

**MOLECULAR DOCKING STUDIES OF SIDDHA MEDICINE INJI CHOORANAM II ON
ANTI HYPERLIPIDEMIC ACTIVITY**

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ABSTRACT

Hyperlipidemia is a condition characterized by increased levels of lipids such as cholesterol and triglycerides in the blood. Hyperlipidemia is a medical disorder characterized by an increase in one or more plasma lipids, plasma lipoproteins and low density-lipoprotein, and decrease in high density-lipoproteins. Several medicinal herbs have been shown in studies to lower blood cholesterol levels by decreasing the action of 3-hydroxy -3-methylglutaryl co enzyme a reductase (HMG-CoA). Molecular docking has become increasingly important as a method for drug discovery. The aim of the study is to evaluate natural products against hyperlipidemia using molecular docking. The increase likely due to a combination of factor, including unhealthy dietary habits, physical inactivity and obesity. Binding of phytocomponents with the core amino acids (Ser 684, Asp690, Lys691, Lys 692) of the target by forming hydrogen bond will hinder the function of the enzyme HMG CoA reductase with PDB-1HWK. These amino acid residues are functionally responsible for HMG CoA reductase enzyme activity in cholesterol biosynthesis. The phytocomponents which inhibit the target enzyme HMG CoA reductase by occupies these active aminoacid could be able to hinder the function of rate limiting enzyme involved in cholesterol biosynthesis.

KEYWORDS: Hyperlipidemia, Molecular Docking, Siddha Herbal Medicine, Inji Chooranam II.

INTRODUCTION

Hyperlipidemia, also is known as dyslipidemia or high cholesterol, means you have too many lipids (fats) in our blood. Liver create cholesterol to help you digest food and make things like hormones. But also eat cholesterol in food from the meat and dairy aisles.

Toomuch cholesterol (200mg/dl to 239mg/dl is borderline high and 240mg/dl is high) isn't healthy because it can create roadblocks in your artery highway where blood travels around to your body. This damage your organs that don't receive enough blood from artery.

Bad cholesterol (LDL) is most dangerous type because it cause hardened cholesterol deposites (plaque) to collect inside of blood vessels. This makes it harder for your blood to get through, which puts to risk of obesity and heart attack.

LOW – DENSITY LIPOPROTEIN(LDL)

LDL is known as bad cholesterol because it can clog the arteries like a large truck that broke down and is blocking a traffic lane.

VERY LOW DNSITY LIPOPROTEIN(VLDL)

VLDL is also called bad because it carries triglycerides that add to artery plaque. This is another type of traffic blocker.

HIGH DENSITY LIPOPROTEIN(HDL)

HDL is known as good cholesterol because it brings cholesterol to liver, which gets rid of it. In this case, its clearing the way for your blood to get through your blood vessels.

In siddha medicine Inji Chooranam II contains 18 herbal plant and it have 18 phytochemicals such as Gingerenone-A 6 Gingerol, Piperic acid, Piperin , sesamin, Nerolidol, Elemicin Gradisin, Chlorogenic acid,

anisaldehyde, Diosgenin, β -sitosterol, Limonene, β -vetivenene, Kaempferol, Myricetin, Coumaric acid, Vitexin. Thereby phytochemicals which inhibit the target enzyme HMG CoA reductase may occupy these

active amino acid could be able to block the HMG CoA enzymatic activity thereby limit the cholesterol synthesis and subsequent helps in control the hyperlipidemia.

SUMMARY OF THE DOCKING STUDY REPORT ON ANTIHYPERLIPIDEMIC ACTIVITY ON INJI CHOORANAM II

Project Id: NRS/AS/1475/02/2025

Name of the Formulation: INJI CHOORANAM II

List of Phytochemicals Selected for docking

| Herbs | Phytochemicals | References |
|--------------------------|---------------------------|---|
| Zingiber officinale | Gingerone-A 6 Gingerol | Sahdeo Prasad. Ginger and Its Constituents: Role in Prevention and Treatment of Gastrointestinal Cancer. <i>Gastroenterology Research and Practice</i> . 2015;1-11 |
| Piper nigrum | Piperic acid | Bahare Salehi. Piper Species: A Comprehensive Review on Their Phytochemistry, Biological Activities and Applications. <i>Molecules</i> . 2019 Apr; 24(7): 1364. |
| Piper longum | Piperine Sesamin | Anshuly Tiwari. Piperine: A comprehensive review of methods of isolation, purification, and biological properties. <i>Medicine in Drug Discovery</i> .2020;7: 100027 |
| Elettaria cardamomum | Nerolidol | Ashokkumar K, Murugan M, Dhanya MK, Raj S, Kamaraj D. Phytochemical variations among four distinct varieties of Indian cardamom <i>Elettaria cardamomum</i> (L.) Maton. <i>Nat Prod Res</i> . 2020 Jul;34(13):1919-1922. doi: 10.1080/14786419.2018.1561687. |
| Myristica fragrans | Elemicin Grandisin | Francis SK, James B, Varughese S, Nair MS. Phytochemical investigation on <i>Myristica fragrans</i> stem bark. <i>Nat Prod Res</i> . 2019;33(8):1204-1208. |
| Nardostachys grandiflora | Chlorogenic acid | Nguyen V, Taine EG, Meng D, Cui T, Tan W. Chlorogenic Acid: A Systematic Review on the Biological Functions, Mechanistic Actions, and Therapeutic Potentials. <i>Nutrients</i> . 2024 Mar 23;16(7):924. doi: 10.3390/nu16070924. PMID: 38612964; PMCID: PMC11013850. |
| Pimpinella anisum | Anisaldehyde | Shojaii A, Abdollahi Fard M. Review of Pharmacological Properties and Chemical Constituents of <i>Pimpinella anisum</i> . <i>ISRN Pharm</i> . 2012;2012:510795. doi:10.5402/2012/510795 |
| Costus speciosus | Diosgenin | Selim, S., & Al Jaouni, S. (2015). Anticancer and apoptotic effects on cell proliferation of diosgenin isolated from <i>Costus speciosus</i> (Koen.) Sm. <i>BMC complementary and alternative medicine</i> , 15, 301. https://doi.org/10.1186/s12906-015-0836-8 |
| Mesua nagassarium | β -sitosterol | Hegde S, Saini A, Hegde HV, Kholkute SD, Roy S. Molecular identification of <i>Saraca asoca</i> from its substituents and adulterants. <i>Biotech</i> . 2018 Mar;8(3):161. |
| Cinnamomum tamala | Limonene | Showkat R. Mir. Chemical composition of essential oil of <i>Cinnamomum tamala</i> Nees et Eberm. <i>Leaves. Flavour and Fragrance Journal</i> .2004;19(2):112 – 114 |
| Vetiveria Zizanioides | β -vetivenene | David A, Wang F, Sun X, Li H, Lin J, Li P, Deng G. Chemical Composition, Antioxidant, and Antimicrobial Activities of <i>Vetiveria zizanioides</i> (L.) Nash Essential Oil Extracted by Carbon Dioxide Expanded Ethanol. <i>Molecules</i> . 2019;24(10):1897 |
| Syzygium aromaticum | Kaempferol | Batiha, G. E., Alkazmi, L. M., Wasef, L. G., Beshbishy, A. M., Nadwa, E. H., & Rashwan, E. K. (2020). <i>Syzygium aromaticum</i> L. (Myrtaceae): Traditional Uses, Bioactive Chemical Constituents, Pharmacological and Toxicological Activities. <i>Biomolecules</i> , 10(2), 202. https://doi.org/10.3390/biom10020202 |
| Abies spectabilis | Myricetin | Vellingiri Vadivel. Chemical Fingerprints of an Indian Traditional Herbal Drug <i>Talisapatra</i> (<i>Abies webbiana</i>) and Comparison with English yew (<i>Taxus baccata</i>). <i>IJPPR</i> . 2018; 10(2); 84-91 Vivek Saravanan. Bioactivities of Isolated Phytochemicals and Extracts of <i>Abies spectabilis</i> (D.Don) Mirb. <i>Matrix Science Pharma</i> .2021,5 (2):42 |
| Cuminum cyminum | Coumaric acid | Ali Esmail Al-Snafi. The pharmacological activities of <i>Cuminum cyminum</i> - A review. <i>IOSR Journal of Pharmacy</i> . 2016;6(6): 46-65 |
| Saccharum officinarum | Vitexin | Singh, A., Lal, U. R., Mukhtar, H. M., Singh, P. S., Shah, G., & Dhawan, R. K. (2015). Phytochemical profile of sugarcane and its potential health aspects. <i>Pharmacognosy reviews</i> , 9(17), 45–54. https://doi.org/10.4103/0973-7847.15634 |

OBJECTIVE

Binding of phytochemicals with the core amino acids (Ser684, Asp690, Lys691, Lys692) of the target by forming hydrogen bond will hinder the function of the enzyme HMG CoA reductase with PDB – 1HWK. These

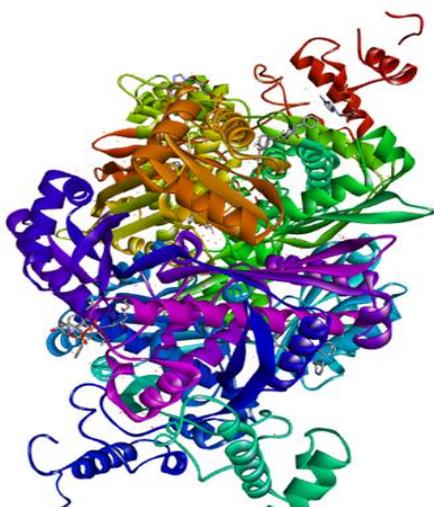
amino acid residues are functionally responsible for HMG CoA reductase enzyme activity in cholesterol biosynthesis. Thereby phytochemicals which inhibit the target enzyme HMG CoA reductase may occupy these active amino acid could be able to block the HMG

CoA enzymatic activity thereby limit the cholesterol synthesis and subsequent helps in control the hyperlipidemia. Compounds that selectively hinders the

action of this enzyme may act as a potential therapeutic agent for management of hyperlipidemia.

| PDB | Name of the Target |
|------|--------------------|
| 1HWK | HMG CoA reductase |

3D- Structure of HMG CoA reductase (PDB) - 1HWK

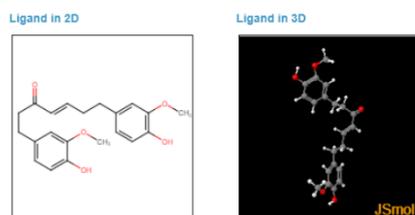


METHODOLOGY

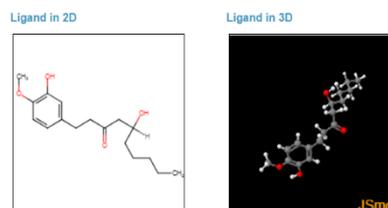
Docking calculations were carried out for retrieved phytocomponents against target enzyme Phospholipases A2. Essential hydrogen atoms, Kollman united atom type charges, and solvation parameters were added with the aid of Auto Dock tools (Morris, Goodsell et al., 1998). Affinity (grid) maps of $\times \times \text{ \AA}$ grid points and 0.375 \AA spacing were generated using the Autogrid program (Morris, Goodsell et al., 1998). Auto Dock 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 \AA , and quaternion and torsion steps of 5 were applied.

2D and 3D Structure of Selected Ligands

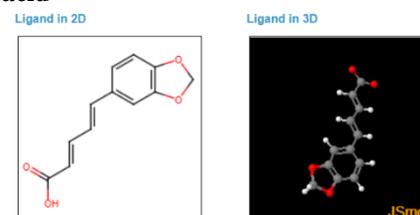
Gingerenone-A



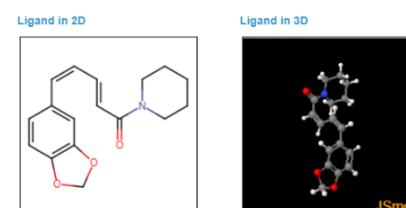
6 Gingerol



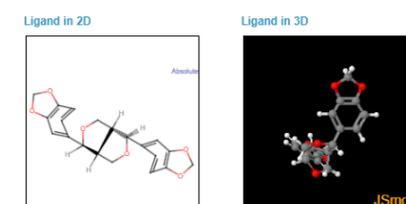
Piperic acid



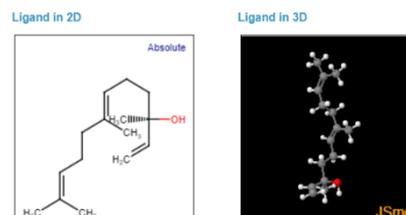
Piperine



Sesamin

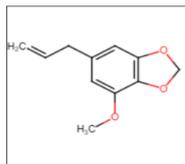


Nerolidol

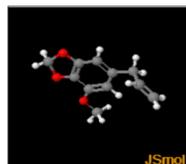


Elemicin

Ligand in 2D

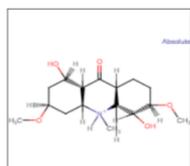


Ligand in 3D

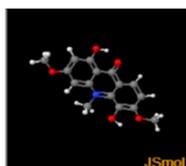


Grandisin

Ligand in 2D

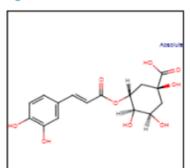


Ligand in 3D

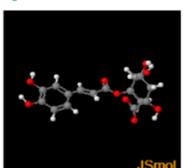


Chlorogenic acid

Ligand in 2D

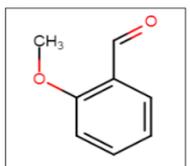


Ligand in 3D



Anisaldehyde

Ligand in 2D

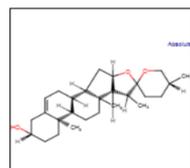


Ligand in 3D

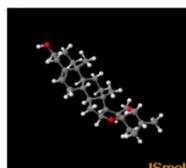


Diosgenin

Ligand in 2D

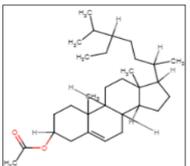


Ligand in 3D

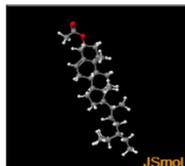


β-sitosterol

Ligand in 2D

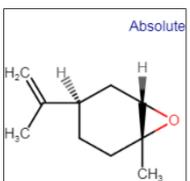


Ligand in 3D

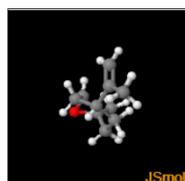


Limonene

Ligand in 2D

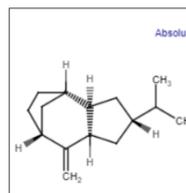


Ligand in 3D



β-vetivenene

Ligand in 2D

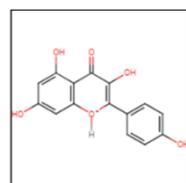


Ligand in 3D

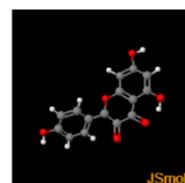


Kaempferol

Ligand in 2D

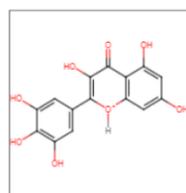


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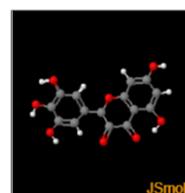


Myricetin

Ligand in 2D

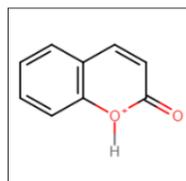


Ligand in 3D



Coumaric acid

Ligand in 2D

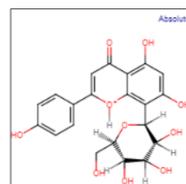


Ligand in 3D

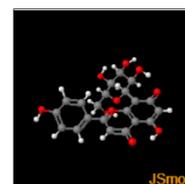


Vitexin

Ligand in 2D

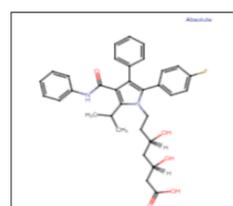


Ligand in 3D

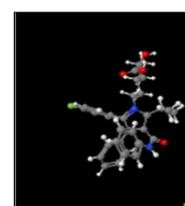


Atorvastatin

Ligand in 2D



Ligand in 3D



Ligand Properties of the Compounds Selected for Docking Analysis.

| Compound | Molar weight g/mol | Molecular Formula | H Bond Donor | H Bond Acceptor | Rotatable bonds |
|------------------|--------------------|---|--------------|-----------------|-----------------|
| Gingerenone-A | 356.4 g/mol | C ₂₁ H ₂₄ O ₅ | 2 | 5 | 9 |
| 6 Gingerol | 294.391g/mol | C ₁₇ H ₂₆ O ₄ | 2 | 4 | 10 |
| Piperic acid | 218.2 g/mol | C ₁₂ H ₁₀ O ₄ | 1 | 4 | 3 |
| Piperine | 285.34 g/mol | C ₁₇ H ₁₉ NO ₃ | 0 | 3 | 3 |
| Sesamin | 354.4 g/mol | C ₂₀ H ₁₈ O ₆ | 0 | 6 | 2 |
| Nerolidol | 222.37 g/mol | C ₁₅ H ₂₆ O | 1 | 1 | 7 |
| Elemicin | 208.25 g/mol | C ₁₂ H ₁₆ O ₃ | 0 | 3 | 5 |
| Grandisin | 276.37 g/mol | C ₁₆ H ₂₄ N ₂ O ₂ | 1 | 4 | 0 |
| Chlorogenic acid | 354.31 g/mol | C ₁₆ H ₁₈ O ₉ | 6 | 9 | 5 |
| Anisaldehyde | 136.148 g/mol | C ₈ H ₈ O ₂ | 0 | 1 | 2 |
| Diosgenin | 414.6 g/mol | C ₂₇ H ₄₂ O ₃ | 1 | 3 | 0 |
| β-sitosterol | 414.7g/mol | C ₂₉ H ₅₀ O | 1 | 1 | 6 |
| Limonene | 136.23 g/mol | C ₁₀ H ₁₆ | 0 | 0 | 1 |
| β-vetivenene | 202.33 g/mol | C ₁₅ H ₂₂ | 0 | 0 | 0 |
| Kaempferol | 286.24 g/mol | C ₁₅ H ₁₀ O ₆ | 4 | 6 | 1 |
| Myricetin | 318.237g/mol | C ₁₅ H ₁₀ O ₈ | 6 | 8 | 1 |
| Coumaric acid | 164.16 g/mol | C ₉ H ₈ O ₃ | 2 | 3 | 2 |
| Vitexin | 432.4 g/mol | C ₂₁ H ₂₀ O ₁₀ | 7 | 10 | 3 |

Summary of the molecular docking studies of compounds against HMG coA reductase (PDB) - 1HWK

| Compounds | Est. Free Energy of Binding | Est. Inhibition Constant, Ki | Electrostatic Energy | Total Intermolec. Energy | Interact. Surface |
|------------------|-----------------------------|------------------------------|----------------------|--------------------------|-------------------|
| Gingerenone-A | -5.05 kcal/mol | 197.75 Um | -0.11 kcal/mol | -6.24 kcal/mol | 709.503 |
| 6 Gingerol | -3.79 kcal/mol | 1.68 mM | -0.12 kcal/mol | -5.93 kcal/mol | 683.722 |
| Piperic acid | -4.01 kcal/mol | 1.14 mM | -1.48 kcal/mol | -4.90 kcal/mol | 402.998 |
| Piperine | -5.43 kcal/mol | 104.25 uM | -0.05 kcal/mol | -5.65 kcal/mol | 648.634 |
| Sesamin | -5.15 kcal/mol | 166.93 uM | -0.03 kcal/mol | -5.69 kcal/mol | 650.568 |
| Nerolidol | -4.48 kcal/mol | 520.16 uM | -0.05 kcal/mol | -6.26 kcal/mol | 596.792 |
| Elemicin | -4.29 kcal/mol | 718.03 uM | -0.10 kcal/mol | -5.13 kcal/mol | 532.473 |
| Grandisin | -3.44 kcal/mol | 3.03 mM | -0.15 kcal/mol | -5.85 kcal/mol | 777.998 |
| Chlorogenic acid | -5.42 kcal/mol | 106.64 uM | -0.75 kcal/mol | -5.07 kcal/mol | 463.408 |
| Anisaldehyde | -3.43 kcal/mol | 3.06 mM | -0.12 kcal/mol | -4.05 kcal/mol | 444.025 |
| Diosgenin | -6.10 kcal/mol | 33.89 uM | -0.03 kcal/mol | -6.40 kcal/mol | 757.767 |
| β-sitosterol | -5.95 kcal/mol | 43.59 uM | -0.02 kcal/mol | -7.75 kcal/mol | 833.892 |
| Limonene | -5.08 kcal/mol | 188.47 uM | -0.01 kcal/mol | -5.38 kcal/mol | 442.813 |
| β-vetivenene | -6.22 kcal/mol | 27.55 uM | -0.18 kcal/mol | -6.52 kcal/mol | 564.724 |
| Kaempferol | -4.91 kcal/mol | 250.57 uM | -0.52 kcal/mol | -5.28 kcal/mol | 575.724 |
| Myricetin | -5.69 kcal/mol | 66.96 uM | -0.47 kcal/mol | -5.00 kcal/mol | 568.58 |
| Coumaric acid | -4.61 kcal/mol | 420.30 uM | -0.09 kcal/mol | -4.61 kcal/mol | 446.404 |
| Vitexin | -7.17 kcal/mol | 5.57 uM | -1.13 kcal/mol | -5.86 kcal/mol | 585.896 |
| | -5.05 kcal/mol | 197.75 uM | -0.11 kcal/mol | -6.24 kcal/mol | 709.503 |
| Atorvastatin | -5.55 kcal/mol | 85.94 uM | -1.30 kcal/mol | -6.17 kcal/mol | 648.525 |

Amino acid Residue Interaction of Lead against HMG coA reductase (PDB) - 1HWK

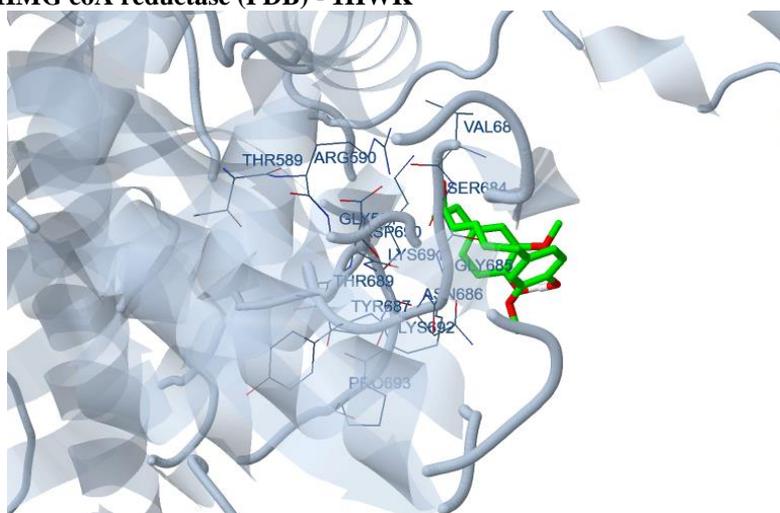
| Compounds | Interaction | Amino Acid Residues | | | | | | | | |
|---------------|-------------|---------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| Gingerenone-A | 4 | 590 | 684 | 686 | 690 | 691 | 692 | | | |
| | | ARG | SER | ASN | ASP | LYS | LYS | | | |
| 6 Gingerol | 3 | 590 | 658 | 661 | 665 | 683 | 684 | 686 | 690 | 692 |
| | | ARG | ASN | SER | GLU | VAL | SER | ASN | ASP | LYS |
| Piperic acid | 4 | 590 | 684 | 690 | 691 | 692 | 769 | | | |
| | | ARG | SER | ASP | LYS | LYS | ALA | | | |
| Piperine | 2 | 691 | 692 | 693 | 769 | 772 | | | | |

| | | | | | | | | | | | | |
|---------------------|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| | | LYS | LYS | PRO | ALA | VAL | | | | | | |
| Sesamin | 2 | 593 | 644 | 684 | 686 | 692 | | | | | | |
| | | VAL | TYR | SER | ASN | LYS | | | | | | |
| Nerolidol | 4 | 590 | 684 | 690 | 691 | 692 | 693 | 772 | | | | |
| | | ARG | SER | ASP | LYS | LYS | PRO | VAL | | | | |
| Elemicin | 3 | 690 | 691 | 692 | 769 | 772 | | | | | | |
| | | ASP | LYS | LYS | ALA | VAL | | | | | | |
| Grandisin | 2 | 590 | 655 | 657 | 658 | 661 | 690 | 691 | 767 | | | |
| | | ARG | MET | MET | ASN | SER | ASP | LYS | ASP | | | |
| Chlorogenic acid | 4 | 590 | 684 | 686 | 690 | 691 | 692 | 769 | | | | |
| | | ARG | SER | ASN | ASP | LYS | LYS | ALA | | | | |
| Anisaldehyde | 0 | 655 | 766 | 767 | 809 | | | | | | | |
| | | MET | GLN | ASP | THR | | | | | | | |
| Diosgenin | 3 | 590 | 655 | 657 | 658 | 684 | 690 | 691 | 767 | | | |
| | | ARG | MET | MET | ASN | SER | ASP | LYS | ASP | | | |
| β -sitosterol | 4 | 590 | 684 | 690 | 691 | 692 | 769 | 772 | | | | |
| | | ARG | SER | ASP | LYS | LYS | ALA | VAL | | | | |
| Limonene | 0 | 655 | 766 | 767 | 770 | 809 | | | | | | |
| | | MET | GLN | ASP | GLN | THR | | | | | | |
| β -vetivenene | 2 | 691 | 692 | 693 | 769 | 772 | | | | | | |
| | | LYS | LYS | PRO | ALA | VAL | | | | | | |
| Kaempferol | 3 | 590 | 682 | 684 | 686 | 690 | 692 | | | | | |
| | | ARG | ALA | SER | ASN | ASP | LYS | | | | | |
| Myricetin | 4 | 590 | 682 | 684 | 686 | 690 | 691 | 692 | | | | |
| | | ARG | ALA | SER | ASN | ASP | LYS | LYS | | | | |
| Coumaric acid | 0 | 655 | 809 | | | | | | | | | |
| | | MET | THR | | | | | | | | | |
| Vitexin | 4 | 590 | 661 | 665 | 682 | 683 | 684 | 686 | 690 | 691 | 692 | |
| | | ARG | SER | GLU | ALA | VAL | SER | ASN | ASP | LYS | LYS | |

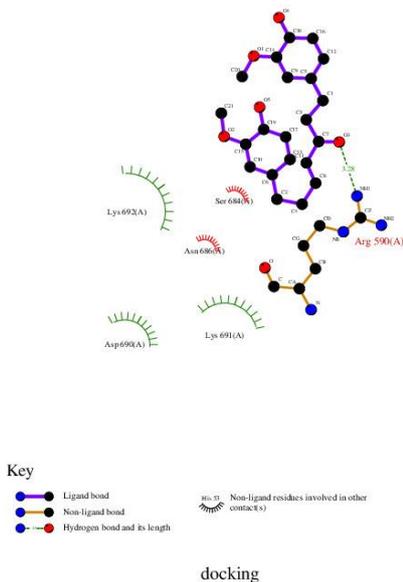
Atorvastatin 4 590 ARG 657 MET 658 ASN 661 SER 683 VAL 684 VAL 690 ASP 691 LYS 692 LYS 767 ASP 770
GLN

Docking Pose

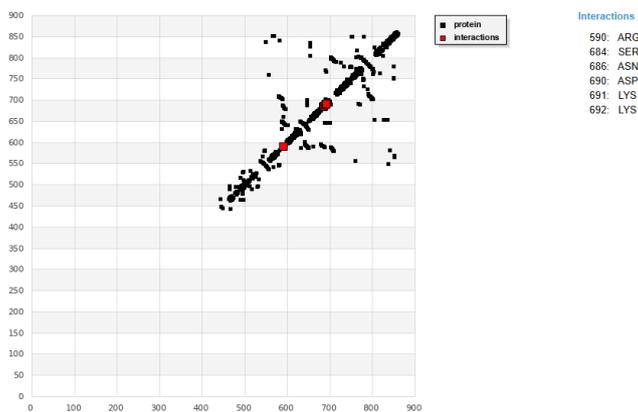
Gingerenone-A with HMG coA reductase (PDB) - 1HWK



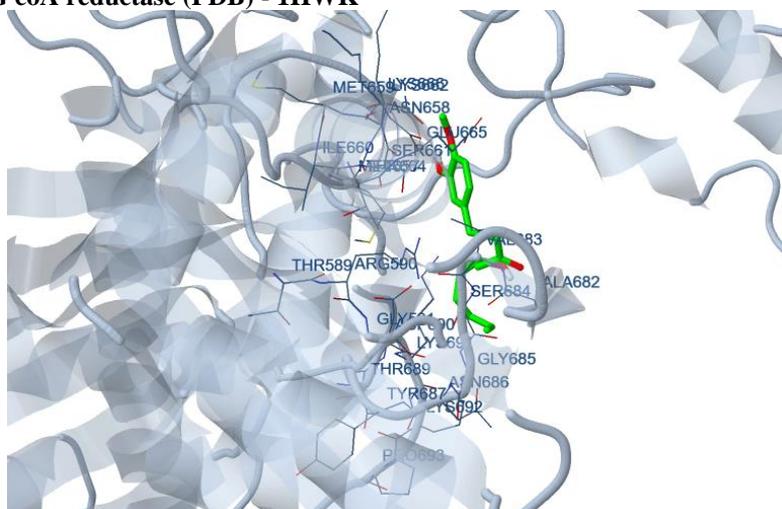
2D Interaction Plot Analysis



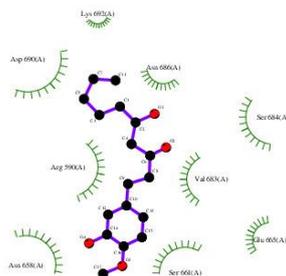
Hydrogen bond plotting with core amino acid Analysis



6 Gingerol with HMG coA reductase (PDB) - 1HWK

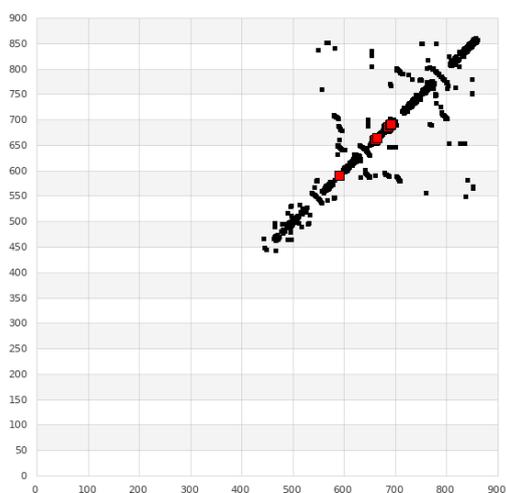


2D Interaction Plot Analysis



docking

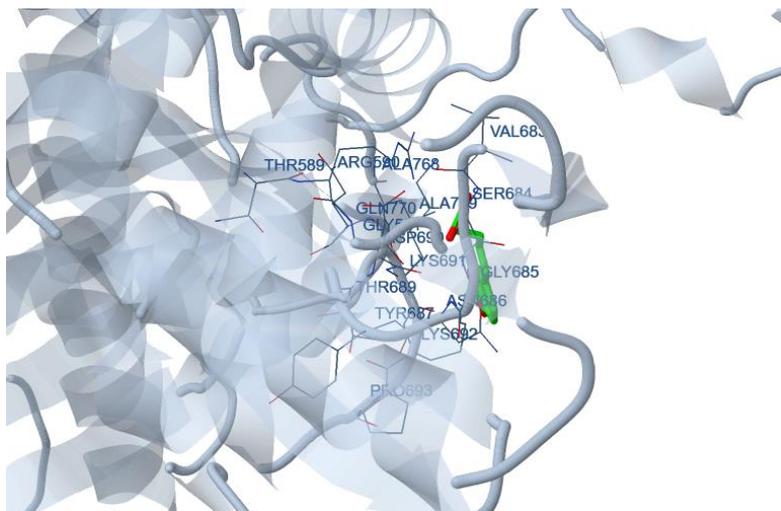
Hydrogen bond plotting with core amino acid Analysis



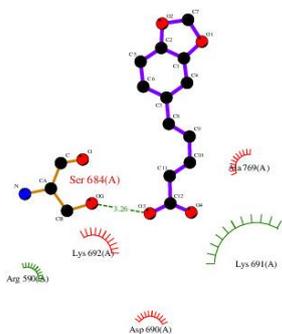
Interactions

- 590: ARG
- 658: ASN
- 661: SER
- 665: GLU
- 683: VAL
- 684: SER
- 686: ASN
- 690: ASP
- 692: LYS

Piperic acid with HMG coA reductase (PDB) - 1HWK



2D Interaction Plot Analysis

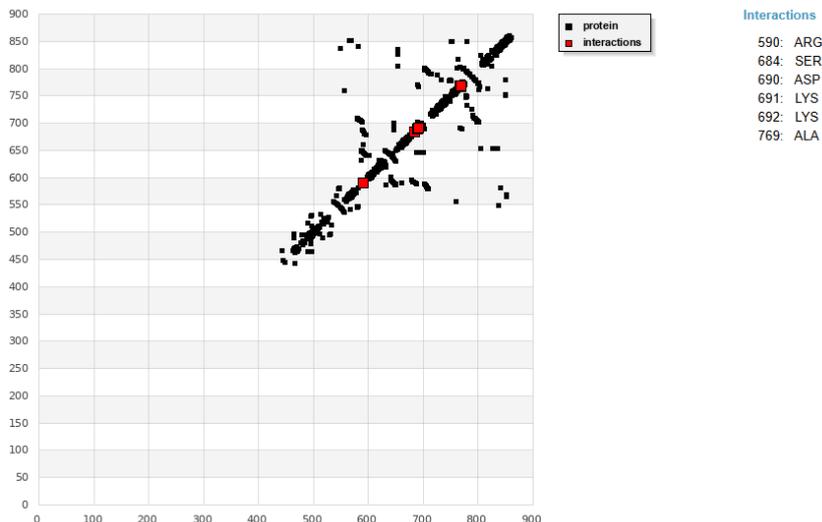


Key

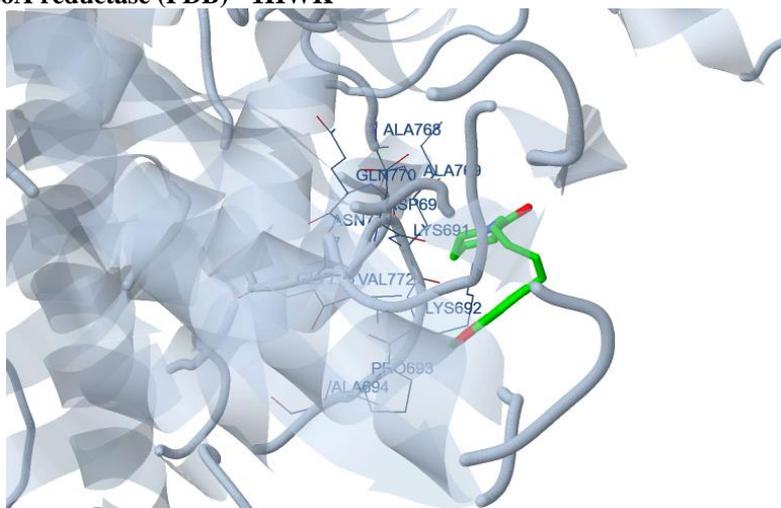
- Ligand bond
- Non-ligand bond
- Hydrogen bond and its length
- Non-ligand residues involved in other contacts

docking

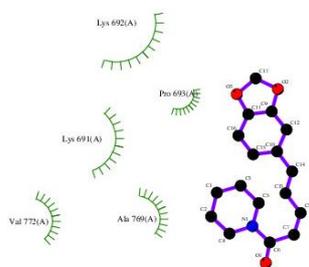
Hydrogen bond plotting with core amino acid Analysis



Piperine with HMG coA reductase (PDB) - 1HWK



2D Interaction Plot Analysis

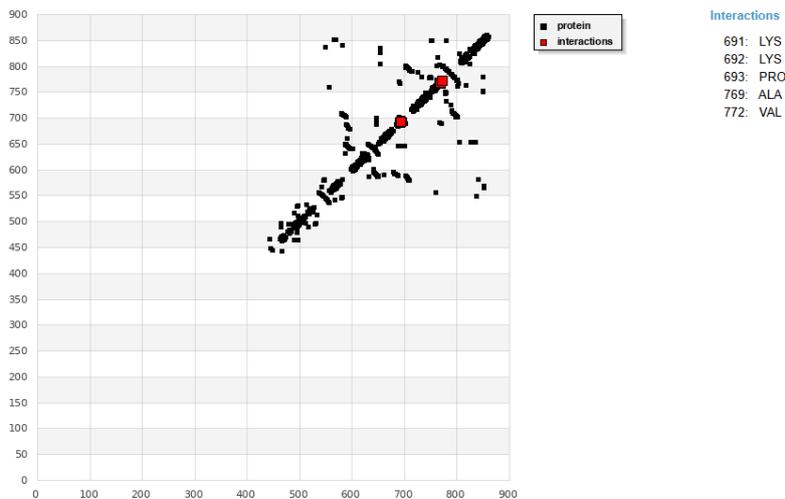


Key

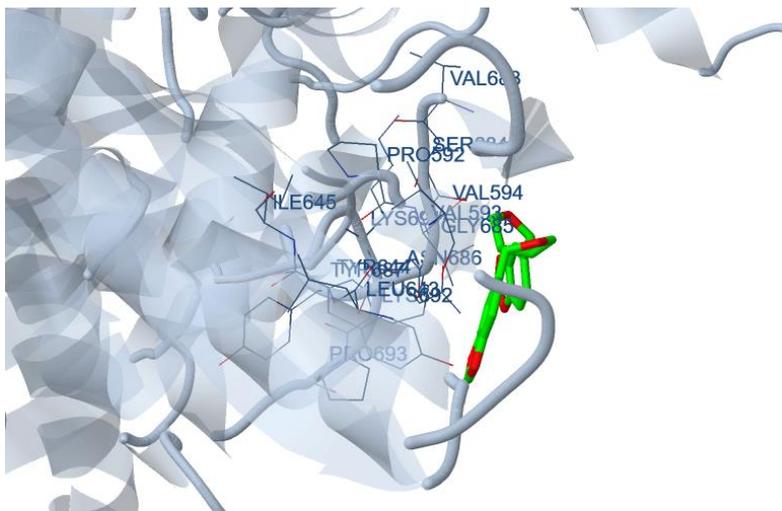
- Ligand bond
- Non-ligand bond
- Hydrogen bond and its length
- Non-ligand residues involved in other contact(s)

docking

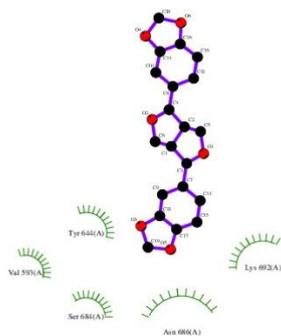
Hydrogen bond plotting with core amino acid Analysis



Sesamin with HMG coA reductase (PDB) - 1HWK



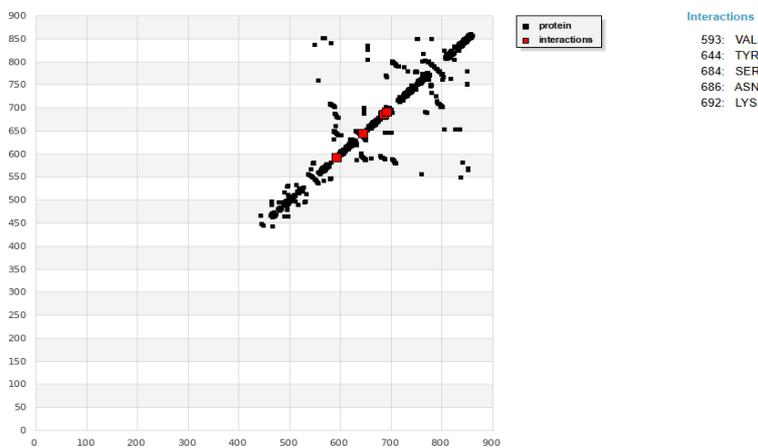
2D Interaction Plot Analysis



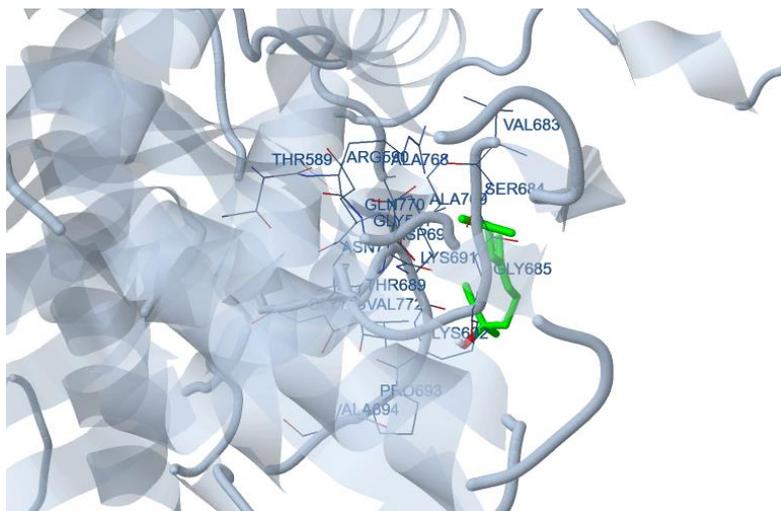
Key
 ●—● Ligand bond
 ●—● Non-ligand bond
 ●—● Hydrogen bond and its length
 ● Non-ligand residues involved in other contact(s)

docking

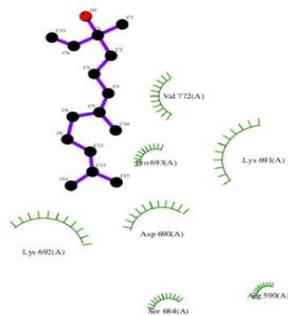
Hydrogen bond plotting with core amino acid Analysis



Nerolidol with HMG coA reductase (PDB) - 1HWK



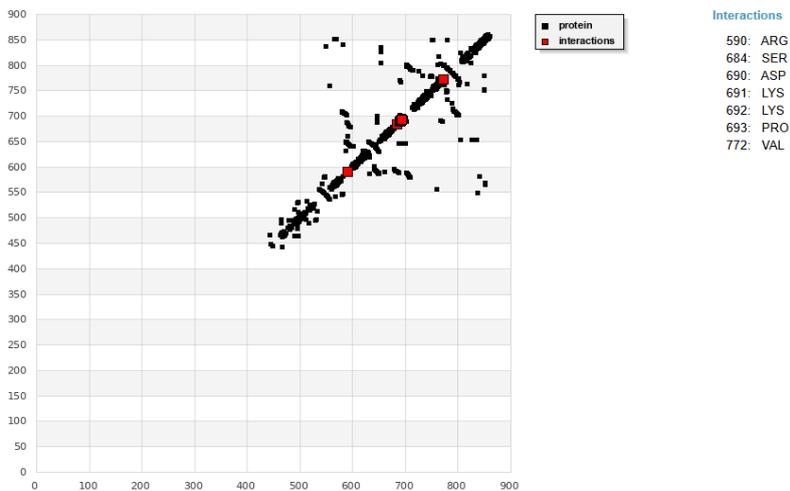
2D Interaction Plot Analysis



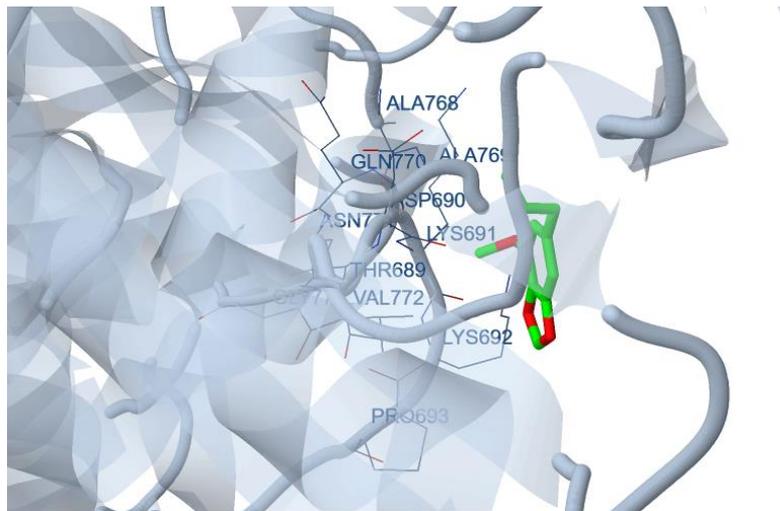
Key
 ●—● Ligand bond
 ●—● Non-ligand bond
 ●—●—● Hydrogen bond and its length
 (A) (B) Non-ligand residues involved in other contact(s)

docking

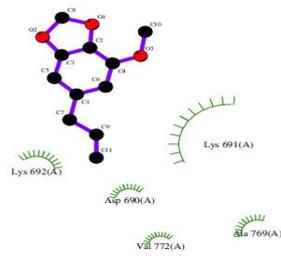
Hydrogen bond plotting with core amino acid Analysis



Elemicin with HMG coA reductase (PDB) - 1HWK



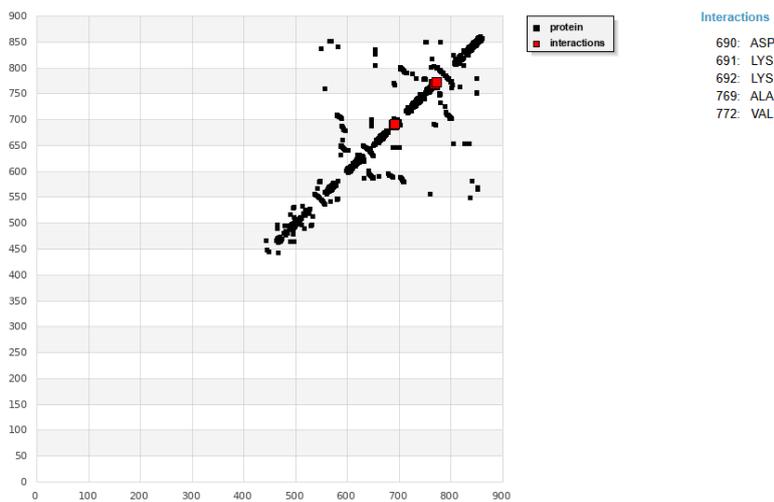
2D Interaction Plot Analysis



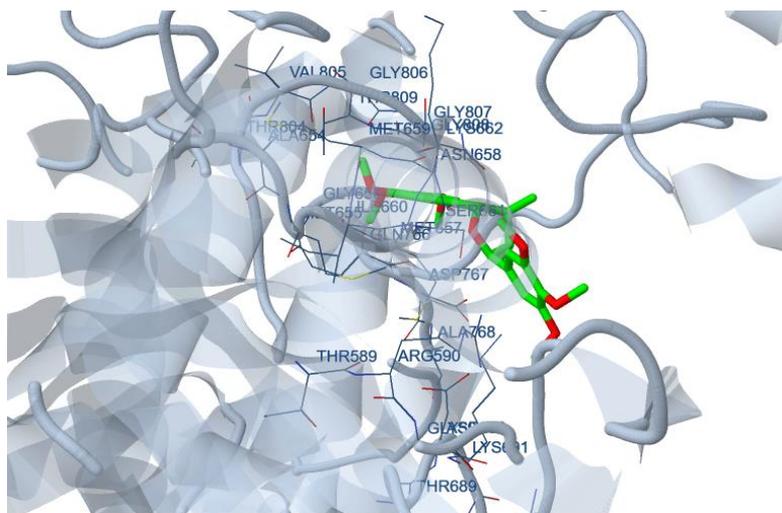
Key
 ● Ligand bond
 ● Non-ligand bond
 ● Hydrogen bond and its length
 (H...O) Non-ligand residues involved in other contacts

docking

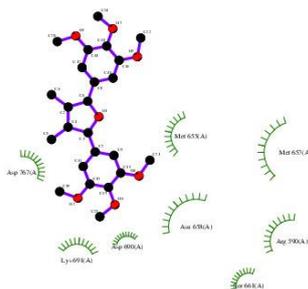
Hydrogen bond plotting with core amino acid Analysis



Grandisin with HMG coA reductase (PDB) - 1HWK



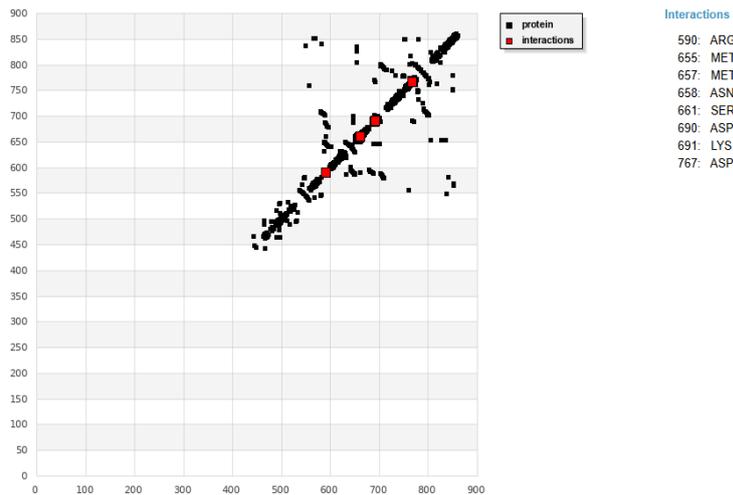
2D Interaction Plot Analysis



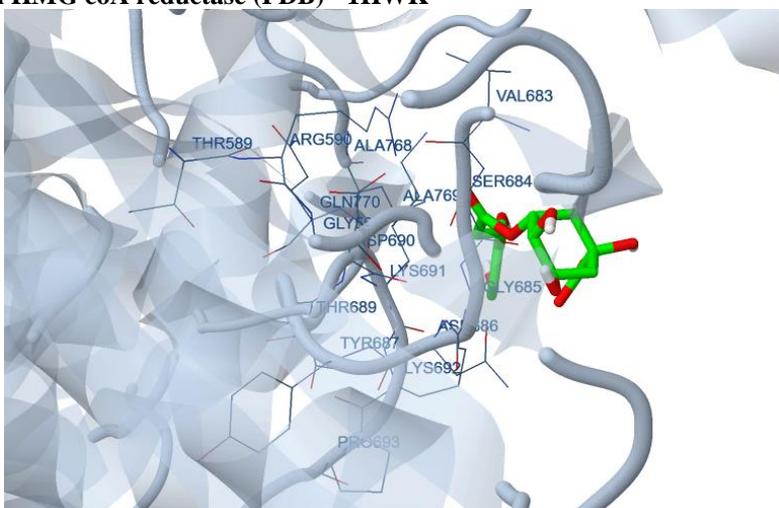
Key
 ●—● Ligand bond
 ●—● Non-ligand bond
 ●—● Hydrogen bond and its length
 H₂O Non-ligand residues involved in other contact(s)

docking

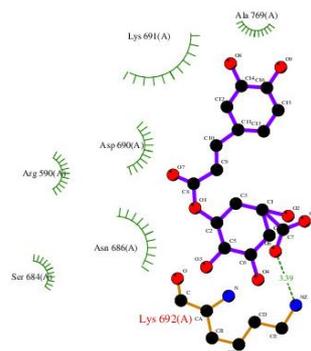
Hydrogen bond plotting with core amino acid Analysis



Chlorogenic acid with HMG coA reductase (PDB) - 1HWK



2D Interaction Plot Analysis

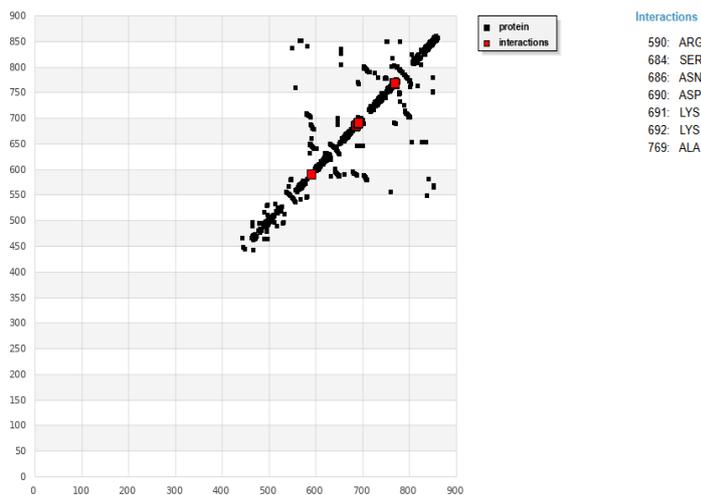


Key

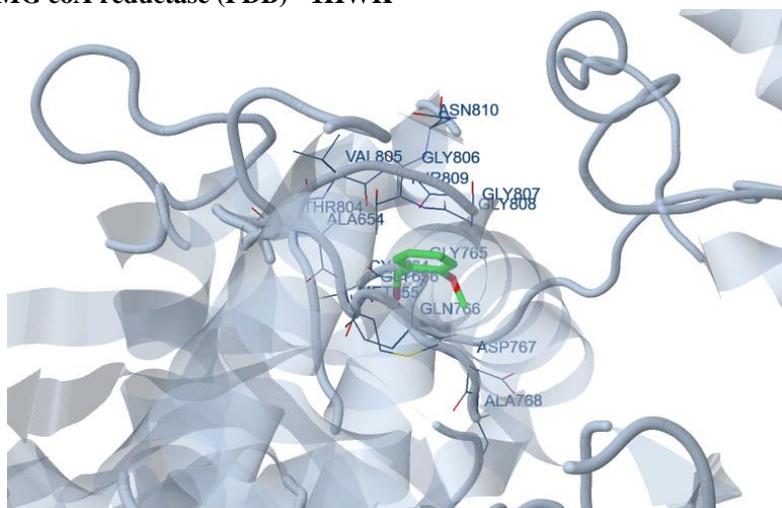
- Ligand bond
- Non-ligand bond
- Hydrogen bond and its length
- Non-ligand residues involved in other contact(s)

docking

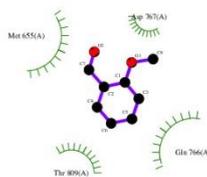
Hydrogen bond plotting with core amino acid Analysis



Anisaldehyde with HMG coA reductase (PDB) - 1HWK



2D Interaction Plot Analysis

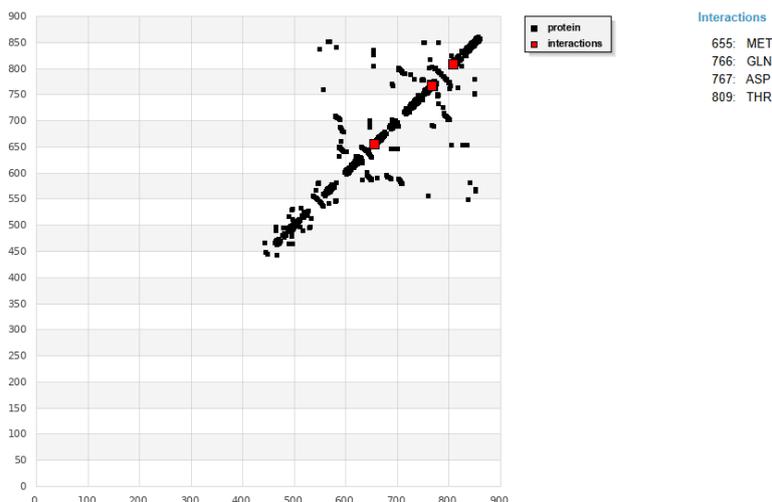


Key

- Ligand bond
- Non-ligand bond
- Hydrogen bond and its length
- Non-ligand residues involved in other contacts

docking

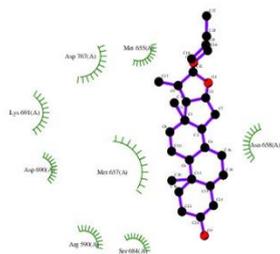
Hydrogen bond plotting with core amino acid Analysis



Diosgenin with HMG coA reductase (PDB) - 1HWK



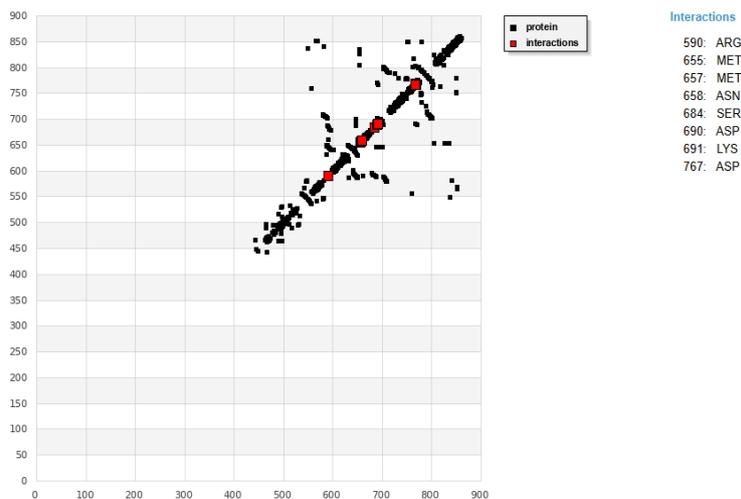
2D Interaction Plot Analysis



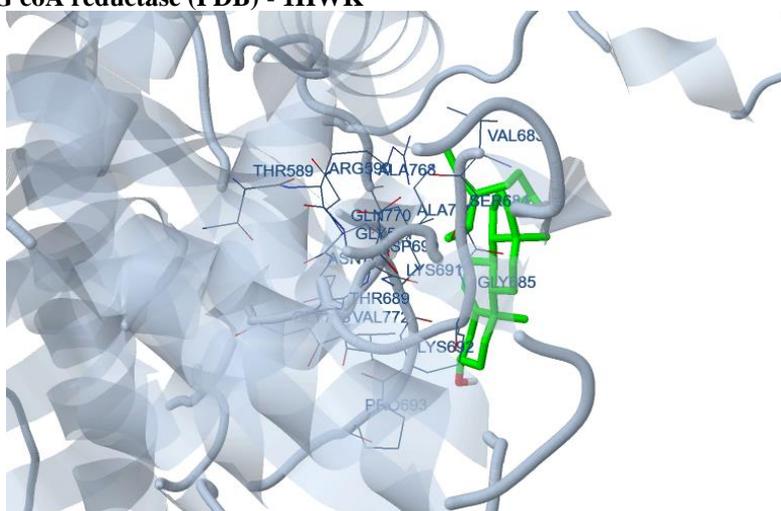
Key
 ● Ligand bond
 ● Non-ligand bond
 ●-○ Hydrogen bond and its length
 ○ Non-ligand residues involved in other contact(s)

docking

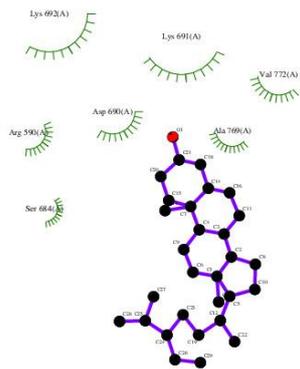
Hydrogen bond plotting with core amino acid Analysis



β-sitosterol with HMG coA reductase (PDB) - 1HWK



2D Interaction Plot Analysis

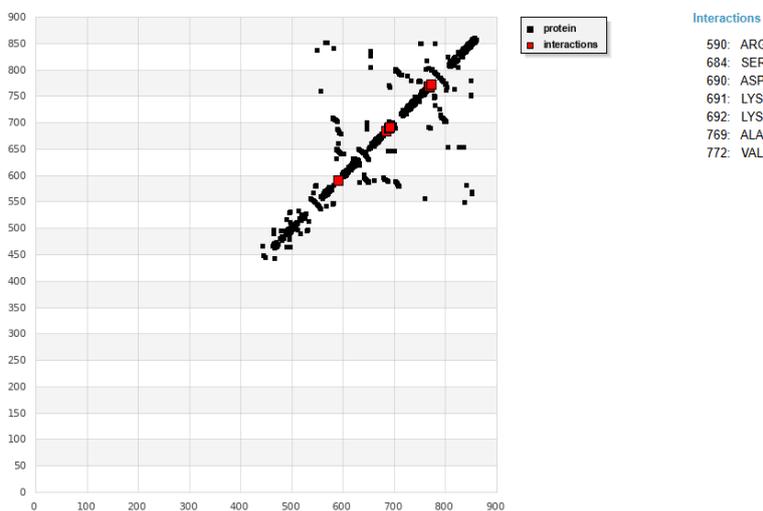


Key

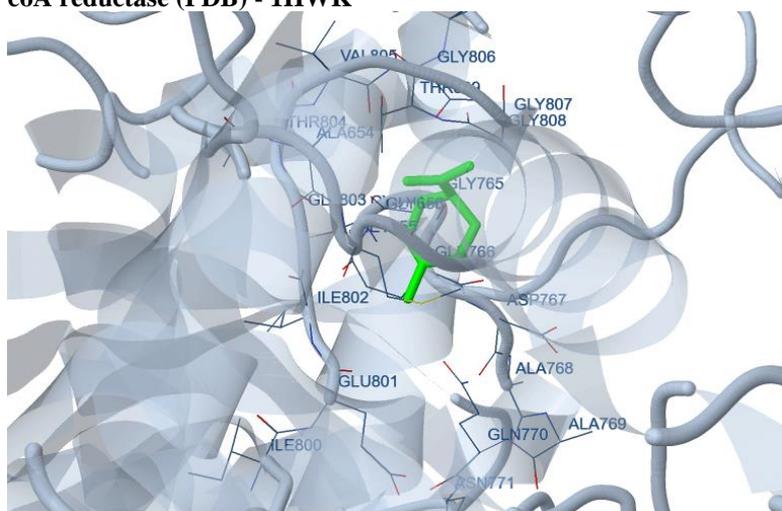
- Ligand bond
- Non-ligand bond
- Hydrogen bond and its length
- Non-ligand residues involved in other contact(s)

docking

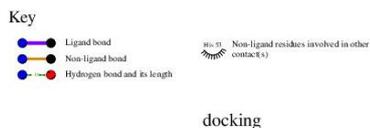
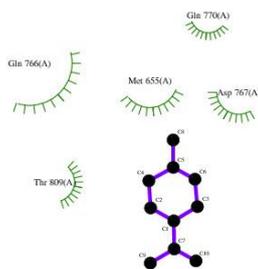
Hydrogen bond plotting with core amino acid Analysis



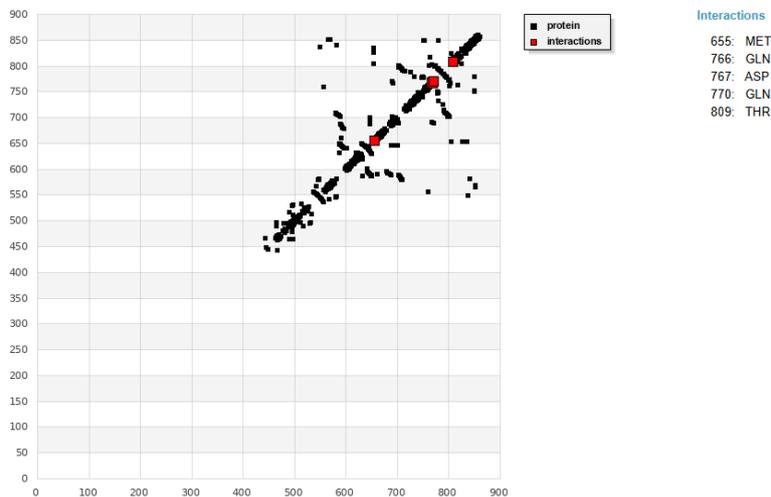
Limone with HMG coA reductase (PDB) - 1HWK



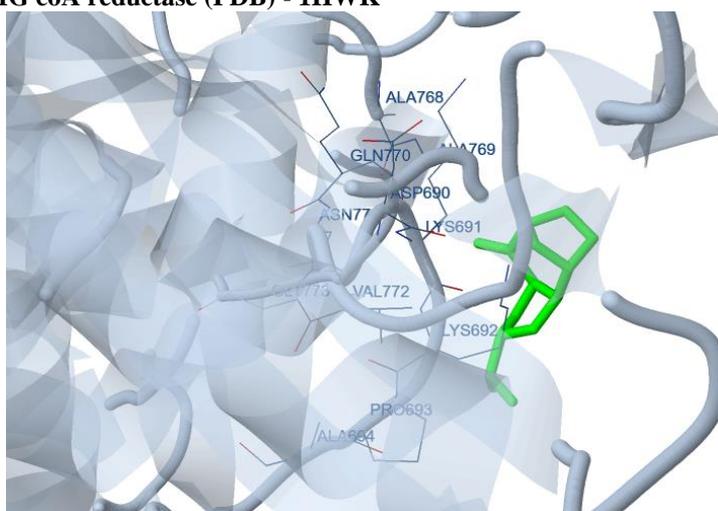
2D Interaction Plot Analysis



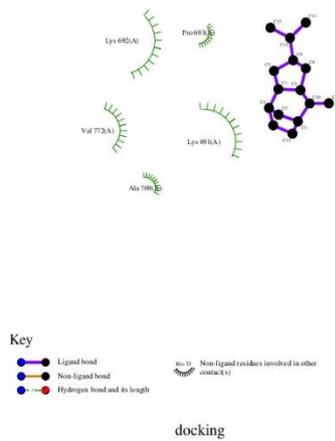
Hydrogen bond plotting with core amino acid Analysis



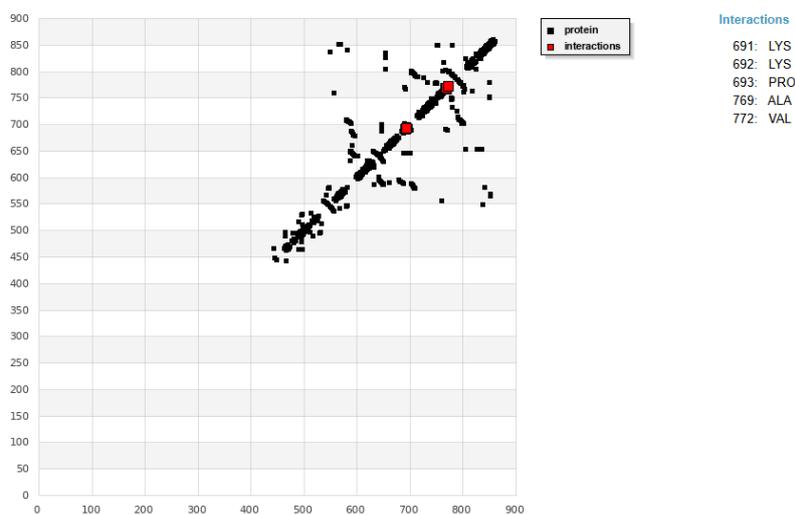
β-vetivenene with HMG coA reductase (PDB) - 1HWK



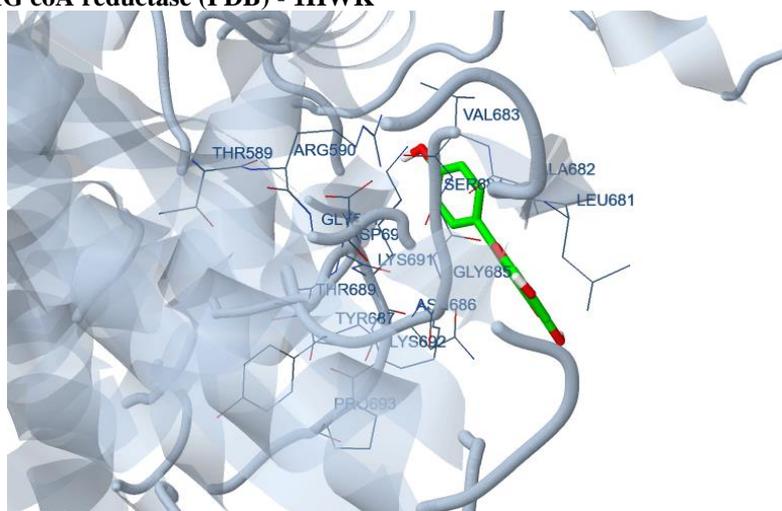
2D Interaction Plot Analysis



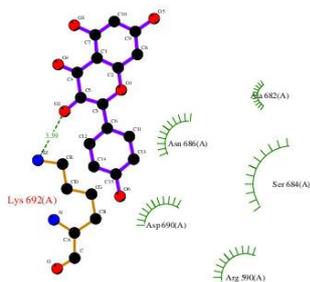
Hydrogen bond plotting with core amino acid Analysis



Kaempferol with HMG coA reductase (PDB) - 1HWK



2D Interaction Plot Analysis

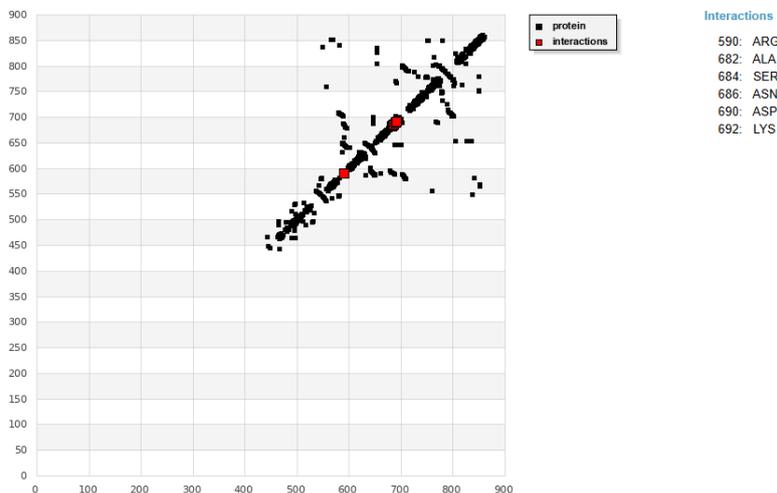


Key

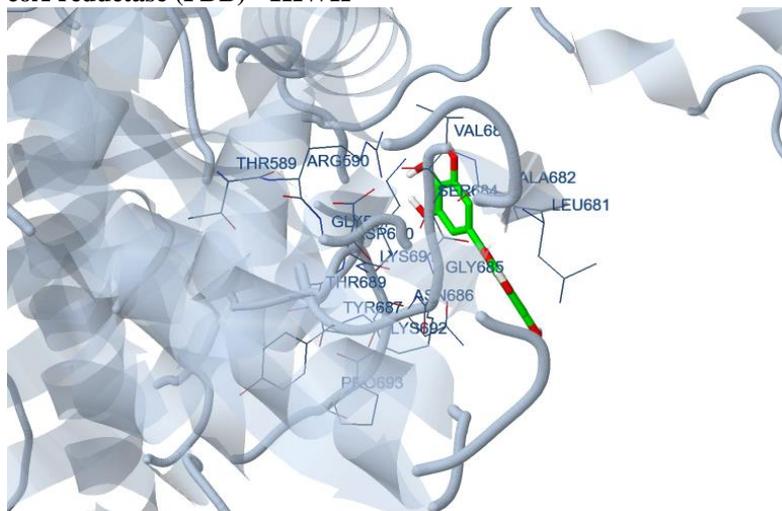
- Ligand bond
- Non-ligand bond
- Hydrogen bond and its length
- Non-ligand residues involved in other contact(s)

docking

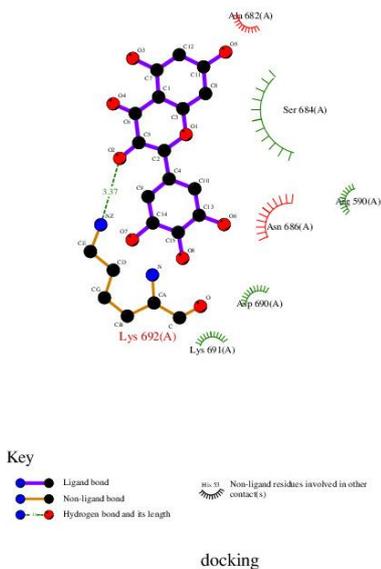
Hydrogen bond plotting with core amino acid Analysis



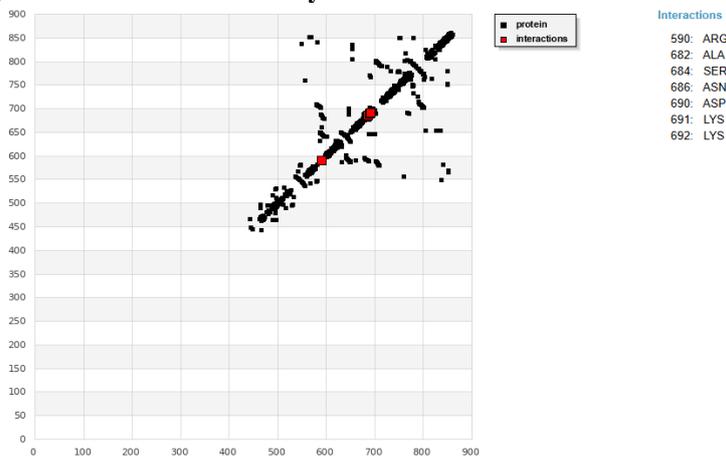
Myricetin with HMG coA reductase (PDB) - 1HWK



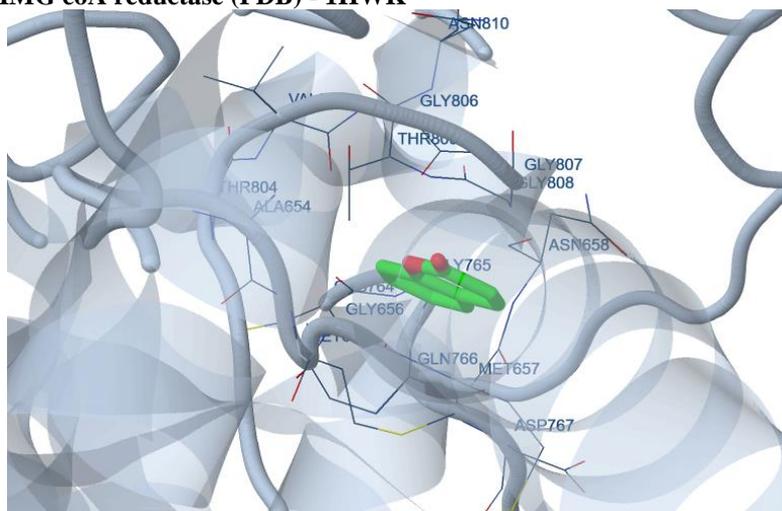
2D Interaction Plot Analysis



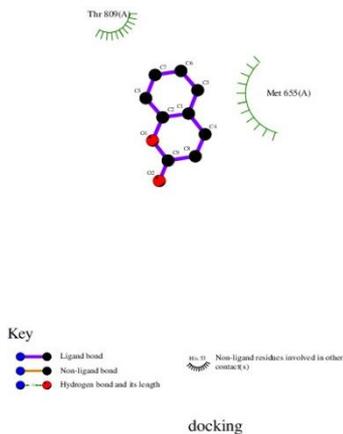
Hydrogen bond plotting with core amino acid Analysis



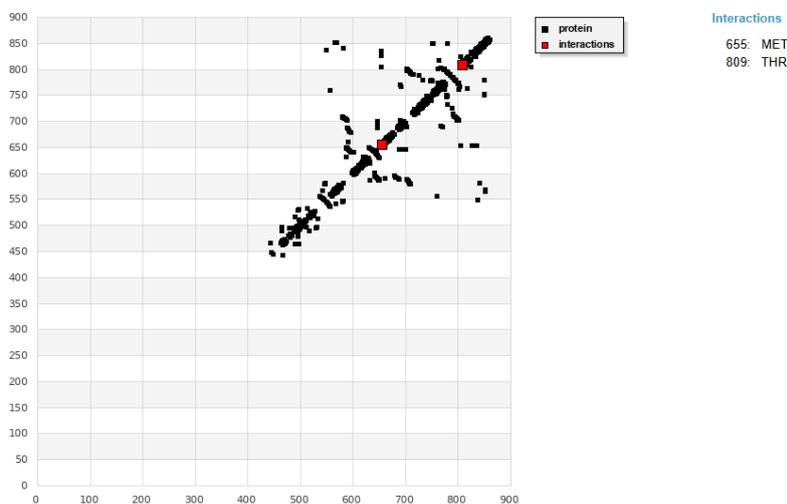
Coumaric acid with HMG coA reductase (PDB) - 1HWK



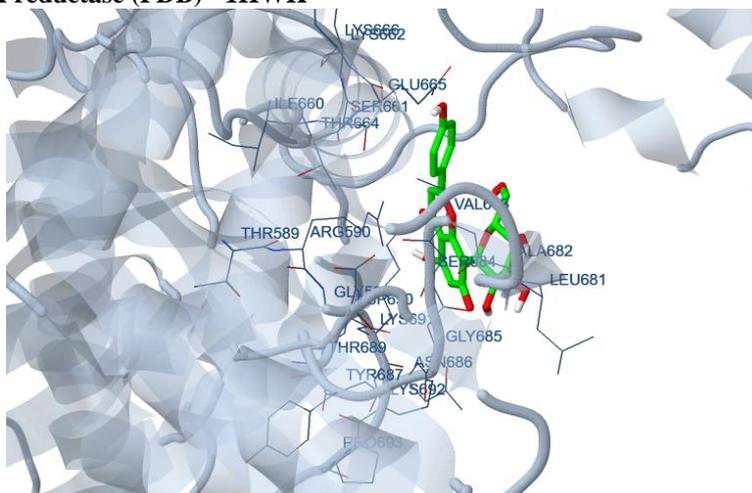
2D Interaction Plot Analysis



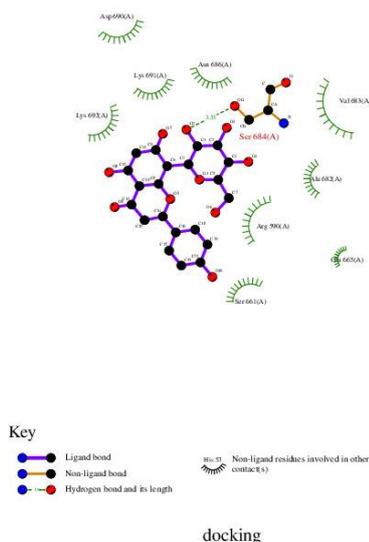
Hydrogen bond plotting with core amino acid Analysis



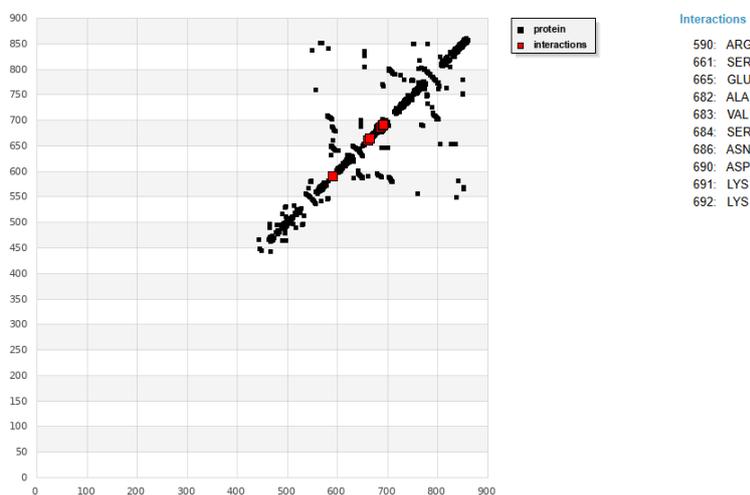
Vitexin with HMG coA reductase (PDB) - 1HWK



2D Interaction Plot Analysis



Hydrogen bond plotting with core amino acid Analysis



OBSERVATION AND INFERENCE

Total of 18 bioactive lead compounds were retrieved from the herbal and other ingredients present in the siddha formulation Inji Chooranam II. From the reported data of the bioactive compounds, the compounds such as Gingerenone-A, 6-Gingerol, Piperic acid, Nerolidol, Elemicin, Chlorogenic acid, Diosgenin, β -Sitosterol, Kaempferol, Myricetin, and Vitexin present in the herbal ingredients reveals maximum of 3-4 interactions with the core active amino acid residues present on the target HMG CoA reductase.

CONCLUSION

Based on the results of the computational analysis it was concluded that the bio-active compound's like Gingerenone-A, 6-Gingerol, Piperic acid, Nerolidol, Elemicin, Chlorogenic acid, Diosgenin, β -Sitosterol, Kaempferol, Myricetin, and Vitexin present in the ingredients possess significant binding against the target enzyme HMG CoA reductase. Thereby phytocomponents which inhibit the target enzyme HMG CoA reductase by occupies these active aminoacid could be able to hinder

the function of rate limiting enzyme involved in cholesterol biosynthesis.

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6. Sivaraman Dhanasekaran, Pradeep Pushparaj Selvadoss, Solomon Sundar Manoharan, Srikanth Jeyabalan, Devi Rajeswari Vijayarangan. Revealing Anti-Fungal Potential of Plant-Derived Bioactive Therapeutics in Targeting Secreted Aspartyl Proteinase (SAP) of *Candida albicans*: A Molecular Dynamics Approach. *Journal of Biomolecular Structure and Dynamics*, 2023; 6: 1-15. <https://doi.org/10.1080/07391102.2023.2196703>