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RESEARCH ARTICLE

DRUG DESIGNING FOR CHICKEN GUNIYA FROM *Andrographis paniculata*

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ABSTRACT

This study provides the detailed investigation of phytochemical extracted from *Andrographis paniculata* using GC-MS and drug designing. We are going to concentrate in docking studies and Protein GSK3ß, which is responsible for chikungunya. Based on docking studies, we can able to calculate the docking scores. The lists of drugs which are treated for chikungunya to be retrieved from drug bank. Based on Lipinski's rule, the absorption capacity of the drug going to be identified. Among those collected drugs, the Dimethylglycine and Nelfinavir have good absorption Capacity.

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INTRODUCTION

Andrographis paniculata is a plant that possesses many medicinal values in treating several diseases and for health care maintenance. *Andrographis paniculata* could be used as a hepatoprotective agent and possesses the potential to treat or prevent degenerative diseases where oxidative stress is implicated. (Ref 1)

Andrographis paniculata

Andrographis paniculata belongs to family Acanthaceae is a medicinal plant used in many countries. It is used to treat infections and some diseases, often being used before antibiotics were created. Mostly the leaves and roots were used for medicinal proposes. Flavonoids present in plant showed potent inhibition of collagen, arachidonic acid, thrombin and platelet activation factor induced platelet aggregation. Furthermore, a diterphenoid demonstrated moderate vasorelaxing effect in isolated rat thoracic aorta. The plant is used as an important ingredient in different medicinal formulations in national and international market. The increased sequencing of pathogen genomes and the subsequent availability of genome-scale functional datasets are expected to guide the experimental work necessary for target-based drug discovery. The plant extracts exhibits anti-typhoid and antifungal activities. Kalmegh is also reported to possess anti-hepatotoxic, antibiotic, anti-malarial, anti-hepatitic, anti-thrombogenic, anti-inflammatory, anti-snake venom, and antipyretic properties. In India medicinal herb used to treat liver disorders, bowel complaints of children, colic pain, common cold and upper respiratory tract infection. (Ref 6)

Chikungunya

Chikungunya virus is an insect borne virus which causes acute febrile illness in humans followed by a prolonged arthralgic disease that affects the joints of the extremities. Re-emergence of the virus in the form of outbreaks in last 6-7 years has posed a serious public health problem. CHIKV has a positive sense single stranded RNA genome of about 12,000 nt. Open reading frame one of the viral genome encodes a polyprotein precursor, nsP1234, which is processed further into different non structural proteins (nsP1, nsP2, nsP3 and nsP4). Sequence based analyses have shown helicase domain at the N-terminus and protease domain at C-terminus of nsP2. A detailed biochemical analysis of NTPase RNA helicase and 5'-RNA phosphatase activities of recombinant CHIKV P2T protein was carried out. The protein could hydrolyze all NTPs except dTTP and showed better efficiency for ATP, dATP, GTP and dGTP hydrolysis. (Ref 2) Chikungunya virus, of the genus Alpha virus, that is transmitted to humans by virus carrying Aedes mosquitoes. There have been recent breakouts of CHIKV associated with severe illness. CHIKV causes an illness with symptoms similar to dengue fever. CHIKV manifests itself with an acute febrile phase of the illness lasting only two to five days, followed by a prolonged

The pain associated with CHIKV

Table 1: In GC-MS Analysis, *Andrographis paniculata* having variety of phytochemical compounds. This table shows that the no of phytochemical compounds present in *Andrographis paniculata.* These Phytochemical compositions can be identified by Gas Chromatography Mass Spectrometry Technique.

S.No.	Peak Name	Retention time	Peak area	% Peak area
1.	2(5H)-Furanone Formula: $C_4H_4O_2$; MW: 84	4.24	359801	0.4706
2.	N,N-Dimethylglycine Formula: $C_4H_9NO_2$; MW: 103	4.54	11071331	14.4794
3.	Glycolaldehyde dimer Formula: $C_4H_8O_4$; MW: 120	4.95	837173	1.0949
4.	Phenyl-á-D-glucoside Formula: $C_{12}H_{16}O_6$; MW: 256	5.21	623893	0.8159
5.	2-Hydroxy-gamma-butyrolactone Formula: $C_4H_6O_3$; MW: 102	5.38	391131	0.5115
6.	2-Hexenoic acid Formula: $C_6H_{10}O_2$; MW: 114	5.48	902897	1.1808
7.	3-Hexanone, 2-methyl- Formula: $C_7H_{14}O$; MW: 114	6.07	421084	0.5507
8.	2,5-Dimethyl-4-hydroxy-3(2H)-furanone Formula: $C_6H_8O_3$; MW: 128	6.21	289450	0.3786
9.	Cyclopentane, 1-acetyl-1,2-epoxy- Formula: $C_7H_{10}O_2$; MW: 126	6.56	1072768	1.4030
10.	1-Propanamine, N,2-dimethyl-N-nitroso- Formula: $C_5H_{12}N_2O$; MW: 116	6.87	542266	0.7092
11.	o-Acetyl-L-serine Formula: $C_5H_9NO_4$; MW: 147	7.50	246707	0.3227
12.	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl- Formula: $C_6H_8O_4$; MW: 144	7.60	425992	0.5571
13.	4-Hydroxy-3-methylacetophenone Formula: $C_9H_{10}O_2$; MW: 150	9.98	547853	0.7165
14.	Sucrose Formula: $C_{12}H_{22}O_{11}$; MW: 342	11.80	10745864	14.0538
15.	Coumarin, 3,4-dihydro-6-methoxy-4,4-dimethyl- Formula: $C_{12}H_{14}O_3$; MW: 206	12.48	108237	0.1416
16.	1,6-Anhydro-á-D-glucopyranose (levoglucosan) Formula: $C_6H_{10}O_5$; MW: 162	12.60	590430	0.7722
17.	Methyl 4-O-acetyl-2,3,6-tri-O-ethyl-à-d-galactopyranoside Formula: $C_{15}H_{28}O_7$; MW: 320	12.81	927308	1.2128
18.	Dodecanoic acid Formula: $C_{12}H_{24}O_2$; MW: 200	13.05	174319	0.2280
19.	1,2,3,5-Cyclohexanetetrol, (1à,2á,3à,5á)- Formula: $C_6H_{12}O_4$; MW: 148	14.34	3250073	4.2505
20.	1-Dodecanol, 3,7,11-trimethyl- Formula: $C_{15}H_{32}O$; MW: 228	16.93	599346	0.7838
21.	3,7,11,15-Tetramethyl-2-hexadecen-1-ol Formula: $C_{20}H_{40}O$; MW: 296	17.04	20007102	26.1659
22.	Andrographolide Formula: $C_{20}H_{30}O_5$; MW: 350	18.25	938057	1.2268
23.	Hexadecanoic acid, methyl ester Formula: $C_{17}H_{34}O_2$; MW: 270(Palmitic acid, methyl ester)	18.40	1521578	1.9900
24.	1,6-Octadiene, 3-ethoxy-3,7-dimethyl- Formula: $C_{12}H_{22}O$; MW: 182	20.68	351119	0.4592
25.	Linolenic acid, methyl ester Formula: $C_{19}H_{32}O_2$; MW: 292	20.86	1215944	1.5902
26.	Phytol Formula: $C_{20}H_{40}O$; MW: 296	21.00	1387437	1.8145
27.	7-Hexadecenoic acid, methyl ester, (Z)- Formula: $C_{17}H_{32}O_2$; MW: 268	21.54	643451	0.8415
28.	26-Deoxy-26-ethylaminodihydroneotigogenin Formula: $C_{29}H_{51}NO_2$; MW: 445	23.05	532485	0.6964
29.	Octadecanal Formula: $C_{18}H_{36}O$; MW: 268	23.59	855047	1.1183
30.	Bicyclo[4.4.0]dec-2-ene-4-ol, 2-methyl-9-(prop-1-en-3-ol-2-yl)- Formula: $C_{15}H_{24}O_2$; MW: 236	24.63	4054080	5.3020
31.	2H-Benzo[f]oxireno[2,3-E]benzofuran-8(9H)-one, 9-[[[2-(dimethylamino)ethyl]amino]methyl]octahydro-2,5a-dimethyl- Formula: $C_{19}H_{32}N_2O_3$; MW: 336	25.06	359129	0.4697
32.	2,2-Dimethyl-6-methylene-1-[3,5-dihydroxy-1-pentenyl]cyclohexan-1-perhydrol Formula: $C_{14}H_{24}O_4$; MW: 256	28.95	6517485	8.5238
33.	2,5,5,8a-Tetramethyl-4-methylene-6,7,8,8a-tetrahydro-4H,5H-chromen-4a-yl hydroperoxide Formula: $C_{14}H_{22}O_3$; MW: 238	30.14	3951716	5.1682
	Total percentage of peak area			100.0000

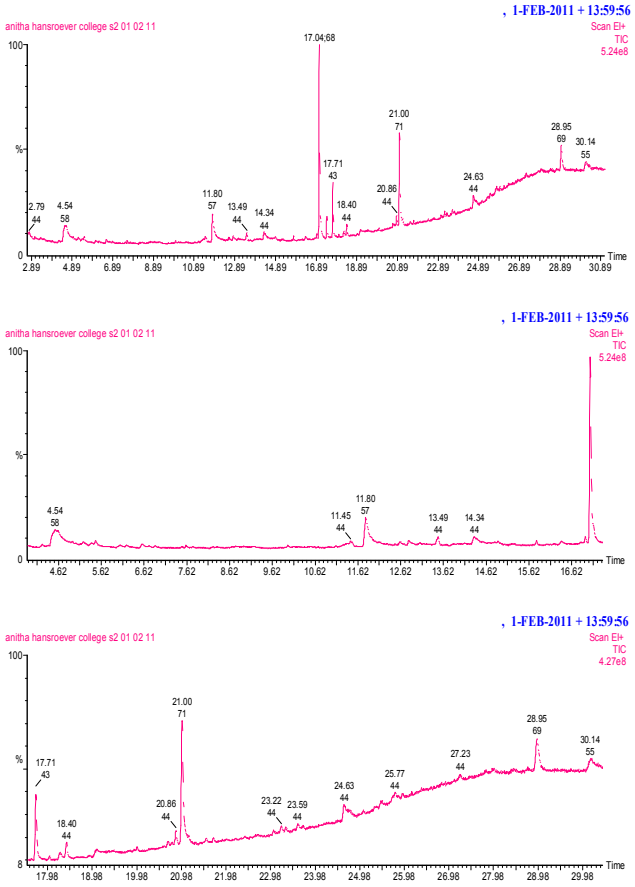

Fig 1: Chromatogram for Phytochemical Compounds

infection of the joints persists for weeks or months, or in some cases years. (Ref 3). There is no antiviral drug or medicine specifically for Cikungunya. But since Chikungunya is cured by immune system in almost all al cases there is no need to worry. Treatment usually is for the symptoms and includes sufficient rest, taking more fluid and medicines to relieve pain (paracetomol). Aspirin should be avoided. Alternative medical systems such as ayurveda and homeopathy have specific treatments for Chikungunya. Many of these treatments are helpful in reducing the symptoms especially the joint pain. In siddha medicine, *Androgaphis paniculata* is widely used to treat fever like Chikungunya.

Drug designing

Drug design is the approach of finding drugs by design, based on their biological targets. Typically a drug target is a key molecule involved in a particular metabolic or signaling pathway that is specific to a disease condition or pathology, or to the infectivity or survival of a microbial pathogen.

MATERIALS AND METHODS

Protein sequences for Chickengunya collected from NCBI Database. The sequences were saved in notepad and submitted in to PROSITE Tool. The Binding sites of the receptor were identified by PROSITE tool. The structure of the receptor and phytochemical compounds were retrieved and subjected to docking studies by Hex tool. We can also docked the structure of artificial drug with phytochemical compound. The docking scores can be calculated from Hex tool. Finally, docked structures were compared and identify the best drug for chickengunya.

Table 2: Absorption Analysis of Natural Drugs treated for Chickungunya

No	Phytochemicals	Hydrogen Bond Donor	Hydrogen Bond Acceptor	Log p (Daltons)	Molecular Weight (g/mol)	Absorption
1	Sucrose	0	1	0	0	Poor
2	Tetramethyl hexadecen	1	0	0	0	Poor
3	Dimethylglycine	1	1	1	1	Good
4	Bicyclo dec ene methyl	1	0	0	0	Poor
5	Tetra methyl methylene tetrahydro chromen hydro peroxide	1	0	0	0	Poor
6	Cyclohexanetetrol	1	0	0	0	Poor
7	Phytol	1	0	1	1	Poor
8	Hexadecanoic acid	1	0	1	1	Poor
9	Cyclopentane acetyl epoxy	0	0	0	0	Poor
10	Cyclopentane	1	0	1	1	Poor

Table 3: Drug Parameters for various artificial drugs treated for Chickungunya

No	Drugs	Hydrogen Bond Donor	Hydrogen Bond Acceptor	Log P	Molecular Weight
1	Nelfinavir	-4	-5	5.7	567.7824
2	Antipyrine	0	2	0.4	188.22578
3	Phenylethylamine	1	1	1.4	121.17964
4	Citalopram	0	4	3.2	324.39198
5	Hyaluronidase	2	5	1	215.21136

Table 4: Absorption Analysis of Artificial Drugs treated for Chickungunya

No	Drugs	Hydrogen Bond Donor	Hydrogen Bond Acceptor	Log P	Molecular Weight	Absorption
1	Nelfinavir	0	0	1	1	Good
2	Antipyrine	0	0	0	0	Poor
3	Phenylethylamine	1	0	0	0	Poor
4	Citalopram	0	0	0	0	Poor
5	Hyaluronidase	1	0	0	0	Poor

RESULTS AND DISCUSSION

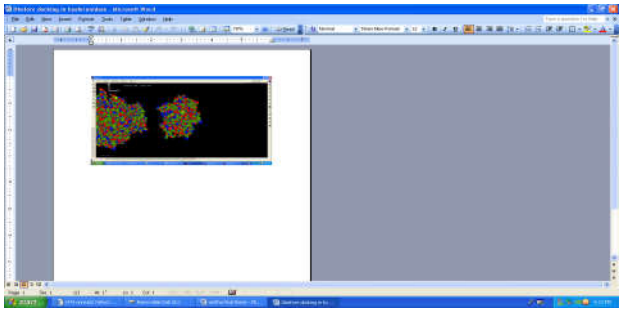

Fig 2: Screenshot of Receptor and Ligand before docking

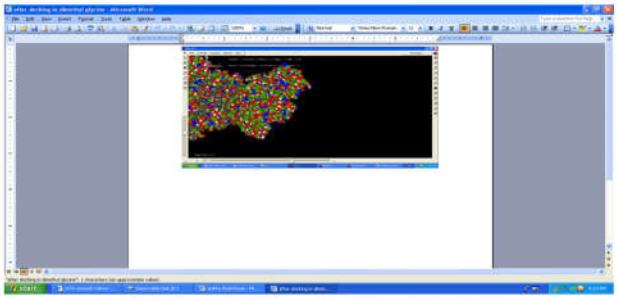

Fig 3: Screenshot of Receptor and Ligand after docking

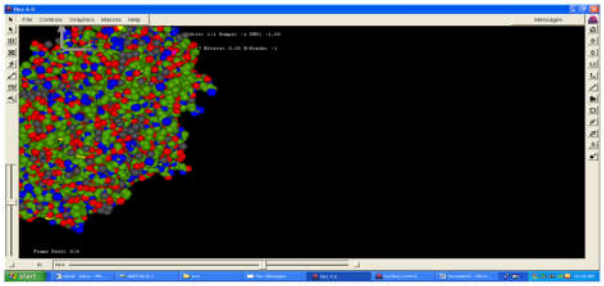

Fig 4: Schematic diagram illustrating the docking of a small molecule ligand to a protein complex receptor to produce a complex.

Table 6: Docking Score Values derived from Hex tool

S. No	Drug Name	Docking Score Value
1	Nelfinavir	85.12
2	Antipyrine	80.02
3	Phenyl ethylamine	81.50
4	Citalopram	78.23
5	Hylarunidase	76.87

Conclusion

This study provides the detailed analysis of phytochemical extracted from *Andrographis paniculata* using GC-MS and drug designing. The phytochemical analysis shows that the compounds present in plant (*Andrographis paniculata*). We are also highly focused on docking studies and Protein GSK3ß, which is responsible for chikungunya. The Protein GSK3ß and the ligand were subjected to docking. Based on docking studies, we can able to calculate the docking scores. The lists of drugs which are treated for chikungunya were retrieved from drug bank. Based on Lipinski's rule, the absorption capacity of the drug can be identified. Among those collected drugs, the Dimethylglycine and Nelfinavir have good absorption Capacity. From these observations, we conclude that the Natural drug Dimethyl glycine has good absorption effect when compared with Nelfinavir.

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