Title: **The Influence of the Background Salt in pKa and log Po/w Parameters of Ionizable Drugs**

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pK_a and lipophilicity are physicochemical parameters that influence key processes such as ADMET properties (adsorption, distribution, metabolism, excretion and toxicity), structure-activity relationships (QSAR), molecular recognition, and xenobiotic patterns. That is why they are so important in environmental and biochemical research and drug discovery.

The log $P_{o/w}$ is one of the most used parameters to study lipophilicity and is defined as the partition of one specie of the compound (usually the neutral form) between the *n*-octanol and water phases. Nevertheless, most drugs are ionizable in aqueous solutions and depending on the pH of the medium they can be found in ionic or neutral form. Then, the lipophilicity is measured through the distribution coefficient, $D_{o/w}$, that relates the concentration of all species of an ionizable compound between *n*-octanol and water to a given pH. To give lipophilicity profiles, the log $D_{o/w}$ value is plotted as a function of pH, usually 2 to 12.

In pharmaceutical research, these parameters are generally measured under physiological conditions of ionic strength I = 0.15 M KCl. However, they are highly dependent on the type and concentration of the background salt.

In this work the influence of ionic strength in pK_a and log $P_{o/w}$ parameters is studied. The experimental obtained values show that the pK_a value doesn't change with the ionic strength until I = 0.15 M in basic compounds, but it does in acidic compounds. For I > 0.15 M the pK_a increase with the ionic strength. Moreover, there is no change in the log $P_{o/w}$ values of both species of chlorpromazine, B and BH^+, with the ionic strength (0.05 M, 0.075 M, 0.1 M, 0.15 M).

The results will help to understand the effect of the salt bottom and to open the door to the study of the partition of compounds in environments with high ionic strength (for example, seawater I = 0.6-0.7 M), which up to now they had not been explored.

Keywords: pK_a, Spectrophotometric, log P_N, log P_i, drug, potentiometry, shake-flask