



Exploring various extracts and compounds of *Grewia velutina* as potential anticancer agents: An in vitro and in silico investigations

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ARTICLE INFO

Keywords:

Grewia velutina
Molecular docking
Chemical profiling
Volatiles
Phytoconstituents

ABSTRACT

This study presents a comprehensive investigation into the potential anticancer properties and chemical constituents of an unexplored plant (*Grewia velutina*) extracts. Three distinct extracts of hexane (GVH), chloroform (GVC) and methanol (GVM) of the plant were used to check their anticancer activity against four prominent cancer cell lines (HepG2, DU145, Hela, A549), and the results were compared with the standard chemotherapeutic agent doxorubicin. Anticancer assays revealed that the GVC extract exhibited highest activity than others, with IC50 values of 61.06 µg/mL, 47.87 µg/mL, 88.76 µg/mL, and 87.99 µg/mL against HepG2, DU145, Hela, and A549 cell lines, respectively and reflected a comparable activity to doxorubicin, highlighting its potential as an effective anticancer agent. With the help of chemical profiling data, molecular docking studies were performed and this study suggested that ionol, present in GVC extract is the most active compound against all the cancerous cells.

1. Introduction

Various plant species with potential anticancer properties have been explored for the prevention of cancer, particularly the plant species which are already being used as herbal medicines are largely considered for scientific endeavor (Khan et al., 2022a). Over the couple of decades, a considerable number of phytochemicals with slight structural modifications have been approved to combat cancer (Iqbal et al., 2018). Particularly, some specific groups of secondary metabolites like terpenes, flavonoids, alkaloids, lignans, saponins etc., have been proved to be highly effective in selectively inhibiting cancer cell proliferation and inducing their death (Agarwal et al., 2020). For example, a methoxylated flavone i.e., xanthomicrol extracted from *Dracocephalum kotschyii* Boiss has been found to inhibit the growth of a variety of malignant cells by inhibiting the proliferation of endothelial cell via decreased vascular endothelial growth factor activity (Fattahi et al., 2014). Similarly, in our recent study, we have demonstrated effective anticancer properties of seed extract of *Citrullus colocynthis* against several cell lines including HepG2, DU145, Hela, and A549 (Khan et al., 2023a). As a result of such medicinal properties, scientists across the globe routinely conduct a

thorough initial screening of plant extracts with the hope of discovering potential anticancer agents from plant sources (Khan et al., 2022a).

Among different regions, the Arabian Peninsula is known for its rich variety of plants from different families which have long been used for medicinal purposes. However, most of these natural products, particularly plants-based materials have not been explored scientifically for their potential anti-cancer properties (Khan et al., 2023b). Indeed, extracts of different families of plants from Saudi Arabia with potential anticancer and other medicinal properties including Tiliaceae, Asteraceae, Lamiaceae etc., have been rarely explored for their anticancer potential (Ullah et al., 2020). One such plant is *Grewia velutina* belonging to the *Grewia* genus of Tiliaceae family, and is commonly found in tropical and subtropical regions, including some African, Arabian, Asian and Australian regions (Ullah et al., 2012). Due to effective medicinal properties, several species of the genus *Grewia* have long been utilized for different therapeutic purposes (Qamar et al., 2021, Suguna and Umesha 2022). For example, the roots and barks of *G. tiliaefolia* are used for the treatment of diarrhea, hypertension, skin, neurodegenerative and inflammatory bowel diseases etc., while the extracts of different parts of *G. asiatica* have shown effective antimicrobial and antioxidant

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<https://doi.org/10.1016/j.jksus.2024.103427>

Received 9 June 2024; Received in revised form 27 August 2024; Accepted 31 August 2024

Available online 2 September 2024

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properties (Shukla et al., 2016, Rajput et al., 2023).

Despite of diverse medicinal applications of different plants species of the genus *Grewia*, there is no recognized scientific reports on the therapeutic potential of *G. velutina*. Indeed, to the best of our knowledge, we did not find any single report in the literature about the phytochemical analysis and medicinal properties of this plant. Thus, detail phytochemical analysis and investigation of the anticancer properties of *G. velutina* is highly desirable. Therefore, in the current study we performed the detail phytochemical analysis of different extracts of *G. velutina* and assess their anticancer properties against various cancer cell lines such as, HepG2, DU145, HeLa, and A549. Moreover, molecular docking study were also performed to identify the anticancer potential of the specific compounds present in different extracts.

2. Materials and methods

2.1. Plant material

The complete aerial components of *G. velutina* were gathered in May 2020 from the Al-Baha region, situated in the southwestern part of Saudi Arabia. The verification and authentication of the plant material were conducted by Dr. Rajakrishnan Rajagopal, a botanist from the herbarium division of King Saud University. A specific specimen labelled as 24,573 of *G. velutina* has been preserved within the herbarium division of King Saud University, Riyadh, Saudi Arabia.

2.2. Extraction of *G. velutina* aerial parts

The plant material of *G. velutina* aerial parts were extracted according to the method described previously (Khan et al., 2023a). Detailed extraction methodology is given in [Supplementary Materials \(Scheme S1\)](#).

2.3. GC and GC-MS analysis of *G. velutina* aerial parts extracts

GC-MS and GC-FID analysis of *G. velutina* extracts were done employing the procedure reported earlier (Khan et al., 2023a). Detailed methodology for the analysis is provided in [Supplementary Materials \(Scheme S2\)](#).

2.3.1. Calculation of linear retention indices (LRIs)

The linear retention indices (LRIs) values of chemical constituents of *G. velutina* extracts were determined according to the procedure described earlier (Khan et al., 2023a). Detailed methodology is provided in [Supplementary Materials \(Scheme S3\)](#).

2.3.2. Identification of chemical constituents of *G. velutina* aerial parts extracts

The identification of phytocomponents in the *G. velutina* extracts (GVH, GVC, and GVM) was achieved employing the methods as described previously (Khan et al., 2023a). Detailed methodology is provided in [Supplementary Materials \(Scheme S4\)](#).

2.4. Evaluation of anticancer activity

Anticancer activity of *G. velutina* extracts was assessed against the human lung adenocarcinoma cell line (A549), human hepatocarcinoma cell line (HepG2), human cervical cancer cell line (HeLa), and human prostate cancer cell line (DU145) using MTT assay as described earlier (Hansen et al., 1989, Khan et al., 2023a). Detailed methodology is provided in [Supplementary Materials \(Scheme S5\)](#).

2.5. Computational methodology for molecular docking study

The three-dimensional structure of the selected proteins considering various cancer cell lines [HepG2, A549, DU145, HeLa] were modeled

Table 1

Receptor details considering selected cancerous cells.

S. No.	Cancerous cell	Receptor name	PDB Id	Reference
1	HepG2	Cysteine-aspartic acid protease-3 (CASPASE-3)	1GFW	(Siddiqui et al., 2021)
2	A549	Epidermal Growth Factor Receptor (Tyrosine kinase)	1 M17	(Muniaraj et al., 2018)
3	DU145	Vascular endothelial growth factor receptor 2 (VEGFR2)	2QU6	(Husain et al., 2021)
4	HeLa	Refined 13pf HeLa Cell Tubulin microtubule	6I2I	(Aydin et al., 2021)

based on the available structures in the Protein Data Bank (<https://www.rcsb.org>) and previous studies. SWISS-MODEL (Waterhouse et al., 2018) web server was used to model the missing residues when the available structures comprise some unsolved region. The PDB IDs considered for different proteins are listed in Table-1 with their structures and supporting studies. Autodock tools were used to clean the structure followed by the removing of heteroatoms and to add necessary hydrogen atoms and charges (Baidya et al., 2021). Optimized structures of the major compounds present in the three distinct extracts (GVH, GVC, GVM) as per chemical profiling were used as ligands in the molecular docking study (Table 1).

A few major compounds (Table 2), present in GVC extract was also considered as GVC extract showed maximum activity against all the cancerous cells (Ghosh et al., 2022). Selected compounds were optimized using Gaussian 09 programme with B3LYP hybrid functional and localized 6-31G(d,p) basis set. Autodock Vina 6. (Seeliger and de Groot 2010) package was used for docking between the selected proteins and ligands. The docking score is a key screening characteristic and plays a crucial role to ensure screening success. PyMOL (Seeliger and de Groot 2010) Discovery Studio (Wang et al., 2015) and LigPlot + (Laskowski and Swindells 2011) platforms were used for docking result analysis and the type of interaction present between the protein and ligand.

3. Results and discussion

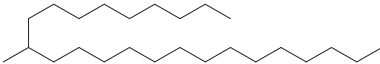
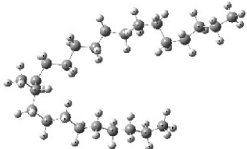
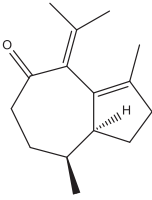
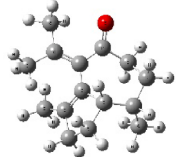
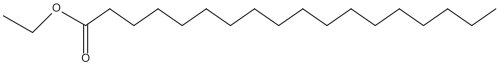
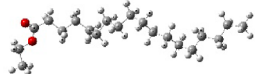
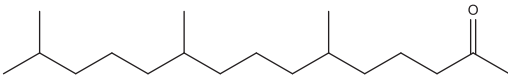
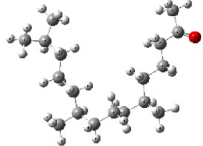
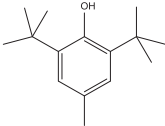
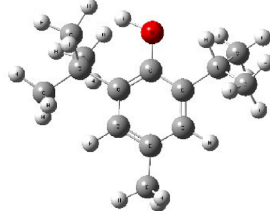
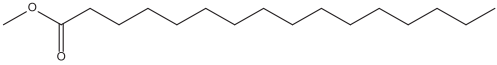

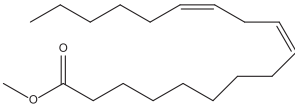

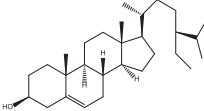
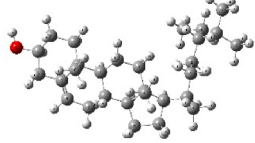

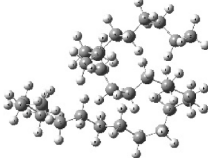
In order to determine chemical constituents of unexplored *G. velutina* and to conduct a comparative phytochemical analysis of various solvent extracts, aerial parts of the plant were extracted in three different solvents including hexane (GVH), chloroform (GVC) and methanol (GVM). Resultant extracts were analyzed using detailed GC-MS and GC-FID analysis. Table 3 exhibits the list of compounds identified in three different extracts of *G. velutina*.

Overall 29 compounds were identified from the GVH, GVC and GVM extracts of *G. velutina*. Notably, each extract does not contain all the identified (29) compounds, and the number of compounds and their quantities varied in all extracts. For example, GVH extract consists of only 12 compounds, while GVC and GVM contain 17 and 19 different types of phytomolecules, representing 97.4 %, 91.1 %, and 96.2 % of the total extract compositions, respectively. The total ion chromatogram from the GC analysis of each extracts of the aerial parts of *G. velutina* are given in Fig. 1.

It is interesting to note that in all the three extracts, the major constituent is triacontane, which is present in ~ 59, 57, and 47 % in GVH, GVC and GVM extracts, respectively. While the second major component in these extracts is nonacosane which is present in the range of 13 to 17 %. Remarkably, another significant constituent found in GVM extract is 1-[(2-Hydroxyphenyl)thioxomethyl]pyrrolidine, accounting for approximately 18 % according to Table 3. Conversely, in GVC and GVH, this compound was detected in mere 1 % of the sample. There were some other notable compounds present in appreciable amounts in these three extracts. For instance, GVH extract contained 2-methylacetophenone, methyl hexadecanoate, 11-butyldocosane, and (8S,8aS)-3,8-dimethyl-

Table 2

List of the selected compounds with structures for using as ligands.

S. No.	Name of the compounds	Structure of the compounds	Optimized structure of the compounds
1	10-Methyltetracosane		
2	(8 <i>S</i> ,8 <i>aS</i>)-3,8-Dimethyl-4-propan-2-ylidene-1,2,6,7,8,8 <i>a</i> -hexahydroazulen-5-one		
3	Ethyl-octadecanoate		
4	Hexahydrofarnesyl-acetone		
5	Ionol		
6	Methyl-hexadecanoate		
7	Methyl-linoleate		
8	Sitosterol		
9	Triacontane		

(continued on next page)

Table 2 (continued)


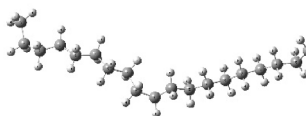
S. No.	Name of the compounds	Structure of the compounds	Optimized structure of the compounds
10	Tricosane		

Table 3

Chemical constituents identified from various extracts of *G. velutina* aerial parts.

No.	Compound	M.F.	CAS No.	R.T. (min)	LRI	GVH %	GVC %	GVM %
1	3-Methyl-2-buten-1-ol	C ₅ H ₁₀ O	556-82-1	5.19	771	–	–	0.6
2	α -Pinene	C ₁₀ H ₁₆	80-56-8	10.76	934	1.9	–	–
3	Isobutyl tiglate	C ₆ H ₁₆ O ₂	66917-61-1	17.09	1099	–	–	1.1
4	2-Methylacetophenone	C₉H₁₀O	577-16-2	18.53	1138	4.0	–	–
5	4-Oxoisophorone	C ₉ H ₁₂ O ₂	1125-21-9	18.84	1147	–	–	0.3
6	Ionol	C ₁₅ H ₂₄ O	128-37-0	31.04	1516	–	0.8	–
7	γ -Dodecalactone	C ₁₂ H ₂₂ O ₂	2305-05-7	35.84	1686	–	–	0.5
8	Aristolone	C ₁₅ H ₂₂ O	6831-17-0	38.62	1791	–	–	0.4
9	Hexahydrofarnesyl acetone	C ₁₇ H ₁₈ O ₂	68607-88-5	39.81	1838	–	1.7	1.7
10	Diisobutyl phthalate	C ₁₆ H ₂₂ O ₄	84-69-5	40.43	1863	–	–	0.6
11	Pentadecanoic acid	C ₁₅ H ₃₀ O ₂	1002-84-2	40.87	1881	–	–	0.9
12	Methyl hexadecanoate	C₁₇H₃₄O₂	112-39-0	41.95	1925	3.4	1.6	4.7
13	<i>n</i> -Hexadecanoic acid	C ₁₆ H ₃₂ O ₂	57-10-3	42.76	1959	–	–	0.6
14	Hexadecanoic acid, ethyl ester	C ₁₈ H ₃₆ O ₂	628-97-7	43.57	1993	–	2.2	0.6
15	8,11-Octadecadienoic acid, methyl ester	C ₁₉ H ₃₄ O ₂	56599-58-7	45.88	2090	–	–	0.8
16	(<i>Z</i>)-9-Octadecenoic acid methyl ester	C ₁₉ H ₃₆ O ₂	112-62-9	46.03	2096	–	–	0.9
17	Methyl linoleate	C₁₉H₃₄O₂	112-63-0	46.29	2107	–	0.9	3.2
18	Methyl octadecanoate	C ₁₉ H ₃₈ O ₂	112-61-8	46.60	2120	1.7	1.3	0.8
19	Ethyl octadecanoate	C ₂₀ H ₄₀ O ₂	111-61-5	48.22	2188	–	0.7	–
20	Tricosane	C ₂₃ H ₄₈	638-67-5	50.65	2300	–	0.6	–
21	10-Methyltetracosane	C ₂₅ H ₅₂	65820-50-0	53.93	2427	–	0.7	–
22	1-[(2-Hydroxyphenyl)thioxomethyl] pyrrolidine	C₁₁H₁₃NOS	1000100-20-2	54.64	2457	1.0	1.2	17.9
23	2,6,10,14,18-Pentamethyl-2,6,10,14,18-eicosapentaene	C ₂₅ H ₄₂	75581-03-2	57.81	2589	2.3	0.7	–
24	Hexacosane	C ₂₆ H ₅₄	630-01-3	58.51	2600	1.7	1.2	–
25	11-Butyldocosane	C₂₆H₅₄	13475-76-8	61.14	2729	3.0	1.5	–
26	Benzo[h]quinoline, 2,4-dimethyl-	C ₁₅ H ₁₃ N	605-67-4	64.25	2859	2.8	2.0	–
27	Nonacosane	C ₂₉ H ₆₀	630-03-5	65.46	2900	13.3	10.0	16.2
28	(8S,8aS)-3,8-Dimethyl-4-propan-2-ylidene-1,2,6,7,8,8a-hexahydroazulen-5-one	C₁₅H₂₂O	6754-66-1	66.31	2945	4.4	7.0	2.2
29	Triacotane	C ₃₀ H ₆₂	638-68-6	67.41	3000	58.9	57.0	41.1
	Total identified					98.4	91.1	95.1

4-propan-2-ylidene-1,2,6,7,8,8a-hexahydroazulen-5-one at concentrations ranging from 3 % to 5 %. GVM included methyl hexadecanoate, methyl linoleate, and (8S,8aS)-3,8-dimethyl-4-propan-2-ylidene-1,2,6,7,8,8a-hexahydroazulen-5-one between 2 % to 5 %, while GVC exhibited the presence of hexadecanoic acid ethyl ester, benzo[h]quinoline, 2,4-dimethyl-, and (8S,8aS)-3,8-dimethyl-4-propan-2-ylidene-1,2,6,7,8,8a-hexahydroazulen-5-one within the range of 2 % to 7 %.

It is quite fascinating to note that two compounds, α -pinene (1.9 %) and 2-methylacetophenone (4.0 %), were exclusively present in GVH extract. Conversely, four compounds, namely ionol (0.8 %), ethyl octadecanoate (1.3 %), tricosane (0.6 %), and 10-methyltetracosane (0.7 %), were solely detected in GVC extracts. On the other hand, three compounds, namely *n*-hexadecanoic acid (0.6 %), 8,11-octadecadienoic acid methyl ester (0.8 %), and (*Z*)-9-octadecenoic acid methyl ester (0.9 %), were specific to GVM extracts.

During the current study, these three extracts of *G. velutina* from Saudi Arabia i.e., GVH, GVC and GVM, were subjected to in vitro anticancer evaluation against different types of cancer cell lines including, HepG2 (hepatic cancer cells), DU145 (prostate cancer cells), Hela (cervical cancer cells) and A549 (human lung cancer cells). On the other hand, doxorubicin, which is commonly prescribed anticancer medicine, is used as a positive control for the study (Table 4). Results revealed significant variations in IC50 values, highlighting the potential of *G. velutina* as a source of bioactive compounds with anticancer properties.

It is significant to mention that the GVC extract demonstrated notable anticancer activity across all tested cell lines, exhibiting IC50 values of $61.06 \pm 1.11 \mu\text{g/mL}$ (HepG2), $47.87 \pm 3.27 \mu\text{g/mL}$ (DU145), $88.76 \pm 0.91 \mu\text{g/mL}$ (Hela), and $87.99 \pm 0.12 \mu\text{g/mL}$ (A549). These findings suggest the presence of potent cytotoxic compounds within the GVC extract that merit further investigation for potential therapeutic applications. In contrast, the GVM extract displayed selective cytotoxicity only against DU145 (IC₅₀ ~ 122 $\mu\text{g/mL}$) cell line, indicating it might be useful in prostate cancer treatment. However, it exhibited no activity against HepG2, Hela, and A549 cell lines. Similarly, the GVH extract exhibited no activity against any of the tested cell lines, indicating a lack of potency against the tested cancer cell lines. It is noteworthy that upon comparing the anticancer activity of the GVC extract with that of standard anticancer agents, it was observed that the anticancer activity of the GVC extract was comparable to that of the standard chemotherapeutic agent doxorubicin at the extract level, particularly against DU145 and HepG2 cell lines. This implies that *G. velutina* extracts, specifically GVC, may harbor some bioactive compounds with cytotoxic potential.

In order to correlate the anticancer activities of all the extracts with their phytochemical constituents, we compared the type of major constituents present in each extract. Notably, the major constituents (more than 5 % of total amount of constituents) are same in all the extract i.e., triacotane is the most abundant constituent, while nonacosane is the second largest component in GVH and GVC. While, GVM consisted of 1-

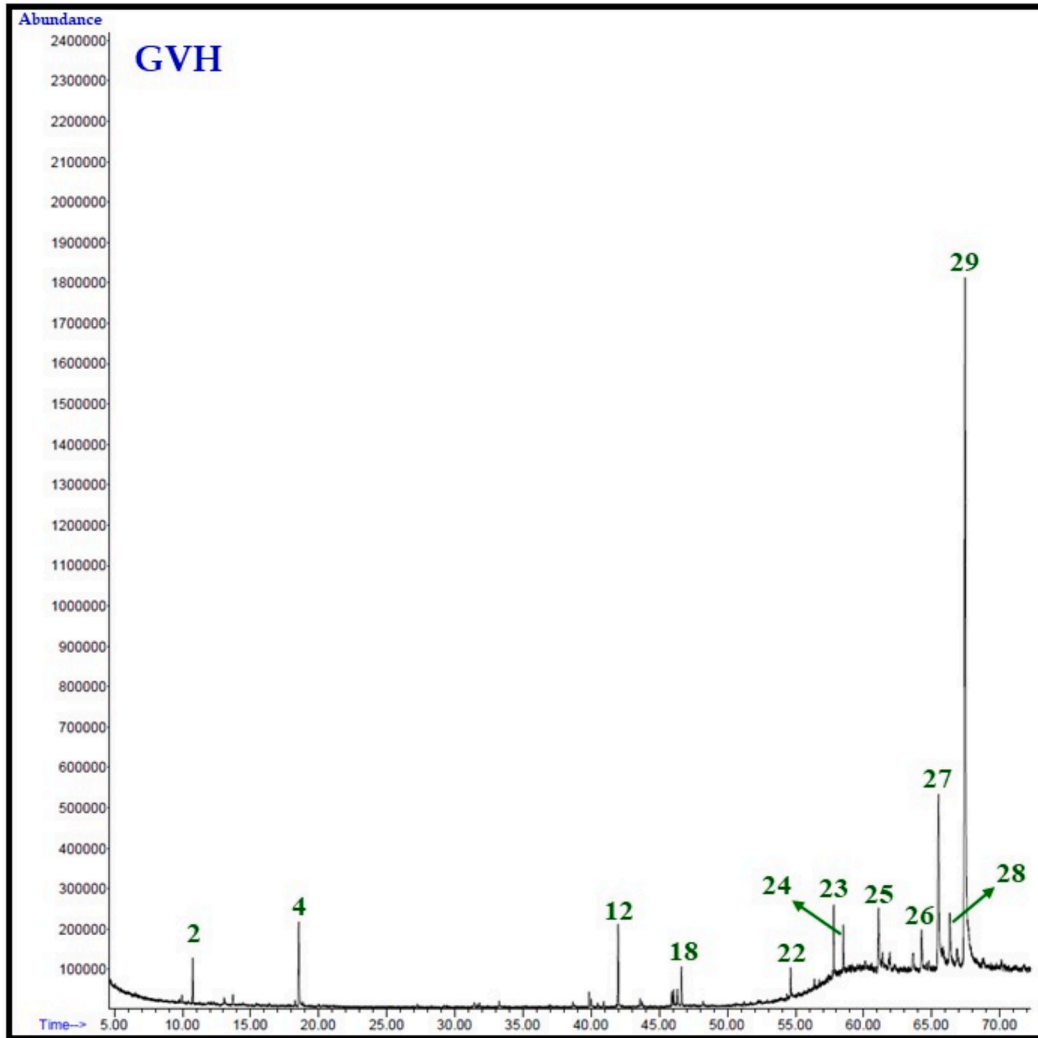


Fig. 1. Total ion chromatogram (TIC) of *n*-hexane (GVH), chloroform (GVC), and methanol (GVM) extracts of aerial parts of *G. velutina*.

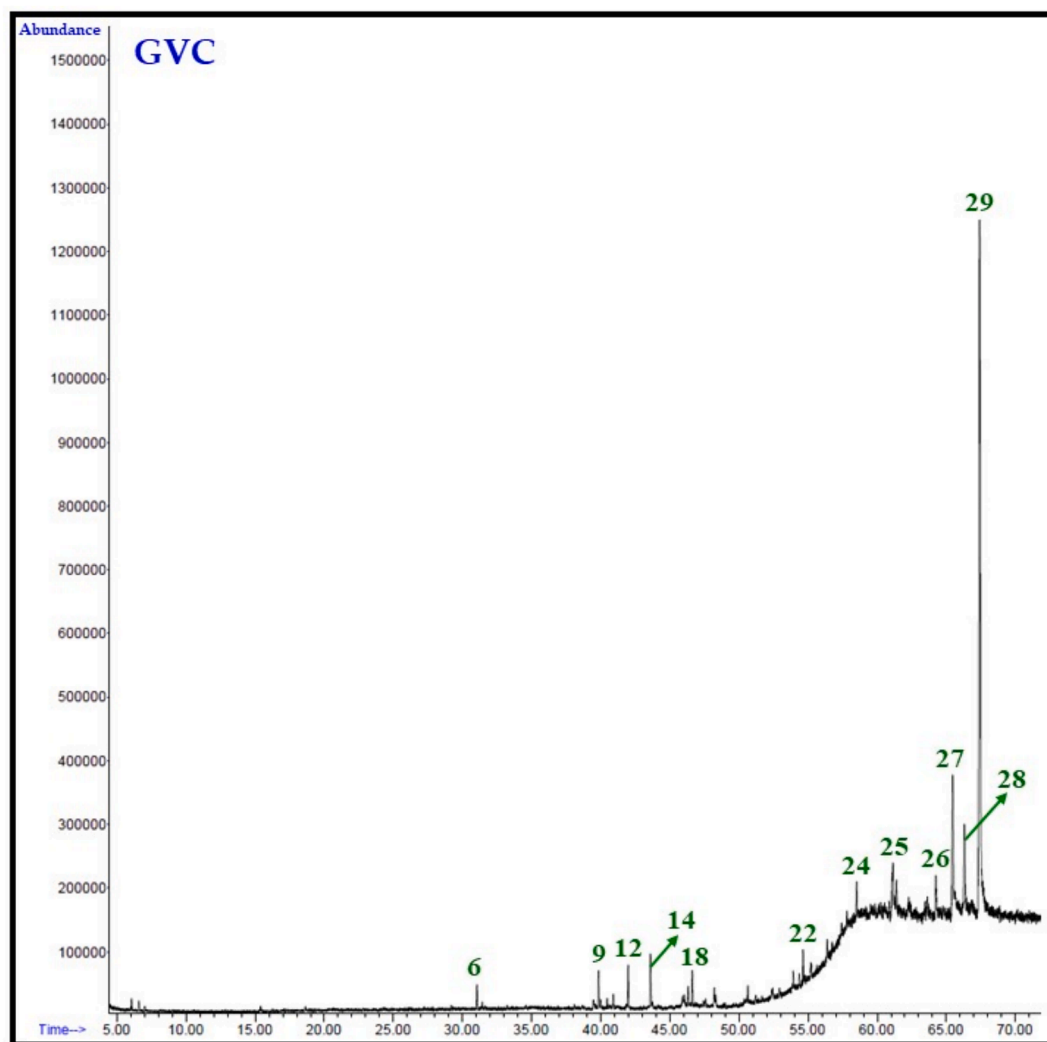


Fig. 1. (continued).

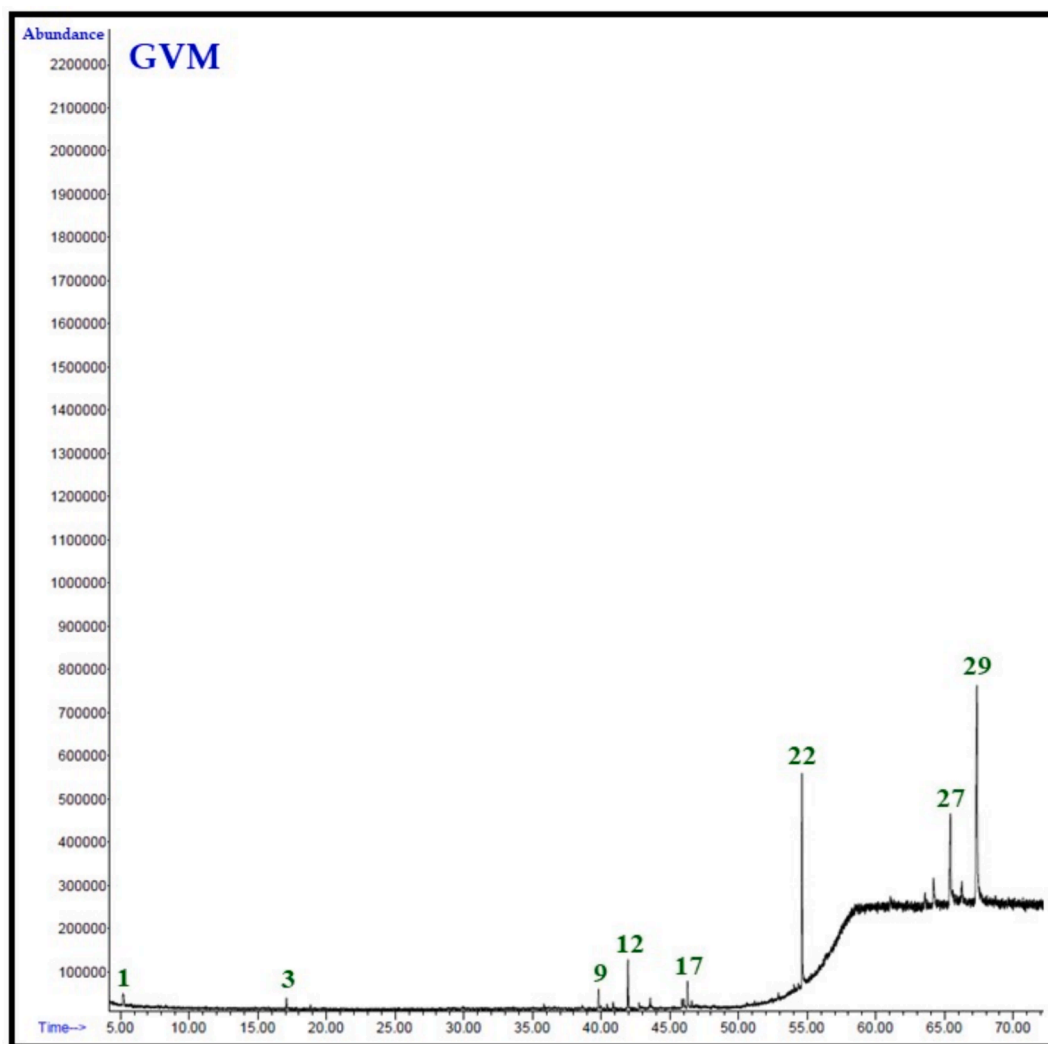


Fig. 1. (continued).

Table 4

Anticancer activity of various extracts of *G. velutina* aerial parts against various cancer cell lines.

Tested Extracts of <i>G. velutina</i> aerial parts	IC ₅₀ (µg/mL)			
	HepG2	DU145	Hela	A549
GVM	NA	121.27 ± 7.56	NA	NA
GVH	NS	NS	NS	NS
GVC	61.06 ± 1.11	47.87 ± 3.27	88.76 ± 0.91	87.99 ± 0.12
Doxorubicin	0.39 ± 0.012	0.19 ± 0.01	0.43 ± 0.71	0.29 ± 0.16

Results are expressed as mean ± SD, NA=No activity, NS=Not soluble.

[(2-hydroxyphenyl)thioxomethyl]pyrrolidine as the second largest component. Since, the highest anticancer activity is exhibited by GVC, there is a minimum chance of the role of major constituents of *G. velutina* towards the contribution to the anticancer properties of this extract. To further confirm this claim, literature was explored to find reports on the anticancer properties of major components, including triacontane and nonacosane which are present in large quantities in all the extracts. However, no references were found which are directly linked to the anticancer properties of these components. On the other hand, the GVC consists of several minor components which are only unique to this

Table 5

Binding score values of the selected compounds (ligands) against selected proteins.

S. No.	Compounds Name	Docking Score			
		HepG2 (PDB Id:1GFW)	A549 (PDB Id:1M17)	DU145 (PDB Id:2QU6)	Hela (PDB Id:6I2I)
1	10-Methyltetracosane	-7.2	-7.1	-4.1	-5
2	Dimethyl-4-propan	-2.8	-4	-3.8	-3.9
3	Ethyl-octadecanoate	-3.8	-5.1	-2.8	-3.2
4	Hexahydrofarnesyl-acetone	-1.5	-1.8	-3.2	-2.4
5	Ionol	-6.8	-8.8	-7	-7.9
6	Methyl-hexadecanoate	-3.3	-3.2	-1.2	-2.8
7	Methyl-linoleate	-3.2	-3.8	-6.7	-4.0
8	Sitosterol	-2.1	-2.2	-3.1	-3.2
9	Triacontane	-3.5	-3.2	-2.7	-3.3
10	Tricosane	-3.5	-5	-3.1	-4.7

particular extract, such as, ionol, ethyl octadecanoate, tricosane, 10-methyltetracosane. Possibly, these constituents may have played a crucial role in the anticancer properties of GVC. To confirm this assessment, we have performed in silico studies to predict cell

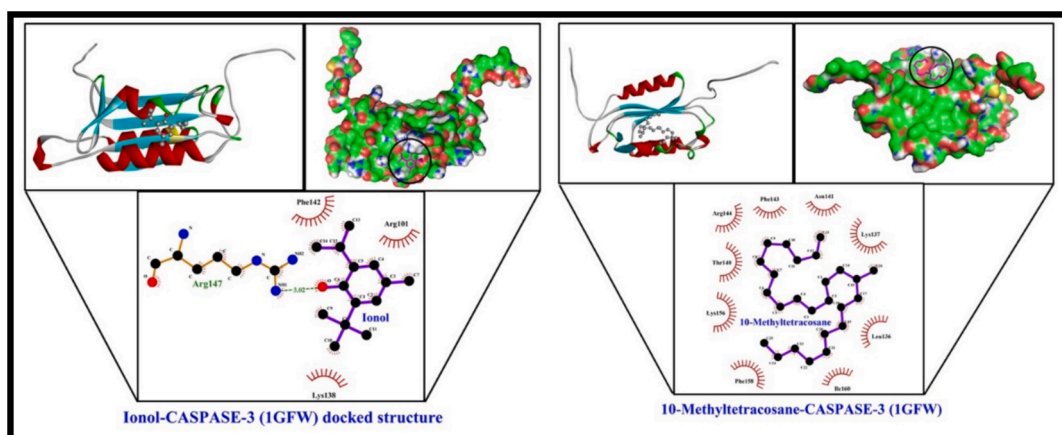


Fig. 2. Docked structure of ionol and 10-methyltetracosane with CASPASE-3 (HepG2).

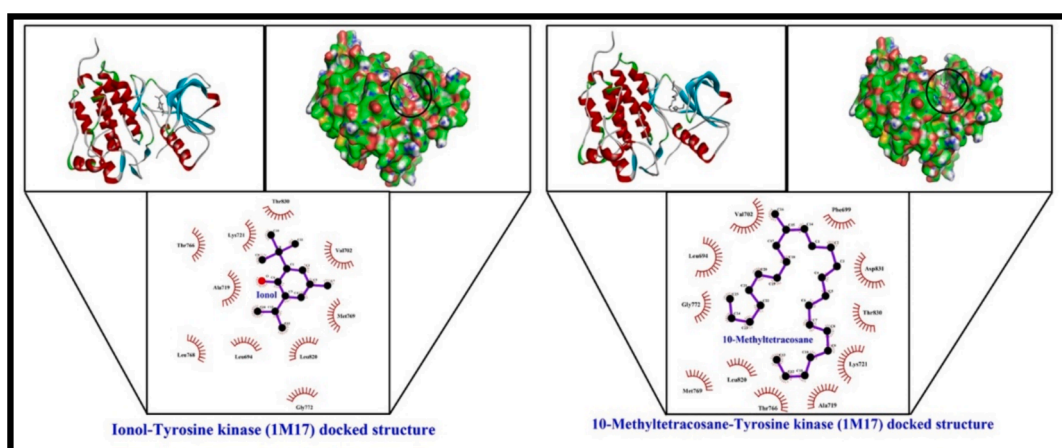


Fig. 3. Docked structure of ionol and 10-methyltetracosane with Tyrosine kinase (A549).

permeability of *G. velutina* constituents.

3.1. Analysis from molecular docking study

The molecular docking results are represented in Table 5 which reflects the Binding affinities of the selected compounds (Fig. 2) against the selected proteins. The more negative binding energy implies best docking score with greater binding affinity (Dutta et al., 2021). Binding pose and binding score are the significant tools to check the ability of a compound to block that protein considering the related disease. As per the docking scores, ionol showed very good activity against the four selected proteins.

Experimental studies revealed that GVC extract showed highest activity against all the cancerous cells and ionol is present only in GVC extract. GVH extract is totally inactive whereas GVM extract only showed weak activity against DU145. Another compound methyl-linoleate also reflects good binding score (−6.7) against DU145, present in very large amount in GVM extract. 10-methyltetracosane is also very active compound against HepG2 (−7.2) and A549 (−7.1) and it is only present in GVC extract.

Ionol forms H-Bonding with CASPASE-3 whereas non-polar interactions dominate in the 10-methyltetracosane and CASPASE-3 docked structure (Fig. 3). Hydrophobic environment also helps to create a strong protein–ligand interaction ‘Ionol-Tyrosine kinase’ and ‘10-Methyltetracosane-Tyrosine kinase’ docked structure (Fig. 3).

Both ionol and methyl-linoleate forms H-bonding with VEGFR but non-polar interaction only present in case of ‘ionol-HeLa’ docked

structure (Fig. 4). Overall, H-bonding and non-polar interaction are majorly responsible for ionol, 10-methyltetracosane and methyl-linoleate to block the selected proteins.

Hence, as per the molecular docking study ionol is the most active compound. 10-methyltetracosane and methyl-linoleate are also showed significant activity. In silico study clearly identifies the specific compounds of *Grewia velutina*, majorly responsible for the anticancer activities as obtained from the experimental observations and the experimental observation is well supported by the in silico study.

4. Conclusion

For the first time, this study provides a comprehensive exploration of the phytochemical composition and anticancer properties of different extracts derived from the aerial parts of *G. velutina*. These extracts showcased significant variations in their chemical profiles, particularly evident from the minor constituents. Notably, the GVC extract revealed several minor components unique to its composition. The difference was also clearly reflected by the results of anticancer properties i.e., only the GVC extract has showed significant activity, with IC₅₀ values ranging from 47 to 88 µg/mL against all the studied cell lines. Furthermore, the molecular docking studies have identified ionol as the most active compound which is only found in GVC as minor component.

CRedit authorship contribution statement

Merajuddin Khan: Writing – review & editing, Writing – original

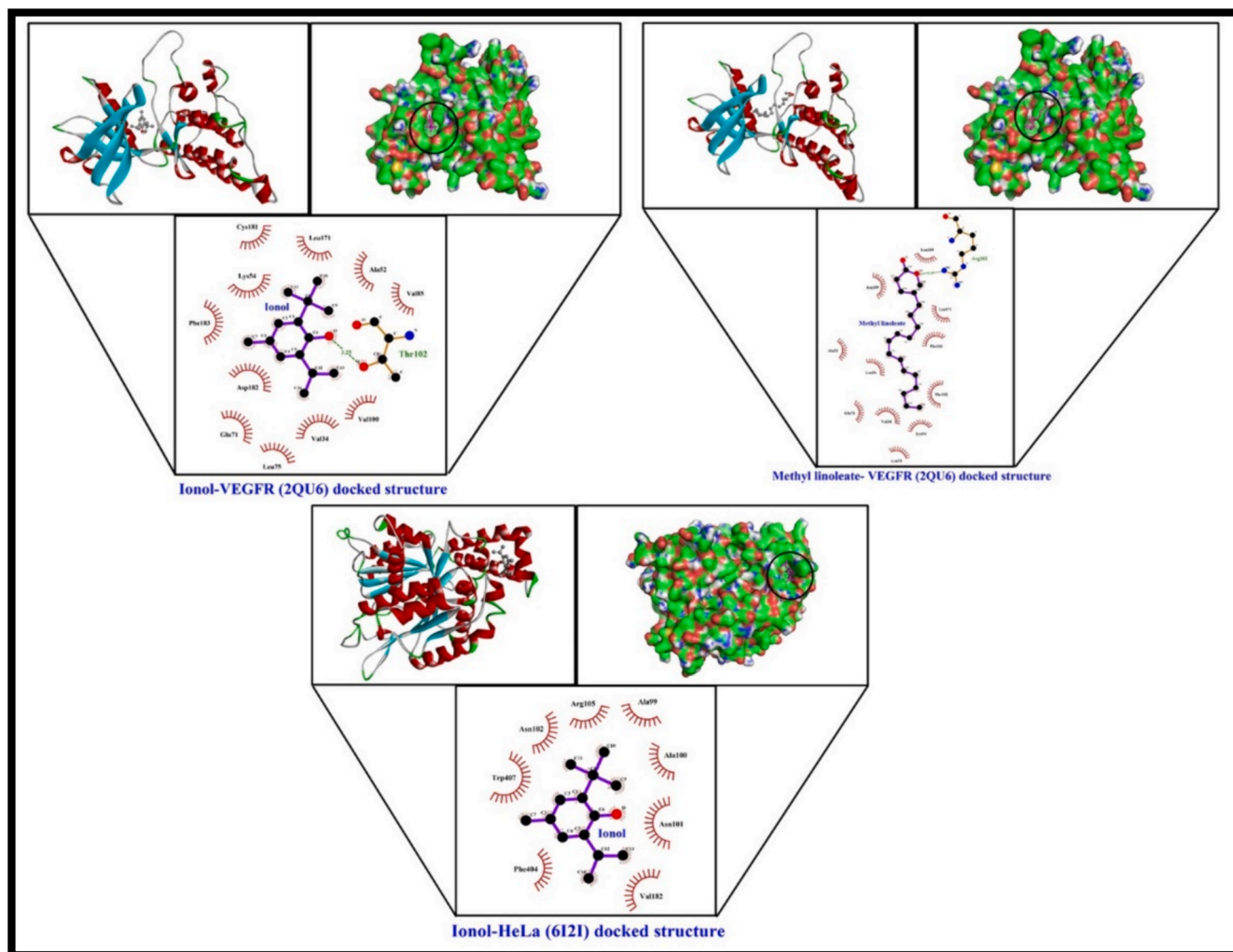


Fig. 4. Docked structure of ionol and methyl-linoleate with VEGFR (DU145) and HeLa.

draft, Validation, Resources, Investigation, Formal analysis, Data curation, Conceptualization. **Tanmoy Dutta:** Supervision, Software, Formal analysis, Data curation. **Mujeeb Khan:** Validation, Data curation, Conceptualization. **Khaleel Al-hamoud:** Visualization, Validation, Methodology, Formal analysis. **Shams Tabrez Khan:** Visualization, Validation, Data curation. **Mahmood M.S. Abdullah:** Validation, Formal analysis, Data curation. **Hamad Z. Alkhathlan:** Supervision, Resources, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This work was funded by the Researchers Supporting Project number (RSPD2024R817), King Saud University, Riyadh, Saudi Arabia.

Appendix A. Supplementary material

The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, Figure S1: title; Table S1: title; Video S1: title. Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jksus.2024.103427>.

References

- Agarwal, G., Carcache, P.J.B., Addo, E.M., et al., 2020. Current status and contemporary approaches to the discovery of antitumor agents from higher plants. *Biotechnol. Adv.* 38, 107337.
- Aydn, A., Okten, S., Erkan, S., et al., 2021. In-vitro anticancer and antibacterial activities of brominated indeno [1, 2-b] quinoline amines supported with molecular docking and MCDM. *ChemistrySelect* 6 (13), 3286–3295.
- Baildya, N., Khan, A.A., Ghosh, N.N., et al., 2021. Screening of potential drug from *Azadirachta Indica* (Neem) extracts for SARS-CoV-2: An insight from molecular docking and MD-simulation studies. *J. Mol. Struct.* 1227, 129390.
- Dutta, T., S. Ghorai, A. A. Khan, et al., 2021. Screening of potential anti-HIV compounds from *Achyranthes aspera* extracts for SARS-CoV-2: An insight from molecular docking study. *Journal of Physics: Conference Series*, IOP Publishing.
- Fattahi, M., Cusido, R.M., Khojasteh, A., et al., 2014. *Xanthomicrol: A comprehensive review of its chemistry, distribution, biosynthesis and pharmacological activity*. *Mini Rev. Med. Chem.* 14 (9), 725–733.
- Ghosh, K., Mridha, N.K., Khan, A.A., et al., 2022. CO2 activation on transition metal decorated graphene quantum dots: an insight from first principles. *Physica E* 135, 114993.
- Hansen, M.B., Nielsen, S.E., Berg, K., 1989. Re-examination and further development of a precise and rapid dye method for measuring cell growth/cell kill. *J. Immunol. Methods.* 119 (2), 203–210.
- Husain, A., Bhutani, M., Parveen, S., et al., 2021. Synthesis, in vitro cytotoxicity, ADME, and molecular docking studies of benzimidazole-bearing furanone derivatives. *J. Chin. Chem. Soc.* 68 (2), 362–373.
- Iqbal, J., Abbasi, B.A., Ahmad, R., et al., 2018. Ursolic acid a promising candidate in the therapeutics of breast cancer: Current status and future implications. *Biomed. Pharmacother.* 108, 752–756.
- Khan, M., Khan, M., Adil, S.F., et al., 2022a. Screening of potential cytotoxic activities of some medicinal plants of Saudi Arabia. *Saudi J. Biol. Sci.* 29 (3), 1801–1807.
- Khan, M., Khan, M., Al-Hamoud, K., et al., 2023. Diversity of *Citrullus colocynthis* (L.) Schrad seeds extracts: detailed chemical profiling and evaluation of their medicinal properties. *Plants* 12 (3), 567.

- Khan, M., Khan, M., Alshareef, E., et al., 2023b. Chemical characterization and chemotaxonomic significance of essential oil constituents of *matricaria aurea* grown in two different agro-climatic conditions. *Plants*. 12 (20), 3553.
- Laskowski, R.A., Swindells, M.B., 2011. LigPlot+: multiple ligand-protein interaction diagrams for drug discovery. ACS. Publications.
- Muniaraj, S., Subramanian, V., Srinivasan, P., et al., 2018. In silico and in vitro studies on Lyngbya majuscula using against lung cancer cell line (A549). *Pharmacogn. J.* 10 (3).
- Qamar, M., Akhtar, S., Ismail, T., et al., 2021. The chemical composition and health-promoting effects of the *Grewia* species—A systematic review and meta-analysis. *Nutrients* 13 (12), 4565.
- Rajput, A., Sharma, P., Kumar, N., et al., 2023. Neuroprotective activity of novel phenanthrene derivative from *Grewia tiliaefolia* by in vitro and in silico studies. *Sci. Rep.* 13 (1), 2444.
- Seeliger, D., de Groot, B.L., 2010. Ligand docking and binding site analysis with PyMOL and Autodock/Vina. *J. Comput. Aided Mol. Des.* 24 (5), 417–422.
- Shukla, R., Sharma, D.C., Baig, M.H., et al., 2016. Antioxidant, antimicrobial activity and medicinal properties of *Grewia asiatica* L. *Med. Chem.* 12 (3), 211–216.
- Siddiqui, S., Upadhyay, S., Ahmad, I., et al., 2021. Cytotoxicity of *Moringa oleifera* fruits on human liver cancer and molecular docking analysis of bioactive constituents against caspase-3 enzyme. *J. Food Biochem.* 45 (5), e13720.
- Suguna, M., Umesha, S., 2022. Phytochemical composition, pharmacological properties, and therapeutic activities of genus: *Grewia*. *Journal of Pharmacognosy and Phytochemistry.* 11 (4), 263–272.
- Ullah, R., Alqahtani, A.S., Noman, O.M., et al., 2020. A review on ethno-medicinal plants used in traditional medicine in the Kingdom of Saudi Arabia. *Saudi J. Biol. Sci.* 27 (10), 2706.
- Ullah, W., Uddin, G., Siddiqui, B.S., 2012. Ethnic uses, pharmacological and phytochemical profile of genus *Grewia*. *J. Asian Nat. Prod. Res.* 14 (2), 186–195.
- Wang, Q., He, J., Wu, D., et al., 2015. Interaction of α -cyperone with human serum albumin: Determination of the binding site by using Discovery Studio and via spectroscopic methods. *J. Lumin.* 164, 81–85.
- Waterhouse, A., Bertoni, M., Bienert, S., et al., 2018. SWISS-MODEL: homology modelling of protein structures and complexes. *Nucleic Acids Res.* 46 (W1), W296–W303.