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Pharmacokinetics/ADME of Large Molecules

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1. INTRODUCTION

As discussed in previous chapters, pharmacokinetics (PK) is the study of the rate processes that are responsible for the time course of the level of an exogenous compound in the body. The processes involved are absorption (A), distribution (D), metabolism (M), and excretion (E). The pharmacokinetics of peptides, proteins, and other biotechnology products are an important factor in their pharmacodynamics, i.e., the time course of their pharmacological effect. Therefore, knowledge of the pharmacokinetics of a pharmaceutical drug in humans and laboratory animals is required when selecting dose levels and dose regimens. Similarly, the toxicokinetics (pharmacokinetics in toxicology studies, including higher doses than used clinically) are important for the design of toxicology studies (dose levels and dose regimens) as well as in determining safety margins and extrapolating toxicological data to humans.

In this chapter, the PK and ADME characteristics of protein therapeutics will be described. The ADME mechanisms for protein drugs that influence the plasma PK and systemic exposure are usually similar to those that handle endogenous proteins. Receptor-mediated uptake mechanisms that may also be involved in the protein's PD effect play an important role. This is generally different from small molecule drugs that are taken up by cells and distribute into organs, including the biophase, in many cases by