BINDING AND PARTITIONING BEHAVIOR OF KETOPROFEN WITH SURFACTANTS: INFLUENCE OF POLOXAMER 188 AND 407 IN PREFORMULATION STUDIES

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Abstract

This study explores the interactions between ketoprofen, a poorly water-soluble NSAID, and three surfactants—sodium cholate (SC), dodecyltrimethylammonium bromide (DTAB), and Brij C10 (BC10)—as well as the modulatory effects of Poloxamer 188 (P188) and Poloxamer 407 (P407). Binding constants were determined using Benesi-Hildebrand analysis below the critical micelle concentration (CMC), while micellar partitioning was assessed above the CMC using Kawamura's approach. Job's plots revealed 1:1 complexation in most systems, with an exception in DTAB/P407 mixtures (1.67:1). DTAB showed the highest affinity for ketoprofen (K_x = 81,386), particularly in combination with P188, likely due to favorable electrostatic and hydrophobic interactions. SC and BC10 showed moderate and low solubilizing capacities, respectively. Poloxamers modulated micelle formation by altering CMCs and binding behaviors: P407 exhibited synergistic effects with SC and DTAB, while P188 showed antagonistic effects with SC and BC10. All Gibbs free energies of partitioning ($\Delta G_x < 0$) indicated spontaneous solubilization, confirming micellar encapsulation as an effective strategy for enhancing ketoprofen solubility. These findings contribute to the rational design of surfactant-based drug delivery systems.

Introduction

Poor aqueous solubility of ketoprofen limits its bioavailability. Micellar solubilization using surfactants and poloxamers offers a promising strategy for preformulation optimization. This work investigates host–guest interactions at molecular and micellar levels in surfactant–ketoprofen systems, with or without poloxamer modifiers.

Experimental

UV–Vis spectrophotometry was used to monitor absorbance changes at $\lambda = 259$ nm. Job's plots, Benesi-Hildebrand, and Kawamura equations were employed to determine complexation stoichiometry, binding (K_b), and partitioning coefficients (K_x). Fluorescence spectroscopy using pyrene probe was used to determine CMCs.

Results and Discussion

DTAB combined with P188 or P407 enhanced ketoprofen solubilization through favorable electrostatic and hydrophobic interactions (Figure 1). SC showed moderate performance, while BC10 was least effective, likely due to its non-ionic nature. The presence of poloxamers modified CMC values and micelle stability. P407 showed synergistic behavior with SC and DTAB, while P188's effect was more antagonistic, possibly due to hydrogen bonding with surfactants [1, 2]. The spontaneity of solubilization was confirmed by negative ΔG_x values across all systems involving micelles. The highest K_x and most negative ΔG_x values were found in DTAB + P188 systems. At higher poloxamer concentrations, steric hindrance and hydrogen bonding limited drug–surfactant interactions.

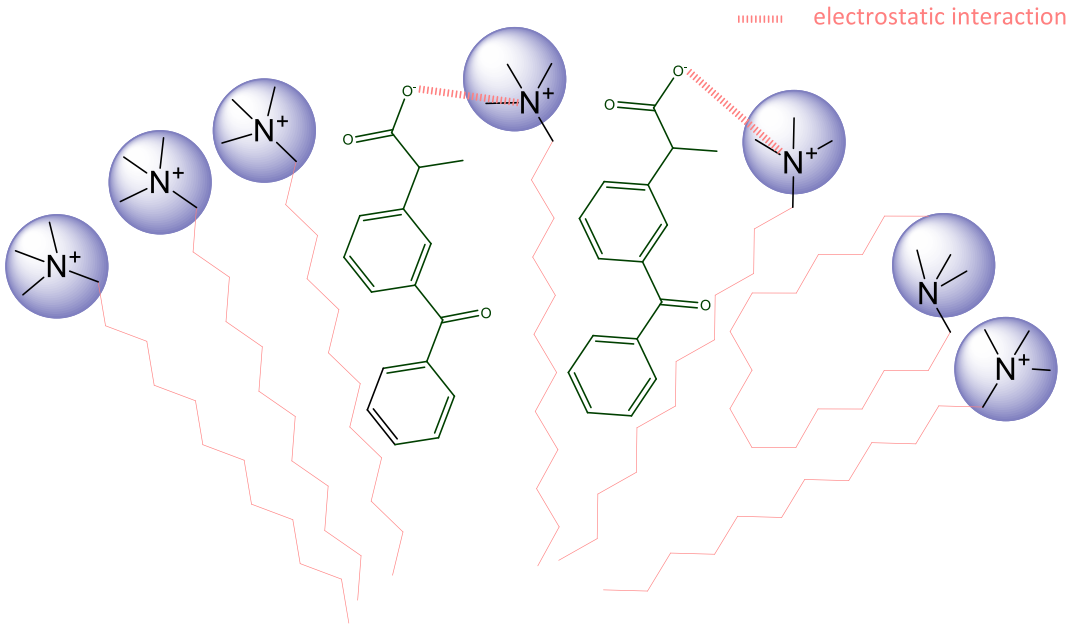

Figure 1. The solubilization of ketoprofen in DTAB micelle

Conclusion

DTAB, particularly in combination with P188 or P407, exhibits the greatest potential for solubilizing ketoprofen. These findings provide a scientific basis for selecting excipients in the development of improved drug formulations.

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References

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