Journal of Applied Botany and Food Quality 96, 148 - 156 (2023), DOI:10.5073/JABFQ.2023.096.019

[1]Institute of Biotechnology and Food Technology, Industrial University of Ho Chi Minh City, Vietnam
[2]Phu Nhuan High School, Ho Chi Minh City, Vietnam
[3]Office of Science Management and International Affairs, Industrial University of Ho Chi Minh City, Ho Chi Minh City, Vietnam
[4]Center of Analytical Services and Experimentation HCMC, Ho Chi Minh City, Vietnam
[5]Binh Chau-Phuoc Buu Nature Reserve, Ba Ria-Vung Tau Province, Vietnam

Chemical profiles and biological activities of acetone extracts of nine Annonaceae plants

Ngoc Duyen Nguyen[1,2#], Sao Mai Dam[1#], Ngoc Nam Trinh[3], Quoc Hung Nguyen[4], Thanh Tho Le[4], Van Son Le[5], Hong Thien Van[1], Ngoc An Nguyen[1], Hanh Thi Dieu Nguyen[1], Tan Viet Pham[1*]

(Submitted: August 1, 2023; Accepted: November 18, 2023)

Summary

This study investigated the chemical components and bioactivities of acetone leaf extracts of nine Annonaceae plants collected in the Binh Chau-Phuoc Buu Nature Reserve, Vietnam. A total of 182 constituents were identified, with linolenic acid, diaeudesmin, germacrene D, 1-octadecenoic acid, 8-(3-octyl-2-oxiranyl)-1-octanol, oleic acid, and phenylmethyl ester being the major compounds. The antimicrobial activity of the extracts was evaluated using a disc diffusion assay. Eight of the nine extracts, except for the *Mitrephora thorelii* extract, showed an inhibition effect against *Bacillus cereus* and *Staphylococcus aureus*. The antioxidant activity of the extracts was determined using DPPH assay, and the cytotoxic activity was determined using SRB assay. The results showed that the acetone extracts of *Artabotrys hexapetalus*, *Uvularia grandiflora*, *Polyalthia luensis*, *Xylopia pierrei*, *Sphaerocoryne affinis*, *Desmos cochinchinensis*, *Uvaria littoralis*, *Mitrephora thorelii*, and *Goniothalamus touranensis* had significant activity with IC_{50} for the DPPH radical scavenging activity ranging from 18.56 to 702.33 µg/mL, and the IC_{50} for the cytotoxic effects ranged from 5.39 to 251.77 µg/mL. Overall, the results obtained provide experimental evidence for the potential use of these plants in medicine and other related fields.

Keywords: Annonaceae, antibacterial activity, antioxidant activity, Binh Chau-Phuoc Buu, chemical composition, cytotoxicity.

Introduction

Annonaceae is a large family of 2,500 species belonging to 135 genera, mainly found in tropical and subtropical regions (Aziz et al., 2016). Annonaceae is known as an economic family, with many species used as sources of edible oils and fruits (Al Kazman et al., 2022). The seeds of some species are used in the production of soap as well as edible oils, while the flowers are used in the perfume industry (Quílez et al., 2018). A large number of Annonaceae species have been used for medicinal properties to treat skin diseases, fever, flu, asthma, wounds, stomachache, and cough (Breuer et al., 1982; Kluza et al., 2007). Accordingly, Annonaceae plants have also been reported to possess many valuable biological activities such as antioxidants, antimicrobial, anti-cancer, and anti-ulcerogenic effects (Leite et al., 2021).

Vietnam is an important and diverse region for Annonaceae, with more than 183 recorded species distributed in 29 genera, 2 subspecies, and 21 varieties (Nguyen et al., 2016). Despite this rich diversity, research on the chemical compositions and bioactivities of Annonaceae species in Vietnam has been limited. Only a handful of studies have explored this area, such as examinations of the chemical compositions of essential oil from the flower *Artabotrys hexapetalus* (Phan et al., 2007), investigations into the chemical constituents of the leaf of *Uvaria grandiflora* (Tran et al., 2017), and the exploration of the potential benefits in ameliorating locomotor disabilities and dopaminergic neuron degeneration through the aqueous extract from *Sphaerocoryne affinis* (Ngo et al., 2022). Species like *Goniothalamus touranensis*, *Polyalthia luensis*, and *Uvaria littoralis*, which are also found in Vietnam, remain largely unexplored on a global scale to date. Moreover, while non-polar solvents (e.g., chloroform and n-hexane) and polar solvents (e.g., water, methanol, and ethanol) are commonly employed for extracting plant active compounds, intermediate-polar solvents such as acetone and dichloromethane have been shown to offer a more comprehensive chemical composition or enhanced yield for flavonoid extraction (Chuo et al., 2022; Dirar et al., 2019).

This study, therefore, seeks to elucidate the chemical constituents, antibacterial, antioxidant, and cytotoxic activities of acetone extracts isolated from nine Annonaceae species including *A. hexapetalus, Desmos cochinchinensis, G. touranensis, P. luensis, Mitrephora thorelii, S. affinis, U. grandiflora, U. littoralis* and *Xylopia pierrei* collected from the Binh Chau-Phuoc Buu Nature Reserve in Vietnam for the first time.

Materials and methods

Plant materials

The leaves of nine studied plants belonging to Annonaceae, including *Artabotrys hexapetalus, Desmos cochinchinensis, Goniothalamus touranensis, Polyalthia luensis, Mitrephora thorelii, Sphaerocoryne affinis, Uvaria grandiflora, Uvaria littoralis* and *Xylopia pierrei* were collected from Binh Chau-Phuoc Buu Nature Reserve, Ba Ria-Vung Tau Province, Vietnam. The vouchered specimens of these species were deposited at the Herbarium of Binh Chau-Phuoc Buu Nature Reserve.

Extraction procedures

Each studied plant's leaves (10 kg) were dried at 50 °C until unchanged weights were achieved. An electric grinder was used to grind the dried samples into the powder, and 100 g of the powder was subsequently macerated in 500 ml of acetone 99% solution (Thermo Fisher Scientific, USA) for 72 hours at room temperature. The Whatman paper was used to filter the extracts. The process was repeated twice. The rotary evaporator concentrated the total filtrate under reduced pressure at 45 °C. Finally, the extracts were dried to remove the remaining acetone completely.

Gas chromatography-mass spectrometry (GC/MS) analysis

The chemical compositions of nine acetone extracts were determined using the gas chromatograph GC TRACE 1310 and a single qua-

* Corresponding author
# Equal contribution in this paper

drupole mass spectrometer ISQ 7000 (Thermo Fisher Scientific Inc., Waltham, MA, USA). A DB-5MS column (30 m × 0.25 mm × 0.25 µm) was employed for this analysis. Helium was the carrier gas with a constant 1.2 mL/min flow rate. The samples were introduced into the GC system with an injection chamber temperature of 270 °C. The samples were injected using split mode, with a divided flow rate of 36 mL/min, a split ratio 30:1, and a splitless time of 1 minute. The column was set at 80 °C for 5 min, then 280 °C for 10 min, and finally 300 °C for 3 min at a constant heating rate of 20 °C/min. The ion source temperature was maintained at 250 °C, while the transfer line temperature was set to 280 °C. Electron impact ionization was employed with an energy level of 70 eV. The mass range for MS acquisition was 29-650 m/z, and the scanning frequency was two scans/sec. The chemical compositions in the samples were identified by comparing their mass spectra with those in the NIST 2017 library.

Determination of the antibacterial activity of the extracts

The antibacterial activities of the acetone extracts from the leaves of the nine studied species were tested against two bacterial pathogens *Bacillus cereus* (ATCC 11774), *Staphylococcus aureus* (ATCC 25923) in order to explore their potentials in medicine and food industries. The strains were preserved in 20% glycerol solution at 20 °C and activated by cultivation in Luria-Bertani broth at 37 °C for 24 h before the antibacterial activity assay.

The CLSI (Clinical and Laboratory Standards Institute) guide performed the antibacterial activity assays. The LB Broth was used to grow the studied bacterial strains until the turbidity of 0.5 McFarland standards. 100 µL of bacterial culture was spread on a sterile Mueller Hinton plate. The sterile paper discs (6 mm diameter) containing 10 µl of the studied extracts solution were placed on the plate surface. The plate was incubated at 37 °C for 24 hours, and the antimicrobial effects of the studied specimens were identified by measuring the inhibition zone diameter of the oral bacterial strains. Gentamycin antibiotic discs (supplied by Nam Khoa BioTek, Vietnam) were used as the positive control, and 5% dimethyl sulfoxide solution (Bio Basic, Canada) was used as a negative control.

Determination of the antioxidant activity of the extracts

DPPH solution of 150 µM was prepared with methanol 80%, and 200 µl was immediately mixed with 25 µl of sample solution at different concentrations in each well on a 96-well plate. The samples were incubated in the dark for 20 minutes. The optical density was measured at 517 nm. Trolox was used as a positive control. All the chemicals were obtained from Thermo Fisher Scientific, USA.

The DPPH free radical scavenging percentage was calculated by the formula: SC% = 1-[ODt/ODc] × 100 (%).ODt stands for the optical density of the test sample after subtracting the blank, and ODc stands for the control sample's optical density after subtracting the blank. The IC_{50} values were determined using Graphpad Prism software with multi-parameter non-linear regression and R2 > 0.9.

Determination of cytotoxicity of the extracts

The nine studied extracts' cytotoxic effects were identified using SRB (Sulforhodamine B) method. The human liver cancer cell line (Hep G2) (ATCC, USA) was cultured in Eagle's minimum essential medium (E'MEM), supplemented with L-glutamine (2 mM), HEPES (20 mM), amphotericin B (0.025 µg/ml), penicillin G (100 UI). /ml), streptomycin (100 µg/ml), 10% (v/v) fetal bovine serum FBS and incubated at 37 °C, 5% CO_2.

Single cells were cultured on 96-well culture plates at 104 cells/well density. After 24 hours of culture, the cell population was incubated with the studied samples at different concentrations for 48 hours. The total proteins from test cells were fixed with a 50% cold trichloroacetic acid (Sigma) and stained with 0.2% sulforhodamine B solution (Sigma). The results were identified by the ELISA reader at 492 nm (OD_{492}) and 620 nm (OD_{620}) and were calculated by using the following formula:

- $OD = OD_{492} - OD_{620}$ (1)
- OD_{492} (or OD_{620}) = $OD_{cell} - OD_{blank}$ (2)

The percentage (%) causing cytotoxicity was calculated according to the formula:

Where

- OD_{cell}: OD values of the well containing cells
- OD_{blank}: OD values of the blank well (no cells)
- OD_{TN}: OD values of the studied samples obtained from formulas (1) and (2)
- OD_C: OD values of the control obtained from formulas (1) and (2).

Data analysis

The experiments were conducted in triplicate, and the results were expressed as a mean±standard deviation (SD). The data were analyzed by the one-way analysis of variance (ANOVA) assay that was used to compare different groups using Fisher's least significant difference (LSD) procedure ($p<0.05$). Statistical analysis was performed using Statgraphics Centurion XV (version 15.1.02, Statgraphics Technologies, Inc., USA).

Results and discussion

Chemical compositions of acetone extracts of nine Annonaceae plants

The chemical components of acetone extracts isolated from the leaves of nine Annonaceae species were presented in Tab. 1, in which a total of 182 compounds have been identified. Accordingly, the extract of *P. luensis* was characterized by the predominance of linolenic acid (24.56%), caryophyllene (10.56%), chondrillasterol (7.45%), phytol (6.27%), and hexadecanoic acid (8.32%). The *U. littoralis* extract mainly contained linolenic acid (13.3%), oleic acid (7.80%), and benzoic acid (5.7%), while diaeudesmin (44.66%), oleic acid (36.61%) were the major compounds in the *M. thorelii* extract. Furthermore, *X. pierrei* extract was found to contain germacrene D (19.79%), 3-hydroxypregn-5-en-20-one (16.23%), kauren-19-oic acid (15.75%), phytol (7.04%) and spathulenol (6.94%) as the dominant constituents whereas *S. affinis* extract was found to be rich in benzoic acid, allyl ester (7.48%), resorcinol monobenzoate (4.87%) and flavone, 5,7-dimethoxy (3.76%). The leaf extract of *G. touranensis* was dominated by 11-octadecenoic acid (18.57%), 2-methoxybenzyl benzoate (10.2%), hexadecanoic acid (7.13%) and 1,5-Diphenyl-2-pentyne-1,5-diol (6.13%) while 8-(3-octyl-2-oxiranyl)-1-octanol (22.30%), benzoic acid (17.46%) and linolenic acid (11.90%) were the major compounds in the *U. grandiflora* extract. Furthermore, the main components of the *A. hexapetalus* extract were oleic acid (58.44%), 3-O-methylhexose (9.00%), hexadecanoic acid (5.71%), and caryophyllene (5.08%). In contrast, *D. cochinchinensis* extract was characterized by large quantities of benzoic acid, phenylmethyl ester (28.08%) and trans-nerolidol (11.80%).

Notably, the acetone extracts of five species such as *U. littoralis, S. affinis, G. touranensis, D. cochinchinensis* and *U. grandiflora* contained several unknown compounds (UC) as the major components in spite of the fact that NIST 2017 library, the most innovative library, was used in this study. As a result, *G. touranensis* extract was found to be rich in UC1 (25.27%) and UC2 (13.88%) while UC3 (35.84%) and UC6 (16.33%) were the major constituents in the *U. littoralis* extract. In addition, UC4 (60.42%) was the most abundant component in the *S. affinis* extract whereas UC7 (9.09%) was the major compound in the *U. grandiflora* extract. Furthermore, the acetone extract of *D. cochinchinensis* contained UC9 (11.88%) and UC10 (10.61%)

Tab. 1: Chemical compositions of the acetone extracts from leaves of the nine Annonaceae species

No.	RT	Compounds	The relative percentage (%)								
			PL	UL	XP	SA	GT	UG	AH	MT	DC
1	3.49	2-Thujene	-	-	0.18	-	-	-	-	-	-
2	3.61	α-Pinene	-	-	0.21	-	-	-	-	-	-
3	4.02	Glycerin	0.91	0.11	-	-	-	-	-	-	-
4	4.06	Caproic acid	-	-	-	-	-	0.12	-	0.04	-
5	4.36	2-Menthene	-	-	1.33	-	-	-	-	-	-
6	4.44	*trans*-3-Hexenoic acid	-	-	-	-	-	-	-	-	0.04
7	4.51	β-Pinene	-	-	1.00	-	-	-	-	-	0.09
8	4.53	*trans*-3-Hexenoic acid	-	-	-	-	-	0.71	-	-	0.02
9	5.05	Ethylidene acetate	-	-	-	-	-	-	-	0.01	0.03
10	5.16	α-Phellandrene	-	-	-	-	-	0.07	0.55	-	-
11	5.58	Benzene	-	-	-	-	-	-	0.09	-	-
12	5.77	Benzenemethanol	-	0.05	-	-	-	-	-	-	4.17
13	5.92	4-Methyl-2-propyl-1-pentanol	-	-	-	-	-	-	0.19	-	-
14	6.40	Ethanone, 1-phenyl	-	-	-	-	-	-	-	-	0.84
15	6.86	Methyl benzoate	-	-	-	-	-	0.04	-	-	0.05
16	6.93	Linalool	-	0.09	0.47	-	0.15	0.15	-	-	0.04
17	7.59	Pinocarveol	-	-	0.4	-	-	-	-	-	-
18	7.62	*cis*-Pinen-3-ol	-	-	0.19	-	-	-	-	-	-
19	7.85	Pinocarvone	-	-	0.20	-	-	-	-	-	-
20	7.97	Benzenecarboxylic acid	-	-	-	3.94	-	-	-	-	-
21	8.11	Benzoic acid	0.18	5.70	-	-	-	17.46	-	-	3.67
22	8.24	Myrtenol	-	-	1.01	-	-	-	-	-	-
23	9.70	α-Cubebene	-	-	0.38	-	-	-	0.36	-	-
24	9.82	Phenol, o-propyl-	-	-	-	0.11	-	-	-	-	-
25	9.96	Copaene	-	0.21	1.24	0.12	0.07	0.05	0.22	0.03	3.35
26	9.99	Ylangene	0.12	-	-	-	-	-	-	-	-
27	10.05	β-elemene	-	-	-	-	-	0.14	-	-	0.32
28	10.26	Cinnamic acid	-	-	-	-	0.08	-	-	-	-
29	10.29	Butyrophenone	-	-	-	0.45	-	-	-	-	-
30	10.33	Caryophyllene	10.56	0.33	1.14	1.11	0.36	2.74	5.08	0.59	2.65
31	10.39	Benzene	0.21	-	-	-	0.11	-	-	-	-
32	10.40	Propionic acid, 3-benzoyl	-	-	-	-	-	-	-	-	0.21
33	10.41	4-n-Propylresorcinol	-	0.02	-	-	-	-	-	-	-
34	10.58	α-Caryophyllene	-	-	0.23	0.14	0.07	-	0.68	-	-
35	10.59	Humulene	4.32	-	-	-	-	0.18	-	0.12	0.44
36	10.63	Methyl 2-(benzoyloxy)ethanoat	-	-	-	0.09	-	-	-	-	-
37	10.68	Cadina-1(10),4-diene	-	-	-	-	-	-	0.11	0.05	-
38	10.69	Naphthalene, 1,2,3,4,4a,5,6,8a-	-	-	0.77	-	-	-	-	-	-
39	10.77	Germacrene D	1.43	0.40	19.79	0.77	0.12	0.13	0.2	-	0.58
40	10.78	Isogermacrene D	-	-	-	-	-	-	0.42	-	-
41	10.82	Anhydro-d-mannosan	-	-	-	-	-	-	0.35	-	0.07
42	10.85	Bicylogermacrene	-	-	-	1.03	-	-	0.52	-	-
43	10.86	γ-Elemene	-	0.22	0.59	-	-	1.22	-	0.19	0.26
44	10.97	γ-Cadinene	-	-	1.07	-	-	-	0.54	-	-
45	11.00	Hedycaryol	-	-	-	-	-	-	-	-	0.21
46	11.01	Cadina-1,3,5-triene	-	-	-	-	-	-	0.34	-	-
47	11.09	δ-Cadinene	-	-	-	-	-	-	0.44	-	-
48	11.14	n-Dodecanoic acid	-	-	0.14	-	-	0.06	-	-	-
49	11.19	trans-Nerolidol	-	-	-	-	0.32	-	-	-	11.8
50	11.20	Phenol, 2,6-dimethoxy-4-vinyl-	-	-	-	-	-	0.07	-	-	-
51	11.41	Spathulenol	-	0.52	6.94	-	-	0.57	-	-	-
52	11.45	4-n-Propylresorcinol	-	-	-	-	-	-	1.06	-	-
53	11.46	Caryophyllene oxide	5.12	-	1.12	-	0.92	0.32	-	-	0.38
54	11.52	Mintketone	-	-	0.34	-	-	-	-	-	-
55	11.62	2-(Acetyloxy)-4-allylphenyl acetate	-	-	-	0.32	-	-	-	-	-
56	11.63	5-Cyclodecen-1-ol, 4,10-bis(methylene)-7-(1-methylethyl)-	-	-	0.76	-	0.11	-	-	-	-
57	11.66	Megastigmatrienone	-	-	-	-	-	0.07	-	-	-
58	11.67	Humulene epoxide II	1.45	-	-	-	-	-	-	-	-
59	11.74	Aromadendrane-4,10-diol	-	-	0.13	-	-	0.10	-	-	-
60	11.75	γ-Eudesmol	-	-	-	-	-	-	-	-	0.54
61	11.79	Cadinol	-	-	1.09	-	-	-	-	-	-
62	11.91	Eudesm-4(14)-en-11-ol	-	-	0.76	-	-	-	-	-	3.40

No.	RT	Compounds	The relative percentage (%)								
			PL	UL	XP	SA	GT	UG	AH	MT	DC
63	11.94	Guai-1(10)-en-11-ol	-	-	-	-	-	-	-	-	0.16
64	12.01	Isoaromadendrene epoxide	0.57	-	-	-	-	-	-	-	-
65	12.06	Ledene oxide-(II)	-	-	0.35	-	-	-	-	-	0.03
66	12.10	6-Isopropenyl-4,8a-dimethyl-1,2,3,5,6,7,8,8a-octahydro-2-naphthalenol	-	-	0.99	-	-	-	-	-	-
67	12.34	Oplopanone	-	-	0.71	-	-	0.20	-	-	-
68	12.36	Myristic acid	-	-	-	-	-	-	0.30	0.06	-
69	12.44	Aromadendrene oxide-(1)	-	-	0.59	-	-	-	-	-	-
70	12.49	(2,2,6-Trimethyl-bicyclo [4.1.0] hept-1-yl)-methanol	-	-	-	-	-	-	-	0.05	-
71	12.51	Benzyl Benzoate	-	0.25	-	-	-	-	-	-	-
72	12.52	2(4H)-Benzofuranone, 5,6,7,7a-tetrahydro-6-hydroxy-4,4,7a-trimethyl	-	-	-	-	0.07	-	-	-	-
73	12.53	3-O-Methylhexose	-	-	-	-	-	-	9.00	-	-
74	12.55	Benzoic acid, phenylmethyl ester	-	-	-	-	-	-	-	-	28.08
75	12.58	4,4,8-Trimethyl-non-7-en-2-one	-	-	-	-	-	-	-	0.07	-
76	12.66	2,3,3a,4,5,6,7,7a-Octahydro-1H-cyclopenta[a]pentalen-7-ol	-	0.12	-	-	-	-	-	-	-
77	12.67	1,3-Benzenedicarboxaldehyde, 2-hydroxy-5-methylOH	-	-	-	-	-	-	0.45	-	-
78	12.77	2-Hexadecene, 3,7,11,15-tetramethyl	-	-	-	-	-	-	-	0.03	-
79	12.80	Neophytadiene	-	0.46	1.40	0.54	-	1.25	1.43	1.09	0.68
80	12.82	Shyobunol	-	-	-	-	0.20	-	-	-	0.53
81	12.83	2-Hexadecene, 3,7,11,15-tetramethyl	1.18	-	-	-	-	-	-	0.09	-
82	12.84	Proximadiol	-	-	-	-	-	-	-	-	0.90
83	12.92	2-Hexadecen-1-ol, 3,7,11,15-tetramethyl	0.45	0.08	-	0.11	-	0.2	0.25	0.16	0.07
84	13.00	Benzoic acid, phenethyl ester	-	-	-	-	0.23	-	-	-	1.03
85	13.03	2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, acetate	0.62	0.12	-	0.18	0.42	0.42	0.44	0.28	0.14
86	13.08	Salicylic acid	-	0.05	-	-	-	-	-	-	-
87	13.17	4,7-Methano-1H-inden-1-ol	-	-	-	-	0.77	-	-	-	-
88	13.20	Farnesyl acetone	-	-	-	-	-	-	-	-	0.16
89	13.22	Clovanediol	-	-	-	-	0.15	-	-	-	-
90	13.26	8-α-11-elemodiol	-	-	-	-	-	-	-	-	0.08
91	13.28	Hexadecanoic acid, methyl ester	0.36	-	-	-	-	-	-	-	-
92	13.33	(9E)-9-Hexadecenoic acid	-	0.05	-	-	-	-	-	-	-
93	13.48	Hexadecanoic acid	8.32	3.28	2.07	0.57	7.13	4.46	5.71	2.89	0.50
94	13.58	Squalene	-	-	-	-	-	-	-	-	0.01
95	13.63	trans-Geranylgeraniol	-	-	-	-	-	-	-	-	0.01
96	13.67	2-Methoxybenzyl benzoate	-	-	-	0.10	10.2	-	-	-	-
97	13.75	2-Propen-1-ol, 3-phenyl-, benzoate	-	-	-	-	-	-	-	-	0.04
98	13.84	Unknown compound 1	-	-	-	-	25.27	-	-	-	-
99	13.88	Benzeneacetic acid	-	-	-	-	0.41	-	-	-	-
100	13.93	n-Heptadecanoic acid	-	-	-	-	-	-	0.17	-	0.01
101	13.95	trans-9-Octadecen-1-ol	-	-	-	-	-	0.87	-	-	0.04
102	13.99	9-Oxatetracyclo [5.3.1.0(2,6).0(8,10)] undec-3-ene	-	-	-	-	3.08	-	-	-	-
103	14.00	o-Methoxyphenyl benzoate	-	0.10	-	-	-	0.23	-	-	-
104	14.05	Ledene oxide-(II)	-	-	0.35	-	-	-	-	-	-
105	14.10	9,12-Octadecenoic acid, methyl ester	-	0.06	-	-	-	-	-	-	0.01
106	14.11	Kaur-16-ene	-	-	0.18	-	-	-	-	-	-
107	14.13	Oleic acid, methyl ester	-	0.05	-	-	-	-	-	-	0.06
108	14.16	Linolenin, 1-mono	0.51	-	-	-	-	-	-	-	-
109	14.17	2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-	-	-	-	0.52	0.95	-	-	-	-
110	14.18	Phytol	6.27	0.14	7.04	-	-	2.56	0.54	0.35	2.39
111	14.27	Linoelaidic acid	-	-	-	-	-	-	-	-	0.11
112	14.31	Linolenic acid	24.56	13.30	2.75	0.54	-	11.90	-	-	0.52
113	14.33	11-Octadecenoic acid	-	-	-	-	18.57	-	-	-	-
114	14.37	Oleic Acid	-	7.80	-	-	4.21	-	58.44	36.61	-
115	14.45	Stearic acid	2.26	1.15	0.33	-	-	0.66	1.25	0.49	0.09
116	14.49	(1R,6S)-6-Hydroxy-6-methyl-4-oxocyclohex-2-en-1-yl benzoate	-	-	-	0.69	-	-	-	-	-
117	14.58	1,5-Diphenyl-2-pentyne-1,5-diol	-	-	-	-	6.13	-	-	-	-
118	14.64	Methyl 2-benzoyl-3-methyl-4H-pyrazole-3-carboxylate	-	-	-	0.17	-	-	-	-	-
119	14.70	Unknown compound 2	-	-	-	-	13.88	-	-	-	-
120	14,78	9-(2-Oxiranyl)-1-nonanol	-	-	-	-	-	0.43	-	-	-
121	14.87	8-(3-Octyl-2-oxiranyl)-1-octanol	-	-	-	-	-	22.30	-	-	-

No.	RT	Compounds	The relative percentage (%)								
			PL	UL	XP	SA	GT	UG	AH	MT	DC
122	14.89	2,2-Dimethyl-1-phenyl-3-buten-1-one	-	-	-	1.40	-	-	-	-	-
123	15.01	Benzoic acid, allyl ester	-	-	-	7.48	-	-	-	-	-
124	15.06	Unknown compound 3	-	35.84	-	-	-	-	-	-	-
125	15.09	Resorcinol monobenzoate	-	-	-	4.87	-	3.08	-	-	-
126	15.14	1H-2,10a-Ethanophenanthrene, kaur-16-en-18-al deriv.	-	-	1.02	-	-	-	-	-	-
127	15.24	Benzoic acid, 3-(3-oxocyclopentyl)-, allyl ester	-	0.47	-	-	-	-	-	-	-
128	15.28	Dehydroabietic acid	-	-	0.19	-	-	-	-	-	-
129	15.29	Unknown compound 4	-	-	-	60.42	-	-	-	-	-
130	15.40	Unknown compound 5	-	-	-	-	-	2.18	-	-	-
131	15.47	1-(3,3-Dimethyl-2-oxobicyclo [4.1.0] hept-7-yl) ethyl benzoate	-	-	-	-	-	1.43	-	-	-
132	15.50	Unknown compound 6	-	16.33	-	-	-	-	-	-	-
133	15.72	Methyl trisporate B	-	-	-	-	-	-	-	-	0.06
134	15.77	Unknown compound 7	-	-	-	-	-	9.09	-	-	-
135	15.84	Kauren-19-oic acid	-	-	15.75	-	-	-	-	-	-
136	15.97	Glycidol oleate	-	-	-	-	-	-	-	0.34	-
137	16.03	(2E)-2-Hexenyl benzoate	-	-	-	-	-	-	-	-	0.06
138	16.04	Dihydrochrysin	-	-	-	0.54	0.34	-	-	-	-
139	16.05	Palmitin, 2-mono-	-	0.21	-	-	1.26	0.30	0.47	0.30	0.24
140	16.10	Glycerol 1-palmitate	-	-	-	-	-	-	-	0.03	-
141	16.11	Palmitin, 2-mono	1.28	-	-	-	-	-	-	-	-
142	16.22	Methyl 5,8,11-heptadecatriynoate	4.72	0.49	-	-	-	-	-	-	-
143	16.26	5,8,11-Eicosatriynoic acid, methyl ester	6.96	-	-	-	-	-	-	-	-
144	16.32	Methyl trisporate B	-	-	-	-	-	-	-	-	0.57
145	16.50	Flavanone, 5,7-dimethoxy	-	-	-	-	-	-	-	-	0.07
146	16.51	Glycidyl palmitate	-	-	-	-	-	-	-	0.12	-
147	16.62	Unknown compound 8	-	1.83	-	-	-	-	-	-	-
148	16.69	Flavone, 5-hydroxy-7-methoxy	-	-	-	0.39	-	-	-	-	-
149	16.89	(2E)-1-(2-Hydroxy-3,4,6-trimethoxyphenyl)-3-phenyl-2-propen-1-one	-	0.60	-	-	-	-	-	-	-
150	16.92	Dihydrooroxylin A	-	1.61	-	-	-	-	-	-	-
151	17.02	3-Hydroxypregn-5-en-20-one	-	-	16.23	-	0.19	-	-	-	-
152	17.17	Linolein, 2-mono-	-	0.42	-	-	-	-	-	-	-
153	17.20	Glyceryl Monooleate	-	-	-	-	-	-	3.93	1.94	-
154	17.26	9-Octadecenoic acid (Z)-, 2-hydroxy-1-(hydroxymethyl)ethyl ester	-	-	-	-	-	-	-	0.42	-
155	17.33	4H-1-Benzopyran-4-one, 5,7-dihydroxy-2-phenyl	-	-	-	3.55	-	-	-	-	-
156	17.36	Stearin, 1-mono	-	-	-	-	-	-	0.16	0.09	-
157	17.81	Flavone, 5-hydroxy-7-methoxy	-	-	-	-	-	-	-	-	0.76
158	17.91	2‘-Hydroxy-3,4,5-trimethoxychalcone	-	0.66	-	-	-	-	-	-	-
159	17.99	Unknown compound 9	-	-	-	-	-	-	-	-	11.88
160	18.00	Icosapentaenoic acid	-	-	-	-	-	-	-	0.33	-
161	18.06	Glycidyl palmitoleate	-	-	-	-	-	-	-	1.31	-
162	18.07	Flavone, 5,7-dimethoxy	-	-	-	3.76	-	-	-	-	-
163	18.16	Supraene	-	0.22	-	-	-	1.31	0.08	-	-
164	18.39	Unknown compound 10	-	-	-	-	-	-	-	-	10.61
165	18.43	Isocryptotanshinone	-	-	-	-	-	-	-	-	2.43
166	18.63	Doconexent	-	-	-	-	-	-	-	0.33	-
167	18.91	O-Arachidonoylglycidol	-	-	-	-	-	-	-	0.11	-
168	19.77	Methyl 6,8-octadecadiynoate	-	-	-	-	-	-	-	0.54	-
169	19.99	Methyl 7,9-octadecadiynoate	-	-	-	-	-	-	-	3.54	-
170	20.09	9,12-Octadecadiynoic acid, methyl ester	-	-	-	-	-	-	-	0.57	-
171	22.14	Vitamin E	7.86	1.30	2.55	3.25	0.62	7.04	2.40	0.61	1.75
172	22.60	3-(Benzoylsulfanyl)-2-methylpropanoic acid	-	-	-	-	-	1.08	-	-	-
173	23.22	Benzil	-	-	-	-	-	1.71	-	-	-
174	23.89	Ergost-5-en-3-ol	-	-	-	0.25	0.14	-	-	-	-
175	23.94	Campesterol	-	0.35	0.40	-	-	0.38	0.45	-	0.37
176	24.51	Stigmasterol	2.10	0.63	0.53	0.30	0.45	0.62	0.61	-	0.52
177	24.68	Diaeudesmin	-	-	-	-	-	-	-	44.66	-
178	25.31	Dipentadecyl ketone	-	-	-	0.14	-	-	-	-	-
179	25.37	16-Hentriacontanone	-	-	-	-	-	-	-	-	0.24
180	25.72	β-Sitosterol	-	1.56	1.99	1.08	0.52	1.60	1.77	0.58	0.64
181	25.85	Chondrillasterol	7.45	-	-	-	-	-	-	-	-
		Total	99.77	97.18	96.90	98.93	97.50	99.50	99.00	99.02	99.01

as the main constituents. Thus, these chemical constituents should be investigated further to determine whether they are new compounds.

As mentioned above, the chemical compositions of acetone extracts obtained from the nine Annonaceae species have yet to be elucidated. However, there were several published data for chemical components of other extracts isolated from some species in this study. Accordingly, the major compounds of the essential oil of *A. hexapetalus* flowers collected from Ha Noi, Vietnam, contained caryophyllene oxide and β-caryophyllene (PHAN et al., 2007). In addition, the dichloromethane extract of the aerial parts of *A. hexapetalus* from Hong Kong contained β-methoxy-γ-methylene-α, β-unsaturated-γ-butyrolactones (WONG and BROWN, 2002).

The chemical components of the essential oils of *D. cochinchinensis* collected from Vietnam have been reported by recent studies. As a result, the flower oil of this plant was characterized by the abundance of camphor, limonene, and α-pinene. The fruit oil of this plant was mainly composed of b-caryophyllene, limonene, and germacrene D, whereas b-caryophyllene, bicyclogermacrene, and benzyl benzoate were the major compounds in the bark essential oil. SUTHIPHASILP et al. (2020) identified 16 chemical compounds in the methanol and ethyl acetate extracts of *D. cochinchinensis* flowers and leaves, in which desmoscochinchinenes A-E were the new polyoxygenated *seco*-cyclohexene derivatives (SUTHIPHASILP et al., 2020). Similarly, a new benzyl benzoate derivative, five new oxepinones, four new flavonoids, and 14 known compounds have been identified in ethyl acetate extracts of *D. cochinchinensis* twigs and leaves (MEESAKUL et al., 2019). Furthermore, the methanol extract of this plant has been reported to contain two new compounds, including 1b,7a-dihydroxyeudesman-4-one, and 5aH-megastigm-7-ene- 3a,4a,6b,9-tetrol (WU et al., 2014).

Previous reports showed six new polyoxygenated cyclohexenes, namely uvarigranol D, C, G, H, I and Grandifloranol obtained from *U. grandiflora* extracts (MACABEO et al., 2021). Moreover, grandionoside A, a new megastigmane glycoside, and (–)-3-O-debenzoylzeylenone, a new polyoxygenated cyclohexene, obtained from the aerial part extract of *U. grandiflora* have also been reported (MACABEO et al., 2021). The methanol extract obtained from *U. grandiflora* twigs has been reported to include six compounds such as aristolactam BI, griffithinam, sinactine, isoursuline, aristolactam AII, and velutinam (KONGKUM et al., 2021). TRAN et al. (2017) demonstrated that the major constituents of the leaf essential oils of *U. grandiflora* were limonene, benzyl benzoate, α-phellandrene, and eugenol (TRAN et al., 2017). MENG et al. (2007) showed that the methanol extract of *M. thorelii* aerial parts and its fractions such as petroleum ether, chloroform and n-butanol contained 6a,16,18-trihydroxycleroda-3(4),13(14)-dien-15,16-olide and 16-hydroxycleroda-3(4),13(14)-dien-15,16-olide, in which the first one was a new compound (MENG et al., 2007). Similarly, GE et al. (2008) firstly reported a new sesquiterpene (thorelinin) and three new lignanamides (thoreliamides A, B, C) in the ethanol extract of *M. thorelii* stems (GE et al., 2008). In addition, one triterpene (polycarpol), three heptenes ((7R)-acetylmelodorinol, (7R)-melodorinol, melodienone) and four flavonoids (pinocembrin, isochamanetin, chrysin, dichamanetin) have been reported in the stem bark extracts of *X. pierrei* for the first time (CHOKCHAISIRI et al., 2017).

Tab. 2a: Antibacterial activity of acetone extract of the eight Annonaceae plants

Scientific name	Concentration (mg/mL)	PL	UL	XP	SA	Gentamicine
B. cereus	100	8.17±0.29^{a}	9.83±1.04^{ab}	8.83±1.26^{a}	11.33±2.08^{bc}	18.50±1.32^{d}
	150	8.83±0.29^{a}	12.83±0.76^{c}	10.67±1.15^{b}	8.33±0.58^{a}	17.33±0.58^{de}
	200	9.00±0.50^{a}	8.50±0.50^{a}	7.33±0.29^{a}	8.67±0.58^{a}	18.83±1.04^{c}
	250	9.17±0.76^{ab}	8.67±1.53^{ab}	7.67±0.58^{a}	13.33±1.15^{c}	19.67±1.53^{e}
	300	9.33±0.58^{a}	12.33±0.58^{b}	11.00±2.64^{ab}	11.33±1.15^{ab}	20.33±0.58^{d}
S. aureus	100	7.67±0.58^{a}	10.67±1.15^{b}	7.17±0.29^{a}	8.17±0.29^{a}	20.67±1.53^{d}
	150	7.83±0.76^{a}	8.33±1.04^{a}	8.33±0.29^{a}	14.33±1.53^{b}	21.17±1.44^{cd}
	200	8.67±1.15^{a}	8.17±0.29^{a}	8.17±0.29^{a}	14.17±0.76^{c}	21.00±1.32^{e}
	250	8.33±1.15^{a}	8.33±0.29^{a}	8.50±0.87^{a}	17.83±0.76^{d}	22.33±0.58^{e}
	300	9.83±0.76^{a}	9.33±0.29^{a}	8.83±0.29^{a}	18.00±0.50^{d}	23.50±0.50^{e}

Different superscript lower-case letters in the same row denote significant difference (p<0.05). PL: *Polyalthia luensis*, UL: *Uvaria littoralis*, XP: *Xylopia pierrei*, SA: *Sphaerocoryne affinis*. (-): no inhibition.

Tab. 2b: Antibacterial activity of acetone extract of the eight Annonaceae plants

Scientific name	Concentration (mg/mL)	GT	UG	AH	DC	Gentamicine
B. cereus	100	13.67±1.53^{c}	-	-	-	18.50±1.32^{d}
	150	19.50±0.50^{f}	18.17±0.76^{ef}	16.33±2.08^{d}	14.17±0.7^{c}	17.33±0.58^{de}
	200	11.33±2.31^{b}	21.33±1.53^{d}	13.33±1.15^{b}	7.67±1.15^{a}	18.83±1.04^{c}
	250	18.33±1.53^{de}	22.67±1.15^{f}	16.67±1.15^{d}	10.67±0.58^{b}	19.67±1.53^{e}
	300	18.33±0.58^{cd}	23.33±1.15^{f}	17.33±0.58^{c}	10.67±1.15^{ab}	20.33±0.58^{d}
S. aureus	100	17.33±1.15^{c}	-	-	-	20.67±1.53^{d}
	150	19.67±3.21^{c}	22.33±0.58^{d}	13.67±0.29^{b}	12.67±1.15^{b}	21.17±1.44^{cd}
	200	17.50±1.32^{d}	23.50±1.32^{f}	14.83±1.04^{c}	10.67±1.15^{b}	21.00±1.32^{e}
	250	18.67±0.29^{d}	24.83±0.76^{f}	15.67±1.04^{c}	12.17±0.29^{b}	22.33±0.58^{e}
	300	19.00±0.87^{d}	25.50±0.50^{f}	16.50±1.32^{c}	12.83±0.76^{b}	23.50±0.50^{e}

Different superscript lower-case letters in the same row denote significant difference (p<0.05). GT: *Goniothalamus touranensis,* UG: *Uvaria grandiflora*, AH: *Artabotrys hexapetalus*, MT: *Mitrephora thorelii*, DC: *Desmos cochinchinensis*. (-): no inhibition.

Antibacterial activity of acetone extracts of the nine Annonaceae plants

The antibacterial activities of the acetone extracts of the nine Annonaceae plants were evaluated by the diameter of the inhibition zone against tested bacteria. Accordingly, eight out of the nine studied extracts (except *M. thorelii* extract) were found to be effective against two tested microorganisms, including *B. cereus* and *S. aureus* (Tab. 2a and 2b). The extracts isolated from four species such as *S. affinis, G. touranensis, U. grandiflora* and *A. hexapetalus* possessed potent antibacterial effects against two studied bacterial strains. Notably, the antibacterial activities of the *U. grandiflora* extract were higher than positive control with gentamycin discs. Accordingly, at doses of 100, 150, 200, 250 and 300 mg/mL, the diameters of inhibition zones of this extract against *B. cereus* were 18.17, 21.33, 22.67 and 23.33 mm while those of positive control were 18.33, 18.83, 19.67 and 20.33 mm, respectively. Similarly, the diameters of inhibition zones of these extracts against *S. aureus* were 22.33, 23.50, 24.83 and 25.50 mm whereas 21.17, 21.00, 22.33 and 23.50 mm, respectively were shown by the positive control towards the same bacterial strain at dose of 100, 150, 200, 250 and 300 mg/mL. Furthermore, the *D. cochinchinensis* extract possessed moderate antibacterial effects while *P. luensis*, *U. littoralis* and *X. pierrei* had weak inhibitory effects on *B. cereus* and *S. aureus* (Tab. 2a and b).

The chemical components in the acetone extracts of the nine Annonaceae plants could be the main factor responsible for their antibacterial activity. For instance, β-caryophyllene has been reported to possess antibacterial effects against many bacterial strains, including *Bacillus cereus, B. subtilis, Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Streptococcus mutans* and *Staphylococcus aureus* (Francomano et al., 2019). Furthermore, oleic acid was found to be effective against *B. subtilis, Micrococcus kristinae, S. aureus, K. pneumonia* (Ghavam et al., 2021). α-Humulene had an inhibitory effect on *Bacteroides fragilis* (Jang et al., 2020) while *S. aureus* was inhibited by hexadecanoic acid (Cartron et al., 2014).

Antioxidant activity of acetone extracts of the nine Annonaceae plants

The antioxidant activity of the nine extracts from this study was determined by using 1,1-diphenyl-2-picrylhydrazol (DPPH). The data in Tab. 3 showed that the leaf extract of *A. hexapetalus* had the strongest antioxidant activity with IC_{50} value of 18.56 μg/mL, followed by the extracts of *U. grandiflora, P. luensis, X. pierrei* and *S. affinis* with IC_{50} value of 49.55, 54.05, 73.57 and 79.73 μg/mL, respectively. Meanwhile, the extracts of four species such as *D. cochinchinensis, U. littoralis, M. thorelii* and *G. touranensis* possessed weak antioxidant effects with IC_{50} values of 171.90, 228.43, 702.33 and 702.33 μg/mL, respectively.

Tab. 3: Antioxidant and cytotoxic activities of acetone extract of the nine Annonaceae plants

	IC_{50} values (μg/mL)	
	DPPH	**HepG2**
Polyalthia luensis	54.05±6.00	75.39±1.05
Uvaria littoralis	228.43±24.07	65.70±5.05
Xylopia pierrei	73.57±3.24	251.77±11.50
Sphaerocoryne affinis	79.73±3.65	72.54±4.07
Goniothalamus touranensis	702.33±37.17	5.39±0.46
Uvaria grandiflora	49.55±3.42	43.55±2.53
Artabotrys hexapetalus	18.56±0.80	83.53±4.42
Mitrephora thorelii	252.27±16.76	243.30±14.2
Desmos cochinchinensis	171.90±2.60	180.13±2.25
Trolox	7.58±0.22	-
Camptothecine	-	0.08± 0.02

The antioxidant activities of the acetone extracts isolated from the nine Annonaceae species in this study may be attributed to the chemical components present in the extracts. For instance, β-caryophyllene inhibited DPPH free radical scavenging and ferric-reducing antioxidant power with IC_{50} values of 1.25 and 3.23 μM, respectively (Dahham et al., 2015). Leite et al. (2021) showed that β-caryophyllene also had antioxidant effects against hydroxyl radicals, superoxide anions, and lipid peroxides (Leite et al., 2021). Furthermore, Santos et al. (2013) showed that phytol possessed potent antioxidant activity. This compound also removed nitric oxide, hydroxyl radicals and prohibited the formation of thiobarbituric acid reactive components (Santos et al., 2013). Spathulenol has been reported as a strong antioxidant effect with IC_{50} values of 85.6, 639.25, and 26.13 μg/mL for the DPPH, ABTS, and MDA assays (Nascimento et al., 2018). Many reports demonstrated that various vitamin E forms such as α, β, γ and δ-tocopherols are considered as strong peroxyl radical scavengers. They are chain-breaking antioxidants and prevent the multiplication of free radical damage in biological membranes (Yamauchi, 1997).

Previous reports showed the antioxidant activity of other extracts isolated from several species in this study. For instance, the methanol-ethyl acetate extracts of *U. grandiflora* and its component, velutinam, showed antioxidant effect using DPPH assay with IC_{50} values of 310 and 240 μg/mL, respectively (Kongkum et al., 2021). By using DPPH free radical scavenging, Ngo et al. (2022) demonstrated that the fruit water extract of *S. affinis* possessed strong antioxidant activity with IC_{50} value of 85.62 μg/mL (Ngo et al., 2022).

Cytotoxic activity of acetone extracts of the nine Annonaceae plants

The cytotoxic activities of the acetone extracts of the nine Annonaceae species against HepG2 cell line are presented in Tab. 3. Results indicated that the extract obtained from *G. touranensis* possessed potent cytotoxicity against HepG2 cells with an IC_{50} value of 5.39 μg/mL. On the other hand, the extracts from five plants, including *U. grandiflora, U. littoralis, S. affinis, P. luensis,* and *A. hexapetalus* showed moderate cytotoxic effects against HepG2 cell with IC_{50} values of 43.55, 65.70, 72.54, 75.39 and 83.53 μg/mL. Meanwhile, the extracts of *D. cochinchinensis, M. thorelii,* and *X. pierrei* exhibit weak cytotoxicity against HepG2 cells with IC_{50} values of 180.13, 243.30, and 251.77 μg/mL

The cytotoxic effects of the acetone extracts isolated from the nine Annonaceae plants in this study may be attributed to the chemical components present in the extracts. For example, α-humulene has been demonstrated to possess strong cytotoxic properties against L-929 and MCF-7 cell lines (Legault et al., 2003). Chen et al. (2019) showed that α-humulene has also been proven to have bioactivity against several tumor cells, including PC-3, DLD-1, A-549, and M4BEU, while HCC cells were also inhibited by these compounds (Chen et al., 2019). In addition, hexadecanoic acid has been reported to have significant cytotoxicity against human colorectal carcinoma (HCT-116) and HT-29 human colon cancer cell lines (Bharath et al., 2021). Previous reports showed that oleic acid combined with partially unfolded human α-lactalbumin has been shown to exhibit a spectrum of tumor cells and effects against several differentiated cells such as mammalian erythrocytes (Hoque et al., 2017). Stigmasterol has been demonstrated to possess potential anti-cancer properties against human hepatoma HepG2 cells, whereas vitamin E also possessed potent cytotoxic activities against human breast cancer cells (Kim et al., 2014a). Furthermore, β-caryophyllene oxide and β-caryophyllene have been reported to possess significant anticancer effects. Accordingly, the first compound has been proven to

have bioactivity against many tumor cells, including HepG2, HeLa, AGS, SNU-1, and SNU-16 (Jun et al., 2011), KBM-5, H1299, A293, U266, and DU145 (Kim et al., 2014b). Meanwhile, the later component showed cytotoxic effects against HTC 116, PANC-1, HT-29, ME-180, PC3, K562, and MCF-7 (Dahham et al., 2015). Also, kauren-19-oic acid has been shown to exhibit against several human cancer cell lines such as HL60, SF295, K562, and MDA-MB435 (Cavalcanti et al., 2009).

The cytotoxicity of other solvent extracts obtained from several species in this study has been reported by previous studies. For instance, the solvent extracts of *D. cochinchinensis* have been reported as the natural sources of tumor inhibitors. For instance, this species' ethanol extract fractions showed cytotoxicity against some human tumor cell lines such as A549, MCF7, U2.51, and RPMI7951 (Sun et al., 1992). The two new compounds, hexapetalines A and B, isolated from the methanol extract of *A. hexapetalus,* possessed potent cytotoxic activity against five human cancer cell lines, including HL-60, A-549, SMMC-7721, SW480, and MCF-7 (Zhou et al., 2015). Similarly, the two components, (8*S*,12*S*)-yingzhaosu C and (8*R*,12*R*)-yingzhaosu C isolated from ethanol extract of *A. hexapetalus,* had significant anticancer activities. Accordingly, the first compound was evaluated for its strong cytotoxic against HCT-116, HepG2, and A2780 cell lines, whereas the latter was highly cytotoxic to A2780 cell line (Xi et al., 2017).

In addition, the two new compounds, 6a,16,18-trihydroxycleroda-3(4),13(14)-dien-15,16-olide and 16-hydroxycleroda-3(4),13(14)-dien-15,16-olide obtained from methanol extract of *M. thorelii* also had cytotoxicity against some human cancer cell lines. Accordingly, both components were effective against human hepatoma BEL-7402 cells while the hepatoma H22 cell was only inhibited by the second compound (Meng et al., 2007). Furthermore, the chloroform, hexane, and ethanol extracts of *U. grandiflora* have been demonstrated to possess potential cytotoxic effects against HTC-116 cell line. In contrast, this species' hexane, ethyl acetate, and methanol extracts also have bioactivity against HepG2 cell (Seangphakdeea et al., 2013). Moreover, some bioactive compounds isolated from the hexane, methanol, and ethyl acetate extracts of *X. pierrei* have been reported to possess highly cytotoxic activities against human small-cell lung cancer cells. Accordingly, (7R)-acetylmelodorinol, isochamanetin, dichamanetin, and melodienone has been shown to exhibit cytotoxicity against both NCI-H187 and Vero cell lines, whereas (7R)-melodorinol has been demonstrated to possess potential cytotoxic effect against Vero cell (Chokchaisiri et al., 2017).

Conclusions

The present study identified 182 chemical components of the acetone extracted from the leaves of the nine Annonaceae species, in which many compounds have been reported to possess biological activities. Eight out of the nine studied extracts inhibited the growth of two tested bacterial strains such as *B. cereus* and *S. aureus*. The nine studied extracts also possessed antioxidant and cytotoxic activities, in which the *A. hexapetalus* extract showed the highest antioxidant effect. In contrast, the extract obtained from *G. touranensis* had the strongest cytotoxic activities against HepG2 cells.

Conflict of interest

No potential conflict of interest was reported by the authors.

Acknowledgement

We acknowledge the Industrial University of Ho Chi Minh City (IUH) for supporting this study.

References

Al Kazman, B.S., Harnett, J.E., Hanrahan, J.R., 2022: Traditional uses, phytochemistry and pharmacological activities of annonacae. Molecules 27(11), 3462. DOI: 10.3390/molecules27113462

Aziz, A., Taha, H., Ismail, N.H., Yusof, F.Z.M., Bakar, M.Z.A., 2016: Therapeutic potential of plant species derived from some *Annonaceae* genus. Int. J. Agricult. Forest. 6(6), 214-221. DOI: 10.5923/j.ijaf.20160606.03

Bharath, B., Perinbam, K., Devanesan, S., Alsalhi, M.S., Saravanan, M., 2021: Evaluation of the anticancer potential of Hexadecanoic acid from brown algae *Turbinaria ornata* on HT–29 colon cancer cells. J. Mol. Struct. 1235, 130229. DOI: 10.1016/j.molstruc.2021.130229

Breuer, H., Rangel, M., Medina, E., 1982: Pharmacological properties of melochinine, an alkaloid producing Central American cattle paralysis. Toxicology 25(2-3), 223-242. DOI: 10.1016/0300-483X(82)90032-4

Cartron, C.L., England, S.R., Chiriac, A.I., Josten, M., Turner, R., Rauter, Y., Hurd, A., Sahl, H.-G., Jones, S., Foster, S.J., 2014: Bactericidal activity of the human skin fatty acid cis-6-hexadecanoic acid on *Staphylococcus aureus*. Antimicrob. Agents Chemother. 58(7), 3599-3609. DOI: 10.1128/AAC.01043-13

Cavalcanti, B.C., Bezerra, D.P., Magalhães, H.I.F., Moraes, M.O., Lima, M.A.S., Silveira, E.R., Câmara, C.A.G., Rao, V.S., Pessoa, C., Costa-Lotufo, L.V., 2009: Kauren-19-oic acid induces DNA damage followed by apoptosis in human leukemia cells. J. App. Toxicol. 29(7), 560-568. DOI: 10.1002/jat.1439

Chen, H., Yuan, J., Hao, J., Wen, Y., LV, Y., Chen, L., Yang, X., 2019: α-Humulene inhibits hepatocellular carcinoma cell proliferation and induces apoptosis through the inhibition of Akt signaling. Food Chem. Toxicol. 134, 110830. DOI: 10.1016/j.fct.2019.110830

Chokchaisiri, R., Kunkaewom, S., Chokchaisiri, S., Ganranoo, L., Chalermglin, R., Suksamrarn, A., 2017: Potent cytotoxicity against human small cell lung cancer cells of the heptenes from the stem bark of *Xylopia pierrei* Hance. Med. Chem. Res. 26, 1291-1296. DOI: 10.1007/s00044-017-1843-8

Chuo, S.C., Nasir, H.M., Mohd-Setapar, S.H., Mohamed, S.F., Ahmad, A., Wani, W.A., Muddassir, M., Alarifi, A., 2022: A glimpse into the extraction methods of active compounds from plants. Crit. Rev. Anal. Chem. 52(4), 667-696. DOI: 10.1080/10408347.2020.1820851

Dahham, S.S., Tabana, Y.M., Iqbal, M.A., Ahamed, M.B.K., Ezzat, M.O., Majid, A.S.A., Majid, A.M.S.A., 2015: The anticancer, antioxidant and antimicrobial properties of the sesquiterpene β-caryophyllene from the essential oil of *Aquilaria crassna*. Molecules 20(7), 11808-11829. DOI: 10.3390/molecules200711808

Dirar, A., Alsaadi, D., Wada, M., Mohamed, M., Watanabe, T., Devkota, H., 2019: Effects of extraction solvents on total phenolic and flavonoid contents and biological activities of extracts from Sudanese medicinal plants. S. Afr. J. Bot. 120, 261-267. DOI: 10.1016/j.sajb.2018.07.003

Francomano, F., Caruso, A., Barbarossa, A., Fazio, A., Torre, C.L., Ceramella, J., Mallamaci, R., Saturnino, C., Iacopetta, D., Sinicropi, M.S., 2019: β-Caryophyllene: a sesquiterpene with countless biological properties. Appl. Sci. 9(24), 5420. DOI: 10.3390/app9245420

Ge, F., Tang, C.-P., Ye, Y., 2008: Lignanamides and sesquiterpenoids from stems of *Mitrephora thorelii*. Helv. Chim. Acta 91(6), 1023-1030. DOI: 10.1002/hlca.200890109

Ghavam, M., Afzali, A., Manca, M.L., 2021: Chemotype of damask rose with oleic acid (9 octadecenoic acid) and its antimicrobial effectiveness. Sci. Rep. 11(1), 8027. DOI: 10.1038/s41598-021-87604-1

Hoque, M., Gupta, J., Saleemuddin, M., 2017: Augmenting the cytotoxicity of oleic acid-protein complexes: Potential of target-specific antibodies. Biochimie 137, 139-146. DOI: 10.1016/j.biochi.2017.03.013

Jang, H.-I., Rhee, K.-J., Eom, Y.-B., 2020: Antibacterial and antibiofilm effects of α-humulene against *Bacteroides fragilis*. Can. J. Microbiol. 66(6), 389-399. DOI: 10.1139/cjm-2020-0004

Jun, N.J., Mosaddik, A., Moon, J.Y., Jang, K.-C., Lee, D.-S., Ahn, K.S.,

Cho, S.K., 2011: Cytotoxic activity of [beta]-Caryophyllene oxide isolated from jeju guava (*Psidium cattleianum* sabine) leaf. Rec. Nat. Prod. 5(3), 242-246.

Kim, C., Cho, S.K., Kapoor, S., Kumar, A., Vali, S., Abbasi, T., Kim, S.-H., Sethi, G., Ahn, K.S., 2014a: β-caryophyllene oxide inhibits constitutive and inducible STAT3 signaling pathway through induction of the SHP-1 protein tyrosine phosphatase. Mol. Carcinog. 53(10), 793-806. DOI: 10.1002/mc.22035

Kim, C., Cho, S.K., Kim, K.-D., Nam, D., Chung, W.-S., Jang, H.-J., Lee, S.-G., Shim, B.S., Sethi, G., Ahn, K.S., 2014b: β-Caryophyllene oxide potentiates TNFα-induced apoptosis and inhibits invasion through down-modulation of NF-ϰB-regulated gene products. Apoptosis 19(4), 708-718. DOI: 10.1007/s10495-013-0957-9

Kluza, J., Marchetti, P., Bailly, C., 2007: Lamellarin Alkaloids: Structure and Pharmacological Properties. In: Fattorusso, E., Taglialatela-Scafati, O. (eds.), Modern Alkaloids: Structure, Isolation, Synthesis, and Biology. Wiley Online Library.

Kongkum, N., Thanasansurapong, S., Surapanich, N., Kumutanat, W., Sukkum, C., Kuhakarn, C., Jaipetch, T., Reutrakul, V., Hongthong, S., 2021: Antioxidant and antimicrobial alkaloids isolated from twigs of *Uvaria grandiflora* Roxb. ScienceAsia 47S, 14-18. DOI: 10.2306/scienceasia1513-1874.2021.S002

Legault, J., Dahl, W., Debiton, E., Pichette, A., Madelmont, J.-C., 2003: Antitumor activity of balsam fir oil: Production of reactive oxygen species induced by α-humulene as possible mechanism of action. Planta Med. 69(05), 402-407. DOI: 10.1055/s-2003-39695

Leite, G.M.D.L., Barbosa, M.D.O., Lopes, M.J.P., Delmondes, G.D.A., Bezerra, D.S., Araújo, I.M., Alencar, C.D.C.D., Coutinho, H.D.M., Peixoto, L.R., Barbosa-Filho, J.M., Felipe, C.F.B., Barbosa, R., Menezes, I.R.A.D., Kerntof, M.R., 2021: Pharmacological and toxicological activities of α-humulene and its isomers: A systematic review. Trends Food Sci. Technol. 115, 255-274. DOI: 10.1016/j.tifs.2021.06.049

Macabeo, A.P.G., Flores, A.I.G., Fernandez, R.A.T., Budde, S., Faderl, C., Dahse, H.-M., Franzblau, S.G., 2021: Antitubercular and cytotoxic polyoxygenated cyclohexane derivatives from *Uvaria grandiflora*. Nat. Prod. Res. 35(23), 5229-5232. DOI: 10.1080/14786419.2020.1741579

Meesakul, P., Richardson, C., Pyne, S.G., Laphookhieo, S., 2019: α-Glucosidase inhibitory flavonoids and oxepinones from the leaf and twig extracts of *Desmos cochinchinensis*. J. Nat. Prod. 82(4), 741-747. DOI: 10.1021/acs.jnatprod.8b00581

Meng, D.-H., Xu, Y.-P., Chen, W.-L., Zou, J., Lou, L.-G., Zhao, W.-M., 2007: Anti-tumour clerodane-type diterpenes from *Mitrephora thorelii*. J. Asian Nat. Prod. Res. 9(7), 679-684. DOI: 10.1080/10286020601103270

Nascimento, K.F.D., Moreira, F.M.F., Santos, J.A., Kassuya, C.A.L., Croda, J.H.R., Cardoso, C.A.L., Vieira, M.D.C., Ruiz, A.L.T.G., Foglio, M.A., Carvalho, J.E.D., Formagio, A.S.N., 2018: Antioxidant, anti-inflammatory, antiproliferative and antimycobacterial activities of the essential oil of *Psidium guineense* Sw. and spathulenol. J. Ethnopharmacol. 210, 351-358. DOI: 10.1016/j.jep.2017.08.030

Ngo, B.T.N., Tran, T.U., Huynh, M.A., Dao, M.L., Dang, T.P.T., 2022: Rumdul (*Sphaerocoryne affinis*) Antioxidant Activity and Its Potential for Parkinson's Disease Treatment. Oxid. Med. Cell. Longev. 2022, 1-12. DOI: 10.1155/2022/8918966

Nguyen, V.N., Tagane, S., Hoang, T.B., Toyama, H., Okabe, N., Nguyen, D.C., Yahara, T., 2016: *Popowia bachmaensis* (Annonaceae), a new species from Bach Ma National Park, Central Vietnam. PhytoKeys(65), 125. DOI: 10.3897/phytokeys.65.8792

Phan, G.M., Phan, S.T., König, W.A., 2007: Chemical composition of the flower essential oil of *Artabotrys hexapetalus* (L. f.) Bhandare of Vietnam. J. Essent. Oil Res. 19(6), 523-524. DOI: 10.1080/10412905.2007.9699321

Quílez, A., Fernández-Arche, M., García-Giménez, M., De la Puerta, R., 2018: Potential therapeutic applications of the genus Annona: Local and traditional uses and pharmacology. J. Ethnopharmacol. 225, 244-270. DOI: 10.1016/j.jep.2018.06.014

Santos, C.C.D.M.P., Salvadori, M.S., Mota, V.G., Costa, L.M., Almeida, A.A.C.D., Oliveira, G.A.L.D., Costa, J.P., Sousa, D.P.D., Freitas, R.M.D., Almeida, R.N.D., 2013: Antinociceptive and antioxidant activities of phytol in vivo and in vitro models. Neurosci. J. 2013, 1-9. DOI: 10.1155/2013/949452

Seangphakdeea, P., Pompimona, W., Meepowpanb, P., Panthongc, A., Chiranthanutd, N., Banjerdpongchaie, R., Wudtiwaie, B., Nuntasaenf, N., Pitchuanchoma, S., 2013: Anti-inflammatory and anticancer activities of (–)-zeylenol from stems of *Uvaria grandiflora*. ScienceAsia 39(6), 610-614.

Sun, N.-J., Ho, D.K., Sneddon, J.M., Stephens, R.E., Cassady, J.M., 1992: New cytotoxic cycloartane triterpenoids from *Desmos cochinchinensis* (Annonaceae). Nat. Prod. Lett. 1(2), 109-115. DOI: 10.1080/10575639208048897

Suthiphasilp, V., Maneerat, T., Duangyod, T., Charoensup, R., Andersen, R.J., Pyne, S.G., Laphookhieo, S., 2020: Polyoxygenated seco-cyclohexenes derivatives from flower and leaf extracts of *Desmos cochinchinensis* and their α-glucosidase inhibitory activity. Heliyon 6(12), 1-7. DOI: 10.1016/j.heliyon.2020.e05791

Tran, T., Luu, H., Nguyen, T., Do, D., Ogunwande, I., Nguyen, H., 2017: Analysis of the leaf essential oils of *Uvaria grandiflora* Roxb. ex Hornem. and *Uvaria microcarpa* Champ. ex Benth. (Annonaceae) from Vietnam. J. Essent. Oil Bearing Plants 20(2), 496-501. DOI: 10.1080/0972060X.2017.1321503

Wong, H.-F., Brown, G.D., 2002: β-Methoxy-γ-methylene-α, β-unsaturated-γ-butyrolactones from *Artabotrys hexapetalus*. Phytochemistry 59(1), 99-104. DOI: 10.1016/S0031-9422(01)00433-2

Wu, T.Y., Cheng, Y.B., Cheng, F.T., Hsu, Y.M., Tran, D.T., Chang, F.R., Wu, Y.C., 2014: Chemical Constituents of the Leaves of *Desmos cochinchinensis* var. *fulvescens* BAN. Helv. Chim. Acta 97(12), 1714-1718. DOI: 10.1002/hlca.201400108

Xi, F.-M., Liu, Y.-B., Qu, J., Li, Y., Tang, Z.-H., Li, L., Li, Y.-H., Chen, X.-G., Ma, S.-G., Yu, S.-S., 2017: Bioactive sesquiterpenoids from the roots of *Artabotrys hexapetalus*. Tetrahedron 73(5), 571-582. DOI: 10.1016/j.tet.2016.12.043

Yamauchi, R., 1997: Vitamin E: Mechanism of its antioxidant activity. Food Sci.Technol. Int., Tokyo 3(4), 301-309. DOI: 10.3136/fsti9596t9798.3.301

Zhou, Q., Fu, Y.-H., Li, X.-B., Chen, G.-Y., Wu, S.-Y., Song, X.-P., Liu, Y.-P., Han, C.-R., 2015: Bioactive benzylisoquinoline alkaloids from *Artabotrys hexapetalus*. Phytochem. Lett. 11, 296-300. DOI: 10.1016/j.phytol.2015.01.017

ORCID
Sao Mai Dam https://orcid.org/0000-0002-3170-0785
Ngoc Duyen Nguyen https://orcid.org/0009-0009-5515-6997
Ngoc Nam Trinh https://orcid.org/0000-0002-7983-7270
Quoc Hung Nguyen https://orcid.org/0000-0003-2668-6293
Thanh Tho Le https://orcid.org/0000-0002-6303-3235
Van Son Le https://orcid.org/0000-0003-0151-0646
Hong Thien Van https://orcid.org/0000-0003-0151-5068
Ngoc An Nguyen https://orcid.org/0000-0002-7574-2952
Hanh Thi Dieu Nguyen https://orcid.org/0000-0002-3735-9127
Tan Viet Pham https://orcid.org/0000-0002-1061-1257

Address of the corresponding author:
Tan Viet Pham, Institute of Biotechnology and Food Technology, Industrial University of Ho Chi Minh City, No. 12 Nguyen Van Bao Street, Go Vap District, Ho Chi Minh City, Vietnam
E-mail: phamtanviet@iuh.edu.vn

© The Author(s) 2023.
This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/deed.en).