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# Molecular docking analysis of phytoconstituents of *Illicium verum* fruit against Caspase 3, MMP-9 and TNF-α

Hima Saila M[1]* & Santhrani Thakur[2]

[1]Department of Pharmacology; & [2]Department of Pharmacology, Institute of Pharmaceutical Technology, Sri Padmavathi Mahila Visva Vidyalayam, Tirupati-517 502, Andhra Pradesh, India

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Present study was designed to evaluate the anti-apoptotic activity and anti-inflammatory of phytocompounds of *Illicium verum* fruits. Bioactive compounds from the alcoholic, chloroform and ethylacteate fractions of *Illicium verum* were selected based on GC-MS analysis, which were *in silico* docked against Caspase 3, Matrix Metalloproteinase 9 and TNF-α. The structures of Caspase 3, Matrix Metalloproteinase 9 (MMP-9) and TNF-α enzymes were obtained from the protein data bank. Molecular docking was done by using Glide XP module of Schrodinger software and binding energies of ligands were also calculated. The phytocompound Strychane,1-acetyl-20α- hydroxy-16-methylene showed good docking score against Caspase 3 and TNF-α. The phytocompound Pyrrolidine, 1-(7-oxo-2,4,6 trimethylheptanoyl) showed good docking score against MMP-9. The results revealed that phytoconstituents obtained from *Illicium verum* showed good docking against Caspase-3, MMP-9 and TNF-α indicating their potential towards apoptosis and inflammation.

**Keywords**: Binding energy, Caspase 3, *Illicium verum*, MMP-9, Molecular docking, TNF-α

Apoptosis or Programmed Cell Death is an energy-dependent process by which undesirable cells undergone self-destruction when the genes of apoptosis are activated[1]. The two apoptotic signaling cascades are the extrinsic and intrinsic pathways, were eminent. The extrinsic pathway is activated by engaging of Fas plasma membrane death receptor to Fas ligand (Fas-L) and other similar receptors, such as TNFR 1. A death complex forms by binding Fas-L with Fas. This death complex recruits death domain-containing protein (FADD) and pro-caspase-8, aggregating to become the death-inducing signaling complex (DISC)[2]. The protein complex activates pro-caspase-8, which proceeds to activate pro-caspase-3, an eventual enzyme for the execution of apoptotic process. Apoptosis also triggers through intrinsic pathway but under the control of pro enzymes of mitochondria. When a cell is stimulated either intracellularly or extracellularly, the mitochondrial outer membrane become permeable to cytochrome C, which is then liberated into the cytosol. Then apoptosome formation takes place when the adaptor protein Apaf-1 associates with cytochrome C, which triggers caspase 9. Once activated, caspases 8, 9, and 10 activates caspases 3 and 7, the executioner caspases. Caspases 3 and 7 cleaves a pair of substrates, resulting in membrane blebbing, nuclear condensation, and genomic DNA fragmentation[3].

MMPs are classified as the matrixins, subfamily of zinc metalloprotease family. Matrix metalloproteinases also called as matrixins which are zinc-dependent endopeptidases and are membrane- bound that have the ability to degrade all the components of the extracellular matrix. MMP enzymes are tangled in normal, pathological, physiological and biological processes such as angiogenesis, normal tissue remodeling, embryogenesis, wound healing and plays a pivotal role in vascular remodeling. Divergent action of MMPs has been involved in numerous disease conditions. MMPs are considered as central participants in management of cell–cell and cell–ECM communications, and the explanation of their potential as medication focuses in illness or as significant features of the repair cycle will be needy upon cautious examination of their part in various cell areas and at various disease level[4].

The inflammatory reaction is an essential body protection defense mechanism in response to unfavorable inflammogens. This complicated reaction entails leukocytes cells which includes neutrophils, macrophages and lymphocytes, additionally referred

*Correspondence:
E-mail: himasaila.spsp@gmail.com

to as inflammatory cells[5]. In response to the inflammatory process, these cells release specialized materials which consists of vasoactive amines, peptides, proinflammatory cytokines, acute-phase proteins, eicosanoids, which mediate inflammation with the aid of preventing tissue harm and ultimately resulting in recuperation and recovery of tissue function[6]. The complete process of the inflammatory reaction ismediated through several key regulators involved within the selective expression of pro-inflammatory molecules. The inflammatory passage varies depends on the nature of stimulants, so are their target tissues. Activation of inflammatory process involves in releasing of mediators such as inflammatory cytokines like interleukin-1 (IL-1), tumor necrosis factor alpha (TNF-α), and interleukin-6 (IL-6) and chemokines. The length of inflammatory responses relying on the extent of injury caused by the infection. The significance of inflammatory conditions in modern generation of clinical technological knowhow cannot be overvalued due to their involvement in many of illnesses inclusive of weight problems, atherosclerosis, allergies, neurodegenerative diseases, cancer, inflammatory bowel disease, type 2 diabetes and rheumatoid arthritis[7].

*Illicium verum* belongs to the family *illiceae.* It possess antioxidant, antimicrobial, antifungal anti-inflammatory, anticancer, diuretic, antirheumatic, treatment of alzhemier's disease[8,9,10] and protection against neuronal cells (*in vitro*)[11].

The goal of the present study was designed to identify bioactive compounds from the alcoholic, ethylacetate and chloroform fractions of *Illicium verum* by gas chromatography and mass spectroscopy analysis followed by *in silico* docking analysis to validate the activity of the compounds against Caspase 3, Matrix metalloproteinase 9 and TNF-α enzymes. The compounds were identified based on NIST along with retention indices. Schrodinger software was used to study molecular docking studies.

## Materials and Methods

### Collection and identification of plant material

The fruits of *Illicium verum* were collected at Tirupati, Andhra Pradesh, India. Dried fruits were coarsely powdered and were extracted using maceration process; briefly first they were soaked in ethanol: water (7:3) for 3 days. The macerate filtrate was concentrated with rotary evaporator under reduced pressure at 40°C. The hydroalcoholic extract was subjected to partial fractionation successively with chloroform and ethylacetate. To this extract 250 mL of water was added and shaken vigorously and 100 mL of ethylacetate was added, the non polar constituents were separated. This procedure was repeated until the appearance of colorless layer. After separation of ethylcetate fraction, 100 mL of chloroform was added to the hydroalcoholic extract and this procedure was repeated till the chloroform layer became colorless. Both the fractions were collected and evaporated to get a concentrated residue. The remaining portion was considered as hydroalcoholic fraction.

GC MS analysis was performed by JOEL-GC MATE II. The equipment has a DB 35-MS capillary standard non polar column with dimensions of 30 mm × 0.25 mm ID × 0.25 µM. Helium gas was used as a carrier at rate of 1 mL/min. Injector was operated at 250º C and the oven temperature was programmed as 110°C hold for 3.50 min, up to 200°C at the rate of 10°C/min-no hold, upto 280°C at the rate of 5°C /min-12 min hold and total running time for GC is 40 min. The compounds were identified based on NSIT library as well as comparison of other retention indices.

### Molecular docking

#### *Methodology*

The software used for this research was Glide tool from Schrodinger molecular drug discovery suite.

### Docking analysis

The compounds identified in GC-MS were docked to the proteins Caspase 3, MMP9, TNF-α from Homo sapiens. The structures of Caspase 3 (PDB Id: 1pau), MMP9 (PDB Id: 2ow1) and TNF-α (PDB Id: 2AZ5) were obtained from PDB database.

### Identification of active site

#### *Preparation of proteins*

The digital structure of Caspase 3, MMP-9, TNF-α proteins were retrieved from the Protein databank website with PDB Ids: 1pau, 2ow1 and 2AZ5, respectively, and the structure was optimized by deleting unbound water molecules which were over 1 Å, hydrogen atoms were added to satisfy the valences, side chains were stabilized by adding missing amino acids and energy of the whole structure was minimized using OPLS-2005 force field using protein Preparation Wizard tool of Schrodinger Suite.

The active site (binding pocket) and functional residues of 1pau, 2ow1 and 2AZ5 were identified and characterized by site map module from Schrodinger software. Site map calculation began with an initial search step that identifies or characterized through the use of grid points. One or more regions on protein surfaces that may be suitable for binding of ligands to the receptor. Counter maps were then generated, hydrophobic, hydrophilic maps, hydrogen binding possibilities guide the protein ligand docking analysis.

**Molecular docking using glide**

Structurally optimized protein structure was used to identify protein-ligand interactions of the ligands using Glide Xp docking. Initially, a 3D grid was established to the binding pocket (active site) of the protein and ligands were docked into the active site of protein. Binding efficiency and binding interactions were calculated as Glide Score, a combination of hydrophobic, hydrophilic, metal binding groups, Vander Waals energy, freezing rotatable bonds and polar interactions with receptor.

**Post docking calculations**

Prime MM/GBSA (molecular mechanics based generalized Born/surface area) module of Schrodinger suite was used to calculate the binding energies of the docked complexes, which is a combination of OPLS molecular mechanics energies (EMM), an SGB solvation model for polar solvation (GSGB), and a non-polar solvation term (GNP) containing non-polar solvent accessible surface area and Vander Waals interactions. In this, docking results were rescored through an energy function with a well-defined description of binding contributions. The total free energy of binding is then expressed in the form of G bind energy as calculated using below mentioned equation:

$\Delta G_{bind}$= Gcomplex – (Gprotein + Gligand)

where, $\Delta G_{bind}$ is ligand binding energy.

## Results and Discussion

In this study we evaluated the interaction of the ligands with one of the markers of inflammation and apoptosis proteins. As shown in (Fig. 1A), the chromatogram of GC MS analysis revealed the presence of six phytocompounds from hydroalcoholic fraction, six phytocompounds from ethylacetate fraction as shown in (Fig. 1B) and eleven phytocompounds from chloroform fraction of *Illicium verum* fruits as shown in (Fig. 1C).The compounds were identified based on retention time and classified in parallel to NSIT library (Table 1A-C).

Molecular docking of ligands against the active site of the enzymes determines the interactions between proteins and ligands. Docking was performed for all twenty three compounds. The target proteins selected were the biomarkers of apoptosis and inflammation. Caspase-3 is the cysteine protease family protein and it is a executioner caspase. Caspase-3, a regulatory caspase, which controls caspase activated DNAse (CAD) activity to complete the process of apoptosis[12]. CAD cleaves DNA at internucleosomal linker sites between nucleosomes, degradation of nuclear DNA into nucleosomal units is one of the hall marks of apoptotic cell[13]. Based on the virtual screening score of the phytocompounds as tabulated in (Table 2), the highest docking score was showed by Strychane, 1-acetyl-20α- hydroxy-16-methylene with −3.66 score for apoptotic marker that is caspase 3 with PDB Id 1Pauas showed in (Fig. 2).

Matrix metalloproteinase-9 (MMP9) has been involved in many diseases like cardiovascular disorders, bipolar illness, schizophrenia, multiple sclerosis and cancer[14]. MMP-9 is one of the important biomarkers, which could be used in combination with other biomarkers to improve diagnosis or accelerate drug discovery[15,16]. In this analysis high score for MMP-9 was showed by the ligand Pyrrolidine, 1-7-oxo-2,4,6 trimethylheptanoyl having −6.506 as shown in (Fig. 3) and the docking scores were tabulated in (Table 3).

Tumor Necrosis Factor alpha, provocative cytokine released by macrophages or monocytes during many inflammatory conditions and is liable for prompting apoptosis and necrosis. TNFα plays a key role in triggering the cytokine cascade in various inflammatory diseases. This is considered as a “master-regulator” of inflammatory cytokine production and it has been suggested as a target for a numerous disorders[17,18]. TNF-α crosses BBB by a receptor-mediated transportation that is upregulated during ischaemic injury[19]. TNF-α activated macrophages are the main components involved in number of autoimmune diseases. As shown in (Fig. 4 and Table 4) the maximum docking score was observed in the compound Strychane,1-acetyl-20α- hydroxy-16-methylene with −5.054 towards TNFα having PDB Id:2AZ5.

The docking studies show the importance of molecular docking approaches in the development and

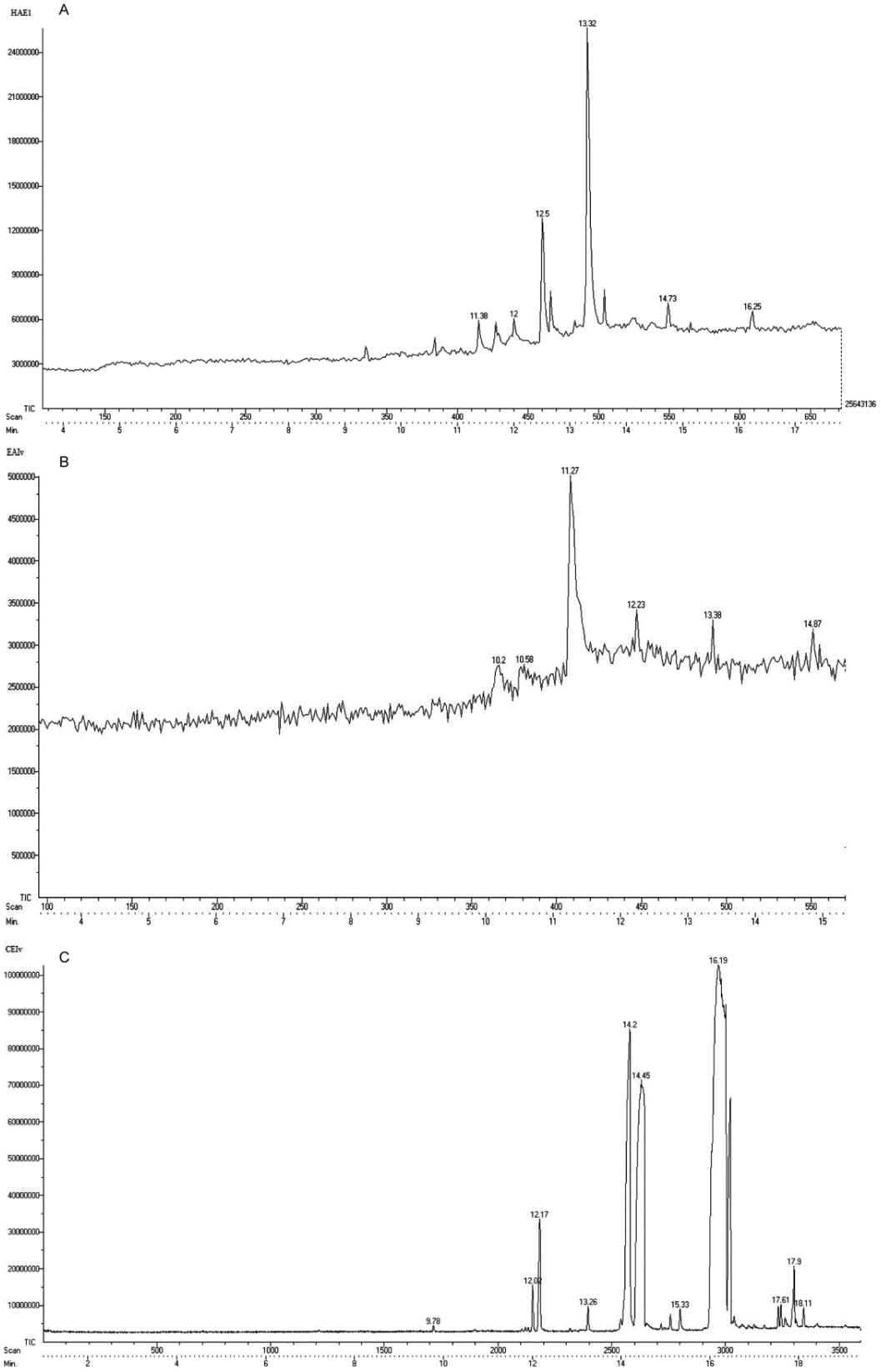


Fig. 1 — GC MS chromatogram of (A) hydroalcoholic fraction; (B) ethylacetate fraction; and (C) chloroform fraction of *Illicium verum*

Table 1 — The phytocompounds present in *Illicium verum* fruit obtained from GC MS analysis

| S. No | Retention time | Compound |
|---|---|---|
| Hydroalcoholic extract | | |
| 1 | 11.38 | Hexadecanoic acid, 14 methyl methyl ester |
| 2 | 12 | Dasycarpidan-1-methanol acetate |
| 3 | 12.5 | 8-11-octadecadienoic acid |
| 4 | 13.32 | 10- Heptadecen-8- enoic acid |
| 5 | 14.73 | Strychane, 1- acetyl-20α- hydroxyl-16-methylene |
| 6 | 16.25 | 4H-cyclopropa(5,6)benz (1,2:7,8) azuleno (5,6b)) Oxiren-4-one |
| Chloroform fraction | | |
| 7 | 9.78 | Trans anethole |
| 8 | 10.8 | 2,2,5- Trimethyl-cyclohexane 1,4 diol |
| 9 | 12.02 | 1,E-8,Z-10- Pentadecatriene |
| 10 | 12.17 | Pyrrolidine, 1-(7-oxo-2,4,6 trimethyl heptanoyl) |
| 11 | 13.26 | 1,5,9,9-Tetramethyl-Spiro (3,5)nonan-5-ol |
| 12 | 14.2 | Cyclohexanone 2,3,3-trimethyl 2-(3- methylene but-1-en-1-yl) |
| 13 | 14.45 | 4 methyl 5,6 tetramethylene- 3-4- dihydro-1,3-oxazine-2-thione |
| 14 | 15.33 | 1-octene, 2-methoxy |
| 15 | 17.61 | 1-hexen-3-ol,5-nitro-1-phenyl |
| 16 | 17.9 | Androstan-6-one,3 (acetyloxy)5-hydroxy, (3a,5a) |
| 17 | 18.11 | Cyclopentadecanone, 2-methyl |
| Ethylacetate fraction | | |
| 18 | 10.2 | Methyl Z-11- tetradeconate |
| 19 | 10.58 | 1-(2- acetoxyethyl)-3,6- diazahomoad- amantan-9-one oxime |
| 20 | 11.27 | p-anasaldehyde |
| 21 | 12.23 | 1-Benzazirene-1-carboxylic acid,2,2,5 a |
| 22 | 13.38 | 4-(5-pentyl-3a,4,5,7a-tetrahydro-4 indanyl) butonic acid, methyl ester (stereoisomer 1) |
| 23 | 14.87 | 12-methyl-e,e-2,13-octadcadien-1-ol |

Table 2 — Molecular docking analysis of bioactive compounds present in fruits of *Illicium verum* against Caspase 3 (PDB Id:1pau) — (*Contd*.)

| Name of the compound | Dock score | No of H-bonds | Interacting amino acids | H-bond distance (A$^o$) | Emodel energy | Binding energy Kcal/mole |
|---|---|---|---|---|---|---|
| Strychane,1-acetyl-20α- hydroxy-16-methylene | −3.66 | 1 | ARG 341 | 1.83 | −26.746 | −41.626 |
| Dasycarpidan-1-methanol acetate | −3.602 | 1 | CYS 285 | 1.91 | −41.967 | −51.902 |
| 1,5,9,9-tetramethyl-spirro(3.5)nonan-5-ol | −3.572 | 1 | SER 339 | 2.02 | −21.531 | −36.256 |
| 2,2,5 –trimethyl-cyclohexane 1,4diol | −3.507 | 1 | SER 339 | 1.66 | −19.981 | −28.051 |
| Pyrrolidine, 1-(7-oxo-2,4,6 trimethylheptanoyl | −3.37 | 1 | ARG 341 | 1.73 | −31.169 | −50.323 |
| Hexadecanoic acid,14 methyl methyl ester | −3.225 | 1 | PHE381B | 1.98 | −34.351 | −62.241 |
| 10-Heptadecen-8-enoic acid | −3.102 | 3 | ARG 179 GLN 283 | 1.89, 2.11 1.81 | −26.663 | −4.87 |
| 1-hexen-3-ol,5-nitro-1-phenyl- | −3.097 | 1 | ARG 341 | 1.81 | −32.301 | −36.819 |
| 4 methyl 5,6 tetramethylene- 3-4- dihydro-1,3-oxazine-2-thione | −3.07 | 1 | HIS237 | 2.02 | −25.907 | −32.041 |
| 8,11-octadecadienoic acid | −3.023 | 1 | PHE381B | 2.05 | −35.55 | −49.288 |
| P anisaldehyde | −2.904 | 2 | ARG 341 CYS 285 | 2.23, 2.06 | −17.759 | −18.047 |
| Trans anethole | −2.751 | 2 | ARG 341 | 2.04, 2.20 | −14.298 | −22.792 |
| Methyl Z-11-tetradecenoate | −2.413 | 2 | TRP 348 ASN 342 | 1.81 2.30 | −33.455 | −58.701 |
| 1-octene, 2-methoxy | −2.328 | 0 | - | - | −19.213 | −36.676 |
| Cyclopentadecanone,2-methyl | −1.136 | 1 | CYS 285 | 2.13 | −15.138 | −30.888 |
| 1-(2- acetoxyethyl)-3,6- diazahomoad-amantan-9-one oxime | −1.123 | 1 | ARG186 | 2.06 | −18.96 | −32.98 |
| 1,E-8,Z-10- Pentadecatriene | −1.085 | 1 | GLN 173 | 1.35 | −19.64 | −24.87 |

(*Contd*.)

Table 2 — Molecular docking analysis of bioactive compounds present in fruits of *Illicium verum* against Caspase 3 (PDB Id:1pau) (*Contd*.)

| Name of the compound | Dock score | No of H-bonds | Interacting amino acids | H-bond distance (Aº) | Emodel energy | Binding energy Kcal/mole |
|---|---|---|---|---|---|---|
| 1-Benzazirene-1-carboxylic acid, 2,2,5 a | −1.183 | 0 | -- | --- | −20.21 | −33.65 |
| 4-(5-pentyl-3a,4,5,7a-tetrahydro-4 indanyl) butonic acid, methyl ester | −1.09 | 1 | PHE 165 | 2.18 | −19.34 | −39.65 |
| Cyclohexanone 2,3,3-trimethyl 2-(3- methylene but-1-en-1-yl) | −0.98 | 1 | SER 234 | 1.87 | −28.43 | −19.32 |
| 4H-cyclopropa(5,6)benz (1,2:7,8) azuleno (5,6b)) Oxiren-4-one | −0.98 | 0 | -- | -- | −26.43 | −16.34 |
| Androstan-6-one,3 (acetyloxy)5-hydroxy, (3a,5a) | −0.78 | 1 | CYS 256 | 1.81 | −23.65 | −29.31 |
| 12-methyl-e,e-2,13-octadcadien-1-ol | −0.69 | 1 | GLN 195 | 1.96 | −32.87 | −27.43 |

Table 3 — Molecular docking analysis of bioactive compounds present in fruits of *Illicium verum* against the enzyme MMP-9 (PDB Id:2ow1)

| Name | Dock score | No of H-bonds | Interacting amino acids | H-bond distance (A) | Emodel energy | Binding energyKcol/mole |
|---|---|---|---|---|---|---|
| Pyrrolidine, 1-(7-oxo-2,4,6 trimethylheptanoyl | −6.506 | 1 | GLN 402 | 1.95 | −39.63 | −55.03 |
| 1-hexen-3-ol,5-nitro-1-phenyl- | −5.831 | 2 | GLN 402 PRO 421 | 1.93 1.96 | −48.096 | −60.737 |
| 10-Heptadecen-8-enoic acid | −5.637 | 1 | ALA 191 | 1.91 | −51.433 | −82.638 |
| Dasycarpidan-1-methanol acetate | −5.109 | 1 | HIS 401 | 2.23 | −36.694 | −48.582 |
| 8,11- octadecadienoic acid | −5.079 | 2 | ARG 424 LEU 418 | 2.46 2.03 | −56.2777 | −50.742 |
| 4 methyl 5,6 tetramethylene-3,4-dihydro-1,3-oxazin-2-thione | −4.618 | 0 | - | - | −38.72 | −42.239 |
| P anisaldehyde | −4.588 | 2 | ALA 189 LEU 188 | 2.12 2.11 | −30.337 | −34.03 |
| 2,2,5 –trimethyl-cyclohexane 1,4diol | −4.5 | 3 | ALA 189 LEU 188 HIS 411 | 2.34 2.09 2.22 | −29.886 | −42.983 |
| Hexadecanoic acid,14 methyl methyl ester | −4.418 | 1 | ALA 191 | 1.89 | −46.57 | −76.64 |
| Cyclopentadecanone,2-methyl | −4.312 | 1 | GLN 402 | 2.01 | −28.683 | −36.791 |
| Trans anethole | −4.128 | 0 | - | - | −32.592 | −45.208 |
| Strychane,1-acetyl-20$^{\alpha}$- 515ydroxyl-16-methylene | −3.943 | 1 | ALA 191 | 2.36 | −31.78 | −44.052 |
| 1,5,9,9-tetramethyl-spirro(3.5)nonan-5-ol | −3.742 | 1 | ALA 189 | 1.77 | −22.95 | −38.3 |
| Methyl Z-11-tetradecenoate | −3.594 | 1 | ALA 191 | 1.94 | −41.412 | −60.229 |
| 1-octene,2-methoxy | −2.914 | 1 | GLN 402 | 2.10 | −24.368 | −50.044 |
| 1-(2- acetoxyethyl)-3,6- diazahomoad-amantan-9-one oxime | −2.834 | 1 | ALA 231 | 1.23 | −23.23 | −64.23 |
| Cyclohexanone2,3,3trimethyl2-(3- methylene but-1-en-1-yl) | −2.49 | 1 | PRO154 | 1.63 | −32.56 | −42.45 |
| 12-methyl-e,e-2,13-octadcadien-1-ol | −2.45 | 1 | LEU169 | 1.74 | −43.92 | −54.21 |
| 1,E-8,Z-10- Pentadecatriene | −2.34 | 1 | GLN 219 | 2.18 | −27.76 | −34.53 |
| 4-(5-pentyl-3a,4,5,7a tetrahydro-4indanyl) butonic acid, methyl ester | −2.41 | 0 | ALA 212 | 1.54 | −28.50 | −35.23 |
| Androstan-6-one,3 (acetyloxy)5-hydroxy, (3a,5a) | −2.12 | 1 | HIS234 | 2.13 | −39.21 | −36.42 |
| 1-Benzazirene-1-carboxylic acid,2,2,5 a | −1.87 | 1 | LEU 176 | 1.76 | −25.43 | −41.34 |
| 4H-cyclopropa(5,6)benz (1,2:7,8) azuleno (5,6b) Oxiren-4-one | −1.45 | 1 | GLN 136 | 2.08 | −36.73 | −45.78 |

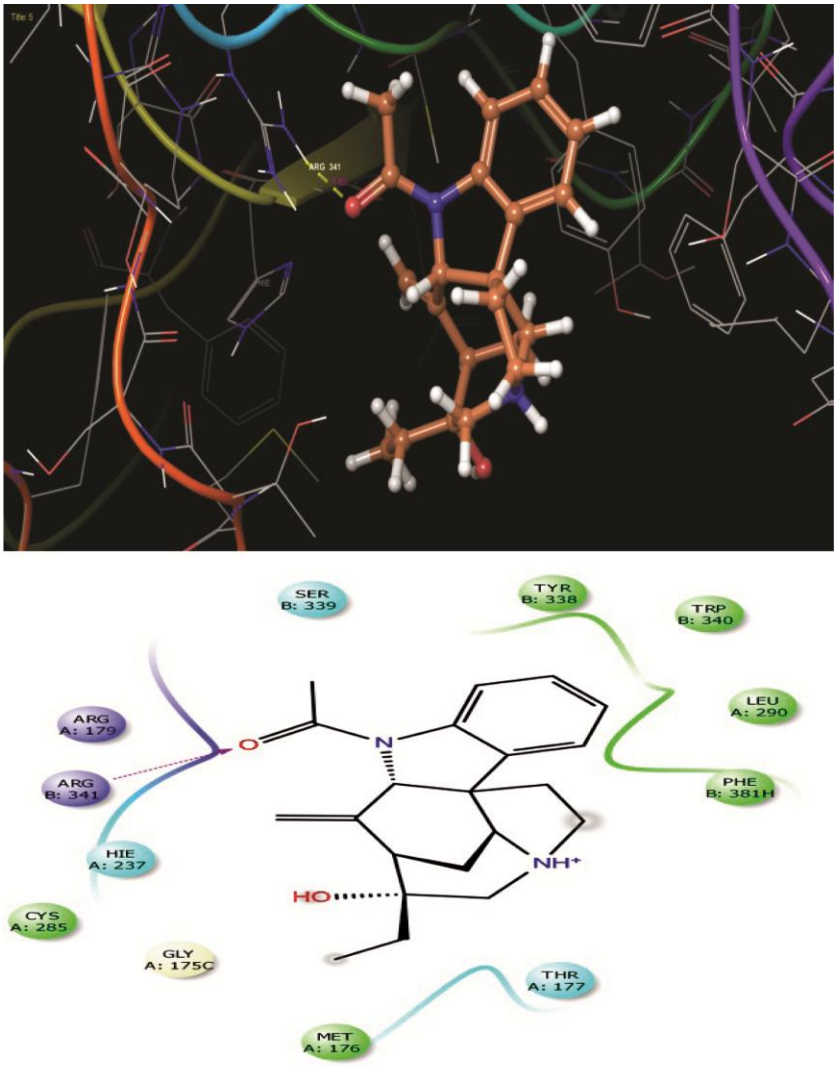


Fig. 2 — 3-Dimensional and 2-Dimensional interaction of Strychane, 1-acetyl-20α- hydroxy-16-methylene against caspase3 (PDB Id:1pau)

Table 4 — Molecular docking analysis of bioactive compounds present in fruits of *Illicium verum* against the enzyme Tumor necrosis factor α (PDB Id:2AZ5) (*Contd*.)

| Name of the compound | Dock score | No of H-bonds | Interacting amino acids | H-bond distance (A) | Emodel energy | Binding energy (Kcal/mole) |
|---|---|---|---|---|---|---|
| *Strychane,1-acetyl-20α- hydroxy-16-methylene* | −5.054 | 1 | TYR 151 | 2.26 | −39.524 | −50.13 |
| 1-hexen-3-ol,5-nitro-1-phenyl- | −5.046 | 1 | TYR 151 | 2.10 | −29.195 | −43.163 |
| Pyrrolidine, 1-(7-oxo-2,4,6 trimethylheptanoyl | −4.733 | 0 | - | - | −33.814 | −54.224 |
| Hexadecanoic acid,14 methyl methyl ester | −4.3 | 1 | TYR 119 | 2.10 | −28.402 | −63.469 |
| 2,2,5–trimethyl-cyclohexane 1,4diol | −4.27 | 1 | TYR 151 | 1.87 | −25.145 | −32.645 |
| Cyclopentadecanone,2-methyl | −4.178 | 0 | - | - | −31.45 | −48.03 |
| 4 methyl 5,6 tetramethylene-3,4-dihydro-1,3-oxazin-2-thione | −4.012 | 0 | - | - | −29.837 | −41.68 |
| 1,5,9,9-tetramethyl-spirro(3.5)nonan-5-ol | −3.962 | 1 | LEU 120 | 1.96 | −22.108 | −35.274 |
| Trans anethole | −3.674 | 0 | - | - | −22.782 | −31.73 |
| P anisaldehyde | −3.383 | 0 | - | - | −21.722 | −23.697 |
| Dasycarpidan-1-methanol acetate | −4.986 | 0 | - | - | −15.707 | −51.468 |
| Methyl Z-11-tetradecenoate | −2.56 | 0 | - | - | −28.184 | −48.291 |
| 1-octene,2-methoxy | −2.456 | 0 | - | - | −16.931 | −42.766 |

(*Contd*.)

Table 4 — Molecular docking analysis of bioactive compounds present in fruits of *Illicium verum* against the enzyme Tumor necrosis factor α (PDB Id:2AZ5) (*Contd*.)

| Name of the compound | Dock score | No of H-bonds | Interacting amino acids | H-bond distance (A) | Emodel energy | Binding energy (Kcal/mole) |
|---|---|---|---|---|---|---|
| 10-Heptadecen-8-enoic acid | −4.479 | 1 | TYR 151 | 1.84 | −35.153 | −65.942 |
| 8,11-octadecadienoic acid | −4.323 | 1 | TYR 151 | 1.80 | −38.498 | −63.345 |
| 1-(2- acetoxyethyl)-3,6- diazahomoad- amantan-9-one oxime | −3.92 | 1 | TYR274 | 1.91 | −25.67 | −51.50 |
| 1-Benzazirene-1-carboxylic acid,2,2,5 a | −3.63 | 0 | - | - | −13.24 | −29.45 |
| 1,E-8,Z-10- Pentadecatriene | −3.12 | 1 | LEU 132 | 2.34 | −27.43 | −41.34 |
| 4-(5-pentyl-3a,4,5,7a-tetrahydro-4 indanyl) butonic acid, methyl ester | −3.09 | 1 | TYR147 | 2.16 | −21.56 | −34.87 |
| Cyclohexanone 2,3,3-trimethyl 2-(3- methylene but-1-en-1-yl) | −2.96 | 0 | - | - | −19.43 | −46.21 |
| 12-methyl-e,e-2,13-octadcadien-1-ol | −2.62 | 1 | TYR168 | 1.98 | −19.34 | −42.38 |
| 4H-cyclopropa(5,6)benz (1,2:7,8) azule34no (5,6b)) Oxiren-4-one | −1.98 | 1 | ALA213 | 1.87 | −34.78 | −51.93 |
| Androstan-6-one,3 (acetyloxy)5-hydroxy, (3a,5a) | −0.89 | 1 | LEU 122 | 1.13 | −18.34 | −38.12 |

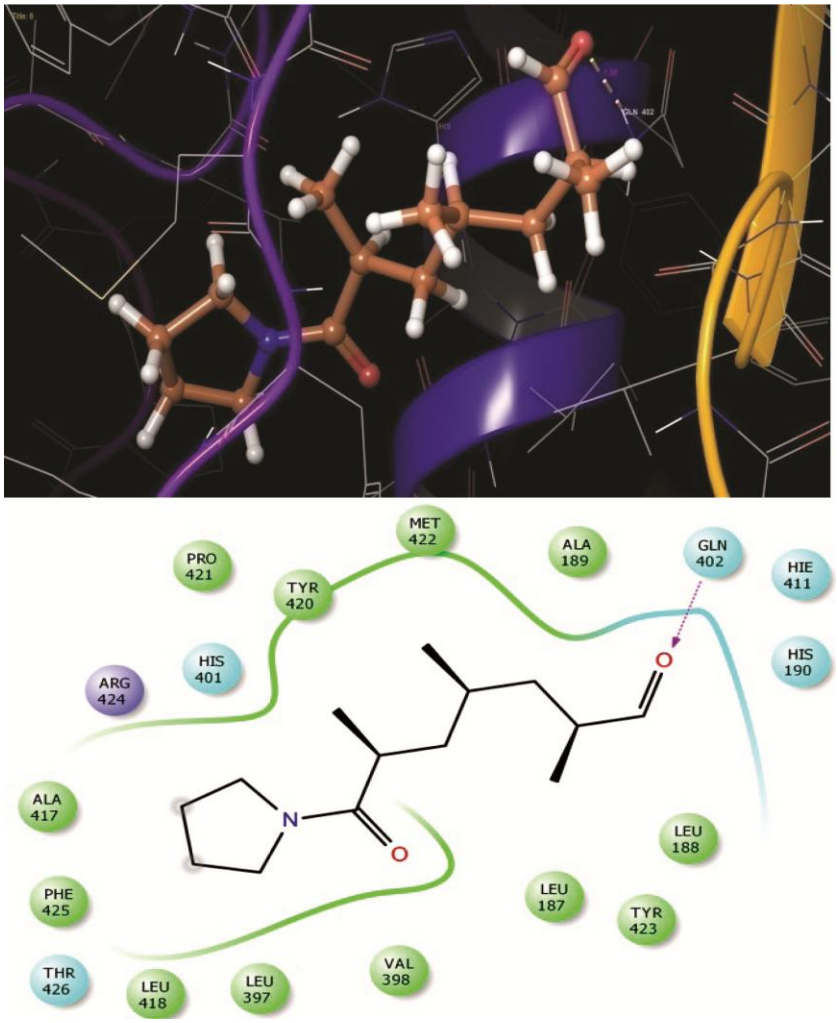


Fig. 3 — 3-Dimensional and 2-Dimensional interaction of Pyrrolidine, 1-(7-oxo-2,4,6 trimethyl heptanoyl against MMP-9 (PDB Id:2ow1)

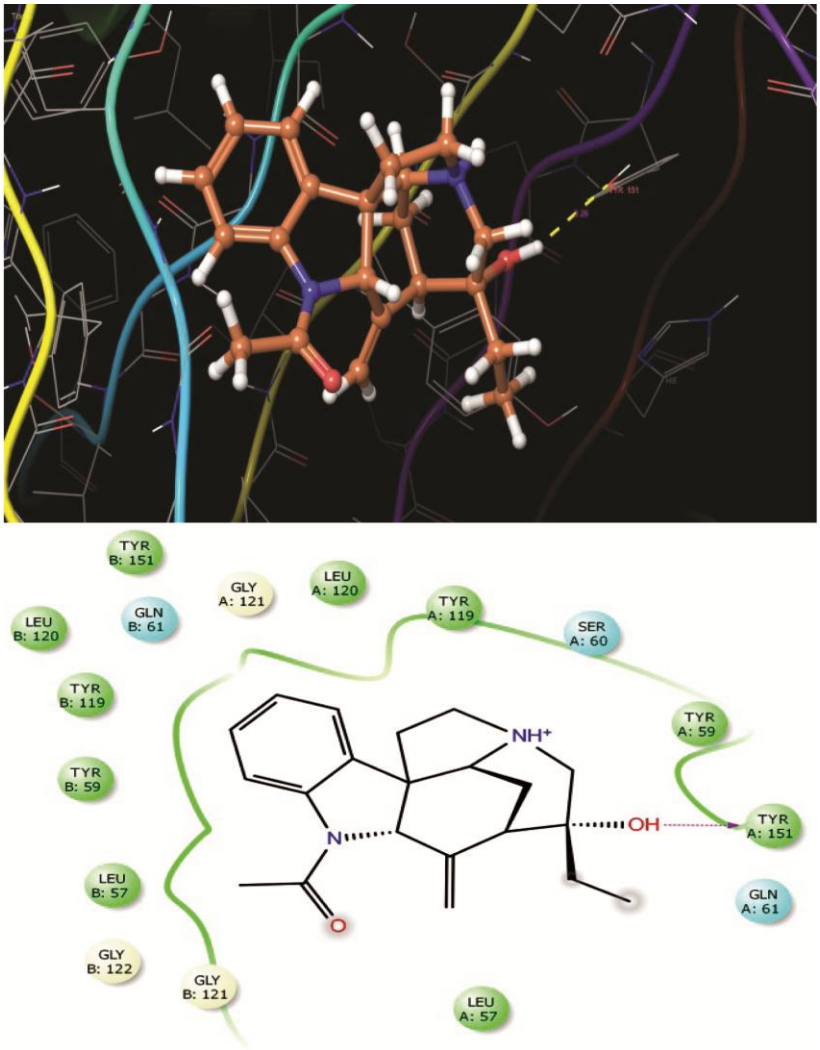


Fig. 4 — 3-Dimensional and 2-Dimensional interaction of Strychane, 1-acetyl-20α- hydroxy-16 methylene against TNF-α (PDB Id:2AZ5)

design development of new compounds with biological activity. This study provides the significance of structure-based drug coming up with strategy towards the development of novel medicine while not victimization of animals.

## Conclusion

Results revealed that phytoconstituents obtained from *Illicium verum* showed good docking against Caspase-3, MMP-9 and TNF-α indicating their potential against apoptosis and inflammation. As apoptosis and inflammation are pathological factors for many diseases, screening of these compounds in animal models may provide further insights into their usefulness to develop novel therapeutic agents.

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## Conflict of Interest

All authors declare no conflict of interest.

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