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# Molecular Docking Studies of Some Phytoconstituents as Anti-Obesity Agent

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**Keywords:** Obesity, gastrointestinal cancers, dyslipidemia, hypertension, BMI, Molecular Docking

**ABSTRACT**

Obesity is now a global problem and is associated with a number of chronic conditions including osteoarthritis, obstructive sleep apnea, gallstones, fatty liver disease, reproductive and gastrointestinal cancers, dyslipidemia, hypertension, type 2 diabetes, heart failure, coronary artery disease, and stroke. Lifestyle modifications such as diet and exercise intervention are essential for both prevention and management of obesity, and pharmacotherapy may be considered if the interventions are ineffective for individuals with a body mass index [BMI] ≥30 kg/m$^2$ or for those with a BMI ≥27 kg/m$^2$ when co-morbidities, such as hypertension or type 2 diabetes mellitus are present. The glide score of the plant constituents and standard drugs are shown in table 2 and table 3. The interaction between the plant constituents and standard drugs are shown in Figure 8 and Figure 9. Best compounds from each plant are identified according to their glide score and interaction with the receptor. It is concluded that those compounds can be effectively used in the treatment of obesity, particularly against **Diet-induced obesity.** Further work can be done to isolate those compounds and formulate into a suitable formulation which can be used effectively in the treatment of obesity.

## INTRODUCTION

### Obesity

Obesity is now a global problem and is associated with a number of chronic conditions including osteoarthritis, obstructive sleep apnea, gallstones, fatty liver disease, reproductive and gastrointestinal cancers, dyslipidemia, hypertension, type 2 diabetes, heart failure, coronary artery disease, and stroke. Lifestyle modifications such as diet and exercise intervention are essential for both prevention and management of obesity, and pharmacotherapy may be considered if the interventions are ineffective for individuals with a body mass index [BMI] ≥30 $kg/m^2$ or for those with a BMI ≥27 $kg/m^2$ when co-morbidities, such as hypertension or type 2 diabetes mellitus are present. However, anti-obesity drugs are a frequent adjunct, because these interventions have limited long-term success and the weight is regained when treatment is discontinued.[1] Various explanations for these increases have been put forward, such as sedentary lifestyles and higher levels of fat intake.[2]

### Risk Factors

The risk of obesity may vary between different ethnic groups. Asians are at greater risk of developing obesity when compared to Afro-Caribbean. South Asians are particularly at risk of developing abdominal obesity and there is also an increased prevalence of insulin resistance in this group. People's risk of obesity varies over the life cycle.

## STANDARD ANTI-OBESITY AGENTS

The existing pharmaceuticals fail to come up with long-term solutions to address this issue, there is an ever-pressing need to find and develop new drugs and alternatives. Natural products, particularly medicinal plants, are believed to harbor potential anti-obesity agents that can act through various mechanisms either by preventing weight gain or promoting weight loss amongst other.[3]

The standard available drugs currently used in the market and their mechanism are listed in table 1.

| GENERIC NAME | MECHANISM OF ACTION |
|---|---|
| Orlistat | It inhibits the lipase enzyme. |
| Danthron | RXR receptor antagonist[13] |
| Fexaramine | FXR receptor antagonist[14] |
| Atorvastatin | It inhibits the HMG-COA reductase enzyme. |
| Bezafibrate | HDL levels are increased. The activity of triglyceride lipase involved in the catabolism of TG rich lipoprotein is increased by bezafibrate. |
| Ezetimibe | It is a lipid lowering agent. |
| Fenofibric acid | It inhibits HMG-COA reductase enzyme. |
| Fluvastatin | It also inhibits the HMG-COA reductase enzyme. |
| Gemfibrozil | It reduces the cholesterol level &TG level in blood. |
| Lovastatin | It also inhibits the HMG-COA reductase enzyme. |
| Rosuvastatin | It acts by inhibiting the HMG-COA reductase enzyme. |

## MATERIALS AND METHODS

### PLANTS USED

#### *1. Alnus hirsuta*

*Alnus* (alders) is an important genus belonging to Betulaceae which comprises 30 species worldwide. Almost all plants of this genus have been traditionally used as folk medicine in Ayurveda, Unani, and Chinese medical systems.[4]


**Figure 1: *Alnus hirsuta***

**Chemical constituents**

- Betulin, Hirsunin, Hirsutanone, Hirsutanolol, Hirsutolide, Oregonian, Platyphyllonol
- Platyphylloside

**Uses**

The bark of *Alnus hirsuta* is used in Korean and Chinese traditional medicine as remedies for fever, hemorrhage, alcoholism, and diarrhea.[4]

Extract of *Alnus hirsuta* inhibited triglyceride (TG) formation by human HepG2 cells.[5]

***2. Artemisia scoparia***

The genus *Artemisia* (commonly wormwood or sagebrush) is one of the largest and most widely distributed genera of the family Asteraceae. It consists of around 300–400 species of herbs and shrubs well-known for their volatile oil. It is distributed from Central Europe to Western Asia (including, China, Japan, India, Afghanistan) and extends up to 2100 m in the western Himalayas.[6]

**Figure 2: *Artemisia scoparia***

**Chemical constituents**

- Acenaphthene, Acetyl Isoeugenol, B- Myrcene, B- Eudesmol, B- Caryophyllene
- Caryophyllene oxide, Citronellol, Geraniol, Isopulegol, Limonene, P- Cymene

**Uses**

Anti-obesity, anti-malarial, hepatoprotective, free radical scavenging agent used in the contemporary medicines.[6][7]

*Artemisia* extracts prevent body weight increase and improve dyslipidemia in HFD-induced obese rats by enhancing their lipid metabolism.[7]

***3. Hoodia gordonii***

*Hoodia gordonii* is a spiny succulent plant with rows of small thorns present along with the fleshy, green gray or gray-brown stem belongs to the family Apocyanacae. It is widely distributed throughout the South Africa and Namibia which can survive at extreme temperature of about more than 40 degrees.[8]

**Figure 3:** ***Hoodia gordonii***

**Chemical constituents**

- Gordonoside B, Gordonoside C, Hoodigoside A, Hoodigoside C, Hoodistanaloside
- Hoodistanaloside B

**Uses**

It is consumed for its purported anti-obesity effect. Traditionally used by the Khoi-San of South Africa and Namibia as a hunger and thirst suppressant while on long hunting trips**.[**8] *Hoodia* extract supplemented rats exhibited significant weight loss (P<0.001).[9]

***4. Murraya koenigii***

It is a small tree, growing 4-6m tall, with a trunk up to 40 cm in diameter. The aromatic leaves are pinnate, with 11-21 leaflets, each leaflet 2-4 cm long and 1-2 cm broad. The plant produces small white flowers which can self–pollinate to produce small shiny blackberries containing a single , large visible seed.

**Figure 4 : *Murraya koenigii***

**Chemical constituents**

- 3- Carene, 3-Thujene, 4-Phenyl butyrophenone, Allyldimethylsilane
- A- Elemene, A-Terpinene, B-Elemene, Caryophyllene, Girinimbine
- Mahanimbine, Murranimbine

**Uses**

The leaves of *Murraya koenigii* are also used as an herb in ayurvedic medicine. The plant is also used in soap making, body lotions, scent, air fresheners, body fragrance, perfume, bath & massage oils, aromatherapy. It significantly lowered the body weight gain as well as plasma TC and TG levels.[11]

***1. Salvia Miltiorrhiza***

*Salvia miltiorrhiza* is a well-known traditional Chinese herb, belongs to the family of Labiatae. It is a perennial flowering plant in the genus Salvia, highly valued for its roots in traditional Chinese medicine. Native to China and Japan, it grows between 90-1200 m elevations. Leaves are simple or divided, depending on their position on the stem. Flower petals are purple or blue held within a dark purple calyx.[12]

**Figure5: *Salvia Miltiorrhiza***

**Chemical constituents**

➢ Arucadiol, Baicailin, β-sitosterol, Cryptotanshinone, Danshensu, Daucosterol, Isoferulic acid, Miltrione, Rosmarinic acid, Salviol, Stigmasterol, Tanshindiol A, Tanshindiol B, Tanshinlactone, Tanshinone ,Urusolic, acid

**Uses**

Anti-cancer, anti-inflammatory, anti-oxidant, anti-microbial, anti-virus and cardioprotective agent[12]. It is reported as an anti-obesity agent which reduces the body weight of the rat.[13]

**Receptors**

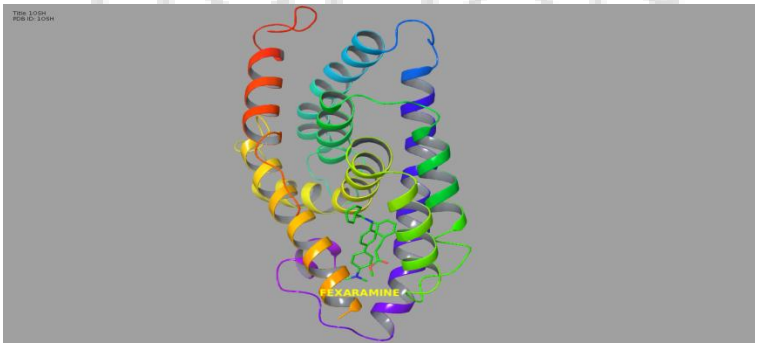


**Figure 6: Farnesoid X receptor**

The farnesoid X receptor (FXR), also known as bile acid receptor (BAR), or NR1H4 (nuclear receptor subfamily 1, group H, member 4) is a nuclear receptor that is encoded by the *NR1H4* gene in humans. FXR is expressed at high levels in the liver and intestine. Chenodeoxycholic acid and other bile acids are natural ligands for FXR. Similar to other nuclear receptors, when activated, FXR translocates to the cell nucleus, forms a dimer (in this case a heterodimer with RXR) and binds to hormone response elements on DNA, which up- or down-regulates the expression of certain genes. One of the primary functions of FXR activation is the suppression of cholesterol 7 alpha-hydroxylase (CYP7A1), the rate-limiting enzyme in bile acid synthesis from cholesterol. FXR does not directly bind to the CYP7A1 promoter. Rather, FXR induces expression of small heterodimer partner (SHP), which then functions to inhibit transcription of the CYP7A1 gene. In this way, a negative feedback pathway is established in which synthesis of bile acids is inhibited when cellular levels are already high. FXR has also been found to be important in regulation of hepatic triglyceride levels. Studies have also shown the FXR to regulate the expression and activity of epithelial transport proteins involved in fluid homeostasis in the intestine, such as the cystic fibrosis conductance transmembrane regulator (CFTR)[IS2].

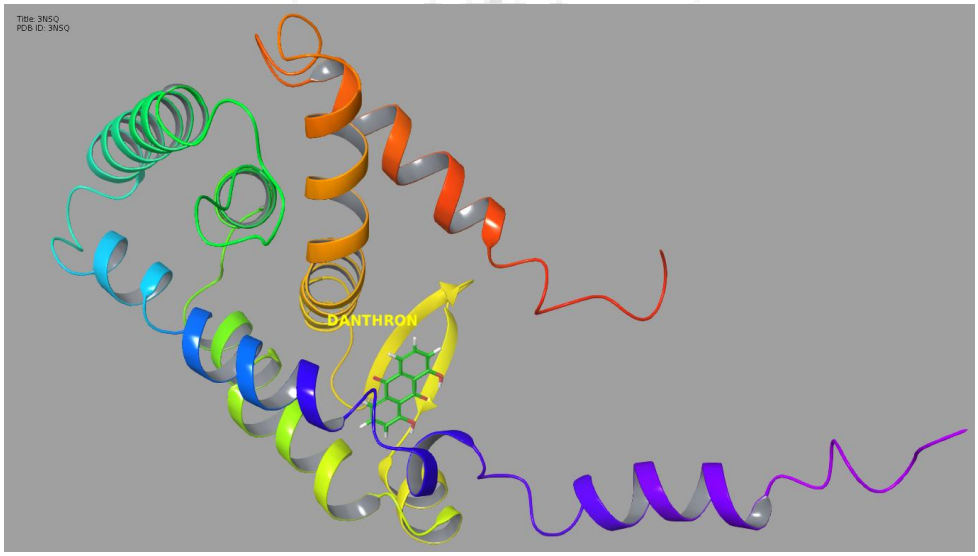


**Figure 7: Retinoic X Receptor**

Retinoid X receptor (RXR), also known as NR2B1 (nuclear receptor subfamily 2, group B, member 1) is a nuclear receptor that in humans is encoded by the *RXRA* gene. Retinoid X receptors (RXRs) and retinoic acid receptors (RARs) are nuclear receptors that mediate the

biological effects of retinoids by their involvement in retinoic acid-mediated gene activation. These receptors exert their action by binding, as homodimers or heterodimers, to specific sequences in the promoters of target genes and regulating their transcription. The protein encoded by this gene is a member of the steroid and thyroid hormone receptor superfamily of transcription factors. In the absence of ligand, the RXR-RAR heterodimers associate with a multiprotein complex containing transcription corepressors that induce histone deacetylation, chromatin condensation and transcriptional suppression. On ligand binding, the corepressors dissociate from the receptors and associate with the coactivators leading to transcriptional activation.[IS1]

**Schrodinger software**

1. **Accurate docking and scoring for lead optimization**

Structure-based virtual screening primarily consists of two key steps: (1) obtaining an accurate structure of the protein-ligand complex (docking) and (2) accurately predicting the ligand binding affinity (scoring). This work describes recent developments at Schrodinger in complimentary methods designed to enhance docking and scoring. We focus on key components in virtual screening, including ligand-induced receptor flexibility, enhanced ligand sampling methods, and an improved scoring function for docking [IS3].

High-quality protein-ligand structures are imperative for understanding the structural basis for ligand binding. Accounting for receptor flexibility is a major challenge in the development of computational methods. Conformational adaptation ranges from subtle side-chain motion to dramatic backbone rearrangements. We present our novel and robust methodology for computing induced-fit effects in protein-ligand complexes [1]. Extensive validations show that the obtained induced-fit structures can be used as members of a target ensemble in virtual screening studies to significantly improve the enrichments in database screens.

To address the scoring problem, we describe results that have been obtained with the extra precision (XP) version of the Glide program [2]. In addition to a number of improvements in the general scoring function, Glide XP accounts for both penalties and rewards upon binding through the explicit docking of water molecules. Finally, we discuss a combinatorial version of the Glide

algorithm (CombiGlide) which can be used for the design of focused libraries. The ability of CombiGlide to rank known active compounds in a high position are presented [IS3].

## 2. Introduction of Quantum Mechanics in protein/ligand docking

The extent to which accuracy of electric charges plays a role in protein-ligand docking is investigated through development of a docking algorithm, which incorporates quantum mechanical/molecular mechanical (QM/MM) calculations. In this algorithm, fixed charges of ligands obtained from force field parameterization are replaced by QM/MM calculations in the protein environment, treating only the ligands as the quantum region. The algorithm is tested on a set of 433 co-crystallized structures taken from the Protein Data Bank (PDB) and provides strong evidence that use of nonfixed charges is important. An algorithm, dubbed "Survival of the Fittest" (SOF) algorithm, is implemented to incorporate QM/MM charge calculations without any prior knowledge of native structures of the complexes. Using an iterative protocol, this algorithm is able in many cases to converge to a native like structure in systems where redocking of the ligand using a standard fixed charge force field exhibits nontrivial errors. The results demonstrate that polarization effects can play a significant role in determining the structures of protein-ligand complexes, and provide a promising start towards the development of more accurate docking methods for lead optimization applications [IS3].

## 3. PHASE: A New Engine for Pharmacophore Perception, 3D QSAR Model Development, and 3D Database Screening.

We introduce PHASE, a highly flexible system for common pharmacophore identification and assessment, 3D QSAR model development, and 3D database creation and searching. The primary workflows and tasks supported by PHASE are described, and details of the underlying scientific methodologies are provided. Using results from previously published investigations, PHASE is compared directly to other ligand-based software for its ability to identify target pharmacophores, rationalize structure-activity data, and predict activities of external compounds [IS3].

## RESULTS AND DISCUSSION

Table 2- Glide score and interactions of Test & Standard compounds with FXR receptor

**Table 2a- *Alnus hirsuta* with FXR receptor**

| Compound Name | H-Bond interaction | II-Cation interaction | II-II interaction | Glide score |
|---|---|---|---|---|
| Fexaramine* | HIS 298<br>SER 336 | - | TRP 473 | -13.427 |
| Platyphylloside | SER 336<br>HIS 298<br>LEU 352<br>TYR 365<br>LEU 291 | - | - | -10.944 |
| Hirsutanone | LEU 352<br>TRP 458<br>THR 293 | - | - | -8.946 |
| Oregonin | ARG 355<br>ASN 287<br>TYR 365<br>LEU 291 | - | - | -8.851 |
| Hirsutanonol | TYR 365<br>HIS 298<br>SER 336<br>TRP 458 | - | TRP 458<br>TRP 473 | -8.789 |
| Rubranoside | HIS 298<br>SER 336<br>LEU 352<br>TYR 365<br>LEU 291 | - | - | -8.773 |
| Platyphyllonol | TYR 365 | - | - | -8.226 |

| | | | | |
|---|---|---|---|---|
| | LEU 352<br>THR 292<br>TRP 473 | | | |
| Retinol | TYR 373 | - | - | -6.932 |
| Rhoiptelol | TYR 365<br>SER 336<br>HIS 298 | - | - | -6.519 |
| Hirsutolide | - | - | - | -5.804 |
| Betulin | X | X | X | X |
| Hirsunin | X | X | X | X |
| Pedunculagin | X | X | X | X |
| Praecoxin | X | X | X | X |
| Rugosin | X | X | X | X |
| Tellimagrandin | X | X | X | X |

***Standard Compound**

**Table 2b- *Artemisia scoparia* with FXR Receptor**

| Compound Name | H-Bond interaction | Π-Cation interaction | Π-Π interaction | Glide score |
|---|---|---|---|---|
| Acenaphthene | - | - | PHE 288<br>TRP 470 | -7.631 |
| P-Cymene | - | - | TRP 473 | -7.234 |
| β-Eudesmol | - | - | - | -7.034 |
| Acetyl isoeugenol | SER 336<br>HIS 298 | - | - | -6.94 |
| Caryophyllene Oxide | - | - | - | -6.627 |
| β-Caryophyllene | - | - | - | -6.275 |
| Isopulegol | - | - | - | -6.031 |
| Limonene | - | - | - | -6.003 |

| | | | | |
|---|---|---|---|---|
| Geraniol | TYR 365 | - | - | -5.157 |
| Citronellol | - | - | - | -4.196 |
| β-Myrcene | - | - | - | -4.159 |

**Table 2c- *Hoodia gordonii* with FXR Receptor**

| Compound Name | H-Bond interaction | Π-Cation interaction | Π-Π interaction | Glide score |
|---|---|---|---|---|
| Gordonoside B | X | X | X | X |
| Gordonoside C | X | X | X | X |
| Hoodigoside A | X | X | X | X |
| Hoodigoside C | X | X | X | X |
| Hoodistanoloside A | X | X | X | X |
| Hoodistanoloside B | X | X | X | X |

**Table 2d- *Murraya koenigii* with FXR Receptor**

| Compound Name | H-Bond interaction | Π-Cation interaction | Π-Π interaction | Glide score |
|---|---|---|---|---|
| 4-Phenyl butyrophenone | - | - | HIS 298<br>TRP 458<br>TRP 473 | -8.3 |
| Mahanimbine | SER 336 | - | PHE 340 | -7.811 |
| α- Elemene | - | - | - | -7.414 |
| Girinimbine | - | - | - | -7.129 |
| α- Terpinene | - | - | - | -6.978 |
| 3- Thujene | - | - | - | -6.977 |
| Murranimbine | - | - | - | -6.606 |
| α- Elemene | - | - | - | -6.238 |
| 3- Carene | - | - | - | -6.058 |
| Limonene | - | - | - | -6.003 |
| Allyl Dimethyl silane | - | - | - | -4.408 |

| | | | | |
|---|---|---|---|---|
| Phytol | THR 292 | - | - | -4.319 |
| Myrcene | - | - | - | -4.159 |
| Carypohyllene | X | X | X | X |
| Sabinene Hydrate | X | X | X | X |

**Table 2e- *Salvia miltiorrhiza* with FXR Receptor**

| Compound Name | H-Bond interaction | Π-Cation interaction | Π-Π interaction | Glide score |
|---|---|---|---|---|
| Stigmasterol | - | - | - | -8.796 |
| β-Sitosterol | - | - | - | -8.7 |
| Cryptotanshinone | HIS 298 | - | - | -6.813 |
| Tanshinlactone | - | - | - | -6.593 |
| Salviol | SER 336 | - | - | -6.593 |
| Miltrione | SER 336<br>HIS 298 | - | - | -6.271 |
| Baicalin | HIS 298<br>SER 336 | - | - | -6.236 |
| Danshensu | HIS 298<br>TYR 365<br>SER 336<br>TYR 373<br>LEU 291 | - | - | -5.708 |
| Tanshinone | X | X | X | X |
| Arucadiol | X | X | X | X |
| Daucosterol | X | X | X | X |
| Isoferulic acid | X | X | X | X |
| Rosmarinic acid | X | X | X | X |
| Ursolic acid | X | X | X | X |
| Tanshindiol A | X | X | X | X |
| Tanshindiol B | X | X | X | X |

**Table 3- Glide score and interactions of Test & Standard compounds with RXR receptor**

**Table 3a- *Alnus hirsuta* with RXR Receptor**

| Compound Name | H-Bond interaction | Π-Cation interaction | Π-Π interaction | Glide score |
|---|---|---|---|---|
| Danthrone* | - | LYS 440 | PHE 437 | -6.523 |
| Platyphylloside | ILE 345<br>PHE 346<br>LYS 440<br>HIS 269<br>GLN 275<br>ASN 306 | - | - | -6.511 |
| Hirtsutanone | ASN 306<br>LYS 440<br>PHE 346<br>ILE 345 | - | - | -6.439 |
| Platyphyllonol | ASN 306<br>LYS 440<br>PHE 438 | - | PHE 437 | -6.36 |
| Hirsutanonol | LYS 440<br>ASN 306 | - | PHE 437 | -6.223 |
| Oregonin | ASN 306<br>CYS 269<br>LYS 440 | - | - | -6.053 |
| Retinol | - | - | - | -5.741 |
| Rubranoside | ALA 327<br>LYS 440<br>CYS 269 | LYS 440 | PHE 437 | -5.45 |
| **Compound Name** | **H-Bond interaction** | **Π-Cation interaction** | **Π-Π interaction** | **Glide score** |
| Danthrone* | - | LYS 440 | PHE 437 | -6.523 |

| | | | | |
|---|---|---|---|---|
| Platyphylloside | ILE 345<br>PHE 346<br>LYS 440<br>HIS 269<br>GLN 275<br>ASN 306 | - | - | -6.511 |
| Hirtsutanone | ASN 306<br>LYS 440<br>PHE 346<br>ILE 345 | - | - | -6.439 |
| Platyphyllonol | ASN 306<br>LYS 440<br>PHE 438 | - | PHE 437 | -6.36 |
| Hirsutanonol | LYS 440<br>ASN 306 | - | PHE 437 | -6.223 |
| Oregonin | ASN 306<br>CYS 269<br>LYS 440 | - | - | -6.053 |
| Retinol | - | - | - | -5.741 |
| Rubranoside | ALA 327<br>LYS 440<br>CYS 269 | LYS 440 | PHE 437 | -5.45 |
| Hirsutolide | LYS 440 | - | - | -4.691 |
| Betulin | - | - | - | -4.161 |
| Rhoiptelol | LYS 440 | - | - | -4.092 |
| Praecoxin | X | X | X | X |
| Hirsunin | X | X | X | X |
| Pedunculagin | X | X | X | X |
| Rugosin | X | X | X | X |
| Tellimagrandin | X | X | X | X |

***Standard Compound**

**Table 3b- *Artemisia scoparia* with RXR Receptor**

| Compound Name | H-Bond interaction | Π-Cation interaction | Π-Π interaction | Glide score |
|---|---|---|---|---|
| Acenapthene | - | LYS 440 | PHE 437 | -6.96 |
| P-Cymene | - | LYS 440 | PHE 437 | -6.248 |
| β- Eudesmol | LYS 440 | - | - | -5.827 |
| Caryophyllene oxide | - | - | - | -5.592 |
| β- Caryophyllene | - | - | - | -5.584 |
| Limonene | - | - | - | -5.451 |
| Acetyl isoeugenol | LYS 440 | - | PHE 437<br>PHE 313 | -5.45 |
| Isopulegol | - | - | - | -5.378 |
| Geraniol | ASN 306 | - | - | -4.183 |
| Citronellol | ASN 306 | - | - | -3.585 |
| β- Myrcene | - | - | - | -2.799 |

**Table 3c- *Hoodia gordonii* with RXR Receptor**

| Compound Name | H-Bond interaction | Π-Cation interaction | Π-Π interaction | Glide score |
|---|---|---|---|---|
| Gordonoside B | X | X | X | X |
| Gordonoside C | X | X | X | X |
| Hoodigoside A | X | X | X | X |
| Hoodigoside C | X | X | X | X |
| Hoodistanoloside A | X | X | X | X |
| Hoodistanoloside B | X | X | X | X |

**Table 3d- *Murraya koenigii* with RXR Receptor**

| Compound Name | H-Bond interaction | Π-Cation interaction | Π-Π interaction | Glide score |
|---|---|---|---|---|
| 4-Phenyl butyrophenone | - | - | PHE 437<br>PHE 313 | -6.922 |
| Girinimbine | - | LYS 440 | PHE 437 | -6.654 |
| Mahanimbine | - | - | PHE 437<br>PHE 313 | -6.6 |
| 3-Thujene | LYS 440 | - | - | -6.263 |
| 3-Carene | - | - | - | -6.198 |
| α- Elemene | - | - | - | -5.934 |
| α- Terpinene | - | - | - | -5.726 |
| Caryophyllene | - | - | - | -5.503 |
| Limonene | - | - | - | -5.454 |
| Murranimbine | - | - | PHE 313 | -5.118 |
| α- Elemene | - | - | - | -5.101 |
| Allyldimethylsilane | - | - | - | -3.708 |
| Myrcene | - | - | - | -2.799 |
| Phytol | ASN 306 | - | - | 2.16 |
| Sabinene Hydrate | X | X | X | X |

**Table 3e- *Salvia miltiorrhiza* with RXR Receptor**

| Compound Name | H-Bond interaction | Π-Cation interaction | Π-Π Interaction | Glide score |
|---|---|---|---|---|
| Cryptotanshinone | - | - | PHE 313<br>PHE 437 | -7.35 |
| Baicalin | LYS 440<br>CIS 269 | - | PHE 437 | -7.088 |
| Tanshinlactone | - | - | PHE 313<br>PHE 437 | -6.932 |

| | | | | |
|---|---|---|---|---|
| Daucosterol | - | LYS 440 | PHE 437 | -6.801 |
| Miltrione | - | - | PHE 313<br>PHE 437 | -6.62 |
| β- Sitosterol | PHE 346 | - | - | -6.344 |
| Stigmasterol | ALA 271 | - | - | -6.051 |
| Salviol | - | LYS 440 | PHE 437 | -5.943 |
| Danshensu | LYS 440<br>ASN 306 | - | - | -5.119 |
| Arucadiol | X | X | X | X |
| Daucosterol | X | X | X | X |
| Isoferulic acid | X | X | X | X |
| Rosmarinic acid | X | X | X | X |
| Ursolic acid | X | X | X | X |
| Tanshindiol A | X | X | X | X |
| Tanshindiol B | X | X | X | X |

**Figure 8: Represents the interactions between the Ligand and FXR Receptor.**

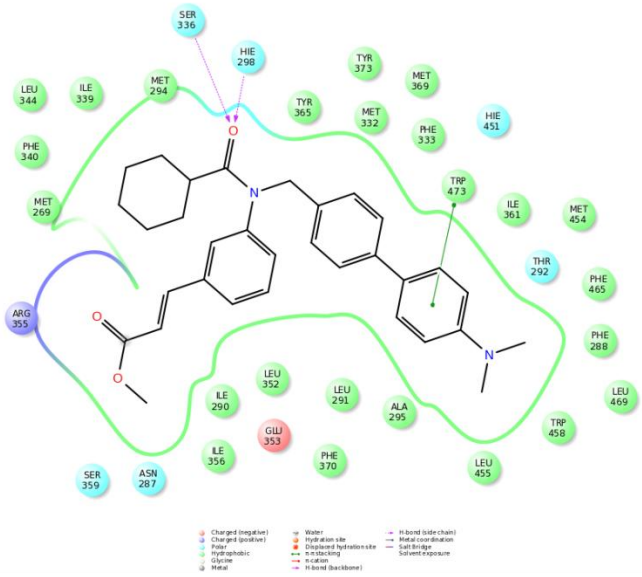


**Fig 8a: Interaction of Fexaramine (Standard) with FXR receptor**

Fexaramine forms H-Bond interaction with HIS 298, SER 336 and Π-Π interaction with TRP-473.

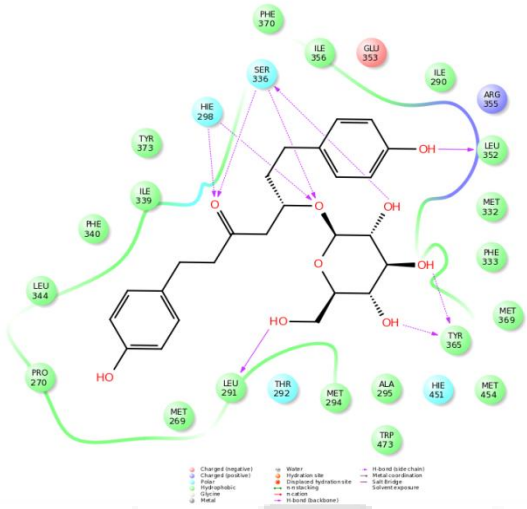


**Fig 8b: Interaction of Platyphylloside with FXR receptor**

Platyphylloside forms H-Bond interaction with SER 336, HIS 298, LEU 352, TYR 365, LEU 291.

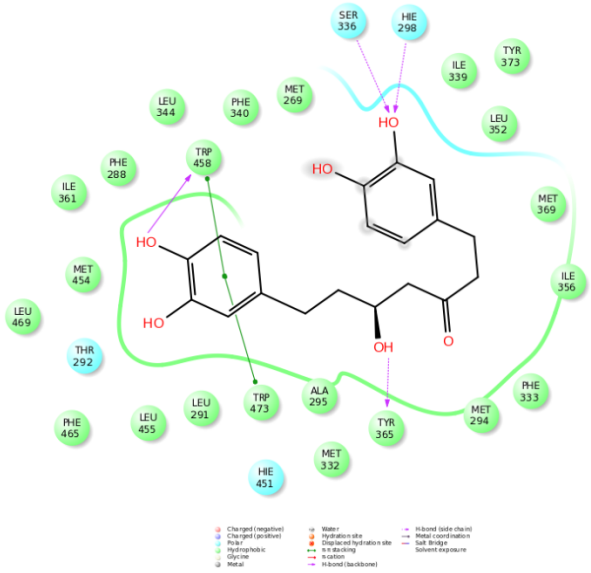


**Fig 8c: Interaction of Hirsutanonol with FXR receptor**

Hirsutanonol forms H-Bond interaction with TYR 365, HIS 298, SER 336, TRP 458 and forms Π-Π interaction with TRP 473, TRP 458.

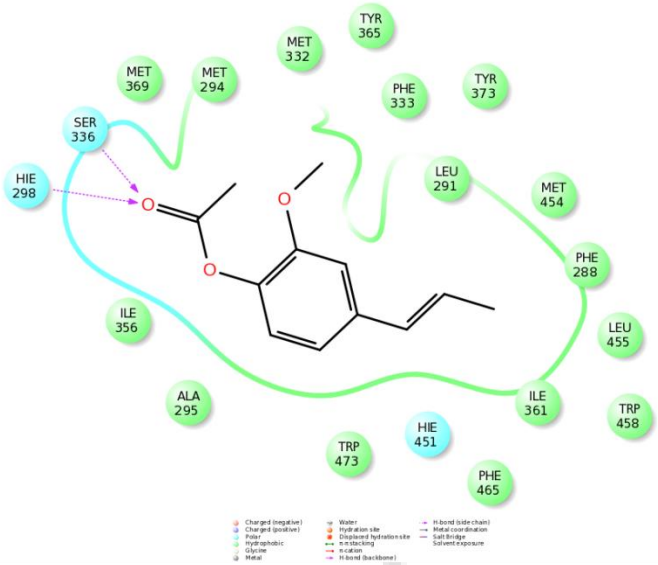


**Fig 8d: Interaction of Acetyl Isoeugenol with FXR receptor**

Acetyl Isoeugenol forms H-Bond interaction with SER 336, HIS 298.

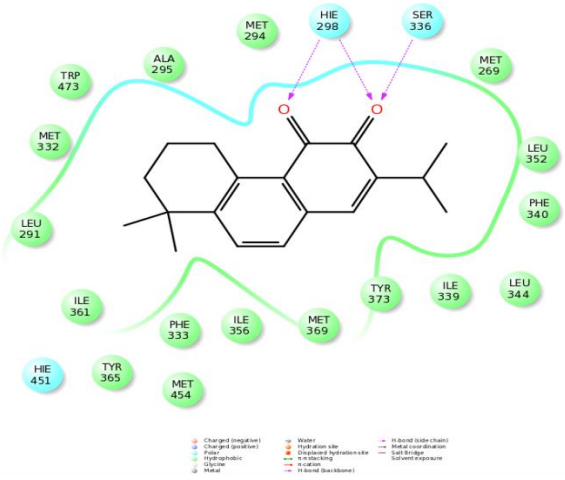


**Fig 8e: Interaction of Miltrione with FXR receptor**

Miltrione forms H-Bond interaction with SER 336, HIS 298.

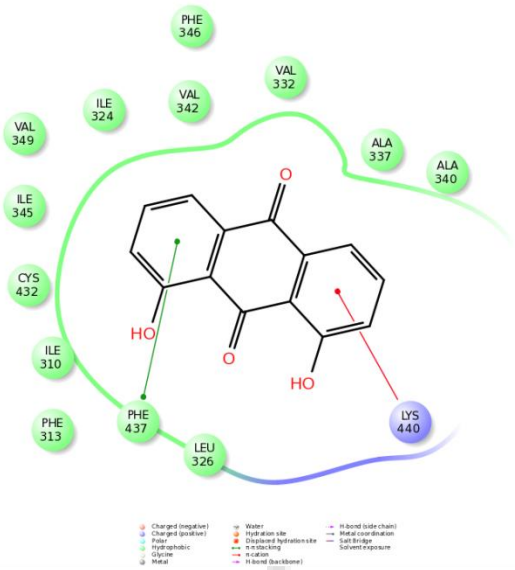


**Fig 9a: Interaction of Danthron (standard) with RXR receptor**

Danthron forms Π-Cation interaction with LYS 440 and Π-Π interaction PHE 437.

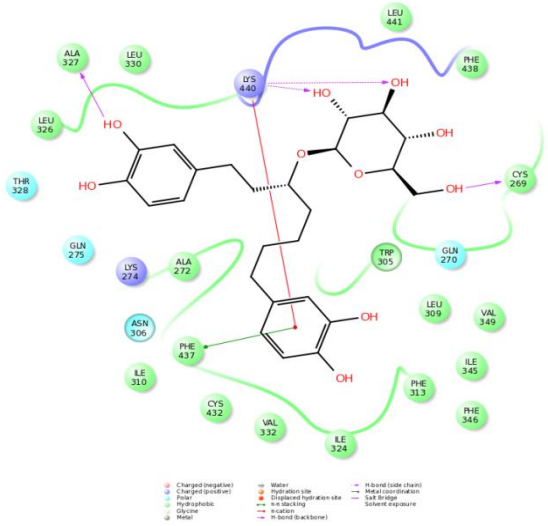


**Fig 9b: Interaction of Rubranoside with RXR receptor**

Rubranoside forms H-Bond interaction with ALA 327, LYS 440, CYS 269, Π-Cation interaction with LYS 440 and Π-Π interaction with PHE 437

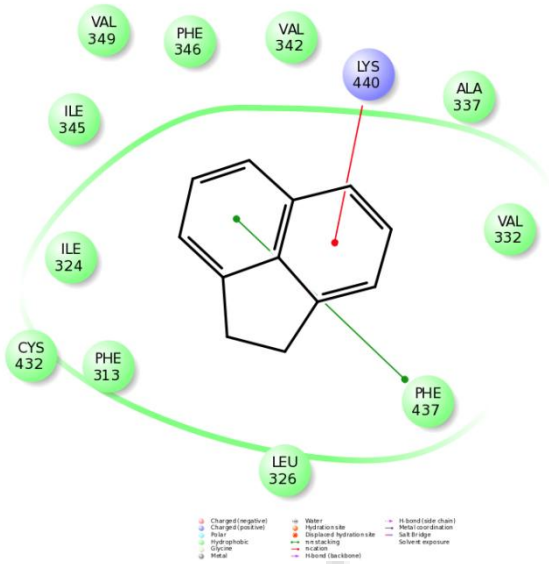


**Fig 9c: Interaction of Acenaphthene with RXR receptor**

Acenaphthene forms Π-Cation interaction with LYS 440 and Π-Π interaction with PHE 437.

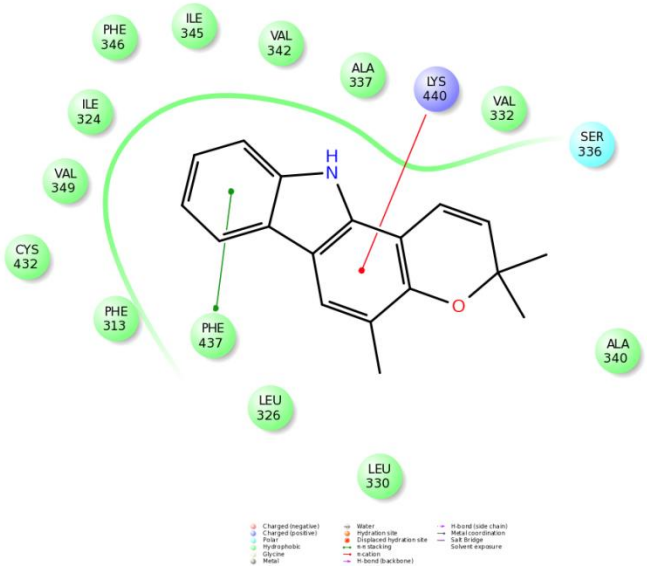


**Fig 9d: Interaction of Girinimbine with RXR receptor**

Girinimbine forms Π-Cation interaction with LYS 440 and Π-Π interaction with PHE 437.

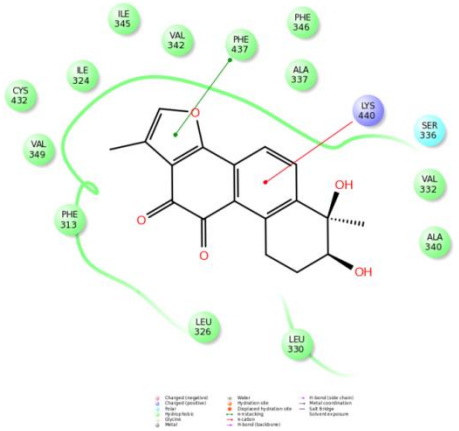


**Fig 9e: Interaction of Entry with RXR receptor**

Entry forms Π-Cation interaction with LYS 440 and Π-Π interaction with PHE 437.

## CONCLUSION

The glide score of the plant constituents and standard drugs are shown in table 2 and table 3. The interaction between the plant constituents and standard drugs are shown in Figure 8 and Figure 9. Best compounds from each plant are identified according to their glide score and interaction with the receptor. It is concluded that those compounds can be effectively used in the treatment of obesity, particularly against **Diet-induced obesity.** Further work can be done to isolate those compounds and formulate into a suitable formulation which can be used effectively in the treatment of obesity.

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