شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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قسم

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كلية علوم

Photostability Studies of Some Analgesic Drugs

Thesis Submitted by

EMAN BANDARY YOUSSOF MOSTAFA

B.Sc. (Chemistry) 2006
M.Sc. (Chemistry) 2011

For the requirement of Ph.D. Degree of Science in Chemistry

To
Department of Chemistry
Faculty of Science, Ain Shams University
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كلية علوم

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Thesis Submitted by

Eman Bandary Youssof Mostafa

For the requirement of Ph.D. Degree of Science in Chemistry

Thesis advisors

1- **Prof. Dr. Mohamed Sabry Abdel-Mottaleb**

Professor of Chemistry, Faculty of Science, Ain Shams University.

2- **Prof. Dr. Marwa Hosny Ahmed Tammam**

Professor of Analytical chemistry, National Organization for Drug control and Research, Giza.

3- **As. Prof. Yousra Mohamed Sabry**

Associate Professor of Pharmacology and toxicology, Faculty of pharmaceutical sciences and industries, Future University in Egypt.

Head of Chemistry Department

Prof. Dr. Ayman Ayoub Abdel-Shafi

ABSTRACT

Name: Eman Bandary youssof Mustafa

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 βcylcodextrin (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 (βCD).The experimentally determined association constants (K) of LRX- βCD and TNX- βCD 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-βCD (-24.19 kcal/mol) over the TNX-βCD (-13.45 kcal/mol) capsulate. 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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