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An Insilico Investigation: Repurposing FDA Approved Drugs Targeting Monkeypox Virus

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Abstract: Monkeypox viral infection is emerging as a significant threat and concern worldwide for the human population. Still, the available treatment options don't meet the requirement, increasing the mortality and morbidity. This fosters the researchers to engage in the development of novel treatment strategies or drug repurposing to overcome the hurdle. With this background, the identification of potential drug targets can significantly amplify the development of potent drug molecules for the treatment. The proteins responsible for viral replication should be targeted, and hindering these proteins should be the key findings to reduce the morbidity and mortality. The literature review provides insight into two viral proteins, viral core Thymidylate Kinase (2V54) and DNA polymerase holoenzyme (8HG1), which are primarily responsible for disease aggravation. Sixty-four antiviral agents approved by the FDA were selected and evaluated against both viral proteins via simulation screening. These antiviral agents possess the capability to obstruct bacterial protein production, rendering them significant candidates for medication repurposing. According to the screening outcomes against DNA polymerase holoenzyme, the two leading compounds, Dolutegravir and Raltegravir, with docking values of –10.0 and –9.7 kcal/mol, respectively, were chosen for further examination. Raltegravir and Etavirine, exhibiting docking scores of −10.0 and −9.6 kcal/mol, respectively, against thymidine kinase are the leading compounds identified following the validation of the protease with the pharmacological library. While investigating medications targeting proteinase, the top two molecules, Dolutegravir and Raltegravir, had the highest docking scores. These two medicinal compounds have significant inhibitory capabilities against MPXV proteinase Thymidine kinase and DNA polymerase protein. Ultimately, the current research illustrates the repurposing of antiviral medicines as a treatment for monkeypox viral infection.

Keywords: *Monkeypox Virus, Thymidylate Kinase, DNA Polymerase Holoenzyme, Antiviral Agents.*

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I. INTRODUCTION

Monkeypox is a zoonotic disease that causes a smallpox-like infection in humans [1]. The human monkeypox virus (MPXV) is a double-stranded DNA virus of the Orthopox virus genus, Poxviridae family [2]. Monkeypox viruses are oval or brick-shaped, measuring 200–400 nm in size [3]. Since the first human case in 1970 in the Democratic Republic of the Congo, the disease has caused occasional outbreaks, mainly in West and Central Africa [4]. Until this year, rising monkeypox cases in Africa were largely ignored, but over 16,000 cases in nonendemic countries led the WHO to declare it a global health emergency. India has reported 30 cases, with one death in Kerala in March 2024 [5]. Rope squirrel (*Funisciurus* spp.), Gambian pouched rat (*Cricetomys gambianus*), and Sooty mangabey monkey (*Cercocebus atys*) are suspected reservoir host for monkey pox [6]. Monkeypox commonly causes fever, headache, myalgia, fatigue, and lymphadenopathy, with skin lesions appearing 1–3 days after fever onset [7].

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Although smallpox and monkeypox are both viral illnesses, monkeypox is generally less severe [8]. Lymphadenopathy, which occurs in monkeypox but not in smallpox, is the key distinguishing feature [9]. Monkeypox spreads through contact with infected skin, fluids, or respiratory droplets, then multiplies at the entry site and spreads to nearby lymph nodes [10]. Person-to-person transmission has become significant, mainly through respiratory droplets, contaminated objects, close contact, and direct contact with rashes [11]. Viral DNA has been detected in blood, urine, and saliva, though this does not confirm the samples are infectious [12]. Risk factors include age, sex, occupation, sexual orientation, and routes of exposure such as close contact, contact with animals, or sexual activity [13]. Monkeypox is dangerous due to complications like blindness, sepsis, and encephalitis, with nearly 1 in 10 cases-especially in children-risking fatal outcomes [14]. Samples must be collected with proper precautions. MPXV diagnosis involves viral culture, electron microscopy, immunohistochemistry, IgG/IgM tests, and PCR, which may be used alone or with sequencing [15]. Early detection, prompt treatment, and widespread prevention are essential. As monkeypox spreads across more than a third of countries, a pandemic is possible, particularly because it resembles measles and chickenpox [16]. Monkeypox is a zoonotic virus maintained in wildlife, which makes eradication difficult. Increasing immunocompromised populations also reduce vaccination effectiveness [17]. Strategies for preventing monkeypox include immunization, health education, and personal protective equipment [18].

Personal protection includes covering lesions, avoiding infected animals, and practicing safe sex [19]. Supportive care is the mainstay of standard treatment, with antivirals being evaluated for severe cases or high-risk individuals [20]. Tecovirimat, brincidofovir, and cidofovir are potential antivirals, with tecovirimat showing the greatest promise. Care includes protecting sensitive areas, preventing infection, and maintaining nutrition and hydration [21]. Symptomatic treatment includes antipyretics, IV fluids, antihistamines, and antibiotics for secondary infections [22]. Mpox has a linear double-stranded DNA genome, approximately 197 kb in size [23]. Thymidylate kinase (2V54) binds thymidine diphosphate and is a unique drug target, as no approved treatments exist, and it differs structurally from the human enzyme at the active site [24]. The MPXV (8HG1) DNA polymerase holoenzyme includes Uracil-DNA glycosylase E4, DNA polymerase F8, and A22. As MPXV replicates in the host cell cytoplasm, this holoenzyme is a key antiviral target [25]. The molecular functions of these viral factors remain unclear, but their structures reveal key aspects of the polymerase life cycle and DNA replication [26]. Drug repurposing finds new uses for existing drugs to treat various diseases [27]. This strategy offers faster approval, lower costs, and reduced health risks since the drugs are already proven safe [28]. This study aims to identify a new monkeypox treatment using computational drug repurposing of approved antivirals [29].

II. PATHOPHYSIOLOGY

MPXV virions are ovoid or brick-shaped and are enclosed by a geometrically corrugated lipoprotein outer membrane. Their size ranges from 200-250 nm [30].

- *The Virus can also Display Two Distinct Morphologies:*

The extracellular enveloped virion (EV) has two membranes, whereas the mature virion (MV) has one membrane. EVs are produced from MVs through a structural remodeling process that includes the addition of host endosomal membranes or components of the Golgi apparatus [31].

Virus transmission begins with close contact between an animal and a human or between humans, entering through the injection site and initiating replication in the respiratory and oropharyngeal mucosa. This process corresponds to an incubation period of 7, 14, or 21 days [32].

Glycosaminoglycans on the membrane surface of the host cell are bound by proteins from the virion membrane [33]. The nucleocapsid is uncoated and enters the cytoplasm, where replication takes place, after the virus is internalized by endocytosis and delivered via vesicles to the proper site of fusion [34].

III. METHOD AND METHODOLOGY

- *Ligand Preparation:*

FDA-approved antivirals are selected for the study. The structures of all the antiviral drugs were retrieved from the PubChem database. The 64 Antiviral drugs and the standard drug Tecovirimat of ‘sdf’ format are converted into ‘pdb’ format by adding polar to the ligands using BIOVIA Discovery Studio Visualizer 4.0, a free viewer software.

- *Molecular Docking:*

All the FDA-approved antivirals were performed for molecular docking studies against the target DNA polymerase holoenzyme (2V54) and Thymidylate kinase (8HG1) with the resolution of 2.40 and 2.80 respectively using the PyRx tool of Autodock Vina software. The prepared protein and ligands in the Biovia discovery studio and all the ligands are minimized and converted to protein and ligands into PDBQT format. Then, the grid parameter configuration file was created, and the docking process was carried out. Then the binding energies for all the compounds were saved and compared with the standard drug. 2D and 3D structures of compounds with the highest binding affinities were visualized using Biovia, and the amino acid interactions were validated.

- *ADMET Prediction Analysis:*

The *in silico* ADME screening and drug-likeness evaluation were performed using the free web tool Swiss ADME, which is developed by the Swiss Institute of Bioinformatics. The compounds with high-ranking binding energy scores were subjected to this part of the screening process. (35,36). Drug development includes evaluating absorption, distribution, metabolism, and excretion (ADME) at a point in the discovery phase when there are many

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compounds under consideration but limited access to physical samples. Computer models are acceptable alternatives for experiments in that situation. (37) The bioactivity prediction was determined by Molinspiration software, and toxicity studies were performed by Protox-II software.

IV. RESULT AND DISCUSSION

Currently, there is no standard treatment for Monkeypox; therefore, this study focuses on drug repurposing for the disease using antiviral drugs. PyRx is a Virtual Screening software that can be used to screen libraries of compounds against potential drug targets.The selected top priority compounds & MPXV protein reference molecules were studied to find the interaction between the protein ligand complex. Three hydrogen bond interactions were formed by dolutegravir are Tyr300, His319, and Phe328 residues. Likewise, arg41, glu142, and lys14 all formed three hydrogen bonds with raltegravir. Ser338, Phe494, and Met656 exhibited strong hydrogen bonding with the reference compound Tecovirimat. Apart from the hydrogen bond, Dolutegravir and Raltegravir also demonstrated Pi-alkyl interactions with residues Tyr B101 and Phe A129, respectively, suggesting stable binding within the MPXV DNA polymerase holoenzyme active site.

When Thymidylate kinase and Raltegravir were docked, the important hydrogen bonds involving residues Arg41, Glu142, Lys14, and Pro39 were found, suggesting stable binding. But no hydrogen bonds were formed in the etavirine-thymidylate kinase complex. However, the reference Tecovirimat shows Ser338, Phe494, and Met656 residues, respectively. Furthermore, Pi-alkyl and hydrophobic interactions were observed in selected ligands including with reference. A comparative investigation of all these bioactive substances is necessary for screening molecules with higher efficacy. [38]. Molecular docking studies were performed to study the treatment for monkeypox by FDA-approved 64 antivirals against DNA polymerase holoenzyme (8HG1) and Thymidylate kinase (2V54). All the ligands exhibit various binding affinities (ΔG kcal/mol) ranging from -10.0 to -1.6 kcal/mol for DNA polymerase holoenzyme (8HG1) and ranging from -10.0 to -1.3 kcal \ mol for Thymidylate kinase (2V54), which is shown in Table 1.

Table 1 The Binding Affinities of Antivirals against the Protein DNA Polymerase Holoenzyme and Thymidylate Kinase

S.NO	***COMPOUNDS***	***8HG1***	***2V54***	***S.NO***	***COMPOUNDS***	***8HG1***	***2V54***
1.	Acyclovir	-6.4	-5.3	33	Entecavir	-8.1	-6.6
2	Ganciclovir	-6.4	-5.6	34	Ribavirin	-7.2	-7.1
3	Vidarabine	-7.6	-5.7	35	Telbivudine	-7.4	-6.6
4	Zidovudine	-7.5	-7.0	36	Zanamivir	-7.3	-6.7
5	Lamivudine	-6.5	-5.5	37	Cabotegravir	-8.8	-7.5
6	Zalcitabine	-6.3	-5.7	38	Rilpivirine	-8.5	-9.2
7	Podofilox	-7.8	-6.6	39	Tenofovir	-6.6	-6.7
8	2 docosanol	-4.8	-4.1	40	Dolutegravir	-10.0	-8.2
9	Abacavir	-7.7	-7.6	41	Imiquimod	-7.1	-6.1
10	Idoxuridine	-7.2	-6.5	42	Trifluridine	-7.7	-6.9
11	Famciclovir	-7.1	-6.4	43	Dasabuvir	-8.8	-7.9
12	Penciclovir	-7.0	-6.7	44	Boceprevir	-1.6	-1.3
13	Efavirenz	-7.8	-7.3	45	Pleconaril	-7.2	-7.0
14	Oseltmavir	-6.5	-5.3	46	Favipiravir	-5.6	-6.0
15	Raltegravir	-9.7	-10.0	47	Maribavir	-6.8	-6.5
16	Nevirapine	-6.9	-6.1	48	Baloxavir	-9.9	-7.9
17	Rimatadine	-5.9	-5.5	49	Brincidifovir	-5.9	-5.6
18	Inosine	-7.3	-6.5	50	EIDD 2801	-8.0	-8.7
19	Emtricitabine	-6.6	-6.7	51	Peramivir	-7.0	-6.7
20	Amprenavir	-7.7	-6.1	52	Nelfinavir	-9.1	-8.3
21	Etavirine	-8.8	-9.6	53	Doravirine	-8.6	-7.2
22	Stavudine	-6.4	-6.0	54	Delavirdine	-9.0	-7.5
23	Cidofovir	-6.2	-6.4	55	Arbidol	-7.9	-7.0
24	Valacyclovir	-6.9	-7.1	56	Brivudine	-7.6	-6.4
25	Didanosine	-6.9	-7.1	57	Tilorone	-6.7	-6.7
26	Indinavir	-9.4	-8.0	58	Tecovirimat	-9.0	-7.5
27	Tipranavir	-9.5	-8.4	59	Clevudine	-7.3	-7.0
28	Foscarnet	-4.1	-4.8	60	Moroxydine	-6.0	-5.7
29	Phosphono acidic acid	-4.8	-4.7	61	Fostemsavir	-8.5	-8.4
30	Darunavir	-8.4	-7.7	62	Enisamium Iodide	-6.5	-6. 3
31	Elvitegravir	-8.8	-6.8	63	Ingavirin	-5.8	-6.2
32	Valganciclovir	-7.7	-7.3	64	Amenamevir	-8.3	-6.9

Compounds were subjected to a second screening where compounds greater than 9.0 kcal/mol were chosen as a threshold criterion, and the binding affinity for the top compounds is listed in Table 2,3. From the results,

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Dolutegravir (-10.1 kcal/mol) and Raltegravir (-10.0 kcal/mol) showed the highest binding affinity against the targets compared to the standard drug Tecovirimat (-9.0 kcal/mol). The 2D and 3D drug interactions against DNA polymerase are shown in Figures 1 to 4.

Table 2 The Binding Affinity of Top Antivirals against DNA Polymerase Holoenzyme

Compound (8HG1)	Hydrogen Bond Interactions	Other Interactions
TECOVIRMAT	**Ser:338, Phe:494, Met:656**	**lys:478, lys:397, Ile:662, Pyr:658**
RALTEGRAVIR	Val:320, Glu:495, Asn:321, Thr:326	Met:492, Phe:9, Asn:322, Phe:494, Phe:329, Ile:327
ETAVIRINE	-	-
INDINAVIR	Asn:322, Asn:321, Phe:318, Asp:330	Pyr:300, His:12, Met:492, His:265, Phe:329, Val:320
TIPRANAVIR	Ser:655, Ser:338, Lys:337	Tyr:486, Ile:501, Phe:494, Pyr:658 Lys:478, Ile:662
RILPIVIRINE	Val:320, Asn:322	His:12, Asn:321, Val:295
DOLUTEGRAVIR	Tyr:300, His:319, Phe:328, Ser:491	Phe:129, Glu:495
BALOXAVIR	Asp:462, Pro:176	Glu:920, Phe:267, Phe:175, Phe:171, Lys:174
NELPINAVIR	Asp:268	Cys:459, Glu:168, Phe:171, Phe:175, Pro:176, Lys:345
DELAVIRDINE	Cys:169	Phe:171, Pro:176, Leu:346

Table 3 The Binding Affinity of the Top Antivirals against Thymidylate Kinase

Compound(2v54)	Hydrogen Bond Interactions	Other Interactions
TECOVIRMAT	**Ser:338, Phe:494, Met:656**	**Tyr:658, Ile:662, Lys:397, Lys:478**
RALTEGRAVIR	Arg:41, Glu:142, Lys:14, Pro:39	Lys:17, Tyr:101, Phe:68, Ser:97
ETAVIRINE	-	-
INDINAVIR	Arg:43, Glu:142, Lys:14, Prd:35	Tyr:101, Phe:68, Ser:97, Lys:17
TIPRANAVIR	Arg:41, Asp:13, Thr:18, Asn:37, Gly:16	Arg:137, Lys:14, Tyr:144, Leu:53
RILPIVIRINE	Asp:13, Glu:142	Leu:53, Arg:93, Lys;14
DOLUTEGRAVIR	Asn:37, Thr:18, Lys:17, Ser:15, Asp:13, Thr:19, Arg:93	Arg:41, Leu:12, Gly:16
BALOXAVIR	Arg:93, Asn:37, Arg:41, Thr:18	-
NELPINAVIR	Tyr:35, Asn:37, Asp:92, Arg:93, Arg:41, Thr:18	Leu:53, Tyr:101, Lys:14
DELAVIRDINE	Thr:18, Gln:20	Gly:16, Ser:15, Arg:137

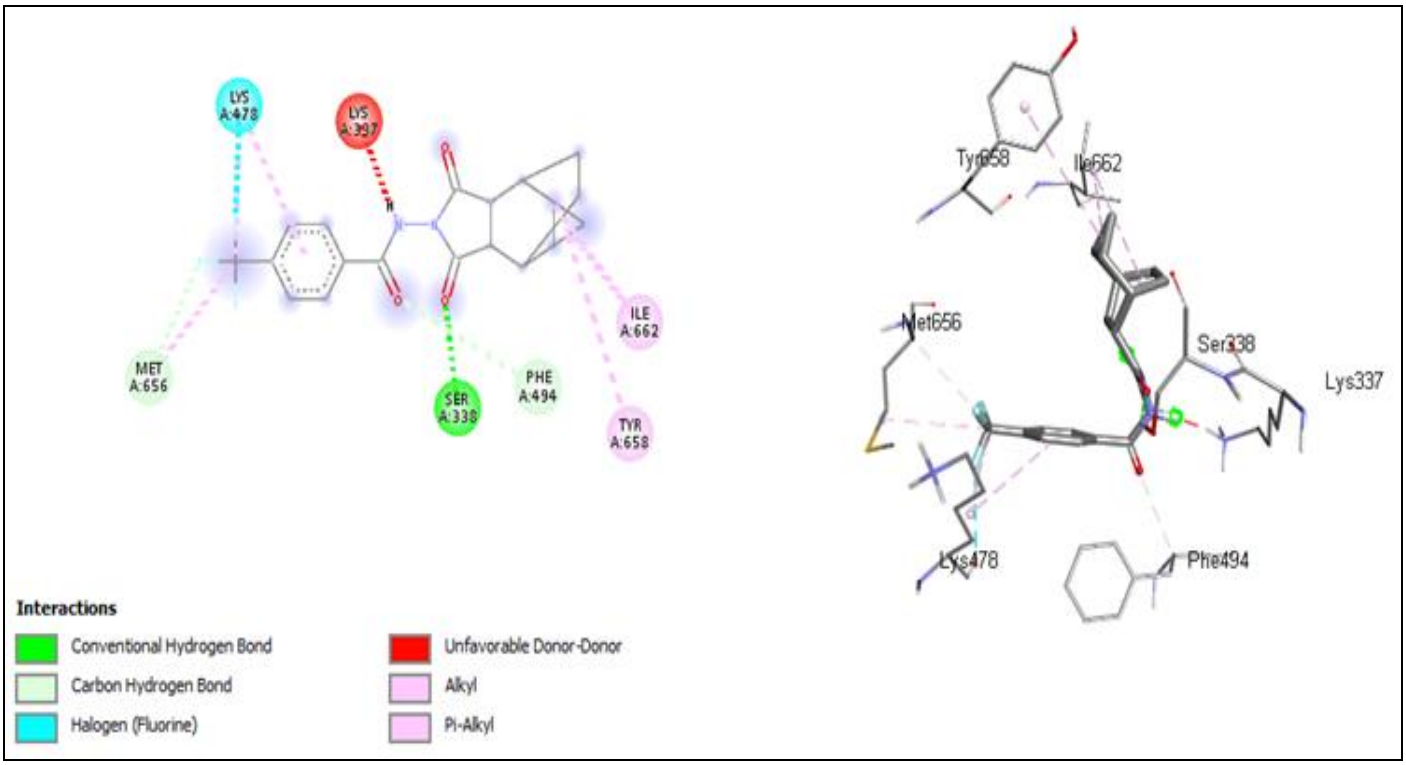

Fig 1 2D and 3D Structure of Tecovirimat against DNA Polymerase Holoenzyme

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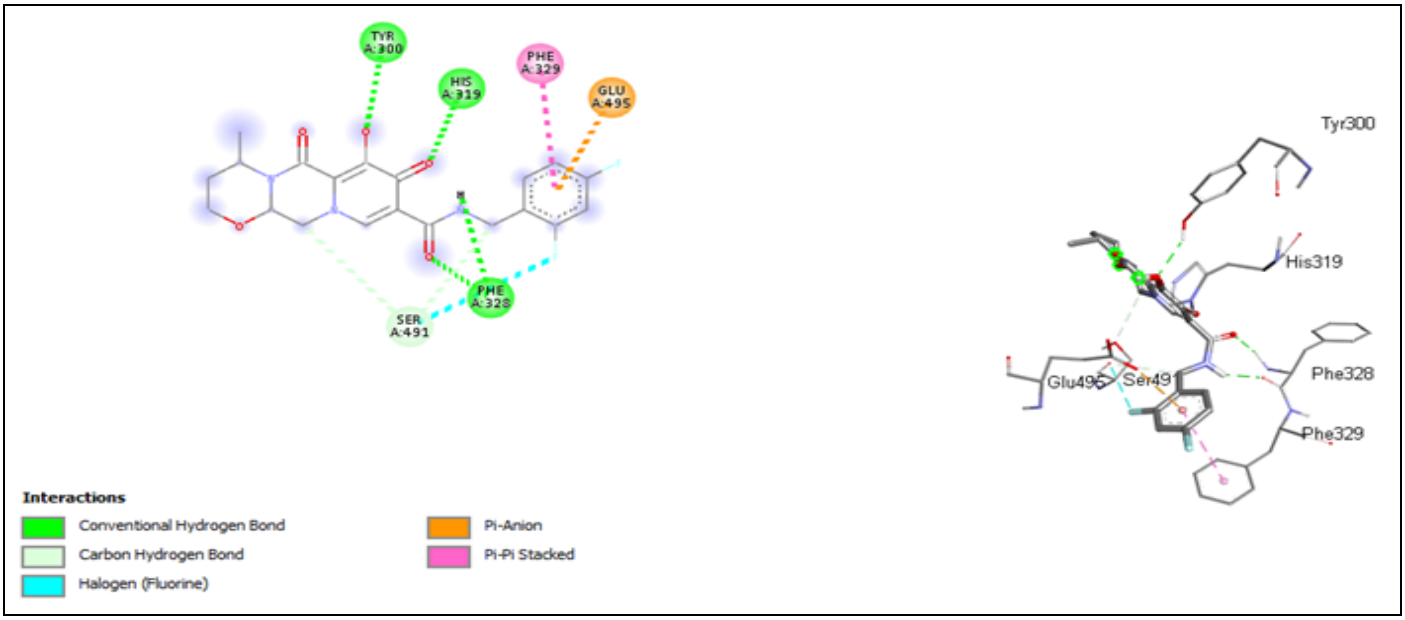

Fig 2 2D and 3D Structure of Dolutegravir against DNA Polymerase Holoenzyme

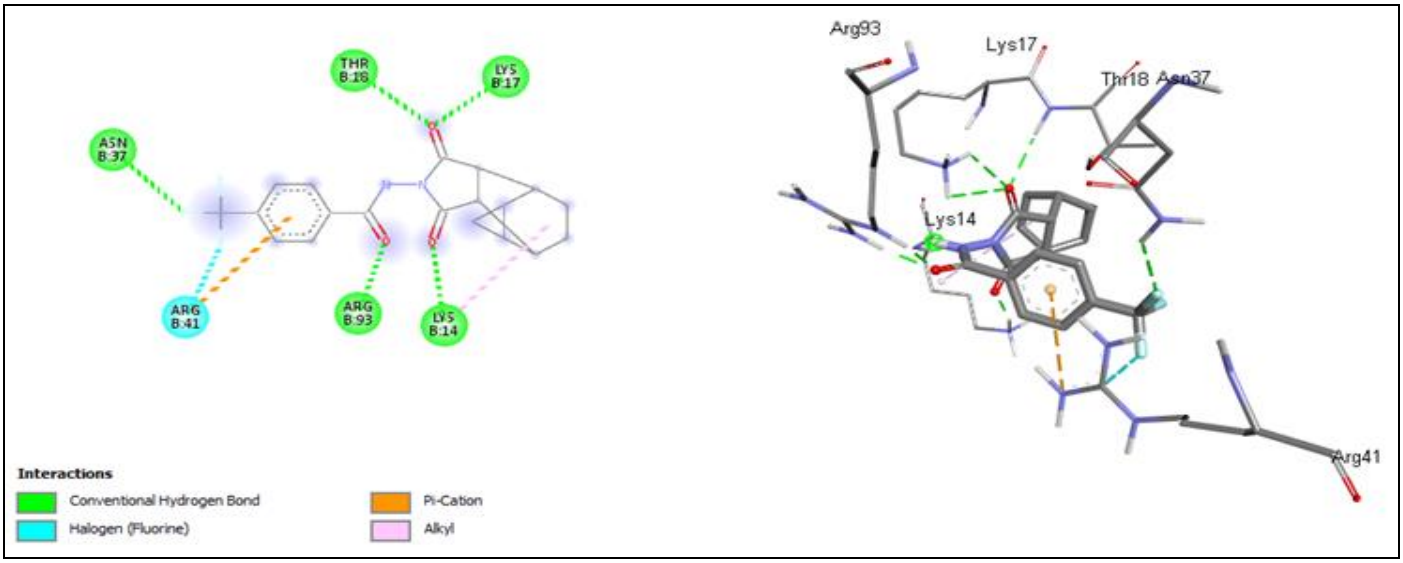

Fig 3 2D and 3D Structure of Tecovirimat against Thymidine Kinase

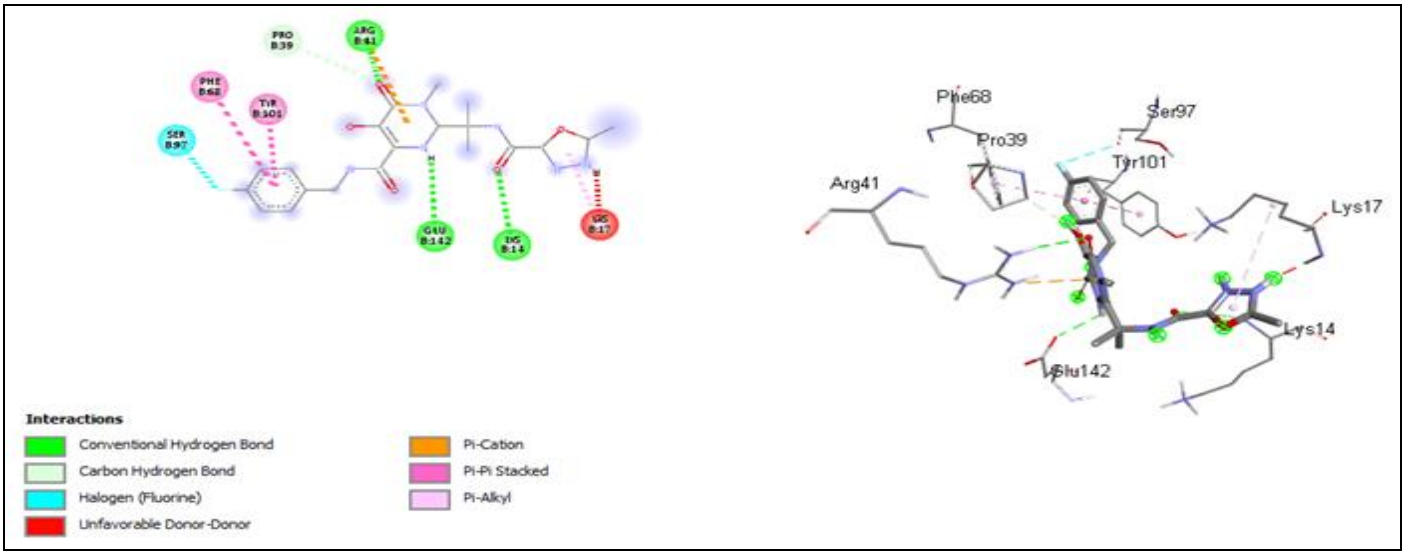

Fig 4 2D and 3D Structure of Raltegravir against Thymidine Kinase

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➢ *Physiochemical and Pharmacokinetic Analysis*

To determine the bioavailability of orally taken medications, follow the Lipinski criteria of five: molecular weight < 500, hydrogen bond acceptor < 10, hydrogen bond donor < 5, and log p < 5. Thorough ADME study throughout the discovery phases helps to avoid pharmacokinetic issues during the clinical phase 2. (39)

The drug likeness property indicates that Dolutegravir, Etavirine, and Raltegravir compounds have drug likeness compared to the reference. The blood-brain barrier is a key factor in analyzing whether the compounds can penetrate the CNS. From the analysis, none of the compounds penetrate the BBB (Blood Brain Barrier), except Tecovirimat, which shows that other drugs do not possess any CNS-related side effects; results are shown in Table 4.

Table 4 ADME Properties of Selected Compounds

S. No	Properties	Raltegravir	Tecovirmit	Etavirine	Indinavir	Tipranavir	Rilpivirine	Dolutegravir	Baloxavir	Nelfinavir	Delaviridine
1.	Molecular weight	444.42	376.33	435.28	613.79	602.66	366.42	419.38	517.55	567.78	456.56
2.	HBA	9	6	5	7	9	4	7	9	5	4
3.	HBD	3	1	2	4	2	2	2	0	4	3
4.	Lipinski violation	1	0	0	1	1	0	0	1	1	0
5.	Molar Refractivity	109.03	90.79	109.56	182.62	153.8	110.41	104.48	144.58	166.17	134.45
6.	TPSA	152.24	66.48	120.64	118.03	113.97	97.42	100.87	125.84	127.2	118.81
7.	BBB	No	Yes	No	No	No	No	No	No	No	No
8.	HIA	76.783948	95.943746	96.380539	93.553818	95.766993	94.695333	94.030881	96.879376	92.670060	90.491872
9.	CaCo2	20.0447	21.1291	20.149	25.4674	18.4144	21.714	20.4148	40.971	40.1713	16.5568
10	PgP substrate	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes
11	Bioavailability score	0.55	0.55	0.55	0.55	0.56	0.55	0.55	0.55	0.55	0.55
12	Synthetic accessibility	3.49	4.17	3.29	5.6	5.29	3.25	4.16	5.41	5.58	3.33

(HBA- Hydrogen bond acceptor, HBD- Hydrogen bond donor, TPSA-Topological polar surface area, BBB- Blood-brain barrier, HIA – Human Intestinal absorption)

Bioavailability prediction refers to the process of estimating the extent and rate at which an active pharmaceutical ingredient is absorbed into systemic circulation and becomes available at the site of action. If the compound has a bioavailability score greater than 0.00, it is considered to be biologically active, and if the range is between -0.50 to 0.00, it is moderately active. When it is less than -0.50, it indicates inactive results listed in Table 5. All the selected compounds were studied for toxicity properties and were listed in Table 6. From that, all compounds are inactive for carcinogenicity, mutagenicity, and cytotoxicity, except for hepatotoxicity and immunotoxicity.

Table 5 Bioactive Prediction for the Selected Compounds

S. NO	Compound Name	GPCR ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1	Raltegravir	-0.03	-0.43	0.00	-0.39	0.11	0.13
2	Etavirine	-0.01	-0.08	0.49	-0.31	0.00	0.22
3	Indinavir	0.18	-0.52	-0.38	-0.70	0.66	-0.20
4	Tipranavir	-0.02	-0.45	-0.62	-0.16	0.22	-0.13
5	Rilpivirine	0.06	-0.13	0.72	-0.27	-0.17	0.20
6	Dolutegravir	0.05	-0.20	-0.04	-0.20	0.04	0.07
7	Baloxavir	-0.22	-0.35	-0.24	-0.20	-0.07	0.05
8	Nelfinavir	0.19	-0.25	-0.28	-0.25	0.58	-0.02
9	Delavirdine	0.33	0.16	0.34	-0.14	0.26	0.22
10	Tecovirimat	-0.11	-0.64	-0.54	-0.19	-0.29	-0.51

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Table 6 Toxicity Properties of the Selected Compounds

S.NO	Compounds	Hepatotoxicity	Carcinogenicity	Immunotoxicity	Mutagenicity	Cytotoxicity
1.	Raltegravir	Active	Inactive	Active	Inactive	Inactive
2.	Etavirine	Active	Inactive	Active	Inactive	Inactive
3.	Indinavir	Active	Inactive	Active	Inactive	Inactive
4.	Tipranavir	Active	Inactive	Active	Inactive	Inactive
5.	Rilpivirine	Active	Inactive	Active	Inactive	Inactive
6.	Dolutegravir	Active	Inactive	Active	Inactive	Inactive
7.	Baloxavir	Active	Inactive	Active	Inactive	Inactive
8.	Nelfinavir	Active	Inactive	Active	Inactive	Inactive
9.	Delavirdine	Active	Inactive	Active	Inactive	Inactive
10.	Tecovirimat	Active	Inactive	Active	Inactive	Inactive

V. CONCLUSION

In the current work, three antiviral medicines were discovered to engage with ligand-binding sites of poxvirus proteins via non-covalent intermolecular bonds and interactions. A comparative examination of docking scores suggested that Dolutegravir and Raltegravir may be the best inhibitors. As a result, Dolutegravir and Raltegravir should be explored in future investigations and clinical trials as lead molecules in drug repurposing for the development of cost-effective anti-MPXV medicines.

REFERENCES

[1]. Jafari K, Woodward GA. Mpox. Pediatr Emerg Care. 2023 Nov 1;39(11):883-889. doi: 10.1097/PEC.0000000000003063. PMID: 37902655.

[2]. Petersen E, Kantele A, Koopmans M, Asogun D, Yinka-Ogunleye A, Ihekweazu C, Zumla A. Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention. Infect Dis Clin North Am. 2019 Dec;33(4):1027-1043. doi: 10.1016/j.idc.2019.03.001. Epub 2019 Apr 11. PMID: 30981594; PMCID: PMC9533922.

[3]. Louten J. Virus Structure and Classification. Essential Human Virology. 2016:19 29. doi: 10.1016/B978-0-12-800947-5.00002-8. Epub 2016 May 6. PMCID: PMC7150055.

[4]. Mitjà O, Ogoina D, Titanji BK, Galvan C, Muyembe JJ, Marks M, Orkin CM. Monkeypox. Lancet. 2023 Jan 7;401(10370):60-74. doi: 10.1016/S0140-6736(22)02075-X. Epub 2022 Nov 17. Erratum in: Lancet. 2022 Dec 3;400(10367):1926. doi: 10.1016/S0140-6736(22)02414-X. PMID: 36403582; PMCID: PMC9671644.

[5]. Singhal T, Kabra SK, Lodha R. Monkeypox: A Review. Indian J Pediatr. 2022 Oct;89(10):955-960. doi: 10.1007/s12098-022-04348-0. Epub 2022 Aug 10. PMID: 35947269; PMCID: PMC9363855.

[6]. KAMARIA, P., & GUHA.. A REVIEW ON MONKEYPOX DISEASE. Innovare Journal Health Sciences, 2022;11(1): 1–5. https://doi.org/10.22159/ijhs.2022.v11i1.46559

[7]. Soheili M, Nasseri S, Afraie M, Khateri S, Moradi Y, Mahdavi Mortazavi SM, Gilzad-Kohan H. Monkeypox: Virology, Pathophysiology, Clinical Characteristics, Epidemiology, Vaccines, Diagnosis, and Treatments. J Pharm Pharm Sci. 2022;25:297-322. doi: 10.18433/jpps33138. PMID: 36130588.

[8]. Sawale Amol V, Ashwini K. Bhilawekar, and Mr. Pratik S. Jadhao. "MONKEYPOX VIRUS: AN OVERVIEW. Journal of Emerging Technologies and Innovative Research. 2021;8(6): 648-654.

[9]. Jezek Z, Szczeniowski M, Paluku KM, Mutombo M. Human monkeypox: clinical features of 282 patients. J Infect Dis. 1987 Aug;156(2):293-8. doi: 10.1093/infdis/156.2.293. PMID: 3036967.

[10]. Kumar N, Acharya A, Gendelman HE, Byrareddy SN. The 2022 outbreak and the pathobiology of the monkeypox virus. J Autoimmun. 2022 Jul;131:102855. doi: 10.1016/j.jaut.2022.102855. Epub 2022 Jun 25. PMID: 35760647; PMCID: PMC9534147.

[11]. Kaler J, Hussain A, Flores G, Kheiri S, Desrosiers D. Monkeypox: A Comprehensive Review of Transmission, Pathogenesis, and Manifestation. Cureus. 2022 Jul 3;14(7):e26531. doi: 10.7759/cureus 26531. PMID: 35928395; PMCID: PMC9345383.

[12]. Sberna G, Rozera G, Minosse C, Bordi L, Mazzotta V, D'Abramo A, Girardi E, Antinori A, Maggi F, Lalle E. Role of Direct Sexual Contact in Human Transmission of Monkeypox Virus, Italy. Emerg Infect Dis. 2024 Sep;30(9):1829-1833. doi: 10.3201/eid3009.240075. Epub 2024 Aug 10. PMID: 39127126; PMCID: PMC11346984.

[13]. Ogoina D, Dalhat MM, Denue BA, Okowa M, Chika-Igwenyi NM, Oiwoh SO, Tobin EA, Yusuff HA, Ojimba AO, Christian UC, Aremu JT, Gomerep SS, Habila KL, Awang SK, Adekanmbi O, Iroezindu M, Onukak A, Falodun O, Sunday M, Johnson SM, Olaitan A, Onyeaghala C, Alasia D, Mmerem J, Unigwe U, Kwaghe V, Adeiza MA; Nigerian Infectious Diseases Society (NIDS) mpox study group. Mpox Epidemiology and Risk Factors, Nigeria, 2022. Emerg Infect Dis. 2024 Sep;30(9):1799-1808. doi: 10.3201/eid3009.240135. Epub 2024 Aug 10. PMID: 39127124; PMCID: PMC11346979.

[14]. Iqbal T. MONKEY POX?A LOOMING HEALTH CRISIS FOR THE WORLD. Pak J Phsyiol [Internet]. 2022 Jun. 30 [cited 2024 Nov. 18];18(2):1-2.DOI: https://doi.org/10.69656/pjp.v18i2.1465

[15]. Karagoz A, Tombuloglu H, Alsaeed M, Tombuloglu G, AlRubaish AA, Mahmoud A, Smajlović S, Ćordić S, Rabaan AA, Alsuhaimi E. Monkeypox (mpox)

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25oct382

virus: Classification, origin, transmission, genome organization, antiviral drugs, and molecular diagnosis. J Infect Public Health. 2023 Apr;16(4):531-541. doi: 10.1016/j.jiph.2023.02.003. Epub 2023 Feb 9. PMID: 36801633; PMCID: PMC9908738.

[16]. Dwivedi M, Gupta CLP, Tiwari RG. Comparative Result Analysis of Optimization Techniques in Convolutional Neural Network for Prediction and Diagnosis of Monkey Pox. 2023 Aug 5;2:1–6. doi: 10.1109/INDISCON58499.2023.10270750.

[17]. Parker S, Nuara A, Buller RM, Schultz DA. Human monkeypox: an emerging zoonotic disease. Future Microbiol. 2007 Feb;2(1):17-34. doi: 10.2217/17460913.2.1.17. PMID: 17661673.

[18]. Sompolwattana C. A Review on Epidemiology of Monkeypox and Prevention in Thailand. International Journal of Research Publications. 2022 Sep 1;109(1).doi :10.47119/ijrp1001091920223900

[19]. Amiri F, Tabassum S, Melika Boroomand-Saboor, Laya Ohadi. Monkeypox and Recommendations for Cancer Patients. Mathews Journal of Emergency Medicine. 2023 Jan 1;8(1). doi:10.30654/mjem.10049

[20]. Rizk, J.G., Lippi, G., Henry, B.M. et al. Prevention and Treatment of Monkeypox. Drugs 82, 957–963 (2022). https://doi.org/10.1007/s40265-022-01742-y

[21]. Reynolds MG, McCollum AM, Nguete B, Shongo Lushima R, Petersen BW. Improving the Care and Treatment of Monkeypox Patients in Low-Resource Settings: Applying Evidence from Contemporary Biomedical and Smallpox Biodefense Research. Viruses. 2017 Dec 12;9(12):380. doi: 10.3390/v9120380. PMID: 29231870; PMCID: PMC5744154.

[22]. PriyadharsiniRaman Palanisamy, Dhivya Elango, Vimala Ananthy, Subramanian U. Recent advances in the treatment of monkeypox drugs and vaccines. National Journal of Pharmacology and Therapeutics. 2023 Jan 1;1(2):65–5.DOI: 10.4103/njpt.njpt_18_23

[23]. Kugelman JR, Johnston SC, Mulembakani PM, Kisalu N, Lee MS, Koroleva G, McCarthy SE, Gestole MC, Wolfe ND, Fair JN, Schneider BS, Wright LL, Huggins J, Whitehouse CA, Wemakoy EO, Muyembe-Tamfum JJ, Hensley LE, Palacios GF, Rimoin AW. Genomic variability of monkeypox virus among humans, Democratic Republic of the Congo. Emerg Infect Dis. 2014 Feb;20(2):232-9. doi: 10.3201/eid2002.130118. PMID: 24457084; PMCID: PMC3901482.

[24]. Ajmal A, Mahmood A, Hayat C, Hakami MA, Alotaibi BS, Umair M, Abdalla AN, Li P, He P, Wadood A, Hu J. Computer-assisted drug repurposing for thymidylate kinase drug target in monkeypox virus. Front Cell Infect Microbiol. 2023 May 29;13:1159389. doi: 10.3389/fcimb.2023.1159389. PMID: 37313340; PMCID: PMC10258308.

[25]. Shen Y, Li Y, Yan R. Structural basis for the inhibition mechanism of the DNA polymerase holoenzyme from mpox virus. Structure. 2024 Jun 6;32(6):654-661.e3. doi: 10.1016/j.str.2024.03.004. Epub 2024 Apr 4. PMID: 38579705.

[26]. Wang X, Ma L, Li N, Gao N. Structural insights into the assembly and mechanism of mpox virus DNA polymerase complex F8-A22-E4-H5. Mol Cell. 2023 Dec 7;83(23):4398-4412.e4. doi: 10.1016/j.molcel.2023.10.038. Epub 2023 Nov 22. PMID: 37995690.

[27]. Li V, Lee Y, Lee C, Kim H. Repurposing existing drugs for monkeypox: applications of virtual screening methods. Genes Genomics. 2023 Nov;45(11):1347-1355. doi: 10.1007/s13258-023-01449-8. Epub 2023 Sep 15. PMID: 37713070; PMCID: PMC10587275.

[28]. Hurle MR, Yang L, Xie Q, Rajpal DK, Sanseau P, Agarwal P. Computational drug repositioning: from data to therapeutics. Clin Pharmacol Ther. 2013 Apr;93(4):335-41. doi: 10.1038/clpt 2013.1. Epub 2013 Jan 15. PMID: 23443757.

[29]. Hashemi M, Zabihian A, Hajsaeedi M, Hooshmand M. Antivirals for monkeypox virus: Proposing an effective machine/deep learning framework. PLoS One. 2024 Sep 12;19(9):e0299342. doi: 10.1371/journal.pon,e.0299342. PMID: 39264896.

[30]. Alakunle E, Moens U, Nchinda G, Okeke MI. Monkeypox Virus in Nigeria: Infection Biology, Epidemiology, and Evolution. Viruses. 2020 Nov 5;12(11):1257. doi: 10.3390/v12111257. PMID: 33167496; PMCID: PMC7694534.

[31]. da Silva GB, de Carvalho Braga G, Simões JLB, Kempka AP, Bagatini MD. Cytokine storm in human monkeypox: A possible involvement of purinergic signaling. Cytokine. 2024 May; 177:156560. doi: 10.1016/j.cyto.2024.156560. Epub 2024 Mar 5. PMID: 38447385.

[32]. Anwar F, Haider F, Khan S, Ahmad I, Ahmed N, Imran M, Rashid S, Ren ZG, Khattak S, Ji XY. Clinical Manifestation, Transmission, Pathogenesis, and Diagnosis of Monkeypox Virus: A Comprehensive Review. Life (Basel). 2023 Feb 14;13(2):522. doi: 10.3390/life13020522. PMID: 36836879; PMCID: PMC9962527.

[33]. Moss B. Poxvirus cell entry: how many proteins does it take? Viruses. 2012 May;4(5):688-707. doi: 10.3390/v4050688. Epub 2012 Apr 27. PMID: 22754644; PMCID: PMC3386626.

[34]. Schmidt FI, Bleck CK, Mercer J. Poxvirus host cell entry. Curr Opin Virol. 2012 Feb;2(1):20-7. doi: 10.1016/j.coviro.2011.11.007. Epub 2011 Dec 27. PMID: 22440962.

[35]. Daina A, Michielin O, Zoete V. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep. 2017 Mar 3;7:42717. doi: 10.1038/srep42717. PMID: 28256516; PMCID: PMC5335600.

[36]. Ali SMA, Helina N, Kumar SV, Varshini E, Ahmad KMFT, Rajamohamed H. Novel Drug Repurposing Strategy as an Alternative Therapeutic Concept for Scrub Typhus Using Computational Studies. J Pure Appl Microbiol. 2024;18(2):1167-1176. doi: 10.22207/JPAM.18.2.35.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25oct382

[37]. Daina, A., Michielin, O. & Zoete, V. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep 7, 42717 (2017). https://doi.org/10.1038/srep42717.

[38]. Gulati P, Chadha J, Harjai K, Singh S. Targeting envelope proteins of poxviruses to repurpose phytochemicals against monkeypox: An in silico investigation. Front Microbiol. 2023 Jan 5;13:1073419. doi: 10.3389/fmicb.2022.1073419. PMID: 36687601; PMCID: PMC9849581.

[39]. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv Drug Deliv Rev. 2001 Mar 1;46(1-3):3-26. doi: 10.1016/s0169-409x(00)00129-0. PMID: 11259830.