431a Mathematical Modeling of Drug Release, Absorption and Clearance after Intramuscular Injection of Suspensions

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Parenteral routes of drug administration are as useful and important as oral ones; Intramuscular (IM) route is especially important for drugs with low aqueous solubility. IM injections are administered via extra-vascular route, where the drug has to leave the site of injection to enter the systemic circulation to distribute throughout the body and produce the desired pharmacological response. There are various factors that can affect the rate of drug clearance from the site of injection. These factors can be associated with properties of the drug and the formulation. Drug concentration, injection volume, site and speed of injection can also lead to different pharmacological responses. Development of a mathematical model will be discussed which can predict the drug clearance rate from the IM injection site based on the different physico-chemical properties of the administered drug suspension. Various transfer processes taking place in the vascular and extravascular spaces are mathematically coupled in the developed model to predict drug release, absorption and clearance rates. These processes are: liquid, protein and lymphatic fluxes; suspended drug dissolution, drug permeation and drug partitioning to muscle tissues. Developed model has been used to predict the drug clearance rate from the injection site. It is observed that the model is able to predict drug clearance rates which correlate with the experimental values reported in literature. Differences in drug clearance rates are also successfully predicted by the model for different injection volumes and concentrations for the same drug. Developed model has also been extended to predict the behavior of oil solutions/suspensions by incorporating drug diffusion across the oil depot.