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Modelling of drug particles behavior near the release boundary: a classical and fractional dynamics approach

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Abstract: In first place, investigation of the evolution of the fraction of drug molecules that are sufficiently close to the release boundary, in order to check the validity of the assumption underlying the theoretical derivation of a stretched exponential (Weibull) release kinetics [1]. Secondly, exploration of the use of fractional order differential equations for the analysis of datasets of various drug processes that present anomalous kinetics, i.e. kinetics that are non-exponential and are typically described by power-laws [2]. This approach takes place also for the drug release behavior near the release boundary. A fractional differential equation corresponds to a differential equation with a derivative of fractional order. The main mechanism that describes the drug release is diffusion. For the aforementioned cases, the Diffusion-controlled drug release from slabs and spheres is considered. Both analytical results and Monte Carlo simulations are used to calculate the evolution of diffusive drug particles.
Both analytical and Monte Carlo simulations data show an inverse power-law time dependence of the fraction of diffusive drug particles near the boundary, after an initial short time, followed by saturation. The power-law dependence starts early during the process, at around 1% of the release and lasts up to at least 80% of the release. The obtained results indicate an agreement between the values of the power-law exponent, m, and the Weibull exponent, b, as predicted from the relation b=1-m [1]. The fraction of drug molecules near to an exit, as a function of time, follows an inverse power-law in a substantial part of the release problem, justifying an approximate description of the release kinetics through a stretched exponential function. Fractional kinetics though, can describe all the cases of drug release systems, including the Weibull classical kinetics and offers an elegant description of anomalous kinetics, i.e. nonexponential terminal phases, the presence of which has been acknowledged in pharmaceutical literature extensively.

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