pKa DETERMINATION OF LEVODROPROPIZINE

Ibrahim NARIN¹, Salih SARIOGLAN¹, Beril ANILANMERT², Hayati SARI³

¹Erciyes University, Faculty of Pharmacy, Dept. Of Analytical Chemistry, Kayseri, TURKEY
tel: +90 352 438 04 86, fax: +90 352 437 91 69, e-mail: narin@erciyes.edu.tr

²Forensic Council of Turkey, İstanbul, TURKEY

³Gazi Osman Pasa University, Faculty of Arts and Sciences, Dept. of Chemistry, Tokat, TURKEY

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The pKa of a drug influences lipophilicity, solubility and permeability which in turn directly affects pharmacokinetic characteristics such as absorption, distribution, metabolism and excretion [1]. pKa is also important in choosing the optimum conditions in developing analysis methods for the drug molecules. The pKa constants and relative abundances of non-ionised and ionized forms of Levodropropizine at various pH’s were determined potentiometrically, to relate their pKa with their bioavailability and to provide chemical data to be used in their analysis.

Levodropropizine is used orally, in symptomatic treatment of cough [2]. It is rapidly absorbed (bioavailability≈75%) and distributed throughout the body, after oral administration. Binding to plasma proteins is low (11 – 14%). No experimental study exists on the determination of pKa constants of Levodropropizine in literature.

In this study, the pKa constants of Levodropropizine were determined potentiometrically, using Irving-Rossotti method. Eleven 50.00 mL aqueous solutions (1) containing 0.010 M HClO₄, 0.100 M NaClO₄, 4.00x10⁻⁴ M Levodropropizine, and their blanks were titrated potentiometrically under N₂ with a 0.1000 M NaOH at 25±1 °C, I=0.11 (NaClO₄). Using the Irving-Rossotti method, .Automation values were calculated from the titration curves of HClO₄, plotted as a function of pH, i.e., A.Automation = f(pH). From the graph, log K values were calculated from the A.Automation values of 0.5 and 1.5 and the relative abundances of the drug species were calculated and plotted in a graph. pKa₁ and pKa₂ values of Levodropropizine were found as 7.12±0.50 and 10.58±0.25 in order. Relative abundances of the ionized and non-ionized species were calculated at various pH values, using the pKa constants.

From the ionization profile of the drug, it’s understood that its presence in stomach is in 100% ionized form. This phenomena is supported by the information in British Pharmacopoeia that the pH of the aqueous solution of the drug is 9.2-10.2 [3]. However, no information exists on the mechanism of absorption of this ionized moiety. But when the bioavailability of Levodropropizine is evaluated regarding pKa constants, the good penetration to body compartments seem to arise merely because of passing through the porous membranes of vessels.

References
2. LEVOPRONT 30 mg/5 ml SYRUP Prospectus, Prospectus Approval Date: 16.04.2007, Istanbul, Abdi Ibrahim İlaç San. ve Tic. A.S. with Dompe International S.A.- Switzerland Licence