Research Article

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Molecular docking of secondary metabolites from *Cyperus rotundus* and *Cyamopsis tetragonolobus* against aldose reductase - A novel drug target for diabetic cataract

Vijayalakshmi Krishnamoorthy[2*], Seema Surendran[1,3], Vadivelan Sankaran[1], Vengatesa Prasanna Vasudevan[1], Sarma JARP[1]

[1]GVK Biosciences Pvt. Ltd. Chennai, Tamil Nadu, India - 600 018

[2]Department of Biochemistry, Bharathi Women's College (Autonomous), North Chennai, Tamil Nadu, India - 600 108

[3]Bharathiar University, Research and Development Centre, Coimbatore, Tamil Nadu, India - 641 046

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ABSTRACT

Diabetic cataract is one of the serious complications of diabetes mellitus, which is a major cause of blindness all over the world. Aldose reductase is the rate limiting enzyme responsible for triggering the pathogenesis of diabetic cataract. Nowadays, natural therapy is gaining more value as alternative medicine. So, it was planned to study the ability of secondary metabolites identified from *Cyperus rotundus* and *Cyamopsis tetragonolobus* to serve as antagonist to aldose reductase that may serve as new drug target. 21 compounds were identified as secondary metabolites of ethanolic extract of *C. rotundus* rhizome by GC-MS analysis and 34 compounds were identified from ethanol extract of *C. tetragonolobus* fruit. These compounds were docked with aldose reductase. Docking analysis was performed using GLIDE. We describe the docking of these identified compounds into the 3D structure of aldose reductase of human. The inhibitor binding positions and affinity were evaluated using scoring functions. The compounds 3-(2-hydroxy-3,4-dimethoxyphenyl)-7-chromanol and 3-bromo-4-(methoxymethyl)-bicyclo[4.2.0]octa-1,3,5,7-tetraene from *C. tetragonolobus* were identified as potential inhibitors of aldose reductase. In addition, camphoric aldehyde and longifolenaldehyde from *C. rotundus* are considered for its effective binding with the target protein. 1,2-cyclopentanedione and (3,8,8-Trimethyl-1,2,3,4,5,6,7,8-octahydro-2-naphthalenyl)methyl acetate showed more hydrogen bond interactions with effective binding to aldose reductase. Thus, it may be concluded that the identified metabolites from both the plants could serve as antagonist to aldose reductase that can be used to treat diabetic cataract.

Key words: *Cyperus rotundus, Cyamopsis tetragonolobus,* aldose reductase, diabetic cataract, molecular docking

INTRODUCTION

Diabetic cataract is one of the serious complications of diabetes mellitus. Patients with diabetic mellitus have every chance of developing cataract. Cataract is a major cause of visual impairment in diabetic subjects. Diabetic cataract formation occurs due to increased glucose accumulation in the lens.[1] Polyol pathway is linked to the development of cataract in diabetic patients. The excess sugar levels present within the lens are usually reduced by aldose reductase to its alcohol.[2] Aldose reductase is a rate-limiting enzyme that catalyzes the reduction of glucose to sorbitol through polyol pathway.[3]

In subjects with normal glucose levels, much of the glucose gets phosphorylated into glucose-6-phosphate by hexokinase enzyme. Only a minor portion of non-phosphorylated glucose enters the polyol pathway. However, under hyperglycemic conditions, aldose reductase gets activated due to saturation of hexokinase enzymes. This leads to increased production of sorbitol which gets accumulated. Increased sorbitol accumulation in retina results in pathogenesis of cataract.[4] Thus, aldose reductase is believed to have a role in developing diabetic cataract. Many aldose reductase inhibitors were developed as drug candidates to fight complications, but they have failed.[5] Consequently, inhibition of aldose reductase will act as a therapeutic strategy to prevent the complications of diabetes.

From ancient times, phytotherapy is employed to control diabetes in various countries. Nowadays, treatment via natural therapy is gaining popularity due to its less or no side effects. *Cyperus rotundus* commonly known as coco-grass or nut sedge or nut grass belongs to Cyperaceae. It is an invasive weed which occurs worldwide. It is a popular folklore medicine employed to treat fever and digestive system defects. It is widely used in ayurvedic treatments. It has good nutritional value and could be an important source of minerals and trace elements.[6]

Cyamopsis tetragonolobus is an annual legume that belongs to Fabaceae family. This plant is the source of guar gum. It is commonly called as cluster bean which is popularly used as food.[7] It is widely used for industrial purpose also. It was also used as a home remedy for treating dyspepsia, anorexia, stomach disorders, etc.

Bioinformatics studies have emerged as new techniques to investi-

***Corresponding author.**
Dr. K. Vijayalakshmi
Associate Professor
Bharathi Women's College (Autonomous)
Department of Biochemistry
North Chennai - 600 108,Tamil Nadu,India

gate diseases at molecular level using *in silico* approaches. Thus, our aim was to carry out the molecular docking analysis to find out the inhibitory effect of secondary metabolites of *Cyperus rotundus* and *Cyamopsis tetragonolobus* on aldose reductase enzyme and to determine the affinity of these ligands using bioinformatics.

MATERIALS AND METHODS

Collection of Plant Material

The rhizome of *Cyperus rotundus* and fruits of *Cyamopsis tetragonolobus* were collected from medicinal vendor, Chennai, Tamil Nadu, India. The selected plant materials were identified and authenticated as PRAC/2010/495 for *Cyperus rotundus* and PRAC/2010/494 for *Cyamopsis tetragonolobus* by Prof. P. Jayaraman, Plant Anatomy Research Center, West Tambaram, Chennai, Tamil Nadu, India.

Preparation of Plant Extracts

C. rotundus rhizome and *C. tetragonolobus* fruit were shade-dried and pulverized to fine powder in a mechanical grinder. The powder (100g) was extracted with ethanol as solvent. The extracts were concentrated under reduced pressure in a rotary evaporator. The ethanolic extracts were subjected to GC-MS analysis.

GC-MS Analysis

GC-MS analysis of selected samples was performed with Shimadzu GC-MS-QP2010. Secondary metabolites of *C. rotundus* and *C. tetragonolobus* were identified. 21 compounds were identified from *C. rotundus* and 34 compounds were identified from *C. tetragonolobus* using the database of National Institute Standard and Technique (NIST), WILEY8 and FAME Libraries as mentioned in our previous study. [8]

Docking

The docking studies were performed using Glide (Grid-based Ligand Docking with Energetics) 5.7 program in Schrodinger Software Suite, 2011 (Schrodinger, Portland, USA). Glide was run in rigid docking mode. In Glide, the initial filters test the spatial fit of the ligand to the defined active site, and examine the complementarity of ligand-receptor interactions using a grid-based method patterned after the empirical ChemScore function. Poses that pass these initial screens enter the final stage of the algorithm, which involves evaluation and minimization of a grid approximation to the OPLS-AA non-bonded ligand-receptor interaction energy. Final scoring was then carried out on the energy-minimized poses. By default, Schrodinger's proprietary GlideScore multi-ligand scoring function is used to score the poses. Emodel which is used to rank the poses combines GlideScore, the non-bonded interaction energy, and, for rigid docking, the excess internal energy of the generated ligand conformation is utilized.

Protein Preparation and Grid Generation

RCSB Protein Data Bank entry, 2PZN of *Homo sapiens* aldose reductase protein was used for protein preparation step. Water molecules were deleted. The formal charges of the ligand and protein atoms were adjusted. The restrained minimization of hydrogen of the protein was done using *protein preparation wizard* and OPLS2005 force field.

The secondary metabolites identified were used as ligands for this study. The two-dimensional structures of these ligands were generated using the ChemSketch tool (ChemDraw Ultra 10.0). The structures were converted into 3D structures with the help of 3D optimization tool.

55 molecules were prepared using ligand preparation step. These 55 compounds were divided into three groups based on the structural similarity and three different grids with sizes 6Å, 9Å, 14Å centered on the centroid of the overlaid crystal ligand on to the modeled 3D structure of protein based on their structure, in order to confine the centroid of the docked inhibitor. Default settings were used for all the remaining parameters.

32 conformations were generated for each input ligand after generating tautomers, removing problematic structures and optimizing ligand geometries. *Epik* was used to generate all possible states of the ligand between pH ranges of 7.0±2.0.

Ligand Docking

Ligand docking was done taking the prepared protein and ligands as inputs. Standard-precision (SP) docking was used for this purpose which is appropriate for screening ligands of unknown quality in large numbers. Conjugate gradient method (100 steps) was used for energy minimization of poses which had passed through the selection of initial poses scoring phase. Top 20 poses were generated per each input ligand with the default values being retained for rest of the parameters.

RESULTS AND DISCUSSION

The structures of the ligands were drawn using ChemSketch tool and converted into Maestro format using molecular converter tool. Table 1 shows 21 compounds identified from *C. rotundus* by GC-MS analysis. Table 2 shows 34 compounds identified from *C. tetragonolobus* by GC-MS analysis. These compounds were divided into three groups based on their structural similarity, i.e., small compounds-13; chain/long compounds -16; bicyclic compounds (more than one ring) -26 and the grids were prepared accordingly. The 3D structure of aldose reductase (PDB ID: 2PZN) was downloaded from the PDB database. Figure 1 shows the structure of aldose reductase protein retrieved from RCSB protein database.

All 55 compounds prepared by LigPrep were subjected to Standard-precision (SP) docking in which 10 compounds showed higher docking score. Table 3 shows the docking score of various inhibitors against aldose reductase. Figure 2 shows the 2D structures of compounds present in *C. rotundus*. Figure 3 shows the 2D structures of compounds identified in *C. tetragonolobus*. These ligands were docked separately using Glide version 5.7. The Glide Score values of available compounds ranged between -7.62 and -6.05 (Table 3).

Table 1: Compounds identified in the extract of *C. rotundus* identified using GC-MS analysis

Compound Name	Molecular Formula
(-)-Alpha-gurjunene	$C_{15}H_{24}$
Camphoric aldehyde	$C_{10}H_{16}O$
7-isopropenyl-4A-methyl-1-methylenedecahydronaphthalene	$C_{15}H_{24}$
Zierone	$C_{15}H_{22}O$
1H-inden-1-one-3a-chlorooctahydro-4,4,7a-trimethyl-	$C_{12}H_{19}ClO$
Longifolenaldehyde	$C_{15}H_{24}O$
5-Amino-2,2-dimethyl-1-[(1-methylethylidene)amino]-1,2-dihydro-3H-pyrrole-3,3,4-tricarbonitrile	$C_{12}H_{14}N_6$
Longiverbenone	$C_{15}H_{22}O$
Longifolene-(V4)	$C_{15}H_{24}$
(E)-Carveol	$C_{10}H_{16}O$
2,4a,5,8a-Tetramethyl-1,2,3,4,4a,7,8,8a-octahydro-1-naphthalenyl acetate	$C_{16}H_{26}O_2$
7-Isopropenyl-1,4a-dimethyl-4,4a,5,6,7,8-hexahydro-3H-naphthalen-2-one	$C_{15}H_{22}O$
Beta-neoclovene	$C_{15}H_{24}$
(3,8,8-Trimethyl-1,2,3,4,5,6,7,8-octahydro-2-naphthalenyl)methyl acetate	$C_{16}H_{26}O_2$
2,2,6-Trimethyl-1-[(1E)-3-methyl-1,3-butadienyl]-5-methylene-7-oxabicyclo[4.1.0]heptane	$C_{15}H_{22}O$
Acetic acid, 3-(2,2-dimethyl-6-methylene-cyclohexylidene)-1-methyl-butyl ester	$C_{16}H_{26}O_2$
1,1,4,7-tetramethyldecahydro-1H-cyclopropa[E]azulen-4-ol	$C_{15}H_{26}O$
Menthol, 1'-(butyn-3-one-1-yl)-, (1S,2S,5R)-	$C_{14}H_{22}O_2$
(+)-Cis-longipinan	$C_{15}H_{26}$
2-Isopropenyl-4,4,6b-trimethyl-4,5,5a,6,6a,6b-hexahydro-2H-cyclopropa[g][1]benzofuran	$C_{15}H_{22}O$
Digitoxigenin-4-en	$C_{23}H_{32}O_4$

Table 2: Compounds identified in the extract of *C. tetragonolobus* identified using GC-MS analysis

Compound Name	Molecular Formula
1,2-Cyclopentanedione	$C_5H_6O_2$
Isopentyl acetate	$C_7H_{14}O_2$
3,5-Dihydroxy-6-methyl-2,3 -dihydro-4H-pyran-4-one	$C_6H_8O_4$
2,3-Dihydro-benzofuran	C_8H_8O
Acetyl monoglyceride	$C_5H_{10}O_4$
1-(p-methoxyphenyl)propene	$C_{10}H_{12}O$
Ethyl alpha-D-glucopyranoside	$C_8H_{16}O_6$
Mome inositol	$C_7H_{14}O_6$
N-(2-heptynyl)-n-hexylamine	$C_{13}H_{25}N$
Palmitic acid	$C_{16}H_{32}O_2$
Ethyl hexadecanoate	$C_{18}H_{36}O_2$
Hexopyranosyl hexopyranoside	$C_{12}H_{22}O_{11}$
Phytol	$C_{20}H_{40}O$
Ethyl (9Z,12Z)-9,12-octadecadienoate	$C_{20}H_{36}O_2$
Ethyl (9Z)-9-octadecenoate	$C_{20}H_{38}O_2$
Ethyl n-octadecanoate	$C_{20}H_{40}O_2$
2-Hexadecanoyl glycerol	$C_{19}H_{38}O_4$
Mono(2-ethylhexyl) phthalate	$C_{16}H_{22}O_4$
Ethyl nonadecanoate	$C_{21}H_{42}O_2$
Aletamine	$C_{11}H_{15}N$
Propyleneglycol monoleate	$C_{21}H_{40}O_3$
alpha-Monostearin	$C_{21}H_{42}O_4$
Ethyl docosanoate	$C_{24}H_{48}O_2$
3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol	$C_{17}H_{18}O_5$
Nonacosane	$C_{29}H_{60}$
3-bromo-4(methoxymethyl)-bicylco [4.2.0]octa-1,3,5,7-tetraene	$C_{10}H_9BrO$
beta-Tocopherol	$C_{28}H_{48}O_2$
N-Tetracontane	$C_{44}H_{90}$
dl-alpha-Tocopherol	$C_{29}H_{50}O_2$
Ergost-5-en-3-ol	$C_{28}H_{48}O$
Stigmasterol	$C_{29}H_{48}O$
gamma-Sitosterol	$C_{29}H_{50}O$
Alpha-amyrin	$C_{30}H_{50}O$
Lupeol	$C_{30}H_{50}O$

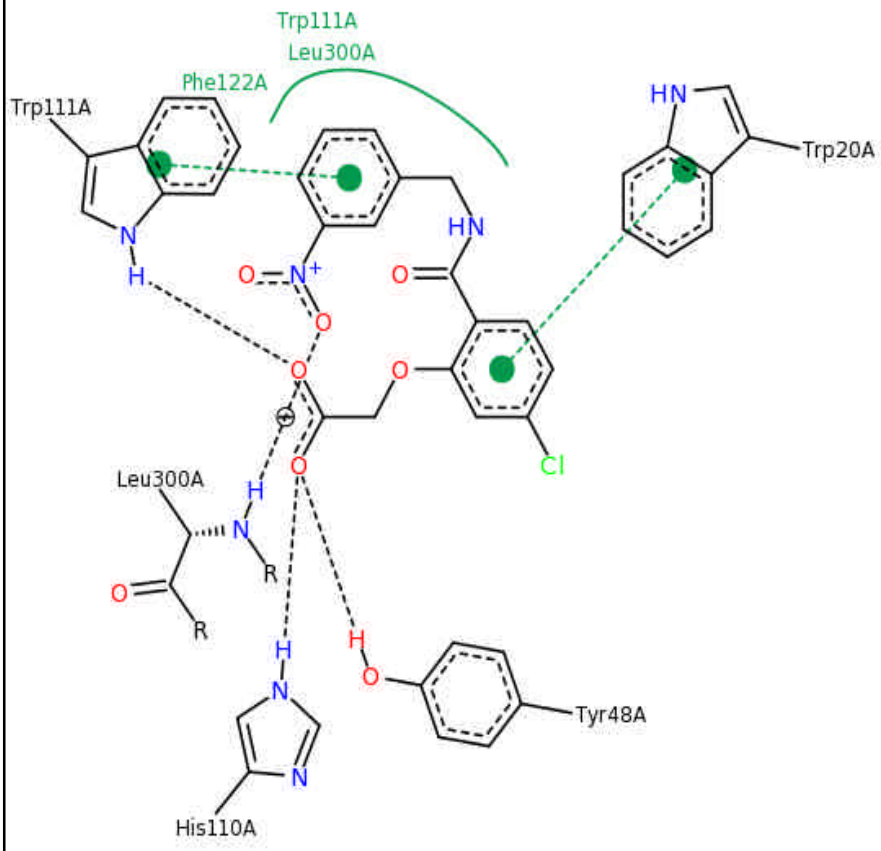


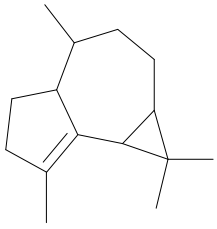
Figure 1: Structure of Aldose Reductase [2PZN- Ligplot from RCSB]

Table 3: Docking score of various compounds from both the plants against aldose reductase

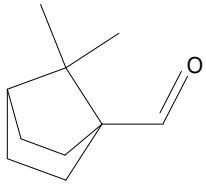
Compound Name	Derived From	G-Score
3-(2-hydroxy-3,4-dimethoxyphenyl)-7-chromanol	*C. tetragonolobus*	-7.62
3-bromo-4-(methoxymethyl)-bicyclo[4.2.0]octa-1,3,5,7-tetraene	*C. tetragonolobus*	-7.30
Camphoric aldehyde	*C. rotundus*	-6.87
Longifolenaldehyde	*C. rotundus*	-6.57
1,1,4,7-tetramethyldecahydro-1H-cyclopropa[E]azulen-4-ol	*C. rotundus*	-6.53
1,2-cyclopentanedione	*C. tetragonolobus*	-6.36
Acetic acid, 3-(2,2-dimethyl-6-methylene- 1-methyl-butyl ester	*C. rotundus*	-6.29
2,3-dihydro-benzofuran	*C. tetragonolobus*	-6.16
(3,8,8-Trimethyl-1,2,3,4,5,6,7,8-octahydro-2-naphthalenyl)methyl acetate	*C. rotundus*	-6.13
(E)-carveol	*C. rotundus*	-6.05

Figure 2: 2D structures of compounds identified from *C. rotundus*

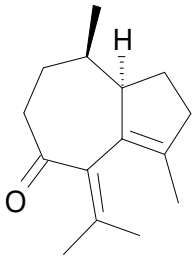
(-)-alpha-



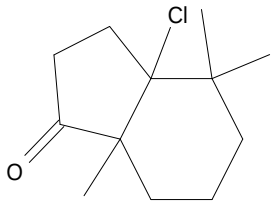
Camphoric



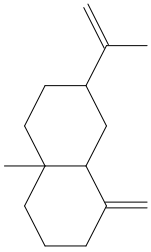
Zieron



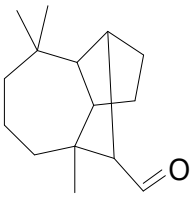
1H-inden-1-one, 3a-chlorooctahydro-4,4,7a-



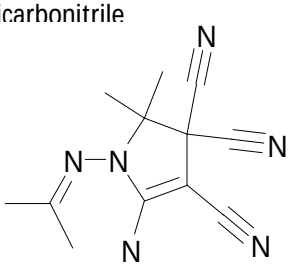
7-isopropenyl-4a-methyl-1-methylenedecahydronaphthalen



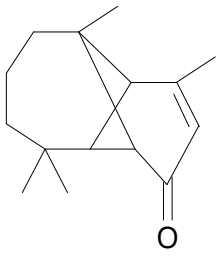
Longifolenaldehyd



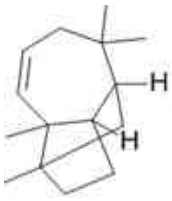
5-Amino-2,2-dimethyl-1-[(1-methylethylidene)amino]-1,2-dihydro-3H-pyrrole-3,3,4-tricarbonitrile



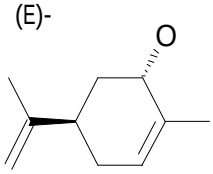
Longiverbenon



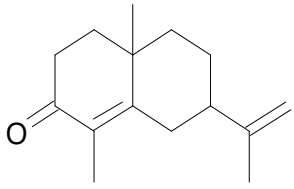
Longifolene-



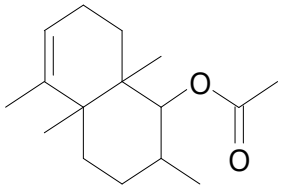
(E)-



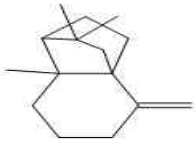
7-Isopropenyl-1,4a-dimethyl-4,4a,5,6,7,8-hexahydro-3H-naphthalen-2-one



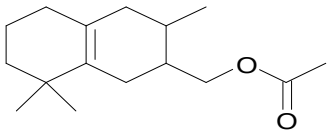
2,4a,5,8a-tetramethyl-1,2,3,4,4a,7,8,8a-octahydro-1-naphthalenyl acetate



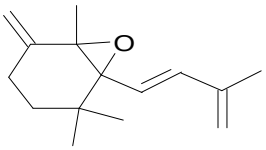
Beta-neoclovene



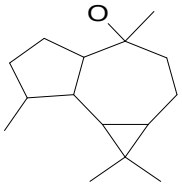
(3,8,8-Trimethyl-1,2,3,4,5,6,7,8-octahydro-2-naphthalenyl)methyl acetate



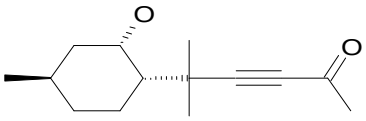
2,2,6-Trimethyl-1-[(1E)-3-methyl-1,3-butadienyl]-5-methylene-7-oxabicyclo[4.1.0]heptane



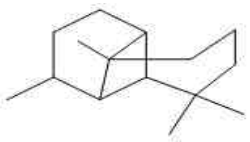
1,1,4,7-tetramethyldecahydro-1H-cyclopropa[E]azulen-4-ol



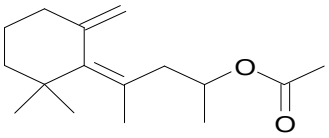
Menthol, 1'-(butyn-3-one-1-yl)-, (1S,2S,5R)-



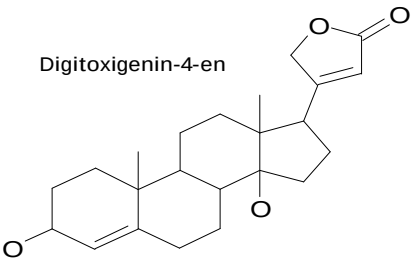
(+)-Cis-longipinan



Acetic acid, 3-(2,2-dimethyl-6-methylene-cyclohexylidene)-1-methyl-butyl ester



Digitoxigenin-4-en



2-Isopropenyl-4,4,6b-trimethyl-4,5,5a,6,6a,6b-hexahydro-2H-cyclopropa[g][1]benzofuran

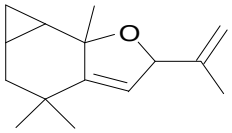
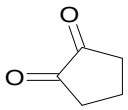
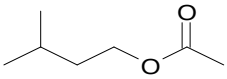


Figure 3: 2D structures of compounds identified from *C. tetragonolobus*

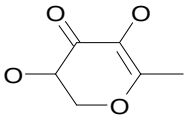
1,2-cyclopentanedione



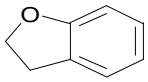
Isopentyl acetate



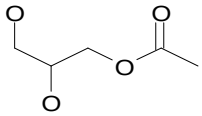
3,5-dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one



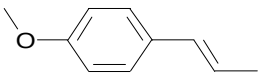
2,3-dihydro-benzofuran



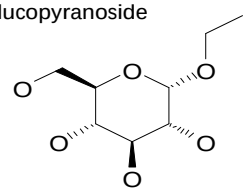
Acetyl monoglyceride



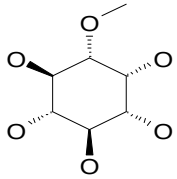
1-(p-methoxyphenyl)propene



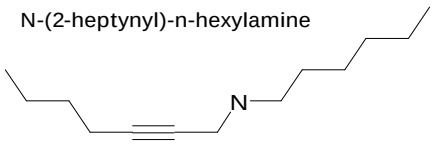
Ethyl alpha-d-glucopyranoside



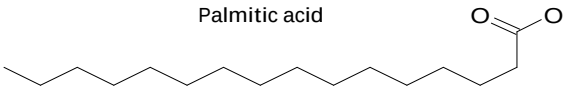
Mome-Inositol



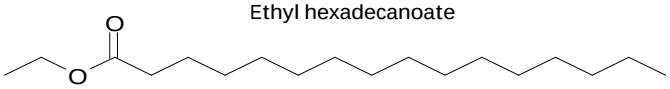
N-(2-heptynyl)-n-hexylamine



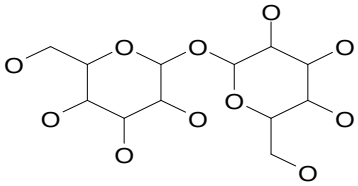
Palmitic acid



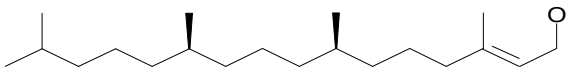
Ethyl hexadecanoate



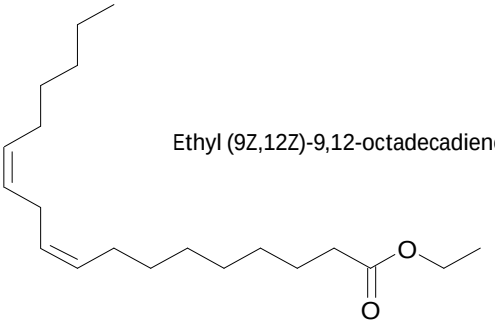
Hexopyranosyl hexopyranoside



Phytol



Ethyl (9Z,12Z)-9,12-octadecadienoate



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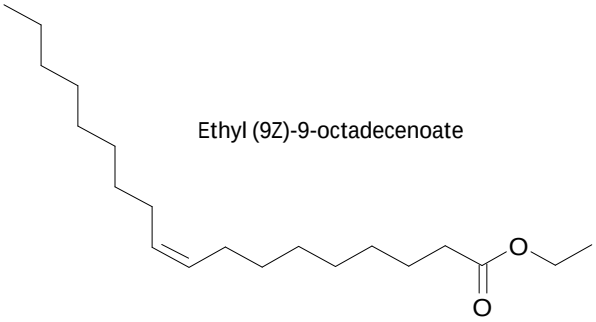

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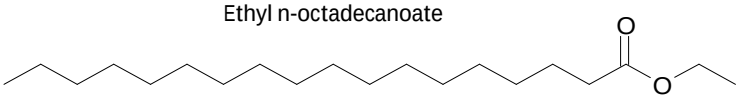
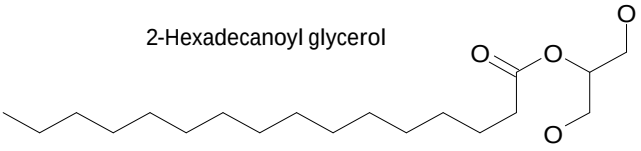
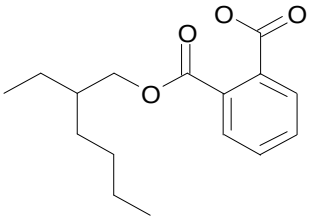


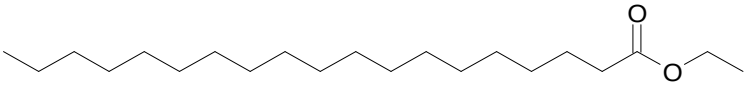
2-Hexadecanoyl glycerol



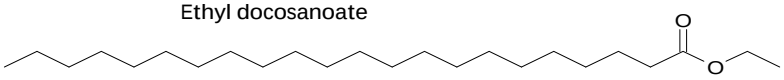
Mono(2-ethylhexyl) phthalate



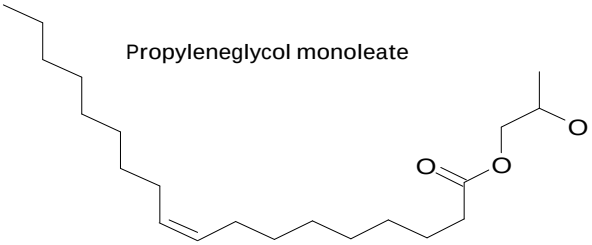
Ethyl nonadecanoate



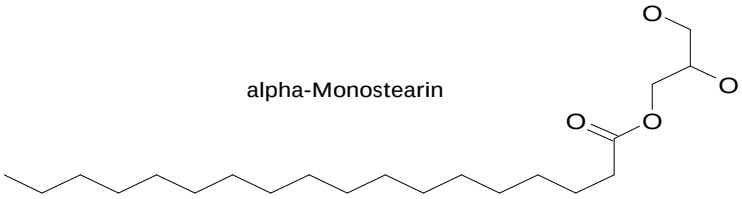
Ethyl docosanoate



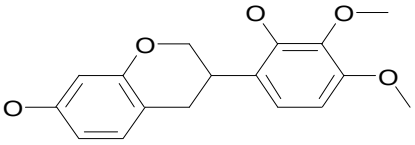
Propyleneglycol monoleate



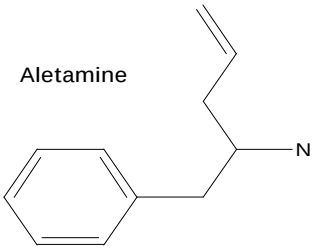
alpha-Monostearin



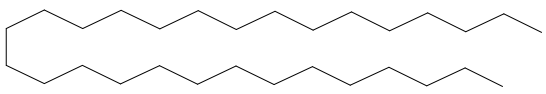
3-(2-Hydroxy-3,4-dimethoxyphenyl)-7-chromanol



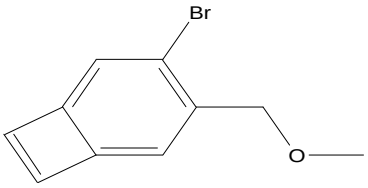
Aletamine



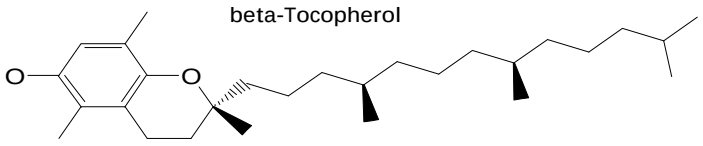
Nonacosane

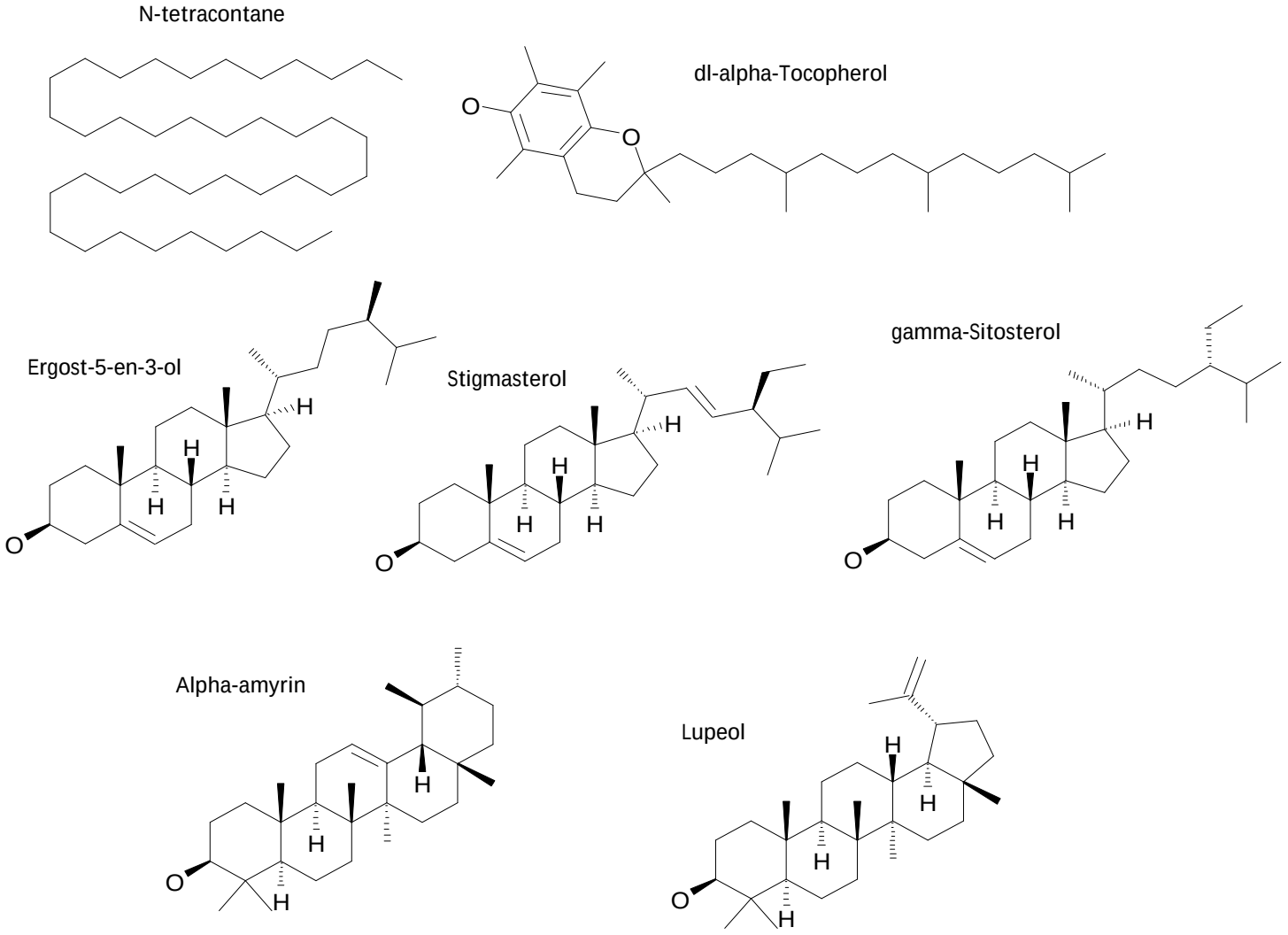


Bicyclo[4.2.0]octa-1,3,5,7-tetraene, 3-bromo-4-(methoxymethyl)-



beta-Tocopherol





The binding mode of active compound 3-(2-hydroxy-3,4-dimethoxyphenyl)-7-chromanol (G-score: -7.62) from *C. tetragonolobus* shows 1 hydrogen bond interaction with TRP 20 against the target protein and the ligand surrounded by TYR 48, HIS 110, TRP 111, PHE 122, LEU 300 and the distance between the 'O' of chromanol and 'NH' of TRP 20 is calculated as 2.153 A^0. The binding region was defined using a grid of 9 Å X 9 Å X 9 Å.The binding mode of the next active compound 3-bromo-4-(methoxymethyl)-bicyclo[4.2.0]octa-1,3,5,7-tetraene, (G-score: -7.30) from *C. tetragonolobus* with 1 hydrogen bond interaction with TRP 111 with the target protein and the ligand surrounded by TYR 48, TRP 20, HIS 110, PHE 122, LEU 300 and distance between the 'O' of ligand and 'NH' of TRP 111 is calculated as 2.639 A^0. The binding region was defined using a grid of 9 Å X 9 Å X 9 Å.

The binding mode of the active compound camphoric aldehyde (G-score: -6.87) from *C. rotundus* with 2 hydrogen bond interaction with HIS 110 i.e., NH of histidine with O of camphoric aldehyde (NH-O=C, 1.79 A^0) and TYR48 i.e. side chain hydroxyl group O of camphoric aldehyde (OH-O=C, 1.969 A^0) with the target protein and the ligand surrounded by TRP 20, TRP 111, PHE 122, LEU 300. The binding region was defined using a grid of 9 Å X 9 Å X 9 Å. The binding mode of the active compound longifolenaldehyde (G-score: -6.57) from *C. rotundus* with 2 hydrogen bond interaction with HIS 110 i.e., NH of histidine with O of longifolenaldehyde (NH-O=C, 2.668 A^0) and TRP 111 i.e. side chain hydroxyl group O of longifolenaldehyde (NH-O=C, 2.177 A^0) with the target protein and the ligand surrounded by TRP 20, TYR 48, PHE 122, LEU 300. The binding region was defined using a grid of 9 Å X 9 Å X 9 Å.

Figure 4 maps the binding mode of 1,2-cyclopentanedione (G-score: -6.36) from *C. tetragonolobus* with 3 hydrogen bond interactions with TRP111, HIS 110 and TYR 48 with the target protein and surrounding ligands. The binding mode of (3,8,8-Trimethyl-1,2,3,4,5,6,7,8-octahydro-2-naphthalenyl)methyl acetate (G-score: -6.13) from *C. rotundus* is depicted in Figure 5.

Fig 4: Docking pose of ligand (1,2-cyclopentanedione) within the active site of aldose reductase (PDB ID: 2PZN)

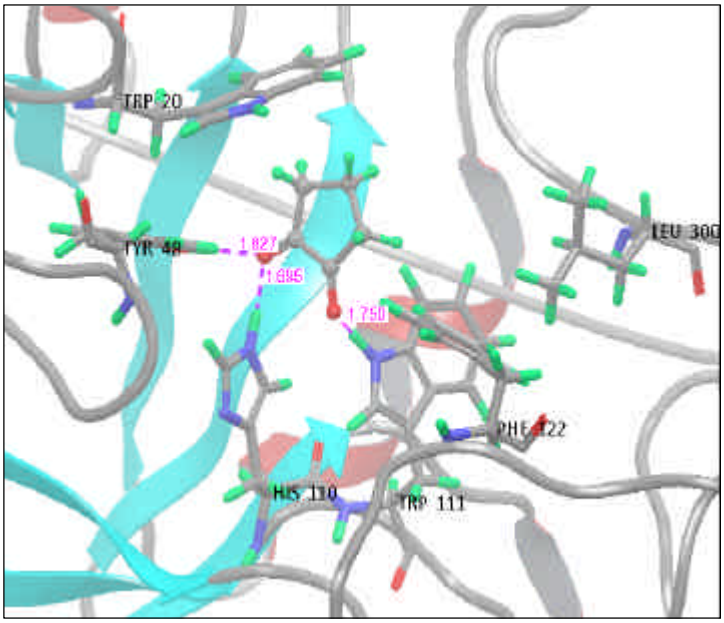
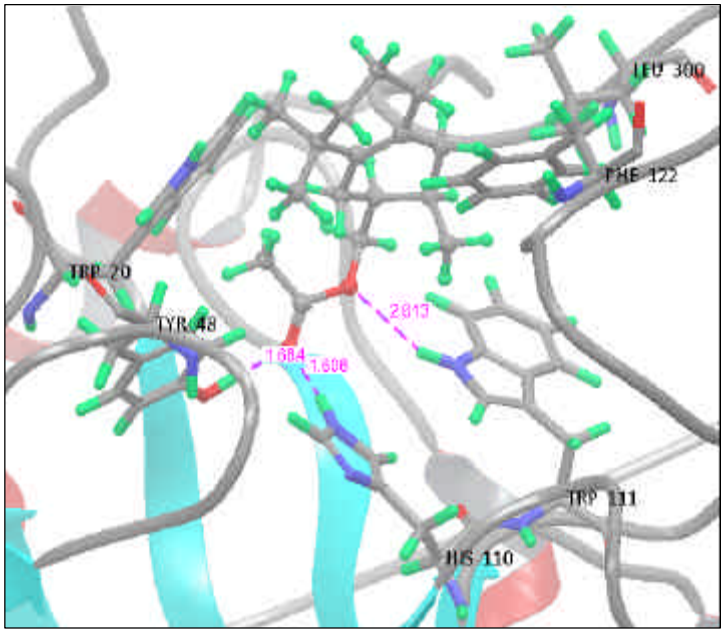


Fig 5: Docking pose of ligand ((3,8,8-Trimethyl-1,2,3,4,5,6,7,8-octahydro-2-naphthalenyl)methyl acetate) within the active site of aldose reductase (PDB ID: 2PZN)



The other compounds such as 1,1,4,7-tetramethyldecahydro-1H-cyclopropa[E]azulen-4-ol, Acetic acid 3-(2,2-dimethyl-6-methylene-1-methyl-butyl ester and (E)-carveol identified from *C. rotundus* showed good docking score revealing the possible binding of such phytochemicals to aldose reductase enzyme, thus serving as antagonists. Likewise, 1,2-cyclopentanedione identified from *C. tetragonolobus* also exhibited good binding affinity for aldose reductase.

Aldose reductase is responsible for the pathogenesis of diabetic cataracts and inhibition of this enzyme represents a therapeutic approach to restore function of lens in patients.[9] The rise in aldose reductase activity occurs due to hyperglycemia. This is the underlying cause of cataractogenesis.[10] Inhibition of aldose reductase prevents hyperglycemic changes in diabetic cataract patients.[11] Increase in aldose reductase activity is caused by hyperglycemia. Polyol pathway inhibition is a promising approach for regulation of diabetic complications.[12]

Aldose reductase inhibitors have already been shown to prevent diabetic complications.[13] There are many orally active aldose reductase inhibitors available for clinical use. Aldose reductase inhibitor blocks the glucose flux via polyol pathway and prevents the intracellular accumulation of sorbitol. This effect can prevent the chronic complication of inducing cataract.[14] There are two general series of aldose reductase inhibitors. One group possesses carboxylic acid group and the other group contains a cyclic imide ring.[15] A variety of aldose reductase inhibitors are available commercially such as epalrestat, tolrestat and zenarestat contains carboxylic acid moiety. Other compounds such as sorbinil, fidarestat and minalrestat have cyclic imide.[16], [17]

Secondary metabolites isolated from many plant species have shown to inhibit aldose reductase activity in previous studies. Polar constituents of *Origanum vulgare* have shown to inhibit aldose reductase.[18] Similarly, it has been proven that many plant-derived extracts and phytochemicals serve as alternatives to available synthetic inhibitors against aldose reductase.[19], [20], [21], [22] Essential phytochemicals obtained from *Cymbopogon citratus* were shown to exhibit inhibitory activity against aldose reductase.[23] Curcumin was found to inhibit aldose reductase.[24] It could be noticed that the compounds identified from our plants of interest also exhibits such inhibitory activity against aldose reductase.

CONCLUSION

Similar to the commercial aldose reductase inhibitors available for the clinical utility, some of the phytochemicals identified from both the plant extracts showed good docking results. *C. rotundus* had more number of compounds that may possibly bind to the target protein aldose reductase to inhibit its action, when compared to *C. tetragonolobus*. But compounds present in *C. tetragonolobus* binds more actively to aldose reductase as observed from their docking scores. It was predicted that the active analogs adopt an acceptable conformation within the active site of Human Aldose Reductase and significant binding interactions were noticed. Therefore, we can conclude that *C. rotundus* and *C. tetragonolobus* contain many active chemical constituents which can inhibit aldose reductase activity. On the basis of the above findings, future studies will aim for the rational design of novel selective inhibitors.

ACKNOWLEDGEMENT

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