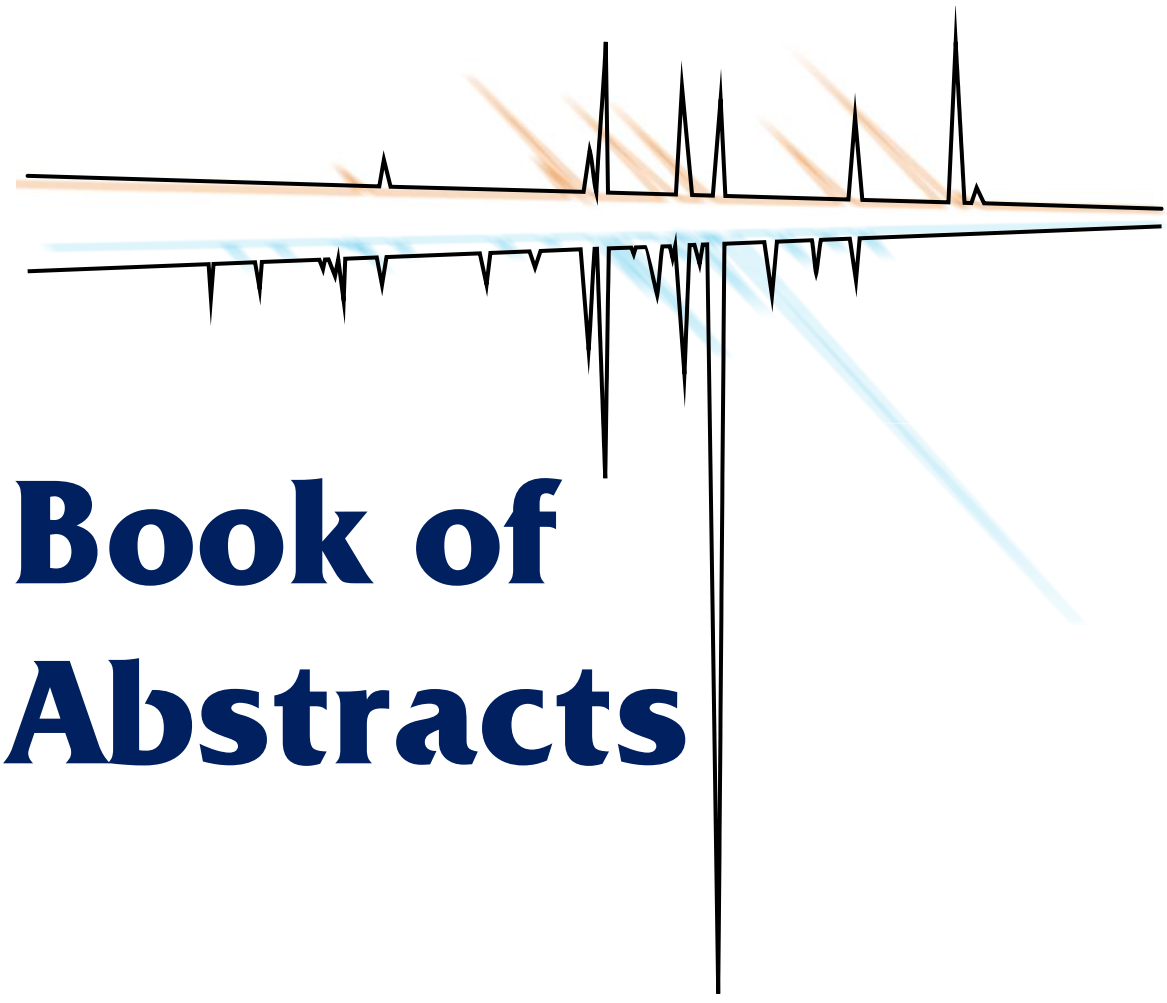
6th IAPC Meeting

Sixth World Conference on Physico-Chemical Methods in Drug Discovery

&

Third World Conference on ADMET and DMPK



Book of Abstracts

Zagreb, Croatia, September 4-7, 2017

6th IAPC Meeting

Sixth World Conference on Physico-Chemical Methods in Drug Discovery
&
Third World Conference on ADMET and DMPK
Zagreb, Croatia, September 4-7, 2017

Book of Abstracts

Published by
International Association of Physical Chemists
E-mail: office@iapchem.org, URL: http://www.iapchem.org

For Publisher
Zoran Mandić

Editor
Zoran Mandić

Design, Page Making and Computer Layout
Aleksandar Dekanski

On Line version only

P 07

Protolytic equilibria of rupatadine in micellar solutions of differently charged surfactants

Marija Popović Nikolić[1], Gordana Popović[2], Danica Agbaba[1]

[1]*Department of Pharmaceutical Chemistry Fauculty of Pharmacy, University of Belgrade*
[2]*Department of General and Inorganic Chemistry, Fauculty of Pharmacy, University of Belgrade*

Rupatadine is selective second-generation H_1 antagonist, used in seasonal allergic rhinitis and chronic urticaria, and reported to be an antagonist to platelet-activating factor. Rupatadine contains three ionizable basic centers, two aromatic and one cyclic aliphatic amine. The pharmaceutical dosage forms for oral administration contain rupatadine fumarate as an active substance. A complex system of protolytic equilibria establishes in the solution of rupatadine fumarate which includes three basic centers of rupatadine and two acidic groups of fumaric acid. The data on the physicochemical properties of drugs determined in aqueous solution is not sufficient for the prediction of solubility and bioavailability in physiological conditions that are significantly more complex. For a better understanding of pharmacological behavior of ionizable drugs their physicochemical properties should be investigated under conditions more similar to physiological. As the biomembrane mimetic systems micellar solutions of surfactants can be used. The aim of this study was to investigate the effect of micellar solutions of differently charged surfactants sodium dodecyl sulfate (SDS), cetyltrimethylammonium bromide (CTAB) and 4-octylphenol polyethoxylate (TX-100), as biomembrane mimetic systems, on protolytic equilibria of rupatadine.

The solutions (5×10^{-4} M) with and without of the 0.01 M surfactants were titrated with standard NaOH solution (0.0983 M) at a constant ionic strength (0.1 M NaCl) and temperature 25°C. Experimental data obtained by potentiometric titration were analyzed in the program Hyperquad.

The pK_a values of rupatadine (pK_{a1} = 3.45, pK_{a2} = 4.72, pK_{a3} = 6.75) were determined and the ionization was defined in aqueous media. The shift in protolytic equilibria was observed based on the pK_a values of rupatadine determined in the presence of surfactants, anionic SDS (ΔpK_a up to +1.44); cationic CTAB (ΔpK_a up to -1.99) and nonionic TX-100 (ΔpK_a up to -0.69). Different types of interactions between rupatadine and micelles were assumed.

Rupatadine ionizable groups participate in electrostatic interactions with the ionic SDS and CTAB micelles and are involved in the interactions with a hydrophilic layer of nonionic TX-100 micelles. Observed shift in protolytic equilibria at biopharmaceutically significante pH values can be considered in the presence of biomolecules with various charge and polarity in physiological conditions.