Phytochemical-based Inhibition of 5-Alpha Reductase Types I and II: A Computational Method for Treating Androgenic Alopecia

Thesis Submitted in Partial Fulfilment of
The Requirements for The Degree of

Master of Science in Biotechnology

by

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I, **Rounak Tailor** hereby certify that the work which is being presented in the thesis entitled "**Phytochemical-based Inhibition of 5-Alpha Reductase Types I and II: A Computational Method for Treating Androgenic Alopecia**" in partial fulfilment of the requirements for the award of the Degree of Master of Science in Biotechnology, submitted in the Department of Biotechnology, Delhi Technological University is an authentic record of my own work carried out during the period from January, 2025 to May, 2025 under the supervision of **Prof. Jai Gopal Sharma**, Department of Biotechnology, Delhi Technological University, Delhi.

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Certified that **Rounak Tailor** (23/MSCBIO/42) has carried out her research work presented in this thesis entitled "**Phytochemical-based Inhibition of 5-Alpha Reductase Types I and II: A Computational Method for Treating Androgenic Alopecia**" for the award of Master of Science from Department of Biotechnology, Delhi Technological University, Delhi, under our supervision. The thesis embodies results of original work, and studies are carried out by the student herself, and the contents of the thesis do not form the basis for the award of any other degree to the candidate or anybody else from this or any other University/Institution.

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Phytochemical-based Inhibition of 5-Alpha Reductase Types I and II: A Computational Method for Treating Androgenic Alopecia

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ABSTRACT

Androgenic alopecia is a disorder affecting both males and females and causes progressive loss of hair, causing a person to become bald. Androgenic alopecia is caused by hyperactivity of the enzyme 5-alpha reductase, which causes it to metabolize more of the androgen testosterone. This increases the metabolism of testosterone, resulting in the formation of more dihydrotestosterone, which is a more potent androgen than testosterone. This dihydrotestosterone binds to the androgen receptors of hair follicles, causing a change in the shape of the receptor. This dihydrotestosterone binds to the androgen receptors of hair follicles, causing a change in the shape of the receptor. Due to this signalling pathway, the hair growth cycle is affected. As a result, the Anagen growth phase gets shortened and the Telogen phase gets longer. Due to the shortening of the Anagen phases, hair growth does not take place, and the follicles shrink, resulting in baldness. Currently, the FDA-approved drug Finasteride is used to treat androgenic alopecia, which inhibits the enzyme 5-alpha reductase and blocks the formation of dihydrotestosterone. But continuous use of Finasteride also shows side effects in the body, such as a decrease in libido, erectile dysfunction, etc. Hence, there is a need for a drug that has minimal side effects and is effective for androgenic alopecia. The two types of 5-alpha reductase, 5-alpha reductase type I and type II, are primarily responsible for androgenic alopecia. Hence, in this study, we inhibit both 5-alpha reductase type I and type II with the help of natural compounds. First of all, we obtain phytochemicals from different medicinal plants, later we do their molecular docking and ADMET analysis, and search for a drug-like compound. In this study, we found that the phytochemical Kaempferol obtained from *Allium cepa* shows higher binding affinity with both 5-alpha reductase enzymes than the control drug (Finasteride). The binding affinity of the phytochemical kaempferol with both 5-alpha reductases was found to be -9.2 kcal/mol. Moreover, this compound also follows all the ADME&T parameters, which makes it a better drug candidate.

Keywords: Androgenic alopecia, 5-Alpha Reductase, Testosterone, DHT, Finasteride, Kaempferol, Computer Aided Drug Design.

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Rounak Tailor

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LIST OF ABBREVIATIONS AND SYMBOLS

ns	Nanosecond
ps	Picosecond
nm	Nanometre
Å	Angstrom
%	Percentage
AGA	Androgenic Alopecia
5AR1	5-Alpha Reductase Type 1
5AR2	5-Alpha Reductase Type II
DHT	Dihydrotestosterone
PDB	Protein Data Bank
ADME	Absorption, distribution, metabolism, and excretion
ADMET	Absorption, distribution, metabolism, excretion, and toxicity

CHAPTER 1: INTRODUCTION

Pattern baldness, another name for androgenic alopecia, is a prevalent kind of gradual hair loss that affects both men and women. Genetic and hormonal factors mainly cause androgenic alopecia. After puberty, androgenic alopecia is characterized by increasing loss of the scalp's terminal hairs in both boys and girls [1]. The main feature of AGA is that it causes progressive miniaturization of hair follicles, which causes the terminal hairs to transform into vellus continuously. In androgenic alopecia, this change occurs due to changes in hair cycle dynamics. In androgenic alopecia, the duration of the hair cycle's anagen phase decreases while the duration of the telogen phase increases. Anagen phase duration determines hair length since the anagen phase becomes short in androgenic alopecia; hence, new anagen hairs remain short, and eventually, baldness progresses [2], [3]. If the father has androgenic alopecia, the risk of his sons having androgenic alopecia increases significantly [4].

The body uses intracellular signalling pathways to carry out the function of androgens, which are essential hormones for growth and development. The main and most active androgen in a man's body is testosterone [5]. Testosterone is converted to dihydrotestosterone (DHT) by the enzyme 5-alpha reductase, which causes androgenic alopecia (AGA). DHT shrinks the hair follicles and changes the terminal hairs into vellus hairs [6]. DHT alters the protein structure of hair follicles' androgen receptors, starting a signaling cascade that modifies the hair growth cycle [7]. Occipital hairs are not much affected by androgenic alopecia because androgen receptors are methylated, which prevents miniaturization of hairs [8].

Both 5-alpha reductase type I and II enzymes are NADPH-dependent and membrane-associated. 5AR1 enzyme is composed of 259 and 5AR2 enzyme is composed of 254 amino acids. These enzymes contain a higher number of hydrophobic amino acid residues, due to which they get embedded in the lipid bilayer [9]. The 5AR1 enzyme is mainly found in the scalp, skin, and liver, while the 5AR2 enzyme is found in hair follicles and the prostate.

Oral finasteride and topical minoxidil are commonly used to treat androgenic alopecia. Finasteride is an FDA-approved drug that is used to treat androgenic alopecia. Finasteride acts as a competitive and specific inhibitor of 5-alpha reductase. Minoxidil is a vasodilator drug used to treat hypertension, but it also promotes hair growth by increasing blood circulation in the scalp. Combined therapy of minoxidil and finasteride gives a better result than the use of one drug alone [10]. But long-term use of these drugs also has adverse effects on the body. Long-term use of finasteride can cause scalp itching, redness, irritation, contact dermatitis, and sexual dysfunction [11]. Long-term use of minoxidil can cause headaches, allergies, and excessive hair growth [12].

So, considering these side effects, there is a need for a good drug that has fewer side effects and is effective so that these drugs can be replaced for the treatment of androgenic alopecia. Natural ingredients may be considered a safe drug candidate for treating hair loss. Plant-based drugs have been used a lot in recent years as they have fewer side effects than synthetic drugs. Currently, different bioactive ingredients, such as caffeine and capsaicin, have been extracted from fungi and plants for hair growth.

The main objective of this study is to find an effective phytochemical that inhibits both 5-alpha reductase type I and type II and blocks DHT formation. At the same time, consumption of this phytochemical has very minimal side effects in the body, and this phytochemical can replace the FDA-approved drug finasteride.

CHAPTER 2: REVIEW OF LITERATURE

2.1. Androgenic Alopecia

Androgenic alopecia is a scalp-related disorder in which there is progressive loss of hair, and a person becomes partially or completely bald. Pattern hair loss, androgenic alopecia, is seen in both males and females [13]. Androgenic alopecia occurs in both males and females in different types and at different rates. Hair loss in androgenic alopecia is a polygenetic condition that depends mainly on age and location of the scalp. In males, hair loss is most commonly seen in the hairs of the male vertex and temporal regions, while the occipital hair is not much affected. An imbalance in the hair development cycle, where the duration of the telogen phase grows and the duration of the anagen phase progressively decreases, is the primary cause of androgenic alopecia, resulting in terminal hairs changing into vellus [1]. The length of hair is determined by its anagen growth phase, in androgenic alopecia, the anagen phase becomes short, hence, hair growth stops, and baldness starts appearing [14]. About 80% of total baldness is caused by androgenic alopecia, which largely depends on genetic factors [15].

Three primary phases make up the hair development cycle: anagen (growing), catagen (transition), and telogen (resting). The most important stage is the anagen phase, during which the majority of epithelial hair follicles multiply and the hair shaft develops [15]. Club hairs, which are easily extracted from the follicle by hair washing and combing, are formed when the hair shaft changes during the telogen phase [15]. There are nine times as many anagen and telogen hairs on the scalp as telogen hairs, which can last anywhere from two to seven years and up to 100 days, respectively [16].

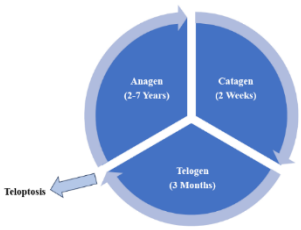


Fig. 2.1: Hair Growth Cycle.

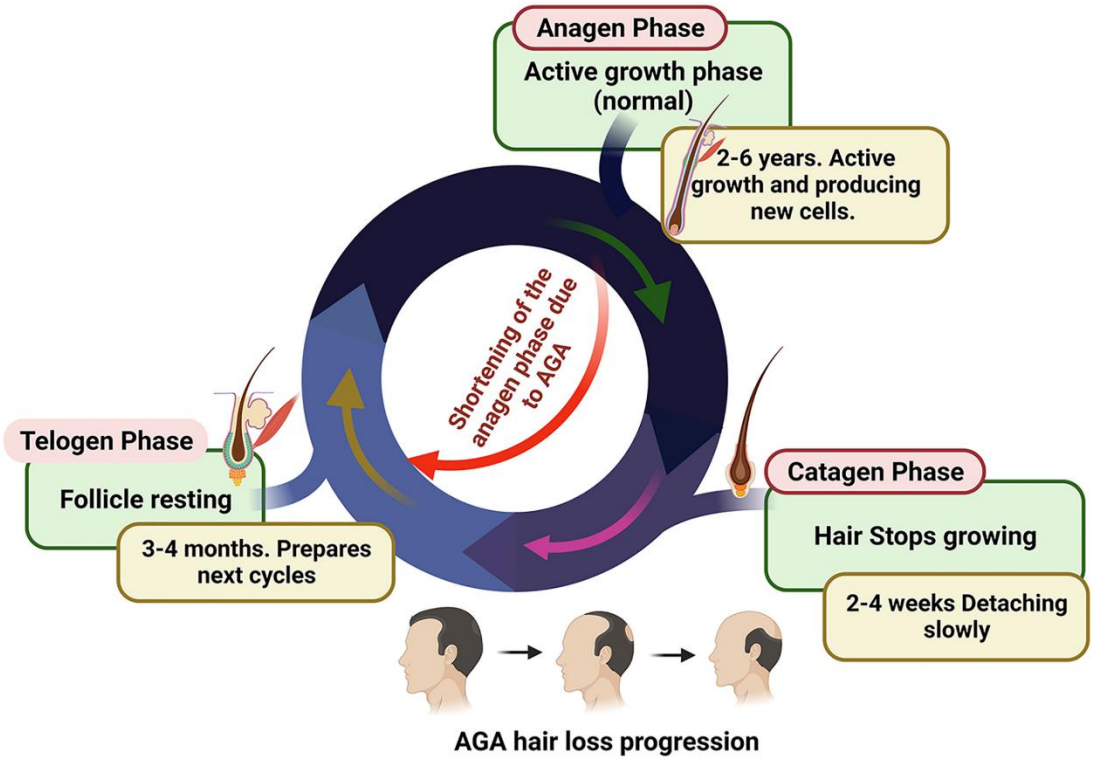
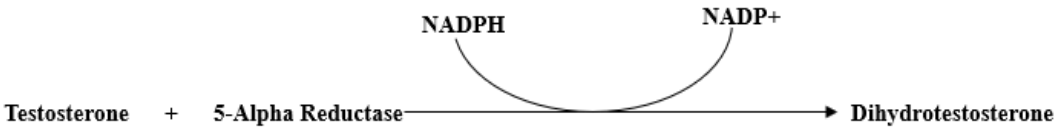


Fig. 2.2: The Cycle of Hair Growth in Androgenic Alopecia [17].

2.2. Causes of Androgenic Alopecia

Androgens control the development of subcutaneous glands in the body, hair growth, and the functions of human skin through intracellular signalling pathways [18]. Androgens can both promote and inhibit hair growth depending on the location in the body, making it a significant regulator [18]. Androgen increases the size of beard, axillary, and pubic hairs while suppressing hair development by shortening the anagen growth phase of scalp follicles [19]. The local bioavailability of androgen determines how androgen acts on hair follicles, usually in those that contain AGA, testosterone is metabolized more locally into DHT, while androgen levels in the body circulation are normal [20]. Testosterone is metabolized by 5-alpha reductase to dihydrotestosterone, which is a much more powerful androgen than testosterone. The two members of the 5-alpha-reductase enzyme, 5AR1 and 5AR2, are primarily responsible for androgenic alopecia. The 5AR1 enzyme is mainly found in the liver, skin, and scalp, while the 5AR2 enzyme is found in the prostate and hair follicles. 5-alpha reductase enzyme

plays an important role in metabolic pathways in the body, such as androgen metabolism, bile acid production, and oestrogen metabolism. 5-alpha reductase uses NADPH to break the 4,5-bond in testosterone, converting it into dihydrotestosterone (DHT), which leads to AGA [21]. High levels of DHT shrink the hair follicles and change the terminal hairs into vellus [22]. When DHT binds to the androgen receptor of the hair follicle, a change occurs in the structure of the androgen receptor, which triggers signalling pathways and finally affects the hair growth cycle [23].



2.3. Current Treatment of Androgenic Alopecia

Currently, oral finasteride and topical minoxidil are the FDA-approved drugs used to treat androgenic alopecia.

2.3.1. Minoxidil

Minoxidil was first used as an antihypertension drug, but when patients experienced that it was causing hypertrichosis, it gained attention as a hair loss treatment. Minoxidil is used as primary therapy to treat androgenic alopecia. Topical minoxidil widens the blood arteries of the scalp, which increases blood circulation in the scalp and provides more nutrients to the follicles, which encourages hair growth [24]. 5% minoxidil solution is more effective than 2% solution [25]. Long-term use of minoxidil can cause redness, itching, and contact dermatitis, which can be treated with a 2% minoxidil solution without propylene glycol [26].

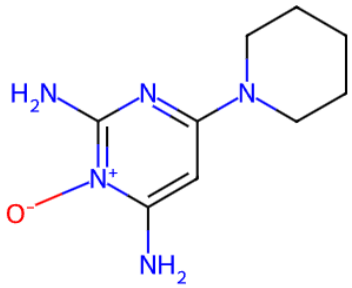


Fig. 2.3: Chemical Structure of Minoxidil.

2.3.2. Finasteride

Finasteride is an FDA-approved drug that acts as a competitive and selective inhibitor of 5-alpha reductase. For mild to severe androgenic alopecia, finasteride is administered. 1mg daily consumption of finasteride was shown to reduce DHT levels in the scalp and prostate by 60-70% [27]. When NADPH is present, finasteride and the enzyme 5-alpha reductase form a stable complex that prevents the production of DHT. Hair regrowth stops one year after discontinuing finasteride [28]. Recent studies have shown that finasteride inhibits the phenyl ethanolamine N-methyltransferase enzyme, which regulates the adrenal hormone. Long-term use of finasteride can cause sexual and psychological side effects [29].

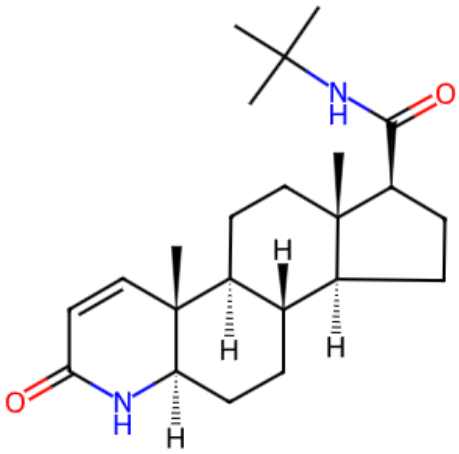


Fig. 2.4: Chemical Structure of Finasteride.

2.4. Kaempferol

Kaempferol is a flavonoid phytochemical [30]. The hydrophobic properties of kaempferol are due to the diphenyl propane present in it [31]. Kaempferol is found in abundance in different plants such as Citrus, Allium, and Brassica [32], [33]. Kaempferol is an anti-inflammatory phytochemical. Kaempferol is an effective phytochemical that reduces inflammation and also has benefits in cancer, heart disease, and neurological diseases.

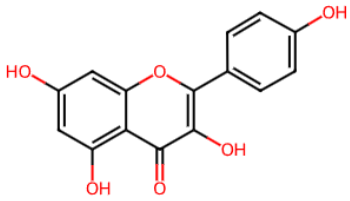


Fig. 2.5: Chemical Structure of Kaempferol.

CHAPTER 3: METHODOLOGY

3.1. 5-Alpha Reductase enzyme structure retrieval

As we know, androgenic alopecia is caused by hyperactivity of 5 alpha reductase, which metabolizes testosterone into DHT. 5-alpha reductase type I and type II are the enzymes primarily responsible for the AGA. There is no three-dimensional structure of type I alpha reductase, whereas a three-dimensional x-ray crystallography structure of type II alpha reductase is available. 5-alpha reductase type II's three-dimensional structure was obtained using PDB ID 7BW1 from the RCSB database [34]. Due to the unavailability of the three-dimensional structure of 5-alpha reductase type I, we predict its structure through homology modelling with the help of the SWISS-MODEL tool [35]. We obtained the FASTA format sequence file of 5-alpha reductase type I from the UniProt database with SRD5A1 gene ID or accession number P18405 for homology modelling. The structure obtained by homology modelling is validated using the PROCHECK [36] Tool, that provides the Ramachandran plot of the structure.

3.2. Chemical Compound Library Preparation

To find an effective phytochemical, we retrieved chemical compounds from 5 different medicinal plants: *Allium cepa, Aloe vera, Eclipta alba, Lawsonia inermis,* and *Bacopa monnieri* from the IMPPAT 2.0 database [37]. We obtained a total of 120 phytochemicals from these medicinal plants. We downloaded these compounds in a 3D SDF file format in this study. In this study, we used the FDA-approved Finasteride as the control drug. Finasteride was acquired using PubChem ID 44338570 from the PubChem database.

3.3. Preparing ligands and proteins for docking

Before molecular docking, the hetero atoms attached to the receptor proteins 5AR1 and 5AR2 and the water molecules are removed, and a polar hydrogen charge is added

with the help of BIOVIA Discovery Studio software. Also, with the help of the Open Babel tool, the phytochemicals retrieved from the database are converted from SDF format to PDBQT format by minimizing their energy to work as ligands [38].

3.4. Molecular Docking

For molecular docking, we use the PyRx 0.8 virtual screening tool [39]. After preparing the protein and ligand, we upload the protein to PyRx and convert it into a macromolecule. Because we have two protein targets, we perform molecular docking twice. Once we take one protein and dock all the compounds, we dock all the compounds using the same method the second time. In PyRx, we do molecular docking with the help of AutoDock Vina, in which we set the grid box dimensions as per our requirement and perform molecular docking [40]. The PyRx tool returns the docking result as a file in .csv format.

3.5. ADME and Toxicity analysis

With the help of the SwissADME tool, compounds' ADME (absorption, distribution, metabolism, and excretion) properties are analyzed [41]. The compounds obtained through molecular docking, whose binding energy was more than -8 Kcal/mol, were subjected to ADME property analysis using SMILES ID. For toxicity analysis, the ProTox 3.0 online tool was used [42]. ProTox server analyses chemical compounds for their toxicity using machine learning methods.

3.6. Interaction Analysis

The best docked compounds having binding energy less than -8 Kcal/mol were subjected to interaction analysis. In interaction analysis, we study the bonds between the ligand and the protein and their types. The study of three-dimensional interaction between protein and ligand was done with the help of Biovia Discovery Studio, and two-dimensional interaction analysis was done with the help of Schrödinger Maestro software [43].

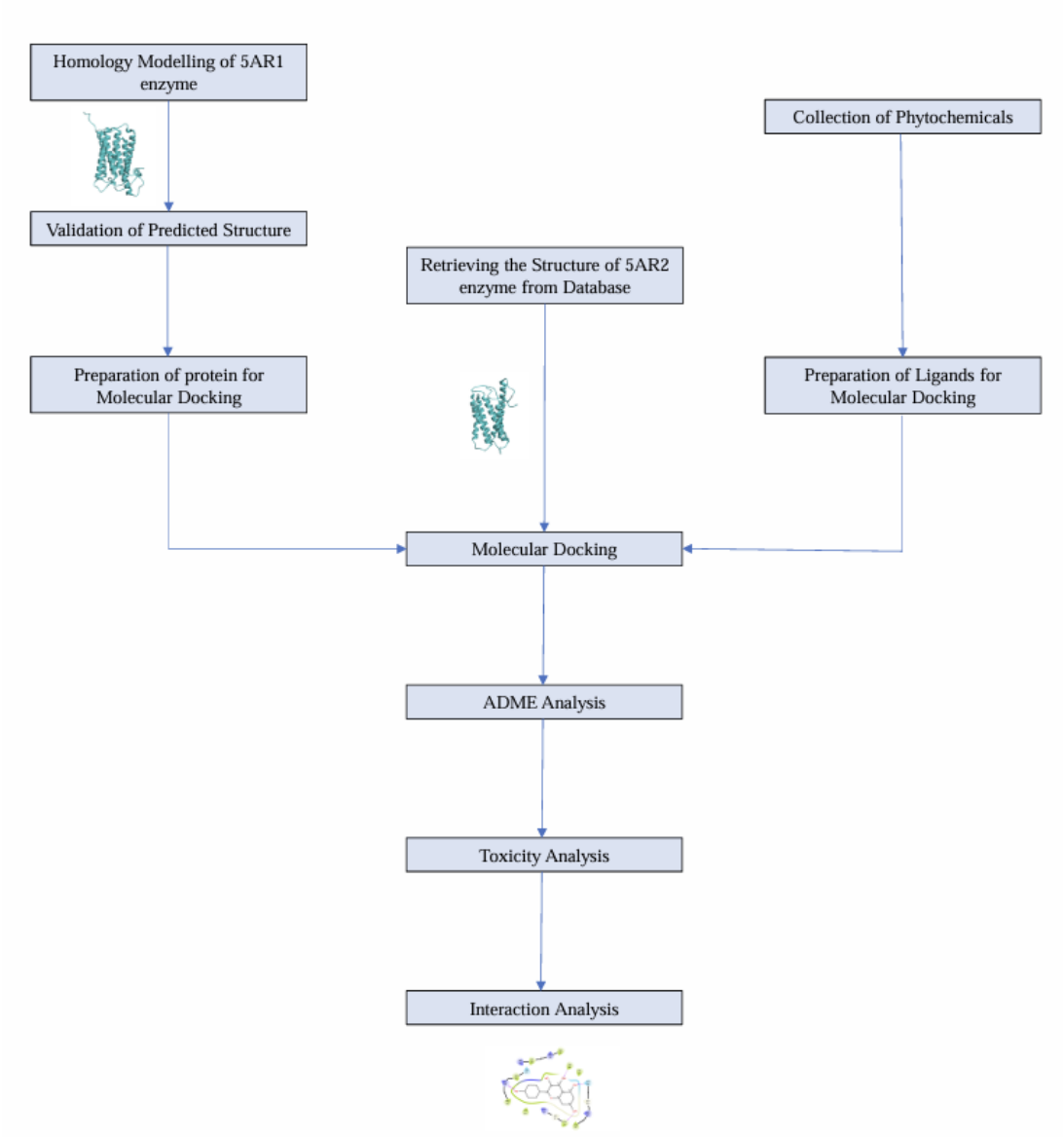


Fig. 3.1: An outline of the methodology.

CHAPTER 4: RESULTS

4.1. Homology Modelling Result and its validation

The Swiss-Model 5AR1's three-dimensional structure is seen in Figure 4.1. Swiss-Model predicts structure with the help of a homology modelling pipeline [44]. Homology modelling by Swiss-Model includes template selection, alignment of target sequences, model building, and refinement steps [44]. Figure 4.2 shows the Ramachandran plot, with the help of which we validate the modelled structure. According to Figure 4.2, all the residues of our 5AR1 protein fall in the allowed region, which shows that the modelled structure is stable and can be used in further studies. Figure 4.3 shows the 5-alpha reductase type I enzymes retrieved from the RCSB database.

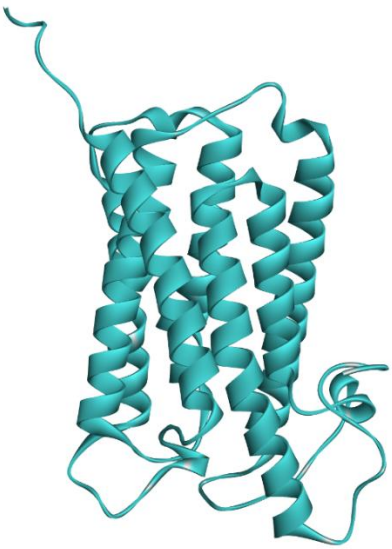


Figure 4.1: Predicted structure of 5AR1 enzyme from homology model.

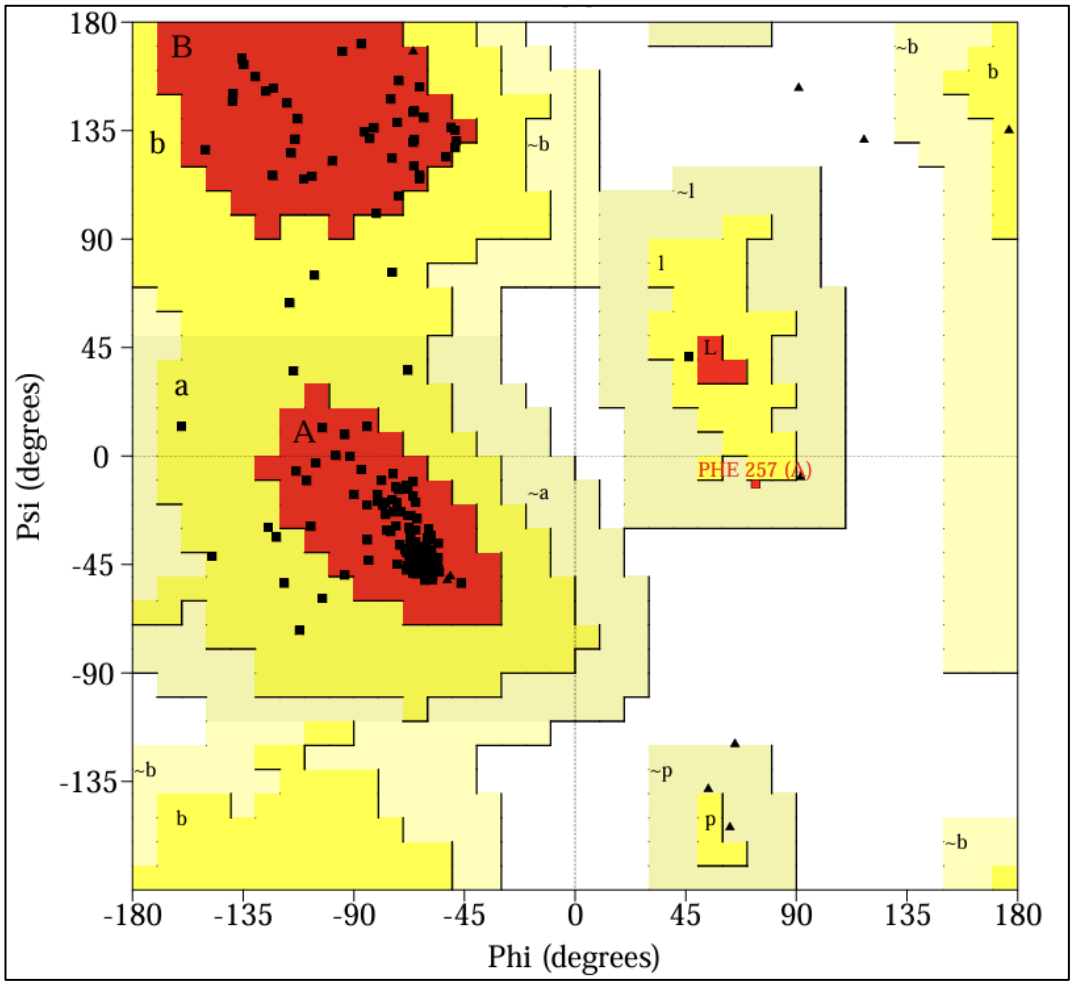


Figure 4.2: Ramachandran plot of the modelled 5-Alpha Reductase enzyme structure.

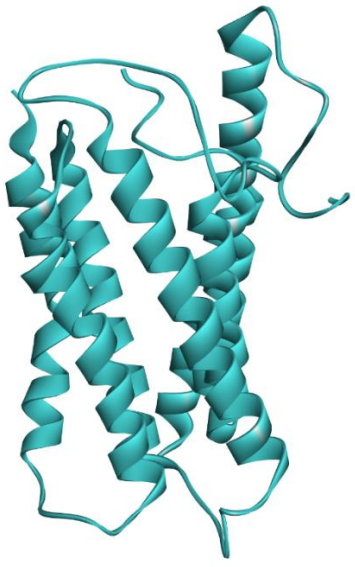


Figure 4.3: Three-dimensional structure of 5-Alpha Reductase Type II enzyme.

4.2. Molecular Docking Results

According to molecular docking data from the PyRx virtual screening tool, the FDA-approved medication finasteride has a binding affinity of -9.0 kcal/mol with 5AR2 and -8.2 kcal/mol with 5AR1. Therefore, we choose the compounds with a binding affinity below -8.2 Kcal/mol from the docking findings. Only seven phytochemicals with a good binding energy with both enzymes were identified out of 120 chemical compounds from five medicinal plants.

The findings of finasteride (control) and the best docked compounds with the 5AR1 enzyme are displayed in Table 4.1.

The findings of finasteride (control) and the best docked compounds with the 5AR2 enzyme are displayed in Table 4.2.

Table 4.1: Molecular Docking Results of Phytochemicals with 5AR1.

Ligand	**Binding Affinity (kcal/mol)**	**Source**	**IMPPAT ID**
Finasteride	-8.2	NA	44338570 (PubChem)
Kaempferol	-9.2	*Allium cepa*	IMPHY004388
Apigenin	-10	*Eclipta alba*	IMPHY004661
Aloesone	-8.2	*Aloe vera*	IMPHY008696
Isorhamnetin	-9.5	*Allium cepa*	IMPHY008724
Apigenin-7-o-glucuronide	-11.5	*Bacopa monnieri*	IMPHY011710
Apigenin 7-glucuronide	-10.7	*Bacopa monnieri*	IMPHY011711
Tilianin	-10.1	*Lawsonia inermis*	IMPHY011742

Table 4.2: Molecular Docking Results of Phytochemicals with 5AR2.

Ligand	Binding Affinity (kcal/mol)	Source	IMPPAT ID
Finasteride	-9	NA	44338570 (PubChem)
Kaempferol	-9.2	*Allium cepa*	IMPHY004388
Apigenin	-9.2	*Eclipta alba*	IMPHY004661
Aloesone	-8.6	*Aloe vera*	IMPHY008696
Isorhamnetin	-9.4	*Allium cepa*	IMPHY008724
Apigenin-7-o-glucuronide	-11.2	*Bacopa monnieri*	IMPHY011710
Apigenin 7-glucuronide	-11.4	*Bacopa monnieri*	IMPHY011711
Tilianin	-10.9	*Lawsonia inermis*	IMPHY011742

4.3. ADME and Toxicity Analysis Results

The seven best docked compounds obtained from molecular docking and finasteride were subjected to ADME analysis using the SMILES ID with the help of the SwissADME tool. The SwissADME program helps us find a suitable medication by analysing the physicochemical and pharmacokinetic characteristics of phytochemicals. The ADME data for finasteride and the top seven phytochemicals are displayed in Table 4.3. Table 4.4 displays the toxicity analysis of each of these chemical substances. ProTox 3.0 online server has been used in this study for toxicity analysis.

Table 4.3: ADME Results of Best Docked Chemical Compounds and Finasteride.

Chemical Compound	ADME Results										
	GI Absorption	**Solubility**	**LogK$_p$ (in cm/s)**	**BBB Permeant**	**Bioavailability**	**Lipinski Rule**	**Veber's Rule**	**PAIN Alerts**	**Brenk Alerts**	**Synthetic Accessibility**	**Leadlikeness**
Finasteride	HIGH	Soluble	-6.42	Yes	0.55	No	No	0	0	5.37	No
Kaempferol	HIGH	Soluble	-6.7	No	0.55	No	No	0	0	3.14	Yes
Apigenin	HIGH	Soluble	-5.8	NO	0.55	No	No	0	0	2.96	Yes
Aloesone	HIGH	Soluble	-6.88	Yes	0.55	No	No	0	0	2.78	No
Isorhamnetin	HIGH	Soluble	-6.9	No	0.55	No	No	0	0	3.26	Yes
Apigenin-7-o-glucuronide	LOW	Soluble	-7.90	No	0.15	Yes (1)	No	0	0	5.06	No
Apigenin-7-glucuronide	LOW	Soluble	-7.90	No	0.15	Yes (1)	No	0	0	5.06	No
Tilianin	LOW	Soluble	-7.5	No	0.55	No	No	0	0	5.23	No

Table 4.4: Results of the Toxicity Analysis of Finasteride and the Best Docked Ligands.

Ligand	Toxicity Class	LD50 Value (in mg/kg)	Hepatotoxicity	Neurotoxicity	Nephrotoxicity	Carcinogenicity
Finasteride	IV	418	×	✓	×	×
Kaempferol	V	3919	×	×	✓	×
Apigenin	V	2500	×	×	✓	×
Aloesone	V	3200	×	×	✓	×
Isorhamnetin	V	5000	×	×	✓	×
Apigenin-7-o-glucuronide	V	5000	×	×	✓	×
Apigenin-7-glucuronide	V	5000	×	×	✓	×
Tilianin	V	5000	×	×	✓	×

4.4. Interaction Analysis

We analyse the interactions of the best compounds docked with 5AR1 and 5AR2 enzymes, including the number and type of bonds formed between the protein and the compound. For this, we use the PDB structure of the docked complex. Two-dimensional interaction analysis is done with the help of Schrödinger Maestro, and three-dimensional interaction analysis is done with the help of the BIOVIA Discovery Studio tool.

Table 4.5: Amino Acid Interaction analysis for 5AR1.

Chemical Compound	Amino Acid Involved in H-Bonding	Amino Acid Involved in Other Interactions
Finasteride	ARG98, GLU202	ARG40, TRP56, TYR199, LEU172
Kaempferol	ALA116	ALA123, PHE123, PHE228
Apigenin	ALA116, THR225, HIS94	GLU202, MET119, PHE228
Aloesone	THR225	TYR38, PHE228
Isorhamnetin	ALA116, GLU202	ALA120, PHE228
Apigenin-7-o glucuronide	ASP169, TYR102	ARG98, PHE228, ALA120
Apigenin-7 glucuronide	ARG40, GLU60, THR225	TRP56
Tilianin	ARG40	LEU229, PHE228, PHE123

Table 4.6: Amino Acid Interaction analysis for 5AR2.

Chemical Compound	Amino Acid Involved in H-Bonding	Amino Acid Involved in Other Interactions
Finasteride	GLU197, TRP201	SER220, ARG114
Kaempferol	ASN193, HIS231, ARG227	GLY34, TRP53, PHE194, PHE223, PHE118, ASP164
Apigenin	TYR98, ARG105, ARG179	ASN102, ARG171, LEU170, TYR178
Aloesone	SER220, TRP201, ASP164, ASN193	LEU224, PHE194
Isorhamnetin	GLU57, GLN56, TYR107, SER220	PHE223, LEU224, TRP201
Apigenin-7-o glucuronide	TYR91, ASN160, ASP164	PHE223, PHE118, GLU57, ASN193
Apigenin-7 glucuronide	ASP164, ASN193, TRP53	PHE194, PHE223, LEU224, ASN102
Tilianin	ASN193, HIS231, ARG227	ASP164, GLY34, TRP53, PHE118

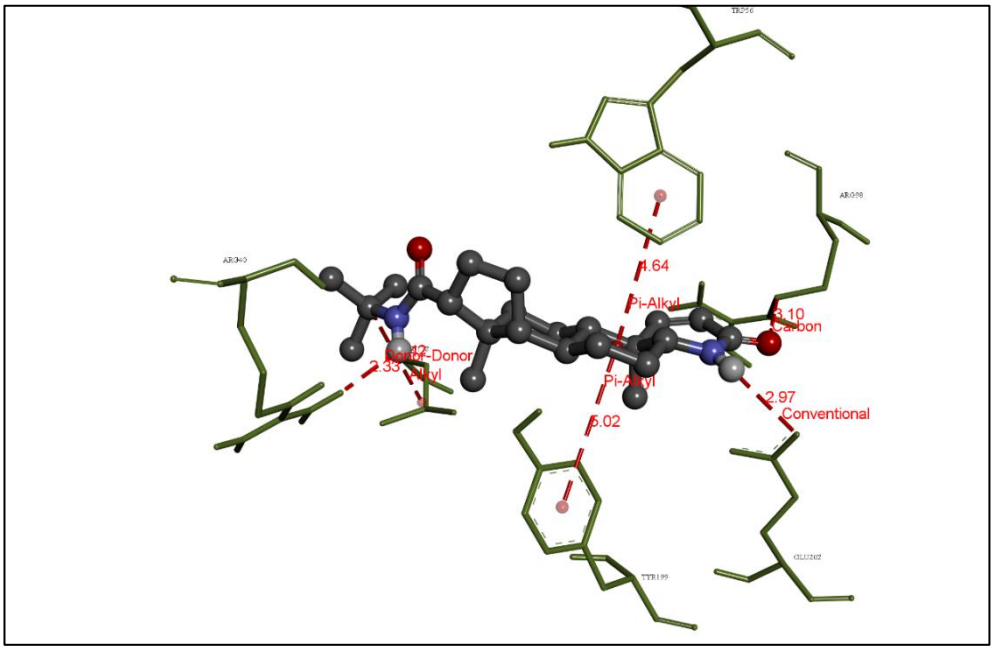


Fig. 4.4: Analysis of 5AR1's three-dimensional interactions with Finasteride

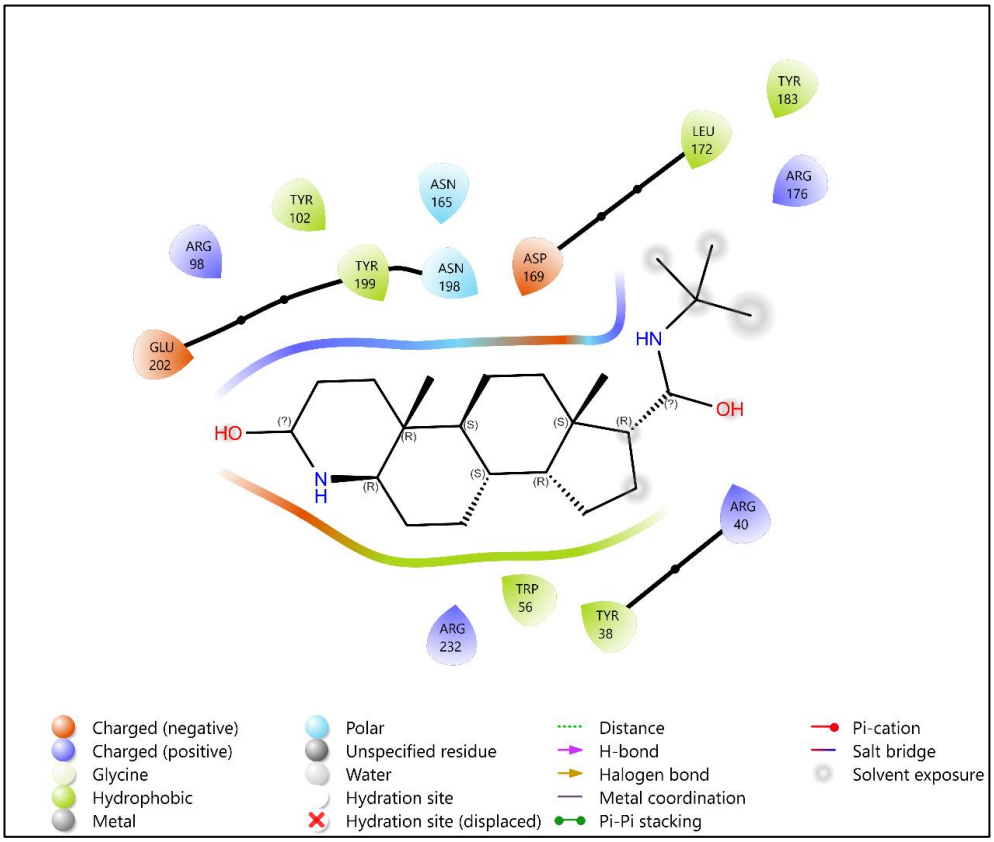


Fig. 4.5: Analysis of 5AR1's two-dimensional interactions with Finasteride.

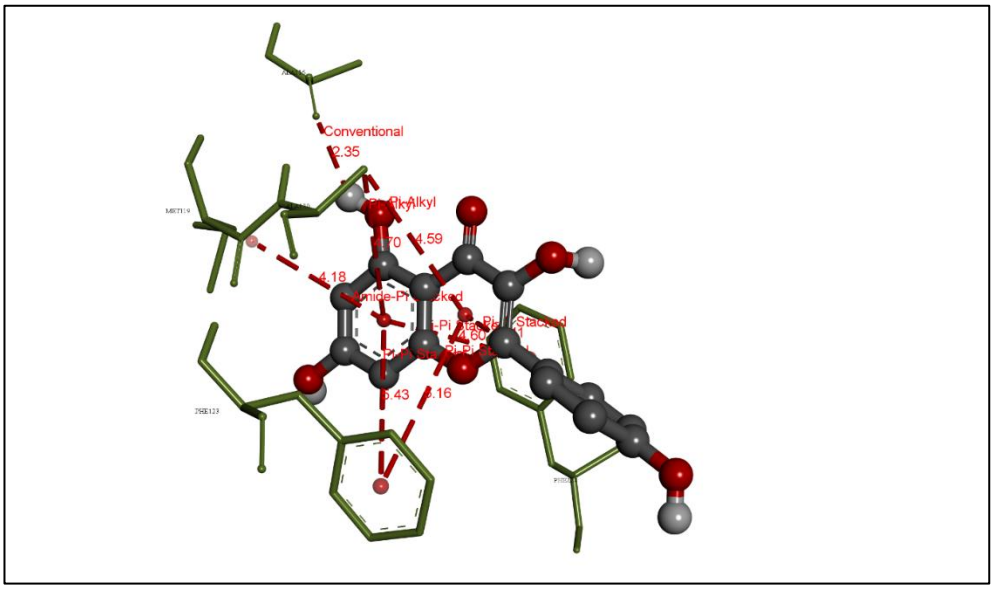


Fig. 4.6: Analysis of 5AR1's three-dimensional interactions with kaempferol

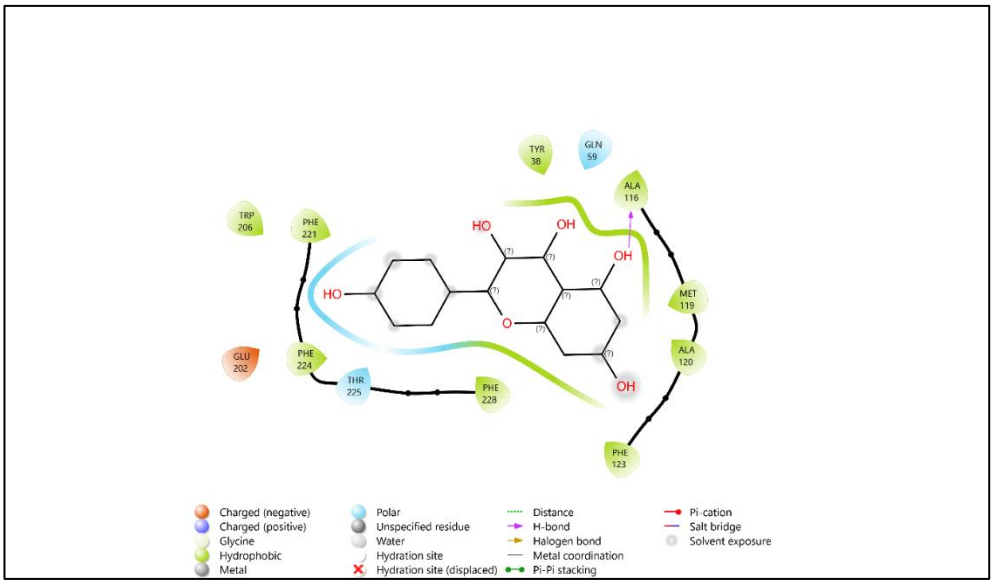


Fig. 4.7: Analysis of 5AR1's two-dimensional interactions with kaempferol

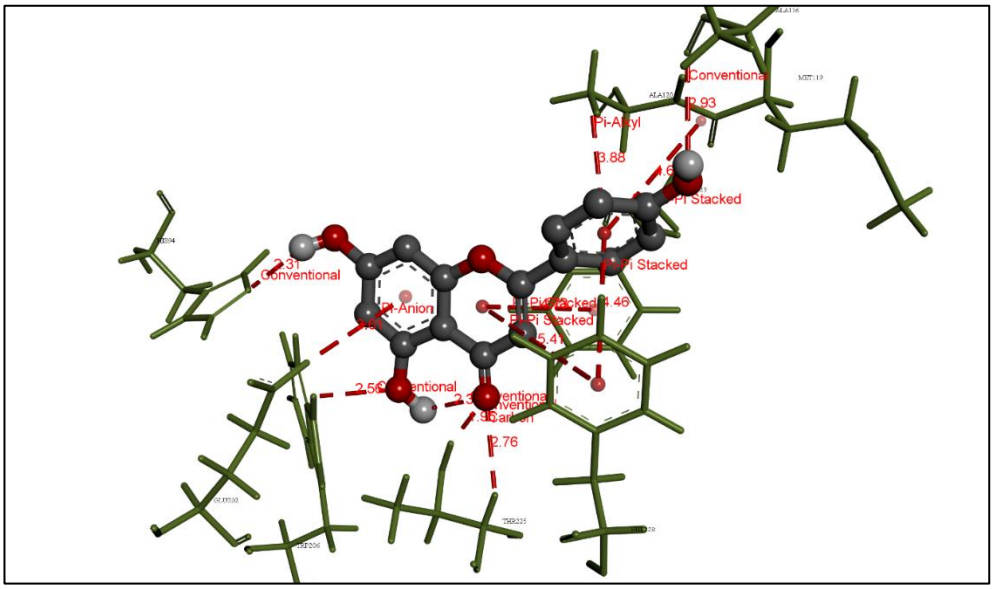


Fig. 4.8: Analysis of 5AR1's three-dimensional interactions with Apigenin

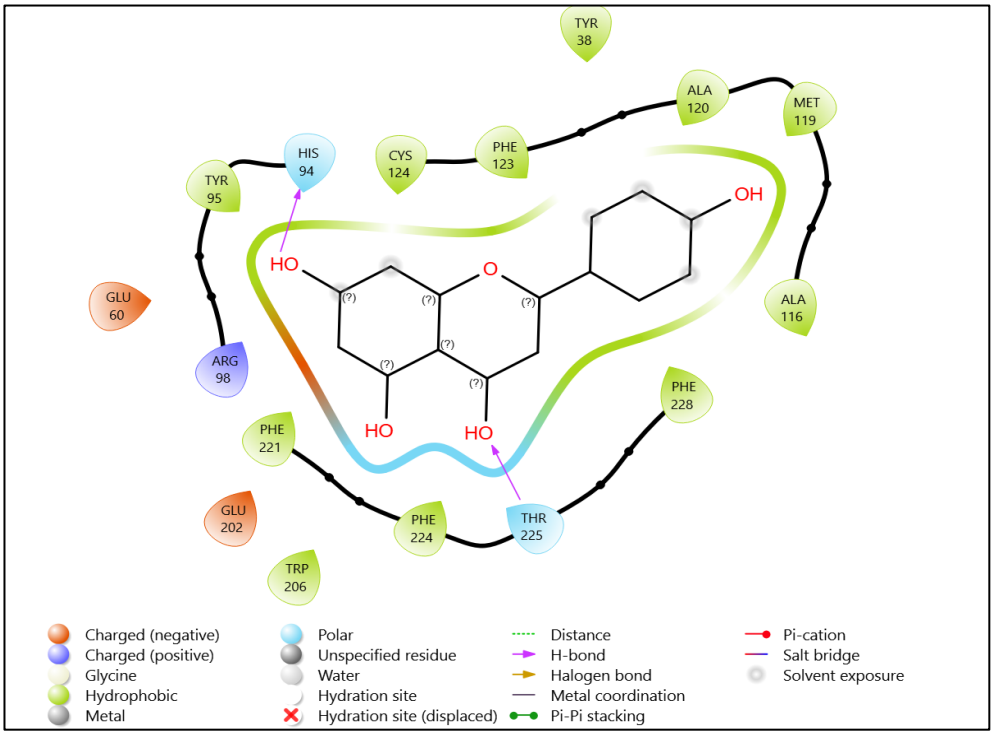


Fig. 4.9: Analysis of 5AR1's two-dimensional interactions with Apigenin

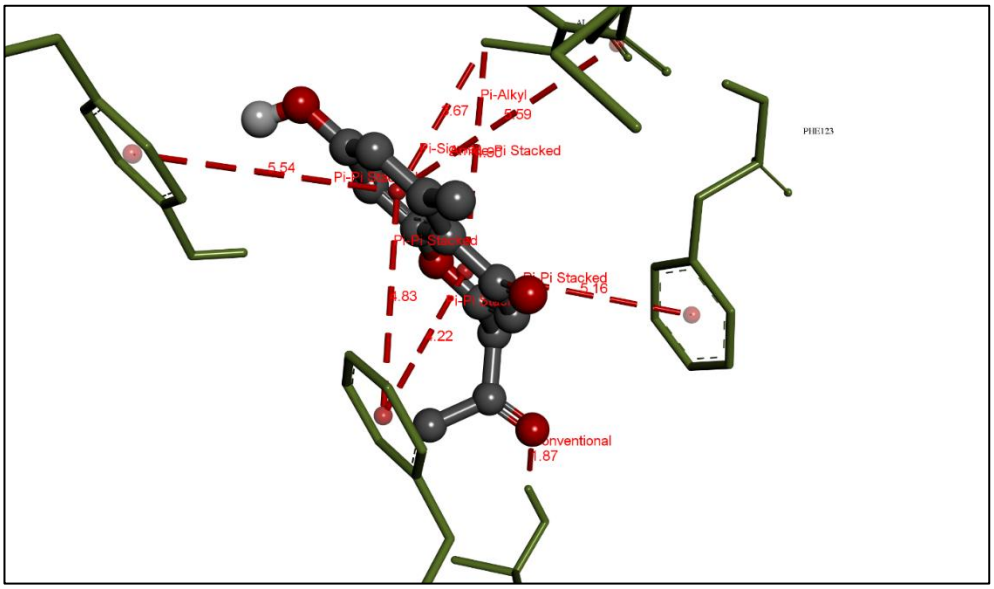


Fig. 4.10: Analysis of 5AR1's three-dimensional interactions with Aloesone

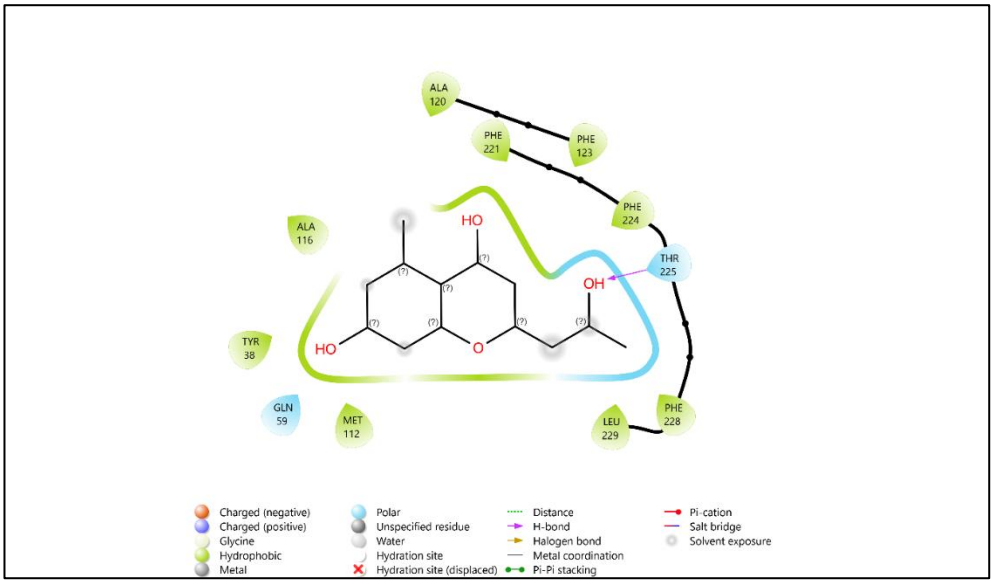


Fig. 4.11: Analysis of 5AR1's two-dimensional interactions with Aloesone

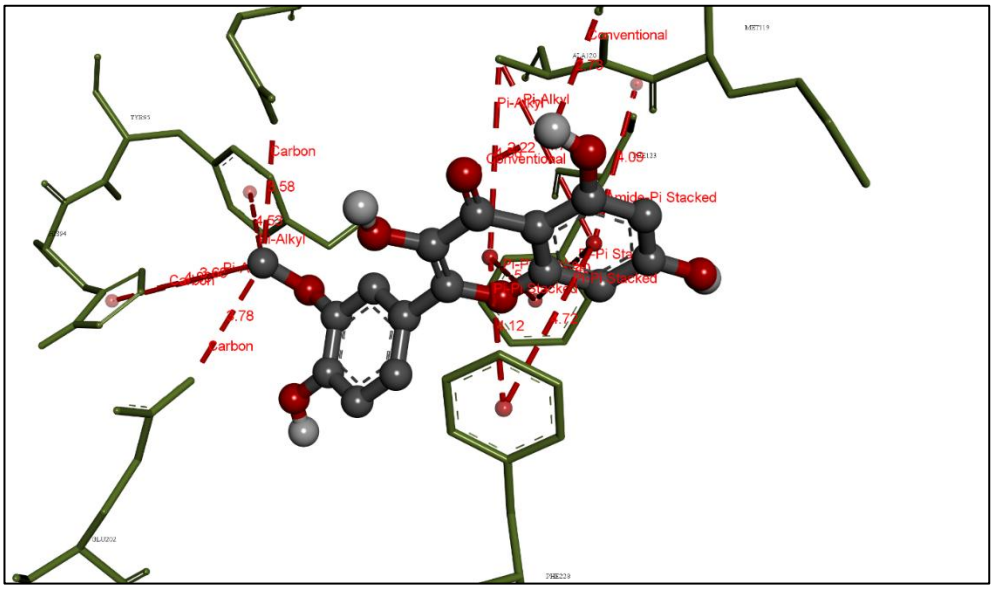


Fig. 4.12: Analysis of 5AR1's three-dimensional interactions with Isorhamnetin

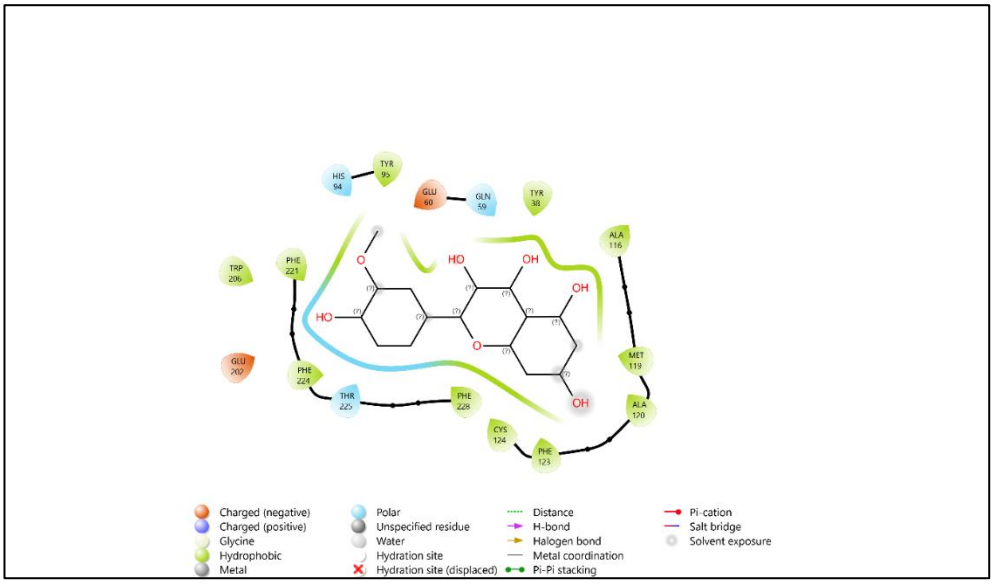


Fig. 4.13: Analysis of 5AR1's two-dimensional interactions with Isorhamnetin

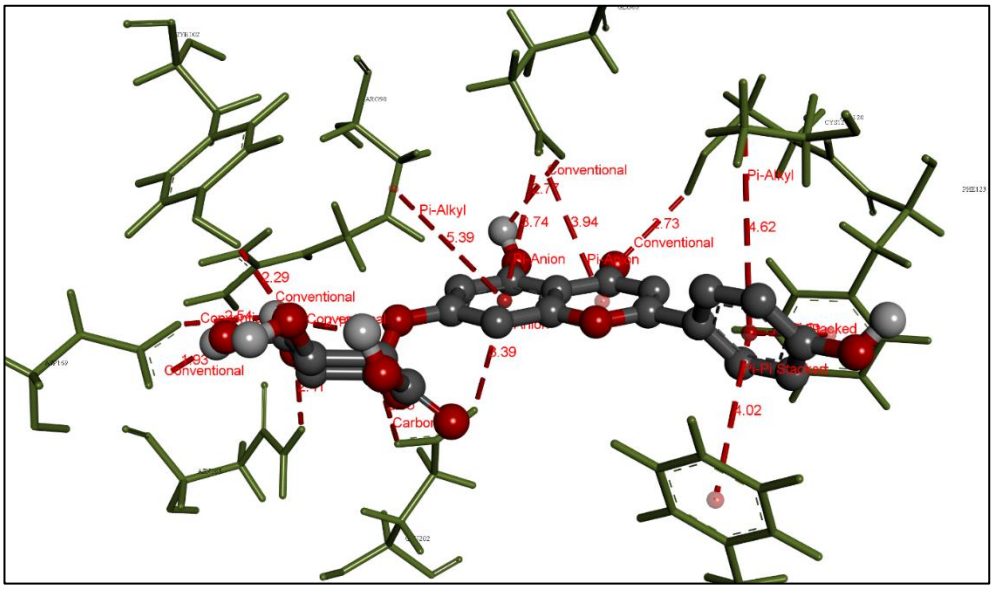


Fig. 4.14: Analysis of 5AR1's three-dimensional interactions with Apigenin-7-o-glucuronide

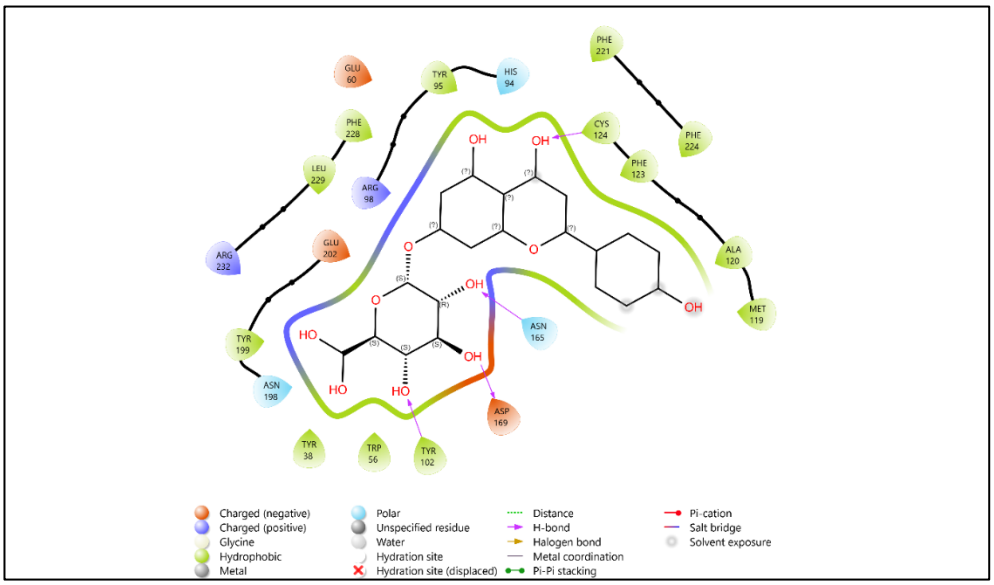


Fig. 4.15: Analysis of 5AR1's two-dimensional interactions with Apigenin-7-o-glucuronide

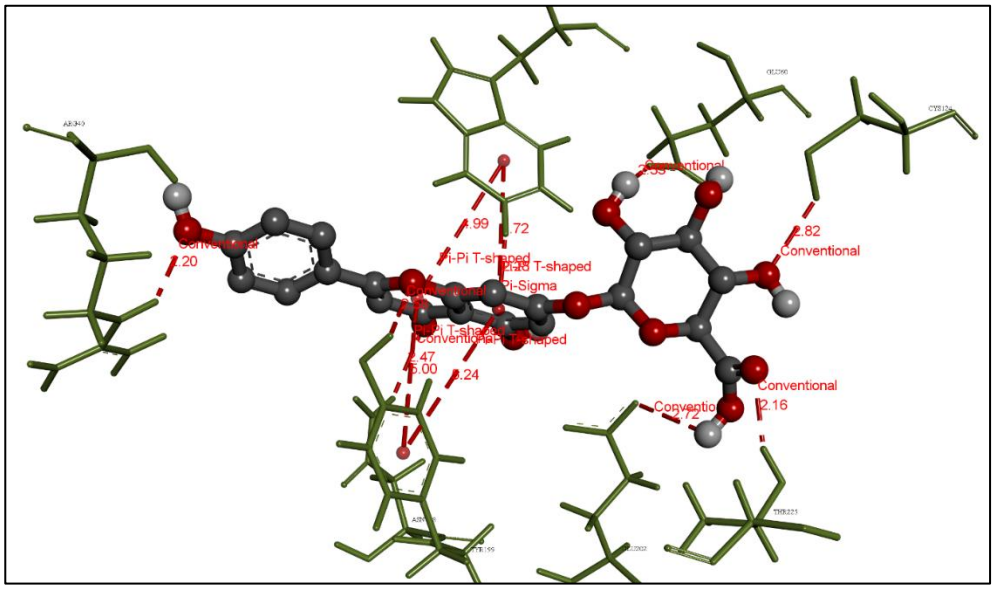


Fig. 4.16: Analysis of 5AR1's three-dimensional interactions with Apigenin-7-glucuronide

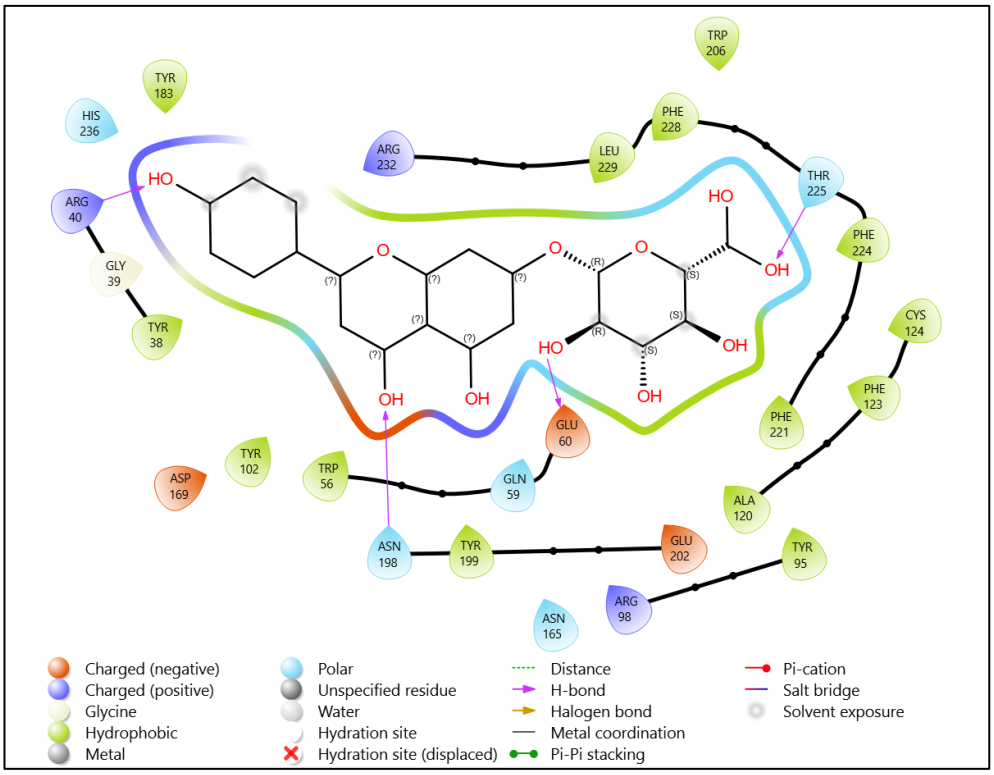


Fig. 4.17: Analysis of 5AR1's two-dimensional interactions with Apigenin-7-glucuronide

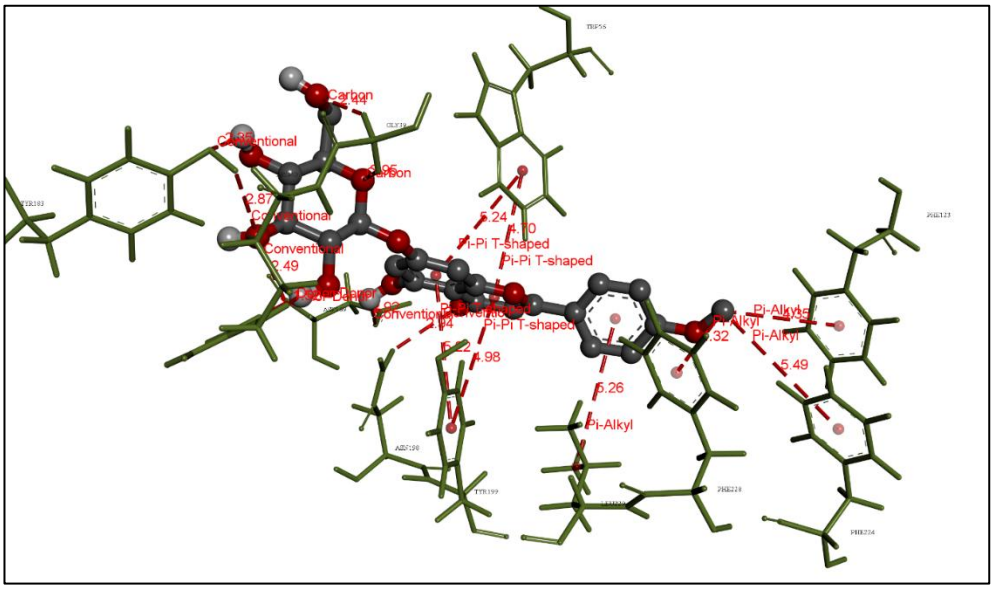


Fig. 4.18: Analysis of 5AR1's three-dimensional interactions with Tilianin

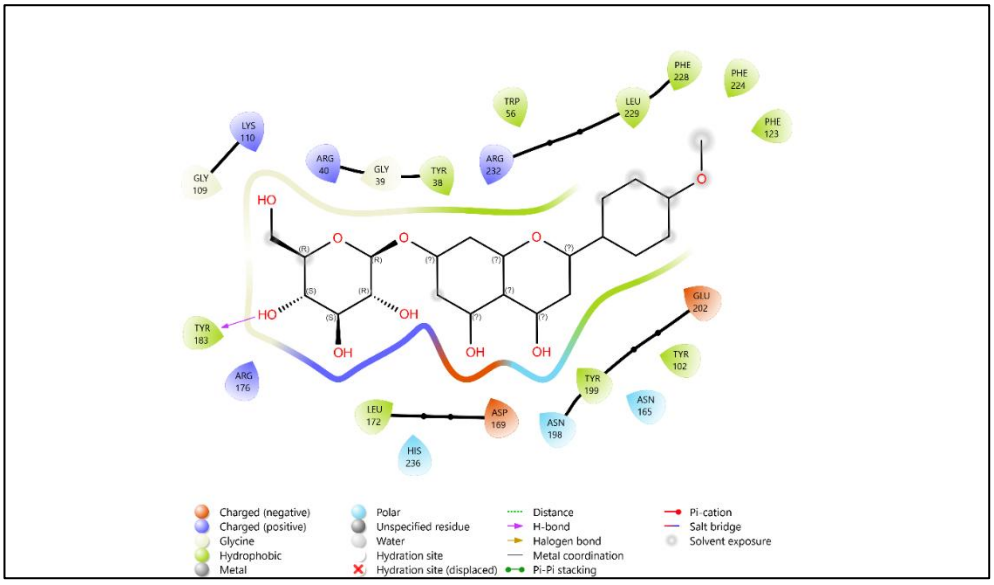


Fig. 4.19: Analysis of 5AR1's two-dimensional interactions with Tilianin

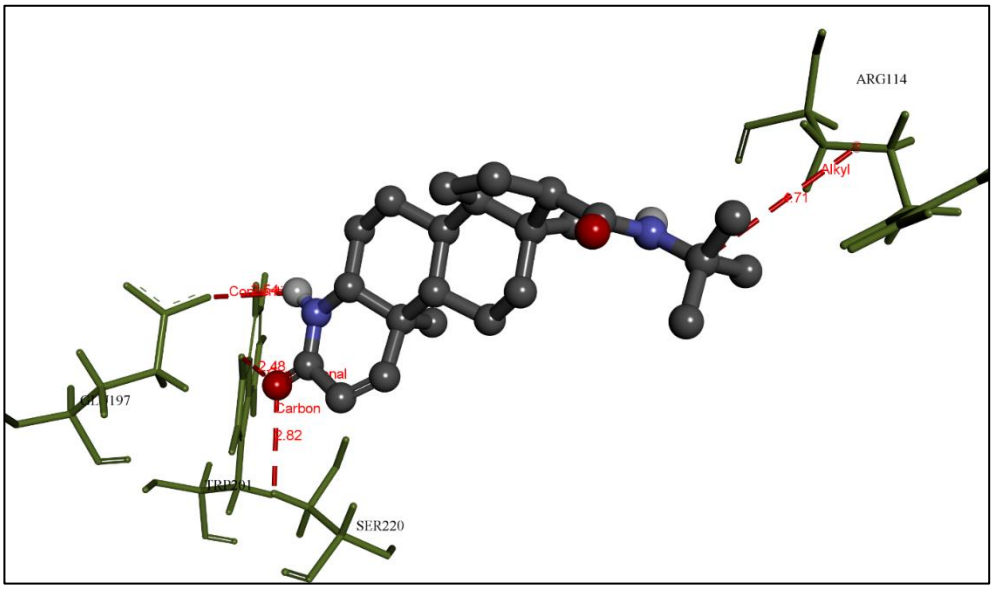


Fig. 4.20: Analysis of 5AR2's three-dimensional interaction with Finasteride.

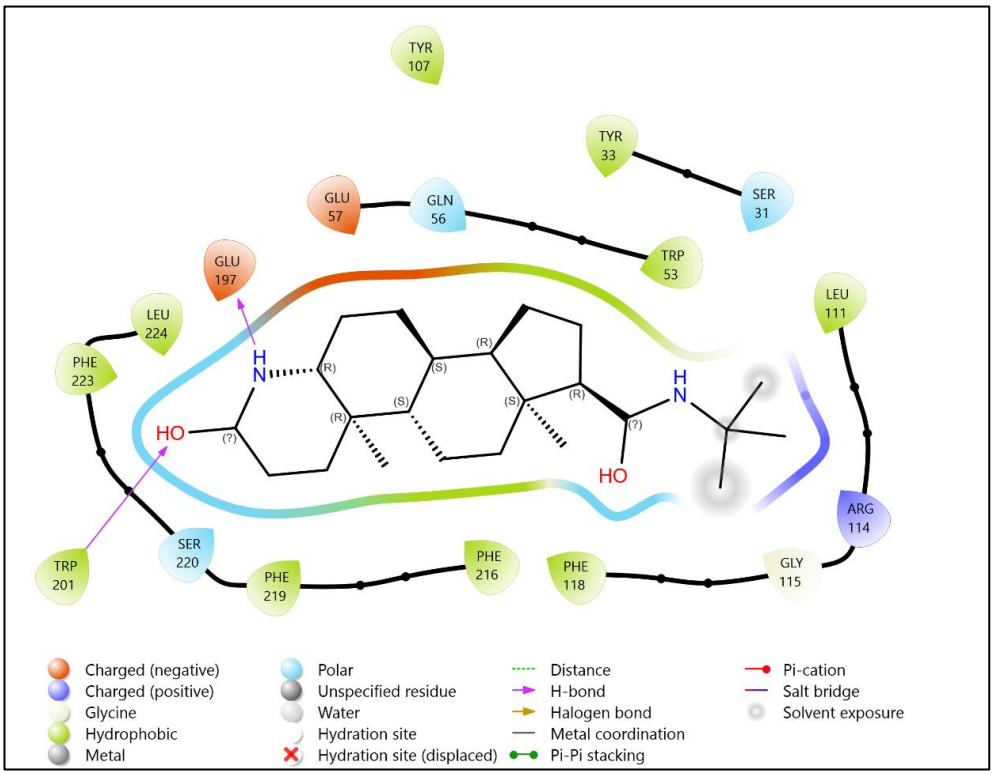


Fig. 4.21: Analysis of 5AR2's two-dimensional interactions with Finasteride

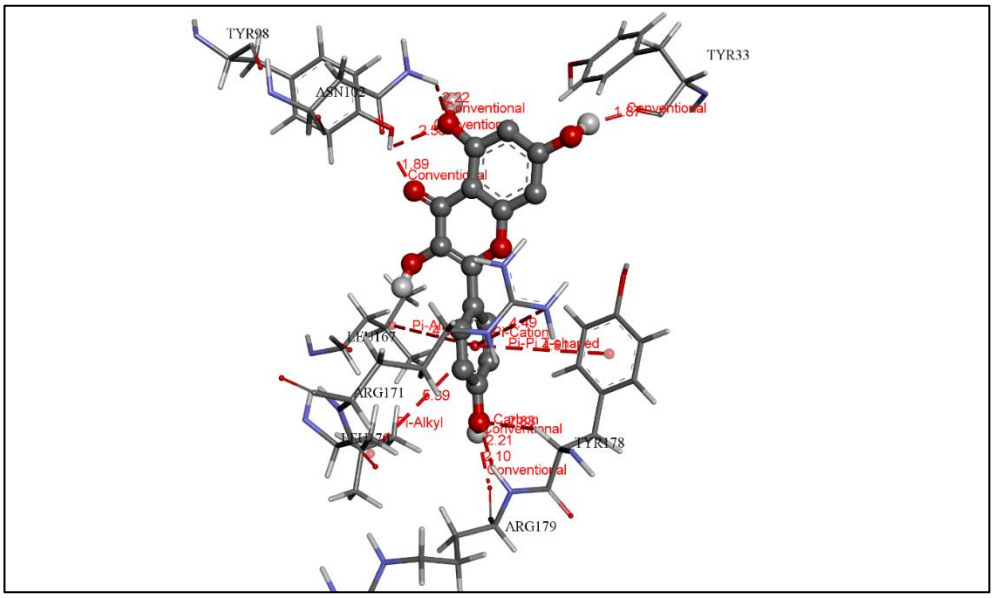


Fig. 4.22: Analysis of 5AR2's three-dimensional interactions with Kaempferol

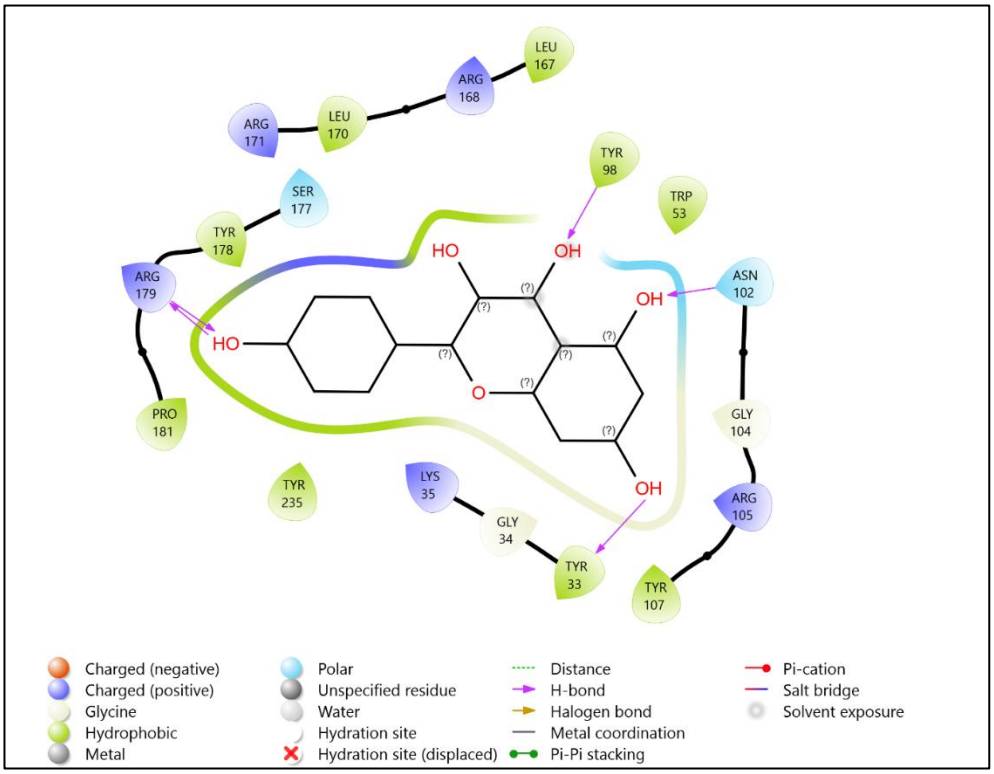


Fig. 4.23: Analysis of 5AR2's two-dimensional interactions with Kaempferol

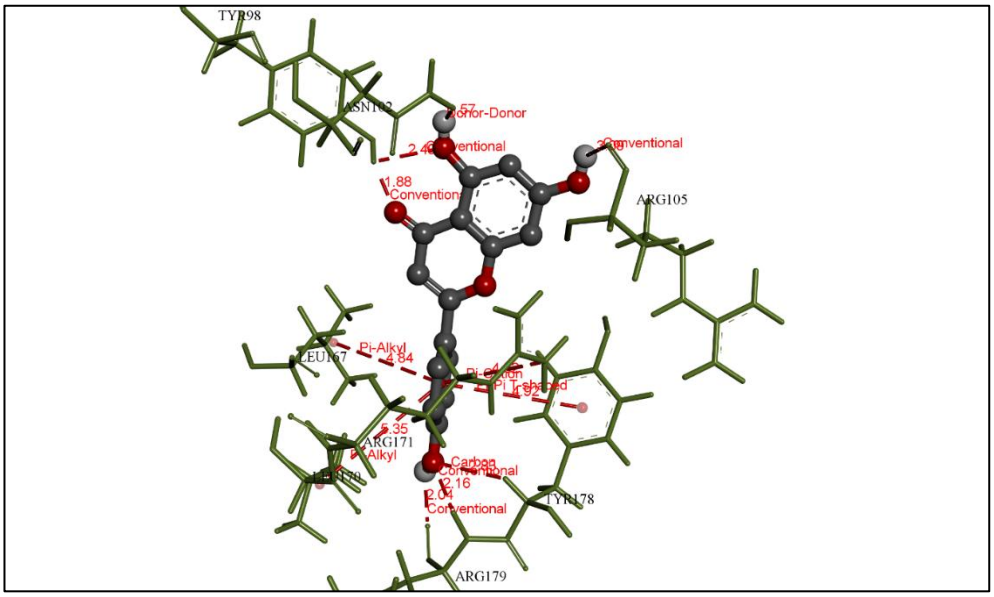


Fig. 4.24: Analysis of 5AR2's three-dimensional interactions with Apigenin

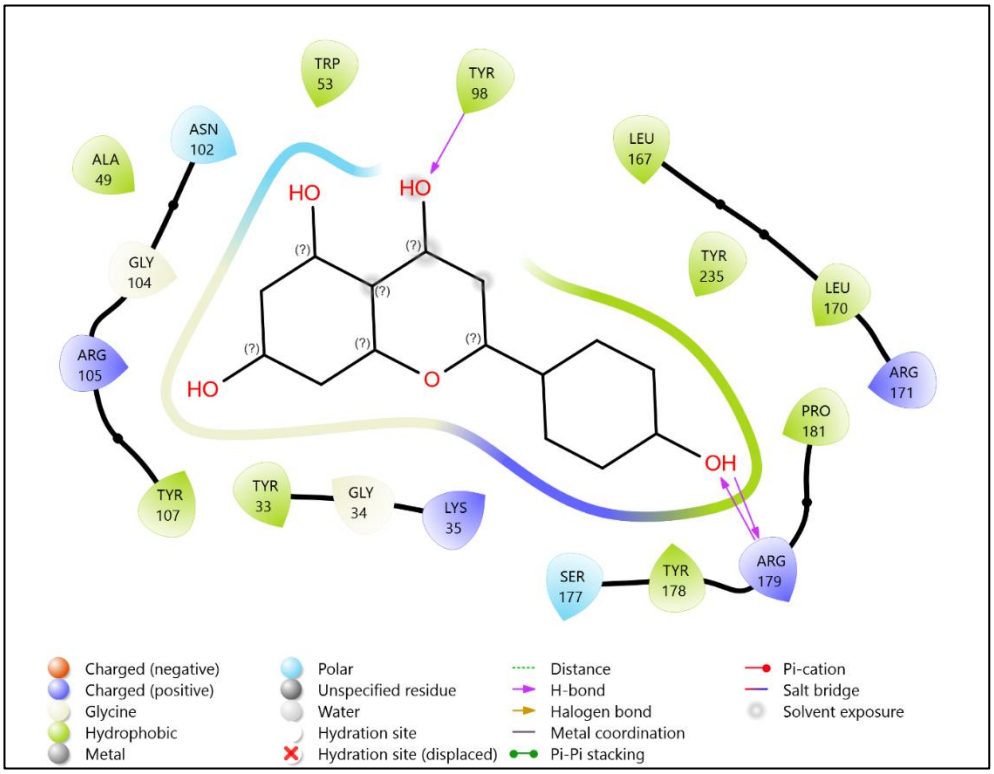


Fig. 4.25: Analysis of 5AR2's two-dimensional interaction with Apigenin.

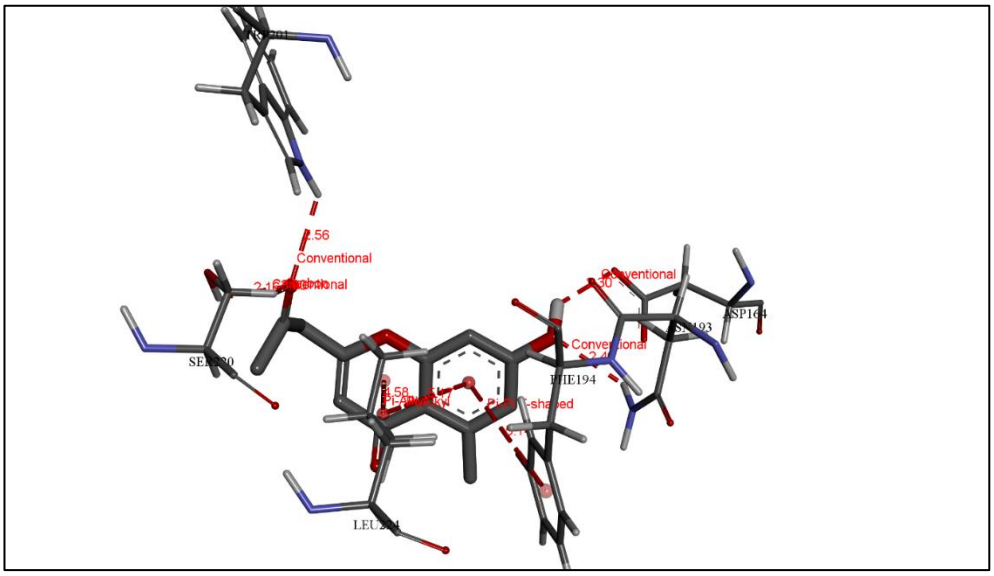


Fig. 4.26: Analysis of 5AR2's three-dimensional interactions with Aloesone

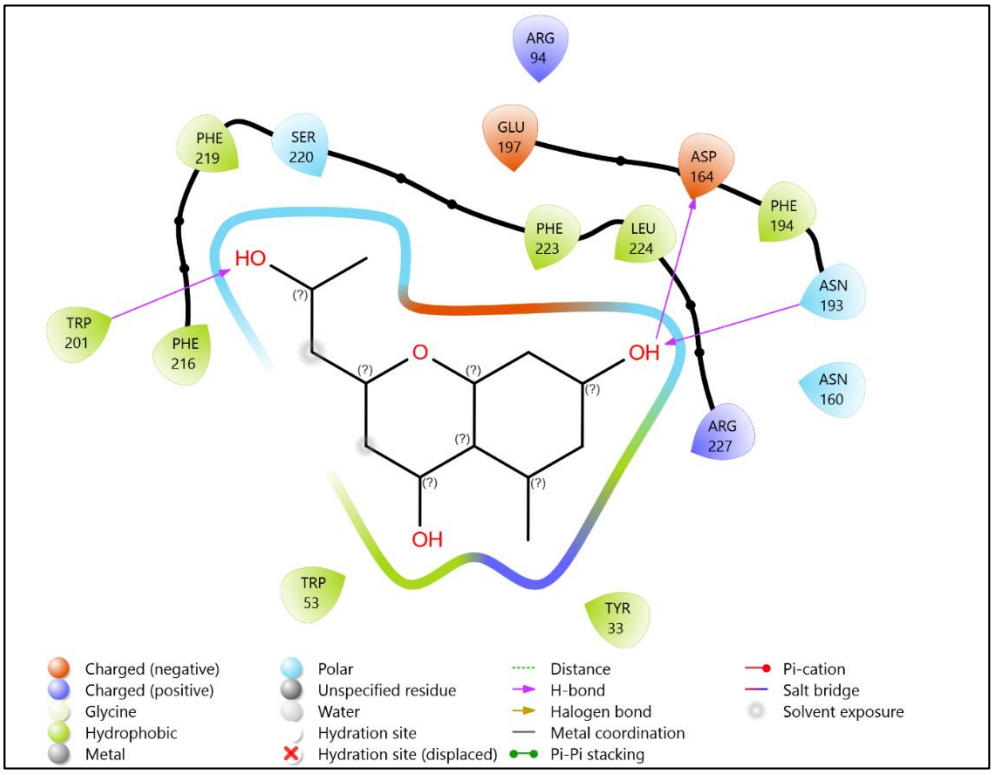


Fig. 4.27: Analysis of 5AR2's two-dimensional interactions with Aloesone

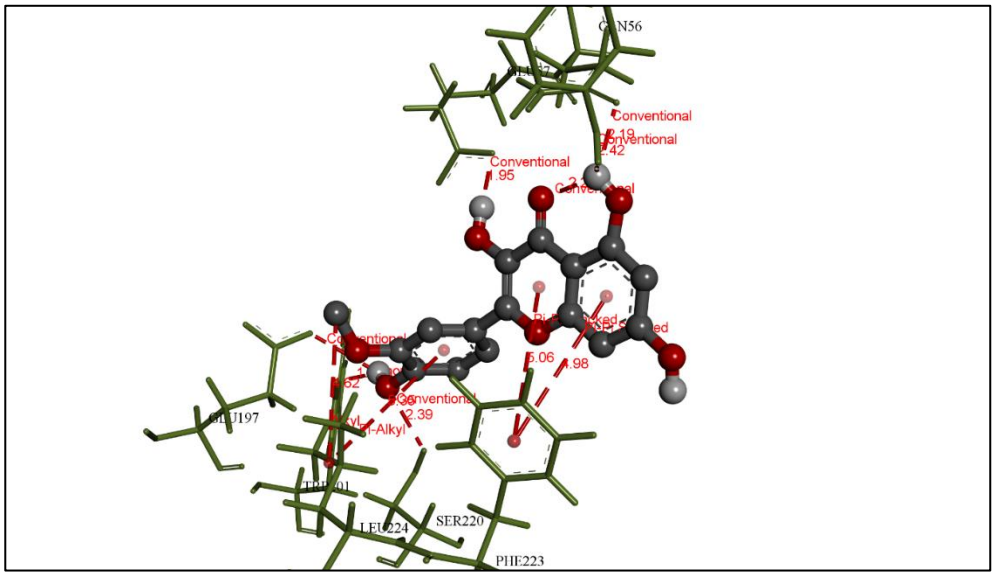


Fig. 4.28: Analysis of 5AR2's three-dimensional interactions with Isorhamnetin

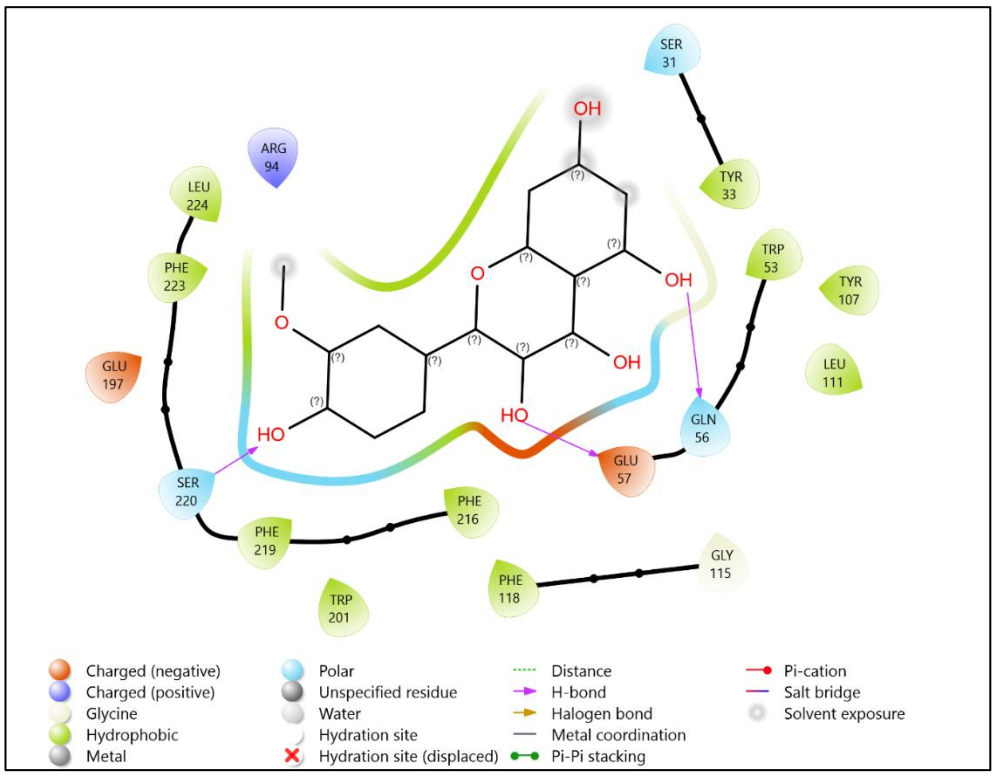


Fig. 4.29: Analysis of 5AR2's two-dimensional interactions with Isorhamnetin

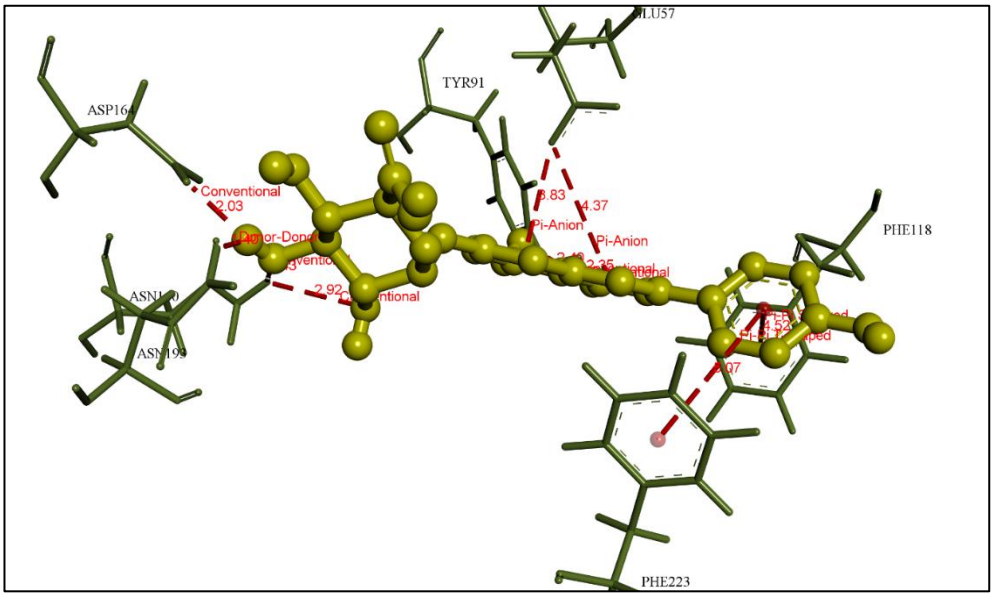


Fig. 4.30: Analysis of 5AR2's three-dimensional interactions with Apigenin-7-o-glucuronide

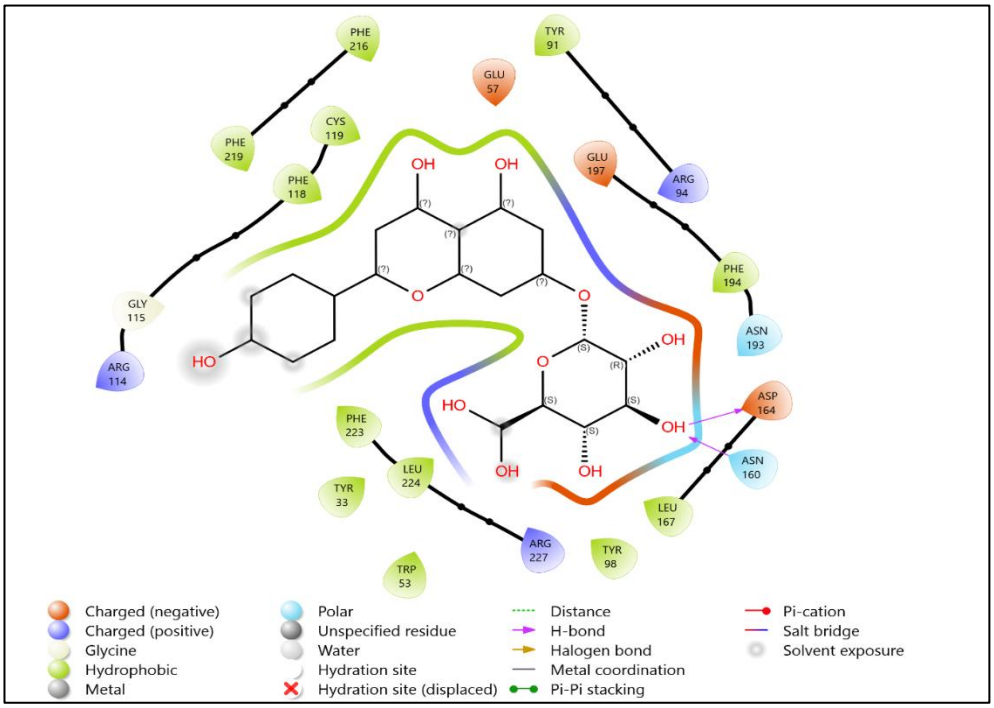


Fig. 4.31: Analysis of 5AR2's two-dimensional interactions with Apigenin-7-o-glucuronide.

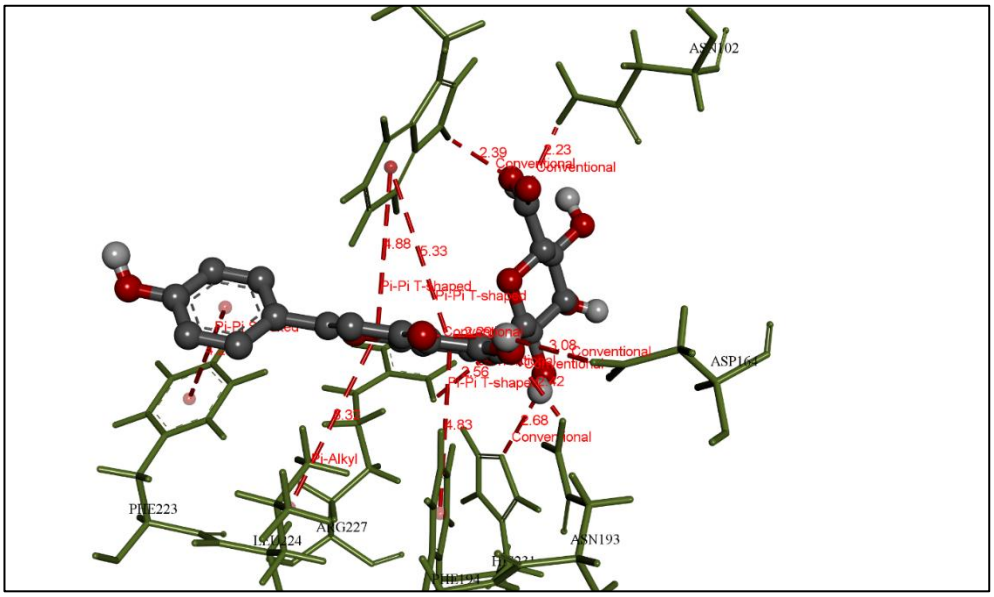


Fig. 4.32: Analysis of 5AR2's three-dimensional interactions with Apigenin-7-glucuronide

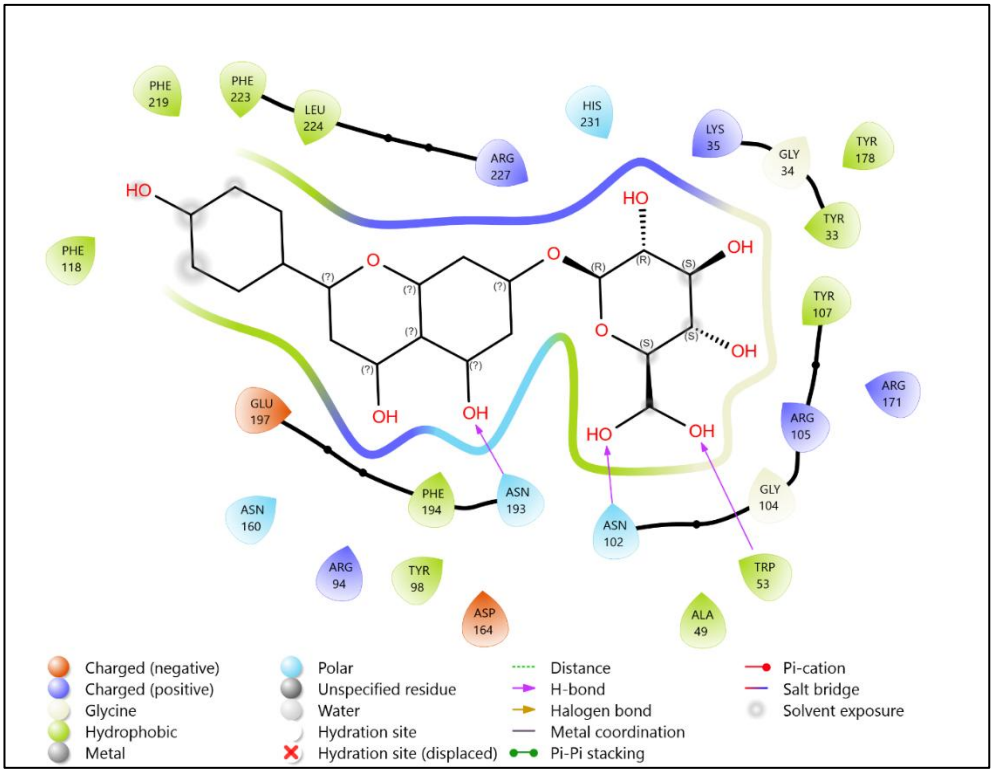


Fig. 4.33: Analysis of 5AR2's two-dimensional interactions with Apigenin-7-glucuronide

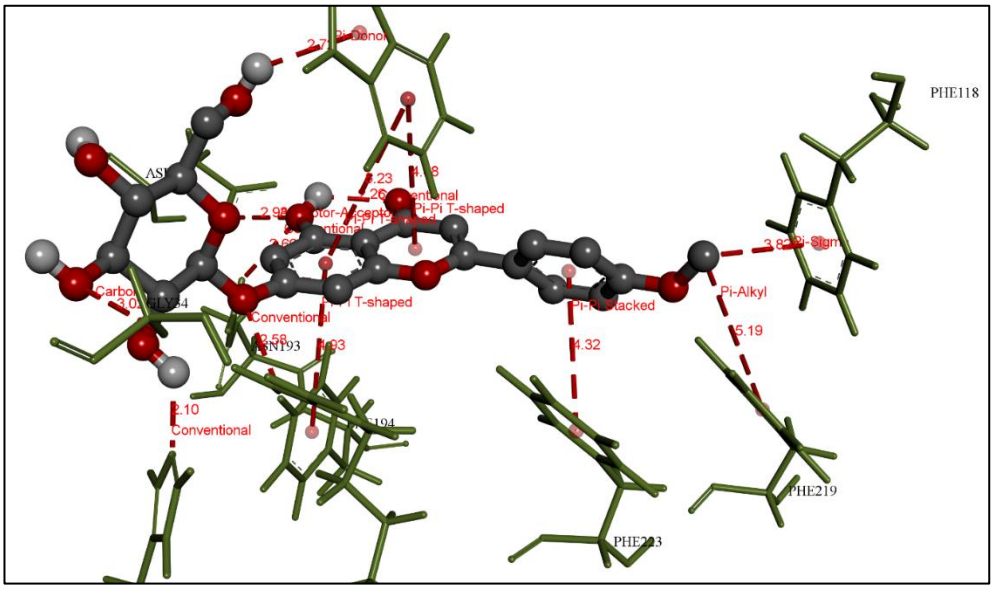


Fig. 4.34: Analysis of 5AR2's three-dimensional interactions with Tilianin

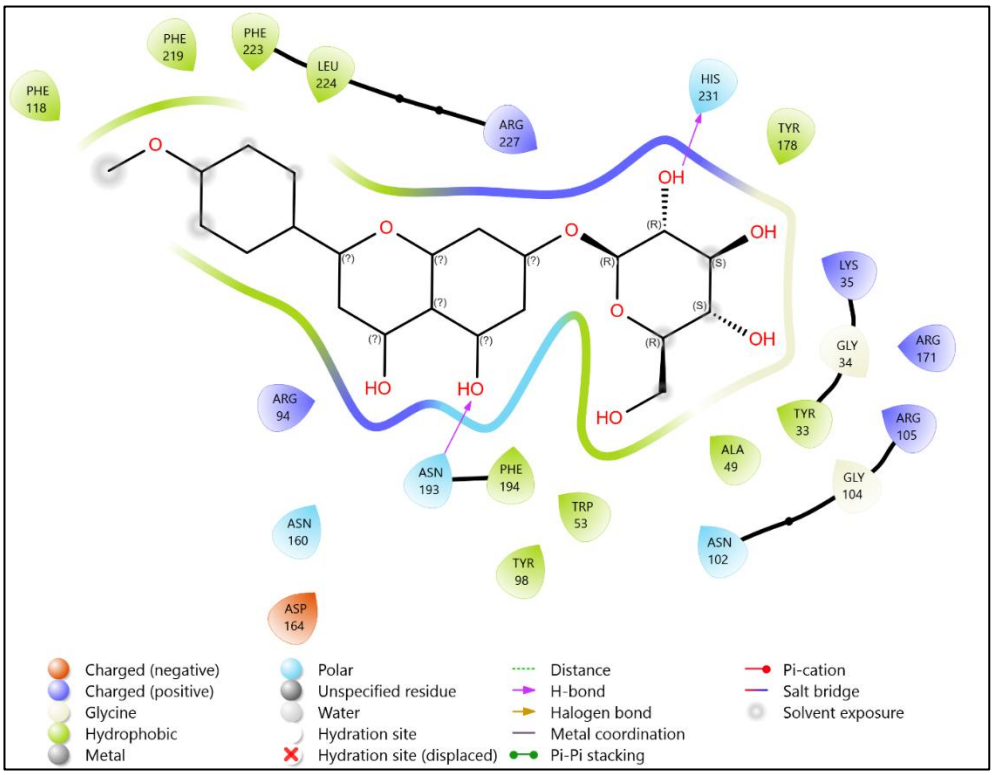


Fig. 4.35: Analysis of 5AR2's two-dimensional interactions with Tilianin

CHAPTER 5: CONCLUSION AND FUTURE DIRECTIONS

As is well known, one of the most prevalent conditions worldwide is androgenic alopecia. Androgenic alopecia is brought on by the 5-alpha reductase enzyme becoming overactive. Due to the hyperactivity of this 5-alpha reductase, the metabolism of testosterone increases in the blood, giving rise to pattern baldness. Currently, the FDA-approved drug finasteride is used to treat androgenic alopecia. Finasteride works as an inhibitor of 5-alpha reductase and blocks DHT formation, but continuous use can cause side effects in the body. Hence, there is a need for a drug that has fewer side effects and is an effective drug for the treatment of androgenic alopecia. In this work, we used computational techniques to identify an effective physical chemical that can replace finasteride, utilizing 120 physical compounds from five medicinal plants. In this study, we used two isoforms of 5-alpha reductase, 5AR1 and 5AR2, as the target enzyme because this is mainly responsible for androgenic alopecia. When we docked these phytochemicals on both 5AR1 and 5AR2 enzymes, seven such phytochemicals were found whose binding energy was higher than that of finasteride with both 5AR enzymes. After docking, ADME and Toxicity analysis revealed that Kaempferol phytochemical obtained from Allium cepa plant was an effective drug candidate. The binding affinity of kaempferol with both 5-alpha reductase enzymes is -9.2 kcal/mol. ADME properties showed that it is a drug-like compound that could be an effective drug for androgenic alopecia. Kaempferol phytochemical follows Lipinski and Veber's rule and does not show PAINS and brain alert, making it a drug-like compound.

Based on the aforementioned research, we may conclude that kaempferol may be a useful medication for treating androgenic alopecia. Because it is a phytochemical, its adverse effects will also be substantially lower than those of finasteride. Before using this phytochemical as an effective drug in the future, we can perform molecular dynamics simulations to understand its dynamic behaviour with both 5-alpha reductase enzymes. By studying molecular dynamics simulations, we can find the stability of the complex formed with the enzyme of this phytochemical. Additionally, we can determine how the binding of phytochemicals alters the protein's structure.

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CONFERENCE

1. Gave a Poster Presentation at the International Conference on **"Health and Agricultural Biotechnology: Interdisciplinary Trends [HABIT-2025]"** at **Motilal Nehru National Institute of Technology Allahabad, Prayagraj.** (28 Feb – 2 March, 2025)


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DTU, delhi has
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in HABIT-2025.
Dr. Joyabrata Mal
(Treasurer)
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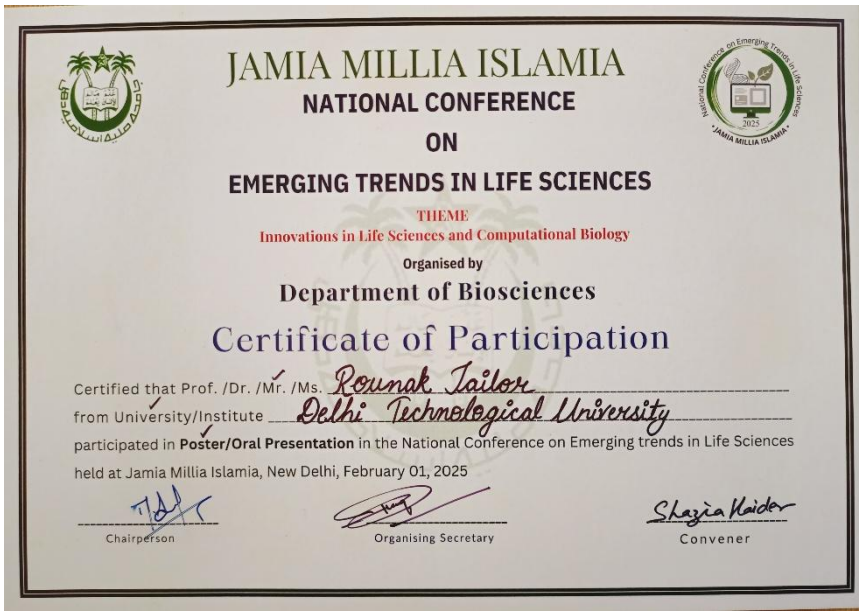
Ministry Science & Technology

2. Gave a Poster Presentation at the National Conference on "**Emerging Trends in Life Sciences**" under the Theme Innovations in Life Sciences and Computational Biology at **Jamia Millia Islamia, New Delhi.** (1 Feb, 2025)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Chairperson
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