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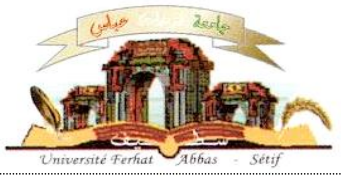

DEPARTMENT OF BIOCHEMISTRY

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Dissertation

Presented by

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THEME

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ADMET and molecular docking studies of organic-inorganic hybrid and phosphonate materials for *in silico* evaluation of anti-inflammatory and antioxidant activities.

By the jury

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Chafia

Dedications

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I dedicate this humble work as a token of my gratitude to all those who have supported, encouraged, and accompanied me, whether closely or from afar, throughout my path.

Nour El Islam

الملخص

يرتكز هذا العمل على دراسات حاسوبية (*in silico*) باستخدام تقنيات رقمية لدراسة الإمكانيات المضادة للالتهابات والمضادة للأكسدة لمواد هجينة عضوية-غير عضوية ومركبات الفوسفونات .تم استخدام برنامجي ChemDraw و ChemSketchلرسم هياكل أربعة وعشرون ممخلبات، ثم أُجريت عليها محاكاة الالتحام الجزيئي مع بروتينين مستهدفين: 1HD2مرتبط بالإجهاد التأكسدي و2AZ5 مرتبط بالالتهاب تمت المحاكاة باستخدام برنامج MOEsoftware. أظهرت النتائج أن هذه المركبات تمتلك خصائص مضادة للالتهاب ومضادة للأكسدة .قيمة Rالناتجة عن تحليل تراكب المجمعات الممخلبة مع البروتين كانت بين 1.5 و2 **Å** ، مما يدل على تطابق جيد داخل المواقع الفعالة للبروتينات.

الكلمات المفتاحية:

MOE software، مضاد للالتهاب، مضاد للأكسدة، المحاكاة الحاسوبية(*In silico*) ، الخصائص الدوائية ADMET ، قواعد ليبينسكي.

Abstract

This study is based on *in silico* analysis using computational tools to explore the anti-inflammatory and antioxidant potential of organic-inorganic hybrid materials and phosphonate compounds. ChemDraw and ChemSketch software were used to draw the structures of twenty-four chelating agents. These were then subjected to molecular docking with two proteins: 1HD2 (related to oxidative stress) and 2AZ5 (involved in inflammation). Docking simulations were performed using MOE (Molecular Operating Environment). The results showed that the compounds exhibited promising anti-inflammatory and antioxidant properties. The RMSD values of the chelator-protein complexes ranged between 1.5 and 2 Å, indicating good binding and alignment within the protein active sites.

Keywords: *MOE software, anti-inflammatory, antioxidant, in silico, ADMET, Lipinski's rules.*

Résumé

Ce travail repose sur des études *in silico*, utilisant des méthodes informatiques pour explorer le potentiel anti-inflammatoire et antioxydant de matériaux hybrides organiques-inorganiques et de composés phosphonates. Les logiciels ChemDraw et ChemSketch ont été utilisés pour dessiner la structure de vingt-quatre chélateurs. Ces structures ont ensuite été soumises à une simulation de docking moléculaire avec deux protéines cibles : 1HD2 (liée au stress oxydatif) et 2AZ5 (impliquée dans l'inflammation). Les simulations ont été effectuées avec le logiciel MOE. Les résultats ont montré que ces composés possèdent des propriétés anti-inflammatoires et antioxydantes prometteuses. Les valeurs RMSD obtenues varient entre 1,5 et 2 Å, ce qui indique un bon ajustement des chélateurs dans les sites actifs des protéines.

Mots-clés *: MOE software, anti-inflammatoire, antioxydant, in silico, propriétés ADMET, règles de Lipinski.*

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Chapter I: Bibliographic Studies

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List of abreviations

2D: 2 dimension.

3D: 3 dimension.

A°: Angstrom.

ADMET: Absorption, Distribution, Metabolism, Excretion, and Toxicity.

Aln: Alanine.

Arg: Arginine.

Asn: Asparagine.

Asp: Aspartic acid.

BBB: blood-brain barrier (BBB) permeability.

CASF: comparative assessment of scoring function.

CLR: C-type lectin receptor.

COX: cyclooxygenase.

CYP450s: Cytochrome P450 proteins.

Cys: Cysteine.

DAMP: danger associated molecular pattern.

DNA: deoxyribonuclei acid.

EPSPsynthase: 5-enolpyruvylshikimate-3-phosphate synthase.

Gln: Glutamine.

Glu: Glutamic acid.

Gly: Glycine.

HBA: hydrogen bond acceptors.

HBD: hydrogen bond donors.

HIF1-α: hypoxia-inducible factor-1α.

His: Histidine.

HIV: human immunodeficiency virus.

IG: gastrointestinal absorption.

IL-1β: interleukin-1β.

IL-6: interleukin-6.

Ile: Isoleucine.

iNOS: nitric oxide synthase.

IR: infrared.

kDa : kilo Dalton.

Leu: Leucine.

LogP: partition coefficient (lipophilicity measure).

Lys: Lysine.

Met: Methionine.

microRNA: ribonucleic acid.

MOE: Molecular Operating Environment.

MSNs: Mesoporous silica nanoparticle.

NADPH: nicotinamide adenine dinucleotide phosphate.

NCBI: National Center for Biotechnology Information.