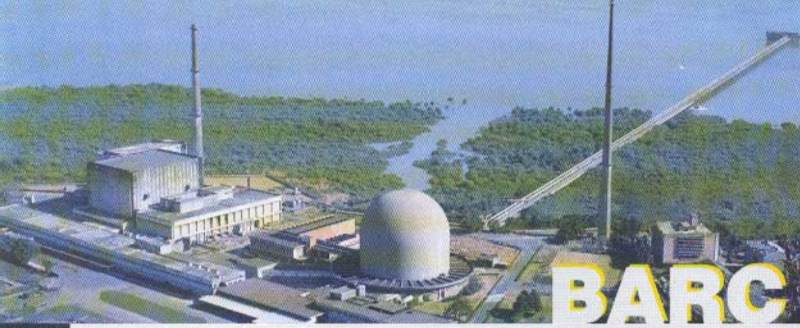

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# $^{166}$Ho-HA : A NEW RADIOPHARMACEUTICAL FOR TREATMENT OF ARTHRITIS

P.R. Unni, S. Chakraborty, Meera Venkatesh, N. Ramamoorthy and M.R.A. Pillai
Radiopharmaceuticals Division, BARC

S.V. Solav,
Ruby Hall Clinic, Pune

and

P.R. Chaudhary
Radiation Medicine Centre, BARC

## Introduction

Application of radioisotopes in the form of radiopharmaceuticals for the efficient diagnosis and management of some malignancies is well established and routinely practised. As an offshoot from its main stream applications, it is possible to develop radiopharmaceuticals for better management of some of the pathological disorders and one such instance is the management of arthritis and arthritis related problems. It is estimated that about 1% of the global adult population suffer from one or the other type of arthritis affecting some of the 264 synovial joints present in the human system. The total expenditure for providing medical treatment and rehabilitation of these patients could be exorbitantly high in addition to the productivity loss and social inequality.

## Management of Arthritis

### *Diagnosis*

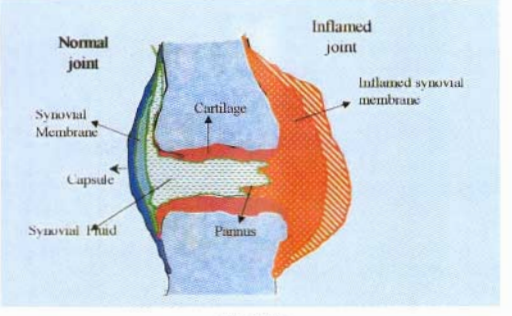
Conventional techniques for diagnosis of synovitis include physical examination along with collection of patient's history. Laboratory and serology tests such as erythrocyte

Contents

## ARTHRITIS

Inflammation of the joints manifesting into reduced joint mobility and associated pain are the main external symptoms of arthritis. Complete destruction and deformation of the joint structure takes place over a period of time resulting in loss of function of the joint. More than 50% of the arthritis patients get their knees involved and are immobilised to different degrees depending upon the severity of the disease. Other susceptible joints include fingers, shoulder, ankles, wrist and hip. A timely diagnosis and proper treatment can reduce the difficulties due to arthritis to a great extent.

Arthritis (or synovitis) is an immunological disorder affecting the joints in the body and the exact cause of the disease is not fully understood. Persistent immunological activity with T lymphocytes and macrophages is seen besides neovascularisation and tissue hypertrophy of the diseased joint region. Synovial membrane of the joint is involved in the disease. Synovial membrane is the tissue that lines the non cartilaginous surfaces of a synovial joint and is composed of a synoviocyte layer (intima) and an underlying subsynoviocyte layer which is a loose connective tissue. The synoviocyte layer in a healthy joint is normally 1-3 cell layer thick. The principle type of cells constituting these layers are Type A (macrophages like cells that expresses CD 68) and Type B cells (fibroblast like cells that expresses uridine diphosphodehydrogenase). Synoviocytes reside in a matrix rich in collagen fibrils and proteoglycans. Subsynoviocyte layer is a rich vascular tissue with a number of small arteries, arterioles, capillaries, venules and lymphatic channels with periarterial nerve fibres. These vascular tissues allow the diffusion of nutrients to the cartilage from the circulating plasma. The cartilage covering the two bone surfaces are made of type II collagen and aggregates of proteoglycans are entrapped within the collagen fibrils. A synovial joint will have at least two bones involved with their meeting surfaces coated with a thin layer of hyleine cartilage. The whole structure is encapsulated in a bag like membraneous tissue called synovial membrane that lines the non-cartilaginous surfaces of the joint. This sack-like structure is filled with synovial fluid secreted by the synovial cells and this helps in the smooth functioning of the joint. This synovial membrane containing the bones, cartilage and the fluid together is referred to as synovial cavity.




## SYNOVITIS

The onset of synovial inflammation depends upon a number of active mediators present such as acid metabolites, reactive oxygen species, proteases and cytokines derived from the circulating plasma and migrating inflammatory cells from the infected joint cells. It is the presence of these mediators that stimulates the proliferation of synovial cells which eventually leads to cartilage erosion and joint destruction. In the case of genetically predisposed persons, the initiation may be through an endogenous or exogenous antigen present in the body. The corresponding antibodies will be produced by the natural defense mechanism of the body and this leads to the formation of an immune complex. The immune complex gets phagocytosised by the polymorphonuclear cells and the macrophage cells present in the synovium resulting in the release of active mediators such as lysosomal enzymes and reactive oxygen species which, in turn, attack the cartilage. These mediators cause synovial tissue oedema and pain. The synovial membrane becomes hyperplastic in nature and starts thickening with the excessive proliferation of synoviocytes. An inflamed synovium could be 1-7 mm thick and the primary zone of attack is the cartilage. The protruding-tongue like synovial structure is called pannus, which causes marginal erosion of the cartilage via the secretions of metalloproteinases. Fig.1 shows the appearance of a normal joint as well as the pathological changes seen in an inflamed synovium.

sedimentation rates, arterioscentesis and determination of rheumatoid arthritis (RA) factor could be carried out. Radiological examinations using X-rays give some information about the disease. However, none of the above mentioned methods conclusively tell about the progression of the disease. Other options such as CT and MRI scan will yield comprehensive information, but these diagnostic procedures are too expensive to be used routinely. Specialized biochemical techniques can also be used for the diagnosis of certain type of arthritis. For example, systemic lupus erythamatosis type disease needs additional tests for the presence of auto antibodies such as anti-nuclear antibody (ANA), anti-double strand DNA (Antids DNA), anti-smith anti-body (Anti-sm), etc. In the case of ankylosing spondylitis, presence of histocompatability leucocyte antigen B 27 (HLA B 27) provides additional information.

### *Radionuclide imaging*

Radionuclide imaging of the affected joint can also yield information with respect to the extent of damage caused to the cartilage and bone by the intruding synovium. Imaging of the inflamed synovial joints using radionuclides involve the use of both non-specific and specific radiopharmaceuticals. Non-specific radiopharmaceuticals are bone seeking agents such as $^{99m}$Tc-MDP (methylene diphosphonate) which provide quantitative information about bone metabolism and inflammation. However, these methods cannot give information about the damage /inflammation due to arthritis separately. Earlier studies used $^{99m}$Tc-leucocytes and human immunoglobulins labelled with $^{99m}$Tc besides $^{99m}$Tc-MDP. Since inflammatory area has got immunoglobulin receptor centres, $^{99m}$Tc-HIG could yield some information. Site specific radiopharmaceuticals for imaging of the inflamed tissues include $^{99m}$Tc labelled CD4 specific antibody and $^{99m}$Tc labelled monoclonal antibodies. Documentation of synovial inflammation is mandatory before contemplating radiation synovectomy.

## Treatment of Arthritis

Rheumatism is a systemic disease and is to be treated systemically. Different modes of treatment are available which include systemic therapy trying to slow down the inflammatory process. Traditional first level agents are gold salts, chloroquine, sulfasazopyridine, d-pencillamine, cyclosporine, luflonoamide, etc. Disease modifying anti-rheumatic drugs (DMARD) which act either by immunosuppression, immunostimulation or immuno-modulation can be used. Immunosuppressive drugs include methotrexate, azathioprine, cyclo-phosphamide, chlorambucil and corticosteroids. Non-steroidal anti-inflammatory drugs (NSAID) such as naproxin, ibuprofen, etc. are also used for treatment of arthritis. Locoregional treatment of the affected joints such as intra-articular corticosteroid injection, chemical synovectomy, surgical synovectomy are also applied after proper evaluation of risk and patient benefit. The current line of treatment of arthritis involves any one or combinations of the above modes of therapy. These are aimed at providing pain relief and improved joint mobility. But none of these arrest the progression of the disease. The treatment practised are economical but prolonged usage and frequent dose adjustments are required. Long term use of the drugs is not advisable due to side effects such as internal haemorrhage and gastric ulceritis. Long term medication also causes considerable damage to liver and kidneys. Immunosuppressive and cytotoxic drugs prescribed also have undesirable side effects.

Recently, antimetabolites have been tried with limited success. Chemicals such as osmic acid, nitrogen mustard and alkylating agents are injected into the affected synovial joint cavity to destroy the proliferating synovium. These chemicals are highly injurious to the cartilage and bones. Even though they succeed in partial prevention of synoviocyte multiplication, the damages caused to the cartilage and bones are the unfavourable factors for their use. The process is painful and normally remission of symptoms lasts for 2-3 years.

Surgical synovectomy involves removal of the inflamed synovial lining. This mode of treatment is expensive, needs hospitalisation and involves long convalescent periods. Also, complete removal of the affected synovial tissue is seldom achieved. Normally, the relief obtained lasts for 3-4 years and, the chances of recurrence are high and, in case of recurrence, surgical re-intervention is not recommended due to the scar tissue and fibrosis from the previous surgery. Hence, the expense to benefit ratio is low for surgical synovectomy. Radiation synovectomy offers a viable and attractive alternative for the effective management of synovitis, especially in the early stages of the disease.

## Radiation Synovectomy (RS)

Radiation synovectomy (otherwise referred to as radiation synoviorthesis, the word 'orthesis' meaning restoration) involves intra-articular injection of a $\beta^-$ emitting radionculide of appropriate nuclear, chemical and biochemical characteristics in the form of a radiopharmaceutical into the affected synovial joint in order to counteract and control the excessive proliferation of the synoviocytes. This mode of therapy was tried several years ago with limited success. The earlier attempts using inorganic colloids of radionuclides such as $^{198}Au$, $^{32}P$, etc. failed due to the excessive leakage of the injected radiopharmaceutical from the joint leading to relatively excessive radiation dose to other organs. Development of colloidal particles such as silicates, citrates and hydroxides of the isotopes $^{90}Y$ and $^{169}Er$ reduced the incidence of leakage from the joint. The radiation exposure to healthy organs due to the labelled particles escaping from the injected joint cavity was still a point of concern. The current approach is to make the particles of appropriate size and then label them with the radionuclide of choice.

A radionuclide for potential application in radiation synovectomy should have a short half life of 1-2 days, having $\beta^-$ emissions of energy adequate to penetrate and ablate the proliferating synovium with minimal radiation dose to the underlying cartilage and bones. Low energy $\gamma$ radiations in low yield, if present, will further enhance the utility of the radionuclide for its biolocalisation using an externally placed gamma camera. Quick clearance of the radionuclide from the system in whatever chemical form it gets released from the tagged particles is also highly desirable. The particles could be made from biodegradable substances having good biocompatability. The particles to be used as carriers for the radioisotopes should be in size range 5-20 $\mu$m and should have appropriate porosity and density. They should get easily phagocytosised and should not turn hostile in the cavity. They should not initiate inflammatory reactions. Once metabolised by the body enzymes, fast clearance from the body is also expected of them. The biological half-life of the particles in the synovial joint should be longer than the physical half-life of the tagged radionuclide.

## Mode of Action

The mode of action of radionuclides in therapeutic applications is due to the cytotoxic effects of the particulate radiation emitted by them while undergoing transmutation. The excessive proliferation of the inflamed synovium under the stimulus from the active mediators present in the system is effectively controlled and counteracted by the radiations emitted by the radionuclide attached to the carrier molecule. Radiation synovectomy is the invasive type of treatment for arthritis. Relief lasts for 3-4 years and, in case of recurrence, the treatment can be repeated. Long term hospitalization of the patient is not required and the injection could be administered under local anesthesia and under fluoroscopic guidance. This method has got high potential as an alternative to the currently available modes of treatment.

The accepted biological mechanism by which radiation synovectomy agents function involves their phagocytosis by the synoviocytes, polymorpho-nuclear cells and macrophages present inside the

synovial cavity. The radionuclide tagged particles are injected intra-articularly into the affected joint. They get phagocytosised and subsequently distributed over the entire synovium and below. Radiation emanating from the radionuclide penetrate and ablate the inflamed synovium and thereby control the excessive proliferation of the synoviocytes by their cytotoxicity. The inflamed synovial lining starts shrinking and ultimately leads to reduction in pain. Typically, 70-100 Gy of radiation dose is delivered by a radio-pharmaceutical preparation (5 mCi $^{90}Y$) used for radiation synovectomy.

## $^{166}$Ho-HA particles for Radiosynovectomy

Radiopharmaceuticals Division has taken up a programme for the development of radio-synovectomy a$_{y}$ents. The radioisotopes of choice are the ones which can be easily produced in large quantities in medium flux reactors. Hence, the target nuclides should have very high neutron absorption cross-section.

$^{166}$Ho was one of the radionuclide selected as it has several advantages. It is short lived (27 h half life), decays by emission of 1.8 MeV ($E_{\beta\text{-max}}$) β-particles, and 81 keV γ rays are also emitted with 6% abundance. $^{166}$Ho could be produced in high specific activity by the thermal neutron bombardment of the stable target $^{165}$Ho which has 100 % natural abundance. The reaction cross-section of 66 barns results in the production of high specific activity $^{166}$Ho. 1.8 MeV $E_{\beta\text{-max}}$ has got a maximum soft tissue penetration of 8.5 mm and hence suitable for large joints. Normal scintigraphic imaging can be carried out with the help of the 81 keV γ emission from $^{166}$Ho.

## Preparation of the Radiopharmaceutical

### *Production of $^{166}$Ho*

$^{166}$Ho was produced by irradiating $^{165}Ho_2O_3$ target in the Dhruva reactor at a neutron flux of 1.8 x $10^{13}$ neutrons/cm$^2$/s for 7 days. Six hours of post irradiation cooling was provided. Irradiated $Ho_2O_3$ was dissolved in HCl by gentle warming inside a lead shielded glove box. The activity was assayed by measuring the ion current of an aliquot in an ion chamber and the radionuclidic (RN) purity of the isotope formed was estimated by high resolution gamma ray spectrometry.

### *Synthesis of hydroxy apatite (HA) particles*

Hydroxyapatite, $Ca_{10}(PO_4)_6(OH)_2$, was synthesised by reacting $Ca(NO_3)_2$ with $(NH_4)_2HPO_4$ at pH 12. The precipitated HA cake was heated for 10 min. at 70°C and cooled to room temperature. The precipitate was filtered and dried at 240°C. After cooling, the HA cake was broken to small lumps and ground to finer particles and sieved in a 100-200 mesh and 200-400 mesh standard sieves. Characterisation of the compound was carried out by X-ray diffractometry. Braggs peaks obtained were compared with the corresponding ASTM standard values to establish the identity of the sample. Fig.2 shows the diffraction profile obtained.

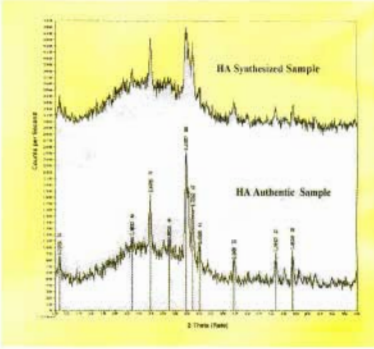



*Fig.2 X-ray diffraction pattern of HA samples*

Particles below 125 μm size were collected and subjected to further attrition in a high speed grinder for 15 min. in order to get smaller HA particles. The powder was sieved through a 200-400 mesh

mechanically vibrated sieve. An aliquot from the sample was suspended in 50 ml d.d water and ultrasonicated for 30 min. Particle size analysis was carried out by feeding the solution into Laser Diffraction particle size analyser.

### *Labelling of hydroxy apatite particles*

HA particles suspended in double distilled water were labelled with $^{166}HoCl_3$. The contents in the test tube were kept mixing for 1 h in a rotary shaker at room temperature and centrifuged at 2000 rpm for 5 min and the supernatant discarded. $^{166}$Ho-HA particles were washed with normal saline solution. Washing step was repeated thrice to ensure that no free $^{166}$Ho activity would leach out from the labelled particles.

## Bio distribution Studies

The biological evaluation of the radiopharmaceutical was done at the Radiation Medicine Centre as follows. Healthy News Zealand white rabbits (n=7) weighing around 3-3.5 kg were selected for this purpose. A knee joint lesion that closely resembles that of a rheumatoid arthritis knee in man was developed in two rabbits by injecting ovalbumin following the procedure reported by Dumonde and Glynn. The inflammed knee joint was cleaned, shaved and $^{166}$Ho-HA particulate suspended in normal saline was intra-articularly injected into the inflamed joint using a 22 gauge needle. Control animals (n=7) having normal joints (no antigen induced arthritis) were also administered with an identical dose of the $^{166}$Ho-HA particulates in a similar way. After the instillation of the radioparticulates, the injected limb was flexed 2-3 times. All the above operations were carried out in aseptic environment. All animal studies were carried out with the approval of Animal Ethics Committee of BARC.

## Imaging Studies

Gamma camera images were acquired with virtual view of the site of injection (knee joint). While acquiring the images, the animal was positioned in such a way that abdominal and thoracic regions are under the field of view. Static images were acquired using a single headed ECIL Medix gamma camera of 256x256 matrix size. The experimental animals were brought under sedation by general anesthesia using Ketamin™ and Xylaxin™ administered through intramuscular route. All the animals were subjected to scintigraphic imaging at the end of 3 h, 24 h, 48 h and 96 h post injection. Blood samples from the animals were also collected at these time intervals. Activity present in the blood was estimated as percentage of injected dose by withdrawing blood samples, measuring the activity in a counter and comparing to the injected dose. Extra-articular leakage was calculated on the basis of activity present in the blood and also based on activity in a non-target site calculated from the scintigraphic images by drawing a region of interest (ROI) at the site of injection and another at the mid-abdomen.

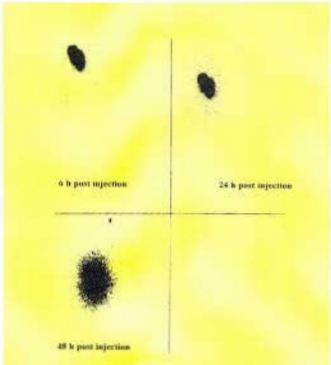



*Fig.3 Scintigrams of the injected joints in the arthritis induced rabbit model*

Counts/pixel in the selected ROIs were taken into consideration for calculating the extra-articular leakage. These animals were monitored over a

period of six months for any physical and skeletal disability. Biodistribution results are shown in the Fig. 3. The injected activity remained at the site of injection even after 48 h post injection. The blood samples taken at different points of time did not show any radioactivity over the bakground activity indicating the integrity of the labelled particles within the joints.

## Clinical Evaluation

All the results of the above experiments were submitted to the Nuclear Medicine Committee (NMC) seeking approval for clinical trials on human beings. NMC cleared the proposal in May, 2000 and Nuclear Medicine Department, Ruby Hall Clinic, Pune (who have been practising radiation synovectomy using imported products) undertook the clinical trials. Earlier reported work has suggested that a radiation dose of about 1 Gy/g of synovial tissue is effective to prevent the cell proliferation. Accordingly, ~185 MBq of the labelled preparation suspended in 300 µl of sterile normal saline was injected intra-articularly under fluroscopic guidance to the affected knee joint of the patients. The knee was flexed 3-4 times post injection. The patients were kept under observation for 1 h post injection. Distribution scintigrams by gamma camera imaging of the injected knee joint was taken to ascertain the localisation of the injected dose. More than 82 knee joints have been treated during the past six months. Patients suffering from rheumatoid arthritis and haemophiliacs have shown good response from the treatment.

Fig.4 shows the procedure followed. A gamma camera image of the knee after injection is also shown. Some patients also underwent delayed

*Fig.4 (Clockwise) Radiation synovectomy procedure and the scintigraphic images of the injected joint*

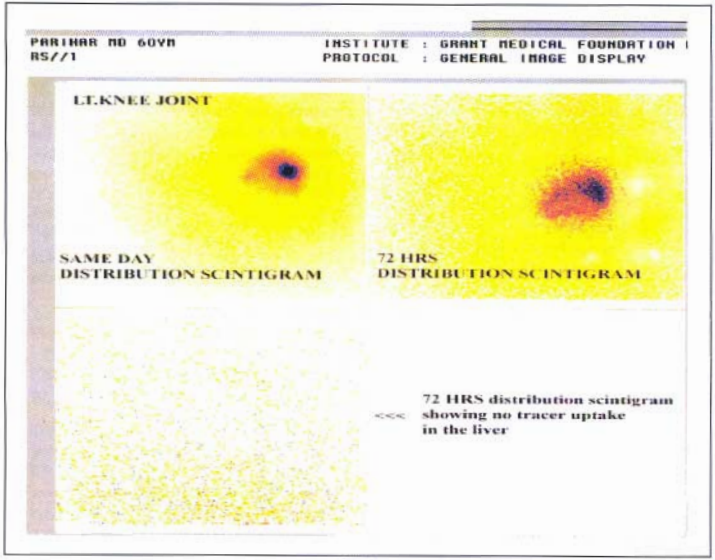



*Fig. 5*

imaging to ensure that there was no leakage of the radiopharmaceutical 72 h post injection. Fig.5 shows the delayed images obtained 72 h after the injection. About 60 patients have been treated with the new radiopharmaceutical out of which 75% of the patients treated reported significant reduction in pain. These clinical evaluation findings are now proposed to be submitted to the Radio-pharmaceutical Committee (RPC) for seeking clearance for regular manufacture and supply to all interested users. The indigenous availability of this product for RS would be an important milestone and render this treatment mode widely available at affordable cost for the needy patients of our country.

## Conclusion

$^{166}$Ho labelled HA particles suitable for radiosynovectomy application has been successfully developed. The biological evaluation and subsequent clinical studies have demonstrated that the present product could be used as a replacement for the expensive commercially available synovectomy agents. The radioisotope $^{166}$Ho can be prepared in adequate quantities in the Dhruva reactor and hence this radiopharmaceutical could be made available to a large number of needy patients. The present work is thus a successful result of R&D on a new therapeutic radiopharmaceutical taken through satisfactory demonstration of clinical utility. The product is earmarked for regular deployment on a large scale through BRIT.

# AUGMENTATION OF ANALYTICAL CHEMISTRY RESEARCH FACILITIES

P.K. Mathur and M.Sudersanan
Analytical Chemistry Division

Quantitative measurements are an integral part of any research program. Measurements are needed for various purposes like identification of a material, its elemental composition and suitability for a given application. It is also needed to investigate the reasons for the failure of any component or process and for other scientific investigations. Analysis of metals or special strategic materials are needed in engineering, science, biology or medicine to study the effect of the role of specific metallic impurities introduced deliberately or through the manufacturing process. The use of various materials in industrial applications has increased the concern about toxic metal ions and organics in drinking water and effluent samples. The use of high purity materials in various specialized applications like lasers, computers, electronics, cryogenics etc also requires the analysis of trace constituents at vanishingly low levels. The demand for analysis is thus increasing in various fields. This demand is more in the nuclear industry in view of the specialized nature of the materials and the stringent specifications for nuclear fuels, moderators, coolants and cladding materials. The concern about the impact of nuclear power generation on the environmental degradation has put further demands on analysis. In order to cope up with these increasing requirements and also to prepare effectively to meet the future challenges in analysis, the Analytical Chemistry Division (ACD) had taken up a program on the augmentation of analytical chemistry research facilities as part of the IX plan project. This article outlines the progress made in this aspect.

Modern chemical analysis is mainly an instrument-based technique using minimum sample processing. This is important since the sample processing is a source of error in the case of high purity materials or in the case of environmental samples. Quality assurance through multiparameter multitechnique approach is also needed to enhance the value of analytical data. The increasing realization that the toxicity of metals depends on their particular form has led to the demand for methods which can provide speciation, in addition to the total analytical concentration. Thus a variety of instruments are needed to fulfil the needs of various categories of users and our IX Plan Project was structured in this manner.

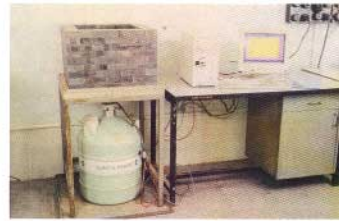


*Fig. 1 γ-spectrometry set up*

Nuclear analytical techniques are of special relevance to Department of Atomic Energy. The easy accessibility and availability of nuclear reactor or accelerator facilities makes ACD an ideal laboratory to carry out analysis using thermal or fast neutrons and charged particles. The Division has built the necessary infrastructural facilities for such sophisticated analytical work. The multielement capability, an almost non-destructive nature of analysis, minimum sample requirements and processing and the freedom from blank has made instrumental neutron activation analysis a highly versatile tool for the characterisation of

environmental and geological materials for trace impurities. The analysis is facilitied by the use of HPGe detector for the measurements. The poor performance of the earlier analyser systems available in the Division was affecting the efficiency of analysis and hence the procurement of a new HPGe detector both for normal and low energy counting was taken up as a priority area. The procurement is complete and the Division has successfully used the technique in connection with the analysis of trace metals in process solutions of Pa recovery project, for the analysis of geological samples for rare earth elements and for platinum group metals.

*Fig. 2 Atomic absorption spectrophotometer*

Analysis of carbon, sulphur and other dissolved gases in metals and alloys is needed for assessing the suitability of these materials for various engineering applications. The use of elemental analysers is valuable for this task. The Division procured a C-S analyser for this purpose. This has helped not only in replacing the ageing C analyser but also in extending the analysis to sulphur which was earlier carried out by a time consuming combustion -volumetric method. This instrument is being used extensively along with the other analysers like H, N and O determinators.

Chromatographic techniques are extremely important for the determination of trace anions and cations in aqueous samples or of organics in water samples. Such measurements are important in many applications like analysis of chloride in heavy water, that of fluoride, nitrate, chloride and sulphate in domestic waters or effluent solutions. The analysis of organic compounds like pesticides, aromatics, etc is also becoming important. Ion chromatography and HPLC are the preferred analytical tools for such work. The Division has procured suitable instruments for this purpose. They are being tested and will be available for the determination of trace impurities in aqueous solutions.

*Fig. 3 Electrochemical system*

Electroanalytical techniques have considerable potential for use in the analysis of metal ions in complex matrices like environmental samples or sea water. The technique has an additional advantage that the information on speciation of metal ions can also be obtained. Various electroanalytical methods like square wave, normal and differential pulse polarography have been used both for analysis and fundamental studies on electrochemistry. Corrosion behaviour of metal ions can also be studied by electrochemical techniques and can provide useful information on the compatibility behaviour of various metals and alloys under normal operating conditions of nuclear reactors. They are also of value in the speciation of metal ions in corrosion product deposits on reactor system constructional materials. Differential pulse anodic stripping voltammetry has application for the determination of trace metal ions at ppb levels. In view of the use of electroanalytical methods in nuclear and analytical research,

versatile electrochemical systems and bipotentiostat with stationary mercury drop electrode and rotating ring disc electrode were procured recently. Analysis of trace metallics in sea water reference material or in high purity arsenic have been carried out. The determination of Cr (iii) and Cr(vi) in effluent samples and of Pd in deoxo catalysts have been carried out by electrochemical techniques. The electroanalytical system serves as a useful comparison to spectrochemical methods for trace analysis.

*Fig. 4 ICPAES Instrument*

Atomic absorption and emission spectrometric techniques have emerged as the workhorse of any modern analytical laboratory. The high sensitivity, specificity and wide working range have made these methods very useful for rapid analysis of solution samples. Considering the needs for such analysis and to strengthen the existing systems, the Division procured an atomic absorption spectrometer with facilities for flame emission and absorption measurements along with hydride generation facility. An inductively coupled plasma emission spectrometer and a spectrofluorimeter were also obtained. These instruments have considerably widened the scope for analysis and are being regularly employed for the analysis of various types of samples. The AAS and ICP ABS serve as good comparison techniques for the analysis of large number of a wide variety of samples. Thus the analysis of solutions for metal ions like Fe, Cu, Zn, Cd, Mg can best be done by AAS while the analysis for Al, Ha, Sr, REE etc can be done by ICPAES. ICPAES is a suitable technique when a large number of metal ions have to be analysed in a single sample while analysis of a single metal ion in a set of solutions can best be carried out by AAS. These instruments are in regular use for the analysis of forensic samples for Pb, Zn, Ni; solutions for Mn, Cr, Fe; uranium samples for Fe and Al; process solutions from Pa recovery for elements like U, Fe, Zr; environmental solutions for various metal ions etc. The procurement of these instruments has helped the Division to actively collaborate in various important projects like intercomparison exercises on U; protactinium recovery project; project on U extraction from sea water; analysis of solutions in connection with the uptake of U by plants; work in connection with thorium utilizational, etc. The large linear dynamic range, multielement capability, absence of chemical interferences and the ability to analyse a large number of elements in the ppm to ppb level has made the investment in these instruments a wise decision.

Fluorimetry is a technique which has special relevance to the nuclear industry since uranium shows a remarkably high sensitivity for fluorescence. Similarly, other important elements like He and Al are also sensitive by fluorimetry. Hence, a spectrofluorimeter was also obtained which has application for the estimation of Uranium from phosphoric acid medium. In view of the interest in the recovery of uranium from rock phosphate, this technique will be of use in such analyses.

Necessary actions have already been taken for the procurement of other instruments like ICPMS, O-N analysers, upgradation of XRF, etc. In addition, a minor equipment like specific ion analyser has also been procured, which will help in the faster analysis of various samples.

The major thrust of the activities of Analytical Chemistry Division is towards providing efficient and accurate analytical service support to various Divisions of BARC and other units of DAB. The fuller utilization of the analytical instruments can be

ensured only by adequate interaction between the users and ACD. Various user Divisions are, therefore, requested to associate ACD in their projects and freely discuss their analytical requirements so as to ensure optimum utilization of the available facilities and scarce resources. This will enable a proper technology transfer and will also provide necessary fillip for further targeted research in developing user specific analytical procedures.

## WORKSHOP ON 'RADIOLOGICAL EMERGENCY PREPAREDNESS'

The 10th Training Workshop on 'Planning, Preparedness & Response to Radiological Emergencies' for DAE scientists and engineers was held at Rajasthan Atomic Power Station (RAPS), Kota, during February 5-9, 2001 and was attended by 48 officers. Engineers and Health Physicists from Tarapur Atomic Power Station (TAPS), Rajasthan Atomic Power Station (RAPS) 1&2, Rajasthan Atomic Power Project (RAPP) 3&4, Madras Atomic Power Station (MAPS), Narora Atomic Power Station (NAPS), Kakrapar Atomic Power Station (KAPS), KGS, Plutonium Plant (PP), Cirus reactor, Dhruva reactor, Power Reactor Fuel Reprocessing Plant (PREFRE), Kalpakkam Fuel Reprocessing Project (KARP), Fast Breeder Test Reactor (FBTR) and Indira Gandhi Centre for Atomic Research (IGCAR), attended the course.

Mr K.P. Ojha, Station Director, RAPS 1-4, welcomed the distinguished guests, faculty members and the participants of the workshop and thanked the Organising Committee for choosing RAPS as the venue for this workshop at a time when RAPP-4 became operational.

In his introductory remarks, Mr B.K. Bhasin, Chairman, Organising Committee and Executive Director (O), NPCIL, gave a brief overview of this programme. He told that the course contents of these workshops were prepared by experts from BARC, NPCIL and AERB. The course contents were drafted on the lines of similar programmes conducted by bodies like the International Atomic Energy Agency (IAEA). He emphasised on the safety aspects being taken into consideration in our reactors. Emergency preparedness is an integral part of the Nuclear Power Programme, he added.


*Inauguration of the Training Workshop on "Planning, Preparedness & Response to Radiological Emergencies". On the dais are (from left to right): Mr K.C.Purohit, Mr A.R. Sundararajan, Mr M.S.R. Sarma, Mr B.K. Bhasin, Mr K.P. Ojha and Mr D.K. Goyal*

In his inaugural speech, Guest of Honour Mr M.S.R. Sarma, ex-Chairman, SARCOP, AERB, pointed out that accidents took place due to cumulative errors and multiple failures. He said that a proper review of all the emergency exercises conducted should be carried out to ensure that the observed deficiencies are removed.

Mr A.R. Sundararajan, Member, Organising Committee and Head, Health & Safety Division, AERB, described in brief the relevance of this workshop in the context of the expanding Nuclear Power Programme.

The inaugural function concluded with the Vote of Thanks proposed by Mr T.S. Marwah, Head, Industrial Safety Section, RAPS 1&2.

# TOTAL HEALTH CARE PROGRAMME FOR BARC STAFF

Recent epidemiological research has shown that Indians are more prone to develop Ischaemic heart disease and that too a decade earlier than their Western counterparts. Indians are also genetically more prone to develop Diabetes mellitus, an important disorder, which can increase the risk of heart, kidney, eye and foot damage. The research also indicates that, despite genetic predisposition, one can significantly reduce the risk and delay the onset of disorders by following certain healthy guidelines regarding life style. USA has demonstrated the reduction in risk by adopting healthier life styles.


*Dr B.J. Shankar, Head, Medical Division, BARC, speaking at the "Healthy Living" programme organised at Anushaktinagar*

Keeping the above in mind, BARC Staff Club - Yoga Circle, DAE Sports & Cultural Council and Medical Division of BARC organised a unique health fitness programme for the benefit of their employees and family members on April 13, 14 and 15, 2001 at Anushaktinagar.

The programme comprised of talks by eminent speakers like Dr P.S. Lamba, Diabetologist, speaking on "Prevention of Complications in Diabetes", Dr Harish Shetty, Psychiatrist, on "Stress Management", Dr N. Patankar, Obesity specialist, on "obesity", and Dr Sheetal Mhamunkar, Dietecian on "Diet Modifications". Dr P.T.V. Nair of BARC Hospital enlightened the audience about high blood pressure and its management. Dr Asha Damodaran gave details of exercises for the management of health. Dr G.A. Ramarao talked about the effect of positive and negative emotions on health. Mr N.K. Porwal and Mr S.G. Markandeya spoke on "Meditation" and "Integrated Approach to Yoga Therapy", respectively.

The programme concluded with a demonstration of Pranayam practices by Mr H.C. Dabral, Veena recital by Ms Prabha Agarawala and humour session by Mr A.J. Singh.

# DAE-BRNS NATIONAL SYMPOSIUM ON NUCLEAR AND RADIOCHEMISTRY (NUCAR-2001 )

The 5th biennial National Symposium on 'Nuclear and Radiochemistry' (NUCAR2001) was organised during February 7-10, 2001 by Board of Research in Nuclear Sciences (BRNS), Department of Atomic Energy, in association with University of Pune, Pune, at the Department of Chemistry. The objective of these biennial symposia has been to provide an effective forum for fruitful interaction among the specialists in the fields of nuclear and radiochemistry, application of radioisotopes and allied research areas to have an objective assessment of current trends and also take stock of the latest developments. The scope of NUCAR2001 was covered under various themes such as nuclear chemistry and instrumentation, chemistry of actinides and reactor materials, spectroscopy of actinides, radioisotope applications, chemistry of fission and activation products, radioanalytical chemistry and radioactivity in environment. Judging from the response in the form of number of papers received, this symposium seems to have provided

the requisite platform for effective interaction. It is heartening to note that more than 230 contributory papers have been received for presentation. In addition, 16 specialists including 7 from overseas have kindly consented to deliver invited lectures in their area of specialisation.

*Prof. N.J. Sonawane, Vice-Chancellor, University of Pune, Pune, lighting the lamp during the inaugural function of NUCAR2001*

The symposium was inaugurated by Dr.D.D.Sood, Director, Division of Physical and Chemical Sciences, IAEA, Vienna, at a function presided over by Prof. N.J.Sonawane, Vice Chancellor, University of Pune, Pune. Prof. R.S.Mali, Head, Department of Chemistry, University of Pune and Chairman, Local Organising Committee, welcomed the honourable guests, delegates and other participants to the symposium. Dr. K.L.Ramakumar, Convener, NUCAR 2001, while welcoming the gathering, spelt out the scope of NUCAR2001 symposium. The importance and the wide recognition of the impact the series of NUCAR symposia have generated has been gauged by the continuous increase in the number of contributory papers and participation. He further recalled the long and sustained association of University of Pune with NUCAR symposia.

In his inaugural address, Dr. Sood emphasized the indispensable role of the symposia like NUCAR, in bringing out interaction among various researchers active in different areas of nuclear and radiochemistry and application of radioisotopes for furthering the scope and understanding of the discipline. The synergic cooperation among the academics and the research institutions will go a long way in extracting maximum benefits out of the applications of radioisotopes in different areas of science and technology.

Prof. Sonawane, in his presidential address, recounted the long-standing association of University of Pune with regards to the research activities in nuclear sciences. In this context, he emphasised the important and the catalytic role of collaboration, which the University has with the Department of Atomic Energy. "Symposia like NUCAR2001 adds further impetus to this collaboration activity", he stressed. Prof. B.S.M.Rao, Co-Convener, Local Organising Committee, and Dr. R.M.Kadam, Secretary, NUCAR2001 proposed vote of thanks.

The symposium took off with a keynote address by Dr.S.B.Manohar, Head, Radiochemistry Division, BARC, on academic interaction in nuclear sciences. The proceedings of NUCAR2001 were divided into 16 sessions, out of which four (one per day) were for poster presentations. In view of large number of contributory papers received, and with a view to having maximum interaction among the participants, poster presentations included a large number of papers. At the same time young researchers have also been encouraged to present their papers in oral presentations.

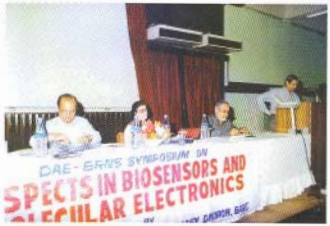
A one-day embedded seminar on "Chemistry of Actinides in Nuclear Fuel Cycle" was also organised during NUCAR2001. Specialists in the respective fields discussed all the aspects of nuclear fuel cycle starting from fuel fabrication to waste immobilisation.

Best paper presentation awards were also given away to young research scholars who have been pursuing research in nuclear and radiochemistry. Local press gave a wide coverage to the event.

In the feedback session, participants suggested of having a video coverage of poster presentations. Delegates from abroad were of unanimous opinion that the nuclear and radiochemistry research in India is far more thriving and active, especially at University level.

# SYMPOSIUM ON 'PROSPECTS IN BIOSENSORS AND BIO-MOLECULAR ELECTRONICS'

Nuclear Agriculture & Biotechnology Division (NA&BTD), BARC, organised a two-day symposium on 'Prospects in Biosensors and Bio-molecular Electronics on February 10 and 11, 2001 at the Multipurpose Hall, Training School Hostel, Anushaktinagar.




*Dr S.F. D'Souza welcoming the participants. Other seated (left to right) are Prof. Sukhatme, Dr (Ms) Samuel and Dr K.K. Surendranathan*

The symposium deliberated on an emerging interdisciplinary area wherein nano or micro level concentrations of biological recognition element will be in intimate contact with transducer devices that could produce a digital electronic signal to monitor/ identify subject of interest. These devices could play a major role in pollution monitoring, clinical diagnostics, and biochemical analysis in food and agriculture, etc.

Prof Phil Warner, Director, Institute of Bioscience and Technology, Cranfield University, U.K., while giving the keynote address, remarked on this multi-disciplinary area which could revolutionise and make in-roads into the monitoring of environment/ health/food quality, etc. Twenty-five speakers from all over the country and abroad presented papers, and over 250 participants actively took part in the deliberations. The symposium deliberated on topics pertaining to biosensors for clinical diagnosis, food and fermentation industry, environment and pesticide monitoring, development of biosensors, optical fibre sensors, three dimensional memories electronic noses, and tongues, molecular electronics and other structural and organisational aspects of biosensors.

Prof S.P. Sukhatme, Chairman, Atomic Energy Regulatory Board, and Chief Guest of the inaugural session, reminded about the requirement of inexpensive and indigenously developed biometers for quality assurance and freshness especially in the changing world commercial scenario.

Dr (Ms) A.M. Samuel, Director, Biomedical Group, BARC, and Chairman, Organising Committee, in her presidential address, highlighted on the role of biosensors in the diagnostics and urged the multidisciplinary participants to interact and synthesise novel interactive programme and products.

Dr S.F. D'Souza, Head, NA&BT Division and Convenor, while welcoming the participants, reminded them of the enviable position biology will be occupying in the 21st century. He also brought out some of the impacts made by biosensors and biomolecules in various fields.

Dr K.K. Surendranathan, NA&BT Division, Secretary, Organising Committee, thanked all those who made the two-day session an excellent mental treat.

# BARC SCIENTISTS HONOURED

A paper entitled "Fluxes and Residence Time of Different Toxic and Trace Elements in Thane Creek", authored by S.K. Jha, G.G. Pandit, Sujata Chavan and B.S. Negi of Environmental Assessment Division, BARC, was presented in the "Second

International Seminar on Analytical Techniques in Monitoring the Environment" held at Sri Venkateswara University, Tirupati, Andhra Pradesh, during December 18-20, 2000, and it won the Best Paper Award at the Seminar.

• Dr S.K. Jha joined the Environmental Assessment Division (EAD), BARC, after completing his M.Sc. in Inorganic Chemistry from Patna University and after graduating through BARC Training School in 1988. His earlier work on physico-chemical behaviour of $_{237}Np$ in marine environment earned his Ph.D. from Mumbai University. Since then, Dr Jha has carried out extensive research work on many aspect of environmental problems using Nuclear Analytical Techniques. At present, he is working on sedimentation rate, behaviour and fluxes of different pollutants affecting marine environment of Mumbai city. His field of interest also includes use of nuclear techniques for monitoring of toxic and trace elements in different environmental samples.

• Dr (Ms) G.G. Pandit joined EAD in 1981 after graduating from 24th batch of BARC Training School. She obtained M.Sc. (Organic Chemistry) from University of Mumbai, in 1980 and Ph.D. (Sciences) from University of Mumbai in 1990 for her thesis entitled, "Sourced Reconciliation of Atmospheric Hydrocarbon". Her specialisation includes development and standardisation of methodologies for monitoring of various organic pollutants such as volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs) and organo chlorine pesticides in the different environmental matrices. At present, she is working on characterisation and risk assessment of persistent organic pollutants (POPs) in indoor and outdoor aerosols and in coastal marine environment. Her field of interest also includes speciation of marine environment.

• Ms S.B. Chavan joined EAD in 1998 after completing her graduation in Physics from Mumbai University. She is associated with use of nuclear and related techniques (EDXRF and INAA) for the measurement of toxic and trace elements of environmental samples. At present, she is working on geochemical peculiarities of sediments in the coastal marine environment around Mumbai city.

• Dr B.S. Negi joined BARC in 1969 after completing one year training course of Training Division. He obtained Ph.D. degree from Mumbai University in 1988. He has been associated with the development and use of nuclear and related techniques (EDXRF and INAA), systems for the measurement of toxic and trace elements of envionmental samples (air particulates, soil, fly ash, coal, etc.) and statistical analysis of the data to identify pollution sources. He is also involved in the R&D activities related to the natural and man-made radionuclides in environmental samples like air filters, dry and wet deposition samples collected at various sampling stations spread all over the country and analysed at low level radioactivity measurement laboratory of EAD. The laboratory is being upgraded under his supervision with an advance system to handle new challenges in the field.

*Edited and published by Dr Vijai Kumar, Head, Library & Information Services Division, Bhabha Atomic Research Centre, Trombay, Mumbai 400 085.*
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