# Medical Isotopes

# Laser based Isotope Selective Photoionization for Enrichment of $^{176}$Yb, $^{174}$Yb and $^{168}$Yb

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Process dye lasers deployed in Yb enrichment experiment

ABSTRACT

Laser based isotope selective ionization is a suitable technique for selective isotope enrichment via atomic route. It has several advantages over conventional techniques such as high single stage selectivity, high energy efficiency and most importantly, its suitability to enrich any specific isotope, including middle isotopes of the element consisting of several isotopes. Of late, focus has been on enrichment of medical isotopes for radiopharmaceutical industry using the available expertise and infrastructure. This article presents in detail the developmental steps in establishing the enrichment process towards realization of >95% enriched $^{176}$Yb from its natural abundance of ~13%. Moreover, the process was successfully employed for enrichment of other Yb isotopes of medical importance, namely, $^{174}$Yb & $^{168}$Yb to realize >98% enriched $^{174}$Yb and ~15% enriched $^{168}$Yb from their natural abundances of ~ 32% and 0.13%, respectively.

KEYWORDS: *Laser based Isotope Selective Ionization, Ytterbium, Enrichment, $^{177}$Lu.*

## Introduction

In recent years, there has been a growing demand of the medical isotope Lutetium-177 in radiopharmaceutical industry. Although not available in nature, $^{177}$Lu can be produced by neutron irradiation of precursor isotopes $^{176}$Lu (direct route) or $^{176}$Yb (indirect route) in isotopically pure form[1]. This necessitates enrichment of the precursor isotope. Both direct and indirect routes have their own advantages and disadvantages. The ATLA Facility of Beam Technology Development Group has focused on both these approaches. This article describes the recent developments in the RIS facility at Engineering Hall-6 on enrichment of Yb isotopes.

Laser based isotope selective excitation followed by ionization and collection using electro-magnetic fields offers one of the most efficient techniques for isotope enrichment/ denaturing[2,3]. The complete process of enrichment requires inputs and expertise from diverse fields of science and technology and in that sense, it is truly multi-disciplinary. Availability of an efficient photoionization (PI) scheme, high power high repletion rate tunable lasers fulfilling the requirements of wavelength, line widths and intensities solicited by the PI scheme, highly collimated low loss atomic beam generation, efficient collection of the photoions as enriched product and well developed post-process treatment for product extraction are the key factors in a successful laser based enrichment process. Further, various aspects in laser-atom interaction affecting selectivity and accessibility of the process, in ion extraction e.g. plasma effects, sputtering of the already deposited product layers by ions and in non-selective pick-up processes deteriorating the selectivity need attention.

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## Isotope Selective Three-step Photoionization Scheme for Ytterbium

At the heart of laser based isotope enrichment lies a proficient multi-step isotope selective photoionization scheme giving optimum selectivity and product yield. Yb has two valence electrons and very few transitions originating from its ground level. Its ionization potential is 6.254eV. This necessitates selection of three-step photoionization scheme for selective photoionization of its isotopes using the availble laser infra-structure supporting visible range of spectrum. Yb has only one transition at 555nm starting from its ground level in visible range. A selective photoionization scheme as depicted in Fig.1 with 555nm as first step is available in literature[4] and has been used in other works on enrichment of Yb isotopes. As is evident from Fig.1, the isotopes shifts of even isotopes are ~500MHz/amu in first step transition and ~1.3GHz/amu for second step transition. However, there are two odd isotopes exhibiting hyperfine structure, with their components spanning over the spectral lines of the even isotopes. Consequently, to achieve requisite selectivity of > 95 %, very narrow line width lasers are indispensable for first and second step excitations. The ionizing transition at 582nm has broad profile and use of multimode laser for the third step is acceptable.

## Development of Single Longitudinal Mode Process Dye Lasers

Dye lasers offer best suitable choice for enrichment process as they suffice to all the requirements of process like wavelength tunability, high power generation (up to tens of W) at high repetition rates (12.5KHz), *etc.* We had already developed process dye lasers pumped by Copper Vapour Laser (CLV) MOPA chains and Diode Pumped Solid State Green Lasers (DPSSGLs) with ~3GHz line width in multi-mode

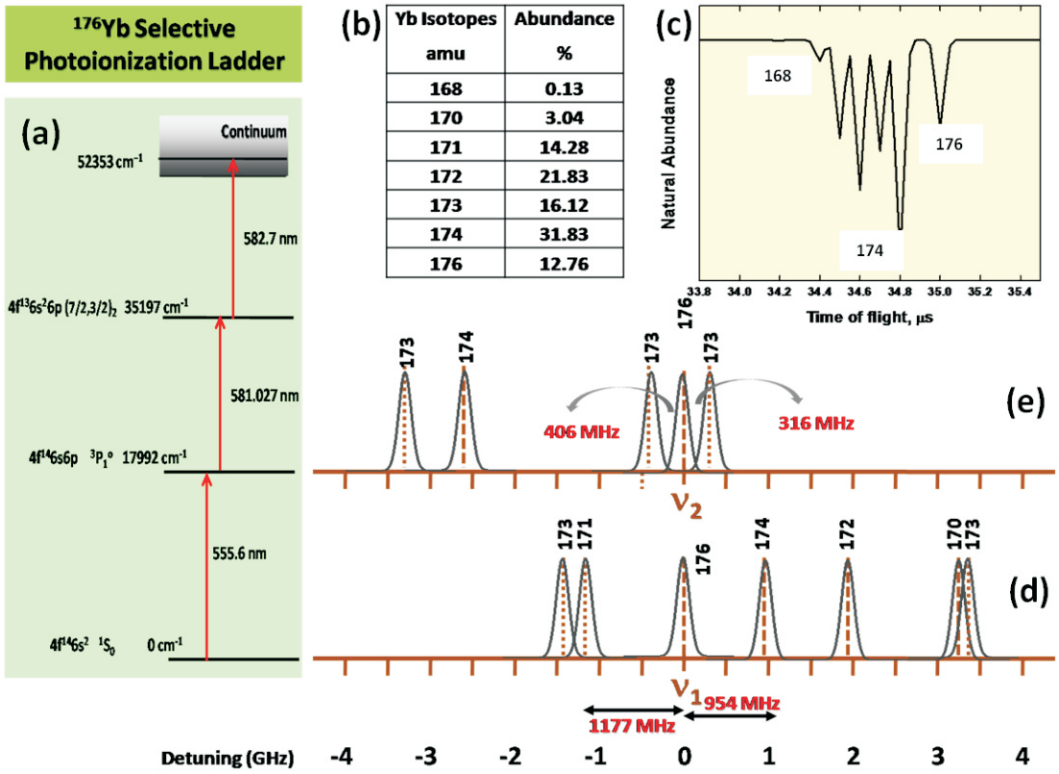


*Fig.1: Three-step photoionization scheme used for selective photoionization of Yb isotopes is shown schematically in (a) with Yb energy levels and corresponding electronic configurations, (b) Presents natural composition of Yb isotopes, (c) Shows mass spectrum of Yb in natural composition when multi-mode lasers were used while (d) and (e) Depict the spectral regions in the vicinity of first and second step transitions respectively of $^{176}$Yb spectral lines where the closeby spectral lines of other Yb isotopes that have maximum effect on selectivity are clearly evident.*

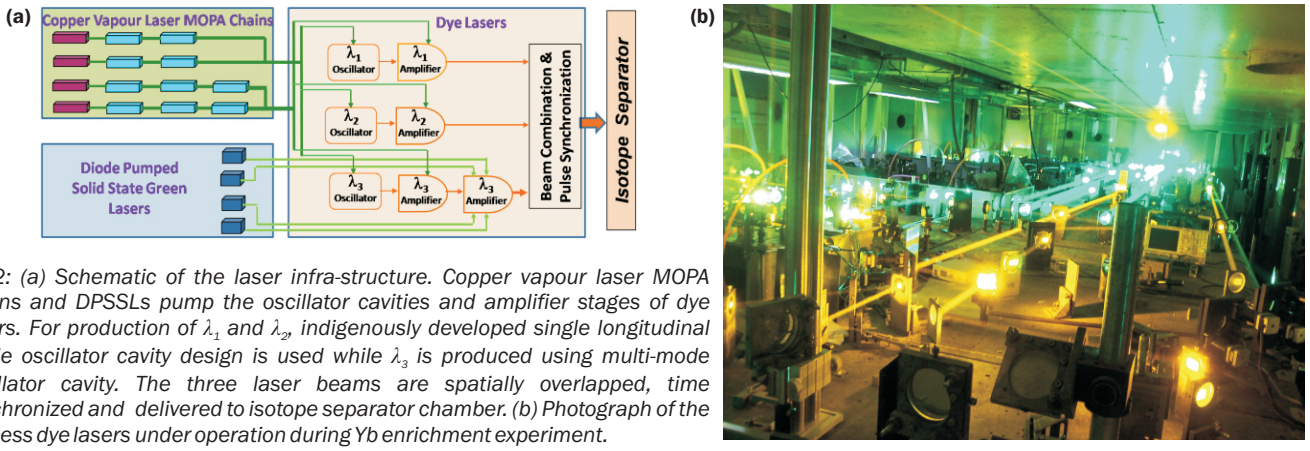


*Fig.2: (a) Schematic of the laser infra-structure. Copper vapour laser MOPA chains and DPSSLs pump the oscillator cavities and amplifier stages of dye lasers. For production of $\lambda_1$ and $\lambda_2$, indigenously developed single longitudinal mode oscillator cavity design is used while $\lambda_3$ is produced using multi-mode oscillator cavity. The three laser beams are spatially overlapped, time synchronized and delivered to isotope separator chamber. (b) Photograph of the process dye lasers under operation during Yb enrichment experiment.*

operation. Schematic of the laser infra-structure is presented in Fig.2 (a) and a photograph shows the dye lasers and beam combination set-up in Fig.2 (b). As a next step, we indigenously developed single longitudinal mode (SLM) dye oscillator cavity generating laser output with line width ~60MHz, time averaged line width ~100MHz and excellent stability over couple of hours[5]. A recording of wavelength and line width stability of the SLM laser over a period of 4 hours is shown in Fig.3 when laser was tuned to 555nm. In SLM laser development, the main challenge faced was the mode hops owing to temperature fluctuations in the oscillator cavity as well as dye solution. To circumvent this, the oscillator cavity was temperature stabilized. Further, various water based binary solvents offering superior thermo-optic properties were explored for their photostability and lasing efficiency and suitable solvent was optimized for process dye laser generation. The aqueous nature of dye solution also offered better safety against fire hazard. The first and second step lasers with average powers of 700mW and 1.5-2W, respectively, and ionizing laser with average power of ~25W were spatially overlapped to make a combined beam with the help of dichroic as well as polarization based beam combiners. The temporal delays between the pulses from the three lasers were arranged to ensure their sequencial arrival in the interaction region with delay of ~ 5ns.

**Qualification of Laser-Atom Interaction and Optimization of Laser and Atomic Parameters**

To ensure high selectivity as well as high product yield, tuning of SLM laser wavelengths precisely to the spectral lines of desired isotope is crucial. Consequently, the transition wavelengths pertaining to first and second step of the $^{176}$Yb PI scheme were precisely determined within ±30MHz for first and second step. Resonance ionization mass spectroscopic technique was employed in a time of flight mass spectrometer (TOFMS) developed in house and a protocol was established

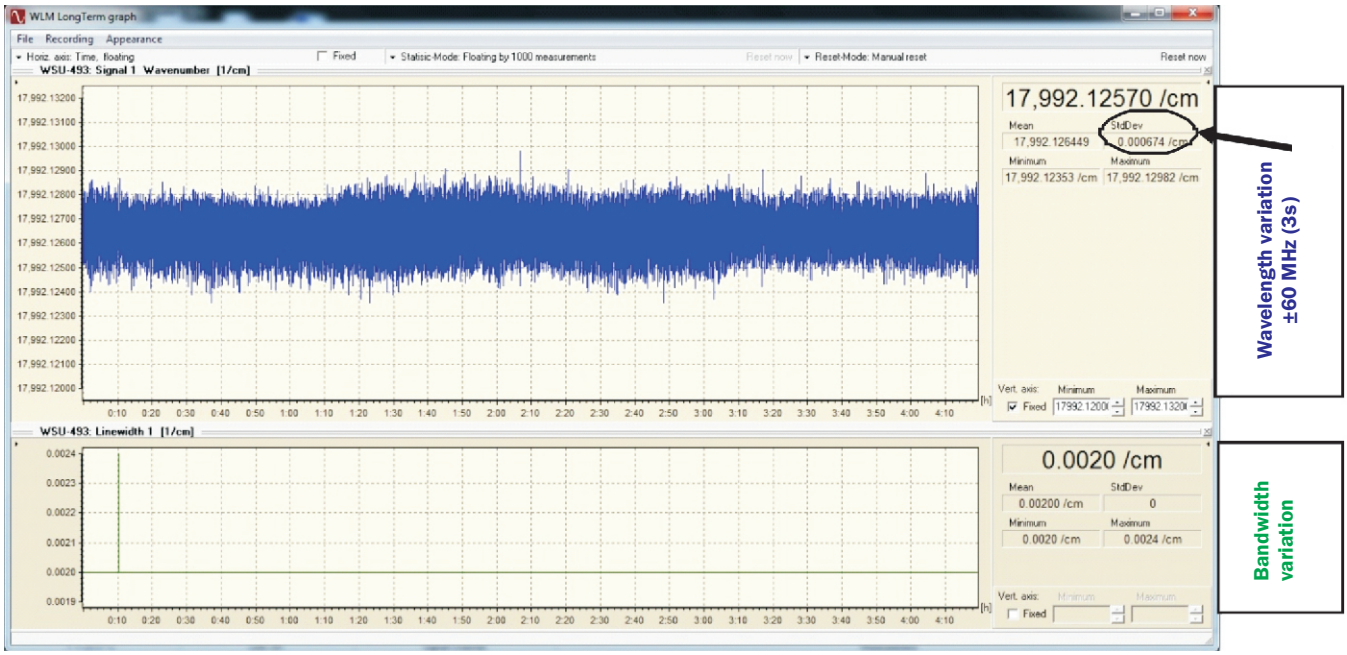


*Fig.3: Wavelength of the indigenously developed SLM dye laser tuned to 555nm recorded over four hours shows highly stable output with standard deviation in wavelength of 0.000674 $cm^{-1}$ i.e. 21MHz with fluctuations (maxima to minima) limited within ± 100MHz.*

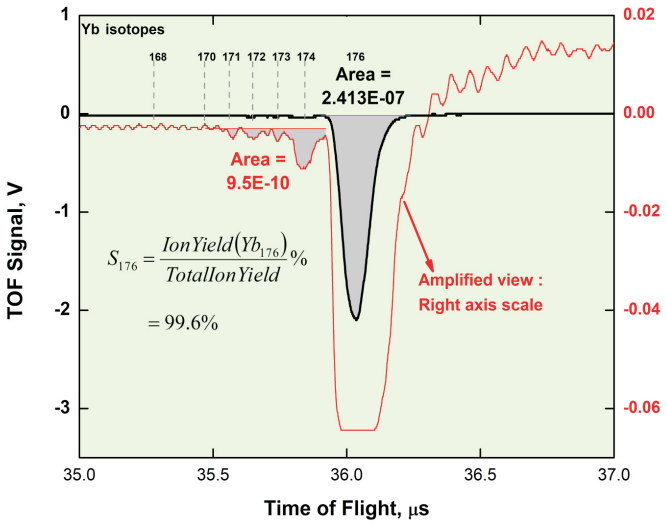


*Fig.4: Mass spectrum of Yb isotopes showing selective ionization of $^{176}$Yb with lasers tuned to its spectral lines at optimized intensities. For clarity amplified view of the spectrum is also plotted (in red) and the relevant scale is shown along the right axis. Further, positions of all Yb isotopes are marked with dashed vertical lines. The spectroscopic selectivity or degree of enrichment of $^{176}$Yb is 99.6 %.*

for precise wavelength determination pertaining to all even isotopes[6]. Further, the same set-up was used for process qualification in terms of spectroscopic selectivity. Towards this, the laser-atom interaction process in enrichment chamber was mimicked in the TOFMS and the effect on selectivity of the laser intensities was evaluated by analyzing the respective mass spectra. The intensities of the precisely tuned lasers were optimized to get maximum ion yield with spectroscopic selectivity of >99 %. The corresponding mass spectrum is presented in Fig.4. For clarity amplified view of the spectrum is also plotted (in red) and the relevant scale is shown along the right axis. Further, positions of all Yb isotopes are marked with dashed vertical lines. The optimum values of laser intensities were used in the actual enrichment experiment, where the lasers selectively ionized $^{176}$Yb atoms from a well-collimated Yb atomic beam having typical atomic number density of ~$10^{11}$/cc in the interaction zone of the enrichment chamber.

**Experimental Chamber for Enrichment Experiments**

The enrichment chamber houses all the modules necessary in enrichment process, *viz*. i) Yb atomic beam generator, ii) collimating structures for shaping the beam to minimize scattering as well as reducing the residual Doppler width in the laser propagation direction, iii) ion extraction assembly which extracts the photoions by using DC electric fields, and delivers them for deposition on the collector plate. A schematic of these modules is shown in Fig.5. The chamber is operated at $10^{-5}$ mbar or better vacuum.

**Atomic Beam Generator**

The atomic beam generator consisted of a tungsten crucible meticulously designed based on extensive thermal analysis, holding small chunks of ytterbium. The crucible was heated to 700K by radiative heat transfer from resistively heated tungsten filaments surrounding it to get atom number density of ~$10^{13}$/cc at source. The evaporated atoms escaped from the crucible slit through collimating structures in the form of smaller compartmentalized channels along beam axis. The channel dimensions were designed for reduction of Doppler width along both laser propagation direction and the direction of ion trajectories during collection to reduce nonselective pick-up of unwanted isotopes. The resulting atomic beam had reduced Doppler width of ~350MHz.

**Multi-pass Arrangement of Lasers to Enhance Atom Accessibility**

The three lasers tuned to $^{176}$Yb transitions having good spatial overlap and optimum temporal synchronization were passed through the ionization region of the enrichment chamber. The combined beam with cross-sectional area of 12mm x 10mm intersected the atomic beam multiple times using a specially designed multi-pass mirror assembly to extend the interaction region along the direction of atomic

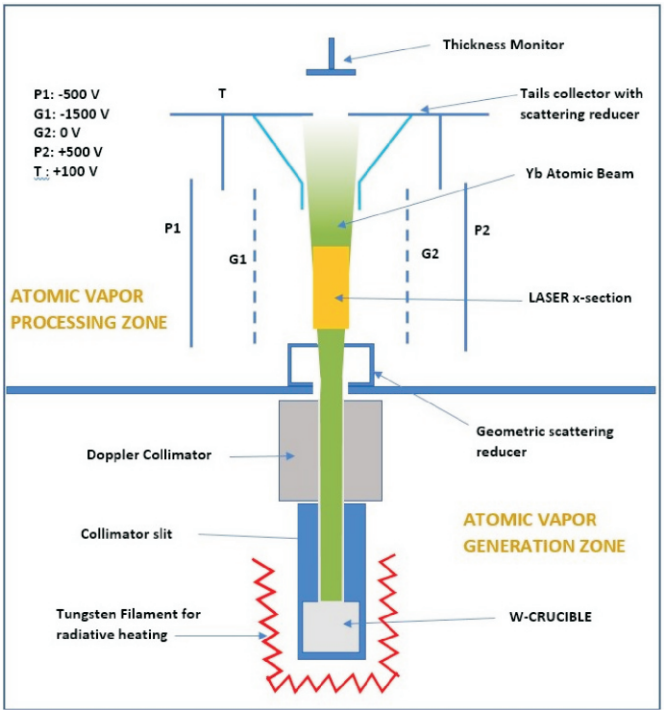


*Fig.5: Schematic of the modules of experimental chamber necessary in enrichment process where vapour generation zone, Doppler width reducer zone and ion generation (laser-atoms interaction zone) and collection zone are marked appropriately. Typical voltages applied to ion collector (P1, G1)) /repeller (P2, G2) grids and plates are also shown.*

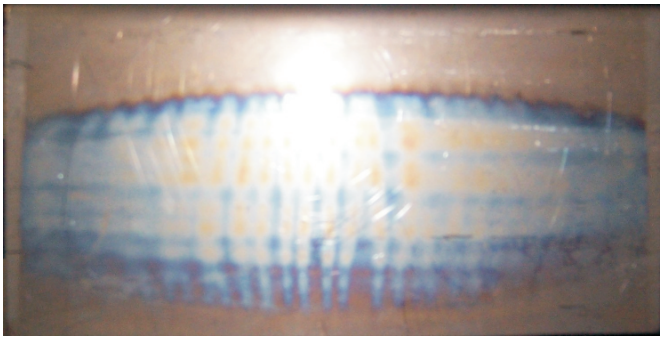

*Fig.6: A photograph showing deposition of photoions on the collector plate.*

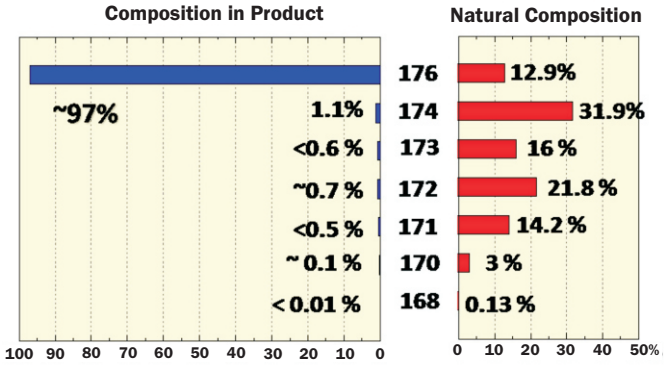


*Fig.7: Graphical representation of the isotopic composition in the feed (right) and product (left).*

beam resulting in total ionization volume of dimensions of 120mm x 12mm x 45mm. The multi-pass arrangement ensured that at least 90% of the atoms in the beam were irradiated by the lasers at least once, thus reducing sample loss and increasing collection rate.

**Ion Extraction and Collection Assembly**

The photoions generated in the process were directed towards collector plate by use of DC electric field. The ion collection assembly as schematically represented in Fig.5 consists of repeller plate, repeller grid, collector grid and collector plate as shown. This design facilitated significant reduction in self-sputtering of product ions as well as non-selective deposition of neutrals due to geometrical scattering from the primary as well as secondary sources. The DC extraction field was set in the range 200-400V/cm in the ionization region located between the collection and repeller grids to minimize the plasma effects. The collection plate was kept at ~500-850V generating a repelling effect on the ions and decelerating them, thus enabling their soft landing on the collector plate, consequently minimizing the self-sputtering[7]. The neutral atomic beam was collected on a tails collector which also had provision to measure atom flux using a quartz crystal based thickness monitor. Typical number density of the Yb atoms in the ionization region was ~$10^{11}$ atoms/cc.

**Results and Analysis**

A photograph of the collector plate is shown in Fig.6 in which Yb ions deposited on the plate are clearly seen. Consequent to the enrichment experiment, the collector plates were eluted with nitric acid to remove the deposited Yb isotope. Small parts of this liquid sample were used for diagnosis to determine the quality and quantity of the product using ICPMS and TIMS techniques at ACD and EmA&ID, BARC, respectively. The isotopic composition of the product based on their evaluation is depicted in Fig.7 along with natural composition of Yb isotopes. After completion of analysis the product was given to RPhD for neutron irradiation in Dhruva reactor for generation of the medical isotope $^{177}$Lu. At present, $^{177}$Lu thus produced is being evaluated for clinical trials.

We have performed a series of enrichment experiments in our test set-up for $^{176}$Yb which yielded better than 95% degree of enrichment from its natural abundance of 12.9% with 5-7mg/hour production rates, showing excellent consistency and reproducibility.

Among other isotopes of Yb, apart from $^{176}$Yb, the isotopes $^{168}$Yb and $^{174}$Yb also have applications in radiopharmaceutical industry as in pure form they can be used to produce the medical isotopes $^{169}$Yb and $^{175}$Yb, respectively. Further, $^{169}$Yb has industrial applications as well. The technology developed for enrichment of $^{176}$Yb is easily extendable to these isotopes. Consequently, we have performed enrichment experiments for production of isotopically pure $^{168}$Yb and $^{174}$Yb as well. Towards this, same methodology developed for $^{176}$Yb was followed to determine the transition wavelengths pertaining to selective photoionization scheme for each isotope[8,9]. Further, the selective laser-atom interaction process was qualified for spectroscopic selectivity better than 99% and the optimized laser parameters were used for actual enrichment experiments, in which 98% enriched $^{174}$Yb and 15% enriched $^{168}$Yb were collected successfully. Fig.8 shows photograph of the enriched product recovered in process runs for the Yb isotopes $^{176}$Yb, $^{174}$Yb and $^{168}$Yb.

Before every enrichment run, the laser-atom interaction is qualified for process parameter optimization for spectroscopic selectivity of >99%. However, the actual selectivity realized in experiments is on lower side. This is credited to two factors. Firstly, the nonselective processes like neutral atom scattering from secondary sources, *etc.* deposit


*Fig.8: Sample product in liquid form recovered from enrichment experiments for Yb isotopes $^{176}$Yb, $^{174}$Yb and $^{168}$Yb, respectively.*

Yb atoms on collector plate non-selectively. Secondly, the residual Doppler broadening inside enrichment chamber (~350MHz) is much more than that during qualification experiment in TOFMS. This results in larger overlap between lasers tuned to the required isotope and spectral lines of unwanted isotopes leading to reduction in spectroscopic selectivity. The first factor is significant in enrichment of $^{168}$Yb, owing to the fact that a small percentage of non-selective deposition on collector from the atomic beam is substantially large in comparison with the selectively deposited $^{168}$Yb photoions, which by abundance are only 0.13% in the atomic beam. The second factor is more important in enrichment of $^{176}$Yb as the separations between spectral lines of $^{176}$Yb and those of odd Yb isotopes are very small, particularly, in second step. Consequently, the degree of enrichment realized in collection of $^{168}$Yb is much smaller as compared to the other two isotopes, albeit it is at par with the enriched $^{168}$Yb product requirement in medical and industrial sector.

## Conclusion

In summary, ATLA Facility has extended the existing capabilities of laser based isotope selective resonance ionization technology to include medical isotopes, $^{176}$Yb, $^{168}$Yb and $^{174}$Yb. Enrichment of Yb isotopes is particularly challenging owing to the overlapping nature of the spectral lines of naturally existing isotopes. It necessitates use of narrow line width lasers to achieve requisite selectivity. To cater to this, we have successfully developed single longitudinal mode process dye lasers indigenously with high average powers and high repetition rates and pumped by CVLs and/or DPSSLs. A protocol is established for precise determination of isotope specific transition wavelengths and qualification of the selective ionization process in terms of laser intensities. Well collimated atomic beam of Yb atoms is generated with residual Doppler width of ~350MHz in the interaction region. The photoions resulting from selective ionization are collected by use of soft landing technique to avoid self-sputtering. We have realized >95% enrichment in $^{176}$Yb with 5-7mg/hr production rate with high reproducibility. Further, same process is employed for enrichment of $^{174}$Yb and $^{168}$Yb to realize >98% enriched $^{174}$Yb and 15% enriched $^{168}$Yb. At present, $^{177}$Lu produced by neutron irradiation of the enriched $^{176}$Yb from our facility is being evaluated in clinical trials.

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