Pharmaceutical Dissolution Testing

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1

Historical Development of Dissolution Testing

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INTRODUCTION

Adequate oral bioavailability is a key pre-requisite for any orally administered drug to be systemically effective. Dissolution (release of the drug from the dosage form) is of primary importance for all conventionally constructed, solid oral dosage forms in general, and for modified-release dosage forms in particular, and can be the rate limiting step for the absorption of drugs administered orally (1). Physicochemically, "Dissolution is the process by which a solid substance enters the solvent phase to yield a solution" (2). Dissolution of the drug substance is a multi-step process involving

heterogeneous reactions/interactions between the phases of the solute–solute and solvent–solvent phases and at the solute–solvent interface (3). The heterogeneous reactions that constitute the overall mass transfer process may be categorized as (i) removal of the solute from the solid phase, (ii) accomodation of the solute in the liquid phase, and (iii) diffusive and/or convective transport of the solute away from the solid/liquid interface into the bulk phase. From the dosage form perspective, dissolution of the active pharmaceutical ingredient, rather than disintegration of the dosage form, is often the rate determining step in presenting the drug in solution to the absorbing membrane. Tests to characterize the dissolution behavior of the dosage form, which per se also take disintegration characteristics into consideration, are usually conducted using methods and apparatus that have been standardized virtually worldwide over the past decade or so, as part of the ongoing effort to harmonize pharmaceutical manufacturing and quality control on a global basis.

The history of dissolution testing in terms of the evolution of the apparatus used was reviewed thoroughly by Banakar in 1991 (2). This chapter focuses first on the pharmacopeial history of dissolution testing, which has led to mandatory dissolution testing of many types of dosage forms for quality control purposes, and then gives a detailed history of two newer compendial apparatus, the reciprocating cylinder and the flow-through cell apparatus. The last section of the chapter provides some historical information on the experimental approach of Herbert Strieker's group. His scientific work in combining permeation studies directly with a dissolution tester, is very much in line with the Biopharmaceutic Classification System (BCS), but was published more than two decades earlier than the BCS (4) and can therefore be viewed as the forerunner of the BCS approach.

FROM DISINTEGRATION TO DISSOLUTION

Compressed tablets continue to enjoy the status of being the most widely used oral dosage form. Tablets are solid oral

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