



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكرو فيلم

بسم الله الرحمن الرحيم



HANAA ALY



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جامعة عين شمس

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Photostability Studies of Some Analgesic Drugs

Thesis Submitted by

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B.Sc. (Chemistry) 2006

M.Sc. (Chemistry) 2011

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Photostability Studies of Some Analgesic Drugs

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ABSTRACT

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Title of thesis: Photostability Studies of Some Analgesic Drugs: Stabilization of Photolabile Drugs by Addition of Some Protective Agents.

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The photostability of lornoxicam (LRX) and tenoxicam (TNX) in bulk, dosage forms in dilute aqueous solution and human plasma were investigated. The results indicated that the photodegradation rate of both analgesics obeyed first order kinetics. LC/MS/MS technique was utilized to elucidate the photodegradation products for each analgesic. The results showed that both LRX and TNX had the same degree of photolability in the dosage form compared to the bulk. Photolability of LRX and TNX was further investigated in the existence of ten photo-protective agents as well as encapsulated in β -cyclodextrin (CD) and the experimental data indicated that citric acid increased the photostability of the two analgesics. The photostability of both analgesics in the existence of citric acid was then validated for linearity, precision, limit of detection (LOD) and limit of quantification (LOQ) appropriate to the international conference on harmonization (ICH) guidelines. LRX and TNX drugs have also been found to create a stable 1:1 inclusion complex in aqueous solution with β -cyclodextrin (β CD). The experimentally determined association constants (K) of LRX- β CD and TNX- β CD are 13.4 and 10.3 M^{-1} , respectively. Quantum chemical computations simulated the preferred orientation of guest molecules in the host.

Geometry optimized results using the ONIOM technique provided more in-depth insights and identified the structure and showed that each drugs were partly encapsulated within the cavity of β -CD. The inclusion binding energy (BE, kcal mol⁻¹) calculations tell the obvious thermal stability of LRX- β CD (-24.19 kcal/mol) over the TNX- β CD (-13.45 kcal/mol) capsule. Furthermore, the photostabilities of the encapsulated drugs were tested. Drug encapsulation did not result in any additional photostability. Moreover, encapsulation of the drugs in the β -CD resulted in noticeable changes in the electronic characteristics of the drugs, as reflected in their reactivity indices. The fact that the water-soluble β -CD formed inclusion complexes with water-insoluble LRX and TNX enables the drug delivery vehicle for oral administration.

Keywords: Lornoxicam, Tenoxicam, Photostability, Citric acid, ONIOM, Binding Energy, Reactivity indices

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