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Companies leverage on Nanomedicine

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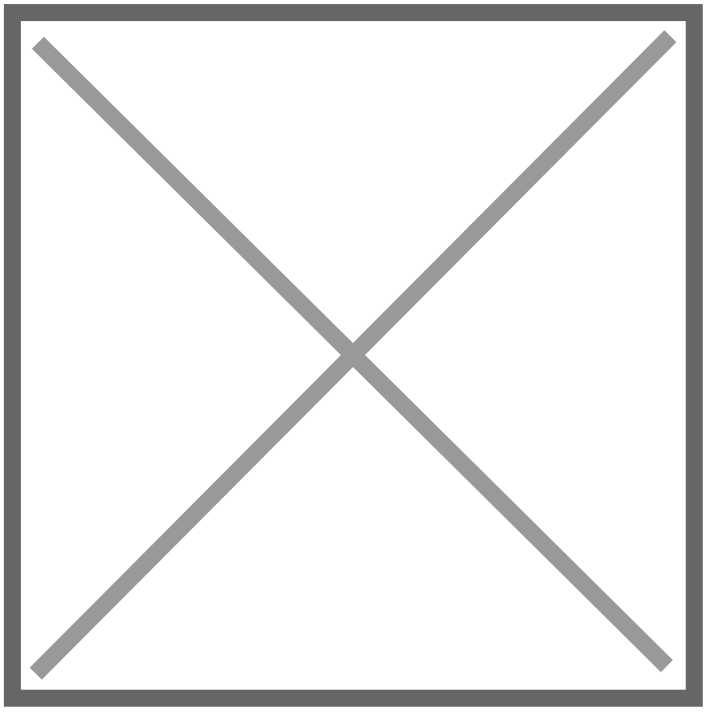

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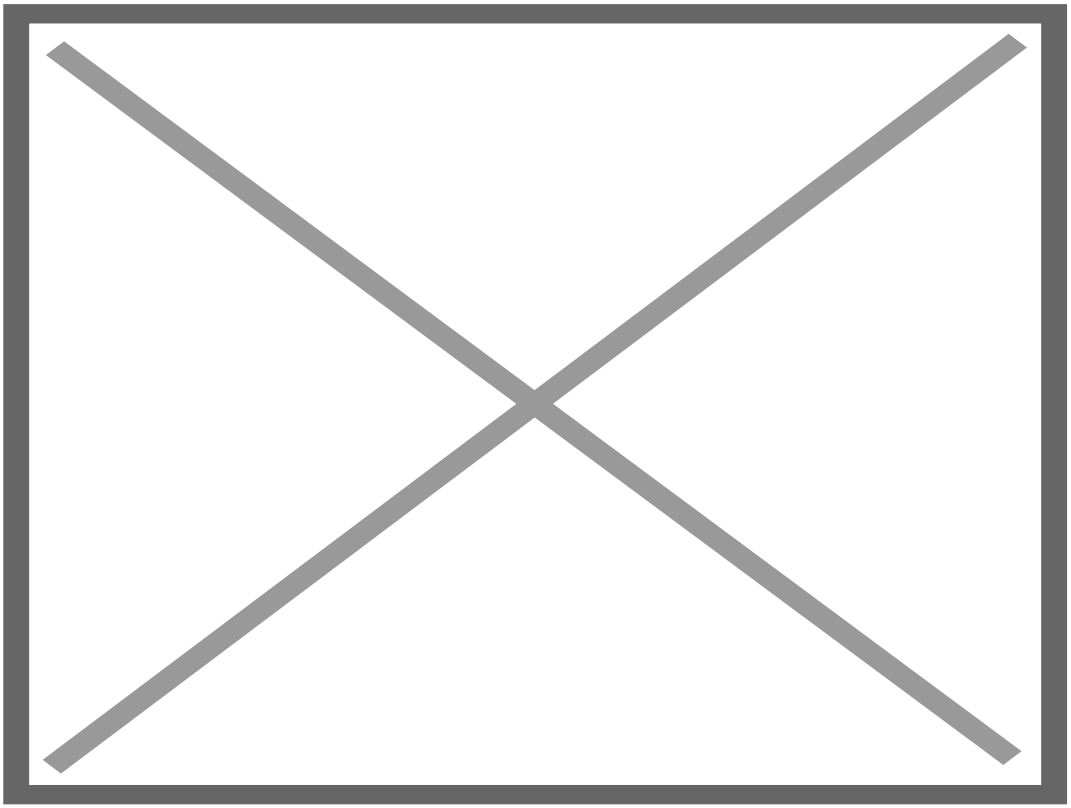


The remarkable properties of various nanomaterials have caught the attention of scientists, researchers, and manufacturers alike. The global market for nanotechnology is expected to reach $1 trillion by 2015. Ongoing research activities harness its potential for the overall betterment of the society.

Ã¢â?¬Å?Nanobiotechnology is an emerging area that provides unlimited opportunities in product development. This new technology speeds up diagnostic processes; develops accurate engineered nanotools for the prevention, diagnosis and

treatment of diseases; facilitates early detection of cancer, heart and other rare diseases; enhances drug discovery; enables targeted drug delivery; opens doors for nanomedicine by imparting stem cell applications; paves way for effective diagnosis and treatment of cardiovascular disease; and strengthens tissue engineering by providing bioactive nanomaterials for smart implantation,Ã¢â?¬? says Mr Puneet Mehrotra, director, Nano Science and Technology Consortium (NSTC).

With over 250 corporate and institutional members, NSTC is one-of-its-kind organization in India. The NSTC focuses on technology transfer; facilitating global and local business opportunities, training, education, publications and collaborative processes in nanotechnology.

The Industry
Indian companies like Lifecare Innovations, Dabur Research Foundation and Imgenex India; and research institutes such as Nichi-In Center for Regenerative Medicine (NCRM) are focused on developing nanomedicine. Nanomedicine makes use of nanoparticles for developing newer drug delivery systems against cancer, diabetes, fungal infections and viral infections.

Since its inception in 2000, Haryana-based Lifecare Innovations has been working on nano drugs. The company has a number of products at different stages of development. Their first product, Fungisome, a nanosomal amphotericin B, is India's first nano drug. The drug offered the opportunity to make a precision targeted delivery of encapsulated amphotericin B to life-threatening fungal infections. Ã¢â?¬Å?In 2003, we started work on application of its proprietary oral sustained release nanotechnology Ã¢â?¬â?? the first application being anti-TB drugs combinations. The preclinical studies were completed four-years ago, but the Drug Controller General of India (DCGI) took three years to understand and grant the company to conduct phase I clinical trial. Promising results of the nano drugs for TB delineated that the long duration sustained release would help reduce dosing frequency from daily to two-three times a month, which would have understandable advantages of logistics, socio-economical and treatment economics. It is a celebrated technology in R&D circles but industry response is lukewarm as TB patients are predominantly served by government-controlled programs and industry is reluctant to invest is neglected diseases,Ã¢â?¬? says Dr Jitendra N Verma, managing director, Lifecare Innovations.

Applications of Nanobiotechnology

Nanopharmaceutical

Drug Discovery

- Gold nanoparticles and quantum dots are used for tracking molecular properties in livening cells.
- NanolaserÂ helps to halt the progression of neurodegenerative diseases.
- Nanoparticles enable cell targeting with attached small molecules.

Drug Delivery

- Protects drug against premature degradation
- Enables sustained release of a drug to maintain a long-lasting drug concentration
- Diminishes adverse side-effects
- Enhances efficacy of a drug by delivering the drug to the diseased tissue.

Drug Production

- Tablet design
- Tablet production system
- Tablet compression

Nanomedicine

- Nanodiagnostic devices
- Nanosurgery tools
- Nanooncology
- Nanoneurology
- Nanocardiology
- Nanoorthopedics
- Nanoophthalmology
- In treatment of infections

Tissue engineering

- In natural musculoskeletal tissues
- Nanofibrous scaffolds are used in bones, cartilages,Â Â Â muscles and ligaments

Ã¢â?¬Å?The experience of sustained Release Nano-TB, however, encouraged more applications. We are working as part of five-organization consortium including ICGEB, New Delhi; BITS, Pilani; and University of Toronto under ISTP Canada-DBT India collaborative program where we are responsible for developing single dose sustained release oral drug for malaria treatment. We have nano-antiinfectives, anti-cancer and anti-inflammatory drugs, and pain killers in pipeline. In the next three-to-five years, we aim to bring these novel drugs to the patients,Ã¢â?¬? adds Dr Verma.

Dabur Research Foundation (DRF), a contract research organization based in Uttar Pradesh, has developed and standardized electron and fluorescence microscopy-based methods, coupled with bioanalytical techniques like HPLC and LC/MS to quantitate intracellular uptake and localization of targeted nanoparticle devices. This technique enables it to evaluate the intracellular accumulation of drugs and its sub-cellular distribution and localization. This in-turn helps to form a correlation with the biological activity of nano-delivery systems. DRF currently offers these models as a service to pharma and biotech industry.

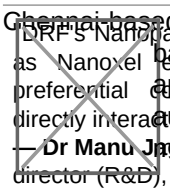
Ã¢â?¬Å?DRF developed and launched nanotech-based chemotherapy in India. This nanoscale drug delivery system for the widely used anti-cancer agent, paclitaxel, was the first-of-its-kind in India. The paclitaxel nano drug is a cremophor-free water soluble formulation and is indicated as a safe therapy for advanced breast, non-small cell lung and ovarian cancers,Ã¢â?¬? says Dr Manu Jaggi, director (R&D), Dabur Research Foundation.DRF's nanoparticle drug delivery devices such as Nanoxel enable the therapy to take a preferential course to cancerous cells and directly interact with tumor causing agents. This opens a larger window for anti-tumor activity. It also ensures that the patient receives full measure of the therapy while limiting the adverse side-effects and toxicity affected by the drug," adds Dr Jaggi.

Orissa-based biotech company Imgenex India is a leading developer of monoclonal antibodies in India. The company has been using nano particles in developing biosimilars, and has a strong program in the development of biosimilar therapeutic monoclonal antibodies (mAbs).

"Imgenex India plans to improve the efficacy of the biosimilar antibodies by encapsulating them in nanoparticles and make them as biobetters or biosuperiors, which may be defined as antibodies that are aimed at similar targets and carry similar indications as existing products, but are with improved stability and dosage," says Mr Sujay Singh, CEO and president, Imgenex India.

"The protein and peptide drugs can exploit the development of innovative systems which provide for controlled, prolonged or targeted delivery, improved stability during storage and delivery, reduced adverse effects, increased bioavailability, improved patient compliance and allow for administration through the desired route while coping with cost-containment therapeutic protocols. These can be achieved using nanotechnology. Delivery of osteoclast inhibitory peptides using nanotechnology-based platform for the treatment of osteoporosis is one of the major projects at Imgenex India," adds Mr Singh.

Imgenex India is also working on formulation of special media supplement to induce pluripotent stem cells (iPS cells) from adult somatic cells. The company plans to add nanoparticle-loaded recombinant transcription factor proteins that are required for iPS cell generation to the cell culture media. These nanoparticles will allow controlled release of transcription factors into the culture media for induction and maintenance of iPS cells from adult somatic cells. This project is being carried out by a SBIRI funding from the Department of Biology, India, in collaboration with Dr Sanjeeb Sahoo from Institute of Life Sciences, Orissa. This technology will provide the ability to create patient specific iPS cells for understanding disease progression and screen for therapeutic strategies.



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— **Dr Manu Jaggi**
director (R&D), Dabur Research Foundation

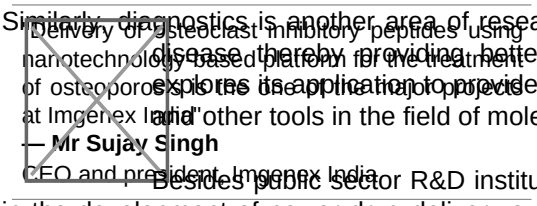
Chennai-based Nichi-In Center for Regenerative Medicine (NCRM) too has been working on developing a nanomaterial-based artificial cornea. NCRM is an Indo-Japan joint venture carrying out research, training and clinical applications protocol development in regenerative medicine, with emphasis on stem cells, progenitor cells and autologous adult cells with regenerative capability. NCRM is also developing a nanomaterial and processing methodology for lab-based expansion of hematopoietic stem cells, which would help blood cancer patients.

Commenting on NCRM's initiatives on nanobiotech, Dr Samuel JK Abraham, director, NCRM says, "NCRM has been working with approximately 270 different nanomaterials and technologies in specialties such as ophthalmology (corneal stem cell

regeneration), orthopedics (cartilage injury repair), and hematology (expansion of hematopoietic stem cells). Recently NCRM along with our global headquarters – Nichi-In International, Japan – and Kawamura Institute of Chemical Research, Japan, have filed a joint patent application on a nano-sheet which promotes the in vitro expansion of corneal endothelial precursors and their application in vivo, in treating corneal blindness."

In the anti-aging research we are working on developing nano-polymer scaffolds to sustain the cells in zero-gravity and micro-gravity so that the damages to cells during lab expansion or storage for longer periods could be minimized so as to preserve their youthfulness," adds
Dr Abraham.

Opportunities
India has a huge potential to market nanotech products. However, careful and selective investments in nanotechnology can certainly catalyze the country's economic development and in near future, could pave way for its transformation into a developed nation. Nanomedicine has bright growth prospects in India with its related research being carried out in various academic and scientific institution. Research includes designing of drugs with greater degree of cell specificity, improved therapeutic efficacy of delivered drug as well as to minimize its cytotoxicity-related adverse effects.


"Delivery of osteoclast inhibitory peptides using nanotechnology based platform for the treatment of osteoporosis is one of the major projects at Imgenex India"
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Similarly, diagnostics is another area of research that is investigated extensively with nanoparticle for early detection of the disease, thereby providing better prognosis. The undergoing research in the field of nanomedicine mainly explores its application to provide targeted drug therapy, diagnostics, tissue regeneration, cell culture, biosensors and other tools in the field of molecular biology.

Besides public sector R&D institutions, various companies in India are researching on nanomedicine, especially in the development of newer drug delivery systems against cancer, diabetes, fungal infections, viral infections and for gene therapy. "The pharmaceutical, biotechnology and biomedical companies in India are concentrating on nano-based platforms like fullerenes, nanotubes, quantum dots, nanopores, dendrimers, liposomes, magnetic nanoprobes and radio-controlled nanoparticles for developing smarter therapeutic and diagnostic modalities," observes Mr Singh of Imgenex India.

India has made significant inroads into the field of nanomedicine in the last decade. This includes areas such as nano-diagnostics (in-vitro and in-vivo sensing and imaging systems capable of quantifying and visualizing the levels of various bio-molecules at the cellular level), targeted drug delivery; and cell and tissue repair (synthetic growth of tissue by targeted delivery). "Other areas include development of nano-bioceramics that can repair bone and tissue; and aerosol sprays that use nanoparticles to deliver drugs for the treatment of lung cancer. This ability to manipulate biological systems at the molecular level and the scientific initiatives taken thus far will certainly contribute to medical advances in the years to come," says Dr Jaggi of DRF.

Challenges
Even though India has several opportunities in the area of nanomedicine, the country faces some challenges in the form of funding, IP and understanding the technology when it comes to global market.

"From my personal opinion, India is still in infancy with the nanomaterial development. When compared to the developed nations, we did not start basic research in nanomaterials well in advance and due to lack of such original technologies in materials, processes and methodologies we need to depend on already patented materials and methodologies to accomplish end-product developments," says Dr Abraham of NCRM.

"Indian researchers and industry both are glued to the generics and biosimiliars bandwagon that does not allow them to think anew and come up with a blockbuster. Regulatory regime also does not improve the situation. On one hand, new things that deserve approvals are hard to understand and so gets delayed, while on the other hand novel drug delivery system in the name of generics get clearance without requisite clinical trials. Same is the situation with clinicians. Any new drug introduced by an MNC despite having well-known and documented narrow activity becomes a drug of choice. For India to take advantage of its full potential of novel technologies, this mindset needs to change, " says Dr Verma of Lifecare Innovations.

According to Dr Verma one important change required is in the area of IP protection. Drugs, biotherapeutics, vaccines and other healthcare products take around 10-15 years from concept to commercialization because of requisite trials and resultant multi-stage regulatory clearance process, whereas non-medical innovations can hit the market immediately. This long duration consumes major part of the patent life that serves as huge disincentive to develop new drugs. If newer solutions are expected, patent life must be granted for a post-marketing period.

Much of the work done until now has been focused on applications of nanomedicine in drug discovery and drug delivery. Sharing his thoughts on the advantages of nanomedicine, Dr Jaggi of DRF says "the miniaturization of analytical, diagnostic

procedures is another important area which results in performing analytical procedures in the lab on a much smaller scale. In the long-term, nanomedicine is expected to provide the ability to undertake in vivo diagnostics coupled with targeted and focused therapy."

Looking at the opportunities and potential applications of nanobiotechnology, the Government of India has been encouraging the growth of the sector by funding nanobiotech projects under various programs of DBT, DST, DSIR and ICMR. The Karnataka government too is promoting nanobiotechnology and has allocated 14 acres of land to set up the Indian Institute of Nano Science and Technology (IINST) in Bangalore to strengthen nanobiotech R&D. Such government initiatives will help India to move ahead in the nanobiotech race.