The Changing Face of the Rate Concept in Biopharmaceutical Sciences: From Classical to Fractal and Finally to Fractional

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ABSTRACT:

Diffusion is one of the main mechanisms of various processes in living organisms and plays an important role in the course of drugs in the body. Processes such as membrane permeation, dissolution of solids and dispersion in cellular matrices are governed by diffusion. Diffusion is classically described by Fick's law, which gives rise to exponential drug concentration vs time curves. However in the last few decades, strong experimental evidence has suggested that diffusional processes may deviate from this law. Specifically in pharmacokinetics, power-law concentration time series have been observed. While the classic representations of rate are applicable under homogeneous conditions where classic diffusion dominates, in heterogeneous confined topologies, fractal concepts need to be introduced to account for anomalous diffusion and memory effects. These effectively introduce time-varying properties for the system. A more elaborate and appealing way to represent these non-classic rates is by fractional calculus, where the phenomena of anomalous diffusion are described naturally, as fractional generalizations of classic laws, without introducing explicit time dependence. In this presentation the changing face of the rate concept in Biopharmaceutical Sciences will be discussed with emphasis on the latest developments in methodology and applications of fractional calculus in pharmacokinetics.