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Entitled

SEQUESTRATION EFFECT ON THE OPEN-CYCLIC SWITCHABLE PROPERTY OF WARFARIN INDUCED BY CYCLODEXTRIN: TIME-RESOLVED FLUORESCENCE STUDY

by

Naji Saleh Ahmed Al-Dubaili

Faculty Advisor

Dr. Na'il Saleh Ibrahim, Chemistry Department
College of Science

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Abstract

In this work, the photophysical properties of the fluorescent anticoagulant drug warfarin (W) were examined in water and inside methyl-β-cyclodextrins (Me-β-CD) through absorption and time-resolved fluorescence measurements at pH 3 and 9 and upon the selective excitation of different isomers of warfarin at 280 and 320 nm. The values of binding constants (2.9×10^3 M^{-1} and 4.2×10^2 M^{-1} for protonated and deprotonated forms, respectively) were extracted from the spectrophotometric data. Both absorption and time-resolved fluorescence results established that the interior of the macromolecular host binds preferentially the open protonated form, red shifts the maximum of its absorption of light at ~305 nm, extends its excited-state lifetime, and decreases its emission quantum yield (Φ_F). Collectively, sequestration of the open guest molecules decreases markedly their radiative rate constants (k_r), likely due to formation of hydrogen-bonded complexes in both the ground and excited states. Due to lack of interactions, no change was observed in the excited-state lifetime of the cyclic form in the presence of Me-β-CD. The host also increases the excited-state lifetime and Φ_F of the drug deprotonated form (W^-). These later findings could be attributed to the increased rigidity inside the cavity of Me-β-CD. The pK_a values extracted from the variations of the UV-visible absorption spectra of W versus the pH of aqueous solution showed that the open isomer is more acidic in both ground and excited states. The positive shifts in pK_a values induced by three derivatives of cyclodextrins: HE-β-CD, Ac-β-CD, and Me-β-CD supported the preferential binding of these hosts to open isomers over cyclic.

Keywords: open-cyclic tautomers, molecular switching, decay-associated spectra, warfarin, excited-state lifetime, cyclodextrins