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# IN SILICO DOCKING AND IN VITRO ENZYME INHIBITION ACTIVITY OF UNRIPE FRUITS OF FICUS RACEMOSA LINN

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## ABSTRACT

*Ficus racemosa,* a versatile medicinal plant, is investigated for many biological activities. The plant is a unique source of various types of compounds having diverse chemical structures. The ethnobotanical and reported studies says it is indicated in hyperglycemia and diabetes. In this study it evaluates relationship between various reported terpenoids in fruit of plant and the targeted protein relating to diabetes in human, it involved docking of 3D structures of ligand (compounds) to selected targeted proteins. The *in silico* docking studies confirmed that the terpenoid contents in the fruit is having good interaction to the specific target proteins, among the terpenoids, the 2 compounds, viz. beta sitosterol and Friedelin are having pronounced docking and interaction with receptors 2QMJ and 2V95 the hyperglycemic targets. In invitro enzyme inhibition studies the extracts of unripe fruits of Ficus racemosa was tested to understand the antihyperglycemic potential. Both extracts were found to inhibit enzymes considerably.The methanol extract showed maximum inhibitory activity with alpha amylase enzyme, whereas aqueous extract signaled a maximum inhibitory action with alpha glucosidase enzyme. Docking study and enzyme inhibition data reveals potent implication of unripe fruits of *Ficus racemosa* in Hyperglycemia and Diabetes.

**KEYWORDS:** Hyperglycemia, *Ficus racemosa*, docking, diabetes mellitus, enzyme inhibition, receptors.

## INTRODUCTION

Diabetes mellitus is a distressing metabolic disorder of great concern to health officials, and its rate is increasing in developing and developed countries.[1] High blood sugar (hyperglycemia) affects people who have diabetes, is a condition in which an excessive amount of glucose circulates in the blood plasma. Several factors which can contribute to hyperglycemia include: poor choices food and physical activity, illness, non-diabetes medications, or skipping or not taking enough glucose-lowering medication The longer blood sugar levels stay high, the more serious the symptoms become.[2] It is a common phenotype of uncontrolled diabetes and leads to severe detriment and deprivation in multiple organs of the body, particularly the nerves and blood vessels Temporary hyperglycaemia is often benign and asymptomatic. Blood glucose levels can rise above normal and cause pathological and functional changes for significant periods without producing any permanent effects or symptoms.[3] The World Health Organization report says that 30 million people were diagnosed with diabetes in 1985, This figure increased to 135 million people in 1995, and approximately 300 million people are estimated to be affected by 2025 (WHO, 2016). Diabetes mellitus is classified as type 1 diabetes (5 – 10% of cases) or type 2 diabetes (approximately 90% of cases) based on whether it is instigated by impairment of insulin secretion in the pancreas or by increased insulin resistance.[4] Type 2 diabetes mellitus (T2DM) is genetically heterogeneous and polygenic disease typecast by altered expression of genes and tissue types. Various enzymes and proteins are considered as targets to manage over T2DM.[5] In recent years, much interest has been focused on biologically active compounds occurring in natural resources. Plants have always been an exemplary source of drugs and many of the currently available drugs have been derived directly or indirectly from them. Although, oral hypoglycemic agents are the main stay of treatment of diabetes and are effectual in regulating hyperglycemia, they have extrussive side effects and fail to significantly alter the course of diabetic aggravations.[6]

The natural product, *Ficus racemosa (*FR) belongs to family Moraceae, widely distributed all over India, China, Australia and Southeast Asia. Many bioactive chemical constituents had been isolated from different parts of this plant.[7]

The plant is frequently found around the water streams and is also cultivated. It is a large deciduous tree up to 18m high, leaves are ovate, ovate-lanceolate or elliptic, sub-acute, entire and petiolate and are shed usually by December and replenished by January and April, when

the tree becomes bare for a short period. It has evergreen leaves; if it is close to a water source. Figs are sub globose or pyriform, red when ripe, borne in large clusters, on short, leafless branches emerging from the trunk and the main branches. The tree is without aerial roots unlike its many family members. It is a member of the 4 sacred trees- "Naalpamara" meant to be planted around home and temples, it grows to the elevation of 1800 metres above sea level.[8]

**Taxonomy**

Kingdom : Plantae
Division : Tracheophyta
Class : Magnoliopsida
Order : Rosales
Family : Moraceae
Genus : Ficus
Species : *Ficus racemosa* linn

As per ethnobotanical and traditional knowledge,The fruit is an astringent, stomachic, carminative given in menorrhea and hemoptysis, fruits are used as a remedy for visceral obstruction, diarrhea and constipation. The fruit is regarded as a good remedy for diabetes.[9]

Fruits are reported to contain sterols, triterpenoids, flavonoids, glycosides, tannins, carbohydrates β-sitosterol, gluanol acetate, hentriacontane, tiglic acid, ceryl behenate, lupeol acetate, α-amyrin acetate, lupeol, friedelin, behanate, stigmasterol, β-sitosterol, β-sitosterol-D-glucoside, gluanol acetate, and quercetin.[10]

The pharmacological approaches to regulate blood glucose level include inhibiting enzymes or agonizing the receptor action, proteins involved in diabetes are selected as targets and checked for inhibition or agonist action. Molecular docking is the in silico method which is used to develop the homology model for the new drug candidate.[11] The terpenoids being the sizable reported compounds in the fruits, so to probe the pharmacological action it is decisive to go for molecular docking of the constituents with anti-diabetic targets and enzyme inhibition – (alpha amylase and alpha glucosidase) activity of the extracts of unripe fruits of *Ficus racemosa* linn.[12] In this notion, the present study entails the insilico docking and invitro enzyme inhibition activity.[13]

## MATERIALS AND METHODS

### Materials

The unripe fruits of the plant *ficus racemosa* linn, the drug of interest was collected from the regions of Thrissur, Kerala.The chemicals used in the study were obtained from sigma Aldrich. The docking was performed by the use of Discovery Studio (4.0) protocol.

### Preparation of extract

Selected fruits were shade dried and powdered. The coarse powder of plant material (700 gms of *ficus racemosa*) was subjected for cold maceration using methanol followed by water, each for 72 h. At the end of respective extraction, the separated filtrate was concentrated in vacuum at 40°C under reduced pressure by means of a rotary evaporator (Buchi, Switzerland). The concentrated extracts were further dried in a desiccator to yield dry methanolic and aqueous extract.

### Qualitative phytochemical analysis

The methanolic and aqueous crude extracts of *Ficus racemosa* Linn unripe fruit was subjected to the chemical tests for identification of presence of various active constituents.[14] The test for alkaloids, carbohydrates were done, the steroids were tested by the Libermann Burchard test which is shown positive by the final bluish green colour. The test for flavonoids were performed by shinoda test which is affirmed positive by the formation of pink-red colour. The phenolic compounds were tested by the ferric chloride test. The test for terpenoids were performed by Salkowaskis test that is confirmed by the presence of red brown colour at the interface of solution.

### *In silico* docking studies

Herbal remedies have been considered as potential medication for hyperglycemia and type 2 diabetes. In view of this our drug unripe fruits of *ficus racemosa* Linn was reported to contain terpenoids like lupeol, beta sitosterol, friedelin[15] etc. From the literature survey says that most of the terpenoids are having the antihyperglycemic/antidiabetic effects. So the purpose of the study is to evaluate whether a relationship exists between various reported compounds and the targeted protein relating to diabetes in human, it involves docking of 3D structures of ligand (compounds) to selected targeted proteins.

The 4 terpenoid compounds having cholesterol like structure were designed using the tool ACD Chemsketch, the compounds used are respectively beta sitosterol, alpha amyrin, lupeol and friedelin. The compounds were docked into the crystal structure of Human maltase-glucoamylase (MGAM) Receptor PDB ID 2QMJ,(fig:1) using acarbose and miglitol as standards, Human maltase-glucoamylase (MGAM) is one of the two enzymes responsible for catalyzing the last glucose-releasing step in starch digestion. MGAM is anchored to the small-intestinal brush-border epithelial cells and contains two homologous glycosyl hydrolase family 31 catalytic subunits: an N-terminal subunit (NtMGAM) found near the membrane-bound end and a C-terminal luminal subunit (CtMGAM). And to Transcortin receptor Corticosteroid-binding globulin PDB ID 2V95 (fig:2) which used cortisol as standard, Corticosteroid-binding globulin (CBG) is a serine proteinase inhibitor (serpin) family member that transports glucocorticoids in blood and regulates their access to target cells The procedure was performed by the use of Discovery Studio 4.0 ("CDOCKER" protocol). The compounds were drawn and saved in mol2 format. Then, the hydrogen bonds were added and the molecule was imported and minimized in Discovery Studio. The obtained structure

was saved in PDB format. The employed docking method CDOCKER used CHARMm-based molecular dynamics (MD) scheme to dock ligands into a receptor binding site[16]. Random ligand conformations were generated using high-temperature MD. The obtained conformations were translated into the binding site and compound poses were created using random rigid-body rotations followed by simulated annealing. A final energy minimization was then used to refine the ligand poses. The CDOCKER ENERGY (sum of the internal ligand strain energy and the receptor-ligand non-bonded interaction energy) and CDOCKER INTERACTION ENERGY (the non-bonded interactions between ligand and receptor) were computed for each pose[17]. The pose with the lowest energy values indicated the most favourable binding mode [DS20 2DOCK].

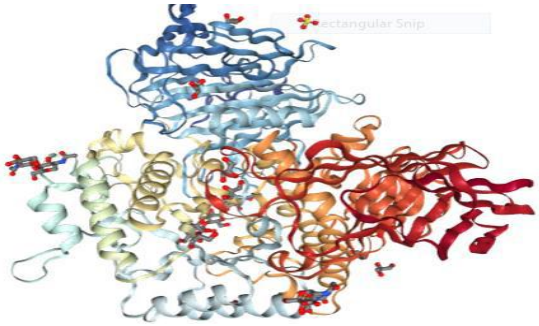


**Fig. 1: Human maltase-glucoamylase (MGAM) Receptor 2QMJ.**

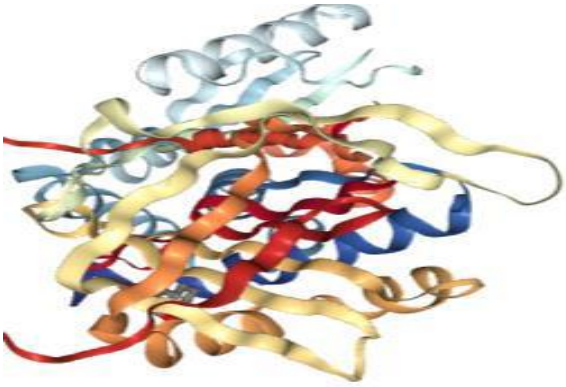
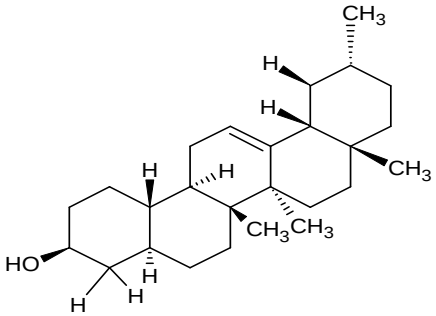
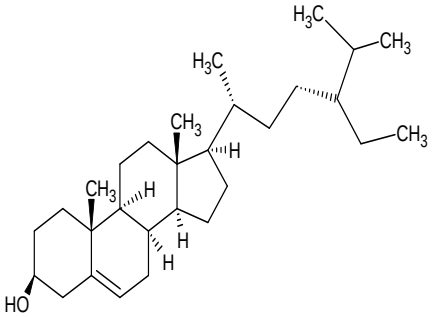


**Fig. 2: Transcortin receptor 2V95.**

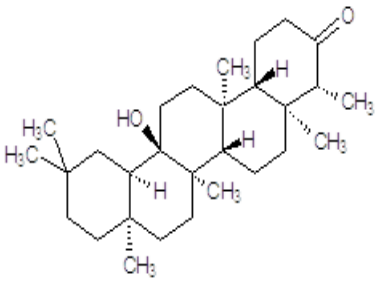
**Structures of ligands**



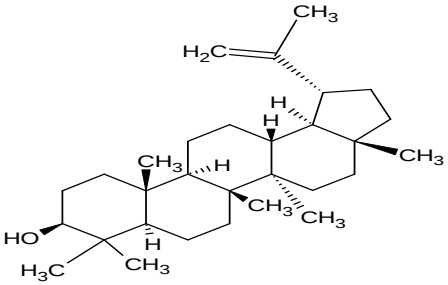
**Alpha amyrin**



**Beta sitosterol**



**Friedelin**



**Lupeol**

***In vitro* enzyme inhibition activity**

**Alpha amylase inhibition assay**

The principle used for the determination of α-Amylase inhibition is that the enzyme acts on substrate and converts to reduced glucose units, and on addition of the inhibitor it acts by arresting the proposed action of enzyme. The spectrophotometric stop reaction determination is based on the following reaction.[18]

$$\text{Starch} + H_2O \xrightarrow{\alpha\text{-amylase}} \text{Reducing Groups (Maltose)}$$

The alpha amylase inhibitory action of extracts (methanolic & aqueous) of the unripe fruits of *Ficus racemosa* linn was evaluated.

Series of concentration of extracts (100, 150 and 200 µg/ml) was prepared and allowed to react with alpha amylase and 0.2M of phosphate buffer (pH- 6.8). After incubation for 20 minutes, to the reaction mixture 80 microlitres of 1% starch solution was added. The same procedure was followed for control samples. Finally, 150 microlitres of dinitro salicylic acid reagent (DNS) - colour reagent was added to both control and test and kept in boiling water bath for 5 minutes. Then, the test tubes were diluted with water and the absorbance was measured at 540 nm using spectrophotometer.The alpha amylase inhibitory activity was estimated by using Acarbose as the standard .The percentage inhibition was calculated using the formula.

(Absorbance Control – Absorbance Test) / (Absorbance Control) X 100

**Alpha glucosidase inhibition assay**

Alpha-glucosidase is a membrane bound enzyme located at the epithelium of the small intestine. It hydrolyzes the terminal, non-reducing 1,4-linked α-D-glucose residues with release of α-D-glucose. It is needed by all animals to hydrolyze maltose to glucose for use as a food. Aberrant activities have been implicated in diseases such as diabetes and pompe disease. α-glucosidase activity can be measured *in-vitro* by determination of the reducing sugar (glucose) arising from hydrolysis by α-glucosidase enzyme.[19] The alpha glucosidase inhibitory action of extracts (methanolic & aqueous) of the unripe fruits of *Ficus racemosa* linn was evaluated.

The concentration of extracts (100,150 and 200 µg/ml) was prepared. The test tubes were taken and labelled as T, C and B. To the test, 0.2M of phosphate buffer (pH 6.8), alpha glucosidase and 1%starch (substrate) solution were added. The contents were mixed well and incubated for 30 mins. Then after incubation trichloroacetic acid (60 microlitre) was added to the tubes. The test tubes were centrifuged for 10 mins, To the above the anthrone reagent (colour reagent) 120 microlitre was added, The contents were boiled for 15 mins. The test tubes were diluted with water and absorbance was measured at 640nm using spectrophotometer. The percentage inhibition was calculated using the formula.

(Absorbance Control – Absorbance Test) / (Absorbance Control) X 100

## RESULTS AND DISCUSSION

**Qualitative phytochemical analysis**

The analysis of plant extracts aids to determine a phytochemical profile indicating the type of constituents present. The phytochemical analysis has affirmed the presence of carbohydrates, protein, tannins and terpenoids in both the extracts. Steroids are present only in methanolic extract, similarly glycosides and flavonoids are present only in methanol extract. Alkaloids, fats & oils are absent in both extracts. The results are given in table 1.

**Table 1:**

| S. No. | Phyto-constituents | Methanol extract | Aqeous extract |
|---|---|---|---|
| 1 | Alkaloid | - | - |
| 2 | Carbohydrate | + | + |
| 3 | Steroid | + | - |
| 4 | Glycoside | + | - |
| 5 | Protein | + | + |
| 6 | Flavonoid | + | - |
| 7 | Tannin | + | + |
| 8 | Terpenoid | + | + |
| 9 | Oils and Fats | - | - |

The presence of flavonoids and glycosides in methanolic extract indicates that it benefit in insulin secretion and modulation of metabolism of glucose and lipid.The tannins present prevents the hyperglycemia, the terpenoid, phenol contents support the antiamylase activity. Analysis of the Phytochemical constituents support the strong anti-hyperglycemic activity.

***In silico* docking studies**

The study of medicinal plants has led to the discovery of new chemical structures for potential development as drugs that act over new or known therapeutic targets. The fruits of *Ficus racemosa* has been used for the treatment of diabetes, hypercholestremia, and other diseases. The triterpenoids are mainly reported in the fruits of the plant, and the fruits have shown anti diabetic activities. In an attempt to find antihyperglycemic agents from the plant, herein went with docking the structures of some selected terpenoids with antidiabetic target proteins. By means of molecular docking, we obtained 3D structures of our targets: MGAM receptor and CBG – Transcortin receptor. Taking into account the structure, we introduced the ligands to explore the influence on the targets. Protein validation is done by Ramachandran plot.

**2QMJ-mgam receptor**

C Docker score

**Table 2:**

| Molecule | Cdocker Energy | Cdocker Interaction Energy |
|---|---|---|
| Beta Sitosterol | -38.8025 | 40.1827 |
| Friedelin | -63.5886 | 26.353 |
| Alpha Amyrin | -67.0318 | 25.2095 |
| Agarbose | -55.7546 | 57.4661 |
| Miglitol | 0.219877 | 35.838 |
| Lupeol | -77.5066 | 25.3743 |

C Docker energy is more for beta sitosterol followed by friedelin. Beta sitosterol was having more energy than miglitol standard, docking ability of beta sitosterol is more and comparable with standard. Friedelin on interaction with receptor forms hydrogen bond (conventional hydrogen bond). Lupeol interacts with receptor forming 2 hydrogen bonds, one is conventional and the other is carbon hydrogen bond depicted in table no: 3&4.

**Table 3:**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 4 | Friedelin | | | | | | | |
| 5 | A:LYS776:HZ1 - Friedelin:O1 | 1.77345 | Hydrogen Bond | Conventional Hydrogen Bond | A:LYS776:HZ1 | H-Donor | Friedelin:O1 | H-Acceptor |
| 6 | A:ALA285 - Friedelin:C31 | 4.40441 | Hydrophobic | Alkyl | A:ALA285 | Alkyl | Friedelin:C31 | Alkyl |
| 7 | A:LYS534 - Friedelin | 5.39157 | Hydrophobic | Alkyl | A:LYS534 | Alkyl | Friedelin | Alkyl |
| 8 | A:ALA780 - Friedelin:C17 | 4.27288 | Hydrophobic | Alkyl | A:ALA780 | Alkyl | Friedelin:C17 | Alkyl |
| 9 | Friedelin:C26 - A:LYS776 | 4.2157 | Hydrophobic | Alkyl | Friedelin:C26 | Alkyl | A:LYS776 | Alkyl |
| 0 | A:HIS115 - Friedelin:C18 | 5.19695 | Hydrophobic | Pi-Alkyl | A:HIS115 | Pi-Orbital | Friedelin:C18 | Alkyl |

**Table 4:**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Lupeol | | | | | | | |
| Lupeol:H76 - A:LYS534:O | 2.43924 | Hydrogen Bond | Conventional Hydrogen Bond | Lupeol:H76 | H-Donor | A:LYS534:O | H-Acceptor |
| Lupeol:H64 - A:LYS534:O | 2.26742 | Hydrogen Bond | Carbon Hydrogen Bond | Lupeol:H64 | H-Donor | A:LYS534:O | H-Acceptor |
| A:ALA285 - Lupeol:C29 | 3.7397 | Hydrophobic | Alkyl | A:ALA285 | Alkyl | Lupeol:C29 | Alkyl |
| Lupeol:C18 - A:LYS534 | 4.31543 | Hydrophobic | Alkyl | Lupeol:C18 | Alkyl | A:LYS534 | Alkyl |
| Lupeol:C28 - A:LYS776 | 3.67456 | Hydrophobic | Alkyl | Lupeol:C28 | Alkyl | A:LYS776 | Alkyl |

The friedelin interacts with Lys776 residue of aminoacid of receptor to form the hydrogen bond, remaining all interactions are hydrophobic in nature, similarly lupeol interacts with residues Lys 534 to form two hydrogen bonds. Among the ligands beta sitosterol demonstrated high Cdocker interaction energy with MGAM receptor, also it showed hydrophobic interaction with receptor which implicates the antihyperglycemic potential is due to this interaction, the amino acid residues being ( Ala 285, Ala 509, Lys 534, Ly 776, Arg 520, Ileu 523, Phe 535 ). The ligand friedelin was having the second highest Cdocker interaction energy, which has hydrophobic interaction other than one hydrogen bond which implicates and justifies the pharmacological action.

**Libdock Score**

**Table 5:**

| Molecule | Libdock Score |
|---|---|
| Beta_Sitosterol | 123.017 |
| Friedelin | 87.5446 |
| Agarbose | 105.421 |
| Miglitol | 98.6303 |

In libdock score is more for beta sitosterol. In this receptor 2QMJ the ligands beta sitosterol and friedelin are having both libdock and C docker interactions.

**Depiction of docking**

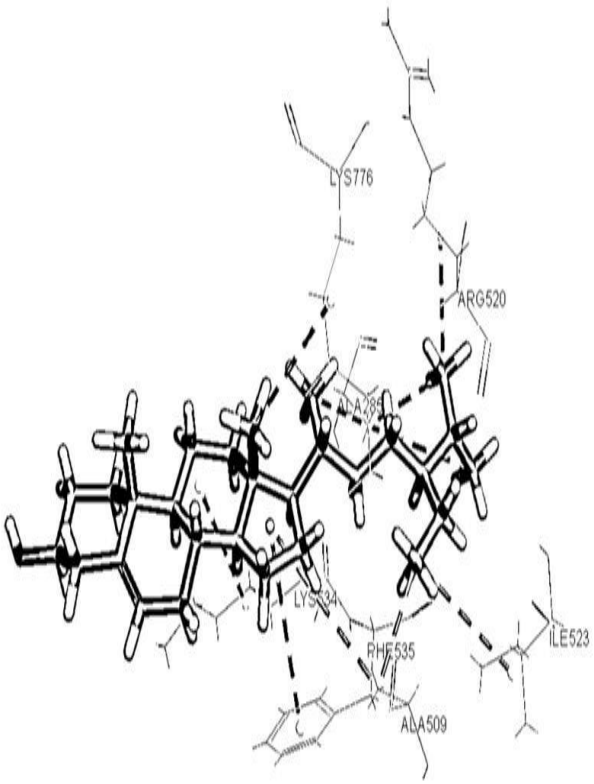



**Figure 3:**

**Beta sitosterol**


**Figure 4:**

**Friedelin**

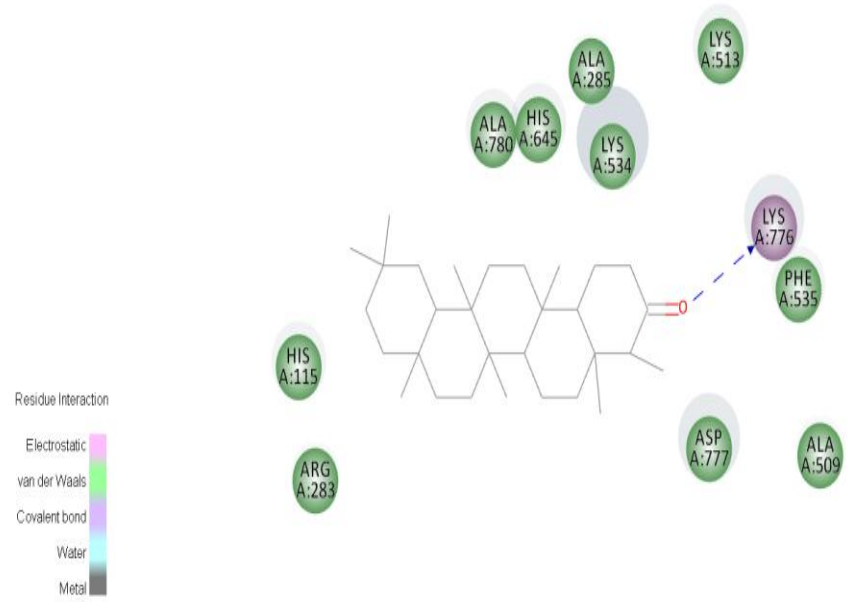



**Figure 5:**

**Lupeol**
**2V95-CBG-transcortin receptor**
C Docker Score

**Table 7:**

| Molecule | Cdocker Energy | Cdocker Interaction Energy |
|---|---|---|
| Friedelin | -42.898 | 45.4215 |
| Alpha Amyrin | -57.0069 | 34.7046 |
| Cortisol | -22.2375 | 47.1353 |
| Lupeol | -66.5796 | 38.2792 |

C Docker interaction energy and binding is more for Friedelin, followed by lupeol.The interaction energy of friedelin is very near to cortisol the standard used.Docking ability is more for Friedelin. In c docker hydrogen bond formation is not shown here the ligand friedelin is having a dominance in docking among the docked poses, the docked images are shown in figure 6 and 7 below.


**Figure 6:**

**Friedelin**

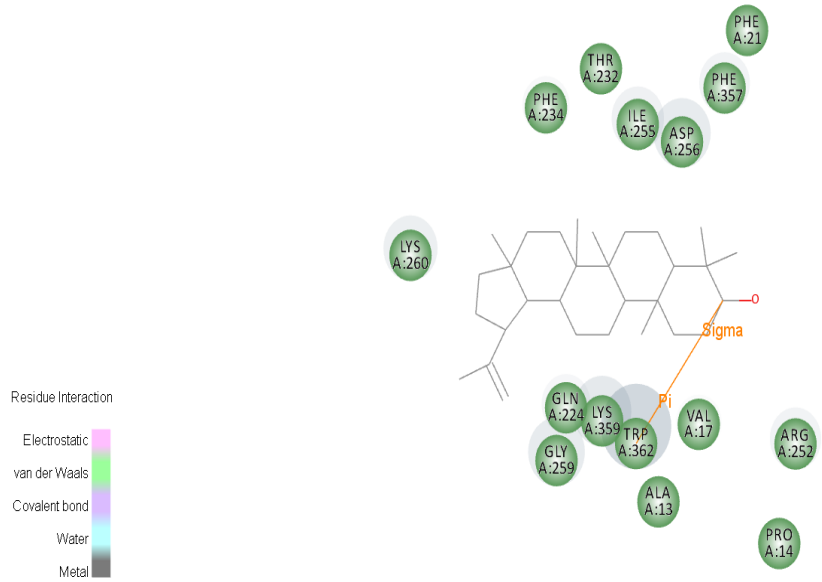



**Figure 7:**

**Lupeol Libdock Score**

**Table 8:**

| Molecule Name | Libdock Score |
|---|---|
| Beta_Sitosterol | 134.417 |
| Friedelin | 111.105 |
| Alpha_Amyrin | 102.689 |
| Cortisol | 125.086 |
| Lupeol | 110.069 |

Here the score is more for Beta sitosterol, followed by friedelin. The score of beta sitosterol is found to be more than the standard .The binding affinity is more for beta sitosterol. Friedelin on interaction with receptor forms 2 hydrogen bonds one is conventional hydrogen bond and other is carbon hydrogen bond. By showing hydrogen bond the docking ability is more for Friedelin. The ligand friedelin interacts with (arg252 h11 and arg 251 hd2) residue of aminoacid to form two hydrogen bonds, the remaining interaction being hydrophobic in nature. The hydrophobic interaction mainly determines the binding affinity and action. The table no 9 shows the hydrogen bonding details.

**Table 9:**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Friedelin | | | | | | | |
| A:ARG252:HH11 - Friedelin:O1 | 1.6694 | Hydrogen Bond | Conventional Hydrogen | A:ARG252 | H-Donor | Friedelin: | H-Acceptor |
| A:ARG252:HD2 - Friedelin:O1 | 2.5524 | Hydrogen Bond | Carbon Hydrogen Bond | A:ARG252 | H-Donor | Friedelin: | H-Acceptor |
| Friedelin:H32 - A:TRP362 | 2.48523 | Hydrophobic | Pi-Sigma | Friedelin: | C-H | A:TRP362 | Pi-Orbital |
| Friedelin:H34 - A:TRP362 | 2.38196 | Hydrophobic | Pi-Sigma | Friedelin: | C-H | A:TRP362 | Pi-Orbital |
| A:ALA13 - Friedelin | 4.96474 | Hydrophobic | Alkyl | A:ALA13 | Alkyl | Friedelin | Alkyl |

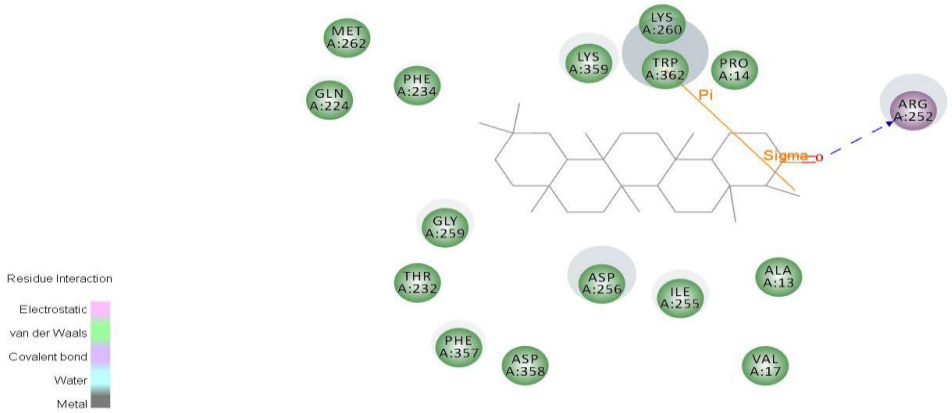



**Figure 8:**

**Docking image of friedelin**

Here in this receptor ligands friedelin, alpha amyrin and Lupeol are having both libdock and Cdocker interactions.So therefore it can be concluded that the binding affinity of the ligands to the receptor as an agonist produce effects similar to that by glucocorticoids, which affects and influences the glucose metabolism, thus this knowledge leads to identifying new targets and ligands for hyperglycemia and diabetes.

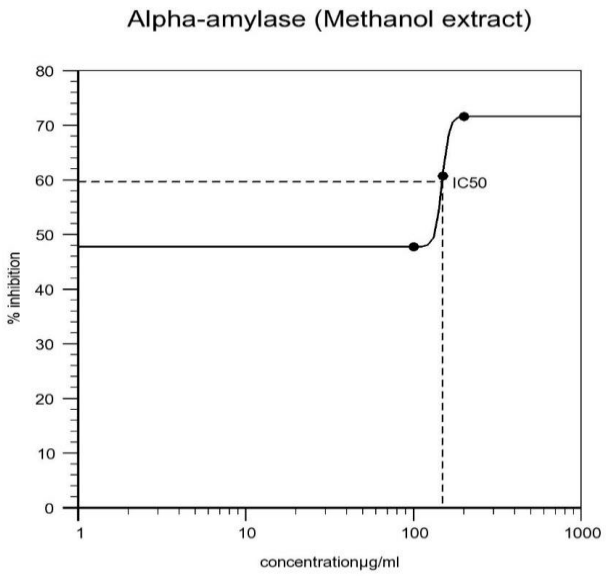
***In vitro* enzyme inhibition activity**

**Alpha amylase inhibition assay**

The alpha amylase inhibition assay was performed for the 2 extracts of the plant- the methanolic and aqueous extracts. Both the extracts had shown inhibition of enzyme. The acarbose is used as the standard. Based on the percentage inhibition of enzyme, the IC50 value is calculated and value should be low for more potent extract. The IC50 value of acarbose is 49.365µg/ml. The IC50value for the methanolic extract is 148.789 µg/ml and is given in table 10 and graph 1 and for the aqueous extract, the IC50 value is 152.36 µg/ml and is given in table no.11 and graph 2.

**Table 10:**

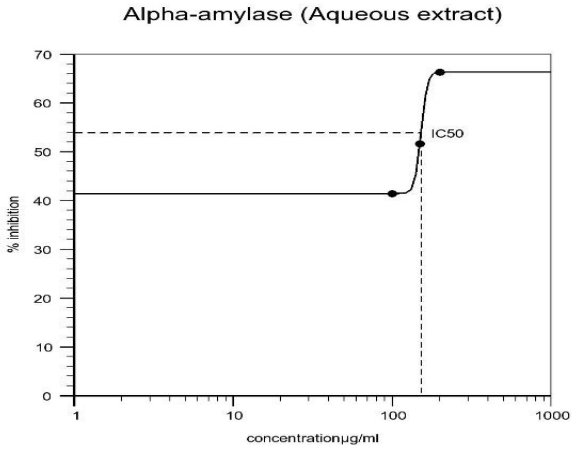
| Concentration µg/ml | % inhibition |
|---|---|
| 100 | 47.73 |
| 150 | 60.71 |
| 200 | 71.58 |
| $IC_{50}$ µg/ml | 148.789 |




**Graph 1:**

**Table 11:**

| Concentration µg/ml | % inhibition |
|---|---|
| 100 | 41.46 |
| 150 | 51.68 |
| 200 | 66.33 |
| $IC_{50}$ µg/ml | 152.36 |




**Graph 2:**

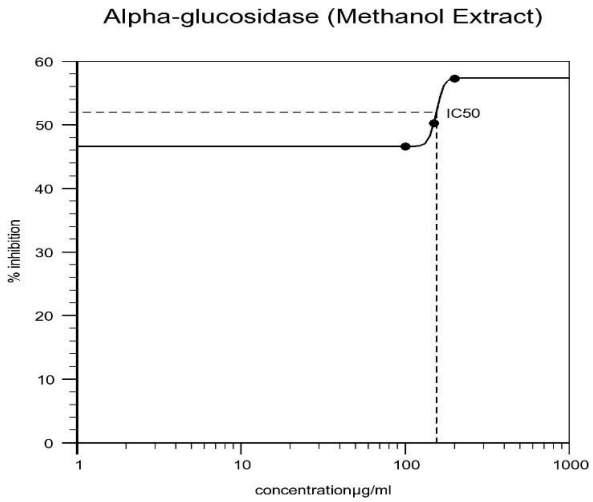
The methanolic extract has shown more percentage of inhibition than the aqueous extract. The IC50 value for the methanolic extract is less compared to aqueous, and hence the methanolic extract has more alpha amylase inhibition.

**Alpha glucosidase inhibition assay**

The alpha glucosidase inhibition assay was performed for the 2 extracts, the methanolic and aqueous extracts. Both the extracts had shown inhibition of enzyme. The acarbose is used as standard. Based on the percentage inhibition of enzyme, the IC50 value is calculated and value should be low for more potent extract. The IC50 value of acarbose is 66.23µg/ml. The IC50 value for methanolic extract is found to be 155.022µg/ml and is given in table 12 and graph 3 below and for aqueous extract the value is found to be 154.449µg/ml and is shown in table 13 and graph 4.

**Table 12.**

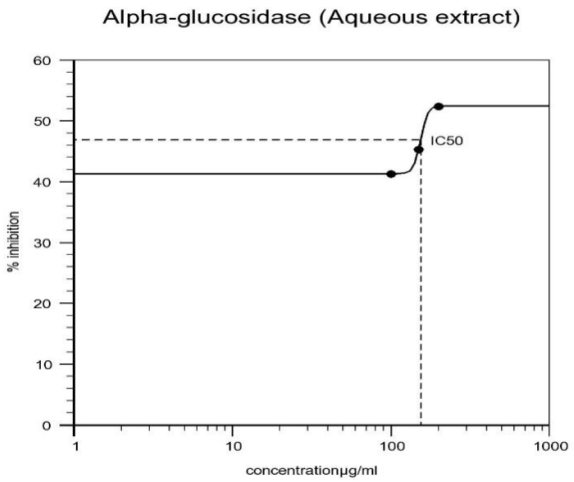
| Concentration µg/ml | % inhibition |
|---|---|
| 100 | 46.6 |
| 150 | 50.3 |
| 200 | 57.3 |
| $IC_{50}$ µg/ml | 155.022 |




**Graph 3:**

**Table 13:**

| Concentration µg/ml | % inhibition |
|---|---|
| 100 | 41.3 |
| 150 | 45.3 |
| 200 | 52.4 |
| $IC_{50}$ µg/ml | 154.449 |




**Graph 4:**

In this assay, both the extracts showed inhibition of alpha glucosidase, the percentage inhibition is high for the methanol extract as compared to the aqueous extract. The IC50 value is less for the aqueous extract.

*In vitro* alpha amylase inhibitory action of unripe fruit extract of *Ficus racemosa* was tested, from the results it is evident that the methanolic extract had potent alpha amylase inhibitory action comparable to standard drug acarbose. Thus we can reach to conclusion that alpha amylase inhibitory action of extracts of unripe fruits of *Ficus racemosa* might play a role in hyperglycemia and diabetes.[20]

So it can be consummated that both extracts of Ficus racemosa can be excellent choice of drug with alpha glucosidase inhibitory action and can reduce the rate of digestion and absorption of carbohydrates.[21]

**CONCLUSION**

Plants, herbs and ethnobotanicals have been used since the early days of humankind and are still used throughout. Plants and natural sources form basis of today's modern medicine, and contribute largely to the commercial drug preparations, the medicinal plants used to treat hyperglycemia are derived from traditional medicine.[22] Over the past few decades herbal medicines have been used as feasible agents for treatment of hyperglycemia and diabetes.[23]

The study confirms that the methanol and aqueous extracts of the unripe fruits of *Ficus racemosa* contains various phytochemicals. the methanolic extract is found to contain more phenolics, terpenoids etc. From the preliminary screening and testings the fruit contains

many terpenoids. The presence of terpenoids have been confirmed qualitatively in methanolic extract.

The *in silico* docking studies confirm that the terpenoid contents in the fruit is having good interaction to the specific target proteins, among the terpenoids, the 2 compounds, viz. beta sitosterol and Friedelin are having pronounced docking and interaction with hyperglycemic targets.

The *in vitro* enzyme inhibition studies shows that both extracts (methanolic & aqueous) are having sound effect on inhibition of alpha amylase and alpha glucosidase. Here it signals the aqueous extract's marked effect on alpha glucosidase inhibition.

The results conclude that the extracts and the terpenoid compounds within, can be considered as persuasive and influential antihyperglycemic agents.

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