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Phytochemical Screening and Molecular Docking-Based Evaluation of *Raphanus sativus* L. Peel Extract as a Prospective Therapeutic Strategy for Diabetic Complications

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Abstract

Radish (Raphanus sativus L.) is a therapeutically important root crop with various medicinal properties. The present study designed to find bioactive compounds from the methanolic peel extract of R. sativus and assess their inhibitory potential against aldose reductase, a key enzyme involved in the pathogenesis of cardiovascular diseases and other diabetic complications. The methanolic peel extract of R. sativus was evaluated by gas chromatography–mass spectrometry (GC-MS), revealing 35 distinct compounds. All compounds were evaluated for drug-likeness and pharmacokinetics using the SwissADME web tool. The results showed full compliance with Lipinski's Rule of Five, with no violations, demonstrating good oral bioavailability and drug-like properties. Additionally, molecular docking was carried out using the PyRx virtual screening tool to determine the binding affinity for aldose reductase. The Discovery Studio Visualizer was used to perform interaction analysis. The docking results exhibited that numerous phytocompounds have strong binding attractions for the active site of aldose reductase. Among the screened compounds, 1,4-benzenedicarboxylic acid, bis(2-ethylhexyl) ester showed the highest binding affinity with docking score of −6.8 kcal/mol, followed by cyclohexanone (−6.5 kcal/mol), lactose (−6.4 kcal/mol), phthalic acid (−6.3 kcal/mol), bis(2-ethylhexyl) phthalate (−5.9 kcal/mol), 4H-pyran-4-one derivative (−5.8 kcal/mol), and 3-deoxy-D-mannoic lactone (−5.5 kcal/mol). The findings validate that Raphanus sativus peel comprises compounds with promising inhibitory potential against aldose reductase, signifying its possible application in the management of diabetic complications. However, additional in vitro and in vivo research is recommended to confirm the identified compounds' therapeutic efficacy.

Introduction

Owing to the universal upsurge in chronic ailments, predominantly diabetes mellitus, there is extensive research on safe and effective natural compounds (Osadebe *et al*., 2014; Sknepnek *et al*., 2025). Vegetables and herbs have conventionally been utilized in traditional healthcare due to their diverse bioactive compounds and pharmacologic effects (Awuchi, 2019). Brassicaceae plants like *Raphanus sativus* are widely cultivated and eaten because of their tremendous health and nutritional benefits (Niar *et al*., 2020; Luo *et al*., 2018; Gao *et al*., 2022).

The common vegetable *Raphanus sativus* L. has antibacterial, antioxidant, and anti-inflammatory, properties in its roots, leaves, and seeds (Gamba *et al*., 2021; Manivannan *et al*., 2019). The plant's therapeutic benefits are attributed to flavonoids, anthocyanins, phenolic acids, and glucosinolates (Rani *et al*., 2021). Radish extracts, in particular, have shown promise in the cure of variety of illnesses, including stomach ulcers, hepatotoxicity, and hypertension (Gamba *et al*., 2021; Mohammed and Hameed, 2018).

The anti-diabetic potential of *R. sativus* is particularly noteworthy. Radish extracts have been shown to improve glucose homeostasis by blocking enzymes like α-glucosidase and α-amylase and protecting against oxidative stress (Vadivelan *et al*., 2012; Manivannan *et al*., 2019). Diabetes is inextricably related to the polyol pathway, particularly the long-term implications. In hyperglycemia, extra glucose is changed into sorbitol via aldose reductase overexpression. This mechanism depletes NADPH, a critical cofactor for antioxidant defense, and accumulates sorbitol.

This raises the risk for diabetes retinopathy, neuropathy, and nephropathy (Ahmed *et al*., 2016). Therefore, discovering natural aldose reductase inhibitors is a promising strategy for alleviating diabetes complications.

Although radish roots and leaves have been thoroughly researched for their phytochemistry and bioactivity (Ibrahim *et al*., 2024; Vityazev *et al*., 2024), the peel is usually discarded as agricultural waste. This by-product may contain concentrated secondary metabolites. Recent studies show that various plant sections accumulate phytochemicals in different ways (Schlering *et al*., 2019). However, no systematic study has examined the methanolic *R. sativus* peel extract, its chemical components, or its ability to interact with diabetes targets such as aldose reductase.

To address this gap, this study uses *in-silico* techniques to investigate *Raphanus sativus* methanolic peel extract. The primary goals of GC-MS analysis are to (1) determine the phytocompounds in the extract, (2) evaluate their drug-likeness and pharmacokinetic properties with the SwissADME tool, and (3) predict their binding affinities and potential as lead molecules for diabetes management through molecular docking with the Aldose reductase enzyme using PyRx. This research aims to prove that radish peel, a common food scrap, could produce novel anti-diabetic medications.

Materials and Methods

Collection of plant material

Fresh vegetables *(Raphanus sativus)* were purchased from the local market and their peels were removed using a peeler. Following that, the peels were cleaned and dried in the shade.

Preparation of methanolic extract of *Raphanus sativus* peel

The shade dried peels were pulverized into powder using an electric grinder. A 50 g peel powder was dissolved in 75% methanol at 1 g: 10mL, then let run in a conical flask on an orbital shaker with the rotational speed of 250 rpm for 72 hours. The mixture was filtered using Whatman filter paper number 1. The extract was then air

dried using rotary evaporator. After drying the extract was kept at 4 °C in a refrigerator for later use (Nauroze *et al.,* 2023).

Gas Chromatography-Mass Spectrometry (GC-MS) Analysis

The gas chromatography-mass spectrometry analysis of the methanolic *R. sativus* extract revealed the presence of diverse compounds. The GC-MS device (Agilent, Model: GC 7890B, MS 5977A) included a nonpolar column DB 5MS. Dimensions of this column were 30 mm long, 0.25 mm diameter, and 0.25 μM film thickness. The mobile phase used helium as the carrier gas, flowing at a rate of 1 mL/min. To reach 280°C, the oven was heated 10 °C per minute. Each injection was 1μL. An electron ionization energy system with 70 eV was used for GC-MS analysis. Duration was 65 minutes. The extract was dissolved in methanol and analyzed with a 10-850 m/z range. Names of the bioactive compounds, along with their molecular weight, structure and molecular formula, were developed for identification. The specific compounds were identified by comparing the m/z ratios with samples validated by Sigma-Aldrich by using mass spectra data from the NIST Mass Spectral Library (Saravanan *et al.*, 2022).

Pharmacokinetics profile

The Phytocompounds derived after GC-MS analysis from *Raphanus sativus* were analyzed for pharmacokinetic profiles using Swiss ADME by entering the SMILES formula of each active compound. The drug-likeness parameters of the Phytocompounds were assessed using the web server of Swiss ADME. Lipinski Rule of Five (LR5) analysis was performed to assess the compound's pharmacokinetic ability.

Study of Ligand-protein docking

Molecular docking of *R. sativus* phytocompounds with aldose reductase was performed to assess their inhibitory potential for the target protein. The docking study carried out using PyRx 0.8 to determine ligand-protein binding interactions. The receptor protein's 3D structure was obtained from the Protein Data Bank (RCSB-PDB). Whereas, PubChem was used to obtain the chemical structures of the phytocompounds as supplemental data files. After removing water molecules and bound ligands, the target protein was structurally prepared followed by adding polar hydrogen atoms. Afterward, BIOVIA Discovery Studio version 21.1.0.20298's was used to create two- and three-dimensional interaction models of the selected phytocompounds with the target protein (Arif *et al*., 2024).

Results

Identification of bioactive compounds of *C. sativus* peel extract by GC-MS

The GC-MS chromatogram of *R. sativus* exhibited thirty-five peaks (35), showing the presence of thirty-five distinct chemicals. Based on the molecular formula, peak area and retention time, the identity of the phytochemicals was verified. The list of these phytochemicals along with their structures, class names, retention times (RT) and peak percentages is given in Table 1. 4-Octanone furanone was the first chemical identified with a short retention time (3.521 min), whereas Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-methyl- was the last compound identified with a long retention period (18.158 min). Fig.1 depicts the chromatogram from the GC-MS.

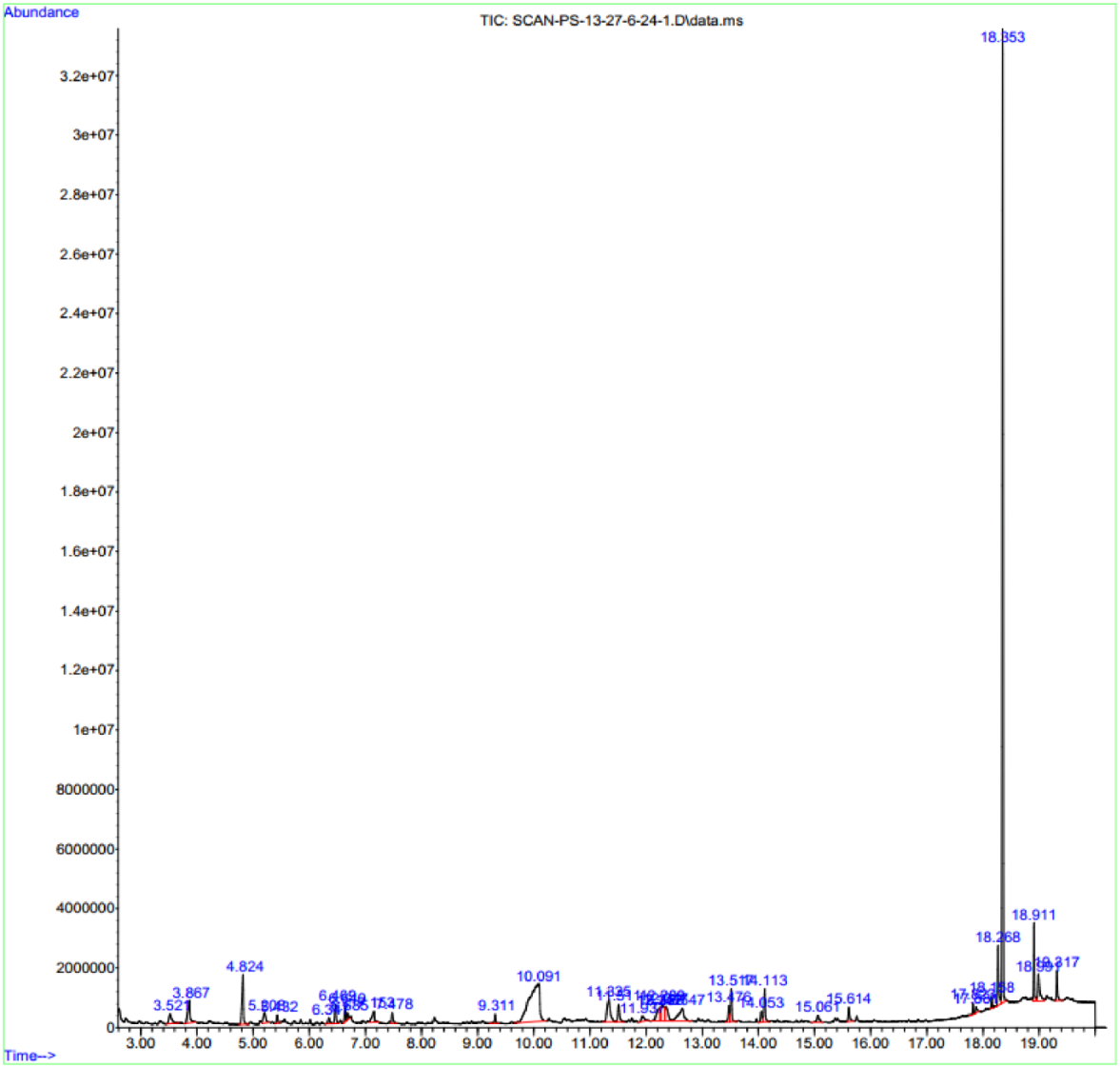

Figure 1. GC-MS chromatogram of methanolic peel extract of *Raphanus sativus*

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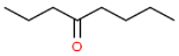
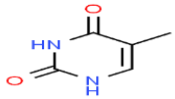
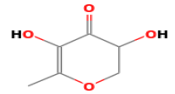
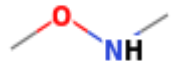
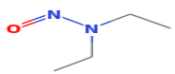
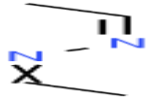
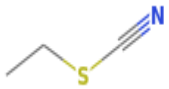
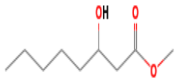
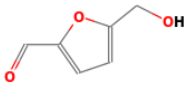
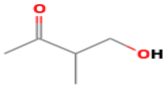
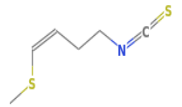
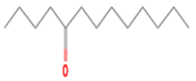
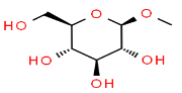
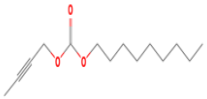
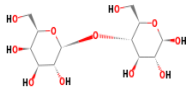
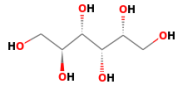
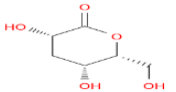
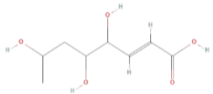
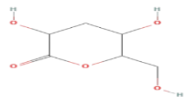
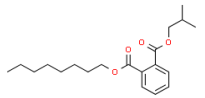
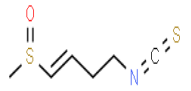
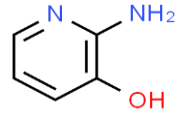
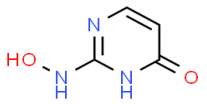
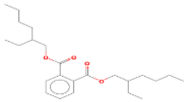
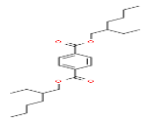
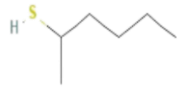
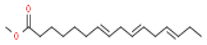
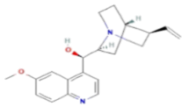
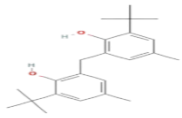
Table 1. Bioactive compounds derived from the methanolic peel extract of *Raphanus sativus* using GC-MS.

Sr. No	Compound name	Class name	Peak area (%)	RT	Structure
1.	4-Octanone	Ketone	1.28	3.521	
2.	Thymine	Pyrimidine	2.12	3.867	
3.	4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	Pyranones	3.53	4.824	
4.	Methanamine, N-methoxy	N-methoxyamines	1.13	5.208	
5.	Ethanamine, N-ethyl-N-nitroso	Primary amine	0.52	5.432	
6.	Acetaldehyde, ethylidenehydrazone	Aldehyde	0.53	6.347	

7.	Thiocyanic acid, ethyl ester	Ester	1.25	6.469	
8.	Octanoic acid, 3-hydroxy-, methyl ester	Hydroxy fatty acid	0.77	6.640	
9.	5-Hydroxymethylfurfural	Furan derivatives	0.36	6.685	
10.	Cyclohexanone, 4-ethyl	Substituted cyclohexanones	1.15	7.153	
11.	2-Butanone, 4-hydroxy-3-methyl	Hydroxy ketones	0.72	7.478	
12.	Cis-Raphasatin	Isothiocyanates	0.50	9.311	
13.	5-Tridecanone	Alkyl ketones	16.77	10.091	
14.	Beta-D-Glucopyranoside, methyl	Glycosides	3.09	11.335	

15.	Carbonic acid, but-2-yn-1-yl nonyl ester	Alkynyl carbonates	1.17	11.511	
16.	Lactose	Disaccharides	0.60	11.937	
17.	Sorbitol	Polyols	1.75	12.242	
18.	3-Deoxy-d-mannoic lactone	Lactones	0.38	12.257	
19.	2-Octenoic acid,4,5,7-trhydroxy	Hydroxy octenoic acids	2.34	12.289	
20.	Propanoic acid, 3-(acetylthio)-2-methyl-, (S)	Carboxylic Acid	1.74	12.347	
21.	n-Hexadecanoic acid	Saturated fatty acids	1.02	13.476	
22.	Phthalic acid, isobutyl octyl ester	Phthalate esters	1.99	13.517	

23.	Sulforaphene	Isothiocyanates	0.66	14.053	
24.	2-Amino-3-hydroxypyridine	Aminopyridines	2.02	14.113	
25.	9,12,15-Octadecatrienoic acid, methyl ester	Polyunsaturated fatty acid methyl esters	0.70	15.061	
26.	4-Hydroxy-2-hydroxyaminopyrimidine	Pyrimidines	0.44	17.823	
27.	Glycerol 1-palmitate	Glycerides	2.81	18.268	
28.	Bis(2-ethylhexyl) phthalate	Phthalate esters	37.39	18.353	
29.	1,4-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester	Esters	2.84	18.911	

30.	Octadecanoic acid, 2-hydroxy-1-(hydroxymethyl) ethyl ester	Fatty acid ethyl esters	2.17	18.911	
31.	13-Docosenamide, (Z)-	Alkenamides	1.53	19.317	
32.	2-Hexanethiol	Thiol group	2.96	12.647	
33.	7,10,13-Hexadecatrienoic acid, methyl ester	Carboxylic acid	1.00	15.614	
34.	Cinchonan-9-ol, 6'-methoxy	Methoxy group	0.34	17.881	
35.	Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-methyl-	Butylated Hydroxytoluene	0.41	18.158	

Pharmacokinetic profile

Lipinski Rule of Five (LR5) was used to assess the pharmacokinetic ability of the compound. The compounds meeting the LR5 criteria were categorized as drug like. Furthermore, we identified the physicochemical features such as molecular weight, hydrogen acceptors, hydrogen donors, and lipophilicity (LogP), as shown in Table 2.

Table 2. Pharmacokinetic analysis of phytocompounds.

Sr No.	Compounds	Molecular weight (g/mol)	Acceptor H	Donor H	LogP	Lipinski
1	4-Octanone	128.21	1	0	2.42	Yes
2	Thymine	126.11	2	2	0.71	Yes
3	4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	144.13	4	2	1.19	Yes
4	Methanamine, N-methoxy	61.08	2	1	1.41	Yes
5	Ethanamine, N-ethyl-N-nitroso	102.14	2	0	1.99	Yes
6	Acetaldehyde, ethylidenehydrazone	84.12	2	0	1.62	Yes
7	Thiocyanic acid, ethyl ester	87.14	1	0	1.58	Yes
8	Octanoic acid, 3-hydroxy-,methyl ester	174.24	3	1	2.47	Yes
9	5-Hydroxymethylfurfural	126.11	3	1	0.91	Yes
10	Cyclohexanone, 4-ethyl	304.39	3	0	2.91	Yes
11	2-Butanone, 4-hydroxy-3-methyl	102.13	2	1	1.10	Yes
12	Cis-Raphasatin	159.27	1	0	2.44	Yes
13	5-Tridecanone	198.34	1	0	3.58	Yes
14	Beta-D-Glucopyranoside, methyl	194.18	6	4	1.25	Yes
15	Carbonic acid, but-2-yn-1-yl nonyl ester	240.34	3	0	4.07	Yes
16	Lactose	342.30	11	8	0.76	No

17	Sorbitol	182.17	6	6	0.34	Yes
18	3-Deoxy-d-mannoic lactone	162.14	5	3	0.72	Yes
19	2-Octenoic acid,4,5,7-trhydroxy	190.19	5	4	1.04	Yes
20	Propanoic acid, 3-(acetylthio)-2-methyl-,(S)	162.21	3	1	1.39	Yes
21	n-Hexadecanoic acid	256.42	2	1	3.85	Yes
22	Phthalic acid, isobutyl octyl ester	334.45	4	0	4.04	Yes
23	Sulforaphene	175.27	2	0	2.17	Yes
24	2-Amino-3-hydroxypyridine	110.11	2	2	0.70	Yes
25	9,12,15-Octadecatrienoic acid, methyl ester, (Z,Z,Z)-	292.46	2	0	4.94	Yes
26	4-Hydroxy-2-hydroxyaminopyrimidine	127.10	3	3	0.45	Yes
27	Glycerol 1-palmitate	330.50	4	2	3.93	Yes
28	Bis(2-ethylhexyl) phthalate	390.56	4	0	4.77	Yes
29	1,4-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester	390.56	4	0	5.24	Yes
30	Octadecanoic acid, 2-hydroxy-1-(hydroxymethyl) ethyl ester	358.56	4	2	4.89	Yes
31	13-Docosenamide, (Z)-	337.58	1	1	5.10	Yes
32	2-Hexanethiol	118.24	0	0	2.30	Yes
33	7,10,13-Hexadecatrienoic acid, methyl ester	264.40	2	0	4.41	Yes
34	Cinchonan-9-ol, 6’-methoxy	324.42	4	1	3.36	Yes
35	Phenol, 2,2’-methylenebis [6-(1,1-dimethylethyl)-4-methyl-	340.50	2	2	4.14	Yes

In Silico-based molecular docking of *Raphanus sativus* peel extract to identify Aldose reductase inhibitors

Table (3) shows the molecular docking of bioactive compounds from *R. sativus* methanolic peel extract against Aldose reductase.

Table 3. Bioactive Compounds with docking score and biological activities

Sr.no	Ligands	CID	Docking score	Biological activity
1	4-Octanone	11516	-4.4	Antimicrobial activity (Oliveira *et al*., 2014).
2	Thymine	1135	-5.1	Antimicrobial and anticancer activity (Kumar *et al*., 2012).
3	4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	119838	-5.8	Antifungal, anti-microbial and anti-inflammatory effects (Fikri *et al*., 2016).
4	Methanamine, N-methoxy	14232	-3.2	Antimicrobial and potential neuroactive effects (Khalid *et al.,* 2019).
5	Ethanamine, N-ethyl-N-nitroso	5921	-4	Carcinogenicity and mutagenicity effects (Sharma *et al*., 2012).
6	Acetaldehyde, ethylidenehydrazone	9571063	-3.8	Antimicrobial, anticancer, anti-tubercular and antioxidant effects (Mohammed *et al*., 2013).
7	Thiocyanic acid, ethyl ester	10968	-3.1	Insecticidal, antimicrobial, anticancer and cytotoxic effects (Ramalakshmi and Muthuchelian, 2013).
8	Octanoic acid, 3-hydroxy-,methyl ester	110974	-4.6	Antifungal, anti-inflammatory, antimicrobial, and antioxidant (Radivojevic *et al*., 2016).
9	5-Hydroxymethylfurfural	237332	-4.7	Gastro protective, antimicrobial and anti-inflammatory (Zhao *et al*., 2013).
10	Cyclohexanone, 4-ethyl	2175947	-6.5	Antibacterial effect (Al-Tufa, 2022).
11	2-Butanone, 4-hydroxy-3-methyl	18829	-4.1	Hepatoprotective, hypocholesteremic, anti-inflammatory, antioxidant, and cancer-preventive properties (Adeyemi, 2023).
12	Cis-Raphasatin	91699052	-3.4	Antiallergic activities (Choi *et al*., 2023).

13	5-Tridecanone	42549	-4.9	Anti-cancer and anti-inflammatory activity (Shanmugam *et al*., 2012).
14	Beta-D-Glucopyranoside, methyl	445238	-5.4	Antimicrobial (Kawsar *et al*., 2022), antibacterial and antifungal (Kawsar *et al*., 2018)
15	Carbonic acid, but-2-yn-1-yl nonyl ester	91692357	-4.8	Antifungal and antimicrobial activity (Kuklev *et al*., 2013)
16	Lactose	6134	-6.4	Antibacterial and prebiotic activities (Sánchez *et al*., 2003).
17	Sorbitol	5780	-5	Anti-diabetic and diuretic Effects (Koyama *et al*., 2000).
18	3-Deoxy-d-mannoic lactone	541561	-5.5	Antimicrobial and anti-diabetic (Wani *et al*., 2024).
19	2-Octenoic acid,4,5,7-trhydroxy	5369339	-5.3	Anti-inflammatory, hepatotoxicity and antioxidant activities (Padmalochana *et al*., 2013).
20	Propanoic acid, 3-(acetylthio)-2-methyl-, (S)	118073	-4.9	Anti-inflammatory activity (Paprocka *et al*., 2023)
21	n-Hexadecanoic acid	985	-5.3	Antibacterial and antioxidant activity (Ganesan *et al*., 2022).
22	Phthalic acid, isobutyl octyl ester	6423815	-6.3	Anti-microbial, insecticidal, immunotoxicity and neurotoxicity effects (Huang *et al*., 2021).
23	Sulforaphene	6433206	-3.9	Herbicidal, anticancer, antimutagenic, antimicrobial, and metabolic activities (Zhang *et al*., 2022).
24	2-Amino-3-hydroxypyridine	28114	-4.4	Anticancer, antioxidant and Neuroprotective effects (Galvan-Hidalgo *et al*., 2020).
25	9,12,15-Octadecatrienoic acid, methyl ester, (Z,Z,Z)-	5367462	-5	Anti-microbial, anti-Inflammatory and cardiovascular effects (Krishnaveni *et al*., 2014).
26	4-Hydroxy-2-hydroxyaminopyrimidine	581456	-5.3	Anti-inflammatory anti-tubercular, anti-malarial anti-fungal anti-bacterial, anti-viral, and anti-cancer (Yerragunta *et al*., 2013).

27	Glycerol 1-palmitate	14900	-5.4	Anti-microbial activity (Siddique *et al*., 2017).
28	Bis(2-ethylhexyl) phthalate	8343	-5.9	Antioxidant, anti-viral, cytotoxicity and anti-tumor activities (El-Sayed *et al*., 2015).
29	1,4-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester	22932	-6.8	Antimicrobial, antifungal and antibacterial activity (Awad *et al*., 2024).
30	Octadecanoic acid, 2-hydroxy-1-(hydroxymethyl) ethyl ester	79075	-5.1	Anti-bacterial, antibiotic and antimicrobial affects (Daniels *et al*., 2021).
31	13-Docosenamide, (Z)-	5365371	-5.1	Anti-inflammatory, antimicrobial, antiviral and antioxidant activity (Adeyemo *et al*., 2024).
32	2-Hexanethiol	519310	-3.4	Antioxidant and antimicrobial activity (Loredana *et al*., 2019).
33	7,10,13-Hexadecatrienoic acid, methyl ester	556196	-5.3	Anti-inflammatory, scavenging activity, antimicrobial and anti-oxidant (Alqahtani *et al*., 2019).
34	Cinchonan-9-ol, 6'-methoxy	3034034	-4.3	Anti-plasmodial, antimalarial and antimicrobial activities (Warhurst *et al*., 2003).
35	Phenol, 2,2'-methylenebis [6-(1,1-dimethylethyl)-4-methyl-	8398	-5.2	Antimicrobial and antibacterial activities (Gupta *et al*., 2021).

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Molecular docking of phytocompounds with Aldose reductase

A total of 35 bioactive compounds, obtained through GC-MS analysis, were docked with Aldose reductase to evaluate their binding affinities. Few of them with best binding energies are shown in the figures (2-8). These are 3-Deoxy-d-mannoic lactone with a binding score of -5.5 in fig.(2), 4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl with a binding score of -5.8 in fig.(3) Bis(2-ethylhexyl) phthalate with a binding score of -5.9 in fig.(4), Phthalic acid, isobutyl octyl ester with a binding score of -6.3 in fig.(5), and Lactose with a binding score of -6.4 in fig.(6), Cyclohexanone, 4-ethyl with highest binding score of -6.5 in fig.(7), and 1,4-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester with binding score of -6.8 in fig.(8). Below, their whole constructions are seen.

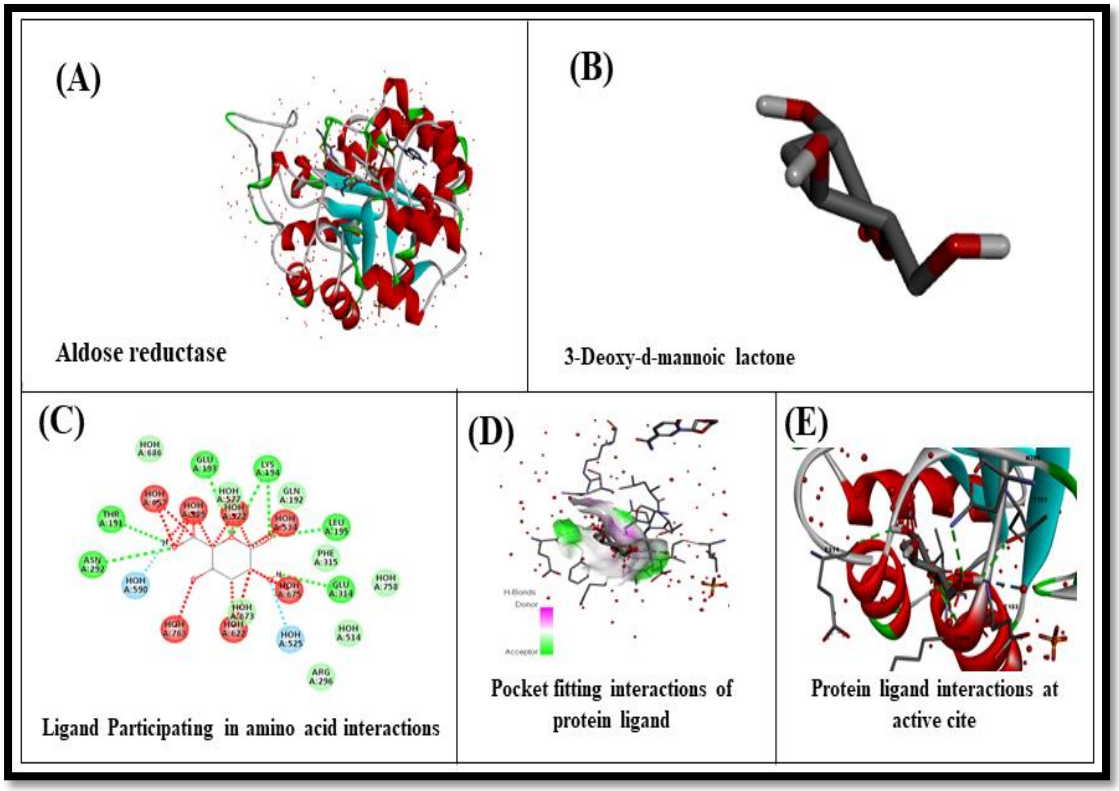

Figure 2. Molecular interaction of 3-Deoxy-d-mannoic lactone with Aldose reductase

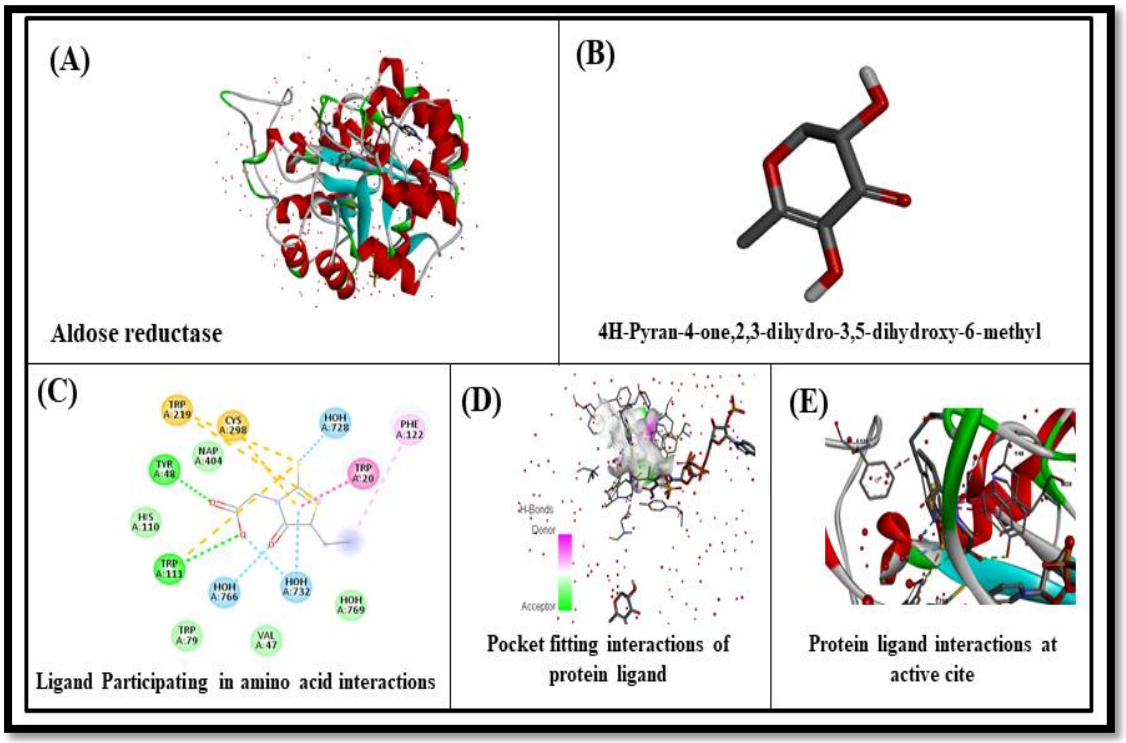

Figure 3. Molecular interaction of 4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6 methyl with Aldose reductase

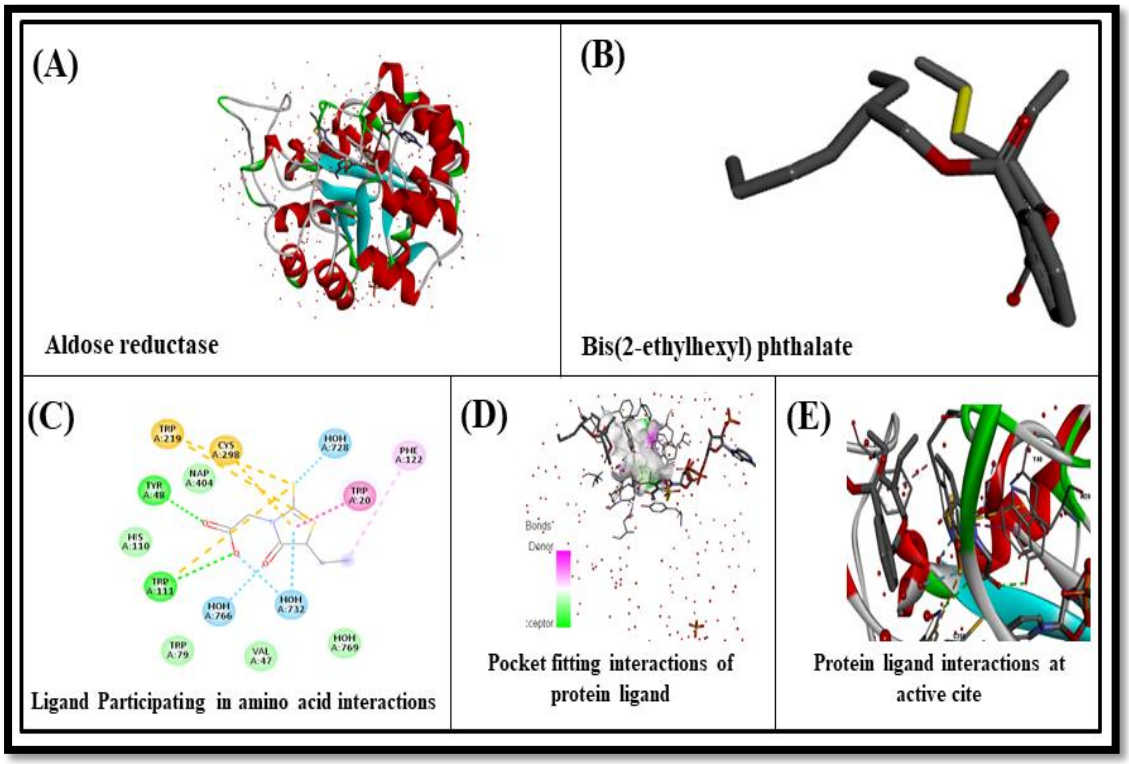

Figure 4. Molecular interaction of Bis(2-ethylhexyl) phthalate with Aldose reductase

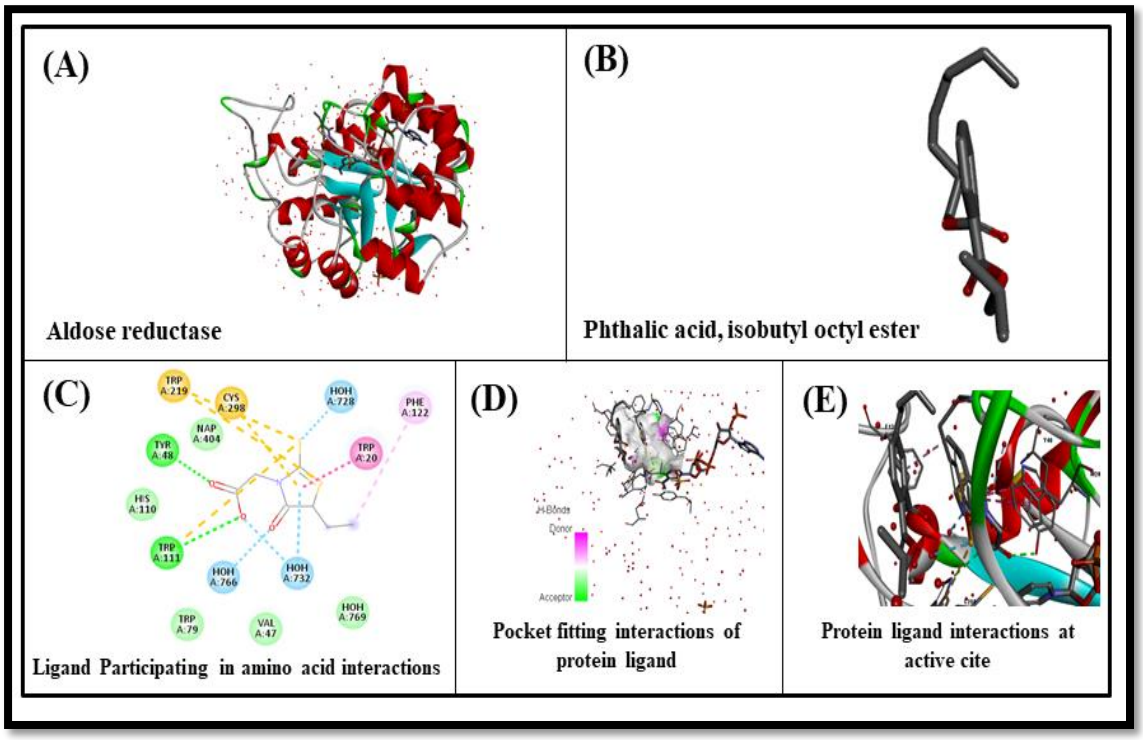

Figure 5. Molecular interaction of Phthalic acid, isobutyl octyl ester with Aldose reductase

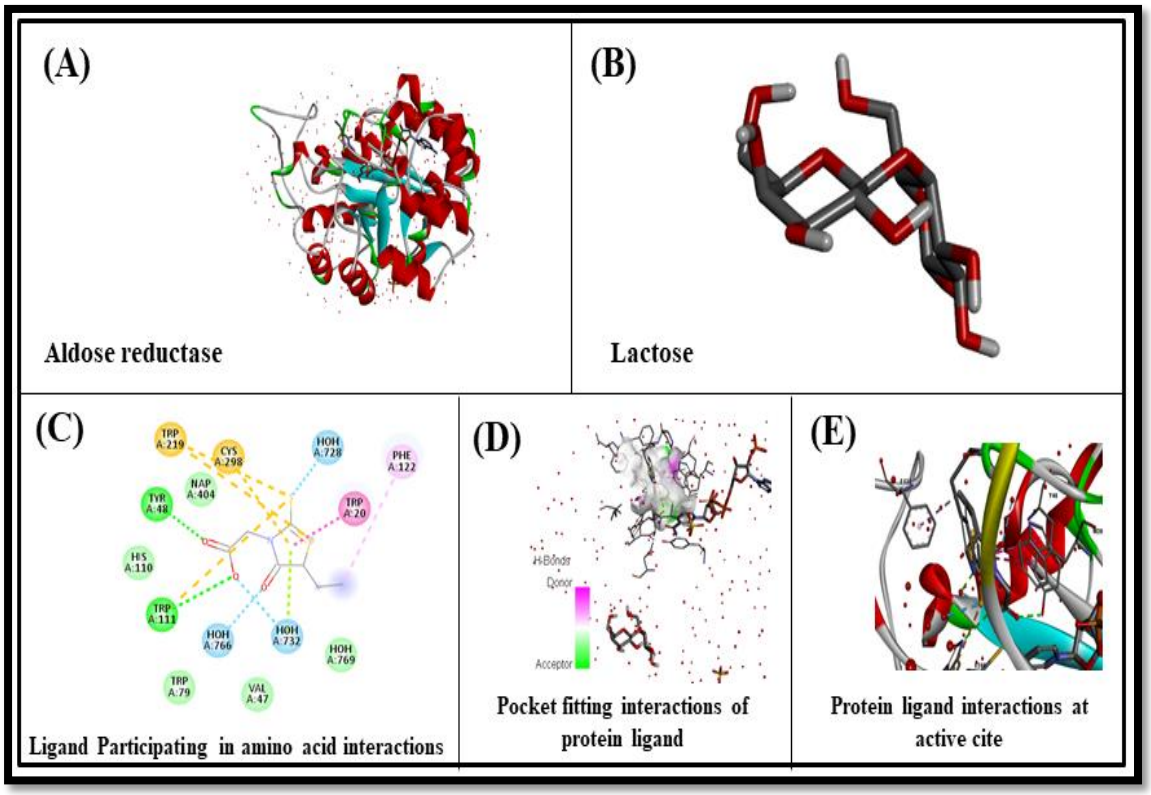

Figure 6. Molecular interaction of Lactose with Aldose reductase

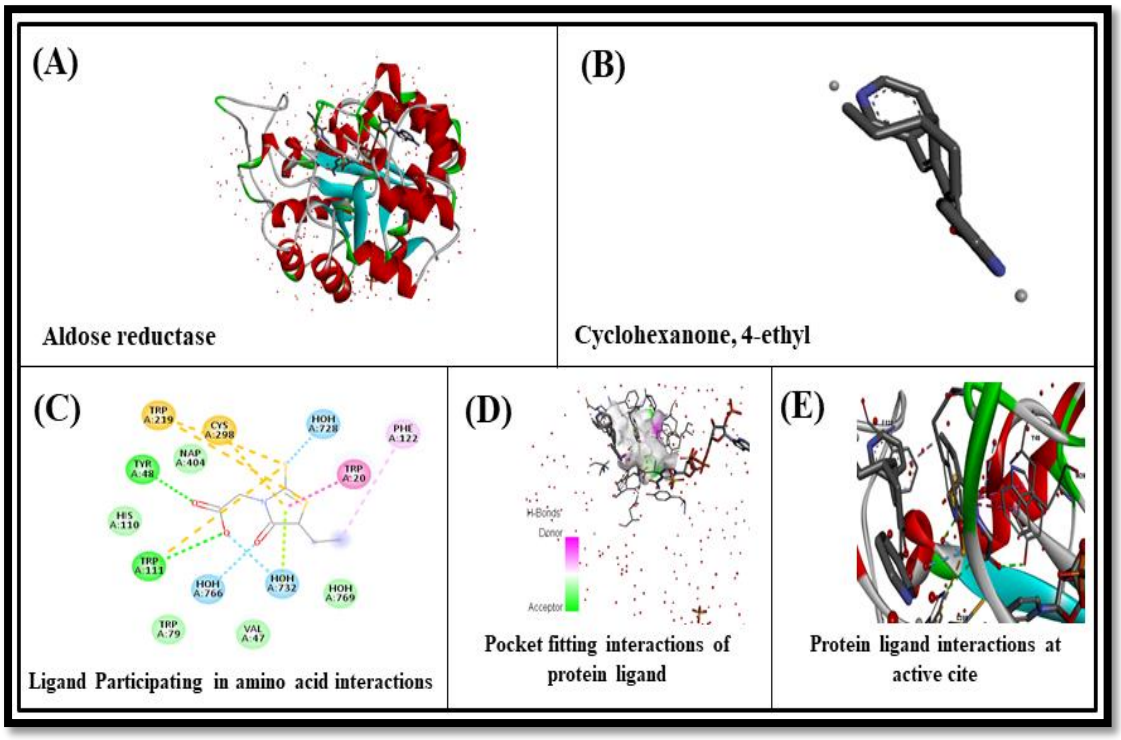

Figure 7. Molecular interaction of Cyclohexanone, 4-ethyl with aldose reductase

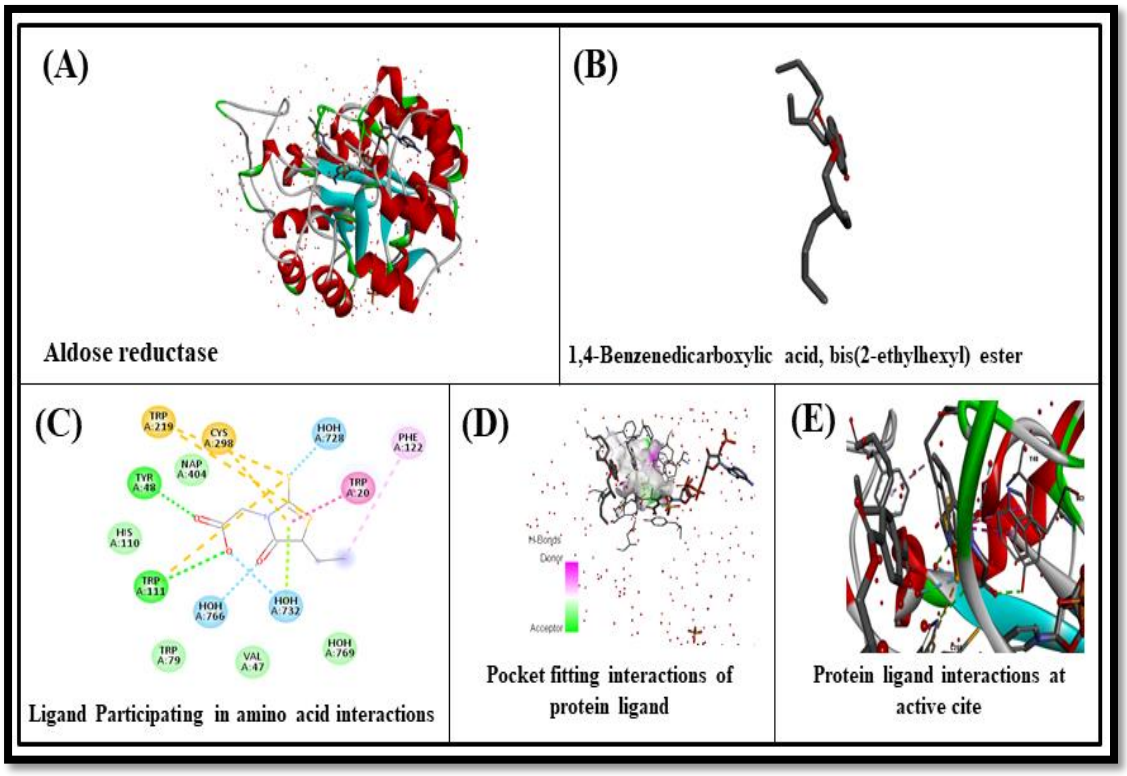

Figure 8. Molecular interaction of 1,4-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester with aldose reductase

Discussion

The current study used an integrated *in-silico* technique to examine the anti-diabetic effects of bioactive chemicals isolated from *Raphanus sativus'* methanolic peel extract. This study presents the first computational proof for radish peel's medicinal potential by combining GC-MS profiling, drug-likeness prediction, and molecular docking against aldose reductase.

GC-MS analysis of methanolic peel extract revealed 35 different phytocompounds. Previous research on *R. sativus* roots and leaves found phenolic acids, flavonoids, and glucosinolates, supporting this phytochemical richness (Gamba *et al*., 2021; Manivannan *et al*., 2019). Our work suggests that plant wastes may contain many nutraceuticals (Rifna et al., 2023). Because it shows that the plant peel contains many bioactive compounds. Brassicaceae vegetables contain phthalic acid esters and 4H-Pyran-4-one derivatives, according to earlier phytochemical study (Agarwal and Varma, 2014).

According to molecular docking tests, seven molecules have binding affinities to aldose reductase between -5.5 and -6.8 kcal/mol, which is advantageous. 1,4-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester had the highest binding score of -6.8 kcal/mol. Cyclohexanone and lactose were second and third with kcal/mol values of -6.5 and -6.4, respectively. These data suggest robust and prolonged enzyme-active site interactions. Aldose reductase overactivation in hyperglycemia causes polyol pathway sorbitol buildup and oxidative damage (Ahmed *et al*., 2012). Thus, treating diabetic complications requires targeting this enzyme. These peel chemicals may reduce diabetes symptoms by binding to this enzyme and inhibiting its activity.

Our study confirmed prior findings that aldose reductase inhibitors have binding affinities. For example, the standard inhibitor binding scores in *in-silico* studies are -7.0 to -8.0 kcal/mol (Schemmel *et al*., 2010). Whereas our top compounds have lower scores, but they are natural and exhibit drug-like properties, making them good candidates for further investigation. Discovery Studio shows hydrophobic and hydrogen bonding with essential amino acid residues in the enzyme binding pocket. This was similar to interaction patterns noted for other plant-derived aldose reductase inhibitors (Chigurupati *et al.*, 2022).

The Swiss ADME pharmacokinetic tool showed excellent oral bioavailability and drug-like characteristics for all seven compounds. Because all seven compounds obeyed Lipinski's rule of five. This result is even more significant because many naturally occurring medicines with strong *in-vitro* activity fail in clinical development. Because these chemicals have low absorption or metabolism profiles (Khan and Ahmad, 2019). These radish peel chemicals should be studied as oral medicinal agents as they follow Lipinski's rule.

Numerous mechanisms have been proposed to explain *R. sativus'* anti-diabetic benefits. These pathways include α-amylase and α-glucosidase inhibition, insulin sensitivity augmentation, and antioxidant action (Vadivelan *et al*., 2012). Our study adds to information by demonstrating that radish components can target the polyol pathway and positively influence aldose reductase. Radish's ability to target many sites makes it a promising diabetes treatment. While our computational findings are promising, there are certain limitations to consider. The dynamic interactions between proteins and ligands in living organisms are overlooked by molecular docking, which makes predictions based on static protein structures. Experimental confirmation using enzymatic testing is needed to confirm that these drugs inhibit aldose reductase.

Future research should isolate and test the inhibitory effects of these selective compounds against Aldose reductase *in vitro*. These compounds need more *in vivo* investigation with diabetic animal models to assess efficacy, safety, and pharmacokinetics. The best leads' binding affinity and selectivity can be improved by modifying their structures.

Conclusion

The present research demonstrated that methanolic peel extract of *Raphanus sativus* contains diverse bioactive phytocompounds with *in-silico* anti-diabetic properties. GC-MS analysis identified 35 distinct compounds, many of which were found to be potent inhibitors of the aldose reductase enzyme, a key diabetes treatment target. These lead compounds' drug-likeness was further confirmed by their favourable pharmacokinetic characteristics and adherence to Lipinski's rule of five. These results demonstrated the untapped potential of radish peel as an origin of nutraceutical compounds and offer a compelling computational justification for the traditional use of radish in metabolic diseases. However, further *in vivo* and *in vitro* investigation is recommended to explain their mechanism of action for therapeutic effect. This type of research could open up the possibilities to the creation of innovative plant-based diabetes treatments.

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