

**Research Article**

**MOLECULAR DOCKING STUDY OF HENTRIACONTANE FOR ANTICANCER AND ANTITUBERCULAR ACTIVITY**

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**ABSTRACT**

**Objective:** The present study discusses the molecular docking study of Hentriacontane for its Anti-tubercular and Anti-cancer activity.

**Methods:** Two protein targets were selected for the study and their structures were taken from RCSB Protein Data Bank in PDB format. Preparation of proteins was done using Discovery Studio 2021 Client. The structure of Hentriacontane was drawn using ChemDraw 20.0 and saved in Mol format. Molecular docking was performed using PyRx software. 3D and 2D docking interactions were visualized by Discovery Studio 2021 Client.

**Results:** Hentriacontane has docked against the selected proteins, namely Extra-cellular regulated kinase-2 (ERK-2; PDB ID: 3QYW) and Shikimate kinase (PDB ID: 1ZYU). The compound has shown the best binding score against Shikimate kinase (-10.4 kcal/mol), and Extra-cellular regulated kinase-2 (-7.4 kcal/mol) than the standard drugs.

**Conclusion:** Molecular Docking study indicates that Hentriacontane could be an effective inhibitor for the proteins under study. Hence, the compound may be considered a lead molecule and further investigation of its analogues may help in the development of novel drugs for the treatment of breast cancer and tuberculosis.

**Keywords:** Hentriacontane, Molecular Docking, Tuberculosis, Extra-cellular regulated kinase-2, Shikimate kinase, Antitubercular, Anticancer, *In silico*

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**INTRODUCTION**

Cancer is the current major leading cause of millions of deaths being reported in the past few years. It has posed a huge threat to humanity. Now there are different forms of cancer affecting most of the body's vital organs and breast cancers are one of them. It is increasing at a tremendous rate and jeopardizing the female population. There have been subsequent treatment development for breast cancer, including chemotherapy, radiotherapy, gene replacement, laser surgery, etc. The most common causes of breast cancer involve defective genes like *ATM*, *BRCA1*, *BRCA2*, *CHEK2*, and *PALB2*. Among European women, approximately 6.8% of the patients and 2.0% of the controls had protein-truncating variants in any of the 9 genes associated with breast cancer risk; in addition, 2.2% of the patients and 1.4% of the controls had missense variants in *CHEK2*. The frequency of protein-truncating variants among Asian women (4.4% of the patients and 1.3% of the controls) was lower than the frequency among European women; this finding is attributable to the much lower frequency of the c.1100delC variant in *CHEK2* among Asian women [1].

Moreover, Tuberculosis is the third major fatal disease rapidly growing worldwide and its resistance to potential therapeutics has become a huge threat to humankind. For example, *M. tuberculosis* resistance towards isoniazid and rifampicin causes multidrug and extensive drug resistance. There were 1-7 million deaths from tuberculosis in 2016, including 0-4 million deaths among people co-infected with HIV (officially classified as deaths caused by HIV/AIDS) [2].

Plants have been a major source of therapeutically active compounds which are modified by various methods to a suitable medicinal regimen with better pharmacodynamic and pharmacokinetic properties. These phytoconstituents can have different pharmacological actions such as anti-microbial, anti-cancer, anti-tubercular, anti-inflammatory, anti-oxidants, immunomodulators, hepatoprotective actions, anti-fungal etc. when administered in the body [3]. Thus, one such phytoconstituent named Hentriacontane is also found to possess some pharmacological action. Hentriacontane is present in small amounts in many medicinal plants like *Gymnema sylvestre*, *Epiphyllum oxypetalum* etc [4]. Hentriacontane is a straight-chain aliphatic alkane compound with 31 carbon atoms. It is highly non-polar and lipophilic in nature [5, 6]. Molecular Docking is a technique used to predict the interactions between the ligand or drug and target proteins and the results of interaction are interpreted in terms of binding affinity, which is called the Docking score [7].

Hence, the present study focuses on anticancer and antitubercular activities of Hentriacontane evaluated by an advanced computational tool called Molecular Docking.

**MATERIALS AND METHODS**

**Selection of ligand and target proteins**

In this study, the ligands chosen were Hentriacontane (test drug), Isoniazid and Ulixertinib (standard drugs). The target proteins for breast cancer and tuberculosis selected were Extracellular regulated kinase-2 (ERK-2) [8] and shikimate kinase [9], respectively. The structures of proteins were extracted from RCSB Protein Data Bank in PDB format.

**Preparation of ligand and target proteins**

The structure of hentriacontane was prepared in ChemDraw 20.0 and structures of Isoniazid and Ulixertinib were taken from Pubchem in 3D conformer. The proteins were prepared by a Discovery Studio 2021 Client. The preparation of proteins involved the removal of unwanted residues

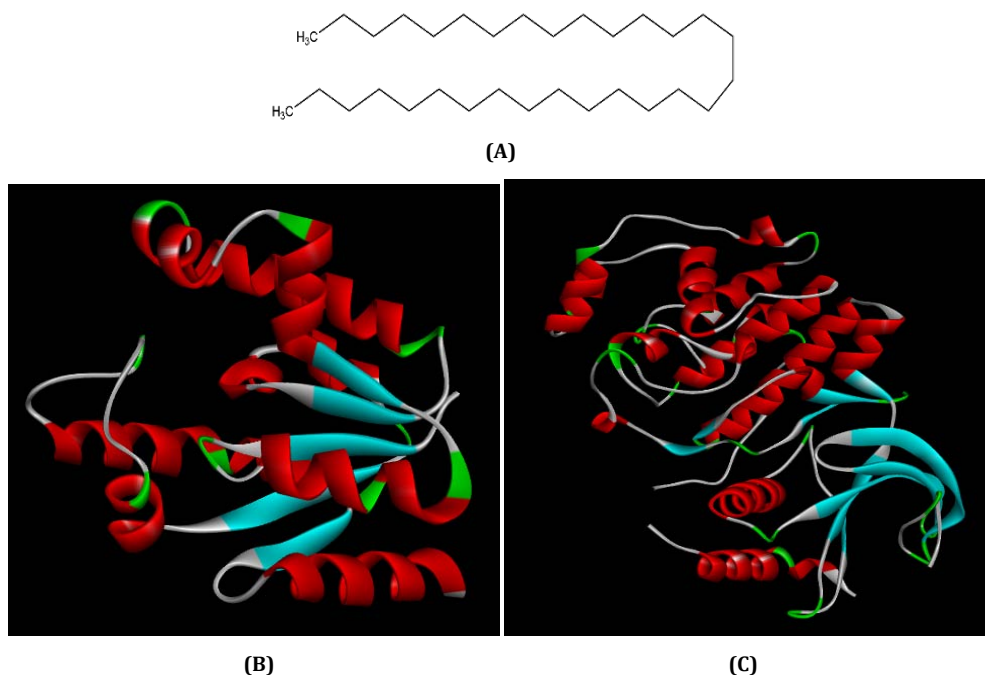
like water molecules, ligands or any other hetero atoms present in protein and also the active site of proteins were defined based on the grid dimensions and the prepared proteins and ligand were saved in PDBQT format. Both the ligand and proteins were prepared for docking. The prepared structures of ligand and both target proteins are shown below in fig. 1.

#### Molecular docking of ligand and target proteins

Hentriacontane was docked against the selected target proteins using PyRx software. The prepared ligand and proteins in PDBQT format are selected in PyRx and then docking is initiated.

#### Visualization of interactions

The docking interactions between ligand and target proteins were visualized in 3D and 2D forms using Discovery Studio 2021 Client.



**Fig. 1: (A) Structure of hentriacontane from ChemDraw 20.0, (B) Structure of ERK-2 protein in breast cancer, (C) Structure of shikimate kinase protein in tuberculosis. Both the protein structures were extracted from RCSB protein data bank**

**Table 1: Molecular docking studies-selected target proteins**

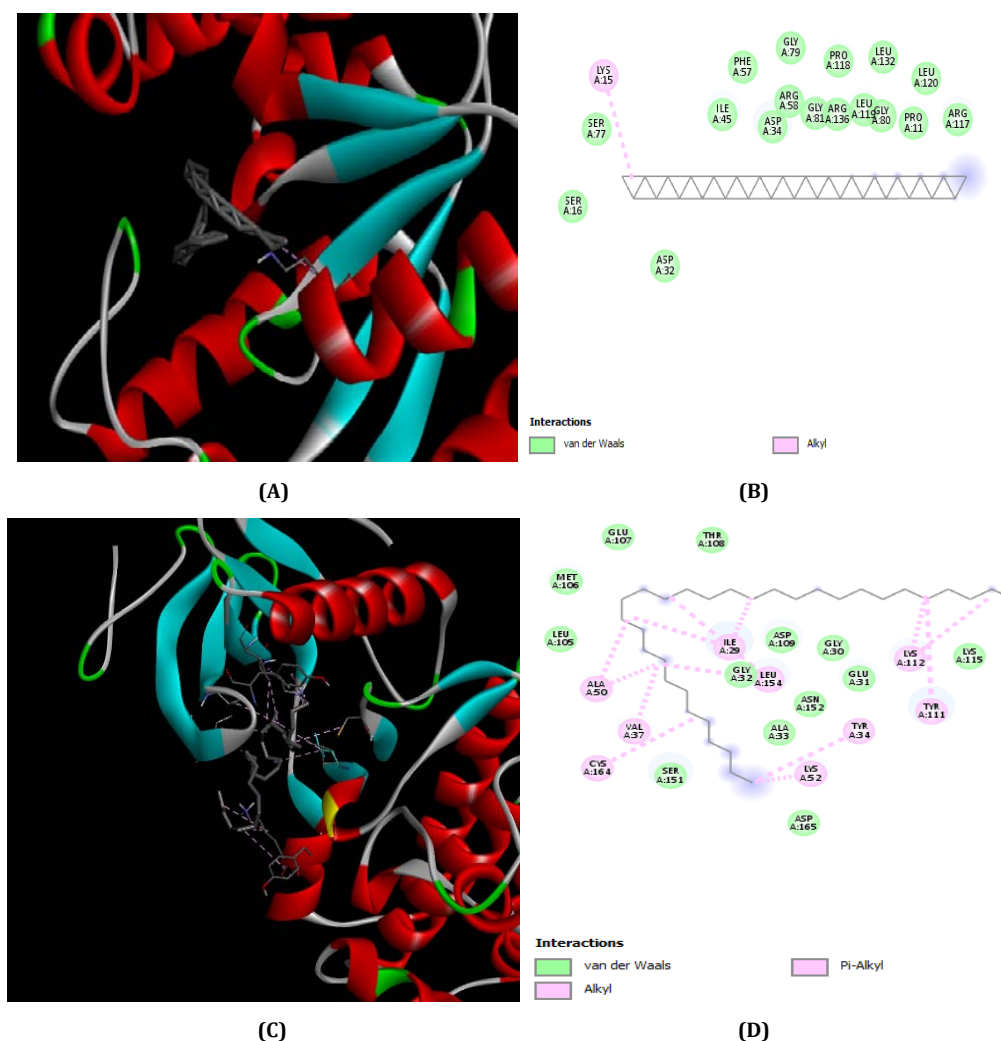
S. No.	Target proteins	PDB ID	Activity
1.	ERK-2	3QYW	Anti-cancer activity
2.	Shikimate kinase	1ZYU	Anti-tubercular activity

#### RESULTS AND DISCUSSION

Molecular docking of hentriacontane resulted in 9 possible modes of interactions with different binding affinity or docking scores. The 2D and 3D interactions having the least docking score for both the proteins were taken from Discovery Studio 2021 Client. Based on the docking score, it showed that the interaction of hentriacontane with the two proteins with the highest negative binding affinity is the most suitable mode of interaction. Because the ligand binds with the protein in different poses with certain binding affinity and the least value of the same gives the most suitable binding. Also, the docking score in the case of shikimate kinase is least as compared to the docking score in the case of ERK-2 protein. This shows that binding of hentriacontane with shikimate kinase more easily took place than with ERK-2, which subsequently indicates that antitubercular activity can be more profound. Further, the molecule Hentriacontane has given better docking results as compared to the compounds discussed in other articles [8-10]. The docking scores for both proteins are tabulated in table 1. The 2D and 3D interactions of the suitable pose of Hentriacontane in both proteins are given in fig. 2.

**Table 2: Docking scores of hentriacontane against selected target proteins**

S. No.	Ligand	Docking scores	
		ERK-2 (3QYW)	Shikimate kinase (1ZYU)
1.	Hentriacontane	-7.4	-10.4
2.	Isoniazid	-	-6.2
3.	Ulixertinib	-6.8	-



**Fig. 2: (A) 3D interaction of hentriacontane with shikimate kinase (B) 2D interaction of hentriacontane with shikimate kinase. (C) 3D interaction of hentriacontane with ERK-2 protein. (D) 2D interaction of hentriacontane with ERK-2 protein**

## CONCLUSION

Molecular docking of hentriacontane was performed against the selected proteins shikimate kinase and ERK-2 for evaluation of its antitubercular and anticancer activity. The results of docking showed that interaction of hentriacontane was more profound in case shikimate kinase than ERK-2, which indicates that hentriacontane can have antitubercular activity. Hence, the antitubercular action of hentriacontane can be further explored for its development as a novel shikimate kinase inhibitor.

## DATA AVAILABILITY

Not applicable

## FUNDING

Nil

## AUTHORS CONTRIBUTIONS

The study protocol was designed by Suma B. V and coordinated the overall project. Molecular docking studies were done by Burhanuddin Madriwala. The manuscript was prepared by Judy Jays and revised by all the authors.

## CONFLICTS OF INTERESTS

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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