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DISCOVERY SCIENTIFIC SOCIETY

Molecular Docking and Pharmacokinetic studies of bioactive compounds from methanolic leaf extracts of *Allium hookeri* against alpha amylase & alpha glucosidase

Deepti Teotia[1], Vijai Malik[1]*

ABSTRACT

Alpha-glucosidase and alpha-amylase inhibitors are widely used oral medication for diabetes. These manage the breakdown of carbohydrates into simple sugars, which are then absorbed by the intestines. This study focuses on the phytochemical analysis and molecular docking studies of GC-MS identified compounds from methanolic extracts of *Allium hookeri*. Through GC-MS analysis, 20 different compounds were identified. These compounds were screened against enzyme alpha-glucosidase and alpha-amylase using Auto Dock Vina. Out of twenty compounds only thirteen shows drug likeness property which are included for further study. The docking studies revealed that 10-Methylundecan-4-olide has a high binding affinity with alpha-amylase (4w93) and alpha glucosidase (3l4w) i.e., -5.6kcal/mol & -6.4kcal/mol respectively, the drug-likeness studies indicate that 10-Methylundecan-4-olide is also the most readily bioavailable phytochemical among the thirteen selected compounds. These findings suggest it could be an effective antidiabetic agent.

Keywords: *Allium hookeri*, phytocompounds, alpha-glucosidase, alpha-amylase, molecular docking, antidiabetic

1. INTRODUCTION

Allium hookeri Thwaites (Amaryllidaceae) is distributed across Sri Lanka, India, Bhutan, Myanmar, Korea, and south western China. Within India, it is mainly found in the north eastern states of Arunachal Pradesh, Manipur, and Meghalaya (Singh & Singh, 2014). It is commonly known as Hooker chive or PhulunZung in India, Dudu sag in Nepal, and Maroi napakpi in Manipur. This species is often cultivated in fields and kitchen gardens. In Manipur, it is used as an onion substitute in various dishes (Ayam et al., 2011). This herb produces white flowers between July and September, & is characterized by a small underground rhizome with fibrous, bright-colored roots. The leaves are evergreen, thick, and linear with prominent midribs. *A. hookeri* is

commonly used in a variety of fermented foods, spices, and seasonings (Pandey et al., 2022). This is due to the presence of secondary metabolites and sulphue compounds. (Teotia et al., 2024).

Gas Chromatography-Mass Spectrometry (GC-MS) is a widely used analytical technique for characterizing the intricate chemical composition of plant extracts. It facilitates the identification and quantification of numerous compounds within a sample, providing detailed information about the plant's phytochemical constituents (Jain et al., 2024).

Diabetes mellitus is a persistent endocrine condition that effect the metabolic processes of carbohydrates, proteins, fats, electrolytes, and water. It includes a range of metabolic diseases marked by hyperglycemia, where elevated blood glucose levels result due to inadequate insulin secretion by the pancreas or cellular resistance to insulin (Nair et al., 2013).

Alpha-amylase and alpha-glucosidase are key enzymes that play a crucial role in carbohydrate metabolism. Alpha-amylase initiates the hydrolysis of complex carbohydrates into smaller oligosaccharides, while alpha-glucosidase further converts these products, including starch and disaccharides, into absorbable glucose units. These enzymes are essential for proper digestion and glucose absorption in the intestinal tract. Inhibiting their activity has emerged as a promising strategy for managing type 2 diabetes, as it can effectively reduce the rapid rise in blood glucose levels following a meal. By targeting these carbohydrate-digesting enzymes, it is possible to delay glucose release and absorption, offering a therapeutic avenue to control postprandial hyperglycemia (Subramanian et al., 2008).

Several invitro & invivo work has been done so far; Singh et al., 2013, demonstrated the anti-hyperglycemic effects of methanolic leaf extract of *A. hookeri* in diabetic Wistar rats, significantly reducing key biochemical parameters to normal levels. Park et al., 202 found that the plant's aqueous extract lowered glycated hemoglobin in prediabetic patients over eight weeks. Deka et al., 2022, observed that in high-fat diet-induced diabetic rats, the methanolic extract reduced body weight and blood glucose levels, improved antioxidant markers, and enhanced glucose metabolism. *A. hookeri* exhibits significant anti-diabetic properties, effectively reducing blood glucose levels and improving various biochemical parameters in both animal and human studies Kim et al., 2015, but it lacks molecular docking studies.

The aims of present study are focused on

- Identification of various bioactive compounds from methanolic leaves extract of *A. hookeri* by GC–MS analysis.
- Investigation of the potential inhibiting efficiency of selected bioactive compounds against alpha glucosidase and alpha amylase, by using drug-likeness characteristics, molecular docking and bioavailability radar assay.

2. MATERIALS AND METHODS

2.1. Collection of Plant Material

Plant sapling of *A. hookeri* were collected from Bhowali station Nanital (Uttrakhand) and grown in Botanical Garden of CCSU, Meerut at month of October. Leaves of plant were harvested in month of April 2024 for experimental purpose.

2.2. Preparation of Plant Extracts

The collected plant material, comprising whole plant were thoroughly cleaned. Each plant part was separated, air-dried, and only leaves were ground into a fine powder for further analysis. The powdered samples were extracted using methanol in soxhlet, to obtain crude extracts rich in bioactive compounds.

2.3. Gas Chromatography-Mass Spectrometry (GC-MS) Analysis

The extracted samples were analyzed using Gas Chromatography-Mass Spectrometry (GC-MS) to identify and measure their chemical constituents. A high-resolution instrument with a fused silica capillary column, specifically the SH-Rxi-5Sil MS column (5% biphenyl and 95% dimethyl polysiloxane), measuring 30 meters in length, 0.25 mm in inner diameter, and with a 0.25 μm film thickness, was employed. The study was conducted at a temperature range of 320-350°C. Helium (He) was used as the mobile phase, flowing at 1.0 ml/min. The gas chromatography process started at 50°C and increased to 300°C at a rate of 5°C/min. A 1 microliter injection volume was used. Samples dissolved in methanol, were analyzed within a mass-to-charge ratio (m/z) range of 50-650. The results were compared using an integrated chemical library search program that identified individual compounds based on their retention times

and mass spectra. Peak integration and area normalization quantified the relative abundance of each compound in the sample (Jain et al., 2024).

2.4. Molecular Docking

2.4.1. Library generation and protein retrieval

All the compounds identified through GC-MS analysis from methanolic extract of *A. hookeri* leaves were used as ligand for molecular docking studies. The 3D conformations of the selected compounds were sourced from the PubChem database (https://pubchem.ncbi.nlm.nih.gov)." in an SDF file format then converted into PDBQT format by using Open Babel GUI (O'Boyle et al., 2011). The 3D protein structure of the target enzyme alpha-glucosidase and alpha-amylase with PDB ids 3L4W and 4W93 respectively were downloaded from protein data bank RCSB PDB (https://www.rcsb.org/) in PDB (Protein Databank) format and converted it into PDBQT format by Autodock 4.2. (Morris et al., 2009). Both protein subjected to Energy Minimization and optimization with the help of SPDBV, to become it stable. Now, both the proteins were used for performing the molecular Docking Process by using Autodock Vina (Morris et al., 2009).

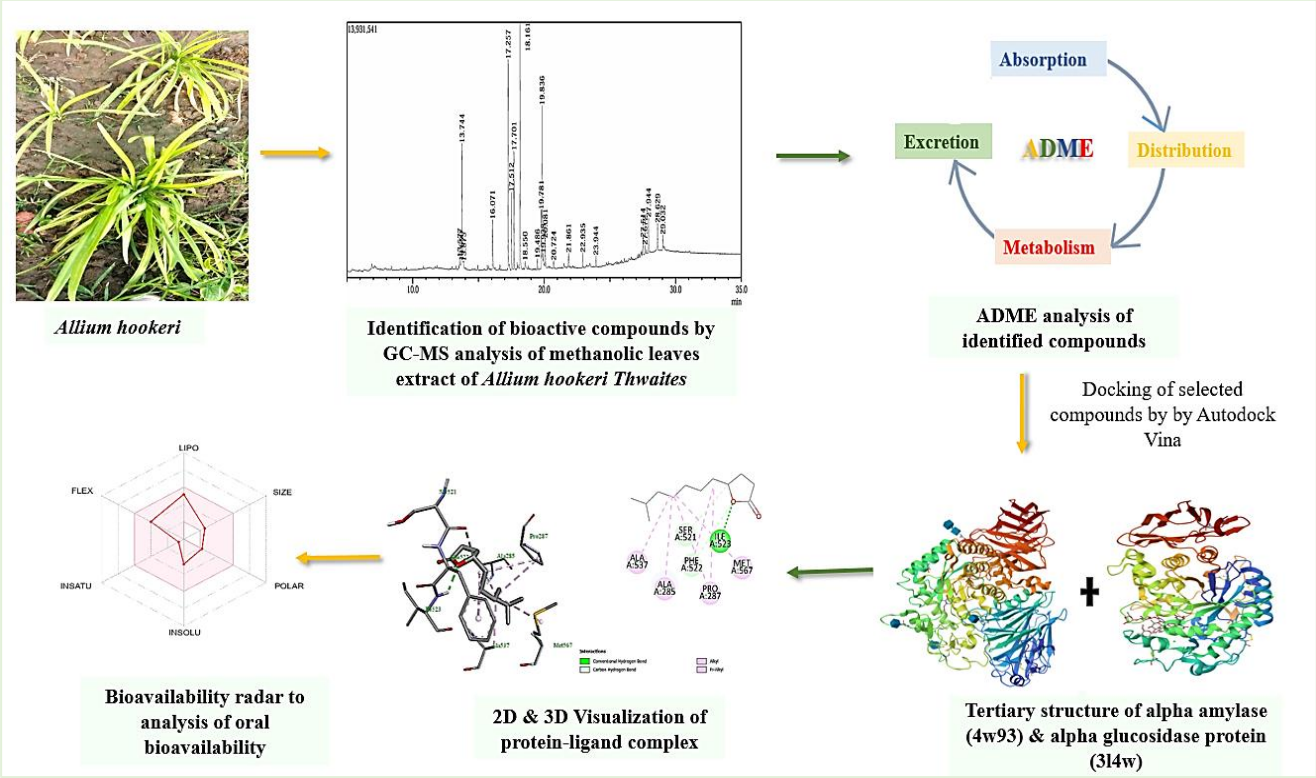


Figure. 1 Workflow of the present study

2.4.2. Physiochemical and ADMET Screening of the Compounds

Swiss-AdME, an online web server was used to measure the physiochemical, pharmacokinetic and toxicological properties of the compounds. Different parameters like Blood-Brain absorption (BBB), Human intestinal absorption (HIA), CaCo2 permeability, and clearance of a drug 9CL) was used to scoring the ADMET properties (Agrawal et al., 2025). Swiss-AdME was used to determination of physiochemical parameters like molecular weight (MW), hydrogen bond donar (HBD), hydrogen bond acceptor (HBA), lipophilicity, log (log p), molar refractivity (MR), number of rotatable bonds (nRot) and drug-likeness (Daina et al., 2017). SwissADME's algorithm is based on Lipinski's rule of five and provides an accessible interface for those unfamiliar with computer-aided drug design (Gulati et al., 2021).

2.4.3. Molecular docking studies

The molecular docking studies of all the selected compounds and proteins were performed by using AutoDock Vina (Morris et al., 2009). The GRID box values for the receptor active site dimensions were set at 45.424 x 92.375 x 34.811 XYZ coordinates for α-glucosidase and -9.682 x 4.274 x -23.145 XYZ coordinates for alpha amylase with 0.375 grid spacing for each atom type and kept box dimension as 40 A^0 x 40 A^0 x 40 A^0 (Amin et al., 2022). Ten confirmations were obtained for each docking experiment, each with a corresponding binding affinity expressed in kcal/mol. For further studies, the ligand-binding position with the lowest binding energy was selected. In our investigation, the phytochemicals that have strong interactions with both target enzymes were further examined.

2.4.4. Visualization of Ligand-Protein interaction

The best possible 2D & 3D structures between ligand and protein were analyzed using Discovery Studio Visualizer for different interactions such as conventional H Bond, Vander wall interactions, Carbon H Bond, Pi-Alkyl, Pi-Sulphur, Pi-Sigma, Pi-Anion and Alkyl are visualized (Design et al., 2014).

2.4.5. Bioavailability radar

The drug-likeness of the selected compounds that shows their binding energy with both enzymes were analyzed by considering six physiochemical properties and forming a bioavailability radar by using the SwissADME tool (https://www.swissadme.ch/). The six evaluated parameters are ligand flexibility, lipophilicity, polarity, saturation, size, and solubility. For a compound to be considered drug-like, its red line must be entirely within the pink area. The pink-shaded regions define the optimal values of all the six parameters, and any deviation from them suggests the ligand not being orally bioavailable (Daina et al., 2017). The workflow of the present study given in figure 1.

3. RESULTS

3.1. Identification of Bioactive compounds through GC-MS analysis

The methanolic extract of *A. hookeri* leaves was subjected to biochemical profiling using GC-MS analysis. A total of 15 peaks corresponding to the bioactive compounds were identified. The identification carried out by correlating their retention times, peak areas, peak heights, and fragmentation patterns with reference spectra from the National Institute of Standards and Technology (NIST) database. Overall, 20 different phytocompounds identified in the methanol extracts from leaves, of *A. hookeri* (Table 2) along with their retention time and reported biological activity. The GC-MS chromatogram which shows peak 1 with an m/z value of 149.00, corresponding to 3-Methylbenzyl alcohol, a TBDMS derivative while Peak 2, with an m/z value of 191.05, 2,4-Di-tert-butylphenol. Peak 3, 4, 5 and 6 with m/z 74.00, 74.00, 73.00, and 74.00 respectively, reveal the presence of Undecanoic acid, Dodecanoic acid, 1,1,1,5,7,7,7-Heptamethyl-3,3-bis(trimethylsiloxy)tetrasiloxane and methyl tetradecanoate which are fatty acid compounds. Peak 7, 8, 9 with an m/z value 68.05, 82.05 and 82.05 are shown the presence of compound Neophytadiene. Peak 10 with an m/z value 74.00, indicates the compound is Hexadenoic acid, methyl ester. Peak 11 and peak 12 with m/z value 85.00 are n-Hexadecanoic acid, and 10-Methylundecan-4-olide respectively. Peak 13 with an m/z value 67.00 is 9,12-Octadecadienoic acid (Z,Z)-, methyl ester, and peak 14 with an m/z value is 55.00 is 9-Octadecenoic acid, methyl ester, (E)-. Peak 15 and peak 16 with m/z value 71.00 and 74.00 represents the presence of Phytol and Methylsterate. Peak 17, 18, 19, 20 with m/z value 73.00 represents Cyclononasiloxane octadecamethyl-repetitively. Peak 21 with an m/z value 147.10 is beta-Sitosterol acetate, and peak 22 with an m/z value 165.00 is Vitamin E. Peak 23, 24 and 25 with an m/z value 430.20, 239.10, 43.05 represents compounds (.+/-.)-.alpha.-Tocopherol acetate, 16-Hentriacontanone and gamma-Sitosterol respectively. The GC-MS chromatogram of different peaks corresponding to their respective compounds are given in figure.2, Table 1. Molecular docking analyses were performed on all the selected compounds against alpha glucosidase & alpha amylase and among them two compounds namely Hexadecanoic acid, methyl ester and Vitamin E are not available on Pubchem database (Kim et al., 2016) Table 3.

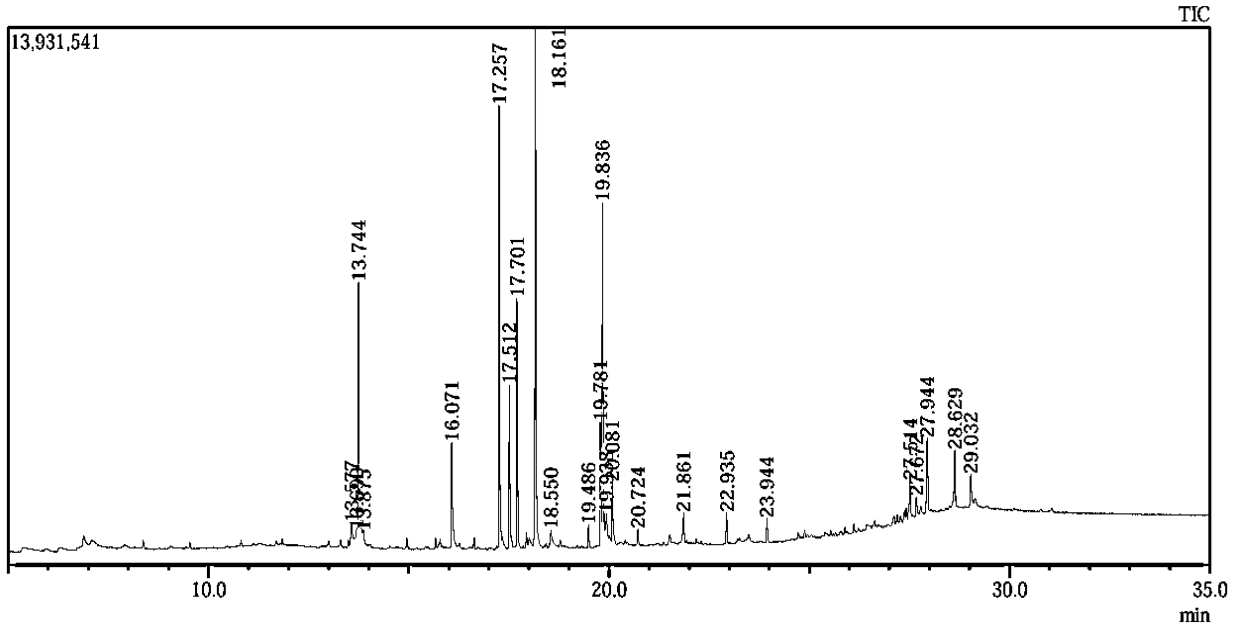


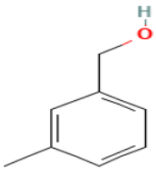
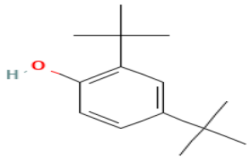
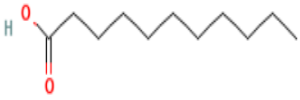
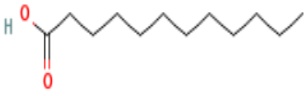
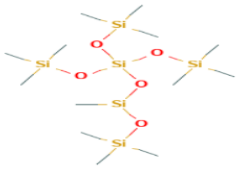
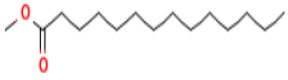
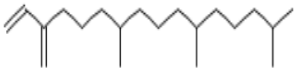
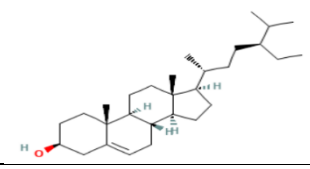
Figure. 2. GC-MS chromatographic profile of the methanolic leaf extract of *Allium hookeri*

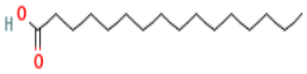
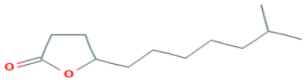
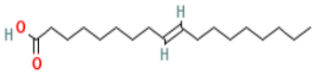
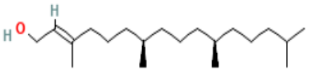
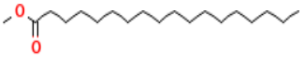
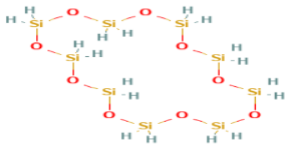
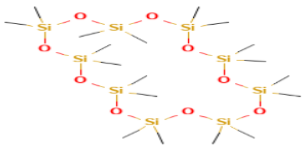
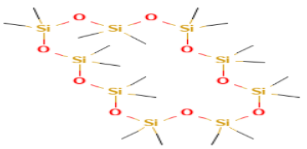
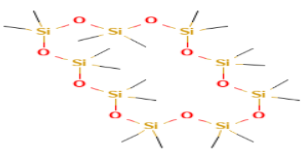
Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	4.140	990307	0.78	442274	0.63	3-Methylbenzyl alcohol, TBDMS derivative	149.00
2	13.577	1520876	1.20	612878	0.87	2,4-Di-tert-butylphenol	191.05
3	13.690	1856936	1.46	406138	0.58	Undecanoic acid, 10-methyl-, methyl ester	74.00
4	13.744	13736631	10.83	6814108	9.70	Dodecanoic acid, methyl ester	74.00
5	13.875	914548	0.72	332805	0.47	1,1,1,5,7,7,7-Heptamethyl-3,3-bis(trimethylsil	73.00
6	16.071	5355851	4.22	2685293	3.82	Methyl tetradecanoate	74.00
7	17.257	18013906	14.20	11406204	16.24	Neophytadiene	68.05
8	17.512	7376771	5.81	4220352	6.01	Neophytadiene	82.05
9	17.701	10062995	7.93	6436807	9.17	Neophytadiene	82.05
10	18.161	21870404	17.24	13417012	19.11	Hexadecanoic acid, methyl ester	74.00
11	18.550	781562	0.62	352566	0.50	n-Hexadecanoic acid	85.00
12	19.486	1036104	0.82	586041	0.83	10-Methylundecan-4-olide	85.00
13	19.781	5267988	4.15	3198729	4.56	9,12-Octadecadienoic acid (Z,Z)-, methyl este	67.00
14	19.836	15719458	12.39	8876578	12.64	9-Octadecenoic acid, methyl ester, (E)-	55.00
15	19.938	2609581	2.06	804685	1.15	Phytol	71.00
16	20.081	3733389	2.94	1607979	2.29	Methyl stearate	74.00
17	20.724	715942	0.56	405471	0.58	Cyclononasiloxane, octadecamethyl-	73.00
18	21.861	1338511	1.06	710708	1.01	Cyclononasiloxane, octadecamethyl-	73.00
19	22.935	1404036	1.11	783943	1.12	Cyclononasiloxane, octadecamethyl-	73.00
20	23.944	1112146	0.88	599945	0.85	Cyclononasiloxane, octadecamethyl-	73.00
21	27.514	1728871	1.36	949312	1.35	.beta.-Sitosterol acetate	147.10
22	27.672	1055359	0.83	491146	0.70	Vitamin E	165.00
23	27.944	4231723	3.34	1897516	2.70	(.+/-.)-.alpha.-Tocopherol acetate	430.20
24	28.629	2551477	2.01	1380637	1.97	16-Hentriacontanone	239.10
25	29.032	1876998	1.48	801582	1.14	.gamma.-Sitosterol	43.05
		126862370	100.00	70220709	100.00		

Table 1. GC-MS Identified compounds with their Peak value, Retention Time, % Area and M/Z ratio

Table 2. List of Bioactive Compounds Identified through GC-MS analysis from methanolic extract of *A. hookeri* leaves

GC-MS identified Compounds	Molecular weight (g/mol)	Molecular formula	Retention Time	Class of compound	Structure	Reported activity	Reference
3-Methylbenzyl alcohol	122.07	C8H10O	4.14	Alcohol		Biodegradation (Toulene, m-xylene, p-xylene)	Duetz et al., 1998
2,4-Di-tert-butylphenol	206.17	C14H22O22	13.577	Phenols		Antioxidant	Choi et al., 2013
Undecanoic acid	186.16	C11H2202	13.69	Fatty acids		Antifungal	Rossi et al., 2021
Dodecanoic acid	200.18	C12H22O2	13.744	Fatty acids		Antiseizure	Sills et al., 1986
1,1,1,5,7,7,7-Heptamethyl-3,3-bis(trimethylsiloxy) Tetrasiloxane	443.149	C13H39O5Si6	13.875	Hydro-carbon		Anti-quorum sensing	Sharma et al., 2023
Methyl tetradecanoate	242.4	C15H30O2	16.071	Fatty acids		Not found	
Neophytadiene	278.5	C20H38	17.257, 17.512, 17.701	Terpene		Neuro-pharmacological effects	Gonzalez-Rivera, et al., 2023
gamma. -Sitosterol	414.5	C29H50O	29.032	Terpene		Antidiabetic	Balamurugan et al., 2011

Hexadeconoic acid, methyl ester			18.161	Fatty acid	-	Not Found	
n-Hexadecanoic acid	256.42	C16H32O2	18.55	Fatty acid		Antiviral	Pal et al., 2024
10-Methylundecan-4-olide	198.3	C12H22O2	19.486	-		Not Found	
9,12-Octadecadienoic acid (Z,Z)-, methyl ester	294.5	C19H34O2	19.781	Fatty acid		Anti-inflammatory	Selvan et al., 2015
9-Octadecenoic acid, methyl ester, (E)	282.5	C18H3402	19.836	Fatty acid		Anti-spasmodic and immune modulators	Al-Marzoqi et al 2016
Phytol	296.5	C20H40O	19.938	Di-terpene		Antioxidant & Antinociceptice	Santos et al., 2013
Methyl stearate	298.5	C19H38O2	20.081	Fatty acid		Nematicidal Effect	Lu et al., 2020
Cyclononasiloxane	414.9	H18O9Si9	20.724	Fatty acid		Not found	
Cyclononasiloxane, octadecamethyl-	667.4	C18H54O9Si9	21.861	Fatty acid		Antiulcer	Syed et al., 2022
Cyclononasiloxane, octadecamethyl-	667.4	C18H54O9Si9	22.935	Fatty acid		Antiulcer	Syed et al., 2022
Cyclononasiloxane, octadecamethyl-	667.4	C18H54O9Si9	23.944	Fatty acid		Antiulcer	Syed et al., 2022

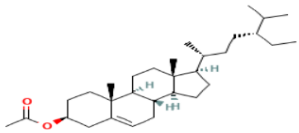
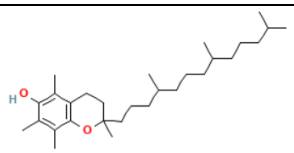
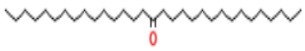
beta.-Sitosterol acetate	456.7	C31H52O2	27.514	Terpenes		Anti-inflammatory & Antioxidant	El-Feky et al., 2023
Vitamin E		Not found	27.672	Vitamin	Not found	Antioxidant	Cahoon et al., 2003
(.+/-.)-.alpha.-Tocopherol acetate	472.7	C31H52O3	27.944	Vitamin		Neural recovery & Protective effect for UVB irradiation	Zhu et al., 2024 & Saral et al., 2002
16-Hentriacontanone	450.8	C31H62O	28.629	Fatty acid		Anxiety	Onofre-Campos et al., 2017

Table 3. Identified compounds with their CID & Canonical smile source (PubChem)

S. no	Compound Name	CID	Canonical smiles
1	3-Methylbenzyl alcohol	11476	CC1=CC(=CC=C1)CO
2	2,4-Di-tert-butylphenol	7311	CC(C)(C)C1=CC(=C(C=C1)O)C(C)(C)C
3	Undecanoic acid	8180	CCCCCCCCCCC(=O)O
4	Dodecanoic acid	3893	CCCCCCCCCCCC(=O)O
5	1,1,1,5,7,7,7-Heptamethyl-3,3-bis(trimethylsiloxy)tetrasiloxane	6329081	C[Si](O[Si](C)(C)C)O[Si](O[Si](C)(C)C)(O[Si](C)(C)C)O[Si](C)(C)C
6	Methyl tetradecanoate	31284	CCCCCCCCCCCCCC(=O)OC
7	Neophytadiene	10446	CC(C)CCCC(C)CCCC(C)CCCC(=C)C=C
8	Hexadeconoic acid, methyl ester	-	Not available
9	n-Hexadecanoic acid,	985	CCCCCCCCCCCCCCCC(=O)O
10	10-Methylundecan-4-olide	21778194	CC(C)CCCCCC1CCC(=O)O1
11	9,12-Octadecadienoic acid (Z,Z)-,	5280450	CCCCCC=CCC=CCCCCCCCC(=O)O
12	9-Octadecenoic acid	637517	CCCCCCCCC=CCCCCCCCC(=O)O
13	Phytol	5280435	CC(C)CCCC(C)CCCC(C)CCCC(=CCO)C
14	Methyl stearate	8201	CCCCCCCCCCCCCCCCCC(=O)OC
15	Cyclononasiloxane	71358777	O1[SiH2]O[SiH2]O[SiH2]O[SiH2]O[SiH2]O[SiH2]O[SiH2]O[SiH2]O[SiH2]1
16	beta-Sitosterol acetate	5354503	CCC(CCC(C)C1CCC2C1(CCC3C2CC=C4C3(CCC(C4)OC(=O)C)C)C(C)C

17	Vitamin E	-	Not available
18	(.+/-.)-.alpha.-Tocopherol acetate	2116	CC1=C(C2=C(CCC(O2)(C)CCCC(C)CCCC(C)CCCC(C)C)C(=C1O)C)C
19	16-Hentriacontanone	94741	CCCCCCCCCCCCCCCC(=O)CCCCCCCCCCCCCCC
20	gamma.-Sitosterol	457801	CCC(CCC(C)C1CCC2C1(CCC3C2CC=C4C3(CCC(C4)O)C)C)C(C)C

3.2. In silico Docking Studies

The GC–MS analysis revealed that *A. hookeri* leaf methanolic extracts contained 20 different bioactive compounds. Out of them Hexadeconoic acid methyl ester and Vitamin E are not avaliabe on Pubchem (Kim et al., 2016). All the available compounds with their Compound ID and Canonical smiles represents in Table 3. All these identified compounds were subjected to molecular docking studies against alpha amylase (4w93) & alpha glucosidase (3l4w) by using Autodock vina (Morris et al., 2009). Out of twenty GC-MS identified compounds, only thirteen compounds namely (n-Hexadecanoic acid, (.+/-.)-.alpha.-Tocopherol, Dodecanoic acid, 2,4-Di-tert-butylphenol, Undecanoic acid, Neophytadiene, 3-Methylbenzyl alcohol, Methyl tetradecanoate, gamma-Sitosterol, 9,12-Octadecadienoic acid (Z,Z)-, 9-Octadecenoic acid, Phytol and 10-Methylundecan-4-olide) shows binding interaction with both enzyme The compound gamma-Sitosterol formed highest binding energy with alpha amylase and alpha glucosidase i.e., -9.3kcal/mol and -8.1 kcal/mol respectively among all selected compounds. However, gamma-Sitosterol formed 1 H-bond on amino acid Asp 474 with alpha amylase and no H-bond formed with alpha glucosidase (figure. 3, Table 4 & 5). Binding interactions of all thirteen selected compounds of *A. hookeri* with interacting amino acid were analysed using Discovery Studio Vizualizer (Design et al., 2014). The different bonding interactions of ligand and protein residues are hydrogen, hydrophobic (alkyl), hydrophobic (pi-alkyl), pi-lone pair (Table 6).

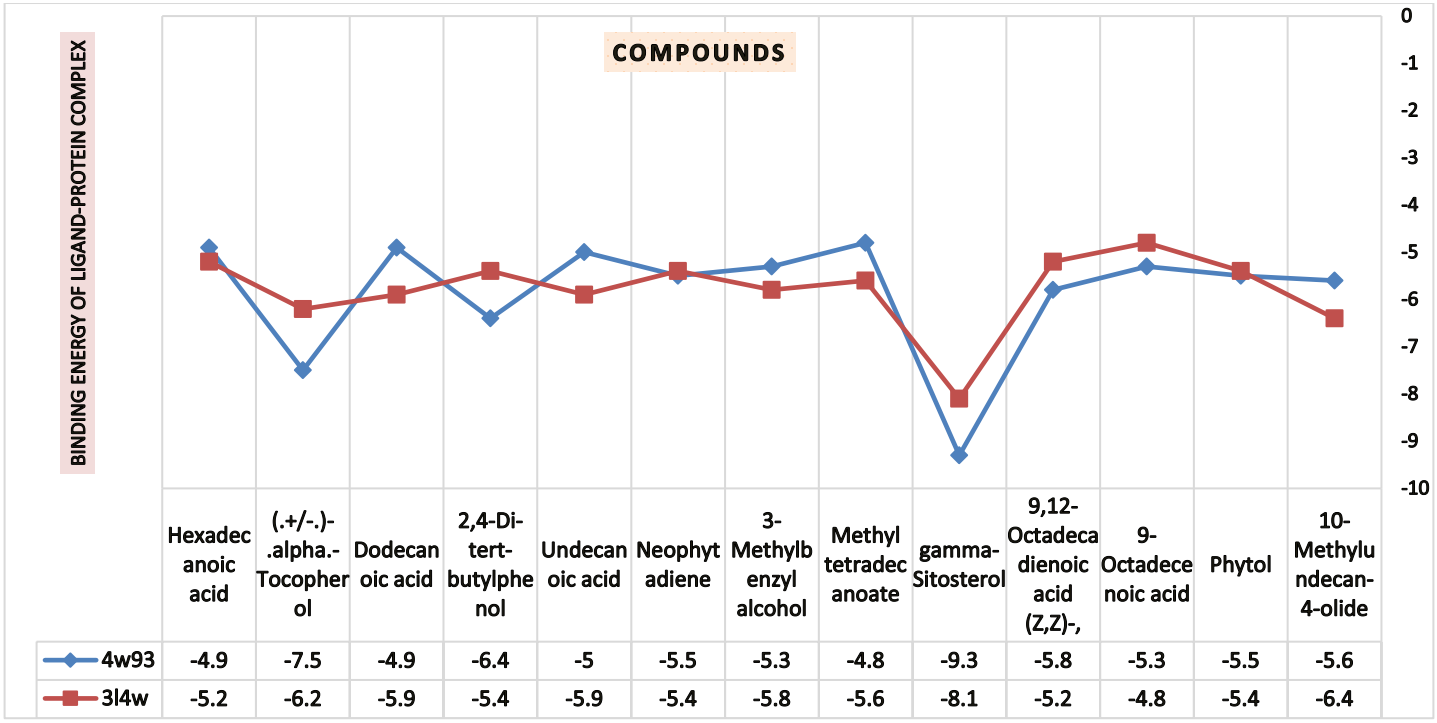


Figure 3. A graphical representation of binding energy between GC-MS identified compounds against alpha amylase (4w93) & alpha glucosidase (3l4w).

Table 4. Docking of alpha amylase with compounds identified through GC-MS analysis

Compound name	Binding Energy with alpha amylase	Number of H bonds involved in bonding	Amino acid involved in H bond
n-Hexadecanoic acid	-4.9	1	His201
(.+/-.)-.alpha.-Tocopherol	-7.5	-	--
Dodecanoic acid	-4.9	2	Asp197, Glu 233
2,4-Di-tert-butylphenol	-6.4	2	Asp197, Glu 233
Undecanoic acid	-5	1	Glu233
Neophytadiene	-5.5	-	--
3-Methylbenzyl alcohol	-5.3	2	Asp197, Arg195
Methyl tetradecanoate	-4.8	1	Gln63
gamma-Sitosterol	-9.3	-	--
9,12-Octadecadienoic acid (Z,Z)-,	-5.8	2	His299, Glu233
9-Octadecenoic acid	-5.3	1	His201
Phytol	-5.5	2	Glu233, Asp197
10-Methylundecan-4-olide	-5.6	1	Arg195

Table 5. Docking of alpha glucosidase with compounds identified via GC-MS analysis

Compound name	Binding Energy with alpha glucosidase	Number of H bonds involved in bonding	Amino acid involved in H bond
n-Hexadecanoic acid	-5.2	-	--
(.+/-.)-.alpha.-Tocopherol	-6.2	-	--
Dodecanoic acid	-5.9	2	Met567, Ala285
2,4-Di-tert-butylphenol	-5.4	-	--
Undecanoic acid	-5.9	2	Met567, Gly533
Neophytadiene	-5.4	-	--
3-Methylbenzyl alcohol	-5.8	2	Leu540, Glu182
Methyl tetradecanoate	-5.6	-	--
gamma-Sitosterol	-8.1	1	Asp474
9,12-Octadecadienoic acid (Z,Z)-,	-5.2	1	Asn449
9-Octadecenoic acid	-4.8	-	--
Phytol	-5.4	2	His600, Asp443
10-Methylundecan-4-olide	-6.4	1	Ile523

3.3. Physiochemical Properties of the Compounds by SwissADME & Bioavailability radar chart

All selected compounds were initially screened using Lipinski's rule of five to assess drug-likeness (Lipinski, 2004), and their ADME (Absorption, Distribution, Metabolism, and Excretion) profiles were predicted using SwissADME (Daina et al., 2017). Canonical SMILES retrieved from PubChem (Kim et al., 2016) were analyzed via the SwissADME tool for physicochemical properties. Table 7 summarizes the ADME predictions, the compounds such as 3-Methylbenzyl alcohol, 2,4-Di-tert-butylphenol, Undecanoic acid, and Dodecanoic acid showed high GI absorption and no Lipinski violations, indicating favorable oral bioavailability. Despite one Lipinski violation, compounds like n-Hexadecanoic acid and 9,12-Octadecadienoic acid (Z,Z) maintained high absorption and bioavailability scores (up to 0.85). In contrast, Neophytadiene, Phytol, and beta-Sitosterol acetate exhibited poor GI absorption and lacked BBB permeability, while some, including Cyclononasiloxane, showed high GI uptake but limited solubility due to lack of hydrogen bond donors.

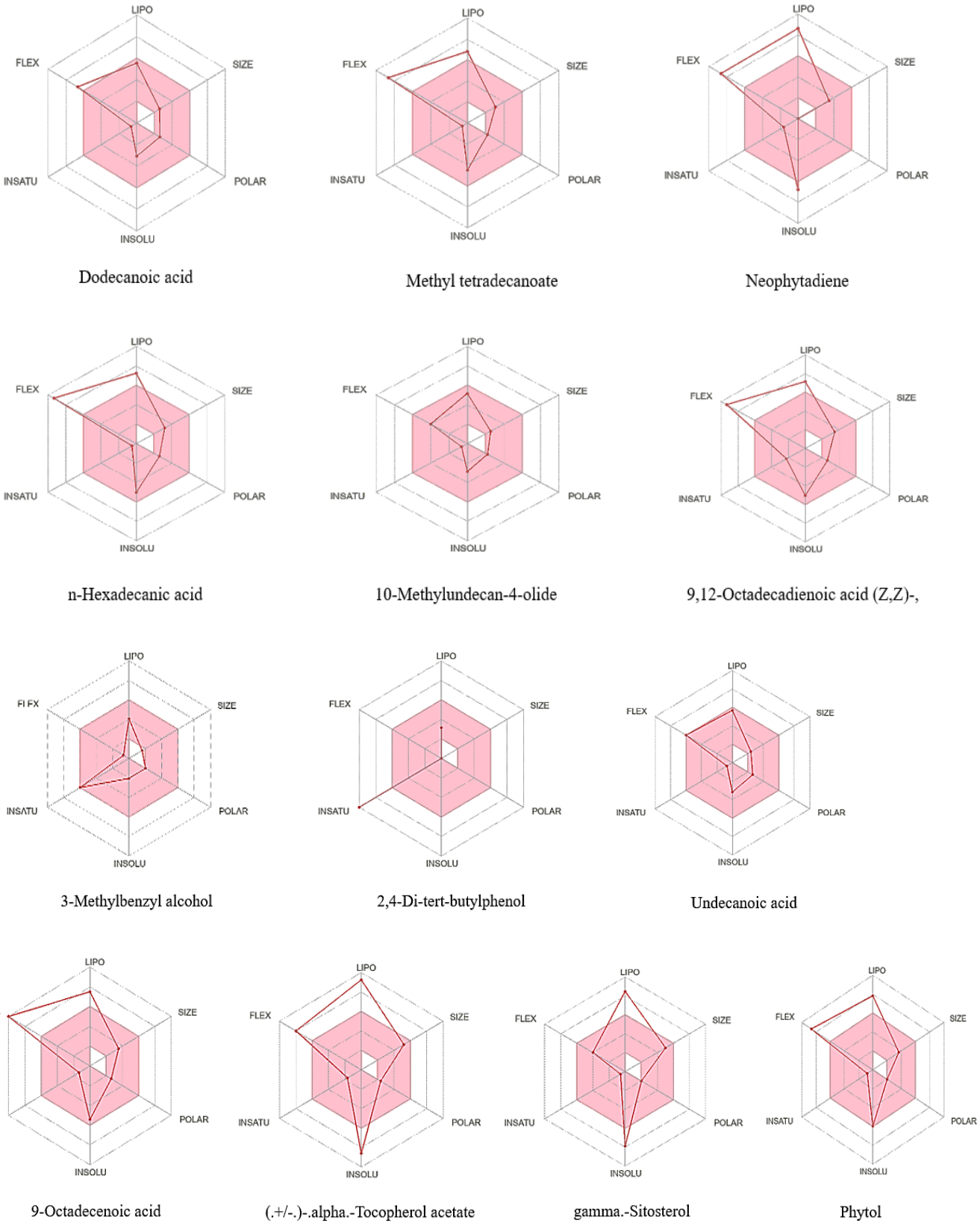
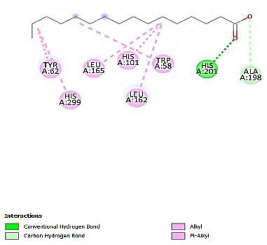
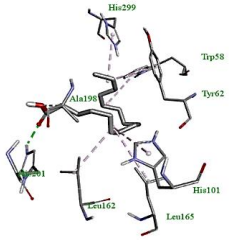
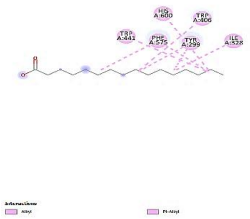
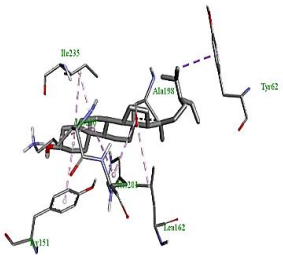
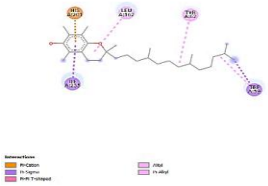
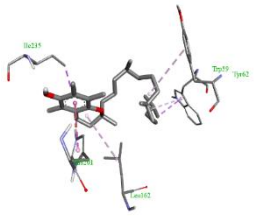
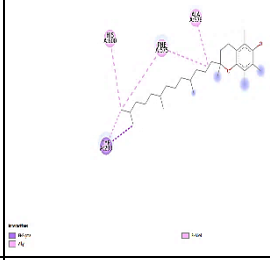
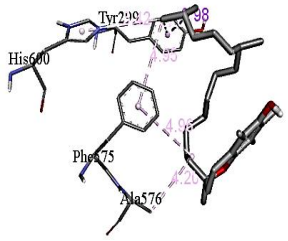
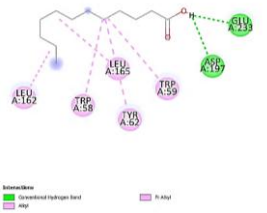
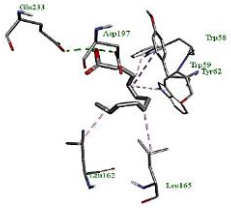
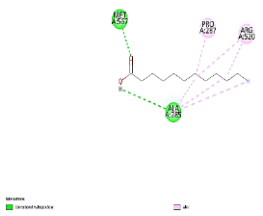
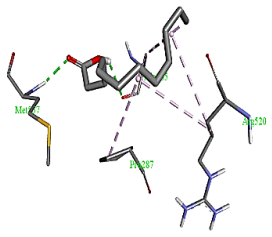
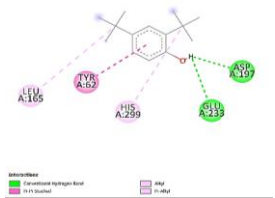
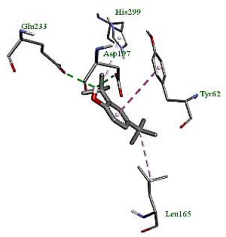
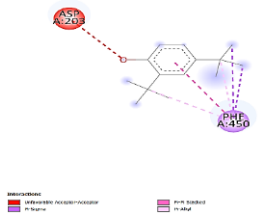
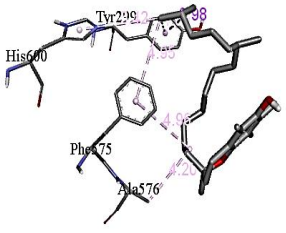
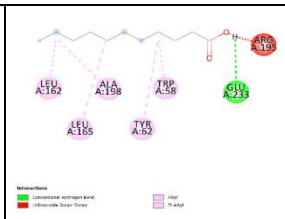
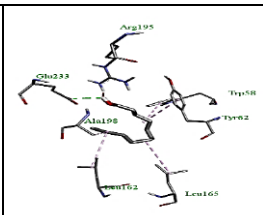
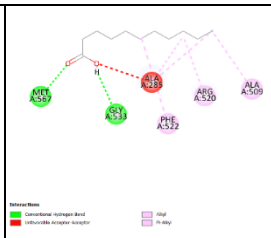
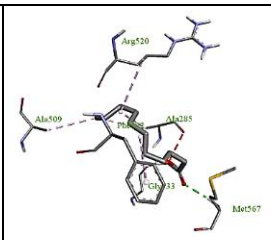
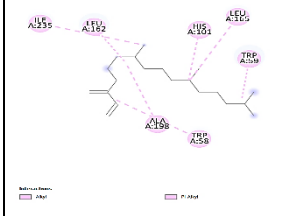
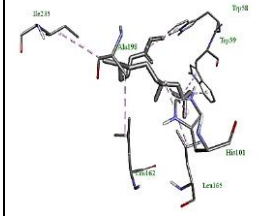
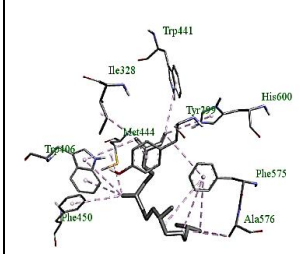
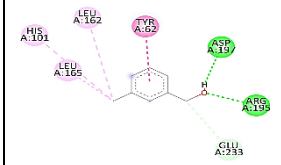
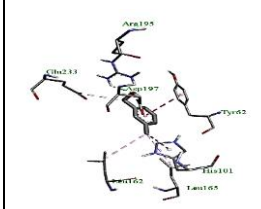
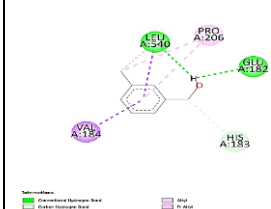
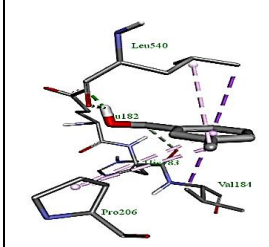
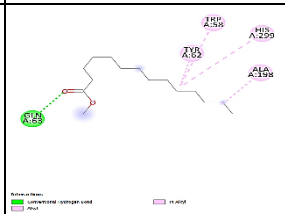
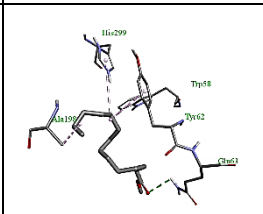
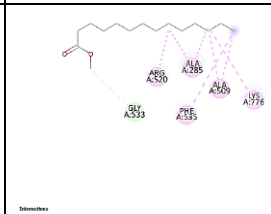
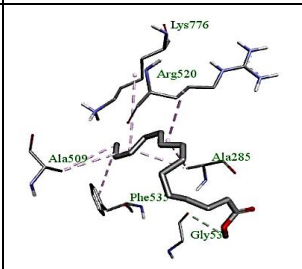
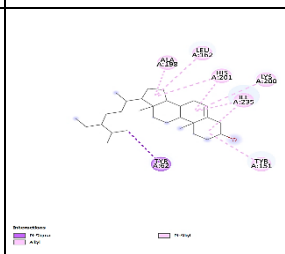
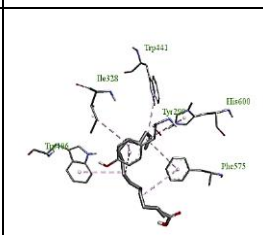
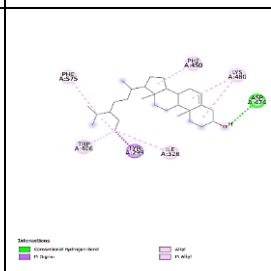
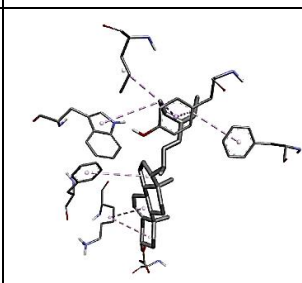
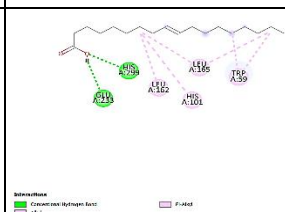
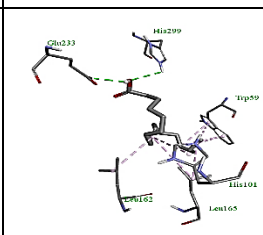
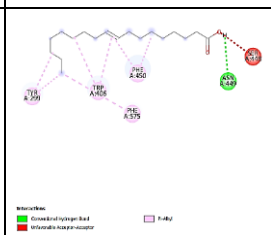
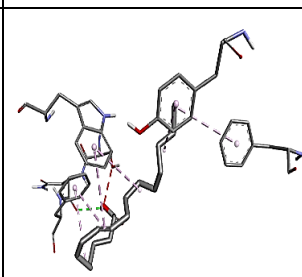


Figure.4. Analysis of drug-likeness property of thirteen compounds shows their binding affinity with enzyme alpha amylase & alpha glucosidase by using bioavailability radar.

Docking studies with AutoDock Vina revealed that 13 out of 18 compounds had binding affinity for both α-amylase (3L4W) and α-glucosidase (4W93), (Figure 4). Among them, 3-Methylbenzyl alcohol, Undecanoic acid, and 10-Methylundecan-4-olide met all physicochemical criteria, falling within the ideal bioavailability radar zone. This zone includes specific limits for lipophilicity, size, polarity, solubility, saturation, and flexibility, confirming their potential as orally bioavailable therapeutic candidates.

Table 6. Diagrams showing 2D & 3D interaction between Ligand-Protein complexes

Compound name	2D interaction with Alpha amylase	3D interaction with Alpha amylase	2D interaction with Alpha glucosidase	3D interaction with Alpha glucosidase
n-Hexadecanoic acid,				
(.+/-.)-alpha.-Tocopherol acetate				
Dodecanoic acid				
2,4-Di-tert-butylphenol				

Undecanoic acid				
Neophytadiene				
3-Methylbenzyl alcohol				
Methyl tetradecanoate				
gamma.-Sitosterol				
9-Octadecenoic acid				

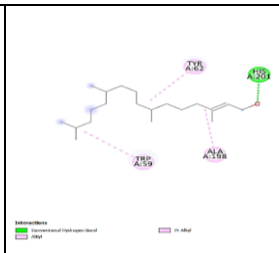
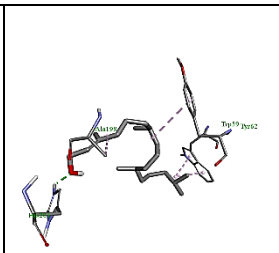
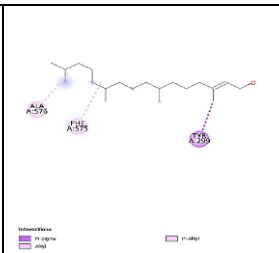
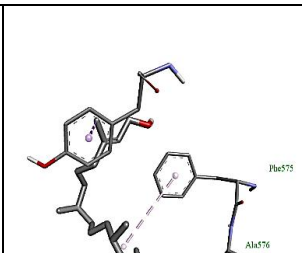
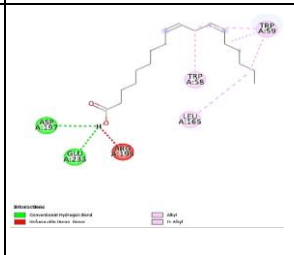
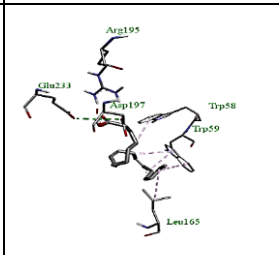
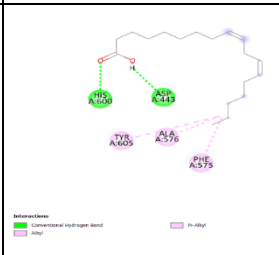
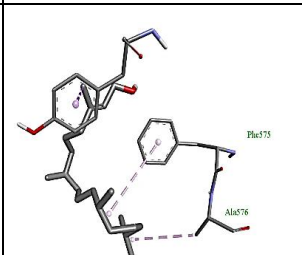
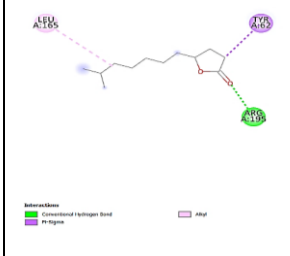
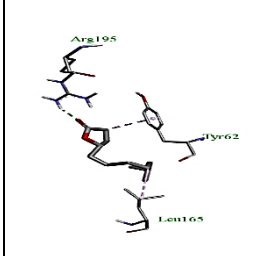
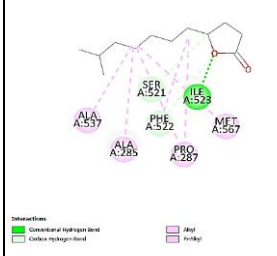
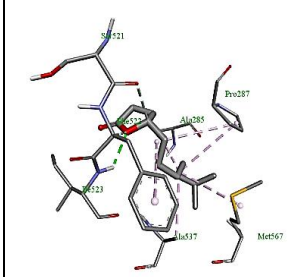
Phytol				
9,12-Octadecadienoic acid (Z,Z)				
10-Methylundecan-4-olide				

Table 7. ADME properties of selected compounds Predicted by SWISS-ADME

Compound name	Formula	MW	Rotatable bonds	H-bond acceptors	H-bond donors	GI absorption	BBB permeant	Lipinski violations	Bioavailability Score
3-Methylbenzyl alcohol	C8H10O	122.16	1	1	1	High	Yes	0	0.55
2,4-Di-tert-butylphenol	C14H22O	206.32	2	1	1	High	Yes	0	0.55
Undecanoic acid	C11H22O2	186.29	9	2	1	High	Yes	0	0.85
Dodecanoic acid	C12H24O2	200.32	10	2	1	High	Yes	0	0.85
1,1,1,5,7,7,7-Heptamethyl-3,3-bis(trimethylsiloxy)tetrasiloxane	C13H39O5Si6	443.96	10	5	0	High	Yes	0	0.55
Methyl tetradecanoate	C15H30O2	242.4	13	2	0	High	Yes	0	0.55

Neophytadiene	C20H38	278.52	13	0	0	Low	No	1	0.55
n-Hexadecanoic acid,	C16H32O2	256.42	14	2	1	High	Yes	1	0.85
10-Methylundecan-4-olide	C12H22O2	198.3	6	2	0	High	Yes	0	0.55
9,12-Octadecadienoic acid (Z,Z)-,	C18H32O2	280.45	14	2	1	High	Yes	1	0.85
9-Octadecenoic acid	C18H34O2	282.46	15	2	1	High	No	1	0.85
Phytol	C20H40O	296.53	13	1	1	Low	No	1	0.55
Methyl stearate	C19H38O2	298.5	17	2	0	High	No	1	0.55
Cyclononasiloxane	H18O9Si9	414.91	0	2	0	High	No	1	0.55
beta-Sitosterol acetate	C31H52O2	456.74	8	2	0	Low	No	1	0.55
(.+/-.)-.alpha.-Tocopherol acetate	C29H50O2	430.71	12	2	1	Low	No	1	0.55
16-Hentriacontanone	C31H62O	450.82	28	1	0	Low	No	1	0.55
gamma.-Sitosterol	C29H50O	414.71	6	1	1	Low	No	1	0.55

4. DISCUSSION

It is well well-known that medicinal plants possess a wide range of chemicals capable of preventing or treating numerous diseases. Notably, the phytocompounds identified through GC-MS profiling of methanolic extracts from *A. hookeri* leaves have demonstrated antidiabetic activity via molecular docking studies against two enzymes alpha glucosidase and alpha amylase. These phytocompounds likely contribute to the medicinal properties attributed to *A. hookeri*. Computational methods are invaluable in pharmaceutical research, assisting the discovery and development of new therapeutic the exploration and formulation of new treatment strategies especially when combined with molecular docking techniques (Sliwoski et al., 2013). Numerous research groups have employed these techniques to screen potential new compounds against various diseases (Sharma et al., 2023). Additionally, in silico predictions have been made regarding the absorption, distribution, metabolism, excretion (ADME), therapeutic potential, and safety profile of these compounds. In the present study, we utilized a molecular docking to evaluate the binding affinities of selected phytocompounds from *A. hookeri* against diabetes targeting enzymes alpha-amylase (4w93) and alpha-glucosidase (3l4w). This investigation aimed to assess the enzyme inhibitory potential of the ligand–protein complexes, as well as the drug-likeness and toxicity predictions of the selected phytocompounds.

5. CONCLUSION

The outcomes of this study show that methanolic leaves extract of *A. hookeri* is abundant in bioactive phytochemicals, which may contribute to its antidiabetic and health-promoting properties. The binding modes and energies of GC-MS identified phytochemicals against the target enzymes alpha amylase (4w93) & alpha glucosidase (3l4w), analyzed through molecular docking studies via Autodock Vina. Total 20 different phytochemicals were identified through GC-MS analysis. These compounds were screened using Lipinski's rule of five and drug-likeness parameters. Only eighteen compounds that obeyed Lipinski's rules were subjected to molecular docking against alpha amylase (4w93) & alpha glucosidase (3l4w). Thirteen phytochemicals showed binding affinity with both enzymes individually, while only three compounds 3-Methylbenzyl alcohol, Undecanoic acid, and 10-Methylundecan-4-olide were found to be orally bioavailable. Among the thirteen compounds, 10-Methylundecan-4-olide has a high binding affinity with alpha-amylase (4w93) and alpha glucosidase (3l4w), i.e., -5.6kcal/mol & -6.4kcal/mol, respectively and it also show that is the most

readily bioavailable phytochemical among the thirteen selected compounds. However, we recommend that future in vivo studies be conducted to explore the therapeutic and beneficial effects of these compounds in diabetic-related disorders.

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Authors Contribution
D.T. performed experimental work, and drafted the manuscript. V. M. supervised the research, data analysis, and reviewed the manuscript critically for important intellectual content.

Ethical Approval
Not applicable.

Informed Consent
Not applicable

Conflicts of interests
The authors declare that there are no conflicts of interests.

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Data and materials availability
All data associated with this study are present in the paper.

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