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Drug-excipient interactions: evaluation of the binding constants

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In pharmaceutical formulations the presence of excipients can affect physicochemical properties of the drug as the ionization degree or the solubility. In fact, some excipients like cyclodextrines or plasdones are used as enhancers of drug solubility, and this enhancement is mainly attributed to interactions between the excipients and the drug. Therefore, the knowledge of the interaction constant may be a key point in the prediction of drug solubility in presence of excipients. Nevertheless, for ionisable compounds, the pH of the medium plays a very important role in both, the excipient-drug interactions and the solubility.
This work is focused on the determination of binding constant between several excipients and an ionisable drug by studying the pK_a-shift of the drug when increasing excipient concentration. The study has been performed with three excipients; two cyclodextrines (captisol and cavasol) and one plasdone (kollidon) and two drugs: diflunisal (containing an acidic group) and trazodone (containing a basic group). The variation of the ionization constant with the concentration of excipient shows different behaviour depending on the type of excipient used and the nature of the drug ionisable centres (acidic or basic).
From the profiles, the binding constant of both species, the neutral and the ionic, with the excipient are obtained. Then, knowing the pK_a of the drug, a model to predict the excipient-drug interaction at any pH has been developed.