Bombay Technologist

INTERVIEW

An interview with Prof. Jayant Khandare

About Prof. Jayant Khandare:

Prof. Jayant Khandare is the MD and Chief Scientific Officer of Pune-based R&D Company, Actorius Innovations and Research Pvt Ltd. (AIR) and also a respected professor of Pharmacy at the Research Cell of MITWPU, Pune. After completing his Bachelors and Masters in Pharmacy, he received a Ph.D. in Polymer Chemistry from NCL, Pune and went on to do two postdoctoral tenures in the USA. He was awarded the prestigious Alexander von Humboldt Experienced Researcher Fellowship in 2011 for his contribution in the field of macromolecular chemistry and worked for a year at the Freie University, Berlin, for the same. As a senior research scientist and founder of the Polymer Chemistry Group at Piramal Healthcare Ltd., he contributed greatly to the development of the organization. Khandare Sir, being extremely prolific in his research, has a whooping number of 45 research papers to his name and a remarkable total of 14 US/PCT filed patents. His areas of interest include cancer biology, chemical engineering, polymer chemistry, macromolecular chemistry, targeted drug delivery systems, cellular imaging, 3D cancer cell scaffolds and nanoparticles. His brainchild, Actorius, has come up with the 'OncoDiscover Liquid Biopsy Technology'; the second of its kind in the world and the first in India. It was the first non-predicative device to receive License for Manufacture under the new Medical Device Rules (MDR 2017). This novel technology aims at combating metastasis and secondary tumor growth of epithelial origin cancers at an earlier stage. Apart from this, Actorius strives for formulating pharmaceutically crucial drug delivery and GI imaging systems. Sir has also worked with several organizations to provide impetus to the field of scientific research.

1. What was the motivating factor behind establishing the Polymer Chemistry Group and AIR?

First of all, I would profusely like to thank Bombay Technologist and the professor faculty who considered me to be a part of this journal. It's a pleasure, privilege and honor to be here today.

Back then, the Polymer innovation or Polymer technology, a drug discovery company, was aspiring to discover new drugs, new chemical entities and the organization was investing a lot of time and funds in bringing the best of the scientific temperaments and minds from all over the world, majorly from the US. I was very fortunate to be under their radar and was called back from the US for the same. I might not have come back to India if that wasn't the case. We all had impressive resumes in medicine and therapeutics. My job in the first tenure was as a drug discovery formulation expertise scientist. However, in the second tenure, I didn't want to come back to the same role after completing the Alexander von Humboldt scholarship. I then took up the role of senior research scientist. The degree of freedom that our Chief Scientific Officer, Dr. Sharma, provided us with was commendable.

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2. You are an epitome of the confluence of academia and industry. Which one do you prefer over the other; and why?

I must say, the questions have been designed very smartly. It's like a wheel. When Newton came up with his observation of gravitational fall, there was lack of fundamental understanding of laws. That is not the case now. From around the past 400 centuries, advances in research have been documented well. At any given point of time, researchers, whether fundamental researchers or applied, do not predict the outcome of their work. As an academician, this is always challenging and inspiring. Once you practice being a researcher for a decade or two, a few are able to convert from research to technology or innovation. You cannot build incremental technology without understanding the fundamental sciences. It helps for an innovator to have a research background in order to enrich and propagate better innovations. Thus, fundamental sciences are catalyst for innovation and I personally enjoy both, academia and industry.

3. How has the chemical industry evolved over the years and where is it headed now?

Post independence, India caught up with the basic needs of society with respect to medicine. Recently, wonderful programs for pharmaceutical sciences have been developed. Even ICT has played a crucial role in building the shape of pharmaceutical and chemical sciences' industry. The legacy that has been built with respect to the drugs and other products that have been synthesized is now process driven. I was happy to read that the Harvard school has named their Chemistry Department after Dr Khwaja Abdul Hamied- Cipla's founder. To name a department in a foreign country after the name of a veteran scientist of India speaks volumes about how much the chemical industry has grown. In pharmaceutical sciences, we have been able to provide and manufacture quality medicines at a very affordable price, which have been made available to the highest and lowest strata of society. The point to improve is that we are still secondary supporters to the innovations. We are the world's second largest pharmaceutical products exporters. However, we still depend on other countries for drugs and other therapeutics. There is still scope to improve through the young innovators. In short, we have come a long way, but there is still a long way to go.

4. What is the (MOA) Mechanism of Action of OncoDiscover and how does it stand out from other tests that determine metastasis due to CTC (Circulating Tumor Cells)?

I am very comfortable in answering this question because it stands in my line. All of us are aware that cancer incidences are on the rise. Published in 2018, the Global Cancer Data showed 18 million plus active cases. Mortality in 2018 was about 9.5 million people. The predictions for the coming decade are terrible. Cases are predicted to be more than 30 million people a year, despite the great research in cancer, with predominant focus from US and European researchers and lot of money being spent by the pharmaceutical companies in discovering new drugs. The main reason for a rise in these cases is the increase in geriatric population because the survival rate is increasing and more people are leading healthier lives. The average survival for Indians used to be 45 years then around 50 years and is now 65 years. As the human body deteriorates, genetic mutations are going to be caused and therefore the numbers are going to stand tall. Head and neck cancer is the most common in India. Breast and uterine cancer is common among females and lung cancer, among males. Early detection of cancer is the key in increasing chances of survival. It is to be noted that 90% of the patients died because of metastasis and not due to the primary cancers. However, treatments are done extensively for the primary cancers. Blood is taken from the patient and the tumor cells are accounted for. The circulating tumor cells enter the peripheral blood in the circulatory system. They tumor then begins to grow in the substrate organs and is many a times undetectable due to a limit on the sensitivity of CT and PET scans. Around 1 gram of a tumor can shed almost 1 million CTC. We are the only company in India to get a Medical Device License in cancer diagnostics for circulating tumor cells detection and isolation. The first objective is detecting

metastasis at an earlier stage, to increase chance of survival. The second is to gauge how well the patient is responding to the treatment. OncoDiscover also helps to identify relapse. In epithelial cancers, if CT scan does not detect any tumor, we will say that the cancer has been cured, which might not be the case, as the CTC will not be determined. Thankfully, a solution came to this in 2004, but its cost was $2,600, thus an unmet need in India. This was the inspiration for our journey. We are able to detect 80% of the epithelial cancers from this technology. An antibody is hooked onto the material which then interacts with these CTC. The concept of immunomagnetic system is applied, wherein the anatomy is reached on is the fluorescent microscope which runs the samples. A group of hospitals in Dubai was surprised to hear that our turnaround time is merely a few hours whereas hey take around 14 to 16 days to produce the results. Thus, this is the mechanism of action of OncoDiscover.

5. You have come up with a DDS that specifically targets ligands for cancer cells and also a gastro-retentive-pulsatile NDDS. What are the characteristics of these DDS?

Targeted therapeutics using regulation system or liposome systems are there in the market, what is not there is an antibody system and it requires billions of Dollars and Phase 1, Phase 2 and Phase 3 studies. On 1st December, we entered into a new phase, with funding from international industries and have begun our thought process in bringing targeted drug therapy therapeutics. I'm very glad that we got good startup funds from the international company in spite of the project having high risk and possibility of failure. Targeted drug delivery systems are going to be the next 3rd generation cancer therapeutics. First is your free form of a drug like a class of palatinates; they are wonderful drugs which are established but not highly efficient, they're not targeted. Therefore, the second line of treatment is using this drug delivery system like liposome drug delivery, which came in 1995. The next one is that can target this therapy to specific cancer cells which has always been a academic thought process. I'm indeed very happy that in two years from now, we will be the pioneers from India, for the anti body based systems in clinical studies. We are very glad to state that we develop a technology which can deliver a drug to colon. In US and Europe about 60 to 70% of the population has intestinal borne diseases or syndromes due to food habits or gastric retention. Hence, inflammation of bowel is highly common. However, therapeutics for this has not been addressed well because you need to carry your drug from stomach to intestine to colon. This process takes about 6 to 8 hours and there are no drug delivery systems which can sustain 6 hours of very vigorous acidic and alkaline pH. Hence, we started our program with this kind of a thought process, where we would make capsules from very ordinary available material which will have a much delayed extend-release profile. The Government of India and Department of Biotechnology funded us for last 4/5 years. We finished India's first novel drug delivery system for this cause with a very profound outcome. But it will take at least two years from now to actually come in the market, and has a travel path of almost 7 years, with a spending of 1 Cr. Another international company has come forward to take up this technology for manufacturing in that country.

As you can see, the starting materials have almost no cost. The pathway of actually transforming any idea to technology is very extensive. We have several other NDDS projects which are being supported by UK based companies and other local inventors.

Around 6 NDDS technologies are in the pipeline and we have filled 2 patents. One technology of ours has been licensed out to Indian pharmaceutical companies, which is a production of sustained-release diabetic drugs that are smaller in size by 25% and are manufactured in tones in 24 hours instead of 10 days. Reduction in product size increases patient compliance. NDDS are one of the key interests of our company.

6. We went through several articles/papers of yours and noticed that you have emphasized on the use of polymer protection for drugs and prodrugs; with a lot of work on dendrimer and PEG as well. What are the pros of these polymer conjugates?

Good question. FDA calls for several standards of what can be injected into the body. We do fundamental research in polymeric delivery systems which are for a systemic delivery. Anticancer drugs are predominantly delivered using FDA polymer, which is polyethylene glycol. It is a liner polymer, hence expensive, but is water soluble and has its own physic-chemical advantages. I have done insightful research on this topic. Cancer therapy requires drugs to be delivered at the cellular level-at the cytoplasm of nuclear sites and dendrimers are a catchy polymer for that. They are hyper branched polymers which possess exceptionally high cationic group charge and hence require an ideal water soluble chemistry which would offer a biocompatibility that includes the lower potential. Many companies considered this pathway to be unsafe and hence dendrimers were pulled off from clinical trials.

7. What are your views on the rapidly growing field of nanomedicine and nanotherapeutics?

Nanotherapeutics includes everything that we inject in blood, whether it is glucose supplements or large volume parenterals. We were not capable of examining the size of the material until 1997. Nanotherapeutics is using a combination of materials, in the size below 16nm. Considering PEG, its radius of gyration would be limited in a oversize, however there are certain materials whose size can be reduced to nano. Nanoparticles are driven by pharmacokinetics and dynamics. From this, we do understand that smaller drug size is preferred by the body, the immunological responses are not triggered and a better implication is provided. The translations in nanomedicine, however, are still not at the level at which they were anticipated. New technologies need regulatory pathways and descriptions and it is not only ideas and concepts written in publications that make your innovations work, billions of dollars are required for putting them in action. Several small-scale companies aboard are focusing on nanotherapeutics. So, in India, nanomedicine is not at the forefront yet, and will require a lot of impetus to do so. However, it is an established field in foreign countries. Young innovators in the future should keep this as one of your goals since nanomedicine is going to be of key importance in technology in future.

8. Which projects of yours are currently in the pipeline?

Great question. I am very happy to share that OncoDiscover is now licensed to Cyprus, Canada, Bangladesh and Thailand. It is one technological challenge that we completed. The next challenge is to make it more widely available in India, in all mainstream hospitals, so that it will reach the masses and that too at an affordable price. On October 12th, we filed a US patent for research regarding diagnostic symptoms of tumor cells. We are collaborating with a company in Los Angeles. The plan is to take the blood of the cancer patient, rid it off CTC and send the blood back into the patient's body, similar to the process seen in diabetes.

The filtering of CTC outside the body is a crucial job. The main aim in cancer treatment is to increase the survival time of the patient, since a progression-free normal life is anyway very rare. If this innovation works out, it will be an asset to cancer management therapeutics, but the cost for the same is around 150 million dollars. Cancer diagnostics are always very expensive. We predict that we will have the money in the coming 4 or 5 years. I am very glad and humbled to say that we are the only ones in the world to be working on this innovation.

9. As an integral part of a novel R&D company and a pharmacy professor, you are an inspiration to all those who wish to place foot in the field of research. What is your advice to these aspirants?

My advice is to not give any advice. Follow your dreams and find your destiny. Do not stop at the Bachelors level, because research is never going to be sufficient, irrespective of how much one does it. The more you research, the better understanding of technology and science, you will gain. As you keep on earning higher degrees, you will meet better advisors and fellow colleagues. Keep learning from what you see around you. Keep your focus on what you plan to do 10 years from now. The innovations we have today are going to limit your abilities 20 years from now and hence it is necessary for science to constantly get updated. This should be a part of

your philosophy as young innovators. Making an innovative product out of a similar one already available in the market is not going to count as an incremental share- you need to address unmet needs of the society. Keep yourself updated- keep reading about what is happening worldwide, in India, in centers like IITB and NCL. My advice would be to not start up with incremental innovations unless you have around 20 years of experience. Great ideas need great teams, network, coordination, cooperation and even great funding. Keep dreaming of your scientific journey and keep trying to use your knowledge to change the world.