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EVALUATION OF BINDING AFFINITY OF THE SELECTED HERBAL BIO-ACTIVE COMPONENTS WITH THE ENZYME CYP- 17A-HYDROXYLASE BY PCOS AMELIORATION ACTIVITY THROUGH MOLECULAR DOCKING *IN- SILICO* APPROACH

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Keywords:

PCOS, Molecular docking, Siddha medicine, CYP- 17α-hydroxylase, Herbs

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ABSTRACT: Polycystic ovarian syndrome (PCOS) known by its name can be correlated with *Soothaga Vaayu* in Siddha classical literature which is one of the most common forms of metabolic and endocrine disorders of women, with a high prevalence among the reproductive age group, often associated with obesity, hypertension, insulin resistance, diabetes mellitus, hyperinsulinemia and dyslipidemia. Current therapeutic management available for PCOS is only moderately effective in controlling symptoms and preventing some of the complications. Hence in recent times, people rely most on alternative complementary treatments for the management of PCOS. The research articles have shown the following bio-active compounds present in the selected herbs used in the Siddha treatment for gynecological problems as Campesterol, Diosgenin, Cinnamic acid, Anethole, Kaempferol, Ferulic acid, Myricetin, Erysovine, β-Sitosterol and Rutin. Molecular docking is a great approach in current trends to identify the possibility of pharmacological effects of medicinal compounds which could be exerted over their corresponding protein targets which are relevant for the disease. Docking simulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method (*Solis and Wets, 1981*). From the reported data of the herbs, the phytochemicals such as Campesterol, Diosgenin, Cinnamic acid, Kaempferol, Ferulic acid, Myricetin, β-Sitosterol and Rutin reveal a maximum of 2 to 3 interactions with the core active amino acid residues present on the target enzyme CYP- 17α-hydroxylase which can be used by multiple ways in reducing glucose thereby decrease the inflammatory reactions in PCOS.

INTRODUCTION: Polycystic ovary syndrome (PCOS) is a common and multifactorial disease associated with both endocrine and metabolic disorders. It affects approximately 4%–18% of all reproductive-aged women in the world. PCOS is characterized by hyperandrogenism and ovarian abnormalities, resulting from a disruption in the hypothalamic-pituitary-ovarian axis.

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Clinically, the main cause of reproductive and metabolic abnormalities in women with PCOS are hyperandrogenism and insulin resistance [1]. The etiology of PCOS is still unknown, although environmental, genetic, and hormonal factors are all thought to be important in its development.

PCOS is a common diagnosis in women presenting with anovulatory infertility and it affects 5–10% of women of reproductive age. Symptoms of PCOS related to ovulation manifest as amenorrhea or oligomenorrhea [2]. Polycystic ovaries are enlarged and contain a large number of immature follicles. There are also metabolic disorders associated with PCOS such as insulin resistance and hyperinsulinemia in women [3]. Recently, herbal remedies for PCOS have received attention as a form of lifestyle management in traditional Medicine clinics, in which the menstrual cycle and normal serum hormone levels can be recovered. Herbal remedies are known to be effective in reducing testosterone as well as increasing FSH and 17 β-estradiol levels and they have been shown to reduce polycystic ovaries and ovarian volume, improve insulin sensitivity, and normalize reproductive cycles [4]. The signs and symptoms of *Soothaga vayu or Karpavayu i.e.*, diseases that prevent pregnancy characterized by multiple ovarian cysts are called *Sinaippai neerkatigal, Soolaga neerkattigal, Karpapai neerkattigal* can be correlated with the Poly Cystic Ovarian Syndrome (PCOS) in which poly means many, cystic means water filled sac-like structure and when many are formed in the ovary called PCOS which is mentioned in theverses of *Thanvanthiri vaidhiya pagam* part -I, *Soothaga vayu* presented with the symptoms of diminished menstrual flow with abdominal pain, when the flow increases the pain is relieved and it may be preventing conception and there is low back pain and constipation will be there as per Siddha text [5, 6]. Molecular docking is a preclinical and *in-silico* approach that can be done before starting the pharmacological and clinical study which can be helpful one to assessing the future outcome whether positive or negative in the management of the particular disease. Even though Molecular docking studies are considered preliminary study, it is significant to other pre-clinical studies done by research scholars from various fields [7].

MATERIAL AND METHODS:

Source of Materials: The herbs were selected as per the Siddha classical textbook *Gunapadam mooligai vaguppu* with the indication for treating the gynecological problems. The following 9 herbs were includedby reviewing the previous research articles which showed their bio-active molecules such as *Caesalpinia Crista (Kazharchikkai), Asparagus racemosus (Thanner vittan kizhangu), Cinnamomum verum (Lavanga pattai), Anethum graveolens (Sathakuppai), Ruta chalapensis (Aruvatha), Ferula asafoetida (Perungayam), Citrulus colocynthis (Aattruthummattikkai), Erythrina varigata (Kalyana murukku) and Melia azedarach (Malai vembu)* [9]. Literature reviews of the selected herbs were noted in **Table 1** and the references of the selected herbs in the management of PCOS were noted in **Table 2.**

TABLE 1: LITERATURE REVIEW OF THE SELECTED HERBS

Sl. no.	The selected herbs in this molecular docking study with their botanical and tamil name	Bio-active components in the selected herbs	List of Siddha medicine prepartions by using the herb
1	*Caesalpinia Crista (Kazharchikkai)*	Sitosterol, steroidal saponins, hydrocarbons, fatty acids, caesalpins, phytosterols, bonducin, flavonoids, isoflavones, caesane, caesalpinianone and 6-O-methylcaesalpinianone, hematoxylin, stereochenol-A, 6-O-acetylloganic acid, 4-O-acetylloganic acid, 2-O-β-D-glucosyloxy-4-methoxybenzenepropanoic acid, diterpenoids, neocaesalpin-H, cordylane-A, caesalpinin-B, bonducellpin-E, caesalpinolide-A, bonducin, Cysteric acid, sassanefurano-diterpene, caesalpinin, caesaldekarins F and G, caesaldekarin A, Bonducellpins A, B, C, and D, steroidal saponin like Diosgenin, 6-o-methylcaesalpinianone, caesalpinianone, hematoxylol, 6-o-acetylloganic acid, 4-o-acetylloganic acid, and 2-o-glucosyloxy-4-methoxybenzenepropanoic acid [21]. Stemcontains peltogynoids, pulcherrimin, 6-methoxypulcherrimin, Natin, Bonducin (Bonducellin), Steroidal saponins, 14-Voucapanepentol derivative, Caesalpin (1-ketone 6, 7-diacetylcassane), vinaticole, caesalpin-F, myristic acid, vouncapen and cassaic acids, caesalpin-Y, Caesalpins-E, phytosterinin,α-caesalpinin 4-o-methyl myoinositol hydrate, bonducellpin E, F and G, amino acids like aspartic acid, lysine, leucine, glycine, L-alanine, histidine, isoleucine, arginine, threonine,	*Kazharchi chooranam, Kazharchi thylam, Kabada mathirai*

		phenylalanine, cysteine, valine, citrulline, tyrosine, glutamic acid, serine, proline, tryptophan, methionine, r-ethylidene glutamic acid, r-ethyl glutamic acid and r-methylene glutamic acid [9]	
2	*Asparagus racemosus (Thanner vittan kizhangu)*	Rutin, asparagan, Asparagamine A, 9,10-dihydro 1, 5 methoxy-Quercetin3 glucouronides, 8-methyl-2, 7-phenenthrenediol, Racemofuron, ncoumertans, Shatavarin V. ShatavarinI, II, III,IV (steroid glycosides), Immunoside, Sitosterol, Undecanyl cellanoate, Shatavari, 4,6-dihydroxy-2-0 (2-hydroxyl isobutyl) benzaldehyde, Secoisolariciresinol, diosgenin, Racemosol, 4-trihydro isoflavine 7-0-beta-D-glucopyranoside, Sterols, Alkaloid, Tannins, carbohydrates, Flavonoids, isoflavones, coumestans, prenylated. Lactones, Amino acids and rutin, Sarsasapogenin and kaempferol Thiophenes, thiazole, aldehyde, ketone, Gamma linoleinic acids, Undecanyl cetamoate,vanillin, asparagusic acid and methyl/ethyl esters, Diosgenin, quercetin-3-glucuronide, Quercetin, rutin, hyperoside, Racemoside A, B, and C and Sarsasapogenin [10]	*Thannervitttan kizhangu chooranam, Thaneervitan nei, Sathavari ilagam, Kanthaga rasayanam, Parangipattai rasayanam*
3	*Cinnamomum verum (Lavanga pattai)*	Camphene, β-pinene, Sabinene, Myrcene, 1,4-Cineole, Limonene, Cis-β-Ocimene, trans-β-Ocimene, p-Cymene, Linalool, γ-Terpinene, α-Terpineol, Piperitone, Geraniol, (E)-Cinnamaldehyde, (Z)-Cinnamaldehyde, Eugenol, (E)-Cinnamyl acetate, Eugenyl acetate and Benzyl benzoate[11]	*Lavangapattai chooranam, Thaneervittan nei, Vilvathy ilagam, Sarapunga vilvathy ilagam*
4	*Anethum graveolens (Sathakuppai)*	α-phellandrene, Dillether, β-phellandrene, Myristicin, p-Cymene, m-Cymene, α- pinene, β-pinene,Limonene, α-thujene, Apiol, Carvone, Transdihydrocarvone, Cis-dihydrocarvone, Dillapiol, R-Carvone, S-carvone, Anethole E,E-2,6dimethyl- 3,5octatetraene, ϒ-terpinene, Myrcene, Linaylacetate, Camphor, Dehydro-p-Cymene, Carveol, Piperitone, βMyrcene, Thujylalcohol, Grandisol, *neoiso*-dihydrocarveol, Dihydrocarveol, *cis*-Carveol, Sabinene, 2-Careneo-Isopropenyltolune, 1,2-diethoxyethane, Diplaniol, Linalool and Bis-1,2 Benzenedicarboxylicacid[12]	*Sathakuppai chooranam*
5	*Ruta chalapensis (Aruvatha)*	Bergapten, imperatorin, xanthotoxin, caffeic acid, chlorogenic acid, cinnamic acid, ellagic acid, gallic acid, gentizic acid, isoferulic acid, neochlorogenic acid, o-coumaric acid, protocatechuic acid, rosmarinic acid, salicylic acid, sinapic acid, syringic acid, apigenin, apigetrin, hyperoside, isoquercetin, isorhamnetin, kaempferol, luteolin, myricetin, populnin, robinin, quercetin, quercitrin, rhamnetin, rutoside, vitexin, umbelliferone, p-coumaric acid, vanillic acid, ferulic acid, p-hydroxybenzoic acid, coumarin, scopoletin, caftaric acid, cryptochlorogenic acid, isochlorogenic acid, catechin, epigallocatechin, epicatechin gallate, epicatechin, epigallocatechin gallate, cinaroside , osthenol, apigetrin, astragalin , avicularin, trifolin, isopimpinellin, isoimperatorin, daphnetin 7-methyl ether, rutaretin, daphnetin, osthenol, bergaptol, daphnetin dimethyl ether, γ-fagarine, and 7-isopentenyloxy-γ-fagarine [13]	*Aruvatha chooranam*
6	*Ferula asafoetida (Perungayam)*	α-Pinene, β-Pinene, Myrcene, Decane, Benzene, α-Phellandrene, Limonene, β-Phellandrene, (Z)-β-ocimene, (E)-β-ocimene, Triethylarsine, (Z)-1-propenyl sec-butyl disulfide, (E)-1-propenyl sec-butyl disulfide, Fenchyl acetate, Phenol, β-Bisabolene, y-bisabolene, α-bisabolene, Elemol, β-Dihydroagarofurane, Guai-1(5)-en-11-ol, β-Calarene and 8-Oxo-neoisolongifolene [14]	*Perungaya chooranam, Attaathi chooranam, Gunma kudori mezhugu, Perungaya kalavai mezhugu, Agathiyar kuzhambu, Kaya moosambara mathirai, Siddhathi ennai.*
7	*Citrulus colocynthis (Aattruthummat tikkai)*	Cucurbitacin-E,I,J,L,T, Coloside A, Colocynthitin, Colocynthin, Isovitexin and Citrullol [15]	*Kalingathi thylam Kalingathi mezhugu, Nava uppu mezhugu*
8	*Erythrina varigata*	3-eicosyne, Squalene, Gallic acid, Caffeic acid, Phytol and Butanoic acid [16]	*Kalyana murukuu poo kudineer*
9	*Melia azedarach*	Terpenoids and limonoids like l-Cinnamoyl-3-acetyl-11-hydroxy meliacarpin,l-Cinnamoyl-3-methacrylyl-l1-hydroxy meliacarpin,	*Malaivembathi chooranam, Kalingathi*

(Malai vembu)	Deacetylsalannin, α & β-Pinene, α-Terpinene & Terpineol, Kaempferol-3-O-β-rutinoside, Kaempferol-3-L-rhamno-D-glucoside and Rutin [17]	*thylam*

TABLE 2: REFERENCE OF THE SELECTED HERBS IN THE MANAGEMENT OF PCOS

Sl. no.	The selected herbs with their botanical and Tamil name	Animal model	Reference of the selected herbs in the management of PCOS
1	*Caesalpinia Crista (Kazharchikkai)*	Letrozole-Induced Polycystic Ovarian Syndrome in Prepubertal female Wistar albino rat Models[18] (aged 4-6 weeks weighing 180-230 g)	Improve the reproductive abnormalities, Normalize the ovulation, Reduces the menstrual irregularities, Histopathological changes associated with PCOS was restored, Normalize the hormone levels of FSH, and LH, also normalized the LH/FSH ratio. Reduces the testosterone level FSH, and LH, also normalized the LH/FSH ratio. Reduces the testosterone level
2	*Asparagus racemosus (Thanner vittan kizhangu)*	Fructose & Letrozole-Induced Prepubertal female Wistar albino rat Models[19] (6 week-old weighing 180-225 g) with regular estrus cyclicity	Increase in graffian follicles, Increased number of corpora lutea with a lower number of cystic follicles, Normal process of folliculogenesis and ovulation, Increase in FSH, estrogen, and progesterone, Decreasing LH and testosterone, Normalization of the hormonal level
3	*Cinnamomum verum (Lavanga pattai)*	DHEA induced Polycystic Ovarian Syndrome in Prepubertal female C57BL/6 mice[20] (aged 21 days weighing 10-15 g)	Improve the reproductive abnormalities, Normalize the ovulation, Reduces the menstrual irregularities, Histopathological changes associated with PCOS was restored
4	*Anethum graveolens (Sathakuppai)*	Letrozole-Induced Polycystic Ovarian Syndrome in Prepubertal female Wistar albino rat Models[21] (aged 5-6 weeks weighing 190-210 g)	Increased number of corpora lutea with a lower number of cystic follicles, Normal process of folliculogenesis and ovulation, Increase in FSH, estrogen, and progesterone, Increased estrous cycle duration, Induces infertility without any significant adverse effects on oocytes development
5	*Ruta chalapensis (Aruvatha)*	DHEA induced Polycystic Ovarian Syndrome in Prepubertal female C57BL/6 mice[22] (aged 18 -25 days weighing 12-15 g)	Improve the reproductive abnormalities , Increase in FSH, estrogen, and progesterone, Decreasing LH and testosterone, Normalize the ovulation, Reduces the menstrual irregularities
6	*Ferula asafoetida (Perungayam)*	Letrozole-Induced Polycystic Ovarian Syndrome in Prepubertal female Wistar albino rat Models[23] (aged 5-6 weeks weighing 190-210 g)	Increase in graffian follicles, Increased number of corpora lutea with a lower number of cystic follicles, Normal process of folliculogenesis and ovulation, Regulating and activating metabolic and ovarian cycle enzymes
7	*Citrulus colocynthis (Aattruthummattikkai)*	Estradiol valerate induced polycystic ovarian syndrome in prepubertal female wistar albino rat models[24] (weighing about 190 – 210 gm)	Histopathological changes associated with PCOS was restored, Normalize the hormone levels of FSH, and LH, also normalized the LH/FSH ratio. Reduces the testosterone level
8	*Erythrina varigata (Kalyana murukku)*	Letrozole-Induced Polycystic Ovarian Syndrome in Prepubertal female Wistar albino rat Models[25]	Reduces the menstrual irregularities, Estrogenic, anti-hyperlipidemic, antioxidant and hypoglycemic effects, Prevent ovarian cell dysfunction, Improving fertility.
9	*Melia azedarach (Malai vembu)*	Estradiol valerate induced polycystic ovarian syndrome in prepubertal female wistar albino rat models[26] (weighing about 190 – 210 gm)	Increase in graffian follicles, Increased number of corpora lutea with a lower number of cystic follicle, Increase in FSH, estrogen, and progesterone, Normalize ovarian cycle through reducing the androgen concentration

TABLE 3: LIST OF SELECTED HERBS IN THIS STUDY WITH THEIRPHYTOCHEMICALS AND ITS REFERENCE

Sl. no.	Herbs	Phytochemicals	References
1	*Caesalpinia crista*	Campesterol	Sasidharan S, Kp S, Bhaumik A, Kanti Das S, Nair J H. Administration of Caesalpinia bonduc Seed Extracts Ameliorates Testosterone-Induced Benign

			Prostatic Hyperplasia (BPH) in Male Wistar Rats. Res Rep Urol. 2022 May 26;14:225-239.
2	*Asparagus racemosus*	Diosgenin	Negi JS, Singh P, Joshi GP, Rawat MS, Bisht VK. Chemical constituents of Asparagus. Pharmacogn Rev. 2010;4(8):215-220.
3	*Cinnamomum verum*	Cinnamic acid	Singh N, Rao AS, Nandal A, Kumar S, Yadav SS, Ganaie SA, Narasimhan B. Phytochemical and pharmacological review of Cinnamomum verum J. Presl-a versatile spice used in food and nutrition. Food Chem. 2021 Feb 15; 338:127773.
4	*Anethum graveolens*	Anethole	Jana, S., & Shekhawat, G. S. (2010). Anethum graveolens: An Indian traditional medicinal herb and spice. Pharmacognosy reviews, 4(8), 179–184.
5	*Ruta chalapensis*	Kaempferol	Alotaibi, S. M., Saleem, M. S., & Al-Humaidi, J. G. (2018). Phytochemical contents and biological evaluation of Ruta chalepennsis L. growing in Saudi Arabia. Saudi pharmaceutical journal: SPJ: the official publication of the Saudi Pharmaceutical Society, 26(4), 504–508.
6	*Ferula asafoetida*	Ferulic acid	Poonam Mahendra, Shradha Bisht. Ferula asafoetida: Traditional uses and pharmacological activity. Pharmacognosy Reviews.2012;6(12):141-146
7	*Citrulus colocynthis*	Myricetin	Benariba, N., Djaziri, R., Bellakhdar, W., Belkacem, N., Kadiata, M., Malaisse, W. J., & Sener, A. (2013). Phytochemical screening and free radical scavenging activity of Citrullus colocynthis seeds extracts. Asian Pacific journal of tropical biomedicine, 3(1), 35–40.
8	*Erythrina varigata*	Erysovine	Kumar, A., Lingadurai, S., Jain, A., & Barman, N. R. (2010). Erythrina variegata Linn: A review on morphology, phytochemistry, and pharmacological aspects. Pharmacognosy reviews, 4(8), 147–152. https://doi.org/10.4103/0973-7847.70908
9	*Melia azedarach*	β-Sitosterol Rutin	Shrestha SS, Ferrarese I, Sut S, Zengin G, Grana S, Ak G, Pant DR, Dall'Acqua S, Rajbhandary S. Phytochemical Investigations and In Vitro Bioactivity Screening on Melia azedarach L. Leaves Extract from Nepal. Chem Biodivers. 2021 May;18(5):e2001070. doi: 10.1002/cbdv.202001070. Epub 2021 Mar 30. PMID: 33682999.

Molecular Docking: Molecular Docking analysis was performed with a commonly well-known established Auto dock tool which is a very convenient and excellent screening tool for identifying binding energy between the 3D structures of each ligand and target proteins. The target protein PDB ID: 2J7U was selected, a Gridfree docking was performed, and the binding energies of each ligand were found [27].

PDB	Name of the Target
3RUK	CYP- 17α-hydroxylase

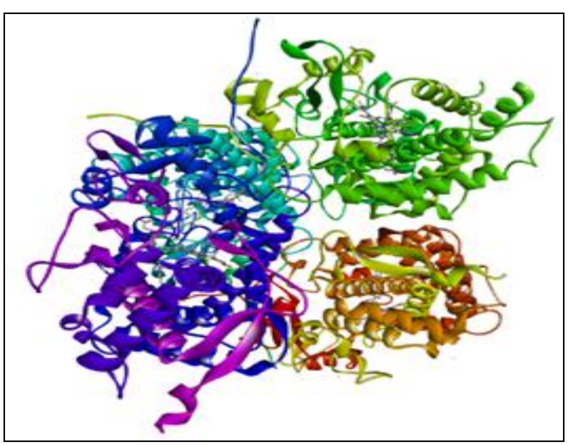


FIG. 1: 3D- STRUCTURE OF CYP- 17A-HYDROXYLASE (PDB) - 3RUK

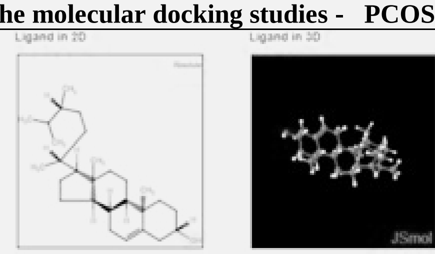
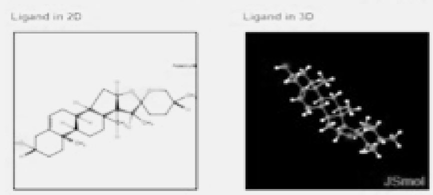
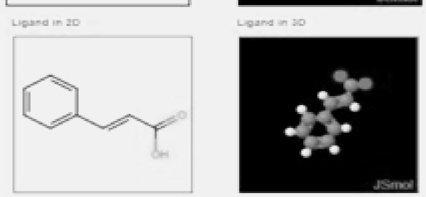
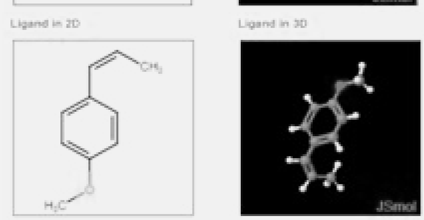
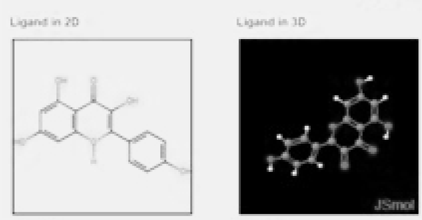
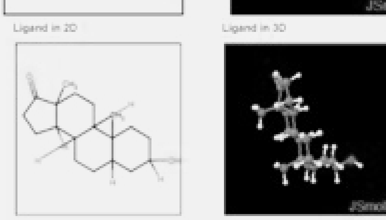
Receptor Structure: The crystalline 3D structure of the target enzyme CYP- 17α-hydroxylase with PDB – 3RUK in **Fig. 1** was retrieved from the protein data bank and protein clean-up process was done and essential missing hydrogen atoms were added. Different orientation of the lead molecules concerning the target protein was evaluated by the Autodock program and the best dock pose was selected based on the interaction study analysis [28].

Objective of the Molecular Docking: The binding of phytocomponents with the core amino acids (Ala105, Arg239 and Asn202) of the target by forming a hydrogen bond will hinder the function of the enzyme CYP- 17α-hydroxylase with PDB – 3RUK. These amino acid residues are functionally responsible for the binding of substrate and inhibitors. Thereby phytocomponents that inhibit the target enzyme CYP- 17α-hydroxylase may act as a potential therapeutic agent for the management of PCOS and can be assessed by this method.

Methodology [29]: Docking calculations were carried out for retrieved phytocomponents against the target enzyme CYP- 17α-hydroxylase. Essential hydrogen atoms, Kollman united atom type charges, and solvation parameters were added with the aid of AutoDock tools (*Morris, Goodsell et al., 1998*). Affinity (grid) maps of ×× Å grid points and 0.375 Å spacing were generated using the Autogrid program (*Morris, Goodsell et al., 1998*). AutoDock 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*). The 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 Å, and quaternion and torsion steps of 5 were applied.

Observation and Inference:

TABLE 4: 2D AND 3D STRUCTURE OF SELECTED LIGANDS WITH ACTIVE PHYTO-COMPONENTS IN EACH HERBS USED IN THE MOLECULAR DOCKING STUDIES - PCOS AMELIORATION ACTIVITY

S. no.	Compound name	2D and 3D Structure of Selected Ligands with active phyto-components in Each herbs used in the molecular docking studies - PCOS Amelioration Activity
1	Campesterol	
2	Diosgenin	
3	Cinnamic acid	
4	Anethole	
5	Kaempferol	
6	Ferulic acid	

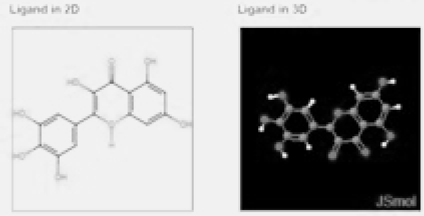
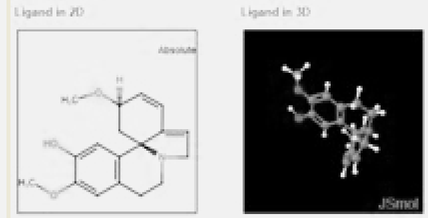
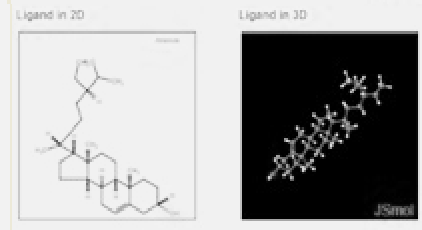
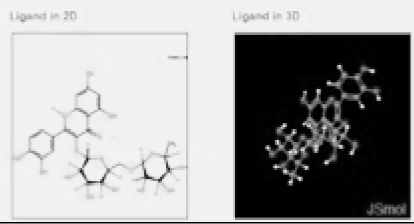
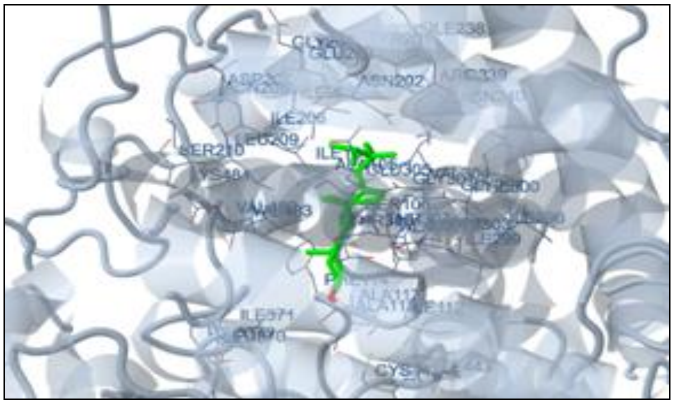
7	Myricetin	
8	Erysovine	
9	β-Sitosterol	
10	Rutin	

TABLE 5: LIGAND PROPERTIES OF THE COMPOUNDS SELECTED FOR MOLECULAR DOCKING ANALYSIS

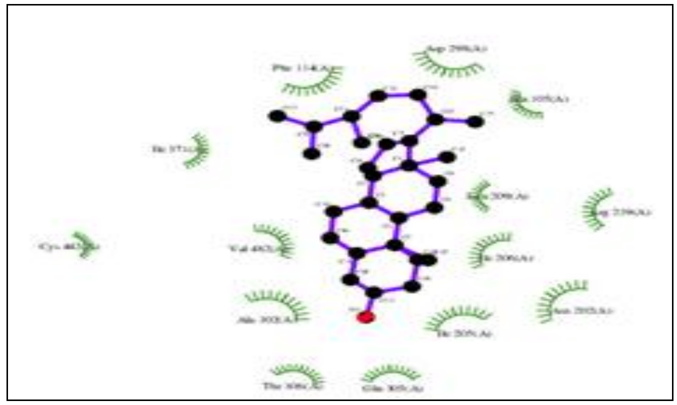
Sl. no.	Compound	Molar weight g/mol	Molecular Formula	H Bond Donor	H Bond Acceptor	Rotatable bonds
1	Campesterol	400.7 g/mol	$C_{28}H_{48}O$	1	1	5
2	Diosgenin	414.6 g/mol	$C_{27}H_{42}O_3$	1	3	0
3	Cinnamic acid	148.16 g/mol	$C_9H_8O_2$	1	2	2
4	Anethole	148.20 g/mol	$C_{10}H_{12}O$	0	1	2
5	Kaempferol	286.239 g/mol	$C_{15}H_{10}O_6$	4	6	1
6	Ferulic acid	194.186 g/mol	$C_{10}H_{10}O_4$	2	4	3
7	Myricetin	318.237g/mol	$C_{15}H_{10}O_8$	6	8	1
8	Erysovine	299.4 g/mol	$C_{18}H_{21}NO_3$	1	4	2
9	β-Sitosterol	414.7g/mol	$C_{29}H_{50}O$	1	1	6
10	Rutin	610.5 g/mol	$C_{27}H_{30}O_{16}$	10	16	6

TABLE 6: SUMMARY OF THE MOLECULAR DOCKING STUDIES OF COMPOUNDS AGAINST CYP- 17α-HYDROXYLASE (PDB) - 3RUK

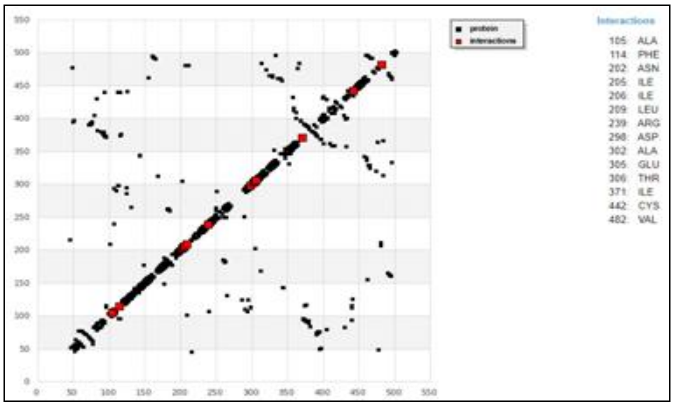
Sl. no.	Compounds	Binding Free energy Kcal/mol	Inhibition constant Ki µM	Electrostatic energy Kcal/mol	Intermolecular energy Kcal/mol	Total Interaction Surface
1	Campesterol	-12.21	1.11 nM	-0.07	-12.75	645.45
2	Diosgenin	-11.08	7.51 nM	-0.08	-11.38	668.143
3	Cinnamic acid	-5.24	144.63 uM	-0.36	-5.83	352.71
4	Anethole	-5.29	131.55 uM	-0.02	-5.92	377.416
5	Kaempferol	-6.14	31.32 uM	-0.22	-6.50	488.26
6	Ferulic acid	-5.24	145.17 uM	-0.45	-5.63	406.324
7	Myricetin	-7.05	6.83 uM	-0.18	-6.33	506.247
8	Erysovine	-8.59	507.85 nM	-0.02	-8.94	526.698
9	β-Sitosterol	-12.68	507.82 pM	-0.12	-14.30	715.992
10	Rutin	-6.38	20.98 uM	-0.58	-6.27	730.585



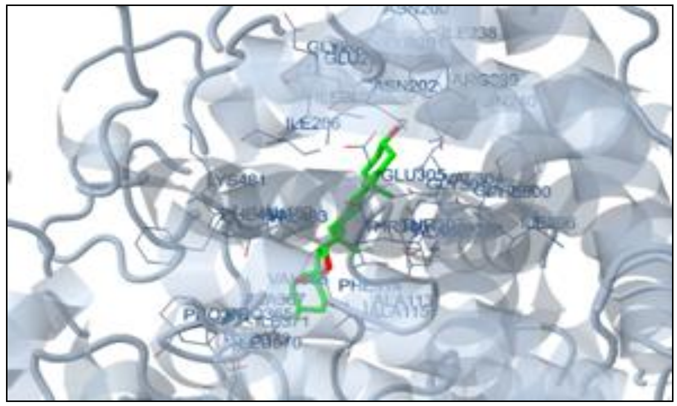
DOCKING POSE CAMPESTEROL WITH CYP- 17A-HYDROXYLASE (PDB) - 3RUK



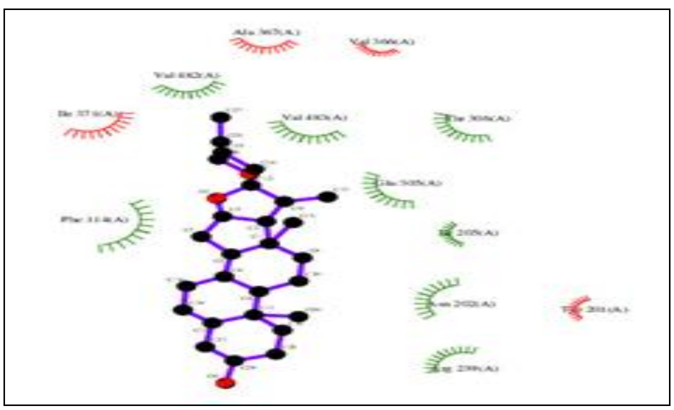
CAMPESTEROL WITH TARGET 2D INTERACTION PLOT ANALYSIS



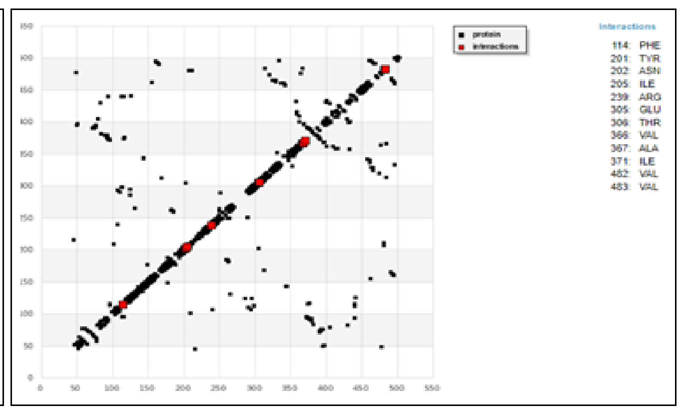
CAMPESTEROL WITH TARGET HYDROGEN BOND PLOTTING WITH CORE AMINO ACID ANALYSIS



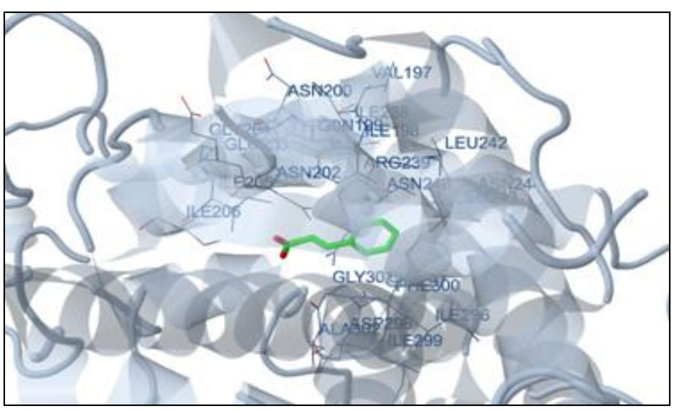
DOCKING POSE DIOSGENIN WITH CYP- 17A-HYDROXYLASE (PDB) - 3RUK



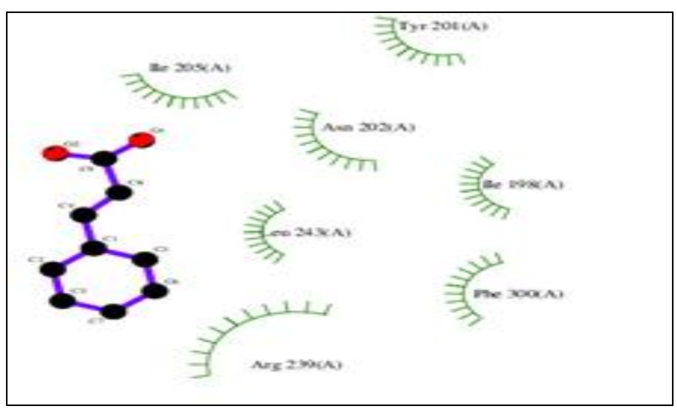
DIOSGENIN WITH TARGET 2D INTERACTION PLOT ANALYSIS



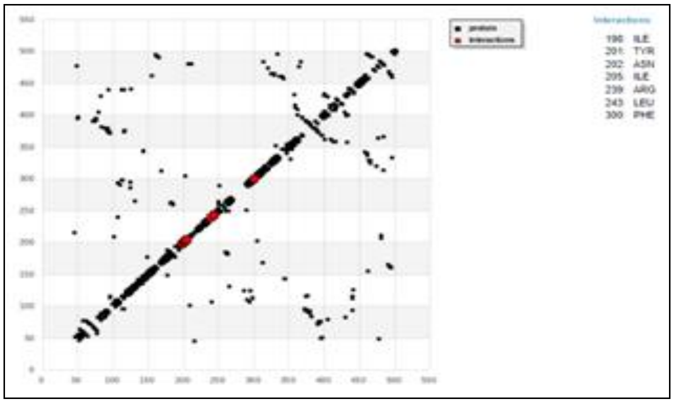
DIOSGENIN WITH TARGET HYDROGEN BOND PLOTTING WITH CORE AMINO ACID ANALYSIS



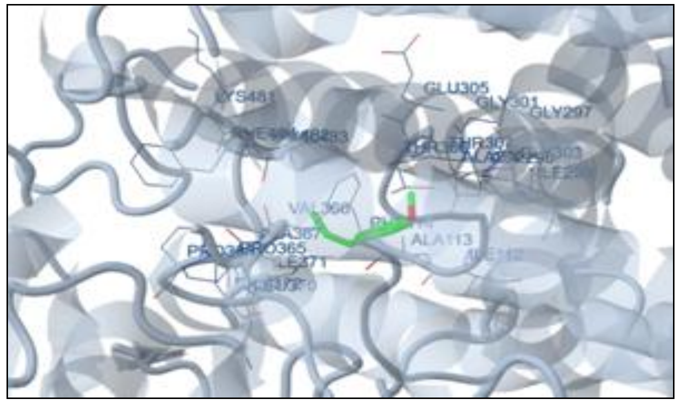
DOCKING POSE CINNAMIC ACID WITH CYP- 17A-HYDROXYLASE (PDB) - 3RUK



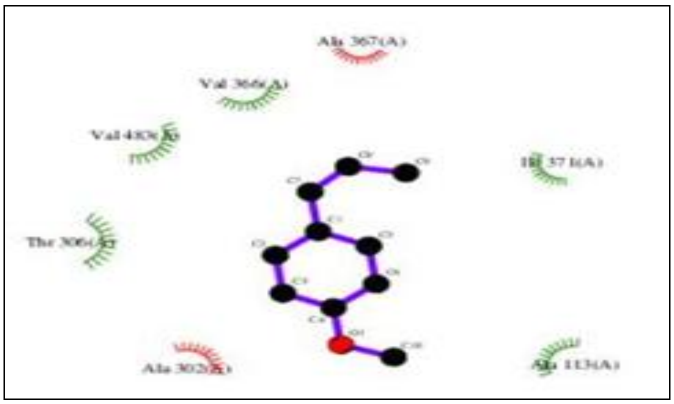
CINNAMIC ACID WITH TARGET 2D INTERACTION PLOT ANALYSIS



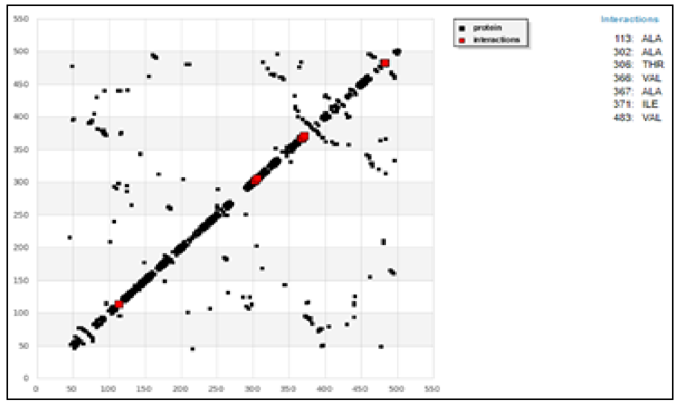
CINNAMIC ACID WITH TARGET HYDROGEN BOND PLOTTING WITH CORE AMINO ACID ANALYSIS



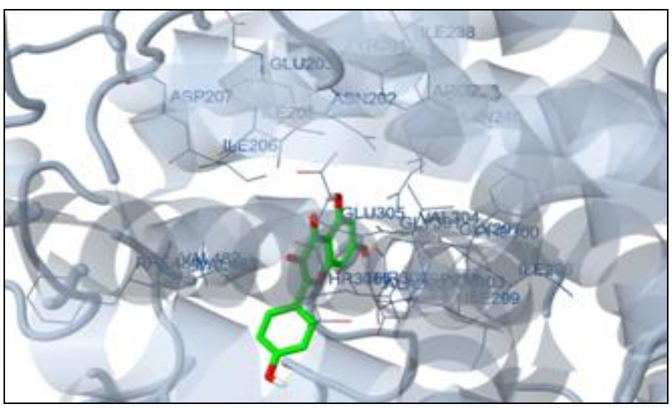
DOCKING POSE ANETHOLE WITH CYP- 17A-HYDROXYLASE (PDB) - 3RUK



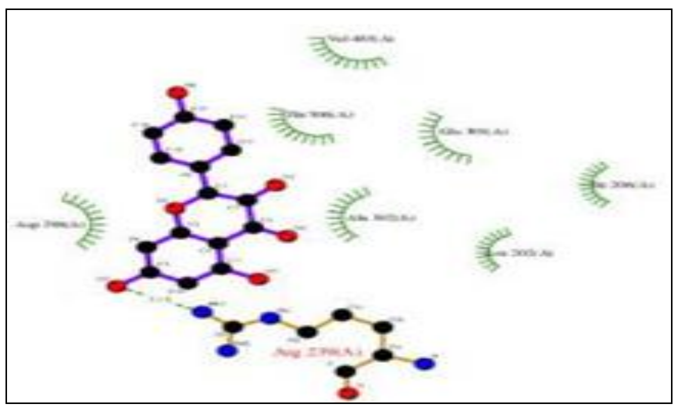
ANETHOLE WITH TARGET - 2D INTERACTION PLOT ANALYSIS



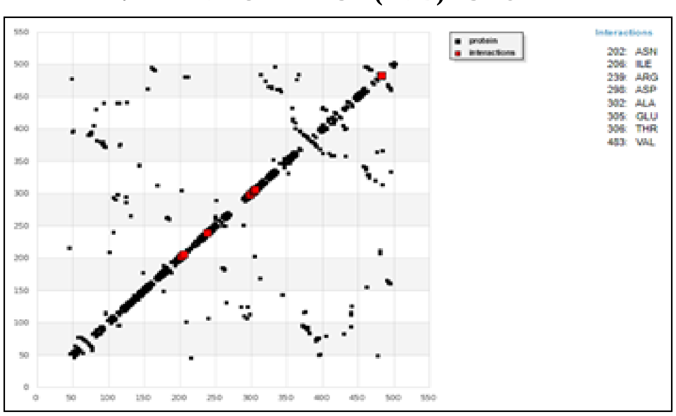
ANETHOLE WITH TARGET - HYDROGEN BOND PLOTTING WITH CORE AMINO ACID ANALYSIS



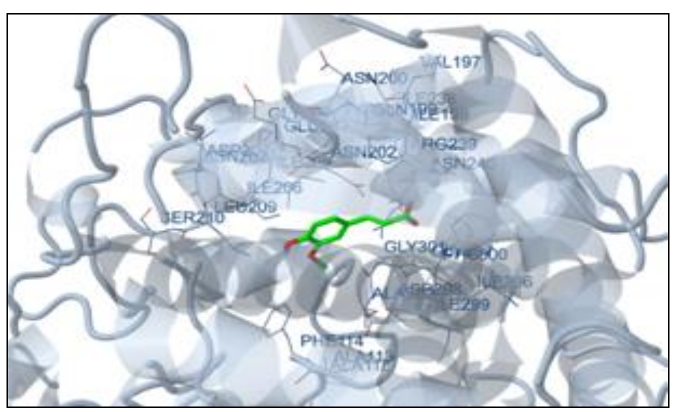
DOCKING POSE KAEMOFEROL WITH CYP-17A-HYDROXYLASE (PDB) - 3RUK



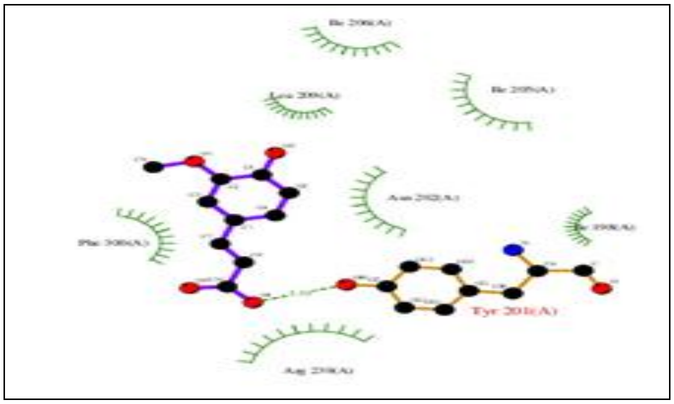
KAEMOFEROL WITH TARGET - 2D INTERACTION PLOT ANALYSIS



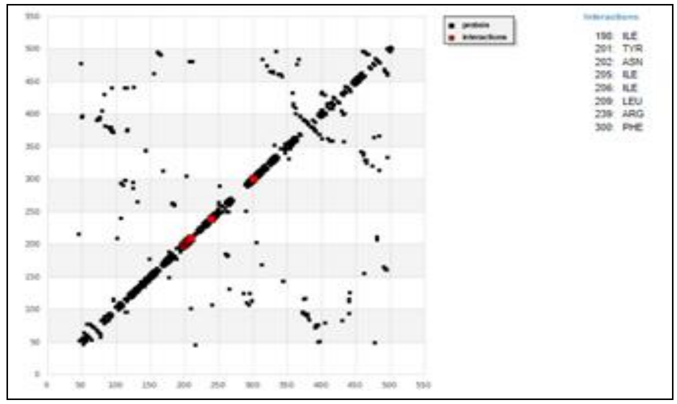
KAEMOFEROL WITH TARGET-HYDROGEN BOND PLOTTING WITH CORE AMINO ACID ANALYSIS



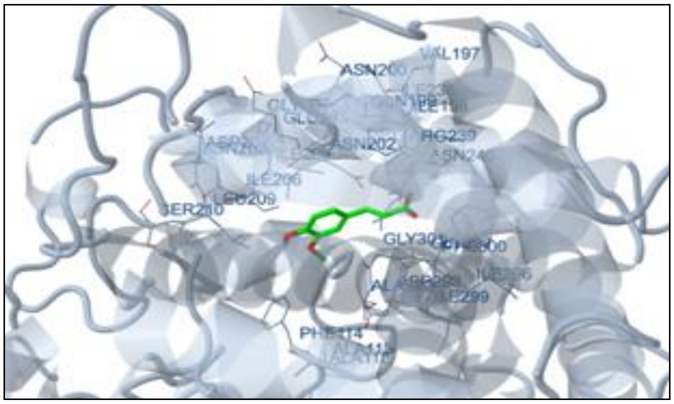
DOCKING POSE FERULIC ACID WITH CYP- 17A-HYDROXYLASE (PDB) - 3RUK



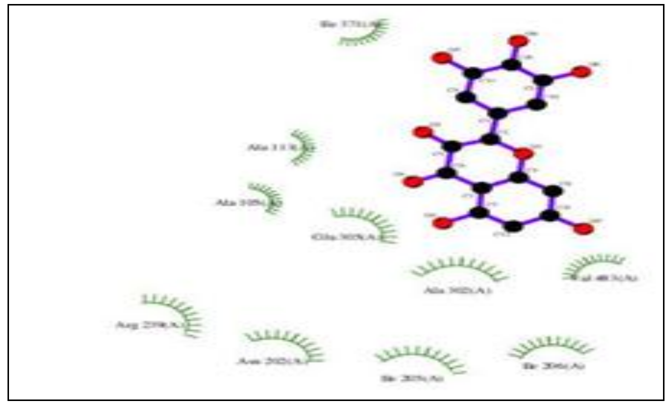
FERULIC ACID WITH TARGET - 2D INTERACTION PLOT ANALYSIS



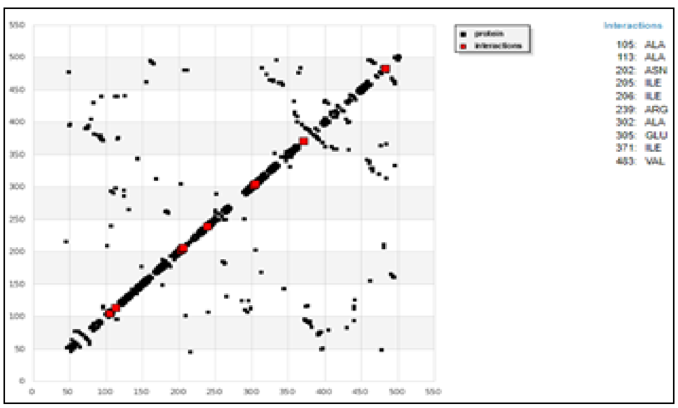
FERULIC ACID WITH TARGET - HYDROGEN BOND PLOTTING WITH CORE AMINO ACID ANALYSIS



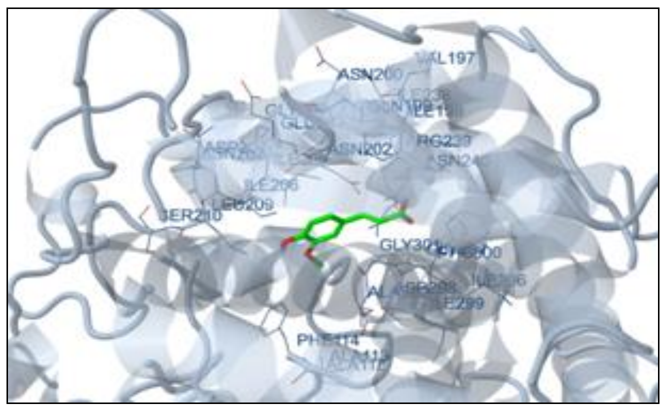
DOCKING POSE MYRICETIN WITH CYP-17A-HYDROXYLASE (PDB) - 3RUK



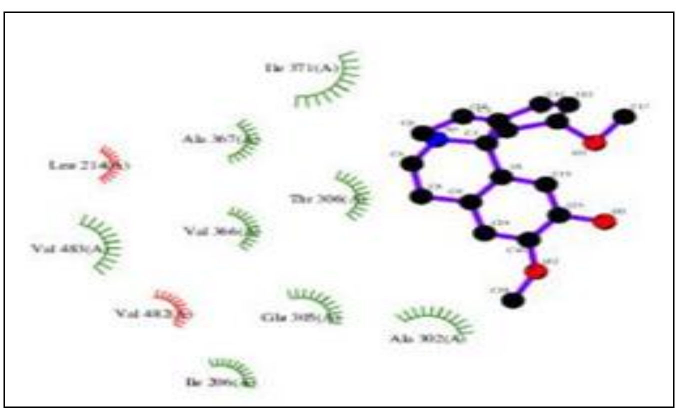
MYRICETIN WITH TARGET - 2D INTERACTION PLOT ANALYSIS



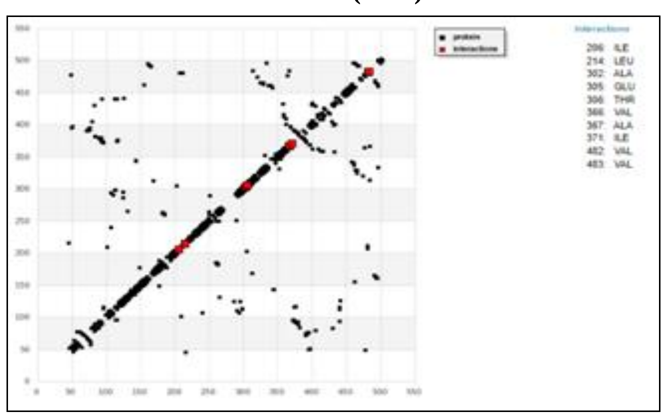
MYRICETIN WITH TARGET -HYDROGEN BOND PLOTTING WITH CORE AMINO ACID ANALYSIS



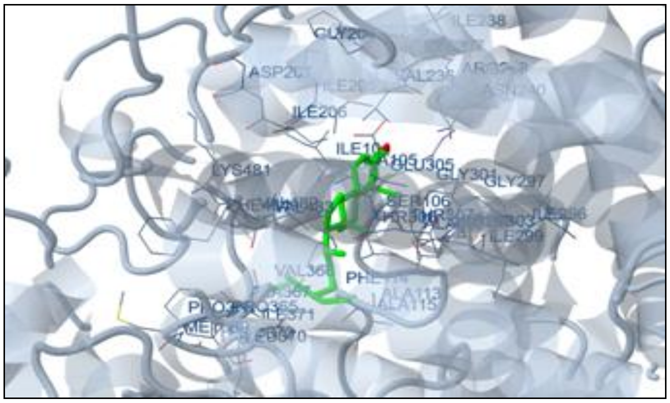
DOCKING POSE ERYSOVINE WITH CYP- 17A-HYDROXYLASE (PDB) - 3RUK



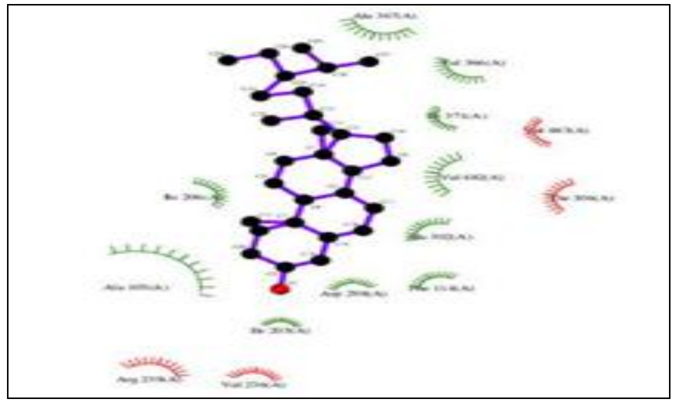
ERYSOVINE WITH TARGET - 2D INTERACTION PLOT ANALYSIS



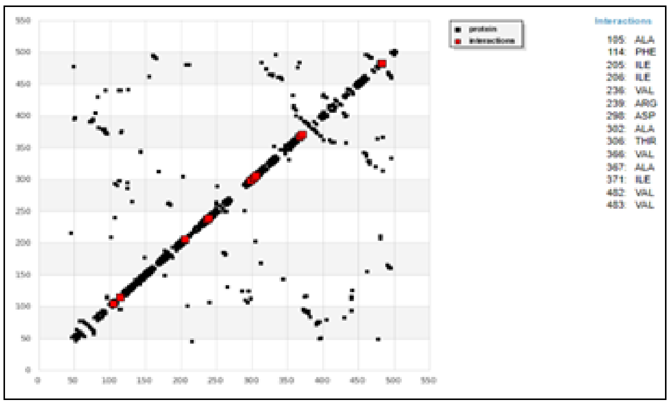
ERYSOVINE WITH TARGET - HYDROGEN BOND PLOTTING WITH CORE AMINO ACID ANALYSIS



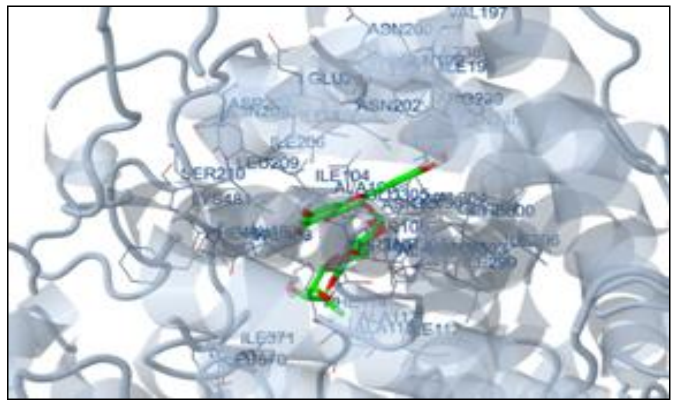
DOCKING POSE β-SITOSTEROL WITH CYP-17A-HYDROXYLASE (PDB) - 3RUK



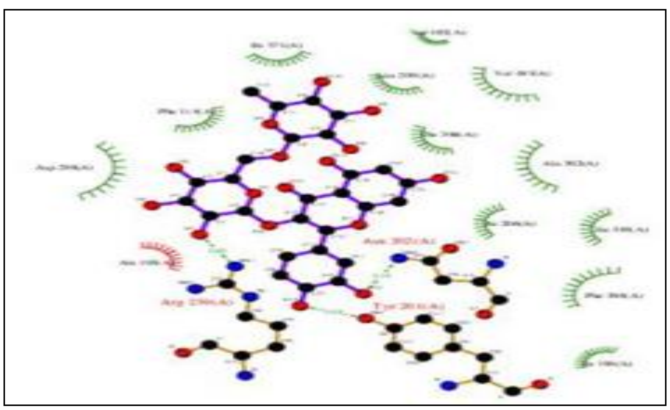
β-SITOSTEROL WITH TARGET - 2D INTERACTION PLOT ANALYSIS



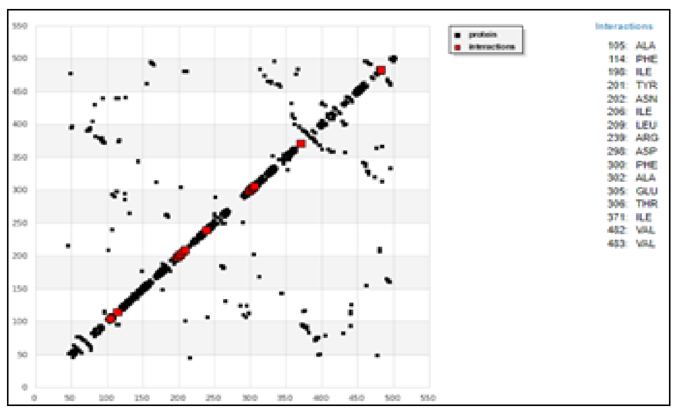
β-SITOSTEROL WITH TARGET -HYDROGEN BOND PLOTTING WITH CORE AMINO ACID ANALYSIS



DOCKING POSE RUTIN WITH CYP- 17α-HYDROXYLASE (PDB) - 3RUK



RUTIN WITH TARGET - 2D INTERACTION PLOT ANALYSIS



RUTIN WITH TARGET - HYDROGEN BOND PLOTTING WITH CORE AMINO ACID ANALYSIS

TABLE 7: AMINO ACID RESIDUE INTERACTION OF LEAD AND STANDARD AGAINST CYP- 17α-HYDROXYLASE (PDB) - 3RUK

Compounds	Interaction	Amino acid Residue												
Campesterol	3	105 ALA	114 PHE	202 ASN	205 ILE	206 ILE	239 ARG	298 ASP	302 ALA	305 GLU	306 THR	371 ILE	442 CYS	482 VAL
Diosgenin	2	114 PHE	201 TYR	202 ASN	205 ILE	239 ARG	305 GLU	306 THR	366 VAL	367 ALA	371 ILE	482 VAL	483 VAL	
Cinnamic acid	2	198 ILE	201 TYR	202 ASN	205 ILE	239 ARG	243 LEU	300 PHE						
Anethole	0	113	302	306	366	367	371							

		ALA	ALA	THR	VAL	ALA	ILE								
Kaempferol	2	202 ASN	206 ILE	239 ARG	298 ASP	302 ALA	305 GLU	306 THR	483 VAL						
Ferulic acid	2	198 ILE	201 TYR	202 ASN	205 ILE	206 ILE	209 LEU	239 ARG	300 PHE						
Myricetin	3	105 ALA	113 ALA	202 ASN	205 ILE	206 ILE	239 ARG	302 ALA	305 GLU	371 ILE	483 VAL				
Erysovine	0	206 ILE	214 LEU	302 ALA	305 GLU	306 THR	366 VAL	367 ALA	371 ILE	482 VAL	483 VAL				
β-Sitosterol	2	105 ALA	114 PHE	205 ILE	206 ILE	209 LEU	236 VAL	239 ARG	298 ASP	302 ALA	306 THR	366 VAL	367 ALA	371 ILE	482 VAL
Rutin	3	105 ALA	114 PHE	198 ILE	201 TYR	202 ASN	206 ILE	209 LEU	239 ARG	298 ASP	300 PHE	302 ALA	305 GLU	306 THR	371 ILE

Observations of Amino acid Residue Interaction of Lead and Standard against the target enzyme CYP- 17α-hydroxylase (PDB) - 3RUK: From the **Table 4, 5, 6** and **7** and **Fig. 2,** a total of 10 bioactive lead compounds were found and the structure of the components from the selected herbs was used in this Molecular docking. From the reported data of the herbs, the phytochemicals such as Campesterol, Diosgenin, Cinnamic acid, Kaempferol, Ferulic acid, Myricetin, β-Sitosterol and Rutin reveal a maximum of 2 to 3 interactions with the core active amino acid residues present on the target enzyme CYP- 17α-hydroxylase.

RESULTS AND DISCUSSION: Based on the results of the computational analysis it was concluded that the bio-active compounds like Campesterol, Diosgenin, Cinnamic acid, Kaempferol, Ferulic acid, Myricetin, β-Sitosterol and Rutin present in the selected herbs possess significant binding against the target enzyme CYP-17α-hydroxylase by interacting with active amino acids. Hence these phytocomponents which inhibit the target enzyme CYP-17α-hydroxylase might act as a potential therapeutic the agent for management of PCOS [30].

CONCLUSION: Based on the findings of docking score values we can strongly suggest these active compounds present in the selected herbs for the better management ofPCOS. Further preclinical and clinical trials have to be conducted to know the exact mechanism and efficacy of the selected herbsin PCOS management.

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CONFLICTS OF INTEREST: The author hereby declares that he has no conflicts of interest to disclose.

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