International Journal of Reverse Pharmacology and Health Research (IJRPHR)

Research article

Evaluation of binding affinity of Seenthil Kudineer with enzyme RNA-dependent RNA polymerase of Dengue virus through molecular docking In-Silico Approach.

Ethel shiny. S[*], Bharath Christian CS[2], Gomathi P[3]

[1*]Associate Professor, Department of Gunapadam Marunthiyal [2]Assistant professor, Department of Maruthuvam,

[3]Assistant Professor, Department of Varmam, Pura maruthuvam & Sirappu maruthuvam,

Santhigiri Siddha Medical College, Thiruvananthapuram, Kerala.

ABSTRACT

Seenthil Kudineer (SK) a classical siddha formulation is used to treat various fevers which cause moderate to severe acute hemorrhagic symptoms as is indicated in the text. The research article has shown the following bioactive compounds such as Tinosporide, Santalic acids, Gingerenone-A, Vasicinone, Beta-santalol, Rutin, Geniposide, Thymol, Ascorbic acid and Gamma-Himachalene. Molecular docking is a great approach in current trends to identify the possibility of pharmacological effects of medicinal compounds which could be exerted over their corresponding protein targets which are relevant for the disease. Docking simulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method (*Solis and Wets, 1981*) against the target protein Dengue virus NS5 RNA dependent RNA polymerase (2J7U) which is responsible for viral replication and transcription. The binding energy observed were of the order: -10.28 Kcal/mol (Rutin), -7.90Kcal/mol (Geniposide),

-7.14 Kcal/mol(Gingerenone), - 6.09 Kcal/mol(Santalic acids),-5.91 Kcal/mol (Gamma Himachalene), -5.80 Kcal/mol(Beta - Santalol), -5.43Kcal/mol (Tinosporide), - 5.32 Kcal/mol(Ascorbic acid), -5.12 Kcal/mol(Vasicinone) and -4.22 Kcal/mol(Thymol), respectively towards for the target 2J7U. These findings confirm that the Siddha formulation *Seenthil Kudineer* has some potent activity against the symptoms produced by Dengue virus.

Keywords:

Seenthil Kudineer, Dengue, Molecular docking, Siddha medicine. .

Address for correspondence:

Ethel shiny S

Associate Professor

CODEN : IJRPHR

To access this article online

Website : http://www.ijrphr.com/

DOI : 10.121/ijrphr/05.0401.580

Quick response code

INTRODUCTION

Throughout the world, dengue ranks as most important mosquito borne viral disease in the world. WHO estimates that 50-100 million dengue infections occur in each year and almost half of the world's population lives in the countries, where dengue is endemic. Close to 75% of global population exposed to dengue are in Asia-Pacific region.There are no antiviral medicines available for dengue. Current conventional management focuses on fluid replacement and management of other metabolic consequences of viral infection.A major problem in fight against virus is rapid adaptation and development of drug resistance as well as emergence of new hybrid viruses. In past few years natural remedies came more and more in centre of interest. Recent studies showing antiviral potential of plant extracts against viral strains resistant to conventional antiviral agents have challenged modern drug discovery practices and deem a very careful look towards exploring natural antiviral components of medicinal plants and exploring traditional medical formulations used in treatment of viral diseases.

Molecular docking is the preclinical and a in-silico approach can be done before starting the pharmacological and the clinical study which can be helpful one to assessing the future outcome whether positive or negative in the management of the particular disease.Eventhough Molecular docking studies are considered as a preliminary study, it is significant with other Pre-clinical studies done by the Research scholars from various fields including in-vivo immuno-modulatory activity against viral infection in backyard chicken and in-vivo safety studies in wistar rats.

Dengue fever is an acute febrile illness caused by virus belonging to Flaviviridae family. Four well defined dengue viruses identified are DENV-1, DENV-2, DENV-3 and DENV-4. Each of them has a distinct genetic structure. Dengue virus is transmitted to humans through bites of infective Ades mosquitos- Ades aegyptii, Ades albopictus. Dengue fever is characterized by biphasic fever, myalgia, arthralgia and rashes. Dengue haemorrhagic fever (DHF) is characterized by abnormality in haemostasis and by marked leakage of plasma from the capillaries. The later may lead to Dengue shock syndrome (DSS).

In siddha medicine, the *Pithasuram* mentioned in the classical siddha text book, *Yugi Vaidhiya Chinthamani* can be correlated with Dengue fever.Most of the symptoms in the p*itha suram* can be matched with the signs and symptoms of dengue clinical presentation as follow.

Table.1. Pitha suram vs Dengue Fever (A Correlation view)

Pitha suram* explanation in *Yugi Vaidhiya Chinthamani	**As per modern Medicine**
Udal sikappu niram adaithal - Reddish discolouration on body	Petechial heamorrhage
Siruneer sikappu niram adaithal -Red colored urination	Hematuria
Malam sikappu niram adaithal - Black colour stools	Melaena
Kan sikappu niram adaithal - Reddish discoloration on eye	Retinal heamorrhage

Manakalakkam, Mayakkam, Padukkaiyil thankamai Confusion, fainting, not sitting in the bed	Restlessness, Symptoms of altered sensorium.
Okaalam - Nausea	Nausea, Vomiting
Neervetkai - Thirst	Thirst due to dehydration
Vayiru kalithal - watery stools	Diarrhoea
Idaividamal athika suram kaaithal - High grade fever	Hyperpyrexia
Mugam Karuppu niram adaithal- Blackish discoloration of face	Cyanosis

2.Materials and Methods

2.1.Source of drug

The Sastric drug Seenthil Kudineer (SK) was prepared as per the Siddha classical text book Gunapadam mooligai vaguppu.

The drug has the following 8 herbals such as ***Tinospora cordifolia (Seenthil), Santalum album(Santhanam), Zingiber officinale (Chukku), Sida cordifolia (Sittramutti), Cyprus rotundus (Korai kizhangu), Hedyotis corymbosa (Parpadagam), Plectranthus vettiveriodes (Vilamichuver) and Chrysopogon zizanioides(Veetiver).***

Table.2. List of herbs present in the SK formulation with their phytochemicals

Sl. No	Herbs	Phyto chemicals	References
1.	***Tinospora cordifolia***	Tinosporide	Krupanidhi S, Abraham Peele K, Venkateswarulu TC, et al. Screening of phytochemical compounds of Tinospora cordifolia for their inhibitory activity on SARS-CoV-2: an in silico study .J Biomol Struct Dyn. 2020;1-5.
2.	***Santalum album***	Santalic acids	Gautam P. Vadnere. Phytochemical Investigation And In Vitro Antimicrobial Screening Of Santalum Album Seeds Extracts. International Journal of Pharmacy and Pharmaceutical Sciences, vol. 9, no. 10, Nov. 2017, pp. 117-24,
3.	***Zingiber officinale***	Gingerenone-A	Rampogu S, Baek A, Gajula RG, et al. Ginger (Zingiber officinale) phytochemicals-gingerenone-A and shogaol inhibit SaHPPK: molecular docking, molecular dynamics simulations and in vitro approaches. Ann Clin Microbiol Antimicrob. 2018;17(1):16.

4.	***Sida cordifolia***	Vasicinone	Momin, M. A., Bellah, S. F., Rahman, S. M., Rahman, A. A., Murshid, G. M., & Emran, T. B. (2014). Phytopharmacological evaluation of ethanol extract of Sida cordifolia L. roots. Asian Pacific journal of tropical biomedicine, 4(1), 18–24. https://doi.org/10.1016/S2221-1691(14)60202-1
5.	***Cyprus rotundus***	Beta-santalol	Yasaman Taheri. Cyperus spp.: A Review on Phytochemical Composition, Biological Activity, and Health-Promoting Effects.2021.https://doi.org/10.1155/2021/4014867
6.	***Hedyotis corymbosa***	Rutin Geniposide	Sridevi SKS. A Review on Phytochemical and Pharmacological Profile of Hedyotis corymbosa Linn. Int. J. Pharm. Sci. Rev. Res., 26(1), May – Jun 2014; Article No. 54, Pages: 320-324
7.	***Plectranthus vettiveriodes***	Thymol	Arumugam G, Swamy MK, Sinniah UR. Plectranthus amboinicus (Lour.) Spreng: Botanical, Phytochemical, Pharmacological and Nutritional Significance. Molecules. 2016;21(4):369
8.	***Chrysopogon zizanioides***	Ascorbic acid, Gamma-Himachalene	Grover, M., Behl, T., & Virmani, T. (2021). Phytochemical Screening, Antioxidant Assay and Cytotoxic Profile for Different Extracts of Chrysopogon zizanioides Roots. Chemistry & biodiversity,18(8),e2100012. https://doi.org/10.1002/cbdv.202100012

2.2.Molecular Docking

Molecular Docking analysis performed with a commonly well-known established software Auto dock Gridfree a very convenient and excellent screening tool for identifying binding energy between the 3D structures of each ligand and target proteins.

The target protein PDB ID: 2J7U was selected, a Gridfree docking performed, and the binding energies of each ligand found.

PDB	Name of the Target
2J7U	Dengue virus NS5 RNA dependent RNA polymerase

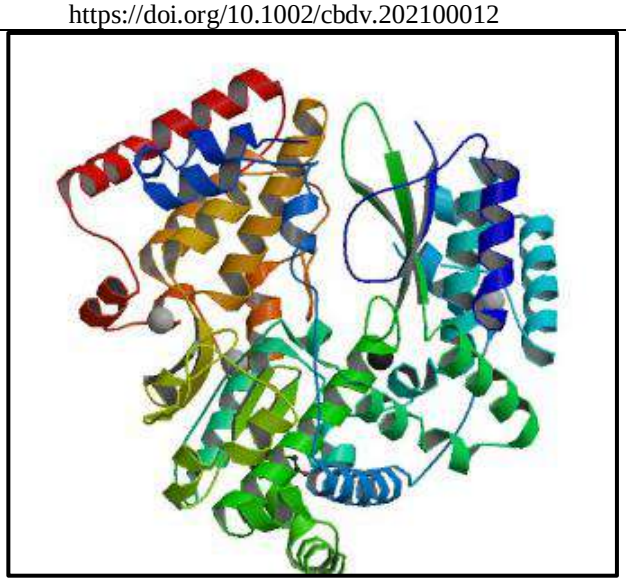


Figure.1.Structure of Dengue virus NS5 RNA dependent RNA polymerase protein

2.3.Receptor Structure :

Crystalline structure of the target protein Dengue virus NS5 RNA dependent RNA polymerase (2J7U) was retrieved from protein data bank and protein clean-up process was done and essential missing hydrogen atom were being added.

Different orientation of the lead molecules with respect to the target protein was evaluated by Autodock program and the best dock pose was selected based on the interaction study analysis.

2.4.Objective of Molecular Docking :

Binding of phytocomponents with the core amino acids (Arg-737, Arg-729 and Ser-710) of the targets by forming hydrogen bond will hinder the function of the enzyme RNA-dependent RNA polymerase since these are the prime mediators for dengue viral replication. Thereby phytocomponents which inhibit this enzyme may act as a potential therapeutic agent for management of dengue fever can be assessed by this method.

2.5. METHODOLOGY:

Docking calculations were carried out for retrieved phytocomponents against target enzyme Dengue virus NS5 RNA dependent RNA polymerase (2J7U). Essential hydrogen atoms, Kollman united atom type charges, and solvation parameters were added with the aid of AutoDock tools (*Morris, Goodsell et al., 1998*).

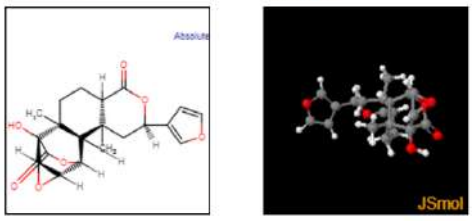
Affinity (grid) maps of ×× Å grid points and 0.375 Å spacing were generated using the Autogrid program (*Morris, Goodsell et al., 1998*). AutoDock parameter set- and distance-dependent dielectric functions were used in the calculation of the van der Waals and the electrostatic terms, respectively.

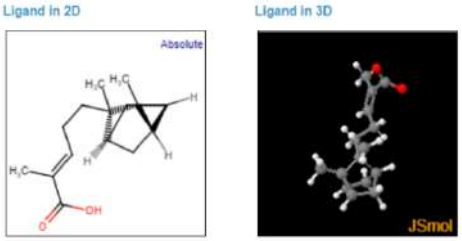
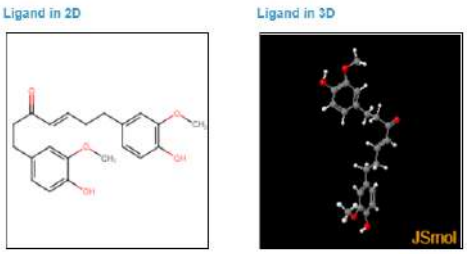
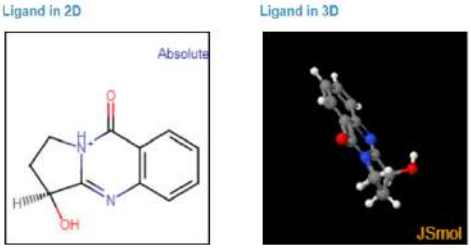
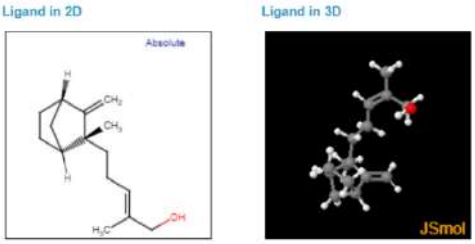
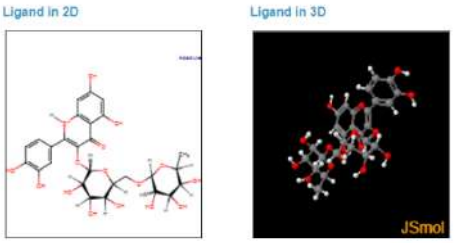
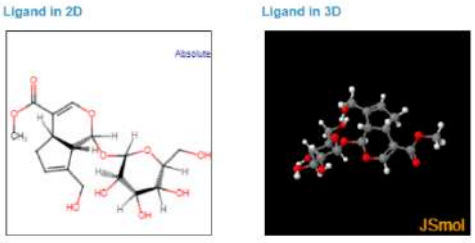
Docking simulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method (*Solis and Wets, 1981*). Initial position, orientation, and torsions of the ligand molecules were set randomly.

All rotatable torsions were released during docking. Each docking experiment was derived from 2 different runs that were set to terminate after a maximum of 250000 energy evaluations. The population size was set to 150. During the search, a translational step of 0.2 Å, and quaternion and torsion steps of 5 were applied

3.Observation and Inference :

Table.3. 2D and 3D Structure of Selected Ligands with active components in Each herbs used in the Seenthil Kudineer preparation

S.No	Compound name	2D and 3D Structure of Selected Ligands With active components in Each herbs used in the Seenthil Kudineer preparation
1.	Tinosporide	

2.	**Santalic acid**	
3.	**Gingerenone-A**	
4.	**Vasicinone**	
5.	**Beta-santalol**	
6.	**Rutin**	
7.	**Geniposide**	

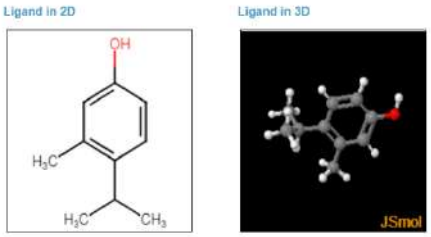
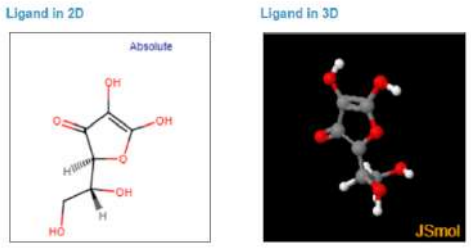
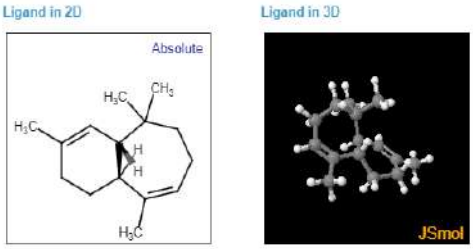
8.	**Thymol**	
9.	**Ascorbic acid**	
10.	**Gamma- Himachalene**	

Table.4. Ligand Properties of the Compounds selected for Molecular docking

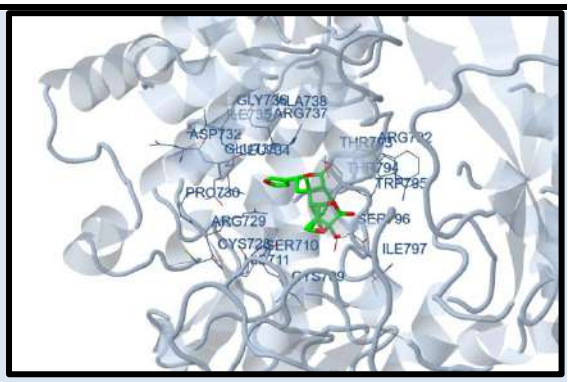
Sl.No	Compound	Molar weight g/mol	Molecular Formula	H Bond Donor	H Bond Acceptor	Rotatable bonds
1.	**Tinosporide**	374.4 g/mol	$C_{20}H_{22}O_7$	1	7	1
2.	**Santalic acids**	234.33 g/mol	$C_{15}H_{22}O_2$	1	2	4
3.	**Gingerenone-A**	356.4 g/mol	$C_{21}H_{24}O_5$	2	5	9
4.	**Vasicinone**	202.21 g/mol	$C_{11}H_{10}N_2O_2$	1	3	0
5.	**Beta-santalol**	220.35 g/mol	$C_{15}H_{24}O$	1	1	4
6.	**Rutin**	610.5 g/mol	$C_{27}H_{30}O_{16}$	10	16	6
7.	**Geniposide**	388.4 g/mol	$C_{17}H_{24}O_{10}$	5	10	6
8.	**Thymol**	150.221 g/mol	$C_{10}H_{14}O$	1	1	1
9.	**Ascorbic acid**	176.12 g/mol	$C_6H_8O_6$	4	6	2
10.	**Gamma- Himachalene**	204.35 g/mol	$C_{15}H_{24}$	0	0	0

Table.5. Summary of the molecular docking studies of compounds against

Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U

Sl. No	Compounds	Binding Free energy Kcal/mol	Inhibition constant Ki µM (*uM)(**nM)	Electrostatic energy Kcal/mol	Intermolecular energy Kcal/mol	Total Interaction Surface
1.	Tinosporide	-5.43	105.16*	-0.31	-5.98	627.235
2.	Santalic acids	-6.09	34.08*	-0.64	-7.50	591.192
3.	Gingerenone-A	-7.14	5.81*	-0.08	-8.21	767.986
4.	Vasicinone	-5.12	176.56*	-0.04	-5.42	519.812
5.	Beta-santalol	-5.80	56.08*	-0.01	-7.18	605.683
6.	Rutin	-10.28	29.35**	-0.04	-5.45	770.183
7.	Geniposide	-7.90	1.63*	-0.01	-7.33	685.726
8.	Thymol	-4.22	804.95*	-0.07	-4.86	454.614
9.	Ascorbic acid	-5.32	126.89*	-0.76	-5.53	419.335
10.	Gamma-Himachalene	-5.91	46.36*	-0.01	-5.91	535.663

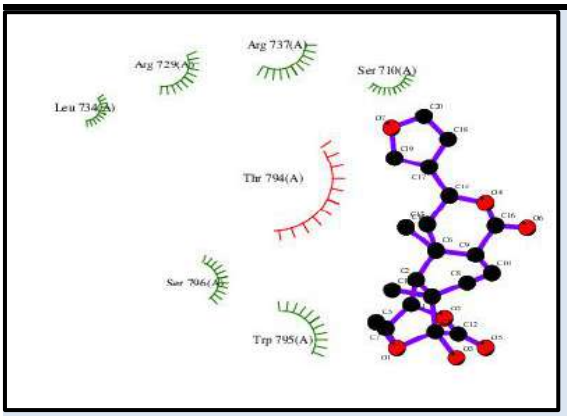
Figure.2. Docking Poses , 2D interaction plot analysis and Hydrogen bond plotting with core amino acid analysis of all the compounds of the molecular docking studies of *Seenthil kudineer* against Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U



DOCKING POSE

Tinosporide with Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U

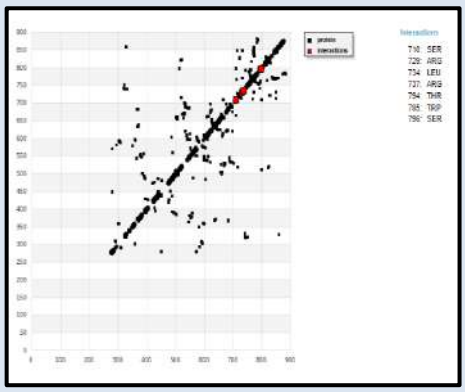
-



Tinosporide with target 2D Interaction Plot Analysis

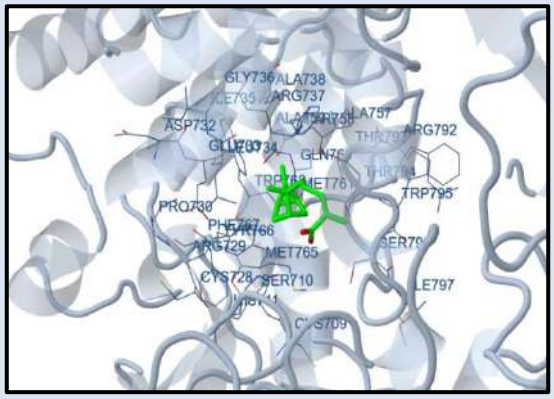
Tinosporide with target-

Hydrogen bond plotting with core amino acid Analysis

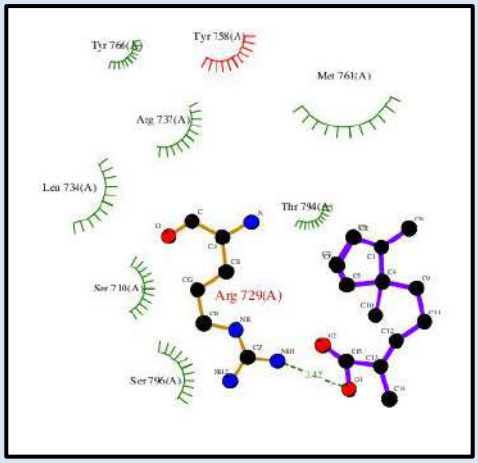


DOCKING POSE

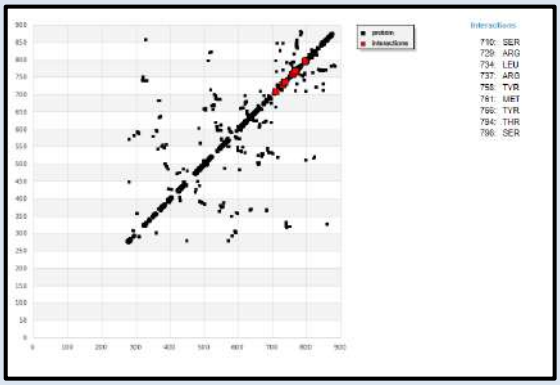
Santalic acid with Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U



Santalic acid with target -2D Interaction Plot Analysis

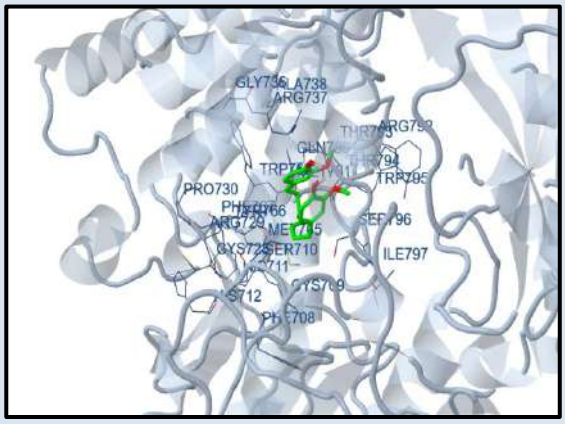


Santalic acid with target -Hydrogen bond plottin g with core amino acid Analysis

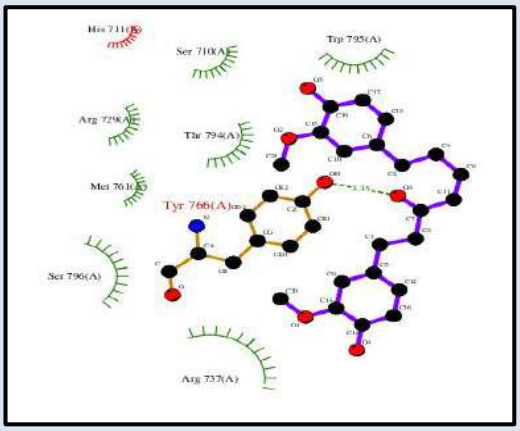


D OCKING POSE

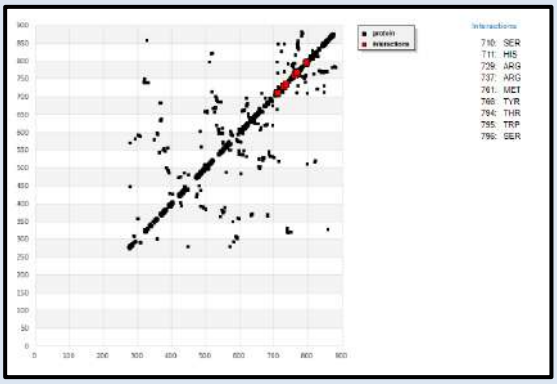
Gingerenone-A with Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U



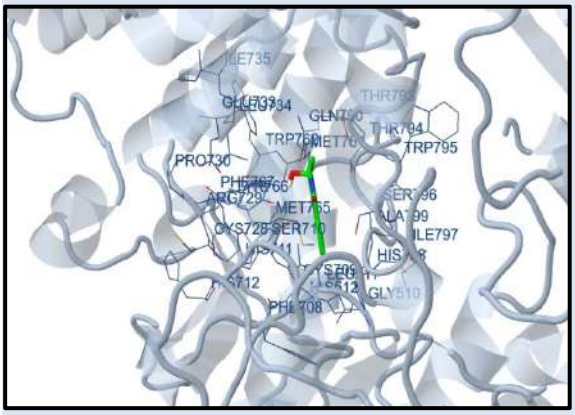
Gingerenone-A with target - 2D Interaction Plot Analysis



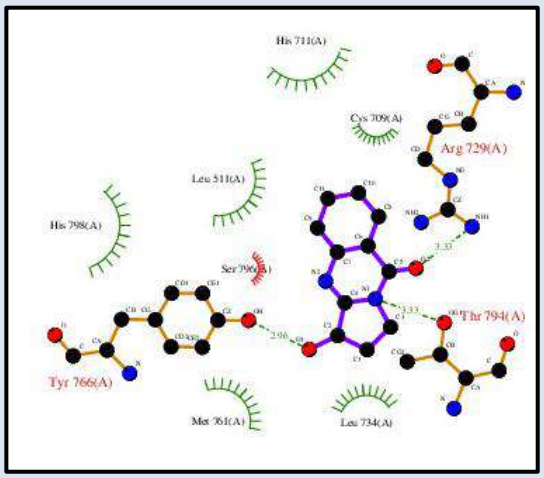
Gingerenone-A with target - Hydrogen bond plotting with core amino acid Analysis



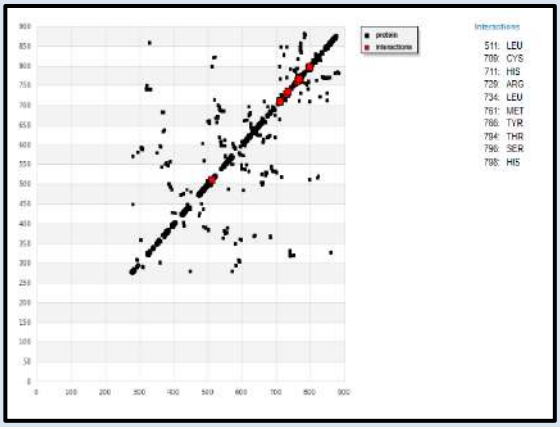
DOCKING POSE
Vasicinone with Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U



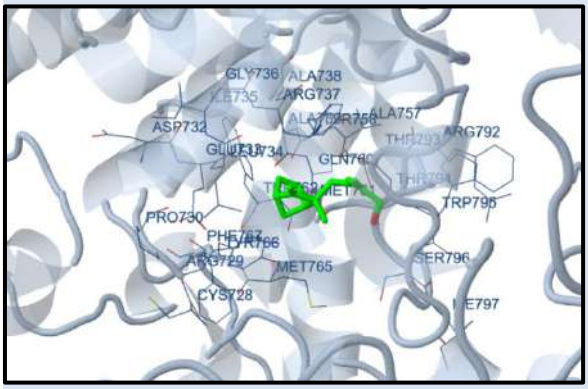
Vasicinone with target -2D Interaction Plot Analysis



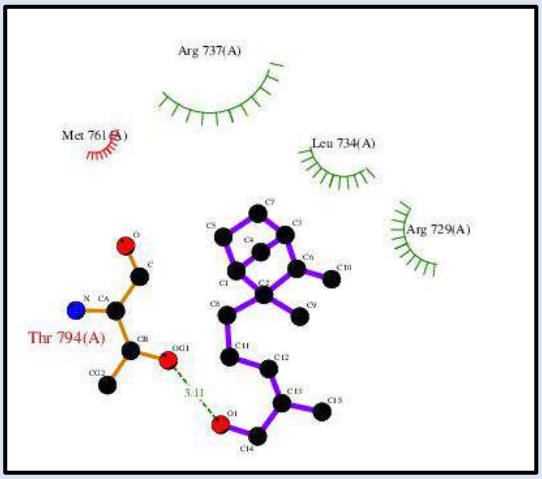
Vasicinone with target -Hydrogen bond plotting with core amino acid Analysis



DOCKING POSE
Beta-santalol with Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U

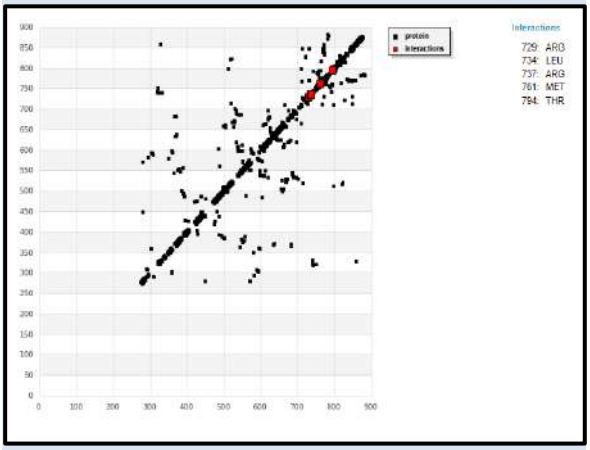


Beta-santalol with target - 2D Interaction Plot Analysis

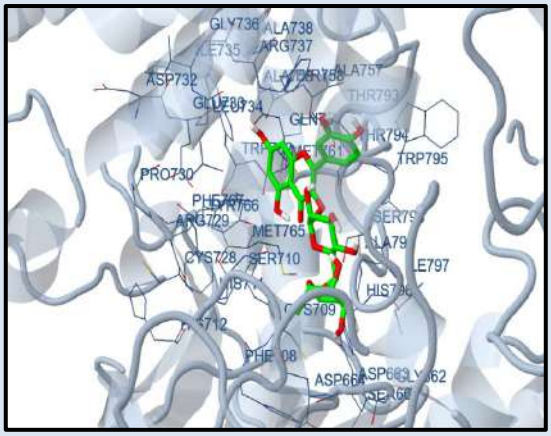


Beta-santalol with target -

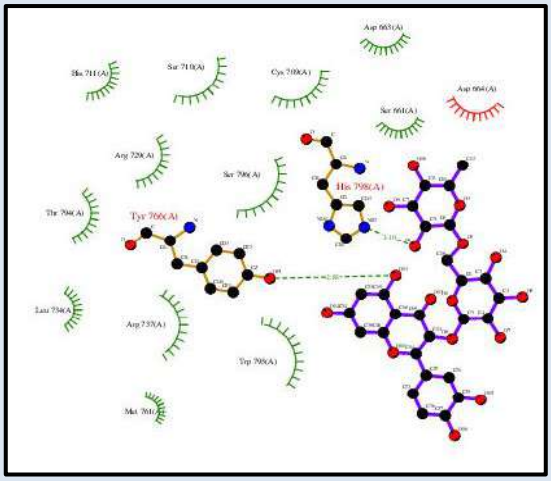
Hydrogen bond plotting with core amino acid Analysis



DOCKING POSE
Rutin with Dengue virus NS5 RNA dependent RNA polymerase -PDB 2J7U

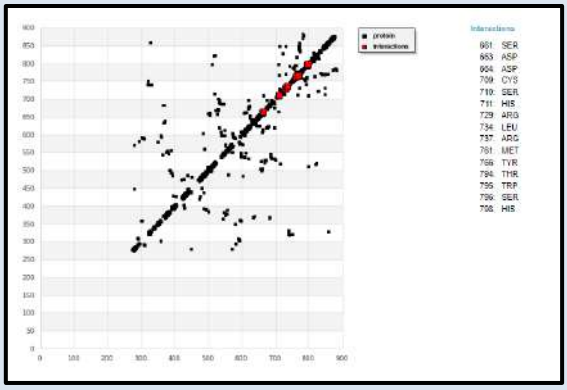


Rutin with target -
2D Interaction Plot Analysis

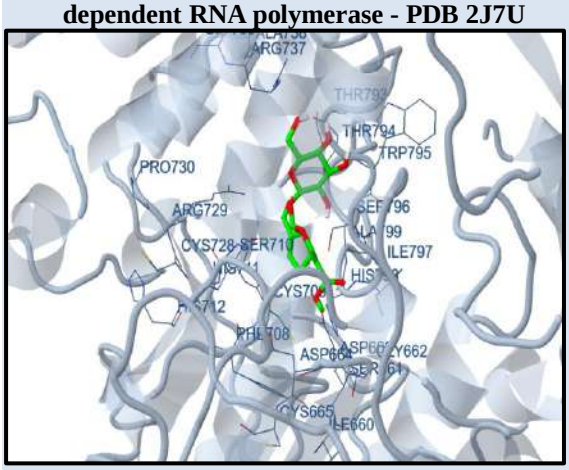


Rutin with target -

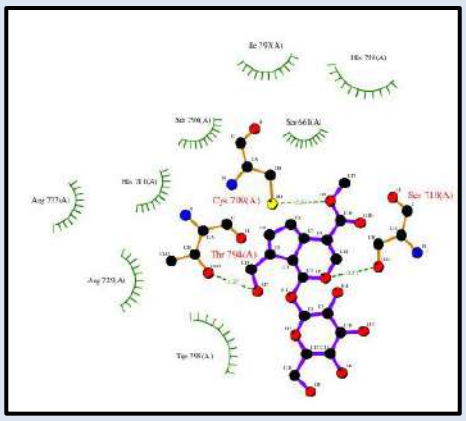
Hydrogen bond plotting with core amino acid Analysis



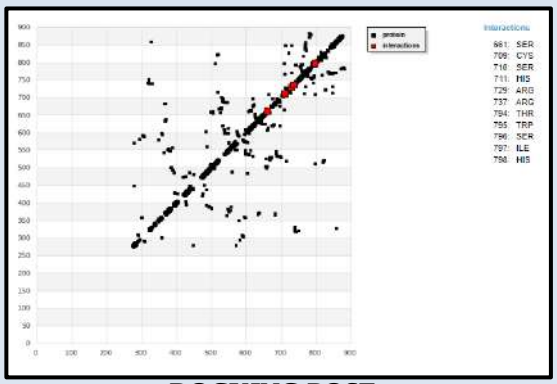
Docking Pose:
Geniposide with Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U



Geniposide with target - 2D Interaction Plot Analysis

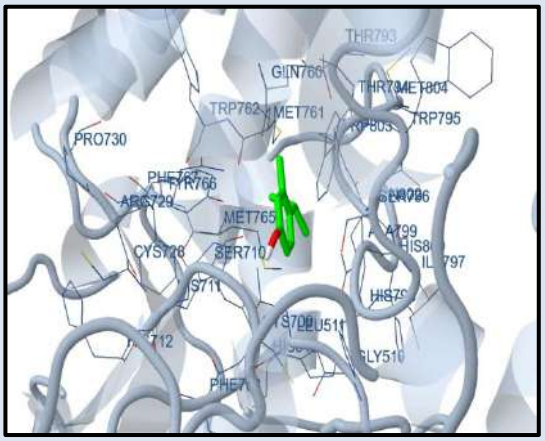


Geniposide with target -Hydrogen bond plottin g with core amino acid Analysis

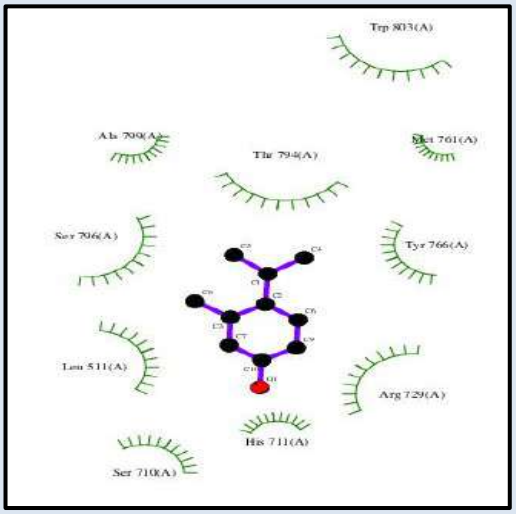


DOCKING POSE

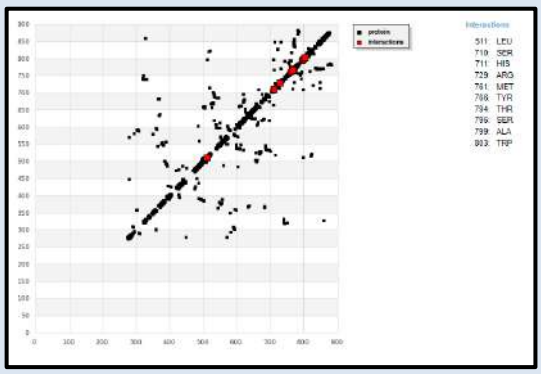
Thymol with Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U



Thymol with target –
2D Interaction Plot Analysis

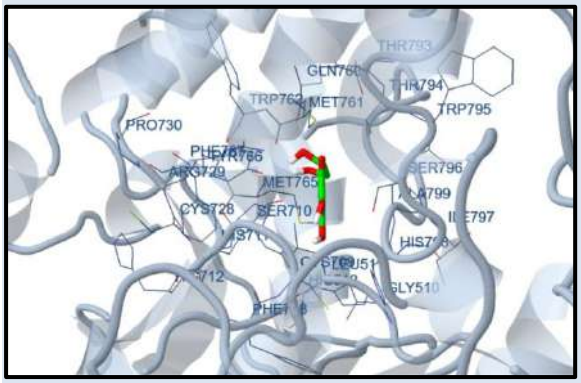


Thymol with target -Hydrogen bond plotting wi th core amino acid Analysis

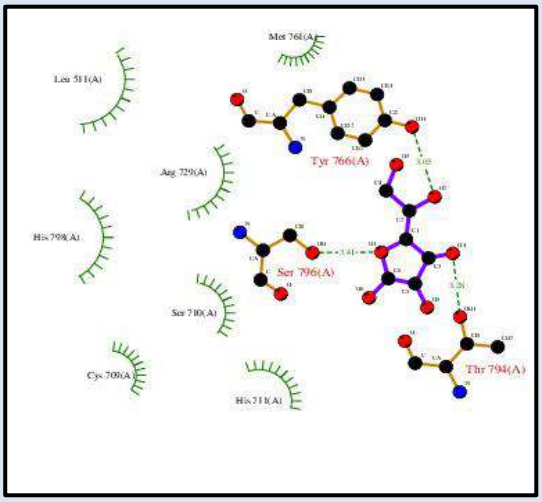


DOCKING POSE

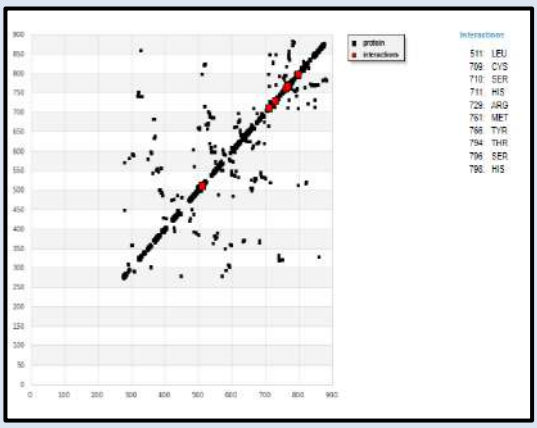
Ascorbic acid with Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U



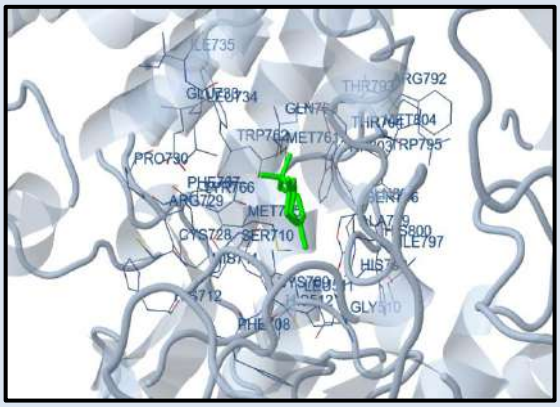
Ascorbic acid with target - 2D Interaction Plot A nalysis



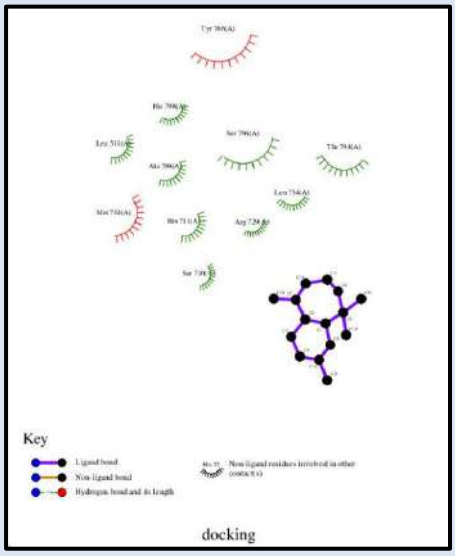
Ascorbic acid with target - Hydrogen bond plotting with core amino acid Analysis



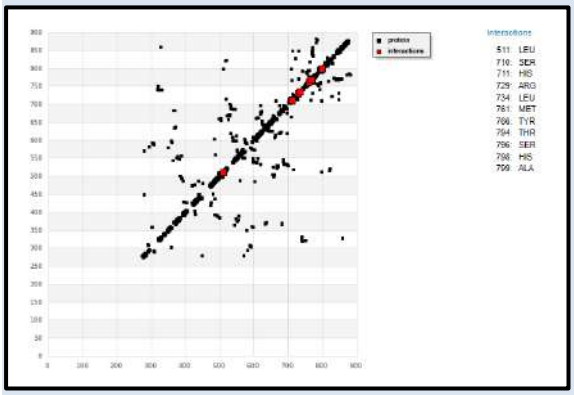
DOCKING POSE
Gamma- Himachalene with Dengue virus NS5 RNA dependent RNA polymerase - PDB 2J7U



Gamma- Himachalene with target - 2D Interaction Plot Analysis



Gamma- Himachalene with target - Hydrogen bond plotting with core amino acid Analysis



3.1.Observations of Amino acid Residue Interaction of Lead and Standard against Dengue virus NS5 RNA dependent RNA polymerase PDB 2J7U :

Total of 10 bioactive lead compounds were retrieved from the herbs present in the siddha formulation - *Seenthil Kudineer*. From reported data the phytochemicals such as Tinosporide, Santalic acids, Gingerenone-A, Beta-santalol, Rutin, Geniposide, Ascorbic acid and Gamma-Himachalene reveals maximum of 2- 3 interactions that accounts of 100 % of the occupancy with the core active amino acid residues present on the target dengue NS5 RNA dependent RNA polymerase enzyme.

4. CONCLUSION

Based on the results of the computational analysis it was concluded that the bio-active compound's like Tinosporide, Santalic acids, Gingerenone-A, Vasicinone, Beta-santalol, Rutin, Geniposide, Thymol, Ascorbic acid and Gamma-Himachalene in *Seenthil kudineer*, possess significant binding against the amino acid residues Arg-737, Arg-729 and Ser-710 present on the active site thereby it was concluded that these compounds may exerts promising anti-viral by

inhibiting the enzyme Dengue NS5 RNA dependent RNA polymerase.

Table.6. Amino acid Residue Interaction of Lead and Standard against Dengue virus NS5 RNA dependent RNA polymerase PDB 2J7U

Compounds	Inter actions	Amino acid Residues													
Tinosporide	3	710 SER	729 ARG	734 LEU	737 ARG	794 THR	795 TRP	796 SER							
Santalic acids	3	710 SER	729 ARG	734 LEU	737 ARG	758 TYR	761 MET	766 TYR	794 THR	796 SER					
Gingerenone-A	3	710 SER	711 HIS	729 ARG	737 ARG	761 MET	766 TYR	794 THR	795 TRP	796 SER					
Vasicinone	1	511 LEU	709 CYS	711 HIS	729 ARG	734 LEU	761 MET	766 TYR	794 THR	796 SER	798 HIS				
Beta-santalol	2	729 ARG	734 LEU	737 ARG	761 MET	794 THR									
Rutin	3	661 SER	663 ASP	664 ASP	709 CYS	710 SER	711 HIS	729 ARG	734 LEU	737 ARG	761 MET	766 TYR	794 THR	796 SER	798 HIS
Geniposide	3	661 SER	709 CYS	710 SER	711 HIS	729 ARG	737 ARG	794 THR	796 SER	797 ILE	798 HIS				
Thymol	1	511 LEU	711 HIS	729 ARG	761 MET	766 TYR	794 THR	796 SER	799 ALA	803 TRP					
Ascorbic acid	2	511 LEU	709 CYS	710 SER	711 HIS	729 ARG	761 MET	766 TYR	794 THR	796 SER	798 HIS				
Gamma-Himachalene	2	511 LEU	710 SER	711 HIS	729 ARG	734 LEU	761 MET	766 TYR	794 THR	796 SER	798 HIS	799 ALA			

Thereby phytocomponents which inhibit the target may act as a potential therapeutic agent for management of dengue viral infection by inhibiting the viral entry into target cellular pathway and replication.

Based on the findings of docking score values we can strongly suggest this Siddha poly herbal formulation *Seenthil Kudineer* for the better management of Dengue. Further preclinical and clinical trials have to be conducted in order to know the exact mechanism and efficacy of *Seenthil Kudineer* in Dengue infection management.

5. REFERENCES

1. Bikadi, Z., Hazai, E. Application of the PM6 semi-empirical method to modeling proteins enhances docking accuracy of AutoDock. J. Cheminf. 1, 15 (2009)
2. T. A. Halgren. Merck molecular force field. I. Basis, form, scope, parametrization, and performance of MMFF94. Journal of Computational Chemistry 17 (5-6), 490-519 (1998)
3. G. M. Morris, D. S. Goodsell, et al. Automated docking using a Lamarckian genetic algorithm and an empirical binding free energy function. Journal of

Computational Chemistry 19 (14), 1639-1662(1998)

4. Halstead S. B. (1988) Pathogenesis of dengue: challenges to molecular biology. *Science* 239: 476–481. pmid:3277268
5. Selisko B., Wang C., Harris E. & Canard B. (2014) Regulation of Flavivirus RNA synthesis and replication. *Curr Opin Virol* 9: 74–83. pmid:25462437
6. Jin Z., Deval J., Johnson K.A. & Swinney D.C. (2011) Characterization of the elongation complex of dengue virus RNA polymerase: assembly, kinetics of nucleotide incorporation, and fidelity. *J Biol Chem* 286: 2067–2077. pmid:21078673
7. Haudecoeur R., Peuchmaur M., Ahmed-Belkacem A., Pawlotsky J.M. & Boumendjel A. (2013) Structure-activity relationships in the development of allosteric hepatitis C virus RNA-dependent RNA polymerase inhibitors: ten years of research. *Med Res Rev* 33: 934–984. pmid:22893620
8. Lim S.P., Noble C.G. & Shi P.Y. (2015) The dengue virus NS5 protein as a target for drug discovery. *Antiviral Res* 119: 57–67. pmid:25912817
9. Dengue: Guidelines for diagnosis, treatment, prevention and control.2nd Edition. Geneva,Swizterland;WHO:1997.5.
10. Ghai OP, Paul VK, Bagga A. Essential Pediatrics, Seventh edition. New Delhi: CBS Publishers; 2010. Page. No : 196-201.3.
11. Global strategy for dengue prevention and control 2012-2020 – Geneva,Swizterland;WHO publication: 20122.
12. Siddha maruthuvam-Pothu (In Tamil).6th edition. Chennai:Indian medicine and Homeopathy department;2004. p 20-23.
13. Boon NA, Colledge NR, Walker BR, Hunter JAA, editors. Davidson's principles and practice of medicine.20th International edition. India: Churchchill Livingstone Elsevier; 2006.p 308-310.4.
14. Harihara mahadevan M, Vanmathi K.P. Literature Review on Siddha Herbal Formulations (Kudineer) Available for The Management of Dengue. Int J Pharmacol and Clin Sci. 2016;5(3):90-96
15. Ralston, Stuart H., Ian D. Penman, Mark W. J. Strachan, and Richard Hobson, eds. 2018. Davidson's Principles and Practice of Medicine. 23rd ed. London, England: Elsevier Health Sciences.Page no: 243,244.
16. Krupanidhi S, Abraham Peele K, Venkateswarulu TC, et al. Screening of phytochemical compounds of Tinospora cordifolia for their inhibitory activity on SARS-CoV-2: an in silico study .J Biomol Struct Dyn. 2020;1-5.
17. Gautam P. Vadnere. Phytochemical Investigation And In Vitro Antimicrobial Screening Of Santalum Album Seeds Extracts. International Journal of Pharmacy and Pharmaceutical Sciences, vol. 9, no. 10, Nov. 2017,Page. No : 117-24.
18. Rampogu S, Baek A, Gajula RG, et al. Ginger (Zingiber officinale) phytochemicals-gingerenone-A and shogaol inhibit SaHPPK: molecular docking, molecular dynamics simulations

and in vitro approaches. Ann Clin Microbiol Antimicrob. 2018;17(1):16.

19. Momin, M. A., Bellah, S. F., Rahman, S. M., Rahman, A. A., Murshid, G. M., & Emran, T. B. (2014). Phytopharmacological evaluation of ethanol extract of Sida cordifolia L. roots. Asian Pacific journal of tropical biomedicine, 4(1), Page. No :18–24.
20. Yasaman Taheri. Cyperus spp.: A Review on Phytochemical Composition, Biological Activity, and Health-Promoting Effects. 2021.https://doi.org/10.1155/2021/4014867
21. Sridevi SKS. A Review on Phytochemical and Pharmacological Profile of Hedyotis corymbosa Linn. Int. J. Pharm. Sci. Rev. Res., 26(1), May – Jun 2014; Article No. 54, Page. No : 320-324
22. Arumugam G, Swamy MK, Sinniah UR. Plectranthus amboinicus (Lour.) Spreng: Botanical, Phytochemical, Pharmacological and Nutritional Significance. Molecules. 2016;21(4):369
23. Grover, M., Behl, T., & Virmani, T. (2021). Phytochemical Screening, Antioxidant Assay and Cytotoxic Profile for Different Extracts of Chrysopogon zizanioides Roots. Chemistry & biodiversity,18(8),e2100012.
24. Vaidhiya Rathanam. Ka. Sa. Murugesa Muthaliyar, Gunapadam - part I(Mooligai Vaguppu), 2022 Edition Page no : 683.