RESEARCH ARTICLE

Exploring Alleviative Effects of *Delonix regia* Extracts on Diabetes Mellitus via Inhibiting α-Amylase, α-Glucosidase and Oxidative Stress: Phytochemical Analysis, *In-silico* and *In-vitro* Studies

Kamica Yadav[1], Monu Yadav[1*], Parveen Kumar Goyal[2], Sumit Kumar[3]

[1]*Amity Institute of Pharmacy, Amity University, Amity Education Valley, Gurugram, Manesar, Panchgaon, Haryana-122413, India*
[2]*Department of Pharmacy, Faculty of Pharmacy, Panipat Institute of Engineering and Technology (PIET), Samalkha, Panipat, Haryana-132102, India*
[3]*Department of Pharmaceutical Sciences, Central University of Haryana, Mahendergarh, Haryana-123031, India*

Received: 2nd Aug, 2025; Revised: 7th Sep, 2025; Accepted: 10th Sep, 2025; Available Online: 25th Sep, 2025

ABSTRACT
Diabetes mellitus is known to elevate oxidative stress, which may lead to the development of complications like cardiomyopathy. As reported by the World Health Organization (WHO), around 830 million individuals worldwide are suffering from diabetes, and about 1.1% of them suffer from diabetic cardiomyopathy. This highlights the importance of managing diabetes effectively to reduce associated risks. This study aimed to explore the antioxidative and antihyperglycemic potential of hydroalcoholic extracted from the leaves (DRL) as well as from flowers (DRF) of *Delonix regia*, using phytochemical screening, *in-vitro* assays, and *in-silico* methods. Plant extracts were analysed for their total phenolic content coupled with flavonoid determination and GC–MS study profiling to identify biologically active compounds. Molecular docking (AutoDock Vina) was used to assess binding interactions of selected phytochemicals with key carbohydrate-hydrolyzing enzymes, α-amylase and α-glucosidase. Drug-likeness as well as ADMET properties were predicted using Swiss ADME. The antioxidant potential was assessed by DPPH free radical inhibition assay, as well as enzyme inhibition assays were conducted for antidiabetic potential. Phytochemical assessment established the presence of phenolic and flavonoid compounds and 55 other metabolites. Docking results showed that Stigmasterol, Lupeol, Betulin, and β-amyrin strongly bind to α-amylase, whereas Stigmasterol, catechol, gamma sitosterol, and Vitamin E showed binding affinity toward α-glucosidase. ADMET analysis indicated good drug-likeness and non-toxicity. Antioxidant activity (IC_{50}) was 92.22 µg/ml (DRL) and 118.1 µg/ml (DRF), compared to 18.19 µg/ml for ascorbic acid. Enzyme inhibition assays demonstrated strong inhibitory activity against α-amylase (IC_{50} 1.806±0.363 µg/ml for DRL, 4.419 ± 0.347 µg/ml for DRF, and 0.1845 ± 0.10874 µg/ml for acarbose) and α-glucosidase (IC_{50} 0.5263 ± 0.0682 µg /ml for DRL, 2.028 ± 0.5506 µg /ml for DRF, and 13.24 ± 0.05337µg/ml for acarbose), revealing their anti-diabetic potential. Hydroalcoholic extracts of *Delonix regia* flower and leaf, along with their phytoconstituents, possess potential antioxidant and antidiabetic activities, suggesting their role in diabetes and associated consequences like cardiomyopathy

Keywords: *Delonix regia*; GCMS analysis; *in-silico* ADMET; DPPH; α-amylase; α-glucosidase
How to cite this article: Kamica Yadav, Monu Yadav, Parveen Kumar Goyal, Sumit Kumar. Exploring Alleviative Effects of *Delonix regia* Extracts on Diabetes Mellitus via Inhibiting α-Amylase, α-Glucosidase and Oxidative Stress: Phytochemical Analysis, *In-silico* and *In-vitro* Studies. International Journal of Drug Delivery Technology. 2025;15(3):1047-64. doi: 10.25258/ijddt.15.3.21
Source of support: Nil.
Conflict of interest: None

INTRODUCTION

Diabetes mellitus refers to a long-lasting metabolic abnormality identified by a hyperglycemic condition of blood due to defects in either insulin synthesis or its function or both, which triggers the generation of free radicals. High levels of free radicals can further encourage oxidative stress, which exacerbates the impairment of pancreatic β cells, coronary arteries, and heart muscles. Epidemiological data found that patients with diabetes are two to five times more likely than those without the disease to experience cardiac dysfunction[1,2]. As per the WHO, approximately 830 million people have diabetes globally, and 1.1 % suffer from diabetic cardiomyopathy[3-4]. A redox imbalance causes diabetes, leading to oxidative tissue damage, which is reported to involve increasing the Ang-II, protein kinase C activation, and transforming growth factor-β (TGF-β) expression[5]. Furthermore, hyperglycemia activates TGF-β further triggers cardiac fibrosis through SMAD pathways. Stimulation of SMAD2/3 proteins encourages the transcription of fibrotic genes contributing to extracellular matrix deposition, which is a potent cause of diabetic cardiomyopathy (DCM)[6]. Furthermore, increased Ang-II levels and TGF-β together contribute to stimulate the production of the mesangial matrix, which can lead to cardiac fibrosis and hypertrophy[7]. Notably, some of the anti-diabetic drugs have been reported to increase the

**Author for Correspondence: monuyadav.pharmacology@gmail.com*

risk of cardiovascular disorders for instance, thiazolidinedione and rosiglitazone are associated with sudden cardiac arrest (SCA) and ventricular arrhythmia (VA)[8]. With these limitations, plants used in traditional medicine and their phytochemical profile are becoming popular as natural sources, by owning antioxidant and anti-inflammatory properties, and are safer options than synthetic antidiabetic agents for diabetes and DCM patients[9]. *Momordica charantia*[10], *Panax ginseng*[11], *Allium cepa*[12], *Allium sativum*[13], *Aloe vera* [14], *Pterocarpus marsupium*[15], *Tinospora cordifolia*[16], *Tinospora crispa*[17], *Gymnema sylvestre*[18], *Eugenia jambolana*[19], *Costus pictus*[20], *Phaseolus vulgaris*[21], *Euphorbia hirta*[22], *Zingiber officinale*[23], *Ocimum sanctum*[24] are the examples of anti diabetic drugs which are widely used in Ayurveda.

"Diabecon, Diasulin, Pancreatic tonic 180 cp, Bitter gourd Powder, Dia-care, Diabetes-Daily Care, Gurmar powder, Epinsulin, Diabecure, Diabeta, Syndrex" are examples of formulated herbal drugs with antidiabetic potential available in the market[25,26]. Plants such as *Cissus quadrangularis*[27], *Artemisia vulgaris*[28], *Lycium chinense*[29], and the compound Tanshinone II[30] have been reported to exhibit activity against diabetic cardiomyopathy. Some Examples of traditional herbal formulations with reported activity against diabetic cardiomyopathy include Vasant Kusumakar Rasa[31], Erzhi Pill (Traditional Chinese Medicine)[32], Guan Xin Dan Shen formula[33], and Tongmai Capsules[34].

Delonix regia (Caesalpiniaceae) has been widely used as medicine in Ayurveda, which is reported to possess multiple biological activities, including anti-inflammatory[35], analgesic[36], antibacterial[37], antifungal[38], wound-healing[39], hepatoprotective[40], gastroprotective[41], antiarthritic[42], antimalarial[43], antifertility[44], diuretic[45], and anthelmintic properties[46]. The phytoconstituents reported from this plant belong to different classes such as carbohydrates (galactomannan), tannins such as propelargonidin[47]and procyanidin[48], flavonoids such as quercetin[49], Leucocyanidin[50] Flavonoids such as Kaempferol-3-rhamnoside[51], Ketocarotenoid such as Astaxanthin[52], Sterols such as β-sitosterol[53], Triterpenoidal Saponin such as Lupeol [54], Phenolic acids like Gallic acid [55], protocatechuic acid[56] have demonstrated potential antidiabetic activity. With these findings, The current research focused on evaluating phytochemical and evaluation of *in-vitro* antioxidant as well as anti-diabetic activities of *Delonix regia* Extracts. Furthermore, docking and ADMET analysis were performed on the phytochemical constituents revealed via GC–MS profiling of hydroalcoholic extracts of *Delonix regia* leaves and flowers to further screen their antidiabetic potential and pharmacokinetics using AutoDock Vina and Swiss ADME software, respectively.

MATERIALS AND METHODS

Collection of Plants and Preparation of Plant Extracts

The flowers and leaves of *Delonix regia* were collected from the botanical garden of Punjabi University and Mahindra College, Patiala, Punjab, India. Authentication of the collected plant specimens was carried out by the Council of Scientific and Industrial Research-National Institute of Science Communication and Policy Research (CSIR- NISCPR), Delhi, with vide authentication number NIScPR/RHMD/Consult/2022/4175-76. To prepare the

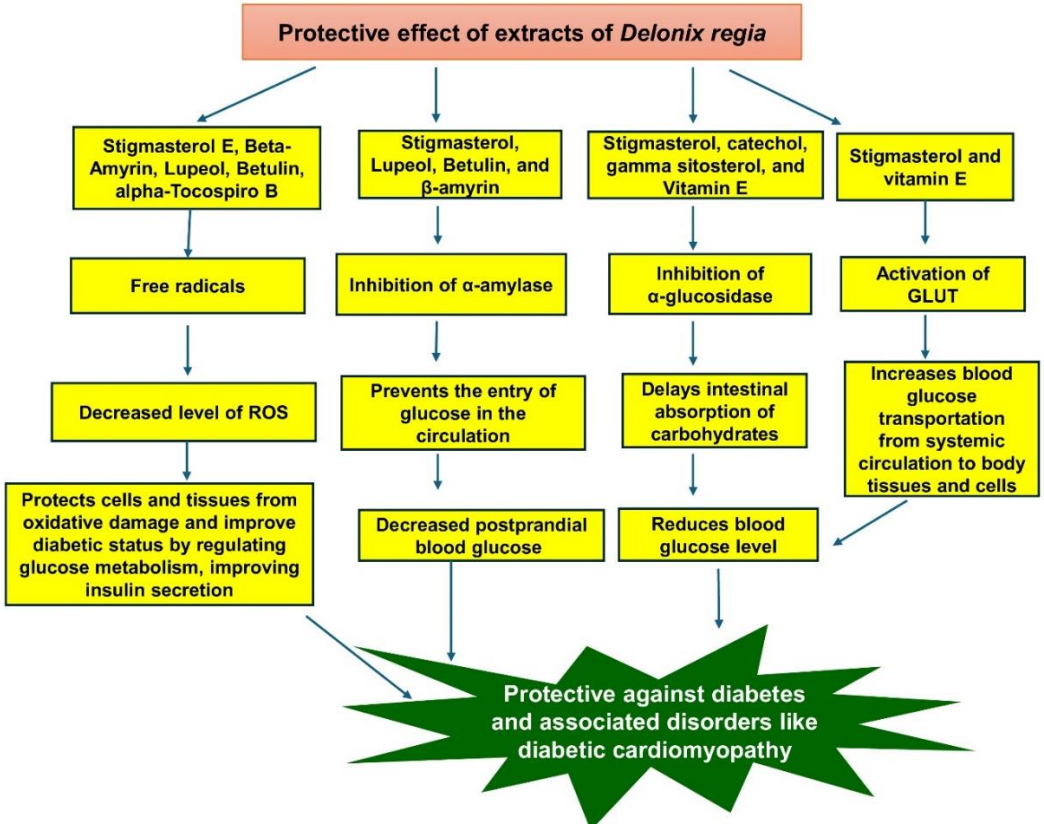


Figure 1: Possible mechanism of action *Delonix regia* in diabetes

extracts, maceration was done using ethanol/water (60/40) for 7 days. Briefly, 100 g of powder of leaves and flowers of *D. regia* was subjected to successive extraction using 300 ml of ethyl alcohol as well as 200 ml of water for 7 days using magnetic stirring. Then, the macerated material was filtered through Whatman filter paper and concentrated to dryness using a rotary evaporator at 50 °C. The dried extracts were then stored at 40 °C until further use. The extract yields from leaves and flowers were found to be 12.29g/100g and 24.72g/100g dry weight, respectively[57].

Phytochemical Analysis

Determination of Total Phenolic Content

The total phenolic contents in DRL and DRF extracts were determined using the Folin-Ciocalteu method as described by Spanos and Wrolstad[58]. Gallic acid served as the standard for the calibration curve, and the results are reported as milligrams of gallic acid equivalents per gram of dried extract (mg Gallic acid/g extract dry weight)".

Determination of Total Flavonoid Content

The total flavonoid contents in DRL and DRF extracts were determined according to the method using aluminum chloride, as described by Dewanto et al,[59]. Rutin served as the calibration standard, and the extract content was expressed as mg rutin equivalents per gram of dry weight(mg Rutin/g extract dry weight)".

Gas Chromatography and Mass Spectroscopic Analysis

Analysis by GC–MS was conducted on extracts of *Delonix regia.* "GCMS-QP2010 Plus system (Shimadzu, Kyoto, Japan)" was used to analyze the extracts.

Antioxidant Activity

DPPH Free Radical Scavenging Activity Assay

Antioxidant capacity for the hydroalcoholic extracts (DRF and DRF) was determined at different concentrations by scavenging the free radicals of the stable 1,1-diphenyl-2-picrylhydrazyl (DPPH)[60]. Ascorbic acid was considered a standard antioxidant agent in the current research. The findings were expressed as % inhibition.

Docking Studies of Target Molecules

Computational Molecular Docking Analysis is used to predict the binding interaction with the active site of α-Amylase (pdb 7TAA) and α-glucosidase (pdb 3A4A) with potential phytoconstituents identified in GC-MS analysis of *Delonix regia* leaves and flowers. The 3D crystal structures of the enzymes were acquired from the Protein Data Bank (https://www.rcsb.org), and the drug structures were sourced from PubChem (https://pubchem.ncbi.nlm.nih.gov/).

ADMET Analysis

The ADME investigation was carried out on potential phytoconstituents, which were analysed by GC-MS analysis of *Delonix regia* leaves and flowers were conducted via Swiss ADME software (http://www.swissadme.ch/). The canonical SMILES were obtained from Pubchem for phytoconstituents (Mome-inositol, Stigmasterol E, Lupeol, Vitamin E, alpha-Tocospiro B, Betulin, Eicosanoic acid, Catechol, Tetradecanoic acid, Gamma-sitosterol, Eicosanoic acid, 1-Heptacosanol,Lauric acid and3-hydroxybenzoic acid) for several Pharmacokinetic parameters, including solubility of the drug, ADME properties, and drug-likeness. Moreover, Predictions were performed via the Protox-II web server (https://tox.charite.de/protox3) to predict the toxicity in terms of hepatotoxicity, immunotoxicity, carcinogenicity, mutagenicity, and cytotoxicity of selected phytoconstituents of *Delonix regia* leaves and flowers.

In-vitro Antidiabetic Activity Assays

α-Amylase Inhibition Assay

Inhibitory assay of α-Amylase for the extracts was studied by the standard method with minor modifications[61]. Dilutions of the samples were prepared with sodium phosphate buffersolution. Enzymatic solution (10 µl) containing 20 mg/ml α-amylase solution (HIMEDIA GRM638-100G) was dispensed into designated wells of a 96-well plate at different concentrations (0,1, 10, 50, 100, 250, 500, 1000 µg/ml). Mixture containing the enzyme solution and sample dilutions was incubated at 37 ℃ for a period of 10 minutes to ensure enzyme-inhibitor interaction. 50 µl of the substrate (0.1% Soluble Starch-Fisher Scientific –Cat no. 20725) was employed to start the reaction, and the mixture was allowed to incubate for another 15 minutes. Following a 15-minute incubation, 100 µL of GOD-POD reagent was added to the mixture of enzyme solution and sample dilutions. The plate was subsequently incubated at room temperature for 10 minutes, and the absorbance of the samples was determined using a microplate reader(iMark, BioRad) at 490 nm. Acarbose (SRL- Cat no. 65457) was used as a positive control. The results were expressed as percentage inhibition.

α-Glucosidase Inhibitory Assay

The inhibitory assay of α-glucosidase for the extracts was studied by the standard method with slight modification[61]. The reaction mixture, consisting of 20 µL of each extract concentration (0, 1, 10, 50, 250, 500, 1000 µg/ml), 10 µL α-glucosidase (1 U/ml), and 50 µL phosphate buffer (100 mM, pH 6.8), was preincubated at 37 °C for 15 minutes. After that, substrate of 20 µL of P-NPG (5 mM) was introduced into the mixture, followed by further incubation for 20 minutes at 7°C. The reaction was terminated by employing 50 µl Na_2 CO_3 (0.1 M). The amount of p-nitrophenol released was determined by measuring absorbance at 405 nm with an ELISA microplate reader (iMark, Bio-Rad). Acarbose (1 mg/ml) served as the positive control, and the IC_{50} was calculated based on the percentage inhibition of α-amylase activity at various concentrations. The results were expressed as percentage inhibition.

In-vitro Glucose Uptake Assay

Assays were carried out using the method described by Lakshmanan *et al.* L6 Cells (Procured from National Centre for Cell Science, Pune) remain arranged in plates with Cells (8×10^4 per well) were plated in 96-well plates and allowed to grow in standard medium for 24 hours[62]. Cultured cells were treated as a control test (Extract), standard I (Insulin), and standard II (Metformin). Cells were washed twice with KRPH buffer (20 mM HEPES, 5 mM KH_2PO_4, 1 mM $CaCl_2$, 136 mM NaCl, 4.7 mM KCl, pH 7.4) and incubated in glucose-free DMEM for 1 hour. The cells were then treated for 40 minutes in the presence or absence of mM 2-DG (2-deoxy-D-glucose) for 20 minutes in a KRPH buffer containing 2% (v/v) bovine serum albumin.

Table 1: GC-MS analysis of hydroalcoholic extracts of *Delonix regia* Leaves (DRL)

S. No.	Retention Time	Area	Area %	Name
1.	3.435	3085489	2.07	3,3-Diethoxypropylamine
2.	4.284	9331642	6.25	1-Butanol, 3-methyl-, acetate
3.	5.650	224007	0.15	2,4-Dimethyl-2-oxazoline-4-methanol
4.	6.436	473848	0.32	2-PROPANONE, 1,1-DIETHOXY-
5.	7.107	292801	0.20	2-METHOXY-4-VINYLPHENOL
6.	8.810	150226	0.10	5,9-Undecadien-2-one, 6,10-dimethyl-, (Z)-
7.	9.609	537873	0.36	PHENOL, 2,4-BIS(1,1-DIMETHYLETHYL)-
8.	9.778	148306	0.10	8-DECEN-2-ONE, 9-METHYL-5-METHYLENE-
9.	9.895	331580	0.22	Phosphoric acid, diethyl octyl ester
10.	10.018	313656	0.21	2(4H)-Benzofuranone, 5,6,7,7a-tetrahydro-4,4,7a-trimethyl
11.	10.378	705507	0.47	(2E,6E)-1,1-DIDEUTERO-3,7,11-TRIMETHYL-2,6,10-D
12.	11.144	149193	0.10	2-Cyclopenten-1-one, 4-hydroxy-3-methyl-2-(2-propenyl)-
13.	12.157	9834445	6.59	MOME INOSITOL
14.	12.786	722953	0.48	6-Hydroxy-4,4,7a-trimethyl-5,6,7,7a-tetrahydrobenzofuran
15.	13.322	4102291	2.75	Neophytadiene
16.	13.772	1283037	0.86	2-HEXADECEN-1-OL, 3,7,11,15-TETRAMETHYL-, [R-[
17.	14.108	140736	0.09	5,9,13-Pentadecatrien-2-one, 6,10,14-trimethyl-, (E,E)-
18.	14.446	745432	0.50	Isophytol
19.	14.629	2417267	1.62	n-Hexadecanoic acid
20.	14.888	496343	0.33	HEXADECANOIC ACID, ETHYL ESTER
21.	15.795	258720	0.17	1-OCTADECANOL
22.	16.049	40941356	27.42	Phytol
23.	16.250	52650	0.04	9-Dodecen-1-ol, acetate, (E)-
24.	16.316	545945	0.37	8,11,14-Eicosatrienoic acid, (Z,Z,Z)-
25.	16.470	82597	0.06	Ethyl 9,12-hexadecadienoate
26.	16.530	283532	0.19	9,12,15-Octadecatrienoic acid, ethyl ester, (Z,Z,Z)-
27.	16.758	148295	0.10	OCTADECANOIC ACID, ETHYL ESTER
28.	17.622	197481	0.13	n-Nonadecanol-1
29.	18.159	143596	0.10	4,8,12,16-Tetramethylheptadecan-4-olide
30.	18.478	169792	0.11	ETHYL PENTADECANOATE
31.	19.132	174236	0.12	1,3,5-TRISILACYCLOHEXANE
32.	19.303	493432	0.33	Hexanoic acid, octadecyl ester
33.	19.479	725743	0.49	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl est
34.	19.621	402929	0.27	Bis(tridecyl) phthalate
35.	19.909	102034	0.07	2-Methyltetracosane
36.	20.124	175672	0.12	Octadecanamide
37.	20.939	460038	0.31	Hexacosyl heptafluorobutyrate
38.	22.062	13699900	9.18	Squalene
39.	22.418	726710	0.49	.alpha.-Tocospiro B
40.	22.653	1036781	0.69	.alpha.-Tocospiro B
41.	23.049	1844302	1.24	1-Heptacosanol
42.	23.284	1374050	0.92	1,6,10,14,18,22-Tetracosahexaen-3-ol, 2,6,10,15,19,23-hex
43.	23.430	656603	0.44	Oxirane, 2,2-dimethyl-3-(3,7,12,16,20-pentamethyl-3,7,11,
44.	24.211	277103	0.19	1,6,10,14,18,22-Tetracosahexaen-3-ol, 2,6,10,15,19,23-hex
45.	24.474	410638	0.28	(6E,10E,14E,18E)-2,6,10,15,19,23-HEXAMETHYL-1,6,1
46.	25.248	1572412	1.05	.gamma.-Tocopherol
47.	26.134	3150755	2.11	1-Heptacosanol
48.	26.656	11369447	7.62	Vitamin E
49.	28.796	1267607	0.85	ERGOST-5-EN-3-OL, (3.BETA.,24R)-
50.	29.406	5425266	3.63	Stigmasterol
51.	30.995	7987430	5.35	.gamma.-Sitosterol
52.	31.235	485734	0.33	4,4,6a,6b,8a,11,11,14b-Octamethyl-1,4,4a,5,6,6a,6b,7,8,8a,
53.	32.125	7046423	4.72	.beta.-Amyrin
54.	33.531	9302553	6.23	Lupeol
55.	34.957	810993	0.54	.alpha.-Tocopherol-.beta.-D-mannoside
		149289387	100.00	

The cells were washed three times with PBS to remove exogenous 2-DG, lysed with extraction buffer, frozen once, heated at 85 °C for 40 minutes to eliminate endogenous NADP, and centrifuged at 500 rpm for 2 minutes. Using the GOD-POD enzyme assay kit, the supernatant was analyzed for 2-DG6P, and readings were taken at 505 nm with a microplate reader. To determine the blank value, lysates of cells that were not treated with 2-DG were examined. Data

were calculated as nanomoles of 2-DG by comparison with a standard. 2-DG6P was used as the reference standard, with insulin (0.1 U/ml) as Standard I and metformin (1 mM) as Standard II.

Table 2: GC-MS analysis of hydroalcoholic extracts of *Delonix regia* flower (DRF)

S. No.	Retention Time	Area	Area%	Name
1.	6.004	5804636	1.51	3-CYCLOPENTEN-1-OL
2.	6.075	1341696	0.35	PHENOL
3.	6.291	758408	0.20	1,2-Cyclooctanedione
4.	6.649	7717826	2.01	2-Cyclohexen-1-one
5.	7.259	711957	0.19	2,5-ANHYDRO-1,6-DIDEOXYHEXO-3,4-DIULOSE
6.	7.649	2054309	0.54	2-FURANMETHANOL, 5-ETHENYLTETRAHYDRO-.A
7.	8.640	5604087	1.46	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-
8.	9.134	853198	0.22	BENZOIC ACID
9.	9.289	2645053	0.69	BENZOIC ACID
10.	9.613	95841385	25.01	Catechol
11.	10.220	1388249	0.36	Methylphosphonic acid, 2TMS derivative
12.	10.526	1123403	0.29	2-FURANMETHANOL, 5-ETHENYLTETRAHYDRO-.A
13.	11.070	1484145	0.39	2-METHOXY-4-VINYLPHENOL
14.	11.936	557726	0.15	2,3-Diazabicyclo[2.2.1]hept-2-ene, 5-ethenyl-4,7,7-trimeth
15.	12.134	1899567	0.50	3,7-DIMETHYLOCT-1-EN-3,6,7-TRIOL
16.	12.246	9477313	2.47	1,2,3-BENZENETRIOL
17.	13.523	1139986	0.30	1,7-Octadien-3-ol, 2,6-dimethyl-
18.	13.628	4978152	1.30	PHENOL, 2,4-BIS(1,1-DIMETHYLETHYL)-
19.	14.041	17950945	4.68	3-HYDROXYBENZOIC ACID
20.	14.292	16108845	4.20	Benzoic acid, 3-hydroxy-
21.	14.361	1526754	0.40	DODECANOIC ACID
22.	15.468	41023119	10.71	.beta.-D-Glucopyranoside, methyl
23.	16.175	1760502	0.46	2-Cyclohexen-1-one, 4-(3-hydroxybutyl)-3,5,5-trimethyl-
24.	16.336	1695251	0.44	1H-[1]Pyrindine-3-carbonitrile, 4-ethyl-2-oxo-2,5,6,7-tetra
25.	16.602	3472474	0.91	Tetradecanoic acid
26.	16.833	2869724	0.75	6-HYDROXY-1,3,4,5-TETRAHYDRO-2H-1-BENZAZEP
27.	17.238	13183330	3.44	MOME INOSITOL
28.	17.808	2420275	0.63	3(2H)-PYRIDAZINONE, 4,5-DIHYDRO-2-METHYL-6-(
29.	18.726	38236368	9.98	n-Hexadecanoic acid
30.	18.897	1713243	0.45	HEXADECANOIC ACID, ETHYL ESTER
31.	18.947	1259575	0.33	Butanoic acid, 2-[2,4-bis(1,1-dimethylpropyl)phenoxy]-
32.	19.297	6994591	1.83	P-(P-AMINOPHENOXY)PHENOL
33.	20.328	7950439	2.07	9,12-Octadecadienoic acid (Z,Z)-
34.	20.382	4533210	1.18	9,12-Octadecadienoic acid (Z,Z)-
35.	20.562	6845419	1.79	Octadecanoic acid
36.	21.632	1032005	0.27	9-(3,3-DIMETHYL-2-OXIRANYL)-2,7-DIMETHYL-2,6-
37.	22.279	1200805	0.31	Eicosanoic acid
38.	23.488	2887817	0.75	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl est
39.	23.897	736526	0.19	Docosanoic acid
40.	24.140	1115230	0.29	4-(2-Hydroxyethyl)-2,2-dimethyl-1,3-dioxolane, pentafluo
41.	24.935	2448112	0.64	9,12-Octadecadienoic acid (Z,Z)-, 2,3-dihydroxypropyl est
42.	26.423	1215413	0.32	.alpha.-Tocospiro B
43.	26.772	1138526	0.30	4,4-DIMETHYL-5.ALPHA.-D1-ANDROSTAN-3.BETA.-
44.	28.986	392477	0.10	.beta.-Tocopherol
45.	29.849	543760	0.14	4,4-DIMETHYL-5.ALPHA.-D1-ANDROSTAN-3.BETA.-
46.	30.674	10362652	2.70	Vitamin E
47.	32.832	4124758	1.08	ERGOST-5-EN-3-OL, (3.BETA.,24R)-
48.	33.465	10767952	2.81	Stigmasterol
49.	35.033	13168655	3.44	.gamma.-Sitosterol
50.	35.418	2321178	0.61	STIGMASTA-5,24(28)-DIEN-3-OL, (3.BETA.,24E)-
51.	36.100	3736603	0.98	METHYL COMMATE D
52.	36.622	1249243	0.33	METHYL COMMATE B
53.	37.546	3720260	0.97	Lupeol
54.	39.159	1132443	0.30	CYCLOPROPA[5,6]-33-NORGORGOSTAN-3-OL, 3',6-D
55.	40.580	4973976	1.30	Betulin
		383193551	100.00	

Table 3: Binding affinity and binding efficacy of phytoconstituents of DRL extract with α-Amylase

S. No	Ligand	Binding Affinity (in kcal/mol)	Binding Efficacy (in kcal/mol)
1.	Mome-inositol	-5.1	-0.43
2.	Stigmasterol E	-9	-0.3
3.	Beta-Amyrin	-9.5	-0.31
4.	Squalene	-6.6	-0.22
5.	Lupeol	-8.4	-0.27
6.	Neophytadiene	-5.5	-0.28
7.	Vitamin E	-7.7	-0.25
8.	Gamma-sitosterol	-8.2	-0.21

Table 4: Binding affinity and ligand efficiency of phytoconstituents of DRL with α-glucosidase

S. No.	Ligand	Binding Affinity (in kcal/mol)	Binding Efficacy (in kcal/mol)
1.	Mome-inositol	-5.9	-0.49
2.	Stigmasterol E	-9.1	-0.3
3.	Beta-Amyrin	-7.7	-0.25
4.	Squalene	-6.6	-0.22
5.	Lupeol	-8.4	-0.27
6.	Neophytadiene	-6.6	-0.33
7.	Vitamin E	-9.3	-0.3
8.	3-hydroxybenzoic acid	-5.8	-4.173

RESULTS

Determination of Total Phenolic Contents

The total phenolic content in DRL and DRF was measured in this study, with gallic acid serving as the standard. The different concentrations between (0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, and 4.0 µg/ml) of gallic acid solutions were confirmed by Beer's Law at 725 nm with a 0.9917 regression coefficient (R^2). The y= 7.614x+0.0855 was obtained for a standard plot to measure total phenolic content. Using this equation total content of phenolics was 1.25 (mg of gallic acid/g of extract) and 0.73 (mg of gallic acid/g of extract) in DRL and DRF extracts, respectively.

Determination of Total Flavonoid Content

By taking rutin as a standard, the total flavonoid content in DRL and DRF was determined in the present study. The different concentrations between 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, and 4.0 (µg/ml) of rutin solutions were confirmed by Beer's Law at 510 nm with a 0.9936 regression coefficient (R^2). The y= 0.0948x+0.1153 was obtained for a standard plot to measure total flavonoid content. Using this equation total content of flavonoid was 5.52 and 3.10 in DRL and DRF extracts, respectively, mg of rutin acid/g of extract.

GC-MS Analysis

In the current study, the GC-MS chromatogram identified a total of 55 phytocompounds in both the hydroalcoholic extracts of DRL and DRF, whose retention time, percent area, area of %, and phytoconstituents are shown in Tables 1 and Table 2, respectively.

Prediction of Binding Interactions of Phytoconstituents of Delonix regia

Using Auto Dock Vina, the binding interactions of phytoconstituents of *Delonix regia* were docked with molecules in the active sites of all the receptors under study. Each receptor was validated by performing a redocking with its co-crystallized ligand. The binding affinity of phytoconstituents of *Delonix regia* of flowers and leaves is shown in Tables 3,4, 5, 6, 7, and 8 by hydrogen bond and has hydrophobic interactions with HIS122, TRP82, TRP83, and LEU173.

Table 5: Binding affinity and ligand efficiency of phytoconstituents of DRF with α-Amylase

S. No.	Ligand	Binding Affinity (in kcal/mol)	Binding Efficacy (in kcal/mol)
1.	Mome-inositol	-7.7	-0.25
2.	Stigmasterol E	-9	-0.3
3.	Lupeol	-8.4	-0.27
4.	Vitamin E	-7.7	-0.25
5.	alpha-Tocospiro B	-7.6	-0.24
6.	Betulin	-8.3	-0.26
7.	Eicosanoic acid	-5.6	-0.25
8.	Catechol	-4.8	-0.6
9.	1-Heptacosanol	-6.2	-0.24
10.	Lauric acid	-5.8	-0.26

Table 6: Binding affinity and ligand efficiency of phytoconstituents of DRF with α-glucosidase

S. No.	Ligand	Binding Affinity (in kcal/mol)	Binding Efficacy (in kcal/mol)
1.	Mome-inositol	-5.9	-0.49
2.	Stigmasterol E	-9.1	-9.1
3.	Lupeol	-8.4	-0.27
4.	Vitamin E	-9.3	-0.3
5.	alpha-Tocospiro B	-8.3	-0.26
6.	Betulin	-6.3	-0.29
7.	Eicosanoic acid	-5.7	-0.71
8.	Catechol	-8.4	-0.26
9.	Tetradecanoic acid	-6.1	-0.29
10.	Gamma-sitosterol	-8.2	-0.27

ADMET Analysis

A molecule's ADME parameters define "how it travels within the body to reach at the appropriate target location at an appropriate concentration, which is necessary for a compound to exert a therapeutic effect". According to Lipinski's rule of five, the pharmacokinetics of a compound are influenced by its physicochemical properties and the possibility that a chemical entity would be orally active (i.e., drug-likeness)". The Swiss-ADME data, like information on blood-brain barrier (BBB) permeability, gastrointestinal (GI) absorption, and how the phytoconstituents interact with drug-metabolizing enzymes (CYPs) and transporters (P-gp) depicted in Table 9. The toxicity of phytoconstituents was tested using a web server (protox-III) to assess the potential they are predicted to have a harmful impact on the body, are shown in Table 10.

Biological Evaluation

Determination of In-vitro Antioxidant Potential via the DPPH Method

In present study, both the extracts (DRL and DRF) have shown their potential to scavenge DPPH free radical by increasing in % inhibition, which revealed their antioxidant potential.

Table 7: The binding interaction of phytoconstituents present in DRL and DRF extracts with amino acids of active sites of the α-Amylase enzyme

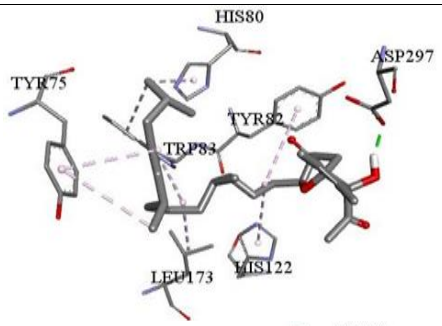
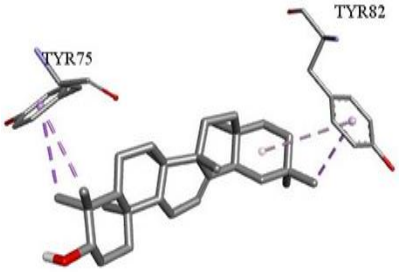
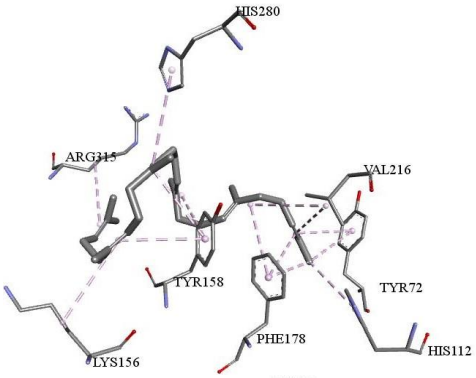
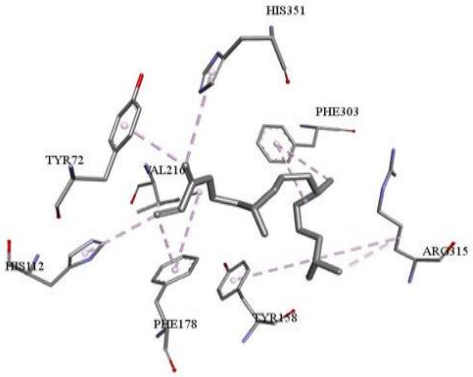
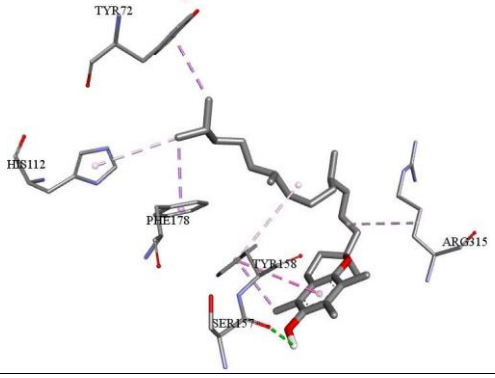
S. No.	Phytocontituents	Docked Poses	Interactions
1.	alpha.-Tocospiro B		H- bonding: ASP297 Hydrophobic interactions: LEU173, HIS122, TRP83
2.	Beta- Amyrin		Hydrophobic interactions: TYR 82, TYR76
3.	Squalene		Hydrophobic interactions: TYR 82, TYR76, TYR 82, HIS80
4.	Neophytadiene		Hydrophobic interactions: HIS351, TYR72, PHE178, TYR158
5.	Vitamin E		H- bonding: SER157 Hydrophobic interactions: TYR72, HIS112, PHE178, TYR158

Table 7: The binding interaction of phytoconstituents present in DRL and DRF extracts with amino acids of active sites of the α-Amylase enzyme

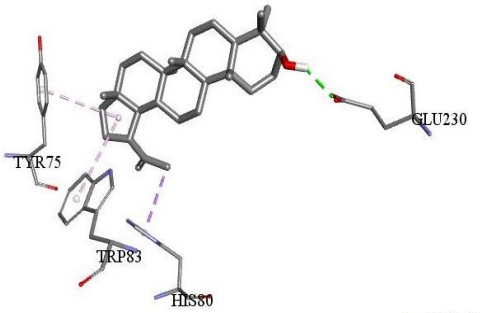
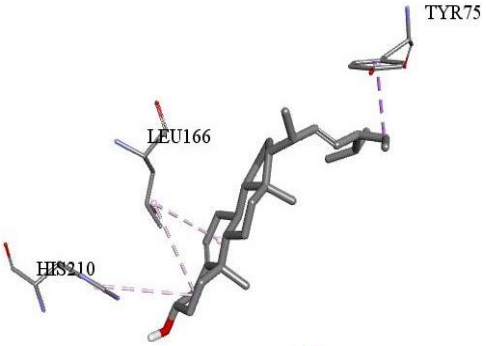
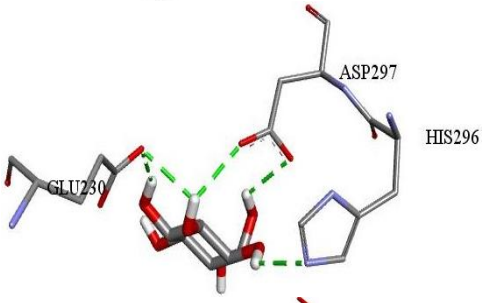
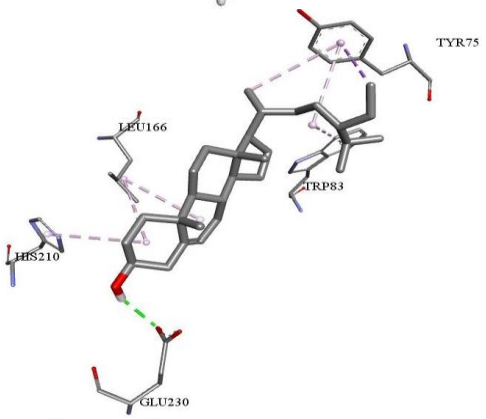
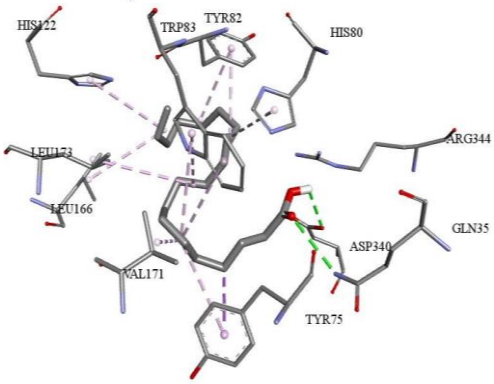
S. No.	Phytocontituents	Docked Poses	Interactions
6.	Lupeol		H- bonding: GLU230 Hydrophobic interactions: HIS80, TRP83,TYR75
7.	Stigmasterol		Hydrophobic interactions: TYR75, LEU166, HIS210
8.	Mome inositol		H- bonding: GLU411, ARG442 Hydrophobic interactions: ARG352
9.	Gamma-sitosterol		H- bonding: GLU230 Hydrophobic interactions: TYR75 LEU166, LEU166 TYR75, TYR75 TRP83, HIS210
10.	Eicosanoic acid		H- bonding: ASP340, TYR 75 Hydrophobic interactions: HIS 122, TRP82,TRP83, LEU173, LEU171, HIS80, ARG344

Table 7: The binding interaction of phytoconstituents present in DRL and DRF extracts with amino acids of active sites of the α-Amylase enzyme

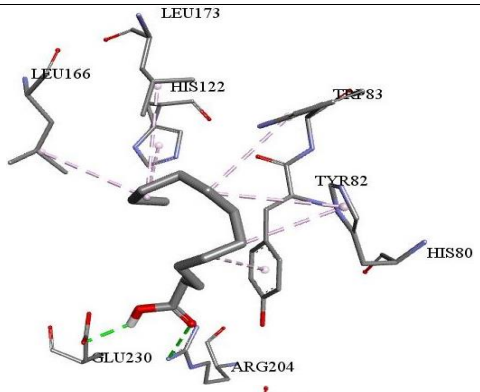
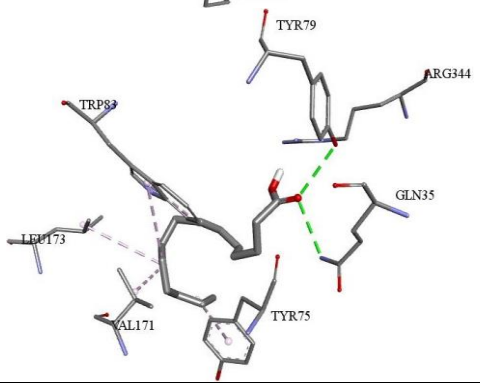
S. No.	Phytocontituents	Docked Poses	Interactions
11.	Lauric acid		H- bonding: GLU230, ARG204 Hydrophobic interactions: LEU166 LEU173,HIS80,HIS80 TYR82, TRP83, HIS122
12.	Tetradecanoic acid		H- bonding: GLN35, TYR79 Hydrophobic interactions: VAL171 LEU173, TYR75, TRP83, TRP83

Table 8: The binding interaction of phytoconstituents present in DRL and DRF extracts with amino acids of active sites of the α-glucosidase enzyme

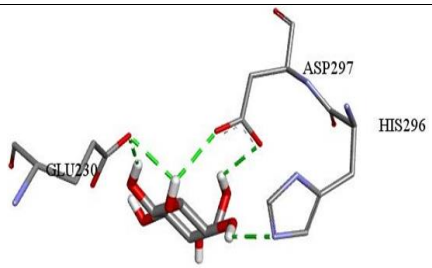
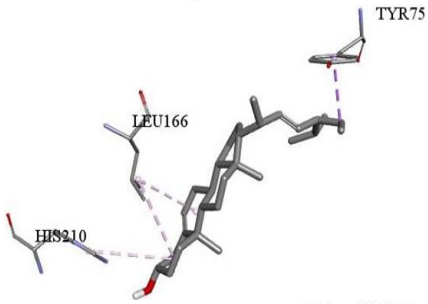
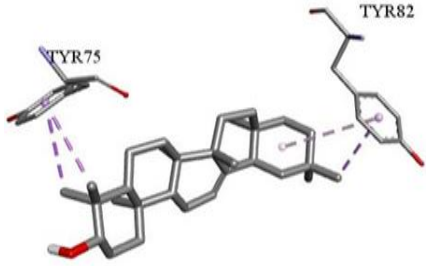
S.No	Phytoconstiuents	Docked Poses	Interactions
1.	Mome-inositol		H- bonding: GLU411, ARG442 Hydrophobic interactions: ARG352
2.	Stigmasterol E		Hydrophobic interactions: TYR75,LEU166, HIS210
3.	Beta-amyrin		Hydrophobic interactions: TYR 82,TYR76

Table 8: The binding interaction of phytoconstituents present in DRL and DRF extracts with amino acids of active sites of the α-glucosidase enzyme

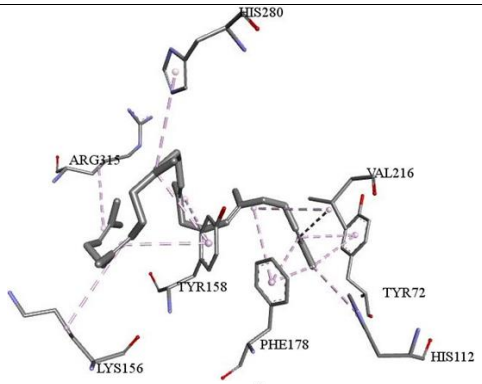
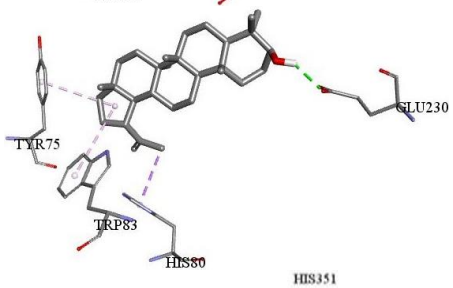
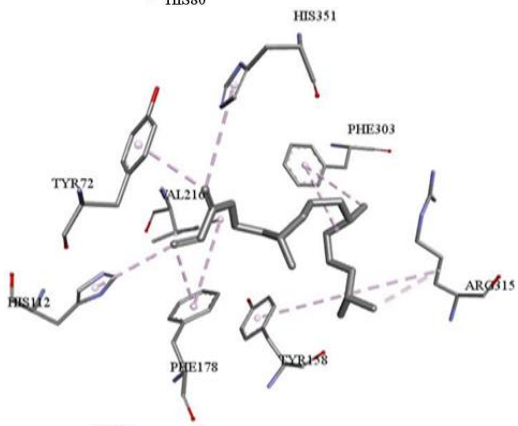
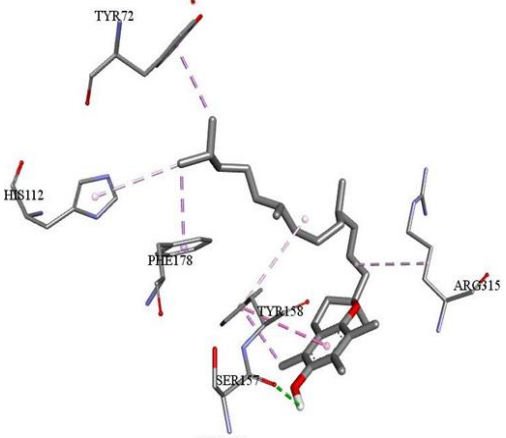
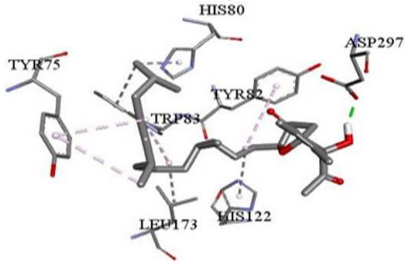
S.No	Phytoconstiuents	Docked Poses	Interactions
4.	Squalene		Hydrophobic interactions: TYR 82,TYR76, TYR 82, HIS80
5.	Lupeol		H- bonding: GLU230 Hydrophobic interactions: HIS80,TRP83,TYR75
6	Neophytadene		Hydrophobic interactions: HIS351, TYR72, PHE178, TYR158
7.	Vitamin E		H- bonding: SER157 Hydrophobic interactions: TYR72, HIS112, PHE178, TYR158
8.	alpha.-Tocospiro B		H- bonding: TYR ASP297 Hydrophobic interactions: LEU173, HIS122, TRP83

Table 8: The binding interaction of phytoconstituents present in DRL and DRF extracts with amino acids of active sites of the α-glucosidase enzyme

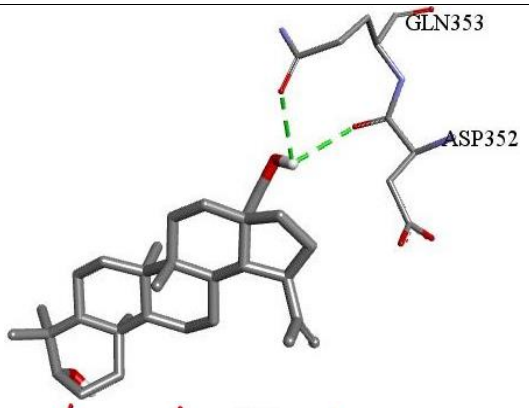
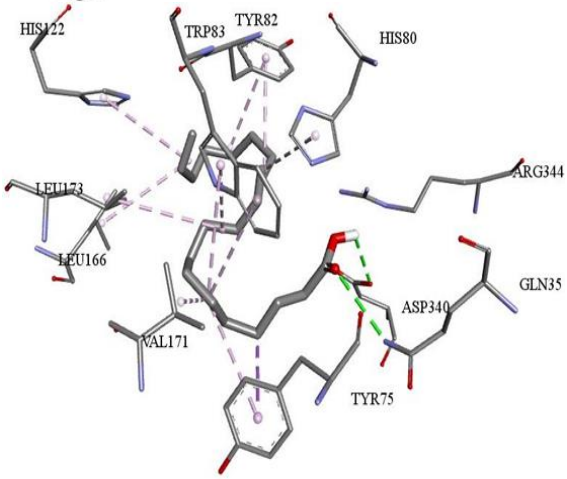
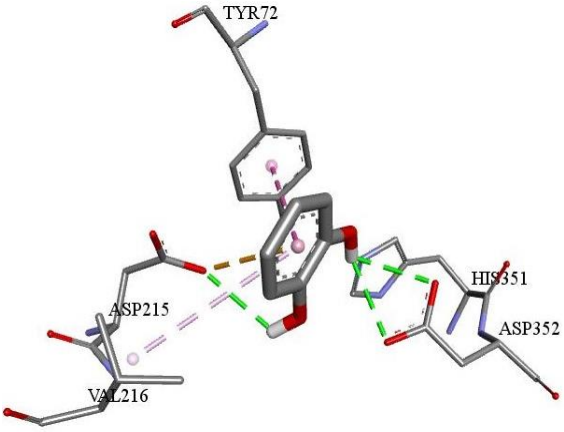
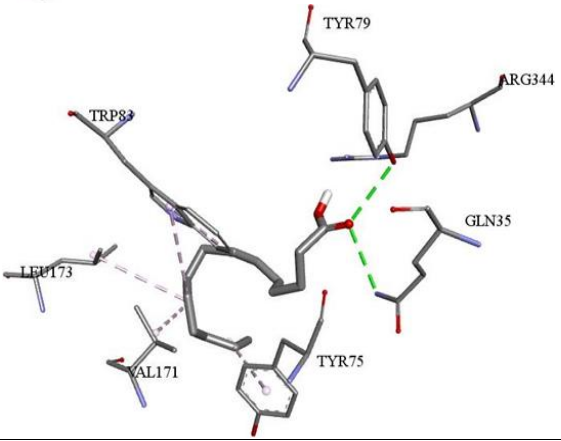
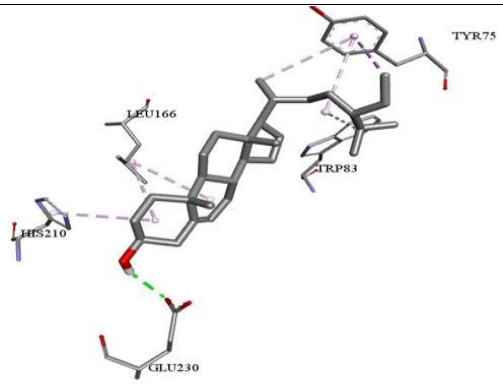
S.No	Phytoconstiuents	Docked Poses	Interactions
9.	Betulin		H- bonding: ASP352 Hydrophobic interactions: GLN353
10.	Eicosanoic acid		H- bonding: ASP340, TYR 75 Hydrophobic interactions: HIS 122, TRP82,TRP83, LEU173, LEU171,HIS80,ARG344
11.	Catechol		H- bonding: HIS351, ASP352,ASP215 Hydrophobic interactions: TYR72,VAL216
12.	Tetradecanoic acid		H- bonding: GLN35, TYR79 Hydrophobic interactions: VAL171 LEU173, TYR75, TRP83, TRP83

Table 8: The binding interaction of phytoconstituents present in DRL and DRF extracts with amino acids of active sites of the α-glucosidase enzyme

S.No	Phytoconstiuents	Docked Poses	Interactions
13.	Gamma- sitosterol		H- bonding: GLU230 Hydrophobic interactions: TYR75 LEU166, LEU166 TYR75, TYR75 TRP83, HIS210

Results of both of the extracts were comparable to ascorbic acid. IC_{50} values of extracts were 92.22 µg/ml (DRL), 118.1µg/ml (DRF), and 18.19µg/ml (ascorbic acid).

In-vitro Anti-diabetic Evaluation via α-Amylase and α-Glucosidase Inhibitory Assay

Both DRF and DRL extracts revealed inhibitory effects on both of the enzymes. It was found that alpha amylase inhibition was observed in both the extracts, with IC_{50} 1.806±0.363 µg/ml for DRL, 4.419 ± 0.347 µg/ml for DRF, and 0.1845 ± 0.10874 µg/ml for acarbose. DRL showed stronger inhibition than DRF but was less potent than the standard inhibitor, acarbose (IC_{50} = 0.1845 ± 0.1087 µg/ml), indicating promising antidiabetic potential. Further, α- Glucosidase inhibition was observed in both the extracts with 0.5263 ± 0.0682 µg /ml for DRL, IC_{50} 2.028.24 ± 0.5506 µg /ml for DRF and 13.24 ± 0.05337µg/ml for acarbose. DRLand DRF extracts demonstrated inhibitory activity against α-glucosidase, with IC_{50} values of 0.5263 ± 0.0682 µg/ml and 2.028.24 ± 0.5506 µg /ml, respectively. Among them, DRL exhibited markedly higher potency than both DRF and the standard drug acarbose (IC_{50} = 13.24 ± 0.053 µg/ml), signifying its strong potential as effective α-glucosidase inhibitor.

In-vitro Anti-diabetic Study using Glucose Uptake Assay

The uptake of glucose by L6 cells following treatment with DRL and DRF at given concentrations (5, 10, and 20 µg/ml) is shown in Table 12. The *in-vitro* glucose uptake assay showed that both DRL and DRF extracts significantly enhanced glucose uptake increasing with dose when compared to the untreated control (129.79 µg/ml). DRL exhibited the strongest effect (112.26 µg/ml) glucose uptake, which is more effective than DRF (73.38 µg/ml) at the same concentration and comparable to metformin (115 µg/ml).

DISCUSSION

Diabetes is 3rd highest prevalent health issue after cancer and CVS disorders. Hyperglycemia contributes to sustained damage, compromised organ function, and organ failure over time like renal function, vision, blood circulation, and brain[63]. Diabetic patients have an increased likelihood of developing peripheral vascular abnormalities, cerebrovascular medical conditions, and coronary heart disease due to lipid abnormalities[64]. Moreover, cellular oxidative stress and inflammatory responses are the prominent drivers in the progression of cardiovascular abnormalities[65].

Over the decades, many medicinal agents have been evaluated against oxidative stress and inflammation-induced DCM, but have shown poor clinical trial success because of insufficient efficacy and undesirable effects. Several phytocompounds have been reported for their contribution to many pharmacological activities with avoidable side effects by decreasing oxidative stress, enhancing the potential of endogenous antioxidants[66] and by reducing inflammation[67]. Hence, it is meaningful to continue studying herbal remedies for DCM, which could ultimately be evaluated in clinical trials. *Delonix regia* contains a variety of phytoconstituents with various therapeutic properties, such as antioxidant[35] and anti-inflammatory activities[40,] but has not been explored against DCM. Based on this background, hydroalcoholic extracts of *Delonix regia* leaves (DRL) and flowers (DRF) were aimed to explore for the *in-silico* and *in-vitro* studies against DCM along with phytochemical analysis.

In the present study, DRL and DRF contain a good amount of phenolic compounds and flavonoids. Furthermore, GC-MS analysis of DRF and DRL revealed total of 55 phytocompounds. In DRF 3-Cyclopenten-1-ol, Mome inositol, beta-tocopherol, hexadecanoic, acid, 2-Methoxy-4-vinylphenol, Octadecanoic acid 1,2-Cyclooctanedione, 2,5-anhydro-1,6-dideoxyhexo-3,4-diulose, Phytol, catechol, dodecanoic acid, vitamin E, stigmasterol, lupeol, betulin are present and whereas in DRL 3,3-Diethoxypropylamine, 1-Butanol, 3-methyl-, acetate, Phytol, lupeol, beta-amyrin, stigmasterol, vitamin E, squalene, neophytadiene, Mome inositol are the therapeutic active constituents. Based on the presence of these bioactive compounds with potential therapeutic roles, molecular docking studies were done to predict their binding affinities and interactions with target proteins relevant to diabetic complications.

In-silico studies were performed against the potential targets. In docking studies, alpha-tocospiro B, Vitamin E, Lupeol, Eicosanoic acid, lauric acid, tetradecanoic acid, and Lupeol bind with α-amylase with ASP 297, SER 157, GLU230, ASP 340, ARG204, GLN 35, residues by hydrogen bonding, respectively.

Table 9: ADME data of the phytoconstituents of *Delonix regia*

Phyto-constituents	GI Absorption	BBB Parameters	P-gp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Log Kp (skin permeation)
Stigmasterol E	Low	No	No	No	No	Yes	No	No	-2.74 cm/s
Beta-Amyrin	Low	No	No	No	No	No	No	No	-2.41cm/s
Squalene	Low	No	Yes	No	No	Yes	No	No	-1.17 cm/s
Lupeol	Low	No	No	No	No	No	No	No	1.90 cm/s
Neophytadiene	Low	No	Yes	No	No	Yes	No	No	1.90 cm/s
Vitamin E	Low	No	Yes	No	No	No	No	No	-1.68 cm/s
Gamma-sitosterol	Low	No	No	No	No	No	No	No	-2.20cm/s
alpha.-Tocospiro B	High	No	No	No	No	No	No	No	-3.90 cm/s
Betulin	No	No	No	No	No	No	No	No	-3.12 cm/s
Eicosanoic acid	No	No	No	Yes	No	No	No	No	-1.61 cm/s
Catechol	High	Yes	No	No	No	No	No	Yes	-6.35 cm/s
1-heptacosanol	Low	No	Yes	No	No	No	No	No	0.56 cm/s
Lauric acid	High	Yes	No	No	No	No	No	No	-4.54 cm/s
Tetradecanoic acid	High	Yes	No	Yes	No	No	No	No	-3.35 cm/s
3-hydroxybenzoic acid	High	Yes	No	No	No	No	No	No	-6.08 cm/s

Table 10: Predicted toxicity of the phytoconstituents of *Delonix regia*

Phyto-constituents	LD_{50} (mg/kg/p.o.)	Toxicity class	Hepatotoxicity	Nephrotoxicity	Cardiotoxicity	Carcinogenecity
Stigmasterol E	890	4	No	No	No	No
Beta-Amyrin	7000	6	No	No	No	No
Squalene	1190	4	Yes	No	No	No
Lupeol	2000	4	No	No	No	No
Neophytadiene	5050	6	No	No	No	No
Vitamin E	5000	5	No	No	No	No
Gamma-sitosterol	890	4	No	No	No	No
alpha.-Tocospiro B	300	3	No	No	No	No
Betulin	2000	4	No	No	Yes	No
Eicosanoic acid	900	4	No	No	No	No
Catechol	100	3	No	No	yes	yes
1-heptacosanol	1000	4	No	No	No	No
Lauric acid	900	4	No	No	No	No
Tetradecanoic acid	900	4	No	No	No	No

Similar residues such as TRP83, ASP 340, ARG 204, and GLU 230 have been reported for molecular docking studies on 1, 2-benzothiazine derivative against α-amylase[68].

Mome inositol, Tetradecoic acid, betulin, and catechol bind with α-glucosidase with ARG 442, GLN 35, ASP 352, and ASP 215 residues by hydrogen bonding, respectively. In one study, THR 306, ASP 352, ARG 213, GLU 277, ASP 215, and ARG 442 were reported most potent α-glucosidase inhibitors that act by interacting with the target protein through hydrogen bonds[69]. Phytoconstituents of both DRF and DRL extracts exhibited notable binding interactions with α-amylase and α-glucosidase, engaging crucial active site residues via hydrogen bonding. These findings are consistent with known inhibitor binding profiles, suggesting their promise as potential antidiabetic agents.

ADME was performed to evaluate the pharmacokinetics and toxicity of the phytoconstituents present in the extract. In the ADME study, alpha-tocospiro b, stigmasterol E, lauric acid, 3-hydroxybenzoic acid, and tetradecoic acid were found to have good oral bioavailability and obey Lipinski's rule of five, Ghose, Veber, Egan, and Muegge rules with no violations, indicating their drug-likeliness. The bioavailability score for phytoconstituents was 0.55. According to medicinal chemistry, there are no PAINS and Brenk alerts for 1-heptacosanol, Lauric acid, Tetradecanoic acid, 3-hydroxybenzoic acid,alpha.-Tocospiro B, vitamin E, eicosanoic acid, and beta-amyrin. The phytoconstituents stigmasterol, Beta β-amyrin, Lupeol, Neophytadiene, Vitamin E, Gamma sitosterol, alpha.-Tocospiro B, Eicosanoic acid, 1- hepatocosanol, and lauric acid are found to be non-toxic and non-irritant, as well as no these phytoconstituents are hepatotoxic, nephrotoxic, cardiotoxic, and carcinogenic.

Table 11: Antioxidant activity of DRL, DRF, and ascorbic acid using the DPPH method

Conc. (µg/ml)	Ascorbic Acid (% inhibition)	DRL (% inhibition)	DRF(% inhibition)
10	0.42059	9.200456	5.07033
50	13.5935	26.00554	24.94275
100	36.38	54.27455	44.81518
250	61.0868	84.75818	72.50572
500	85.16	87.62417	87.73307

In literature, it has been reported that a hyperglycemic state of blood can lead to the production of free radicals[69]. High levels of free radicals can encourage oxidative stress that can exacerbate the damage to pancreatic β cells, coronary arteries, cancer, and heart muscles. Furthermore, an excess amount of free radicals is reported to cause oxidative stress, which further contributes to worsening the diabetic condition. Antioxidants help to prevent or reduce tissue damage by scavenging ROS and RNS[70]. Therapeutically, polyphenols and flavonoids are the secondary metabolites that exhibit inhibition of free radical breakdown of peroxide, inactivation of metal, and scavenging of oxygen, which contributes to preventing or reducing various disorders[71,72].

Therefore, antioxidant-containing therapeutic agents can be effective against such diseases. In the present study, hydroalcoholic extracts of DRF and DRL exhibited significantly high DPPH scavenging activities, suggesting the potent antioxidant effect of the extracts, which may be due to the presence of phenols and flavonoids. Furthermore, GC-MS analysis of a hydroalcoholic extract of DRF and DRL revealed the presence of pharmacologically important constituents such as 3-Cyclopenten-1-ol, catechol, Mome inositol, Octadecanoic acid, Phytol, Squalene, which are previously reported to have antioxidant properties; thereby, these compounds are likely to contribute to the radical scavenging activity[73-76].

The digestive enzymes, such as alpha amylase and alpha glucosidase, have been revealed to play an important role in the metabolism of carbohydrates. The breakdown of polysaccharides is catalyzed by alpha amylase[77]. Whereas, alpha-glucosidase cleaves disaccharides into glucose, which is absorbable into the intestinal lumen. So, inhibition of enzymes is a potential strategy to treat hyperglycemia[78]. Therefore, the alpha amylase and glucosidase inhibitory *in-vitro* activities of hydroalcoholic extracts of DRL and DRF were investigated, and the results of both the extracts are comparable to acarbose with IC50 values (0.1845 ± 0.1087 µg/ml) and (13.24 ± 0.05337 µg/ml), respectively. The inhibitory activities observed by both DRL and DRF extracts in this study may be associated with the presence of compounds such as Mome inositol, hexadecanoic acid, 2-Methoxy-4-vinylphenol, and Octadecanoic acid, which have previously been reported to possess α-glucosidase and α-amylase inhibitory activities[79]. Moreover, these results suggested that the *Delonix regia* could be a potential candidate for the search for a new alpha amylase and alpha glucosidase inhibitory agent to treat diabetes.

Table 12: Effect of hydroalcoholic extracts of DRL and DRF using the Glucose uptake assay for antidiabetic activity

Sample	*In-vitro* Glucose Uptake (µg/ml)
Control	129.79
Metformin	115.05
Insulin	170.0438
DRL (5 µg/ml)	112.2673
DRL (10 µg/ml)	94.7426
DRL (20 µg/ml)	80.2300
DRF (5 µg/ml)	85.7065
DRF (10 µg/ml)	73.3844
DRF (20 µg/ml)	70.8368

Uptake of glucose by muscle is mostly mediated by GLUT-4. It has been shown that GLUT-4 recruitment from cytosol to the cell surfaces of muscles stimulated by insulin, which ultimately decreases the blood glucose level and potentially reduces the risk of diabetes [70]. L6 is a skeletal muscle cell line that has been used to investigate insulin action in glucose uptake via GLUT-4. Hence, L6 muscle cell line is an appropriate *in-vitro* model for studying the activity of glucose transport since skeletal muscle is the primary location of glucose disposal and utilization[80]. Previous studies using L6 myotubes showed that troglitazone and rosiglitazone have their maximal capacities for glucose absorption[81].

Therefore, in the present study, the glucose uptake potential of the hydroalcoholic extract of DRL and DRF was performed on L6 cells. It has been observed that the hydroalcoholic extract of DRL and DRF possesses glucose uptake in L6 cells. DRL extract shows dose-dependent inhibition in glucose uptake-higher doses result in less uptake. DRF showed significant glucose uptake that was comparable to metformin and insulin. Metformin has been reported to enhance glucose uptake in muscle and adipose tissue via translocation of GLUT4 transporters to the cell membrane and improve insulin sensitivity[82]. The significant increase in glucose uptake observed with DRF treatment suggests that the extract may facilitate GLUT4 translocation to the plasma membrane, potentially activating insulin-mimetic signaling pathways. Further molecular validation is required to explore this mechanism. These results agreed with the previous reports that phytoconstituents such as phytol, squalene, lupeol, and stigmasterol possess antidiabetic activity via the glucose uptake process[83].

To confirm these observations, the *in-vitro* and *in-silico* studies suggested that the hydroalcoholic extracts of *Delonix regia* flower and leaves possessed phenolics and flavonoid content, which exhibited antioxidant and anti-diabetic effects. Furthermore, it is anticipated that the mechanism of action contributing to the anti-diabetic effect of both extracts is the boost of glucose uptake by the muscles. As both the extracts exhibited good free radical–scavenging and blood glucose–modulating activity, and may have a potential effect in cardiovascular disorders. Therefore, identification of lead bioactive compounds which is responsible for antidiabetic activity in the pathophysiology of diabetes, with its molecular mechanism

as well as *in vivo* studies also required to be conducted for further investigations involved in cardiovascular disorders. The possible mechanism of action for the protective effect of *Delonix regia* in diabetes is depicted in Figure 1.

CONLUSION

In the current study, hydroalcoholic extracts of *Delonix regia* leaves (DRL) as well as flowers (DRF) demonstrated significant antioxidant and antidiabetic activities, as evidenced by *in-vitro* DPPH radical scavenging, α-amylase as well as α-glucosidase inhibition, and glucose uptake in L6 muscle cells. These effects are likely due to the presence of phytoconstituents like phenols, flavonoids, and a range of other bioactive substances (e.g., phytol, lupeol, squalene, mome inositol). *In-silico* docking and ADME analyses further supported the therapeutic potential and safety of these compounds. The findings suggest that extracts of *Delonix regia* may act via enhancement of GLUT-4 translocation and inhibition of key carbohydrate-metabolizing enzymes, positioning it as a promising natural candidate for diabetes management and possibly for associated cardiovascular complications. However, further in vivo and molecular studies are warranted to validate these effects and elucidate the precise mechanisms of action.

Acknowledgements

We are thankful to Amity University Haryana, India for providing us with facilities to conduct the present study. The authors sincerely acknowledge Akaar Biotechnologies, Lucknow**,** for providing laboratory facilities and technical support throughout the experimental work. We are also grateful to Jawaharlal Nehru University (JNU), New Delhi, for its academic

Author Contributions

Dr Monu Yadav and Dr Parveen Kumar Goyal have designed the present study. Ms Kamica Yadav and Dr Monu Yadav have done material preparation, data collection, analysis, *in-vitro* and *in-silico* studies from the section 2 to 3.6.4 . Ms. Kamica Yadav and Dr Sumit Kumar wrote the manuscript under supervision of Dr. Monu Yadav and Dr. Parveen Kumar Goyal from section 1 to 4. Dr Monu Yadav and Dr Anjali Dhillon proof read the final vesion of the manuscript. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

REFERENCES

1. Singh H, Singh R, Singh A, Singh H, Singh G, Kaur S, Singh B. Role of oxidative stress in diabetes-induced complications and their management with antioxidants. Archives of Physiology and Biochemistry. 2024 Nov 1;130(6):616-41.
2. Burgess, S., Juergens, C.P., Yang, W., Shugman, I.M., Idris, H., Nguyen, T., McLean, A., Leung, M., Thomas, L., Robledo, K.P. & Mussap, C. Cardiac mortality, diabetes mellitus, and multivessel disease in ST elevation myocardial infarction. *International Journal of Cardiology*, Vol. 323, 2021, pp.13-18
3. Gulsin GS, Athithan L, McCann GP. Diabetic cardiomyopathy: prevalence, determinants and potential treatments. Therapeutic advances in endocrinology and metabolism. 2019 Mar;10:2042018819834869.
4. Swiatkiewicz I, Patel NT, Villarreal-Gonzalez M, Taub PR. Prevalence of diabetic cardiomyopathy in patients with type 2 diabetes in a large academic medical center. BMC medicine. 2024 May 14;22(1):195.
5. Peng ML, Fu Y, Wu CW, Zhang Y, Ren H, Zhou SS. Signaling pathways related to oxidative stress in diabetic cardiomyopathy. Frontiers in endocrinology. 2022 Jun 15;13:907757.
6. Saadat S, Noureddini M, Mahjoubin-Tehran M, Nazemi S, Shojaie L, Aschner M, Maleki B, Abbasi-Kolli M, Rajabi Moghadam H, Alani B, Mirzaei H. Pivotal role of TGF-β/Smad signaling in cardiac fibrosis: non-coding RNAs as effectual players. *Frontiers in cardiovascular medicine*. 2021 Jan 25;7:588347.
7. Leask A. Potential therapeutic targets for cardiac fibrosis: TGFβ, angiotensin, endothelin, CCN2, and PDGF, partners in fibroblast activation. Circulation research. 2010 Jun 11;106(11):1675-80.
8. Leonard CE, Brensinger CM, Dawwas GK, Deo R, Bilker WB, Soprano SE, Dhopeshwarkar N, Flory JH, Bloomgarden ZT, Gagne JJ, Aquilante CL. The risk of sudden cardiac arrest and ventricular arrhythmia with rosiglitazone versus pioglitazone: real-world evidence on thiazolidinedione safety. Cardiovascular Diabetology. 2020 Feb 25;19(1):25.
9. Ansari P, Akther S, Hannan JM, Seidel V, Nujat NJ, Abdel-Wahab YH. Pharmacologically active phytomolecules isolated from traditional antidiabetic plants and their therapeutic role for the management of diabetes mellitus. Molecules. 2022 Jul 3;27(13):4278.
10. Cortez-Navarrete M, Martínez-Abundis E, Pérez-Rubio KG, González-Ortiz M, Méndez-del Villar M. Momordica charantia administration improves insulin secretion in type 2 diabetes mellitus. Journal of medicinal food. 2018 Jul 1;21(7):672-7.
11. Vuksan V, Sung MK, Sievenpiper JL, Stavro PM, Jenkins AL, Di Buono M, Lee KS, Leiter LA, Nam KY, Arnason JT, Choi M. Korean red ginseng (Panax ginseng) improves glucose and insulin regulation in well-controlled, type 2 diabetes: results of a randomized, double-blind, placebo-controlled study of efficacy and safety. Nutrition, Metabolism and Cardiovascular Diseases. 2008 Jan 1;18(1):46-56.
12. Ojieh AE, Adegor EC, Okolo AC, Lawrence EO, Njoku IP, Onyekpe CU. Hypoglycemic and hypolipidaemic effect of allium cepa in streptozotocin-induced diabetes. International Journal of Science and Engineering. 2015;6(10):23-9.
13. Jiang Y, Yue R, Liu G, Liu J, Peng B, Yang M, Zhao L, Li Z. Garlic (Allium sativum L.) in diabetes and its complications: Recent advances in mechanisms of action. Critical Reviews in Food Science and Nutrition. 2024 Jun 21;64(16):5290-340.
14. Rajasekaran S, Sivagnanam K, Subramanian S. Antioxidant effect of Aloe vera gel extract in

streptozotocin-induced diabetes in rats. Pharmacol Rep. 2005 Jan 1;57(1):90-6.
15. Mishra A, Srivastava R, Srivastava SP, Gautam S, Tamrakar AK, Maurya R, Srivastava AK. Antidiabetic activity of heart wood of Pterocarpus marsupium Roxb. and analysis of phytoconstituents. Indian J Exp Biol. 2013 May 1;51(5):363-74.
16. Rajalakshmi M, Eliza J, Priya CE, Nirmala A, Daisy P. Anti-diabetic properties of *Tinospora cordifolia* stem extracts on streptozotocin-induced diabetic rats. Afr J Pharm Pharmacol. 2009 May 1;3(5):171-80.
17. Klangjareonchai T, Roongpisuthipong C. The effect of Tinospora crispa on serum glucose and insulin levels in patients with type 2 diabetes mellitus. BioMed Research International. 2012;2012(1):808762.
18. Devangan S, Varghese B, Johny E, Gurram S, Adela R. The effect of Gymnema sylvestre supplementation on glycemic control in type 2 diabetes patients: A systematic review and meta-analysis. Phytotherapy Research. 2021 Dec;35(12):6802-12.
19. Jana K, Bera TK, Ghosh D. Antidiabetic effects of Eugenia jambolana in the streptozotocin-induced diabetic male albino rat. Biomarkers and Genomic Medicine. 2015 Sep 1;7(3):116-24.
20. Gireesh G, Thomas SK, Joseph B, Paulose CS. Antihyperglycemic and insulin secretory activity of Costus pictus leaf extract in streptozotocin induced diabetic rats and in *in vitro* pancreatic islet culture. Journal of ethnopharmacology. 2009 Jun 25;123(3):470-4.
21. Luka CD, Olatunde A, Tijjani H, Olisa-Enewe IA. Effect of aqueous extract of Phaseolus vulgaris L.(red kidney beans) on alloxan-induced diabetic Wistar rats. Int. J. of Science Invention Today. 2013;2(4):292-301.
22. Tuhin RH, Begum MM, Rahman MS, Karim R, Begum T, Ahmed SU, Mostofa R, Hossain A, Abdel-Daim M, Begum R. Wound healing effect of Euphorbia hirta linn.(Euphorbiaceae) in alloxan induced diabetic rats. BMC complementary and alternative medicine. 2017 Aug 24;17(1):423.
23. Shidfar F, Rajab A, Rahideh T, Khandouzi N, Hosseini S, Shidfar S. The effect of ginger (Zingiber officinale) on glycemic markers in patients with type 2 diabetes. Journal of complementary and integrative medicine. 2015 Jun 1;12(2):165-70.
24. Malapermal V, Botha I, Krishna SB, Mbatha JN. Enhancing antidiabetic and antimicrobial performance of Ocimum basilicum, and Ocimum sanctum (L.) using silver nanoparticles. Saudi journal of biological sciences. 2017 Sep 1;24(6):1294-305.
25. Patel DK, Kumar R, Laloo D, Hemalatha S. Diabetes mellitus: an overview on its pharmacological aspects and reported medicinal plants having antidiabetic activity. Asian Pacific Journal of Tropical Biomedicine. 2012 May 1;2(5):411-20.
26. Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TP. Indian herbs and herbal drugs used for the treatment of diabetes. Journal of clinical biochemistry and nutrition. 2007;40(3):163-73.
27. Syed AA, Reza MI, Shafiq M, Kumariya S, Katekar R, Hanif K, Gayen JR. Cissus quadrangularis extract mitigates diabetic cardiomyopathy by inhibiting RAAS activation, inflammation and oxidative stress. Biomarkers. 2022 Nov 17;27(8):743-52.
28. Liza, Hussain G, Malik A, Akhtar S, Anwar H. Artemisia vulgaris extract as a novel therapeutic approach for reversing diabetic cardiomyopathy in a rat model. Pharmaceuticals. 2024 Aug 8;17(8):1046.
29. Wen C, Liu C, Li Y, Xia T, Zhang X, Xue S, Olatunji OJ. Ameliorative potentials of the ethanolic extract from Lycium chinense leaf extract against diabetic cardiomyopathy. Insight into oxido-inflammatory and apoptosis modulation. Biomedicine & Pharmacotherapy. 2022 Oct 1;154:113583.
30. Tao S, Chen L, Song J, Zhu N, Song X, Shi R, Ge G, Zhang Y. Tanshinone IIA ameliorates diabetic cardiomyopathy by inhibiting Grp78 and CHOP expression in STZ-induced diabetes rats. Experimental and Therapeutic Medicine. 2019 Jul 1;18(1):729-34.
31. Singh AD, Chawda MB, Kulkarni YA. Cardioprotective effects of 'Vasant Kusumakar Rasa,'a herbo-metallic formulation, in type 2 diabetic cardiomyopathy in rats. Cardiovascular Toxicology. 2024 Sep;24(9):942-54.
32. Peng M, Xia T, Zhong Y, Zhao M, Yue Y, Liang L, Zhong R, Zhang H, Li C, Cao X, Yang M. Integrative pharmacology reveals the mechanisms of Erzhi Pill, a traditional Chinese formulation, against diabetic cardiomyopathy. Journal of Ethnopharmacology. 2022 Oct 5;296:115474.
33. Zhang B, Zhang CY, Zhang XL, Sun GB, Sun XB. Guan Xin Dan Shen formulation protects db/db mice against diabetic cardiomyopathy via activation of Nrf2 signaling. Molecular Medicine Reports. 2021 Jul;24(1):531.
34. Zeng JQ, Zhou HF, Du HX, Wu YJ, Mao QP, Yin JJ, Wan HT, Yang JH. Tongmai hypoglycemic capsule attenuates myocardial oxidative stress and fibrosis in the development of diabetic cardiomyopathy in rats. Chinese Journal of Integrative Medicine. 2025 Mar;31(3):251-60.
35. Patra S, Muthuraman MS, Meenu M, Priya P, Pemaiah B. Anti-inflammatory effects of royal poinciana through inhibition of toll-like receptor 4 signaling pathway. International immunopharmacology. 2016 May 1;34:199-211.
36. Ezeja MI, Ezeigbo II, Madubuike KG, Ekpe IJ. Analgesic activity of the methanol leaf extract of *Delonix regia*. Nigerian Veterinary Journal. 2012;33(2).
37. Sachidananda Swamy HC, Asha MM, Chaithra M, Vivek MN, YoshodaKambar PK. Antibacterial activity of flower extract of Caesalpinia pulcherrima, *Delonix regia* and Peltaphorum ferrugineum against urinary tract pathogens. Int Res J Biol Sci. 2014;3(4):80-3.
38. Salem MZ, Abdel-Megeed A, Ali HM. Stem wood and bark extracts of *Delonix regia* (Boj. Ex. Hook): Chemical analysis and antibacterial, antifungal, and antioxidant properties. BioResources. 2014 Jan 1;9(2):2382-95.

39. Sunday AG, Ifeanyi OE, Ezeja MI. Wound healing potentials of leaf and bark extracts of *Delonix regia*. World J Pharm Pharm Sci. 2014 Feb 19;3:133-42.
40. Elhassaneen YA, Khader SA, Gharib MA, Abd-ElAziz YE. Possible protective roles of poinciana (*Delonix regia*) seeds against carbon tetrachlorideinduced biochemical and histological disorders in rat liver. American J. of Medical Sciences and Medicine. 2024;12(1):1-5.
41. Sachan N, Chandra P, Pal D. Effect of *Delonix regia* (Boj. Ex Hook.) Raf. stem bark extract against experimentally induced ulcers in rats. Indian J Exp Biol. 2017 Jan 1;55(1):49-54.
42. Chitra V, Ilango K, Rajanandh MG, Soni D. Evaluation of *Delonix regia Linn.* flowers for antiarthritic and antioxidant activity in female wistar rats. Annals of Biological Research. 2010 Aug 25;1(2):142-7.
43. Amalia A, Syafitri I, Prasasty VD. Antimalarial effect of flamboyant (*Delonix regia*) bark and papaya (Carica papaya L.) leaf ethanolic extracts against plasmodium berghei in mice. Biomedical and Pharmacology Journal. 2017 Sep 25;10(3):1081-9.
44. Garg M, Sharma A, Choudhary M, Kaur P. Antifertility potential of leaves and seeds of *Delonix regia* in female rats. Asian Pacific Journal of Reproduction. 2023 May 1;12(3):117-23.
45. Jayanthi MK, Amoghimath S. To evaluate the diuretic activity in ethanolic extract of leaves of *Delonix regia* in wistar albino rats. Biomedical and Pharmacology Journal. 2018 Jun 25;11(2):959-63.
46. Shaikat MA, Parvin MN, Ranjan P. Evaluation of anthelmintic activity of aqueous leaf extract of *Delonix regia*. J. Med. Plants Stud. 2023;11(4):01-2.
47. Sathya A, Siddhuraju P. Role of phenolics as antioxidants, biomolecule protectors and as anti–diabetic factors–Evaluation on bark and empty pods of Acacia auriculiformis. Asian Pacific journal of tropical medicine. 2012 Oct 1;5(10):757-65.
48. Gonzalez-Abuin N, Pinent M, Casanova-Marti A, Arola L, Blay M, Ardevol A. Procyanidins and their healthy protective effects against type 2 diabetes. Current medicinal chemistry. 2015 Jan 1;22(1):39-50.
49. Bule M, Abdurahman A, Nikfar S, Abdollahi M, Amini M. Antidiabetic effect of quercetin: A systematic review and meta-analysis of animal studies. Food and chemical toxicology. 2019 Mar 1;125:494-502.
50. Geetha BS, Mathew BC, Augusti KT. Hypoglycemic effects of leucodelphinidin derivative isolated from Ficus bengalensis (Linn.). Indian journal of physiology and pharmacology. 1994 Jan 1;38:220-.
51. Aodah AH, Alkholifi FK, Alharthy KM, Devi S, Foudah AI, Yusufoglu HS, Alam A. Effects of kaempherol-3-rhamnoside on metabolic enzymes and AMPK in the liver tissue of STZ-induced diabetes in mice. Scientific Reports. 2024 Jul 13;14(1):16167.
52. Zhuge F, Ni Y, Wan C, Liu F, Fu Z. Anti-diabetic effects of astaxanthin on an STZ-induced diabetic model in rats. Endocrine Journal. 2021;68(4):451-9.
53. Ponnulakshmi R, Shyamaladevi B, Vijayalakshmi P, Selvaraj J. *In silico and in vivo* analysis to identify the antidiabetic activity of beta sitosterol in adipose tissue of high fat diet and sucrose induced type-2 diabetic experimental rats. Toxicology mechanisms and methods. 2019 May 4;29(4):276-90.
54. Malik A, Jamil U, Butt TT, Waquar S, Gan SH, Shafique H, Jafar TH. *In silico* and *in vitro* studies of lupeol and iso-orientin as potential antidiabetic agents in a rat model. Drug design, development and therapy. 2019 May 6:1501-13.
55. Variya BC, Bakrania AK, Patel SS. Antidiabetic potential of gallic acid from Emblica officinalis: Improved glucose transporters and insulin sensitivity through PPAR-γ and Akt signaling. Phytomedicine. 2020 Jul 15;73:152906.
56. Alegbe EO, Teralı K, Olofinsan KA, Surgun S, Ogbaga CC, Ajiboye TO. Antidiabetic activity-guided isolation of gallic and protocatechuic acids from Hibiscus sabdariffa calyxes. Journal of food biochemistry. 2019 Jul;43(7):e12927.
57. Pirbalouti AG, Mahdad E, Craker L. Effects of drying methods on qualitative and quantitative properties of essential oil of two basil landraces. Food chemistry. 2013 Dec 1;141(3):2440-9.
58. Boulfia M, Lamchouri F, Toufik H. Chemical analysis, phenolic content, and antioxidant activities of aqueous and organic Moroccan Juglans regia L. Bark extracts. Current Bioactive Compounds. 2020 Dec 1;16(9):1328-39.
59. El-Gizawy HA, Alazzouni AS, El-Haddad AE. Pharmacognostical and Biological Studies of *Delonix regia* growing in Egypt: HPLC Profiles. Pharmacognosy Communications. 2018 Jul 1;8(3).
60. Yadav M, Parle M, Sharma N, Dhingra S, Raina N, Jindal DK. Brain targeted oral delivery of doxycycline hydrochloride encapsulated Tween 80 coated chitosan nanoparticles against ketamine induced psychosis: behavioral, biochemical, neurochemical and histological alterations in mice. Drug delivery. 2017 Jan 1;24(1):1429-40.
61. Telagari, M. and Hullatti, K. *In-vitro* α-amylase and α-glucosidase inhibitory activity of Adiantum caudatum Linn. and Celosia argentea Linn. extracts and fractions. *Indian journal of pharmacology*, Vol.47, No.4, 2015, pp.425-429.
62. Lakshmanan J, Elmendorf JS, Özcan S. Analysis of insulin-stimulated glucose uptake in differentiated 3T3-L1 adipocytes. Diabetes Mellitus: Methods and Protocols 2003 Jan 1 (pp. 97-103). Totowa, NJ: Humana Press.Forbes JM, Cooper ME. Mechanisms of diabetic complications. Physiological reviews. 2013 Jan;93(1):137-88.
63. Marso SP, Hiatt WR. Peripheral arterial disease in patients with diabetes. Journal of the American College of Cardiology. 2006 Mar 7;47(5):921-9.
64. Steven S, Frenis K, Oelze M, Kalinovic S, Kuntic M, Bayo Jimenez MT, Vujacic-Mirski K, Helmstädter J, Kröller-Schön S, Münzel T, Daiber A. Vascular inflammation and oxidative stress: major triggers for cardiovascular disease. Oxidative medicine and cellular longevity. 2019;2019(1):7092151.

65. Muscolo A, Mariateresa O, Giulio T, Mariateresa R. Oxidative stress: the role of antioxidant phytochemicals in the prevention and treatment of diseases. International journal of molecular sciences. 2024 Mar 13;25(6):3264.
66. Fakhri S, Piri S, Moradi SZ, Khan H. Phytochemicals targeting oxidative stress, interconnected neuroinflammatory, and neuroapoptotic pathways following radiation. Current Neuropharmacology. 2022 May 1;20(5):836-56.
67. Kimani NM, Ochieng CO, Ogutu MD, Yamo KO, Onyango JO, Santos CB. Inhibition kinetics and theoretical studies on Zanthoxylum chalybeum engl. Dual inhibitors of α-glucosidase and α-Amylase. Journal of Xenobiotics. 2023 Feb 21;13(1):102-20.
68. Riyaphan J, Pham DC, Leong MK, Weng CF. *In silico* approaches to identify polyphenol compounds as α-glucosidase and α-amylase inhibitors against type-II diabetes. Biomolecules. 2021 Dec 14;11(12):1877.
69. Engwa GA, Nweke FN, Nkeh-Chungag BN. Free radicals, oxidative stress-related diseases and antioxidant supplementation. Alternative Therapies in Health & Medicine. 2022 Jan 1;28(1).
70. Hernández-Rodríguez P, Baquero LP, Larrota HR. Flavonoids: Potential therapeutic agents by their antioxidant capacity. InBioactive compounds 2019 Jan 1 (pp. 265-288). Woodhead Publishing.
71. Chaudhary P, Janmeda P, Docea AO, Yeskaliyeva B, Abdull Razis AF, Modu B, Calina D, Sharifi-Rad J. Oxidative stress, free radicals and antioxidants: potential crosstalk in the pathophysiology of human diseases. Frontiers in chemistry. 2023 May 10;11:1158198.
72. Wickramaratne MN, Punchihewa JC, Wickramaratne DB. *In-vitro* alpha amylase inhibitory activity of the leaf extracts of Adenanthera pavonina. BMC complementary and alternative medicine. 2016 Nov 15;16(1):466.
73. Mansouri F, Ben Moumen A, Richard G, Fauconnier ML, Sindic M, Serghini-Caid H, Elamrani A. Flavor profiles of monovarietal virgin olive oils produced in the Oriental region of Morocco. Oilseeds and fats, Crops and Lipids. 2017;24.
74. Vazifedoost M, Didar Z, Hajirostamloo B. Identification of Chemical Compounds, radical scavenging activity and Antimicrobial Properties of Seed Extract of Securigera securidaca L. Journal of food science and technology (Iran). 2019 Dec 10;16(94):13-22.
75. Luo Y, Huang Y, Yuan X, Zhang L, Zhang X, Gao P. Evaluation of fatty acid composition and antioxidant activity of wild-growing mushrooms from Southwest China. International journal of medicinal mushrooms. 2017;19(10).
76. Li X, Bai Y, Jin Z, Svensson B. Food-derived non-phenolic α-amylase and α-glucosidase inhibitors for controlling starch digestion rate and guiding diabetes-friendly recipes. Lwt. 2022 Jan 1;153:112455.
77. Kashtoh H, Baek KH. Recent updates on phytoconstituent alpha-glucosidase inhibitors: An approach towards the treatment of type two diabetes. Plants. 2022 Oct 14;11(20):2722.
78. Wahid A, Hamad R, Manik S, Mohapatra D. Processing-Mediated Changes in Micro-and Macro-nutrients. In Colored Cereals (pp. 170-194). CRC Press.
79. Jaiswal N, Maurya CK, Pandey J, Rai AK, Tamrakar AK. Fructose-induced ROS generation impairs glucose utilization in L6 skeletal muscle cells. Free radical research. 2015 Sep 2;49(9):1055-68.
80. Yonemitsu S, Nishimura H, Shintani M, Inoue R, Yamamoto Y, Masuzaki H, Ogawa Y, Hosoda K, Inoue G, Hayashi T, Nakao K. Troglitazone induces GLUT4 translocation in L6 myotubes. Diabetes. 2001 May 1;50(5):1093-101.
81. Herman R, Kravos NA, Jensterle M, Janež A, Dolžan V. Metformin and insulin resistance: a review of the underlying mechanisms behind changes in GLUT4-mediated glucose transport. International journal of molecular sciences. 2022 Jan 23;23(3):1264.
82. Hairani MA, Abdul Majid FA, Zakaria NH, Hudiyanti D, Fadhlina A, Sheikh HI. Anti-diabetic properties of traditional herbal concoction containing Eleutherine palmifolia (L.) Merr., Momordica charantia L., and Syzygium polyanthum (Wight.): a bibliometric analysis. Food Production, Processing and Nutrition. 2023 Jul 10;5(1):60.
83. Wang J, Huang M, Yang J, Ma X, Zheng S, Deng S, Huang Y, Yang X, Zhao P. Anti-diabetic activity of stigmasterol from soybean oil by targeting the GLUT4 glucose transporter. Food & nutrition research. 2017 Jan 1;61(1):1364117.