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A MOLECULAR MODELING STUDY OF PHYTOCONSTITUENTS ANALYSED *VIA* GC-MS TECHNIQUE IN THE RHIZOME PART OF *HEDYCHIUM SPICATUM* (ZINGIBERACEAE)

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Keywords:

Antidiabetic, Aldose reductase, *In-silico*, GC-MS analysis, 7-hydroxyhedychenone, Spicatanol

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ABSTRACT: *Hedychium spicatum* is one of the plant species reported from the northern Himalayan ranges of India, belonging to the family Zingiberaceae, with ethnobotanical values and is well-known for their ethnomedicinal applications. In the present investigation, pet ether and ethanolic rhizome extracts of *Hedychium spicatum* were Analyzed by gas chromatography-mass spectrometry (GC–MS) to identify the important phytochemical constituents. The GC–MS analysis of pet ether and ethanolic extracts from rhizomes of *Hedychium spicatum* detected the presence of numerous phytochemical compounds. Further, the literature review reported rhizome extracts of H. spicatum to have remarkable anti-inflammatory, antioxidant, cardioprotective, and antibacterial activities. The results of DPPH and ferric reducing antioxidant power assay recorded maximum antioxidant activity in *Hedychium spicatum* ethanolic rhizome extract at 500mg/kg dosage. As well as the ethanolic extract exhibited maximum α-amylase inhibition activity followed by exhibiting aldose reductase inhibition. Subsequently, the six identified compounds were analyzed for their bioactivity through *in-silico* molecular docking studies. Results revealed that 7-hydroxyhedychenone might have maximum antioxidant and antidiabetic properties among the phytochemical compounds identified, followed by spicatanol and spicatanol methyl ether. To our best knowledge, this is the first description of some of the phytochemical constituents of rhizomes of H. spicatum, which show pharmacological significance, as there has been no literature available yet on *in-silico* molecular docking of 7-hydroxyhedychenone was also performed to confirm its pharmacological antidiabetic activity based on the binding interactions with the aldose reductase target proteins. The present study results will create an understanding of the antidiabetic pharmacological mechanism of action, which may lead to the development of novel drugs.

INTRODUCTION: "Atharvaveda" (around 1600-1000 B.C) in which comparatively more number of plants have been mentioned than in "Rig-Veda" (around 3500-1800 BC). This evidently proves that preservation of health and prevention from diseases has been the instinctive necessity of humankind from the very beginning of creation.

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An estimated 2, 50,000 species of higher plant and in total around 30 million species are present. The World Health Organization has identified 3,000 plants from the forests of India and other tropical countries, which can be used as medicine [1]. Various phytochemical constituents of medicinal plants exhibit stimulating pharmacological actions such as

cardioprotective, renal, hepatic, neuronal protections [2-4]. These bioactive constituents should be explored widely in isolation, characterization, and identification of compounds responsible for the activity and pathophysiological mechanism of action in curing chronic ailments [5]. The herbal-derived drugs are often prepared from different plant extracts comprising of different phytoconstituents. These phytoconstituents have unique and complex structures and are used in treating prolonged as well as contagious diseases. Extractions and characterizations of numerous such bioactive compounds from various medicinal plants have led to certain medicines with high-activity profiles [6].

The preliminary screening of medicinal plants by spectrometric and chromatographic methods provides basic information on chemical and pharmacological activities, which Helps to select biologically active plants [7]. In recent years, gas chromatography-mass spectrometry (GC–MS) has commonly been employed to identify various bioactive therapeutic compounds present in medicinal plants [8]. Hence, in the present study, GC–MS technique was adopted for detection and identification of phytochemical compounds present in the medicinal plant, *H. spicatum* rhizome belonging to Zingiberaceae, is mentioned as shati in Ayurveda classics and has been used in various dosage forms to treat cough, wound ulcer, fever, respiratory problems and hiccough [9].

Thus, *H. spicatum* is known for its economic, medicinal, aromatic, and aesthetic values. Besides, the rhizome of the species is used is in preparation of Chyawanprash, which is recognized as a tonic and food supplement [10]. The unique topography of Indian Himalayan region of around 250,000 km, is found to have diverse habitats of flora and fauna [11]. The 50 species contain the most famous genra of Zingiberaceae [12-14]. The sesquiterpene alcohols, sesquiterpene hydrocarbons, drimane and labdane [15], 7-hydroxyhedychenone [16], 7-hydroxyl hedychenal and spicatanoic acid [17] and spicatanol and spicatanol methyl ether [18]. Many drugs have failed to enter the market due to their poor pharmacokinetics, which incurs huge losses to pharmaceutical companies. Computer-aided tools have emerged as advanced methods for drug discovery, which can be applied to screen the drugs from phytochemicals found in various medicinal plants. Currently, molecular docking is an effective and inexpensive method for designing and testing drugs. This technique provides information about drug-receptor interactions that are useful to predict the binding orientation of drug candidates to their target proteins [19, 20].

To the best of our knowledge, the pet ether and ethanolic extract composition *Hedychium spicatum* rhizome, an essential oil-bearing plant, has not been reported previously. In this paper, we report the composition of pet ether and ethanolic extract from the rhizomes of *Hedychium spicatum*, occurring in Himalayan ranges and analyzed by GC-MS. Finally, the *in-sillico* studies of six major compounds already reported in the literature were evaluated for aldose reductase molecular docking via the GLIDE algorithm.

MATERIAL AND METHOD:

Plant Material Collection and Authentication: Procurement of plant raw material: Fresh aerial parts of *H. spicatum* were collected from Khari Baoli, Delhi, and were dried and coarsely powdered using a grinder. Authentication and identification of plant were done by Dr. H. B. Singh at National Institute of Science Communication And Information Resources (NISCAIR), New Delhi (References ID: NISCAIR/RHMD/Consult /-2012- 13/2154/160). The voucher specimen has also been deposited in the botany department of Kurukshetra University, Kurukshetra, and voucher specimen no. IPS/012/578 was submitted for future reference.

Preparation of Extract: Shade dried coarsely powdered rhizomes of *H. spicatum* were packed in Soxhlet extractor and a sufficient volume of solvent was added to the reservoir, and the hot continuous extraction process was continued for about 48 h or until solvent came down from the siphoning tube became colorless, firstly the powdered drug was treated with petroleum ether (60-80 °C) and then with alcohol (ethanol).

A Rotatory vacuum evaporator was used to distill excess alcohol under reduced pressure. A brown residue was recovered from the flask with a 48.17% yield and stored in the refrigerator for further pharmacological studies.

Quantification Analysis of Extract *via* GC-MS Analysis:

Preparation of Extract: The respective extracts were weighed, transferred to a flask, treated with the Methanol until the powder was fully immersed, incubated overnight, and filtered through a Whatmann No. 41 filter paper along with Sodium sulphate was wetted with absolute alcohol. The filtrate is then concentrated to 1ml by bubbling nitrogen gas into the solution. The extract contains both polar and non-polar components of the material, and a 2µl sample of the solution was employed in GC-MS to analyze different compounds.

GC–MS Analysis: The GC–MS analysis was carried out using Agilent Chem station Gas Chromatograph equipped and coupled to a mass detector with a polar column. The instrument was set to an initial temperature of 60 °C and maintained at this temperature for 2 min. At the end of this period, the oven temperature was rose up to 210 °C, at the rate of an increase of 3 °C/min, and maintained for 9 min. Injection port temperature was ensured as 250 °C and Helium flow rate as one ml/min. The ionization voltage was 70eV. The samples were injected in split mode as 1:40. Using computer searches on a NIST Ver.2.1 MS data library and comparing the spectrum obtained through GC-MS, compounds present in the plant's sample were identified.

Identification of Phytocompound: Interpretation on Mass-Spectrum GC-MS was conducted using the National institute Standard and Technology (NIST) database having more than 62,000 patterns. The spectrum of the unknown components was compared with the spectrum of known components stored in the NIST library. The name, molecular weight, and structure of the components of the test materials were ascertained (Abhirami *et al.*, 2012).

Aldose Reductase Molecular Docking Studies: Molecular docking is a frequently used tool in computer-aided structure-based rational drug design. It evaluates how small molecules called ligands (terpenoids), and the target macromolecule (aldose reductase enzyme) fit together. Besides generating binding energies in these docking studies, the position of the ligand in the enzyme binding site can be visualized. It can be useful for developing potential drug candidates and also for understanding the binding nature [20-22].

Protein Preparation Wizard: The PDB file (1EL3) was imported from the PDB website. The protein preparation wizard of Schrödinger's suite (Maestro, version 9.3, Schrödinger, LLC, New York, NY, 2012) has processed the protein. The minimal protein preparation steps were followed to process the protein 1EL3, including deleting substrate cofactor and co-crystallized water molecules and addition of missing hydrogen, *etc*.). An extended PDB format termed PDBQT file was used for coordinate files, including atomic partial charges. AutoDock Tools was used for generating PDBQT files from traditional PDB files [19]. Even though there are thousands of structures of aldose reductase enzymes are present in the database. Still, the 3EL3 were selected for the present study due to its similarity with the human enzyme [23].

Ligand Preparation: The 3D structure of the compound labdane diterpenes was drawn in marvin sketch, and standard aldose reductase inhibitor zopolrestat was downloaded from Pubchem. Lig. Prep. of Schrodinger utility software has been used to generate energy minimized 3D molecular structure. The 2D structure was drawn with the help of ChemSketch and downloaded from www.acdlabs.com.

Docking: Molecular docking study was carried out to evaluate the inhibitory potential of terpenoids against AR. The docking study was performed in the binding site of the 1EL3 in the standard precision mode of GLIDE algorithm. The protein preparation utility tool of Schrödinger suite relaxes the protein making it flexible to accommodate the ligand or inhibitor. The receptor grid files were generated around the active site of 1EL3 using the Grid Receptor generation program.

The docking process has been started after ensuring that the protein and ligand in the correct position. For a prepared set of ligands, the best pose and mol dock score was taken. AutoDock4.2 was downloaded from www.scripps.edu. The AutoDock was run several times to get various rigid docked conformations and analyze the predicted docking energy. The binding sites for these molecules were selected based on the ligand-binding pocket of the

templates. AutoDock Tools provide various methods to analyze the results of docking simulations such as, conformational similarity, visualizing the binding site and its energy and other parameters like intermolecular energy and inhibition constant. For each ligand, ten best poses were generated and scored using AutoDock 4.2 scoring functions [19].

RESULTS:

Chemical Composition of *Hedychium spicatum* Rhizome: The yield of rhizome extract was obtained by Soxhlet extraction from *Hedychium spicatum* was 5.98%. 61 component chromatographic peaks of the extracts were detected, and many components of the respective extracts were identified.

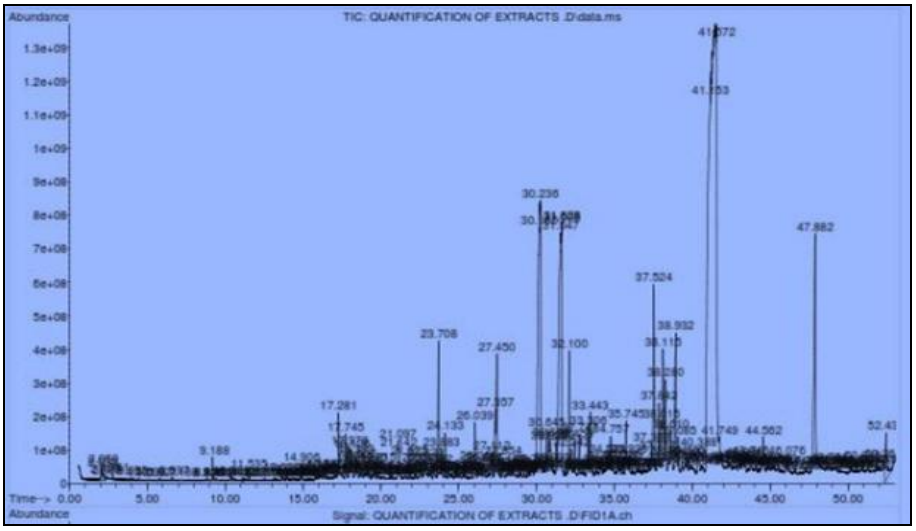

FIG. 1: CHROMATOGRAPH SHOWING AREA% OF COMPOUND PRESENT IN PET ETHER EXTRACT

TABLE 1: CHEMICAL COMPOSITION OF PET ETHER EXTRACT OF RHIZOME *HEDYCHIUM SPICATUM*

S. no.	Chemical Constituents	Rt	Qual	Area %	Cas no.#
1	Benzofuran, 3-methyl	30.164	70	0.97	#14360
2	Quinoline, decahydro-, trans	31.548	46	1.24	#17674
3	Epizonarene	32.458	78	0.89	#62258
4	Epizonarene	32.744	83	0.83	#62258
5	alpha.-Cubebene	33.305	55	0.87	#62286
6	2-Naphthalenemethanol, 1,2,3,4,4a,8a hexahydro-.alpha.,.alpha.,4a,8-tetramethyl-, [2R-(2.alpha.,4a.alpha.,8a.alp	34.129	87	0.82	#74862
7	Hexahydro-5-methyl-1-phenyl-1,3,5-triazine 2-thione	37.522	47	1.24	#64457
8	E-2-Octadecadecen-1-ol	38.117	50	0.90	#112028
9	Maleimide, N-allyl	38.277	60	0.80	#1643
10	Cyclohexane, 1,2-dimethyl-3-pentyl-4-propyl	38.609	87	1.16	#78219
11	Octahydropyrano[3,2-b]pyridin-6-one	38.830	41	1.26	#27553
12	(+)-2-Carene, 4-.alpha.-isopropenyl	39.084	59	0.96	#41642
13	3-Chloro-4-(dichloromethyl)-5-hydroxy 2(5H)-furanone	39.559	12	0.87	#71875
14	Distannoxane, hexabutyl	39.971	10	1.71	#217834
15	2-Methoxybenzoic acid, cyclopentyl ester	40.389	72	1.25	#74442
16	2-(2-Furyl)pyridine	41.156	89	2.73	#21203
17	2-(2-Furyl)pyridine	41.573	83	4.20	#21203
18	2-Propenoic acid, 3-(4-methoxyphenyl)-, ethyl ester	41.751	96	1.58	#63709
19	3-Hydroxypropionic acid, 3-(1H benzoimidazol-2-yl)	42.454	64	0.88	#63397
20	1H-1,3-Diborole, 1,3,4,5-tetraethyl-2,3- dihydro-2-methyl	42.632	18	0.79	#51683
21	1H-Indene, 1-ethylideneoctahydro-7a-methyl- , (1E,3a.alpha,7a.beta.)	43.050	38	0.85	#33116
22	p-Hydroxycinnamic acid, ethyl ester	43.296	93	1.06	#52780
23	Bicyclo[3.1.1]heptane, 2,6,6-trimethyl	43.748	64	0.84	#16757
24	Oleyl alcohol, heptafluorobutyrate	46.076	90	1.46	#209404
25	Hexadecanoic acid, methyl ester	46.614	97	0.87	#113689
26	9-Octadecenoic acid (Z)-, 9-hexadecenyl ester, (Z)	47.289	15	0.82	#213688
27	Kaur-16-ene, (8. beta, 13. beta.)	47.885	55	1.85	#115432

Note: Rt is retention time, Cas # indicates library reference number, Qual. indicates quality.

The content of the identified components was more than 94.03% of the oil. 2-(2-Furyl) pyridine (6.93) and Kaurene (1.85) were the most abundant components in the pet ether extract. Benzofurazan, 5-methyl-4-nitro (5.03) and Anisole, m-(2-nitrovinyl) (2.58), 1-8 cineole were the most abundant compounds in ethanolic extract. The rhizome ethanolic extract was predominantly made up of monoterpenoids and sesquiterpenoids, mainly labdane diterpenes as the principal components and other phenolic compounds in trace amounts.

While the pet ether extract contained monoterpenoids and sesquiterpenoids as the major components with diterpenoids and other phenolic compounds as minor ones. The extract's constituents were comparatively the same the ethanolic extract contains quantitatively more. Out of total components reported, the 1-8 cineol, spathulenol, hedychenone, 7-hydroxyhedychenone, linalool, and terpineol were found to be major components in both extracts.

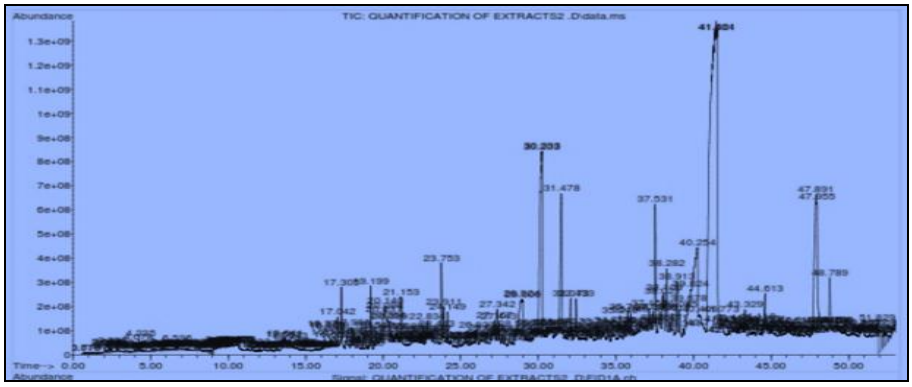

FIG. 2: CHROMATOGRAPH SHOWING AREA % OF COMPOUNDS PRESENT IN ETHANOLIC EXTRACT

TABLE 2: CHEMICAL COMPOSITION OF ETHANOLIC EXTRACT OF RHIZOME *HEDYCHIUM SPICATUM*

S. no.	Chemical Constituents	Rt	Qual.	Area %	Cas#
1	trans-Cinnamic acid	28.922	60	1.17	#22885
2	Benzofuran, 3-methyl	30.304	70	1.16	#14360
3	1-Methylcyclopropanecarboxylic acid	31.480	43	0.97	#3714
4	Naphthalene, 1,2,4a,5,8,8a-hexahydro-4,7-dimethyl-1- (1-methyl-ethyl) -, [1S(1.alpha.,4a.beta.,8a.alpha.)]161.0	32.435	64	0.94	#62497
5	alpha.-Calacorene	33.202	95	0.85	#59547
6	(-)-Spathulenol	34.535	95	0.83	#74725
7	endo-2-Methylbicyclo[3.3.1]nonane	35.743	76	0.96	#16733
8	Lactose	36.669	49	0.80	#166318
9	2-Propenoic acid, 3-(4-methoxyphenyl)	37.156	94	1.24	#42590
10	Coumarin-3-carboxylic acid	37.533	80	0.98	#51429
11	1,4,9-Decatriene, (Z)	38.283	55	0.83	#15537
12	Oleyl alcohol, trifluoroacetate	38.615	60	1.04	#179539
13	1-Tetradecene	38.912	53	0.95	#56562
14	Nonadecyl trifluoroacetate	39.084	91	1.07	#187548
15	2-Propenoic acid, 3-(4-methoxyphenyl)	39.679	93	1.42	#42590
16	Anisole, m-(2-nitrovinyl)	40.251	78	2.58	#43979
17	2-Propenoic acid, 3-(4-methoxyphenyl)	40.418	46	1.48	#42590
18	Benzofurazan, 5-methyl-4-nitro	41.464	48	5.03	#43869
19	2-(2-Furyl)pyridine	41.522	83	1.46	#21203
20	3-Hydroxypropionic acid, 3-(1H-benzoimidazol-2-yl)	41.876	42	1.05	#63397
21	p-Hydroxycinnamic acid, ethyl ester	43.330	64	0.94	#52780
22	Benzenemethanol, 4-methoxy	44.612	30	0.81	#17129
23	Kaur-16-ene	47.890	43	0.94	#115428
24	Adipic acid, hexyl propyl ester	47.953	70	0.84	#114994

Note: Rt is retention time, Cas# indicates library reference number, Qual. indicates quality.

The oil composition of *Hedychium spicatum* from different parts of India already reported terpinen-4-ol (31.15 %), cis-sabinene hydrate (15.76 %), p-cymene (6.83 %), sabinene (6.91 %), trans-sabinene hydrate (3.86 %) and α-terpineol (3.71 %) as the main constituents. So it was concluded that

depending on the geographical origin of marjoram, its quality and quantity varies considerably, as influenced by genotype or the environmental conditions. The identified components where the content is more than 0.80% were given in **Tables 1 & 2.**

***In-silico* Studies:** The molecular docking (*In-silico* studies) of the selected compounds (ligands) with the amino acids are shown in **Tables 3** and **4**. The six compounds were selected on the basis of literature and their binding in the cavity of *Aldose reductase* enzyme was examined.

The compound that shows the maximum docking score and hydrogen bond interactions were the most effective compound in alleviating diabetic nephropathy.

TABLE 3: STRUCTURES OF SIX COMPOUNDS USED FOR *IN-SILICO* STUDIES ARE GIVEN BELOW

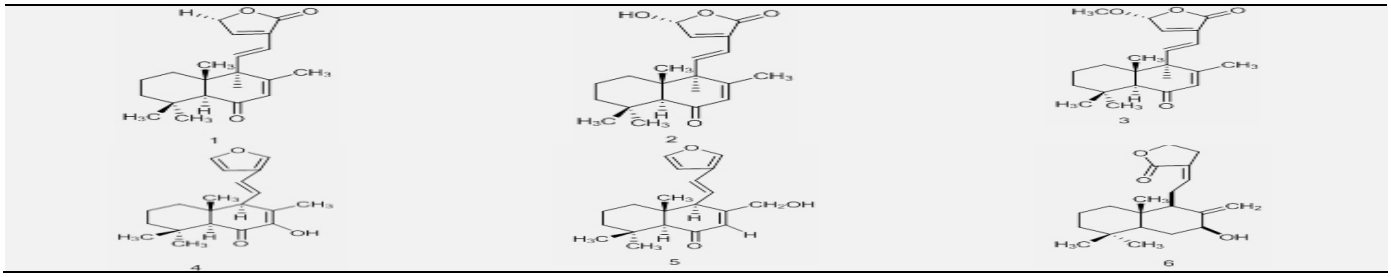

TABLE 4: TABLE SHOWING THE MOL DOCK SCORE AND H BOND INTERACTIONS

S. no.	Name	Mol. dock score	Docking score	H-bond interaction	H-bond distance	Interacting residue	Interacting atom
1	Internal Standard	-178.961	-178.442	6	2.60, 3.55	Ser 210, Cys 298,	O-N, O-S
					2.84, 3.47	Tyr 209, Ser 159,	O-O, O-O
					2.93, 3.12	Asn 160, Trp 111	O-N, O-N
2	6-oxo-7,11,13-labdatrien-16,15-olide	-140.505	-138.604	5	3.17	Lys 77	O-N
					2.68	Try 48	O-O
					3.10	Lys 262	O-N
					2.37	Asn 216	O-O
					1.96	Asp 43	O-O
3	Spicatanol	-145.755	-146.469	6	3.34	Gln 183	O-O
					2.85	Lys 77	O-N
					1.71	Asp 43	H-O
					2.10	Try 48	O-O
					3.41	Lys 21	O-N
					3.01	Leu 212	O-N
4	Spicatanol methyl ether	-146.443	-146.335	4	2.54	Asp 43	O-O
					2.58	Tyr 48	O-O
					3.31	Ser 214	O-N
					3.42	Leu 212	O-N
5	7- hydroxyl hedychenone	-147.32	-147.565	6	3.12	Ser 214	O-N
					3.37	Leu 212	O-N
					3.20	Lys 77	O-N
					2.27	Asp 43	O-O
					3.08	Thr 99	O-N
					2.83	Asp 43	O-O
6	Yunnacoronarin D	-141.122	-143.921	7	3.48	Gln 183	O-O
					3.08	Lys 77	O-N
					2.60	Asp 43	O-O
					3.13	Ser 214	O-N
					3.48	Leu 212	O-N
					2.16	Ile 260	O-O
					2.29	Tyr 48	O-O
7	Hedychia Lactone B	-144.399	-142.196	4	2.66	Cys 298	O-S
					2.84	Ser 210	O-O
					2.95	His 110	O-N
					3.22	Trp 111	O-N

The compound 6-oxo-7,11,13-labdatrien-16,15-olide showed the molecular docking score of -140.50 and bound with Aldose Reductase enzyme to its active site amino acid Lys 77, Try 48, Lys 262, Asn 216, Asp 43 that formed 5 Hydrogen bonds along with their hydrogen bond distance 3.17, 2.68, 3.10, 2.37, 1.96A^0 respectively. The interactions between the atoms of compound 6-oxo-7,11,13-labdatrien-16,15-olide and amino acids of Aldose reductase enzyme was Oxygen-Nitrogen and dioxide in nature, suggesting the strong bonds between the cavity of aldose reductase and the compound.

The compound named Spicatanol had the molecular docking score(-145.75) to active site amino acids Gln 183, Lys 77, Asp 43, Try 48, Lys 21, Leu 212 by forming 6 Hydrogen bonds along with their hydrogen bond distance 3.34, 2.85, 1.71, 2.10, 3.41, 3.01A^0 respectively. The interactions between the atoms of Spicatanol and amino acids of the enzyme were dioxide, Oxo-Nitro, oxo-Hydrogen in nature. The compound Spicatanol methyl ether showed the molecular docking score (-146.44) to active site amino acids Asp 43, Tyr 48, Ser 214, Leu 212, forming 4 Hydrogen bonds along with their hydrogen bond distance 2.54, 2.58, 3.31, 3.42$A^{0,}$ respectively. Thus the compound named 7-hydroxyhedychenone showed the best mol doc score of -147.32 as compared to internal standard zoporlestat with mol doc score of -178.68 and a maximum number of interactions *i.e.*, 7 with protein residue Ser 214, Leu 212, Lys 77, Asp 43, Thr 99, Asp 43 along with their hydrogen bond distance 3.12, 3.37, 3.20, 2.27, 3.08, 2.83 A^0 respectively. The best molecular posture of 7-hydroxyhedychenone in the aldose reductase cavity is shown in **Fig. 3.** The compound Yunnacoronarin D shows the molecular docking score (-141.12) to active site amino acids Gln 183, Lys 77, Asp 43, Ser 214, Leu 212, Ile 260, Tyr 48 by forming 7 Hydrogen bonds along with their hydrogen bond distance 3.48, 3.08, 2.60, 3.13, 3.48, 2.16, 2.29 in A^0 respectively.

The interactions between the atoms of the compound (Yunnacoronarin D) and amino acids of Aldose reductase enzyme were Oxygen-Oxygen, Oxygen-Nitrogen, Oxygen-Oxygen, Oxygen-Nitrogen, Oxygen-Nitrogen, Oxygen-Oxygen, Oxygen-Oxygenrespectively. The compound Hedychia Lactone B shows the molecular docking score (-144.39) to active site amino acids Cys 298, Ser 210, His 110, Trp 111 by forming 4 Hydrogen bonds along with their hydrogen bond distance 2.66, 2.84, 2.95, 3.22 in $A^{0,}$ respectively. The interactions between the atoms of compound (Hedychia Lactone B) and amino acids of Aldose reductase enzyme were Oxygen-Sulphur, Oxygen-Oxygen, Oxygen-Nitrogen, Oxygen-Nitrogen, respectively. All the compounds showed comparable aldose reductase inhibition, leading to inhibition of sorbitol conversion to glucose, consequently lowering the glucose load in renal tissues that might helped in protection of kidney in chronic diabetic patients.

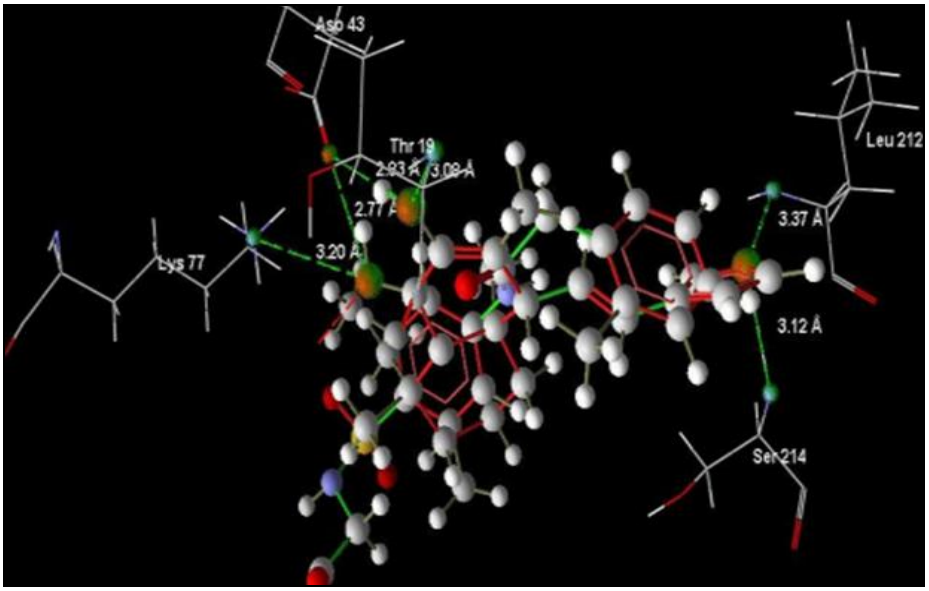

FIG. 3: SHOWING THE BEST RESULTING INTERACTION BY A MOLECULE 7- HYDROXYHEDYCHENONE

DISCUSSION: Diabetes is a multifactorial disease that leads to several complications; it demands multiple therapeutic approaches. Many hypoglycaemic/ antidiabetic plants and herbs are known in traditional medicine, but their introduction in modern therapy waited for pharmacological testing by recent methods. Thus it offers a natural key to unlock a diabetologist's for the future. Streptozotocin-induced diabetes mellitus causes the destruction of beta cells of islets of Langerhans [24] which leads to the reduction in insulin release. An insufficient release of insulin causes high blood glucose levels, namely hyperglycaemia, which results in the development of diabetic complications [25] because of oxidative damage caused by the generation of reactive oxygen species (ROS). STZ-induced diabetic animals may exhibit many other diabetic complications such as myocardial, cardiovascular, gastrointestinal, nervous, and urinary bladder dysfunctions. We believe that Hedychium spicatum having properties such as antioxidant [26], hypoglycaemic [17], anti-inflammatory, and cytotoxic activity [18], showed good results against diabetic nephropathy

In the present view of GC-MS, sesquiterpenes are studied for their various biological activities like antioxidant, antidiabetic, anticholesterolemic, *etc*. It can be seen that the volatile components in the dry rhizome *Hedychium spicatum* are mainly unsaturated organic compounds, such as monoterpenes, sesquiterpenes, and their oxygenous derivatives, triterpenoids, and other aliphatic compounds. Most of the identified volatile components, such as pinene, camphene, camphor, borneol, caryophyllene, *etc*., are similar to that of the references cited therein.

The coumarins chain-breaking antioxidants, display a remarkable array of biochemical and pharmacological actions, some of which suggest that certain members of this group of compounds may significantly affect the function of various mammalian cellular systems. Thus the compounds reported in the respective pet ether extract are mainly found to possess antidiabetic, antioxidant activity, which will help us to confine the activity of our respective extract to possess antidiabetic activity, and free radical scavenging activity of some extract will greatly influence the protective effect on kidneys, *i.e.*, diabetic nephropathy. The phenolic compounds can act as free radical scavengers, removing reactive oxygen species (ROS), which can initiate oxidative stress and chronic inflammation. Novel bioactive flavonoid compounds are currently in trial for combating many oxidative stress-related diseases such as diabetes, cancer, arthritis, alzheimer's, and parkinson's diseases [27]. A variety of phenolic and flavanoids have been purified from the rhizomes of *Hedychium spicatum*, such as eugenol, chavicol analogues, cinnamic, coumaric acid derivatives which show the ability to inhibit nitric oxide (NO) or reactive oxygen species (ROS). Thus, the compounds reported in the respective ethanolic extract were mainly found to possess antidiabetic, antioxidant activity, which will help us confine our respective extract's activity to possess' antidiabetic activity and free radical scavenging activity extract will greatly influence the protective effect on kidneys, *i.e.*, diabetic nephropathy.

CONCLUSION: The present investigation focused on identifying various bioactive compounds from the rhizome extracts of *Hedychium spicatum* for the first time by GC–MS analysis and in silico Molecular modelling. These compounds are responsible for the different therapeutic and pharmacological properties. We have also provided evidence of rhizome extracts of *Hedychium spicatum* as antidiabetic activities. The 7-hydroxyhedychenone compound showed promising binding affinity toward different proteins in molecular docking experiments, and their drug-like features were demonstrated through autodock analysis. Using the 7-hydroxyhedychenone compound may enable us to develop an effective drug against diabetic diseases.

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