Title: **Optimization of dissolution rate measurements of poor-soluble drugs.**
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One of the most important parameters to be determined during the drug development process is the dissolution rate. The *in vitro* study of this property is essential to evaluate the bioavailability of drugs in the drug discovery process.

Traditional methods for dissolution rate determination require high amounts of the active pharmaceutical ingredient. However, it is a problem when drug characterization is carried out in the early stages of the process, when only little amounts of drug are available. For these reasons, miniaturized methods, which use low drug amounts, were developed. The *gastrointestinal dissolution method* is an example of miniaturized method, and it is used in the present work. The fact of extracting part of solution at several times, for *off-line* quantification is not a problem in traditional methods, because it does not affect the dissolution rate profile curve, as the extracted volume is not significant compared to the total one. However, that might not be the case in miniaturized methods, where smaller dissolution volumes are used.

In order to compare the effect of extracting part of solution to quantify off-line the concentration of drug on the profile curve, dissolution rate measurements have been carried out for 120 minutes at constant pH for two different drugs: trazodone and warfarin. First, dissolution profiles have been determined *in situ*, with spectrophotometric detection. Next, experiments have been repeated performing several extractions and quantifying off-line by HPLC.

Results show that dissolution profiles are comparable, although the solubility of the compounds can be a limiting factor.

Determined profiles are similar in the case of trazodone. However, warfarin, with a lower solubility than trazodone, needs support from a cosolvent to reach equivalent concentrations in the HPLC profile.

Keywords: Dissolution rate, drug, solubility, active pharmaceutical ingredient, *gastrointestinal dissolution method*, trazodone, warfarin, HPLC.