[S2-2] [10/10/2003(Fri) 10:00-10:25/ Grand Ballroom 103]

Recent Trends in the Development of Sustained-Release Dosage Forms

Jung Ju Kim

Pharmaceutical & Health Research Institute, AmorePacific R&D Center,

AmorePacific Corporation

Development of drug delivery systems has been recognized as one of portfolios to gain a competitive edge in pharmaceutical industry over 30 years. The application of drug delivery technologies offers pharmaceutical companies and patients several therapeutic benefits, including improving efficacy and adverse effect profiles, enhancing patient compliance and potentially regenerating unsuccessful drugs. With controlled-release technologies drug levels remain within the therapeutic window and do not fluctuate the peaks and troughs seen in regular oral dosing. Furthermore, drug targeting that results in a concentrated dose at the site of action, and low systemic concentrations can also improve the safety and efficacy profile of the drug treatment. Drug delivery technologies have made it possible to enhance patient compliance. If a dosage formcan be prepared into a once-daily tablet vs. a three-times daily therapy, or a patch that is applied once a week, or a depot injection that can deliver drug for up to months, then there is a significantly higher chance that patients will follow the dosing regimen, leading to an improved treatment outcome. Especially, sustained-release technologies have been widely applied to gain a competitive edge and have proven big market potential.

Transdermal drug delivery

Transderm-Scop patch (scopolamine for motion sickness) developed by Alza in 1982 opened new era and impacted pharmaceutical industry and healthcare society. Until the seventies transdermal drug delivery was not familiar terminology and percutaneous absorption was more popular in investigation of drug transport through skin layers. Systemic drug circulation via skin was regarded as a big adventure overcoming strong skin barrier function. In 1994, Pacific Pharm. Co. launched Ketotop developed by AmorePacific R&D Center. Then the competitive edge gained resulted in strong Ketotop sales and made transdermal drug delivery boom in Korea. Today transdermal patches are widely used to

deliver hormones and pain management medications. The world wide sales of Duragesic (J&J) reached 1.2 billion dollars in 2002. Although technological advances caused significant market shifts, it has done little to expand the overall potential of the transdermal market. The lack of market expansion may be largely blamed on failing to receive approval for more drugs and newer applications. The result is that transdermal technology is largely restricted today to pain management, hormone replacement therapy, and cardiovascular therapy. Although transdermal technology offers the advantage of sustained drug delivery, reduced dosing and improved patient compliance, its limitations, such as skin irritation and poor adhesion must be solved. The newer generations must be smaller, more efficient, stick better and cause less skin irritation to hold competitive edge in comparison with other drug delivery technologies. Likewise to the introduction of patches for contraception (Ortho Evra) and overactive bladder (Oxytrol), more drugs are likely to be developed by utilizingadvances in transdermal technologies.

Oral drug delivery

Oral delivery has been the gold standard from the past to the present in the pharmaceutical industry. It has been regarded as the safest, most convenient and ease of preparation of dosage forms. Patient preference or compliance is typically higher among orally administered medicines than the alternatives. Oral delivery products share market more than fifty five percent of sales amount due to those advantages. Disadvantages of oral delivery include variable bioavailability, the limited absorption of macromolecules, food effects, first pass metabolism necessitating the administration of larger doses to reach the systemic circulation.

To overcome the major problems associated with oral delivery, controlled-release and sustained-release products have been widely introduced. Procardia XL (nifedipine) applied Oros technology was recognizedas an example of extending product lifecycles by utilizing drug delivery technology. It is worth to mention that Adalat Oros tab distributed by Bayer Korea has sharply increased its market potential in recent years. The cardiovascular market is particularly well suited to oral controlled release technologies, and there has been a proliferation of such products in the hypertension market in particular. The products suffixed such as XL, ER, SR and CR can be differentiated in the crowded market as value-added formulations to conventional dosage forms.

Many drug delivery companies own their proprietary technologies including Alza's Oros and SkyePharma's Geomatrix system and aggressively apply those to a series of drugs.

Kontram XL (tramadol hydrochloride) launched by Pacific Pharma will be introduced in the lecture.

Injectable drug delivery

Even though injectable drug delivery is the least preferred method of drug delivery, patient preference may not often be taken into account. For the delivery of large molecular weight compounds, such as most biotechnological products injection may be the only viable method currently. Injectable sustained-release formulations have a wide range of beneficial effectsin comparison with traditional dosage forms. Obviously reduced dosage requirement means greater convenience for the patient and increase compliance. Controlled-release manner of administered dose for several months can provide plasma drug concentration within optimal range, called a therapeutic window, which results in increased efficacy while avoiding the onset of side effects.

Sustained-release systems normally involve biodegradable polymers or lipid materials impregnated with the drug. Injected to the body, the material degrades or eliminates in a controlled fashion, releasing drug over a prolonged period. Particulate delivery system involving PLGA or liposome is most popular in this category. It is noteworthy that this technology is likely to be applied to wider range of drugs as well as macromolecular drugs. The increasingcommercialization of biotechnology and gene based products, which are by their nature difficult to administer without injection, represents an emerging opportunity for this technology.