Majalah Obat Tradisional (Trad. Med. J.), January-April 2026
Vol. 31(1), p 83-93
ISSN-p : 1410-5918 ISSN-e : 2406-9086

Submitted : 14-09-2024
Revised : 05-02-2025
Accepted : 09-04-2026

Secondary Metabolites Analysis and Anti-Cancer Potential of *Lansium parasiticum* Extract

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ABSTRACT

Cancer is a non-communicable disease characterized by uncontrolled growth of malignant cells. The leaves and stems of *Lansium parasiticum* have been recognized for their potential as an anti-cancer agent. However, research reporting secondary metabolite profiles and anti-cancer activity in these plants remains limited. This study aimed to identify compounds, compare compound profiles, and predict the anti-cancer activity of secondary metabolites present in the leaves and stem bark of *Lansium parasiticum*. The secondary metabolite profile was analyzed using UPLC-MS/MS (Ultra-Performance Liquid Chromatography-Tandem Mass Spectrometry) chromatogram data interpretation, while the prediction of anticancer activity was made by referencing the Probability Activity value obtained through the PASS (Prediction of Activity Spectra for Substances) Server. The results revealed 24 bioactive compounds successfully identified from the *Lansium parasiticum* leaf extract, with Emindole Sb as the major compound comprising 19.3% of the total chromatographic area. Meanwhile, the analysis identified 23 bioactive compounds in the stem bark extract of *Lansium parasiticum*, with Moronic Acid as the major constituent, representing 14.29% of the total chromatographic area. The examination of the anticancer potential utilizing a probability activity method suggests that both the leaves and stem bark of *Lansium parasiticum* demonstrate antineoplastic, chemopreventive, and apoptosis-inducing activities.
Keywords: Antineoplastic; Apoptosis; Chemopreventive; Emindole Sb; Moronic Acid

INTRODUCTION

Cancer worldwide ranks as the second leading cause of death. Among men, lung, prostate, colorectal, stomach, and liver cancers prevail, while breast, colorectal, lung, cervix uteri, and thyroid cancers are predominant among women (Krieghoff-Henning et al., 2017). Various factors including age, gender, and environmental influences contribute to the incidence, prevalence, and mortality rates (Sung et al., 2021). The utilization of tobacco, alcohol consumption, exposure to hazardous chemicals, along with other environmental factors, escalates the risk of developing cancer (Sawicki et al., 2021). Developed nations exhibit higher cancer incidence rates, primarily attributed to population aging, advancements in diagnostic techniques, and lifestyle changes (Xi & Xu, 2021).

The success of cancer treatment remains a significant challenge, particularly due to the often accompanying side effects of chemotherapy (van den Boogaard et al., 2022). With advancements in science and technology, research on the development of alternative therapies for cancer is expanding, including the utilization of natural substances such as medicinal plants (Gutte & Deshmukh, 2023). *Lansium parasiticum*, commonly known as langsat, is one such plant that has long been used in traditional medicine in various regions of Indonesia. The leaves and stem bark of langsat have drawn attention as potential sources for the development of alternative cancer therapies due to their potential secondary metabolite content (Mutiah & Suryadinata, 2024; Mutiah et al., 2024).

Previous studies have reported that the leaves of *Lansium parasiticum* contain alkaloids, saponins, flavonoids, and polyphenols (Pithonah et al., 2023). Meanwhile, the stem bark of *Lansium parasiticum* has been reported to contain flavonoids, saponins, and terpenoids (Mutiah & Suryadinata, 2024). Additionally, it has been reported that the stem bark exhibits antibacterial activity and can dissolve kidney stones (Lubis et al., 2022) (Ramadhani et al., 2018). However, previous studies have not specifically compared the secondary metabolite profiles between the leaves and stem bark of *Lansium parasiticum*. Furthermore, there is still very little research exploring the potential anticancer activity of these phytochemicals, creating a significant gap in understanding the pharmacological relevance of the active compounds. Therefore, there is still

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a critical need for the identification of compounds present in the leaves and stem bark of Lansium parasiticum.

The UPLC/MS technique is a variation of LC/MS that utilizes Ultra-Performance Liquid Chromatography (UPLC) instead of High-Performance Liquid Chromatography (HPLC). The main difference lies in UPLC's ability to operate at significantly higher pressure compared to HPLC, enabling better resolution, faster analysis, and improved sensitivity in identifying and analyzing the metabolite profiles of the extracts under investigation. (van Dooren et al., 2018). Its utilization has gained popularity in recent natural product research due to its capability to provide qualitative and quantitative metabolite profile data simultaneously (Mutiah et al., 2019) (Taleuzzaman et al., 2015). Quantitative data from LC-MS are typically represented as intensity or ion count within the mass spectrum, reflecting the abundance of detected ions. While chromatogram peak areas may provide relative quantification, they must be interpreted alongside mass spectral data to accurately determine the concentration of compounds in the sample. LC-MS/MS was selected for this study due to its high sensitivity, precision, and ability to analyze polar and thermally labile compounds without the need for derivatization, unlike GC-MS. It also requires smaller sample amounts and provides better detection of trace components compared to NMR. The combination of liquid chromatography for separation and tandem mass spectrometry for precise identification makes LC-MS/MS a superior tool for profiling complex plant metabolites, as supported by its widespread application in metabolomics (Chawla & Ranjan, 2016; Smith et al., 2020; Johnson & Peterson, 2021). Understanding the bioactivity potential of secondary metabolite compounds contained in the leaves and stem bark of *Lansium parasiticum* is crucial in their development into herbal medicines. Bioinformatics analysis, such as the use of PASS (Prediction of Activity Spectra for Substances) software, can significantly expedite drug development by predicting potential bioactive properties of compounds based on their structural features. PASS software is a computational tool that utilizes a large database of over 250,000 compounds and more than 4,000 types of biological activities, including therapeutic mechanisms, enzyme interactions, toxicity, and side effects. By analyzing structure-activity relationships, PASS predicts the probability of compounds exhibiting specific bioactivities, providing valuable insights into their pharmacological potential (Lagunin et al., 2000; Poroikov et al., 2003).

The present study aims to identify secondary metabolite in leaf and stem bark extracts of *Lansium parasiticum* using the UPLC/MS/MS method, and predict their anti-cancer activities. These predictions, supported by PASS software, bridge the gap between metabolite identification and potential therapeutic applications, particularly in cancer treatment.

MATERIALS AND METHODS

Preparation of 70% ethanol extract samples from leaves and bark of *Lansium parasiticum*

The leaves and bark of *Lansium parasiticum* were obtained from the Malang region in East Java at an altitude of 400 meters. Plant identification was conducted at the Materia Medika with the number 067/566/102.20/2023. The area experiences an annual rainfall of 125.49 mm and an average temperature of 25 degrees Celsius. Leaf and bark powders were extracted using a 1:10 ratio with 70% ethanol and the Ultra Assisted Extraction (UAE) method. This process lasted for 20 minutes at a temperature of 40°C. Evaporation was carried out using a Rotary evaporator. Drying was performed in an oven at 40°C until a constant weight was obtained (Mutiah et al., 2023).

Compound Identification with Thin Layer Chromatography (TLC)

The compound identification procedure commenced by weighing 10 mg of the extract and dissolving it in 96% ethanol pa. From each dissolved extract, 2 µl was extracted using a capillary pipette and applied onto a TLC plate (CAMAG, Switzerland) with specified distances and boundaries. Subsequently, 10 ml of chloroform: methanol (9:1) was introduced into the chamber, and its saturation was confirmed using a sealed paper. The TLC plates were then developed using the chamber-saturated eluent until the mobile phase reached the marked measurement limit. Post-development, the TLC plates were sprayed with a 10% H2SO4 solution and subjected to heating on a TLC Heater (CAMAG, Switzerland) at 105°C for 5 minutes. The Rf values and stain patterns formed on the TLC plates were observed using a TLC Visualizer (CAMAG, Switzerland).

Compound identification with UPLC-MS/MS

Analysis was conducted using UPLC-MS equipped with QToF and ESI in positive ionization mode. An Acquity C18 column with 1.8 µm particle size (2.1 × 150 mm) was used along with a gradient elution system, consisting of two types of water (HPLC grade) and formic acid with a ratio of 99.9/0.1 [v/v] and 99.9/0.1 [v/v] for acetonitrile, respectively. The comparison is presented in Table I.

Table I. The Ratio of eluent used

Time (Minuts)	% Eluent A	% Eluent B
0,00	95.00	5.00
2,00	75.00	25.00
3,00	75.00	25.00
14,00	0.00	100.00
15,00	0.00	100.00
19,00	95.00	5.00
23,00	95.00	5.00

The source temperature was set at 100°C and desolvation temperature at 350°C. A 10 mg extract was dissolved in a 10 ml volumetric flask using absolute methanol and then injected into the UPLC-MS instrument with 5 µl. Spectra were obtained in the mass range of m/z 120 to 1000, using positive ion mode for analytical parameters. PubChem (https://pubchem.ncbi.nlm.nih.gov/) and Mass Lynx software version 4.1 were used for chemical identification and chromatogram processing. Validation was conducted by comparing MS/MS fragment results with an error tolerance below 5 ppm (Mutiah et al., 2019).

Prediction of anticancer activity with PASS Server

Compounds that were detected were then subjected to pharmacological activity prediction using the PASS Server web tool available at (http://www.way2drug.com/passonline/index.php). The compounds that were successfully detected were extracted for their Canonical SMILES for further identification of their Pa values. A Pa value above 0.7 indicates that the predicted activity aligns accurately with actual laboratory-scale activity. If the value ranges between 0.5-0.7, the accuracy decreases, and it diminishes further if the value is less than 0.5(Mutiah et al., 2023) .

RESULTS

The identification of metabolite profiles using TLC method in this study aims to determine the classes of compounds present in both extracts and to identify differences in metabolite profiles between them. Figure 1 illustrates the contrasting metabolite profiles of the two extracts. The parasitic lansium leaf extract exhibits 11 spots, whereas the stem extract shows only 7 spots. Sample identification from the spot analysis reveals the presence of alkaloid compounds indicated by the appearance of blue or blue-green spots, flavonoids identified by red spots, and terpenoids characterized by green and purple spots.

Identification of active compounds by UPLC-MS/MS

The analysis in this study utilized the UPLC separation technique followed by mass spectrometry (MS) analysis to identify active compounds in the leaf and stem bark samples of Lansium parasiticum. The UPLC-MS/MS separation technique generated chromatograms showing peaks representing the specific identities of each compound. From these results, the chromatograms indicated a total of 24 compounds present in the 70% ethanol extract of *Lansium parasiticum* leaves (Figure 2) and 23 compounds in the 70% ethanol extract of *Lansium parasiticum* stem bark (Figure 3).

Interpretation of the chromatograms by MassLynx yielded data on Retention Time (Rt), peak height, % area, measured and calculated mass, spectra, and the molecular formula of a compound. The name of a compound was obtained by converting the molecular formula minus 1 hydrogen atom (1.0078), as one hydrogen atom is lost during ESI ionization [17]. Compound names were determined using PubChem software and their structures were depicted using ChemDraw Ultra version 19.0. The percentage area representing the concentration of a compound was obtained by the ratio of the area under the compound's peak to the total ion chromatogram (TIC) multiplied by 100%. The profiles of compounds in *Lansium parasiticum* leaves and stem bark are presented in Tables II and III below.

The phytochemical analysis of *Lansium parasiticum* leaves presented in Table II reveals a diversity of compounds contained therein. The Table III unveils that *Lansium parasiticum* leaves harbor a variety of active compounds, including 10 compounds classified as alkaloids, 3 compounds classified as flavonoids, 2 phenolic compounds, 3 terpenoid compounds, 5 steroid compounds, and 1 indole alkaloid terpenoid compound.

The anticancer activity of 70% ethanol extracts from the leaves and bark of *Lansium parasiticum* was analyzed using the PASS Server

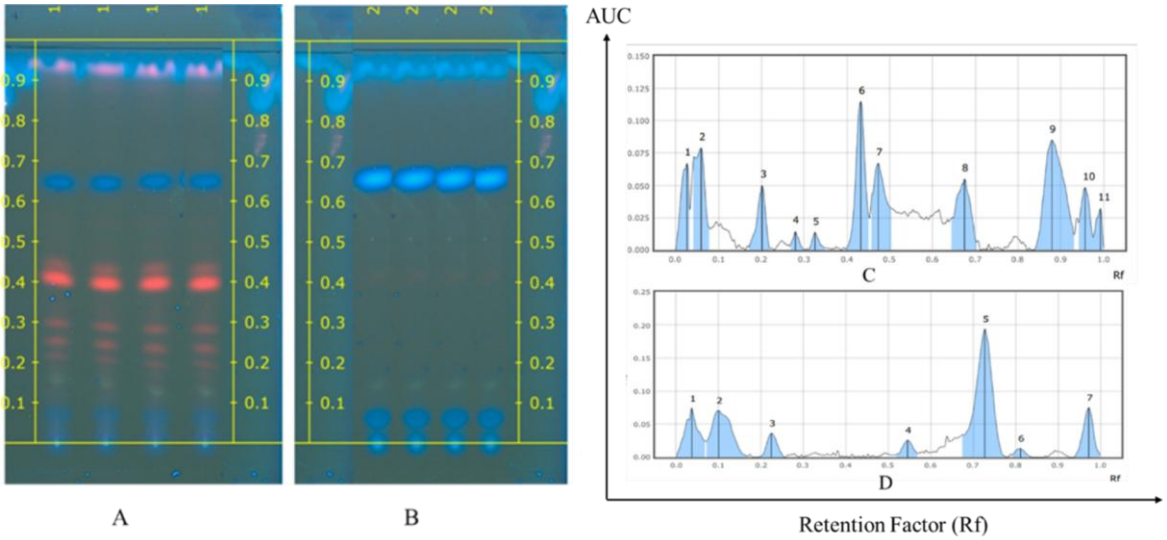

Figure 1. A) The identification results of the parasitic lansium leaf extract are observed on the TLC Visualizer monitor under 366 nm UV light. B) The identification results of the parasitic lansium bark extract are observed on the TLC Visualizer monitor with 366 nm UV light. C) The peak outcomes of the Rf values of the TLC from the *Lansium parasiticum* leaf extract. D) The peak outcomes of the Rf values of the TLC from the *Lansium parasiticum* bark extract.

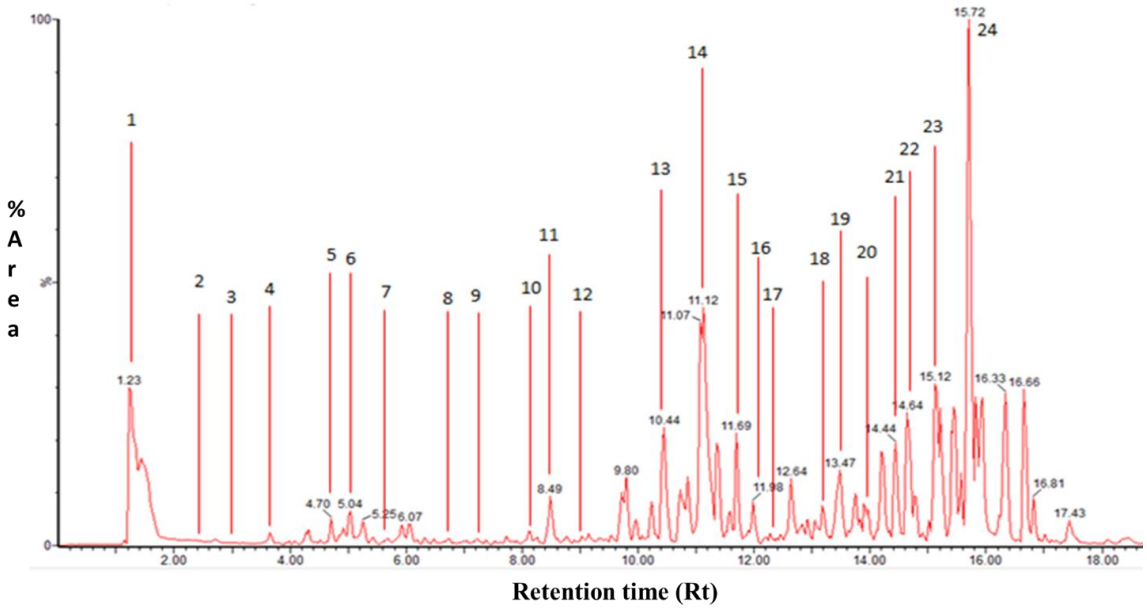

Figure 2. Chromatogram of *Lansium parasiticum* leaf extract separated by UPLC-MS/MS. C18 was used as the stationary phase, while the mobile phase consisted of acetonitrile/formic acid 99.9/0.1 (v/v) and water/formic acid 99.9/0.1 (v/v).

database, which generated outputs in the form of Probability Activity values for each compound in the sample (Tables IV and V).

The Heatmap Analysis of Anticancer Activity Probability (pa)

The heatmap analysis of anticancer activity aims to visually elucidate the level of potential compounds in their activities as antineoplastic, apoptosis agonists, chemopreventive agents, antimetastatic agents, and MAPK inhibitors. The color scale reflects the level of potential of these compounds, where dark red indicates high anticancer potential, while dark blue indicates low potential. The darker the red color of the compound, the stronger its potential as an anticancer agent, whereas if the compound exhibits a darker blue color, it indicates that the

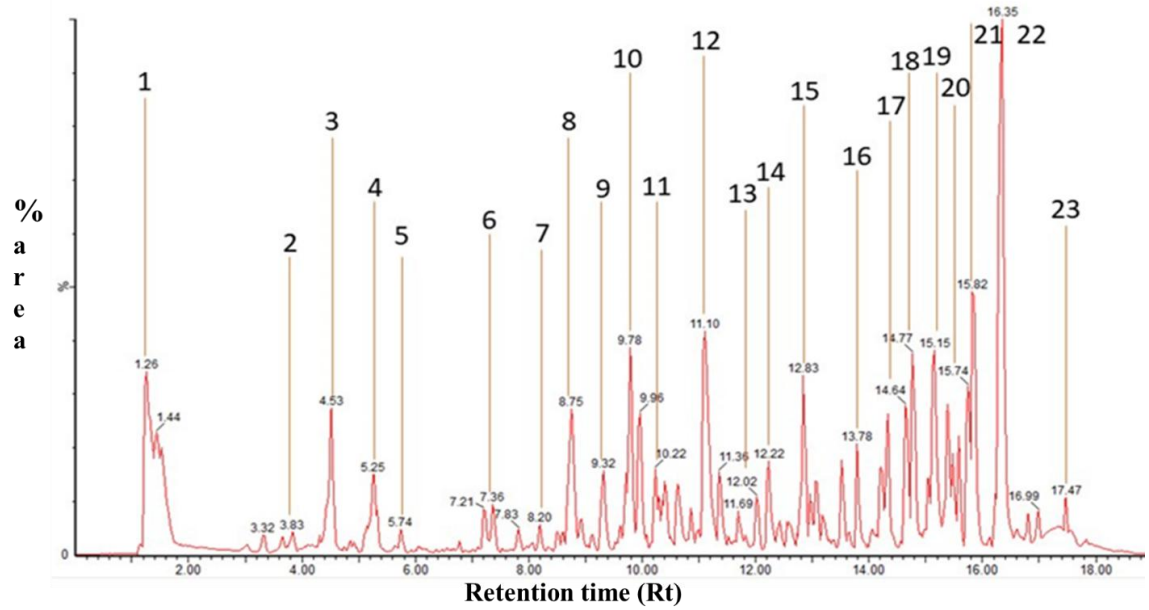

Figure 3. Chromatogram of *Lansium parasiticum* stem bark extract separated by UPLC-MS/MS. C18 was used as the stationary phase, while the mobile phase consisted of acetonitrile/formic acid 99.9/0.1 (v/v) and water/formic acid 99.9/0.1 (v/v).

predicted compound has no potential as an anticancer agent (Figure 4).

DISCUSSION

This study aims to compare the profiles of secondary metabolites as well as the anticancer activities of ethanol extracts from the leaves and stem bark of Lansium parasiticum. The differences in the composition of secondary metabolite compounds between these two plant parts can provide a deeper understanding of their pharmacological potential.

In this study, the identification of compounds was performed using MS 1 spectra obtained from chromatogram analysis. Each chromatogram peak is assumed to represent one compound, and the Masslynx 4.1 software was used to process the chromatogram and obtain the m/z spectrum needed to predict the molecular formula of the compound. Although MS 1 data only provides information on the mass of the compound, not fragments, it still provides an initial overview of the possible compound composition based on the detected molecular mass.

To predict the compound names, the PubChem software was used by entering the calculated molecular formula. In this process, the molecular formula obtained from MS 1 must be corrected by subtracting one hydrogen atom, because the positive ESI ionization source will add an H (proton) charge to the compound, resulting in a higher m/z value than the actual molecular mass. Therefore, the mass of H, which is 1.0078, needs to be subtracted from the total m/z to obtain a more accurate molecular mass.

After obtaining the predicted molecular formula, the measured m/z is compared with the calculated m/z, and the compound structure is drawn using ChemDraw Ultra 12.0 software. This process ensures that the difference between the measured and calculated m/z is very small, ≤ 0.0005. If this difference is met, the chromatogram peak is considered to represent the predicted compound. However, it is important to note that while this process provides useful information for predicting compound identities, more accurate and complete identification, including detailed compound structures, requires further analysis techniques such as MS/MS or NMR to confirm the molecular structure in greater detail.

A total of 24 compounds were identified from the ethanol extract of *Lansium parasiticum* leaves based on MS analysis., primarily alkaloid, flavonoid, and steroid groups. Among these compounds, 7 of them show significant probabilities of anticancer activity (Pa>0.7). Quercetin, kaempferol, and scortechinon stand out as compounds with strong anticancer potential, with scortechinon exhibiting the highest antineoplastic activity. On the other hand, several compounds in *Lansium parasiticum* leaves have potential as chemopreventive agents, such as Quercetin, Orbiculin D, and Pregnenolone. Orbiculin D shows the most potential in

Table II. Results of the profile of secondary metabolite compounds in *Lansium parasiticum* leaf extract

No	Rt	%Area	*Measured Mass*	*Calculated Mass*	Formula	Compounds	Groups of compounds
1.	1.303	13.57	146,0818	146,0817	$C_6H_{12}N0_3$	4-Acetamidobutyric acid	Alkaloid
2.	2.709	0.35	166,0867	166,0868	$C_9H_{12}NO_2$	L-phenylalanine	Alkaloid
3.	3.650	0.3	188,0711	188,0712	$C_{11}H_{10}N0_2$	methylquinoline-6-carboxylate	Alkaloid
4.	4.311	0.36	408,1764	408,1804	$C_{15}H_{11}O_7$	Quercetine	Flavonoid
5.	4.726	0.58	303,05	303,0505	$C_{15}H_{11}O_6$	Kaemferol	Flavonoid
6.	5.035	1.67	287,0558	287,0556	$C_{11}H_{17}O_3$	5-methoxyeugenol	Fenol
7.	5.977	1.31	197,1186	197,1178	$C_{21}H_{22}N0_4$	oxoberberine	Alkaloid
8.	7.237	0.17	352,1541	352,1549	$C_{31}H_{40}NO_{10}$	CID 216134	Alkaloid
9.	7.735	0.13	275,2024	275,2011	$C_{29}H_{38}N_7O_9$	CID 101220820	Alkaloid
10.	8.136	0.3	586,2692	286,2652	$C_{11}H_{17}O_2$	Olivetol	Fenol
11.	8.488	1.22	628,2778	628,2731	$C_{27}H_{33}O_{10}$	orbiculin D	Sesquiterpen (terpenoid)
12.	9.12	0.16	181,1229	181,1229	$C_{25}H_{31}N_6O_7$	CID 22988024	Alkaloid
13.	10.442	3.08	527,23	527,2254	$C_{29}H_{35}O_9$	Territrem B	Terpenoid
14.	11.124	13.93	527,2283	527,2281	$C_{18}H_{29}O_2$	Bolandiol (19-Nor-4-androstenediol)	Steroid
15.	11.694	2.84	694,4018	694,3987	$C_{21}H_{35}O_3$	Tetrahydrodeoxycorticosterone	Diterpen (terpenoid)
16.	11.982	0.79	277,2155	277,2168	$C_{27}H_{50}NO_9$	AAL Toxin TE2	Alkaloid
17.	12.28	0.04	335,2593	335,2586	$C_{26}H_{46}N_3O_6$	8-phenyl-octanecarboxamie peptidomimetic	Alkaloid
18.	13.163	0.95	496,3403	496,3387	$C_{19}H_{31}O_2$	dihydrotestosterone	Steroid
19.	13.472	2.35	453,3376	453,3371	$C_{30}H_{45}O_3$	Moronate	Alkaloid
20.	13.761	2.01	291,2324	291,2324	$C_{21}H_{33}O_2$	pregnenolone	Steroid
21.	14.443	1.64	317,2483	317,2481	$C_{35}H_{60}NO_7$	CHEMBL4748940 (CID 162650677)	Steroid
22.	14.661	4.45	634,4494	636,4449	$C_{31}H_{33}N_{10}O_4$	CHEMBL4855226 (CID 153347580)	Alkaloid
23.	15.167	6.41	606,4373	606,437	$C_{34}H_{41}O_9$	Scortechinone B	Xanthones (flavonoid)
24.	15.715	19.3	593,2731	593,2751	$C_{28}H_{40}NO$	Emindole Sb	Terpenoid indol Alkaloid

chemopreventive activity, as evidenced by its Pa value. Quercetin and kaempferol have also been proven to induce apoptosis in *Lansium parasiticum* leaves, with Quercetin being the most accurate apoptosis agonist among them. However, *Lansium parasiticum* leaves have not shown significant potential as anticancer agents through the mechanisms of antimetastasis and MAPK inhibition, as indicated by their Pa values.

Compounds with high potential as anticancer agents, as mentioned above, predominantly originate from the flavonoid group. The antioxidant properties in healthy cells and pro-oxidant properties in tumor cells of these compounds play a crucial role in modulating Reactive Oxygen Species (ROS) within tumor cells, inhibiting carcinogens, pro-inflammatory pathways, inducing apoptosis, and inhibiting tumor cell proliferation and development (Kopustinskiene et al., 2020) (Pithonah et al., 2023)Additionally, Orbiculin D, derived from the Sesquiterpene group, has also been proven as an anticancer agent through its capabilities in anti-proliferative and apoptosis induction. This is attributed to its unsaturated carbonyl functional groups, acting as electrophiles and forming covalent bonds with Keap 1 to activate Nrf2 (Kim et al., 1998; Kim et al., 1999; Feng et al., 2023)

Meanwhile, the ethanol extract from the stem bark of *Lansium parasiticum* contains 23

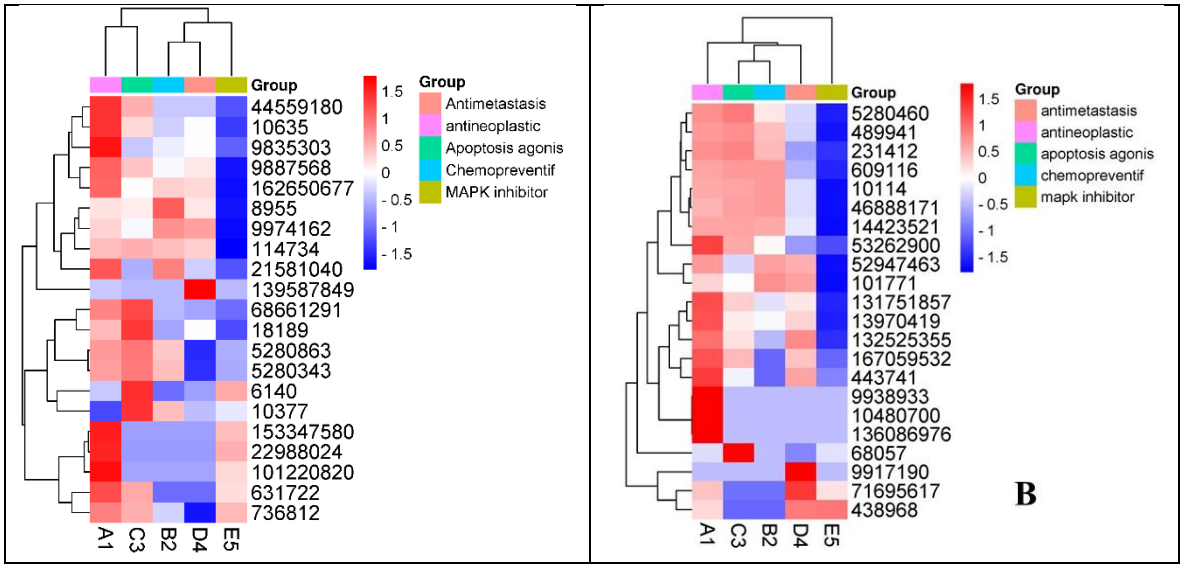

Figure 4. A) Heatmap of Anticancer Activity Results of *Lansium parasiticum* Leaves. B) Heatmap of Anticancer Activity Prediction Results of *Lansium parasiticum* Stem Bark

Table III. Results of the profile of secondary metabolite compounds in *Lansium parasiticum* stem bark extract

No	Rt	%Area	*Measured Mass*	*Calculated Mass*	Formula	Name	Groups
1.	1,324	12,2%	146,0821	146,0817	C6H12NO3	4-Morpholineacetic Acid	Alkaloid
2.	3,826	0,57%	310,093	310,0927	C14H16 NO7	7-Deoxypancratistatin	Alkaloid
3.	4,529	3,5%	352,1613	352,1608	C14H26 NO9	Validoxylamine B	Alkaloid
4.	5,253	2,41%	193,0498	193,0501	C10H9O4	Scopoletin	Coumarin
5.	5,739	0,44%	502,1724	502,176	C23H28N5O6S	CID 136086976	Alkaloid
6.	7,32	1,75%	520,2156	520,2183	C26H34NO10	CID 38585	Alkaloid
7.	8,199	0,48%	175,1489	175,1487	C13H19	1,1,6- Trimethyltetral	Coumarin
8.	8,747	4,50%	485,1828	485,1812	C26H29 O9	Dukunolide E	Terpenoids
9.	9,296	1,34%	486,213	486,2128	C26H32 NO8	Saccharothriolide D	Alkaloid
10.	9,802	6,65%	517,2096	517,2074	C27H33 O10	Ananolignan F	Alkaloid
11.	10,639	0,44%	469,1882	469,1862	C26H29 O8	Dukunolide D	Triterpenoids
12.	11,124	6,88%	439,2137	439,2121	C26H31 O6	3,6-Dimethylmangostin	Flavonoid
13.	12,024	0,46%	618,2916	618,2888	C28H40 N7O9	Rotigaptide	Alkaloid
14.	12,242	1,72%	627,2805	627,2779	C30H39 N6O9	Tripeptide-based inhibitor	Alkaloid
15.	13,535	1,28%	453,3378	453,3402	C30H45O3	Ganoderic acid SZ	Steroid
16.	13,803	1.35%	604,3877	604,3849	C34H54NO8	CID 167059532	Alkaloid
17.	14,309	3,59%	335,2578	335,2586	C21H35O3	Tetrahydrodeoxycorticosterone	Steroid
18.	14,744	5,29%	471,3492	471,3474	C30H47 O4	Enoxolone	Steroid
19.	15,117	4,50%	606,4395	606,437	C35H60NO7	CID 52947463	Alkaloid
20.	15,405	4,63%	490,3912	490,3896	C30H52NO4	CID 10480700	Alkaloid
21.	15,82	8,37%	441,3753	441,3733	C30H49 O2	Ursolic aldehyde	Steroid
22.	16,326	14,29%	455,3551	455,3525	C30H47O3	Moronic acid	Triterpenoids
23.	17,452	2,69%	469,3964	469,3682	C31H49O3	CID 609116	Steroid

Table IV. Probability values of anticancer activity of compounds in *Lansium parasiticum* leaves with PASS Server

No.	Compound name	Anti-neoplastic (Pa)	Chemopre-ventive (Pa)	Apoptosis Agonist (Pa)	Antimetastasis (Pa)	MAPK Inhibitor (Pa)
1.	4-Acetamidobutyric acid	0,291	0,148	0,409	0,223	0,065
2.	L-phenylalanine	0,220	0,166	0,303	0,186	0,256
3.	methyl quinoline-6-carboxylate	0,264	0,141	0,233	-	0,224
4.	Quercetin	0,797 *	0,717*	0,887*	-	0,327
5.	Kaempferol	0,791*	0,669	0,881*	-	0,331*
6.	5-methoxyeugenol	0,586	0,313	0,673	0,286	0,201
7.	Oxoberberine	0,538	-	0,384	-	0,298
8.	CID 216134	-	-	-	-	-
9.	CID 101220820	0,380	-	-	-	0,149
10.	Olivetol	0,128	0,350	0,476	0,235	0,269
11.	Orbiculin D	0,881	0,774*	0,242	0,321	-
12.	CID 22988024	0,247	-	-	-	0,137
13.	Territrem B	0,452	0,453	0,478	0,435	-
14.	Bolandiol (19-Nor-4-androstenediol)	0,754*	0,448	0,406	0,467	0,278
15.	Tetrahydrodeoxycorticosterone	0,498	0,559	0,458	0,545	0,235
16.	AAL Toxin TE2	0,009	-	-	0,233	-
17.	8-phenyl-octanecarboxamide	-	-	-	-	-
18.	peptidomimetic, dihydrotestosterone	0,806*	0,454	0,576	0,514	0,255
19.	Moronate	-	-	-	-	-
20.	pregnenolone	0,496	0,747*	0,479	0,489	-
21.	CHEMBL4748940 (CID 162650677)	0,884	0,648	0,541	0,631*	-
22.	CHEMBL4855226 (CID 153347580)	0,436	-	-	-	0,222
23.	Scortechinone B	0,988*	0,318	0,662	0,322	-
24.	Emindole Sb	0,802*	0,499	0,621	0,558	0,097

compounds, with the majority originating from alkaloid, coumarin, triterpenoid, and steroid groups. In this study, 11 compounds in the stem bark extract showed significant Pa values, indicating strong potential for anticancer activity with Pa>0.7. Ursolic aldehyde exhibited the highest antineoplastic activity with a Pa value of 0.895. Additionally, the compound with the highest chemopreventive and apoptosis induction effects was Enoxolone (p=0.944). Dukunolid E and dukunolid D, also found in the stem bark, showed strong antineoplastic activity. However, no compounds were found to have potential as antimetastatic agents or MAPK inhibitors.These results indicate that both parts of the *Lansium parasiticum* plant have the potential to serve as sources of bioactive compounds with significant anticancer activity. The differences in the secondary metabolite profiles between the leaves and stem bark can be linked to variations in the growing environment and physiological functions of each plant part.

Differences in the content of metabolite compounds between different parts of the plant can be attributed to several interrelated factors. Firstly, physiological factors play a key role, considering that each plant part has distinct physiological functions (Dos Santos et al., 2022) (Bhatla & Lal, 2023). For example, leaves tend to play a role in photosynthesis and may produce compounds such as chlorophyll and phytochemicals, while stem bark may contain compounds involved in protection and structural support. Secondly, genetic differences among plant parts can also be significant factors. Variations in the genetic code can lead to different gene expressions, resulting in diverse metabolite compound production (Efendi et al., 2022).

Table V. Probability values of anticancer activity of compounds in the bark extract of *Lansium parasiticum* with PASS Server.

No.	Compound name	Anti-neoplastic (Pa)	Chemopre-ventive (Pa)	Apoptosis Agonist (Pa)	Antimetastasis (Pa)	MAPK Inhibitor (Pa)
1.	4-Morpholineacetic Acid	0,200	-	-	0,299	0,308
2.	7-Deoxypancratistatin	0,633	0,166	0,354	0,491	0,208
3.	Validoxylamine B	0,321	-	-	0,549	0,274
4.	Scopoletin	0,723*	0,606	0,750*	0,520	0,273
5.	CID 136086976	0,166	-	-	-	-
6.	CID 38585	-	-	-	-	-
7.	1,1,6-Trimethyltetralin	0,282	0,264	0,437	0,231	0,283
8.	Dukunolide E	0,777*	0,370	0,519	0,472	-
9.	Saccharothriolide D	0,582	0,231	0,397	0,539	-
10.	Ananolignan F	0,885*	0,447	0,634	0,187	-
11.	Dukunolide D	0,702*	0,384	0,423	0,468	-
12.	3,6-Dimethylmangostin	0,828*	0,715*	0,862*	0,291	-
13.	Rotigaptide	0,361	-	-	-	-
14.	Tripeptide-based inhibitor, 14m	-	-	-	0,259	-
15.	Ganoderic acid SZ	0,798*	0,866*	0,853*	0,529	-
16.	CID 167059532	0,382	-	0,259	0,247	-
17.	Tetrahydrodeoxycorticos terone	0,498	0,559	0,458	0,545	0,235
18.	Enoxolone	0,890*	0,944*	0,904*	0,568	-
19.	CID 52947463	0,599	0,590	0,356	0,561	-
20.	CID 10480700	0,328	-	-	-	-
21.	Ursolic aldehyde	0,895*	0,879*	0,896*	0,597	-
22.	Moronic acid	0,825*	0,740*	0,862*	0,476	-
23.	CID 609116	0,880*	0,902*	0,909*	0,412	-

Notes: Pa: Probability Activity value indicating the likelihood of activity of a compound; *: Compounds with Pa values above 0.7

Thirdly, environmental factors such as light, temperature, humidity, and soil type can contribute to these differences. This variability may even occur within the same plant, depending on the growth conditions imposed. Finally, the plant's growth stage in its life cycle can play a crucial role, with certain metabolite compounds potentially (Bhatla & Lal, 2023).This study provides a significant contribution to understanding the potential of *Lansium parasiticum* as a source of bioactive compounds for the development of anticancer therapy. However, further research is needed to identify specific active compounds and understand their mechanisms of action in anticancer activities, as well as clinical trials to confirm their effectiveness and safety in human use.

CONCLUSION

Based on the research, 24 secondary metabolite compounds were identified in *Lansium parasiticum* leaves, with dominance from the alkaloid, flavonoid, terpenoid, and steroid groups. Emindole Sb compound emerged as the major compound with a percentage area of 19.3%. Meanwhile, 23 secondary metabolite compounds were found in the stem bark of Lansium parasiticum, with Moronic Acid as the major compound with a percentage content of 14.29%. The differences in compound composition between the leaves and stem bark indicate the specific nature of each sample. Analysis of anticancer activity using probability activity approach indicates that both the leaves and stem bark of *Lansium parasiticum* exhibit antineoplastic, chemopreventive, and apoptosis agonist activities.

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