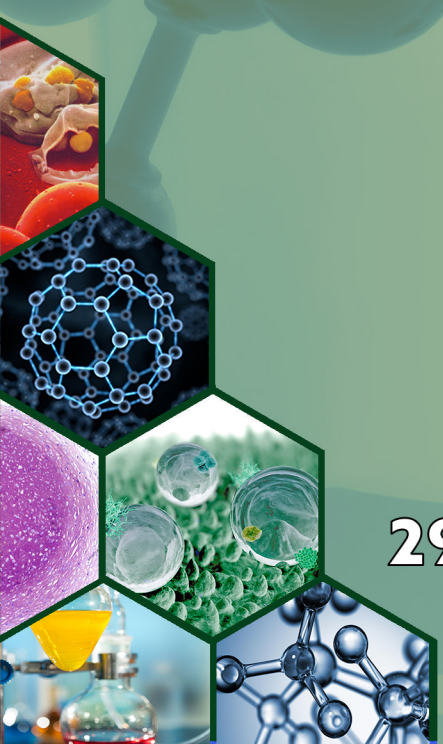
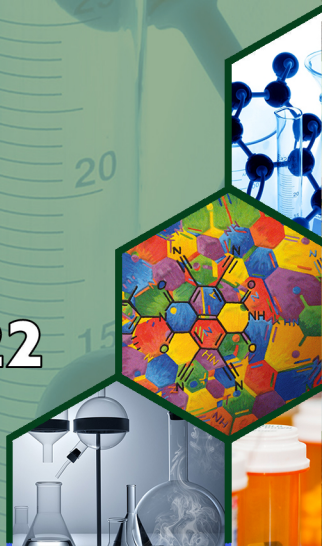
Serbian Chemical Society
Serbian Young Chemists' Club

Eight Conference
of the Young Chemists of Serbia

Book of Abstracts





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Poster presentations

Analytical chemistry

AC PP 04

The influence of competing counterions on the solubility of imipramine

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Experimental studies of solubility are important in all phases of drug design and development. Solubility data are used to screen out drug-like candidates, biopharmaceutical classification and formulation optimization. The development of oral and parenteral dosage forms can be challenging, especially when drugs are poorly soluble, ionizable, exhibiting pH-dependent solubility and when multiple counterions are present in drug suspension. The influence of different counterions on the existing equilibria and on pH-dependent drug solubility must be defined in such systems. To investigate the effect of multiple ions on the solubility of a model basic drug – tricyclic antidepressant imipramine (Im), we conducted a systematic study of the Im solubility as a function of pH in the presence of both chloride and phosphate ions as well as in chloride-free and phosphate-free suspensions. The pH–Ramp *shake–flask* method[1,2] was used for solubility determination. The computer program *p*DISOL–X was used for data analysis. It is shown that distinct pH-dependent solubility profiles were obtained in studied systems. Depending on the pH and the total concentration of chloride and/or phosphate ions, Im can precipitate as chloride and phosphate salt or free base. Furthermore, pH values of solid phase transitions (pH_{max}) varied as well. For instance, pH_{max} of solid phase transition of $(ImH)H_2PO_{4(s)}$ to $(ImH)_2HPO_{4(s)}$ change from 5.15 (chloride and phosphate-containing suspensions) to 5.73 (chloride-free suspensions). The intensive self-aggregation of Im in acidic region was suppressed by raising chloride or phosphate ions concentration (I_{avg} 1.42–1.64 M). In that way, solubility of Im was decreased due to the common-ion effect. This study illustrates the influence of competing counterions on Im solubility and on interconversions in solid phase. Hence, such factors must be taken into account during formulation optimization in drug research.

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