

Developing improved oral reformulations of poorly soluble drugs using the LipoCeramic™ nanoparticle encapsulation technology



The commercialisation company
of the University of South Australia

Researchers at The University of South Australia have developed revolutionary drug delivery technology that has the potential to reformulate and significantly improve the delivery of poorly soluble drugs and cosmetics.

Technology Background

It is generally accepted that over 40% of therapeutic drugs available on the market are poorly soluble. While these drugs have efficacy and safety, their performance is far from optimal in terms of bioavailability and dose variability. Even at a late stage, many novel development programs are abandoned due to poor solubility of the therapeutic and difficulties with acceptable delivery parameters within a biological system. Solving the solubility issues of therapeutics is a priority area for the pharmaceutical industry because this leads to better therapeutics with lower doses, fewer side effects, and greater control.

The LipoCeramic™ technology addresses these issues and was developed by Prof. Clive Prestidge's team at the University of South Australia's Ian Wark Research Institute. The technology comprises methods of preparing micro-sized capsules composed of nano-scale particles, bio-compatible oils and other polymers. The solvent-free production process can load the capsules with poorly soluble (lipophilic) compounds of interest at high levels.

This controllable encapsulation process produces formulations in which the active compounds have greatly improved stability, solubility, and bioavailability with the added benefit of engineerable rates of release.

A number of rat in vivo studies have been conducted in which the delivery system performed significantly better than commercial products. The latest study involved the NSAID indomethacin and results showed:

- Loading levels up to 10% - significantly above drug solubility in the oil
- The drug in a stable molecular dispersion
- Solid state storage stability > 6 months under accelerated conditions
- Excellent capsule redispersibility in simulated body fluids
- Significantly increased release rate
- Superior *in-vivo* pharmacokinetics in comparison with indomethacin and Indocid®
- Bioavailability is significantly increased, up to 100% (versus 75% for Indocid®)
- Increased C_{max} and reduced T_{max} (less time to get more drug in system)

Application

The LipoCeramic™ nanoparticle encapsulation platform technology solves solubility problems for an incredibly wide range of drugs. The technology possesses a useful combination of competitive advantages over other drug delivery technologies. These advantages include:

1. A cold and solvent-free production process
2. Components that are already widely approved and used in industry and foods
3. Highly controllable drug release profiles (from slow to rapid)
4. Effective encapsulation for enhanced stability and solubility properties
5. Maintenance of active ingredient in its preferred (in this case hydrophobic) environment
6. In vivo drug bioavailability of 100%

Also, many blockbuster and other high-earning drugs on the market are in the process of coming off-patent with many others to follow over the coming years (patents of drugs worth \$37 Billion expired in 2005), with the result being the introduction of the drug in generic form by competitors and massive erosion of drug revenues.

As such there exists very strong demand from pharmaceutical companies for reformulating these drugs in novel value-added ways by improving the pharmacokinetics, solubility, and bioavailability of the drugs, and patenting these new formulations of their old drugs to effectively extend the patent life of the old compound.

The US drug delivery market was \$41 Billion in 2007 and oral delivery accounted for over half of this. The first model drug, celecoxib, is a well-known block buster drug marketed by Pfizer (as Celebrex) that is currently worth \$2.1 Billion annually. It suffers from some of the problems discussed and is a compound that is an excellent candidate for reformulation.

IP Position

On-going development of the technology has created a patent portfolio that covers the preparation of the delivery system, drug release properties, and specific applications for oral and dermal delivery.

There are currently two national phase patent applications active in Australia, Japan, Europe, USA, and Canada, in addition to patents 3 (a PCT application) and 4 (a provisional application) that cover specific embodiments of the underlying platform.

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