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Towards better understanding of drug interactions with mesoporous silica carriers by using inverse gas chromatography and molecular modelling

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Drug adsorption onto silica carriers is an attractive formulation principle because of non-crystalline drug stabilization in the mesopores and supersaturation upon release for enhancement of drug absorption [1]. Much research has already been invested and commercial products of are under development [2]. However, despite intensive previous work, there is a research gap on the surface energetics and molecular interactions for drugs and non-ordered mesoporous silica surfaces. Therefore, the present study attempts to better understand drug-silica interactions. We compare results from Inverse Gas Chromatography (IGC) using non-ordered mesoporous silica and volatile solvents with calculations obtained from molecular modelling. As a result, a model is presented which includes enthalpic interactions by a molecular mechanics approach and an entropic part estimated by an empirical relationship with molecular descriptors (τ and HBN, see Myrdal et al. [4]). Based on the IGC desorption energies, a simple regression model was proposed for volatile molecules. In case of drugs, it is proposed to have a first approximation of the intrinsic surface affinity based solely on the enthalpic interactions as obtained from molecular mechanics. The intrinsic surface affinity holds for a binary interaction of drug and surface, which is an important characterization especially when an additional liquid phase in pharmaceutical practice complicates the adsorption process upon drug loading or release. The combination of molecular modelling and IGC provided valuable insights into how volatiles or drugs interact with surfaces of disordered mesoporous silica. The introduced concept may help to identify early in development which compounds could be candidates for a drug product using mesoporous silica.

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