

Title: Reconciling the ITIES and Ion-Pair theories through partition experiments with Indomethacin.

Student: Kilian German Muria

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Supervisor/s: Dra. Clara Ràfols Llach
Departament d'Enginyeria Química i Química Analítica
Dr. William Zamora Ramírez
Departament de Nutrició, Ciències dels Aliments i Gastronomia

The capacity of a drug to reach the desired target is key in order to optimize its activity.

Lipophilicity is a property used to describe this capacity. This descriptor is mathematically represented using the partition coefficient P , which reflects the quantity of the sample that transfers from the aqueous phase to the organic one in a biphasic system, giving information about what portion of the substance can pass through the biological membranes. For this reason, there's a high interest in the determination and quantization of this parameter in many investigation areas.

At extreme pH conditions (in respect of the studied substance's pK_a), the ionic species exercise the major contribution of partitioning of the drug, so the determination of the ionic partition coefficient (P_i) has the most relevance in this kind of environments.

Some reports have demonstrated that the value of this parameter varies depending on the salt background concentration, concluding that exists a relationship between these two variables, which is usually described using the widely accepted Ion-Pair Theory. However, this theory can't predict the behavior of the ionic species under conditions of low salt background concentration, where the ITIES Theory (Ion Transfer between two Immiscible Electrolyte Solutions) describes more precisely a situation that the ion-pair formation doesn't occur.

The aim of this work is to find a point of connection between these theories in order to know which of them must be used depending on the background conditions.