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RESEARCH ARTICLE

Identification of Novel Compounds from *Cissus quadrangularis* L. by Gas Chromatography-Mass Spectrometry Analysis

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Abstract

Cissus quadrangularis (L.) commonly known as Asthisamharaka, Hadjod or Bonesetter, is a medicinal plant belonging to the family Vitaceae. The roots and stems of this plant have traditionally been used for the management of bone fractures and various musculoskeletal disorders, including osteoarthritis, rheumatoid arthritis and osteoporosis. In the present study, an ethanolic extract of *C. quadrangularis* stem was prepared and subjected to gas chromatography-mass spectrometry (GC-MS) analysis for the characterization of its phytoconstituents. The analysis resulted in the tentative identification of seventeen compounds. Based on an extensive literature survey and comparison with previously reported GC-MS profiles of *C. quadrangularis*, these compounds were not found to have been previously reported from the stem extract of this species. The physicochemical, drug-likeness and pharmacokinetic properties of the tentatively identified compounds were further evaluated using *in silico* ADMET analysis. Among the identified constituents, four compounds namely (5α)-Pregnane-3,20α-diol, 14α,18α-[4-methyl-3-oxo-(1-oxa-4-azabutane-1,4-diyl)], [1,2,4] Triazolo[4,3-a] quinoxalin-4-amine, N-(2,3-dihydro-1,4-benzodioxin-6-yl), 4H-Pyrido[1,2-a] pyrimidin-4-one, 6-methyl-3-phenyl-2,3-dihydroxypropyl(E)-Docos-13-enoate diacetate, and 2-Ethoxy-6,6-dimethyl-9-thioxo-6,9-dihydro-7,8-dithia-5a-azabenzothiazole-6-sulfonic acid, (4-methoxyphenyl) showed comparatively favourable predicted physicochemical and pharmacological characteristics, including parameters related to drug-likeness, absorption, distribution, solubility and toxicity. These compounds may therefore represent potential candidates for further pharmacological investigation. However, their identities and biological activities require confirmation through isolation and structural characterization, followed by appropriate *in vitro*, *in vivo* and toxicological studies. The findings provide preliminary information on the phytochemical composition of *C. quadrangularis* stem and identify candidate constituents that warrant further investigation for their potential therapeutic relevance.

Keywords: Bone disorders, *C. quadrangularis*, GC-MS, Hadjod, Wound healing

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Introduction

Medicinal and spice plants are important sources of diverse secondary metabolites, including phenolic compounds and other bioactive constituents (Waman *et al*., 2024; Naik *et al*., 2025). *C. quadrangularis* L., commonly known as asthisamharaka, veldt grape, or winged treebine, is a perennial, dicot succulent climber with quadrangular fleshy twigs. It is widely distributed in the tropical and subtropical countries and indigenous to India, West Africa, Sri Lanka, Thailand and Bangladesh (Bhuvanasree *et al*., 2013; Sawangjit *et al*., 2017). It has a long history of use in traditional systems of medicine, particularly Ayurveda, where it is particularly used to cure bone fractures (Azam *et al*., 2023), haemorrhoids, scurvy, tumours, menstrual disorders, diarrhoea, dysentery, gout, leucorrhea (Jainu and Devi, 2004; Jainu *et al*., 2006; Rex and Ravi, 2020), musculoskeletal disorders, inflammation, and pain (Ghosh *et al*., 2021). The plant's wide reputation as *Asthisamharaka* or a bone-healing herb has instigated extensive pharmacological investigation, particularly its effects on bone healing and repair. According to Ayurveda, hadjod has sandhania property,

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so if hadjod juice is given with cow ghee, it cures a bone fracture. However, excessive consumption may cause dry mouth, headache, and diarrhoea, etc. In the Siddha system of medicine, this plant is used for weight loss (Oben, 2006). The herb helps in managing weight by improving the metabolism of the body and reducing obesity by preventing fat and lipid accumulation in the body and reducing triglyceride levels. This plants also possess antioxidant, antibacterial, antifungal, anti-inflammatory (Sarkar *et al*., 2016), antiflatulence, and anti-cancerous activities (Joseph and Rai, 2011). The stem of the plant cures scurvy, otorrhoea, epistaxis and its limewater paste cures asthma (Sundaran *et al*., 2020). The extract of *C. quadrangularis* also helps in wound healing due to its astringent and wound-healing properties (Abate *et al*., 2017).

Different plant parts of *C. quadrangularis,* particularly the stem, roots and aerial parts, have been used to cure different medical conditions. Ethnomedicinal studies report that the stem and root preparations have been traditionally employed for bone injuries and inflammatory conditions, whereas other preparations are used for digestive, dermatological and gynaecological complaints. However, ethnopharmacological rationale only does not provide relevance for clinical efficacy because it depends on many factors such as plant part, extraction method, preparation and dose. Phytochemical investigations of *C. quadrangularis* have demonstrated the presence of different chemical constituents such as triterpenoids, phytosterols, phenolics, flavonoids, stilbenes, iridoids, tannins, saponins, vitamins and other lipid-derived constituents. One systematic study (Bafna *et al*., 2021) documented the extensive phytochemical and pharmacological literature on *C. quadrangularis* and emphasized that the relationship between individual constituents and biological effects remains incompletely resolved. There is a need to explore more chemical constituents and investigate biological properties. The long history of medicinal use of *C. quadrangularis,* along with its diverse chemical profile, positions the species as a promising source of bioactive natural products. However, researchers have reported that variation in phytochemical composition depends on geographical origin, plant part, maturity, extraction solvent and analytical methodology, emphasizing the need for standardized phytochemical characterization (Mehta *et al*., 2001; Avula *et al*., 2021). Previous studies have reported the presence of compounds such as β-sitosterol, α-/β-amyrin, δ-amyrone, friedelin, taraxerol, taraxeryl acetate, onocer-7-ene-3α,21β-diol and onocer-7-ene-3β,21α-diol (Bhutani *et al*., 1984; Mehta *et al*., 2001). Besides this, the plant also possesses stilbenoid compounds such as resveratrol, piceatannol, pallidol, parthenocissine and quadrangularin derivatives, including quadrangularins A-C (Avula *et al*., 2021). The spectrometric and chromatographic analysis of the plant extracts provides information on the chemical constituents present in plants, which is useful in investigating the pharmacological activities (Konappa *et al*., 2020). These techniques are fast, accurate, and need a small amount of extract to detect bioactive compounds, including alkaloids, phenolics, flavonoids, and other plant metabolites (Baeshen *et al*., 2023). Modern chromatographic and mass-spectrometric investigations have considerably expanded knowledge of the phytochemical composition of *C. quadrangularis*. The UHPLC-PDA-MS analysis of stem and leaf extracts enabled the characterization and quantitative determination of several polyphenolic constituents, such as catechin, epicatechin, quercetin-3-O-β-glucopyranoside, kaempferol-3-O-glucoside, quercetin-3-O-rhamnoside, leachianol F, amurensin A, pallidol, resveratrol and quadrangularin A (Avula *et al*., 2021). Many of these compounds possess antioxidant, anti-inflammatory and other pharmacological properties. Previous GC–MS analysis of *C. quadrangularis* stem extracts has demonstrated the presence of several fatty acids and fatty-acid derivatives, including palmitic acid, stearic acid and linoleic acid, highlighting the chemical diversity of the stem and the utility of chromatographic-spectroscopic approaches for its phytochemical characterization (Chanda *et al*., 2013). More recently, untargeted GC-MS/MS metabolite profiling of *C. quadrangularis* stem detected 36 compounds, of which 21 were identified using the NIST14 mass-spectral library (Purohit *et al*., 2023). These mass spectrometric metabolite profiles obtained through different extraction and analytical conditions have shown considerable variation depending on the analytical conditions. Besides traditional uses, *C. quadrangularis* also possess diverse ethnomedicinal applications such as use in dietary supplements and herbal formulations, particularly for bone and musculoskeletal health. Recent studies have explored the incorporation of *Cissus quadrangularis* extracts and phytobioactives into advanced biomaterial systems for bone regeneration. These approaches include 3D-printed β-tricalcium phosphate scaffolds functionalized with *C. quadrangularis* extract-loaded polydopamine coatings, chitosan-collagen hybrid scaffolds, β-tricalcium phosphate-reinforced natural polymer composites, and nano-hydroxyapatite-based ceramic nano-cement

for localized delivery of phytobioactives. Collectively, these studies demonstrated enhanced osteogenic differentiation, biomineralization, cellular proliferation, and new bone formation, highlighting the increasing potential for translating *C. quadrangularis*-derived bioactives into pharmaceutical and biomedical applications (Nagarajan *et al*., 2015; Robertson *et al*., 2020; Nair *et al*., 2021; Liao *et al*., 2023; Gupta *et al*., 2023). Despite extensive investigation, important gaps remain in the chemical characterization of *C. quadrangularis*. Published studies have used different plant parts, extraction solvents, extraction procedures and analytical platforms, resulting in substantially different chemical profiles. Moreover, GC-MS identification is frequently based on comparison with commercial spectral libraries, whereas authentic-standard comparison, retention-index determination and orthogonal spectroscopic confirmation are not consistently reported. Therefore, systematic characterization of the phytochemical profile of *C. quadrangularis* stem using a clearly defined extraction and GC-MS analytical workflow remains relevant. In the present study, the stem extract of *C. quadrangularis* was subjected to GC-MS analysis to characterize its detectable chemical constituents and to provide a preliminary profile of its phytochemical composition. The identified compounds were evaluated through comparison with available mass-spectral library data and published information. Because library-based GC-MS matching does not by itself establish definitive molecular identity, compounds for which authentic-standard or orthogonal confirmation was unavailable were considered tentative identifications. The study therefore aims to contribute additional chemical information on *C. quadrangularis* stem while providing a basis for subsequent targeted isolation and structural confirmation of potentially bioactive constituents. The phytoconstituents present in the ethanolic stem extract were tentatively identified using gas chromatography-mass spectrometry (GC-MS). The identified compounds were subsequently subjected to assessment of their physicochemical and pharmacokinetic properties, including absorption, distribution, metabolism, excretion and toxicity (ADMET), using computational platforms such as ADMETlab 3.0 and pkCSM. These computational approaches provide a preliminary assessment of the drug-likeness, pharmacokinetic characteristics and potential safety profiles of the detected compounds and can assist in prioritizing promising candidates for further experimental investigation. By reducing the number of compounds requiring initial experimental screening, *in silico* approaches can help streamline the early stages of natural-product research and potentially reduce time, resource consumption and experimental costs.

Materials and Methods

Plants collection

The plants of *C. quadrangularis* were gathered from the campus of Allahabad University in the post-rainy season from September to December. The plant was identified by an eminent taxonomist, Professor Satya Narain, at the Department of Botany, Allahabad University, Allahabad. The voucher specimen was deposited in the Duthie Herbarium 'SID collection 'AU-101' in the Botany Department, Allahabad University. Plants were photographed using a Nikon L-310 (Fig. 1).



Fig. 1: The plants of *C. quadrangularis.*

Extract preparation

The collected stem was shade-dried for extraction and then ground to make powder. 10 g of powdered material was mixed with 250 ml of 90% ethanol and extracted by Soxhlet apparatus at the boiling point of the solvent for 6 h and 6 cycles h (*Lin et al*., 1999). After filtering, the extract was dried in the rotary evaporator at a temperature not exceeding 40°C and stored in airtight amber glass vials at -20°C until further analysis. The percentage yield was calculated by dividing the weight of dried extract residue by the initial weight of the dried powdered sample and then multiplying by hundred.

Per cent yield = weight of dried extract residue/ weight of the dried powdered sample × 100

GC-MS analysis

GC-MS was carried out at Chandigarh University using the Thermo GC model Trace-1300. The column

dimension was 30 m × 0.25 mm × 0.25 um (5% phenyl methyl polysiloxane). The column was injected with 1.0 µL extract, and the temperature program was set from 50°C for 5 minutes to 280°C for 10 minutes. The injector temperature was set at 250°C while the temperature of the MS transfer line was fixed at 280°C. The helium gas was used as the carrier with a flow rate of 1ml/min. Identification of various compounds present in samples was based on calculated fragmentations. The identified compounds were evaluated through comparison with available mass-spectral library data and published information.

Screening of physiological and pharmacological properties of the compounds

ADMETlab3 (Fu *et al*., 2024) and pkCSM (Pires *et al*., 2015) were used to screen the physiochemical, pharmacokinetic, and toxicity properties of compounds. Different parameters like blood-brain barrier (BBB) penetration, human intestinal absorption (HIA), CaCo2 permeability, virtual decoy sets (VDS), skin permeability and water solubility were used to determine the pharmacological properties. Different physiochemical parameters such as molecular weight (MW), hydrogen bond donor (HBD), hydrogen bond acceptor (HBA), molecular log P, topological polar surface area (TPSA), acid dissociation constant (pKa), and drug-likeness were determined to assess the druggability of the phytochemicals.

Results and Discussion

The percentage yield (w/w) of the ethanolic extract was calculated by dividing the dry weight of the extract by the initial weight of the coarse powder used for extraction. The extraction yield was approximately 16.89%. In recent years, GC-MS has been widely employed for the qualitative characterization and tentative identification of volatile and semi-volatile phytoconstituents based on their mass spectral profiles (Ouandaogo *et al.,* 2023). In the present study, GC-MS analysis of the ethanolic stem extract of *C. quadrangularis* resulted in the tentative identification of seventeen compounds (Table 1). The details of the tentatively identified compounds, including their molecular weight, molecular formula, retention time and peak area percentage, are presented in Table 1. The corresponding chemical structures and GC-MS

Table 1: List of compounds identified by GC-MS analysis

Sr.	Compound Name	RT	Probability	Molecular Formula	Biological activity	References
1	Cyclononasiloxane, octadecamethyl-	17.25	57.38	C18H54O9Si9		
2	Tetracosamethyl cyclodode casiloxane	17.25	26.13	C24H72O12Si12	-	
3	1,1,1,5,7,7,7-Heptamethyl-3,3-bis (trimethylsiloxy) tetrasiloxane	17.25	6.36	C13H40O5Si6	-	
4	Octasiloxane, 1,1,3,3,5,5,7,7,9,9,11,11, 13,13,15,15-hexadecamethyl-	17.59	8.28	C16H50O7Si8	Reported antimicrobial activity	More *et al.,* 2022
5	Prosta-5,13-dien-1-oic acid, 9,11,15-tris [(trimethylsilyl)oxy]-, trimethylsilyl ester, (5Z,9α,11α,13E,15S)-	17.59	7.31	C32H66O5Si4	-	
6	Glycine, N-[(3α,5β,7α,12α)-24-oxo-3,7,12-tris [(trimethylsilyl) oxy] cholan-24-yl]-, methyl ester	17.59	7.03	C36H69NO6Si3	-	
7	(5α)-Pregnane-3,20α-diol, 14α,18α-[4-methyl-3-oxo-(1-oxa-4-azabutane-1, 4-diyl)]-, diacetate	17.64	11.70	C28H43NO6	-	
8	D-Glucopyranosiduronic acid, 3-(5-ethylhexahydro-1,3-dimethyl-2,4,6-trioxo-5-pyrimidinyl)-1-methylbutyl 2,3,4-tris-O-(trimethylsilyl)-, methyl ester	17.64	9.89	C29H56N2O10Si3	-	
9	Cyclodecasiloxane, eicosamethyl-	18.11	70.83	C20H60O10Si10	Reported antimicrobial activity	Ganesh and Mohankumar (2017)
10	[1,2,4] Triazolo[4,3-a] quinoxalin-4-amine, N-(2,3-dihydro-1,4-benzodioxin-6-yl)-	19.61	44.07	C17H13N5O2	-	

11	2-Tetrazaboroline, 5-methyl-1,4-diphenyl-	19.61	7.82	C13H13BN4	
12	4H-Pyrido[1,2-a] pyrimidin-4-one, 6-methyl-3-phenyl-	19.61	7.82	C15H12N2O	
13	2,3-Dihydroxypropyl cis-13-docosenoate	21.57	7.45	C25H48O4	-
14	2-Ethoxy-6,6-dimethyl-9-thioxo-6,9-dihydro-7,8-dithia-5a-azabenzothiazole-6-sulfonic acid (4-methoxyphenyl) amide	21.57	4.36	C14H12N2O3S2	-
15	1-Cyclopentene-1-propanoic acid, 2-[3,7-bis[(trimethylsilyl)oxy]-1-octenyl]-5-oxo-, methyl ester	26.63	26.63	C23H42O5Si2	-
16	Butane, 1,4-bis[benzo[h]chroman-6-ol-5-yl]-	26.63	20.44	C30H30O4	-
17	Cholestano[7,8-a] cyclobutane, 3-methoxy-6-oxo-2′-methylene-	26.63	19.65	C31H50O2	-

chromatograms are presented in Figs. 2-5. At a retention time (RT) of 17.25 min (Fig. 4A), three compounds were tentatively identified: Cyclononasiloxane, octadecamethyl, Tetracosamethyl cyclododecasiloxane and 1,1,1,5,7,7,7-heptamethyl-3,3-bis (trimethylsiloxy) tetrasiloxane. Among these compounds, Cyclononasiloxane, octadecamethyl showed the highest library match value (57.38), followed by tetracosamethyl cyclododecasiloxane (26.13) and 1,1,1,5,7,7,7-heptamethyl-3,3-bis (trimethylsiloxy) tetrasiloxane (6.36). None of the above compound have previously reported biological activity. Similarly, three compounds were tentatively identified at RT 17.59 min (Fig. 4B), namely Octasiloxane, 1,1,3,3,5,5,7,7,9,9, 11,11,13,13,15,15-hexadecamethyl; Prosta-5,13-dien-1-oic acid, 9,11,15-tris[(trimethylsilyl)oxy], trimethylsilyl ester, (5Z,9α,11α,13E,15S); and Glycine, N-[(3α,5β,7α,12α)-24-oxo-3,7,12-tris [(trimethylsilyl) oxy]cholan-24-yl], methyl ester. Octasiloxane, 1,1,3,3,5, 5,7,7,9, 9,11,11,13,13,15,15- hexadecamethyl showed the highest library match value (8.28), followed by Prosta-5,13-dien-1-oic acid, 9,11,15-tris [(trimethylsilyl) oxy], trimethylsilyl ester, (5Z,9α,11α,13E,15S) (7.31) and Glycine, N-[(3α,5β,7α,12α)-24-oxo-3,7,12-tris [(trimethylsilyl) oxy] cholan-24-yl], methyl ester (7.03). Antimicrobial activity has previously been reported for Octasiloxane, 1,1,3,3,5,5,7,7,9,9,11,11,13,13,15,15-hexadecamethyl (More *et al*., 2022), whereas the biological activities of the other two tentatively identified compounds have not been adequately established. At RT 17.64 min (Fig. 4C), two compounds, namely 5α-Pregnane-3,20α-diol, 14α,18α-[4-methyl-3-oxo-(1-oxa-4-azabutane-1,4-diyl)]-diacetate and D-glucopyranosiduronic acid, 3-(5-ethylhexahydro-1,3-dimethyl-2,4,6-trioxo-5-pyrimidinyl)-1-methylbutyl 2,3,4-tris-O-(trimethylsilyl), were tentatively identified. No specific biological activity of these compounds could be established from the literature consulted. Cyclodecasiloxane, eicosamethyl was tentatively identified at RT 18.11 min (Fig. 4D). Previous studies have reported antimicrobial; anthelmintic and antioxidant activities associated with this compound. At RT 19.61 min (Fig. 5A), three compounds were tentatively identified, namely [1,2,4] triazolo[4,3-a] quinoxalin-4-amine, N-(2,3-dihydro-1,4-benzodioxin-

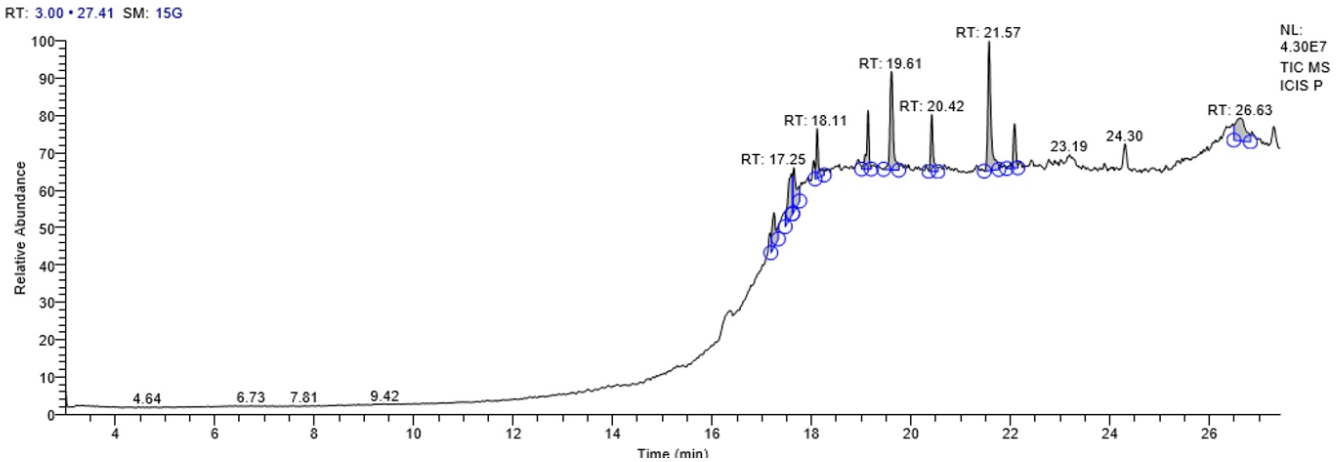


Fig. 2: GC-MS chromatogram of ethanol extract of *Cissus quadrangularis* L stem extract.

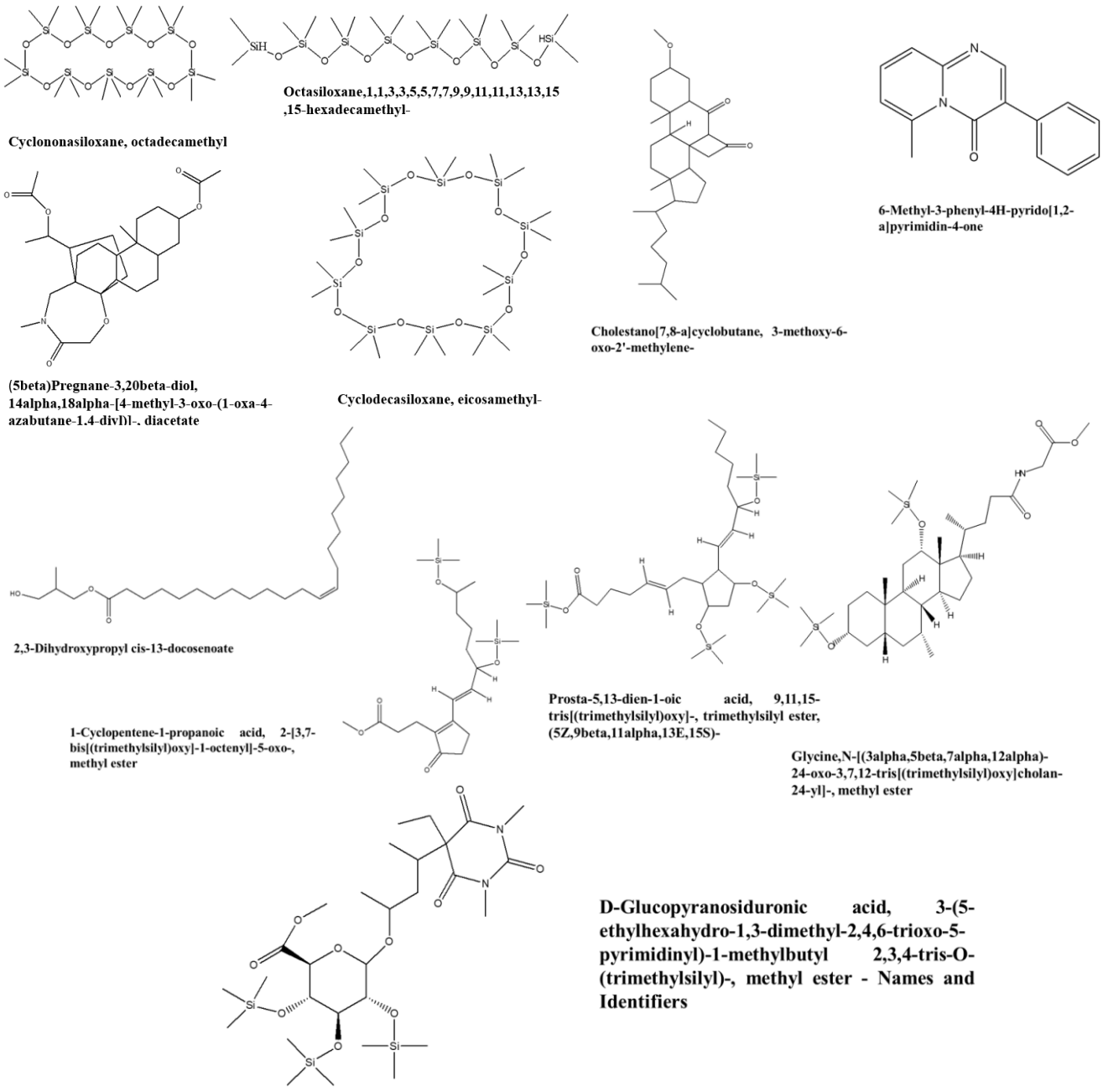


Fig. 3: Chemical structure of identified compounds.

6-yl); 2-tetrazaboroline, 5-methyl-1,4-diphenyl; and 4H-pyrido[1,2-a] pyrimidin-4-one, 6-methyl-3-phenyl. Among these, [1,2,4] triazolo[4,3-a] quinoxalin-4-amine, N-(2,3-dihydro-1,4-benzodioxin-6-yl) showed the highest library match value (44.07), whereas the other compounds showed lower match values (7.82). The biological activities of these compounds have not been adequately reported. At RT 21.57 min (Fig. 5B), three compounds were tentatively identified, namely 2,3-dihydroxypropyl, cis-13-docosenoate; cyclopenta[e]acenaphthylene- 4,5-dione, 2-ethoxy-6,6-dimethyl-9-thioxo-6,9-dihydro-7,8-dithia-5a-aza; and 2-ethoxy-6,6-dimethyl-9-thioxo-6,9-dihydro-7,8-dithia-5a-azabenzothiazole-6-sulfonic acid (4-methoxyphenyl) amide. The biological activities of these compounds have not been sufficiently characterized. Finally, three compounds, namely 1-cyclopentene-1-propanoic acid, 2-[3,7-bis [(trimethylsilyl) oxy]-1-octenyl]-5-oxo-, methyl ester; Butane, 1,4-bis[benzo[h] chroman-6-ol-5-yl]; and cholestano[7,8-a] cyclobutane, 3-methoxy-6-oxo-2′-methylene, were tentatively identified at RT 26.63 min

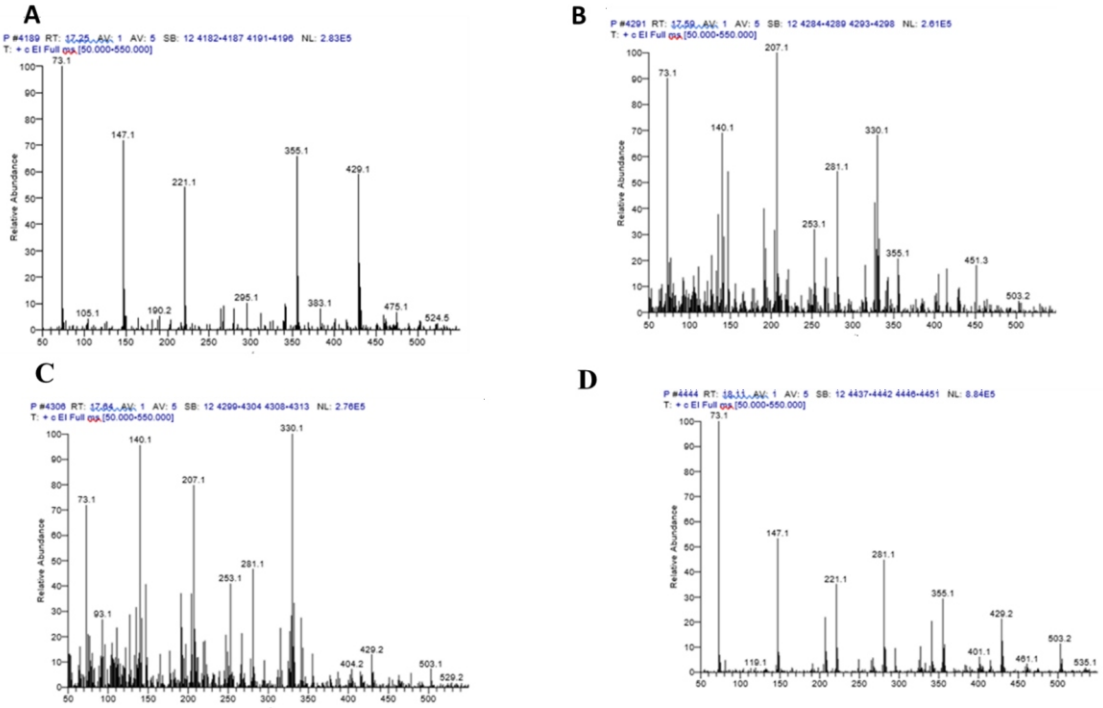


Fig. 4: Mass spectrum of compounds identified at retention time A-17.25; B-17.59; C-17.64; D-18.11.

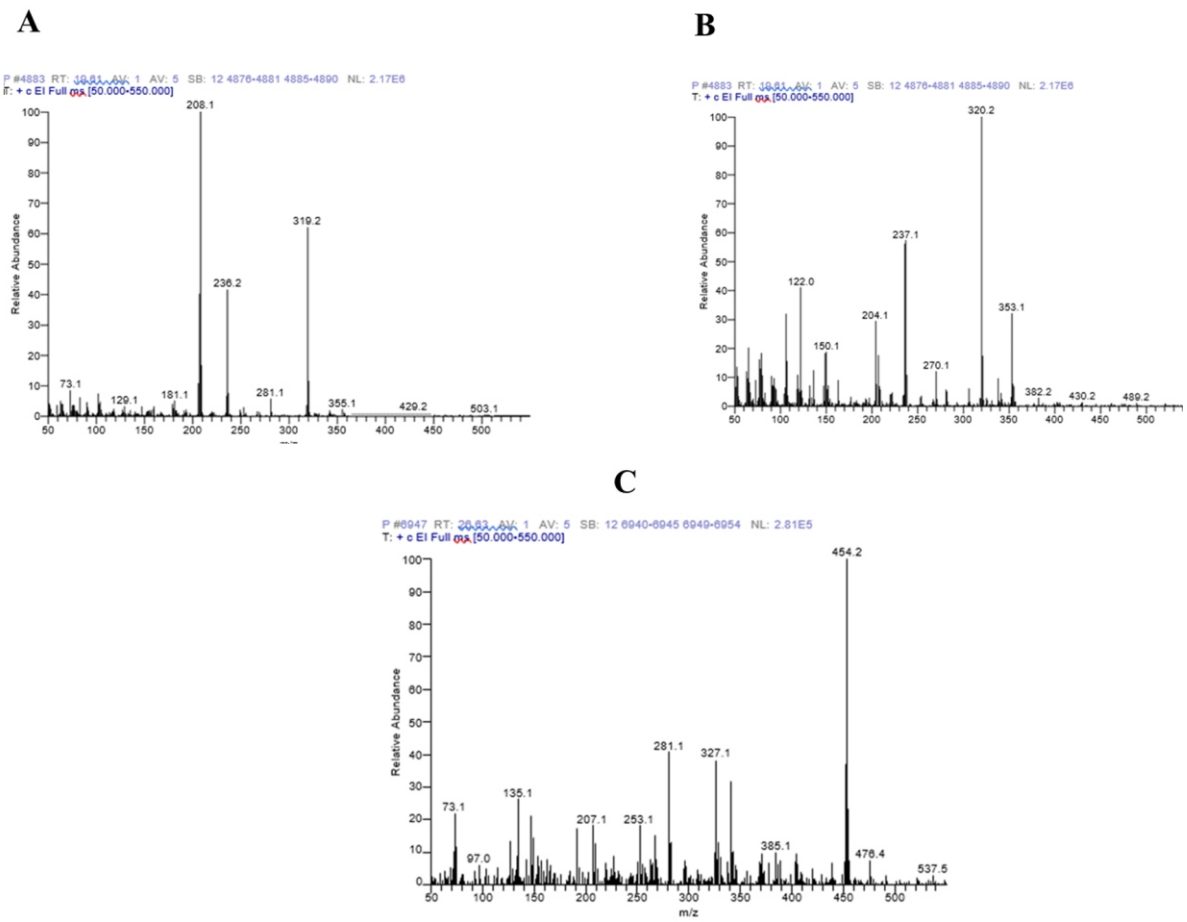


Fig. 5: Mass spectrum of compounds identified at retention time A-19.61; B-21.57; C-26.63.

(Fig. 5C). No specific biological activities of these compounds could be established from the literature consulted. The phytochemical profile obtained in the present study is broadly consistent with the chemically diverse nature of *Cissus quadrangularis* L. reported in previous investigations; however, considerable differences are evident in the composition and relative representation of individual constituents. More comprehensive LC-based investigations indicate that the phytochemical composition of *C. quadrangularis* extends considerably beyond compounds readily amenable to GC-MS analysis. Kaur *et al*., (2022) performed LC/MS-guided profiling of petroleum ether, chloroform, ethanol and aqueous extracts and demonstrated marked differences in metabolite distribution among extracts of different solvent polarities. Phytosterols were reported predominantly in petroleum ether and ethanolic extracts, while terpenoids, flavonoids, alkaloids and glycosides were detected across different extracts. In the ethanolic extract, campesterol, β-sitosterol, stigmasterol, pterostilbene, resveratrol, apigenin-glucoside, genistein, luteolin and a prenylated chalcone were reported. These findings emphasize the importance of extraction solvent and solvent polarity in determining the phytochemical profile recovered from *C. quadrangularis* (Kaur *et al.,* 2022). Similarly, Avula *et al*., (2021) investigated stem and leaf samples of *C. quadrangularis* using UHPLC-PDA-MS, LC-QToF and HPTLC. The study characterized polyphenolic constituents including catechin, epicatechin, quercetin-3-O-β-glucopyranoside, kaempferol-3-O-β-glucoside, quercetin-3-O-rhamnoside, leachianol F, amurensin A, pallidol, resveratrol and quadrangularin A. LC-QToF analysis enabled structural correlation of more than 40 components, demonstrating the broader metabolite coverage achievable using LC-based approaches (Avula *et al*., 2021). Thus, the absence of these compounds from the present GC-MS profile should not be interpreted as evidence of their absence from the plant material, because many polar, non-volatile or thermolabile constituents are not readily amenable to conventional GC-MS analysis. Earlier HPLC and HPTLC investigations further established characteristic marker constituents of *C. quadrangularis*, including onocer-7-ene-3α,21β-diol, δ-amyrin, δ-amyrone and 3,3′,4,4′-tetrahydroxybiphenyl (Mehta *et al*., 2001). Importantly, the quantities of these marker constituents were determined in samples collected from five different geographical regions of India, demonstrating variation among geographically distinct samples and suggesting that geographical origin may contribute to phytochemical variability in *C. quadrangularis* (Mehta *et al*., 2001). The differences between the present GC-MS profile and previously reported phytochemical profiles should therefore not necessarily be interpreted as contradictory findings. Plant part, genotype, geographical location, developmental stage, environmental conditions, harvesting conditions, extraction solvent, solvent-to-sample ratio, extraction temperature and duration, sample preparation and analytical platform can all influence the metabolites detected. In particular, GC-MS preferentially detects volatile and semi-volatile compounds and compounds that can be rendered amenable to gas chromatographic analysis, whereas LC-MS provides substantially broader coverage of polar, non-volatile and thermolabile metabolites. The present findings should therefore be considered a GC-MS-based qualitative profile of the investigated ethanolic stem extract, rather than a comprehensive representation of all phytoconstituents occurring in *C. quadrangularis*. Accordingly, differences from earlier studies may reflect a combination of genuine biological variation and methodological differences. Complementary LC-MS/MS, HPLC and spectroscopic investigations, together with authentic-standard comparison and, where appropriate, isolation and structural elucidation, would be required to establish a more comprehensive chemical fingerprint of the species.

The drug-development potential of a compound depends on its physicochemical, pharmacokinetic and pharmacological characteristics. Therefore, preliminary *in silico* assessment of physicochemical, drug-likeness and absorption, distribution, metabolism, excretion and toxicity (ADMET) parameters can assist in prioritizing compounds for subsequent experimental investigation. Such analyses may also provide preliminary insights into the pharmacological potential of phytoconstituents and facilitate the identification of candidate molecules for further drug-discovery studies (Upadhyay and Tiwari, 2023). In the present study, the predicted physicochemical and pharmacological properties of the tentatively identified phytochemicals are presented in Tables 2 and 3. Among the seventeen tentatively identified compounds, four compounds showed comparatively favourable predicted physicochemical and drug-likeness characteristics, including hydrogen-bond donor and acceptor properties, molecular lipophilicity (logP), acid dissociation constant (pKa) and other parameters evaluated according to commonly used drug-likeness criteria, including the Lipinski Rule, Pfizer Rule, GSK Rule

and Golden Triangle (Table 2). These four compounds also demonstrated favourable predicted pharmacokinetic characteristics, including absorption, distribution, aqueous solubility and skin permeability (Table 3). The predicted volume of distribution (VDs) and Caco-2 permeability values were also considered as indicators of the potential distribution and intestinal permeability of the compounds, respectively. A favourable Caco-2 permeability prediction may indicate the potential for intestinal absorption; however, such computational values should not be interpreted as direct measurements of *in vivo* permeability. The toxicity profile of a candidate molecule is an important consideration during drug

Table 2: Physiochemical properties of the compounds identified through GC-MS analysis

Sr.	Compound Name	IUPAC	HBA	HBD	MLOGP	TPSA	pKA(acid)	DL	MW
1	Cyclononasiloxane, octadecamethyl-	2,2,4,4,6,6,8,8,10,10,12,12,14,14, 16,16,18,18-octadecamethy l-1,3, 5,7,9,11,13,15,17-nonaoxa-2,4,6,8,10,12,14,16,18-nonasilacyclooctadecane	9.0	0.0	12.469	83.07	3.179	No (2)	666.17
2	Tetracosamethyl cyclododecasiloxane	2,2,4,4,6,6,8,8,10,10,12,12,14,14, 16,16,18,18,20,20,22,22,24,24-tetracosamethyl-1,3,5,7,9, 11,13,15,17,19,21,23-dodecaoxa-2,4,6,8,10,12,14,16,18,20,22,24-dodecasilacyclotetracosane	12	0	16.368	11076	2.60	No (3)	889.8
3	1,1,1,5,7,7,7-Heptamethyl-3,3-bis (trimethylsiloxy) tetrasiloxane	5 trimethyl-[methyl-[methyl-bis (trimethylsilyloxy)silyl] oxy-trimethylsilyloxysilyl]oxysilane	0	4.9626	46.15	7.469	No (2)	458.16	
4	Octasiloxane, 1,1,3,3,5,5,7,7, 9,9,11,11,13,13,15,15-hexadecamethyl-	1,1,3,3,5,5,7,7,9,9,11,11,13, 13,15,15-Hexadecamethyl octasiloxane	7	0	5.8156	64.61	6.6	No (3)	576.16
5	Prosta-5,13-dien-1-oic acid, 9,11,15-tris [(trimethylsilyl) oxy]-, trimethylsilyl ester, (5Z,9α,11α,13E,15S)-	trimethylsilyl (E)-7-[3,5-bis (trimethylsilyloxy)-2-[(E)-3-trimethylsilyloxyoct-1-enyl] cyclopentyl] hept-5-enoate	5	0	9.914	53.99	10.967	No (3)	642.4
6	Methyl 2-[[(4R)-4-[(3R,5S,7R, 8R,9S,10S,12S,13R,14S,17R)-10,13-dimethyl-3,7,12-tris (trimethylsilyloxy) -2,3,4,5,6, 7,8,9,11,12,14,15,16,17-tetradecahydro-1H-cyclope nta[a]phenanthren-17-yl] pentanoyl] amino] acetate	7	1	8.2309	83.09	9.153	No	695.44	
7	(5α)-Pregnane-3,20α-diol, 14α,18α-[4-methyl-3-oxo-(1-oxa-4-azabutane-1,4-diyl)]-, diacetate	[22-(1-acetyloxyethyl)-10,16-dimethyl-17-oxo-19-oxa-16-azapentacyclo [12.5.3.0.0.0] docosan-7-yl] acetate	7	0	2.771	82.14	8.251	Yes	489.6
8	D-Glucopyranosiduronic acid, 3-(5-ethylhexahydro-1,3-dimethyl-2,4,6-trioxo-5-pyrimidinyl)-1-methylbutyl 2,3,4-tris-O-(trimethylsilyl)-, methyl ester	Methyl (2S,3R,4S,5R,6S)-6-[4-(5-ethyl-2,4,6-trioxo-1,3-diazinan-5-yl)-2-methylbutan-2-yl] oxy-3,4,5-tris (trimethylsilyloxy) oxane-2-carboxylate	12	2	3.8824	147.72	7.678	No (2)	648.29
9	Cyclodecasiloxane, eicosamethyl-	2,2,4,4,6,6,8,8,10,10,12,12,14,14, 16,16,18,18,20,20-icosamethyl-1,3,5,7,9,11,13,15,17,19-decaoxa-2,4,6,8,10,12,14,16,18,20-decasilacycloicosane	10	0	7.184	92.3	2.938	No (2)	740.19

10	[1,2,4] Triazolo[4,3-a] quinoxalin-4-amine, N-(2,3-dihydro-1,4-benzodioxin-6-yl)-	1-methyl-8-nitro-6-pyridin-2-yl-4H- [1,2,4] triazolo[4,3-a] [1,4] benzodiazepine	8	0	1.3	99.1	7.582	Yes	320.31
11	2-Tetrazaboroline, 5-methyl-1, 4-diphenyl-	2,3-dihydroxypropyl (E)-docos-13-enoate	4.0	2.0	6.197	66.76	6.921	No (2)	412.36
12	4H-Pyrido[1,2-a] pyrimidin-4-one, 6-methyl-3-phenyl-	6-methyl-3-phenylpyrido [1,2-a] pyrimidin-4-one	8	2	2.67	103.99	8.38	Yes	397.17
13	2,3-Dihydroxypropyl cis-13-docosenoate	2,3-dihydroxypropyl (E)-docos-13-enoate	4	2	6.19	66.76	6.921	No (2)	412.6
14	2-Ethoxy-6,6-dimethyl-9-thioxo-6,9-dihydro-7,8-dithia-5a-azabenzothiazole-6-sulfonic acid (4-methoxyphenyl) amide	6-(2-Hydroxy-ethoxy)-benzothiazole-2-sulfonic acid (2-amino-acetyl)-amide	8	4	-0.336	131.61	6.165	Yes	331.03
15	1-Cyclopentene-1-propanoic acid, 2-[3,7-bis [(trimethylsilyl)oxy]-1-octenyl] -5-oxo-, methyl ester	1-Cyclopentene-1-propanoic acid, 2-[3,7-bis [(trimethylsilyl)oxy]-1-octenyl]-5-oxo-, methyl ester	5	0	4.63	61.83	8.66	No (2)	454.7
16	Butane, 1,4-bis[benzo[h] chroman-6-ol-5-yl]-	1,4-bis(2-chloroethylthio) butane	0	0	3.314	00	6.555	Yes	246.01
17	Cholestano[7,8-a] cyclobutane, 3-methoxy-6-oxo-2'-methylene-	Cholestano[7,8-a] cyclobutane, 3-methoxy-6-oxo-2'-methylene-	2	0	6.77	26.3	10.217	No (2)	454.38

Table 3: Pharmacological properties of the compounds identified through GC-MS analysis

Sr.	Compound Name	Skin Permeability	Water Solubility	Caco2	HIA	VDs	BBB	Carcinogenicity	Human hepatotoxicity
1	Cyclononasiloxane, octadecamethyl-	-2.717	4.302	-4.677	excellent	0.976	poor	Yes	No
2	Tetracosamethylcyclododecasiloxane	-2.735	-3.557	4.655	excellent	0.95	poor	Yes	No
3	1,1,1,5,7,7,7-Heptamethyl-3,3-bis (trimethylsiloxy) tetrasiloxane	-2.014	-4.348	-4.816	excellent	0.037	excellent	Yes	No
4	Octasiloxane, 1,1,3,3,5,5,7,7,9,9,11,11, 13,13,15,15-hexadecamethyl-	-2.189	-4.551	-4.657	excellent	0.717	poor	Yes	No
5	Prosta-5,13-dien-1-oic acid, 9,11,15-tris [(trimethylsilyl)oxy]-, trimethylsilyl ester, (5Z,9α,11α,13E,15S)-	-2.746	-6.625	-5.017	excellent	3.67	poor	Yes	No
6	Glycine, N-[(3α,5β,7α,12α)-24-oxo-3,7,12-tris[(trimethylsilyl)oxy] cholan-24-yl]-, methyl ester	-2.808	-6.523	-5.032	excellent	2.515	poor	Yes	No
7	(5α)-Pregnane-3,20α-diol, 14α,18α-[4-methyl-3-oxo-(1-oxa-4-azabutane-1, 4-diyl)]-, diacetate	-3.495	-5.521	-4.809	excellent	-0.144	poor	No	No
8	D-Glucopyranosiduronic acid, 3-(5-ethylhexahydro-1,3-dimethyl-2,4, 6-trioxo-5-pyrimidinyl)-1-methylbutyl 2,3, 4-tris-O-(trimethylsilyl)-, methyl ester	-2.72	-4.177	-5.082	excellent	0.647	poor	No	No
9	Cyclodecasiloxane, eicosamethyl-	-2.731	-4.075	-4.67	excellent	0.96	Poor	Yes	No
10	[1,2,4] Triazolo[4,3-a] quinoxalin-4-amine, N-(2,3-dihydro-1,4-benzodioxin-6-yl)-	-2.714	-3.066	-4.667	excellent	1.019	poor	No	No
11	2-Tetrazaboroline, 5-methyl-1,4-diphenyl-			-5.01	excellent	0.447	excellent	No	No
12	4H-Pyrido[1,2-a] pyrimidin-4-one, 6-methyl-3-phenyl-	-2.73	-2.89	-5.21	excellent	1.089	poor	No	No
13	2,3-Dihydroxypropyl cis-13-docosenoate	-2.77	-6.62	-5.099	excellent	0.447	excellent	No	No

14	2-Ethoxy-6,6-dimethyl-9-thioxo-6, 9-dihydro-7,8-dithia-5a-azabenzothiazole-6-sulfonic acid (4-methoxyphenyl) amide	-2.73	-2.25	-4.959	excellent	2.40	excellent	No	No
15	1-Cyclopentene-1-propanoic acid, 2-[3,7-bis[(trimethylsilyl)oxy]-1-octenyl]-5-oxo-, methyl ester	-2.45	-5.41	-4.95	excellent	0.38	poor	yes	No
16	Butane, 1,4-bis[benzo[h] chroman-6-ol-5-yl]-	-1.92	-5.09	-4.97	poor	0.89	poor	Yes	No
17	Cholestano[7,8-a] cyclobutane, 3-methoxy-6-oxo-2'-methylene-	-2.71	-6.14	-4.929	excellent	2.48	poor	No	No

discovery because adverse toxicological properties may limit its further development. In the present study, toxicity-related parameters were therefore evaluated computationally. The four prioritized compounds did not show predicted carcinogenic or hepatotoxic liabilities under the computational models used (Table 3). However, computational toxicity predictions cannot establish the absence of toxicity, and these findings require confirmation through appropriate experimental toxicological studies (Sun *et al.,* 2022). Overall, the *in silico* analysis suggests that the four prioritized compounds may possess favourable molecular and pharmacokinetic characteristics and could therefore serve as candidate molecules for further pharmacological investigation. However, their potential as lead compounds cannot be established solely from computational predictions. Further experimental studies involving isolation, structural confirmation, *in vitro* and *in-vivo* bioactivity evaluation, pharmacokinetic assessment and toxicological investigation are required. Considering the traditional medicinal importance of *C. quadrangularis* in the management of bone-related disorders and its reported osteogenic, anti-inflammatory and antioxidant activities, the prioritized compounds may warrant further investigation for their potential relevance to bone health and bone-repair-related biological processes. Nevertheless, their specific contribution to bone healing or fracture repair cannot be established solely based on GC-MS-based tentative identification and computational predictions. Future activity-guided isolation and mechanistic studies may help elucidate the contribution of individual constituents to the therapeutic properties of *C. quadrangularis*.

Conclusion

The study resulted in the tentative identification of seventeen compounds from the ethanolic extract of *C. quadrangularis* stem using GC–MS analysis. Among these, only three compounds have previously been reported to possess biological activities, whereas the bioactive potential of the remaining tentatively identified compounds has not yet been adequately investigated. Therefore, further studies are warranted to evaluate the biological activities of these compounds. Among the seventeen tentatively identified compounds, four compounds, namely, 5α-Pregnane-3,20α-diol,14α,18α-[4-methyl-3-oxo-(1-oxa-4-azabutane-1,4-diyl)]-diacetate; [1,2,4]triazolo[4,3-a]quinoxalin-4-amine, N-(2,3-dihydro-1,4-benzodioxin-6-yl); 4H-pyrido[1,2-a]pyrimidin-4-one, 6-methyl-3-phenyl-2,3-dihydroxypropyl (E)-docos-13-enoate; and 2-ethoxy-6,6-dimethyl-9-thioxo-6,9-dihydro-7,8-dithia-5a-aza-benzothiazole-6-sulfonic acid (4-methoxyphenyl)amide, exhibited favorable predicted physicochemical and pharmaceutical properties in the computational analyses. These findings suggest that these compounds may serve as potential candidates for further pharmacological investigation. However, the predicted physicochemical and pharmacokinetic properties alone are insufficient to establish their biological efficacy. Therefore, these compounds require further validation through isolation, structural characterization, in vitro and *in vivo* bioactivity assays, and appropriate toxicological studies. Considering the traditional medicinal importance of *C. quadrangularis* in the management of bone-related disorders and its reported osteogenic, anti-inflammatory, and antioxidant properties, the identified compounds may have potential relevance to bone health and bone-repair-related biological processes. Nevertheless, their specific contribution to bone healing or fracture repair cannot be established solely based on GC-MS identification and computational predictions. Further experimental studies are therefore required to elucidate their biological activities, mechanisms of action, safety, and therapeutic potential.

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