Republic of Iraq
Ministry of Higher Education and Scientific Research
University of Basrah
College of Pharmacy

Preparation, Characterization and Biological Activity of Acyl hydrazone derivatives of NSAIDs

A Thesis
Submitted to the Department of Pharmaceutical Chemistry and the Committee of Graduate Studies of the College of Pharmacy-University of Basrah in Partial Fulfillment of the Requirement for the Degree of Master in Pharmaceutical Chemistry

By
Mustafa Qusay Ali
(B.Sc. Pharmacy 2013)

Supervised by

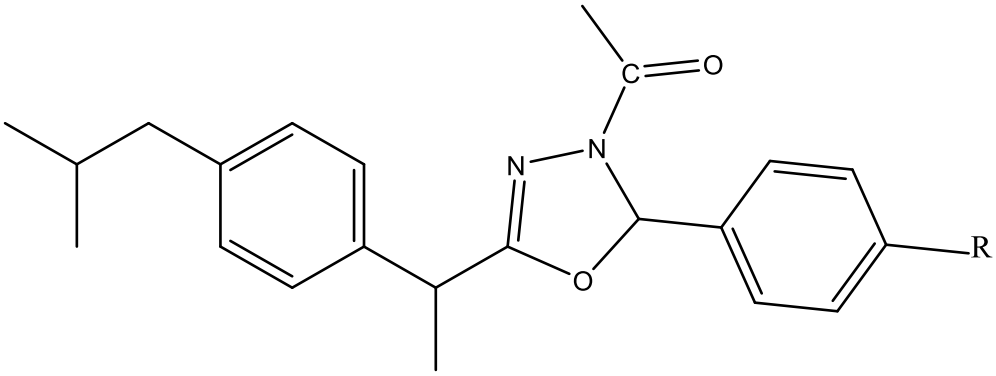
Assist. Prof.
Dr.Leaqaa Abdul-Redha

Assist Prof.
Dr.Falah Hasan Shari

2020 AD **1441 AH**

Abstract

Our study includes the synthesis of new series of Ibuprofen 1,3,4-Oxadiazoline derivatives.



Compound	R
OX1	-H
OX2	$-NO_2$
OX3	-F
OX4	-Cl
OX5	$-OCH_3$

The final compounds synthesized through four steps starting from ibuprofen as acid to prepare the ethyl ester of ibuprofen, followed by the ibuprofen hydrazide synthesis, then the acyl hydrazone of ibuprofen synthesized and finally cyclized to 1,3,4-Oxadiazoline of the ibuprofen.

Abstract

The synthesized compounds characterized by FT.IR, proton-NMR and elemental microanalysis (CHN) techniques. The intermediates and final compounds were investigated for their physicochemical properties including the melting point, color, the yield percent, and thin-layer chromatography (TLC) to identify the purity of the products and to know the reaction end- point and the elution by using the following systems: ethyl acetate: hexane (3:7), ethanol:dioxan (1:1) and methanol: chloroform (1:9). The biological study was performed using Swiss albino mice (25-30 g) for the analgesic and anti-inflammatory activity assessment and cytotoxicity study by using MCF7 cell line.

Hind edema template of carrageenan used for anti-inflammatory activity assessment and the analgesic activity evaluated using (writhing induced by acetic acid) and hot plate method, the results show that all the finally synthesized compounds present with anti-inflammatory plus analgesic activities lower than that in ibuprofen exhibited in the animal model of our experimental work , we observed that the standard compound and the synthesized derivatives substantially reduced carrageenan-induced edema at all-times (2,4,6,24) hours, all chemically synthesized new compounds actually significantly reduced the number of acetic acid writhings induced in mice and there is high increase in the reaction time to painful stimulation in hot plate method.

Anticancer study is achieved using MCF-7 cell line for breast cancer, the results show very potent cytotoxic activity with significant reduction in the viable cells.

To identify potential anti-inflammatory and COX selectivity of the synthesized compounds docking calculations were performed using VINA software, the results show good affinity without significant differences in selectivity towards COX-1 and COX-2 isozymes.