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Comparison of the activities of Hyoscyamus niger L. extracts against SARS-CoV-2 virus

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Abstract: In this study, the antiviral potential of ethanol (80%) extracts of *Hyoscyamus niger* L. leaves and seeds was theoretically investigated against SARS-CoV-2 proteins (PDB IDs: 7MRV, 7QO7, and 7U0N) using molecular docking and ADME/T analysis. The chemical composition of the extracts was determined by GC-MS, revealing significant variations in phytochemical profiles between plant organs. Docking simulations were performed on 31 major compounds identified from the extracts. Among them, 6-Amino-2,4-dimethyl-5-methoxyquinoline, Isosteviol methyl ester, and 6-Hydroxy-1,4-dimethylisoquinoline exhibited the most favorable binding affinities and interaction profiles across all target proteins. The ADME/T properties of 6-Amino-2,4-dimethyl-5-methoxyquinoline were further analyzed, demonstrating ideal pharmacokinetic characteristics such as high membrane permeability, good solubility, and excellent oral absorption potential. The results suggest that specific bioactive components in *H. niger* may serve as promising lead compounds for antiviral drug development against SARS-CoV-2 and warrant further in vitro and in vivo validation.

Keywords: *Hyoscyamus niger* L., Molecular docking, ADME/T, Drug, GC-MS

1. Introduction

The COVID-19 disease, caused by the SARS-CoV-2 virus, which was first identified on 13 January 2020, has been effective worldwide since it was declared a pandemic and has been recorded as an extremely serious infectious disease that caused the death of approximately seven million people between 2019-2025 alone, according to World Health Organization (WHO) data [1]. While the majority of patients experience the infection with mild symptoms, a certain group of patients may develop acute respiratory distress syndrome, multiple organ failure and hyperimmune response defined as 'cytokine storm', which is associated with excessive release of various cytokines and chemokines, imbalance in the distribution of T-cell subsets and poor prognosis. The clinical symptomatology of COVID-19 usually includes fever, cough, dyspnoea, fatigue, loss of sense of taste or smell, sore throat and diarrhoea [2]. Although the prevalence of the disease has been brought under control thanks to the vaccines

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developed as of 2021, it is known that thousands of people are still infected with coronavirus, more than seasonal influenza [1,3,4]. There is still no antiviral treatment method for COVID-19 with proven efficacy and safety. For this reason, today, prophylactic approaches and especially plant-based therapeutic strategies have been focused on both in the treatment of the disease and in breaking the chain of transmission [5].

It is known that medicinal plants are effective in the treatment of many viral diseases [6]. Studies conducted in China have revealed that the society effectively utilizes medicinal plants in the prevention, treatment and rehabilitation processes of COVID-19 infection [7]. Similarly, studies conducted in Iran reported that 69% of patients with COVID-19 used aromatic herbs such as ginger, black cumin and thyme for supportive purposes [8]. *Hyoscyamus niger* L. (Solanaceae) is a medicinal plant widely used in traditional medicine and known for its richness in tropane alkaloids such as atropine, scopolamine, and hyoscyamine [9]. These alkaloids exhibit mydriatic, antispasmodic, anticholinergic, analgesic and sedative effects [10]. Today, such secondary metabolites represent a key focus in pharmacological research and natural product-based drug development. Hyoscyamoside is a steroidal glycoside found in *H. niger* and is defined as a flavonoid with potential antioxidant activity. Studies have reported that this compound can support the regeneration of lung tissue, accelerate repair processes and show a phytoprogesterone property that may be effective in alleviating asthma symptoms [11,12].

In recent years, the interaction potential of plant-derived bioactive compounds with various viral targets has been investigated through theoretical calculations [13]. In particular, molecular docking studies are an effective and cost-effective approach to predict the binding affinity and interaction modes of natural compounds with the essential proteins of SARS-CoV-2 [14]. In this context, phytochemicals such as flavonoids, alkaloids and terpenoids found in extracts obtained from various medicinal plants are theoretically evaluated against vital enzymes of the virus such as the main protease (Mpro), spike protein or RNA-dependent RNA polymerase (RdRp) [15]. This study aims to contribute to the drug design process by analysing the possible interactions of compounds in selected plant extracts with SARS-CoV-2 target proteins using only theoretical methods [16].

In this study, in order to develop a therapeutic response against the coronavirus infection, which is currently widespread on a seasonal basis, the chemical constituents of the ethanol (80%) extracts of *Hyoscyamus niger* L. leaf and seed organs, known for its high antiviral activity, were identified. The effects of chemical compounds in *H. niger* L. leaf and seed organs on SARS-CoV-2 virus proteins (PDB IDs: 7MRV, 7QO7, and 7U0N) [17-19] were examined. An ADME/T study was conducted on the compounds exhibiting the highest activity.

2. Computational Method

2.1. Plant Material Collection and Extraction Method

The plant samples used for the analyses were collected from the natural flora of the Sivas region. Firstly, the leaves and seeds of the plant were dried in the shade. These dried plant organs were carefully ground with the help of a blender (Bluehouse) to form a homogenous powder. After weighing 10 g each of the powdered samples, 50 mL of 80% ethanol (Sigma) solution was added to each sample. The mixtures were kept for 48 hours with shaking at regular intervals to ensure effective extraction. After the extraction process was

completed, the mixtures were filtered through filter paper and the filtrates were concentrated in three parallel samples under reduced pressure and at 37 °C using a rotary evaporator until completely dry [20]. Thus, the chemical components extracted from the plant materials with ethanol were obtained in a form suitable for further analyses.

2.2. Chemical components

In this study, the chemical components of the plant extract prepared with 80% ethanol from *H. niger* organs, leaves, and seeds were comprehensively determined. The crude extracts were analysed by gas chromatography-mass spectrometry (GC-MS) for quantitative analysis of chemical compounds. During the analysis process, the extracts were prepared appropriately with minor modifications to the procedure applied by Eruygur and Dural (2019), loaded into the GC-MS device using an injector system, and the components were identified by comparing them with mass spectrum library databases [21]. This method enabled the detailed identification of the main phytochemical compounds present in the extracts, thereby contributing to an understanding of the plant's therapeutic potential.

2.3. Molecular docking calculations

Molecular docking computations are utilized to assess the biological activities of molecules in relation to biological materials. Molecular docking simulations were performed using Schrödinger's Maestro Molecular Modeling platform (version 13.4) [22]. Calculations include several stages. Each process is done separately. Proteins were produced in the preliminary phase using the protein preparation module [23]. This module included the active sites of the proteins. The next phase involves the production of the chemicals being studied. The LigPrep module [24] is configured for computations utilizing optimized structures after the molecules have been preliminarily optimized in the Gaussian software program. Following preparation, the interactions between the drugs and the cancer protein were analyzed using the Glide ligand docking module [25,26]. All computations were performed using the OPLS4 approach. The pharmacological potential of the drugs under examination will be evaluated using an ADME/T study (absorption, distribution, metabolism, excretion, and toxicity). The effects and reactions of drugs in human metabolism were predicted using the Qik-prop module of the Schrödinger software [27].

3. Results and discussion

In this study, the chemical composition of the ethanol (80%) extracts obtained from the leaf and seed parts of the plant was comparatively analysed. The GC-MS results revealed a notable variation in the distribution and abundance of bioactive compounds between the two plant parts. In the leaf extract, phytol was the most dominant component (16.52%), followed by cyclododecane (9.98%), hexahydrofarnesyl acetone (5.86%), and methyl steviol (6.65%), indicating a rich profile of diterpenes and terpenoid derivatives. These compounds are known for their antioxidant, anti-inflammatory, and antimicrobial properties. In contrast, the seed extract exhibited a higher content of fatty acid methyl esters, particularly 6-octadecenoic acid (6.38%), 9-octadecenoic acid methyl ester (6.36%), and dodecanoic acid (6.05%), along with alkaloid derivatives such as tropine (3.31%) and 6-hydroxy-1,4-dimethylisoquinoline (5.90%). Both extracts contained steviol derivatives, including methyl steviol and isosteviol methyl ester, indicating their widespread presence

throughout the plant. Overall, the leaf extract appears to be richer in secondary metabolites with pharmacological potential, while the seed extract is characterized by a higher concentration of fatty acid derivatives, suggesting its value in nutritional or cosmetic applications.

Table 1. Chemical components of 80% ethanol extracts *H.niger* leaf and seed organs

RT	Components	Leaf	Seed
4.208	1-(trideuterio)methyl-2-(.gamma.-hydroxy)propylacetylene	4,58	
12.952	Coniine	1,33	
16.745	Camphor		0,93
17.380	Borneol		1,45
18.691	1,4:3,6-Dianhydro-.alpha.-d-glucopyranose		1,37
19.103	4-vinylphenol		3,80
19.314	Tropine	1,71	3,31
26.347	2-(1-Pyrrolidinyl)-2-cyclopenten-1-one		2,04
28.275	n-Pentadecanol	2,14	
28.916	6-Amino-2,4-dimethyl-5-methoxyquinoline	1,29	
29.368	3a-Methyl-1,2,3,3a,4,5,8,9-octahydrocyclopenta[a]naphthalen-7-one	3,58	
29.631	Methyl laurate	1,85	2,44
29.391	Phenol, 2,4-bis(1,1-dimethylethyl)		1,87
29.923	Dihydroactinidiolide	1,36	
29.929	2(4H)-Benzofuranone, 5,6,7,7a-tetr ahydro-4,4,7a-trimethyl		1,57
30.741	2,6-Dimethyl-3-(methoxymethyl)-p-benzoquinone	1,50	
30.810	Dodecanoic acid		6,05
31.130	3-Methyl-4-phenyl-1H-pyrrole	1,38	
32.635	Maltoxazine		1,32
33.339	6-Hydroxy-1,4-dimethylisoquinoline		5,90
33.471	Cyclododecane	9,98	5,37
35.141	(-)-Loliolide	2,51	2,20
36.229	Myrtanal	1,02	
36.354	Hexahydrofarnesyl acetone	5,86	
37.733	Hexadecanoic acid, methyl ester	2,47	2,86
38.849	Tridecanoic acid ethyl ester	1,31	1,97
39.421	Thieno(2,3-b)quinoline	2,26	
40.457	1,3,12-Nonadecatriene		1,09
40.543	9-Octadecenoic acid, methyl ester		6,36
40.743	Phytol	16,52	
40.920	Methyl stearate		1,05
41.132	4-methoxy-4-methyl-2-(3-methylphenyl)cyclohexa-2,5-dienone	1,28	
41.195	6-Octadecenoic acid, (Z)		6,38
41.538	10-Octadecenoic acid, methyl ester		2,02
45.950	Isosteviol methyl ester	3,12	3,83
46.059	Methyl steviol	6,65	3,92
Total		**73,7**	**69,1**

Table 2. Numerical values of the docking parameters of molecule against protein

7WRV	Docking Score	Glide ligand efficiency	Glide hbond	Glide evdw	Glide ecoul	Glide emodel	Glide energy	Glide einternal	Glide posenum
(-)-Loliolide	-5.23	-0.37	-0.48	-17.71	-4.65	-29.34	-22.36	0.38	381
1,3,12-Nonadecatriene	0.46	0.02	0.00	-26.58	-2.93	-26.15	-29.51	5.07	143
1,4:3,6-Dianhydro-.alpha.-d-glucopyranose	-5.33	-0.53	-0.30	-15.00	-7.29	-29.22	-22.29	0.13	204
10-Octadecenoic acid, methyl ester	1.07	0.05	0.00	-26.39	-1.03	-22.87	-27.43	4.45	237
2-(1-Pyrrolidinyl)-2-cyclopenten-1-one	-5.01	-0.46	0.00	-17.92	-8.21	-33.93	-26.13	0.04	329

2,6-Dimethyl-3-(methoxymethyl)-p-benzoquinone	-5.08	-0.39	-0.37	-18.28	-4.89	-30.20	-23.17	1.10	267
3-Methyl-4-phenyl-1H-pyrrole	-4.77	-0.40	-0.32	-16.38	-4.70	-27.23	-21.07	0.31	327
4-vinylphenol	-4.21	-0.47	-0.32	-12.96	-6.05	-23.72	-19.01	0.26	7
6-Amino-2,4-dimethyl-5-methoxyquinoline	-5.67	-0.38	-0.17	-19.42	-9.79	-38.99	-29.21	0.46	224
6-Hydroxy-1,4-dimethylisoquinoline	-5.92	-0.46	-0.59	-14.70	-9.11	-32.85	-23.80	0.00	136
6-Octadecenoic acid, (Z)	1.19	0.06	-0.31	-21.11	-6.56	-20.50	-27.67	7.83	357
9-Octadecenoic acid, methyl ester	0.89	0.04	0.00	-27.32	-1.46	-24.65	-28.78	4.55	351
Coniine	-5.09	-0.57	0.00	-10.91	-8.03	-24.26	-18.94	1.15	293
Cyclododecane	-3.28	-0.27	0.00	-14.28	-0.12	-17.21	-14.40	0.00	286
Dihydroactinidiolide	-4.60	-0.35	-0.21	-17.87	-2.12	-25.73	-19.99	0.00	128
Dodecanoic acid	1.63	0.12	-0.26	-16.91	-6.33	-15.49	-23.24	7.58	21
Hexadecanoic acid, methyl ester	1.88	0.10	-0.13	-25.84	-3.24	-21.70	-29.09	7.63	276
Hexahydrofarnesyl acetone	-0.42	-0.02	-0.31	-27.59	-4.81	-30.87	-32.40	4.67	315
Isosteviol methyl ester	-4.46	-0.19	-0.66	-18.40	-6.61	-30.31	-25.01	2.54	332
Maltoxazine	-5.10	-0.39	-0.35	-13.59	-9.60	-29.72	-23.19	0.00	93
Methyl laurate	1.16	0.08	-0.32	-21.83	-4.10	-21.96	-25.93	3.77	188
Methyl stearate	2.28	0.11	-0.30	-26.27	-2.19	-20.71	-28.45	6.32	182
Methyl steviol	-4.56	-0.19	-0.48	-18.61	-7.72	-33.57	-26.33	0.23	268
Myrtanal	-4.78	-0.43	-0.20	-15.85	-2.64	-23.29	-18.49	0.55	44
n-Pentadecanol	3.05	0.19	-0.32	-21.24	-4.36	-17.87	-25.60	5.00	41
Phenol, 2,4-bis(1,1-dimethylethyl)	-3.50	-0.15	0.00	-25.59	-6.51	-36.22	-32.10	3.55	221
Phytol	0.11	0.01	-0.32	-25.62	-3.81	-27.49	-29.42	3.47	97
Thieno(2,3-b)quinoline	-4.74	-0.36	0.00	-20.29	-2.95	-30.43	-23.24	0.00	45
Tridecanoic acid ethyl ester	0.86	0.05	-0.32	-23.91	-4.90	-23.11	-28.81	8.19	237
Tropine	-4.98	-0.50	-0.30	-9.77	-10.14	-25.41	-19.91	0.01	248

7QO7	Docking Score	Glide ligand efficiency	Glide hbond	Glide evdw	Glide ecoul	Glide emodel	Glide energy	Glide einternal	Glide posenum
(-)-Loliolide	-4.78	-0.34	-0.05	-19.06	-4.49	-29.88	-23.55	0.41	17
1,3,12-Nonadecatriene	0.80	0.04	0.00	-28.42	-2.32	-25.20	-30.74	8.20	341
1,4:3,6-Dianhydro-.alpha.-d-glucopyranose	-5.48	-0.55	-0.29	-9.48	-11.54	-27.49	-21.02	0.78	73
10-Octadecenoic acid, methyl ester	0.13	0.01	-0.19	-28.22	-2.06	-25.98	-30.28	8.17	93
2-(1-Pyrrolidinyl)-2-cyclopenten-1-one	-4.23	-0.38	0.00	-14.19	-8.29	-26.27	-22.48	2.40	231
2,6-Dimethyl-3-(methoxymethyl)-p-benzoquinone	-4.86	-0.37	-0.32	-17.87	-4.11	-27.25	-21.99	1.33	239
3-Methyl-4-phenyl-1H-pyrrole	-4.56	-0.38	-0.32	-16.36	-4.29	-26.26	-20.64	0.06	370
4-vinylphenol	-4.15	-0.46	-0.32	-11.37	-5.94	-21.59	-17.31	0.09	241
6-Amino-2,4-dimethyl-5-methoxyquinoline	-5.49	-0.37	-0.32	-16.81	-9.57	-34.25	-26.38	0.00	112
6-Hydroxy-1,4-dimethylisoquinoline	-4.99	-0.38	-0.32	-15.44	-5.23	-26.85	-20.66	0.00	157
6-Octadecenoic acid, (Z)	1.41	0.07	-0.16	-20.09	-4.47	-18.60	-24.56	6.00	103
9-Octadecenoic acid, methyl ester	0.14	0.01	-0.32	-26.66	-3.10	-26.52	-29.76	5.96	102
Borneol	-4.10	-0.37	-0.32	-11.33	-3.03	-17.16	-14.36	1.09	178
Camphor	-3.94	-0.36	-0.15	-12.42	-2.95	-18.89	-15.37	0.00	257
Coniine	-4.78	-0.53	0.00	-12.31	-5.23	-19.50	-17.54	4.26	233
Cyclododecane	-3.51	-0.29	0.00	-13.21	-0.28	-16.22	-13.49	0.00	205
Dihydroactinidiolide	-4.35	-0.33	0.00	-16.32	-3.15	-24.43	-19.47	0.00	294
Dodecanoic acid	1.72	0.12	-0.08	-16.81	-1.55	-11.83	-18.37	5.74	389
Hexadecanoic acid, methyl ester	0.76	0.04	-0.32	-23.53	-4.32	-23.57	-27.85	5.93	14
Hexahydrofarnesyl acetone	0.21	0.01	-0.04	-22.98	-2.54	-21.41	-25.52	7.62	363
Isosteviol methyl ester	-6.28	-0.26	-0.47	-25.38	-6.73	-38.58	-32.11	0.57	258
Maltoxazine	-4.83	-0.37	-0.32	-18.65	-2.73	-27.90	-21.37	0.00	319
Methyl laurate	1.30	0.09	-0.25	-19.32	-3.85	-18.26	-23.17	6.39	90
Methyl stearate	0.81	0.04	-0.25	-25.68	-2.48	-23.64	-28.17	6.46	179
Methyl steviol	-5.28	-0.22	-0.23	-19.15	-5.55	-25.62	-24.70	9.71	98

Myrtanal	-4.26	-0.39	-0.32	-13.47	-2.26	-19.42	-15.73	0.18	110
n-Pentadecanol	1.88	0.12	-0.61	-17.00	-7.95	-20.21	-24.95	3.94	72
Phenol, 2,4-bis(1,1-dimethylethyl)	-3.59	-0.16	0.00	-19.93	-4.28	-28.63	-24.21	1.72	253
Phytol	-1.03	-0.05	-0.61	-20.19	-8.30	-27.84	-28.49	4.74	44
Thieno(2,3-b)quinoline	-4.34	-0.33	0.00	-15.28	-3.41	-23.69	-18.69	0.00	215
Tridecanoic acid ethyl ester	1.14	0.07	0.00	-23.64	-0.33	-17.98	-23.97	8.77	135
Tropine	-4.30	-0.43	-0.32	-6.25	-8.68	-17.87	-14.92	0.33	91

7U0N	Docking Score	Glide ligand efficiency	Glide hbond	Glide evdw	Glide ecoul	Glide emodel	Glide energy	Glide einternal	Glide posenum
(-)-Loliolide	-5.62	-0.40	-0.29	-22.53	-4.52	-34.95	-27.05	0.39	251
1,3,12-Nonadecatriene	1.24	0.07	0.00	-10.06	-0.17	-5.57	-10.24	8.75	148
1,4:3,6-Dianhydro-.alpha.-d-glucopyranose	-5.88	-0.59	-0.50	-12.15	-10.66	-30.32	-22.80	0.37	350
2-(1-Pyrrolidinyl)-2-cyclopenten-1-one	-5.73	-0.52	-0.28	-17.94	-7.64	-35.62	-25.58	1.27	278
2,6-Dimethyl-3-(methoxymethyl)-p-benzoquinone	-5.32	-0.41	-0.37	-24.18	-2.32	-34.64	-26.50	1.17	364
3-Methyl-4-phenyl-1H-pyrrole	-5.07	-0.42	0.00	-23.67	-2.06	-33.38	-25.73	0.11	372
4-vinylphenol	-4.41	-0.49	-0.01	-17.81	-3.26	-26.15	-21.07	0.82	342
6-Amino-2,4-dimethyl-5-methoxyquinoline	-6.20	-0.41	-0.32	-23.83	-7.74	-43.92	-31.57	0.40	121
6-Hydroxy-1,4-dimethylisoquinoline	-5.69	-0.44	0.00	-24.50	-1.63	-34.81	-26.13	0.00	194
6-Octadecenoic acid, (Z)	0.57	0.03	-0.01	-6.84	-1.12	-4.52	-7.97	6.22	34
9-Octadecenoic acid, methyl ester	0.13	0.01	-0.14	-17.42	-1.76	-16.93	-19.18	4.45	196
Borneol	-4.64	-0.42	-0.35	-4.45	-4.49	-11.48	-8.94	1.31	382
Camphor	-4.35	-0.40	-0.18	-10.12	0.02	-11.75	-10.10	0.00	179
Coniine	-5.44	-0.60	0.00	-12.86	-7.42	-28.18	-20.29	1.15	74
Cyclododecane	-5.82	-0.49	0.00	-24.31	-0.58	-33.53	-24.89	0.00	374
Dihydroactinidiolide	-4.84	-0.37	0.00	-21.07	-1.08	-27.77	-22.15	0.00	192
Dodecanoic acid	0.88	0.06	-0.16	-12.57	-2.18	-10.52	-14.75	8.00	96
Hexadecanoic acid, methyl ester	0.17	0.01	-0.32	-8.84	-4.15	-9.89	-13.00	5.89	258
Hexahydrofarnesyl acetone	0.75	0.04	0.00	-6.26	0.95	1.55	-5.31	6.97	169
Isosteviol methyl ester	-4.76	-0.20	-0.32	-13.63	-3.32	-17.42	-16.95	0.77	3
Maltoxazine	-5.44	-0.42	0.00	-25.72	-0.97	-35.99	-26.69	0.00	193
Methyl laurate	0.47	0.03	-0.32	-11.33	-3.31	-12.57	-14.64	3.99	198
Methyl steviol	-4.87	-0.20	-0.61	-12.54	-5.73	-22.85	-18.27	3.53	241
Myrtanal	-5.46	-0.50	-0.30	-19.22	-2.76	-28.18	-21.98	0.00	274
Phenol, 2,4-bis(1,1-dimethylethyl)	-4.80	-0.21	0.00	-29.85	-1.78	-38.79	-31.63	3.49	104
Thieno(2,3-b)quinoline	-5.30	-0.41	0.00	-25.34	-0.19	-33.91	-25.52	0.00	285
Tridecanoic acid ethyl ester	1.85	0.11	0.00	-9.90	-0.01	-7.07	-9.91	5.37	370
Tropine	-5.68	-0.57	-0.47	-12.18	-7.69	-26.93	-19.87	0.78	167

Due to the extensive application of theoretical research and technological advancements, current studies indicate that the comparison of molecular biological activities has been significantly accelerated and simplified [28]. This results from the widespread availability of technological breakthroughs. The application of these two study methodologies has significantly contributed to this outcome. This premise is corroborated by the findings of the latest study undertaken. The process of determining the most successful and effective therapies before trying these pharmaceuticals in experimental settings has been significantly accelerated and streamlined due to calculations [29]. Throughout the theoretical computations, several distinct aspects were revealed. This technique enables the identification of the relationship between the numerical values of these parameters and the operation of molecules in biological systems. This link is identified by the

application of this procedure. This method is conducted to guarantee the accurate evaluation of biological parameters. A multitude of elements impact the activities mentioned [30], although the most critical element is the interactions among diverse proteins and molecules. Due to the extensive dispersion of these connections, the proteins are ultimately obstructed. This particular system is accountable for the inhibitory process you are encountering. The interaction of chemicals with a protein dictates the energy content of that protein. Various forms of interactions between molecules and proteins including hydrogen bonds, polar and hydrophobic contacts, π-π interactions, and halogen interactions [31-34]. These interactions can be categorized into many classifications. Molecular interactions are essential for maintaining equilibrium at a stable level. Extensive analyses of these chemical interactions have shown a multitude of ways in which proteins and chemicals engage with one other. This was uncovered throughout the investigations. All figures are located in Figures 1-3, while Table 2 encompasses all aspects. Figures 1-3 encompass all the illustrations.

The Glide ligand efficiency estimate is the most critical metric derived from molecular docking simulations. These traits are not only complimentary but also numerous. This numerical chart indicates the efficiency of the ligand against certain bacterial proteins. An illustrative example of this may be located here. The Glide Hbond [35] allows for the quantification of hydrogen bonds formed due to interactions between chemicals and proteins. The Van der Waals interaction number, also known as Glide Evdw [36], serves as a statistic that exemplifies the interactions between chemicals and proteins. Glide Ecoul is a measure utilized to conduct an impartial evaluation of the Coulomb interactions occurring between pharmaceuticals and proteins. This assessment is conducted to guarantee its objectivity. The Glide Einternal is the last parameter obtained from these computations. It is a numerical value obtained by integrating several components [37]. Upon achieving this parameter, the calculations are finalized.

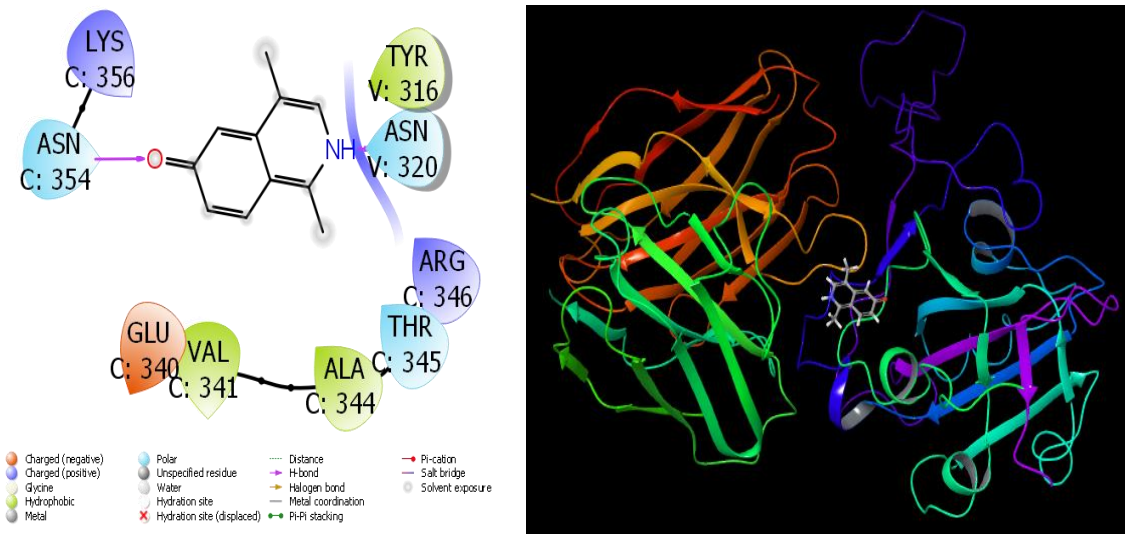

Figure 1. Presentation interactions of 6-Hydroxy-1,4-dimethylisoquinoline with 7mrv protein

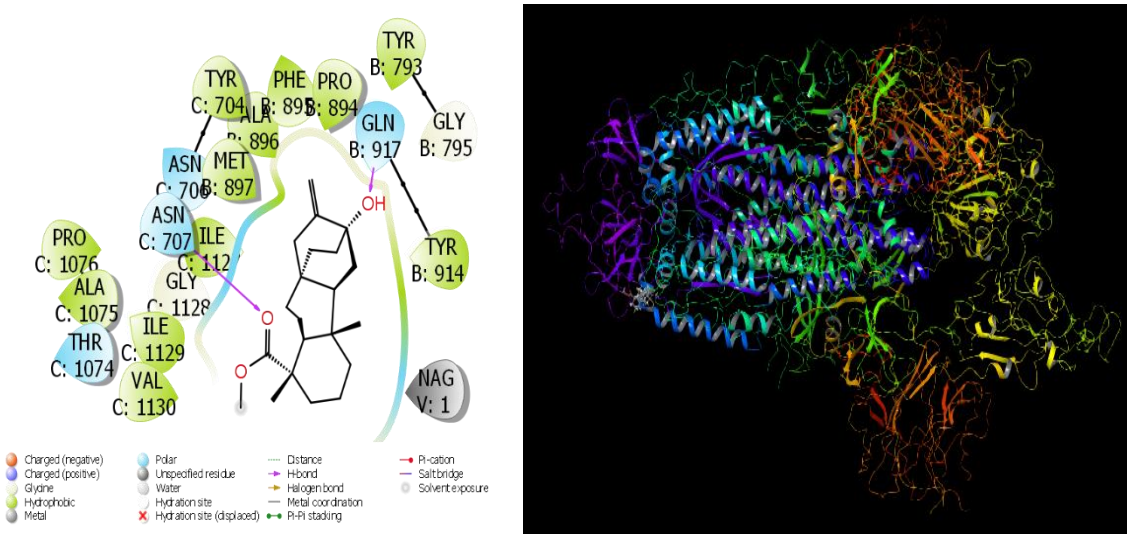

Figure 2. Presentation interactions of Isosteviol methyl ester with 7QO7 protein

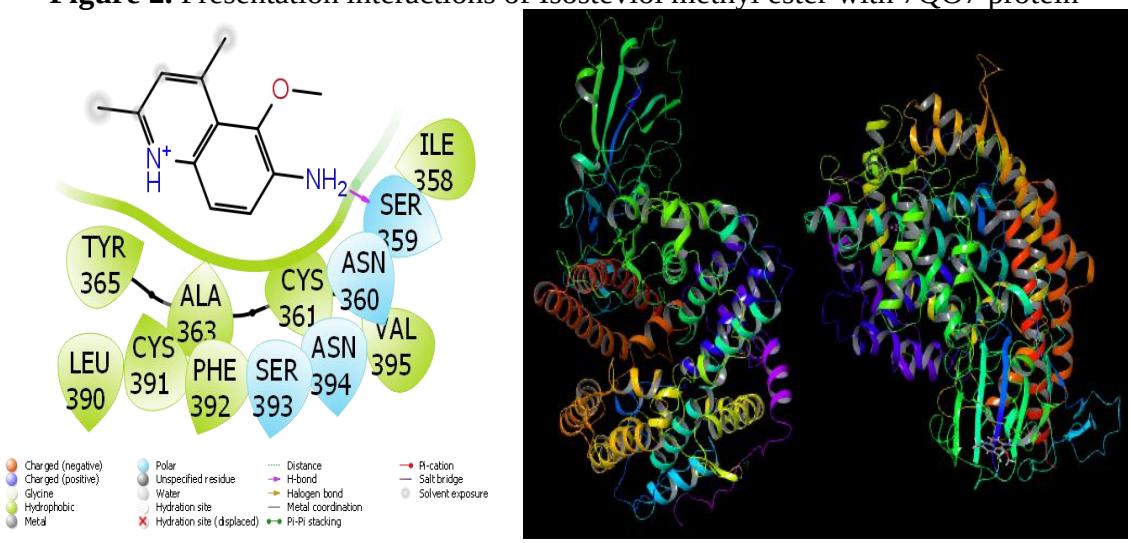

Figure 3. Presentation interactions of 6-Amino-2,4-dimethyl-5-methoxyquinoline with 7U0N protein

Table 3. ADME properties of molecule

	6-Hydroxy-1,4-dimethylisoquinoline	Isosteviol methyl ester	6-Amino-2,4-dimethyl-5-methoxyquinoline	**Referance Range**
mol_MW	-	-	**202**	130-725
dipole (D)	-	-	**3.5**	1.0-12.5
SASA	-	-	**425**	300-1000
FOSA	-	-	**229**	0-750
FISA	-	-	**59**	7-330
PISA	-	-	**136**	0-450
WPSA	-	-	**0**	0-175
volume (A^3)	-	-	**706**	500-2000
donorHB	-	-	**1.5**	0-6
accptHB	-	-	**2.8**	2.0-20.0
glob (Sphere =1)	-	-	**0.9**	0.75-0.95
QPpolrz (A^3)	-	-	**22.1**	13.0-70.0
QPlogPC16	-	-	**6.6**	4.0-18.0
QPlogPoct	-	-	**10.5**	8.0-35.0
QPlogPw	-	-	**6.5**	4.0-45.0
QPlogPo/w	-	-	**2.2**	-2.0-6.5

QPlogS	-	-	**-2.7**	-6.5-0.5
CIQPlogS	-	-	**-2.8**	-6.5-0.5
QPlogHERG	-	-	**-3.8**	*
QPPCaco (nm/sec)	-	-	**2712**	**
QPlogBB	-	-	**0.0**	-3.0-1.2
QPPMDCK (nm/sec)	-	-	**1455**	**
QPlogKp	-	-	**-1.9**	Kp in cm/hr
IP (ev)	-	-	**8.0**	7.9-10.5
EA (eV)	-	-	**0.7**	-0.9-1.7
#metab	-	-	**4**	1-8
QPlogKhsa	-	-	**-0.087**	-1.5-1.5
Human Oral Absorption	-	-	**3**	-
Percent Human Oral Absor.	-	-	**100**	***
PSA	-	-	**39.591**	7-200
RuleOfFive	-	-	**0**	Maximum is 4
RuleOfThree	-	-	**0**	Maximum is 3
Jm	-	-	**4.6**	-

In this study, theoretically calculated ADME/T parameters were examined to evaluate the pharmacokinetic suitability of the compound called 6-Amino-2,4-dimethyl-5-methoxyquinoline in table 3 [38].

According to the calculated values, the molecular weight (mol_MW) of this compound is 202 g/mol and is fully compatible with the 130–725 g/mol reference range accepted for drug-like molecules. The dipole moment is 3.5 Debye, indicating that the molecule has a moderate polarity. This value may positively affect the solubility of the molecule in aqueous environments and its interaction with biological membranes [39].

Among the parameters related to surface area, the SASA (total solvent accessible surface area) value is 425 Å² and is in the range of 300–1000 Å², indicating that the biological membrane permeability of the compound is suitable. FOSA and FISA values were determined as 229 and 59 units, respectively; The low FISA suggests that the molecule has a low hydrophilic surface area and may exhibit lipophilic properties. PSA (polar surface area) was calculated as 39.5 Å², which is between the reference limit of 7–200 Å² and indicates good oral bioavailability potential [40].

Hydrogen bond donation and acceptance capacities (donorHB: 1.5, acceptHB: 2.8) are suitable values for drug-like molecules. The sphericity parameter (glob = 0.92) is very close to the ideal range (0.75–0.95), indicating that the three-dimensional structure of the molecule is compact enough to support interaction with biological targets [41].

Among the parameters related to permeability, the QPPCaco value was calculated as 2712 nm/s and the QPPMDCK value was calculated as 1455 nm/s. These values are quite high and show that the passage of the compound through the intestinal and cell membrane is quite effective. The QPlogBB value is 0.0, indicating that the compound has no potential to cross the blood-brain barrier. In addition, the QPlogKp value is –1.9, indicating that skin permeability is low [42].

The QPlogHERG value, which is associated with cardiotoxicity, is –3.8; this value is above the safe limit of –5.0, so it can be said that the compound is safe in terms of the risk of HERG channel inhibition [43].

The QPlogS (–2.7) and CIQPlogS (–2.8) values of the solubility parameters indicate that the compound is moderately soluble in water. In the evaluation made according to the Lipinski rules, the

compound shows a violation of "0" (RuleOfFive: 0) [44-46], supporting that it is a good drug candidate. In addition, the Human Oral Absorption value was calculated as "3" and 100%; this shows that the compound has an excellent oral absorption potential.

In conclusion, when the 6-Amino-2,4-dimethyl-5-methoxyquinoline compound is evaluated in terms of theoretical ADME/T analyses, it is a promising candidate in terms of pharmacokinetics with its properties such as ideal molecular weight, suitable dipole moment, high intestinal permeability, good solubility and excellent oral bioavailability. These findings indicate that the molecule may be a potential drug candidate if confirmed by advanced experimental studies.

4. Conclusions

This study presents a theoretical evaluation of the phytochemical constituents of *Hyoscyamus niger* L. for their potential inhibitory effects against SARS-CoV-2 proteins. Through molecular docking simulations, several compounds—particularly 6-Amino-2,4-dimethyl-5-methoxyquinoline and Isosteviol methyl ester—demonstrated strong binding affinities to the viral proteins 7MRV, 7QO7, and 7U0N, indicating their potential as antiviral agents. The ADME/T analysis further confirmed the pharmacokinetic suitability of 6-Amino-2,4-dimethyl-5-methoxyquinoline,

highlighting its high oral absorption rate, acceptable solubility, and favorable drug-likeness characteristics. These findings suggest that *H. niger* extracts contain bioactive molecules with promising antiviral profiles. However, experimental validation is required to confirm the in silico predictions and to evaluate the therapeutic applicability of these compounds in clinical contexts.

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