

# Insilico Interaction of Bioactive Compounds from Clove against Oral *Candida albicans* biofilm drug targets

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## **Abstract:**

**Aim:** *Insilico Interaction of Bioactive Compounds from Clove against Oral Candida albicans biofilm drug targets.*

**Materials and methods:** *All the 3D models were obtained from PubMed and the final analysis was produced by two systems, mainly chemsketch and GOLD protein-ligand docking.*

**Results :** *Here in this study we have tried to find the best compatible bio active compound of clove towards the target. Out of 5 Bioactive compounds from clove Eugenol acetate O4,O3 showed the highest docking score having h bond score to be 2.888(O4) , 2.653(O3).*

**Conclusion:** *In most of the cases the docking the H bond value must be considered must be considered because the hydrogen bonds are stronger than van-der-walls bond and weaker than covalent bond as H bonds have the ability to create a bond or break a bond easily in this study we r trying to read the compatibility between the bioactive compounds and the target compound in this case its Candida albicans biofilm. Further the the research can be extended to wet lab work for further details.*

**Keywords:** *Insilico, hydrogen bonds, biofilm, Candida albicans, bioactive, Eugenol*

## **1. Introduction:**

An assemblage of microbial cells that are irreversibly associated with a non mobile surface and with the matrix of primarily polysaccharide material. Biofilm-associated organisms also differ from their planktonic counterparts with respect to the genes that are transcribed. Biofilms form on a wide range of surfaces, including living tissues, indwelling medical devices, etc<sup>[1]</sup>

*Candida albicans* a polymorphic yeast and a pathogen. In the oral cavity, it is associated with caries<sup>[2]</sup>

and it can cause infections on oral soft tissues, as a superficial overgrowth or deep-seeded invasion, this results in disseminated disease. Nevertheless, *C. albicans* colonizes the oral cavity as a commensal in 50–70% of individuals. It has the ability to interact with many bacterial species on different levels forming ma bioflim it increases the biomass of the dual-species biofilms<sup>[3]</sup>

*C. albicans* complex interaction with the cariogenic organism *S. mutans*. The glucan binds to the cell wall of *C. albicans*. The yeast provides adhesion sites for the bacterium, resulting in increased biofilm.

*Acacia seeds* belongs to family Leguminosae<sup>[4,5]</sup> possesses antioxidant, anticancer, anti-haemolytic, anti-inflammatory, antipyretic, analgesic and antidepressant potentials. *Acacia catechu* Willd (*Fabaceae*), commonly known as catechu, cachou, and black cutch, is a moderate size deciduous, thorny tree widely distributed in India.

The name of the plant has recently been changed to *Vachellia karroo*<sup>[6]</sup>. The gum produced by *A. karroo* is used against oral thrush and can also be harvested for food during hard times. *Acacia* is also effective against fever, malaria, cholera, diarrhoea, dysentery and high blood pressure. *Acacia* species are rich sources of polyphenolic compounds, known to have strong antioxidant properties that help in the prevention of various oxidative stress. These activities might attribute to the presence of various active secondary metabolites i.e. gallic acid, catechin, rutin, caffeic acid, 7-*O*-galloyl catechin, +catechin and methyl gallate. Flavonoids, a type of water-soluble plant pigments, are the major class of compounds isolated from *Acacia* plants. Catechin is a major flavan in *Acacia* bark and heartwood, found primarily in green tea.

Various parts of this plant have been used since ancient times in Ayurvedic medicine.<sup>[7,8]</sup> Numerous natural bioactive compounds for instance 4-hydroxybenzoic acid, kaempferol, quercetin, 3,4,7-trihydroxyl-3,5-dimethoxyflavone, catechin, rutin, isorhamnetin, epicatechin, afzelechin, epiafzelechin, mesquitol, ophioglonin, aromadendrin, and phenol have been isolated from heartwood, bark, roots, leaves and stem of *A. catechu* and presence of the above active compounds have been implicated for its myriad biological effects. The phytochemical isolated from this plant have been widely studied for their cytotoxic potentials against variety of cancer cell lines and came out with good results<sup>[9]</sup>. *A. catechu* has been studied for its hepatoprotective, antipyretic, antidiarrheal, hypoglycaemic, anti-inflammatory, immunomodulatory, antinociceptive, antimicrobial, free radical scavenging, and antioxidant activities.

Extensive animal in vivo studies and human clinical trials compositions containing *Acacia* extract indicate that *Acacia* has great potential as a therapeutic agent for inflammatory diseases such as arthritis, irritable bowel syndrome, and inflammatory bowel syndrome<sup>[10]</sup>. Catechu black extract has been approved by the US FDA for food use as a natural flavouring substance and/or natural substance used in conjunction with flavour.

Fatty acid is a carboxylic acid with a long aliphatic chain, which is either saturated or unsaturated. Most naturally occurring fatty acids have an unbranched chain of an even number of carbon atoms, from 4 to 28. Fatty acids are usually derived from triglycerides or phospholipids. Two essential fatty acids are linoleic acid (LA) and alpha-linolenic acid (ALA)<sup>[11]</sup>. These fatty acids are widely distributed in plant oils. The human body has a limited ability to convert ALA into the longer-chain omega-3 fatty acids — eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which can also be obtained from fish. Omega-3 and omega-6 fatty acids are biosynthetic precursors to endocannabinoids with antinociceptive, anxiolytic, and neurogenic properties.

Medicinal plants are currently of considerable importance because of their fatty acids which has potential therapeutic value that leads them to the path of development of novel drugs. Presence of beneficial fatty acids and the shift towards natural products in pharmaceutical and cosmeceutical industry made medicinal plant research equally important to conventional drug. Methods like conventional solvent extraction, steam distillation, and sublimation, etc., are developed for extraction fatty acids.<sup>[12]</sup> However, these methods are based on sequential extraction, including one or more organic solvents. Such phytochemical extracts need to be processed for the removal of traces of the organic solvents.

Furthermore, the mixture has to be purified for individuality. While such methods are useful for extraction and purification of small quantities of fatty acids for research purposes, completely removing the organic solvents from the extracts is a problematic issue. Furthermore, the types and concentrations of organic solvents must be carefully selected to avoid structural changes to the target phytochemical during extraction. Such changes adversely affect one or more of their desirable physical, chemical, and biological properties. Water, is an inexpensive, environment-friendly and an ideal solvent for the industrial extraction of medicinal plants, but its use is limited due to poor extraction efficiency for most organic compounds. The aim of this study is to assess and determine the amount of fatty acids in acacia seed extract.

## **2. Materials and method:**

ACDLabsChemsketch

ACD/ChemSketch is an advanced chemical drawing tool and is the accepted interface for the industries best NMR and molecular property predictions, nomenclature, and analytical data handling software.

ACD/ChemSketch is also available as freeware, with functionalities that are highly competitive with other popular commercial software packages. The freeware contains tools for 2D structure cleaning, 3D optimization and viewing, InChI generation and conversion, drawing of polymers, organometallics, and Markush structures—capabilities that are not even included in some of the commercial packages from other software producers. Also included is an IUPAC systematic naming capability for molecules with fewer than 50 atoms and 3 rings. The capabilities of ACD/ChemSketch can be further extended and customized by programming.

GOLD - Protein-Ligand Docking

GOLD is a program for calculating the docking modes of small molecules in protein binding sites and is provided as part of the GOLD Suite, a package of programs for structure visualisation and manipulation (Hermes), for protein-ligand docking (GOLD) and for post-processing (GoldMine) and visualisation of docking results. Hermes acts as a hub for many of CCDC's products, for more information please refer to the Hermes product page.

The product of a collaboration between the University of Sheffield, GlaxoSmithKline plc and CCDC, GOLD is very highly regarded within the molecular modelling community for its accuracy and reliability.

GOLD features include:

- A genetic algorithm (GA) for protein-ligand docking
- An easy to use interface with interactive docking set-up via Hermes
- A comprehensive docking set-up wizard
- Full ligand flexibility
- Partial protein flexibility, including protein side chain and backbone flexibility for up to ten user-defined residues
- Energy functions partly based on conformational and non-bonded contact information from the CSD
- A variety of constraint options
- Improved flexible ring handling
- Automatic consideration of cavity bound water molecules
- Improved handling and control of metal coordination geometries
- Improved parameterisation for kinases and heme-containing proteins
- Automatic derivation of GA settings for particular ligands
- A choice of GoldScore, ChemScore, Astex Statistical Potential (ASP) or Piecewise Linear Potential (PLP) scoring functions
  - Extensive options for customising or implementing new scoring functions through a Scoring Function Application Programming Interface, allowing users to modify the GOLD scoring-function mechanism in order to either: implement their own scoring function or enhance existing scoring functions; customise docking output
  - A ChemScore Receptor Depth Scaling (RDS) rescore option so that the score attributed to hydrogen bonds is scaled depending on the depth in the binding pocket
  - Automatic rescoring with an alternate scoring function at the end of a docking run.

GOLD's genetic algorithm parameters are optimised for virtual screening applications. GOLD is optimised for parallel execution on processor networks; a distributed version of GOLD is available for use on commercial PC GRID systems

Active site of N-myristoyltransferase enzyme of *Candida albicans*

The active site of the crystal structure of N-myristoyltransferase enzyme of *Candida albicans* (PDB id: 1NMT) ASN 74, TYR 107, ASP 110, TYR 119, ASP 136, LYS 161, LEU 162, ASN 163, LYS 164, GLU 173, ILE 174, ASN 175, PHE 176, ARG 198, ARG 199, THR 211, PRO 217, THR 218, TYR 225, TYR 283, LYS 284, TYR 285, GLN 286, GLU 287, ARG 288, PHE 289, ASP 290, ILE 291, VAL 292, GLN 293, LEU 294, TRP 303, ASN 314, LYS 317, LEU 336, LEU 337, TYR 354, LEU 355, PHE 356, TYR 357, PHE 386, PHE 414, LEU 415, TYR 418, PHE 420, ARG 423, VAL 449, LEU 451.

### 3. Structure of Ligands:

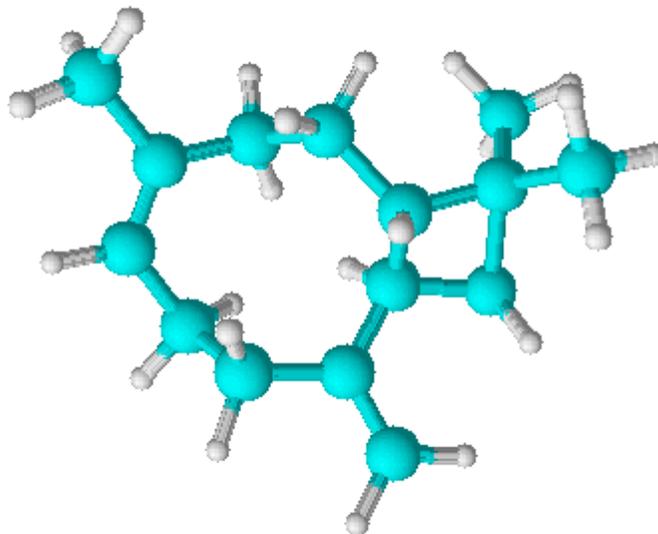


Fig1:Structure of Caryophyllene

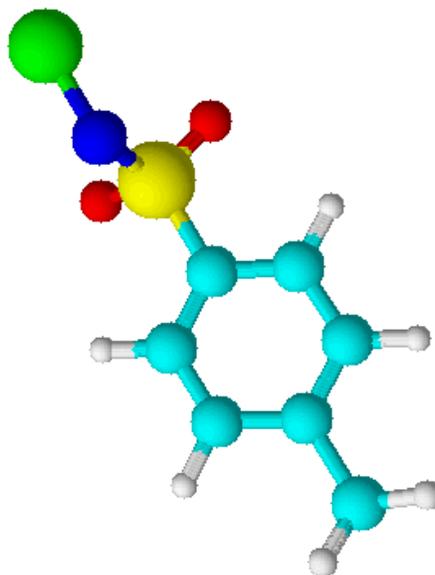


Fig 2: Structure of Chloramine T

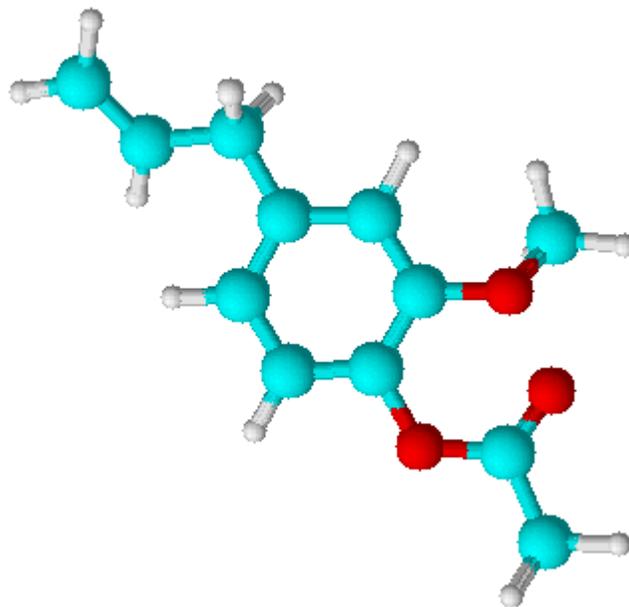


Fig 3: Structure of Eugenol acetate

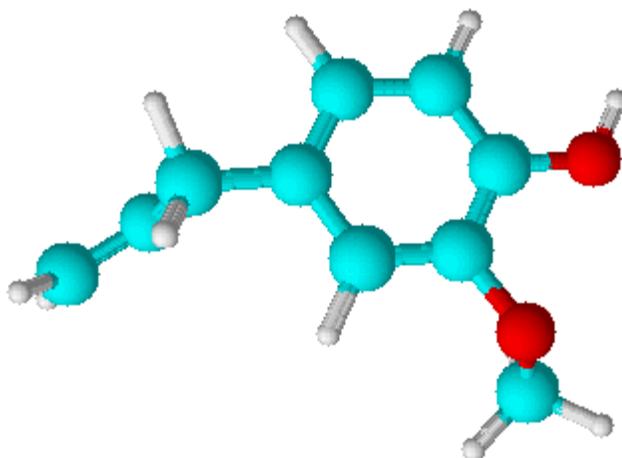


Fig4: Structure of Eugenol

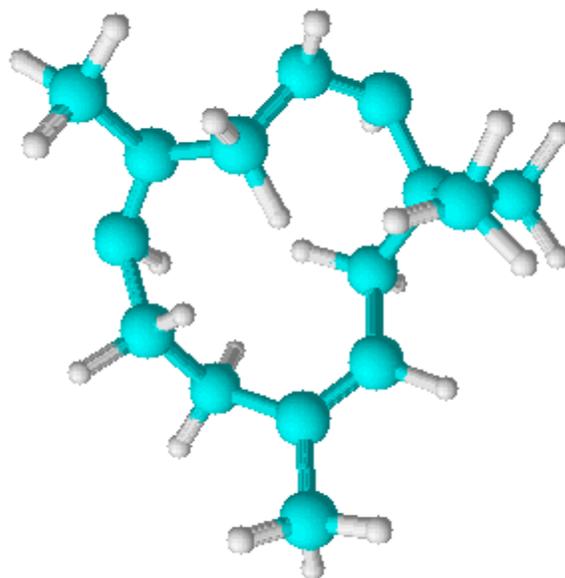


Fig 5: Structure of Humulene

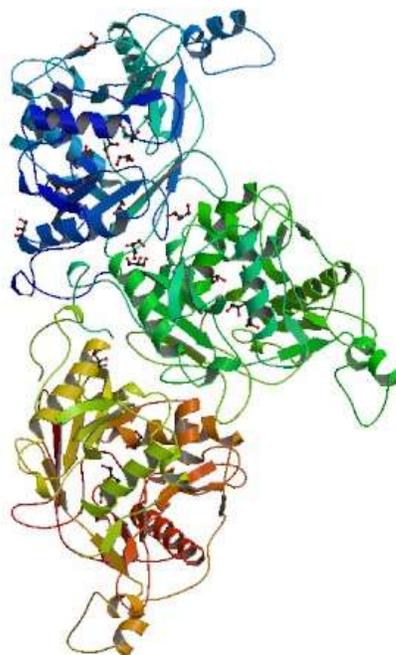


Fig 6: Crystal Structure of 1NMT

#### 4. Results and Discussion

##### Docking Result

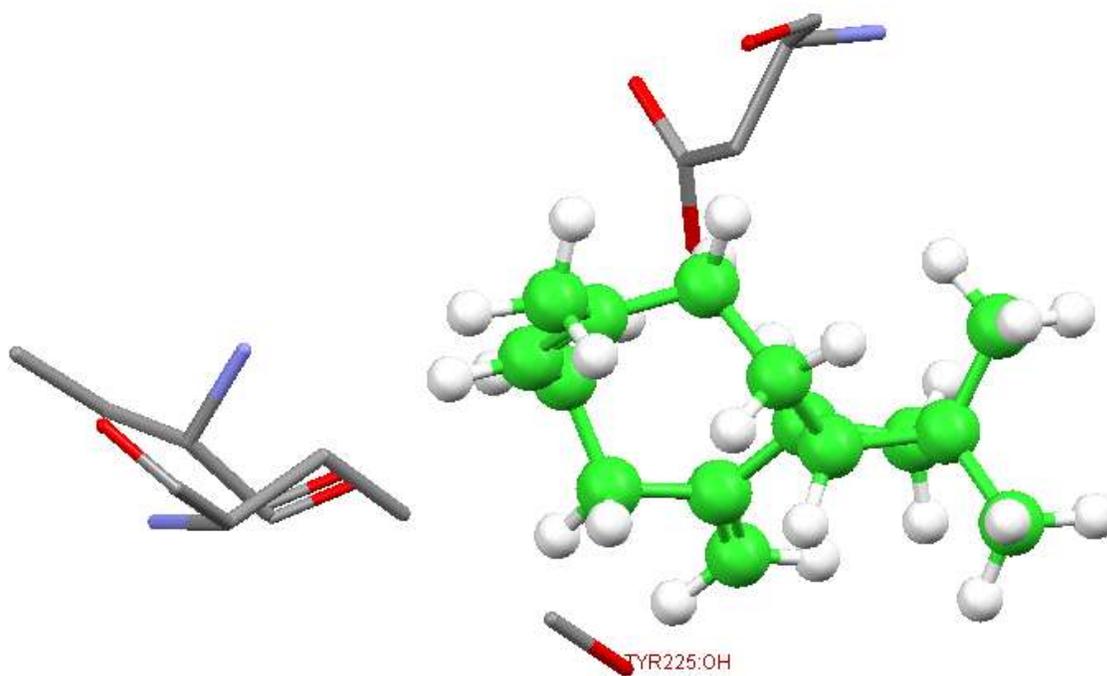


Fig7:1NMT in complex with caryophyllene

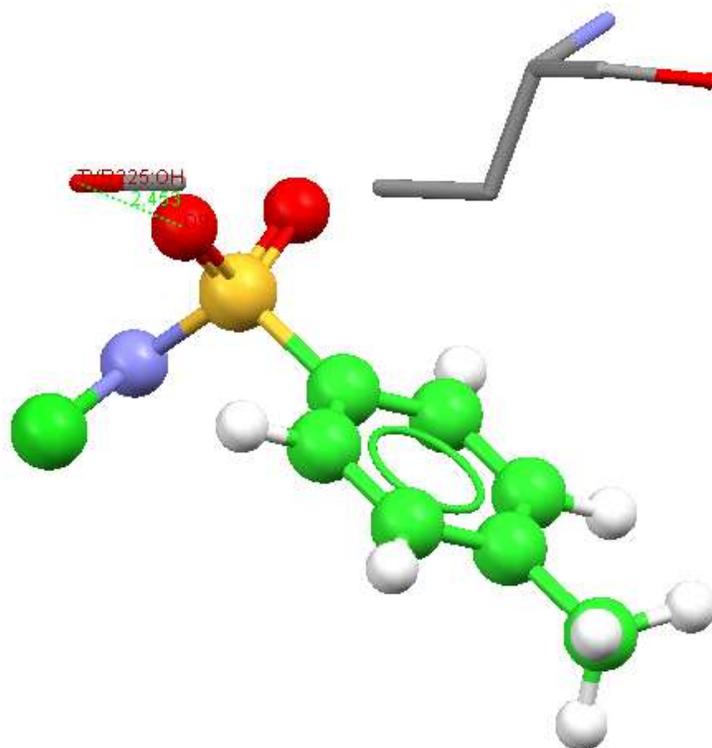


Fig8: 1NMT in complex with chloramine T

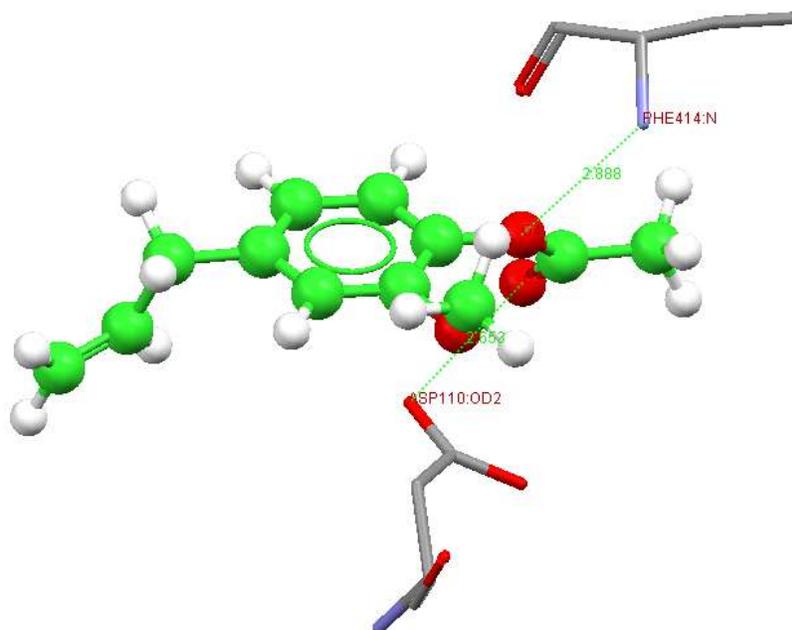


Fig9: 1NMT in complex with EUGENOL ACETATE

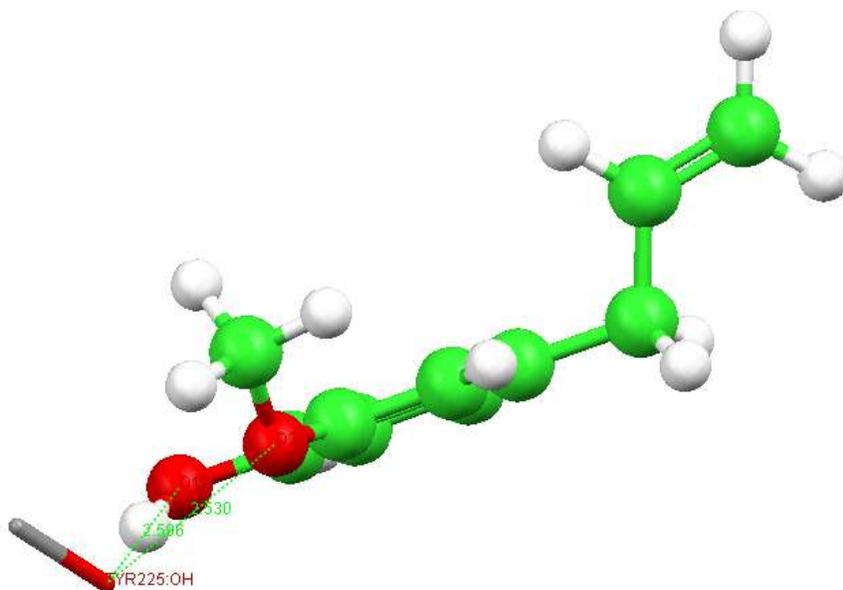


Fig10: 1NMT in complex with EUGENOL

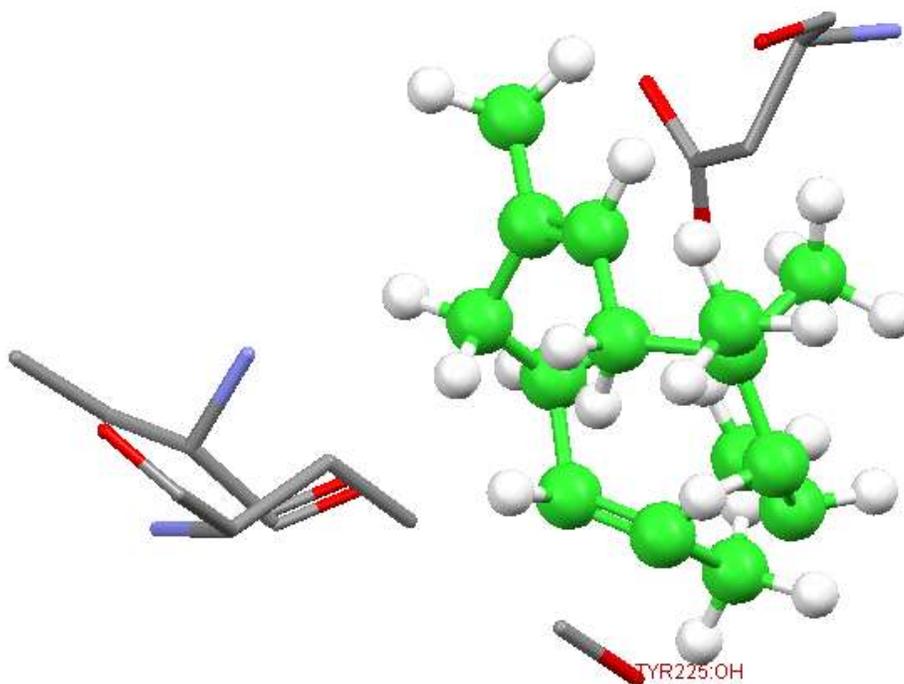


Fig11: 1NMT in complex with HUMULENE

Ligand Name	Atom in Ligand	Atom in Protein	H-Bond Distance	Score
caryophyllene	NO HBONDS			37.13
chloramine T (Standard)	O9	TYR225:OH	2.453	29.56
eugenol acetate	O4	PHE414:N	2.888	32.84
	O3	ASP110:OD2	2.653	
eugenol	O2	TYR225:OH	2.53	33.57
	O12	TYR225:OH	2.586	
humulene	NO HBONDS			19.89

Table1: Docking Scores of H-Bond Formation

## 5. Conclusion:

Here in this study we have tried to find the best compatible bio active compound of clove towards the target. Out of 5 Bioactive compounds from clove Eugenol acetate O4, O3 showed the highest docking score having h bond score to be 2.888(O4) , 2.653(O3)<sup>[13]</sup>. In most of the cases the docking the H bond value must be considered because the hydrogen bonds are stronger than van-der-walls bond and weaker than covalent bond as H bonds have the ability to create a bond<sup>[14,15]</sup> or break a bond easily in this study we are trying to read the compatibility between the bioactive compounds and the target compound in this case its Candida albicans biofilm. Further the the research can be extended to wet lab work for further details.

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