شبكة المعلومات الجامعية

بسم اللّه الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم باللّه العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

Ain Shams University

Faculty of Science

Chemistry Department

Synthesis and Biological Evaluation of Nitrogen and Sulfur Heterocycles

Thesis submitted by

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Approval Sheet

"Synthesis and Biological Evaluation of Nitrogen and Sulfur Heterocycles"

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MANGOUD MOHAMED MANGOUD

AIM OF THE WORK

AIMS AND OBJECTIVES

In the pharmaceutical field, there is a need for new and novel chemical compounds of biological activities. Our efforts are focused on synthesizing pharmacologically interesting heterocyclic compounds of widely different composition. During the course of research, several heterocyclic compounds have been designed, generated and characterized using spectral studies. The aims and objectives of the work carried out are:

1- Synthesis of compounds of predicted pharmacological activity like chalcones, cyanopyridines, pyrazolines, pyrazoles.

2- Characterization of these products for structural elucidation using spectroscopic techniques like IR, ^{1}H-NMR and Mass spectrometry.

3- Evaluation of the biological activity of these new products against the appropriate human cancer cell lines.

4- Prediction of preferred binding orientation of the biologically active synthesized compounds to the appropriate receptor, when both interact with each other in order to form a stable complex. Information gained from the preferred orientation of bound molecules may be used to predict the energy profiling (such as binding free energy), strength and stability (like binding affinity and binding constant) of complexes.

5- Assessing of drug-likeness, pharmacokinetics and toxicity of the synthesized compounds computationally on the basis of *in silico* studies.

Key Words:

Chalcones; Pyrazoles; Pyrazolines; Pyridines; Breast Cancer; Melanoma; *IN SILICO* studies; Molecular Docking.

ABSTRACT

Synthesis and Biological Evaluation of Nitrogen and Sulfur Heterocycles

By

Mangoud Mohamed Mangoud

Abstract:

Novel series of pyrazoline carbothioamides, acetyl pyrazoles, pyridine-3-carbonitriles, pyridine-2-carbonitriles, and nicotinonitriles were synthesized. The structures of the newly synthesized compounds were established based on their spectral data, elemental analyses and alternative synthetic routes whenever possible. Also, the newly synthesized compounds were screened for their *in vitro* anticancer activity against T-47D (breast cancer human cell line) and UACC-257 (melanoma human cell line) by MTT assay (a colorimetric assay for assessing cell metabolic activity). Experimental results demonstrated that all the synthesized compounds exhibited moderate to high activity against T-47D breast cancer cell line, especially compounds **C5**, **D1**, **H6** and **I6** surpassed that of cisplatin surpassed that of cisplatin. Compounds **F3**, **F4** and **F5** showed potent activity against UACC-257 melanoma cancer cell line and surpassed the potency of cisplatin, while the most potent compound against UACC-257 melanoma human cancer cell line was **C4**. Molecular docking studies were performed on compounds **C5**, **D1**, **H6** and **I6** in 6I5K active site. Also, molecular docking studies were carried out for compounds **C4**, **E5**, **F3** and **F4** in 1M17 active site using Molecular Operation Environment (MOE 2008.10) software. Also, drug-likeness, pharmacokinetics, and toxicity assessment studies were carried out.

Key Words:

Chalcones; Pyrazoles; Pyrazolines; Pyridines; Breast Cancer; Melanoma; *IN SILICO* studies; Molecular Docking.