Banyu Pharmaceutical R&D Symposium Presentation
September 2002

Biopharmaceutics of Nanoparticle Formulations

Gloria Y. Kwei
Pharmaceutical Research, Merck Research Laboratories

Abstract

Poorly water soluble compounds present significant challenges during preclinical assessment, and later during formulation of dosage forms. Since oral drug delivery has always been the most convenient route of administration for medications for laboratory animals and humans, many different strategies have been tested to improve the oral delivery and bioavailability of new medications.

For compounds with inherent high intestinal permeability, increasing rate of dissolution is often sufficient to allow complete absorption of compound along the gastrointestinal tract. Decreasing drug molecule particle size, and hence enhancing surface area for dissolution is hardly a new concept, however, nanoparticle delivery for pharmaceuticals is a relative new technology developed in the early 1990s. Particle size reduction by appropriate milling and stabilization of the particles with GRAS polymers have produced aqueous suspensions that behave like solutions (fine colloidal dispersions). Over the past decade, understanding the milling process and key attributes of the drug molecule has allowed preparation of these suspension in volumes as small as 5 mL. Compound requirement for physical and chemical stability characterization and for a set of animal experiments can be readily accommodated by medicinal chemistry groups. This technology is now commonly accepted by basic research and development scientists in the pharmaceutical industry and applied to address absorption issues.

Among the biopharmaceutical characteristics that have improved with the use of nano technology include:
Faster absorption and hence onset of drug action, reducing the variability in absorption, minimization of food effect and attenuation of hepatic first pass metabolism leading to a change in parent: metabolite ratios in the circulation. Examples of these effects from early development and from clinical trials from MRL will be shown in this presentation.