Available online www.unicrossjournals.com

JOURNAL OF CONTEMPORARY RESEARCH (JOCRES)

RESEARCH ARTICLE VOL. 3 (3) ISSN:2814-2241

Date Published: September 30, 2024

Pages 22- 37

BIOCHEMICAL INVESTIGATION OF THE ANTI-NOCICEPTIVE AND ANTI-INFLAMMATORY MECHANISMS OF *NAPOLEONAEA IMPERIALIS* SEED EXTRACT

Moses M. Edim[1] and Hannah Edim Etta[2]

[1] Department of Chemistry, Faculty of Physical Sciences, University of Cross River State

[2]Department of Animal and Environmental Biology, University of Cross River State

E-mail: mosesedim@unicross.edu.ng

Abstract

Globally, pain and inflammation have become one of the most challenging issues facing many individual and health practitioners. Even though the exact causes of these challenges are unknown, it is generally believed that a combination of environmental, lifestyle, and hereditary variables are to blame. These conditions in all stages will in extension cause discomforts, skin condition, and chronically, autoimmune diseases such as multiple sclerosis, Myasthenia gravis, Hashimoto thyroiditis and others. The efforts to proffer adequate anti-inflammatory and anti-nociceptive drugs still remains a quest; wherefore, this study was aimed at investigating the Anti-nociceptive and Anti-inflammatory mechanism of *Napoleonaea imperialis* seed extract interacting with the target proteins (4DO3 and 4Z69), employing the DFT/B3LYP/6-311G++g(2d,2p) method and function with molecular docking approach and ADMET studies. On the evaluation of the electronic properties of the compounds, FMO analysis showed the reactivity of the study compounds depicting energy gap values of 6.857 eV and 6.912 eV for tetradecene and Butyl-MA respectively. More so, NBO analysis showed the stability of Butyl-MA over tetradecene with a perturbation energy of 51.93 Kcal/mol over that of tetradecene 6.86 Kcal/mol. Consequently, molecular docking analysis revealed the binding affinities of the studied compounds, on binding with protein 4DO3, tetradecene had the binding affinity of -4.8 Kcal/mol as Butyl-MA showed a binding affinity of -4,1 Kcal/mol with one conventional hydrogen bond (SER:387), whereas the standard drug acetaminophen stood out with an affinity of -5.1 Kcal/mol with two conventional hydrogen bonds (VAL:270 and CYS:269). Conversely, tetradecene was docked with 4Z69, it recorded -5.1 Kcal/mol binding affinity, while Butyl-MA showed a binding affinity of -4.0 Kcal/mol with one hydrogen bond, just as the standard dominated with -6.1 Kcal/mol binding affinity with a single conventional hydrogen bond. Likewise, the studied compounds were examined for their drug likeness via ADMET studies and they demonstrated potency to serve as drug with good adsorption properties, good metabolism and other properties favorably to Butyl-MA and the both derivatives showed no violation to the Lipinski rule of 5 and Ghose rule for determining the efficacy of drug candidates.

Keywords: Anti-Inflammation, Antinociception, DFT, ADMET, *Napoleonaea Imperialis.*

1.0 Introduction

Across the globe, pain and inflammation have emerged as one of the most difficult issues facing clinicians today. Although pain can be initiated by a combination of lifestyle, environmental, and hereditary variables are to blame [1]. Inflammation, on the other hand, causes the body's immune system to react to injury, infection, or irritation by attacking healthy tissues [2]. In addition, inflammatory illnesses like rheumatoid arthritis, an autoimmune disorder that typically affects women, can cause severe pain, swelling, discomfort, and stiffness in the joints [3]. A further inflammatory disease that is linked to skin conditions like red, scaly skin patches is psoriasis [4]. Multiple sclerosis is another chronic autoimmune disease that results in inflammation due to damage to the myelin sheath surrounding the central nervous system [5]. As a result, nociceptive discomfort and inflammatory diseases impact the body's major organs, including the blood vessels, brain, gut, kidney, joints, skin, and lungs [6-7]. Contrarily, nociception is the process by which the body reacts through the sensory nerves to potentially toxic stimuli that are damaging to human health, such as dangerous substances, mechanical injuries, and extreme temperatures [7].

Although there is no long-term treatment for inflammatory disorders, various defense mechanisms have been developed over time to help reduce both the discomfort and the rapid progression of inflammation. As a result, a variety of anti-inflammatory drugs have been used, which may be beneficial in the therapeutic management of diseases linked to inflammatory responses [8]. Chemical therapeutics that are available for the clinical treatment of inflammatory diseases can be classified as either non-steroidal or steroidal [8]. NSAIDs, or non-steroidal anti-inflammatory medicines, include ibuprofen, aspirin, and indomethacin. Nevertheless, due to non-selective inhibition of both isoforms of the COX enzyme, the currently available anti-inflammatory drug has been shown to have negative side effects, including gastrointestinal injury and ulceration that results in nociception, renal damage, and bronchospasm [9]. However, because of their numerous negative effects, steroidal anti-inflammatory drugs are questioned [10]. As a result of the underlying issues, researchers have tried to create novel therapeutic compounds that can aid in the fight against a variety of diseases.

Researchers have used a variety of medicinal plants because of their rich therapeutic characteristics, abundant in nature, and inexpensive to use in their efforts to provide improved therapeutic agents [11]. Presumably, a great deal of medical plant derivatives has been reported to show exceptional medicinal characteristics. Plants like *Diospyros lotus L*. *Cheiranthus farinosa*, *Napoleonaea Imperialis*, *Hellenia speciosa*, and a few others are still used for their medicinal benefits [12]. For instance, Yonathan *et al* (2006), in their work on in vivo anti-inflammatory and anti-nociceptive activities of *Cheiranthus farinosa* reported that the studied derivatives exhibited good anti-inflammatory properties [8]. Additionally, Uddin *et al* (2014), studied the anti-nociceptive and anti-inflammatory activities *of Diospyros lotus L* and reported that the roots of the studied plant are efficient herbal medicine for subsiding pain and inflammation [13].

Certainly, the effectiveness of medicinal plants as therapeutic agents is increasing, and there is a growing body of research calling for the exploration of medicinal plants as a reliable path to drug discovery [14]. For this reason, in this research, we explore the biological activity of *Napoleonaea Imperialis*, a native of Nigeria, the Congo, and Angola, and a member of the family Lecythidaceae. *Napoleonaea Imperialis* is primarily 6m tall with a dense, low branching crown [15]. Several studies have demonstrated *Napoleonaea Imperialis*' inhibitory action against bacterial and fungal isolates [16], there may be saponin in *Napoleonaea Imperialis* seeds [17]. In addition, it has been reported that *Napoleonaea Imperialis* roots and leaves contain significant phytochemicals like alkaloids, flavonoids, tannins, steroids, glycosides, saponins, carbohydrates, resin, and proteins, as well as having the ability to scavenge free radicals and act as antioxidants [18]. Therefore, using computational density functional theory (DFT), molecular docking, and ADMET prediction, we examine the anti-nociception and anti-inflammatory mechanism of (R)-sec-butyl 2-methoxyacetate (Butyl-MA) and tetradecene derivatives of *Napoleonaea Imperialis* seeds against proteins (4DO3, 4Z69). The outcome of this study provided insight into the electronic properties of these compounds and their potential as promising therapeutic agents.

2.0 Methodology

2.1 Experimental methodology

2.1.1 Identification and collection of plant material

The *Napoleonaea Imperialis* seed was harvested from a tree in an open area of the staff quarters at the University of Cross River State in Calabar, Nigeria. It was verified at the University of Cross River State, Calabar, Nigeria in the Department of Plant and Biotechnology.

2.1.2 Extract preparation

After rinsing the seed in clean water, it was allowed to air dry at room temperature. It was left to dehydrate for 14 days at room temperature; this extended drying time guarantees complete evaporation of the water content, inhibiting the growth of microorganisms and preserving the integrity of the sample. The possibility of sample composition denaturing or thermal deterioration is reduced by carefully drying the sample at room temperature. After that, the sample was crushed into smaller pieces. It was then blended into an extremely fine particle size using an electric blender. The resulting powder was then extracted with ethanol using a Soxhlet extractor. The ethanol was completely evaporated and concentrated using rotary evaporator.The *Napoleonaea Imperialis* seed was subjected to GC-MS analysis using the methodology described by Raju and Kumar (2020) [19]. Utilizing BUCK M910 Gas Chromatography with HP-5MS section (30 m length × 250 µg in width × 0.25 µg in film thickness), the analysis was carried out. High-energy electrons (70 eV) were used in the electron ionization framework for spectroscopic identification by GC-MS. The carrier gas was 99.995% pure helium gas flowing at a rate of 1 mL/min. The starting temperature was adjusted to be between 50 and 150 °C, rising at a pace of 3 °C per minute, and held for around 10 minutes. At last, the temperature was raised to 300 °C at a rate of 10 °C per minute. In a splitless mode, one microliter of the previously prepared 1% extract solution that had been diluted with certain solvents was injected. Based on the peak area produced in the chromatogram, the relative

quantity of the chemicals included in each of the extracts was represented as a percentage.

2.2 Computational procedure

The computational work was performed employing the DFT/B3LYP/6-311G++g(2d,2p) method which is very appropriate for evaluation of the compound's properties and for gaining insight with accurate predictions of molecular geometries energies, and providing detailed information into the assessment of reactivity and stability of the study derivatives and their biological potency with the target's receptors. Optimization of the compounds was achieved utilizing Gaussian 09W [20], and the sketching of the structures was achieved via Gauss View 6.0.16 [21]. The molecular docking technique which evaluates the level of bonding between ligands and target proteins, and the visualization in 2d and 3d were aided by the Biovia discovery studio, Autodock tools and PyMOL software [22-24]. Furthermore, other analyses were carried out in this study, of such analyses like Frontier molecular orbital (FMO) is engaged with calculations of the quantum descriptors to determine the reactivity and stability of a compound [25], natural bonding orbital analysis was also carried out to evaluate bond types and strengths with perturbation energy of a system [26], more so, Density of State of analysis was achieved using the Multiwfn 3.8 software and OriginPro 2018 [27-28]. Finally, the compounds were subjected to the Lipinski rule of 5 and the Ghose rule under the ADMET studies to determine the drug efficacy of the studied compounds by utilizing three web-based tools: SwissADME, ADMET lab, and ProTox-II [29-31].

2.3 Molecular docking procedure

The molecular docking process is an insilico-based technique that predicts the binding mode and binding affinity of small molecules, like potential drugs, to a target protein [32]. Basic important software and tools for performing molecular docking simulations include Autodock and Auto Dock Vina 1.5.6, [33]. In this protocol, the studied compound Tetradecene and (R)-sec-butyl 2-methoxyacetate derivatives from *Napoleonaea Imperialis* seed was docked with two selected proteins with codes 4DO3 and 4Z69 which are inflammatory and nociception receptors, these proteins were downloaded from the protein data bank website (https://www.rcsb.org/) in PDB format. Using the Biovia Discovery Studio program, these proteins were made ready for docking simulations by eliminating ligand groups, water, and heteroatoms. Charges were given to the compounds after protein production in order to transform them from PDB to PDBQT. Following successful docking via vina command, 2D and 3D visualization were made available via PyMOL software and Biovia Discovery Studio, respectively [34]. The standard drug Acetaminophen was also docked with the proteins to compare its binding affinity with the affinities of the studied compounds. Generally, this protocol is designed to identify potential drug candidates for the treatment of inflammation and pain by studying the binding interactions with the studied compound. Hence, the results of molecular docking simulations provide valuable insights into the mechanism of drug action and aid in the design of more effective drugs [35].

3.0 Results and discussion

3.1 Electronic properties

3.1.1 Frontier Molecular Orbital (FMO) analysis

In order to assess the reactive and stable characteristics of compounds, frontier molecular orbitals (FMO) analysis is performed [36]. FMO computations of the quantum descriptors are based on the values of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The HOMO serves as an electron donor, while the LUMO serves as an electron acceptor [37]. However, the energy gap (Eg), which is the difference between the two orbitals (LUMO, HOMO), is a useful parameter for assessing the reactive and stable properties of compounds [38] **Table 1** shows the calculated results for HOMO, LUMO, energy gap, and other quantum descriptors. Moreover, the HOMO and LUMO values are used to compute the global reactivity descriptors, which include Chemical potential (μ), Chemical softness (S), Chemical hardness (η), Electronegativity (χ), and Electrophilicity index (ω) [39]. In the current study, the FMO analysis was computed to gain insight into the electronic properties of selected bioactive compounds, tetradecene and Butyl-M. The computed outcomes for the energy gap, HOMO, LUMO, and additional quantum descriptors are presented in the table, where tetradecene has an energy gap of 6.857 eV, which is marginally less than that of butyl-MA, which is 6.912 eV. This suggests that butyl-MA is more stable and less reactive than tetradecene, which is more reactive and less stable. The compounds under study exhibit polarizability, as indicated by their chemical hardness and softness values (c) of 3.429 and 3.456 eV, respectively, for tetradecene and Butyl-MA. Consequently, tetradecene has a global softness (S) of 1.715 eV while Butyl-MA has a softness (S) of 1.728 eV. Accordingly, we may conclude that the chemicals under study show biological action, which is consistent with recent findings. **Figure 1** displays the HOMO, LUMO issosurface illustrating the regions of electron dispersion for the investigated compounds from *Napoleonaea imperialis.*

Table 1. Result Frontier Molecular Orbitals (FMO) analysis for studied compounds

Parameters	Symbol	Compounds	
		Butyl-MA	Tetradecene

HOMO (eV)	E_{HOMO} (eV)	-7.293	-7.102
LUMO (eV)	E_{LUMO} (eV)	-0.381	-0.245
Energy Gap	(Eg)	6.912	6.857
Ionization Potential	(IP)	7.293	7.102
Electron Affinity	(EA)	0.381	0.245
Global Hardness	(η)	3.456	3.429
Global Softness	(S)	1.728	1.715
Chemical Potential	(μ)	-3.837	-3.674
Electrophilicity	(ω)	-2.130	-1.968
Electronegativity	(χ)	3.837	3.674

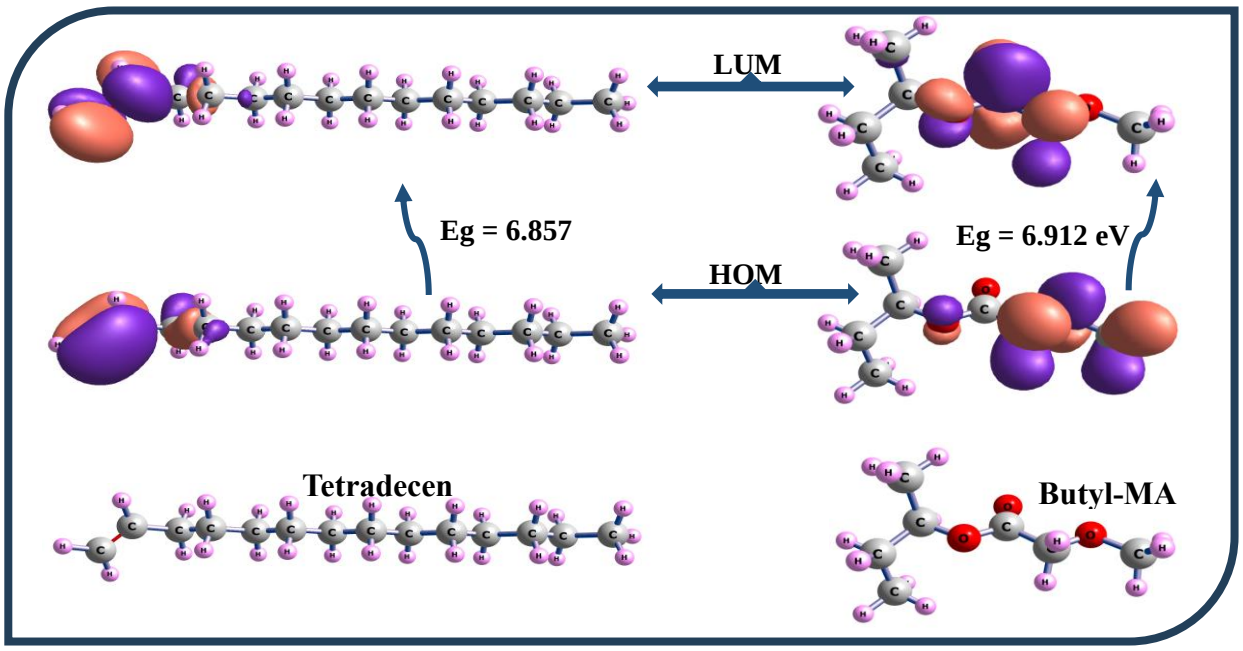


Figure 1: FMO Issosurface plot of Tetradecene and Butyl-M

3.1.2 Natural Bonding Orbitals (NBO) analysis

Natural Bond Orbitals (NBOs) are localized molecular orbitals that provide a chemical interpretation of bonding in terms of Lewis-like electron pairs. They offer insight into the nature and strength of chemical bonds within molecules [40]. NBO analysis provides valuable insights into the nature, strength, and directionality of chemical bonds, aiding in the interpretation of molecular structure and stability [40]. In line with previous research, high perturbation or stabilization energies indicate stronger donor and acceptor interaction and entail a stable compound or molecule [41]. The selected second-order perturbation energies for studied compounds are presented in Table 2. From the table,

Butyl-MA showed its strongest interaction LP-O1 to O3-C8 and bond transition LP → π* with perturbation energy of 51.93 Kcal/mol, while tetradecene showed its strongest interaction of C14 - H41 to C11 - C13 in the transition of σ → σ* with a significantly low energy value of 6.86 Kcal/mol. Similarly, Butyl-MA's least interaction is shown to be LP-O1 to O3 - C8 in a transition LP → σ* with a recorded perturbation energy value of 9.54 Kcal/mol, on the other hand, the least interaction for tetradecene is C11 - H35 to acceptor C13 - H40, with a bond transition σ → σ* and an energy value of 4.68 Kcal/mol. Butyl-MA has shown stronger bonds of interaction and higher perturbation energy over tetradecene, it is therefore indicative that Butyl-MA is more stabilized than tetradecene.

Table 2: Showing natural bonding orbital of Butyl-MA and tetradecene.

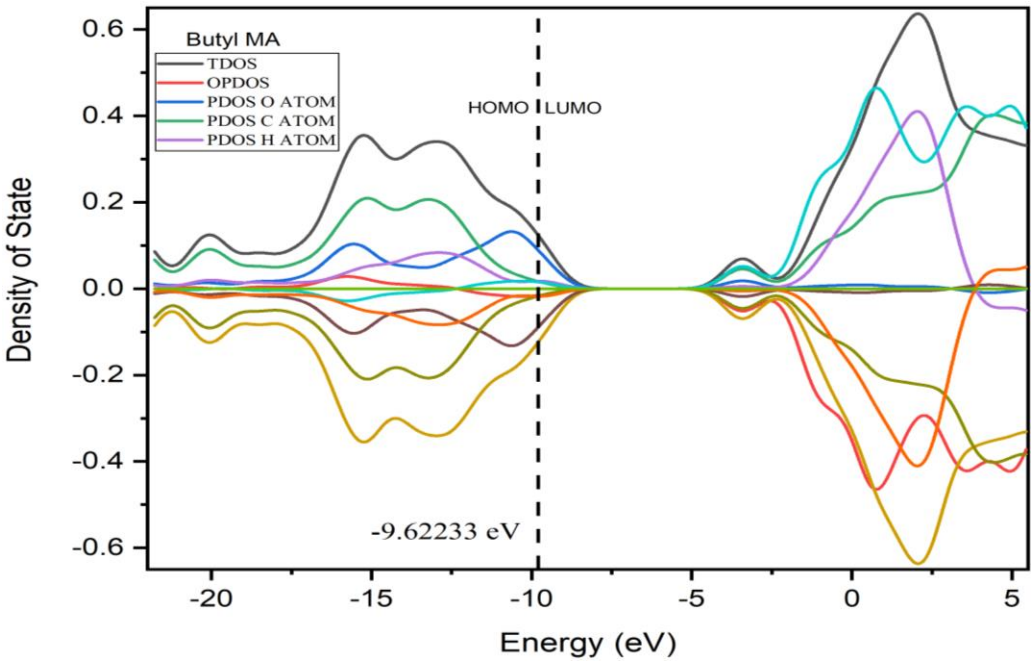
Compounds	Donor (i)	Acceptor (j)	Transition	E2 Kcal/mol	E (j)-E(i) a.u.	F (I, j) a.u.
Butyl-MA	LP - O1	O3-C8	LP → π*	51.93	0.49	0.142
	LP - O3	O1 - C8	LP → σ*	40.76	0.76	0.160
	LP - O3	C8 -C9	LP → σ*	21.84	0.82	0.122
	LP - O1	O3 - C8	LP → σ*	9.54	1.29	0.099
Tetradecene	C14 - H41	C11 - C13	σ → σ*	6.86	1.13	0.079
	C11 - H36	C13 - C14	σ → π*	5.86	0.69	0.057
	C13 - H40	C14 - H42	σ → σ*	5.49	1.16	0.072
	C11 - H35	C13 - H40	σ → σ*	4.68	1.14	0.065

3.1.3 Density of State (DOS) analysis

Density of States (DOS) analysis is a computational technique used in drug design to understand the electrical characteristics of molecules. The number of states, or energy levels, that electrons in a molecule can access at a particular energy range is shown graphically [42]. Figure 2 is a graph for the Density of State analysis of the studied compound Butyl-MA and Tetradecene. Butyl-MA graph has its Total Density of States (TDOS) marked at the range of 0.36 peak level, it has three PDOS atoms (oxygen, carbon, and hydrogen) with Partial Density of State of oxygen atom exhibiting an overlap over other fragments, and having obtained the highest peak level over Carbon and Hydrogen atoms, the PDOS oxygen atom shows dominance over the other PDOS atoms. The Butyl-MA curve also shows its Fermi energy of -9.62233 eV. On the other hand, Tetradecene depicts its Total Density of state (TDOS) at 0.72 peak level, it also projected the Partial Density of State of carbon atom characterized with an overlapping peak level over its other fragment Hydrogen atom. Notably, Fermi energy is an important parameter which distinguishes the HOMO and LUMO of the states and this would characterize the properties of a compound, wherefore, tetradecene shows its Fermi energy to be -

10.59918 eV which is slightly lower comparatively to that of Butyl-MA, this therefore is indicative that Butyl-MA is more reactive because it with would have more available states for electrons to occupy.

Figure 2: Density of State graph for the studied compounds



3.2 Fourier Transform InfraRed (FT-IR) Spectroscopy Analysis

Fourier transform infrared spectroscopy analysis, another name for Vibrational analysis, is a useful technique for characterizing a compound's functional group by using the molecule's vibrational mode [43]. The purpose of this research was to obtain important information regarding the vibrational and frequency modes of certain molecular structures of the compounds Tetradecene and Butyl-MA derivative from *Napoleonaea Imperialis* that were under investigation. The values used in this analysis are compared with the standard range value for every functional group. The computed outcome is displayed in **Table 3** the values on the table increase progressively down the table with each corresponding functional group and assignment. On the frequencies of 1202.25 cm^{-1} and 3274.77 cm^{-1}, Butyl-MA exhibited a CH_2 similar functional group with twisting and asymmetric assignments respectively. Similarly, CH_3 functional group was shown with scissoring and asymmetric assignments for the frequency values of 1486.84 cm^{-1} and 3299.91 cm^{-1}, respectively. Notably, the frequency value of 3267.72 cm^{-1} recorded a methoxy group with an antisymmetric assignment. Consequently, tetradecene showed varying assignments with similar CH_3 functional groups,

indicating only a difference at the first and last frequency values with CH_2 and C_2H_3 functional groups as indicated in the table.

Table 3: FT-IR analysis of the studied compounds

Compounds	Theoretical values (CM^{-1})	Assignment
Butyl-MA	1202.25(CH_2)	Twisting
	1486.84(CH_3)	Scissoring
	3267.72(C_2H_5O)	Anti-symmetric
	3274.77(CH_2)	Anti-symmetric
	3299.91 (CH_3)	Anti-symmetric
Tetradecene	1309.49(CH_2)	Wagging
	1513.77(CH_3)	Scissoring
	2909.90(CH_2)	Anti-symmetric
	2943.45(CH_3)	symmetric
	2993.20(CH_3)	Anti-symmetric
	3029.64(C_2H_3)	symmetric

3.3 Molecular docking analysis

A molecular docking technique was carried out to investigate the biological potential of tetradecene and (R)-sec-butyl 2-methoxyacetate (Butyl-MA) compounds, derivatives from *Napoleonaea imperialis*. This method provides insights into the level of ligand-protein interaction, hydrogen bond formation, and generally predicting the properties of the studied compounds as drug agents [44**]**. Herein, the compounds were assessed as potential anti-inflammation and anti-nociception agents targeting specific proteins (4DO3 and 4Z69). The results from the docking simulation of these compounds against anti-inflammation and anti-nociception are summarized in **Table 4** which shows the data for the docking while the 2D and 3D visualization are shown in **Figure 3.** On docking with protein 4DO3, tetradecene exhibited a binding affinity of -4.8 Kcal/mol with no record of a conventional hydrogen bond, consequently, Butyl-MA attained a binding affinity of -4.1 Kcal/mol with one conventional hydrogen bond (SER:387). while the standard drug Acetaminophen depicts a binding affinity of -5.1 Kcal/mol with two conventional hydrogen bonds (VAL:270 and CYS:269). Also, on docking with protein 4Z69, tetradecene had a binding affinity of -5.1Kcal/mol with no conventional hydrogen bond as Butyl-MA showed docking score of -4.0 Kcal/mol having one conventional hydrogen bond (ARG A:257), whereas, docking the standard drug with the same

protein 4Z69 depicted binding affinity of -6.1 Kcal/mol with one conventional hydrogen bond (TYR A:30). Thus, from the docking scores, although, it can be inferred that the studied compounds showed potency to act as drug candidates, nevertheless, tetradecene exhibited better drug potency over Butyl-MA having shown consistently higher bond level with the target proteins affinities compared to Butyl-MA, Hence, tetradecene can be considered to have better therapeutic potentials compared to Butyl MA.

Table 4: Bonding interactions between studied compounds, the standard and selected proteins

Interaction	Binding affinity (Kcal/mol)	Conventional hydrogen bond	Amino residue
4DO3_Tetradecene	-4.8	nil	Nil
4DO3_Butyl-MA	-4.1	1	SER:387
4DO3_ Acetaminophen	-5.1	2	VAL:270, CYS:269
4Z69_Tetradecene	-5.1	nil	Nil
4Z69_ Butyl-MA	-4.0	1	ARG A:257
4Z69_Acetaminophen	-6.1	1	TYR A:30

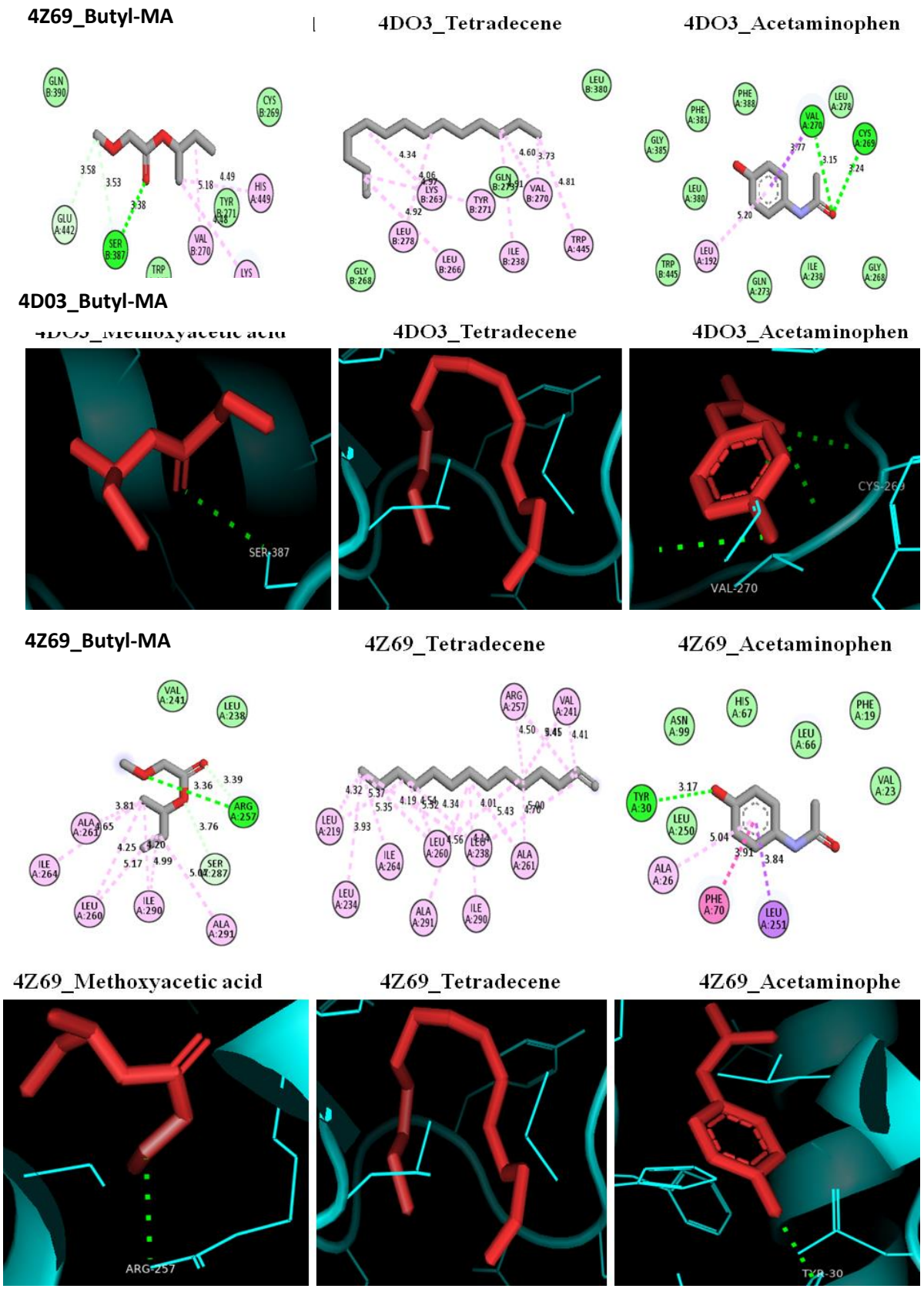


Figure 3: showing 2D and 3D visualization of the studied compounds and the standard

3.4 ADMET Studies

Pharmacokinetics involves studying how a drug behaves in the human body [45]. This

method includes processes that affect drug concentration over time, known as ADMET Adsorption.

Table 5: ADMET studies for the studied derivatives of *Napoleonaea imperialis*.

	Tetradecene		**Butyl-MA**	
Parameters	**Results**	**Color code**	**Results**	**Color code**
Absorption				
Caco-2 Permeability	-4.596	Green	-4.269	Green
MDCK Permeability	1.2e-05	Green	7.6e-05	Green
Pgp-inhibitor	---	Green	---	Green
Distribution				
PPB	98.23%	Red	12.342%	Green
VD	3.683	Green	0.849	Green
BBB Penetration	- -	Green	+++	Red
Metabolism				
CYP1A2 inhibitor	-		-	
CYP2C19 inhibitor	-		---	
CYP2C9 inhibitor	--		---	
CYP2D6 inhibitor	--		---	
CYP3A4 inhibitor	--		---	
Gastrointestinal absorption	Low		high	
Excretion				
Clearance	4.415 mL/min	Red	6.466 mL/min	Green
$T_{1/2}$	0.103s		0.831	
Toxicity	**Probability**	**Prediction**	**Probability**	**Prediction**
Hepatotoxicity	0.69%	Active	0.84 %	Inactive
Carcinogenicity	0.62%	Inactive	0.50%	Active
Immunotoxicity	0.96%	Active	0.99%	Inactive
Mutagenicity	0.97%	Inactive	0.77%	Inactive
Cytotoxicity	0.93%	Inactive	0.80%	Inactive
Physicochemical properties				
Formula	$C_{14}H_{28}$		$C_7H_{14}O_3$	
Molecular weight (MW)	196.37 g/mol		146.18g/mol	
Num. of heavy atoms	14		10	
TPSA	0.00 Å^2		35.53Å^2	

Drug-likeness	prediction	prediction
Lipinski	Accepted	Accepted
Ghost	Accepted	Accepted

Distribution, Metabolism, and Elimination), which is crucial for understanding drug behavior [46]. In this study, our studied compounds were subjected to ADMET studies and the result is displayed in Table 5. Topological polar surface areas (TPSA) for physicochemical parameters were found to be 0.0 A2 for tetradecene and 35.53 A2 for butyl-MA, respectively. Tetradecene shown a low gastrointestinal absorption in terms of metabolism, while Butyl-MA exhibited a high gastrointestinal absorption. Moreover, inhibitors of CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4 are notably inactive in both compounds. For absorption caco-2 assays and MDCK Permeability in both compounds show favorable absorption value for (Tetradecene and Butyl-MA) which is excellent in transport to the intestine. Also, P-glycoprotein inhibitions were not found in both compounds with a color code green. This indicates that there is no interference with absorption indicating that both compounds are excellent. Tetradecene shown a poor attachment to blood proteins inside the blood plasma, with a value of 98.23%, on the distribution measure known as plasma protein binding (PPB), whereas butyl-MA demonstrated a good adhesion, with a value of 12.342%. Additionally, tetradecene demonstrated an inactive blood brain barrier (BBB) penetration result, whereas butyl-MA demonstrated an active BBB penetration result. Furthermore, the chemicals butyl-MA and tetradecene also had good volume of distribution (VD). Tetradecene demonstrated a low clearance capacity under the excretion parameter, represented by a red color code, whereas butyl-MA demonstrated an outstanding clearance ability, indicated by a green color code. Additionally, tetradecene exhibits highly active hepatotoxicity and immunotoxicity, although butyl-MA show significantly active carcinogenicity in the toxicity parameter. Tetradecene and Butyl-MA both adhere to the Lipinski and Ghose rules for evaluating the efficacy of drug candidates, and upon this evaluation, both of the investigated compounds show promising potential as pharmacological agents.

4.0 Conclusion

The analyses in this study were aimed at investigating the biological potency of the derivatives, investigation of the electronic properties of the compounds on FMO analysis showed the reactivity of the studied compounds depicting energy gap values of 6.857 eV and 6.912 eV for tetradecene and Butyl-MA respectively additionally, both compounds showed showcases polarizability as shown by the values of the chemical hardness (η) (3.456 eV to 3.429 eV) and softness (S) (1.728 eV to 1.715 eV). NBO analysis revealed the stability of Butyl-MA over tetradecene with its highest and lowest perturbation energies values shown to be of 51.93 Kcal/mol and 9.54 Kcal/mol with transition of LP $\rightarrow \pi^*$ and LP $\rightarrow \sigma^*$ over tetradecene' 6.86 Kcal/mol highest and 4.68 Kcal/mol lowest perturbation energies with transition of $\sigma \rightarrow \sigma^*$ and $\sigma \rightarrow \sigma$. The number of fragmented atoms of Butyl-MA is more than those of tetradecene with two fragments as depicted by the Density of State (DOS) analysis with a record of -9.62233 eV Fermi energy for Butyl-MA and -10.59918 eV for tetradecene. Consequently, molecular docking analysis revealed the binding affinities of the studied compounds, on binding with protein 4DO3, tetradecene had

a binding affinity of -4.8 Kcal/mol as Butyl-MA showed a binding affinity of -4,1 Kcal/mol with one conventional hydrogen bond (SER:387), whereas the standard drug acetaminophen stood out with an affinity of -5.1 Kcal/mol with two conventional hydrogen bonds (VAL:270 and CYS:269). Conversely, tetradecene was docked with 4Z69, it recorded -5.1 Kcal/mol binding affinity, while Butyl-MA showed a binding affinity of -4.0 Kcal/mol with one hydrogen bond, just as the standard dominated with -6.1 Kcal/mol binding affinity with a single conventional hydrogen bond. Likewise, the studied compounds were examined for their drug likeness via ADMET studies and they demonstrated potency to serve as drug with good adsorption properties, partial distribution and toxicity properties, with good metabolism and other properties favorably to Butyl-MA. Notably, both derivatives showed no violation of the Lipinski rule of 5 and Ghose rule for determining the efficacy of drug candidates. wherefore, it is indicative that the studied compounds have potency to serve as anti-inflammatory and anti-nociceptive drug agents

References

Abbasi, M. M. and Janjua, S. Y. (2016). The Mediating Effect of Job Stress on Work Overload and Organizational Performance in the Banking Industry. *Abasyn University Journal of Social Sciences* (AJSS). 9 (2): 376-387.

Abdel Rahman, A. G., Al Hashim, B. N., Al Hiji, N.K., and Al-Abbad, Z. (2013). Stress among medical Saudi students at College of Medicine, King Faisal University. *Journal of Preventive Medicine and Hygiene*. 54(4):195-199.

Ahmad Ezane, H., Zarina I., Faridah I., Nor Rima M. A., Natasha K. and Normazwin, I. (2012) workplace stress and behavior studies of other space: Commercial Complex, *Procedia – Social& Behavioural Sciences*, (36): 752-769.

Bab.B (2002) Scientific Research Method for Mass Communication Abeokuta Debabs

Bacharach S. B., Bamberger P, and Conley, S. (1991). Work-home conflict among nurses and engineers: Mediating the impact of role stress on burnout and satisfaction at work. *Journal of Organizational Behaviour*.; 12: 39–53.

Bangun, W, 2012, "*ManajemenSumber Daya Manusia*", Jakarta: Erlangga.

Barkhuizen N., Rothmann, S, and van de Vijver, F. J. (2014). Burnout and work engagement of academics in higher education institutions: effects of dispositional optimism. *Stress Health.*30(4):322-332.

Barkhuizen, N. and Rothmann, S. (2008). Occupational stress of academic staff in South African higher education institutions. *South African Journal of Psychology*, 38(2): 321-336.

Basowitz, H., Persky, H., Korchin, S. J., and Grinker, R. R. (1995). *Anxiety and Stress.* New York: McGraw-Hill Book Company, Inc.

Beehr, T. A. and Glazer, S. (2005). Organizational role stress. In J. Barling, K. Kelloway, & M. Frone (Eds.), Handbook of work stress (pp. 7–33). Thousand Oaks, CA: Sage.

Befort, N., Hattrup, K. (2003). Valuing Task and Contextual Performance: Experience, Job Roles, and Ratings of the Importance of Job Behaviors, *Applied HRM Research*, 8(1): 17-32.

Beheshtifar M, Hoseinifar, H, Moghadam, M. (2011). Effect procrastination on work-related stress. *European Journal of Economics, Finance and Administrative Sciences*, 38(38): 59-64.

Hanaysha, J. (2016). Improving employee productivity through work engagement and Job Stress: Empirical evidence from higher education sector. *Management Science Letters* 6 (2016) 61–70

Hasibuan, M. S. P. (2017). *Job Stress Management Revised Edition.* Jakarta: Earth Literacy.

Herr, E. L., Cramer, S. H. & Niles, S. G. (2004). *Job Stress guidance and counselling through the lifespan: Systematic approaches.* (6th Ed). London: Prentice-Hall.

Hulleman, C. S., Schrager, S. M., Bodmann, S. M., &Harackiewicz, J. M. (2010). A meta-analytic review of achievement goal measures: different labels for the same constructs or different constructs with similar labels? *Psychological Bulletin*, 136, 422–449

Ikechukwu D. &Adighije P. J. N. (2017). Effects of Job Stress Growth on Employees Performance: A Study of Non-Academic Staff of Michael Okpara University of Agriculture Umudike Abia State, Nigeria. *World Journal of Entrepreneurial Development Studies*, 1(1), 1-12

Indra, P., Nabilah, A., Heru, T., Nawang, K.&Arif, S. R. (2021). Vocational Training Has an Influence on Employee Career Development: A Case Study Indonesia. *Academy of Strategic Management Journal*, 20(2), 1-8

Irianto, J. (2001). *Main themes of human resource management*. Jatim: Cendikia people.

Izlem, G. (2017). From Mentoring to Career Satisfaction: The Roles of Distributive Justice and Organizational Commitment. *Journal of Management and Strategy*, 8(1), 61– 73.

Kinman, G. and Court, S. (2010). Psychosocial hazards in UK universities: adopting a risk assessment approach. *Higher Education Quarterly*. 64(4): 413-428.

Kozusznik, M., Rodriguez, I. and Peiro, J.M. (2012). Cross national outcomes of stress appraisal. *Cross Cultural Management: An International Journal*, 19(4):507-525.

Lucey.T (2003) Management Accountancy (5th Edition) New York Book Power.

Mchunu, G. (2012). Proposed guidelines for a workplace health promotion policy and implementation framework. *Occupational Health Southern Africa*, 18(2): 5-12.

Olusanya O (2003) Auditing and Investigating (1st Edition). Lagos Agbo Communication Press

Osuala E.C (1982) Introduction to Research Methodology. Lagos Remi Ade Press.

Purwanto, A., Purba,J.T, Bernarto,I., Sijabat,R (2021). effect of transformational leadership, job satisfaction, and organizational commitments on organizational citizenship behavior. *Inovbiz: Journal InovasiBisnis* 9 61-69.

Wood Fand Sangster A. (1996) Business Accounting (7th Edition). Great Pitman Publishing.