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HR-LCMS based metabolite profiling of methanolic leaf extract of *Terminalia Pallida Brandis* and its antioxidant potential

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ABSTRACT: *Terminalia* species are being reported as medicinally useful. *Terminalia pallida Brandis* is one of the plants of the family *Combretaceae*. The aim of the present study is to catalog the phytochemical distribution and to validate the antioxidant potential of methanolic leaf extract (METP). Antioxidant potential of methanolic leaf extract was estimated by DPPH assay and phytochemical distribution was assessed by HR-LCMS analysis. The antioxidant test result of leaf extract displayed a potential free radical scavenging effect at test concentrations ($p<0.001$). In HR-LC-MS study a total of 29 bioactive compounds of a variety of chemical classes like flavanoids, alkaloids, fatty acids, diterpenoids, glycosides, amino acids and polyphenols etc were identified in both positive & negative ion mode, and among these few compounds possessed various biological activities. Based on these obtained results, it is concluded that METP constitute 29 bioactive compounds and possess potential antioxidant property in concentration dependent manner.

KEYWORDS: Antioxidant activity; HR-LCMS; Methanol; *Terminalia pallida Brandis*.

1. INTRODUCTION

Terminalia pallida Brandis is a plant belongs to the family of *Combretaceae,* found in tropical and subtropical countries [1]. Due to the availability of certain bioactive chemicals, plants are employed as medicines in many different cultures and are a source of many powerful pharmaceuticals [2,3]. Due to its bioavailability, accessibility, efficacy, cost, and lack of related side effects, it is estimated that more than 80% of the world's population uses medicinal plants and their phyto therapeutic agents as an alternative to conventional primary healthcare [4]. The prospect of segregating chemical substances from plants gave rise to the contemporary scientific field of ethnopharmacology, which aims to differentiate potential lead medications from medicinally significant plants [5]. Initially, extracting, isolating, and characterising novel bioactive chemicals presented substantial technological challenges to pharmacological researchers. Despite substantial challenges, scientists have made progress in understanding the intricate chemistry of plants, which has helped them overcome methodological challenges in characterising plant metabolites from chemically divergent complicated crude mixtures [6]. It was made feasible by the use of LC-MS methods for untargeted phytochemical profiling [7]. The ability of liquid chromatography with tandem mass spectrometry to couple with other chromatographic methods offers several benefits in investigating and characterising the phytoconstituents of medicinal plants due to its accuracy, sensitivity, speed, and specificity [8]. Developments in computational bioinformatics approaches and the creation of online metabolite databases, chromatographic techniques for characterising plant metabolites have developed during the past few decades, greatly aiding in the cataloguing of many metabolites from pharmacologically significant plants. However, for a number of medicinally important plants that have remained unidentified owing to conventional extraction and identification techniques, there is still a need to apply chromatographic-based chemical fingerprinting widely. HR-LCMS is a sophisticated analytical technique that combines the separation capabilities of high-resolution liquid chromatography (HPLC) with the sensitive and accurate mass analysis of mass spectrometry. HR-LCMS is crucial in identifying and characterizing novel compounds present in plant extracts [9]. In order to identify the pharmaceutically powerful bioactive and make attempts to comprehend its effect on the target simpler, it is essential to reveal the intricate chemistry of bioactive crude extracts utilizing HR-LCMS. The present research work was carried

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out to cataloging the bioactive constituents of methanolic leaf extract of *terminalia pallida Brandis* (METP) and to validate its antioxidant potential by DPPH assay.

2. RESULTS & DISCUSSION

2.1 DPPH activity of METP

DPPH has been widely used to evaluate the antioxidant activity of phytoconstituents due to their free radical scavenging ability [10]. Natural antioxidants may be found in abundance in plants, and some phytochemicals also have antioxidant capabilities. Their main function is to safeguard against oxidative damage caused by free radicals. [11]. Free radicals have a role in a number of illnesses, including cancer, atherosclerosis, neurological disorders, and myocardial infarction. [12]. The antioxidant activity of METP was quantified using the DPPH assay. The % inhibition at a dosage of 40 µg/mL was found to be nearly similar to 10 µg/mL of ascorbic acid. IC_{50} value was compared to that of normal ascorbic acid. Reduced DPPH with the addition of METP in a dose-dependent manner and the results were statistically significant (**Figure 1**). Plants are utilized in traditional medicine to cure a wide range of illnesses. The traditional uses of plants may be scientifically analysed using current methods, which may lead to the discovery of promising substances that can be used to treat a variety of disorders. Phytochemical substances found in medicinal plants are a plentiful supply and can be used to treat a variety of ailments [13]. In recent years, a wide range of therapeutic compounds were produced from medicinal plants [14]. The presence of numerous secondary metabolites was revealed by phytochemical analysis of different solvent leaf extracts, and it is clear that phenolic compounds are the predominant chemical elements of many herbal plants. Due to their advantageous antioxidant properties, phenolic compounds have gained a great deal of public and scientific interest. Screening plants for polyphenolic, flavonoid, and anti-oxidant activities is therefore valuable [15]. Natural antioxidants are a great supply found in plants, and their main purpose is to provide safety from oxidative stress caused by generation of free radicals [16]. The development of free radicle plays a significant role in the development of oxidative stress, and previous literature reports suggested that quercetin and gallic acid can suppress the development of oxidative stress, which can lead to a variety of diseases [17,18]. In this study, methanolic leaf extract of *T. pallida Brandis* exhibited potential antioxidant activity ($p<0.001$) in a concentration-dependent manner.

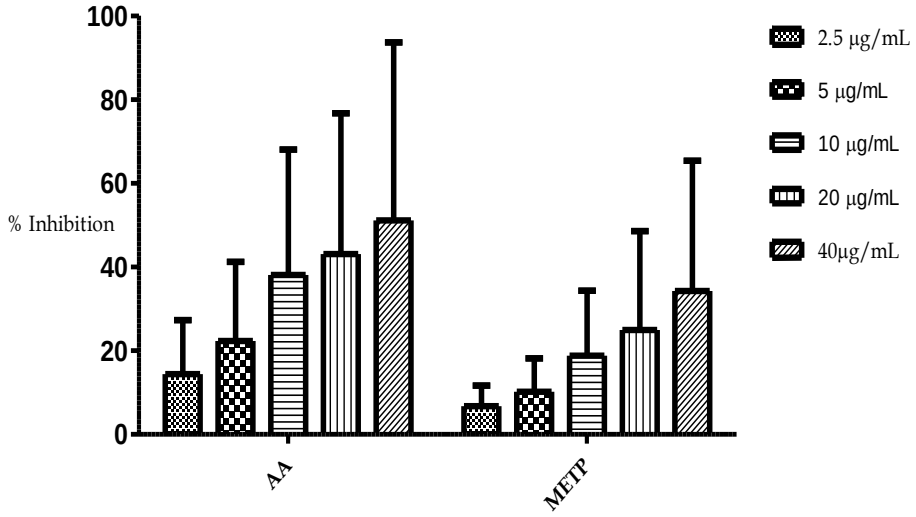


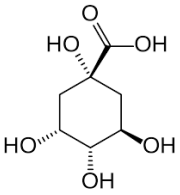
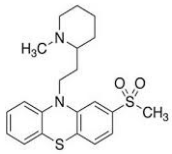
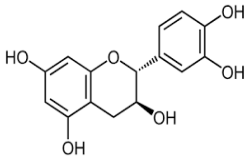
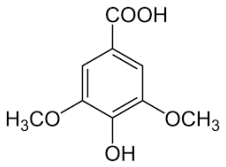
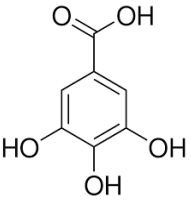
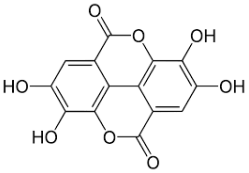
Figure 1. Graphical representation of % inhibition of DPPH free radical of METP.

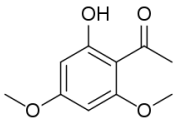
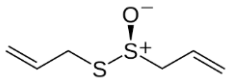
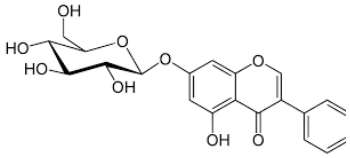
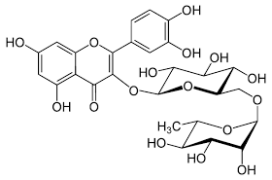
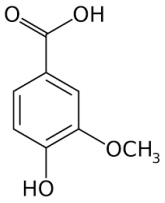
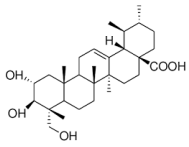
2.2 HR-LCMS study of METP

The typical HR-LCMS chromatogram of METP was shown in Figures 2 (negative mode) and 3 (positive mode). In which about 29 compounds were identified (Tables 1 and 2) and they were characterised based on the Rt, mass (*m/z*), metabolite name, chemical formula, and reported activity. Various secondary metabolites, such as polyphenols, flavonoids, diterpenoids, fatty acids, glycosides, alkaloids, and amino acids have been

identified by the current metabolite profiling. The presence of one or more phenolic rings in their structure differentiate polyphenols, a significant class of phytochemicals. METP was shown to be a rich source of polyphenolic substances such quinic acid, -(-) Catechin, syringic acid, genistin, rutin, and vanillic acid with molecular ion [M-H]-peaks at *m/z*-191.05, *m/z*-289.07, *m/z*-197.04, *m/z*-431.09, *m/z*-609.14, and *m/z*-487. Flavonoids, which have a variety of biological effects. Flavonoids such as 6-C-fucosylluteolin with a molecular ion (M+H) + peak at m/z-433.11 and cicerin with a molecular ion [M+Na]- peak at m/z-601.12 were discovered to be present in METP. METP also included terpenoids including delcosine (*m/z*-476.26) and oleanolic acid (*m/z*-457.36; Rt-22.92 min). It is well recognised that diterpenes have a variety of medicinal properties, including anti-inflammatory, anti-microbial, and cardioprotective action. The LC chromatogram also showed the presence of the alkaloids retronecine (*m/z*-156.10) and the glucoside Multifidol (*m/z*-211.09, Rt-11.18 min). Other classes of compounds, such as cicerin (*m/z*-601.12, Rt-9.42 min), thioridazole-2-sulfone (*m/z*-481.06, Rt-1.14 min), Rhamnalpinogenin (*m/z*-329.06, Rt-8.18 min), Stenocerol (*m/z*-437.34, RT-21.55), and gambirin C (an isoflavone), were also discovered. It has been claimed that the buxamine and alpha-linoleic acid have strong anti-inflammatory properties. In this experiment, it was shown that the METP contains several different classes of phytoconstituents.

Table 1. List of phytochemicals identified in METP by negative ion mode of HR-LCMS.

S. No	Compound	*m/z*	Rt (min)	Formula	Structure
1	Quinic acid	191.0556	1.085	$C_7H_{12}O_6$	
2	Thioridazole-2-sulfone	481.0603	1.142	$C_{21}H_{26}N_2O_2S_2$	
3	(-)-Catechin	289.0711	4.688	$C_{15}H_{14}O_6$	
4	Syringic acid	197.0446	7.005	$C_9H_{10}O_5$	
5	Gallic acid	169.0137	8.357	$C_7H_6O_6$	
6	Ellagic acid	300.9992	8.735	$C_{14}H_6O_8$	

7	Xanthoxylin	195.0657	9.022	$C_{10}H_{12}O_4$	
8	Allivicin	609.1481	9.08	$C_{27}H_{30}O_{16}$	
9	Genistin	431.0983	9.401	$C_{21}H_{20}O_{10}$	
10	Rutin	609.1461	9.418	$C_{27}H_{30}O_{16}$	
11	Vanillic acid	167.0345	11.426	$C_8H_8O_4$	
12	Asiatic acid	487.3426	16.94	$C_{30}H_{48}O_5$	

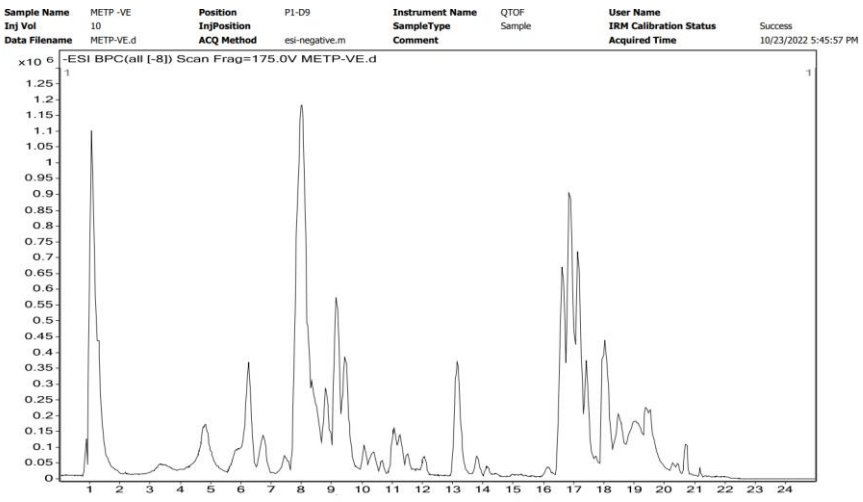
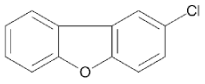
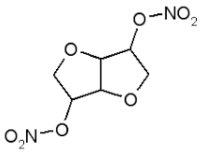
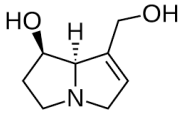
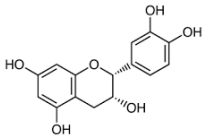
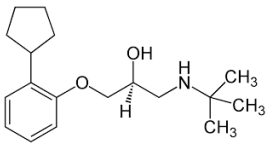
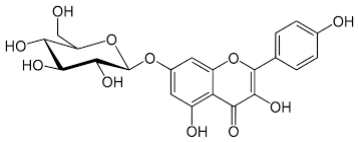
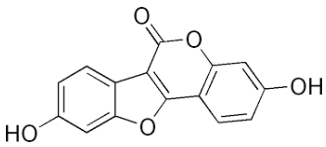
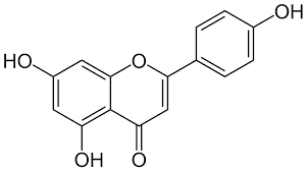
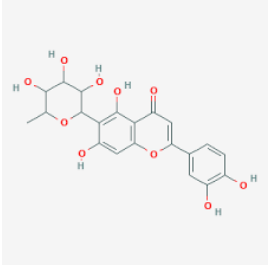


Figure 2. LC chromatogram (negative mode) of METP.

Table 2. List of phytochemicals identified in METP by positive ion mode of HR-LCMS.

Compound Name	*m/z*	Rt	Formula	Structure

2-Chlorodibenzofuran	241.0054	0.821	$C_{12}H_7ClO_2$	
Isosorbide dinitrite	259.0162	0.837	$C_6H_8N_2O_8$	
Dihydroxynortropane	144.1027	1.053	$C_7H_{13}NO_2$	
Retronecine	156.1028	1.125	$C_8H_{13}NO_2$	
(-)-Epicatechin	291.0873	6.286	$C_{15}O_{14}O6$	
Penbutolol	314.2082	7.651	$C_{18}H_{29}NO_2$	
Kaempferol 7-O-g	449.1094	7.705	$C_{21}H_{20}O_{11}$	
Coumestrin	431.0983	7.77	$C_{21}H_{18}O_{10}$	
Rhamnalpinogenin	329.0662	8.183	$C_{17}H_{12}O_7$	
6-C-Fucosylluteolin	433.1146	8.645	$C_{21}H_{20}O_{10}$	

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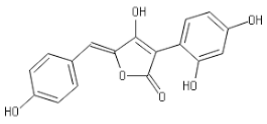
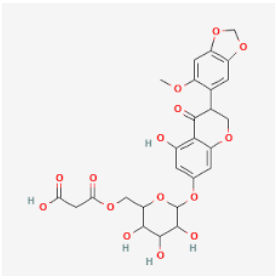
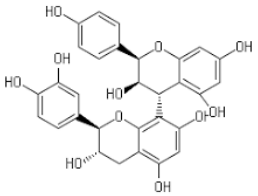
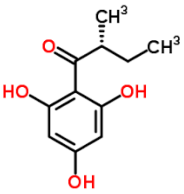
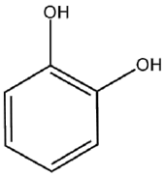
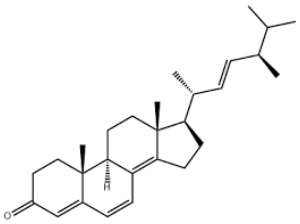
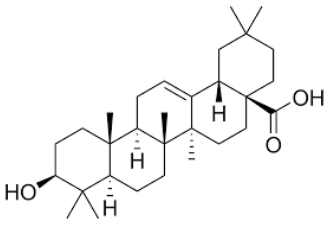
Aspulvinone G	313.0716	9.079	$C_{17}H_{12}O_6$	
Cicerin	601.1213	9.422	$C_{26}H_{26}O_{15}$	
Gambiriin C	585.1259	10.236	$C_{30}H_{26}O_{11}$	
Multifidol	211.0968	11.184	$C_{11}H_{14}O_4$	
catechol	181.1226	15.764	$C_{11}H_{16}O_2$	
Stenocerol	437.3427	21.55	$C_{28}H_{46}O_2$	
Oleanolic acid	457.3686	22.92	$C_{30}H_{48}O_3$	

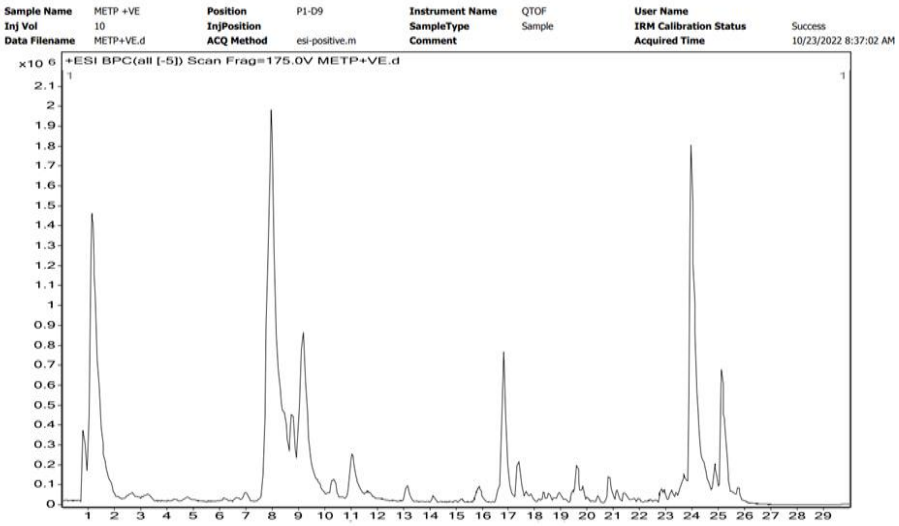


Figure 3. LC chromatogram (positive mode) of METP.

As per one of the recent studies, one of the compounds identified in HR-LCMS analysis, quinic acid has reported as antioxidant and antidiabetic activities [22]. Syringic acid possess potential anti-microbial, anti-inflammatory and anti-endo toxic properties [23]. Rutin is one of the polyphenolic compounds presents in various plant extracts has proved as diversed pharmacological properties includes anti-oxidant, neuroprotective, anticonvulsant, analgesic, antiarthritic, anticoagulant and antiplatelets [29]. List of few phytochemicals identified in HR-LCMS analysis and their reported biological properties were represented in Table 3. The application of untargeted profiling techniques to analyze phytochemicals derived from plant extracts has the potential to facilitate the investigation of diverse compound groups and contribute to the discovery of novel bioactive compounds. This approach can effectively minimize the duplication in compound identification processes. According to extensive research, throughout the long history of civilization on this planet, dependency on plants for survival or treatment was unavoidable. In the health care system, plants play a significant role as a source of bioactive chemicals [30]. Chromatographic techniques for characterizing plant metabolites have developed during the past few decades, greatly aiding in the cataloging of many metabolites from pharmacologically significant plants [31]. The investigation of multiple groups of compounds and the identification of new bioactive compounds would be aided by the untargeted profiling of phytochemicals from plant extracts, decreasing the amount of duplication in compound identification [34]. This research encourages additional research into the separation and structural characterization of various therapeutically beneficial phytochemicals since there has been minimal progress in the identification and isolation of phytoconstituents of the entire plant.

Table 3. List of few compounds identified in HR-LCMS and their reported biological activities.

S. No	Name of the compound	Biological activity
1	Quinic acid	Anti-oxidant, anti-diabetic, anti-cancer, analgesic [19]
2	Syringic acid	Anti-microbial, anti-inflammatory [20]
3	Gallic acid	Anti-inflammatory [21]
4	Ellagic acid	Anti-oxidant [22]
5	Xanthoxylin	Fungicide, fungistatic [23]
6	Allivicin	Anti-oxidant, Cardioprotection, anti-diabetic [24]
7	Genistin	Immunosuppressor [25]
8	Rutin	Neuroprotective, anti-coagulation [26]

9	Vanillic acid	Neuroprotective, anti-oxidant [27]
10	Asiatic acid	Anti-cancer [28]

3. CONCLUSION

In light of the present findings of this research, it was found that methanolic leaf extract could be a probable source for anti-oxidative potential. The application of HR-LCMS in the comprehensive analysis of bioactive components within plant-derived substances is widely acknowledged as a validated methodology. The elucidation of the intricate chemical composition of bioactive crude extracts through the utilisation of high throughput and high-resolution methodologies is crucial in identifying the pharmacologically powerful bioactive compounds and streamlining the endeavours to comprehend their mechanism of action on the intended target. The secondary bioactive compounds like alkaloids, tannins, glycosides, phenols, flavonoids, and many more were found by HR-LCMS analysis, among many others.

4. MATERIALS AND METHODS

4.1 Chemicals

Ascorbic acid and DPPH were procured from Himedia labs., Pvt. Ltd. Mumbai. Thiobarbituric acid and trichloroacetic acid were acquired from SD Fine chemicals Ltd., Mumbai. All the solvents and chemicals were utilized in this work were obtained from SD Fine chemicals, Mumbai and Merck India, Mumbai.

4.2 Collection and authentication of plant leaves

Dr. K. Madhava Shetty, Taxonomist, who works as a Professor in the Department of Botany, Sri Venkateswara University, Tirupati, Andhra Pradesh, India, certified the collected (collected from the Talakona forest in Chittoor, Andhra Pradesh, India) leaves of *T. pallida Brandis* in the laboratory. Specimen vouchers of plants coded as *T. pallida Brandis* -0821 were preserved for future reference.

4.3 Preparation of leaf extract

The gathered leaves were pulverized after being dried (in the air) at room temperature. The 250-gm powdered plant material was macerated for 24 to 72 hours before being fractionated with methanol to generate extract. The resulting solvent extract was concentrated using a rotary evaporator (*in vacuo*) and refrigerated for further investigation [32].

4.4 Antioxidant activity by DPPH assay

The DPPH test technique was used to assess the free radical scavenging activity of leaf extracts of *T. pallida Brandis*. Separate solutions of leaf extract and the reference standard (ascorbic acid) were produced. Plant extract (0.1mL) was mixed with 3 mL of DPPH (0.004%) methanolic solution. The mixture was oscillated and allowed to stand for 30 minutes before measuring optical density at 517 nm with a UV-visible spectrophotometer (Shimadzu 1501). The IC_{50} value was computed using the equation of line obtained by drawing a graph of concentration (g/mL) versus% inhibition [33].

$$(\%)\ \text{Radical scavenging} = \{(A_0 - A_1)/A_0\} \times 100$$

Where, A_0=absorbance of the control; A_1=absorbance of the extract.

4.5 HR-LCMS analysis

The plant extract used in the HR-LCMS study were dissolved in methanol. HR-LCMS study of plant extracts (METP) carried out at Sophisticated Analytical Instrument Facility (SAIF), IIT Bombay, Pawai, Mumbai. An Agilent high-resolution LCMS model-G6550A (Component name: MSQ-TOF, Model: G6550A, Ion source: Dual AJS ESI) was used to analyze the chemical fingerprints of METP. The acquisition mode (Acquisition Mode AutoMS2) was configured to scan at a rate of one spectrum per second across a mass-to-energy (M/Z) range of 120 to 1500 Dalton. A steady gas flow of 13 psi/min was used to keep the LC at 250˚ C. We employed a G4226A hip sampler, which specified a flow rate of 100 l/min for the auxiliary, 100 l/min for the ejection, 5 l for the flush-out factor, and 10 l for the analysis injection volume. For the first two minutes of the 30-minute collecting period, the solvent composition A: B flow remained at 95:5. In HR-LCMS, water, and acetonitrile are two common solvents [34].

4.6 Statistical analysis

Using GraphPad Prism software (Version 5.0), Tukey's multiple comparison tests were used to statistically indicate the experiment outcomes. The acquired data were expressed with SEM (±), and $p<0.05$ was used to indicate the degree of significance.

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REFERENCES

[1] Guguloth SK, Malothu N, Kulandaivelu U, Rao KG, Areti AR, Noothi S. Phytochemical investigation and In-vitro Thrombolytic activity of *Terminalia pallida* Brandis leaves. Res J Pharm Technol. 2021;14(2):879-882. https://doi.org/10.5958/0974-360X.2021.00156.6.

[2] Guguloth SK, Malothu N, Parasanth DSNBK. GC-MS analysis and thrombolytic property of methanolic leaf extracts of *Terminalia pallida* brandis against carrageenan instigated tail thrombosis model in mice. Pharmacogn Res. 2022;14(1):53-60. https://doi.org/10.5530/pres.14.1.9.

[3] Tsugawa H. Advances in computational metabolomics and databases deepen the understanding of metabolisms. Curr Opin Biotechnol. 2018; 54:10-17. https://doi.org/10.1016/j.copbio.2018.01.008.

[4] Tabudravu JN, Pellissier L, Smith AJ, Subko K, Autréau C, Feussner K, Hardy D, Butler D, Kidd R, Milton EJ, Deng H, Ebel R, Salonna M, Gissi C, Montesanto F, Kelly SM, Milne BF, Cimpan G, Jaspars M. LC-HRMS-Database Screening Metrics for Rapid Prioritization of Samples to Accelerate the Discovery of Structurally New Natural Products. J Nat Prod. 2019;82(2):211-220. https://doi.org/10.1021/acs.jnatprod.8b00575.

[5] Noumi E, Snoussi M, Anouar EH, Alreshidi M, Veettil VN, Elkahoui S, Adnan M, Patel M, Kadri A, Aouadi K, De Feo V, Badraoui R. HR-LCMS-Based Metabolite Profiling, Antioxidant, and Anticancer Properties of *Teucrium polium* L. Methanolic Extract: Computational and In Vitro Study. Antioxidants (Basel). 2020;9(11):1089. https://doi.org/10.3390/antiox9111089.

[6] Olivia NU, Goodness UC, Obinna OM. Phytochemical profiling and GC-MS analysis of aqueous methanol fraction of *Hibiscus asper* leaves. Future J Pharm Sci. 2021; 7:59. https://doi.org/10.1186/s43094-021-00208-4.

[7] Marulasiddaswamy KM, Nuthan BR, Channarayapatna RS, Bajpe SN, Sekhar S, Kini KR. In-silico evaluation of Fragransol B from *Myristica dactyloides* for anti-inflammatory potential. J Appl Pharm Sci. 2021;11(11):112-120. https://dx.doi.org/10.7324/JAPS.2021.1101115.

[8] Christenhusz MJ, Byng JW. The number of known plants species in the world and its annual increase. Phytotaxa. 2016;261(3):201-217. https://doi.org/10.11646/phytotaxa.261.3.1

[9] Guguloth SK, Malothu N, Ganta NM, Ramakrishna K, Guntupalli C. Antiplatelet and antithrombotic properties of methanolic leaf extract of *Plumbago zeylanica* L.GC-MS and HR-LCMS metabolite profiling. S Afr J Bot. 2023; 159:627-634. https://doi.org/10.1016/j.sajb.2023.06.027.

[10] Guguloth SK, Malothu N, Prasanth DS, Areti AR. Evaluation of thrombolytic and antioxidant activity of leaf extracts of *Plumbago zeylanica* L. Indian J Pharm Educ Res. 2022;56(4):1181-1189. https://doi.org/10.5530/ijper.56.4.200.

[11] Hsu CY. Antioxidant activity of extracts from *Polygonum aviculare* L. Biol Res. 2006; 39: (2): 281-288. https://doi.org/10.4067/s0716-97602006000200010.

[12] Guguloth SK, Malothu N, Ganta NM, Ramakrishna K, Guntupalli C. Antiplatelet and antithrombotic properties of methanolic leaf extract of *Plumbago zeylanica* L. GC-MS and HR-LCMS metabolite profiling. S Afr J Bot. 2023; 159:627-634. https://doi.org/10.1016/j.sajb.2023.06.027.

[13] Sampaio BL, Edrada-Ebel R, Da Costa FB. Effect of the environment on the secondary metabolic profile of *Tithonia diversifolia*: A model for environmental metabolomics of plants. Sci Rep. 2016;6(1):29765. https://doi.org/10.1038/srep29265.

[14] Rakib A, Ahmed S, Islam MA, Haye A, Uddin SN, Uddin MM, Hossain MK, Paul A, Emran TB. Antipyretic and hepatoprotective potential of *Tinospora crispa* and investigation of possible lead compounds through in-silico approaches. Food Sci Nutr. 2020 ;8(1):547-556. https://doi.org/10.1002/fsn3.1339.

[15] Adnan M, Chy MNU, Kama ATMM, Azad MOK, Chowdhury KAA, Kabir MSH, Gupta SD, Chowdhury MAR, Lim YS, Cho DH. Comparative study of *Piper sylvaticum* Roxb. leaves and stems for anxiolytic and antioxidant properties through in vivo, in vitro, and in silico approaches. Biomedicines. 2020;8(4):68. https://doi.org/10.3390/biomedicines8040068.

[16] Al Mahmud Z, Emran TB, Qais N, Bachar SC, Sarker M, Uddin MM. Evaluation of analgesic, anti-inflammatory, thrombolytic and hepatoprotective activities of roots of *Premna esculenta* (Roxb). J Basic Clin Physiol Pharmacol. 2016;27(1):63-70. https://doi.org/10.1515/jbcpp-2015-0056.
[17] Slevin MN, Ahmed Q, Wang G, Dowell Mc, Badimon L. Unique vascular protective properties of natural products: supplements or future main-line drugs with significant anti-atherosclerotic potential. Vasc Cell. 2012 Apr 30;4(1):9. https://doi.org/10.1186/2045-824x-4-9.
[18] Blokhina O, Virolainen E, Fagerstedt KV. Antioxidants, oxidative damage and oxygen deprivation stress a review. Ann Bot. 2003; 91(2):179-194. https://doi.org/10.1093/aob/mcf118.
[19] Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. Oxid Med CellLongev. 2009; 2(5):270-278. https://doi.org/10.4161/oxim.2.5.9498.
[20] Kim YJ. Antimelanogenic and antioxidant properties of gallic acid. Biol Pharm Bull. 2007; 30 (6):1052–1055. https://doi.org/10.1248/bpb.30.1052.
[21] Iacopini P, Baldi P, Storchi P, Sebastiani L. Catechin, epicatechin, quercetin, rutin and resveratrol in red grape: content, in-vitro antioxidant activity and interactions. J Food Compos Anal.2008;21(8):589-598. https://doi.org/10.1016/j.jfca.2008.03.011.
[22] Benali T, Bakrim S, Ghchime R, Benkhaira N, El Omari N, Balahbib A, Taha D, Zengin G, Hasan MM, Bibi S, Bouyahya A. Pharmacological insights into the multifaceted biological properties of quinic acid. Biotechnol Genet Eng Rev. 2024;40(4):3408-3437. https://doi.org/10.1080/02648725.2022.2122303.
[23] Srinivasulu C, Ramgopal M, Ramanjaneyulu G, Anuradha CM, Kumar CS. Syringic acid (SA) a review of its occurrence, biosynthesis, pharmacological and industrial importance. Biomed Pharmacother. 2018; 108:547-557. https://doi.org/10.1016/j.biopha.2018.09.069.
[24] Kahkeshani N, Farzaei F, Fotouhi M, Alavi SS, Bahramsoltani R, Naseri R, Momtaz S, Abbasabadi Z, Rahimi R, Farzaei MH, Bishayee A. Pharmacological effects of gallic acid in health and diseases: A mechanistic review. Iran J Basic Med Sci. 2019 ;22(3):225. https://doi.org/10.22038/ijbms.2019.32806.7897.
[25] Zhu H, Yan Y, Jiang Y, Meng X. Ellagic acid and its anti-aging effects on central nervous system. Int J Mol Sci. 2022;23(18):10937. https://doi.org/10.3390/ijms231810937.
[26] Cechinel FV, Lima EO, Morais VM, Gomes ST, Miguel OG, Yunes RA. Fungicide and fungiostatic effects of xanthoxyline. J Ethnopharmacol. 1996; 53(3): 171-173. https://doi.org/10.1016/0378-8741(96)01436-5.
[27] Savairam VD, Patil NA, Borate SR, Ghaisas MM, Shete RV. Allicin: A review of its important pharmacological activities. Pharmacol Res Mod Chin Med. 2023;13:100283. https://doi.org/10.1016/j.prmcm.2023.10028.
[28] Ganai AA, Farooqi H. Bioactivity of genistein: A review of in vitro and in vivo studies. Biomed Pharmacother. 2015;76:30-38. https://doi.org/10.1016/j.biopha.2015.10.026.
[29] Ganeshpurkar A, Saluja AK. The pharmacological potential of rutin. Saudi Pharm J. 2017 ;25(2):149-164. https://doi.org/10.1016/j.jsps.2016.04.025.
[30] Ingole A, Kadam MP, Dalu AP, Kute SM, Mange PR, Theng VD, Lahane OR, Nikas AP, Kawal YV, Nagrik SU, Patil PA. A review of the pharmacological characteristics of vanillic acid. J Drug Deliv Ther. 2021;11(2):200-204. https://doi.org/10.22270/jddt.v11i2-S.4823.
[31] Lv J, Sharma A, Zhang T, Wu Y, Ding X. Pharmacological review on asiatic acid and ıts derivatives: A potential compound. SLAS Technol. 2018;23(2):111-127. https://doi.org/10.1177/2472630317751840.
[32] Herath HB, Priyadarshani AA. Two lignans and an aryl alkenone from *Myristica dactyloides*. Phytochem. 1996;42(5):1439-1442.
[33] Marulasiddaswamy KM, Nuthan BR, Sunilkumar CR, Bajpe SN, Kumara KK, Sekhar S, Kini KR. HR-LC-MS based profiling of phytochemicals from methanol extracts of leaves and bark of *Myristica dactyloides* Gaertn. from Western Ghats of Karnataka, India. J Appl Biol. 2021; 9(5):124-135. https://doi.org/10.7324/JABB.2021.9517.
[34] Chang SS, Lee VS, Tseng YL, Chang KC, Chen KB, Chen YL, Li CY. Gallic acid attenuates platelet activation and platelet-leukocyte aggregation: involving pathways of Akt and GSK3β. Evid Based Comple Altern Med. 2012; 1:2012. https://doi.org/10.1155/2012/687832.