The Theory and Practice of Industrial Pharmacy

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Sustained Release Dosage Forms

NICHOLAS G. LORDI

With many drugs, the basic goal of therapy is to achieve a steady-state blood or tissue level that is therapeutically effective and nontoxic for an extended period of time. The design of proper dosage regimens is an important element in accomplishing this goal. A basic objective in dosage form design is to optimize the delivery of medication so as to achieve a measure of control of the therapeutic effect in the face of uncertain fluctuations in the in vivo environment in which drug release takes place. This is usually accomplished by maximizing drug availability, i.e., by attempting to attain a maximum rate and extent of drug absorption; however, control of drug action through formulation also implies controlling bioavailability to reduce drug absorption rates. In this chapter, approaches to the formulation of drug delivery systems, based on the deliberate control of drug availability, are considered with emphasis on peroral dosage forms.

The Sustained Release Concept

Sustained release, sustained action, prolonged action, controlled release, extended action, timed release, depot, and repository dosage forms are terms used to identify drug delivery systems that are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. In the case of injectable dosage forms, this period may vary from days to months. In the case of orally administered forms, however, this period is measured in hours and critically depends on the residence time of the dosage form in the gastrointestinal (GI) tract. The term "controlled release" has become associated with those systems from which therapeutic agents may be automatically delivered at predefined rates over a long period of time. Products of this type have been formulated for oral, injectable, and topical use, and include inserts for placement in body cavities as well.[1]

The pharmaceutical industry provides a variety of dosage forms and dosage levels of particular drugs, thus enabling the physician to control the onset and duration of drug therapy by altering the dose and/or mode of administration. In some instances, control of drug therapy can be achieved by taking advantage of beneficial drug interactions that affect drug disposition and elimination, e.g., the action of probenicid, which inhibits the excretion of penicillin, thus prolonging its blood level. Mixtures of drugs might be utilized to potentiate, synergize, or antagonize given drug actions. Alternately, drug mixtures might be formulated in which the rate and/or extent of drug absorption is modified. Sustained release dosage form design embodies this approach to the control of drug action, i.e., through a process of either drug modification or dosage form modification, the absorption process, and subsequently drug action, can be controlled.

Physicians can achieve several desirable therapeutic advantages by prescribing sustained release forms. Since the frequency of drug administration is reduced, patient compliance can be improved, and drug administration can be made more convenient as well. The blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced, because a more even blood level is maintained. A less obvious advantage, implicit in the design of sustained release forms, is that the total amount of drug administered can be reduced, thus maximizing availability with a minimum dose. In addition, better control of drug absorption can be attained, since the high blood level peaks that may be observed after administration of a dose of a high-availability drug can be reduced by formulation in an extended action form. The safety margin of

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