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"INSILICO DOCKING STUDY OF CURCUMA LONGA WITH THROMOSPONDIN 2 RECEPTOR"

A. Vijaya Kumar*[1], R. Sachin Samuel Raja[1], J. Vasanth Nirmal Bosco[1], J. Saleth Mary Serena[1], K. Madhumitha[1]

[1*]Department of Bioinformatics, Sri Krishna Arts and Science College, Coimbatore, India.

ABSTRACT

Wound is defined as the damage of epidermic cells either by a cut or by any other damage. Wound healing responses to involving migration, proliferation, differentiation, and apoptosis of cell types. There are millions of plants in India to cure the diseases since ancient times. These plants were used because of their antioxidant property. 80% of world's population depends upon herbal plants, according to WHO. The origin of Curcumalonga was found in southern part of Asia. Curcumalonga is also known as turmeric. Curcumalonga belongs to ginger family (*Zingiberaceae*). The medicinal value of curcumalonga is high. Curcumalonga also has the effect of invigorating the circulation of blood, relieving pain, clearing heat of heart and cooling blood, and curing jaundice. The presence of anti-inflammatory, anti-human immunodeficiency properties, anti-bacterial property, antioxidant effects and nematocidal activities made it as of high medicinal value. Turmeric powder consumption reduces the risk of various types of cancers. Curcumalonga helps the cells to grow faster.

KEYWORDS

Epidermic Cells, Curcuma longa, Medicinal Value and Antioxidant Property.

Author for Correspondence:

Vijaya Kumar A,
Department of Bioinformatics,
Sri Krishna Arts and Science College,
Coimbatore, India.

Email: salethmaryserena@gmail.com

INTRODUCTION

Wound healing is subdivided into four phases like acute inflammation, epithelialization, granulation tissue formation, and tissue remodelling. There are millions of plants in India to cure the disease since ancient times. Some methods like Ayurveda, Unani, Siddha, etc., used to cure the disease by using extracts of plants. This method is still used in modern Ayurveda. These plants were used because of their antioxidant property. We use only few plants, rest of them are unrecognised. These plants

are available on hills and in forests. The origin of Curcuma longa was found in southern part of Asia. Curcuma longa is also known as Turmeric. Curcuma longa belongs to ginger family (*Zingiberaceae*). The medicinal value of Curcuma longa is high. Curcuma longa also has the effect of invigorating the circulation of blood, relieving pain, clearing heat of heart and cooling blood, and curing jaundice. The presence of anti-inflammatory, anti-human immunodeficiency properties, anti-bacterial property, antioxidant effects and nematocidal activities made it as of high medicinal value.

Thrombospondin protein is responsible for the healing of wounds in the body naturally. This Thrombospondin family is classified into Thromospondin 1 and Thrombospondin 2. Thrombospondin 1 has an antiangiogenic property whereas Thrombospondin 2 has a wound healing property. Hence, Thrombospondin 2 was used as a receptor in this project. Thrombospondin 2 is a protein which is responsible for wound healing activity. The function of TSP 2 is skin regeneration. Thrombospondins (THBSs) are glycoproteins that have key roles in interactions between cells and the extracellular matrix.

MATERIAL AND METHODS

Softwares Used

Biovia Studio

Structures and sequence analysis was done by Biovia visualizer software. Biovia is used to visualise the structures and edit the data with the options available. The data generated by other soft wares can also be visualised through Biovia hence it is anopen source. This allows us to view the data in an attractive manner to gain more viewers. This software allows us to work on both windows and Linux platforms.

iGEM Dock

iGEM is an automated docking tool. The two types of tags in iGEM is docking/screening tags or post analysing tag. The binding of chemical molecules were predicted by docking/screening tags. The proteins and ligands that were prior found can also be taken for post analysis under the post-analysis tag. IGEM allows you to performs you compound to docking in either standard docking or quick docking.

Protein data bank (pdb)

Protein data bank contains 3D structures of proteins and nucleic acids. PDB is an open source database that can be accessed anywhere.PDB help us to understand the shape of the molecule. Detailed Information about any protein can be retrieved by its PDB id. Every protein has a unique id maintained by PDB. PDB id is a four letter alpha numeric id. We can also search for ligand, sequence, macromolecule author or all categories. PDB is the standard format for the protein structures.

Preparation of receptor

- Using Biovia visualizer studio the PDB structure was viewed.
- Ctrl+H was selected to visualise all the molecules.
- Water molecules were removed.
- For the stable structure hydrogen and polar molecules were added.
- Save the structure using PDB format

Preparation of Ligand

- The 3d structure of the compound was retrieved from pubchem and save it in SDF format.
- Biovia visualizer studio is used to view the compound with graphics mode.
- Using MOL2 format structure was stored.

Docking

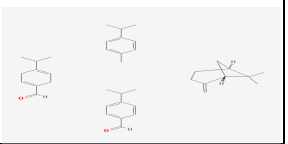
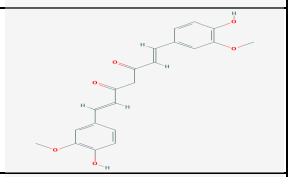
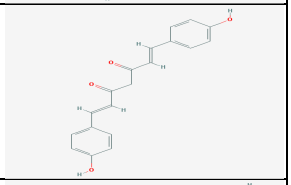
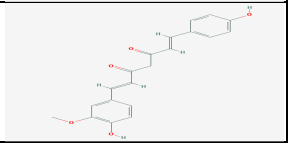
After setting the protein ligand output path and parameters to start the docking process. start docking selected to start the docking process. The status will be displayed on the screen. The docking by screening can be viewed and post analysis can be carried out. The result of the docking process can be examined by selecting the “view docked poses and the post analysis”. The list of energy of the poses will be saved into the “best pose” and “fitness. text” of the output location.

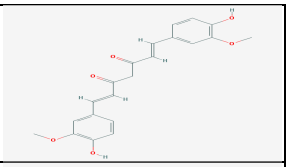
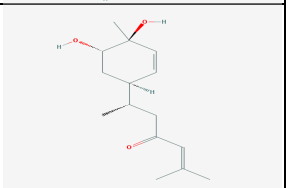
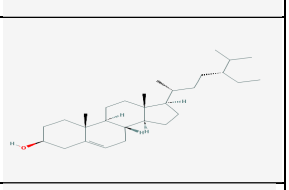
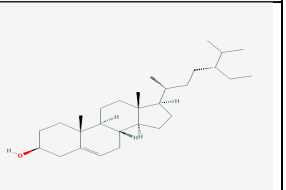
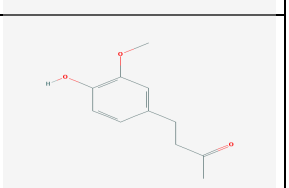
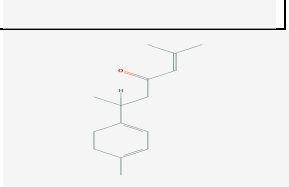
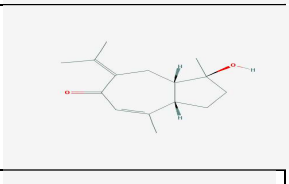
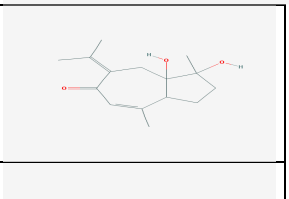
DISCUSSION

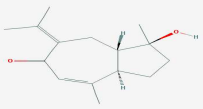
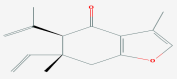
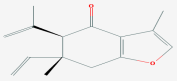
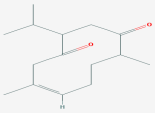
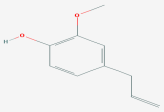
Wound occurs due to a cut or damage of cells in our body. Thromospondin 2 protein has the capacity to

cure the wound where Curcuma longa is taken as a ligand to bind with thrombospondin 2 to heal the cells. Insilico process is used here to evaluate the compounds and its activity towards wound healing. Compounds were visualised through Biovia visualizer tool and 3d structure of ligands were retrieved through PDB. When docking was carried on with the various compounds and the studied receptor Thrombospondin 2, it was observed that Curmins and Thrombospondin 2 had the least binding energy and so was selected as the best ligand receptor pair. The first five compounds (least binding energy) were Curmins, Diferuloylmethane, Bisdemethoxycurcumin, Demethoxy Curcumine, Curcumine in iGEM dock. These five compounds showed least binding energy so that it can act efficiently.

We have selected Curmins as a ligand for further suggestions due to its high wound healing activity ofthe compound. Wound healing and tissue repair are different process. Curcuma longa treated animal results faster healing of wounds than untreated controls.

NAME	PUBCHEM ID	IUPAC NAME	2D STRUCTURE
CURMINS	6850782	(1S, 5S)-6, 6-dimethyl-4-methylidenebicyclo [3.1.1] heptane;1-methyl-4-propan-2-ylbenzene; 4-propan-2-ylbenzaldehyde; 4-propan-2-ylcyclohexa-1, 4-diene-1-carbaldehyde	- 
DIFERULOYLMETHANE	969516	(1E,6E)-1,7-bis (4-hydroxy-3-methoxyphenyl) hepta-1, 6-diene-3,5-dione	
BISDEMETHOXY CURCUMIN	5315472	(1E,6E)-1,7-bis (4-hydroxyphenyl) hepta-1, 6-diene-3, 5-dione	
DEMETHOXY CURCUMINE	5469424	(1E,6E)-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl) hepta-1, 6-diene-3, 5-dione	

CURCUMINE	969516	(1E, 6E)-1,7-bis(4-hydroxy-3-methoxyphenyl) hepta-1, 6-diene-3, 5-dione	
CURONE	14287397	(6S)-6-[(1R, 4S, 5S)-4, 5-dihydroxy-4-methylcyclohex-2-en-1-yl]-2-methylhept-2-en-4-one	
BETA SITOSETROL	222284	(3S, 8S, 9S, 10R, 13R, 14S, 17R)-17-[(2R, 5R)-5-ethyl-6-methylheptan-2-yl]-10, 13-dimethyl-2, 3, 4, 7, 8, 9, 11, 12, 14, 15, 16, 17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol	
ATLANTONE	13967857	6-methyl-2-(4-methylcyclohex-3-en-1-yl) hepta-1, 5-dien-4-one	
ZINGIBERONE	31211	4-(4-hydroxy-3-methoxyphenyl)butan-2-one	
TUMERONE	558173	2-methyl-6-(4-methylcyclohexa-1, 3-dien-1-yl)hept-2-en-4-one	
EPIPROCURCUMENOL	10263440	(3S, 3aS, 8aS)-3-hydroxy-3, 8-dimethyl-5-propan-2-ylidene-2, 3a, 4, 8a-tetrahydro-1H-azulen-6-one	
PROCURCUMADIOL	14633011	3,3a-dihydroxy-3, 8-dimethyl-5-propan-2-ylidene-1, 2, 4, 8a-tetrahydroazulen-6-on	
CURCUMENONE	153845	(1R, 6S, 7R)-6-methyl-7-(3-oxobutyl)-3-propan-2-ylidenebicyclo [4.1.0] heptan-4-one	

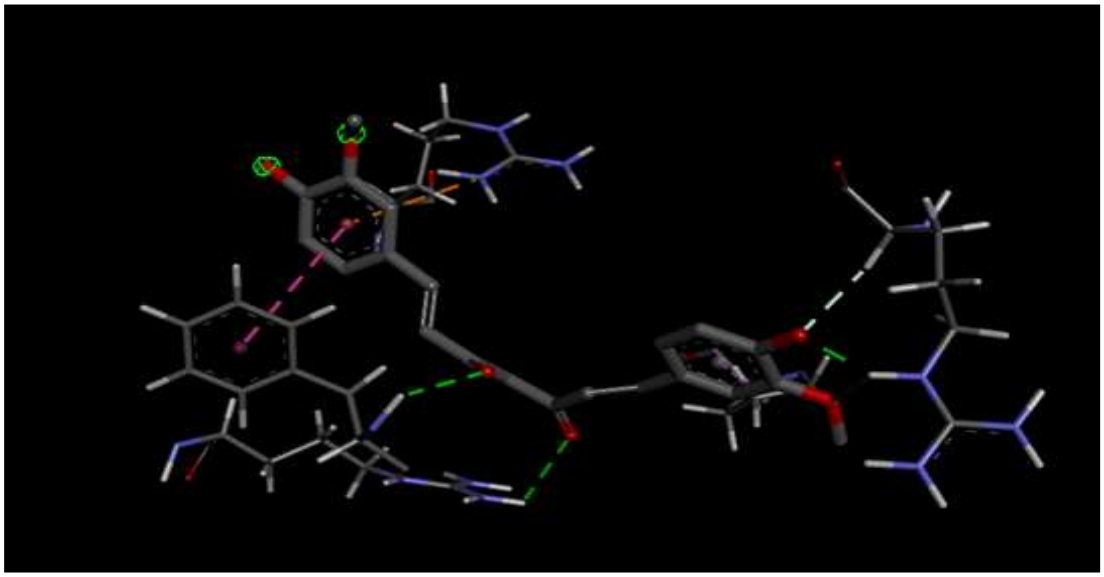
PROCURCUMENOL	189061	(3S, 3aS, 8aR)-3-hydroxy-3, 8-dimethyl-5-propan-2-ylidene-2, 3a,...	
CURZERENONE	3081930	(5R, 6R)-6-ethenyl-3, 6-dimethyl-5-prop-1-en-2-yl-5, 7-dihydro-1-benzofuran-4-one	
CURIDONE	5362828	(6Z)-6, 10-dimethyl-3-propan-2-ylcyclodec-6-ene-1, 4-dione	
BORNOL	64685	4, 7, 7-trimethylbicyclo [2.2.1] heptan-3-ol	
EUGENOL	3314	2-methoxy-4-prop-2-enylphenol	
CAMPHOR	2537	4, 7, 7-trimethylbicyclo [2.2.1] heptan-3-one	
CINEOLE	10106	1-methyl-4-propan-2-yl-7-oxabicyclo [2.2.1] heptane	
CAMPHENE	6616	3, 3-dimethyl-2-methylidenebicyclo [2.2.1] heptane	

DOCKING RESULT

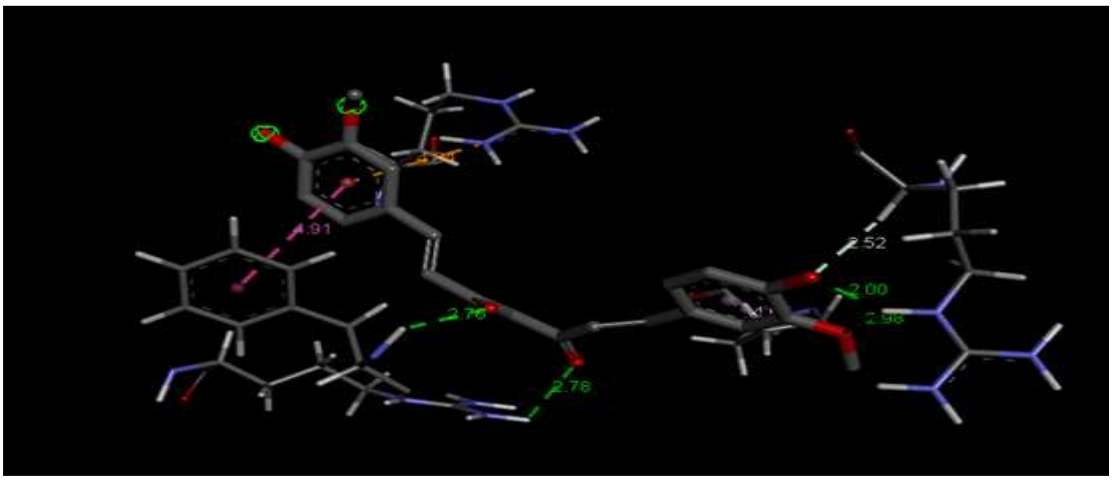
LIGAND	TOTALENERGY	VDW	HBOND	ELEC	AVERCONPAIR
CURMINS	-111.629	-97.6443	-13.9843	0	26.1111
DIFERULOYLMETHANE	-108.976	-83.2824	-25.6936	0	23.2963
BISDEMETHOXYCURCUMIN	-103.914	-83.3732	-20.5412	0	26.0435
DEMETHOXY CURCUMINE	-103.037	-94.6222	-8.41486	0	24.2
CURCUMINE	-98.9123	-75.2714	-23.6409	0	23.2963
CURONE	-91.695	-74.8764	-16.8186	0	29.5
BETA SITOSETROL	-90.4273	-87.9832	-2.44404	0	21.8333
ATLANTONE	-86.3905	-80.638	-5.75252	0	33.75
ZINGIBERONE	-84.7213	-68.8306	-15.8907	0	35.5714
TUMERONE	-83.7552	-77.7552	-6	0	30.25
EPIPROCURCUMENOL	-82.3926	-67.8926	-14.5	0	28.8824
PROCURCUMADIOL	-80.8701	-61.4326	-19.4375	0	25.4444
CURCUMENONE	-78.0266	-68.243	-9.78359	0	27.2941
PROCURCUMENOL	-75.029	-64.3251	-10.7039	0	27.1765
CURZERENONE	-71.8415	-68.3415	-3.5	0	28
CURIDONE	-71.7949	-62.6385	-9.15642	0	31.4706
BORNOL	-71.3685	-56.8685	-14.5	0	35.5455
EUGENOL	-67.522	-57.9199	-9.60204	0	31.25
CAMPHOR	-64.9715	-56.6857	-8.28583	0	38.0909
CINEOLE	-59.4839	-53.8323	-5.65169	0	30.6364
CAMPHENE	-55.2933	-55.2933	0	0	35

3D STRUCTURE

CURMINS



CURMINS WITH DISTANCE



CONCLUSION

Wound is defined as the damage of epidermic cells either by a cut or by any other damage. Thrombospondin 2 was used as a receptor in this project. Thrombospondin 2 is a protein which is responsible for wound healing activity. The function of TSP 2 is skin regeneration. Thrombospondins (THBSs) are glycoproteins that have key roles in interactions between cells and the extracellular matrix.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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