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PHYTOCHEMICAL PROFILING AND IN SILICO PREDICTION OF ANTI-DIABETIC COMPOUNDS FROM *ASPARAGUS RACEMOSUS* (SHATAVARI): A COMPARATIVE ANALYSIS WITH CONVENTIONAL DIABETIC DRUGS

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ABSTRACT

The study explores the in silico anti-diabetic potential of phytochemicals from *Asparagus racemosus* (Shatavari) through molecular docking analysis with Aldose reductase, a key enzyme involved in diabetic complications. Using AutoDock 4.2, the binding interactions of 15 phytochemical compounds were analyzed, and their docking scores were compared with standard anti-diabetic drugs, Glibenclamide and Metformin. The results revealed that several compounds exhibited strong binding affinity to Aldose reductase, with Quercimeritrin showing the lowest interaction energy, suggesting a stable complex with the enzyme. Furthermore, hydrogen bonding and van der Waals interactions played significant roles in ligand-enzyme interactions. The compounds demonstrated favorable pharmacokinetic properties, adhering to Lipinski's Rule of Five, indicating their potential as orally active drugs. The study highlights the promising anti-diabetic effects of *Asparagus racemosus* phytochemicals, especially in the context of Aldose reductase inhibition, which is crucial for mitigating diabetic complications.

KEYWORDS: In silico screening, Anti-diabetic potential, *Asparagus racemosus* (Shatavari), Molecular docking.

1. INTRODUCTION

Diabetes mellitus is a prevalent metabolic disorder characterized by abnormal carbohydrate metabolism, leading to either insufficient insulin production or reduced insulin sensitivity in target organs. It affects approximately 25% of the global population, with alarming statistics highlighting a growing public health concern. Particularly in India, the

country has earned the distinction of being the "diabetic capital" of the world, with over 20 million people affected by the disease. This number is projected to rise significantly, reaching an estimated 57 million by 2025. Due to the chronic nature of diabetes and its association with various complications, there is a pressing need for alternative medicine and novel therapeutic strategies. The Indian Council of Medical Research (ICMR) recognizes diabetes mellitus as a refractory disease, prompting research into alternative therapies, particularly through the use of medicinal plants.

Diabetes mellitus is a group of metabolic disorders characterized by chronic high blood sugar levels, either due to insufficient insulin production or cellular resistance to insulin. This condition leads to the classical symptoms of polyuria (frequent urination), polydipsia (excessive thirst), and polyphagia (increased hunger). Additionally, diabetes significantly increases the risk of vascular problems, particularly cardiovascular diseases. The concept of diabetes dates back to ancient India, where Sushruta (6th century BCE) identified the condition and classified it as "Madhumeha." He linked it to obesity and a sedentary lifestyle, recommending exercises as a cure. Interestingly, ancient Indian physicians diagnosed diabetes by observing whether ants were attracted to a person's urine, hence the term "sweet urine disease."
There are two broad classifications of diabetes: Diabetes Mellitus (DM) and Diabetes Insipidus (DI). The former is associated with the excretion of "sweet urine," while the latter is characterized by the passage of tasteless urine with low sodium content. Diabetes Mellitus is further divided into four major types: Type I**,** Type II**,** Gestational Diabetes**,** and Other Specific Types. Understanding these classifications helps in tailoring appropriate treatment strategies for individuals affected by this chronic condition.

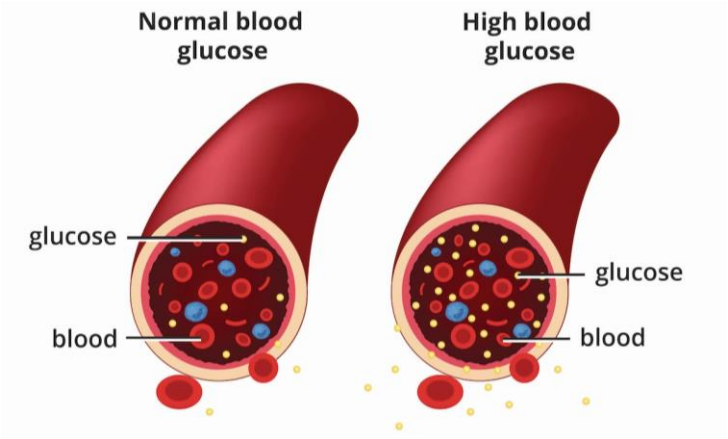


Fig: 1 Diabetes Mellitus.

2. PLANT PROFILE

2.1 Introduction To Asparagus Racemosus In Traditional Medicine

Asparagus racemosus, commonly known as Shatavari, has been a part of Ayurvedic medicine for centuries and holds an esteemed place in traditional Indian healing practices. Its usage dates back to the Pre-Vedic period and is prominently mentioned in several ancient Ayurvedic texts, signifying its long-standing importance in the treatment of various ailments. Ayurveda, one of the oldest holistic healing systems in the world, originated in India around 5000 years ago. It is deeply rooted in the belief that health is a result of balance among the body, mind, and spirit, and it emphasizes the use of natural herbal remedies to achieve this balance. Initially confined to specific regions of India, Ayurveda has spread across the world and is now recognized globally as an alternative and complementary system of medicine. Its methods include a variety of therapies, including herbal remedies, dietary guidelines, yoga, and

meditation. Ayurveda offers a comprehensive approach to health, focusing not only on the physical aspects but also on the emotional and spiritual well-being of individuals.

2.2 The Rich Heritage Of Herbal Medicine In India

India’s ancient medical history is rich and diverse, with a deep-rooted tradition of herbal medicine. Many of the herbs and plants used in Ayurveda have been utilized for their medicinal properties for thousands of years. Asparagus racemosus, or Shatavari, is among these revered herbs. Its benefits have been highlighted in texts like the Charaka Samhita and Sushruta Samhita, where it is described as a powerful herb for treating various conditions, including digestive disorders, respiratory issues, and women's health problems.

In Ayurveda, Asparagus racemosus is recognized for its adaptogenic, immunomodulatory, and anti-inflammatory properties. The herb is believed to have the ability to rejuvenate the body and promote longevity. It is particularly valued for its positive effects on the reproductive system, where it is used to treat conditions like infertility, menstrual disorders, and postpartum recovery.

2.3 Ayurvedic Approach To Wellness

In Ayurvedic philosophy, every individual has a unique constitution, or Prakriti, which governs their physical and mental health. Ayurveda tailors treatments to these individual constitutions, aiming to bring about a state of balance or homeostasis. Herbs like Asparagus racemosus are often chosen based on their ability to restore balance to a person’s system, particularly in cases where the Doshas (Vata, Pitta, and Kapha) are out of harmony.

Asparagus racemosus is considered especially beneficial for balancing the Vata and Pitta doshas, making it a popular remedy for conditions related to the nervous system, digestive tract, and reproductive organs. It is also classified as a "Brahmi Rasayana", meaning it is considered a tonic that supports brain health and cognitive functions.

2.4 Global Spread & Modern Relevance

While Ayurveda was initially restricted to certain regions of India, its global popularity has grown exponentially over the last century. This can be attributed to the increasing recognition of the benefits of natural remedies and the shift towards more holistic health practices worldwide. The rise of Ayurvedic products in international markets, particularly in the wellness and personal care sectors, highlights its global appeal. Today, Asparagus racemosus is widely cultivated and utilized in countries across the globe, with an increasing number of people seeking its therapeutic benefits. As modern research continues to explore the pharmacological and therapeutic properties of Shatavari and other Ayurvedic herbs, the scientific validation of their effects strengthens their credibility. Today, Shatavari is not only used in Ayurvedic medicine but also in modern alternative medicine to treat a range of conditions such as diabetes, anxiety, digestive issues, and hormonal imbalances.

2.5 Taxonomical Classification

- **Kingdom:** Plantae
- **Division:** Angiosperms
- **Class:** Monocots
- **Order:** Asparagales
- **Family:** Asparagaceae; Liliaceae

- **Genus:** Asparagus
- **Species:** Racemosus

2.6 Other Regional Names

- **Bengali -** Shatamuli
- **Gujrati** -Satawari
- **Hindi -** Satmuli
- **Madhya Pradesh -** Narbodh or atmooli
- **Kannada -** Aheruballi
- **Malayalam -** Chatavali
- **Rajasthan -** Norkanto or satawar
- **Marathi -** Shatavari or shatmuli
- **Sanskrit -** Shatavari
- **Tamil-** Thanneer vittaan
- **Himachal Pradesh –** Sanspayiin

2.7 Botanical Description

The genus *Asparagus* comprises of more than 250 species distributed throughout the world out of which 22 species of *Asparagus* are recorded in India. The plant ranges up to 1500 m of altitude range and present in tropical and subtropical regions. The plant is under-shrub and grows to up to 3 metre in height. It is a spinous herb bearing numerous succulent shortrootstocks. The roots are elongated, tuberous brown in colour with tapering ends at both sides. It is 1-2 cm in thick and 25-90 cm long that appears ash silver white colour internally or externally. The plant is a woody climber known as liana bearing brown or may be whitish to grey coloured and small protective spines.

Asparagus leaves having resemblance with pine needles. The flowering occurs in month of February-March. The flowers are uniform and small in size. It appears white in colour having small spikes. The flower is hermaphrodite in nature and mainly pollinated by Bees. The flowers are aromatic nature with a mild fragrance by the end of April. Fruits can be seen with attractive red berries. Its fruits are small, round in shape and changes from green to red colour on maturity. The Shatavari prefers to grow in moist, humid and arid conditions. Its ability to store and capture maximum moisture from dry soils is reflects its potential for replenishing fluids and bringing balance to stress in human body. Usually this plant prefers Black, well drained and fertile soil at a temperature of 20-30 0C. The fruits contain 2 to 3 lobed and globular in shape and changes from green to purple which appears to purple black on ripening and seeds appear to be brittle and hard. Use of *Asparagus racemosus* was mentioned by charka in Charaka samhita (the ancient literature of Ayurveda). It shows the activities of anticancer hypertensive response, Anti-abortifacient, antidysenteric, antioxytoxic, antibacterial anti-inflammatory, spasmodic, hypoglycemic, anticoagulant, antiulcer, antioxidant, antifungal and in reproductive problems.

2.8 Phytochemical Constituents

The Shatavari plant contains a large group of isoflavones, polysaccrides and steroidal saponins. The saponins are present in predominant form such as Shatavarin I-IV. Others phytoconstituents are 8-methoxy-5, 6, 4'-trihydroxyisoflavone 7-O-beta-D-glucopyranoside. Asparagamine, Racemosol, 9, 10- dihydrophenanthrene),

Shatavaroside, Secoisolariciresinol Shatavari Immunoside this is a glycoside of Sarsasapogenin, Racemoside A Ursolic Acid, Beta-Sitosterol and Stigmaterol Genistein and Daidzein, Racemosides A-C.

Fig. 2: Shatavari Plant.

3. MATERIALS AND METHODS

3.1 Natural Compounds Selection

A series of fifteen natural compounds were selected as common reported anti -diabetic property of various parts of *Asparagus racemosus.*(Shatawari) plant from various database and literature. All chemical structures of these compounds were sketched in Chem Draw Ultra 12.0 (Cambrigde Soft) as shown in Table No.1

Table: 1 List of Studied Compounds & Parts of *Asparagus Racemosus.* (Shatawari).

S. No	Compound	Mol. formula	Category	Parts of *Asparagus racemosus*
1.	Asparagamine	$C_{21}H_{25}NO_5$	Alkaloid	Root
2.	Cyanidine 3 galatoside	$C_{22}H_{24}O_{11}$	Flavonoid	Woody portions of tuberous roots
3.	Diosgenin	$C_{27}H_{42}O_3$	Steroidal	Root
4.	Hyperoside	$C_{22}H_{22}O_{11}$	Flavonoid	Flowers and Fruit
5.	kaempferol	$C_{15}H_{10}O_6$	Flavonoid	Woody portions of tuberous roots
6.	Polycyclic alkaloid	$C_{22}H_{27}NO_5$	Alkaloid	Root
7.	Quercetin 3 glucuronide	$C_{21}H_{18}O_{13}$	Flavonoid	Leaves
8.	Quercetin	$C_{15}H_{10}O_7$	Flavonoid	Flowers and Fruit
9.	Racemofuran	$C_{17}H_{16}O_4$	Furan derivatives	Root
10.	Racemosol	$C_{17}H_{18}O_3$	Dihydropheanthrenene	Root
11.	Rutin	$C_{27}H_{32}O_{15}$	Flavonoid	Flowers and Fruit
12.	Sarsasapogenin	$C_{29}H_{48}O$	Steroidal	Root
13.	Shatavarin IV	$C_{53}H_{90}O_{22}$	Steroidal	Root
14.	Sitosterol	$C_{30}H_{52}O$	Steroidal	Root
15.	Stigmasterol	$C_{28}H_{46}O_2$	Steroidal	Root

3.2 Preparation of Protein Structure

The crystal structure of the Human Aldose reductase (PDB ID: 2pdb) mutant F121P complexed with zopolrestat (Fig.No.3) solved by X-ray crystallography at 2.30Å was retrieved from the Protein Data Bank (http://www.pdb.org/pdb/home/home.do). Before initiating the docking simulations, all non-protein molecules were removed from 2pdb; for any alternative atom locations only the first location (A) was retained. All the docking calculations were performed by using Autodock 4.0. 2pdb was modified by adding polar hydrogens and then kept rigid in the docking process, whereas all the tensional bonds of ligands were set free by Ligand module in Autodock Tools-ADT.

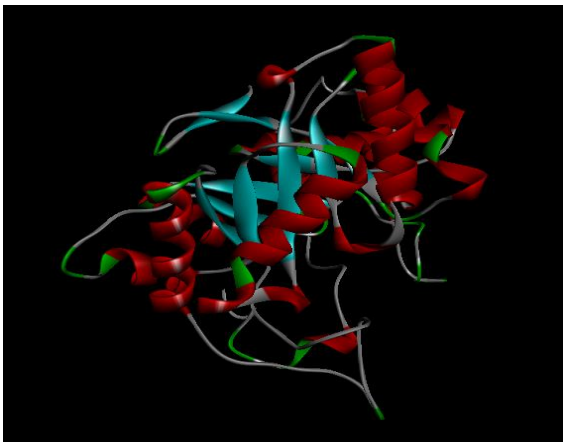
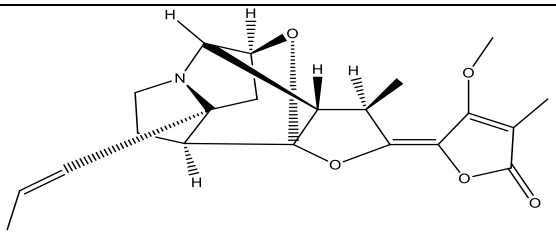
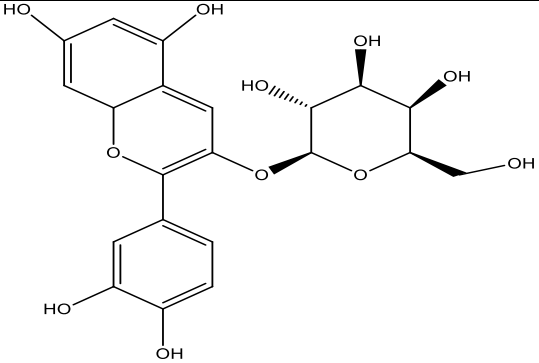


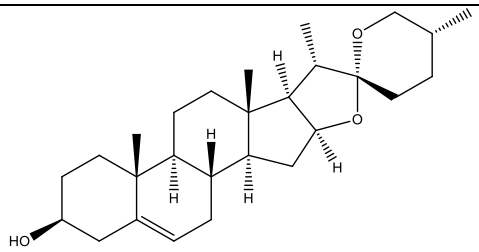
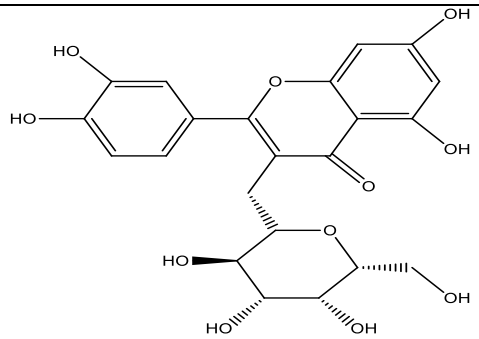
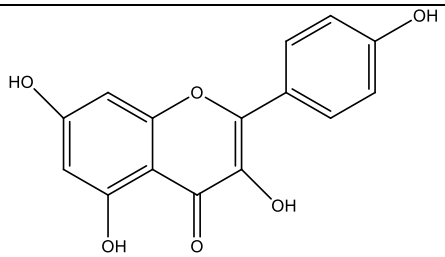
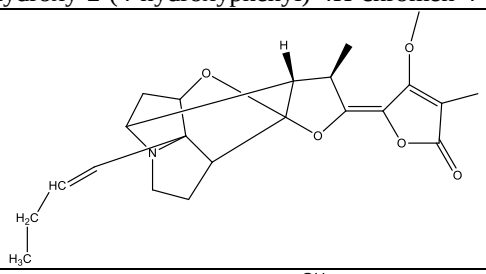
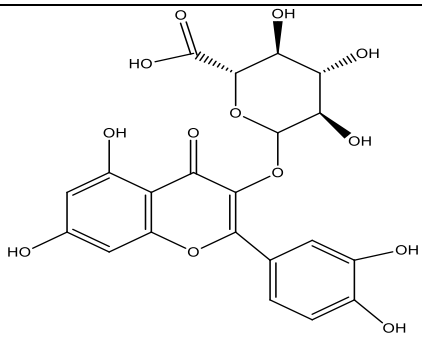
Fig. 3: The Crystal Structure of the Aldose Reductase (PDB ID: 2pdb).

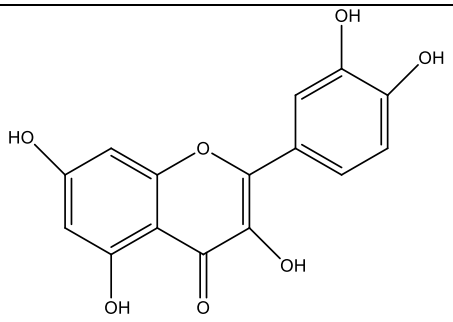
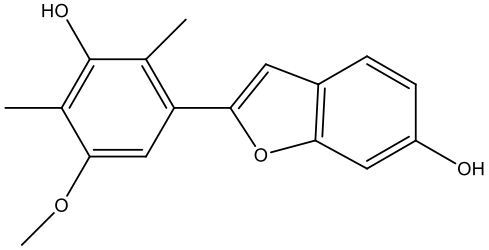
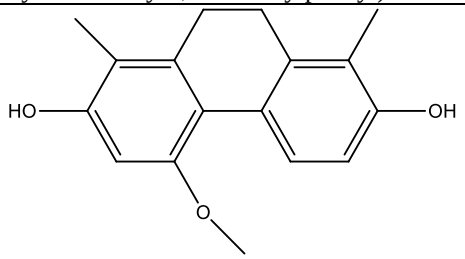
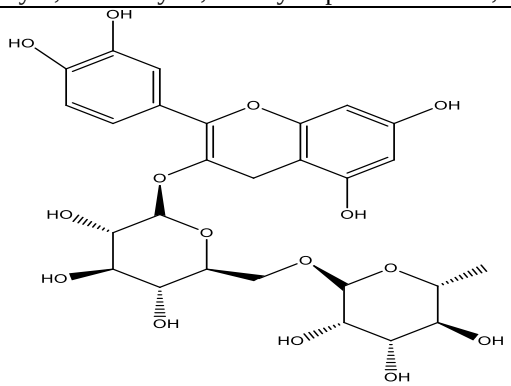
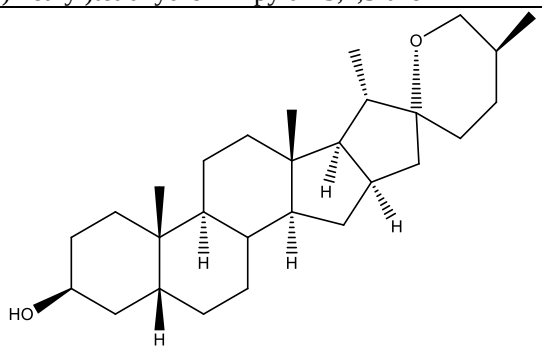
3.3 Preparation of Ligand Structures

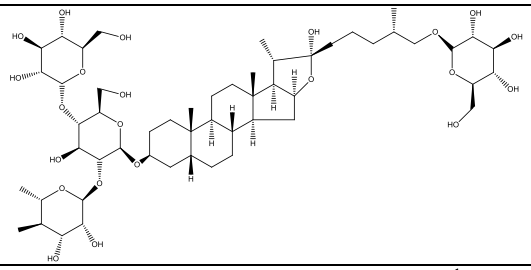
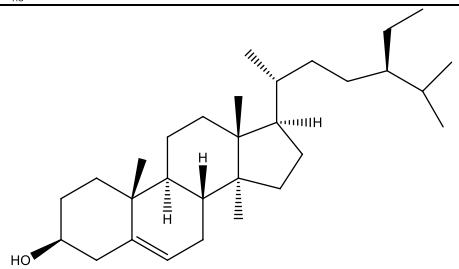
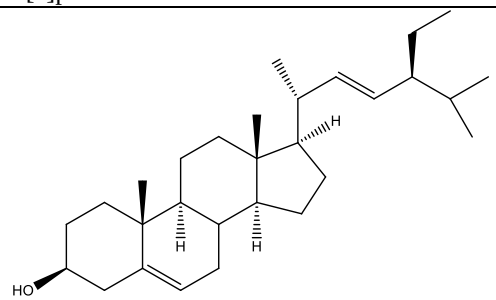
The phytochemicals from various parts of *Asparagus racemosus* (Shatawari) plant were considered as ligand molecules. The phytochemical structure of all the 15 compounds were drawn in Marvinsketch is a tool, adding or deleting functional group or atoms, queries and reactions. Assigning stereochemistry, charge, valence, radicals and isotopes to each atom can be done and moreover single, double, triple bonds and aromatic forms can also be created **(**Table No.2)

Table 2: Structure and Properties of Ligands Used For Docking Analysis.

S. No.	Name of the compound	Structure	Properties
1.	Asparagamine	 (Z)-4-methoxy-3-methyl-5-((1S,2R,3aS,4aR,7R,7bR,8S)-7-methyl-2-((Z)-prop-1-en-1-yl)tetrahydro-2H-2,4a,1-(epipropane[1,1,3]triyl)furo[3',2':4,5]furo[3,2-b]pyrrol-6(7bH)-ylidene)furan-2(5H)-one	Chemical Formula: $C_{21}H_{25}NO_5$ Molecular Weight: 371.43
2.	Cyanidine 3 galatoside	 (2S,3R,4S,5R,6R)-2-((2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-8aH-chromen-3-yl)oxy)-6-(hydroxymethyl)tetrahydro-2H-pyran-3,4,5-triol	Chemical Formula: $C_{22}H_{24}O_{11}$ Molecular Weight: 448.42

3.	Diosgenin	 (2'R,4S,5'R,6aR,6bS,8aS,8bR,9S,11aS,12aS,12bS)-5',6a,8a,9-tetramethyl-1,3,3',4,4',5,5',6,6a,6b,6',7,8,8a,8b,9,11a,12,12a,12b-icosahydrospiro[naphtho[2',1':4,5]indeno[2,1-b]furan-10,2'-pyran]-4-ol	Chemical Formula: $C_{27}H_{42}O_3$ Molecular Weight: 414.62
4.	Hyperoside	 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-(((2S,3R,4R,5R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)methyl)-4H-chromen-4-one	Chemical Formula: $C_{22}H_{22}O_{11}$ Molecular Weight: 462.40
5.	kaempferol	 3,5,7-trihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one	Chemical Formula: $C_{15}H_{10}O_6$ Molecular Weight: 286.24
6.	Polycyclic alkaloid		Chemical Formula: $C_{22}H_{27}NO_5$ Molecular Weight: 385.45
7.	Quercetin 3 glucuronide	 (2S,3S,4S,5R)-6-((2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4H-chromen-3-yl)oxy)-3,4,5-trihydroxytetrahydro-2H-pyran-2-carboxylic acid	Chemical Formula: $C_{21}H_{18}O_{13}$ Molecular Weight: 478.36

8.	Quercetin	 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one	Chemical Formula: $C_{15}H_{10}O_7$ Molecular Weight: 302.24
9.	Racemofuran	 2-(3-hydroxy-5-methoxy-2,4-dimethylphenyl)benzofuran-6-ol	Chemical Formula: $C_{17}H_{16}O_4$ Molecular Weight: 284.31
10.	Racemosol	 4-methoxy-1,8-dimethyl-9,10-dihydrophenanthrene-2,7-diol	Chemical Formula: $C_{17}H_{18}O_3$ Molecular Weight: 270.32
11.	Rutin	 (2S,3S,4R,5R,6S)-2-((2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4H-chromen-3-yl)oxy)-6-((((2R,3S,4S,5S,6R)-3,4,5-trihydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)methyl)tetrahydro-2H-pyran-3,4,5-triol	Chemical Formula: $C_{27}H_{32}O_{15}$ Molecular Weight: 596.53
12.	Sarsasapogenin	 (2aR,2'R,4S,5'S,6aS,6bS,8aS,8bR,9S,11aR,12aS)-5',6a,8a,9-tetramethyldocosahydro-1H-spiro[pentaleno[2,1-a]phenanthrene-10,2'-pyran]-4-ol	Chemical Formula: $C_{28}H_{46}O_2$ Molecular Weight: 414.66

13.	Shatavarin IV		Chemical Formula: $C_{53}H_{90}O_{22}$ Molecular Weight: 1079.27
14.	Sitosterol	 (3S,8R,9S,10R,13R,14S,17R)-17-((2R,5R)-5-ethyl-6-methylheptan-2-yl)-10,13,14-trimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-ol	Chemical Formula: $C_{30}H_{52}O$ Molecular Weight: 428.73
15.	Stigmasterol	 (3S,9S,10R,13R,14S,17R)-17-((2R,5S,E)-5-ethyl-6-methylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-ol	Chemical Formula: $C_{29}H_{48}O$ Molecular Weight: 412.69

3.4 Basic Pharmacokinetics Parameters Calculation

A compound has to be passed through multiple filters to be considered a novel drug. Most of the compounds that fail in pre-clinical trials do so because they do not show the required pharmacological properties to be a drug molecule. Pharmacokinetics properties such as absorption, distribution, metabolism, excretion, and toxicity (ADMET) have played a very crucial role in development of drug design to the final clinical success of a drug candidate. Therefore, prediction of ADMET properties was done earlier with the aim of decreasing the failure rate of the compound for further process in future. Pharmacokinetics properties of natural compounds such as MW (molecular weight), LogP, Hbd (number of hydrogen bond donors), Hba (number of hydrogen bond acceptors), TPSA (topological polar surface area), nrtB (number of rotatable bonds), nViolation (violations of Lipinski's rule of five) were calculated by OSIRIS Data Warrior (Drug LiknessTool) and Molinspiration Online tool (http://www.molinspiration.com/).

4. RESULTS AND DISCUSSION

4.1 Docking Analysis

To ensure the interaction between the natural compounds and diabetic disorder associated targets, we performed molecular docking analysis using Autodock 4.2. Each of the compounds was docked with Aldose reductase targets individually. The output of all ligands was given by energy values in kcal/mol as shown in Table No.3.These compounds showed very good binding affinity with targeted Aldose reductase receptor when compared to standard

drugs. Docking score of the compounds targeted Aldose reductase enzyme receptor was compared with the score of the drug Glibenclamide and Metformin which is used as a potent drug for the diabetic disorder. Table No.3 shows the results obtained through the docking study between the 10 compounds and standard drugs Glibenclamide and Metformin with the Aldose reductase enzyme. Table No.3 shows that all compounds involved in this study interacted with the Aldose reductase enzyme in an attractive manner when compared with standard drug, and the compound Quercimeritrin obtained lower interaction energy, being shown to be more stable in complex with the site of the macromolecule. It can also be observed that the ligand compounds obtained van der waals interaction, hydrogen bonding and solvation energies as satisfactory as the Quercimeritrin, but with higher torsional energies, directly affecting the free energy of the docking.

Fig.No.8,9,10,11, &12 shows the more stable conformation of the compounds Cyanidine, withanolides, Charatin, and Myricetin at the active site of the Aldose reductase. It can be observed that in addition to interacting with the amino acids of the active site, all compounds studied interact ion-dipole with the zinc ion (Zn ++). In Table No.6 the main characteristics of the hydrogen bonds formed between the binding compounds and the active site amino acids of the enzyme can be observed. Ligands interacted through hydrogen bonds with similar active site amino acids, such as Thr 19(A), Trp 20(A), Lys 21 (A), Asp 43(A), Ser 159(A), Asn160(A), Gln183(A), Ser 210(A), Leu 212(A), Ser 214(A), Val 264(A), Thr 265(A), Arg 268(A), Glu 271(A), Asn272(A), and others. This shows the importance of the polar groups of these compounds for the interaction with the active site of the enzyme, because in addition to the large number of hydrogen bonds, all interact with the zinc ion, as already mentioned above In Auto dock the analogues were examined for their binding energies and hydrogen bonding. The conformations with highest binding energies and greater number of hydrogen bonds of all the ligands were taken in consideration for ranking the analogues. The interactions were stronger (energetically lesser) for all the ligands which are used for docking simulation.

Table 3: Value of The Molecular Docking Energy Of The Compounds Against The Aldose Reductase And The Standard Drug.

S. No	Compound Name	2pdb				
		Binding Energy (kJ mol^{-1})	**Vdw, Hydrogen Bond and Solubility Interaction Energy (kJ mol^{-1})**	**Eletrostatic Energy (kJ mol^{-1})**	**Torsional Energy (kJ mol^{-1})**	**Inhibition Constant (µM)**
1.	Asparagamine	-6.96	-7.92	-0.39	0.6	7.92
2.	Cyanidine 3 galatoside	Small molecule	-	-	-	-
3.	Diosgenin	-7.35	-7.36	0.01	0.0	4.07
4.	Hyperoside	-7.94	-9.25	0.02	1.19	1.51
5.	kaempferol	-5.91	-7.0	0.19	0.89	46.48
6.	Polycyclic alkaloid	Small molecule	-	-	-	-
7.	Quercetin 3 glucuronide	molecule	-	-	-	-
8.	Quercetin	molecule	-	-	-	-
9.	Racemofuran	molecule	-	-	-	-
10.	Racemosol	-7.24	-7.46	-0.07	0.3	4.95
11.	Rutin	-5.68	-7.44	-0.04	1.79	68.11
12.	Sarsasapogenin	-7.61	-7.64	0.03	0.0	2.62
13.	Shatavarin IV	-5.71	-10.38	-0.11	4.77	64.97
14.	Sitosterol	-6.75	-8.55	0.01	1.79	11.34
15.	Stigmasterol	-7.04	-8.54	0.03	1.49	6.87
16.	Glibenclamide	-5.3	-7.67	-0.02	2.39	130.71
17.	Metformin	-4.92	-3.29	-1.63	0.0	248.05

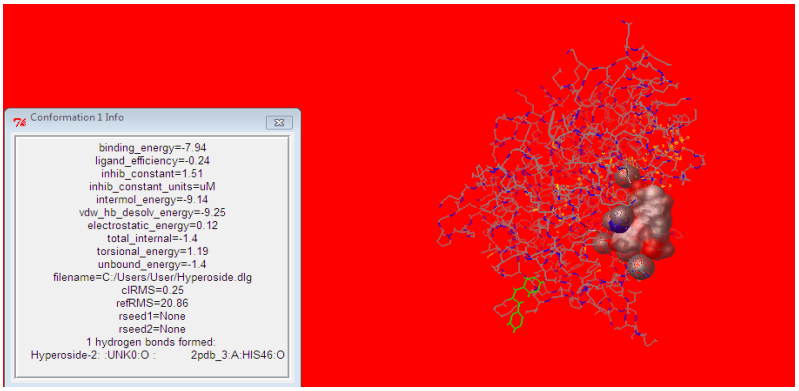


Fig. 4: Compound *Hyperoside* Docked At The Receptor Of Aldose Reductase Enzyme.

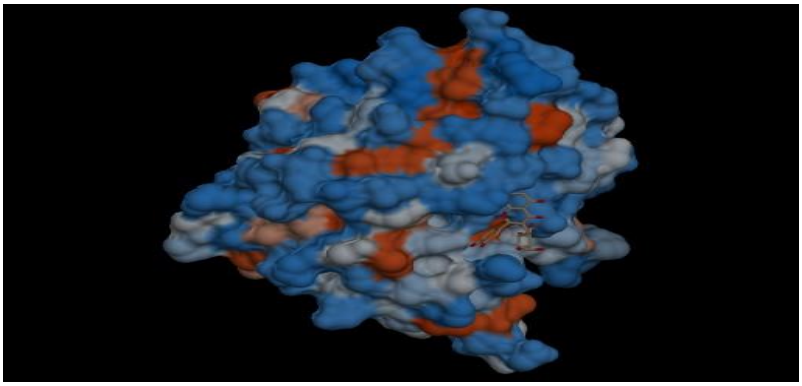


Fig. 5: Compound *Hyperoside* Docked At The Receptor Of Aldose Reductase Ase Enzyme In Chimera View.

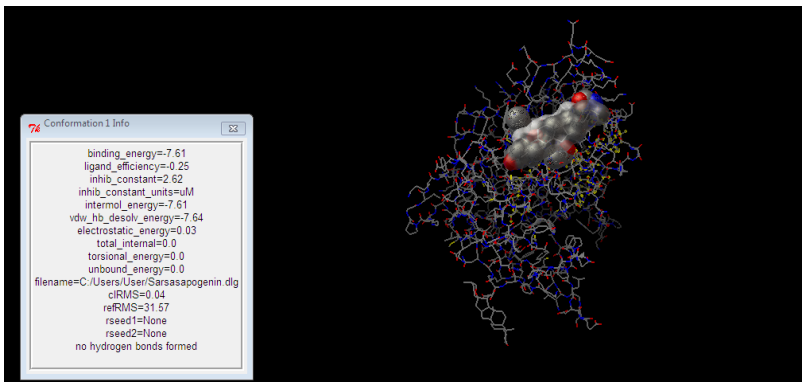


Fig. 6: Compound *Sarsasapogenin* Docked At The Receptor Of Aldose Reductase Enzyme.

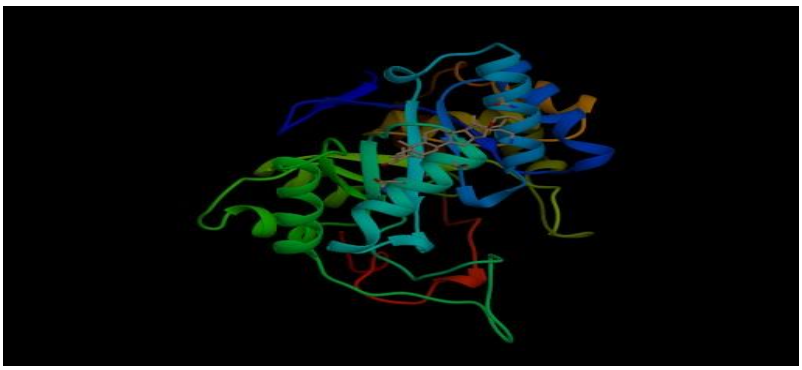


Fig. 7: Compound *Sarsasapogenin* Docked At The Receptor Of Aldose Reductase Enzyme In Chimera View.

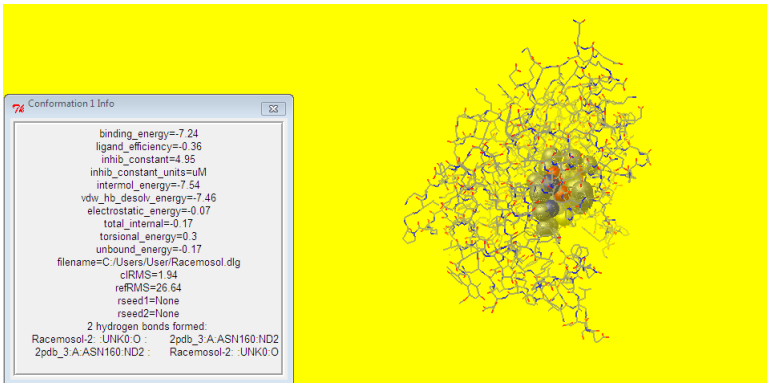


Fig: 8 Compound *Racemosol* Docked At The Receptor Of Aldose Reductase Enzyme.

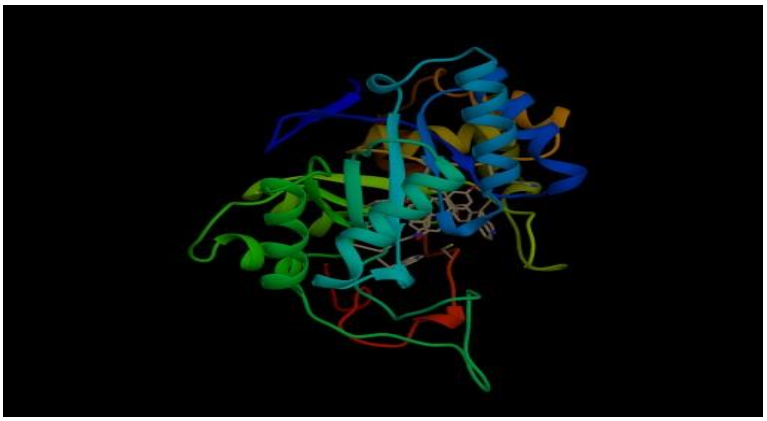


Fig. 9: Compound *Racemosol* Docked At The Receptor Of Aldose Reductase Enzyme In Chimera View.

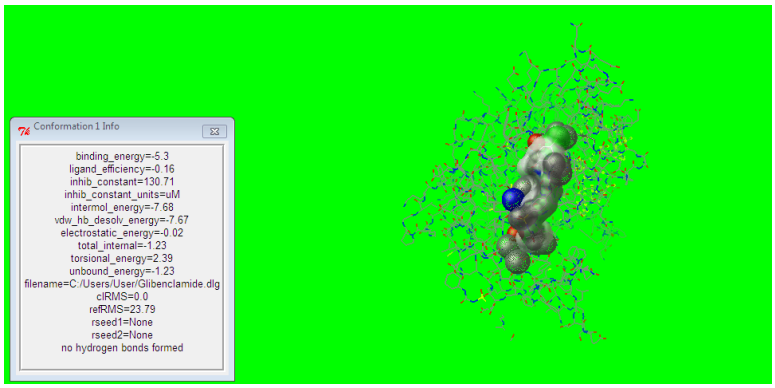


Fig. 10: Compound *Glibenclamide* Docked At The Receptor Of Aldose Reductase Enzyme.

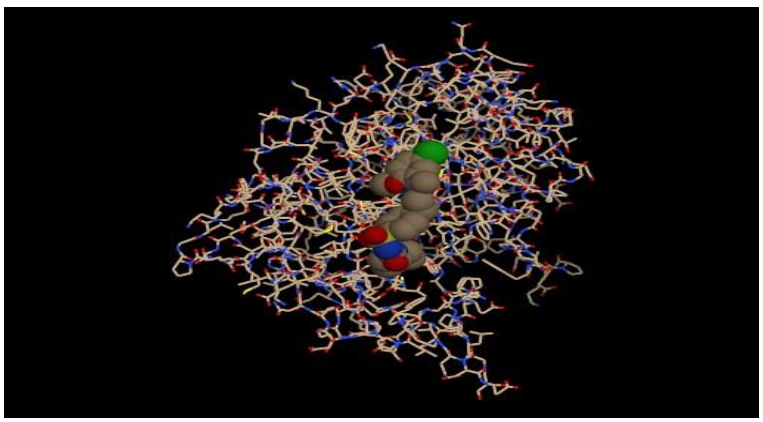


Fig. 11: Compound *Glibenclamide* Docked At The Receptor Of Aldose Reductase Enzyme In Chimera View.

4.2 Validation Of Ligands

QSAR and toxicity studies were performed to obtain the molecular properties of all ligands as shown in Table No.4. QSAR studies reveal that all ligands was passed and acted as a drug molecule by their adherence to the properties such as Absorption, Distribution, Metabolism and Excretion (ADME) as per the Lipinski Rule of 5. The result shows that all the values of analogues were relays within the optimal range. Also the compounds have molecular weight less than 500 Daltons and number of hydrogen bond donors and hydrogen bond acceptors of all the analogues is below 5 and 10 respectively. All the values of partition coefficient and number of rotatable bonds were coming under the limit of 5. All these data indicates that the analogues show no more violations likely to be an orally active drug.

4.3 Assessment Of Toxicities, Drug Likeness, And Drug Score Profiles

Osiris program used for prediction of the overall toxicity of the designed derivatives as the prediction process relies on a predetermined set of structural fragments that give rise to toxicity alerts in case they are encountered in the structure. All target compounds showed low in-Silico possible toxicity risks as shown in Table No.5. Osiris program was also used for calculating the fragment-based druglikeness of the designed compounds and a positive value indicates that the designed molecule contains fragments which are frequently present in commercial drugs.

Table 4: Analysis Of Lipinski Rule Of 5 For The Natural Compounds.

S.No	Compound Name	Molecular weight	ClogP	ClogS	No. of Hba	No. of Hbd	No. of Rot.b
1.	Asparagamine	371.43	-1.1142	-1.916	11	8	4
2.	Cyanidine 3 galatoside	448.42	4.8814	-5.579	3	1	0
3.	Diosgenin	414.62	4.5082	-6.133	7	2	7
4.	Hyperoside	462.40	2.1045	-4.228	8	1	3
5.	kaempferol	286.24	1.99	-2.56	6	4	1
6.	Polycyclic alkaloid	385.45	-0.6965	-2.173	13	8	4
7.	Quercetin 3 glucuronide	478.36	1.4902	-2.491	7	5	1
8.	Quercetin	302.24	3.7878	-4.667	4	2	2
9.	Racemofuran	284.31	3.718	-4.368	3	2	1
10.	Racemosol	270.32	-0.7065	-2.217	15	10	6
11.	Rutin	596.53	5.6266	-6.163	2	1	0
12.	Sarsasapogenin	414.66	-0.2201	-5.498	22	13	16
13.	Shatavarin IV	1079.27	8.1867	-6.846	1	1	6
14.	Sitosterol	428.73	1.0456	-3.554	6	5	4
15.	Stigmasterol	412.69	2.2546	-5.455	5	1	3
Drugs commonly prescribed in treatment of diabetics mellitus							
16.	Glibenclamide	492.03	-0.0382	-2.283	11	8	4
17.	Metformin	129.16	1.8607	-3.568	6	0	4

Table 5: Analysis Of Drug Likeness For The Natural Compounds.

S.No	Compound Name	Molecular formula	Drug Likeness	Muta-genic	Tumo-rigenic	Irritant	Shape Index	TPSA
1.	Asparagamine	$C_{21}H_{25}NO_5$	-4.1025	low	low	none	0.40625	299.37
2.	Cyanidine 3 galatoside	$C_{22}H_{24}O_{11}$	0.84396	none	none	none	0.53333	38.69
3.	Diosgenin	$C_{27}H_{42}O_3$	4.0436	none	none	none	0.60606	105.24
4.	Hyperoside	$C_{22}H_{22}O_{11}$	-1.39	none	none	none	0.44	234.65
5.	kaempferol	$C_{15}H_{10}O_6$	0.28194	none	none	none	0.52381	107.22
6.	Polycyclic alkaloid	$C_{22}H_{27}NO_5$	-0.2337	none	low	none	0.38235	223.67

7.	Quercetin 3 glucuronide	$C_{21}H_{18}O_{13}$	-0.082832	high	high	none	0.5	127.45
8.	Quercetin	$C_{15}H_{10}O_7$	-0.9125	high	none	none	0.52381	62.83
9.	Racemofuran	$C_{17}H_{16}O_4$	-3.0075	none	none	none	0.5	49.69
10.	Racemosol	$C_{17}H_{18}O_3$	1.396	none	none	none	0.42857	248.45
11.	Rutin	$C_{27}H_{32}O_{15}$	-0.07573	none	none	none	0.53333	29.46
12.	Sarsasapogenin	$C_{29}H_{48}O$	-3.9501	none	none	none	0.44	346.06
13.	Shatavarin IV	$C_{53}H_{90}O_{22}$	-4.535	none	none	none	0.51613	20.23
14.	Sitosterol	$C_{30}H_{52}O$	-3.8375	none	none	none	0.34732	157.32
15.	Stigmasterol	$C_{28}H_{46}O_2$	0.2857	none	none	none	0.4	61.25
Drugs commonly prescribed in treatment of diabetics mellitus								
16.	Glibenclamide	$C_{24}H_{30}ClN_3O_4S$	-1.8636	none	none	none	0.39394	197.37
17.	Metformin	$C_4H_{11}N_5$	1.0356	none	none	none	0.46429	57.23

Table 6: Description Of The Hydrogen Bonds Formed Between Ligands And Active Site Of The Enzyme.

S. No	Compound Name	No. of Non H-Atoms (n)	No. of Non-C/H Atoms	No. of Stereo centers	No. of Rotatable Bonds
1.	Asparagamine	32	11	6	4
2.	Cyanidine 3 galatoside	30	3	11	0
3.	Diosgenin	33	9	0	7
4.	Hyperoside	25	8	0	3
5.	kaempferol	21	6	0	1
6.	Polycyclic alkaloid	34	13	5	4
7.	Quercetin 3 glucuronide	22	7	0	1
8.	Quercetin	21	4	0	2
9.	Racemofuran	20	3	0	1
10.	Racemosol	42	15	10	6
11.	Rutin	30	2	12	0
12.	Sarsasapogenin	75	22	32	16
13.	Shatavarin IV	31	1	9	6
14.	Sitosterol	18	2	8	4
15.	Stigmasterol	22	8	4	2
Drugs commonly prescribed in treatment of diabetics mellitus					
16.	Glibenclamide	33	11	5	4
17.	Metformin	28	6	9	4

DISCUSSION

The docking studies conducted in this research emphasize the promising role of phytochemicals from *Asparagus racemosus* in managing diabetes through Aldose reductase inhibition. The results indicated that the binding energies of several compounds were comparable or even superior to the widely used diabetic drugs, Glibenclamide and Metformin. Among the tested compounds, Quercimeritrin exhibited the lowest binding energy, which implies a higher affinity and stability at the active site of Aldose reductase, highlighting its potential as a therapeutic agent.

The docking analysis also revealed that most of the compounds formed stable interactions with the enzyme, characterized by van der Waals forces, hydrogen bonds, and solvation energies. These interactions play a critical role in stabilizing the enzyme-ligand complex, ultimately influencing the binding affinity. The hydrogen bonds formed between the phytochemicals and the active site amino acids such as Thr 19**,** Trp 20**,** and Ser 210 are crucial, as they help to maintain the integrity of the enzyme-inhibitor complex, making it difficult for the enzyme to regain its original state.

Additionally, the QSAR and toxicity analysis conducted in this study suggest that these phytochemicals satisfy the pharmacokinetic criteria outlined by Lipinski's Rule of Five**,** supporting their viability as oral drug candidates. The compounds showed favorable molecular properties, such as low toxicity, optimal molecular weight, and appropriate hydrogen bonding capacity, which further strengthens their candidature as anti-diabetic agents.

The in-silico analysis of Aldose reductase inhibitors provides valuable insights into the molecular interactions between bioactive compounds and diabetic disorder-associated targets. This study could pave the way for future in vitro and in vivo experiments to validate the anti-diabetic properties of these compounds. Moreover, the use of *Asparagus racemosus* extracts as a therapeutic strategy could lead to the development of new, natural-based drugs with minimal side effects.

5. CONCLUSION

Natural products have been used since ancient times and are well recognized as sources of drugs in several human ailments. The healing ability of these herbs and medicinal plants draw attention to study natural products as a potentially valuable resource of drug molecules, they are evolutionarily optimized as drug-like molecules and remain the best sources of drugs and drug leads . In our study, we chose 15 natural compounds that have remarkable anti diabetics' property.

In the present study, we have demonstrated the binding interactions between the phytochemicals obtained from various parts of *Asparagus racemosus.* (Shatawari) plant such as Asparagamine, Diosgenin, Hyperoside, kaempferol, Racemosol, Rutin, Sarsasapogenin, Shatavarin IV, Sitosterol and Stigmasterol with Aldose reductase using Autodock. Based on the binding energies obtained, it can be concluded that the phytochemicals have enhanced binding sites, interactions and potent inhibitory effect on aldose reductase activity. The results also indicate that the significant antidiabetic properties of these phytochemicals may attribute to its aldose reductase inhibitory effects.

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