STUDIES ON THE SEPARATION OF CARRIER FREE Y-90 FROM Sr-90 USING DIGLYCOLAMIDE EXTRACTANTS

By

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STATEMENT BY THE AUTHOR

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Subrata Dutta

DECLARATION

I, hereby declare that the investigation presented in the thesis has been carried out by me. The work is original and has not been submitted earlier as a whole or in part for a degree/diploma at this or any other Institution/University.

Subrata Dutta

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Here is my acknowledgement page of my Ph.D. thesis. Well, the list of the people I need to thank will not fit to a single Acknowledgement Section. I will just mention some people whose contribution is obvious.

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SUBRATA DUTTA

Dedicated to

My Beloved father

Late Shri Sudhir K. Dutta

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List of Publications

The work described in the thesis was planned and carried out by me under the supervision of Prof. P.K. Mohapatra. A part of the work reported in this thesis has been published in the following International Journals and National / International Symposia.

List of Publications

1. Separation of ^{90}Y from ^{90}Sr by a solvent extraction method using N,N,N′,N′-tetraoctyl diglycolamide (TODGA) as the extractant, **S. Dutta**, P.K. Mohapatra and V.K. Manchanda. *Appl. Radiat. Isot.,* 69 (**2011**) 158-162.

2. Preferential extraction of ^{90}Y from ^{90}Sr using N,N,N′,N′-tetra-2-ethylhexyl diglycolamide (T2EHDGA) as the extractant, **S. Dutta**, P.K. Mohapatra, D.R. Raut and V.K. Manchanda. *J. Radioanal. Nucl. Chem.,* 288 (**2011**) 389-394.

3. Chromatographic separation of carrier free ^{90}Y from ^{90}Sr using a diglycolamide based resin for possible pharmaceutical applications, **S. Dutta**, P.K. Mohapatra, D.R. Raut, V.K. Manchanda, *J. Chromatogr.,* 1218 (37) (**2011**) 6483-6488.

4. Role of Diluent on the Separation of ^{90}Y and ^{90}Sr by Solvent Extraction and Supported Liquid Membrane Using T2EHDGA as the Extractant, **S. Dutta**, P.K. Mohapatra, D.R.Raut and V.K. Manchanda. *Appl. Radiat. Isot.*, (In press).

5. Separation of ^{90}Y and ^{90}Sr by TODGA as the carrier extractant: Solvent extraction and supported liquid membrane studies, **S. Dutta**, P.K. Mohapatra, D.R. Raut and V.K. Manchanda. *Sep. Sci. Technol.,* (communicated).

Symposia:

1. Studies on diluent effect on extraction and facilitated transport of Y(III) from nitric acid medium using TODGA, **S. Dutta**, P.K. Mohapatra, D.R. Raut and V.K. Manchanda, *In proceedings of DAE-BRNS Symposium on Nuclear and Radiochemistry (NUCAR-2011), held at GITAM University, Visakhapatnam during February* 22-26, **2011**, pp. 316-317.

2. Separation of carrier free ^{90}Y using supported liquid membrane containing TODGA as the carrier, **S. Dutta**, P.K. Mohapatra, D.R. Raut and V.K. Manchanda, *In proceedings of*

DAE-BRNS Symposium on Nuclear and Radiochemistry (NUCAR-2011), held at GITAM University, Visakhapatnam during February 22-26, **2011**, pp. 471-472.

3. Separation of ^{90}Y from ^{90}Sr using N,N,N',N'-tetra-2-ethylhexyl diglycolamide (T2EHDGA) as the Extractant, **S. Dutta**, P.K. Mohapatra, D.R. Raut, V.K. Manchanda, *In proceedings of DAE-BRNS Symposium on Emerging Trends in Separation Science and Technology (SESTEC-2010) held at IGCAR, Kalpakkam, India, during March 1* -4, **2010**, pp. 605-606.

4. Modifier optimization and separation of carrier free ^{90}Y using N,N,N',N'-tetra-2-ethylhexyl diglycolamide (T2EHDGA), **S. Dutta**, P.K. Mohapatra, D.R. Raut, V.K. Manchanda, *In proceedings of DAE-BRNS Symposium on Emerging Trends in Separation Science and Technology (SESTEC-2010) held at IGCAR, Kalpakkam, India, during March* 1 -4, **2010**, pp. 607-608.

5. Separation of ^{90}Y from ^{90}Sr Using a TODGA Sorbed Extraction Chromatography Resin Material, S. Dutta, P.K. Mohapatra and V.K. Manchanda, *In proceedings of 'Indian Analytical Science Congress'- IASC-2009 held at Lonvala, Maharashtra, during Nov.* 12-13, **2009**, pp 42.

6. Studies on Relative Transport Behavior of ^{90}Y and ^{90}Sr across Supported Liquid Membrane Containing T2EHDGA as the Carrier, **S. Dutta**, D.R. Raut, P.K. Mohapatra and V.K. Manchanda, *In proceedings of 2nd International Conference on 'Application of Radiotracers in Chemical, Environment and Biological Science' - ARCEB - 10 held at Saha Institute of Nuclear Physics, Kolkata, during Nov.* 7-13, **2010**, pp 164.

Synopsis

"Studies on the separation of carrier free Y-90 from Sr-90 using diglycolamide extractants"

Nuclear Medicine is a branch of medicine that uses radiation to provide information about the functioning of a person's specific organs or to treat disease. In Therapeutic Radiopharmaceuticals which is one specialized branch in Nuclear Medicine, for some medical conditions like in case of cancer treatment, it is useful to destroy or weaken malfunctioning cells using radiation. The radioisotope that generates the radiation can be localized in the required organ in the same way it is used for diagnosis - through a radioactive element following its usual biological path, or through the element being attached to a suitable biological compound. In most cases, it is beta radiation which causes the destruction of the damaged cells. This is radionuclide therapy (RNT) or radiotherapy.

Considerable effort has been made in recent times to develop site specific methods for treatment of different types of cancer using radionuclides. The suitability of a given radionuclide for such application is determined by a number of factors viz. its mode of production, availability of effective methods for its attachment to a site specific agent, its potential toxicity if detached from the agent, its therapeutic effectiveness along with the requirement that the isotope has suitable half life and decay scheme. The above requirements severely limit the number of radionuclides which can be considered for cancer therapy.

Among the radioisotopes, P-32, Sr-89, I-131, Y-90 etc are routinely used for therapeutic application in clinic, and Y-90 has been envisaged as one of the most promising radioisotope. The reasons are very many namely, **i)** it is a pure β-emitter with no associated gamma rays and decays to stable daughter ^{90}Zr, ii) has short half-life ($t_{1/2}$ = 64.2 hrs) and high β emissions (E_{max} = 2.28 MeV), iii) yields high complex formation constants with chelating ligands which are acceptable radiopharmaceuticals [**1,2**] and iv) has wide applications in cancer therapy viz. liver cancer therapy, radiation synovectomy, bone metastasis palliation, superficial tumor therapy, targeted tumor cell membrane receptor, control effusion in the pleural and peritoneal cavities after surgery, leukemia and polycythemia therapy etc.

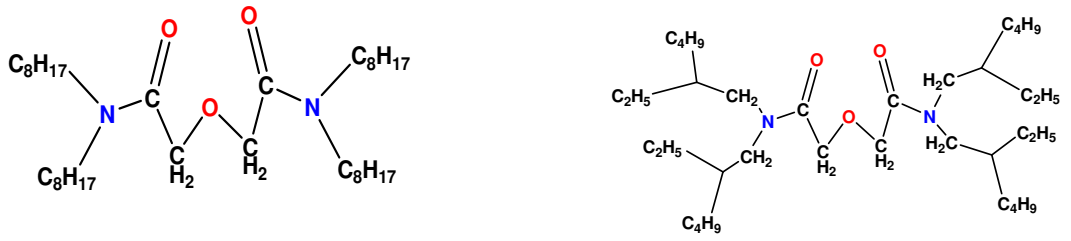
^{90}Y can be obtained either by neutron irradiation of natural yttrium or as the daughter product of ^{90}Sr which is abundantly available in spent nuclear fuel. The neutron activation method yields ^{90}Y with low specific activity due to the presence of large amount of the carrier (^{89}Y), which is a

major limitation in its therapeutic applications. On the other hand, separation of ^{90}Y from ^{90}Sr which is produced in nuclear fission makes a viable alternative source with very high specific activity.

This is due the fact that ^{90}Sr ($t_{1/2}$=28.5yrs) attains secular equilibrium with ^{90}Y in a period of one month and can serve as a long term source for the latter isotope because of relatively long half-life of the parent isotope. Thus it can serve as radiochemical generator similar to the ^{99}Mo-^{99m}Tc generator. However, due to long half-life of ^{90}Sr and its bone seeking nature, it is required to efficiently separate ^{90}Sr from its daughter product, ^{90}Y. Maximum permissible body burden of ^{90}Sr is reported to be 74 kBq or 2μCi and consequently for radiopharmaceutical purposes, the separation of ^{90}Y from ^{90}Sr demands decontamination factor values as high as 10^6.

Separation methods employed for the radiochemical separation of ^{90}Y from ^{90}Sr, involve techniques such as precipitation, solvent extraction [**3,4**], ion exchange [**5**], extraction chromatography [**6**], liquid membrane [**7**] and electrochemical method [**8**]. However, these methods are not free from disadvantages and hence there are always attempts for more efficient methods. Recently, a liquid membrane method using PC-88A as the extractant for the separation of ^{90}Y, after using CMPO sorbed extraction chromatographic resin from high level waste [**9**].

In the past decade, a new class of diglycolamide extractants (containing ether linkage between two amide groups) has been the focus of many separation groups working on actinide partitioning. This class of extractants exhibit higher extraction of minor actinides as compared to malonamides due to their tridentate nature. Amongst various derivatives of diglycolamides, N,N,N′,N′tetra-octyl diglycolamide (TODGA Fig. 1 A) has shown reasonably high extraction of trivalent actinides (viz. Am(III)) and lanthanides and very low extraction of divalent Sr(II) in 1-3 M HNO_3 and also that the extraction efficiency in case of Sr decreases further beyond 6M HNO_3.This has prompted us to evaluate these extractants for the separation of ^{90}Y from ^{90}Sr as a function of mineral acid (HCl or HNO_3) by different separation techniques. It is well known that reagents with branched alkyl groups lead to more efficient separation as compared to their analogs with linear alkyl groups. Moreover, 'actinide partitioning' studies using N,N,N′,N′tetra-(2-ethyl hexyl)diglycolamide (T2EHDGA Fig 1B) have shown promise though the extraction efficiency of TODGA was higher. Therefore, it was pertinent to understand the extraction as well as separation behavior of T2EHDGA as compared to TODGA for the separations of carrier free ^{90}Y.



(A) (B)

Fig.1 Structural formula of the diglycolamide extractants used in the present study (A) TODGA, (B) T2EHDGA

Main objective of the present work is to develop suitable methodologies for the successful separation of carrier free ^{90}Y from ^{90}Sr-^{90}Y mixture under acidic condition using DGA extractants viz. TODGA and T2EHDGA under different experimental conditions. The experimental conditions were optimized by initial solvent extraction studies. The feed and strip condition were used for better separation process of Y(III) from S(II) by low solvent inventory methods such as extraction chromatography and liquid membrane.

Chapter I: General Introduction

In this Chapter, the importance of ^{90}Y in the field of nuclear medicine and its comparison with other radioisotopes prevalently used in cancer therapy is elaborated. The different sources of recovery of ^{90}Y and associated advantages and disadvantages in general and advantages of recovery of ^{90}Y from a mixture of ^{90}Sr-^{90}Y mixture in particular are described in this Chapter.

This Chapter also gives a brief account of the nuclear data pertaining to Sr and Y which includes radioactive decay scheme for all possible radioisotopes of Sr and Y; giving further elucidation of involved secular and transient equilibrium. Also described in this Chapter are the basic chemistry of Strontium and Yttrium, comparison of the chemistry of later with actinides, the complex chemistry of Y^{3+} with different ligands/chelates of radiopharmaceutical interest in general with TODGA and T2EHDGA in particular; also mentioned and discussed the unique characteristics of both TODGA [**10**] and T2EHDGA [**11**] as novel extractants.

This Chapter also includes various prevalent methods applied for the separation of ^{90}Y

from ^{90}Sr and their merits and demerits. Various experimental techniques namely solvent extraction, extraction chromatography and supported liquid membrane method which have been used for the separation of ^{90}Y and ^{90}Sr in this work and their limitations have been included in this Chapter. This Chapter gives the derivation of transport equation and method of calculation of permeability coefficient which will be needed in SLM studies. Various methods employed to estimate the purity of the product (^{90}Y) are also included in this Chapter. This Chapter gives a brief account of the basics of extraction chromatography, expression of distribution ratio in batch method involving the extractant loaded chromatographic resin. Also included in this Chapter are various reagents used for this purpose and their roles in separation science in general and that in recovery of trivalent species like Yttrium from Strontium Yttrium mixture in particular.

Chapter II: Experimental Techniques

This Chapter describes different experimental techniques and instrumental methods used in the present work. The gamma ray emitting radionuclide were estimated by gamma counting using NaI(Tl) scintillator and HPGe detector and the β emitting radionuclide (^{90}Y) was estimated by liquid scintillation counter using dioxane based liquid scintillator solution . The fundamental principles of these detectors and precaution to be taken during measurement of activity have been explained in this Chapter. The preparation and purification of various radiotracers used has also been included.

In solvent extraction experiments, distribution studies were performed by equilibrating the equal volume of suitable organic and aqueous phases in stopperred glass tubes using a thermostated water bath. Calculation of distribution coefficient, separation factors are included in this chapter. In extraction chromatography studies, TODGA impregnated resins were prepared by a method reported in literature. Both batch as well as column method for chromatographic separation of ^{90}Y and ^{90}Sr are described in the Chapter. The procedure for impregnated resins by γ cell having ^{60}Co source was also given. The flat sheet supported liquid membrane studies were performed using a Pyrex glass cell with 20 irradiating TODGA ml of both feed and receiver solution volume. The experimental procedure pertaining to the supported liquid membrane studies are also included in this chapter.

Chapter III: Distribution Studies on Y(III) and Sr(II) by Solvent Extraction Technique

Solvent extraction techniques are rapid and have been employed for many analytical separations. This Chapter describes the liquid-liquid extraction studies on Yttrium and Strontium carried out using two diglycolamide extractants viz., tetraoctyldecyl diglycolamides(TODGA, Fig.1 A) and tetra-2-ethylhexyl diglycolamides (T2EHDGA, Fig.1B). The stoichiometry of the extracted species with Y (III) was determined by measuring the distribution coefficient values at varying concentration of carrier concentration. The effect of feed acidity and diluent composition on the distribution behaviour of Y (III) has also been described in this Chapter. Temperature variation studies were carried out to understand the effect of temperature on the extraction behavior and thermodynamic parameter such as ΔH, ΔS and ΔG were calculated. The results are explained in the present Chapter. The effect of different mineral acids has also been investigated. Phase modifier concentration was also varied and the results of studies on separation behavior of Y (III) with respect to Sr (II) have been presented in this Chapter. Based on these studies a methodology was developed to obtain pure ^{90}Y from ^{90}Sr-^{90}Y mixture. The purity of the product was checked by half life measurement and the method has been used for ascertaining the purity of recovered ^{90}Y and discussed in detail in the present Chapter.

Chapter IV: Chromatographic Separation Studies on Y(III) from Sr(II) using TODGA Based Resin

Due to the growing concern for the environment, solvent extraction methods are not preferable as they use large volumes of volatile organic compounds and generate large amounts of secondary wastes and there is a search for alternative ‘green’ separation methods. Techniques such as extraction chromatography and liquid membrane, on the other hand, are becoming increasingly popular as they thrive on very low volumes of the solvent.

In this present work, an attempt was made to use N,N,N’,N’-tetraoctyl diglycolamide (TODGA) as the stationary phase in an extraction chromatography resin (XCR) material prepared for evaluating the uptake and the separation behaviour of ^{90}Y and ^{90}Sr from acidic

feeds. The batch sorption studies indicated almost no Sr(II) uptake while Y(III) uptake increased with acidity up to 4 M acidity, beyond which a decrease in the $K_{d,w}$ values were observed. Column studies were carried out and breakthrough profiles were obtained for both Y(III) and Sr(II). No breakthrough of Y(III) was noticed even when >50 column volumes of the feed (carrier free ^{90}Y at 4 M HNO_3) was passed through the column while about 20 column volumes were required for the breakthrough of Y(III) when the feed contained 1 g/L Y in 4 M HNO_3 spiked with ^{90}Y tracer. The reusability of the column was also studied which indicated in the deterioration of the column performance as shown by the sharp fall in the breakthrough volumes and was attributed to the probable leaching of the reagent from the support material. The role of absorbed dose was also investigated for Y(III) uptake and the results indicated rapid deterioration of the uptake capacity with increasing in absorbed dose. Separation of carrier free ^{90}Y tracer was also studied by loading the column with ^{90}Sr and eluting with 0.01 M solutions of HNO_3 as well as EDTA. The purity of the product was ascertained by half-life method.

Chapter V: Separation Studies on Y(III) From Sr(II) using Supported Liquid Membrane Techniques

In view of low carrier requirement, and simultaneous extraction and stripping, liquid membrane method appears to be an attractive green technique which is now-a-days finding increasing attention of separation scientists. Membrane based separation methods are explored in this Chapter for separation of Y(III) from Sr(III) using various selective extractants.

In this Chapter, the studies on the transport of Y(III) and Sr(II) by liquid membrane under various experimental conditions have been described. Two different mineral acids viz., HCl and HNO_3 were evaluated for effective separation of Y(III) and Sr(II). Acid variation studies have also been carried out. The detailed description of results has been given in this chapter. Two extractants (TODGA and TEHDGA) have been used for extraction of Y(III) from mixture containing Y(III) and Sr(II). Role of diluents on the transport behaviour was investigated and the results have been correlated to parameters such as diluents polarity and viscosity. Different diluents and diluent mixtures have been used examined and the findings are presented in this chapter.

Based on these studies a methodology was developed to obtain pure ^{90}Y from ^{90}Sr-^{90}Y

mixture. The purity of product was checked by half life measurement and method has been explained in the present chapter.

Chapter VI: Summary and Conclusions

The present thesis deals with the development of methods for the separation of carrier free radionuclide ^{90}Y of radiopharmaceutical importance from ^{90}Sr-^{90}Y mixture having nuclear waste as the potential source using commercially available diglycolamides ligands, viz., N,N,N′,N′-tetra-octyl diglycolamide (TODGA) and its branched homolog, N,N,N′,N′-tetra-2-ethylhexyl diglycolamide (T2EHDGA) respectively. Various techniques evaluated for the separation of radionuclide ^{90}Y from ^{90}Sr-^{90}Y mixture includes solvent extraction, the column chromatography and supported liquid membrane.

This chapter lists the following conclusions drawn from the studies carried out during the present work.

- Solvent extraction studies using both TODGA as well as T2EHDGA extractants gives a viable separation method for the recovery of pure ^{90}Y (DF 10^4) from a mixture of ^{90}Y + ^{90}Sr. It requires two stages of extraction of Y(III) from 6 M HCl medium in case of TODGA and 4 M HCl medium in case of T2EHDGA followed by stripping with distilled water. The extraction kinetics of Y(III) was fast and association of 3-4 ligand molecules with Y(III) was revealed.

- Studies on extraction chromatography using TODGA resin suggests it is possible to separate ^{90}Y from ^{90}Sr using a column containing the XCR material with reasonable purity when the elution of ^{90}Sr and ^{90}Y is done by 0.01 M HNO3 and 0.01 M EDTA at pH 2.0, respectively. Marginal contamination due to the presence of ^{90}Sr in the product is not ruled out and can be possibly separated by loading on to a crown ether column as reported earlier.

- Supported liquid membrane studies with TODGA in xylene as the carrier gives a viable separation method for ^{90}Y from ^{90}Sr from 6 M HCl feed solution.

- From our works, it can also be concluded that combination of two separation techniques viz. extraction chromatography followed by supported liquid membrane can give rise to a better purification scheme for ^{90}Y with higher and better decontamination factor.

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Chapter I

General Introduction

General Introduction

With the passage of time, the field of nuclear medicine has become enriched due to contributions of many eminent scientists from various disciplines of science viz. physics, chemistry, engineering, and medicine. Even though it is difficult to ascertain the exact date and year from which nuclear medicine had come into use, it can probably be guessed between the discovery of artificial radioactivity in 1934 and the production of radionuclides by Oak Ridge National Laboratory for medicine related use, in 1946 [**1.1**]. .

Followed by the earlier discoveries of X-ray by W. K. Roentgen, radioactive uranium salts by Henri Becquerel, and radioactive thorium, polonium by Marie Curie, in February 1934, Frédéric Joliot-Curie and Irène Joliot-Curie reported the first artificial production of radioactive material in the journal *Nature*, after discovering radioactivity in aluminum foil that was irradiated with a polonium preparation. This discovery may probably be considered as the most significant achievement in nuclear medicine. In this context, it is worth mentioning that the eminent Japanese Scientist, Taro Takemi [**1.2**] was the first one to study the application of nuclear physics to medicine in the 1930s.

In 1946, an article [**1.3**] on the successful treatment of a patient with thyroid cancer metastases using radioiodine (^{131}I) started the recognition of nuclear medicine as a potential speciality. Although the earliest use of ^{131}I was devoted to therapy of thyroid cancer, its use was later expanded to include imaging of the thyroid gland, quantification of the thyroid function, and therapy for hyperthyroidism.

Multi-directional clinical use of nuclear medicine started in the early 1950s, as more and more knowledge gained about radionuclides, detection of radioactivity, and using certain radionuclides to trace biochemical processes. Development of the first rectilinear scanner by Benedict Cassen and scintillation camera by Hal O. Anger led the young discipline of nuclear medicine into a full-fledged medical imaging specialty [**1.4**].

In successive years, the growth of nuclear medicine was found to be remarkable. As a consequence, 'The Society of Nuclear Medicine' was formed in 1954 in Spokane, Washington, USA. Within in a span of four years, the Society began publication of the 'Journal of Nuclear Medicine', a premier scientific journal for the discipline in America.

Thus, there started a flurry of research and development of new radionuclides and radiopharmaceuticals for use with the imaging devices and for in vitro studies. Amongst the many radionuclides those were discovered for medical use, the discovery and development of Technetium-99m (^{99m}Tc) is most mentionable. It was discovered in 1937 by C. Perrier and E. Segre as an artificial element and in the 1960s, the development of generator system to produce ^{99m}Tc became a practical method for medical use. Today, ^{99m}Tc is the most utilized element in nuclear medicine and is used in 20 million diagnostic nuclear medical procedures, half of which are bone scans, and the other half are roughly divided between kidney, heart and lung scans. Approximately 85 percent of diagnostic imaging procedures in nuclear medicine use this isotope

Thereafter, the unbound journey of nuclear medicine can be summarized as follows. By the 1970s, most organs of the body could be visualized using nuclear medicine procedures. In 1971, American Medical Association officially recognized nuclear medicine as a medical speciality [**1.5**].

In the 1980s, radiopharmaceuticals were used in the diagnosis of heart diseases. The development of single photon emission tomography, around the same time, led to three-dimensional reconstruction of the heart and establishment of the field of nuclear cardiology. Further developments in nuclear medicine include the invention of the first positron emission tomography scanner (PET). In the late 1950s, David E. Kuhl and Roy Edwards based on the concept of emission and transmission tomography, developed into single photon emission computed tomography (SPECT). Based on their work, several tomographic instruments were constructed at the University of Pennsylvania and during the same period, tomographic imaging techniques were further developed at the Washington University School of Medicine. Further research in nuclear imaging led to the development of first PET/CT prototype in University of Pittsburgh in 1998.

Even though, in its early years, PET and PET/CT imaging experienced sluggish growth mainly due to the requirement for an on-site or nearby cyclotron, at present PET/CT imaging is now an integral part of oncology for diagnosis, staging and treatment monitoring.

1.1. Nuclear Medicine

Nuclear medicine is a special branch of medicine that uses radiation to provide information about

the functioning of a person's specific organs or to treat disease. Usually, the information, thus obtained, help the physicians to make a quick and accurate diagnosis of the patient's illness. Employing this technology, organs like thyroid, bones, heart, liver and many other organs can be easily imaged, and disorders in their function revealed. In some cases, radiation can be used to treat diseased organs, or tumors. The importance of nuclear medicine can be easily guessed by the fact that five Nobel Prizes have so far been awarded to scientists working in this area. Also, over thousands of hospitals worldwide use radioisotopes in medicine, and about 90% of the procedures are for diagnosis.

The following statistics will help us to understand the importance of nuclear medicine all over the world.

- In developed countries which is ~26 % of world population, the frequency of diagnostic nuclear medicine: 1.9 % per year
- The frequency of therapy with radioisotopes: 0.2% per year
- In the USA, number of nuclear medicine procedures per year: 18 million
- In Europe, number of nuclear medicine procedures per year: 10 million
- In Australia, number of nuclear medicine procedures per year: 0.56 millions
- The rate of growth in the use of radiopharmaceuticals in diagnosis: 10% per year

1.2. Radiation Therapy in Nuclear Medicine

Radiation therapy is a branch of nuclear medicine. For certain medical conditions, it becomes useful to destroy or weaken malfunctioning cells using radiation. The radioisotope that produces the radiation, can be localized in the desired organ in the same way it is used for diagnosis i.e., through a radioactive element following its usual biological path, or through the element being attached to a suitable biological compound. Radiation therapy is also sometimes termed as radionuclide therapy (RNT). In most cases, it is the beta radiation which causes the destruction of the damaged cells. Short-range radiotherapy is known as brachytherapy, and this is becoming the main means of treatment.

Although, compared to diagnostic use of radioactive material in medicine, radiotherapy is less common, but now it has become widespread and gaining importance as well as steady growth. An ideal therapeutic radioisotope is a strong beta emitter with just enough γ to enable

imaging, e.g. lutetium-177. This is prepared from ytterbium-176 which is irradiated by neutrons in a reactor to yield Yb-177 which decays rapidly to Lu-177. Yttrium-90 is another important radionuclide used for treatment of cancer, particularly non-Hodgkin's lymphoma, and its more widespread use is envisaged, including for arthritis treatment. Thus, from application and availability view point, Lu-177 and Y-90 are very promising RNT agents in the field of radiation therapy. Some of the other RNT agents along with their scope of therapeutic applications are listed below.

Some RNT agents obtained either by neutron irradiation or by separation method

- **Iodine-131:** Iodine-131 is mainly produced from nuclear reactor by neutron-irradiation of a natural tellurium target.It is used to treat the thyroid for cancer and other abnormal conditions such as *hyperthyroidism* (over-active thyroid). [**1.6**]
- **Phosphorus-32:** Phosphorus-32 can be generated synthetically by irradiation of sulphur-32 with moderately fast neutrons. It is used in a disease called *Polycythemia Vera* in order to control an excess of red blood cells produced in the bone marrow. [**1.7**]
- **Boron-10:** Boron-10 is produced by separation method from natural boron which contains 20% lighter isotope Boron-10. Its use is a new approach in which boron-10 is first concentrated in the tumor and then the patient is then irradiated with neutrons which are strongly absorbed by the boron, to produce high-energy alpha particles which kill the cancerous cells. [**1.8**]

Some RNT agents from Nuclear Reactor Source

- **Bismuth-213:** It is readily available from ^{225}Ac (via 3 alpha decays) to label targeting molecules. This is known as targeted alpha therapy (TAT). ^{213}Bi ($t_{1/2}$= 46min) is obtained by elution from a ^{225}Ac/^{213}Bi generator similar to the ^{99}Mo/^{99m}Tc one. The ^{225}Ac ($t_{1/2}$ =10 days) is formed from the radioactive decay of ^{225} Ra, the decay product of long-lived ^{229}Th, which is obtained from decay of ^{233}U, being produced from ^{232}Th by neutron capture in a nuclear reactor [**1.9**].
- **Lead-212:** With a half-life of 10.6 hours, it can be attached to monoclonal antibodies for cancer treatment. Its decay chain includes the short-lived isotopes ^{212}Bi by beta decay, ^{212}Po

by beta decay and ^{208}Tl by alpha decay of the bismuth, with further alpha and beta decays, respectively to ^{208}Pb, all over about an hour.

Considerable medical research is being conducted worldwide into the use of radionuclides attached to highly specific biological chemicals such as immunoglobulin molecules (monoclonal antibodies). The eventual tagging of these cells with a therapeutic dose of radiation may lead to the regression - or even cure - of some diseases.

1.3. Importance of ^{90}Y in Radiation Therapy

In developing therapeutic radiopharmaceuticals, the most important consideration is the selection of appropriate radionuclides [**1.10 -1.15**] and that requires weighing a variety of factors given below.

- Feasibility of tumor uptake and tumor retention
- Blood clearance
- Rate of radiation delivery
- Half-life and specific activity of the radionuclide
- The feasibility of large scale production of the radionuclide in an economic fashion

The key point for a receptor-based therapeutic radiopharmaceutical is to deliver a tumorcidal dose of radiation while not causing unmanageable side effects.

Amongst various radionuclides, ^{90}Y and lanthanide radionuclides are of particular interest. There are several lanthanide isotopes to choose from, including the low energy β^- emitter, ^{177}Lu, medium energy β emitters such as ^{149}Pm and ^{153}Sm and high energy β^- emitters such as ^{166}Ho similar to ^{90}Y.

Amongst all the above mentioned radionuclides, ^{90}Y has been recognized as one of the most promising due to the following facts.

- It can be used to treat several types of unresectable neoplasm as a complement or a substitute to the classical conventional therapies (external beam radiation therapy, chemotherapy, immunotherapy, or a combination of these)
- It can be used as current loco-regional physical-chemical techniques such as hyperthermia, transarterial chemoembolization (TACE), radiofrequency thermal ablation (RFA) [**1.16-1.18**] stop-flow perfusion with mitomycin-C [**1.19, 1.20**] simultaneous TACE and RFA for hepatic

malignancies (so called single step therapy) [**1.21, 1.22**] and precision pulmonary TACE plus percutaneous RFA [**1.23**].

Due to its capacity to release high energy and its long penetration power, ^{90}Y is able to deliver β radiation not only to the target cell but also to immediate surrounding cells (the cross fire effect) [**1.24**]. Indeed, more than 90% of emitted radiation is absorbed within an effective path length of 5 mm (corresponding to a diameter of 100-200 cells) [**1.25**]. The therapeutic β particles affect cell integrity both directly and indirectly; directly (10%) through the so called primary radiation effect which induces irreparable damage to the structure of double stranded nuclear DNA and indirectly (90%), through the so called secondary radiation effect which increases the amount of toxic free radicals in the cytosol by radiolysis of water[**1.26**].

The cytocidal properties of ^{90}Y [**1.27**] along with its ability to coordinate with a variety of ligands, have allowed us to consider this radionuclide as an important therapeutic tool. The power of the pure high energy β emitter radionuclide ^{90}Y lies in its encouraging capacity in terms of tumour regression, tumour stabilization and patient lifespan prolongation and nonetheless in its interesting ability to coordinate with great variety of ligands. As a consequence, it has been shown to be a promising new tool in the management of patients with unresectable neuroendocrine tumours (NETS), non-Hodgkin's lymphomas (NHL) and liver metastatic colorectal cancer (MCRC), when targeted by an appropriate ligand. In future, the identification of new ligand-receptor systems present in various human tissues, or of more suitable immuno-molecules to be radiolabeled, will allow novel therapeutic applications of ^{90}Y in oncology to be defined.

1.4. ^{90}Y – as Target Specific Radiopharmaceutical

There is a great deal of current interest in developing target-specific radiopharmaceuticals for early detection of diseases and radiotherapy of cancers. Radiopharmaceuticals are those special drugs which contain suitable radionuclides and used routinely in nuclear medicines for the diagnosis or therapy of various diseases. In most of the cases, radiopharmaceuticals are administered *via* intravenous injection. Chemically, they are mostly small organic or inorganic compounds with definite composition. They can also be macromolecules such as monoclonal antibodies and antibody fragments that are not stoichiometrically labeled with a radionuclide.

Radiopharmaceuticals can be divided into two primary classes depending on their medical applications: diagnostics and therapeutics. They can also be classified according to their bio-distribution characteristics: those whose bio-distribution is determined exclusively by their chemical and physical properties; and those whose ultimate distribution is determined by their receptor binding or other biological interactions. The latter class is often termed as target-specific radiopharmaceuticals. Therapeutic radiopharmaceuticals are molecules designed to deliver therapeutic doses of ionizing radiation to specific diseased sites.

Radiotherapy has been in practice for over four decades starting with the use of radioiodine for the treatment of thyroid disorders. The main obstacles for using radiotherapy in clinical practice are the availability of therapeutic isotopes and techniques for their specific localization in diseased tissues, such as tumors. Therapeutic doses of radiation can be delivered to sites of disease in three ways: external beam irradiation, implantable "seeds" or systemic administration. Brachytherapy involves the use of "seeds", which are physically placed at the tumor site and will remain there unless they are surgically removed. The systemic administration of radiopharmaceuticals that are designed for specific localization at tumor sites provides opportunities for treatment of the disseminated metastatic tumors. Ideally, therapeutic radiopharmaceuticals should localize at the diseased site in sufficient concentration to deliver a cytotoxic radiation dose to the tumor cells, and clear rapidly from the blood and other normal organs to minimize radiation damage to normal tissues.

1.5. General Chemistry of Yttrium

Yttrium is a chemical element with symbol Y and atomic number 39. Yttrium is the first d-block element in the fifth period with electronic configuration [Kr] $4d^1$ $5s^2$. Yttrium, which lies above La in Group IIIA, is an analogous +3 ion with a noble gas core; because of the effect of the lanthanide contraction, the Y^{3+} radius is close to the values of Tb^{3+} and Dy^{3+}. Yttrium similar to the lanthanide metals favors the +3 oxidation state. Due to its similar charge, ionic radii and coordination chemistry to those of lanthanides, yttrium is often treated as a "pseudo-lanthanide" metal.

As a trivalent transition metal, yttrium forms various inorganic compounds, generally in the oxidation state of +3, by giving up all three of its valence electrons. Yttrium oxide (Y_2O_3),

also known as yttria, is a white solid and can be used to prepare water-insoluble fluoride, hydroxide, and oxalate, and water soluble bromide, chloride, iodide, nitrate and sulfate. The Y^{3+} ion is colorless in solution because of the absence of electrons in the *d* and *f* electron shells. Water readily reacts with yttrium and its compounds to form Y_2O_3.

1.5.1. Complex Chemistry of Yttrium

Y^{3+} ions in the aqueous solutions exhibit strong tendency to form complexes. This property is widely exploited in devising methods for their separation and purification. One of the most important factors that determines the strength of the complex formed is the ionic potential (or charge density) of the metal ions, which is the ratio of ionic charge to ionic radius. Higher the ionic potential, greater is the electrostatic attraction between the cations and the anions and hence stronger is the complex, formed. For metal ions in a particular oxidation state, the complexing ability increases with the atomic number due to increase in the ionic potential as a result of lanthanide contraction [**1.28**]. However, the above generalized statement may be valid when complexation is primarily ionic in nature. For anions the tendency to form complex generally vary in the same manner as their abilities to bind with hydrogen ion [**1.29**]. For monovalent ligands, the complexing tendency decreases in the order: $F^- > CH_3COO^- > SCN^- > NO_3^- > Cl^- > Br^- > I^- > ClO_4^-$. The divalent anions usually from stronger complexes than the monovalent anions and their complexing ability decrease in the order: $CO_3^{2-} > SO_3^{2-} > C_2O_4^{2-} > SO_4^{2-}$.

The stability of complexes between metal ions and ligands can be discussed on the basis of a scheme based on the concept of hard and soft acids and bases as proposed by Pearson [**1.30**]. Those metal ions are called hard which have a small radius and high charge and do not possess valence shell electrons that are easily distorted. The soft metal ions have the opposite characteristics. When similar classification is applied to the ligands it is observed that the hard metal ions form stronger complexes with hard ligands and soft metal ions with soft ligands. Yttrium ions behave as “hard acids” and interact strongly with hard bases such as “O” or “F” as compared to ligands containing soft donors such as “N”, “S” or “P”. The complex formation reactions involving hard acids and bases are endothermic whereas the reverse is true for soft ions. This is because the complex formation between hard metal ions and hard ligands require the breaking of strong bonds between these metal ions and water molecules in the primary

hydration sphere which require large energy. The process of removal of water molecules, however, results in large increase in entropy which contributes to the driving force of these reactions. When the primary hydration shell is broken during complex formation, the complex formed is referred as "inner sphere complex". In contrast "outer sphere complexes" do not require breaking of the primary hydration shell. The actinide ions interact with soft bases in organic solvents of low solvating power, but not in aqueous solutions where the soft bases would have to replace inner sphere water molecule which is a hard base.

1.5.2. Some Common Labeled Compounds of ^{90}Y

Yttrium, like the lanthanide ions, is coordinated by a number of water molecules in aqueous solutions. The metal chelate formation involves replacement of water molecules by a chelating ligand. Due to their large size, coordination numbers of yttrium and lanthanide ions are typically between 7 and 10. Very few six coordinate species are known while coordination numbers of 8 and 9 are common [**1.31**].

The success of tumor radiotherapy using ^{90}Y depends largely on the high concentration of radioactivity in the tumor for a long duration. Thus, the therapeutic radiopharmaceutical having ^{90}Y must have the following characteristics:

- High uptake at the tumor site
- High tumor-to-background ratio
- Long tumor residence time and fast renal clearance.

High tumor uptake and fast renal clearance are important to improve the tumor-to-background ratio and to reduce radiation burden to organs such as kidneys and bone marrow. The radiopharmaceutical containing ^{90}Y must have high radiochemical purity (RCP $\geq$ 90%) and high solution stability. Since the radiopharmaceutical is manufactured in a centralized facility, it must retain its chemical and biological integrity during storage and transportation. This requires that the labeling with bio-molecule should form a metal chelate with high thermodynamic stability and kinetic inertness. Once again, the coordination chemistry of Y(III) plays a significant role in the development of therapeutic radiopharmaceuticals. Some common labeled compounds of ^{90}Y are listed below.

a) Normal labeled compounds: $^{90}Y(OH)_3$ colloid[**1.32**], ^{90}Y-citrate colloid[**1.33**], ^{90}Y-DTPA[**1.34**]
b) Labeled peptide, receptor: ^{90}Y-DOTA-octreotide[**1.35**], ^{90}Y-DOTA-lanreotide[**1.36**], ^{90}Y-DOTA-RC-160[**1.37**], ^{90}Y-DOTA-VIP
c) Labeled ODN, antisense gene: ^{90}Y-P-SCN-Bz-DTPA-ODN, ^{90}Y-DOTA-ODN.

1.5.3. Different Isotopes of Yttrium

Yttrium isotopes are among the most common products of the nuclear fission of uranium occurring in nuclear reactors. The most important isotopes of yttrium are ^{91}Y and ^{90}Y, with half-lives of 58.51 days and 64 hours, respectively [**1.38**]. Though, ^{90}Y has short half life, it has significance from radioactive waste management point of view as it is present in the high level waste being constantly generated from ^{90}Sr. Yttrium itself has only one stable isotope, ^{89}Y,which is also its only naturally occurring one.

Apart from ^{91}Y and ^{90}Y, about 30 synthetic isotopes of yttrium have been observed, and these range in atomic mass number from 76 to 108. The least stable of these is ^{106}Y with a half-life of ~150 ns (^{76}Y has a half-life of ~200 ns) and the most stable (apart from the naturally occurring ^{89}Y) is ^{88}Y with a half-life of 107 days. Besides ^{91}Y, ^{87}Y, and ^{90}Y, with half lives of 58.5 days, 79.8 hours, and 64 hours, respectively, the remaining isotopes of Y have half lives of less than a

Table 1.1: Stability data of some Y isotopes

Nuclide	Abundance [%]	Mass	Spin	Half-life	Decay mode
^{86}Y	0	86	4	14.74 h	EC,β^+
^{87}Y	0	86.91	1/2	3.35 d	EC,β^+
^{88}Y	0	87.91	4	106.6 d	EC,β^+
^{89m}Y	0	89	0	15.7 s	IT
^{90}Y	0	90	2	2.67 d	β^-
^{90m}Y	0	90	7	3.19 h	IT
^{91}Y	0	90.91	1/2	58.51 d	β^-
^{91m}Y	0	91	9/2	49.71 m	IT

day and most of those have half-lives of less than an hour. Important characteristics of some isotopes of Y are presented in Table 1.1.

1.5.4. Different Sources of ^{90}Y

^{90}Y can be obtained in the following two ways viz. neutron activation of ^{89}Y and decay product of ^{90}Sr.

1.5.4.1. Neutron Activation

^{90}Y can be produced by irradiating ^{89}Y in fast neutron flux of 10^{14}/ cm^2/s for 45-50 days. However, due to very low neutron absorption cross section (0.001b) of ^{89}Y for the (n,γ) reaction, this process results in low yields and hence is not suitable for pharmaceutical purpose due to high carrier concentration (^{89}Y) in the product.

1.5.4.2. ^{90}Sr as Source

Table 1.2: Major contributors to the radioactivity in the spent fuel after a cooling period of 50 days [1.40]

Nuclides	Half life	Nuclides	Half life
^{3}H	12.3 years	^{131}I	8.05 days
^{85}Kr	10.8 years	^{137}Cs	30.2 years
^{89}Sr	50.6 days	^{140}Ba	12.8 days
^{90}Sr	28.5 years	^{140}La	40.2 days
^{90}Y	64.1 hours*	^{141}Ce	32.4 days
^{91}Y	58.8 days	^{143}Pr	13.6 days
^{95}Zr	65 days	^{144}Ce	285 days
^{95}Nb	35 days	^{144}Pr	17.3 minutes**
^{103}Ru	39.6 days	^{147}Nb	11.1 days
^{106}Ru	367 days	^{147}Pm	2.62 years
^{129m}Te	34 days		

* in equilibrium with ^{90}Sr ; ** in equilibrium with ^{144}Ce

Another source of ^{90}Y is ^{90}Sr which is a product of nuclear fission. It is present in significant amount in spent nuclear fuel and in high level radioactive waste emanating from the PUREX process. For thermal neutron fission, the fission product yield from ^{235}U is 5.8%, while it is 6.8% and 2.1% from ^{233}U and ^{239}Pu, respectively. These sources are viable alternatives with very high specific activity and with a possibility of unlimited availability. Even though, spent nuclear fuel which is a potential source of ^{90}Y along with other radionuclides (shown in Table 1.2), is reprocessed only in a small number of countries, but these countries have the capability to develop the process chemistry required for large scale isolation of ^{90}Sr from fission product waste. It is worth mentioning here that there is a facility for the recovery of ^{90}Sr (and other fission products) at Mayak, Russian Federation and a facility for the recovery of 55 500 GBq (1500 Ci) of pure strontium was set up at the Pacific Northwest National Laboratory, United States of America (USA) [**1.39**].

1.5.5. Decay Scheme of ^{90}Sr and ^{90}Y

The decay scheme of ^{90}Sr and ^{90}Y along with emitted β energy and half life can be represented as shown in Fig. 1.1.

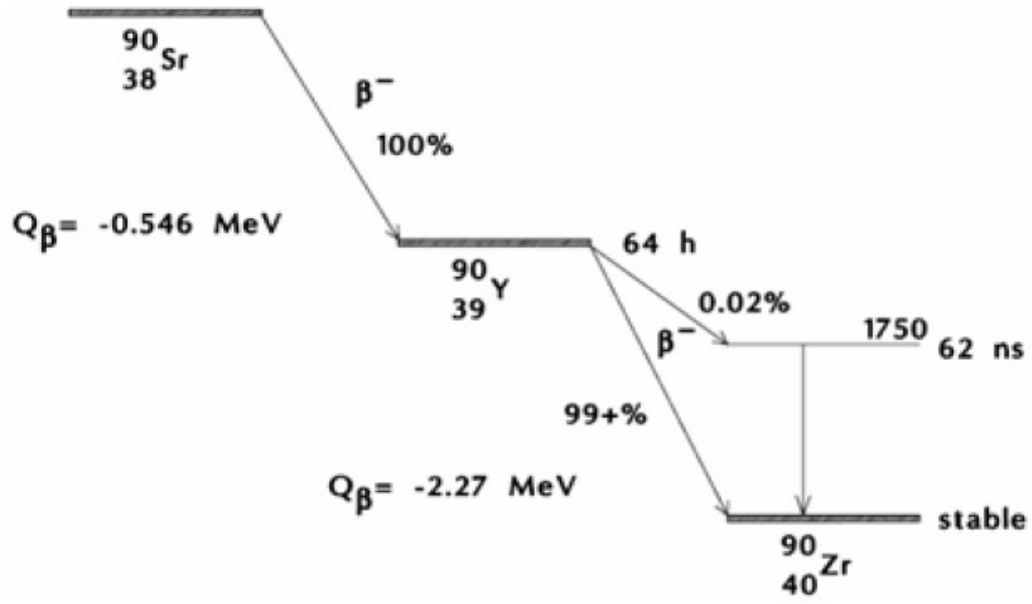

Fig. 1.1: Decay scheme of ^{90}Sr and ^{90}Y

Due to the long half-life of ^{90}Sr and its bone seeking nature, it is required to efficiently separate ^{90}Sr from its daughter product, ^{90}Y. Maximum permissible body burden of ^{90}Sr is reported to be 74 kBq or 2 μCi (maximum permissible body burden and maximum permissible concentrations of radionuclides in air and water for occupational exposure) [**1.41**] and as is in secular equilibrium with ^{90}Sr, for a radiopharmaceutical containing Ci level radioactivity, decontamination factor value as high as 10^6 is required in an efficient separation process.

1.5.6. Radioactive Decay Equilibrium

A simple case of chain decay is the decay of a radionuclide (Parent) to a second radionuclide (Daughter), which then decays to a stable element. The chain decay and decay equation of the parent and daughter can be represented by the following equations.

$$A \xrightarrow{\lambda_A} B \xrightarrow{\lambda_B} C \tag{1.1}$$

$$\frac{dN_p}{dt} = -\lambda_p N_p \tag{1.2}$$

$$\frac{dN_d}{dt} = \lambda_p N_p - \lambda_d N_d \tag{1.3}$$

Equilibrium is a condition established in a parent/daughter mixture when both parent and daughter are radioactive and when the daughter's half-life is shorter than that of the parent. If the daughter's half-life exceeds that of the parent, equilibrium will never be reached.

There are two types of equilibrium [**1.42**]:

- Secular Equilibrium
- Transient Equilibrium

1.5.6.1. Secular Equilibrium

Secular Equilibrium is that condition in serial radioactive decay where the ratio of activities of the parent and daughter radionuclides is a constant and where there is no important decay of the parent nuclide during the time interval of interest.

Mathematically, the secular equilibrium equation, derived from equations 1.2 and 1.3 can

be represented as follows by equation 1.4:

When, $Tp_{1/2} >> T_{d1/2}$

$A_d(t) = A_{p,0}\ (1\text{-}e^{-\lambda t})$ or after several half-lifes

$$A_d(t) = A_{p,0} \quad (1.4)$$

Where $A_d(t)$ and $A_{p,0}$ are activities of daughter at time interval t and that of parent at t = 0

Some examples of secular equilibrium are given below.

^{90}Sr → ^{90}Y

($t_{1/2=}$ 28.5 yrs) ($t_{1/2=}$ 64hrs)

^{226}Ra → ^{222}Rn

($t_{1/2=}$ 1620 yrs) ($t_{1/2=}$ 64hrs)

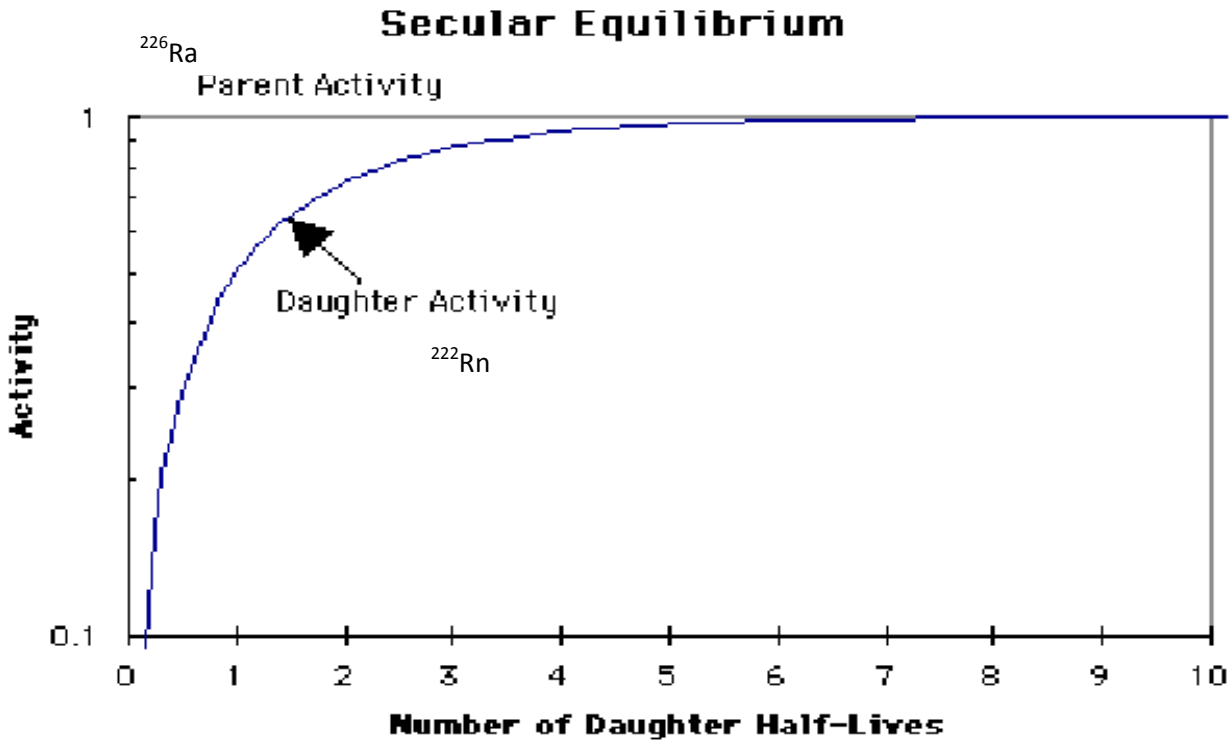

Fig. 1.2. Typical plot of secular equilibrium

In case of secular equilibrium, during 10 half-lives of the daughter, decay of the parent is negligible. For example, in case of decay of the ^{226}Ra, the parent nuclide ^{226}Ra exists in secular equilibrium with daughter ^{222}Rn and is represented by the Fig. 1.2.

From the Fig.1.2, it can be concluded that in the equilibrium mixture, the daughter appears to have same activity as that of the parent. The simplest explanation for their appearing to be equal is that the daughter can't decay until it is formed, and so the rate of formation of the daughter equals the rate of decay of the parent, which is very slow. Therefore, the parent and daughter appear to have the same half-lives. In the case of the decay of ^{226}Ra to ^{222}Rn, the decay constant of the parent 1.2×10^{-6} day^{-1} (only 1 millionth decays per day). Similarly it can be seen in the case of ^{90}Sr-^{90}Y that after nearly 10 half-lives, ^{90}Y will be in secular equilibrium with ^{90}Sr i.e., both parent and daughter nuclide will have same physical half life.

1.5.6.2. Transient Equilibrium

Transient Equilibrium is a condition reached when the $t_{1/2}$ of the parent is greater than the $t_{1/2}$ of the daughter by an order of less than 10. Mathematically, it can be derived from the basic decay

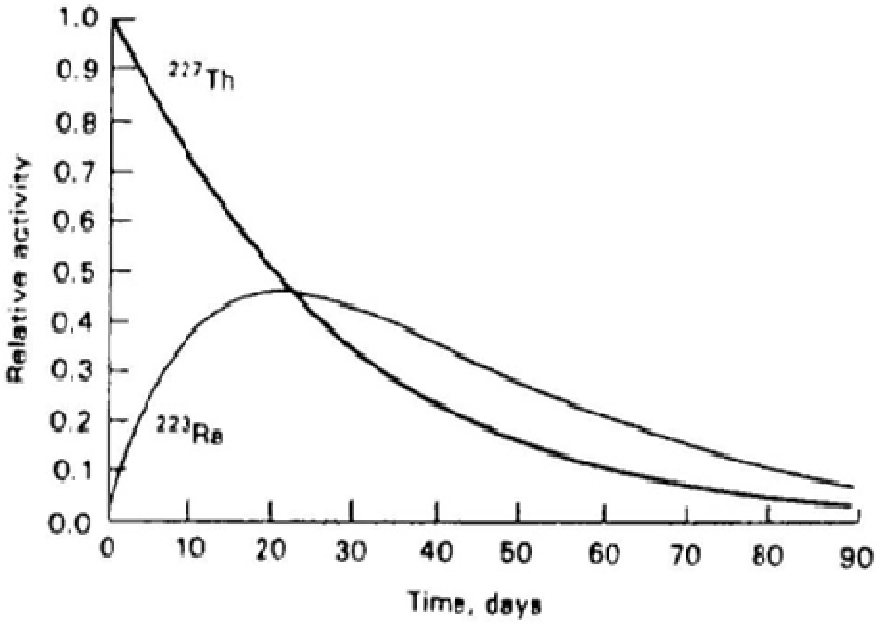

Fig.1.3. Transient equilibrium showing the growth of ^{223}Ra having half life 11.43 days from ^{227}Th having half life 18.5day

equation and can be represented by the following equation:

Condition for transient equilibrium: $T_p > T_d$

$$A_d(t) = A_{p,0}\frac{\lambda_d}{\lambda_d - \lambda_p}\left(e^{-\lambda_p t}\right) = A_p(t)\frac{\lambda_d}{\lambda_d - \lambda_p} \quad (1.5)$$

A classical example is the ^{223}Ra /^{227}Th, where the ratio of the half-lives is 18.5/11.4 hr = 1.7 and the transient equilibrium with daughter is represented by the Fig.1.3.

1.5.7. β Spectrum of ^{90}Sr and ^{90}Y[1.43]

^{90}Sr remains in secular equilibrium with ^{90}Y and the beta spectrum of ^{90}Sr/^{90}Y and that of ^{90}Y are shown in Fig.1.4 (a) and 1.4 (b) respectively. According to Fig. 1.4 (a), it is observed that the two beta components in the compound spectra (^{90}Sr/^{90}Y) can be easily resolved. In Fig. 1.4 (b) it is recorded single beta spectra from ^{90}Y to be used as a reference in order to check the elution efficiency of the generator. The energy channel used was between 50 and 800 kev.

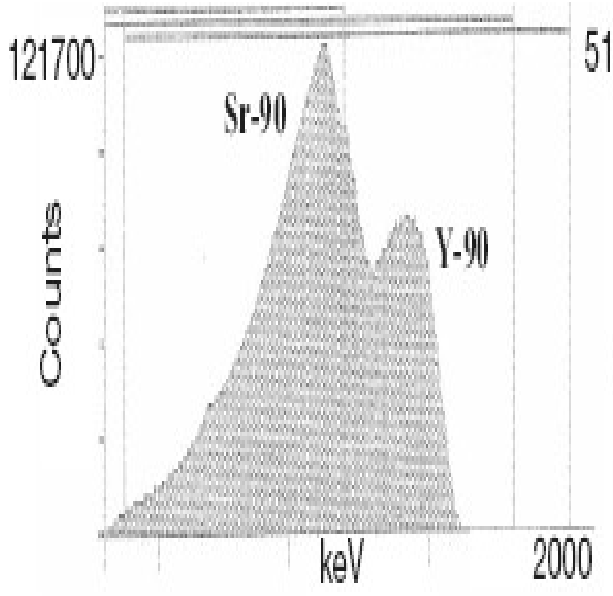

Fig. 1.4 (a): β spectrum of ^{90}Sr & ^{90}Y

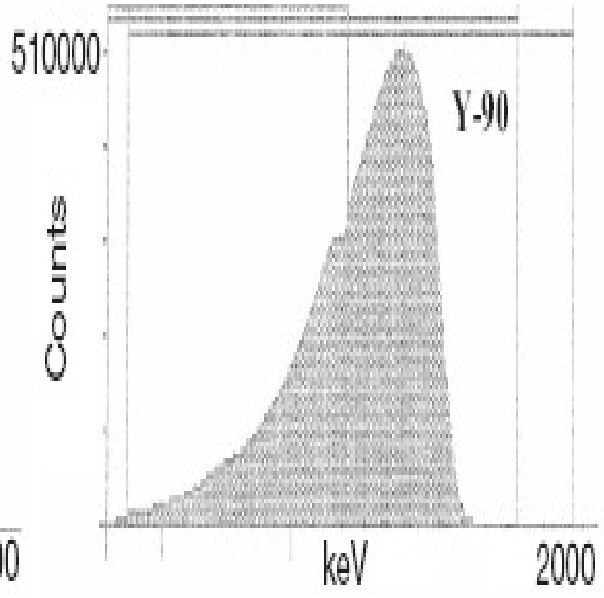

Fig. 1.4 (b): β spectrum of ^{90}Y

1.5.8. Estimation of Radionuclide Purity of ^{90}Y

Yttrium-90 used for therapy should be of very high radionuclide purity (> 99.998 %), as the most probable contaminant, ^{90}Sr, is a bone seeker with a maximum permissible body burden (MPBB) of only 74 kBq (2 mCi). Hence, it is necessary to determine the purity of ^{90}Y and this can be done in a number of ways:

- Paper Chromatography
- Extraction Paper Chromatography (EPC)
- Extraction Chromatography Resin
- Monitoring the half-life of ^{90}Y

A brief description of different types of methodology used for the estimation of radionuclide purity of ^{90}Y is given below.

1.5.8.1. Paper Chromatography

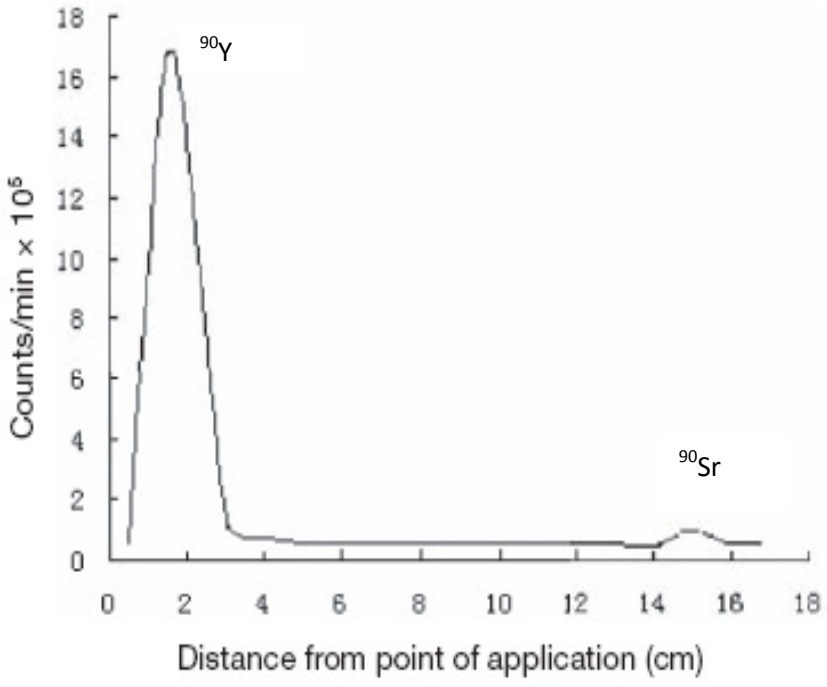

Fig.1.5: Typical paper chromatogram of ^{90}Y- ^{90}Sr

In this method, chromatography paper (30 ± 2.5 cm) eluted with 0.9% saline solution is used for the analyses. During the chromatography, ^{90}Sr moved with the solvent front, while ^{90}Y stayed at the origin. A typical chromatographic pattern of ^{90}Y-acetate is shown in Fig.1.5 [**1.44**].

1.5.8.2. Extraction Paper Chromatography

Extraction Paper Chromatography (EPC) [**1.45**] is a combination of solvent extraction and paper chromatography techniques. A chromatography paper impregnated with a ^{90}Y specific chelate, KSM-17 (2-ethylhexyl-2-ethylhexylphosphonic acid) at the point of application is used as the support for chromatography. Owing to its selective retention by KSM-17, Y^{+3} remains at the point of spotting while Sr^{+2} moves with the solvent front. The activity at the solvent front is estimated in a liquid scintillation counter and compared with the total spotted activity. A typical extraction paper chromatogram is shown in Fig.1.6.

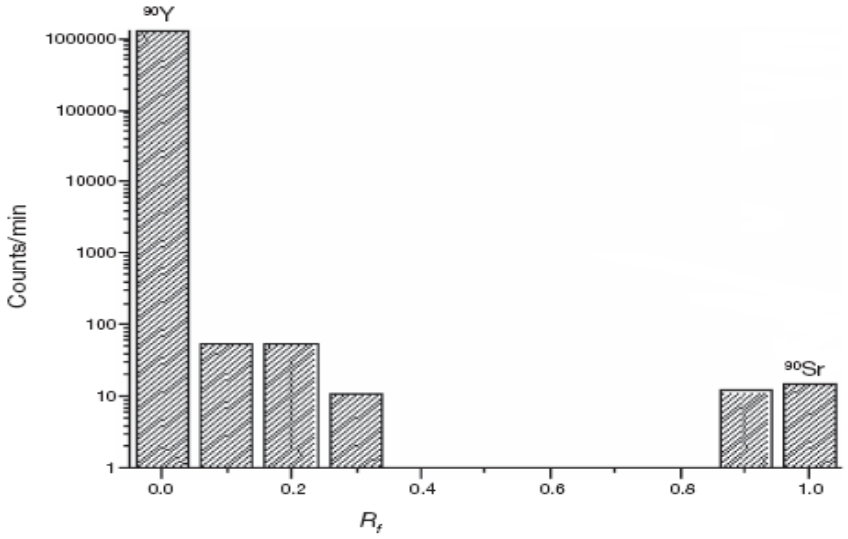

Fig.1.6: Extraction paper chromatogram of ^{90}Y and ^{90}Sr using KSM-17 [1.45]

1.5.8.3. Extraction Chromatographic Resin [1.46]

To determine the traces of ^{90}Sr in ^{90}Y the following procedure can be followed. Two extraction chromatography columns are connected in series. The first column is filled with 1 g of Sr specific resin (Sr.Spec®) and the second column with 1 g of diglycolamide (DGA) Resin. The ^{90}Y solution in 3 M HNO_3 (about 100 mCi) is fed onto the first column. ^{90}Sr is retained on the first column and ^{90}Y on the second one. The columns are separated, and the ^{90}Sr is eluted with

water from the first column and measured using a liquid scintillation counter. The liquid emerging from the tandem columns should contain the rest of the ^{90}Sr. When necessary, the residual amount of ^{90}Y is removed on the additional DGA column

.

1.5.8.4. Monitoring the Half-life of ^{90}Y

The purity of ^{90}Y can be assayed by the radiometric method followed by experimental half life determination. The β activity of the product is estimated as a function of time. The initial β activity on the planchette, (~10^5 counts/min) is found to decay to the background activity after about 26 d. The half-life of the product was estimated to be approximately 64 h, confirming the absence of ^{90}Sr in the product. A typical decay curve is shown in Fig.1.7.

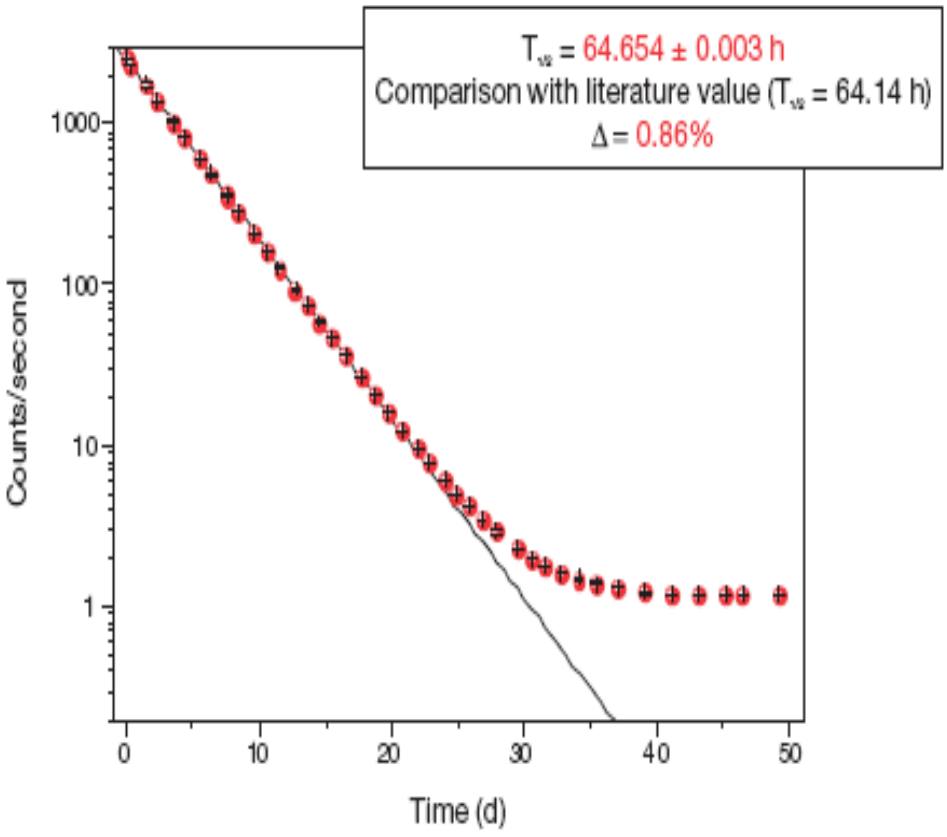

Fig.1.7: A typical decay curve of ^{90}Y contaminated with ^{90}Sr

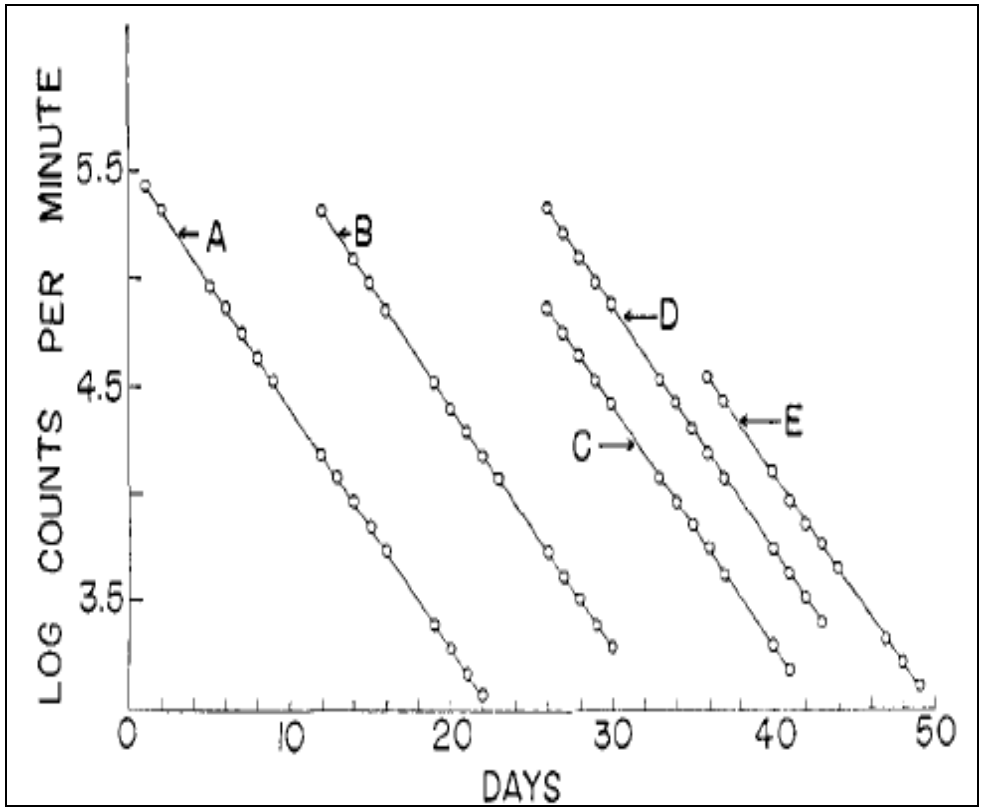

Fig. 1.8: A typical decay plot of five ^{90}Ysamples of sample of same source

An alternative half life methodology known as telescoping half life technique, [**1.47**] which can be can be used to determine the purity of ^{90}Y. In this method, a radioactive material can be counted for many half lives without loss of counting precision, as illustrated in Fig. 1.8. In this method, (say) five samples of ^{90}Y of ascending magnitude are to be prepared, for beta counting and each sample starting with the sample having least activity will be counted daily for less than 8 half lives in an overlapping manner. Thus, while no one sample is counted for more than 8 half lives, their composite decay spans a period of 18.4 half lives. The mean half life can thus be obtained by weighing the five determinations.

1.5.9. A Brief Survey of Separation Methods used for Radiochemical Separation of ^{90}Y

Separation methods used for the radiochemical separation of ^{90}Y from ^{90}Sr involves techniques such as precipitation, solvent extraction, ion exchange, extraction chromatography, liquid

membrane and electrochemical methods. This section gives a brief account of literature methods on ^{90}Y - ^{90}Sr separation.

In last five decades, substantial amounts of work has been carried out for the development of a suitable scheme for obtaining carrier free ^{90}Y of pharmaceutical grade from ^{90}Sr – ^{90}Y mixture. In the seventies, most of the studies were based on either ion-exchange separation or chromatographic separation. In this context, the works of Suzuki's [**1.48**] and that of Kuroda, *et al* [**1.49**] can be mentioned. Suzuki carried out cation exchange separation ^{90}Y from ^{90}Sr using column containing Dowex 50W X-8, 200-400 mesh. One percent ammonium oxalate solution as eluant was found to be quite efficient for producing almost carrier-free ^{90}Y. There are a number of advantages in this method viz.,

I. in the preparation of the eluant, no pH adjustment is necessary
II. there is no risk of the growth of bacteria in the solution
III. volume required to elute 80% of yttrium is less compared to citrate and lactate
IV. the most important one is that the oxalate effluent can easily be decomposed

Kuroda, *et al*, [**1.49**] utilized the isotopic exchange reaction in thin layer chromatography, so that the separation of carrier-free ^{90}Y and its parent ^{90}Sr can be achieved in a rapid and simple way. By using equilibrium mixture of ^{90}Sr and ^{90}Y on a $SrSO_4$ layer and developing with dilute H_2S0_4, ^{90}Sr is retained, while ^{90}Y advances upward almost to the H_2SO_4 front, so that a clear separation can be accomplished rapidly.

In the following two decades, most of the reported work was based on either solvent extraction or extraction chromatographic methods. T.W. Lee et al [**1.50**] separated carrier-free ^{90}Y from ^{90}Sr by solvent extraction method using di-(2-ethylhexyl) phosphoric acid (HDEHP) as extractant in *n*-dodecane as the diluent. The extraction equilibrium time, the effect of temperature, concentration of extractant, and hydrochloric acid concentration on this extraction system were examined. Based on the studies, the chemical procedure for the separation of carrier-free, ^{90}Y from its parent ^{90}Sr have been established. The chemical yield of ^{90}Y is about 80% and the ^{90}Sr impurity is less than 1×10^{-4} %. The trace of extractant presented in the final product can be removed by fuming with HNO_3. Consequently, the preparation of millicurie of ^{90}Y is quite satisfactory for the adsorption in microsphere resin for radiotherapy. With respect to

extraction chromatographic methods, separation of carrier-free ^{90}Y from ^{90}Sr using strontium specific resin (Sr.Spec®) by M.L. Dietz and E.P. Horwttz [**1.51**] is worth mentioning. In their work, a novel extraction chromatographic resin was developed for the separation of ^{90}Y from ^{90}Sr using Sr.Spec® resin comprised of Amberchrom CG-71m being impregnated with 1-octanol solution of di-*tert*-butylcyclohexano-I8-crown-6 (Sr.Spec®) followed by further purification using rare earth specific resin (RE Spec™) comprised of Amberchrom CG-71m being impregnated with CMPO (octyl(phenyl)-N,N-diisobutylcarbamoylmethy-l-phosphine oxide in TBP. The underlying principle of this method is that Sr.Spec® resin column retains ^{90}Sr when the mixture solution at 3 M HNO_3 is passed through it and when the effluent containing mostly ^{90}Y. The yttrium purification scheme is shown in Fig.1.9. In the last decades, vast amount of R and D work were carried out with an objective to produce carrier free ^{90}Y from $^{90}Sr/^{90}Y$ generator, mainly based on supported liquid membrane (SLM) methods using novel extractants and electrochemical methods.

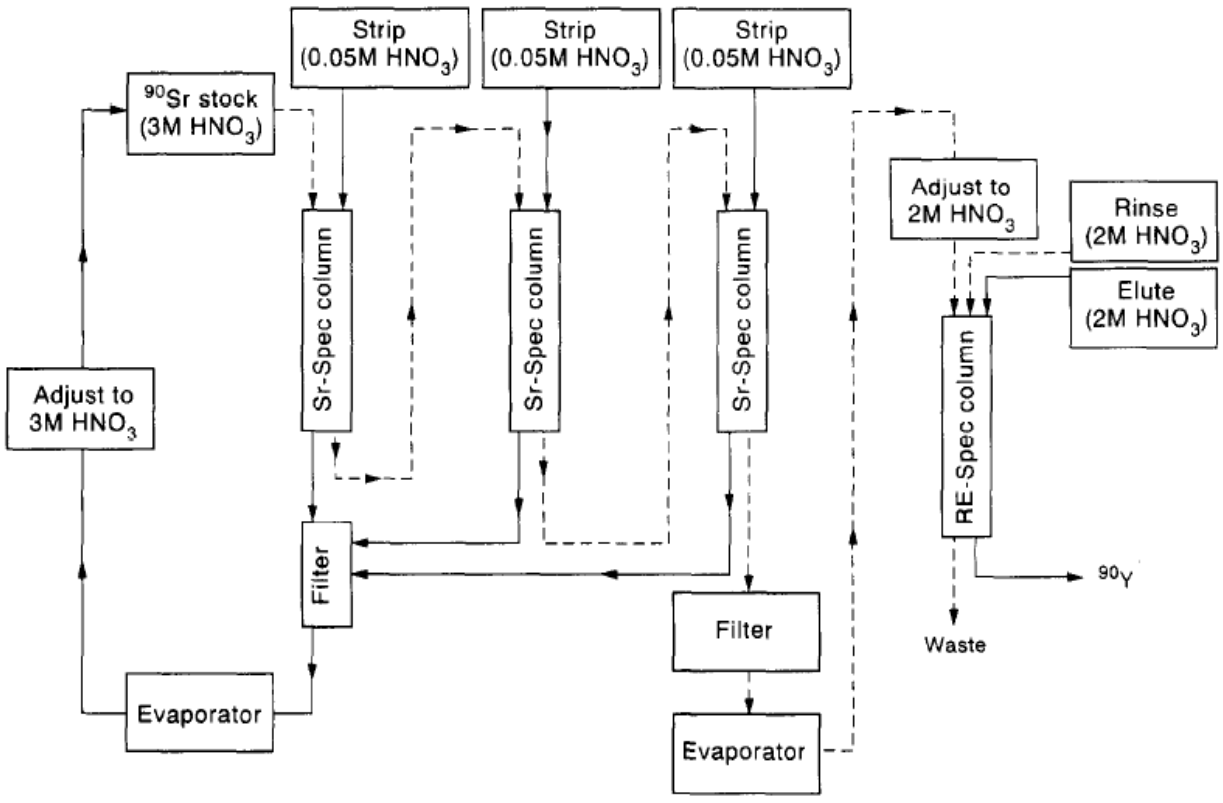

Fig. 1.9: Yttrium-90 purification scheme used by Horwitz et.al. [1.51]

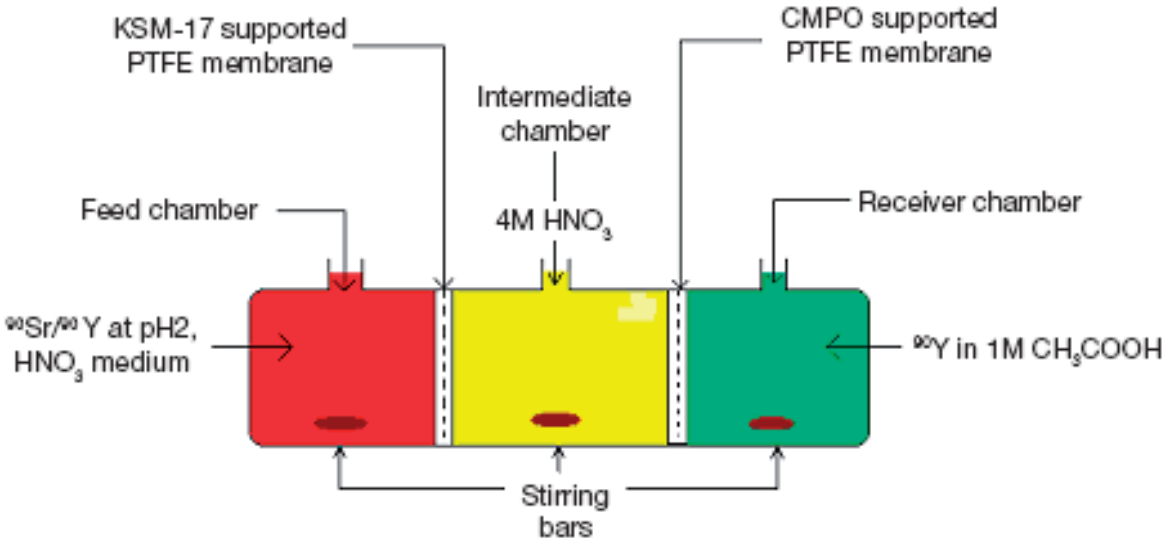

Fig.1.10: Schematic diagram of two stage SLM cell used for the separation of carrier free ^{90}Y by Dhami et al [1.52]

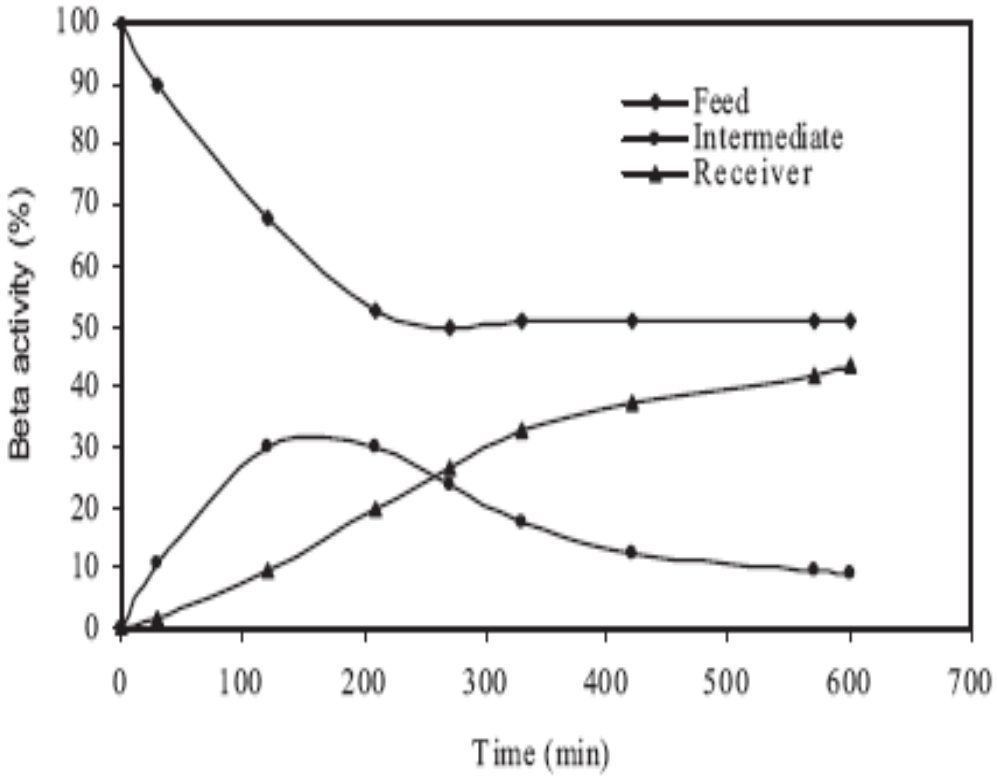

Fig.1.11: Typical plot of activity transport in the two stages SLM studies [1.52]

Based on the solvent extraction properties of KSM-17 and CMPO under different acidity conditions a two stage Supported Liquid Membrane (SLM) generator system was developed for generating carrier free ^{90}Y from $^{90}Sr/^{90}Y$ [**1.52**]. In this system, the generator consists of three 5 mL chambers (feed, intermediate and receiver chambers). Two PTFE membranes are used; one is impregnated with KSM-17 and the other with CMPO. The schematic diagram of the cell is shown in Fig. 1.10. The PTFE membrane containing KSM-17 is inserted between the feed and intermediate chambers, and the PTFE membrane with CMPO is inserted between the intermediate and receiver chambers. Known volume of the mixture of ^{90}Sr (in equilibrium with ^{90}Y) as nitrate adjusted to pH 1–2 was taken as the feed while 1 M acetic acid and 4 M HNO_3 was used in the intermediate and receiver chambers respectively. The system is operated for about 10 h with continuous stirring, and the ^{90}Y solution transported into the receiver chamber is available as ^{90}Y acetate for use. Fig. 1.11 depicts the transport of activity in the two stage SLM generator system. The activity in the feed, intermediate and receiver chambers, as a percentage of the total activity, is plotted versus time. Typically, about 85% of the ^{90}Y is transported to the final receiver chamber in 10 hrs.

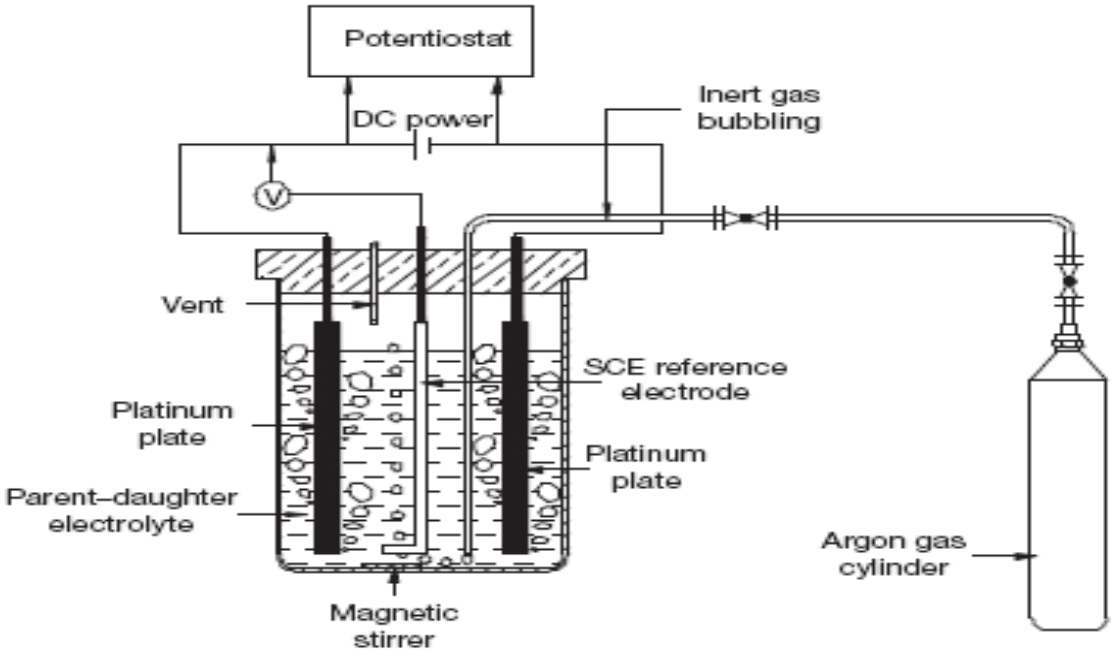

Fig. 1.12: The schematic diagram of the electrolysis cell used for the $^{90}Sr/^{90}Y$ generator [1.53]

In the development of an electrochemical ^{90}Sr-^{90}Y generator for carrier free separation of ^{90}Y [**1.53**], the method consists of two-cycle electrolysis. The first electrolysis is to be performed for 90 min in $^{90}Sr(NO_3)_2$ feed solution at pH 2-3 at a potential of - 2.5 V with 100-200 mA current using platinum electrodes. Subsequently, the second electrolysis is to be performed for 45 min in 3 mM HNO_3 at a potential of -2.5 V with 100 mA current. In this step, the cathode from the first electrolysis containing ^{90}Y (due to first cycle of electrolysis) is used as anode along with a fresh circular platinum electrode as cathode. The carrier - free ^{90}Y which is deposited on the fresh circular cathode after the second electrolysis is dissolved in acetate buffer to obtain ^{90}Y acetate, suitable for radiolabeling. The schematic diagram of the electrolysis cell used for the ^{90}Sr/^{90}Y generator is shown in Fig.1.12. These methods are, however not free from disadvantages and there is always a search for more efficient separation methods. An extraction chromatographic separation method based on a crown ether extractant (di-*tert*-butylcyclohexano-18-crown-6) has also been reported [**1.54**]. However, the crown ether is fairly expensive and it is required to develop separation methods with relatively inexpensive commercial reagents. N,N,N'N'-tetraoctyl diglycolamide (TODGA) has been found to be a more efficient extractant than CMPO and displays unique extraction behavior as the trivalent actinides/lanthanides are extracted to much higher extent as compared to the tetra- and hexa-valent actinide ions. Also, though Sr (II) extraction [**1.55**] is reported to be appreciable at lower acidities (1−3 M HNO_3), it decreased significantly at higher acidities.

1.6. Separation of Metal Ions

The separation of metal ions from solutions is governed by a number of scientific principles, viz., chemical reaction equilibrium kinetics, fluid mechanics and mass transfer from one phase to another. The theory of separation utilizes these principles in different processes viz.; solvent extraction, ion-exchange, extraction chromatography and liquid supported membrane. Amongst these techniques, solvent extraction is the most versatile technique and is extensively used for separation, preparation, purification, enrichment and analysis on micro scale to large industrial processes. The principles underlying these techniques are briefly discussed in this section.

1.6.1. Solvent Extraction

Solvent extraction or liquid-liquid extraction is based on the principle that a solute can distribute itself in a certain ratio between the two immiscible solvents, one of which is usually water and the other is an organic solvent. In certain cases, the solute can be more or less completely transferred into the organic phase. The liquid–liquid distribution can be thermodynamically explained with the help of the phase rule [**1.56**] which is usually stated as,

$$P + V = C + 2 \tag{1.6}$$

where, P, V and C denote the number of phases, variances and components, respectively. In general, a binary liquid-liquid distribution system has two phases (P =2) and contains three or more components (two solvents and one or more solutes). When a system contains only one solute (C = 3), according to the phase rule the variance is three, which means that by keeping any two variables constant the system can be defined by the third variable. In other words, at fixed temperature and pressure, the concentration of solute in the organic phase is dependent on the concentration of solute in the aqueous phase. Thus, when molecular species of the solute is same in the two phases, its concentration in one phase is related to that in the other phase (Nernst's distribution law). Consider following equilibrium reaction involving the distribution of metal ion.

$$M\ (aq.) \rightleftharpoons M\ (org.) \tag{1.7}$$

where, the subscripts (aq.) and (org.) represent species in aqueous and organic phases, respectively.

According to the Nernst's distribution law, the distribution coefficient (K_d) is represented as

$$k_d = \frac{[M]_{(org.)}}{[M]_{(aq.)}} \tag{1.8}$$

However, it has been observed that, in most cases, the molecular species of metal ions are not the

same in both the phases. Therefore, the term "distribution ratio (D)" is used in the solvent extraction which takes into account different species present in both the phases. D is defined as the ratio of the total concentration of metal ion (in all forms) in the organic phase to that in the aqueous phase.

In general, D is expressed as,

$$D=\frac{[M]_{total,org.}}{[M]_{total,aq.}} \quad (1.9)$$

The % extraction (% E) is given by,

$$\% E = \frac{100\ D}{(D + \frac{V_{aq.}}{V_{org.}})} \quad (1.10)$$

If the volume ratio is kept as 1, then equation (1.10) becomes

$$\% E = \frac{100\ D}{(D + 1)} \quad (1.11)$$

The solubility of the uncomplexed metal ions in the organic solvents is not feasible and they tend to remain in the aqueous phase as hydrated ions. For the extraction of metal ions in the organic phase, the charge on the metal ions must be neutralized so as to enhance the solubility in the organic solvents. Therefore, a suitable extractant (ligand) molecule is generally added in the organic solvent which upon complexation with metal ions forms neutral hydrophobic species which is subsequently extracted in the organic phase. In such cases, the extraction of metal ions may follow one of the following extraction mechanisms.

- ***Solvation****:* The extraction of metal ions by neutral ligands, are followed by solvation mechanism. The extraction process proceeds via replacement of water molecules from the co-ordination sphere of metal ions by basic donor atoms such as 'O' or 'N' of the ligand molecules. The well known example is the extraction of U (VI) by tri-*n*-butyl phosphate (TBP) from nitric acid medium as illustrated by the Eq. 1.12 [**1.57**].

$$UO_2^{2+} + 2NO_3^- + 2TBP \rightleftharpoons UO_2(NO_3)_2.2TBP \quad (1.12)$$

- ***Chelation:*** The extraction of metal ions proceeds via the formation of metal chelates with chelating ligands. The example of this type is the extraction of Pu (IV) by thenoyl trifluoro acetone (HTTA) in benzene as shown in Eq. 1.13 [**1.58**].

$$Pu^{4+} + 4HTTA \rightleftharpoons Pu.4TTA + 4H^+ \quad (1.13)$$

- ***Ion- pair extraction:*** This type of extraction proceeds with the formation of ion-pair species between the metal ions and ionic organic ligands. Acidic ligands such as sulphonic acids, carboxylic acids and organophosphoric acids provide anions by liberating protons which then complexed with the metal cation to form ion-pair. On the other hand, basic ligands provide cations which complex with aqueous anionic metal complex to form ion-pair. The best examples of basic extractants are quaternary ammonium salts as is the case in extraction of uranium in 6 M HNO_3 by Aliquot 336 (shown in Eq. 1.14).

$$UO_2Cl_4^{2-} + 2\,R_3NH^+ \rightleftharpoons [UO_2Cl_4]^{2-}\,[R_3NH]_2^+ \quad (1.14)$$

- ***Synergistic extraction:*** Synergism refers to the phenomenon where the extraction of metal ions in the presence of two or more extractants is more than that expected from the sum of extraction employing individual extractants. Well known example of synergistic extraction is the extraction of Pu(IV)from nitric acid medium by a mixture of HTTA and tri-*n*-octyl phosphine oxide (TOPO)in benzene [**1.59**]

1.6.2. Extraction Chromatography

Extraction chromatography is a particular form of liquid-liquid column chromatography. It is a technique that combines the selectivity of solvent extraction and ease of operation of column chromatography with the multistage character of a chromatographic process. Over the last decade, extraction chromatography (XC) has emerged as a versatile and effective method for the

separation and preconcentration of a number of metal ions. The method is now competing favourably with ion exchange chromatography in many separation problems, and is particularly advantageous when micro amounts are concerned [**1.60**]. The difference between extraction chromatography and normal partition chromatography lies in the fact that in the process of partition the solute species undergo only chemical exchange with the exchangeable cation / anion radicals of the chromatographic material (ion exchange resin), while extraction involves the transfer of the initially ionic solute from an aqueous to an organic phase, most often accompanied by complex chemical changes. The term extraction chromatography is generally used when the stationary phase is an organic liquid, and the mobile phase is an aqueous solution. The other difference is the non-attainment of thermodynamic equilibrium when extraction chromatography is performed in a column. Nevertheless, this does not influence the transfer of solutes from one phase to another [**1.61**]. Several extractants such as tri-*n*-butyl phosphate (TBP) [**1.62**], octyl(phenyl)-N,N-di-isobutyl carbamoyl methyl phosphine oxide (CMPO) [**1.63**], N,N′-dimethyl-N,N′-dibutyl tetradecyl malonamide (DMDBTDMA) [**1.64**], trialkyl phosphine oxide (TRPO) [**1.65**] and di-2-diethylhexyl phosphoric acid (D2EHPA) [**1.66, 1.67**] have been used in XC for the recovery of trivalent actinides and other metal ions from aqueous solutions. XC is much more attractive when the material of interest is in very small amount as compared to the impurities or unwanted materials. It is, therefore, very logical to employ the EXC for the separation of Y(III) from the Sr(II).

Excellent separations of elements from aqueous solutions containing high acid concentrations have been achieved by this technique [**1.68**]. XC plays an increasingly prominent role in the separation and pre-concentration of a number of radionuclides, including actinides and fission products [**1.69, 1.70**]. In XC, the selectivity of solvent extraction is combined with the ease of operation of liquid chromatography. Recently, Horwitz *et al*, [**1.71**] demonstrated some of the significant similarities and differences between XC and SX systems.

1.6.2.1. Principle of extraction chromatography

Extraction chromatography (XC) resembles reverse phase LC technique which is based on the preferential extraction of metal ions from an aqueous solution by organic ligands physically impregnated or chemically anchored on an inert solid support. The extractant molecules are

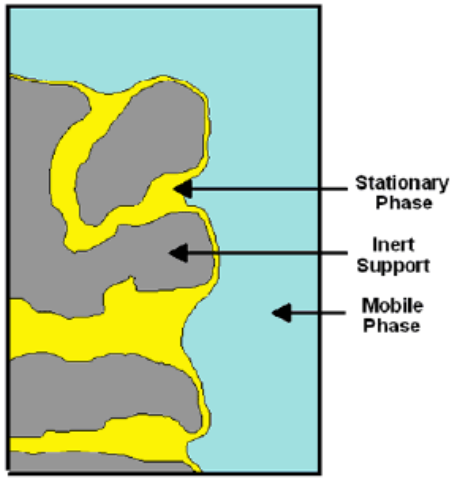

Fig. 1.13: Surface of a porous bead

sorbed into the pores of the solid support through interaction between the surface of the support containing moderate polar groups (e.g. C=O, Si=O) and hydrophobic regions of the extractant molecules by Van der Waal's interactions. The possibility of varying the capacity of extraction chromatographic resins by loading varying amount of extractants on the solid support is another interesting feature of these resins. It is also possible to remove the entire amount of loaded extractants from the support material, which would help in disposing off the resin materials after their useful life.

Fig. 1.13 is a simplified depiction of a cross section of an extraction chromatography resin bead showing the three major components of an XC system, the support, the stationary phase and the mobile phase. The inert support usually consists of the porous silica or an organic polymer ranging in size from 50 to 150 µm in diameter. Extractants, either single compounds or a mixture of compounds are used as the stationary phase. Diluents can also be used to help solubilize the extractant and to increase the hydrophobicity of the stationary phase. The mobile phase is usually an acid solution, for example nitric acid. Complexants, such as oxalic acid or hydrofluoric acid are frequently used to enhance selectivity or elute the impurities (to strip the strongly retained metal ions from the columns).

The mass distribution ratio (K_d) is given by

$$K_d = [(C_t - C_0)/ C_0].V/g \qquad (1.15)$$

where, C_o is the initial concentration of metal ion present in the aqueous phase, C_t is the concentration of metal ion in the aqueous phase at time t, V is volume of the aqueous phase, g is the weight of the resin.

1.6.3. Membrane Based Separation

Membrane based technique for the separation and concentration of metal ions are advantageous due to the following reasons.

- Ease of operation
- Low operation costs
- Energy conservation
- Continuous nature
- Possible large feed to strip volume ratio
- While considering nuclear separation, it can reduce the personnel exposure to radiations which is very crucial.

From a practical point of view, membrane based separations have found wide applications in industrial, biomedical and analytical fields as well as in waste water treatment [**1.72**]. Today's membrane industry is very much diversified. For example, industrial applications are divided into six main categories namely, reverse osmosis, ultra filtration, microfiltration, gas separation, pervaporation and electro-dialysis. Similarly, medical applications are divided into three main categories viz., artificial kidneys, blood oxygenators and controlled drug release. In membrane science, the key property that is exploited is the ability of a membrane to control the permeation of a chemical species through the membrane. In case of separation science and technology, the aim is to allow one component of a mixture to permeate the membrane freely while hindering the permeation of other components. Hence, in essence, membrane can be defined as a discrete thin interface that moderates the permeation of chemical species in contact with it. Membranes can be in biological or synthetic in nature. In separation science, synthetic membranes are mostly used and they can be isotropic or anisotropic in nature. The separation properties of membrane are determined exclusively by the nature of membrane surface layers.

In membrane based separation, two aqueous phases, one from which separation of metal ion is required (referred to as the feed phase or the source phase) and the other to which the

separated metal ion gets stripped (referred to as the receiver or the strip phase) are kept in contact with the membrane by sandwiching the extractant solution. Liquid membranes may be divided into two categories: non-supported liquid membranes and supported liquid membranes (SLM). In the case of non-SLMs the most common types are emulsion liquid membranes (ELM) and bulk liquid membranes (BLM). Supported liquid membrane again can be categorized into two types, flat sheet supported liquid membrane and hollow fiber liquid membrane.

1.6.3.1. Non Supported Liquid Membranes

There are three main types of non supported Liquid Membranes which are discussed below in brief**.**

1.6.3.1.1. Bulk Liquid Membranes

In case of bulk liquid membrane (BLM), the source phase and the receiving phase are separated from each other by a bulk organic ligand solution (Fig. 1.14). For BLM in such a configuration, density of organic carrier solution needs to be higher than both the aqueous phases. Otherwise, a different design has to be adopted. The transported amount of the material is determined by its concentration in the receiving phase. Stability is maintained so long as the stirrer is not spinning too vigorously.

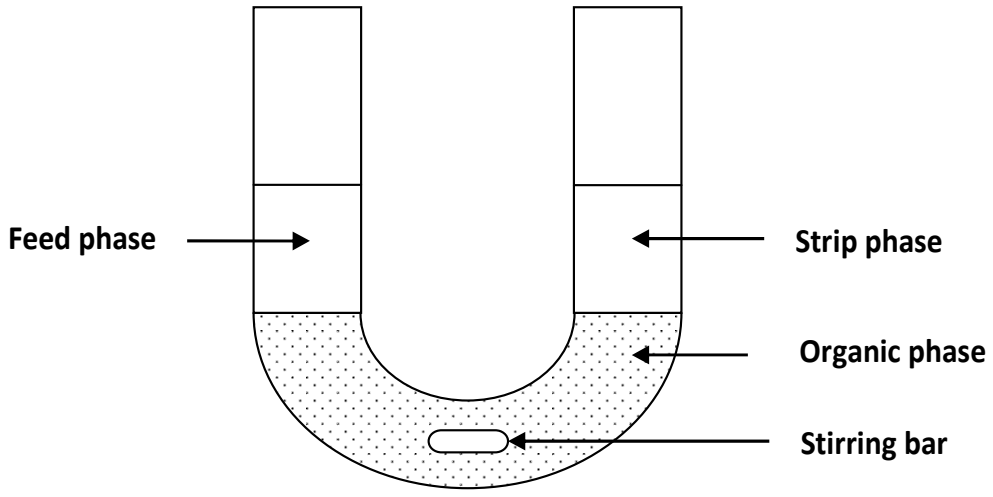

Fig.1.14: Bulk liquid membrane (BLM) set up

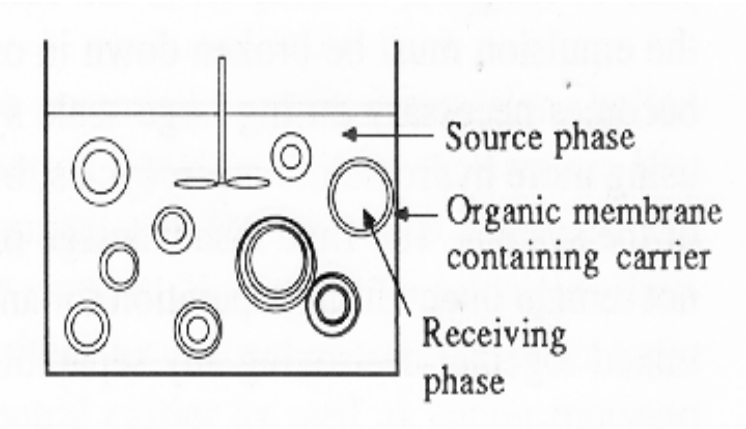

Fig. 1.15: Schematic diagram of emulsion liquid membranes set up

1.6.3.1.2. Emulsion Liquid Membranes

This setup (Fig.1.15) has a very thin membrane and a large surface area per unit source phase volume, which enhances the transport rate of this membrane. In this type of liquid membrane, the emulsion contains the receiver solution as the internal phase. The organic phase or the emulsion also containing a surfactant is added to a source phase or the external phase and mass transfer is determined similar to a two phase extraction system. The membrane stability is the same as the stability of the emulsion. In order to recover the receiving phase, and in order to replenish the carrier phase, it is required to break the emulsion by a process called as demulsification. However, anything affecting emulsion stability like ionic strength, pH, etc. must be controlled as it is vital for the success of the experiment.

1.6.3.2. Supported Liquid Membranes

In this membrane system, the feed and the receiver phases are separated by the organic phase containing carrier ligand supported on a polymeric support material. There are two types of supported liquid membranes viz.; flat sheet supported liquid membrane (FSSLM) and hollow fiber supported liquid membrane (HFSLM).

1.6.3.2.1. Flat Sheet Supported Liquid Membranes

In case of flat sheet supported liquid membrane (FSSLM), the feed and receiver phases are

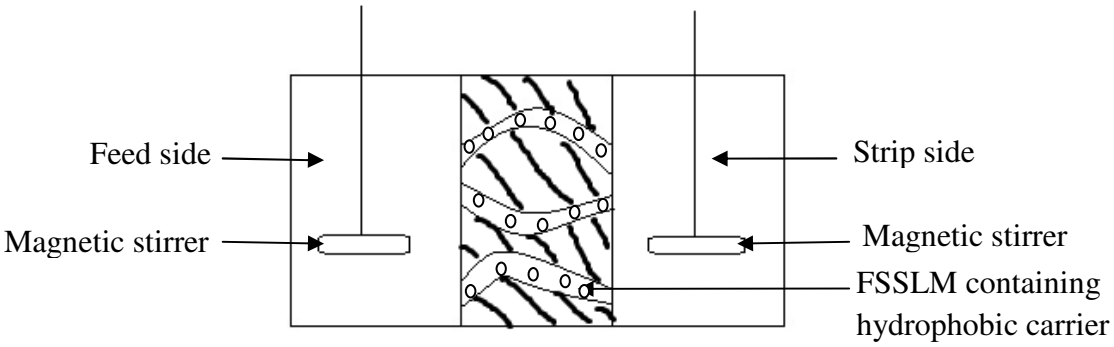

Fig.1.16: Flat sheet supported liquid membrane (FSSLM) set-up

separated using the organic extractant solution supported on the flat sheet polymeric support material. A schematic presentation of FSSLM system is given in Fig.1.16. The feed and the receiver phases are constantly stirred using magnetic stirrers in order to minimize the aqueous diffusion layer. FSSLM systems are usually associated with slow transport rates.

1.6.3.2.2. Transport Mechanisms in Liquid Membranes

In liquid membranes, the permeating species can be transported across the membrane against their concentration gradient as a consequence of an existing concentration gradient of a second species present in the system (coupled transport). Furthermore, the transport process may take place in the presence of an extractant or carrier contained within the membrane (facilitated transport). Facilitated transport originated in biochemistry where natural carriers contained in cell walls are involved. In, 1970, Bloch [**1.72**] first proposed the use of organic extractants immobilized on microporous inert supports for the separation of metal ions from a mixture. Subsequently, other researchers observed that the carrier could assist in the transport process (facilitated transport) by reacting competitively with the two species which were being transported across the membrane [**1.73, 1.74**]. Depending on the nature of the extractant, facilitated coupled transport can be of two types, viz. counter- and co-transport. When the extractant exhibits acidic properties, coupled counter transport takes place and the extraction reaction proceeds via:

$$M^+ + HX_{(membrane)} \rightleftharpoons MX_{(membrane)} + H^+ \qquad (1.16)$$

However, when neutral extractants are used, coupled co-transport takes place according to,

$$M^+ + L^- + E_{(membrane)} \rightleftharpoons EML_{(membrane)} \quad (1.17)$$

where, pH and counter ion concentration are used as driving forces, respectively and L represents the carrier ligand.

1.7. Criteria for Selection of Extractants

A number of factors are taken into consideration while selecting or designing a particular extractant for the separation of metal ions for industrial applications [**1.75**]. Some of the important considerations are listed as follows:

I. High solubility in paraffinic solvents (non-polar solvents)
II. Low solubility in the aqueous phase
III. Non-volatility, non-toxicity and non-inflammability
IV. High complexation ability with the metal ions of interest
V. High solubility of the metal-ligands complex in the organic phase, i.e. high metal loading capacity in the organic phase
VI. Ease of stripping of metal ions from the organic phase
VII. Reasonably high selectivity for the metal ion of interest over the other metal ions present in the aqueous solution
VIII. Optimum viscosity for ease of flow and optimum interfacial tension (IFT) to enable a faster rate of phase disengagement
IX. Ease of regeneration of the extractant for recycling
X. High resistance to radiolytic and chemical degradation during operation and
XI. Ease of synthesis / availability at a reasonable cost.

1.8. Digylycolamides: A Class of Promising Extractants

Diglycolamide are a class of extractants with unusually high extraction efficiency for trivalent actinides vis-avis the tetra valent and hexavalent actinides. The malonamides extractants such as DMDBTDMA (N,N′-dimethyl-N,N′-dibutyl tetradecyl malonamide) and DMDOHEMA (N,N′-

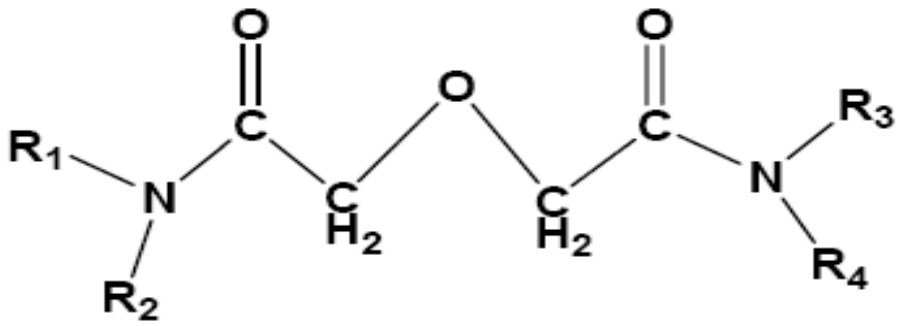

Fig. 1.17: Structural formulae Tetra alkyl diglycolamide

dimethyl-N,N′-dioctyl-2-(2-hexylethoxy) malonamide) are known to extract the actinides in the order: $M^{4+} > MO_2^{2+} > M^{3+}$. On the other hand, diglycolamides extract the actinides in the order: $M^{3+} > M^{4+} > MO_2^{2+}$.

It has been observed that the introduction of etheric oxygen between the two amide groups as shown in Fig. 1.17 causes significant enhancement in the extraction of trivalent actinides / lanthanides. The work on diglycolamides was started after Stephan *et al*, reported the extraction of various metal ions with multidentate amido podands [**1.76, 1.77**]. Sasaki and Choppin were probably the first to report the extraction of lanthanides and actinides with diglycolamides [**1.78-1.82**]. They used dimethyl dihexyl diglycolamide and its analogous compounds for the solvent extraction studies on lanthanides and actinides. These preliminary studies, however, were focused on the extraction of metal ions from aqueous solutions of pH ranging from 1 to 4. Narita *et al*, studied the extraction of lanthanides from acidic solutions employing dimethyl diphenyl diglycolamide [**1.83**]. They proved by XRD and EXAFS studies that diglycolamide form tridentate complex with lanthanides in solid as well as in solution. Sasaki *et al* [**1.84**] synthesized a series of diglycolamides having same central frame with different alkyl chains (ranging from *n*-propyl to *n*-dodecyl) attached to amidic nitrogen atoms. Various properties of the synthesized diglycolamide derivatives are represented in Table 1.3. They found that the diglycolamide derivatives with lower alkyl chain (*n*-propyl and *n*-butyl) were not soluble in paraffinic solvents like *n*-dodecane due to presence of three polar oxygen atoms. Though the higher homologues of diglycolamide were freely soluble in *n*-dodecane, the distribution ratio values for Am(III) were found to decrease due to the steric hindrance during

Table 1.3: Various properties of tetra- *n*-propyl, *n*-butyl, *n*-amyl, *n*-hexyl, *n*-octyl, *n*- decyl and *n*-dodecyl diglycolamide

Diglycolamide (DGA)	Solubility in water [mM]	Solubility in *n*-dodecane	D_{Am} by 0.1M DGA in *n*-dodecane (1M HNO_3)
TPDGA	57.0	Very poor	--
TBDGA	2.3	poor	--
TADGA	0.27	Soluble	100
THDGA	0.11	Soluble	40
TODGA	0.042	Freely soluble	30
TDDGA	0.042	Freely soluble	18
TDDDGA	0.040	Freely soluble	11

complexation of the bulky molecules.

Amongst different derivatives synthesized, N,N,N',N' tetra-*n*-octyl diglycolamide (TODGA) was demonstrated to be the best candidate with reference to its free solubility in *n*-dodecane and significantly high distribution values for trivalent actinides. Along with TODGA, Sasaki *et al* synthesized a series of diglycolamides with varying alkyl substituents on the amidic nitrogen [**1.84**]. Among these, tetra-2-ethylhexyl diglycolamide (T2EHDGA), was found to be competent to TODGA with respect to trivalent actinides extraction [**1.85**]. T2EHDGA is just structural modification of TODGA where, substituent *n*-octyl group of TODGA was replaced by 2-ethyl hexyl group. Though, its extraction efficiency for trivalent ions is slight lower than TODGA, it was quite successful towards actinide partitioning studies.

1.8.1. Main Features of Diglycolamides

Diglycolamides exhibit the excellent properties required for an extractant which can be exploited for the partitioning of radionuclides from HLW. Salient features of diglycolamides are listed as follows,

I. High extraction of trivalent lanthanides/actinides from moderate acidic aqueous solutions
II. Ease of stripping of trivalent lanthanides/actinides

III. High solubility in paraffinic solvents (freely soluble in *n*-dodecane)
IV. Low concentration of diglycolamides to be used (~ 0.1 M)
V. Good radiolytic and hydrolytic stability
VI. Possibilities of complete incineration as the constituent elements are C, H, N and O
VII. Ease of synthesis.

1.9. Scope of the Thesis

Though there are a number of methods using different techniques as well as different extractants viz. CMPO and malonamide based extractants for the separation of ^{90}Y from ^{90}Sr, but they certain limitations either in terms of purity of ^{90}Y or due to complexity of the process. It is, therefore, desirable to develop a simple separation methodology for the separation of ^{90}Y from ^{90}Sr, using alternative extractants with better performances. In this context, two diglycolamides viz. N,N,N'N'- tetra *n*-octyl diglycolamide (TODGA) and N,N,N'N'- tetra-2ethylhexyl diglycolamide (T2EHDGA) have been identified as most powerful ligands being considered for the separation of ^{90}Y from ^{90}Sr. In the present thesis, in solvent extraction studies, effort has been made to explore the efficiency of TODGA and T2EHDGA for preferential extraction of ^{90}Y from its mixture with ^{90}Sr from HNO_3 as well as HCl medium. From the experiments with varying concentration of ligands, both in HNO_3 and HCl, the nature of extracted species was determined. Also, a detailed insight into the thermodynamics of extraction, the effect of the concentration of phase modifiers (particularly for T2EHDGA) on the separation factor has been discussed. Based on these studies, attempt was made to evolve separation schemes for carrier free ^{90}Y using both TODGA and T2EHDGA as the extractant. Finally, the purity of ^{90}Y, thus obtained, was examined by following the half lives.

Solid phase extraction has been increasingly used for the separation of trace as well as ultra trace amounts of metal ions from complex matrices employing chelating polymers. The extraction chromatographic separation studies on separation of ^{90}Y from its mixture with ^{90}Sr were performed by impregnation of TODGA on an inert solid support. A detailed study on the relative sorption behavior of Y(III) and Sr(II) in nitric acid and hydrochloric acid was carried out and based on the elution profile obtained using different eluents, a separation scheme was developed for obtaining carrier free ^{90}Y.

In this work, supported liquid membrane (SLM) based separation of ^{90}Y from its mixture with ^{90}Sr has been explored both with TODGA and T2EHDGA and in SLM studies, the role of diluents and that of feed acidity on the transport behavior were investigated. Based on these studies, attempt was made to develop suitable separation schemes using both TODGA and T2EHDGA as carrier in suitable diluents.

In conclusion, the work reported in this thesis has relevance to the separation chemistry giving rise to some developmental work in the separation of the important radionuclide ^{90}Y from its mixture with ^{90}Sr available in plenty in nuclear waste. Basic as well as applied aspects of the extraction / sorption behavior of metal ions have been explored in the present work.

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Chapter II

Experimental

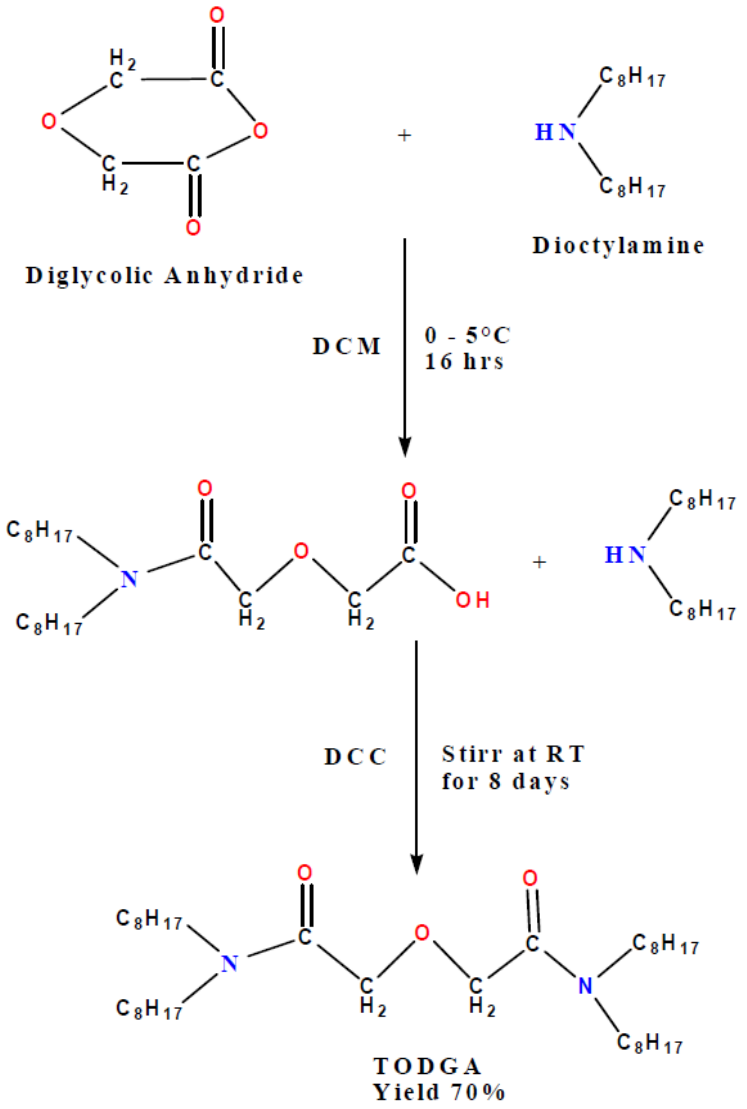
EXPERIMENTAL

In the present studies, the extraction behavior of the Y(III) and Sr(II) have been investigated using under different experimental conditions employing N,N,N′,N′-tetra-*n*-octyl diglycolamide (TODGA) and its branched homolog, N,N,N′,N′-tetra-2-ethylhexyl diglycolamide (T2EHDGA) as the extractants. The techniques used for the separation studies of Y(III) and Sr(II) were solvent extraction, extraction chromatography and supported liquid membrane. This Chapter, therefore, deals with details of various apparatus, materials, experimental techniques as well as analytical techniques used in the present studies along with brief descriptions on materials and apparatus.

2.1. Synthesis of N, N, N′ N′-Tetraoctyl Diglycolamide (TODGA)

In this study, the novel extractant, synthesis of N,N, N′ N′-tetra-*n*-octyl diglycolamide (TODGA) was done with slight modifications compared to the method reported in the literature [**2.1**]. To 1 mol of diglycolic anhydride (dissolved in 600 mL of dichloromethane) taken in a reaction flask connected to moisture and oxygen free nitrogen gas stream 1 mol of di-*n*-octyl amine, dissolved in~300mL of dichloromethane was added drop wise, with a constant stirring and the temperature of the reaction mixture was maintained at 0-5^{o}C. Once the addition of di-*n*-octyl amine was over, the mixture was kept under continuous stirring condition for about 16 hours at room temperature. Subsequently, the reaction mixture was cooled to 0-5^{o}C and 1.3 mol of N,N′-dicyclohexyl carbodiimide (DCC) dissolved in 100mL dichloromethane was added drop wise with constant stirring. The reason for adding ~30% extra DCC (DCC was used as a dehydrating agent) is due to the fact that it can complete the reaction and the remains can be easily decomposable. After the complete addition of DCC, the reaction mixture was stirred at the same temperature for another 30 minutes, followed by the addition of the next batch of di-*n*-octyl amine (1 mol dissolved in dichloromethane) drop wise with constant stirring and maintaining the temperature at 0 - 5°C. After the complete addition of di-*n*-octyl amine, the reaction mixture was stirred for eight days at room temperature. One of the reaction product, N, N′-dicyclohexyl urea, appeared as white precipitate, was discarded after filtering and washing with excess of dichloromethane.

The dichloromethane was subsequently removed from the filtrate by rotavaporator to get the crude product. In the subsequent step, the crude product was purified by ethyl acetate followed by removal of the insoluble impurities. The other soluble volatile impurities were removed by vacuum distillation (2.5mm) at 120-140°C to get the product in the flask. The product was further purified by silica gel column. The final product of (TODGA) was obtained as a pale yellow viscous liquid with about 70% yield. The synthesis scheme for TODGA is represented in Scheme 2.1.



Scheme 2.1.: Synthesis scheme of TODGA

Fig. 2.1: C, H, N & S Elemental analyzer

2.2. Characterization of TODGA

Characterization of TODGA was done by a number of analytical instrumental methods viz., by PMR, FT-IR as well as by elemental analysis. The C, H, N & S elemental analyzer used in the present work is shown in Fig. 2.1. Analysis of the PMR spectrum of TODGA showed that the signal peaks were multiplets at 1.26 and 1.56, triplets at 0.92 and 3.18 and singlet at 4.39 ppm. These peaks were assigned to the protons of different groups and are listed in Table 2.1. Similarly, elemental analysis data of the synthesized TODGA are given in Table 2.2. The values,

Table 2.1: PMR spectral data of TODGA

Functional Groups	No. of protons	#Chemical Shift (ppm)
-N-CH_2-CH_2-$(CH_2)_5$-**CH_3**	12	0.92(t)
-N-CH_2-(**CH_2)$_5$**-CH_2-CH_3	40	1.26(m)
-N-CH_2-$(CH_2)_5$-**CH_2**-CH_3	8	1.56(m)
-N-**CH_2**-$(CH_2)_5$-CH_2-CH_3	8	3.18(t)
-CO-CH_2-O-**CH_2**-CO-	4	4.39(S)

#s: singlet, t: triplet, m: multiplet

Table 2.2: Analytical data of TODGA

Formula	$C_{36}H_{72}N_2O_3$
Product Yield	~70%
C (%)	73.1 (74.5)#
H (%)	12.8 (12.4)#
N (%)	5.2 (4.8)#
Frequency of >C=O	1640 cm^{-1}

Values in parenthesis are the theoretical values

thus obtained in the CHN elemental analysis of the synthesized product were found to be very close to those of the expected values, suggesting the successful synthesis of TODGA. The presence of carbonyl groups of diglycolamide was confirmed by the appearance of characteristic vibrational frequency at 1640 cm^{-1} in FT-IR spectrum.

2.3. Synthesis and Characterization of Tetra (2-Ethylhexyl) Diglycolamide (T2EHDGA)

This extractant, which is a branched derivative of TODGA was synthesized by the condensation of diglycolylchloride and bis (2-ethylhexyl) amine in presence of triethyl amine by a procedure, similar to that described above [**2.2**]. The product was characterized by GC-MS, PMR, FT-IR and elemental analyzer. GC-MS was performed on Thermo Finnigan Trace DSQ instrument with a single quadruple mass spectrometer at 70 eV using 15 m×0.25 mm DB5 fused silica capillary column.

As carrier gas, helium was used and the temperature program was 100 °C for 1 minute, increased to 280 °C at the rate of 10 °C per minute rise and held at 280 °C for 20 minutes. The injector temperature was 300 °C. Elemental analysis was performed on Thermo Finnigan Flash EA TM1112 analyzer. The characterization data are as follows:

GC-MS: 9.05 min, 1.89%, *m/z* 241 calculated for $HN(C_8H_{17})_2$; 22.00 min, 28.13 min, 98.11%, *m/z* 582 calculated for $O[CH_2C(O)N(C_8H_{17})_2]_2$. Elemental analysis: C: 74.471%, H: 12.488%, N: 5.108%, and O: 8.0%; calculated C: 74.41%, H: 12.5%

2.4. Radiotracers

^{90}Y tracer was obtained from two sources viz. i) from ^{90}Sr and ^{90}Y mixture using a crown ether column known as Sr.Spec® resin column and ii) by irradiating natural Y_2O_3 in Dhruva reactor (100MW Indian Research Reactor) at a flux of $1x10^{13}$ neutrons / cm^2 /s.

$^{85,89}Sr$ tracer was procured from Board of Radiation & Isotope Technology (BRIT), Mumbai and was used as a surrogate for ^{90}Sr. For the actual separation studies, ^{90}Sr (procured from BRIT, Mumbai) was used.

2.4.1. Preparation of ^{90}Y Stock Solution from Sr.Spec® Column

The principle of obtaining (also known as milking) ^{90}Y from Sr.Spec® column is based on extraction chromatography [**2.3**]. The extraction chromatographic resin material i.e., Sr.Spec® is prepared by impregnating Amberlite XAD-7, using a solution of 4,4/ (5/) – bis (*tert*-butyl cyclohexano) -18-Crown-6 in 1-octanol by procedure reported earlier[**2.4**].

In our study, Sr.Spec® column was procured from Eichrom Industries, Inc. As per the literature report [**2.4**], D_{Sr} shows the maximum value at 3 M HNO_3 as compared to other divalent and trivalent ion. The following procedure was followed for obtaining ^{90}Y tracer from ^{90}Sr and ^{90}Y mixture using the Sr.Spec® column. First, the column was conditioned by passing 5 ml 3 M HNO_3 solution followed by passing slowly the required amount of ^{90}Sr + ^{90}Y activity taken in measured volume of 3 M HNO_3. In this process, ^{90}Sr was fully retained by the Sr.Spec® column and pure ^{90}Y was obtained as eluate. The stock activity of this eluate after proper dilution was measured by β counting. Subsequently, the ^{90}Sr loaded Sr.Spec® column was used a number of times for milking ^{90}Y just by eluating with 3 M HNO_3 since loaded ^{90}Sr tend to attain secular equilibrium with ^{90}Y.

2.4.2. Preparation ^{90}Y Stock Solution from Neutron Irradiated Y_2O_3 in Dhruva Reactor

After irradiating 200 mg of natural Y_2O_3 for required period of time in Dhruva reactor at a flux of $1x10^{13}$ neutrons / cm^2 /s, the oxide was digested in conc. HNO_3 solution and then evaporated to dryness followed by addition of 3 M HNO_3 solution for making the stock solution. The

Table 2.3: Chemical reagents used in the present studies and their Make

Chemical reagents	Make	Purity
Yttrium Oxide	Apex chemicals, Mumbai	>99.99%
1-Octanol	BDH, Mumbai	>99 %
Toluene	BDH, Mumbai	>99 %
Xylene	Lancaster, U.K.	>99 %
Methyl iso butyl ketone	S.D. Fine Chemicals, Mumbai	>99 %
Chloroform	S.D. Fine Chemicals, Mumbai	>99 %
Carbon tetrachloride	S.D. Fine Chemicals, Mumbai	>99 %
Nitric Acid	S.D. Fine Chemicals, Mumbai	65 %
Hydrochloric Acid	S.D. Fine Chemicals, Mumbai	70 %

activity of the stock solution was measured by β counting in a Liquid Scintillation Counter.

2.5. Chemicals

A list of the chemicals used for the experiments are given in Table 2.3 along with their make. The reagents are used as such while the organic diluents are purified using literature methods [**2.5**].

2.6. Membranes

Polytetrafluoroethylene (PTFE) membranes were procured from Sartorius, Germany. The membrane thickness was measured by a Mitutoyo Digital micrometer while porosities of the membranes were measured by an Electroscan 2020 environmental scanning electron microscope (ESEM). The images of 2 mm × 2 mm membrane pieces glued to aluminium stub were subsequently analyzed by image analyzer [**2.6**]. The porosity of membrane with pore size 0.45µm was determined as 64 % with an effective area (computed from the geometric area and the membrane porosity) as 3.14 cm^2. The porosity of membrane was also determined by measuring the volume of *n*-dodecane that the membrane could hold in the pores. The porosities obtained by these two methods agreed within ± 4 %.

2.7. Solution Preparations

Analytical Grade (A.R) reagents were used throughout the present studies. Millipore deionized water (specific conductivity ~0.05 × 10^{-6} S·cm^{-1}) was used in all the experiments. Solvent solutions were prepared using required diluent mixtures. The dilution was done up to the mark using diluent mixtures prepared earlier.

Acidity of the sample solution, whenever required, was carried out titrimetrically by taking a measured volume of aliquot and titrated against standard alkali in the presence of phenolphthalein indicator.

2.8. Preparation of TODGA Resin

TODGA impregnated extraction chromatographic resin made with Chromosorb W (dimethyl dichlorosilane treated acid washed celite diatomaceous silica, mesh size 60–80) as the solid support was prepared in the following way. Chromosorb W (60–80 mesh) was obtained from Johns Manville, USA and was cleaned by thorough washing with methanol, dilute nitric acid and deionized water. The resin beads were dried at 60^{o}C to constant weight before loading the

Table2.4. Characteristics of the TODGA chromatographic resin material and the corresponding packed column

Resin material	Parameter	Packed Column	Parameter
Stationary phase	TODGA	Bed volume, mL	1.269
Support material	Chromosorb-W	Bed density, g/mL	0.629
Mesh size	60–80	Density of stationary phase, g/mL	0.891
Extractant loading, % w/w	47	Vol. of stationary phase: mL/mL of bed	0.252
Average density of resin, g/mL	1.08	Vol. of mobile phase: mL/mL of bed	0.558

extractant. The extraction chromatographic resin material was prepared by equilibrating 6 g of the solid support material (Chromosorb W) with 4 g TODGA in methanol for 24 hours. The solvent was evaporated by flushing nitrogen gas and the resultant solid was kept under vacuum in desiccators till constant weight. The loading of TODGA in the resin material was 40% which was confirmed from weight measurements. Characteristics of the TODGA chromatographic resin material and the corresponding packed column are given in Table 2.4.

2.9. Methods and Equipments

Though several techniques for the separation of metal ions are known, technique such as solvent extraction, extraction chromatography and liquid membrane were employed in the present studies. The aqueous metal-ligand complexation, ligand nitric acid complexation, thermodynamics of metal ion extraction etc. were studied by the solvent extraction technique. The extraction chromatographic studies on metal ions were performed by impregnation of the ligand on the inert solid support. The basic studies on the transport of metal ions through liquid membrane were carried out by batch studies using a transport cell. Various experimental setups and methodologies used in the present work are briefly mentioned below.

2.10.1. Solvent Extraction Studies

This section deals with the experimental methodology adopted in the solvent extraction studies carried out in the present work.

In order to study metal ion distribution, a suitable volume of aqueous phase (in the range of 0.5-2 ml) at the desired acidity, spiked with the required radiotracer was equilibrated in Pyrex glass stoppered equilibration tube with equal volume of organic phase containing the desired concentration of the extractant in the chosen diluent. In all the experiments, except stated otherwise, the organic phases were pre-equilibrated with the respective acid solutions. In order to have thorough contact between the reactants of both phases, the glass tubes were agitated in a thermostated water bath maintained at 25±0.1°C for about 60 minutes. For studies, carried out to determine thermodynamic parameters however, the temperature of the water bath was maintained between 15-45°C (Fig. 2.2). Proper care was taken to maintain the required temperature of the tubes containing the organic and aqueous phases till the completion of

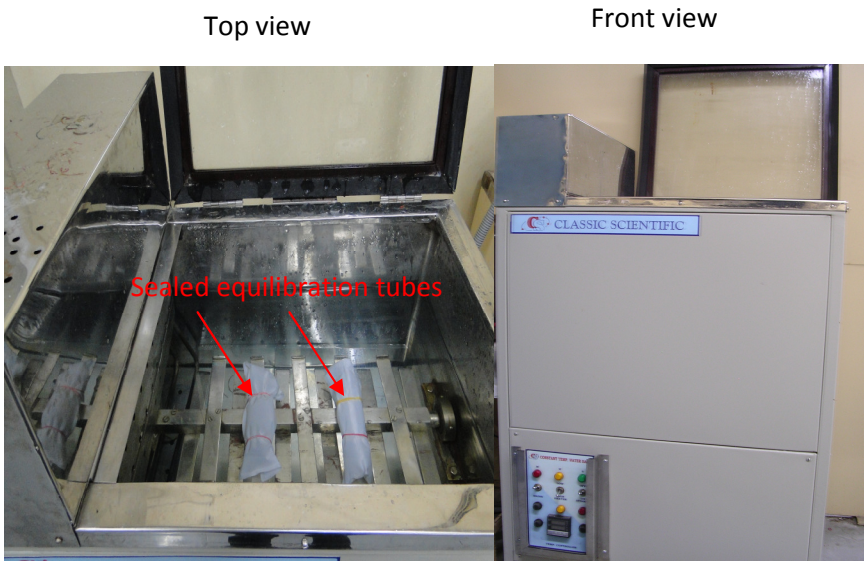


Fig. 2.2: Constant temperature water bath used for carrying out the solvent extraction studies

aliquoting of the sample. After completion of the equilibration, the two phases were centrifuged and assayed by taking out suitable aliquots (25-500 µL) from both the phases. Subsequently, the distribution ratio values were calculated as the concentration of metal ions (in terms of counts of radionuclides per unit time per unit volume) in the organic phase to that in the aqueous phase. Also, during acid distribution studies the hydrogen ion concentrations in the two phases were obtained by titration with standard alkali solution using phenolphthalein as the indicator. The organic phase was titrated in aqueous ethanol medium using standard alkali solution using phenolphthalein as indicator. Each distribution value was obtained in duplicate or triplicate and the agreement between these values was within ±2%. A good material balance (≥95%) was usually obtained in all the experiments.

2.10.2. Extraction Chromatography Studies

2.10.2.1. Batch Distribution Studies

The investigation on the uptake of radionuclides on the extraction chromatographic resin materials in batch studies was carried out by equilibrating about 1-2 ml of the aqueous solutions at the desired acidity containing the radiotracer with a known amount of resin (30-50mg) in glass

stoppered equilibration tubes. The two phases were equilibrated in a thermostated water bath maintained at 25 ± 0.1°C for 45 minutes. The time to attain equilibrium K_d values was about 60 minutes for all the experiments. Since the aqueous phase needs to be clear and free from any floating resin particles, the tubes were centrifuged and the aqueous layer was separated from the resin phase into another tube. Subsequently, the clear aqueous layer was centrifuged for the second time for obtaining resin free aqueous layer. Suitable aliquots of the aqueous phases were taken for assaying the metal ions. The distribution coefficient (K_d) of the metal ions was calculated by employing the following formula,

$$K_d = \frac{(C_0 - C)}{C} x \frac{V}{W} (mL/g) \qquad (2.1)$$

where, C_0 and C represent the concentrations of metal ions (in counts per unit time per unit volume) before and after equilibration, V is the volume of aqueous phase used (mL) and W is the weight of the resin material employed (g). For determining $K_{d\text{-}HNO3}$, equilibration experiments were carried out in similar way in the absence of the metal ions. The concentration of HNO_3 in the aqueous phase was determined volumetrically before and after equilibration. The determined value and the calculated value were found to be within an error limit of ± 5 % error.

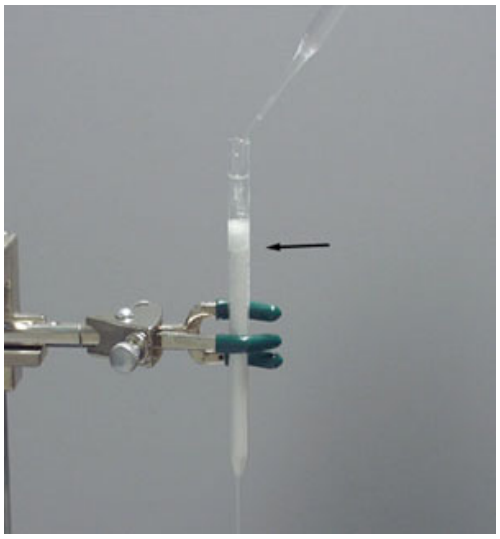


Fig. 2.3: Photograph of a typical column used for extraction chromatographic studies

2.10.2.2. Column Studies

The chromatographic columns were prepared by packing about 0.5 mg to 1.0 g of resin material in borosilicate glass column of 4mm inner diameter. The bed volume and the bed density were calculated from the column dimensions and the weight of the packed chromatographic resin material. The flow rate of eluant through the column was controlled with the help of a pinch cock. The volume of the stationary phase (Vs) and volume of the mobile phase (Vm) were estimated by a reported method [**2.4**]. The columns were pre-conditioned by passing excess of appropriate nitric acid solutions prior to the introduction of the sample solutions. All the column operations were carried out at ambient temperature (24.0 ± 1.0°C) at the required flow rate. The breakthrough curves and elution profiles were obtained by plotting radioactivity in the effluent / eluent vs volume of solution passed. Fig.2.3 represents a typical column used in the present experiments.

2.10.3. Supported Liquid Membrane Studies

This section deals with the methodology adopted in the supported liquid membrane transport experiments using a two component Pyrex glass cell. A typical membrane transport cell used in the present studies is shown in Fig. 2.4. In this type of transport cell, both the compartments of the glass cell are joined by glass flanges with the SLM contained in polymeric PTFE filters placed in between.

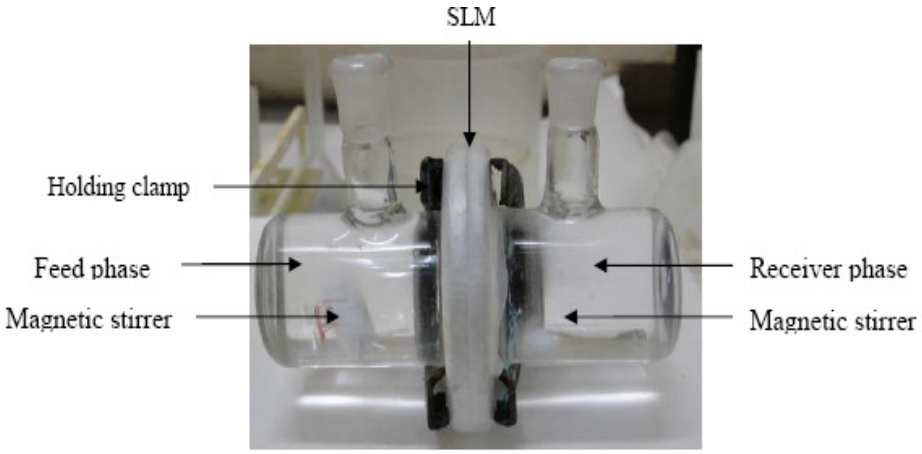


Fig. 2.4: Photograph of a typical supported liquid membrane transport cell used in the present studies

The two aqueous phases viz. feed and receiver were stirred at 200 rpm using high speed magnetic stirrer equipped with precise speed control. The stirring rate of 200 rpm was set to ensure minimal thickness of the aqueous boundary layers without causing any damage to the membrane [**2.7**]. The volumes of the aqueous feed and strip solutions were kept constant (20mL) during all the experiments. For the preparation of the SLM, the microporous PTFE membranes were soaked in the carrier solution (e.g. 0.1M TODGA in *n*-dodecane or 0.2 M T2EHDGA) for about 10 minutes prior to their use. Subsequently, the submerged membrane was removed from the solution and wiped carefully with a tissue paper to remove the excess fluid at the outer surface of the support. This impregnation technique leads to SLMs which were reproducible within 5% with respect to their transport behavior.

The cumulative transport (%T) of the metal ions at a given time was determined by the following equation,

$$\%T = \frac{100(C_0 - C_t)}{C_0} \tag{2.2}$$

where, C_0 and C_t are the concentration of metal ions in the aqueous feed at the start of experiment (t =0) and at time t, respectively.

The permeability coefficient, P is obtained using the following equation,

$$\ln\left(\frac{C_t}{C_0}\right) = P\left(\frac{Q}{V}\right)t \tag{2.3}$$

P is related with the flux of metal ions, C_0 as follows:

$$P = J/C_0 \tag{2.4}$$

where, Q is the effective membrane area obtained from the total exposed membrane surface area, A (4.12cm^2) and porosity, ε (72%) and V is the volume of the feed solution in cm^3. The effective surface is related to the exposed membrane area by the following equation.

$$Q = A \cdot \varepsilon \tag{2.5}$$

A plot of ln (C_t/C_0) versus time allowed calculating the P value from the slope of the linear fit. It should be noted that the above equation is valid only when the carrier is not saturated and the flux decreases linearly with time. In the present work, since all the experiments were carried out at tracer metal concentrations, equation (2.3) was applicable for the calculation of P.

2.10.4. Irradiation Studies

In order to study the irradiation stability of the resins, a ^{60}Co gamma source of ~ 2KGy/hr dose rate was used. TODGA resins were kept in gamma chamber equipped with ^{60}Co source (shown in Fig.2.5) till the required irradiation dose was received. The gamma dose was estimated by Fricke dosimetry [**2.8**].

Fig. 2.5: Photograph of the gamma chamber used in the present studies

2.10.5. Other Equipments

Elemental (C, H, N) analysis was performed using an elemental analyzer EA 1110 from Carlo-Erba Instruments. The FT-IR spectra were recorded as thin film in IR spectrophotometer in the range 4000 – 400 cm^{-1}. The PMR spectra of the amide products were recorded in $CDCl_3$ medium using Bruker 200MHz instrument employing TMS (tetramethyl silane) as an internal standard.

Jasco V-530 UV-Spectrometer was employed for UV-Visible spectrophotometeric analysis. Viscosity of the samples was determined using a digital viscometer from DJ Scientific, model AV250VAC.

2.11. Analytical Instruments / Techniques

The radioanalytical techniques employed for the analysis of β^- emitting radionuclides were liquid scintillation counter and the β^- spectra were taken by coupling the liquid scintillator counter to a multichannel analyzer. NaI (Tl) scintillation counter and HPGe detector were used for the estimation of gamma emitting radionuclides.

2.11.1. Liquid Scintillation Counter

Liquid scintillation counter as shown in Fig. 2.6 [**2.9**] is the most widely used detector for the quantitative analysis of β^- emitters. Nearly 100% detection efficiency of this detector is of great advantage and even as low as few Bq of beta activity can be assayed with good precision. A scintillator is a material that luminesces in a suitable wavelength region when ionizing radiation interacts with it. Interaction of the charged particles (beta particles) with the scintillator results in the emission of photons and the intensity of the emitted light is a quantitative measure of the incident radiation. The light emitted from the scintillator is then collected by the photomultiplier

Fig. 2.6: Photograph of the liquid scintillation counter used in the present study

tube (PMT) which produces signal detected by the detector system. Usually the scintillator emits photons in the UV region and a wavelength shifter is added to the scintillator which has intermediate energy levels. In such cases the de-excitation takes place via these intermediate energy levels and hence the wavelength of the emitted photons is shifted from the UV to the visible region which is subsequently recorded in the PMT (as photocathodes of most PMTs are compatible with visible light). The liquid scintillation counter is used to monitor gross β activity as it cannot distinguish between β energies. Many organic compounds are versatile scintillators for radiation measurements [**2.10, 2.11**].The liquid scintillation cocktail comprises of a solvent like dioxane or toluene, while PPO (2,5-diphenyl oxazole) acts as the scintillator and POPOP [1,4-bis-2-(5-phenyl oxazolyl)-benzene] acts as a wavelength shifter. The solvent is the main stopping medium for radiation and must be chosen to give efficient energy transfer to the scintillating solute. In case of toluene based scintillator a suitable extractant such as di (2-ethylhexyl) phosphoric acid (HD2EHP) is also added which facilitates the transfer the radionuclides from the aqueous phase to the organic phase. In the present work, generally toluene based liquid scintillator was employed which consisted of 10 %(v/v) HD2EHP, 0.7 %(w/v) PPO and 0.03 %(w/v) POPOP. Suitable aliquots (25- 100μL) containing beta activity were taken in glass vials containing liquid scintillator solution. When aqueous phase was added to the toluene scintillator, the two phases were mixed vigorously for ~2 min using an ultrasonic agitator to transfer the radionuclides into the organic phase. Each sample was counted for sufficient time so that the counting statistics was less than 1 % .

2.11.2. NaI (Tl) Scintillation Counter

Sodium iodide activated with 0.1–0.2% of thallium, NaI(Tl), is by far the most widely used inorganic scintillator for the assay of gamma ray emitting radionuclides. Salient features of the detectors are the low cost, ease of operation and ruggedness [**2.12, 2.13**]. The band gap in NaI crystal is of the order of 5-6eV. When gamma ray falls on the detector its energy is used up either for excitation of electrons from the valence band to the conduction band or for the ionization of atom. De-excitation of the electrons from the conduction band to the valence band leads to the emission of photons in the UV region as the band gap is large. To shift the energy of the emitted photons into the visible region, which is requisite of PMT, NaI crystal is doped with

Fig. 2.7: Photograph of the NaI(Tl) detector assembly used for gamma ray counting

activator impurity like Tl which forms the intermediate level conduction band. The resolution of NaI(Tl) detector is about 7% at 662 keV. In the present work, a 3" x 3" well type NaI(Tl) detector coupled with a multi-channel analyzer (Fig. 2.7) has been used for gamma counting. Nearly 100% detection efficiency for moderate energy photons in a well type Na(Tl) detector offers great advantages for the counting of low activity samples. A suitable aliquot (0.1 - 0.5 mL) of the desired analyte solution was taken in glass counting tubes which was then placed in the well of the detector coupled with PMT and associated electronics. Each sample was counted for sufficient time so as to get more than 10,000 counts to restrict the statistical counting error within ±1%.

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Chapter III

DISTRIBUTION STUDIES ON Y(III) AND Sr(II) BY SOLVENT EXTRACTION TECHNIQUE

DISTRIBUTION STUDIES ON Y(III) AND Sr(II) BY SOLVENT EXTRACTION TECHNIQUE

3.1. Introduction

Radioactive ^{90}Y isotope was found to be effective in the treatment of various cancers, including lymphoma, leukemia, ovarian, colorectal, pancreatic, and bone cancers. It works by adhering to monoclonal antibodies, which in turn bind to cancer cells and kill them via the intense β-radiations emanating from the ^{90}Y. Needles made of ^{90}Y, which can cut more precisely than scalpels, have been used to sever pain-transmitting nerves in the spinal cord and ^{90}Y is also used to carry out radionuclide synovectomy in the treatment of inflamed joints, especially knees, in sufferers of conditions such as rheumatoid arthritis [**3.1-3.6**]. Due to its short half life (64.1 h), it serves as an effective radioisotope for medicinal use and therefore, it should be available easily and in large quantities. Two routes, followed worldwide, for obtaining ^{90}Y are neutron activation of natural Y_2O_3 technique and separation of ^{90}Y from the ^{90}Sr which is present in high level radioactive waste which is a concentrate of the PUREX (Plutonium Uranium Reduction Extraction) raffinate. Though ^{90}Y can be made from neutron activation of naturally occurring ^{89}Y salt, its low absorption cross section can result in tracers of very low specific activity. On the other hand, ^{90}Sr has very high fission yield and hence is produced in nuclear reactor as a fission product in large quantities. A typical pressurized heavy water reactor with a burn up of 7000 MWd/te results in production 0.030g/L of Sr, in the high level waste. As discussed in Chapter 1, ^{90}Y is the daughter product of ^{90}Sr and is in secular equilibrium with it. However, direct use of ^{90}Y-^{90}Sr mixture is prohibited due to considerable long half life of ^{90}Sr (28.5 yrs) and chemical similarities of Sr and Ca which results in replacement of Ca by ^{90}Sr, especially in the bone, thereby causing adverse effects to the patients [**3.7**]. It is, therefore, required to efficiently separate ^{90}Sr from its daughter product, ^{90}Y. Maximum permissible body burden of ^{90}Sr is reported to be 74 kBq or 2 μCi [**3.8**] and for a radiopharmaceutical use of ^{90}Y having Ci level radioactivity, decontamination factor values as high as 10^6 is required in an efficient separation process.

Literature reports are available on the separation of ^{90}Y from a mixture of ^{90}Y-^{90}Sr using techniques such as precipitation [**3.9**], solvent extraction [**3.10, 3.11**], ion exchange [**3.12-3.14**], extraction chromatography [**3.15-3.18**], liquid membrane [**3.19**] and electrochemical methods

[**3.20**]. Researchers at the Pacific Northwest National Laboratory developed a process to make ultrapure ^{90}Y for treatment of cancer [**3.21**]. In this method, raw $^{90}Sr/^{90}Y$ source is purified to a fresh $^{90}Sr/^{90}Y$ source "cow" by removing impurities by the addition of sodium hydroxide and by removing ^{137}Cs by further addition of sodium carbonate. The "cow" is set aside to allow in growth. The "cow" is then dissolved in nitric acid and the purified extractant di(2-ethylhexyl) phosphoric acid (HDEHP) is washed with nitric acid and scrubbed with either nitric or hydrochloric acid. The dissolved "cow" and scrubbed HDEHP are combined in an organic extraction, separating ^{90}Y from ^{90}Sr, resulting in a $^{90}Sr/^{90}Y$ concentration ratio of not more than 10^{-7}, and a metal impurity concentration of not more than 10^{-5} curie per curie of ^{90}Y. The separated ^{90}Y may then be prepared for delivery. However, solvent extraction methods are attractive due to their large throughput, rapidity, possibility of scrub contact to get ultrapure product and hence are attractive options for industrial use.

Though a number of extractants were evaluated for the separation of ^{90}Y from ^{90}Y-^{90}Sr mixture, only a few of them were found to be effective. These separations were purely on the basis the divalent and trivalent nature of Sr and Y respectively which strongly affects their complexation behaviour. 2-Ethylhexyl phosphonic acid (PC-88A), octyl(phenyl)-N,N-diisobutyl carbamoyl methyl phosphine oxide (CMPO), and newly developed diglycolamides such as N,N,N'N'-tetraoctyl diglycolamide (TODGA) and tetra-2-ethylhexyl diglycolamides (T2EHDGA) are some extractants which preferentially extract trivalent lanthanides and actinides [**3.22**]. Out of these, TODGA and T2EHDGA display unique extraction behaviour as the trivalent actinides / lanthanides are extracted to a much higher extent as compared to the tetra- and hexavalent actinide ions. Moreover, the extraction efficiency is reported to be exceptionally high as compared to the other extractants mentioned above [**3.23**]. Also, Sr (II) extraction is reported to be significant at lower acidities (1 – 3 M HNO_3) which decreased at higher acidities (> 6 M HNO_3) suggesting possibility of developing separation scheme based on suitable variation in the feed acid strength [**3.24**].

However, there is lack of systematic study about preferential extraction of trivalent ions such as Y(III) over divalent ions such as Sr(II) by diglycolamides which can be utilized for their mutual separation and this has been attempted in the present studies. This Chapter elaborates the extraction behavior of these two diglycolamide viz.; TODGA and T2EHDGA towards Sr (II) and

Y (III) present in different aqueous medium and at variable acidities. The data obtained was utilized to develope a separation method for them. The effect of feed acidity and diluent composition on the distribution behavior of Y(III) and Sr(II) has been investigated.

Based on the results obtained, a methodology has been developed to obtain pure ^{90}Y from ^{90}Sr-^{90}Y mixture. The purity of the product was checked by half life measurement and the method has been used for ascertaining the purity of the recovered ^{90}Y.

3.2. Effect of Counter Anion

The extraction of lanthanides by diglycolamides was found to be affected by the nature of the counter anion. Preliminary studies carried out by S. Tachimori, et.al. [**3.25**], on the distribution of Am(III) from HCl, HNO_3 and $HClO_4$ medium have shown that for a given concentration of TODGA, the distribution values vary in the order: HCl < HNO_3 < $HClO_4$ (Fig.3.1).

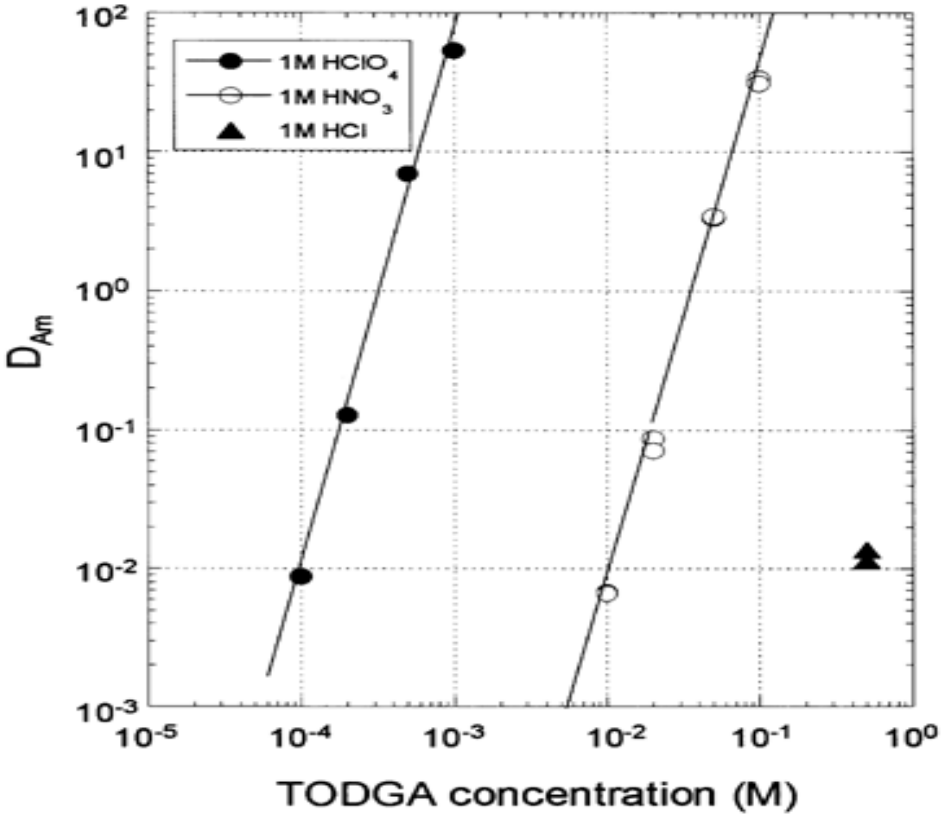

Fig.3.1: Extraction of Am(III) from different acid solutions as a function of TODGA concentration (Ref. [3.25])

In the case of HNO_3, they found that the D_{Am} value increased sharply with nitric acid concentration up to 3 M, beyond which a plateau was observed. Increase in the distribution value with acidity can be explained by the law of mass action due to increased nitrate concentration and the plateau can be explained in the following way. Beyond 3 M acidity, free ligand concentration was decreased due to the formation of TODGA-HNO_3 adduct, thereby giving plateau at higher acidity. On the other hand, lower D_{Am} value observed in HCl medium did not show any significant change upto 2 M HCl. However, there was a steep increase in D_{Am} values beyond 2 M HCl. Lower distribution value in HCl medium was attributed to the weaker aqueous complexation of Am(III) with Cl^- ion as compared to that with NO_3^- ion during formation of the neutral extracted species. Jensen, et al. [**3.26**] has reported that the extraction of metal ions by TODGA is facilitated by the extraction of acid and water in the organic phase. The extraction of mineral acids and water by common extractants is known to vary greatly with the nature of acid, as recently described for TBP extraction system [**3.27**]. In the case of TODGA extraction system, both acid and water are poorly extracted from HCl solutions than from HNO_3 solutions. Ansari *et al*, [3.28] reported that despite considerably higher aqueous acidity of 4 M HCl system, only 0.002 M acid and 0.008 M of H_2O are extracted as compared to HNO_3 system where 0.02 M acid and 0.025 M H_2O are extracted even at 1 M HNO_3. Lower extraction of Am(III) from HCl solution is associated with this behaviour. In this work it is also observed that the distribution values in perchloric acid medium were relatively higher and displayed minor variation (195 ± 20) with aqueous phase acidity (0.01 - 6 M). High D_{Am} in $HClO_4$ was attributed to the perchlorate effect where large perchlorate ions disrupt the ordered hydrated aqua-metal complex in the aqueous phase, thereby promoting the phase transfer of metallic cations from aqueous to organic phase. Therefore, the extraction behaviour of TODGA for Y(III) and Sr(II) in HNO_3 and HCl medium are studied and subsequently, similar studies were carried out using T2EHDGA as the extractant.

3.3. Separation of Sr and Y by TODGA in HCl and HNO_3 Medium

3.3.1. Extraction Behavior of Sr(II) and Y(III) from HNO_3 Medium

The extraction of Sr(II) from HNO_3 medium was also studied by several authors who have also reported an increase in the D_{Sr} values up to 3 M HNO_3 beyond which a decrease was observed

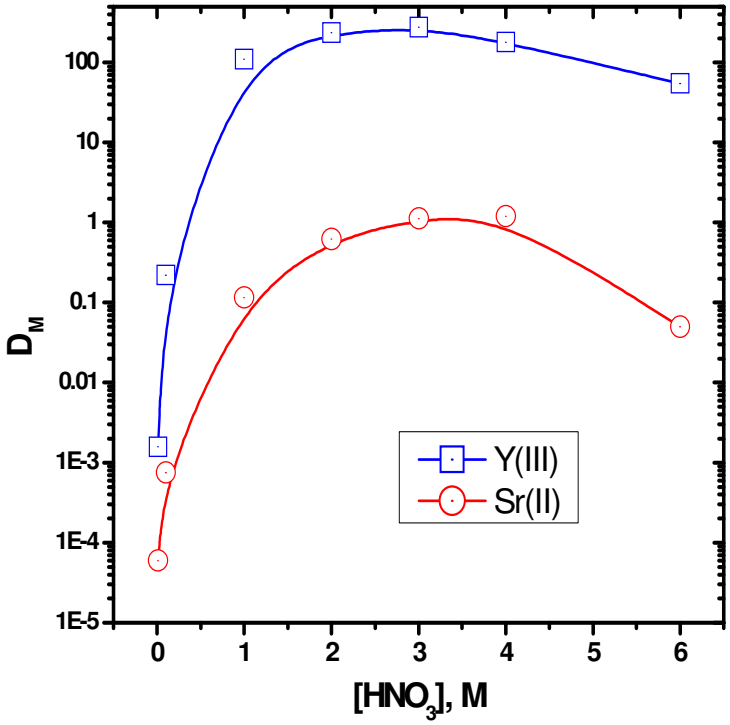

Fig. 3.2: Extraction profiles of Sr (II) and Y (III) from varying concentration of nitric acid. Organic phase: 0.1 M TODGA in *n*-dodecane.

with different ligands [**3.25-3.29**]. Ramírez, *et al.,* revealed that substituted calixarenes with phosphinoyl pendant arms in lower rims also extracts Y from 1 M HNO_3–3.5 M $NaNO_3$ at a metal ion concentration of 1.19 x 10^{-4} M while no extraction was observed with 3 M HNO_3 – 0.5 M $NaNO_3$ as the aqueous phase [**3.30**]. At the same time, it extracts tetravalent Th more efficiently than trivalent Y from 1 M HNO_3–3.5 M $NaNO_3$. However, no data was provided with divalent Sr in this case. Also equilibration time in this work was reported to be as high as 7 hrs. Makrlík, *et al.,* demonstrated separation of Sr (II) from Y(III) from HCl medium, using 15-crown-5 (15C5) and hydrogen di-carbollylcobaltate (H^+B^-) in the two-phase water – nitrobenzene extraction system [**3.31**]. However, in this case also separation factor was found to be low (10).

Parent - daughter separation between ^{90}Sr and ^{90}Y, using ammonium phosphomolybdate has been reported by Amphlett who reported very low yield [**3.32**]. Roy, *et al.,* studied sorption behavior of Sr along with different radionuclides with zirconium vanadate as an ion-exchanger at

variable acidities [**3.13**]. The degree of sorption was found to follow the order; $Cs^{+} > Eu^{3+} > Am^{3+} > Y^{3+} > UO_2^{2+}$, while Sr^{2+} was not at all sorbed by the resin material. A drastic decrease in K_d values was, however, observed with increase in the feed acidity. At 10^{-4} M HCl, K_d for Y (III) was reported as 237 while at 1 M HCl same value falls to 0.4. At all acidities, k_d for Sr (II) was below 0.04. In this work, the purity of the product was reported to be quite satisfactory. Happel, *et al*, demonstrated the ^{90}Y generator that produces ^{90}Y of sufficient purity for their subsequent application in radionuclide therapy [**3.19**]. In such case, the secular equilibrium is re-established few days after separating ^{90}Y from its parent nuclide, making ^{90}Y available approximately twice a week, depending on the desired activity. They measured the distribution ratios for Y and Sr with varying HDEHP/TBP ratios in order to optimize the extractant mixture composition. As HDEHP is a cation-exchanging extractant, the extraction is strongly dependent on the pH of the medium. Accordingly, the influence of the acid concentration on the distribution ratios of a particular mixture was examined by them. It was observed that, HDEHP/TBP System showed synergetic extraction for Y(III) with HDEHP contents between 50 % and 80 % of the extraction mixture for low acid concentrations. As expected, the HDEHP/TBP extraction system was found to be well suited to extract Y selectively from aqueous solutions with low acid concentrations, e.g. 0.1 M to 1 M HNO_3. Thus, the extracted Y can easily back-extracted from the HDEHP/TBP phase into the aqueous phase by higher concentrated acids, like 3 M HNO_3. Thus cation-exchanging property of the HDEHP was successfully used for the separation of Y (III) and Sr (II). HDEHP alone was also used in a report by Naik, *et al.,* for separation of Y (III) from Sr(II)-Y(III) mixture [**3.33**].

In case of pure TODGA solutions, Zhu, *et al* [**3.24**] and Suzuki, *et al* [**3.34**], have reported an increase in the Sr(II) extraction with nitric acid concentration to about 3 M HNO_3 beyond which a decrease was observed. Ansari, *et al* [**3.28**], have shown similar extraction pattern using a mixture of 0.1 M TODGA + 0.5 M DHOA (N,N-dihexyloctanamide), suggesting that the extraction behaviour was largely influenced by TODGA and probably not much dependent on the concentration of phase modifiers such as DHOA. Jensen, *et al*, have reported aggregation of TODGA to form reverse micelles which extracts the metal ions from nitric acid medium [**3.26**]. Apparently, the cavity sizes of the aggregate matches with the ionic size of Sr(II) at 3 M HNO_3 beyond which much larger aggregates are formed with bigger cavity sizes, thereby

decreasing the extraction of Sr (II). The extraction profiles of Sr (II) and Y(III) from nitric acid media are shown in Fig. 3.2. The extraction of Sr(II) increased with acidity up to 3 M and decreased thereafter. Y(III) extraction, on the other hand, was found to be much larger and slight decrease in D_Y values was observed at higher HNO_3 concentration.

The distribution ratio values of Y(III) show an initial increase with nitric acid concentration apparently due to the following extraction equilibrium:

$$M^{n+} + n\ NO_3^- + mL_{(o)} \rightleftharpoons M(NO_3)_n \cdot mL_{(o)} \qquad (3.1)$$

Zhu et al. [**3.24**], have reported a TODGA concentration dependence of ~3.0 suggesting the extraction of species of the type, $Y(NO_3)_n \cdot$ 3TODGA into the organic phase. Decrease in the D_Y values at higher nitric acid concentration has been ascribed to partial formation of non-extracting species. The overall effect is reflected in the separation factor (S.F.) values which do not show any appreciable change with acidity (Table 3.1). The values were compared with work carried out with HDEHP as the extractant [**3.33**]. The data obtained with this reagent along with our reagent was included in Table 3.1. A comparison was made with the current extraction system. With 20 % HDEHP as an extractant, the extraction of yttrium was much higher compared to that

Table 3.1: Distribution data for Y(III) and Sr(II) in HNO_3 medium with different organic phases

[Acid],	0.1 M TODGA in *n*-dodecane			20 % HDEHP in *n*-dodecane [3.24]		
HNO_3,M	Y(III)	Sr(II)	S. F. (D_Y/D_{Sr})	Y(III)	Sr(II)	S. F. (D_Y/D_{Sr})
0.01	0.002	0.000	26.3	1772.60	3.20	5.54×10^2
0.1	0.22	0.000	293	959.16	1.47	6.52×10^2
1	110	0.115	957	70.06	$< 10^{-3}$	$> 7.01 \times 10^4$
2	237	0.620	382	7.63	$< 10^{-3}$	$> 7.63 \times 10^3$
3	274	1.125	244	-	-	-
4	181	1.210	150	0.84	$< 10^{-3}$	$> 8.40 \times 10^2$
6	55	0.050	1140	0.35	$< 10^{-3}$	$> 3.50 \times 10^2$

of strontium which was found to increase substantially with decrease in acidity. Practically negligible extraction of Sr(II) was observed from feed solutions at nitric acid concentrations greater than 1.0 M. However, with HDEHP as the extractant, D_Y was quite low at higher acidities. On the other hand, TODGA was quite promising at these acidities. Reasonable separation factors at higher acidities indicate the usefulness of TODGA.

Kandwal, *et al.,* used 0.63 M PC-88A for the separation of Y from ^{90}Y-^{90}Sr mixture [**3.22**]. However, the separation factor decreased with increasing feed acidity and D_Y was quite low at higher acidities. The reported separation factors were 644, 67 and 100 at 1 M, 2 M and 3 M feed HNO_3 which was lower than those reported in the present work.

3.3.2. Extraction Behavior of Sr and Y from HCl Medium

3.3.2.1. Effect of Acidity

It has been reported that both hydrochloric acid and water are poorly extracted by TODGA from HCl solutions as compared to those seen in HNO_3 solutions. Lower extraction of Am(III) from

Table 3.2: Distribution data for Y(III) and Sr(II) in HCl medium, organic phase: 0.1 M TODGA in *n*-dodecane.

[Acid], HCl, M	0.1 M TODGA in *n*-dodecane		
	Y(III)	Sr(II)	S. F. (D_Y/D_{Sr})
0.01	3.1×10^{-4}	8.2×10^{-4}	0.38
0.1	3.4×10^{-4}	5.2×10^{-4}	0.65
1	0.001	4.55×10^{-3}	0.27
2	0.024	4.53×10^{-3}	5.30
3	0.442	3.39×10^{-3}	130
4	133	5.4×10^{-3}	24705
6	912	0.0152	60178

HCl solution is reported in the literature [**3.28**] and the reason can be attributed to the weaker aqueous complexation of Am(III) with Cl^- and larger hydration of Cl^- ions. Analogous trend was observed for Y(III) extraction in the present studies. The distribution experiments were carried out under identical conditions as HNO_3 medium using carrier free ^{90}Y. The distribution data for Y(III) and Sr(II) are listed in the Table 3.2. Distribution ratio values obtained with various extractants are also included in the Table. In the present work, the extraction profiles in the HCl medium showed continuous increase for both Y(III) and Sr(II), albeit to a much lower extent for the latter (Fig. 3.3) which was in sharp contrast to the data shown above for nitric acid medium. Here, not only the D_{Sr} values were relatively unaffected with the increasing concentration of HCl, the D_Y values also showed nearly monotonous increase with the aqueous phase acidity which resulted in the distribution ratio values for Y(III) in the excess of 1000. In order to check the nature of the extracted species, distribution ratio of Y (III) were measured at varying TODGA concentrations.

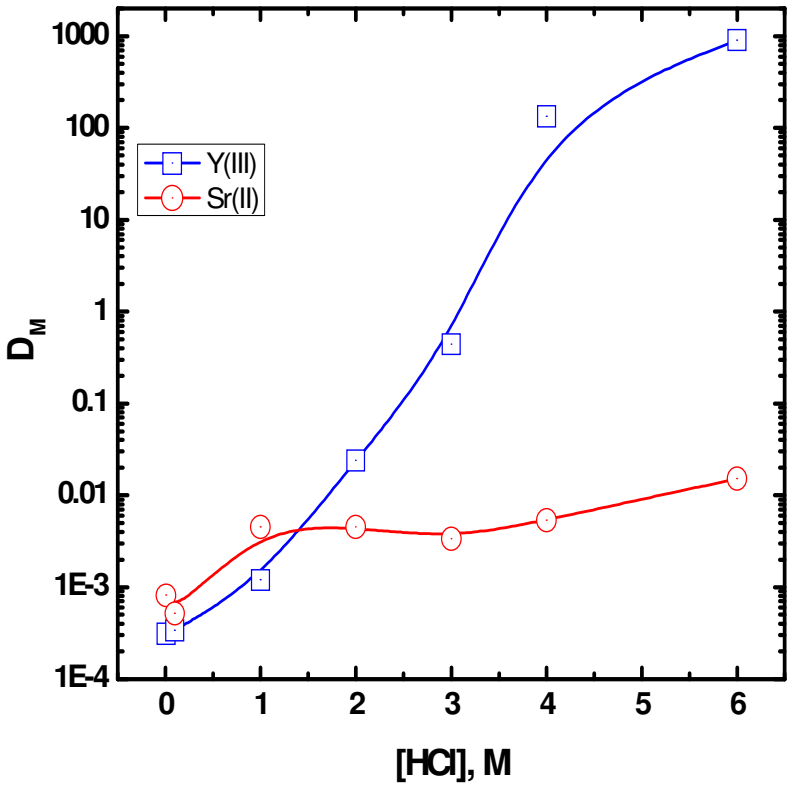

Fig. 3.3: Extraction profiles of Sr(II) and Y(III) from varying concentration of hydrochloric acid. Organic phase: 0.1 M TODGA in *n*-dodecane

3.3.2.2. Ligand Concentration Variation Studies

The stoichiometry of the extracted species of Y(III)-TODGA/*n*-dodecane from hydrochloric acid medium was investigated by determining the D_Y values at different ligand concentrations. The two phase equilibrium of Y(III) between organic (TODGA/*n*-dodecane) and aqueous phase (HCl) can be represented by the following equation (3.2).

$$M^{n+} + n\ NO_3^- + m\ TODGA_{(o)} \overset{Kex}{\rightleftharpoons} M(NO_3)_n \cdot m\ TODGA_{(o)} \qquad (3.2)$$

As a simplified case for equilibrium reaction, the two phase extraction constant (K_{ex}) for the extraction of Y(III) by TODGA from hydrochloric acid medium can be represented by the following equation (3.3).

$$K_{ex} = \frac{[Y(Cl)_3.nTODGA]_{(org.)}}{[Y^{3+}]_{(aq.)}.[Cl]^3.[TODGA]^n_{(org.)}} \qquad (3.3)$$

Since, the distribution ratio of the metal ions (D_M) is the ratio of total concentration of metal ions in the organic phase to that in the aqueous phase, Eq. (3.3) can be modified as follows,

$$K_{ex} = \frac{D_{Am}}{[Cl]^3.[TODGA]^n} \qquad (3.4)$$

Here the subscripts have been omitted to simplify the equation. Taking logarithm of the Eq. (3.4) and rearranging one would obtain:

$$\log D_Y = \log K_{ex} + 3 \log [Cl^-] + n \log [TODGA] \qquad (3.5)$$

The slope analysis of Eq. (3.5) allows the interpretation of stoichiometry of the extracted metal complex. The plot of log D_Y versus log [TODGA] is shown in Fig. 3.4. The value of 'n' was estimated from the slope of the linear fit as 3.02 ± 0.16 (Fig. 3.4) for the extraction of Y(III) suggesting the extraction of the species of the type YCl_3.3TODGA which is similar to the species

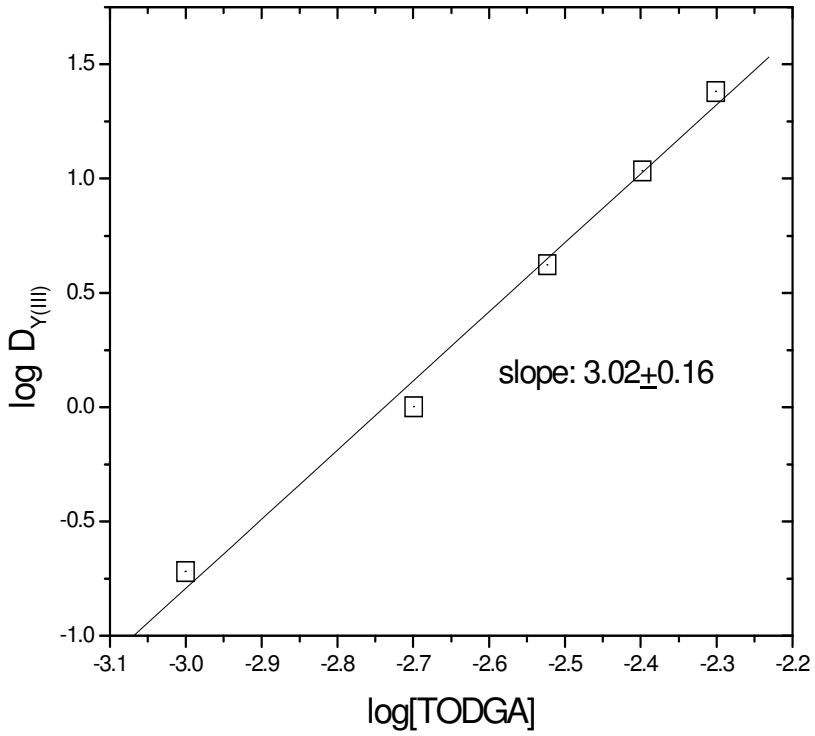

Fig. 3.4: Dependence of distribution ratio values of Y(III) on the TODGA concentration. Aqueous phase: 6 M HCl

reported for Eu^{+3} extraction in case of nitric acid as the aqueous phase (Table 3.3). On the other hand, the species extracted with Am^{+3} was entirely different. However, increasing trend in the D_Y values with increasing HCl concentration could be ascribed to lower complexation by Cl^- ions or a change in the aggregation behaviour at higher acidity in case of HCl medium [**3.26**]. With TODGA as an extractant, the separation factors calculated for both aqueous HCl and HNO_3 medium are listed in Table 3.4.

Table 3.3: Nature of the extracted species with TODGA as extractant

Metal ion	Slope of TODGA variation studies	Expected species	Reference
Y^{3+}	3.02 ± 0.16	YCl_3.3TODGA	Present work
Am^{3+}	4.1 ± 0.40	$Am(NO_3)_3$. 4TODGA	[**3.35**]
Eu^{3+}	3.15 ± 0.25	$Eu(NO_3)_3$. 3TODGA	[**3.36**]

Table 3.4: Separation factor values as a function of aqueous phase acid type and concentration, Organic phase: 0.1 M TODGA in *n*-dodecane

[Acid], M	Separation factor	
	HNO_3	HCl
0.01	26.3	0.38
0.1	293	0.65
1	957	0.27
2	382	5.30
3	244	130
4	150	24705
6	1140	60178

3.3.2.3. Comparison of Separation Factors of Sr and Y in Nitric Acid and Hydrochloric Acid Medium

The separation efficiency is measured in terms of separation factor (S.F.) which is defined as the ratio of the distribution ratio of Y (III) to that of Sr(II). The S.F. values for HNO_3 medium were moderate (a few hundred) in most part of the acidity range studied and a low value of 26.3 was observed at 0.01 M HNO_3 while a high value of 1140 was observed at 6 M HNO_3 (Table 3.4). Though an overall increase in the S.F. values was observed with increasing HNO_3 concentration, the pattern was irregular. On the other hand, the S.F. values in case of HCl solutions showed very low values (< 1) up to 1 M HCl beyond which a sharp increase was observed (Table 3.3). The S.F. value, in case of 6 M HCl as the feed was about 2 orders of magnitude larger than that obtained with equivalent concentration of nitric acid. The high S.F. value (> 60,000) in case of 6 M HCl prompted us to carry out the further separation studies using this acidity as the feed. Happel, *et al.,* carried out systematic investigation of Sr(II) and Y(III) extraction at variable feed acidities with HCl as the aqueous phase using HEDHP in TBP [**3.19**]. However, D_Y was limited to ~ 40 at 0.1 M HCl as feed while drastic decrease in D_Y was noted with increase in feed acidity where 60 % HEDHP in TBP was used as extractant with *n*-dodecane as solvent. D_{Sr} was negligible (< 0.1) under the same experimental condition.

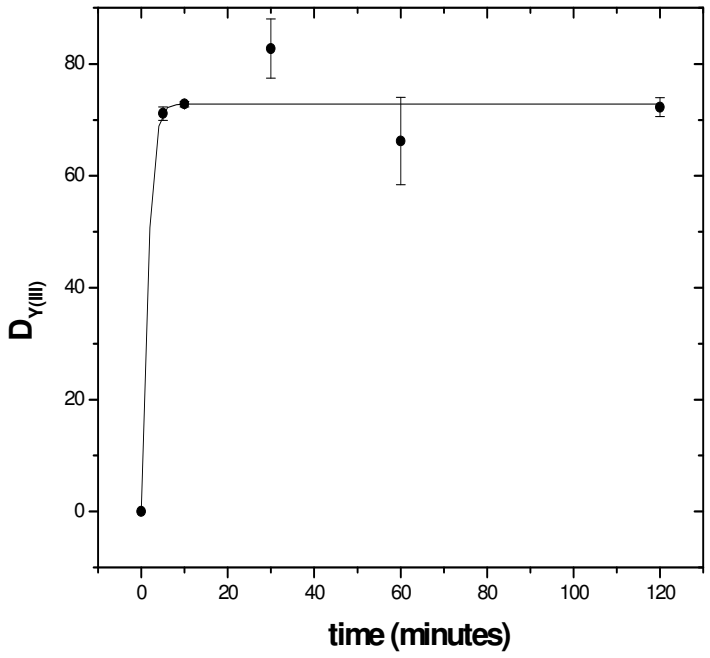

Fig. 3.5: Effect of equilibrium time in D_Y values. Organic phase: 0.1 M TODGA in *n*-dodecane, aqueous phase: 6 M HCl.

3.3.2.4. Kinetics of Extraction

In order to optimize the time required to attain equilibrium in the D values, studies were carried out by equilibrating the aqueous (containing ^{90}Y tracer in 6 M HCl) and the organic phases (0.1M TODGA in *n*-dodecane) for different time interval. The extraction kinetics of the Y(III) was evaluated by determining the time dependence of D_Y with 0.1 M TODGA/*n*-dodecane and 6 M HCl. The results as shown in Fig. 3.5, suggested that 5 minutes of equilibration was sufficient for the extraction of Y(III) implying fast attainment of equilibrium. Similar fast extraction kinetics was reported for the extraction of other actinide ions using TODGA as the extractant (2.8).

3.3.2.5. Separation of ^{90}Y from ^{90}Sr

Based on the solvent extraction studies, a separation method was developed for the recovery of pure ^{90}Y from a mixture of ^{90}Y-^{90}Sr. The method involved three cycles of preferential extraction of ^{90}Y at 6 M HCl followed by its stripping using distilled water.

3.3.2.6. Purity of the Separated Product

The purity of the product can be ascertained by several methods including liquid scintillation counting [**3.34**] of the sample after allowing sufficient time to decay the ^{90}Y and half life method [**3.13**]. In case of half life method, the decay profile of the product (mainly ^{90}Y) was followed with time as per equation (3.6). In this study, the purity of the product was ascertained from its half-life measurements. Three different fractions such as organic and aqueous strip fraction after extraction were monitored for the purity of ^{90}Y. the product samples of ^{90}Y were collected i) after extraction from 6 M HCl, ii) after extraction from 6 M HCl followed by stripping with distilled water and iii) after three cycles consisting of the extraction and stripping steps. The decay profile of the separated ^{90}Y for a typical case is shown in Fig. 3.6. The half-life was calculated from the slope of the semi-log plot as follows:

$$\text{Half life} = \frac{0.301}{\text{slope}} \qquad (3.6)$$

As indicated in Table 3.5, the product obtained after the single extraction and after an extraction and stripping step was contaminated with some amount of ^{90}Sr which was reflected in the measured half-lives. On the other hand, a purification step involving three cycles of extraction from 6 M HCl followed by stripping using distilled water showed reasonable purity as the half life obtained was 64.1 ± 0.2 hrs.

Table 3.5: Purity of the product as indicated by their half-lives as calculated from the slopes of the semi-log plots

Steps of Method	Slope (hrs^{-1})	Half-life (hrs)
Single extraction	0.0041	73.2 ± 1.2
Single extraction followed by stripping	0.0042	71.4 ± 0.9
Two cycles of extraction and stripping	0.0046	64.8 ± 0.4
Three cycles of extraction and stripping	0.0047	64.1 ± 0.2

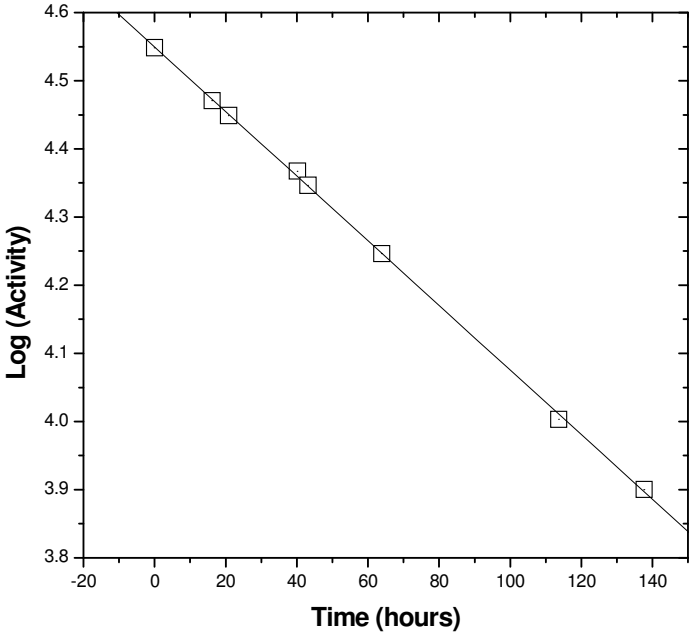

Fig. 3.6: Decay profile of the purified product obtained (^{90}Y) after second extraction followed by stripping used for half-life calculation

3.3.2.7. Thermodynamics of Extraction

The favourable extraction of Y(III) as compared to that of Sr(II) is responsible for the high separation factors in case of HCl medium. The mechanism for Y(III) extraction appears to be similar in both HNO_3 and HCl medium as indicated by the nature of the extracted species. This is in sharp contrast to the species extracted in case of trivalent actinides such as Am (III) which form tetra-solvates [**3.28**]. Even in cases where the extracted species are similar, the nature of bonding can be different. The two phase extraction equilibrium constant for Y(III) extraction as presented by the general eqn. (3.1) is given by the following equation,

$$K_{ex} = \frac{[Y(X)_3.3TODGA]}{[Y^{3+}]\{X^-\}^3\ [TODGA]_n} \qquad (3.7)$$

where, X^- is the anion Cl^- or NO_3^- and the parameters in braces are the activities. As tracer quantity of ^{90}Y was used in the extraction experiments, for all Y bearing species, the activities

are equal to the concentrations.

The distribution ratio of Y(III), D_Y is presented as:

$$D_Y = \frac{[Y(X)_3.3TODGA]}{[Y^{3+}](1+\sum \beta_i [X^-]^i)} \quad (3.8)$$

The extraction constant can thus be expressed as:

$$K_{ex} = \frac{D_Y (1+\sum \beta_i [X^-]^i)}{\{X^-\}^3 [TODGA]^n_{org,\,free}} \quad (3.9)$$

$[TODGA]_{org.free}$ is assumed to be equal to the activity of the free amide. The activities of nitrate and chloride ions were taken from the literature for the calculation of equilibrium constants [**3.37**]. As reported in the literature, the activity of TODGA was assumed to be the concentration of the free TODGA concentration [**3.38**] and the conditional extraction constants were calculated. For calculation purpose, the factor $(1+\sum\beta_i[X^-]^i)$ for Y^{3+} with nitrate and chloride ions were determined by an ion exchange method. In this method, overall complexation constant of YX_3, $[(1+\sum \beta_n^M [X^-]^n)]$ can be evaluated by determining the distribution coefficient (K_d) of metal ions with cation exchange resin from perchloric acid, nitric and hydrochloric acid medium [**3.39**]. Distribution coefficient (K_d) values of Y(III) were obtained at 6 M HNO_3, 6 M HCl and 6 M $HClO_4$ with a cation exchange resin. The values of the overall complexation constants of $Y(NO_3)_3$ and YCl_3 were then obtained from the ratio of K_d value in $HClO_4$ to that in HNO_3 and HCl. If K_d^{HClO4} and K_d^{HCl} are the distribution coefficients of the given metal ions from $HClO_4$ and from HCl media, following equation can be derived as described earlier [**3.39**].

$$\frac{K_d^{HClO4}}{K_d^{HCl}} = 1 + \sum_1^n \beta_n^M \left[Cl^-\right]^n \quad (3.10)$$

Similar expression will hold good for HNO_3 medium. In this experiment, a known volume of aqueous phase (1 mL) containing ^{90}Y was equilibrated with cation exchange resin (~25 mg) in

stoppered glass tubes. Agitation of the two phases was carried out in a thermostated water bath maintained at 25 ± 0.1°C for 45 minutes. Subsequently, the tubes were centrifuged and suitable aliquots of the aqueous phase were taken before and after equilibration for radiometric assay. The K_d value of Y(III) was calculated by employing the following formula,

$$K_d = \frac{(C_0 - C)}{C} x \frac{V}{W} \text{ (mL/g)} \qquad (3.11)$$

where, C_o and C are the concentrations of metal ions (in counts per unit time per unit volume) before and after equilibration, V is the volume of aqueous phase used (mL) and W is the weight of the resin employed (g). In our experiment, the overall stability constant of Y $(NO_3)_3$ and YCl_3 were found to be 2.11 and 2.53, respectively. The conditional extraction constants are listed in Table 3.6 and for the nitric acid medium are reported to be three orders of magnitude lower than that reported for the trivalent actinide ion, Am(III).

Extraction experiments were carried out at varying temperatures and the distribution data were determined (shown in Table 3.6). Using the D values, values of log K_{ex} were calculated and plotted vs 1/T (shown in Fig. 3.7) in order to calculate thermodynamic parameters like change in enthalpy (ΔH), change in entropy (ΔS) and change in free energy (ΔS) by using the following standard thermodynamic equations.

$$\text{Log } K_{ex} = - \frac{\Delta H^o}{2.303R} \frac{1000}{T} + \frac{\Delta S^o}{2.303R} \qquad (3.12)$$

Table 3.6: Variation of Distribution ratio with temperature for the extraction of Y^{3+} from 6 M HCl and 6 M HNO_3 in to TODGA in *n*-dodecane

Temp, (°K)	D_Y	D_Y
	(6 M HNO_3 + 0.005 M TODGA)	(6 M HCl + 0.005 M TODGA)
283	55.0	0.16
293	21.0	0.10
303	13.0	0.05
313	6.9	0.01

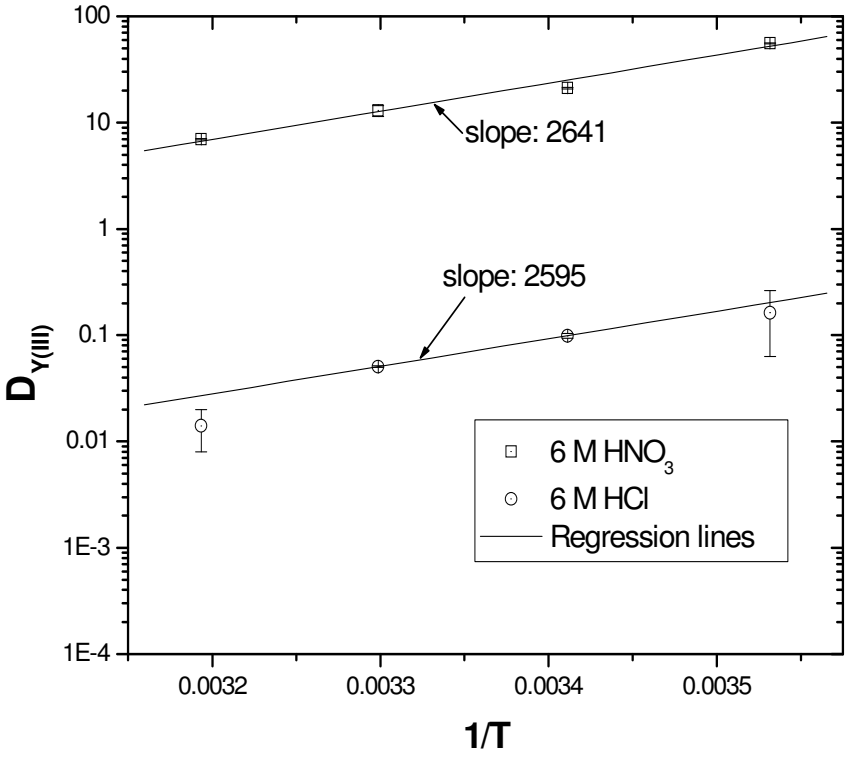

Fig. 3.7: Van'f Hoff plot for the extraction of Y(III) using 0.1 M TODGA in *n*-dodecane as the extractant. Aqueous phase: 6 M HCl and 6 M HNO_3

$$\Delta G = -RT \ln K_{ex} \quad (3.13)$$

$$\Delta G = \Delta H - T\Delta S \quad (3.14)$$

Table 3.7: The conditional extraction constants and thermodynamic parameters for the extraction of Y^{3+} from 6 M HCl and 6 M HNO_3 in to TODGA in *n*-dodecane and that of Am^{3+} from 1 M HNO_3 in to TODGA in *n*-dodecane [3.39]

System	Log K_{ex}	ΔG (kJ·Mol^{-1})	ΔH (kJ·Mol^{-1})	ΔS (J·Mol^{-1}·K^{-1})
Y^{3+} - HNO_3	6.05	-34.5	-50.6	-53.7
Y^{3+}- HCl	4.52	-25.8	-49.7	-80.1
Am^{3+}- HNO_3	9.40	-53.6	-87.6	-114.1

The ΔH values for Y(III) extraction from 6 M HNO_3 as well as 6 M HCl were calculated to be - 50.6 kJ/mol and - 49.7 kJ/mol, respectively. The free energy change and entropy change values were also calculated and are listed in Table 3.7. The enthalpy change values are comparable with the data reported by Ansari, *et al*, for Am(III) though a less negative entropy change is reported in the present case [**3.40**].

3.3.3. Separation of Sr and Y by T2EHDGA

It is well known that reagents with branched alkyl groups lead to more efficient separation as compared to their analogs with linear alkyl groups [**3.39**]. Moreover, 'actinide partitioning' studies using T2EHDGA have shown promise though the extraction efficiency of TODGA was higher [**3.40**]. It was pertinent, therefore, to understand the extraction as well as separation behaviour of T2EHDGA as compared to TODGA for the separation of carrier free ^{90}Y.

Solvent extraction studies were carried out to investigate the distribution behaviour of Y(III) and Sr(II) from nitric as well as from hydrochloric acid media using T2EHDGA as the extractant. 0.2M T2EHDGA in *n*-dodecane was used as the extractant with *iso*-decanol as the phase modifier in order to avoid third phase formation. The third phase formation is a phenomenon arising due to the incompatibility of the polar metal solvate species with non-polar diluents (such as *n*-dodecane) recommended for industrial processes. The third phase is often eliminated by the addition of diluent modifiers such as long chain alcohols, monoamides, organic phosphates, etc., which are capable of solvation of metal-ligand / acid-ligand complexes through either dipole-dipole interaction or hydrogen bonding. In the present case *iso*-decanol was found to be an efficient phase modifier for Y- T2EHDGA in *n*-dodecane system. The separation efficiency and the purity of the product (^{90}Y) were measured by half-life method.

3.3.3.1. Relative Extraction Behavior of Sr and Y

The extraction profiles of Sr(II) and Y(III) from nitric acid feeds using 0.2 M T2EHDGA as the extractant are shown in Fig. 3.8 and those from HCl are presented in Fig. 3.9. The extraction of Sr(II) increased with acidity up to 3 M where D value of 0.24 was observed which rapidly fell thereafter to 0.03 at 6 M HNO_3. This observation is similar to that reported in Section 3.3.2.3 and

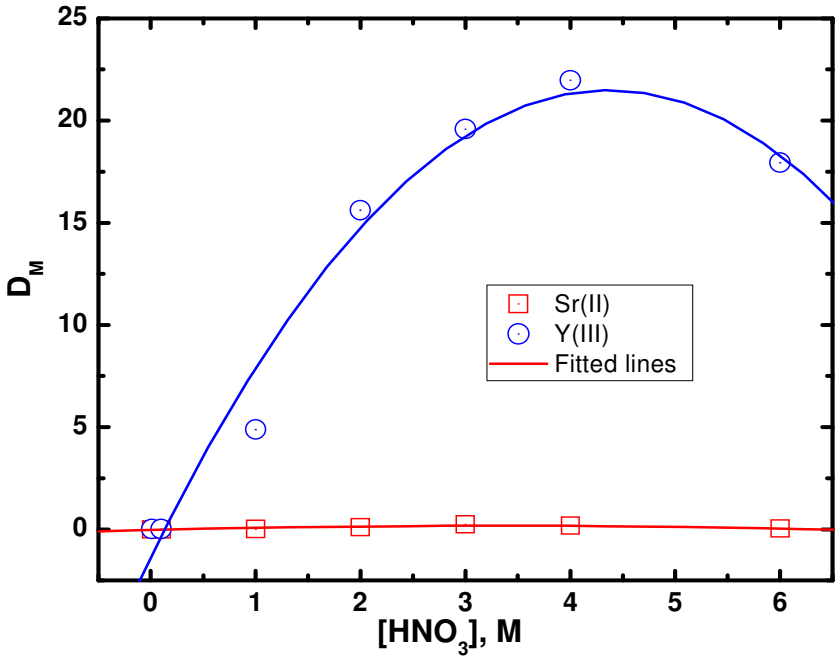

Fig. 3.8: Distribution behavior of Y(III) and Sr(II) as a function of varying nitric acid medium. Organic phase: 0.2 M T2EHDGA and 30% *iso*-decanol as the phase modifier

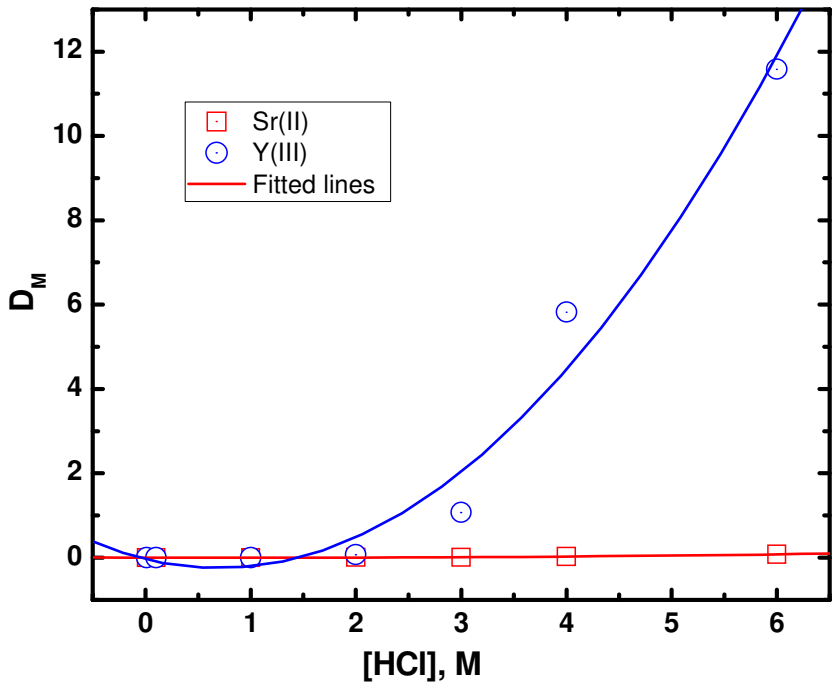

Fig. 3.9: Distribution behaviour of Y (III) and Sr(II) as a function of hydrochloric acid concentration. Organic phase: 0.2 M T2EHDGA in n-dodecane containing 30% *iso*-decanol as the phase modifier.

also to that reported by Suzuki *et al*, while using TODGA as the extractant [**3.34**]. Y(III) extraction, on the other hand, increased with nitric acid concentration to a much larger extent and increased up to 4 M HNO_3 and decreased slightly at higher HNO_3 concentration. The separation factor (S.F.) values with nitric acid concentration show an increase at lower acidity followed by a decrease and finally a sharp rise at 6 M HNO_3. On the other hand, the extraction profiles in the HCl medium showed continuous increase for both Y(III) and Sr(II), albeit to a much lower extent for the latter (Fig. 3.8). Accordingly, the S.F. values in case of HCl solutions showed a continuous increase up to 4 M HCl and a slight decrease afterwards (Fig. 3.10). The S.F. value in case of 6 M HCl was reported to be > 60,000 for TODGA while a value of ~ 145 is reported in the present work using T2EHDGA as the extractant. On the other hand, S.F. value of ~ 200 was observed in the present work at 4 M HCl.

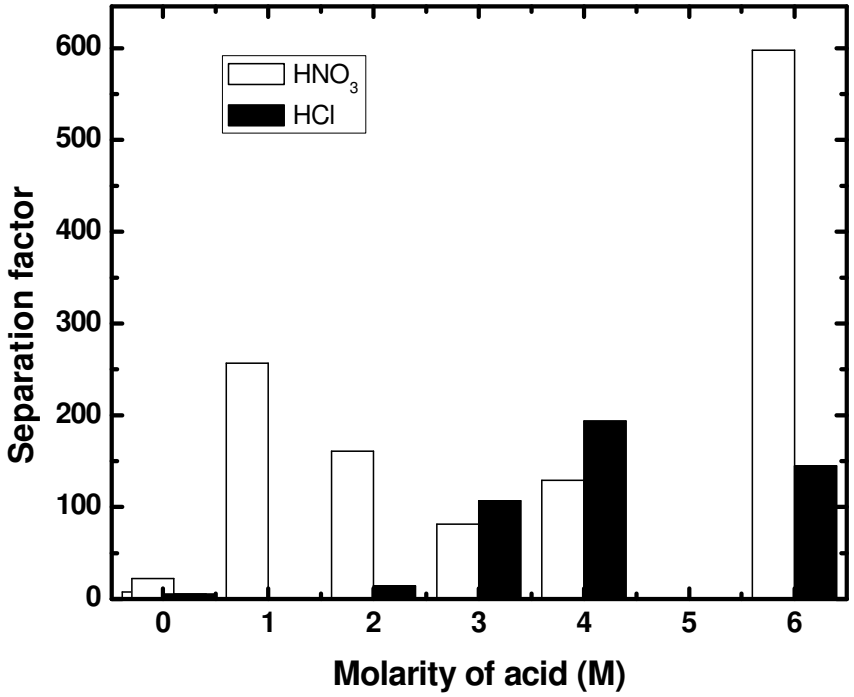

Fig. 3.10: Effect of mineral acid type and molarity on separation factor values

3.3.3.2. Stoichiometry of the extracted species

Extraction studies were further carried out in order to ascertain the nature of the species extracted into the organic phase. Though the trivalent lanthanides and actinides form tetra-solvated

extracted species with TODGA, we had reported tri-solvate complexes with Y(III). The extraction equilibrium is presented as:

$$Y^{3+} + 3(NO_3^-) + nT2EHDGA_{(o)} \rightleftharpoons Y(NO_3)_3.n(TEHDGA)_{(o)} \quad (3.15)$$

where, the species with the subscript '(o)' indicate those in the organic phase and those without any subscript indicate species in the aqueous phase. Distribution studies carried out with T2EHDGA concentration variation at fixed aqueous phase acidity indicated extraction of tri-solvated species for both HNO_3 as well as HCl as the aqueous medium (Fig. 3.11) suggesting that the extracted species conformed to $Y(X)_3.3T2EHDGA$ where X is NO_3^- or Cl^-.

In view of this, the two-phase extraction equilibrium is represented as:

$$Y^{3+} + 3(NO_3^-) + 3T2EHDGA_{(o)} \rightleftharpoons Y(NO_3)_3.3(TEHDGA)_{(o)} \quad (3.16)$$

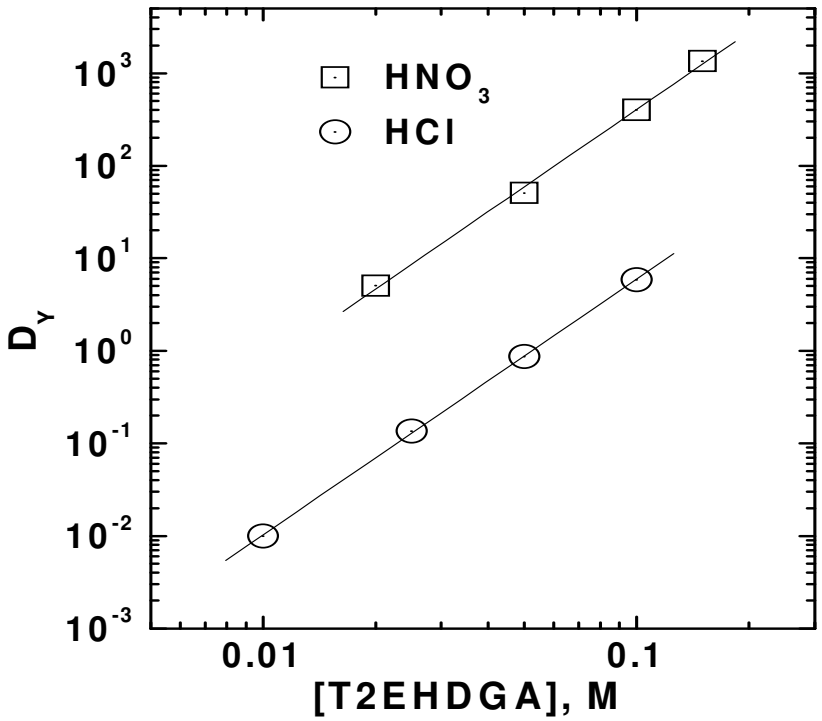

Fig. 3.11: Extraction of Y(III) at varying T2EHDGA concentration; Diluent: *n*-dodecane; Aqueous phase: 4 M acid; Temperature: 25°C

The two-phase extraction equilibrium constant for the above extraction equilibrium can be given as:

$$K_{ex} = \frac{[Y(X)_3.3T2EHDGA]}{[Y^{3+}]\{X^-\}^3\{T2EHDGA\}^n} \quad (3.17)$$

where, the parameters in braces are the activities. As tracer quantity of ^{90}Y was used in the extraction experiments, for all Y bearing species, the activities are equal to the concentrations. The distribution ratio of Y(III), D_Y is presented as:

$$D_Y = \frac{[Y(X)_3.3T2EHDGA]}{[Y^{3+}]\ (1+\sum \beta_i [X^-]^i} \quad (3.18)$$

The extraction constant can thus be expressed as:

$$K_{ex} = \frac{D_Y (1+\sum \beta_i [X^-]^i}{\{X^-\}^3 [T2EHDGA]^n_{org,\ free}} \quad (3.19)$$

where, $[T2EHDGA]_{org.free}$ is assumed to be equal to the activity of free diglycolamide, i.e. [T2EHDGA]. The activities of nitrate and chloride ions were used from the literature for the calculation of the equilibrium constants [**3.37**].

As reported in the literature, the activity of T2EHDGA was assumed to be the concentration of the free T2EHDGA concentration [**3.41**] and the conditional extraction constants were calculated considering the factor $(1+\sum\beta_i[X^-]^i)$ for Y^{3+} with nitrate and chloride ions as 2.11 and 2.53, respectively. The conditional extraction constants are listed in Table 3.8 along with similar data for Y(III)-TODGA extraction system. It is surprising to note that the extraction constants with T2EHDGA system is about 5 orders of magnitude lower as compared to the respective TODGA system. This is ascribed to both lower basicity and greater steric hindrance (experienced during complexation) of T2EHDGA than TODGA.

Table 3.8: The conditional extraction constants for the extraction of Y from 3 M and 6 M HCl and HNO_3 by T2EHDGA / TODGA in *n*-dodecane

Metal ion	Medium	Extractant	Log K_{ex}
Y(III)	3 M HNO_3	T2EHDGA	2.28 ± 0.02
Y(III)	6 M HNO_3	T2EHDGA	1.34 ± 0.02
Y(III)	3 M HCl	T2EHDGA	1.10 ± 0.02
Y(III)	6 M HCl	T2EHDGA	1.23 ± 0.01
Y(III)	6 M HNO_3	TODGA	6.21± 0.03 [a]
Y(III)	6 M HCl	TODGA	6.07 ± 0.02 [a]

Note: [a]: Data obtained at 298^{o}K

3.3.3.3. Kinetics of Extraction

The extraction kinetics of the metal ions was required to obtain equilibrium D_Y values by determining the time with 0.2 M T2EHDGA +20% *iso*-decanol in *n*-dodecane and 4 M HCl. It

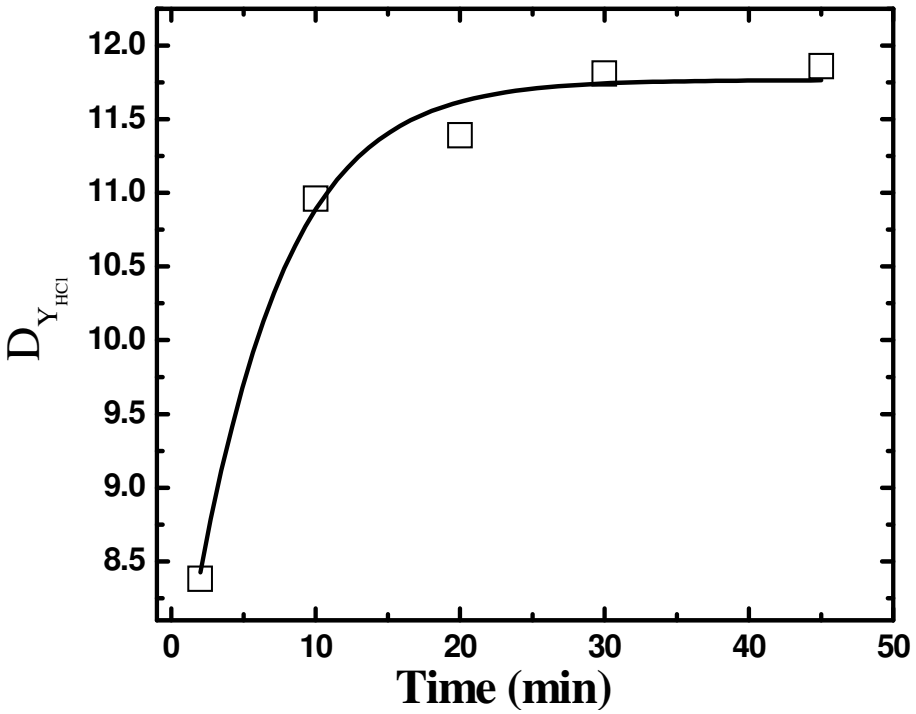

Fig.3.12: Studies carried out to determine the time of equilibrium D_Y value; Organic phase: 0.2 M T2EHDGA + 20% *iso*-decanol in *n*-dodecane, aqueous phase: 4 M HCl

was observed that the equilibrium condition was attained within 5 minutes of the equilibration (shown in Fig. 3.12) implying the fast reaction between TODGA and yttrium. This observation is similar to that in case extraction of Y (III) in TODGA based solvent system discussed above (Section 3.3.2.4).

3.3.3.4. Effect of Temperature on D_Y for T2EHDGA+ *iso*-decanol in Dodecane System from 6 M HNO_3 and 4 M HCl

In order to have an insight into the mechanism of extraction, thermodynamic parameters were determined from the temperature variation studies for the T2EHDGA based solvent system. Similar exothermic nature of extraction process like TODGA system was found for both extraction Y(III) for both 0.2 M T2EHDGA+ 30 % *iso*-decanol in *n*-dodecane from 6 M HNO_3 as well as for 0.2 M T2EHDGA+ 20 % *iso*-decanol l in *n*-dodecane from 4 M HCl (shown in Table 3.9). As will be seen below, the % composition of the phase modifier has a very important role to play in Y(III) extraction.

Table 3.9 Effect of temperature on D_Y, Org. phases: 0.2 M T2EHDGA+ 30 % *iso*-decanol in *n*-dodecane and 0.2 M T2EHDGA+ 20 % *iso*-decanol in *n*-dodecane, aq. phases: 6 M HNO_3, 4 M HCl.

Temp (°K)	D_Y	D_Y
	0.2 M T2EHDGA + 30 % *iso*-decanol in *n*-dodecane from 6 M HNO_3	0.2 M T2EHDGA+ 20 % *iso*-decanol in *n*-dodecane from 4 M HCl
283	7.3	0.049
293	4.5	0.023
303	3.3	0.007
313	2.5	0.004

3.3.3.5. Effect of Phase Modifier Concentration

Though solvent extraction is a versatile technique used for the bulk separation of metal ions on industrial scale, one of the major limitations of the technique is the formation of third phase.

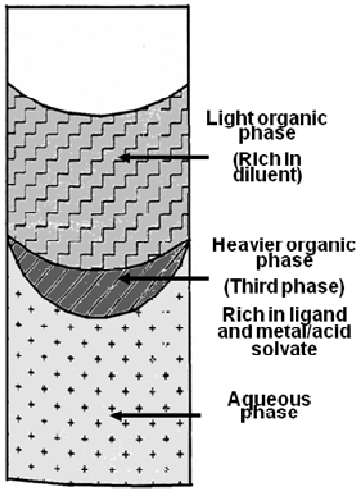

Fig.3.13: Phenomena of third phase formation

Third phase formation (Fig.3.13) is a phenomenon of splitting of the organic phase into two parts, one rich in the metal/ligand or acid/ligand complex and the other is lean in ligand and rich in diluent. When the concentration of polar metal-ligand complex (or acid-ligand complex) in the organic phase exceeds certain limit, it becomes insoluble in the non-polar aliphatic diluents, thus forming third phase.

The maximum concentration of the metal ions that can be loaded in the organic phase without third phase formation is referred to as the Limiting Organic Concentration (LOC). It is well known that a phase modifier is required for the diglycolamides without which third phase was observed [**3.42**]. In the case of TODGA/*n*-dodecane, though D_{Am} value is high, yet it shows third phase formation at very low concentration of metal ions in the organic phase [**3.28**]. In case of T2EHDGA, 30 % *iso*-decanol was used as the phase modifier in an earlier report [**3.40**]. In order to optimize the modifier concentration, distribution studies were carried out as a function of *iso*-decanol content using 4 M HCl and 6 M HNO_3 as the feed solutions which give relatively high separation factors. As indicated in Fig. 3.14, the D_Y values decreased with increasing *iso*-decanol content in both 6 M HNO_3 as well as 4 M HCl media. The increase was to a much larger extent in case of the 6 M HNO_3 and a sudden drop in the D_Y was also observed at 30 % *iso*-decanol, suggesting 20 % *iso*-decanol as the optimum phase modifier concentration. On the other hand, the increase, in case of 4 M HCl was monotonous. This may be attributed to the differences in their aggregation tendencies [**3.26**].

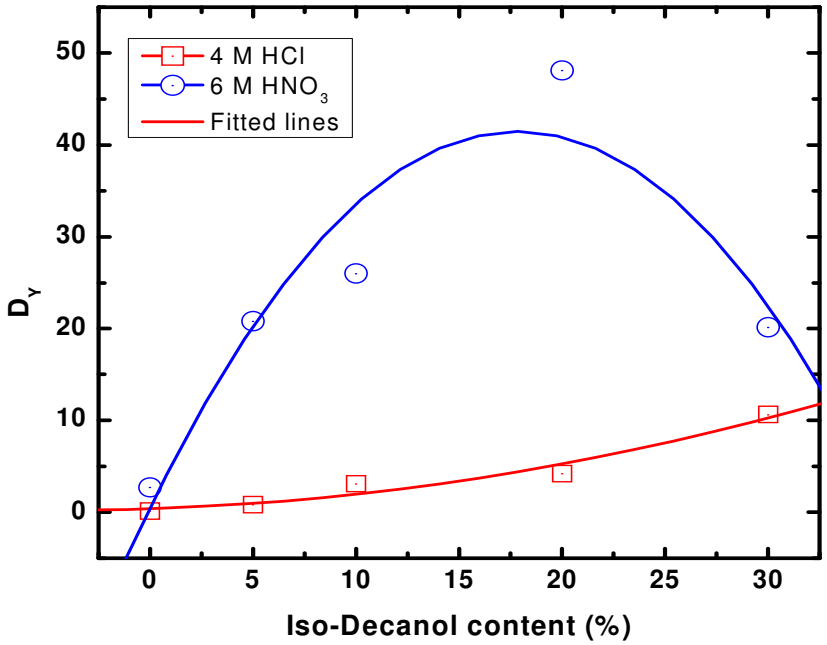

Fig. 3.14: Effect of phase modifier concentration on distribution behaviour of Y by 0.2M T2EHDGA in *n*-dodecane; Temperature: 25°C

Distribution studies were also carried out using ^{85,89}Sr tracer from both 6 M HNO_3 and 4 M HCl. The results in 6 M HNO_3 medium indicated an increase in the D_{Sr} values from 0.03 (no modifier) to 0.32 (5 % *iso*-decanol) which subsequently continuously decreased with increasing *iso*-decanol content.

Table 3.10: Separation factor (SF) between Y and Sr at varying *iso*-decanol concentration. Organic phase: 0.2 M T2EHDGA in *n*-dodecane; Temperature: 25° C

***Iso*-decanol fraction (%)**	**SF (D_Y/D_{Sr})**	
	HCl	**6 M HNO_3**
--	2	104
5	11	64
10	28	105
20	106	405
30	85	495

$D_{Sr,}$ values were in the range of 0.03 to 0.1. The separation factor values are indicated in Table 3.10. As indicated, the maximum separation factor values were obtained for 20 % and 30 % *iso*-decanol for 6 M HNO_3 and 4 M HCl, respectively.

3.3.4. Separation Studies with a Mixture of ^{90}Sr and ^{90}Y

Based on the separation data shown above, ^{90}Y was separated from ^{90}Sr using the following methods.

3.3.4.1. Method-A

^{90}Sr (containing ^{90}Y in secular equilibrium) was taken in 6 M HNO_3 and was equilibrated with 0.2 M T2EHDGA in *n*-dodecane and 20% *iso*-decanol. The organic phase was stripped in to pH 2 solution (to avoid hydrolysis of Y(III)) and part of it was assayed for ^{90}Y purity following the half-life measurement. The remaining portion of the strip solution was acidity adjusted to 6 M and the cycle was repeated three times.

3.3.4.2. Method-B

The separation was carried out in an identical manner as mentioned in Method A as above, in 4 M HCl and 0.2 M T2EHDGA in *n*-dodecane and 30 % *iso*-decanol.

The results of Method A and Method B are summarized in Table 3.11. The decay profiles of the separated ^{90}Y (with possible contamination from ^{90}Sr) following the separation methods are shown in Fig. 3.15. A representative case is presented in the figure using the product

Table 3.11: Purity of the product as indicated by their half-lives as calculated from the slopes of the semi-log plots

Method	Half-life (hrs)	
	6 M HNO_3	**4 M HCl**
One cycle of extraction followed by stripping	86.1 ± 0.4	65.4 ± 0.2
Two cycles of extraction and stripping	70.1 ± 0.2	64.5 ± 0.1
Three cycles of extraction and stripping	66.6 ± 0.1	64.3 ± 0.1

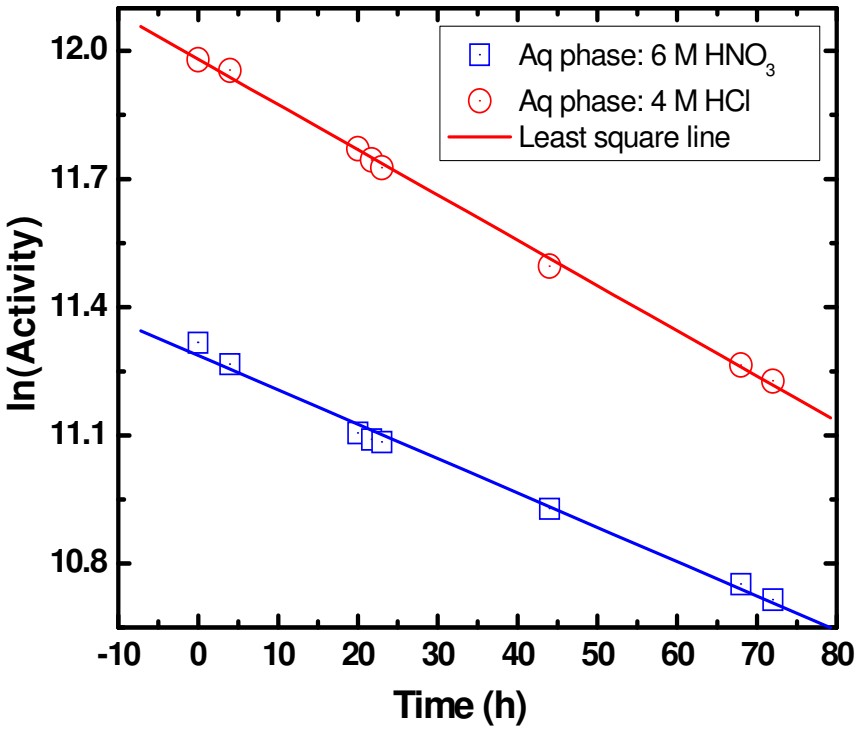

Fig. 3.15: Decay profiles for the separated ^{90}Y activity after separation from ^{90}Sr using METHOD-A (6 M HNO_3) and METHOD-B (4 M HCl)

obtained after one extraction and stripping only. As indicated in Table. 3.11, separation following Method B gave relatively pure form of ^{90}Y with a half-life of 65.4 h while the product obtained following Method A gave a half-life of 86.1 hrs after one cycle of extraction and stripping. Therefore, for separation from both the 6 M nitric acid and 4 M HCl medium were subjected to two additional cycles of separation and the resultant half-lives of 66.6 h and 64.3 h were obtained which indicated acceptable purity for the HCl method (Method B).

3.4. Conclusions

In conclusion, though it is expected that the branched DGA derivative T2EHDGA should display better separation efficiency as compared to TODGA, our studies have indicated an entirely opposite behaviour. The S.F. values are about 100 and 2 times lower for T2EHDGA in 6 M HCl and 6 M HNO_3 medium, respectively as compared to the corresponding values reported for TODGA. Moreover, separation of ^{90}Y from 4 M HCl using 0.2 M T2EHDGA in 30 % *iso*-

decanol in dodecane can result in a relatively pure form of ^{90}Y while the product obtained from 6 M HNO_3 medium using 0.2 M T2EHDGA in 20 % *iso*-decanol in *n*-dodecane has slight amount of ^{90}Sr contamination even after three cycles of purification. No phase modifier was used for TODGA system while role of *iso*-decanol as phase modifier was well executed for the T2EHDGA system. Separation factors were quite high in case of TODGA system than T2EHDGA system especially with HCl medium where it ranges over few thousands at higher feed acidities. This was reflected in the purity of the product obtained. In general, purity of product was reasonably good after first extraction; however, it was well improved after repeated cycles of extraction and stripping. Pure product with half life of 64.1 ± 0.2 was obtained after three repeated cycles of extraction and stripping using 0.1 M TODGA from 6 M HCl medium while with 0.1 M T2EHDGA + 30 % *iso*-decanol system, product half life was 64.3 ± 0.1 hrs under identical conditions. This was due to the contamination of product with unrecovered ^{90}Sr.

Finally, we have developed a solvent extraction based method for recovery of pure ^{90}Y from mixture of ^{90}Y-^{90}Sr using TODGA as an extractant. The pure product was the result of three repeated stages of extraction from 6 M HCl medium followed by stripping with distilled water. T2EHDGA also stands a candidate for ^{90}Y recovery though the product obtained was fairly pure with this system. However, considering large ligand inventory needed for these processes, we have switched over low ligand inventory methods like extraction chromatography and liquid membrane. Chapter IV and V elaborates these techniques.

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Chapter IV

CHROMATOGRAPHIC SEPARATION STUDIES ON Y(III) AND Sr(II) USING TODGA BASED CHROMATOGRAPHIC RESIN

CHROMATOGRAPHIC SEPARATION STUDIES ON Y(III) AND Sr(II) USING TODGA BASED CHROMATOGRAPHIC RESIN

4.1. Introduction

Solvent extraction (SX) processes have been extensively employed in industrial scale operations for the recovery of valuable metal ions due to its continuous nature of operation. However, the major problem associated with SX technique is the generation of large volume of secondary waste and handling of large volume of volatile organic compounds (VOCs) which are inflammable. Also, SX technique is not economical when the material to be recovered is present in sub millimolar concentrations. There are other techniques which are of relevance if the recovery / separation of metal ions are required to be carried out from limited volume of solutions of low concentrations and in case of these techniques, the secondary waste volume and VOCs are reduced significantly. Such techniques include liquid membrane (LM) [**4.1-4.3**], magnetically assisted chemical separation (MACS) [**4.4-4.6**] and extraction (or partition) chromatography (XC) [**4.7-4.10**].

The underlying principle of solvent extraction is based on relative solubility of metal ions in two different immiscible liquids, usually water and an organic solvent while in extraction chromatographic methods; it is based on the differential partitioning of metal ions between the mobile and the stationary phases. In extraction chromatography, the mixture is dissolved in a fluid called the "mobile phase", which carries it through a structure, holding another material called the "stationary phase". The various constituents of the mixture travel at different speeds, causing them to separate. We can separate different constitutes of a mixture using the same column. Chromatographic method of separation can be categorized in different types like paper chromatography, thin layer chromatography, column chromatography. Liquid chromatography (LC) is a separation technique in which the mobile phase is a liquid and can be carried out either in a column or a plane.

In classical normal phase LC, the stationary phase is polar and mobile phase is non-polar. On the contrast, the reverse phase LC utilizes a hydrophobic bonded stationary phase and a polar (usually aqueous) mobile phase [**4.11**]. Extraction chromatography (XC) resembles reverse phase

LC technique which is based on the preferential extraction of metal ions from an aqueous solution by organic ligands physically impregnated or chemically anchored on an inert solid support [**4.12, 4.13**]. The extractant molecules are sorbed into the pores of the solid support through interaction between the surface of the support containing moderate polar groups (e.g. C=O, Si=O) and hydrophobic regions of the extractant molecules by Van- der Waal's interactions. The possibility of varying the capacity of extraction chromatographic resins by loading varying amount of extractants on the solid support is another interesting feature of these resins. It is also possible to remove the entire amount of loaded extractants from the support material, which would help in disposing off the resin materials after their useful life. Excellent separations of elements from aqueous solutions containing high acid concentrations have been achieved by this technique [**4.14**]. XC plays an increasingly prominent role in the separation and pre-concentration of a number of radionuclides, including actinides and fission products [**4.15, 4.16**]. In XC, the selectivity of solvent extraction is combined with the ease of operation of liquid chromatography. A general relationship between the SX and XC has been discussed by several authors [**4.17-4.19**]. Recently, Horwitz et al., [**4.20**] demonstrated some of the significant similarities and differences between XC and SX systems. It was shown that the selectivities for all lanthanides were similar for the two techniques for a given extractant. However, one difference between SX and XC is the change in the activities of the extractant and the extracted complex due to the influence of solid support. The other difference is the non-attainment of thermodynamic equilibrium when extraction chromatography is performed in a column. Nevertheless, this does not influence the transfer of solutes from one phase to another [**4.17**]. XC is much more attractive in cases where the material of interest is in very small amount as compared to the impurities or unwanted materials. Therefore it will be beneficial to employ extraction chromatographic method for separation of ^{90}Y from ^{90}Y-^{90}Sr mixture.

In view of better acceptability of the extraction chromatography based methods over the solvent extraction based methods, N,N,N'N'-tetraoctyl diglycolamide (TODGA) impregnated extraction chromatographic resin (XCR) materials have been studied for metal ion uptake in a variety of systems [**4.19, 4.21**]. Out of these, Horwitz, et al. [**4.20**] have carried out several separation studies including one involving ^{90}Y separation from ^{90}Sr. However, it was required to make a systematic investigation of ^{90}Y and ^{90}Sr separation using TODGA-impregnated XCR and

evaluation of this system for any practical application.

In Chapter III, the preferential extraction of Y (III) with respect to Sr(II) by TODGA and N,N,N',N'-tetra-2-ethylhexyl diglycolamides (T2EHDGA) in different aqueous medium have been elaborated. Utilizing the data obtained in Chapter III, an attempt was made to explore the use of N,N,N',N'-tetraoctyl diglycolamide (TODGA) as the stationary phase in an extraction chromatography resin material. The present work deals with the relative sorption behaviour of Y(III) and Sr(II) in nitric acid and hydrochloric acid using a TODGA impregnated XCR made with Chromosorb W as the solid support. On the basis of the batch uptake data, column studies have also been carried out and breakthrough profiles were obtained for both Y(III) and Sr(II). The separation of ^{90}Y from ^{90}Sr was also investigated and the reusability and radiation stability of the resin was evaluated. Comparison of the results with those obtained by Horwitz et al. using a similar extraction chromatographic material has also been made. Separation of carrier free ^{90}Y tracer was also studied by loading the column with ^{90}Sr and eluting with 0.01 M solutions of HNO_3 as well as EDTA. The purity of the product was ascertained by half-life method.

4.2. Preparation of Chromatographic Resin

The extraction chromatographic resin (XCR) material was prepared by impregnating TODGA on Chromosorb-W, an inert solid support. Chromosorb-W (di-methyl di-chlorosilane treated acid washed celite diatomaceous silica, 60-80 Mesh), obtained from Johns Manville, was washed with distilled water and acetone to remove any adsorbed matter followed by air-drying before use. Chromosorb-W has been reported to be an excellent solid support for actinide-partitioning employing DMDBTDMA as the stationary phase [**4.22**]. In a flask containing a known amount of TODGA diluted in acetone (1:1) was mixed with equal weight of the solid support. The slurry was then equilibrated for 24 hrs in a mechanical shaker followed by the removal of solvent by flushing nitrogen gas with gentle stirring. The resultant resin was vacuum dried to constant weight to get TODGA impregnated resin. This method of resin preparation has been reported in literature using volatile solvents such as methanol, acetone, dichloromethane, toluene etc. [**4.21-4.24**]. Mohapatra, et al. [**4.22**] prepared the malonamide impregnated resin in acetone as well as in methanol and shown that the material prepared by the two methods displayed comparable extraction behaviour. The weight percentage of the TODGA loaded on the Chromosorb-W

support was calculated from the difference in the weight of the resin before and after impregnation and was found to be ~ 50 % w/w. The loading percentage of the extractant on the solid support was confirmed by elemental (C, H, N) analysis. Since Chromosorb-W does not contain any nitrogen, determination of nitrogen content of the impregnated resin could be used for the calculation of the amount of TODGA loaded on the support. Elemental analysis results gave 2.27 % of nitrogen which corresponded to 47 % w/w loading of the extractant on the Chromosorb-W. The density of the TODGA impregnated XCR was determined by water displacement method. A weighed amount of the impregnated resin (~ 2 g) was suspended in water in a narrow neck standard calibrated volumetric flask (25 mL). Care was taken to allow the resin to wet completely to ensure that all the air bubbles were excluded. Finally, the volume of the displaced water was measured by weighing the same. The average density of the prepared TODGA XCR was found to be 1.08 g/mL. The characteristics of the TODGA XCR used in the present work are listed in Table 4.1.

Table 4.1: Characteristics of the TODGA extraction chromatographic resin used in the present work

Parameter	Specification
Stationary phase	TODGA
Support material	Chromosorb-W
Mesh size	60-80
Extractant loading	47 % w/w
Average density of resin	1.08 g/mL
Density of TODGA	0.891 g/mL

4.3. Batch Sorption Studies

Batch sorption studies were performed to explain the extraction behaviour of various metal ions by TODGA XCR. Batch studies are also important for the optimization of various parameters for column chromatography. The extraction of metal ions from different acid medium by TODGA impregnated resin can be expressed by the following equilibrium reaction,

$$M^{n+} + n\,X^{-} + x\,\text{TODGA} \rightleftharpoons MX_n.\,x\text{TODGA} \qquad (4.1)$$

where, TODGA is the ligand moiety impregnated on the resin and X stands for NO_3^- or Cl^-. The above equilibrium reaction is an indication that the extraction of metal ions by TODGA impregnated resin is influenced by aqueous nitric acid concentration as well as the extent of loading of the extractant on the solid support. In this work, ^{90}Y and $^{85,89}Sr$ were used as the radioactive tracers and the distribution studies were performed in a tube containing about 100 mg of the resin coated with TODGA with the desired aqueous phase (containing the requisite quantities of ^{90}Y or $^{85,89}Sr$ tracers in the desired concentration of HCl or HNO_3) and equilibrating with for 30 minutes in a thermostated water bath for an hour at 25.0 ± 0.1 ◦C.

The weight distribution ratio ($K_{d,w}$) values were determined by the following formula,

$$K_{d,w} = \frac{(C_0 - C)/W}{C/V} \qquad (4.2)$$

Where, C_0 and C are the initial and equilibrium concentration of metal ion, W, the weight of the resin (in g) and V, the volume of the aqueous phase (in mL). Assaying of the radiotracers was done as described above. Decay corrections were made for 90Y counting measurements. All the experiments were carried out in duplicate and the distribution data represent the average of the two results. The material balance in all the experiments was within an error limit of ± 5 %.

4.3.1. Uptake Behavior of Resin towards Sr and Y: Batch Mode

4.3.1.1. Effect of Equilibration Time

Prior to the batch sorption and column studies, it was required to study the kinetics of metal ion uptake which is very important in extraction chromatography studies. The optimum equilibration time for Y(III) ion (Sr(II) has much lower extraction with TODGA as the extractant) uptake by the extraction chromatographic resin material was studied by agitating the tubes containing the resin with the feed containing the radiotracer (^{90}Y) in 3 M HNO_3 and 4 M HCl for different time intervals. As listed in Table 4.2, the extraction equilibrium was rapidly achieved and constant $K_{d,w}$ values were observed after only 5 minutes of equilibration as evident from Fig. 4.1. For all subsequent experiments an equilibration time of 30 minutes was used. The time taken for attaining equilibrium metal ion uptake value was significantly lower than that reported earlier

Table 4.2: Kinetics of sorption of Y(III) by TODGA/Chromosorb-W resin; Aqueous phase: 3 M HNO_3 and 4 M HCl; Temperature: 25°C

Time (minutes)	$K_{d,w}(HNO_3)$	$K_{d,w}(HCl)$
0	0	0
5	586	993
10	590	1052
30	583	1012
40	523	1046
60	592	1053
120	575	-

by us for the uptake of Am(III) ion (similar in chemical behavior to Y(III)) with DMDBTDMA, a tetra alkyl malonamide extractant [**4.22**]. However, the results obtained in the present studies agreed fairly well with that reported by Horwitz et al., in an analogous system using a different solid support material [**4.19**].

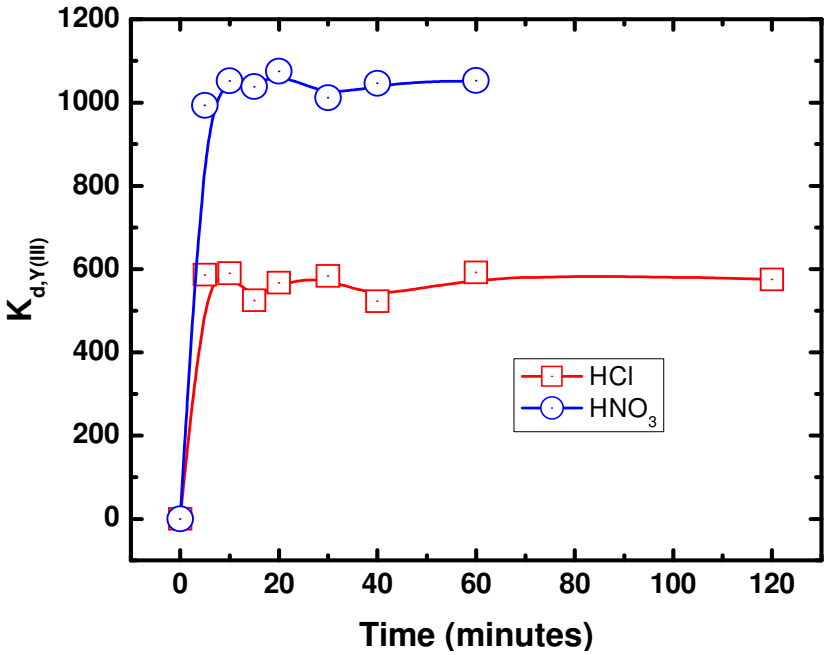

Fig. 4.1: Effect of equilibration time on the batch uptake of Y(III) from 3 M HNO_3 and 4 M HCl

Table 4.3: Effect of acidity on $K_{d,w}$ of Sr(II) and Y(III), aq. phases: HNO_3 and HCl at variable acidities, Temperature: 25 ± 1 °C

HNO_3, M	$K_{D,W}$ Y(III)	$K_{D,W}$ Sr(II)	HCl, M	$K_{D,W}$ Y(III)	$K_{D,W}$, Sr(II)
0.01	2.2	1.04	0.01	0.99	1.1
0.1	127	0.89	0.1	1.14	2.4
1	519	0.7	1	12.4	2.6
2	700	0.9	2	177	2.8
3	1053	0.9	3	347	2.5
4	170	0.9	4	562	3.0
6	281	0.4	6	334	5.4

4.3.1.2. Batch Sorption Studies at Varying Acidities

Solvent extraction studies presented in Chapter III indicated that HCl medium was more suitable for the separation studies involving ^{90}Y and ^{90}Sr as compared to HNO_3 medium using TODGA as the extractant. Similar extraction studies were carried out in batch method at different acidity of two mineral acids viz. nitric and hydrochloric acids in order to investigate the effect of acidity. The batch sorption data (shown in Table 4.3) from nitric acid and hydrochloric acid media indicated that the sorption of Sr(II) was insignificant with nitric acid as the feed and slightly higher $K_{d,w}$ values were reported with HCl at almost the entire range of acidity. The $K_{d,w}$ values for Y(III) were much higher as compared to those for Sr(II) and this was in the same line of their solvent extraction behaviour discussed earlier in Chapter III. It was intriguing to note that the $K_{d,w}$ values for Y(III) are significantly lower as compared to those reported by Ansari et al. involving Am(III) which was attributed to lower loading of the present XCR [**4.21**].

Higher $K_{d,w}$ values of Y(III) were obtained with HNO_3 as the feed solution as compared to HCl up to 3 M HNO_3 beyond which a crossover was seen (Fig. 4.2). However, in case of HCl medium, peak values of $K_{d,w}$ were attained at 4 M acidity though the decrease beyond 4 M acidity was less steep for HCl medium as compared to that in HNO_3 medium. This is reflected in the S.F. (separation factor, defined as the ration of the $K_{d,w}$ values) values which also peaked at 4 M for both the mineral acid medium (Table 4.4). Though the decrease in the $K_{d,w}$ values for Y(III) was to a much lower extent in HCl medium as compared to that observed in HNO_3

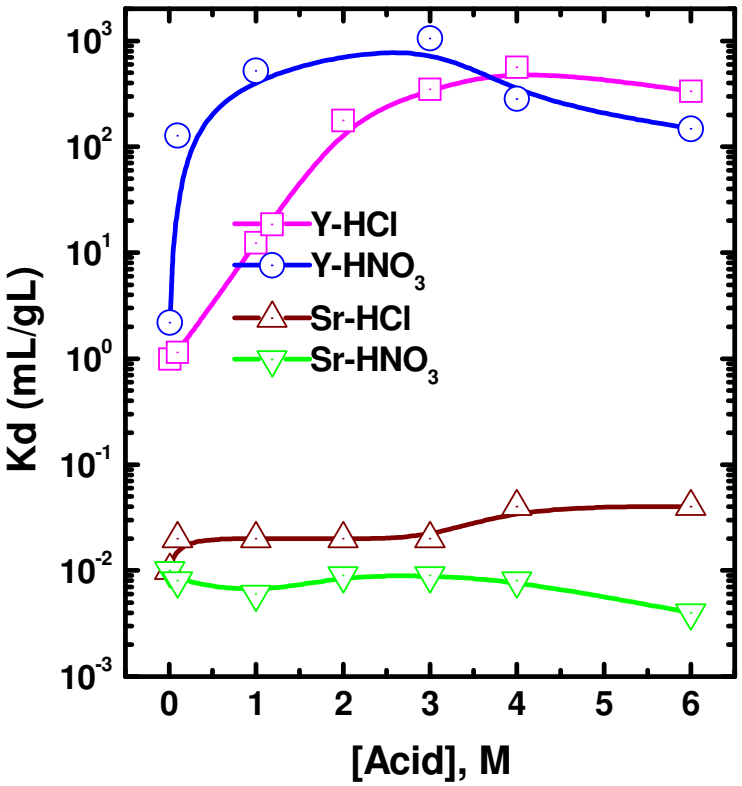

Fig. 4.2: Batch distribution data of Sr and Y using the extraction chromatographic resin material from varying concentrations of HCl and HNO_3

Table 4.4: Separation behaviour of ^{90}Y and ^{90}Sr (studied using $^{85,89}Sr$ as the surrogate) from HCl and HNO_3 feed solutions

Acid concentration (M)	Separation factor (S.F.) values	
	HCl	HNO_3
0.01	0.9 ± 0.01	2.11 ± 0.02
0.1	0.48 ± 0.01	143 ± 0.99
1	4.77 ± 0.05	741 ± 0.5.76
2	63.2 ± 0.03	863 ± 3.32
3	139 ± 1.12	1170 ± 6.71
4	95 ± 0.91	189 ± 1.22
6	62 ± 0.71	702 ± 3.55

medium, the monotonous increase in $K_{d,w}$ value of Sr(II) in HCl medium resulted in a peak S.F. value at 3 M HCl. In view of the higher separation factor values observed at 3 M HNO_3 as the feed solution, separation studies using columns were attempted subsequently at this acidity.

4.3.1.3. Saturation Uptake Capacity

The saturation metal ion uptake capacity with respect to Y(III) sorption was estimated by equilibrating 5 mL of the feed solution (containing 1 g/L Y in 3 M HNO_3 spiked with ^{90}Y tracer) with 500 mg of the resin for 48 hrs. The radioactivity in the feed at the start of the experiment and the supernatant after equilibrating for 48 hrs were used for calculating the saturation uptake capacity of the TODGA resin which was found to be 0.7 meq/g of the extraction chromatography resin material. In view of low $K_{d,w}$ values encountered with Sr(II) no such uptake data was generated for Sr.

4.3.1.4. Effect of Temperature on Distribution Ratio ($K_{d,w}$) in 3 M HNO_3 and 3 M HCl

In case of solvent extraction studies involving extraction of Y(III) from both HNO_3 and HCl medium using TODGA as extractant, the processes were found to be exothermic in nature in our earlier experiments. Similar experiments were carried out to understand the effect of temperature on the distribution ratio of Y(III) between the TODGA resin and aqueous phase. In this experiment, ~0.1 g of TODGA loaded resin along with 2 mL nitric acid and hydrochloric acid of 2 M strength spiked with ^{90}Y activity were taken in Pyrex glass tubes and equilibrated at

Table 4.5: Temperature effect on sorption of Y(III) by TODGA / Chromosorb-W resin; Aqueous phase: 3 M HNO_3 and 3 M HCl

Temperature (^0K)	$K_{d,w}(HNO_3)$	$K_{d,w}(HCl)$
283	12343	7762
288	7804	5125
293	3801	2430
298	1385	933

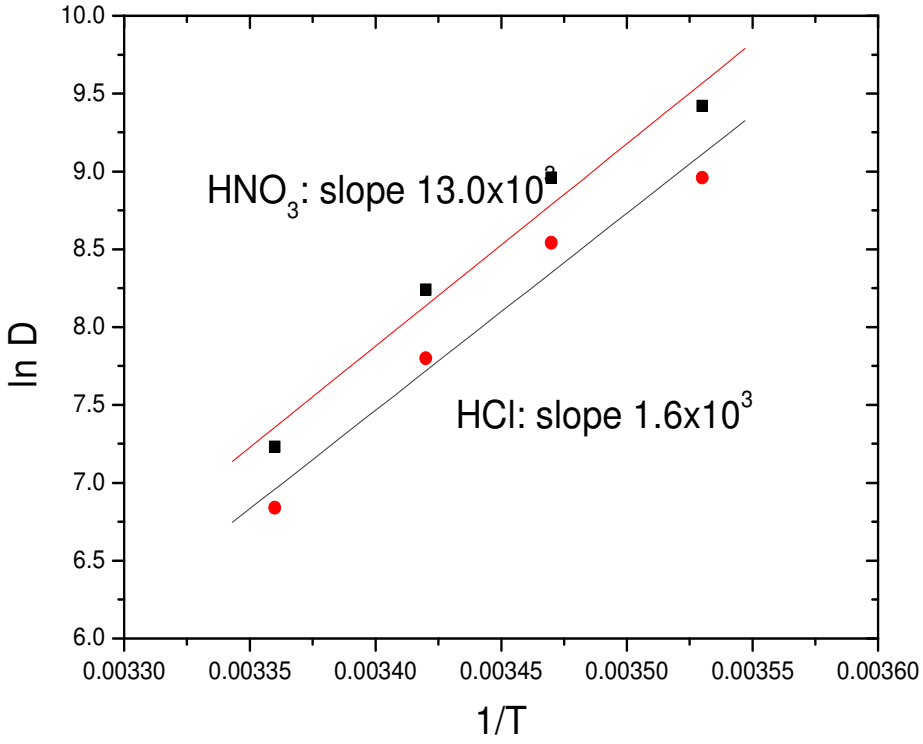

Fig.4.3. Plot of log D versus 1/T in case of sorption of Y(III) by TODGA/chromosorb-W resin; Aqueous phase: 3 M HNO_3 and 3 M HCl

different temperatures. From the data (shown in Table 4.5), it can be concluded that like the solvent extraction process, the distribution process is also exothermic in nature and the plot of log D versus 1/T yielded straight line (shown in Fig. 4.3).

4.4. Column studies

The chromatography column was prepared by packing ~ 1.0 g of TODGA XCR in a borosilicate glass column of 4.0 mm diameter. In the present studies the flow rate was adjusted to about 4–6 drops (0.3 mL/min) by changing the packing density of the glass wool plug in the column and the liquid column height above the glass wool plug. Various column parameters were estimated by the method reported in the literature [**4.25**]. The bed volume and the bed density were calculated from the column dimensions, bed height and the weight of the packed XCR. The volume of mobile phase (V_m), referred to as the free column volume, was calculated from the

Table 4.6: Characteristics of TODGA chromatographic resin packed column

Wt. of resin	1.0 g
Bed volume	1.257 mL
Bed density	0.398 g/mL
Density of stationary phase	0.891 g/mL
Volume of stationary phase	0.210 mL/mL of bed
Volume of mobile phase	0.632 mL/mL of bed

difference in the bed volume and the volume of resin in the bed, the latter being the weight of resin material in bed divided by its density. The volume of liquid stationary phase (V_s) was estimated from the weight of the extractant impregnated on the support material packed in the column divided by the density of the extractant. The former was obtained from the weight of the resin packed in the column and the percentage of extractant loaded on the resin. The calculated parameters and specifications of the packed XCR column are summarized in Table 4.6. The column was preconditioned by passing excess of appropriate nitric acid solution, prior to the introduction of the sample solution. The breakthrough curves and elution profiles were obtained by plotting radioactivity (in terms of counts per unit time per unit volume) in the effluent versus volume of the solution passed.

4.4.1. Breakthrough Profiles

In columnar studies, it is essential to determine the breakthrough capacity of the resin column in order to optimize the extraction chromatographic process. Hence the breakthrough profiles of Sr (II) and Y (III) from 3MHCl and 3 M HNO_3 medium using a 0.4 x 13.8 cm column containing about 1 g of resin material (Table 4.6) were determined. From the data (shown in Table 4.7), it can be suggested that both in case of 3MHCl and 3 M HNO_3, $^{85,89}Sr$ comes out of the column almost immediately after being loaded on to the column suggesting negligible uptake in the resin which was in conformity with the batch sorption data presented above. As the $^{85,89}Sr$ tracer used to carry out these experiments contained significant amount of carrier (concentration of Sr in the solutions was about 10^{-4} M) only slight retention was seen. As will be seen in subsequent studies, ^{90}Sr retained in the column was not eluted in the loading and washing stages using 3 M HNO_3.

Table 4.7: Breakthrough data of $^{85-89}$Sr and ^{90}Y in 3 M HNO_3 and 3 M HCl

Column volume	3 M HNO_3		3 M HCl	
	$^{85-89}$Sr, % BT	^{90}Y, % BT	$^{85-89}$Sr, % BT	^{90}Y, %BT
0	0	0	0	0
2.5	8	1.2	6	1.1
5.0	22	1.4	15	1.2
7.5	42	1.3	32	1.1
10.0	78.5	1.3	70	1.3
12.5	98	1.4	90	1.2
15	100	1.5	93	1.2
20.0	101	1.3	101	1.3
25.0	102	1.4	102	1.3

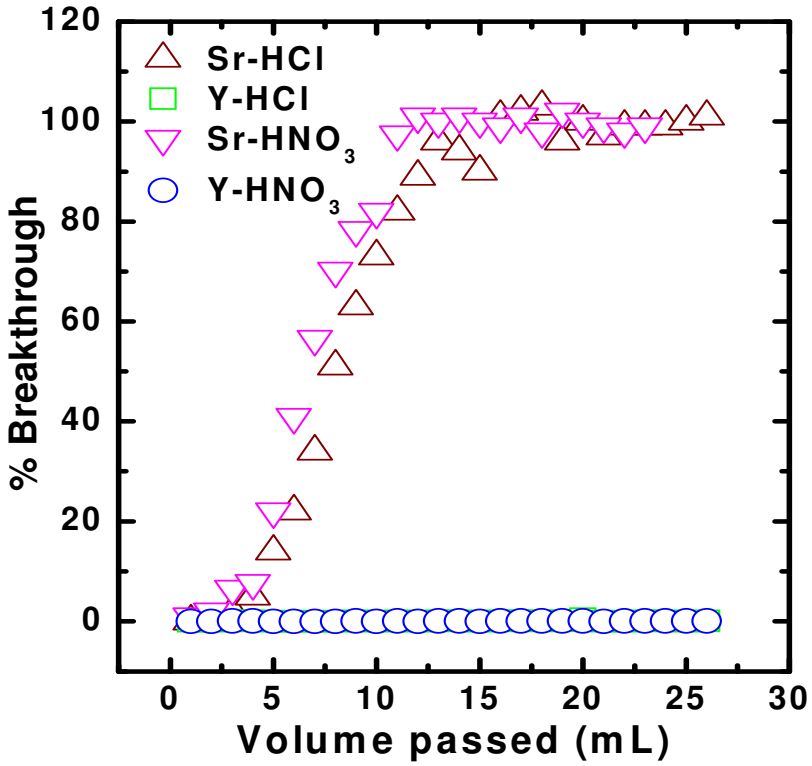

Fig. 4.4: Breakthrough profiles of Sr (using ^{85,89}Sr tracer) and Y (using carrier free ^{90}Y) from 3 M HCl and 3 M HNO_3 feed solutions. Flow rate: 0.3 mL /min

On the other hand, no breakthrough was observed even after passing 50 column volumes when carrier free ^{90}Y was used in the feed (3 M HNO_3 and 3 M HCl). The breakthrough profiles are plotted together in Fig. 4.4. As no breakthrough of ^{90}Y was seen, a feed containing 1 g/L Y in 3 M HNO_3 which was spiked with ^{90}Y tracer was used for the subsequent breakthrough studies. Similar to the results published by Ansari et al. who used Eu(III) carrier in their extraction chromatography studies [**4.19**], about 20 column volumes were required before any breakthrough of ^{90}Y (as shown in Run 1 of Fig. 4.5) as evident from the data given in Table 4.8.

Table 4.8: Breakthrough data of ^{90}Y in column experiment with 3 M HNO_3 feed solution

Column vol. passed	% BT of ^{90}Y	Column vol. passed	% BT of ^{90}Y
2	1.3	16	4.5
4	1.7	18	3.7
6	3.6	20	3.0
8	3.5	24	38.0
10	3.5	28	85.2
12	3.7	30	94.8
14	4.3	40	95.0

4.4.2. Column Capacity and Elution Behavior

The capacity of the column with respect to Y(III) was evaluated using the feed solution containing 1 g/L Y spiked with ^{90}Y. In a triplicate experiment it was observed that 0.65 $\pm$ 0.01 meq of Y could be loaded on the column at 3 M HNO_3 without any discharge of the ^{90}Y activity which is in agreement with the saturation uptake capacity reported above. Elution experiments were performed after loading the column with the desired pure tracers. The elution behavior of Y(III) was investigated by employing 0.01 M HNO_3 and 0.01 M EDTA (pH 2.0) . The elution with 0.01 M HNO_3 was found to be extremely slow and a broad band was observed and about 20 % elution was in 15 bed volumes when dilute HNO_3 solution was used as the eluent (Fig. 4.5). On the other hand, a sharp band with quantitative elution in about 6 bed volumes was noticed when 0.01 M EDTA was used as the eluant (Fig. 4.5).

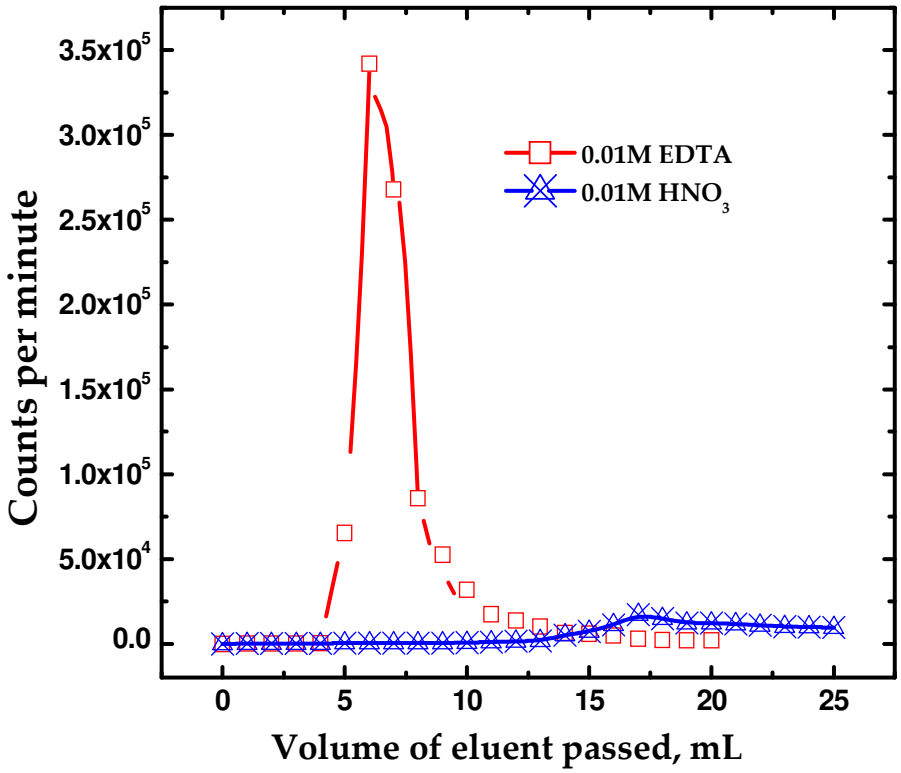

Fig. 4.5: Elution profiles of Y from the column using 0.01 M HNO_3 and 0.01 M EDTA at pH 2.0. Flow rate: 0.3 mL /min

4.4.3. Reusability of the Column

In case of extraction chromatographic method of separation, it is essential to the extent of reusability of the extraction chromatographic resin material i.e, how many times the same column can be used for the same separation purpose. The reusability of the extraction chromatographic resin material was investigated by repeatedly loading and eluting ^{90}Y; loading of Y(III) followed by elution was considered as one cycle. The feed solution contained 1 g/L Y(III) solution in 3 M HNO_3 spiked with ^{90}Y tracer. The breakthrough profiles from the column studies are superimposed in Fig. 4.6 from 3 successive runs which indicated that the breakthrough capacity decreased steadily with continuous use from 20 column volumes in the first run to 8 column volumes in the third run (shown in Table 4.9). This observation indicated possible leaching of the loaded extractant. It is required, therefore, to develop resin materials with the diglycolamide (DGA) moiety grafted to the resin surface.

Table 4.9: Data on breakthrough in terms of column volume passed, in three cycles of reuse of same extraction chromatographic column

No. of Run	Appearance of BT in terms of column volume passed
1	20
2	17
3	8

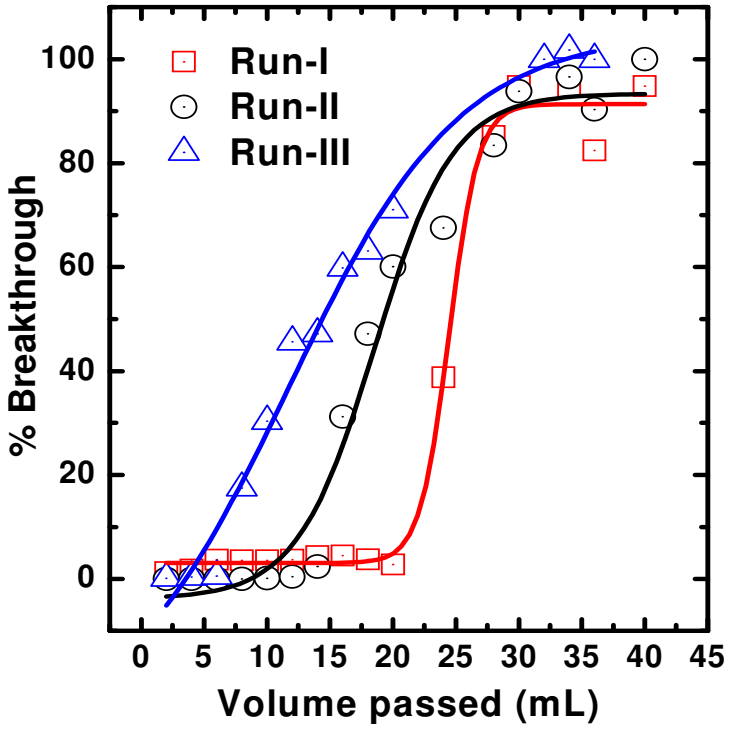

Fig. 4.6: Reusability data of the extraction chromatographic resin as indicated by successive runs. Feed: 1 g/L Y in 3 M HNO_3. Flow rate: 0.3 mL /min

4.4.4. Effect of Absorbed Dose

During the residence of radionuclides viz. ^{90}Sr and ^{90}Y, the TODGA loaded resin column suffers radiation damage due to the high energy beta particles associated with them. Hence, it was pertinent to study the performance of the resin after it was exposed to varying amounts of the dose in ^{60}Co irradiator with a dose rate of 0.32 MRad per hour. Effect of gamma irradiation on the resin performance was studied up to an absorbed dose of 50 MRad. The experiment was

Table 4.10: Effect of absorbed dose on the breakthrough in columnar experiment

Absorbed Dose (Mrad)	Appearance of BT in terms of column volume passed
0	20
10	17.5
20	15
50	10

carried out by taking in each of three vials 2g TODGA resin and kept in gamma cell having exposure dose of 1.6kGy/hr for different period of time. The results in terms no. of column volume passed at the appearance of breakthrough in various absorbed dose are given in Table 4.10 and the breakthrough plots shown in Fig. 4.7. The decrease in the breakthrough volumes with the increase of absorbed dose conclusively proved degradation of the resin with increasing absorbed dose. Zhang et al. [**4.24**] have also reported significant degradation of the TODGA based XCR from batch uptake studies involving Nd(III).

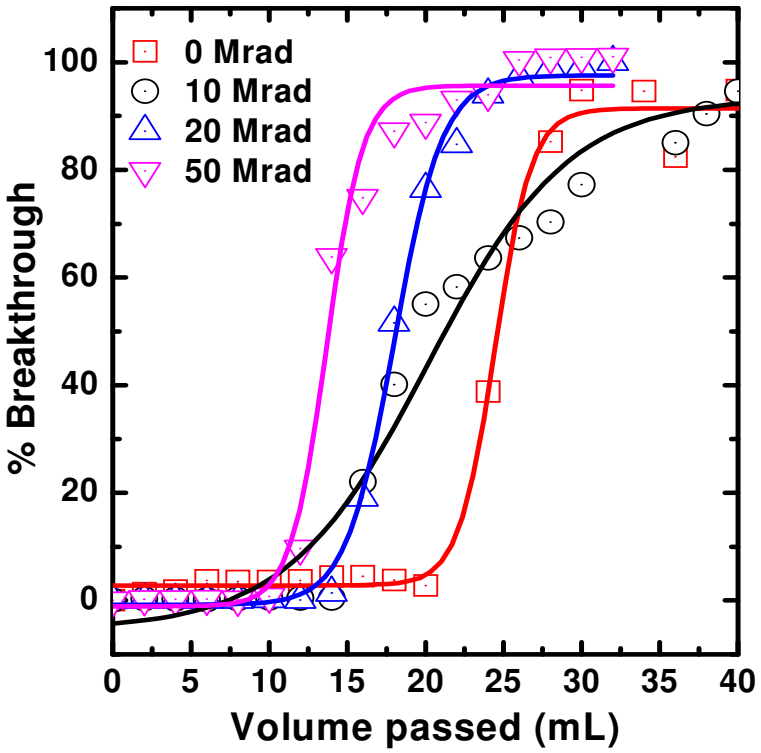

Fig. 4.7: Irradiation stability of the resin as indicated by the breakthrough profiles as a function of absorbed dose. Feed: 1 g/L Y in 3 M HNO_3. Flow rate: 0.3 mL/min.

4.5. Separation of Carrier Free ^{90}Y from ^{90}Sr

Based on the batch studies and column studies on the sorption behavior of ^{90}Y and $^{85\text{-}89}$Sr on TODGA resin, a separation scheme for generating carrier ^{90}Y from ^{90}Sr and ^{90}Y mixture was developed. In this experiment, separation of carrier free ^{90}Y from the mixture of ^{90}Sr and ^{90}Y (present as the daughter product of ^{90}Sr) was accomplished by loading a known amount of the tracer mixture onto a column containing about 1 g of the XCR as mentioned above. Loading of the tracer mixture was done at 3 M HNO_3 and washing up to 10 column volumes indicated negligible activity coming out of the column. Subsequently, elution was carried out using 0.01 M HNO_3 and the profiles of elution are given in Fig. 4.8. The first peak was due to ^{90}Sr and the second broad peak was due to ^{90}Y. Lack of getting a sharp ^{90}Y peak suggested possible contamination of the product. Moreover, large eluent volume was required for getting quantitative elution of the product making this method unsuitable. The half-lives of the product obtained in the 10th, 15th and 20th fractions (of 1 mL each) were obtained from slope of the ln(activity) vs time plots (Fig. 4.9) using equation (4.3) and the data are listed in Table 4.11.

$$\text{Half life } (t_{1/2}) = \text{slope}/\ 0.693 \qquad (4.3)$$

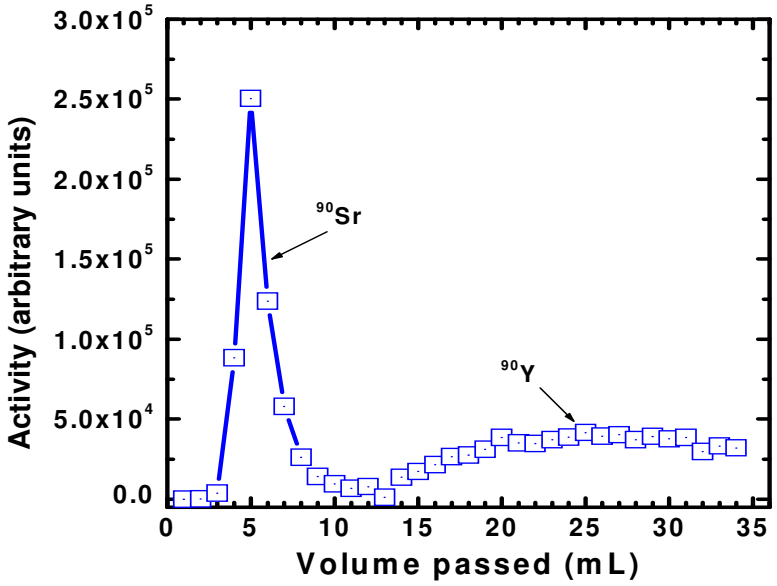

Fig. 4.8: Elution profiles of ^{90}Sr and ^{90}Y from the column. Loading and washing: 3 M HNO_3; Elution: 0.01 M HNO_3. Flow rate: 0.3 mL /min

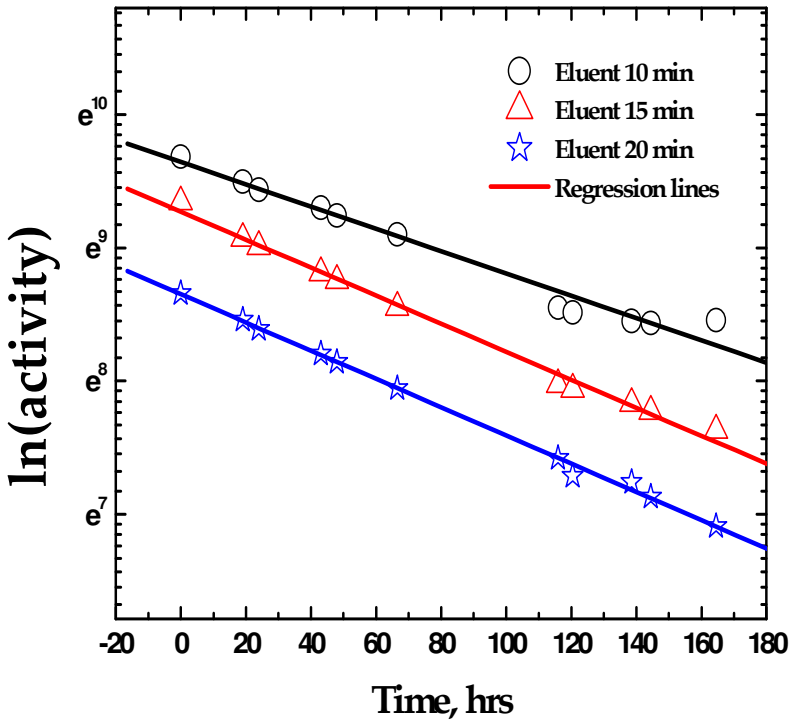

Fig. 4.9: Decay profile of the purified ^{90}Y after second extraction followed by stripping used for half-life calculation

As indicated, the products are contaminated with small fractions of ^{90}Sr making them unsuitable for use. A combination of the eluent, 0.01 M HNO_3 for ^{90}Sr elution and 0.01 M EDTA (at pH 2.0) for ^{90}Y elution was used for a better product separation as indicated in Fig. 4.10. The ^{90}Y

Table 4.11: Purity test data of the eluted fractions as checked by the half-life method

Eluent	Sample identification[a]	Half-life (hrs)	Remarks
0.01M HNO_3	10 mL	82.9	Contaminated
	15 mL	65.9	Contaminated
	20 mL	65.4	Contaminated
0.01M EDTA	17 mL	64.0	Acceptable purity
	22 mL	64.4	Acceptable purity
	25 mL	65.6	Contaminated

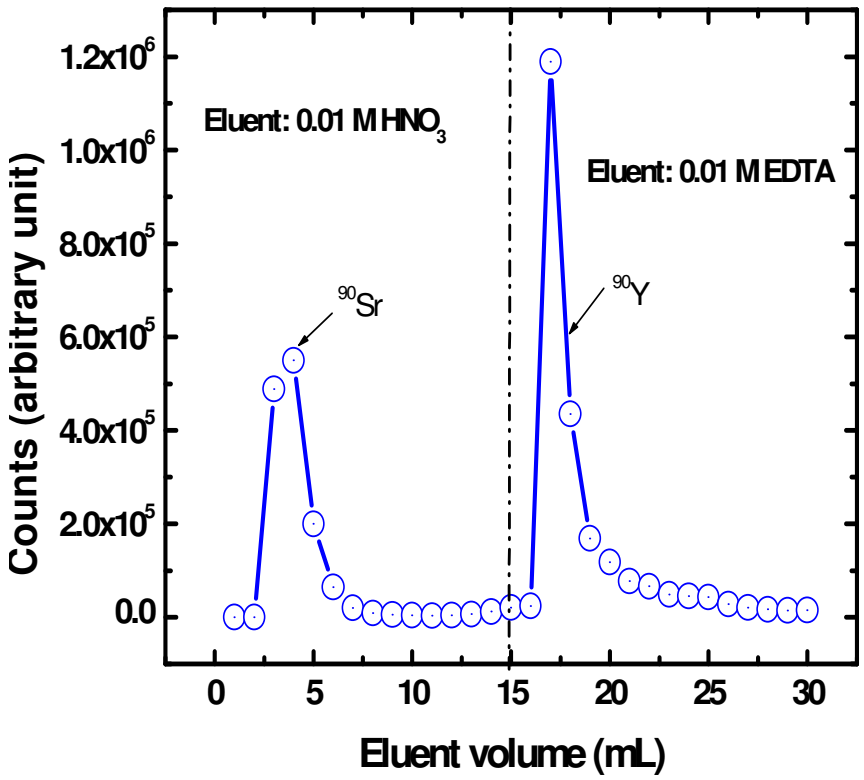

Fig. 4.10: Elution profiles of ^{90}Sr and ^{90}Y from the column. Loading and washing: 3 M HNO_3; Elution: 0.01 M EDTA at pH 2.0. Flow rate: 0.3 mL /min

fraction is recovered in about 3 column volumes or about 6 mL. The recovered products for the 17th, 22nd and 25th fractions (of 1 mL each) were assayed continuously for about 10 days and the half- life of ^{90}Y are also listed in Table 4.11. The half-life data for the 17th and 22nd fractions indicated reasonably good purity of the product. This separation method, therefore, can find possible application for the separation of ^{90}Y from ^{90}Sr for subsequent use in radiopharmaceuticals. The present separation method is far superior to the separation method reported by Horwitz et al. [**4.25**] using a similar resin but 0.1 M HCl as the eluant.

4.6. Conclusions

We have developed N,N,N'N'-tetraoctyl diglycolamide containing chromatographic resin for separation of ^{90}Y from mixture of ^{90}Y-^{90}Sr. The uptake capacity of resin for Y and Sr was studied using solid-liquid extraction mode and column mode. Solid-liquid extraction studies

reveals rapid extraction kinetics and requires only 5 minutes to attain the equilibrium. The batch sorption data from nitric acid and hydrochloric acid media revealed higher extraction affinity towards Y(III) in HCl medium than HNO_3 over entire range of acidity which was consistent with solvent extraction studies discussed in Chapter III. In case of both acidic mediums, separation factor value reaches maximum at 3 M feed acidity, 1170 was reported in case of HNO_3 while in case of HCl, it was just 139. Loading capacity of resin at 4 M HNO_3 was found to be 0.7 meq/g for Y(III). Extraction process was found to be exothermic in nature and observations were consistent with solvent extraction studies discussed in Chapter III. With these promising facts, column studies were carried out with inactive Y spiked with ^{90}Y tracer at 3 M HNO_3. Loading capacity revealed by breakthrough curve at respective column parameters was 0.65 ± 0.01 meq/g for Y(III) in HNO_3 medium. EDTA was found to be quite effective eluant while performance of 0.01M HNO_3 was poor when it was used for same purpose. However, the reusability of the column has serious limitations as a fresh column needs to be used for each separation. Rapid detoriation of column performance was observed with repetitive runs was carried out on same column. The loading of Y was half at 50 MRad irradiation dose as compared to unirradiated one. The results suggested that it is possible to separate ^{90}Y from ^{90}Sr using a column containing the XCR material with reasonable purity when the elution of ^{90}Sr and ^{90}Y is done by 0.01 M HNO_3 and 0.01 M EDTA at pH 2.0, respectively. Marginal contamination due to the presence of ^{90}Sr in the product is not ruled out and can be possibly separated by loading on to a crown ether column as reported earlier. Overall performance of resin was satisfactory, but needs to be improved. In this regards, supported liquid membrane technique will be interesting where stability of membrane was stable over repeated runs for a number of days without affecting the separation efficiencies [**4.26**]. The next Chapter V elaborates the same.

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Chapter V

STUDIES ON SEPARATION OF Y(III) FROM Sr(II) USING SUPPORTED LIQUID MEMBRANE TECHNIQUES

STUDIES ON SEPARATION OF Y(III) FROM Sr(II) USING SUPPORTED LIQUID MEMBRANE TECHNIQUES

5.1. Introduction

Membranes are physical / chemical barriers which allow selective permeation of certain species. Membrane technology has contributed significantly for the production of potable water from sea water in the last few decades. In the recent years, membrane processes have been found to be effective in the treatment of industrial effluents and gas purifications [**5.1-5.3**]. Advantages of membrane based separation techniques are low energy requirements, low capital and operating costs, the possibility of achieving high separation factors and simple modular design [**5.4, 5.5**]. The use of liquid membranes containing a carrier has been proposed as an alternative to solvent extraction for selective separation and concentration of metal ions from dilute aqueous solutions [**5.6, 5.7**]. The important feature of liquid membrane is that unlike solvent extraction the extraction and stripping of the metal ions as well as regeneration of the carrier are combined in a single stage.

Liquid membrane usually consists of a water immiscible (organic) layer held on a polymeric support separating a source aqueous phase (feed) containing mixture of metal ions and a receiving aqueous phase (receiver), where the metal ions of interest gets concentrated preferentially. The liquid membrane may be a stirred organic phase separated by aqueous feed and receiver phases (Bulk Liquid Membrane, BLM) or a dispersion of water (strip phase) containing oil droplets in aqueous feed phase (Emulsion Liquid Membrane, ELM). In contrast, supported liquid membrane (SLM) consists of water immiscible organic phase immobilized in the pores of microporous polymeric film (which acts as inert support) separating the two phases, the feed and the receiver phases. Commonly two types of membrane support are used in SLM, a flat sheet (FSSLM) or a hollow fibre (HFSLM). The performance of different types of liquid membranes, viz. BLM, ELM, FSSLM and HFSLM has been reviewed by Izatt, et al. [**5.8**]. Facilitated transport of metal ions through SLM has been described in a number of papers [**5.9 - 5.23**]. In such transport systems, the metal ions can be transported across the membrane against their concentration gradient, i.e. “uphill” transport. The driving force in such processes is provided by the chemical potential difference of the chemical species present on the two opposite sides of the membrane. The permeability of the transported species is decided by the parameters

such as membrane thickness, pore structure, aqueous diffusion coefficient of metal ions, aqueous diffusion layer thickness, distribution and diffusion coefficients of the metal bearing species in the organic liquid membrane phase, etc. [**5.22 - 5.24**]. While diffusion coefficient of the metal bearing species in the carrier solvent depend upon the chosen membrane and the aqueous diffusion coefficient of the metal ions depend on the stirring rate, the transport rates can be controlled through various parameters, viz. feed acidity, solute concentration, carrier concentration, nature of diluent, strip phase composition etc. [**5.25**]. The preferential extraction of Y(III) as compared to Sr(II) by diglycolamide extractants using solvent extraction studies has been investigated and discussed in Chapter 3. Though the straight chain ligand, N,N,N',N'-tetra-*n*-octyl diglycolamide (TODGA) has been found promising, N,N,N',N'-tetra-2-ethyl-hexyl diglycolamide (T2EHDGA), its branched analog, can also be a candidate for the separation of trivalent Y over Sr (II) in nitric acid medium over a range of acidity (2 - 6 M HNO_3). In Chapter III, we have also discussed the solvent extraction method for the separation of ^{90}Y from ^{90}Sr using TODGA as the extractant in *n*-dodecane and T2EHDGA as the extractant in *n*-dodecane containing 30 % *iso*-decanol as the phase modifier. The role of *iso*-decanol is not only to prevent third phase, but also to change the solvent polarity which can seriously affect the aggregation behaviour of these extractants and hence the relative extractability of these metal ions [**5.26**]. Therefore, it was required to carry out a systematic study on the role of the organic diluent on the extraction behaviour of Y(III) and Sr(III). This behaviour of T2EHDGA can be exploited for the separation of ^{90}Y from ^{90}Sr.

In view of the growing concern for the environment, it is necessary to evaluate separation methods which dwell on low ligand inventory. In Chapter IV, we have discussed the development of an extraction chromatographic method containing N,N,N',N'-tetra-*n*-octyl diglycolamide (TODGA) as the extractant. However, column stability was found to be poor as repetitive column runs indicated fast degrading separation efficiency. In this context, supported liquid membrane based methods are attractive where not only a very small quantity of the extractant was used but also the stability of membrane was found to be good over 20 days of operations [**5.27, 5.28**]. Other advantages of liquid membrane can be listed as the simultaneous extraction and stripping and generation of carrier [**5.29**]. Moreover, serious drawbacks of solvent extraction methods such as third phase formation, phase entrainment and phase separation

limitations can be alleviated by the supported liquid membrane methods.

In this Chapter, the studies on the transport of Y(III) and Sr(II) by liquid membrane under various experimental conditions have been described. Two different mineral acids viz., HCl and HNO_3 were used as the feed and the separation of Y(III) and Sr(II) was investigated. Acid variation studies have also been carried out. Two extractants (TODGA and T2EHDGA) have been used as the carrier extractant for the selective transport of Y(III) from mixture containing Y(III) and Sr(II). Role of diluents on the transport behaviour was investigated and the results have been correlated to parameters such as diluents polarity and viscosity. Different diluents and diluent mixtures have been used examined and the findings are presented in this Chapter. Based on these studies a methodology was developed to obtain purified ^{90}Y from ^{90}Sr - ^{90}Y mixture. The purity of product was checked by the half life measurement which has been described in the Chapter IV.

5.2. Theory of Facilitated Transport

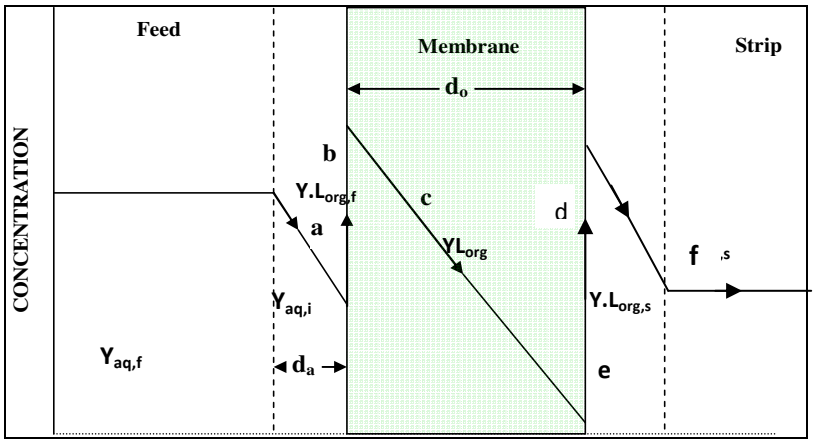
In the facilitated transport process, the metal ion diffuses through the aqueous feed boundary layer and reacts with the carrier molecule (present in the pores of the solid support) at the aqueous feed-membrane interface resulting into the formation of metal-carrier complex. The metal-carrier complex then diffuses through the liquid membrane to the receiver phase because of its negative concentration gradient. Finally, the metal-carrier complex dissociates and releases the metal ion into the strip solution at the membrane-aqueous strip interface. The quantitative description of the facilitated transport, therefore, requires a detailed knowledge of the processes like (a) diffusion of the metal ions through the aqueous feed boundary layer, (b) reversible chemical reaction at the aqueous feed-membrane interface, (c) diffusion of the 'metal-carrier complex' in the membrane phase, and (d) dissociation reaction of the metal-carrier complex at the membrane-aqueous strip interface. The mathematical relationships for the permeation of metal ions in the facilitated transport can be derived by simple assumptions. The model described by Danesi, et al. [**5.23**] assumes that the chemical reactions (process (b) and (d) in Fig.5.1) between the metal ions and the ligand occur instantaneously (relative to other rate controlling processes (a) and (c) in Fig.5.1) at the aqueous-membrane interface. It implies that the local equilibrium always occurs at the aqueous-membrane interface and the metal ion

transport rate will be determined by the diffusion rate through the aqueous stagnant layers (Nernst films) and the diffusion rate through the liquid membrane.

To quantify the transport phenomena, one needs to have a detailed knowledge of the following:

- ✓ Distribution coefficient of metal ion
- ✓ Diffusion coefficient of carrier
- ✓ Kinetics of extraction and stripping
- ✓ Viscosity of the medium
- ✓ Temperature
- ✓ Stirring speed

5.3. Flux Equations for Permeation



a: Aqueous diffusion; b: Chemical reaction c: Membrane diffusion

Fig. 5.1: Schematic presentation of the processes controlling the permeation of Y(III) ion through an SLM containing DGA extractant when the distribution ratio at the membrane-receiver solution interface is much lower than that at the feed-membrane solution interface.

The chemical reaction involved during the extraction of metal ions (M^{n+}) from aqueous nitrate medium by neutral ligand, diglycolamide (L), can be described as,

$$M^{n+}_{(aq)} + n\ NO_3^-{}_{(aq)} + x\ L_{(org)} \rightleftharpoons M(NO_3)_n \cdot xL_{(org)} \quad (5.1)$$

where, the subscripts (aq) and (org) represent the aqueous and the organic phases, respectively. The term $M(NO_3)_n \cdot xL$ represents the extracted species in the organic phase. For simplicity, we will represent this term as [M·L] in this Chapter. The stoichiometry of the extracted species of DGA and various actinide ions are described in Chapter 3. At the aqueous feed-membrane interface, the equilibrium reaction (5.1) is shifted to right and the [M·L] complex species then moves towards the receiving phase within the membrane as a consequence of concentration gradient. On the other hand, at the membrane-strip interface, the equilibrium reaction (5.1) is shifted to the left because of unfavourable conditions in the strippant phase. This results in the dissociation of the [M·L] complex leaving behind free ligand molecules in the membrane phase. The free carrier molecules then move towards the feed solution due to negative concentration gradient to complete the cycle. The equations describing flux across the stagnant aqueous diffusion layer and membrane can be derived by applying Fick's diffusion law with simple assumptions: (a) the composition of the strip solution is such that the complex of Y(III) and DGA (also referred to as L) is completely dissociated at membrane-receiver strip interface, (b) the membrane polarity is low enough to neglect the concentration of charged species in comparison to the uncharged one, and (c) there is no extraction of Y(III) by the pure diluent, (d) the concentration gradients are linear, and (f) feed concentration of NO_3^- is constant, the equations describing the flux, J_a (feed phase) and J_o (membrane phase) under steady state are given by equations (5.2, 5.3),

$$J_a = \frac{D_a}{d_a}\left([M]_{a,fb} - [M]_{a,fi}\right) = \frac{\{[M]_{a,fb} - [M]_{a,fi}\}}{\Delta_a} \quad (5.2)$$

$$J_o = \frac{D_o}{d_o \tau}\left([M]_{o,fi} - [M]_{o,si}\right) = \frac{\{[M]_{o,fi} - [M]_{o,si}\}}{\Delta_o} \quad (5.3)$$

where D_a is the aqueous diffusion coefficient of Y(III), D_o the membrane diffusion coefficient of M·L, d_a, the thickness of the aqueous stagnant film, d_o the membrane thickness, $[M]_{a,fb}$ and

$[M]_{a,fi}$ is the metal concentrations in the bulk aqueous feed phase and at the aqueous feed-membrane interface, respectively, τ is the tortuosity of membrane material. The symbol, Δ represents the mass transfer resistances of respective phases given by $\Delta = d / D$. All these parameters are shown in Fig. 4.1. The symbol, $[M.L]_{o,fi}$ denotes the concentration of metal-ligand complex ion at feed side interface inside the membrane while $[M.L]_{o,si}$ denotes the metal-ligand complex ion concentration at strip side interface inside the membrane. The distribution coefficient (k_d) of M at the feed-membrane interface is reasonably high under the chosen experimental conditions. However, experimental conditions on the strip side are such that the k_d value of the given metal ion at the membrane-receiver interface is very low i.e. $[M.L]_{o,si} << [M.L]_{o,fi}$.

Therefore, Eq. (5.3) can be rewritten as,

$$J_o = \frac{[M.L]_{o,fi}}{\Delta_o} \tag{5.4}$$

If we assume that the carrier in the liquid membrane is not saturated with the metal ions, then the concentration terms $[M{\cdot}L]_{o,fi}$ and $[M]_{a,fi}$ are related to the k_d by the following equation,

$$k_{d,f} = \frac{[M.L]_{o,fi}}{[M]_{a,fi}} \tag{5.5}$$

Equation (5.5) can be rearranged as,

$$[M.L]_{o,fi} = [M]_{a,fi} k_{d,f} \tag{5.6}$$

Substituting equation (5.6) in equation (5.4) we get,

$$J_o = \frac{1}{\Delta_o} k_{d,f} \; [M]_{a,fi} \tag{5.7}$$

Rearranging equation (5.7) we get,

$$[M]_{a,fi} = J_o \frac{\Delta_o}{k_{d,f}} \tag{5.8}$$

From equation (5.2)

$$J_a \Delta_a = [M]_{a,fb} - [M]_{a,fi} \tag{5.9}$$

From equations (5.8) and (5.9), we get,

$$[M]_{a,fi} = J_a \Delta_a + J_o \frac{\Delta_o}{k_{d,f}} \tag{5.10}$$

If the chemical reaction between ligand and the metal nitrate is assumed to be fast compared to the diffusion rate, a local equilibrium at the interface is reached. Thus, at steady state,

$$J_a = J_o = J \tag{5.11}$$

Using equation (5.11) in equation (5.10), we get,

$$[M]_{a,fi} = J\left(\Delta_a + \frac{\Delta_o}{k_{d,f}}\right) \tag{5.12}$$

Rearranging equation (5.12) we get,

$$J = \frac{k_{d,f}[M]_{a,fb}}{k_{d,f}\Delta_a + \Delta_o} \tag{5.13}$$

$$\text{or,} \qquad J = \frac{k_{d,f}[M]_{a,fb}}{k_{d,f}\left(\frac{d_a}{D_a}\right)+\left(\frac{d_o\tau}{D_o}\right)} \tag{5.14}$$

where, τ is the tortuosity factor of the membrane. Here the value of membrane thickness (d_o) can be assumed to be equal to the nominal thickness of the membrane support. Membrane permeability coefficient (P) is written as,

$$P = \frac{J}{[M]_{a,fb}} \tag{5.15}$$

Substituting equation (5.14) in equation (5.15), we get,

$$P = \frac{k_{d,f}}{k_{d,f}\left(\frac{d_a}{D_a}\right)+\left(\frac{d_o\tau}{D_o}\right)} \tag{5.16}$$

Above equation can be used for calculating P using $k_{d,f}$ and diffusion coefficient data. The membrane diffusion coefficient (D_o) can be calculated from the knowledge of permeability coefficient (P) and the distribution ratio of the metal ions ($k_{d,f}$) as per the above equation (5.16). Assuming that the rate determining step is diffusion of the bulky complex across the membrane, the first term in the denominator of equation (5.16) (which refers to the transport of hydrated metal ions across aqueous diffusion layer) can be ignored. Therefore, Eq. (5.16) can be rearranged as follows,

$$P = \frac{D_o.k_{d,f}}{\tau.d_o} \tag{5.17}$$

In the present studies, PTFE membranes of 85 μm thickness (d_o) were employed and the tortuosity factor (τ) for the membrane is reported as 2.4 [**5.30**]. Thus, from the knowledge of P

and D_M, the value of D_o of the metal-ligand complex in the membrane can be obtained. Alternatively, D_o can also be obtained experimentally by determining the P value of metal ions for varying thickness of the membrane (d_o). A plot of P vs $1/d_o$ would be a straight line and the value of D_o can be obtained from the slope of the linear fit.

Permeability is described as amount of metal ion (in terms of concentration) transported through membrane per unit area per unit time and related to membrane flux as per following equation (5.18) and (5.19).

$$J = \left(- \frac{V}{Q} \frac{d\,[M]_{a,fb}}{dt} \right) \tag{5.18}$$

$$J = P.[M]_{a,fb} \tag{5.19}$$

Rearranging above equations (5.18) and (5.19) we get,

$$\left(\frac{d\,[M]_{a,fb}}{dt} \right) = - \frac{Q}{V} P.[M]_{a,fb} \tag{5.20}$$

Integrating above equation we get,

$$\int_{C_0}^{C_t} \frac{d\,[M]_{a,fb}}{dt} = - \frac{Q}{V} \int_0^t P.[M]_{a,fb} \tag{5.21}$$

C_t and C_o are the concentration of metal ion in the aqueous feed solution at time t and initial concentration (t = 0), respectively.

$$\ln \left(\frac{[M]_t}{[M]_0} \right) = - P \left(\frac{Q}{V} \right) t \tag{5.22}$$

In general, P is obtained experimentally using above equation (5.22). Here, Q is the effective membrane area obtained from the total exposed membrane surface area A and the porosity ε (Q = A·ε), V is the volume of the feed solution in cm^3, and t is the permeation time (seconds). A plot of $\ln([M]_t / [M]_0)$ versus time allows one to calculate the P value from the slope of the linear fit. It should be noted that the above equation is valid only when the carrier is not saturated and the flux decreases linearly with time. In the present work, since all the experiments were carried out at tracer concentration of the metal ion, Eq. (5.22) was applied for the calculation of P. The cumulative % *T* at a given time was determined by the following equation (5.23).

$$\% \text{ Transport} = \frac{\left([M]_0 - [M]_t\right)}{[M]_0} \times 100 \qquad (5.23)$$

5.4. Effect of the Nature of the Diluent in Solvent Extraction Studies with T2EHDGA as Extractants

From equation (5.1), we can write,

$$Y^{3+} + 3\ NO_3^- + n\ \text{T2EHDGA}_{(o)} \rightleftharpoons Y(NO_3)_3 \cdot n\ \text{T2EHDGA}_{(o)} \qquad (5.24)$$

where, the subscript '(o)' indicates species in the organic phase and those without any subscript indicate species in the aqueous phase. It is expected that the extractability of the Y- T2EHDGA complex depend on the nature of the extracted species (stoichiometry including number of T2EHDGA and water molecules) and the polarity of the medium. It is well known that the nature of the extracted species change depending on the organic phase characteristics. While non-polar diluents like n-dodecane can favor the extraction of charge neutralized species, polar diluents like nitrobenzene stabilize charge separated or ion-pair species. Solvent extraction studies were carried out using several commonly used diluents namely 1-decanol, xylene, MIBK, chloroform, carbon tetrachloride along with T2EHDGA as extractant.

In this study, solutions of the desired concentration of T2EHDGA (0.2 M) prepared in the desired diluents were agitated with an equal volume of the aqueous phase (containing the requisite quantity of ^{90}Y and $^{85,89}Sr$ tracer) in a rotary thermostated water bath for

Table 5.1: Effect of diluents on the distribution behaviour of Sr(II) and Y(III) by T2EHDGA; Org. phase: 0.2 M T2EHDGA; Aq. phase: 6 M HNO_3

Diluent	$K_{d,Y}$	$K_{d,Sr}$	SF
MIBK (Hexone)	26	0.03	866
CCl_4	60	0.24	250
$CHCl_3$	50	0.01	5000
1-decanol	2.56	0.01	256
Xylene	29	0.05	580
n-dodecane + 30 %-*iso*-decanol	20	0.04	500

an hour at 25.0 ± 0.1°C. The two phases were then centrifuged and assayed by taking suitable aliquots from both the phases. The distribution ratios (K_d) of Sr(II) and Y(III) which is the ratio of the concentration of metal ion in the organic phase to that in the aqueous phase, were determined. As shown in Table 5.1, chloroform gave the best results with $K_{d,Y}$ and $K_{d,Sr}$ values of 50 and 0.01, respectively with a separation factor value of ~5000.Solvent extraction studies using 30% *iso*-decanol in *n*-dodecane also yielded encouraging results. The effect of diluent parameter on the separation factor $SF_{Sr/Y}$ is shown as Fig. 5.2.

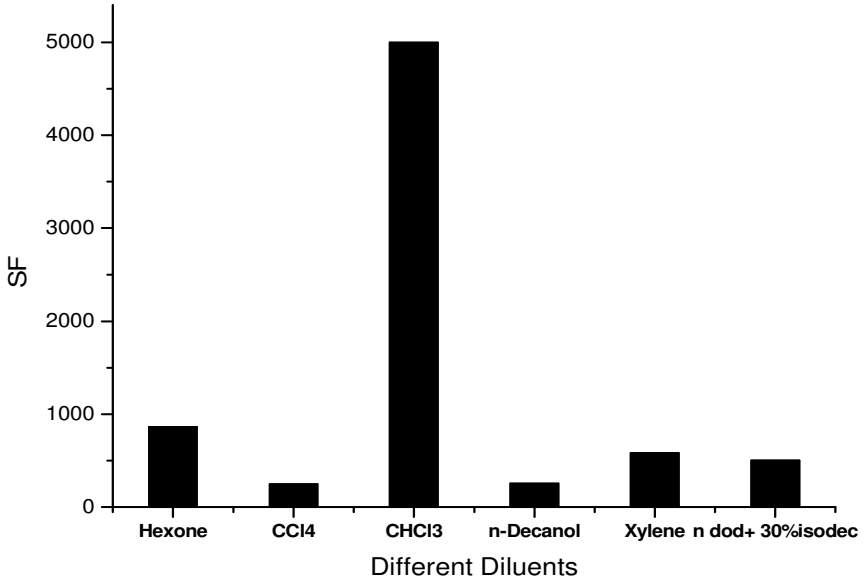


Fig. 5.2: Effect of Diluents on Separation Factor (SF = $K_{d,Y}$/ $K_{d,Sr}$); Org. phase: 0.2 M T2EHDGA; Aq. phase: 6 M HNO_3

5.5. Flat Sheet Supported Liquid Membrane Studies

5.5.1. Role of the Nature of the Diluents in SLM Studies With T2EHDGA as Extractant

The diluent property has a major role in the transport of the metal-extractant complex. The diluent polarity helps in stabilizing the extracted species in the organic phase which can lead to higher extraction and hence higher transport rates. Further, the viscosity of the diluent decides the diffusivity of the complex as per the Stokes-Einstein equation:

$$D_o = \frac{kT}{6\pi R\eta} \tag{5.25}$$

where, D_o is the membrane diffusion coefficient, R, the radius of the diffusing species and η, the dynamic viscosity of the extractant solution, k is the Boltzmann constant and T is absolute temperature.

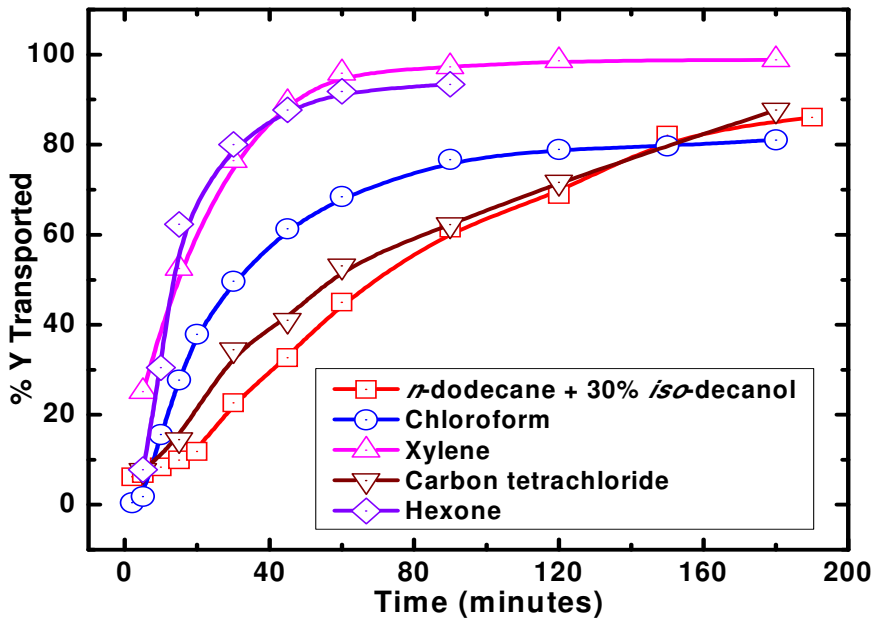


Fig. 5.3: Role of organic diluent on Y(III) transport using 0.2 M T2EHDGA. Feed: 6 M HNO_3; Receiver: 0.01 M HNO_3

Table 5.2: Correlation of physical parameters with Y(III) transport data. Extractant concentration: 0.2 M T2EHDGA. Feed: 6 M HNO_3; Receiver: 0.01 M HNO_3

Diluent system	Viscosity[a] ($mPa.s^{-1}$)	Density[a] ($g.cm^{-3}$)	Dielectric constant[b]	% Y transport (1 hr)	P x 10^3 ($cm.s^{-1}$)
Xylene	0.9043	0.8705	2.57	95.9	1.58 ± 0.08
Chloroform	0.8648	1.3876	4.81	68.5	1.84 ± 0.05
CCl_4	1.4633	1.4868	2.24	53.1	0.53 ± 0.01
Hexone	0.8198	0.8142	13.1	91.9	1.60 ± 0.02
n-dodecane + 30 % *iso*-decanol	3.5382	0.7938	3.26	45	1.09 ± 0.03

Note: [a]: The viscosity and density values are for 0.2 M solution of T2EHDGA in the diluent; [b]: The dielectric constant values are for the diluents or their mixture as indicated in the table

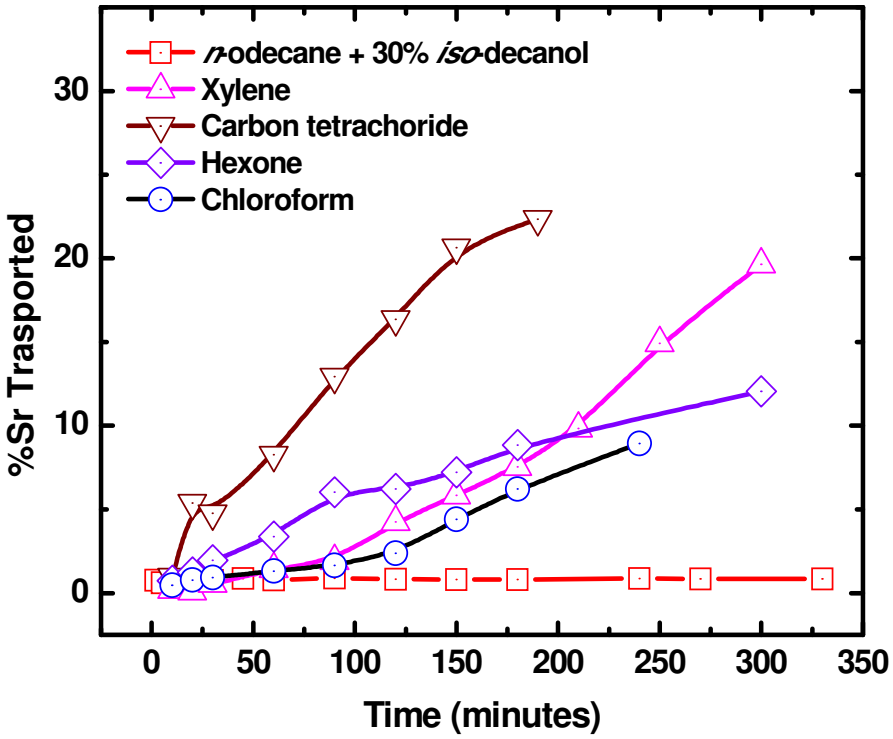


Fig. 5.4: Role of organic diluent on Sr(II) transport using 0.2 M T2EHDGA. Feed: 6 M HNO_3; Receiver: 0.01 M HNO_3

Fig. 5.3 gives the relative Y(III) transport profiles with several diluents used in the present study. With the exception of xylene, which showed highest transport rate in the five diluents used, the transport rates were mainly governed by the polarity of the diluent. The *n*-dodecane + 30 % *iso*-decanol solvent system has a dielectric constant of 3.26 (calculated using [**5.31**]) and hence was seen to yield relatively poor transport rate which was compared to that with carbon tetrachloride as the diluent. The permeability coefficient values for Y(III) transport using T2EHDGA as the carrier extractant were computed with different diluent systems and are listed in Table 5.2. The Y(III) transport trend was found to be xylene ~ hexone > chloroform > carbon tetrachloride > *n*-dodecane + 30 % *iso*-decanol. The transport rates of Sr(II) was also investigated and the results are presented in Fig. 5.4. Though the solvent extraction data indicated poor Sr(II) extraction as compared to Y (III) extraction, the transport rates of Sr(II) was surprisingly large for diluents and the trend for 6 M HNO_3 as the feed was carbon tetrachloride > hexone > xylene > chloroform >> *n*- dodecane + 30 % *iso*-decanol mixture. It was noticed, however, that the % Sr transported was negligible for *n*-dodecane + 30 % *iso*-decanol mixture while relatively lower transport was seen with chloroform and subsequent studies were carried out with these diluents and not with carbon tetrachloride, hexone and xylene which were found to be not suitable for the subsequent studies aimed at the separation of carrier free ^{90}Y from ^{90}Sr.

5.5.2. Role of Feed Acidity

The acidity of the feed has been reported to have a major influence on the transport of metal ions in analogous systems [**5.27, 5.32 - 5.34**]. Though % Y transported was higher with chloroform as the diluent as compared to the *n*-dodecane + 30 % *iso*-decanol mixture at 6 M HNO_3 up to 150 minutes, a reversal was seen subsequently. It was required to carry out transport studies at lower acidities. Results obtained with 3 M HNO_3 are presented in Fig. 5.5. Chloroform was clearly seen as the superior diluent system so far as the Y(III) transport rates were concerned. A close look at the transport profiles indicate that they are comparable up to 50 minutes while after that Y(III) transport increased significantly for chloroform as the diluents. However, it was required to see the relative transport rate at this feed condition (3 M HNO_3). The plot of $\ln(C_t/C_0)$ vs time is presented in Fig. 5.6 and indicates that the transport of Sr(II) though much lower as compared to that of Y(III) cannot be ignored and is going to decide the purity of the product.

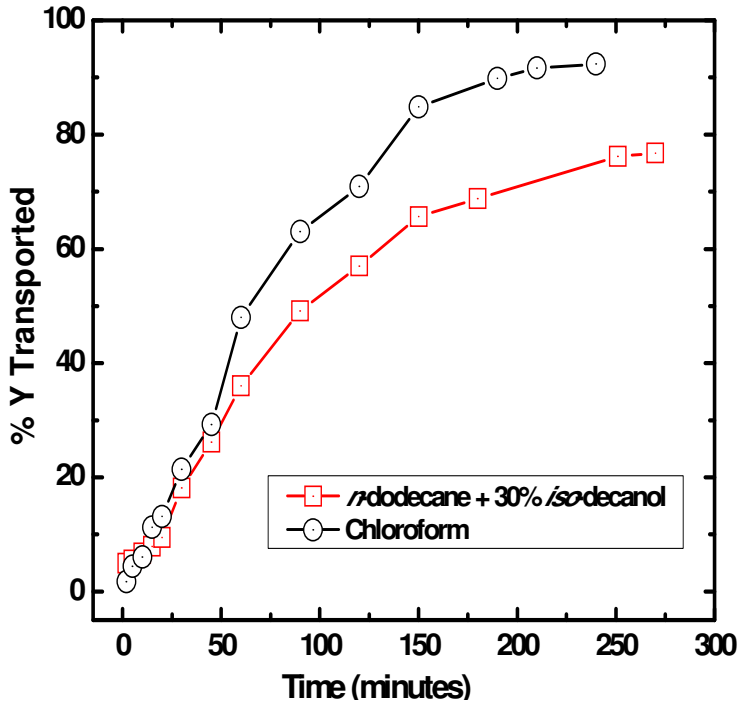


Fig. 5.5: Relative transport behaviour of Y(III) using 0.2 M T2EHDGA in $CHCl_3$ and *n*-dodecane. Feed: 3 M HNO_3; Receiver: 0.01 M HNO_3; Temp.: 24 ± 1°C

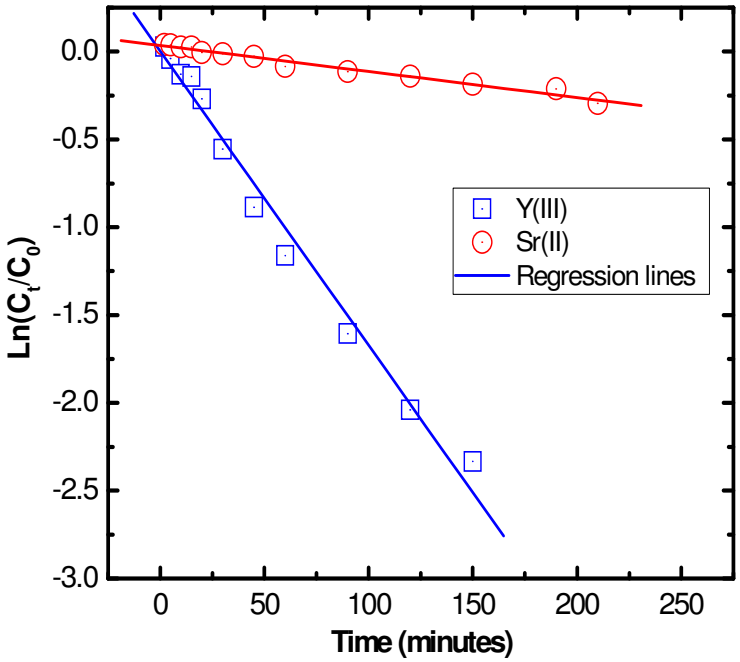


Fig. 5.6: Plot of $\ln(C_t/C_0)$ vs time for 0.2 M T2EHDGA in $CHCl_3$ and *n*-dodecane. Feed: 3 M HNO_3; Receiver: 0.01 M HNO_3; Temp.: 25 ± 1°C

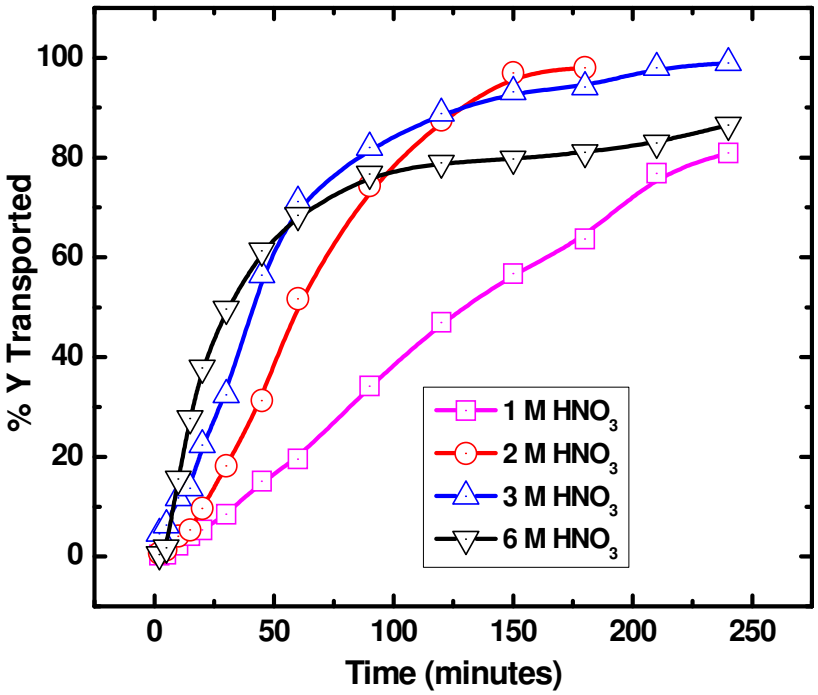


Fig. 5.7: Effect of acidity on the transport of Y(III) by T2EHDGA-SLM; Carrier: 0.2 M T2EHDGA in $CHCl_3$; Strip phase: 0.01 M HNO_3.

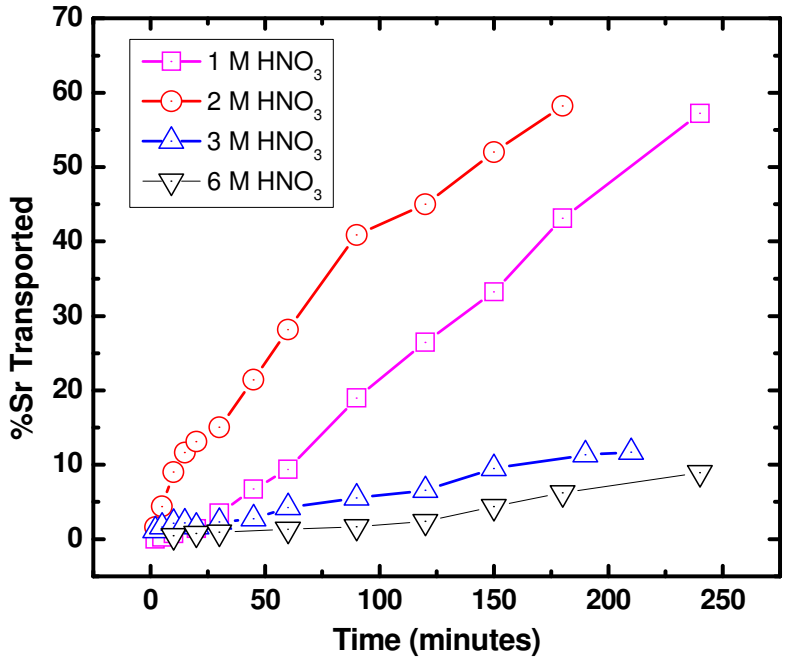


Fig. 5.8: Effect of acidity on the transport of Sr(II) by T2EHDGA-SLM; Carrier: 0.2 M T2EHDGA in $CHCl_3$; Strip phase: 0.01 M HNO_3

Fig. 5.7 shows the effect of feed acidity, in the range of 1- 6 M HNO_3, on the transport of Y using 0.2 M T2EHDGA in chloroform as the carrier solvent. It was found that the transport rate of Y(III) increased with feed acidity from 1 M HNO_3 to 2 M HNO_3 and beyond which a decrease was observed. However, the trend was found to change with transport time. For example, after 30 minutes the trend was 6 M > 3 M > 2 M > 1 M which changes after 2 hrs to 3 M > 2 M > 6 M > 1 M which further changed after 3 hrs to 2 M > 3 M > 6 M > 1 M. After 3 hrs, the Y transport was 65 %, > 99.99 %, 95 % and 80 % at 1 M, 2 M, 3 M and 6 M HNO_3, respectively. At the same time, the transport of Sr was 43 %, 58 %, 10 % and 6 %, respectively (Fig. 5.8). This observation is quite interesting as increasing acid concentration usually enhances the metal ion transport [**5.27, 5.32-5.34**]. The possible reason could be due to 18-crown-6 type cavity formation by two T2EHDGA molecules with 6 'O' donor atoms which is stabilized at lower acidity [**5.35**]. It is proposed that due to possible reverse micelle formation similar to that in case of TODGA destabilizes the 18-crown-6 type dimeric structure leading to lower Sr(II) transport at higher acidities. The separation factor (SF, defined as the concentration of Y(III) over concentration of Sr(II) in the strip solution which was taken from the % transport data) was found to increase with increased feed acidity from 2.09 (at 1 M HNO_3) to 51.9 (at 6 M HNO_3) after 1 hour of transport (Table 5.3). Similar observations have been reported in a solvent extraction study using TODGA as the extractant [**5.36**]. The separation factor values decreased further with time suggesting that Sr contamination in the product would increase making it unsuitable for pharmaceutical applications.

Table 5.3: Transport parameters as a function of the nitric acid concentration in the feed; Support: 0.45 micron PTFE; Extractant: 0.2 M T2EHDGA in chloroform; Receiver: 0.01 M HNO_3

$[HNO_3]$, M	% Transport (1 hr)		Permeability coefficient (cm/s)		S.F. ($\%T_Y/\%T_{Sr}$)
	Y(III)	Sr(II)	Y(III)	Sr(II)	
1.0	19.6	9.36	$(0.53 \pm 0.02) \times 10^{-3}$	$(3.63 \pm 0.21) \times 10^{-4}$	2.09
2.0	51.7	28.2	$(1.79 \pm 0.06) \times 10^{-3}$	$(7.62 \pm 0.35) \times 10^{-4}$	1.83
3.0	71.3	4.26	$(1.87 \pm 0.07) \times 10^{-3}$	$(1.57 \pm 0.07) \times 10^{-4}$	16.7
6.0	68.5	1.32	$(1.84 \pm 0.05) \times 10^{-3}$	$(0.64 \pm 0.08) \times 10^{-4}$	51.9

Table 5.4: Comparative acid transport data with 0.2 M T2EHDGA in chloroform / *n*-dodecane + 30% *iso*-decanol as the carrier solvent systems; Feed: 3 M HNO_3; Receiver: 0.01 M HNO_3

Time (minutes)	% Acid transport in the following solvent systems	
	0.2 M T2EHDGA in *n*-dodecane + 30% *iso*-decanol	0.2 M T2EHDGA in chloroform
10	0.38	0.44
20	0.49	0.57
30	0.56	0.62
60	1.03	1.11
120	1.85	1.59
300	4.09	2.83

The low SF values are due to saturation in Y transport data (at lower acidities) and increase in Sr transport data with time. Relative acid transport data is presented in Table 5.4 which suggested that relatively lower acid transport rate was seen with *n*-dodecane + 30 % *iso*-decanol diluent mixture as compared to chloroform as the diluent.

5.5.3. Separation of ^{90}Y from ^{90}Sr Using T2EHDGA as Extractant

Keeping these observations in mind, viz. Y(III) transport rates, Sr(II) transport rates and acid transport rates two separate experiments were carried out using a mixture of ^{90}Y + ^{90}Sr in the feed, and the product was monitored for ^{90}Y purity by the half life method.

The radioactive decay equation is given by:

$$N_t = N_0 e^{-\lambda t} \qquad (5.26)$$

where, N_0 and N_t are the initial activity and the activity at a time 't' and λ is the decay constant. Therefore, from semi-log plot of ln N(t) vs time, the half-life of the radioisotope can be calculated. One set of experiment involved 0.2 M T2EHDGA in *n*-dodecane + *iso*-decanol as the carrier solvent and ^{90}Y + ^{90}Sr in 6 M HNO_3 as the feed while the second experiment involved

0.2 M T2EHDGA in chloroform as the carrier solvent and ^{90}Y + ^{90}Sr in 3 M HNO_3 as the feed. The product in the receiver phase was assayed after 0.5, 1.0 and 2.0 h and the half-lives were measured from the semi-log plots as mentioned before (*vide supra*) and the data are presented in Table 5. Apparently, ^{90}Sr in the product increases with time when chloroform was used as the diluent. As the half-life of ^{90}Y is 64.1 hrs, higher half-life of the product obtained in the receiver phase was indicative of contamination due to the presence of traces of ^{90}Sr. It is interesting to note that the half-life of the product decreases with transport time for the system with *n*-dodecane + *iso* decanol as the diluent while an opposite trend was seen for the chloroform system. The samples were kept aside for 100 days to enable the ^{90}Y to decay completely and were counted for the residual ^{90}Sr (and ^{90}Y generated out of it as its daughter product).

Decontamination factor (DF) values in the range of 98 to 120 were obtained with the products obtained in the present study (all the three fractions from the *n*-dodecane + *iso*-decanol system and the first fraction from the chloroform system as shown in Table 5.5) indicating that the products obtained by both the systems may not be suitable for radiopharmaceutical use (recommended DF: 10^6) and purification using other method is recommended as discussed in Chapter III. We have reported product with better purity using solvent extraction using TODGA

Table 5.5: Purity test data of the samples taken from the receiver phase as checked by the half-life method

Carrier solvent	Assaying time[c]	Half-life (h)	Remarks
0.2 M T2EHDGA in *n*-dodecane + *iso*decanol[a]	0.5 h	67.7	DF = 98.2 (Reasonably pure[d])
	1.0 h	67.3	DF = 114 (Reasonably pure[d])
	2.0 h	67.0	DF = 120 (Reasonably pure[d])
0.2 M T2EHDGA in Chloroform[b]	0.5 h	67.5	DF = 103 (Reasonably pure[d])
	1.0 h	73.2	Contaminated[d]

Note: [a]: Feed: 6 M HNO_3; [b]: Feed: 3 M HNO_3; [c]: 100 µL samples taken from the receiver phase; [d]: Contaminated with small traces of ^{90}Sr

in Chapter III and extraction chromatographic separation methods with DF values in the range of 10^3 - 10^4 as discussed in Chapter IV. The poor decontamination of the product in the present case is attributed to the co-transport of Sr(II). However, coupling to another separation method may result in the product with the required purity.

5.6. Effect of the Nature of the Diluents in Solvent Extraction Studies with TODGA as Extractants

In the previous section (Section 5.4), we have seen the effect of the nature of diluents on the solvent extraction and supported liquid transport of Y(III) and Sr(II) with T2EHDGA as the extractant. Similar studies were carried out with TODGA as extractant. In this study, solutions of desired concentration of TODGA (0.1 M) were prepared in several diluents viz. 1-decanol, xylene, MIBK, chloroform and carbon tetrachloride, and solvent extraction experiments were carried out in the same manner as described in the previous section. Distribution ratio values of ^{90}Y and $^{85\text{-}89}Sr$ were measured using 0.1 M TODGA in different diluents as organic phase at three different feed conditions viz., 6 M and 3 M $HNO_3$and 6 M HCl. The D_Y and D_{Sr} values are listed in Table 5.6 - 5.8 along with the separation factors (SF). Comparing the data given in Table 5.6 and Table 5.7, it can be stated that in the case 6 M HNO_3, with the exception of xylene, for all other diluents the SF values are 10-1000 fold higher as compared to 3 M HNO_3. Hence the Supported Liquid Membrane (SLM) studies were carried out with 0.1M TODGA as carrier ligand in the above mentioned diluents (except xylene), 6 M HNO_3 as feed phase spiked with ^{90}Y

Table 5.6.Variation of diluents on the solvent extraction of ^{90}Y and $^{85\text{-}89}Sr$ with 0.1M TODGA as extractant from 3M HNO_3

Diluents	$K_{d,Y}$	$K_{d,Sr}$	SF
Xylene	181	0.08	$2.26x10^3$
$CHCl_3$	178	0.003	$5.9x10^5$
CCl_4	229	0.104	$2.2x10^3$
MIBK (Hexone)	161	0.031	$5.3x10^3$
n-Decanol	89	0.02	$4.4x10^3$

Table 5.7: Variation of Diluents on the solvent extraction of ^{90}Y and $^{85-89}Sr$ with 0.1 M TODGA as extractant from 6 M HNO_3

Diluents	$K_{d,Y}$	$K_{d,Sr}$	SF
Xylene	44.8	0.006	7.4×10^3
$CHCl_3$	2188	0.0004	5.4×10^6
CCl_4	6319.2	0.025	2.5×10^5
MIBK(Hexone)	101.3	0.0005	2.0×10^5
n-Decanol	35.5	0.0005	7.1×10^4

Table 5.8: Variation of Diluents on the solvent extraction of ^{90}Y and $^{85-89}Sr$ with 0.1 M TODGA as extractant from 6M HCl

Diluents	$K_{d,Y}$	$K_{d,Sr}$	SF
Xylene	67.3	0.0013	51546
$CHCl_3$	2.62	0.0014	1907
CCl_4	49.4	0.0019	26013
MIBK(Hexone)	4.6	0.0158	291
n-Decanol	229	0.0146	15667

Table 5.9: Transport behavior of ^{90}Y in SLM studies with 0.1 M TODGA in different diluents; Feed: 6 M HNO_3 and strip: pH 2

Time (min)	$\%Y_{CCl4}$ Feed	$\%Y_{CCl4}$ Strip	$\%Y_{CHCl3}$ Feed	$\%Y_{CHCl3}$ Strip	$\%Y_{Hexone}$ Feed	$\%Y_{Hexone}$ Strip	%Y 1-decanol Feed	%Y 1-decanol Strip
0	100	0	100	0	100	0	100	0
15	42.26	18.36	56.13	3.43	53.34	0.49	84.02	1.04
30	22.71	27.94	36.48	4.66	33.12	0.52	70.71	2.12
45	14.07	41.84	24.22	6.86	19.03	0.60	57.49	3.15
60	12.04	58.18	15.35	7.77	4.94	0.50	54.98	4.55
90	11.43	59.28	5.49	10.12	2.23	0.42	48.65	5.29
120	9.15	61.52	1.28	11.05	2.15	0.48	43.16	6.54

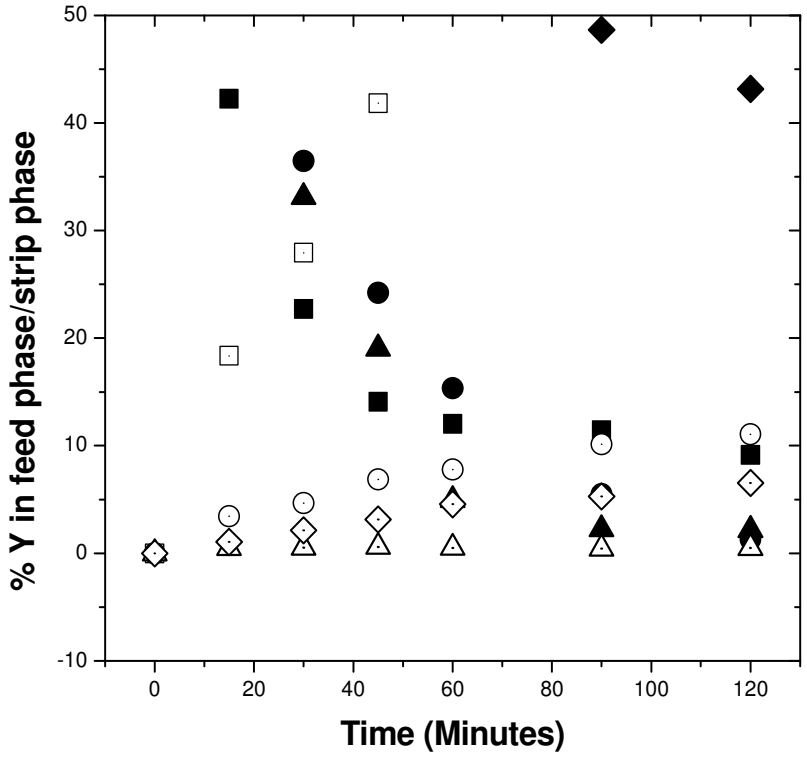


Fig. 5.9: Transport profiles of Y(III) from 6 M HNO_3 feed solutions. Receiver: 0.01 M HNO_3. Carrier: 0.1 M TODGA. Square: CCl_4; Circle: $CHCl_3$; Triangle: Hexone; Diamond: 1-decanol. Closed symbol: As observed in feed phase; Open symbol: As observed in receiver phase.

radiotracer and nitric acid of pH 2 as the strip phase. The results are given in Table 5.9 and the graphical presentation is shown in Fig. 5.9. Except in the case of CCl_4, where ~61%Y(III) transport was observed in 120 minutes, in all the other cases, even though the feed activity was decreasing with time, the strip was not increasing proportionately. The possible reason for such anomalous behavior could attributed to inefficient stripping, slow diffusion of the Y-TODGA complex or both.

From the experiments on the solvent extraction of ^{90}Y and $^{85\text{-}89}Sr$ with 0.1 M TODGA as extractant from 6 M HCl using different diluents (Table 5.8), xylene was found to be most efficient diluent (SF = 5.15 x 10^4) and hence further separation studies were carried out using xylene as the diluent.

Table 5.10: Impurity analysis of ^{90}Y product obtained by solvent extraction; Feed: 6 M HCl. Organic phase: 0.1 M TODGA in xylene.

Source of Product	Half life (hrs)	Source of Product	Half life (h)	Remarks
Strip 1	64.17	Strip 4	64.47	Reasonably pure
Strip 2	64.35	Strip 5	64.42	Reasonably pure
Strip 3	64.41	Extract 1	66.89	Contaminated with ^{90}Sr

Based on this, a separation method was developed for the recovery of pure ^{90}Y from a mixture of ^{90}Y + ^{90}Sr. The method involved preferential extraction of ^{90}Y by 0.1 M TODGA in xylene from 6 M HCl followed by its stripping using 0.01 M HCl. The purity of the product was ascertained from its half-life measurements. Several products samples of ^{90}Y such as: i) after extraction from 6 M HCl, ii) after extraction from 6 M HCl followed by stripping with distilled water and iii) after several cycles consisting of the extraction and stripping steps were obtained. The half-lives of the products from the strip fractions were calculated from the slope of the semi-log plot and were found to be in the range 64.17 hrs to 64.47 hrs suggesting reasonably high purity of the product (Table 5.10). On the other hand, the ^{90}Y containing extract resulted in much higher half-life suggesting partial ^{90}Sr contamination.

Based on the promising solvent extraction result, the SLM studies were carried out with 0.1 M TODGA / xylene using a microporous PTFE membrane as a polymeric support. The transport of Sr and Y by TODGA-SLM for a feed phase containing 6 M HCl and receiver phase containing 0.01 M HCl suggested >99% transport of ^{90}Y in 2 h while ^{85,89}Sr transport was almost negligible. The results of the transport experiments indicated the feasibility of the separation of ^{90}Y from ^{90}Sr using a simple transport cell (Fig.5.10).

^{90}Y samples were removed from the receiver phase after different time intervals (after 40, 60 and 120 minutes) from an SLM experiment carried out using ^{90}Sr and ^{90}Y mixture and the purity of the product was ascertained as a function of time by the half-life method as indicated above under the solvent extraction studies. The half lives were found to be in the range of 64 hrs to 70 h rs(Fig. 5.11) suggesting that the product was contaminated small quantity of ^{90}Sr with increasing sampling time (from receiver phase). This is due to permeation of increasing quantity

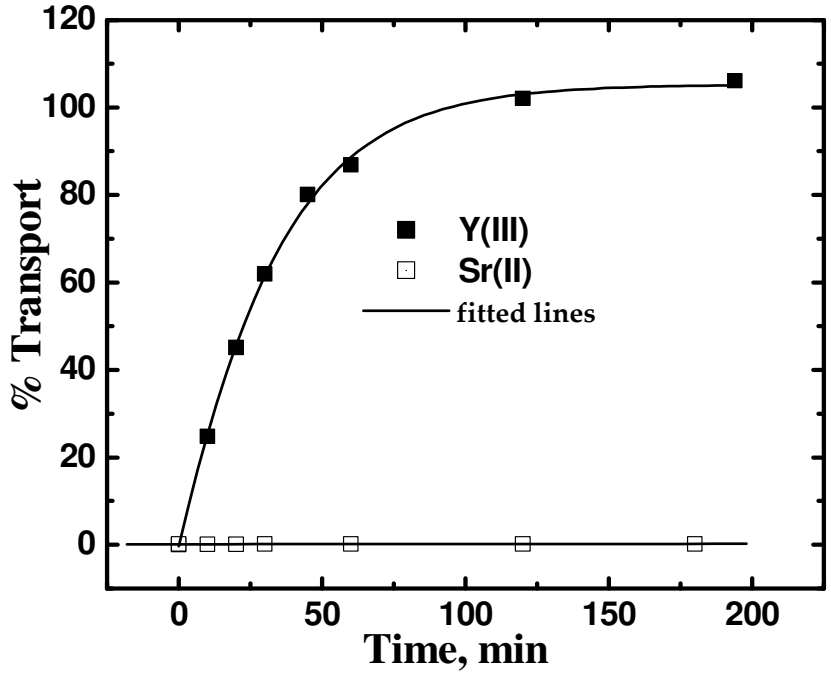


Fig. 5.10: Transport of Y(III) and Sr(II) through SLM, carrier ligand: 0.1 M TODGA xylene, feed solution: 6 M HCl, receiver solution:0.01 M HCl support: PTFE, dip time: 30 min.

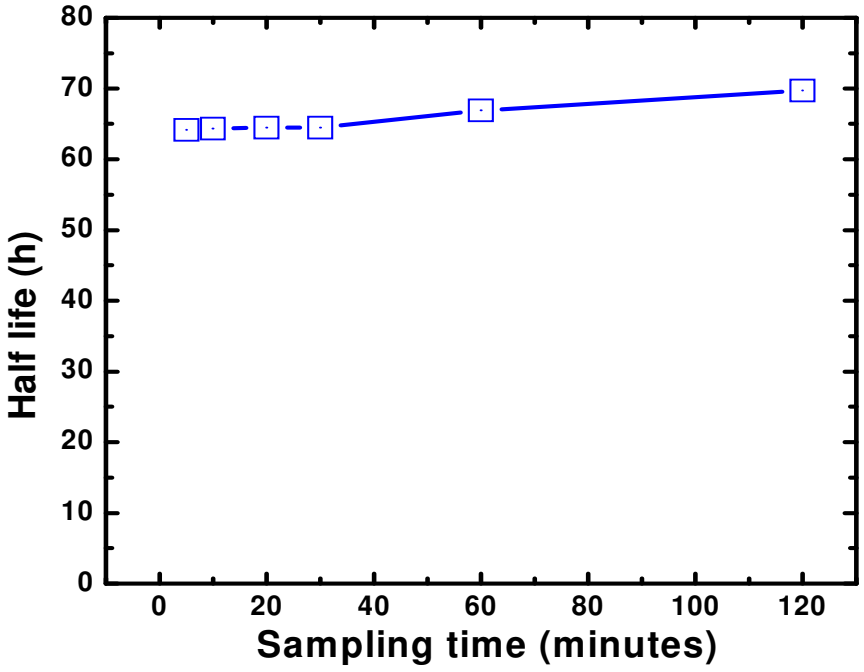


Fig. 5.11: ^{90}Y half life variation in SLM studies as a function of the sampling time.

of ^{90}Sr from the feed side to the receiver side. The product can be purified by passing through a crown ether column as mentioned in previous report [**5.37**].

5.7. Conclusions

Solvent extraction studies suggested chloroform as the most suitable diluent of those used in the present study as a large separation factor value of 5000 was obtained. On the other hand, the transport studies indicated relatively high Y(III) transport rates with xylene and hexone which also facilitated significant Sr(II) transport making these diluents unusable from separation point of view. The studies on the effect of feed acidity though indicated increased Y transport with increasing feed acidity, an entirely opposite trend was observed with respect to Sr(II) transport suggesting 3 M HNO_3 should be the optimum feed to be used for the separation studies. The present studies suggested that T2EHDGA-SLM though do not appear promising, may be used for the separation of Sr and Y only at lower transport times. The product gets contaminated with ^{90}Sr as time increases. Similarly solvent extraction studies on extraction of yttrium and strontium employing carrier extractant TODGA in different diluents from two mineral acids namely nitric acid and hydrochloric acid suggested xylene to be promising diluents in case of 6 M HCl as aqueous phase having separation factor ($SF^{Y/Sr}$ ~ 50,000). The SLM studies using TODGA in xylene in separation Sr-Y suggested solvent extraction method was more promising as compared to the supported liquid membrane based separation method. The product obtained from the SLM method can be purified further by passing through a crown ether column for possible applications.

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Chapter VI

SUMMARY AND CONCLUSIONS

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Radiopharmaceuticals based on ^{90}Y are widely used for radio labeling various targeting molecules for the treatment of cancer as well as in radiation synoviorthesis. The broad interest for use of ^{90}Y in therapeutic nuclear medicine is due to its suitable nuclear characteristics ($t_{1/2}$ = 64.1 h, β - max 2.28 MeV, no gamma emission) and favorable complex chemistry. The availability of ^{90}Y with very low levels of ^{90}Sr contamination (with SF $> 10^6$) is essential for its therapeutic applications, since ^{90}Sr localizes in the skeleton and owing to its long half-life (28.5 years), has very low maximum permissible body burden of 74 kBq. Nowadays, radioisotopes used for nuclear medicine are produced either in cyclotrons or nuclear reactors. ^{90}Y produced by neutron activation of natural ^{89}Y in a nuclear reactor provides activity at low level; however, ^{90}Y of very high specific activity is required for the preparation of labeled antibodies. This can be achieved by separating ^{90}Y from ^{90}Sr-^{90}Y mixture (always present in secular equilibrium) produced in nuclear fission. Once, ^{90}Y of high activity is available, a radionuclide generator is designed to supply in suitable form to the hospital radio pharmacies. The availability of short-lived radioisotopes from radionuclide generators is an inexpensive and convenient alternative to 'in-house' radioisotope production facilities like reactors or cyclotrons. To fulfill the increasing demand of ^{90}Y for radiopharmaceutical applications, a variety of methods like liquid-liquid extraction, chromatographic separations, liquid membrane, etc were developed to design ^{90}Y radionuclide generator. However, there is always scope for further development in this regard for obtaining a neat, clean, efficient, and cheaper method with easy setups and inexpensive ligands which can yield ultrapure ^{90}Y as per radiopharmaceutical requirement.

In present work, we have evaluated liquid-liquid extraction, chromatographic separations and supported liquid membrane methods for obtaining radiopharmaceutical grade ^{90}Y from ^{90}Sr-^{90}Y mixture using two substituted diglycolamides as the extractants. These separations were purely on the basis of the divalent and trivalent nature of Sr and Y, respectively which influence their complexation behaviour. The property of preferential extraction of trivalent ions such as Y(III) over divalent ions such as Sr(II) by two diglycolamides viz.; N,N,N'N'-tetraoctyl diglycolamide (TODGA) and tetra-2-ethylhexyl diglycolamides (T2EHDGA) was successfully utilized for this purpose. Purity of product obtained was determined by half life measurements. The highlights of works are summarized as follows;

I. Extraction behaviour of Sr(II) and Y(III) was investigated using two diglycolamides viz., N,N,N′,N′-tetraoctyl Diglycolamide (TODGA) and tetra-2-ethylhexyl diglycolamides (T2EHDGA). The stoichiometry of the extracted species of Y(III) from HNO_3 and HCl medium conformed to $Y(NO_3)_3.$ 3L and $YCl_3.$ 3L (where L = TODGA or T2EHDGA). The conditional extraction constants (log K_{ex}) for Y(III) with both the extractants from HNO_3 and HCl medium were found to be; Y^{3+} -TODGA - HNO_3 = 6.05, Y^{3+} -TODGA – HCl = 4.52, Y^{3+} - T2EHDGA - HNO_3 =2.28 and Y^{3+} - T2EHDGA – HCl = 1.34. The extraction of Y(III) by both TODGA as well as T2EHDGA was found to be exothermic in nature. Based on the solvent extraction studies, two solvent extraction based methods were developed with an aim to recovery radiopharmaceutical grade ^{90}Y from a mixture of ^{90}Y-^{90}Sr using TODGA and T2EHDGA as extractants. In case of TODGA as the extractant, relatively pure form of ^{90}Y as ascertained by half life (64.1 ± 0.2 hrs of the product) was obtained after three repeated extraction and stripping cycle from 6 M HCl medium followed by stripping with distilled water. It was observed that S.F. values are about 100 and 2 times lower for T2EHDGA in 6 M HCl and 6 M HNO_3 medium, respectively as compared to the corresponding values reported for TODGA. The products obtained with T2EHDGA as the extractant after similar three cycles of extraction followed by stripping are found to be of slightly lesser purity (half life = 66.6 ± 0.1 hrs in case of 6 M HNO_3 as the feed phase and of acceptable purity in case of HCl.

II. Chromatographic resin (using Chromosorb-W resin as the support material) containing TODGA as extractant was used for the separation of ^{90}Y from a mixture of ^{90}Y-^{90}Sr. Extraction kinetics in batch method was found to be fast and require only 5 minutes to attain the equilibrium both in case of HNO_3 and HCl as feed phases. The batch sorption data from nitric acid and hydrochloric acid media revealed higher extraction affinity towards Y(III) in HCl medium than HNO_3 over entire range of acidity. In batch studies, it was observed that SF(Y(III)/Sr(II)) increased with acidity for both HNO_3 and HCl as feed solutions and showed maxima at 3 M acid concentration. Distribution ratio ($K_{d,w}$) of Sr(II) in both HNO_3 and HCl medium was found to be very low (1.04 to 0.4 for HNO_3 and 1.1 to 5.4 for HCl) in the entire acidity range of 0.01 M to 6 M. From temperature variation studies carried out at 3 M HNO_3 and 3 M HCl, it can be concluded that the

extraction process is exothermic in nature. Column capacity was reported as 0.65 ± 0.01 meq of Y(III) per gram of the resin. Compared to 0.01 M HNO_3 solution, 0.01 M EDTA solution was found to effective eluant with respect to chromatographic separation of Y(III) from Sr (II). Based on this observation, a chromatographic separation scheme was developed using HNO_3 and EDTA as the eluants and with EDTA as eluent, relatively pure form of ^{90}Y was obtained in the first 10 bed volumes as evident from the measured half life values (64.0 – 64.5 hrs). In terms of reusability, it was found that the column stability was poor and rapid detoriation of column performance was observed with just second consecutive run carried out on same column. Radiation stability of resin showed that the loading of Y(III) was half at 50 MRad irradiation dose as compared to unirradiated one. Overall performance of resin was satisfactory, but needs to be improved.

III. Supported liquid membrane (SLM) studies which requires low ligand inventory, were carried out to separate ^{90}Y from ^{90}Y-^{90}Sr mixture using 0.1 M TODGA and 0.2 M T2EHDGA as as carrier ligands. Based on the effects of a number of diluents on the solvent extraction of ^{90}Y and $^{85\text{-}89}Sr$ with 0.1 M TODGA as extractant from 3M HNO_3, 6 M HNO_3 and 6 M HCl and also based on acidity variation studies, a SLM based separation scheme using 0.1 M TODGA / xylene loaded on microporous PTFE membrane as a polymeric support from 6 M HCl as feed phase and 0.01 M HCl as the strip phase was developed and the strip side was found to yield reasonably pure ^{90}Y (as evident from half life values) up to 20 minutes of transport and thereafter it became contaminated with ^{90}Sr.

Similar parameter optimization (as mentioned in case of TODGA) in solvent extraction studies was carried out using 0.2 M T2EHDGA. Liquid-liquid extraction studies revealed $CHCl_3$ as an effective diluent towards the extraction of Y(III) and Sr(II) from 3 M HNO_3 with separation factor as of 5000 which resulted higher permeability coefficient values in SLM studies.

With other diluents, the transport studies indicated relatively high Y(III) transport rates with xylene and hexone which also facilitated significant Sr(II) transport making these diluents unsuitable from separation point of view. In the strip phase, the transport of

Y(III) as well as of Sr(II) was monitored. The product was found to be increasingly contaminated with Sr(II) with time which was more prominent at lower acidities. The possible reason could be due to 18-crown-6 type cavity formation by two T2EHDGA molecules with 6 'O' donor atoms which was stabilized at lower acidity. Based on the optimization study, a separation scheme using 0.2 M T2EHDGA / $CHCl_3$ loaded on microporous PTFE membrane as a polymeric support from 3 M HNO_3 as feed phase and 0.01 M HNO_3 as strip was developed and the strip phase was found to be reasonably pure ^{90}Y.

Though the results from these separation studies suggested relatively pure form of ^{90}Y can be obtained from ^{90}Sr, the modest DF values indicated that they cannot be used for radiopharmaceutical application as such. However, coupling to another separation method can result in obtaining the product radionuclide in the required purity. Similar two consecutive separation methods have been developed by researchers including Dhami et al. [**1.52**] and Horwitz et al [**4.20**].

The present study, however, suggests that the diglycolamide based extractants can be used as potential separation agents for ^{90}Y from ^{90}Sr. Further, diglycolamide based extractants are CHON type and can be easily recycled without the generation of hazardous non-incinerable wastes as obtained with CMPO or PC-88A.

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