Media Coverage

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Competitive Edge through NDDS

Severe competition, the need to maximize revenues, & combating patent expiries are forcing pharmaceutical companies to roll up their sleeves & seek out novel drug delivery systems. It is estimated that NDDS products consitute 17% of the world's pharma market, amounting to $104 billion. Similar trends are visible in India. The main segments include controlled release, needle-less injection, injectable/impantable polymer systems, transdermal, transnasal, pulmonary, transmucosal, rectal, liposomal drug delivery, cell/gene therapy & others. Once a small market, the NDDS market is now poised for significant growth & holds great opportunities for both current players & new entrants.

Increasing losses due to patient expiries are leading pharmaceutical & biotech companies to invest in new drug delivery system (NDDS) technologies in a major way. New drug delivery technologies are becoming a critical strategy for them to maintain a strong presence in these cutthroat markets as they offer the potential to enhance the life cycle of established drugs.

Novel Drug Delivery Systems (NDDS) is a new drug delivery technology, which improves patient compliance, raises the drugs pharmacokinetics (absorption, distribution & metabolism) profile reduces the dosage frequency or adverse effects & combines therapeutically complementry drugs into one formulation. With the help of this novel method, a drug delivered can have a significant effect on its efficacy. Some drugs have an optimum concentration range within which maximum benefit is derived & concentrations above or below this range can be toxic or produce no therapeutic benefit at all.

On the other hand, the very slow progress in the efficacy of the treatment of severe diseases, has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, non specific toxicity, immunogenicity, biorecognition & efficacy of drugs were generated. These new strategies , often called drug delivery system (DDS), are based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry & molecular biology.

Controlled drug release & subsequent biodegradation are important for developing successful formation. Potential release mechanisms involve desoption of surface bound/absorbed drugs, diffusion through the carrier matrix, diffusion (in the case of manocapsules) through the carrier wall, carrier matrix erosion & a combined erosion/diffusion process. The mode of delivery can make the difference for a drugs success & failure, as the choice of a drug is often influenced by the way the medicine is administered.
Sustained or continuous release of a drug involves polymers that release the drug at a controlled rate due to diffusion out of the polymer or by degradation of the polymer over time. Pulsatile release is often the preferred method of drug delivery, as it closely mimics the way by which the body naturally produces hormones such as insulin. It is achieved by using drug carrying polymers that respond to specific stimuli (e.g. Exposure to light, changes in pH or temperature).

Drug Delivery Carriers

Colloidal drug carrier systems such as micellar solutions, veside & liquid crystal dispersions, as well as nanoparticle dispersions, as well as nanoparticle dispersions consisting of small particles of 10-400 nm diameters show great promise as drug delivery systems. When developing these formulations, the goal is to obtain systems with optimized drug loading & release properties, long shelf life & low toxicity. The incorporated drug participates in the microstructure of the system, & may even influence it due to molecular interactions, especially if the drug possesses amphiphilic and/or mesogenic properties.

Troikaa Pharmaceuticals Ltd, one of the fastest growing Ahmedabad based healthcare companies, has been focusing on NDDS in a major way & has filed patents for six products in the parenteral, oral, buccal & transdermal segments.

Mr. Ketan Patel, Managing Director, Troikaa Pharma, says, "NDDS for tablet dosage forms has been steadily evolving. Several companies have marketed slow/extended release tablets with an objective or reducing the number of doses. However, there have been very few developments in drug delivery systems for parenteral & topical preparations. In fact, the NDDS portfolio contributes 30% of our sales turnover."

Recent Trends

The global market for advanced drug delivery systems was more than $ 37.9 billion in 2000 & is estimated to grow & reach $ 75 billion by 2005. The main segments include controlled release, needle-less injection, injectable/impantable polymer systems, transdermal, transnasal, pulmonary, transmucosal, rectal, liposomal drug delivery, cell/gene therapy & others. Developments within this market are continuing at a rapid pace, especially in the area of alternatives to injected macromolecules, as drug formulations seek to cash in on the $ 6.2 billion worldwide market for genetically engineered protein & peptide drugs & other biological therapeutics.

In recent times, certain Indian pharma companies have made inroads in developing NDDS for parenteral preparations. Amphotericin injection by Troikaa Pharma is a classic example. Commenting on the recent trends in NDDS, Dr. Brajesh Varshney, Senior Scientist, NDDS department, Intas Biopharmaceuticals Limited said, "The current trends in NDDS have been to evaluate & develop formulations, which can be used to circumvent invasive administrations. These are expected to increase the drug bioavailability (e.g. Transmucosal delivery route). Clearly, to achieve this, the focus has been shifted to biodegradable carriers (polymers) using nanotechnology."

Intas Biopharmaceuticals Ltd (IBPL) is one of the largest growing biopharmaceutical companies in India. As an independent entity of the Intas group, the company has carved a niche in the biotechnology sector in the country. The company has fully integrated biopharmaceutical operations at Ahmedabad, Gujarat with a dedicated multidisciplinary team of more than 200 young & experienced personnel with diversified educational & technical backgrounds.

Echoing the same sentiment, Dr. Brajesh Varshney, Senior Scientist, NDDS department, IBPL, added, "There are certain parameters that biopharmaceutical companies need to follow before forging alliances with drug delivery companies. Drug delivery companies need to have a track record of working on FDA-approved excipients, which will not infringe on any patents. The company should have wide-ranging experience in working with various oils, polymers, surfactants, stabilizers, preservatives, etc." An insulin pump is a classic example of NDDS. It is a medical device used for the administration of insulin in the treatment of diabetes mellitus, also known as continuous subcutaneous insulin infusion therapy.

Current market for NDDS in India

It is estimated that NDDS products constitute 17% of the world's pharma market, amounting to $104 billion. Similar trends are visible in India. The current market for NDDS in India stands at around 4to6% of the total pharmaceutical market. Dr. Ajay Kumar Gupta, Scientist, NDDS department, IBPL, reveals, "NDDS for protein/peptide drugs is at a very nascent market in India. The first FDA-cleared PLGA product was the Lupron Depot drug-delivery system (TAP Pharmaceutical Inc.) Sun Pharma has been in the market with this drug."

Nano-enabled drug delivery system

Nanotechnology is one of the most promising areas for drug delivery. For the past two decades, researchers have appreciated the potential benefits of nanotechnology in providing vast improvements in drug delivery & drug targeting. Improving delivery techniques that minimize toxicity & improve efficacy offers great potential benefits to patients, & opens up new markets for pharmaceutical & drug delivery companies. Other approaches to drug delivery are focused on crossing particular physical barriers, such as the blood brain barrier, in order to better target the drug & improve its effectiveness; or on finding alternative & acceptable routes for the delivery of protein drugs other than via the gastro-intestinal tract, where degradation can occur.

Mr. Ketan Patel, MD of Troikaa Pharma, says, "One clearly defined advantage of nanotechnology in oral dosing is to provide augmented absorption of water insoluble drugs from GI tract. At the moment, however, no Indian company has come up with any such NDDS. Other advantages of nanotechnology could be to improve targeted drug delivery to carcinogenic tumors. This is now deeply investigated in the US, since such NDDS would

be able to target the tumors & hence reduce the side effects of anti-cancer drugs."

Dr. Ajay Kumar Gupta, Scientist, NDDS department, IBPL, opined, "Nano-enabled drugs confer advantages on the solubility of poorly-soluble drugs, avoidance of first-pass metabolism, controlled release, enhanced bio-availability & minimizing the dose as well as the dosing frequency, thereby increasing the patient compliance."

"We have a special focus on R&D initiatives, which concentrates on Future Novel Technology Development. The company has filed patents for six of its products," said Dr. Rustom Mody, Director (Quality & Research), IBPL. The company's NDDS portfolio includes:

- Dynapar Tablets: A pain reliever.
- Dynapar Injections: These are painless as compared to conventional Diclofenac injections & also provide uncompromised bioavailability in obese patients.
- Feno TG: This is a supra bioavailable version of Fenofibrate Tablets. Each tablet of Feno TG contains 160 mg of fenofibrate with augmented absorption. Hence, it is bioequivalent to conventional 200 mg fenofibrate capsules.
- Tess Buccal Paste: It is buccal paste designed to adhere to the oral mucosa, which is wet & slippery & thereby provides rapid healing to mouth ulcers.
- Currently, IBPL is working on the polymer-based particulate delivery system & micro emulsion based transmucosal delivery system. The perceived advantages are – controlled release, reduction in dosing frequency, non-invasive administration & increased patient compliance, "informed Dr. Brajesh Varshney, Senior Scientist, NDDS department, IBPL.

Awareness about NDDS & its advantages compared to normal drugs.

To minimize drug degradation & loss, to prevent harmful side effects & to increase the drug bioavailability & the fraction of the drug accumulated in the required zone, various drug delivery & drug targeting systems are currently under development.

A patient consuming a drug three to four times a day can now, on account of NDDS, needs to take the same medicine only once or twice daily. NDDS has become very popular in patients suffering from chronic diseases such as AIDS & Cancer.

"There is no denying that the awareness about benefits of NDDS amongst medical professionals is very low. We at Troikaa have a team of 600 representatives. Our representatives are trained to educate the doctors on the merits of NDDS products promoted by our company," said Mr. Ketan Patel.

Dr. Varshney added, "NDDS is a new initiative at IBPL. Within a short span of time, a quantifiable progress has been made in the projects. Two patent applications have already been made. Having recognized the importance of this new field, the Government of India has funded around two projects in NDDS."

Technology development in NDDS.

NDDS for patients, means more safety, efficacy & a better compliance; whereas, for drug companies, product innovation in the form NDDS is a big opportunity to rejuvenate their brands by making products easier to administer, more patient-friendly & ultimately more effective, while augmenting their revenues at the same time.

"We are evaluating various biodegradable polymers & excipients to develop micro-particles as potential drug carriers. The polymers are of the polyester family, which includes polyglycolides & polylactides, studies revolve around the stability of the drug loaded micro-particles, in release kinetics, PK/PD profiles etc. & evaluation of various oils & surfactants to develop micro-emulsion based transmucosal delivery systems. These systems, being novel in nature, the compatibility of the protein/peptide drug with various oils/surfactants is under study, " said Sumit Shah & Sumita Paul, Research Associates, NDDS department, IBPL.

Future of NDDS

Once a small market, the NDDS market is now poised for significant growth & holds great opportunities for both current players & new entrants. "NDDS is not meant to replace the conventional methods of drug delivery. Besides, NDDS is not restricted to oral drug delivery. NDDS becomes the preferred dosage form when conventional drug delivery leaves shortcomings, in such cases, an appropriate NDDS can eventually replace the conventional drug delivery," said Mr. Patel. "Troikaa intends to file more patents in the NDDS domain. We will be commercializing the NDDS products, which are found to provide distinct advantages over conventional formulations in clinical trials. New NDDS products will therefore remain the mainstay of our future business plans," he added.

Dr. Gupta, IBPL, explained, "further, the potential for NDDS is very high. We are already seeing a trend of a switchover from the conventional oral delivery system for small drug molecules. Matrix tablets, gastro-retentive tablets, fast dissolving tablets, transdermal patches etc, are gaining prominence. Biotech drugs are likely to follow the trend."

Dr. Rustom Mody, Director (Quality & Research), IBPL, informed "We intend to work on various innovative platforms in the NDDS laboratory. Beginning with polymer-based micro-particles & micro-emulsions, the laboratory intends to go a step further & exploit areas of pegylation, nanoparticles, dendrimers & liposomes, as well as evaluate & develop alternate routes for drug delivery."
