Project on: Modified psoralidin and its derivatives for the treatment of monkeypox by computational chemistry.

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Approval

This project paper, "***Modified psoralidin and its derivatives for the treatment of monkeypox by computational chemistry.***" is submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfilment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

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Declaration

I am Md. Amir Hamja Niloy, hereby declare that, this project is done by me under the supervision of Dr. Sharifa Sultana, Associate Professor & Associate Head, Department of Pharmacy, Daffodil International University, in impartial fulfilment of the requirements for degree of bachelor of Pharmacy. I am also declaring that the results embodied in this project have not been submitted to any other university or institute for the award of any degree or bachelor.

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Dedication

The project paper is Dedicated to -

My Parents, Teachers and Supervisor.

Modified psoralidin and its derivatives for the treatment of monkeypox by computational chemistry

Abstract: Human monkeypox is caused by a zoonotic disease caused by the monkeypox virus, an orthopoxvirus and close relative of the variola virus (smallpox). The first countries to report it were in central Africa. There are currently no clinically proven treatments for monkey pox infections. Once the crusts on the lesions have naturally come off and a new skin layer has developed, the infected individual should remain in isolation, wear a surgical mask, and keep the lesions covered as much as possible. Psoralidin, a derivative of prenylated coumestans, has showed promise as a therapeutic agent in animal studies. As adjuvant drugs, the most notable and generally applicable of these effects are: anti-osteoporotic and cancer-preventing. Psoralen and ultraviolet A radiation are effective therapies for the monkeypox virus (PUVA). Quantum calculations have been progressively undertaken to assess pharmacokinetics characteristics such as drug-likeness and Lipinski's principles, ADMET parameters, and the entire quantum calculation of computational techniques by Density Functional Theory (DFT). After the analysis of docking score, The maximum docking score was found to be -9.6 kcal/mol against Monkeypox virus profilin-like protein (PDB ID 4QWO), while the highest binding energy was found to be -10 kcal/mol against Monkeypox virus DNA polymerase (PDB: 8HG1). Finally, the ADMET properties have been determined, ensuring minimal toxicity and non-carcinogenicity for aquatic and non-aquatic species alike. We conclude that the Psoralidin compounds we've chosen all have significant antifungal potential.

Keywords: Pass prediction; molecular dynamics; DFT calculation; ADMET

List of Figures

List of Tables

CONTENTS

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CHAPTER 1

INTRODUCTION

1.1 Introduction

The monkeypox virus, an orthopoxvirus and close relative of the variola virus is responsible for the zoonotic disease known as "human monkeypox" (smallpox). Central African countries were the first to report it[31]. Around 1970, it has a long history of affecting the world's poorest and most disadvantaged people[32][33]. The virus was first identified in monkeys in a 1958 Danish laboratory experiment, which is where the name "monkeypox" was coined[34]. In 2003, the virus was first detected in areas of the world other than Africa[35]. The World Health Organization (WHO) has received reports of 3413 laboratory-confirmed illnesses and one fatality from 50 countries/territories across five WHO Regions since January 1 of 2022[36]. We have identified a group of monkeypox viruses that we call clade 3 as the cause of the present outbreak (derived from the West African clade)[37]. On July 23, 2022, the World Health Organization issued a worldwide health emergency declaration[38].

A large number of mammal species are susceptible to monkeypox, although the virus has only ever been isolated once, from a Funisciurus squirrel in the Democratic Republic of the Congo[39]. It is unclear how widespread the virus is or what animal species may be carriers, although there is mounting evidence that rats are a plausible reservoir[40]. Human diseases have been related to contact with animals, however pinpointing the exact exposure of a human case can be challenging in locations where contact with animals is widespread due to domestic rodent infestations and the hunting or preparation of bushmeat from a range of species. It is assumed that transmission takes place through saliva/respiratory excretions or through contact with lesion exudate or crust material[41][42]. The symptoms include a rash that looks like smallpox but isn't as severe and some milder indicators that may indicate the beginning of the disease called prodromal symptoms (e.g., fever, lymphadenopathy, and flu-like symptoms)[43]. The rash may or may not spread to other parts of the body, and the total number of lesions may be anything from a handful to thousands[44]. Within the subsequent 2–4 weeks, the lesions progress through macular, papular, vesicular, and pustular phases, each lasting 1–2 days. The characteristics of the lesion change simultaneously and include its firmness, depth, and size, which range from 2 to 10 mm. Pustular lesions stay in this state for around 5–7 days before forming crusts. In most cases, the illness clears itself within three to four weeks after the commencement of symptoms, during which time crusts form and desquamate. Once all crusts have fallen off, a patient is no longer contagious[45].

At the present time, there are no effective therapies for monkey pox infections that have been shown in clinical trials It is recommended that the infected person stay in isolation, wear a surgical mask, and keep lesions covered as much as possible until the crusts on the lesions have naturally fallen off and a new skin layer has grown. Compounds that have shown promise against orthopoxviruses in animal tests and severe vaccinia vaccine effects may be worth testing in extreme instances[46].

It's becoming increasingly likely that several of these naturally occurring chemicals could be used as medicines. Psoralidin, a prenylated coumestans derivative, has been shown to have many therapeutic effects in preclinical trials. The most significant and widely applicable of these effects, as adjuvant medicines, are: anti-cancer and anti-osteoporotic[47]. The Monkeypox virus can be treated with psoralen and ultraviolet A radiation (PUVA)[48].

Thus, the goal of this computational work is to highlight the important bioactive natural components of Modified Psoralidin and its derivatives for the treatment of Monkeypox viral infections. The primary motivation for a computational study is the desire to save time and money.Since there is a bigger risk of failure during the development of any medicine. Therefore, it may be helpful to first determine the potentiality of the biomolecules in order to save time, resources, and money in carrying out our further research on the biochemules in order to find out their practical beneficial applications in designing and developing drugs against Monkeypox virus.

CHAPTER 2

Literature review of Psoralidin and its derivatives

2.1 Literature review of Psoralidin and its derivatives

Psoralidin is one of the most active ingredients identified in *P. corylifolia*. The extracts from seeds of *P. corylifolia*, as well as psoralidin, possess antimicrobial, antioxidant, anti-inflammatory, antimutagenic and anticancer activities [1]. Studies have shown that PSO has the following pharmacological properties: it is an antidepressant [2] , it can alter the signaling pathway[3] for the apoptosis-inducing molecule tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), and it may also affect the estrogen receptor [4]. Many in vitro models have been employed to analyze PSO's anticancer effects and the mechanisms underlying them [5]. The percentage of dead cells and the IC50, or the concentration of PSO that inhibits by 50% cell death, are used to determine cytotoxicity following cell interaction with PSO [6]. PSO modulates autophagy in the lung, prevents cancer cells from multiplying (in prostate, breast, and liver cancers as well as in the colon and esophagus), and induces cellular death [7]. PSO has been shown in multiple studies to counteract the effects of forskolin on the transcription of genes encoding hormones such CRH and ACTN3 [8]. In a recent study, it was found to be highly active in vitro against various cancer cell lines. A significant inhibitory effect on protein tyrosine phosphatase 1B, a key metabolite in insulin signaling, has been demonstrated [9]. Coumarins'which ism anti-cancer action arises from a number of biological processes. Bioactive coumarins may be effective against cancer by targeting the TRAIL-mediated apoptotic pathway, as TRAIL is thought to be a tumor-selective cytokine that induces cell death. In order to make TRAIL-resistant cancer cells vulnerable to TRAIL-mediated cytotoxicity, researchers have identified a number of chemicals that can overcome this resistance. The growth of human cancer cell lines SNU-1 and SNU-16 from the stomach, HT-29 from the colon, and MCF-7 from the breast were all shown to be suppressed by PSO in prior research [10]. Coumarins' anti-cancer action arises from a number of biological processes. Bioactive coumarins may be effective against cancer by targeting the TRAIL-mediated apoptotic pathway, as TRAIL is thought to be a tumor-selective cytokine that induces cell death. In order to make TRAIL-resistant cancer cells vulnerable to TRAIL-mediated cytotoxicity, researchers have identified a number of chemicals that can overcome this resistance [11]. Additionally, other coumarins increase sensitivity of cancer cells to TRAIL-mediated apoptosis. Esculetin, also known as 6,7-dihydroxy-coumarin, is a coumarin found in Artemisia capillaries, Citrus limonia, and Euphorbia lathyris, and it has been shown to have chemopreventive and anticancer effects in animal studies. For oral cancer cells from the SAS, Kok et al. showed that esculetin could increase apoptosis triggered by TRAIL [12]. There have been a number of research on the cytotoxicity of PSO, and the results have revealed that it has the capacity to produce cytotoxicity against a variety of cell types, including breast (MCF-7) cancer, colon (HT-29), and stomach (SNU-1, SNU-16) cells. Both androgen-independent (DU-145, PC-3) and androgen-dependent (LNCaP, C4-2B) prostate cancer cells responded to PSO therapy by undergoing apoptosis. PSO was similarly effective in preventing the growth of PC-3 xenograft tumors in naked mice [13]. In addition to its beneficial effects on cell proliferation, autophagy, and apoptosis, PSO has been proven to have a protective effect against diabetes complications, oxidative stress, obesity, and osteoporosis [14]. PSO is

associated with the regulation of the autophagy process, inhibition of cadmium-transformed prostate epithelial cell xenograft growth through placenta-specific 8 inhibition expression, downregulation of nuclear factor kappa B (NF-kappa B) and B-cell lymphoma-2 (Bcl-2), and upregulation of apoptotic gene expression [15]. PSO has been demonstrated to reduce cell proliferation and promote apoptosis by inhibiting Bcl-2 activity and inducing Bax and caspase-3 activity through the PI3K/Akt pathway [16]. Controlling the death of tumor cells may have therapeutic value since it is a key homeostatic mechanism involving the activation, expression, and regulation of a number of genes [17]. As a result, apoptosis induction in tumor cells is a potential tactic in the creation of anticancer medications. We found that PSO dramatically boosted the apoptotic rate of OS cells using flow cytometry. Caspase-3 is the primary executor of apoptosis and is involved in the initiation of this cell death process [18]. Antiapoptotic members of the Bcl-2 family, including Bcl-2, and proapoptotic members of the Bcl-2 family, like Bax, are critical regulators of mitochondria-mediated apoptosis [19]. We discovered that PSO markedly raised the rate of apoptosis in OS cells, boosted the protein levels of Bax and cleaved caspase-3, and downregulated the levels of Bcl-2. PSO's ability to hasten apoptosis in OS cells was traced back to several well-established mechanisms [20].

Significant alterations in PI3K/Akt and FAK signaling were observed in 143B and MG63 cells treated with PSO, suggesting that these pathways may be involved in the anticancer effects of PSO in OS cells. We used GSEA and Kaplan-Meier analysis to dig deeper into the root reasons of these shifts. The findings highlighted the significance of DEG and ITGB1, two genes frequently linked to cancer. Membrane receptors belonging to the integrin family are involved in cell adhesion and recognition, as well as embryogenesis, hemostasis, tissue repair, the immunological response, and the dissemination and metastasis of malignant cells. Activation of kinases FAK and SRC follows the binding of most integrins to the actin cytoskeleton through talin and other proteins. Despite our results showing a molecular docking interaction between PSO and ITGB1, we feel it is important to point out that other regulatory pathways, such as mitochondrial pathways involved in DNA repair [21][22] also regulate ITGB1 gene expression in specific processes. This indicates that there may be additional modes of action or feedback mechanisms that influence the final expression of ITGB1, beyond those at the protein level. These steps link integrins to signal effectors such as phosphoinositide 3-kinase (PI3K) and Akt (protein kinase B) and Ras-extracellular signal-regulated kinase (ERK) and Yes-associated protein (YAP) and transcriptional co-activator with PDZ-binding motif (TAZ) [23]. Multiple studies have shown that FAK is significantly involved in tumor cell survival, migration, invasion, angiogenesis, and metastasis, and that ITGB1 is the primary activator of FAK. Furthermore, integrin ligand binding increases FAK tyrosine (Tyr) 397 phosphorylation [24][25]. FAK is activated by PI3K after ITGB1 phosphorylates Tyr397; this complex is formed with SRC, which binds the PI3K P85 subunit. In response to ITGB1-induced Tyr397 phosphorylation, FAK can associate with SRC and bind to the P85 subunit of PI3K, triggering downstream Akt activation and cellular proliferation regulation [26][27]. Multiple

investigations have demonstrated that inhibiting ITGB1 expression reduces tumor spread and invasiveness. Inhibiting ITGB1 expression is thus important to enhance OS therapy. Experiments with molecular docking demonstrated that PSO specifically binds to ITGB1. In addition, western blot results confirmed the decreased ITGB1 protein expression in OS cells following PSO treatment, supporting the conclusions of the molecular docking study. As a result, our results show that PSO therapy may impede OS development and progression by decreasing ITGB1 expression via the FAK and PI3K/Akt signaling pathways [28]. Psoralidin, which was extracted from P. corylifolia seeds, increased swimming and decreased immobility time, but had no effect on climbing. Significant increases in 5-HT and 5-HIAA levels were observed after psoralen administration, and striatal DA alterations were reversed. Psoralidin reduced the elevated levels of CRF, ACTH, and corticosterone that were caused by swim stress and restored normal HPA axis function in mice [29]. Psoralidin has been shown to have a strong inhibitory effect on OS, and this anti-OS action may be achieved via down-regulating ITGB1 expression through the FAK and PI3K/Akt signaling pathways. Further, ITGB1 was shown to be a promising therapeutic target for treating OS in this study. When it comes to creating selective anti-OS medications, psoralen stands out as a promising option [20].

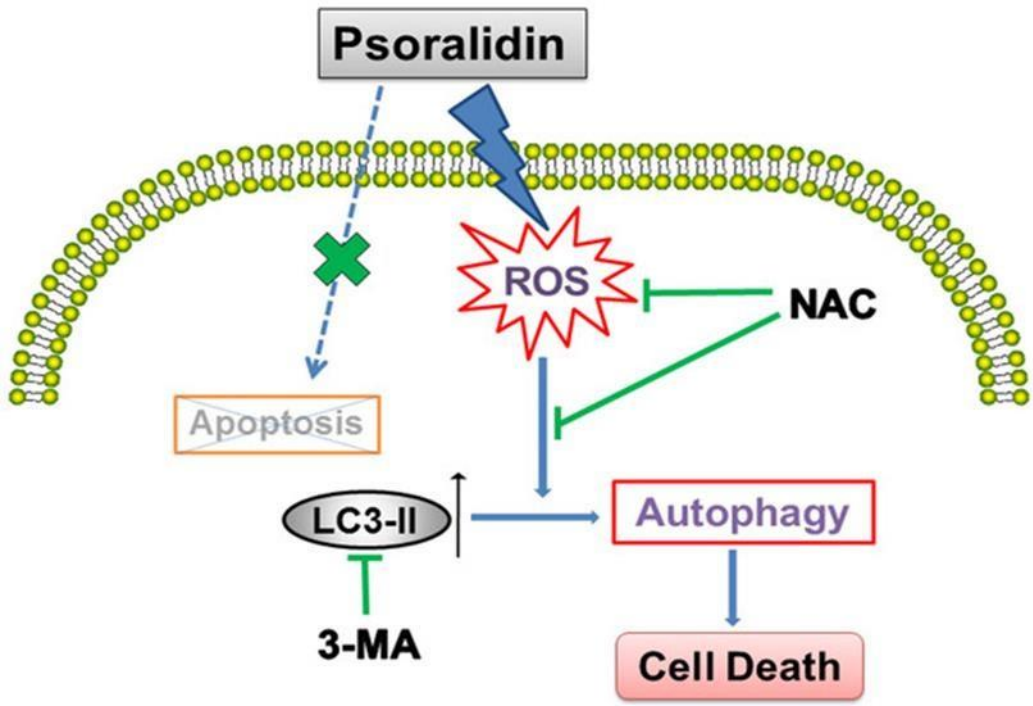

Figure 1: Schematic diagram illustrates the underlying mechanism of psoralidin-induced cell death in A549 cell [30].

CHAPTER 3

Purpose of the study

3.1 Purpose of the study

Computer-aided drug design (CADD) includes computational chemistry, molecular modeling, molecular design and rational drug design.

The main purpose is to identify effective natural source of
anti-viral property and develop a potential lead compound which is effective against monkeypox virus and which is more active specific and less toxic.

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CHAPTER 4

Method and materials

4.Computational method and working procedure

4.1 Determination of the Data of ADMET

ADMET studies are vital for understanding the pharmacokinetic features of ligand molecules, which can then be applied to improving their medicinal efficacy or bioactivity. AmdetSAR, available at "http://lmmd.ecust.edu.cn/admetsar2," is now the go-to resource for forecasting AMDET characteristics, and it is where we get our ADMET data from[49]. Water solubility Log S, human intestinal absorption, Caco-2 permeability, blood-brain barrier, renal OCT2 substrate, total clearance (ml/min/kg), and acute microsomal enzyme toxicity are some of the most important pharmacokinetics features discovered by ADMET investigations.

4.2. Preparation of Ligand and molecular optimization

To begin,

- We used Chemdraw Professional to create accurate representations of all of the chemical structures.
- These compounds have been optimized using vibrational frequencies from the B3LYP functional and DND basis (diffused basis set) semi-core pseudo-potentials[50] and the resulting series of derivative molecules of ketal and non-ketal have been saved to the pdb file for use in subsequent computational studies such as molecular docking, molecular dynamics, and ADMET properties, etc.

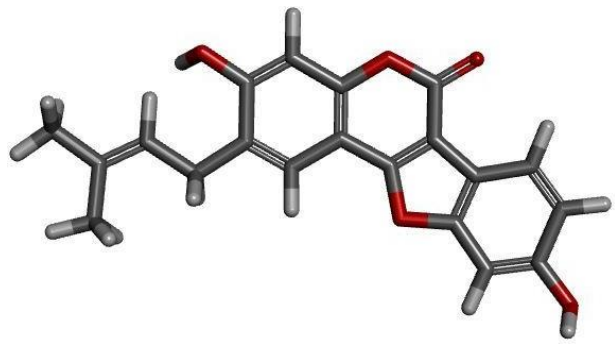


Figure 2: Optimized molecular structure 1

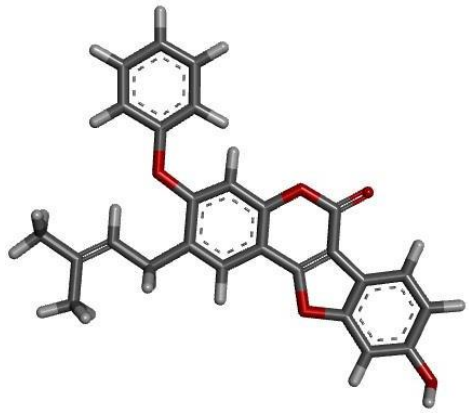


Figure 3: Optimized molecular structure 2

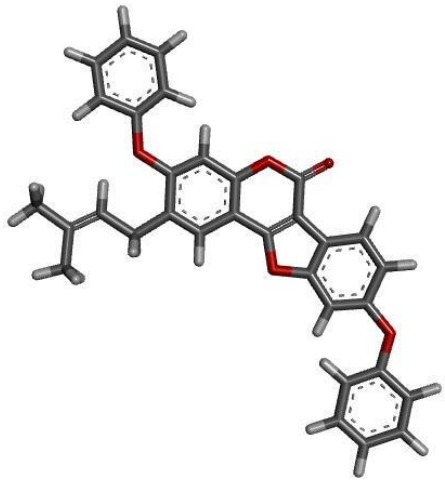


Figure 4: Optimized molecular structure 3

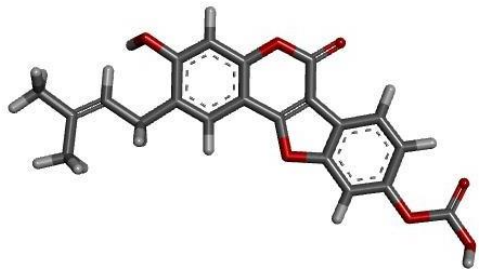


Figure 5: Optimized molecular structure 4

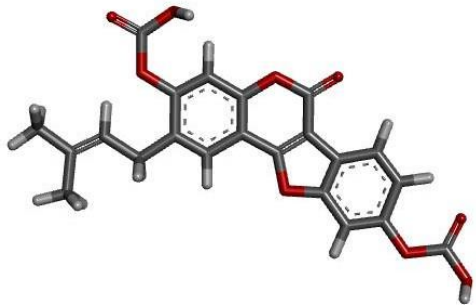


Figure 6: Optimized molecular structure 5

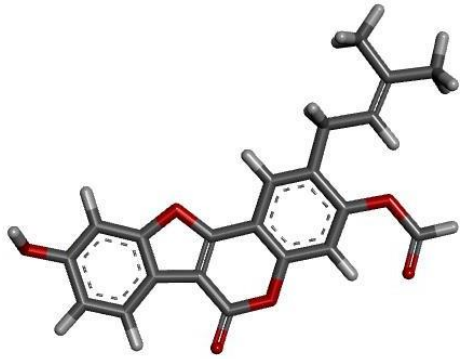


Figure 7: Optimized molecular structure 6

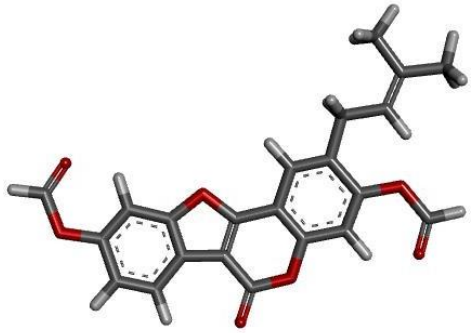


Figure 8: Optimized molecular structure 7

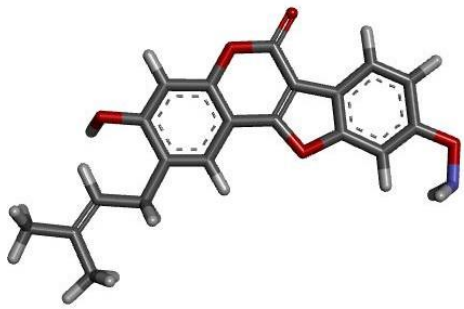


Figure 9: Optimized molecular structure 8

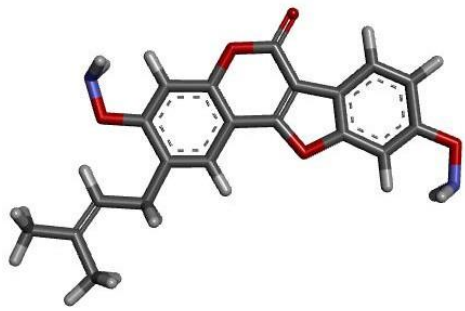


Figure 10: Optimized molecular structure 9

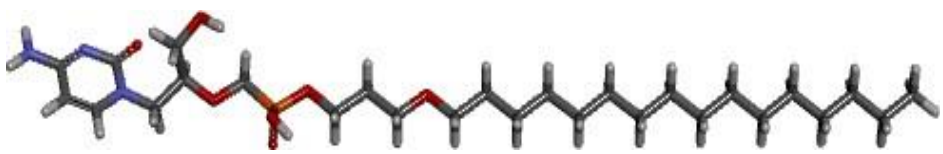
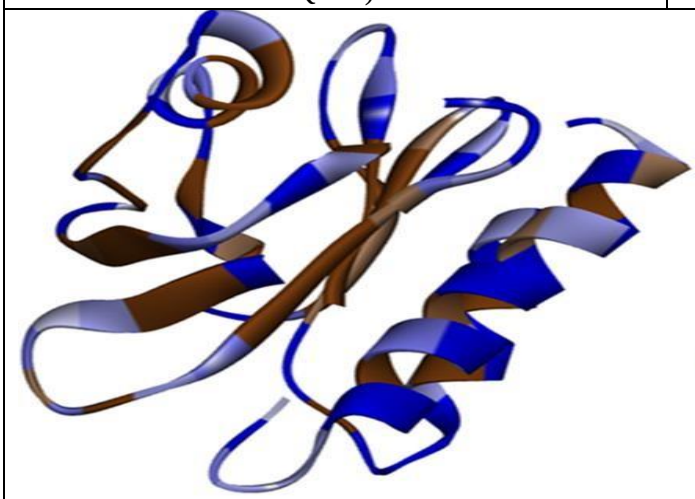
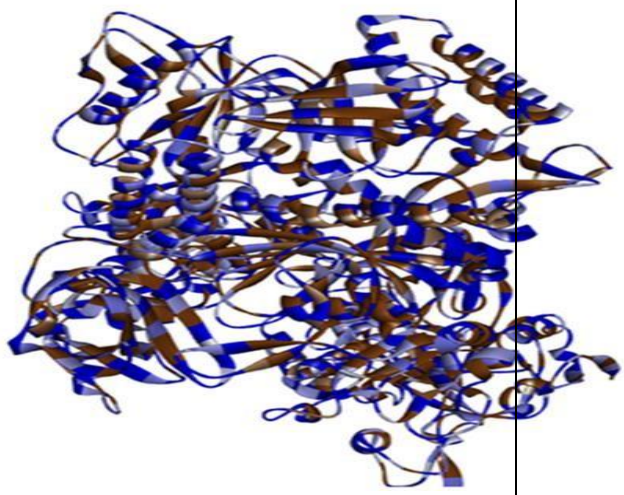


Figure 11: Optimized molecular structure 10

4.3. Preparation of protein, and molecular docking studies.

- The pdb files containing the three-dimensional structures of the monkeypox virus profilin-like protein (PDB ID 4QWO) and the MERS-CoV DNA polymerase (PDB: 8HG1) were downloaded from the protein data bank (https://www.rcsb.org/)[51].
- With version 1.3 of the application PyMol, all heteroatoms and water molecules are eliminated[52].
- The Swiss-Pdb viewer software, version 4.1.0, was used to optimize proteins for lowest energy levels[53].
- After the optimal compounds were identified, molecular docking studies were conducted on them against the various protein targets**.**
- The molecular docking interaction between the protein and ligand was designed using the PyRx program (version 0.8)[54].
- For docking analysis, we imported proteins and their ligands using AutodockVina Tools (ADT) from the PyRx software suite. If you need a reliable and genuine open-source tool to run docking simulations, go no further than AUTODOCK Vina. Vina is mostly used as a platform for single-molecule docking, while Auto Dock Tools can assist with docking simulations[55].

Figure 12: Three-dimensional protein structure of the monkeypox and MERS-CoV virus

Monkeypox virus profilin-like protein (PDB ID 4QWO)	Monkeypox virus DNA polymerase (PDB: 8HG1)
	
[56]	[57]

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4.4 Lipinski rule, Pharmacokinetics and Drug likeness

- Lipinski Rule data is collected from SWISADMETSAR[58] a reputable online resource for calculating pharmacokinetic parameters (http://www.swiss-adme.ch/index.php).
- When studying the pharmacokinetics of a bioactive chemical, the Lipinski Rule is a crucial factor to consider.
- Table 1 displays the range of molecular values, and their applicability is further explored in the following discussion.
- Drugs have typically been tiny molecules that adhere to Lipinski's rule of five (i.e., have a molecular mass of less than 500 Da, include no more than 5 hydrogen bond donors, no more than 10 hydrogen bond acceptors, and have an octanol-water partition coefficient log P of no more than 5).

CHAPTER 5

Result and Discussion

5. Result and Discussion

5.1 Structural activity relationship

We synthesized a Psoralidin analogue by employing structural activity relationship (SAR) analysis. To continue our research, we drew the Psoralidin analog's structure using the DFT tool in Material Studio 08, and then we colored it in. These Psoralidin derivative structures are then investigated using a wide range of computational and biological activity factors.

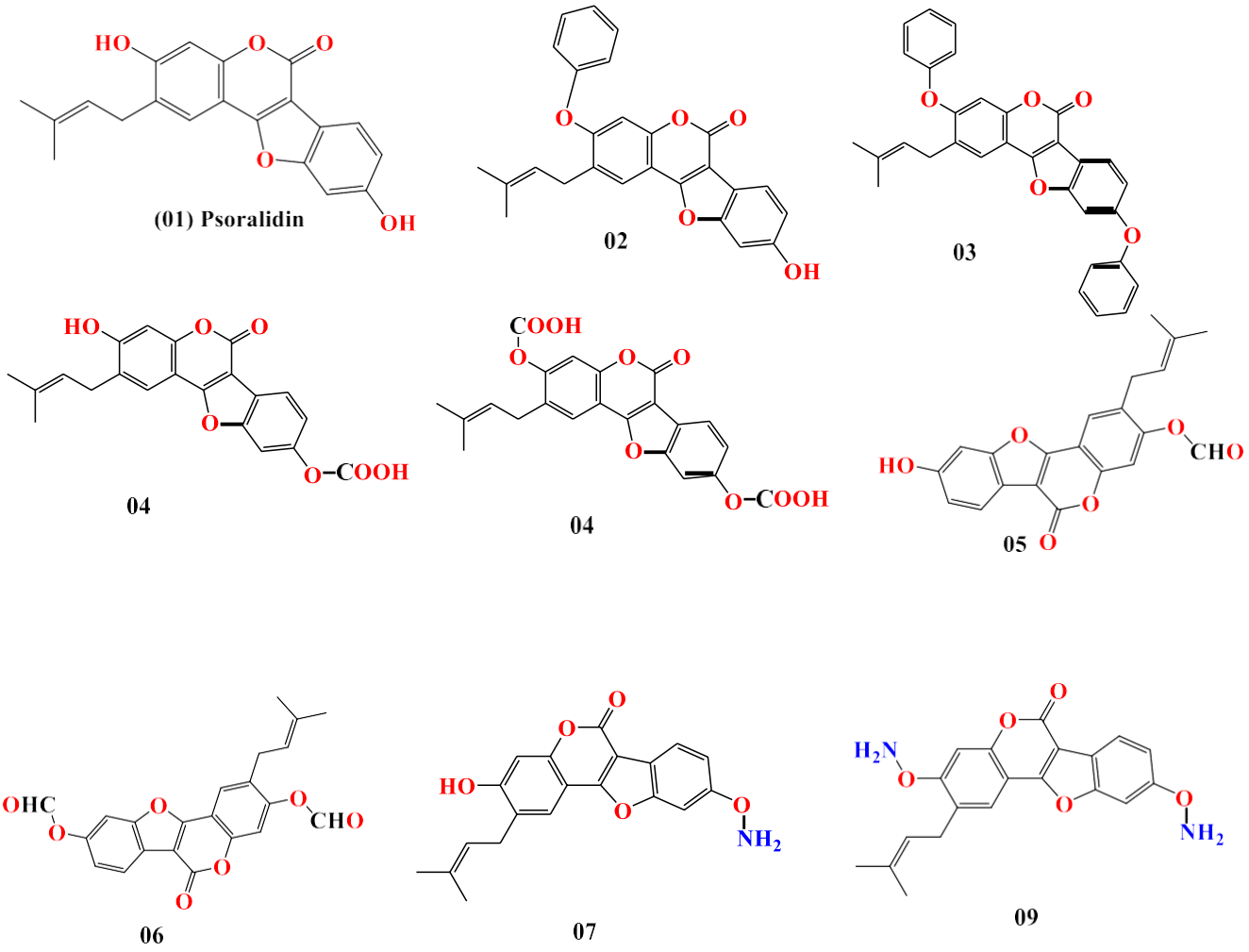


Figure 13. Chemical structure

5.2 Lipinski rule, Pharmacokinetics and Drug likeness

Lipinski's five-rule is widely used as a starting point for investigating drug-like compounds[59]. All of the medication candidates evaluated here have met the established criteria, and it has been determined that the drug candidate has excellent bioavailability and intestinal absorption in humans (HIA). Compounds have been recorded to have molecular weights between 336.34 and 561.69 g/mol, with the lower molecular weight being 336.34 g/mol and the higher molecular weight being 561.69 g/mol. The range of measured molar refractivity was 97.81- 154.16. Except for compounds 2 ,3 and 10, all of these results strictly followed the

Lipinski rule. Since all of the reported compounds have good GI absorption rates, high bioavailability, and conformed to the Lipinski rule, we concluded that they are safe for human consumption.

NO	Molecular Weight (g/mol)	Hydrogen bond acceptor	Hydrogen bond donor	Molar Refractivity	Consensus Log $P_{o/w}$	Lipinski rule		Bioavailability Score
						Result	violation	
01	336.34	5	2	97.81	3.98	Yes	0	0.55
02	412.43	5	1	122.02	5.54	Yes	1	0.55
03	488.53	5	0	146.51	7.15	Yes	1	0.55
04	380.35	7	2	104.16	3.90	Yes	0	0.56
05	424.36	9	2	110.79	3.82	Yes	0	0.56
06	364.35	6	1	102.59	4.04	Yes	0	0.55
07	392.36	7	0	107.64	4.15	Yes	0	0.55
08	351.35	6	2	99.90	3.70	Yes	0	0.55
09	366.37	7	2	102.27	3.37	Yes	0	0.55
Brincidofovir	561.69	8	5	154.16	4.17	Yes	1	0.55

Table 1: Data of Lipinski rule, Pharmacokinetics and Drug likeness

5.3 Molecular docking and interaction analysis

Since the average binding energy of approved drugs is estimated to be -6.0 kcal/mol[60][61]. The identified therapeutic candidate compounds against monkeypox virus profilin-like protein (PDB ID: 4QWO) and Monkeypox virus DNA polymerase (PDB: 8HG1) have showed good and greatest binding affinity. Based on the results of the binding affinity study, it is clear that compound 03 is far more effective than the others in inhibiting the activity of these two monkeypox proteins. The highest binding affinity was measured at -9.6 kcal/mol for compound no. 03 for the monkeypox virus profilin-like protein (PDB ID 4QWO), and at -10 kcal/mol for the monkeypox virus DNA polymerase (PDB: 8HG1). In that regard, the highest docking score recorded was -9.6 kcal/mol against Monkeypox virus profilin-like protein (PDB ID 4QWO), and the greatest binding energy acquired was -10 kcal/mol against Monkeypox virus DNA polymerase (PDB: 8HG1).

No	Monkeypox virus profilin-like protein (PDB ID 4QWO)	Monkeypox virus DNA polymerase (PDB: 8HG1)
	Binding affinity (Kcal/mol)	Binding affinity (Kcal/mol)
1.	-8.5	-8.5
2.	-8.6	-9.1
3.	-9.6	-10
4.	-8.3	-8.5
5.	-7.8	-8.6
6.	-8.1	-8.4
7.	-7.0	-8.2
8.	-8.4	-8.9
9.	-8.1	-8.3
Brincidofovir	-5.5	-5.7

Table 2 : Molecular docking and interaction analysis

5.4 Protein-ligand interaction and Molecular docking poses

Fischer's lock-and-key theory, in which the ligand locks into the receptor, provided an early explanation for this process [62]. This hypothesis formed the basis for the earliest documented docking approaches, in which the ligand and receptor were modeled as rigid entities [63]. Modeling the atomic-level interaction between a small molecule and a protein via the molecular docking approach allows us to define the behavior of small molecules at the binding site of target proteins and provide light on key biological processes [64]. Docking consists of two primary steps: predicting the ligand shape and position/orientation within these sites (often referred to as pose), and then evaluating the binding affinity.

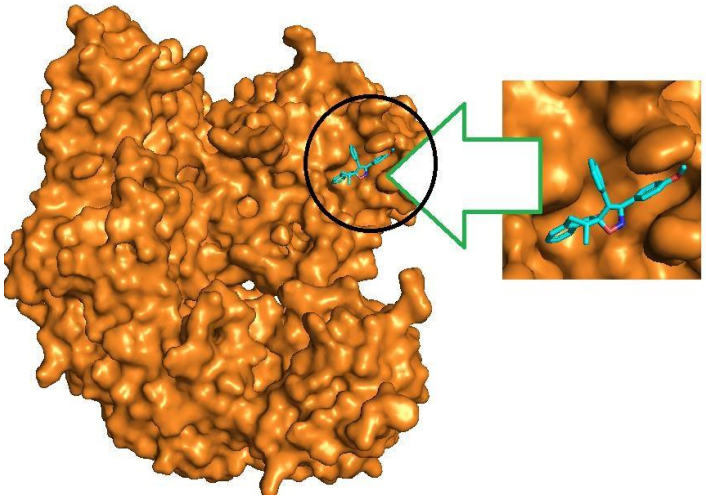
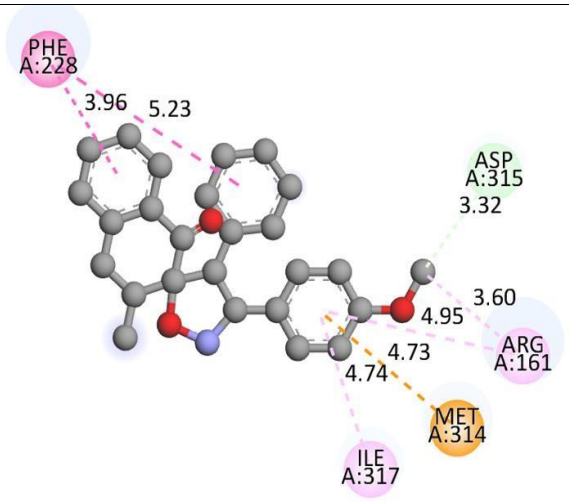
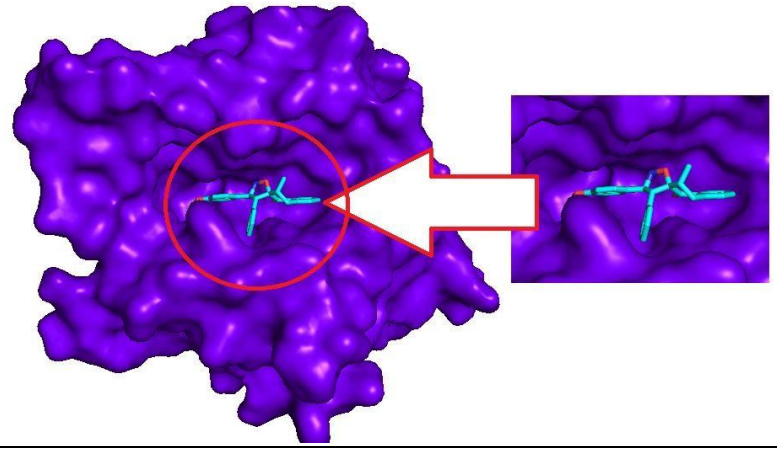
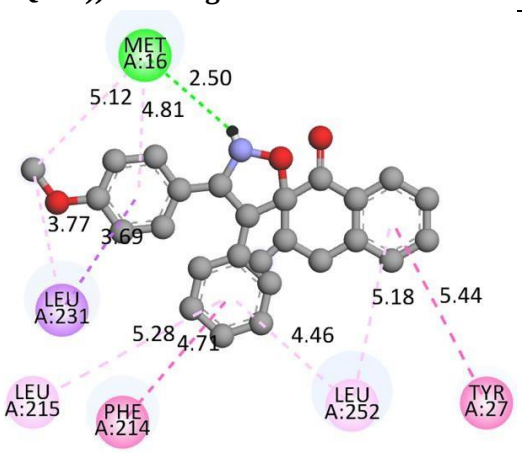
Protein ligands binding pocket	2D picture of active sites.
	
Monkeypox virus profilin-like protein (PDB ID 4QWO)) **with Ligand 03**	
	
Monkeypox virus DNA polymerase (PDB: 8HG1) with Ligand 03	

Figure 14: Docking interactions between the proposed compound and Monkey Pox disease, hydrogenbonding, and 2D picture of active sites.

5.5 ADMET Data Investigation

Absorption, distribution, metabolism, elimination, and toxicity (ADMET) are some of the most critical features of a therapeutic agent or a new drug candidate. Table 6 provides the results of admetSAR's analysis of the chemical's absorption, distribution, metabolism, and excretion (ADMET) parameters, such as the human intestinal absorption (HIA), blood-brain barrier (BBB), Caco-2 permeability, and so on. All of the medications we've designed have been well-absorbed in the digestive tract, but they have failed tests for BBB permeability and negative response in renal OCT2 substrate. All most all compounds are shown a positive effect against CYP450 1A2 Inhibitors and except compound no 04, 05 and Brincidofovir. Except for compounds 1,4 and Brincidofovir, the most majority of compounds have been found to be effective against CYP450 2C9 substrate inhibitors. It has been determined that no medications exhibit hypertoxicity. Acute oral toxicity values for these substances vary widely, from 0.407 kg/mol to 1.046 kg/mol. Acute maximum tolerated doses vary by chemical, with values ranging from 0.302 (ml/min/kg) to 1.046 (ml/min/kg).

NO	Absorption			Distribution		Metabolism		Excretion		Toxicity		
	Water solubility Log S	Caco-2 Permeability x 10^{-6}	Human Intestinal Absorption (%)	VDss (human)	BBB Permeability	CYP450 1A2 Inhibitor	CYP450 2C9 Substrate	Total Clearance (ml/min/kg)	Renal OCT2 substrate	Max. tolerated the dose ((log mg/kg/day)	AMES Toxicity	Hepatotoxicity
1	-3.892	1.017	93.229	-0.112	No	Yes	No	0.832	No	0.448	Yes	No
2	-4.466	0.995	95.903	-0.802	No	Yes	Yes	0.938	No	0.536	Yes	No
3	-3.85	1.089	95.517	-0.884	No	Yes	Yes	0.938	No	0.536	Yes	No
4	-3.561	0.498	77.517	-0.983	No	No	No	1.046	No	0.495	No	No
5	-2.895	0.998	53.949	-1.476	No	No	Yes	0.407	No	0.947	No	No
6	-4.465	1.07	96.271	-0.003	No	Yes	Yes	0.762	No	0.416	Yes	Yes
7	-5.265	1.207	100	0.076	No	Yes	Yes	0.737	No	0.302	No	No
8	-3.837	0.382	100	-0.023	No	Yes	Yes	0.805	No	0.358	Yes	No
9	-3.805	1.019	97.805	-0.062	No	Yes	Yes	0.837	No	0.396	Yes	No
Brincidofovir	-4.523	-0.083	61.172	-0.284	No	No	No	0.926	No	1.081	No	No

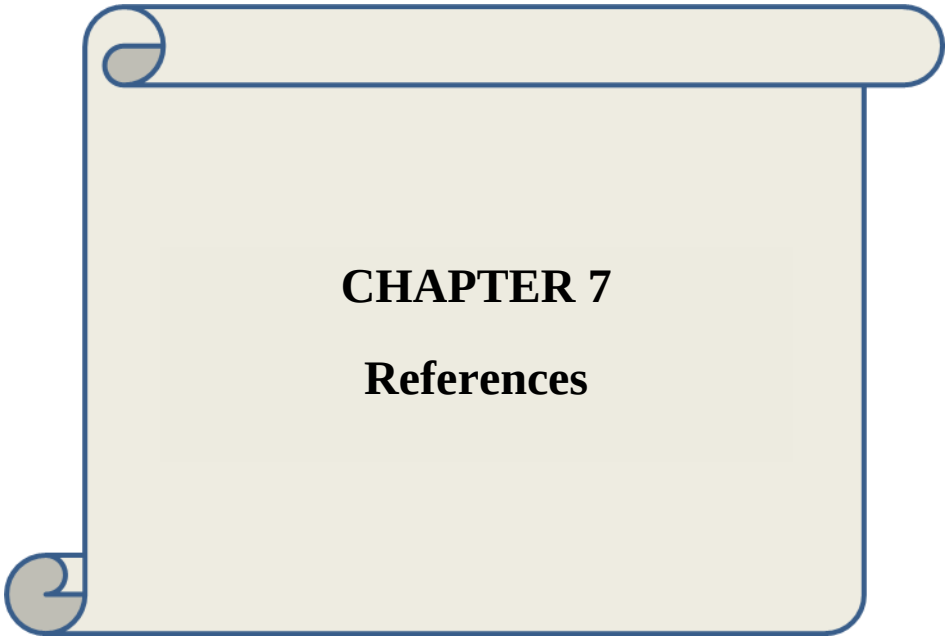
Table 3 : ADMET Data Investigation

CHAPTER 6

Conclusion

6.1 Conclusion

The study's objective is to identify a drug or inhibitor that can prevent the spread of the lethal white spot illness, which is monkeypox. In the search for a cure for monkeypox, researchers have turned to both computational and experimental methods.The monkeypox virus is an orthopoxvirus and a close relative of the variola virus that causes human monkeypox, a zoonotic disease (smallpox). It was originally reported in central African countries. The virus that causes monkey pox has no currently effective treatments. Infected individuals should remain in isolation, use a surgical mask, and keep the lesions covered as much as possible until the crusts have naturally fallen off and a new skin layer has grown. The prenylated coumestan derivative psoralidin has shown effectiveness in animal trials as a potential medicinal drug. Anti-osteoporotic and cancer preventative properties are the most well-known and widely applicable to adjuvant medicines**.**The computational studies of Monkeypox have used Psoralidin and its derivatives, and molecular modeling from computational tools has been used to build new functionalized compounds. The PASS hypothesis hypothesized that they are somewhat antifungal rather than pathogenic. Molecular docking has been used to determine the binding affinity of compounds to mokeypox for more accurate research. In that regard, the highest docking score recorded was -9.6 kcal/mol against Monkeypox virus profilin-like protein (PDB ID 4QWO), and the greatest binding energy acquired was -10 kcal/mol against Monkeypox virus DNA polymerase (PDB: 8HG1). In addition, all derivatives had very high rates of total clearance (renal and non renal). Because of this, it is believed that modified psoralidin and its derivatives can effectively prevent monkeypox.



CHAPTER 7

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