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In Vitro Antioxidant and α-Glucosidase Inhibitor Metabolites of *Chrysanthemum indicum* Flower Represented by Molecular Networking

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ABSTRACT. *Chrysanthemum indicum* flower is known as a Chinese medicinal plant and is consumed as a tea or food supplement. Several research reported the profiling metabolites of this flower using High-Performance Liquid Chromatography (HPLC) or Liquid Chromatography Mass Spectroscopy (LC-MS). However, there is a limitation of those methods, which are the yields several formula obtained by searching in database based on parent masses so give less effectiveness identify of compound. This study aimed to identify the metabolites in the ethanolic extract of *C. indicum* using a de-replication strategy by coupling Liquid Chromatography Orbitrap HRMS with a molecular network approach. This study also evaluated the total phenolic contents (TPC) using Folin-Ciocalteu method, Fourier Transfer Infrared (FTIR) Spectroscopy, while the scavenging activity against DPPH radical method was used to determine the antioxidant activity and the inhibition of α-glucosidase was conducted using α-glucosidase assay. The studies showed that there were diverse families of metabolites were putatively identified in *C. indicum* such as flavonoids and derivates, amino acids, fatty acids and derivates, phenol and derivates, terpenoids, and glucose. The detailed metabolites in extract were approached using application of molecular networking. In agreement with the molecular networking, the extract exerted strong antioxidant activity with % inhibition value of 76.20±1.35 at 100 μg/mL. Whereas, the α-glucosidase inhibitory activity showed good activity with % inhibition value of 83.04±0.52 at 50 μg/mL. The results of this study provide a new metabolite library for *C. indicum* ethanol extract as well as the confirmation of some of its biological activities.

Keywords: *Chrysanthemum*, profiling metabolites, LC-HRMS

INTRODUCTION

Chrysanthemum indicum flower is known as medicinal plant and consumed as tea or food supplement. In China and Korea, this flower has been used for treatment some diseases such as headache, dizziness, hypertension, angina pectoris, arrhythmia, and cardiovascular (He et al., 2016) *Chrysanthemum* flowers have been reported to contain several classes of metabolites including essential oils, flavonoids and derivates, phenolic compounds and derivates, terpenoids, amino acid and derivates, fatty acids, and glucose (Hodaei et al., 2021; Ryu et al., 2019; Yang et al., 2019). Those metabolites exhibited diverse pharmacological activities i.e., antidiabetic, antioxidant, anti-inflammatory, hepatoprotective, antinociceptive, and antiepileptic activities (M. Chen et al., 2019; Hu et al., 2017; Salem et al., 2019; Zhan et al., 2022)).

Profiling and identification of metabolites in plant extract using a conventional method take long time and high cost and sometimes re-isolation of known compounds (Wibowo et al., 2019). Previously, isolation and identify several compounds in *Chrysanthemum* flower was conducted using High Performance Liquid Chromatography (HPLC) (L. Chen et al., 2023; Hu et al., 2017). Others research reported identification and screening of metabolites in this flower using LC-MS/MS (Han et al., 2019; Peng et al., 2019). The LC- MS/MS has limitation some limitation among other the dereplication technique that several molecular formulas were obtained from parent masses according to the database this leads to some uncertainty in compound identification (Mohimani et al., 2018). Due tho this limitation, in this study, we proposed the new method in profiling metabolites via molecular networking (MN) combined

with the liquid chromatography (UHPLC-MS/MS). The sample used in this study was *C. indicum* flower ethanolic extract. In MN, grouping of the compounds contained in the sample was based on the similarity of mass fragmentation. This method provides new way to identify the metabolites in the extracts by providing information about similarity between tentative identified compounds. Through molecular networking analysis, MS/MS spectra can be employed to identify the metabolites contained in the extract and with its biological activity such as antioxidant and inhibition of α-glucosidase.

EXPERIMENTAL SECTION

Plant Material and Extraction

C. indicum flower were obtained from Bandung, West Java, Indonesia. The flower was then dried on the oven at 50 °C. Furthermore, the dried flower was grinded and extracted by maceration method using ethanol (EtOH) 70% (3x24 h). The sample was filtered and the crude extract of *Chrysanthemum* were obtained by evaporating the solvent at rotary evaporator at 40 °C.

LC-Orbitrap HRMS Analysis

Methanol (HRMS grade) was used to dissolve the extract of *C. indicum* (1 mg/1 mL) and then filtered through 0.22 μm and transferred into 2 mL LC vial. The UHPLC column used in this study was Thermo Scientific™ Accucore™ Phenyl-Hexyl 100 mm × 2.1 mm ID × 2.6 μm (Thermo Scientific). The elution applied in the LC-HRMS was gradient elution. Detail method of analysis the sample and filtering of data was set up following : Compound add group based on background is false; name is not blank , MS2 is equal to DDA for prefered ion; and Annotation Δmass (ppm) is between -5 and 5. Detailed method of LC-HRMS analysis according to Anjar et al with some modification. (Windarsih et al., 2022)

Molecular Networking

MS/MS data convertion

MS/MS data was convereted to MzXML using ProteoWizard. Detail paramaters were used in this method following the study performed by Azizah et al (Azizah et al., 2020).

Molecular networking analysis by global natural products social molecular networking (GNPS)

The converted MS/MS data in MzXML format was trasnfered automatically to the GNPS website (http://gnps.ucsd.edu) by uploading the data using WinSCP with the host ost ccms-ftp01.ucsd.edu. Parameters were set up in the GNPS following to (Azizah et al., 2020). The detail setting of the advance networking system according to (Aron et al., 2020) and for further analysis of spectra following Azizah et al(Azizah et al., 2020).

Molecular networking visualization using cytoscape

Visualization and simplification of molecular networking was displayed by Cytoscape 3.7.2. Profiling metabolites in ethanolic extract of *C. indicum* and correlation between their analogs were analysed using Cytoscape.

Measurement of Fourier Transfer Infrared (FTIR) Spectroscopy

Vibration of functional groups in extract was evaluated using The Attenuated Total Reflectance (ATR) FTIR (Bruker Vertex 80). The measurement instrument was set up with the infrared region (4000-300 cm^{-1}), with a resolution of 6 cm^{-1}, and the number of scans was 32. The OMNIC software was used to analyze the vibration of functional group from identified molecule.

The Total Phenolic Contents (TPC)

Ethanolic extract of *C. indicum* was determined for TPC by Follin-Cicalteu assay. The extract 10 μL/mL (1 mg/mL) on microtube was added with the Folling-Cicalteu reagent (50 μL) and then incubated at dark room for 8 min. The mixture was subjected with 20% Na_2CO_3 solution (150 μL) and distilled water. Furthermore, the mixture was incubated in a darkroom for 2h. This analysis following to Ayele at al (Ayele et al., 2022) with modification. A microplate reader was used to measure the absorbance of mixture at 765 nm.

Scavenging Activity Toward DPPH Radicals

The scavenging activity of extract against DPPH radicals at 125 μg/mL was evaluated using DPPH assay according to (Al-Rifai et al., 2017). The mixture of extract (1 mL) and 0.4 mM DPPH solution was incubated for 30 min. The UV-Visible spectrophotometer was used to measure the absorbance the mixture at 517 nm. Equation (1) was used to calculate the % inhibition of extract.

$$\%inhibition = \frac{(A_{control} - A_{sample})}{A_{control}} \times 100 \quad (1)$$

Inhibition of α-Glucosidase Assay

The α-glucosidase inhibitory of *C. indicum* extract was evaluated according to Indrianingsih with slight modification (Indrianingsih et al., 2023). 40 μL of α-glucosidase enzyme (0.1 U/mL) was subjected into a 96-microplate containing 20 μl of extract (50 μg/mL in 10% of dimethyl sulfoxide). 3mM p-nitrophenyl α-D-glucopyranoside (p-NPG) (40μL) was added to the mixture after pre-incubation time at 37 °C for 5 min. Furthermore, the mixture was subjected with 200 μL of 0.1 M sodium carbonate (Na_2CO_3) and incubated at 37 °C for 20 min. A microplate reader was used to measure the absorbance of the mixture at 405 nm.

RESULTS AND DISCUSSION

Metabolite Profiling and Molecular Networking of *C. indicum* Flower Extract

The dried flower of *C. indicum* was extracted using 70% ethanol. The extract was analysed using LC-MS/MS with positive and negative MS ionization mode. Sesquiterpene compounds were detected in a positive ionization, whereas compounds detected in negative ionization mode such as flavonoids, phenolic

acids, and quinic acids (Ruan et al., 2019). The TIC chromatogram of ethanolic extract from this flower is shown in **Figure 1**. The tentative identified compounds were annotated by local and online databases, including MzCloud (www.mzcloud.org) and ChemSpider (www.chemspider.com); they are listed in **Table 1**. The annotated compounds anayzed using LC-MS/MS were clasified belongs to flavonoid, glucose, amino acid and derivates, fatty acid, terpenoid, and phenolic. Both positive and negative ionization mode identified several compounds in the *C. indicum* extract. The tentatively compounds in extract are shown in **Table 1**. Among the phenolic compounds, chlorogenic acid, neochlorogenic acid, quinic acid, and 4,5-Dicaffeoylquinic acid at m/z 354.09449 $[M-H]^-$, m/z 354.09465 $[M-H]^-$, m/z 192.06254 $[M-H]^-$, and m/z 516.12596 $[M-H]^-$, were putatively identified. Another metabolite identified in *C. indicum* extract was linolenic acid at m/z 278.22432 $[M+H]^+$. These finding is in agreement with the previous study. In addition to that, previous study reported the presence of chlorogenic acids and other caffeic acid derivative compounds in *C. indicum* extract such as p-coumaroylquinic acids, feruloylquinic acids, caffeoylquinic acids, dicaffeoylquinic acids, tricaffeoylquinic acids, caffeoyl-hexose esters and caffeic acid-4-β-d-glucose, caffeoylquinic acid glycosides, dicaffeoylquinic acid glycosides, succinic acid-containing chlorogenic acids, and chlorogenic acids based on epi-quinic acid (Clifford et al., 2007). Another research reported that extracts of this flower contained mixtures of flavonoids, volatile oils, organic acids, polysaccharides and other minor components (Liang et al., 2020).

We conducted a molecular networking analysis for profiling the metabolites in ethanolic extract of *C. indicum* flower. The crude extract was analysed in a positive and negative ionization mode (**Figure 1**). Visualization of precursor ion was displayed in Cytoscape 3.10 that resulting a network with cluster corresponding to different compound class. Clusters are groups of nodes and the connecting lines constitute edges (cosine values that expressed the similarity between nodes). In this study, the molecular networking revealed 191 precursor ion with 19 clusters (nodes >2) and 91 nodes. The clustering of compounds were grouped based on structural similarities. The most interesting cluster (cluster A) was composed of 4 nodes displaying the phenolic compounds and derivates such as Phellopterin, 3,4-Di-O-caffeoylquinic acid, (1r,3R,4s,5S)-4-{[(2E)-3-(3,4-Dihydroxyphenyl) -2-propenoyl]oxy}-1,3,5 trihydroxycyclohexanecarboxylic acid, (2S,3R,4S)-4-(2-{[(2E) -3-(3,4-dihydroxyphenyl)-2-propenoyl]oxy} ethyl)-2-(beta-D-glucopyranosyloxy) -3-vinyl-3,4-dihydro-2H-pyran-5-carboxylic acid or known as grandifloroside. Previously, caffeoylquinic acid compound was isolated from *Chrysanthemum morifolium* (L. Chen et al., 2023; Hu et al., 2017; Yang et al., 2019). A separate study suggested that the chlorogenic acid, 3,5-dicaffeoylquinic acid exhibited excellent cellular antioxidant activity (Peng et al., 2019). The molecular networking of 3,4-Di-O-caffeoylquinic acid (m/z 551.095 [M+Cl]- showed the node of MS/MS spectra correlated to the ion at m/z 353.087 [M-H]- with cosine similarity score of 0.96. A known compound was identified at m/z 353.087 [M-H]- had a mass difference of 198.01 from 3,4-Di-O-caffeoylquinic acid, calcd for $[C_{25}H_{24}O_{12} - H]^-$, suggesting that a putative known compound was (1r,3R,4s,5S)-4-{[(2E)-3- (3,4-Dihydroxyphenyl)-2-propenoyl]oxy} -1,3,5-trihydroxycyclohexane carboxylic acid.

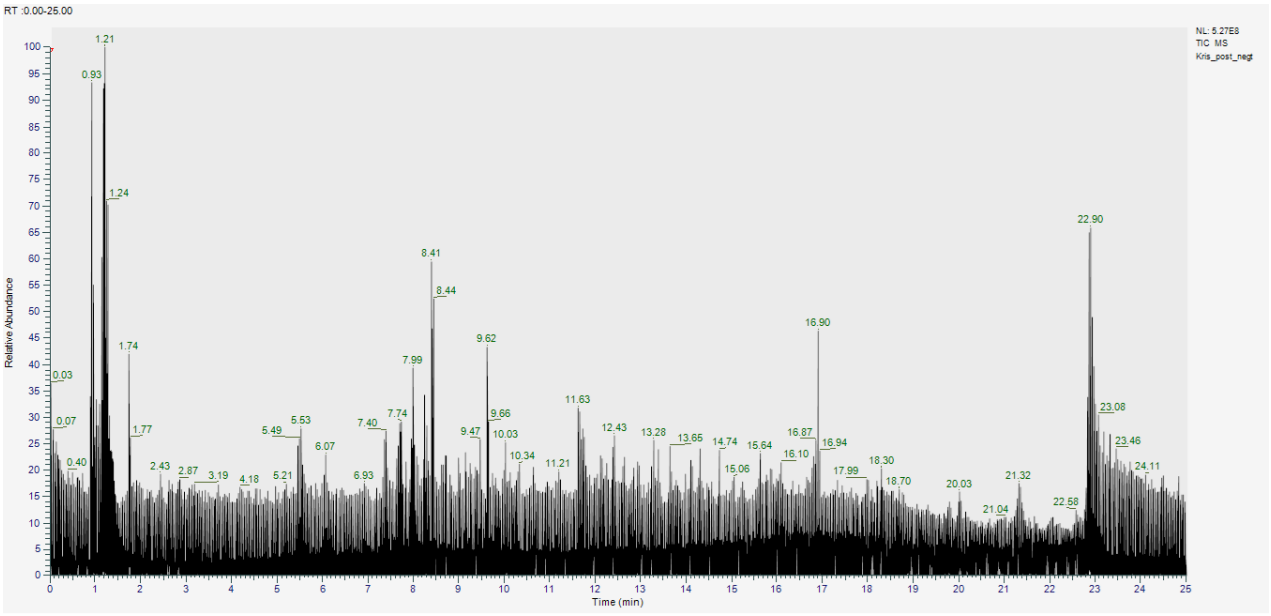

Figure 1. Total ion chromatogram (TIC) of the ethanolic extract of *C. indicum*.

Table 1. Annotated compounds of ethanolic extract of *C. indicum*

No	Annotated compounds	Formula	Adduct	Calculated mass	Rt (min)
1	6-(alpha-D-glucosaminyl)-1D-myo-inositol	$C_{12}H_{23}NO_{10}$	$[M+H]^+$	341.13161	1.037
2	DL-Arginine	$C_6H_{14}N_4O_2$	$[M+H]^+$	174.11159	1.040
3	1-[(3-Carboxypropyl)amino]-1-deoxy-beta-D-fructofuranose	$C_{10}H_{19}NO_7$	$[M+H]^+$	265.11613	1.106
4	L-Glutamic acid	$C_5H_9NO_4$	$[M+H]^+$	147.05301	1.150
5	Glucoheptonic Acid	$C_7H_{14}O_8$	$[M-H]^-$	226.06827	1.159
6	Muramic acid	$C_9H_{17}NO_7$	$[M+H]^+$	251.10036	1.161
7	D-(-)-Fructose	$C_6H_{12}O_6$	$[M-H]^-$	180.06259	1.187
8	β-Angelica lactone	$C_5H_6O_2$	$[M+H]^+$	98.03697	1.207
9	5-Hydroxymethyl-2-furaldehyde	$C_6H_6O_3$	$[M+H]^+$	126.03167	1.217
10	Pipecolic acid	$C_6H_{11}NO_2$	$[M+H]^+$	129.07892	1.23
11	DL-β-Leucine	$C_6H_{13}NO_2$	$[M+H]^+$	131.09453	1.275
12	(-)-threo-isodihomocitric acid	$C_8H_{12}O_7$	$[M-H]^-$	220.05763	1.303
13	2-Furoic acid	$C_5H_4O_3$	$[M+H]^+$	112.01621	1.317
14	10-methoxy-4H-benzo[4,5]cyclohepta[b]thiophen-4-one	$C_{14}H_{10}O_2S$	$[M+H]^+$	242.04016	1.351
15	D-Glucose 6-phosphate	$C_6H_{13}O_9P$	$[M-H]^-$	260.02919	1.365
16	L-Phenylalanine	$C_9H_{11}NO_2$	$[M+H]^+$	165.07903	2.682
17	Chlorogenic acid	$C_{16}H_{18}O_9$	$[M-H]^-$	354.09449	5.53
18	D-(-)-Quinic acid	$C_7H_{12}O_6$	$[M-H]^-$	192.06254	5.524
19	4,5-Dicaffeoylquinic acid	$C_{25}H_{24}O_{12}$	$[M-H]^-$	516.12596	7.718
20	Neochlorogenic acid	$C_{16}H_{18}O_9$	$[M-H]^-$	354.09465	7.724
21	2,4-Octadienal	$C_8H_{12}O$	$[M+H]^+$	124.08878	9.383
22	Turmerone	$C_{15}H_{20}O$	$[M+H]^+$	216.15094	9.801
23	Diosmetin	$C_{16}H_{12}O_6$	[M-H]-	299.0560	10.631
24	Naproxen	$C_{14}H_{14}O_3$	$[M+H]^+$	230.09398	12.098
25	(-)-Caryophyllene oxide	$C_{15}H_24O$	$[M+H-H_2O]^+$	220.1824	12.425
26	Cosmene	$C_{10}H_14$	$[M+H]^+$	134.10944	12.426
27	3-Methyl-1-phenyl-2-butene	$C_{11}H_{14}$	$[M+H]^+$	146.10942	12.427
28	Glycitein	$C_{16}H_{12}O_5$	$[M+H]^+$	284.06786	12.58
29	2-(3-phenylpropyl)oxolane	$C_{13}H_{18}O$	$[M+H]^+$	190.13561	14.067
30	Heptanophenone	$C_{13}H_{18}O$	$[M+H]^+$	190.13561	14.387
31	Germacra-1(10),4,11(13)-trien-12-al	$C_{15}H_{22}O$	$[M+H]^+$	218.16672	14.482
32	9-Hote	$C_{18}H_{30}O_3$	$[M-H]^-$	294.21907	14.875
33	Stearidonic acid	$C_{18}H_{28}O_2$	$[M+H]^+$	276.20882	14.887
34	Bifemelane	$C_{18}H_{23}NO$	$[M+H]^+$	269.17787	14.962
35	3',4'-Trimethylene-α-pyrrolidinovalerophenone	$C_{18}H_25NO$	$[M+H]^+$	271.19344	15.247
36	α-Eleostearic acid	$C_{18}H_{30}O_2$	$[M+H]^+$	278.22432	15.783
37	9-Oxo-10(E),12(E)-octadecadienoic acid	$C_{18}H_{30}O_3$	$[M+H]^+$	294.2191	16.429
38	S-Curcumene	$C_{15}H_{22}$	$[M+H]^+$	202.17185	16.646
39	1-Linoleoyl-2-Hydroxy-sn-glycero-3-PC	$C_{26}H_{50}NO_7P$	$[M+H]^+$	519.33165	18.313
40	α-Linolenic acid	$C_{18}H_{30}O_2$	$[M+H]^+$	278.22432	18.682
41	Stearamide	$C_{18}H_{37}NO$	$[M+H]^+$	283.28707	22.149

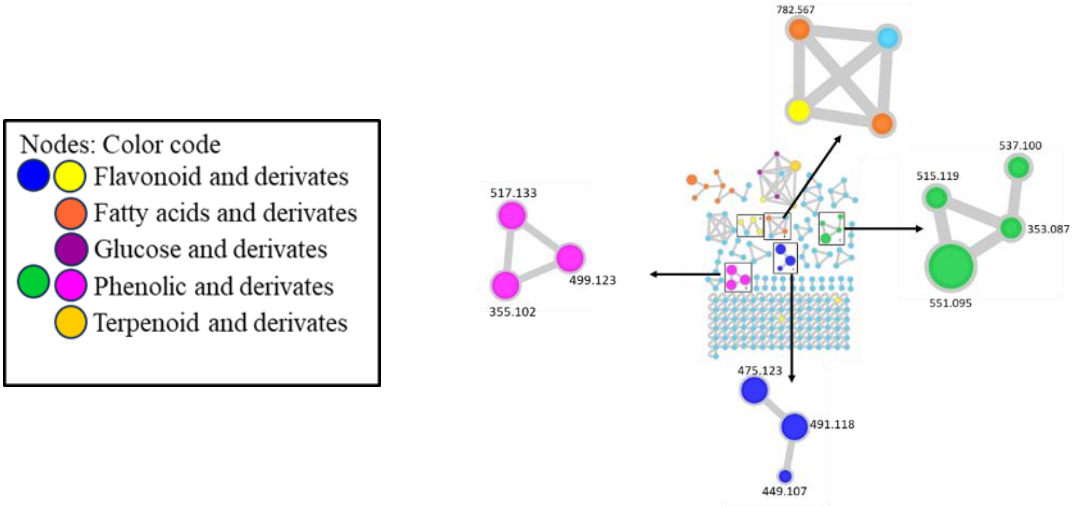

Figure 2. The ethanolic crude extract of *C. indicum* molecular networking

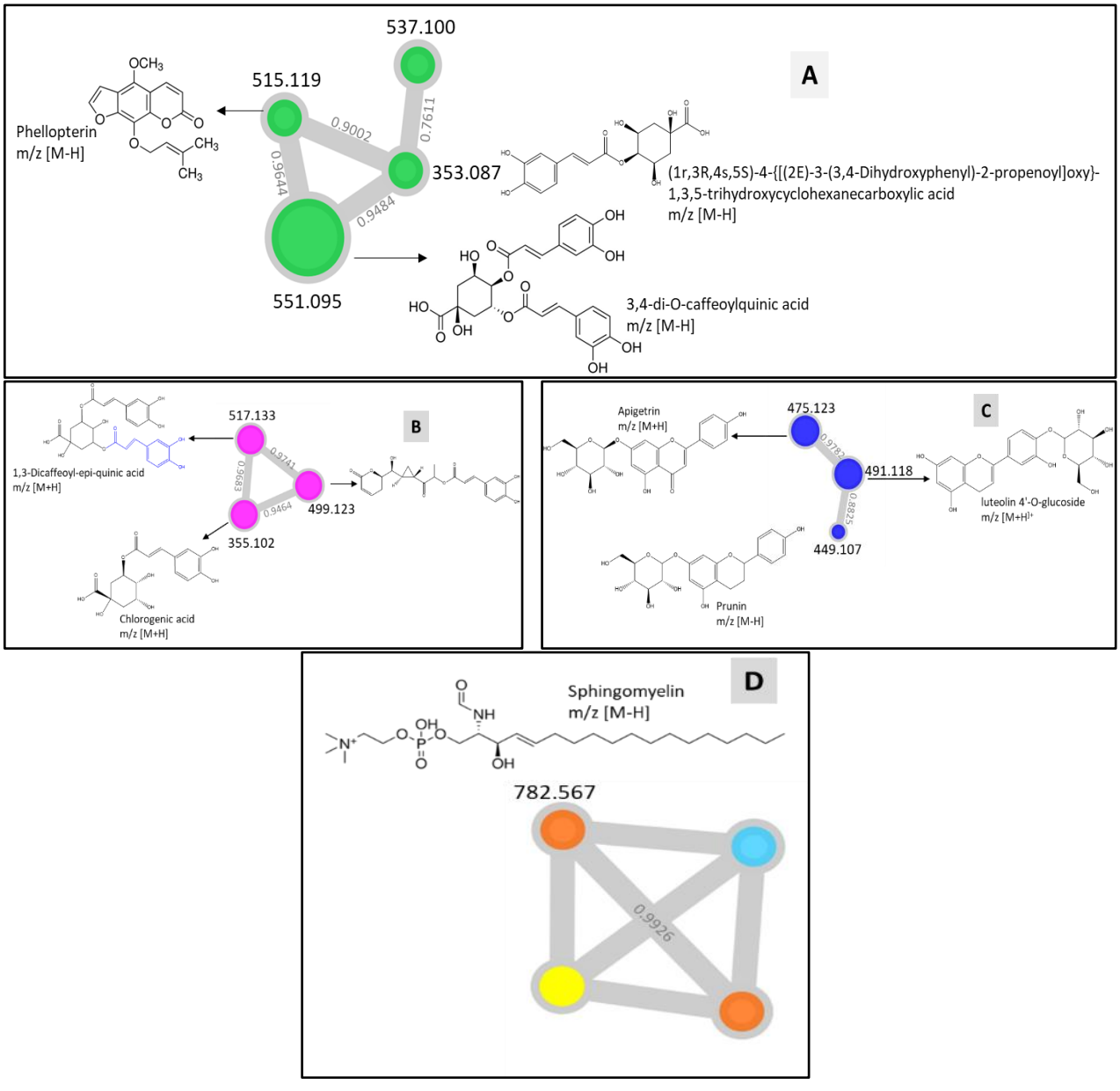

Figure 3. Molecular networking of compounds structure in extract

Table 2. The tentatively compounds of *C. indicum* extract

No	m/z	Molecular formula	Adduct	Cosine score	Compounds
1	449.107	$C_{21}H_{22}O_{10}$	[M-H]	0.88	Prunin
2	475.123	$C_{21}H_{20}O_{10}$	[M+H]	0.98	Apigetrin
3	551.095	$C_{25}H_{24}O_{12}$	[M-H]-	0.95	3,4-Dicaffeoyl-O-quinic acid
4	515.119	$C_{17}H_{16}O_5$	[M-H]-	0.96	Phellopterin
5					(1r,3R,4s,5S)-4-{[(2E)-3-(3,4-Dihydroxyphenyl)-2-propenoyl]oxy}-1,3,5-trihydroxycyclohexanecarboxylic acid
6					Caffeic acid phenethyl ester
7	517.133	$C_{25}H_{24}O_{12}$	[M+H]	0.97	1,3-Dicaffeoyl-epi-quinic acid
8	355.283	$C_{18}H_{32}O_2$	[M+H]	0.75	Linoleic acid
9	239.199	$C_{14}H_{26}O_2$	[M+H]	0.81	Myristoleic acid
10	217.158	$C_{15}H_{22}O$	[M+H-H_2O]	0.76	Nootkatone
11	203.179	$C_{14}H_{26}O_2$	[M+H-2H2O]	0.73	2,4,7,9-Tetramethyl-5-decyne-4,7-diol
12	415.197	$C_{21}H_{34}O_{10}$	[M-H]-	0.77	(Z)-2,6-dimethyl-7-(4-methyl-5-oxooxolan-2-yl)-3-[[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxymethyl]hept-5-enoic acid
13	345.155	$C_{16}H_{28}O_7$	[M-H]-	0.88	(3R,4S,5S,6R)-2-(6-hydroxy-2,6-dimethylocta-2,7-dienoxy)-6-(hydroxymethyl)oxane-3,4,5-triol
14	782.567	$C_{47}H_{93}N_{2O6}P$	M	0.99	Sphingomyelin (d18:1/18:0)

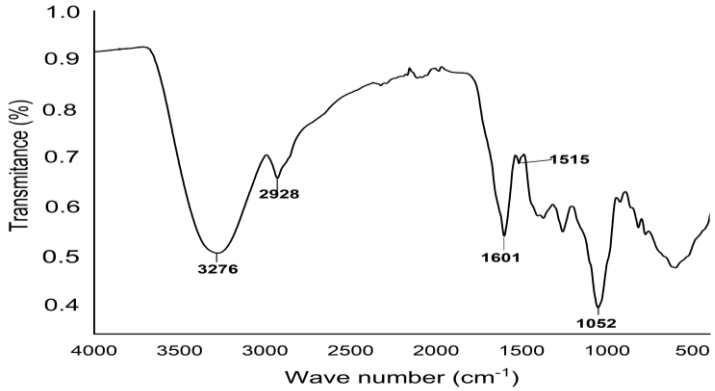

Figure 4. FTIR spectra of ethanolic extract of *C. indicum* flower

Table 3. The TPC, antioxidant, and α-glucosidase inhibition of ethanolic extract of *C. indicum* flower

Sample	Total phenolic contents (TPC) (mg GAE/mg dry extract)	% scavenging activity againts DPPH radicals at 100 μg/mL (%)	Inhibitory activity of α–glucosidase at 50 μg/mL (%)
Ethanolic extract	2.81±0.17	76.20±1.35	83.04±0.52
Ascorbic acid at 6 μg/mL	-	72.55±0.12	-

The tentative known derivate was identified at m/z 353.087 [M-H]-, calculated for [$C_{16}H_{18}O_9$ – H, and the molecular formula of this compound was $C_{16}H_{18}O_9$. In cluster B (**Figure 3**), node of MS/MS spectra connected to chlorogenic acid (m/z 355.102 [M+H]+), possessed a precursor ion of 1,3-Dicaffeoyl-epi-quinic acid at m/z 517.133 with a cosine similarity score of 0.97. In the previous research, the chlorogenic acid was isolated from yellow *C. indicum* flower (Ryu et al., 2019). This compound was higher than in purple colour and it exhibited various pharmacological effects such as antioxidant, protection of liver and kidney, anti-bacterial, anti-tumor, antidiabetic, anti-inflammatory, nervous system protection, and blood vessel regulation (Wang et al., 2022). The interesting result from molecular network analysis was identification of putative compound, sphingomyelin (cluster D,

Figure 3). The fact that, this compound can be found in animal cell membranes, suggested that there was contamination on the flower or in the extract of *Chrysanthemum*.

Measurement of FTIR Spectroscopy

Once the constituent of *C. indicum* were profiled using LC HRMS study were continued to indentify the fingerprint identity of the extract. The functional groups of the molecules in ethanolic extract of *C. indicum* was analysed using FTIR (**Figure 4**). The results suggested that ethanolic extract contain phenolic compound. It was expressed from peaks at 3100-3400 cm^{-1} corresponding to the O-H groups. Peak at 2928 belongs to the aliphatic CH, CH_2, and CH_3 stretching vibrations in asymmetric mode whereas peaks at 1601 corresponded strecthing vibration of carbonyl (C=O). Stretching vibration of alkene or aromatic C=C was observed at 1515 cm^{-1}. The presence of C-O functional groups was identified from the strecthing vibration of C-O observed at 1052 cm^{-1}. The vibration of C-O was suggested from alcohols, phenols, esters, ethers, aldehydes, and carboxylic acids (Raju et al., 2016). The result from FTIR confirming the LC HRMS result regarding the presence of phenolic or phenolic derivates in ethanolic extract the sample examined.

The Total Phenolic Content (TPC), Antioxidant, and Inhibition of α-Glucosidase

As both LC HRMS and FTIR data suggested the presence of phenolic compound, the quantification of total phenolic content is conducted. The scavenging activity toward DPPH radicals was represented the antioxidant activity of *C. indicum* extract. Several mechanism of antioxidant have been reported including enzymatic, metal chelating and free radical scavenging activities (Lü et al., 2010). The antioxidant agent will change the colour of DPPH solution into yellow colour when they are mixed. The difference of color change when the samples were reacted with DPPH solution indicates that the level of metabolites ability contained in the sample to donate hydrogen atoms binding with DPPH radicals (Ruslin et al., 2022). The scavenging activity of ethanolic extract of *C. indicum* against DPPH radicals is shown in **Table 3**. The result revealed that extract from this flower exhibited the greatest antioxidant activity with %inhibition value of 76.20 at 100 μg/mL. The result of this study was in line to the previous research which stated that papain hydrolysate from rabbit meat showed the greatest antioxidant against DPPH and ABTS with % inhibition values of 51.50% and 61.50% at a concentration of 100 μg/mL (Yang et al., 2025). The antioxidant activity might be contributed by both phenolic (TPC) and flavonoid (TFC) compounds. Profiling metabolites of *C. indicum* by LC-HRMS suggested the presence of phenolic compounds such as curcumene, chlorogenic acid, quinic acid, 4,5 dicaffeoylquinic acid, and neochlorogenic acid. The flavonoid compounds such as apigetrin, quercetin, and luteolin and derivates were identified in the current study using LC HRMS. This result similar to the previous study that phenolic and flavonoid compounds contributed on antioxidant activity of *C. indicum* flower (Hodaei et al., 2021).

This study also provided data that *C. indicum* extract exhibited strong activity to inhibit α-glucosidase with % inhibiton value of 83.04±0.52% at 50 μg/mL. Confirming to the previous studies (M. Chen et al., 2019; Luyen et al., 2013), which reported that a new endoperoxysesquiterpene lactone, 10α-hydroxy-1α,4α-endoperoxy-guaia-2-en-12,6α-olide contained in *Chrysanthemum morifolium* flowers extract exerts strong inhibitory effects against α-glucosidase with IC_{50} of 161.0 μM (Luyen et al., 2013). Whereas Chen et al. reported that natural flavonoid contained in *Chrysanthemum sp*. flower extract among other diosmetin 7-glucoside, diosmin, diosmetin, luteolin, apigenin, and acacetin) exhibited inhibition activity toward α-glucosidase by regulating the α-glucosidase and the PTP-1B signal pathway (Chen et al., 2019). Together this study confirming the activity of *Chrysanthemum sp*. flower extract in inhibiting α-glucosidase, an enzyme which is play important role in the pathophysiology of diabetes mellitus.

CONCLUSIONS

The molecular networking method using GNPS and Cytoscape provide a suitable method to identify the known compounds in the extract of plant, and the related analogues. The metabolites contained in the *C. indicum* extract supports the ethnobotanical of this plant as a medicinal herb for cephalalgia, antidiabetic, migraine, coronary heart disease, and chronic inflammation. Thes results also suggest the ethanolic extract of *C. indicum* was potential as natural antioxidant and antidiabetic as inhibition of α-glucosidase.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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