Trop J Nat Prod Res, December 2025; 9(12): 6166 – 6174

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Antioxidant Activity and Phytochemical Composition of Thai Traditional Cannabis Longevity Recipes: *In Vitro* Evaluation of the Phontecho Remedy

Chawalit Yongram[1], Panupan Sripan[2]*, Suwadee Chokchaisiri[2], Orawan Wonganan[2], Rumrada Meeboonya[2], Thavatchai Kamoltham[2], Sasipen Krutchangthong[3], Panyada Panyatip[4]

[1]*Regulatory Technical Support Division, Office of Atoms for Peace, Bangkok 10900, Thailand*
[2]*Division of Cannabis Health Sciences, College of Allied Health Sciences, Suan Sunandha Rajabhat University, Samut Songkhram 75000, Thailand*
[3]*Division of Applied Thai Traditional Medicine, College of Allied Health Sciences, Suan Sunandha Rajabhat University, Samut Songkhram 75000, Thailand*
[4]*Department of Pharmacognosy, Faculty of Pharmacy, Srinakharinwirot University, Nakhon Nayok 26120, Thailand*

ARTICLE INFO

Article history:
Received 26 October 2025
Revised 27 November 2025
Accepted 29 November 2025
Published online 01 January 2026

ABSTRACT

Thai traditional medicine has historically incorporated cannabis-based remedies to treat fever, pain, inflammation, insomnia, and to promote longevity. Because antioxidant activity is associated with anti-aging effects, this study investigated the antioxidant potential and phytochemical composition of the Phontecho remedy using 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS), and ferric reducing antioxidant power (FRAP) assays. Phytochemical profiling was performed by high-performance liquid chromatography and gas chromatography–mass spectrometry. Phontecho exhibited notable antioxidant capacity, with a DPPH half-maximal inhibitory concentration (IC_{50}) of 50.33 ± 0.83 µg/mL, an ABTS IC_{50} of 9.51 ± 0.36 µg/mL, and a FRAP of 382.47 ± 8.61 mmol Fe^{2+}/100 g extract. The extract contained high total phenolic content (85.74 ± 2.49 mg gallic acid equivalents/g extract) and moderate total flavonoid content (34.51 ± 0.11 mg quercetin equivalents/g extract). HPLC analysis identified cannabinoids (THCV, Δ^9-THC, CBDV, CBGA, CBC) and phenolic compounds (gallic acid, quercetin), while GC–MS profiling revealed eugenol, (+)-2-bornanone, γ-sitosterol, and vitamin E. Antioxidant activity correlated with cannabinoid and phenolic acid contents. These phytochemicals provide a mechanistic basis for the antioxidant efficacy of the Phontecho remedy. The findings support its traditional use as a longevity-promoting remedy and highlight potential as a natural antioxidant for pharmacological applications.

Keywords: Phontecho, Antioxidant Activity, Thai Traditional Medicine, Longevity, High-Performance Liquid Chromatography, Gas Chromatography–Mass Spectrometry.

Introduction

Synthetic pharmaceuticals play a crucial role in modern medicine; however, their rising costs and associated risks underscore the importance of identifying safer and more sustainable alternatives. Medicinal plants, which are rich in diverse bioactive compounds, are highly valued for their relative safety, affordability, and enduring relevance in both traditional and contemporary healing practices. Thailand exemplifies this integration, where cannabis has long been embedded within traditional medicine and cultural heritage. Historical records trace the use of cannabis in Thailand back approximately 300 years to the reign of King Narai the Great, when it was prescribed for various ailments and incorporated into food, underscoring its cultural significance.[1] Cannabis-infused formulations have traditionally been employed to alleviate inflammation, fever, insomnia, and pain, and to promote energy and longevity.[2]

*Corresponding author. E mail: panupan.sr@ssru.ac.th
Tel: +66649898958

Citation: Yongram C, Sripan P, Chokchaisiri S, Wonganan O, Meeboonya R, Kamoltham T, Krutchangthong S, Panyatip P. Antioxidant Activity and Phytochemical Composition of Thai Traditional Cannabis Longevity Recipes: *In Vitro* Evaluation of the Phontecho Remedy. Trop J Nat Prod Res. 2025; 9(12): 6166 – 6174
https://doi.org/10.26538/tjnpr/v9i12.33

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

In 1950, international regulations classified cannabis as a category V narcotic, leading to its removal from the Thai traditional pharmacopoeia and its exclusion from medical applications for several decades. Recent legal reforms, however, have reinstated its medical use and commercial potential, reaffirming its role in both cultural heritage and modern healthcare.[3] Ancient Thai pharmacopoeias also contain numerous herbal formulations believed to promote health and delay aging, highlighting the longstanding importance of longevity medicine in Thai culture.

Medicinal plants are key sources of bioactive compounds that can be employed as safe, affordable, and long-lasting alternatives to synthetic pharmaceuticals. Natural antioxidants, such as polyphenols, flavonoids, carotenoids, and vitamins, are free radical scavengers that inhibit lipid peroxidation and protect biomolecules from oxidative stress.[4] Their importance in combating aging and chronic disease pathways is widely recognized and further supported by the recent identification of over 200 anti-aging phytochemicals and the mechanisms by which they extend lifespan .[5]

Several Thai traditional remedies have been scientifically validated. For example, the *Tri-ka-tuk* remedy exhibits synergistic antioxidant and α-glucosidase inhibitory activities, primarily attributed to its high levels of piperine, phenolic compounds, and flavonoids.[6] The *Ya-Kae-Kasai-Lin-Kra-Bue* (KLB) remedy, traditionally prescribed for liver disorders, has demonstrated strong antioxidant properties and cytotoxic effects against HepG2 hepatocellular carcinoma cells, with mechanistic insights provided by GC–MS and FTIR profiling.[7] More recently, the *Suk-Sai-Yasna* remedy, a traditional royal Thai formulation containing cannabis, was shown to alleviate stress-induced cognitive impairment

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

via activation of the Keap1–Nrf2 pathway, underscoring its potent antioxidative and neuroprotective properties.[8] Among cannabis-based remedies, the Phontecho remedy stands out and has traditionally been recommended for vitality and longevity. It is documented in the classical manuscript *Tamra Ya Kret*,[9] preserved at the National Library of Thailand, thereby highlighting the historical roots of cannabis-based medicine.

Numerous ingredients found in these remedies have demonstrated effectiveness in combating free radicals and reducing the risk of cancer. *Zingiber officinale* Roscoe (ginger) contains [6]-gingerol and shogaols, compounds that promote health by reducing inflammation and neutralizing free radicals.[10] *Syzygium aromaticum* (L.) Merr. & L.M. Perry (clove) contains a high concentration of eugenol, which is recognized for its strong antioxidant properties and potential role in cancer prevention.[11] *Plumbago indica* L. (red leadwort) produces plumbagin, a compound that induces apoptosis through reactive oxygen species.[12] Methanolic extracts of *Piper retrofractum* Vahl. (long pepper) have also shown significant antioxidant activity in various studies.[13] Collectively, these phytochemicals provide a strong mechanistic basis for the longevity-promoting qualities of the Phontecho remedy. However, the pharmacological activities of this remedy remain underexplored, leaving a gap in scientific evidence regarding its potential therapeutic benefits.

This study evaluated the antioxidant properties by 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radical scavenging, and the ferric reducing antioxidant power (FRAP) assays. The phytochemical composition of the Phontecho remedy of phenolic acids, flavonoids, and cannabinoids were quantified by high-performance liquid chromatography (HPLC). Gas chromatography–mass spectrometry (GC–MS) was used to characterized the chemical composition.

Materials and Methods

Chemicals and reagents

1,1-diphenyl-2-picrylhydrazyl (DPPH), 6-hydroxy-2,5,7,8-tetramethylchroman carboxylic acid (Trolox), 2,4,6-tris(2-pyridyl)-S-triazine (TPTZ), Folin-Ciocalteu reagent were purchased from Sigma-Aldrich (Buchs, Switzerland). 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), Potassium persulfate ($K_2S_2O_8$), Glacial acetic acid, Ferric chloride hexahydrate ($FeCl_3{\cdot}6H_2O$), Sodium Carbonate (Na_2CO_3) were purchased from Sigma-Aldrich (Hamburg, Germany). Sodium acetate (NaOAc) was purchased from Sigma-Aldrich (Bangalore, India). Hydrochloric acid (HCl) was purchased from Carlo Erba (Milan, Italy). Iron (II) sulfate ($FeSO_4$) was purchased from Thermo Scientific (Mumbai, India). Aluminium chloride ($AlCl_3$) was purchased from QReC™ (New Zealand). Gallic acid (GA), protocatechuic acid (PCCA), p-hydroxybenzoic acid (p-HO), chlorogenic acid (ChA), vanillic acid (VA), p-coumaric acid (p-CA), ferulic acid (FA) and sinapic acid (SnA), syringic acid (SyA), rutin (RN) and Quercetin (QE) were products of Sigma Aldrich (St. Louis, MO, USA). The ethanol was purchased from ACI Labscan (Bangkok, Thailand). Cannabidivarin (CBDV), cannabidiolic acid (CBDA), cannabigerolic acid (CBGA), cannabigerol (CBG), cannabidiol (CBD), tetrahydrocannabivarin (THCV), cannabinol (CBN), delta-9-tetrahydrocannabinol (Δ^9-THC), tetrahydrocannabinolic acid (THCA), and cannabichromene (CBC) were products of Cerilliant® (Round Rock, TX, USA).

Preparation of the Phontecho remedy

The Phontecho remedy, a traditional Thai longevity formulation, was prepared according to the National Thai Traditional Remedies with Ganja.[9] All plant materials were collected from Healthy Hills Farm Co., Ltd., Bangkok, Thailand (GPS coordinates: 13.723497° N, 100.460446° E) in October 2023. All plant materials were taxonomically verified in accordance with the Thai Herbal Pharmacopoeia.[14] The scientific names of all botanical ingredients were verified and cross-checked using the online taxonomic database Plants of the World Online (https://powo.science.kew.org/). Cannabis leaves were supplied by Taratera Corporation Co., Ltd. Voucher specimens (Voucher Nos. SSRU NO 040–052) were deposited at the Division of Cannabis Health Sciences, College of Allied Health Sciences, Suan Sunandha Rajabhat University, Samut Songkhram, Thailand. Details of the botanical ingredients and voucher information are provided in Table 1.

Extraction

Briefly, 50 g of Phontecho powder was sonicated 3 × 30 min with 100 mL of 95% ethanol using an ultrasonic extraction bath (GT Sonic®, Guangdong, China) at an ultrasonic frequency of 40 kHz and 220 V. The extract was filtered with Whatman No. 1 filter paper, the filtrate was dried using rotary evaporator to obtain the Phontecho ethanolic extract, with a yield of 11.6%.

DPPH radical scavenging

DPPH (200 µM) and extract (10-500 µg/mL) were added to the wells of a 96-well plate. The plate was incubated at room temperature for 30 min in the dark. The absorbance was read at 517 nm using a microplate reader (EZ Read 2000, Biochrom Ltd., Cambridge, UK). The half maximal inhibitory concentration (IC_{50}) was determined as the concentration of the extract that was capable of scavenging 50% of DPPH free radicals. Trolox was used as the positive control, and the Trolox equivalent antioxidant capacity (TEAC) was calculated.[15] The experiment was measured in triplicate.

ABTS radical scavenging

The reagents used for this assay: 7 mM ABTS and 2.45 mM potassium persulfate were prepared in deionized water for 18 h before use. The ABTS reagent was mixed with the extract (10-500 µg/mL) in the wells of a 96-well plate, which was incubated at room temperature for 10 min in the dark. After incubation, the absorbance was read at 735 nm using a microplate reader (EZ Read 2000, Biochrom Ltd., Cambridge, UK). The IC_{50} was determined as the concentration of the extract that was capable of scavenging 50% of ABTS free radicals. Similarly to the DPPH radical scavenging assay, Trolox was used as the positive control, and the TEAC was calculated.[16] The experiment was measured in triplicate.

FRAP assay

The FRAP reagent was freshly prepared by mixing of 300 mM acetate buffer (pH 3.6), 10 mM tripyridyltriazine (TPTZ) in a solution of 40 mM HCl and 20 mM $FeCl_3$ in a 10:1:1 (v/v/v) ratio. For the analysis, the extract was mixed with the FRAP reagent in the wells of a 96-well plate, which was incubated at room temperature for 4 min in the dark. The absorbance was read at 595 nm using a microplate reader (EZ Read 2000, Biochrom Ltd., Cambridge, UK). Trolox was used as the positive control.[17] The experiment was measured in triplicate.

Total phenolic content (TPC)

The TPC was determined by Folin-Ciocalteu assay. The Folin-Ciocalteu reagent was diluted 10-fold with distilled water before use. Then, the extract was mixed with the diluted Folin-Ciocalteu reagent in the wells of a 96-well plate. After 5 min, 7% sodium carbonate was added and incubated for 30 min. The absorbance was read at 760 nm using a microplate reader (EZ Read 2000, Biochrom Ltd., Cambridge, UK). The TPC was presented as gallic acid equivalents per gram extract (mg GAE/g extract).[18] The experiment was measured in triplicate.

Total flavonoid content (TPC)

For this assay, 2% $AlCl_3$ and extract were mixed in the wells of a 96-well plate, which was incubated at room temperature for 20 min. After incubation, the absorbance was read at 415 nm using a microplate reader (EZ Read 2000, Biochrom Ltd., Cambridge, UK). The TFC was presented as quercetin equivalents per gram extract (mg QE/g extract).[19] The experiment was measured in triplicate.

HPLC analysis

HPLC was used to determine the contents of phenolic acids including gallic acid, protocatechuic acid, *p*-hydroxybenzoic acid, vanillic acid, syringic acid, chlorogenic acid, sinapinic acid, *p*-coumaric acid, and ferulic acid and flavonoids: rutin and quercetin. The procedure utilized a Prominence-i LC-2030C 3D device (Shimadzu, Kyoto, Japan) with a

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Unisol C18 column (5 µm particle size, 250 × 4.6 mm; Phenomenex, Torrance, CA, USA). The mobile phase consisted of purified water with 1% acetic acid (v/v) (solvent A) and acetonitrile (solvent B). The gradient program was: from 0 to 5 min, 5% solvent B; from 5 to 15 min, 9% solvent B; from 15 to 22 min, 11% solvent B; from 22 to 38 min, 18% solvent B; from 38 to 43, 23% solvent B; from 43 to 44 min, 90% solvent B; from 44 to 45 min, 80% solvent B; from 45 to 55 min, isocratic at 80% solvent B; from 55 to 65 min, re-equilibration at 5% solvent B; and a linear gradient from 65 to 70 min of 5% solvent B. The flow rate was 0.8 mL/min, the column temperature was 40°C, and the injection volume was 20 µL. The diode array detection wavelengths were 280 nm (hydroxybenzoic acids), 320 nm (hydroxycinnamic acids), and 370 nm (flavonoids). The chromatogram for the extract was compared with the chromatograms of standard phenolic compounds and flavonoids. The presence of phenolic compounds in the extract was determined based on the retention time.[18] The experiment was measured in triplicate. HPLC was also used to determine the content of the following cannabinoids: cannabidivarin (CBDV), cannabidiolic acid (CBDA), cannabigerolic acid (CBGA), cannabigerol (CBG), cannabidiol (CBD), tetrahydrocannabivarin (THCV), cannabinol (CBN), delta-9-tetrahydrocannabinol (Δ^9-THC), tetrahydrocannabinolic acid (THCA), and cannabichromene (CBC). The procedure used the same HPLC device (Prominence-i LC-2030C 3D, Shimadzu, Kyoto, Japan), but with a NexLeaf CBX for potency C18 column (2.7 µm particle size, 150×4.6 mm; Shimadzu, Columbia, MD, USA) to achieve reverse phase separation. The column was maintained at 35°C, with a mobile phase flow rate of 1.6 mL/min and an injection volume 5 µL. The mobile phase consisted of 0.085% H_3PO_4 (v/v) in purified water (solvent A) and 0.085% H_3PO_4 (v/v) in acetonitrile (solvent B). The gradient program was: from 0 to 3 min, 70% solvent B; from 3 to 7 min, 85% solvent B; from 7 to 8 min, 95% solvent B; and from 8 to 12 min, 70% solvent B. The diode array detection wavelength was 220 nm. The chromatogram of the extract was compared with the chromatograms of standard cannabinoids. The presence of cannabinoid in the extract was determined based on the retention time.[20] The experiment was measured in triplicate.

Table 1: Plant materials used in the preparation of the Phontecho remedy

Botanical name (Family)	Part used	Proportion (%)	Source	Voucher No.	Collector No.
Cannabis sativa L. (Cannabaceae)	Leaves	1.98	Taratera Corp., Bangkok	SSRU NO 047	PS. 009
Piper nigrum L. (Piperaceae)	Fruits	2.99	Healthy Hills Farm Co., Ltd., Bangkok	SSRU NO 048	PS. 010
Camphor	-	3.25	Healthy Hills Farm Co., Ltd., Bangkok	-	-
Zingiber officinale Roscoe (Zingiberaceae)	Rhizomes	3.95	Healthy Hills Farm Co., Ltd., Bangkok	SSRU NO 041	PS. 003
Syzygium aromaticum (L.) Merr. & L.M. Perry (Myrtaceae)	Flower buds	4.94	Healthy Hills Farm Co., Ltd., Bangkok	SSRU NO 042	PS. 004
Piper ribesioides Wall. (Piperaceae)	Stems/wood	5.95	Healthy Hills Farm Co., Ltd., Bangkok	SSRU NO 045	PS. 007
Piper retrofractum Vahl. (Piperaceae)	Fruits	6.94	Healthy Hills Farm Co., Ltd., Bangkok	SSRU NO 046	PS. 008
Crystalline sugar	-	7.90	Local source, Samut Songkhram	-	-
Wurfbainia vera (Blackw.) Škorničk. & A.D. Poulsen	Leaves	8.91	Healthy Hills Farm Co., Ltd., Bangkok	SSRU NO 044	PS. 006
Cinnamomum verum J. Presl (Lauraceae)	Bark	10.89	Healthy Hills Farm Co., Ltd., Bangkok	SSRU NO 043	PS. 005
Pinus kesiya Royle ex Gordon (Pinaceae)	Wood	11.79	Healthy Hills Farm Co., Ltd., Bangkok	SSRU NO 049	PS. 011
Plumbago indica L. (Plumbaginaceae)	Roots	13.18	Healthy Hills Farm Co., Ltd., Bangkok	SSRU NO 040	PS. 002
Iresine herbstii Hook. (Amaranthaceae)	Leaves	17.31	Healthy Hills Farm Co., Ltd., Bangkok	SSRU NO 052	PS. 014

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

GCMS analysis
GC-MS analysis of the extract was performed using a QP-2010 instrument (Shimadzu, Kyoto, Japan) equipped with a J&W DB-5MS column (30 m × 0.25 mm, 0.25 µm; Agilent Technologies, Santa Clara, CA, USA). The temperature program was: 70°C for 2 min; an increase from 70 to 200°C at 5.0°C/min, then held at 200°C for 10 min; an increase from 200 to 230°C at 5.0°C/min, then held at 230°C for 10 min; an increase from 230 to 250°C at 5.0°C/min, then held at 250°C for 5 min; and an increase from 250 to 320°C at 5.0°C/min, then held at 320° for 20 min. The column flow was 1 mL/min. The carrier gas was helium 5.5. The ionization energy was set at 70 eV. A 1-µL aliquot of the sample solution was injected with a split ratio of 1:20. The peaks were analyzed based on the retention time and comparison to the NIST17.LIB library.[21]

Statistical analysis
IBM SPSS Statistics Version 23.0 for Windows (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The results are presented as the mean ± standard deviation. The data were analyzed with one-way analysis of variance followed by Tukey's honestly significant difference test for pairwise comparisons. Pearson correlation coefficients were used to examine the correlations between the antioxidant activities and the TPC; the TFC; and the contents of individual phenolic acids, flavonoids, and cannabinoids. A p-value < 0.05 was considered to indicate a statistically significant difference for all analyses.

Results and Discussion

Antioxidant activity
Table 2 presents the antioxidant activity of the Phontecho remedy based on three assays. For DPPH radical scavenging, the Phontecho extract showed an IC_{50} value of 50.33 ± 0.83 µg/mL, higher than that of Trolox, the positive control (IC_{50} = 4.89 ± 0.03 µg/mL). In the ABTS radical scavenging assay, the Phontecho extract had an IC_{50} value of 9.51 ± 0.36 µg/mL, notably lower than that of Trolox (IC_{50} = 2.97 ± 0.06 µg/mL. The antioxidant activity can be classified as very strong (IC_{50} < 50 µg/mL), strong (50-100 µg/mL), moderate (101-150 µg/mL), and weak (IC_{50} > 150 µg/mL).[22]

Table 2: The antioxidant activity, TPC, and TFC of the Phontecho extract

Parameter	Phontecho (TEAC)	Trolox
DPPH; IC_{50} (µg/mL)	50.33±0.83^{b} (0.10)	4.89±0.03^{a}
ABTS; IC_{50} (µg/mL)	9.51±0.36^{b} (0.31)	2.97±0.06^{a}
FRAP (mmol Fe^{2+}/100 g extract)	382.47±8.61^{b}	2506.15±13.60^{a}
TPC (mg GAE/g extract)	85.74±2.49	-
TFC (mg QE/g extract)	34.51±0.11	-

Note: Data are expressed as mean ± SD (n = 3). Different superscript letters within the same row indicate significant differences between Phontecho and Trolox as determined by one-way ANOVA followed by Tukey's HSD test ($p < 0.05$).

Thus, the Phontecho extract demonstrated strong antioxidant capacity based on DPPH radical scavenging and very strong activity based on ABTS radical scavenging. The variations between the assays highlight their distinct detection specificities. The ABTS assay is capable of detecting both hydrophilic and lipophilic antioxidants, while the DPPH assay shows a greater selectivity for hydrophobic compounds.[17] The TEAC was calculated from the IC_{50} of Trolox divided by IC_{50} of the Phontecho extract.[23] Although the Phontecho extract demonstrated a notable TEAC, it was still below that of Trolox. The FRAP assay validated these observations, revealing that the Phontecho extract exhibited significant reducing power (382.47 ± 8.61 mmol Fe^{2+}/100 g extract), whereas Trolox displayed the highest overall FRAP.

Total phenolic and total flavonoid contents
The TPC and TFC of the Phontecho extract are also presented in Table 2. The TPC can be classified into three categories: low (<10 mg GAE/g extract), medium (10-50 mg GAE/g extract), and high (>50 mg GAE/g extract).[24] The Phontecho extract exhibited a TPC of 85.74 ± 2.49 mg GAE/g extract, which falls into the high content according to the classification. Phenolic compounds act as reducing agents, hydrogen donors, and are capable of scavenging free radicals,[25] and the TPC in traditional Thai cannabis recipes for longevity correlate with antioxidant activity. The total flavonoid content (TFC) of the Phontecho extract was 34.51 ± 0.11 mg QE/g extract, placing it within the medium category according to the established TPC classification. Flavonoids are major components of medicinal plant polyphenols and one of the most important antioxidant materials in many medicinal plants.[26]

HPLC analysis of phenolic acids, flavonoids, and cannabinoids
HPLC analysis of the Phontecho extract revealed a wide range of phenolic acids and flavonoids, namely gallic acid, protocatechuic acid, *p*-hydroxybenzoic acid, vanillic acid, syringic acid, chlorogenic acid, *p*-coumaric acid, ferulic acid, rutin, and quercetin (Table 3). The total relative abundance was 2,103.29 ± 4.16 µg/g extract, with gallic acid as the most abundant phenolic component (509.56 ± 1.77 µg/g extract). Medicinal herbs are rich sources of phenolic acids, which contribute to the health benefits of these plants. Moreover, the strong antioxidant and biochemical potential of these natural plant preparations may be linked to the synergistic effects of individual phenolic compounds.[27] In addition, a high content of phenolic compounds in plants are responsible for anti-aging properties.[28] Phenolic compounds and flavonoids have been reported the correlate with the antioxidant activity in medicinal plants.[29] Table 4 presents the contents of 10 cannabinoids in the Phontecho extract. The total cannabinoid content was 17806.67 ± 59.07 µg/g extract. THCV was the most abundant cannabinoid in the Phontecho extract, while CBDA and CBG were not detected. In addition, the Phontecho extract contained a notable amount of Δ9-THC (3,360.00 ± 72.57 µg/g), CBC (896.67 ± 9.43 µg/g), and CBDV (1,436.67 ± 9.43 µg/g). CBG, CBD, Δ^{9}-THC, CBN, CBGA, CBDA, and Δ9-THCA exhibit antioxidant activity and the ability to scavenge free radicals, actions that prevent oxidation and reduce metal ions.[30]

GC-MS analysis of Phytochemical composition
The Phontecho ethanolic extract was analyzed using GC-MS, with the results shown in Table 5 and Figure 1. Eleven compounds were identified with a relative abundance of more than 1%: eugenol (33.67%), (+)-2-bornanone (17.03%), γ-sitosterol (5.97%), eugenol acetate (4.00%), THC (3.95%), caryophyllene oxide (2.18%), caryophyllene (1.88%), copaene (1.75%), (-)-globulol (1.17%), endo-borneol (1.10%), and vitamin E (1.02%). Several of these substances have a wide range of pharmacological characteristics.
Eugenol exhibits antioxidant, anti-inflammatory, antimicrobial, and antitumor effects,[31] while eugenol acetate also contributes antioxidant potential.[32] Piperine analogs are associated with antioxidant, immunomodulatory, and anticancer effects.[33-34] γ-Sitosterol demonstrates anticancer activity through growth inhibition, cell cycle arrest, and apoptosis of two cancer cell lines (MCF-7 and A549).[35] THC exhibits anti-inflammatory and antioxidant potential in metabolic disorders.[36]

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Table 3: HPLC analysis of the phenolic acid and flavonoid contents in the Phontecho extract.

Compound	Chemical content (μg/g extract)
Gallic acid	509.56±1.77[a]
Protocatechuic acid	143.67±0.06[f]
p-Hydroxybenzoic acid	111.55±1.02[h]
Vanillic acid	225.51±0.42[d]
Syringic acid	110.16±0.27[h]
Chlorogenic acid	216.94±0.19[e]
Sinapinic acid	ND[j]
p-Coumaric acid	100.49±0.22[i]
Ferulic acid	115.97±0.23[g]
Rutin	281.16±1.14[c]
Quercetin	288.28±0.17[b]

Note: Data are expressed as mean ± SD (n = 3). Different letters indicate a significant difference between compounds in the same column ($p < 0.05$). ND = Not detected.

Table 4: HPLC analysis of the cannabinoid contents in the Phontecho extract.

Compounds	Chemical content (μg/g extract)
CBDV	1436.67±9.43[c]
CBDA	ND[h]
CBGA	843.33±4.71[d]
CBG	ND[h]
CBD	543.33±4.71[e]
THCV	10096.67±4.71[a]
CBN	363.33±4.71[f]
Δ^9-THC	3360.00±72.57[b]
CBC	896.67±9.43[d]
THCA	266.67±4.71[g]

Note: Data means SD (n = 3). Different superscript letters in the same column indicate significant differences ($p < 0.05$). ND = Not detected.

Table 5: The chemical constituents identified by GC–MS in the Phontecho extract

No.	Retention time	Compound name	CAS number	KI[a]	KI[b]	%Peak area
1	9.84	(+)-2-Bornanone	464-49-3	1121	1121	17.03
2	10.30	Isoborneol	124-76-5	1138	1156	0.27
3	10.53	endo-Borneol	507-70-0	1138	1168	1.10
4	15.42	Eugenol	97-53-0	1392	1348	33.67
5	16.02	Copaene	3856-25-5	1221	1375	1.75
6	17.16	Caryophyllene	87-44-5	1494	1420	1.88
7	18.06	Humulene	6753-98-6	1579	1453	0.35
8	19.32	2,4-Di-tert-butylphenol	96-76-4	1555	1502	0.27
9	19.61	Eugenol acetate	93-28-7	1552	1520	4.00
10	21.18	Caryophyllene oxide	1139-30-6	1507	1581	2.18
11	21.28	Oxalic acid, butyl 1-menthyl ester	0-00-0	1592	-	0.75
12	21.84	Humulene oxide II	19888-34-7	1592	1606	0.26
13	22.48	Caryophylla-4(12),8(13)-dien-5α-ol	19431-79-9	1490	1631	0.79
14	22.91	(-)-Globulol	489-41-8	1530	1580	1.17
15	23.25	ent-Germacra-4(15),5,10(14)-trien-1β-ol	81968-62-9	1699	1694	0.47

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

No.	Retention time	Compound name	CAS number	KI[a]	KI[b]	%Peak area
16	27.83	β,9α-Clovanediol	2649-64-1	1840	1885	0.25
17	34.79	Sandaracopimarinal	1686-63-1	2114	-	0.81
18	42.50	Methyldehydroabietate	1235-74-1	2271	2335	0.87
19	48.39	Tetrahydrocannabinol	1972 08 3	2475	2470	3.95
20	68.55	Stigmast-5-en-3-ol, oleate	0-00-0	4469	-	0.75
21	69.86	Vitamin E	59-02-9	3149	3112	1.02
22	73.10	γ-Sitosterol	83-47-6	2731	-	5.97

Note: KI[a] is the relative retention index; n-alkanes (C_8-C_{40}) were used as references to calculate the relative retention index. KI[b] is the relative retention index obtained from https://webbook.nist.gov/chemistry/.

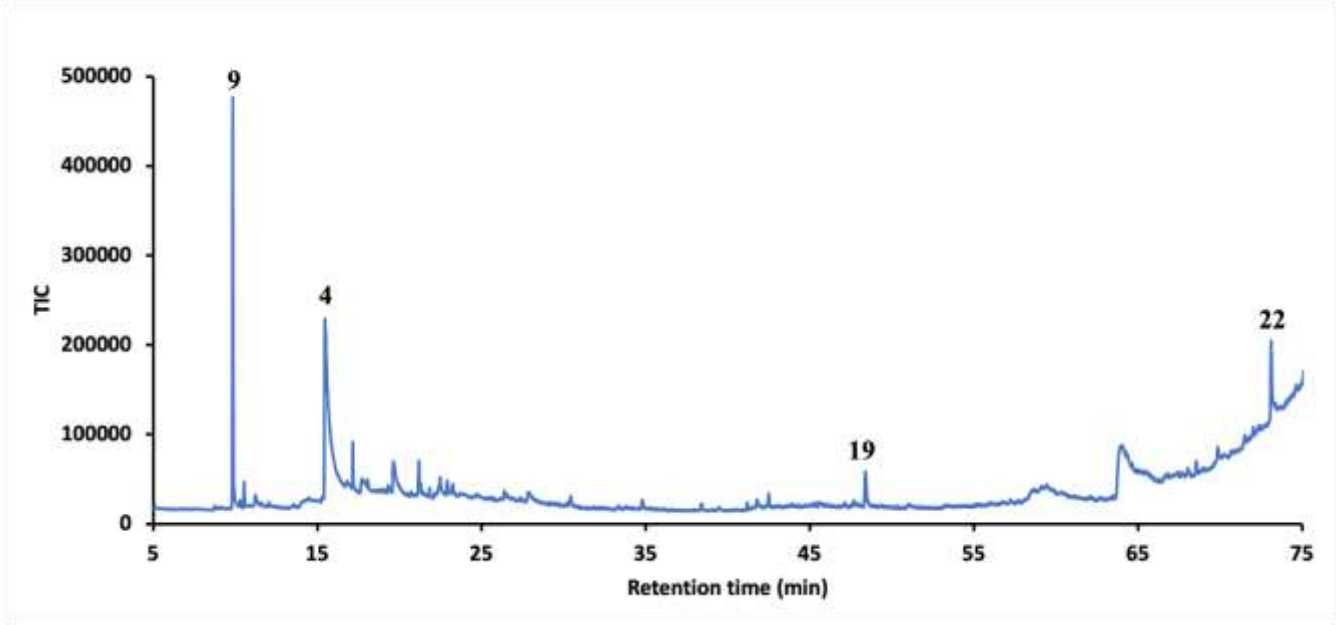

Figure 1: The GCMS chromatogram of Phontecho remedy

Caryophyllene oxide exerts anticancer activity on lung cancer by promoting apoptosis.[37] In addition, caryophyllene has antioxidant potential and anti-inflammatory activity *in vitro*.[38] Copaene increases the antioxidant capacity in human lymphocyte cultures.[39] Globulol demonstrates antimicrobial and antioxidant properties.[40] Borneol presents analgesic, anti-inflammatory, and antioxidant properties.[41] Moreover, vitamin E is one of the essential antioxidants and its main role is to protect lipids from oxidative damage.[42] Taken together, these chemical constituents have several pharmacological activities that might contribute to the antioxidant properties of the Phontecho remedy

Correlation analysis of antioxidant capacity and phytochemical composition

Table 6 presents the results of Pearson correlation analysis. There was a strong negative correlation between the DPPH IC_{50} and the syringic acid (r = -0.961) and Δ^9-THC (r = -0.980) contents in. In addition, the ABTS IC_{50} correlated negatively and with the rutin (r = -0.998), quercetin (r = -0.989), TFC, hydroxybenzoic acid, and THCA (r = -0.977) contents. FRAP correlated positively with quercetin (r = 0.999). These results indicate that higher phytochemical contents are associated with stronger radical scavenging activity.

Table 6: Correlation analysis of the antioxidant capacity and phytochemical composition of the Phontecho remedy

Phytochemical composition	Pearson's correlation coefficient (r)		
	Antioxidant capacity		
	DPPH	ABTS	FRAP
TPC	0.213	0.854	-0.791
TFC	-0.521	-0.977	0.948
Gallic acid	0.322	-0.462	0.362
Protocatechuic acid	0.896	0.940	-0.972
Hydroxybenzoic acid	-0.521	-0.977	0.948
Vanillic acid	0.354	-0.431	0.329
Syringic acid	-0.961	-0.864	0.914
Chlorogenic acid	-0.745	-0.032	0.142
Coumaric acid	-0.035	-0.747	0.669

Phytochemical composition	Pearson's correlation coefficient (r)		
	Antioxidant capacity		
	DPPH	ABTS	FRAP
Ferulic acid	0.995	0.618	-0.701
Rutin	-0.646	-0.998*	0.986
Quercetin	-0.788	-0.989	0.999*
CBDV	0.521	0.977	-0.948
CBGA	0.521	0.977	-0.948
CBD	0.479	-0.304	0.197
THCV	-0.479	0.304	-0.197
CBN	0.479	-0.304	0.197
Δ^9-THC	-0.980	-0.822	0.880
CBC	0.521	0.977	-0.948
THCA	-0.521	-0.977	0.948

Note: * indicates that the result is significant ($p < 0.05$).

On the other hand, there were negative correlations FRAP and the TPC, protocatechuic acid, ferulic acid, CBDV, CBGA, THCV, and CBC contents. These negative correlations may indicate antagonistic or synergetic effects of phytochemicals or the existence of some non-phenolic chelators.[43]

The findings indicate that the Phontecho remedy has a strong antioxidant capacity, substantiated by its varied phytochemical composition. The high levels of phenolic acids, TFC, hydroxybenzoic acid, syringic acid, chlorogenic acid, rutin, quercetin, and Δ^9-THC highlight the essential function of polyphenols in the modulation of oxidative stress. The presence of bioactive cannabinoids, including THCV and Δ^9-THC, as well as terpenoids and other compounds identified by GC-MS, such as eugenol, γ-sitosterol, caryophyllene oxide, and vitamin E, underscores a synergistic phytochemical network that enhances antioxidant and cytoprotective effects. These mechanisms are significant for longevity, as oxidative stress serves as a primary factor in cellular aging, DNA damage, and age-related disorders. The phytochemicals in the Phontecho remedy may contribute to delay oxidative damage and extending the healthspan by modulating reactive oxygen species, maintaining redox balance, and activating endogenous defense pathways. These findings support the application of Phontecho remedy as a longevity-enhancing, anti-aging treatment.[5,44]

Conclusion

This study determined the antioxidant activity and chemical content of the Phontecho remedy, a traditional Thai cannabis recipe. The formulation exhibited strong antioxidant effects based on the DPPH and ABTS radical scavenging assays, consistent with its high phenolic content, particularly gallic acid, quercetin, and rutin. These findings demonstrate a clear correlation between phenolic constituents and antioxidant potential in the ethanolic extract. To the best of our knowledge, this is the first report to scientifically validate the antioxidant properties of the Phontecho remedy, underscoring its pharmacological relevance and potential as a natural source for longevity-promoting medicine. Importantly, the findings from this study will be of great relevance in the development of evidence-based Thai traditional formulations, natural antioxidant supplements, and early-stage pharmaceutical prototypes targeting oxidative stress, aging-related conditions, and wellness applications. The results also provide a scientific basis for further preclinical investigations, mechanistic studies, and formulation development to maximize the therapeutic potential of this traditional remedy.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgements

This work was supported by the Institute of Research and Development, Suan Sunandha Rajabhat University, Thailand (Grant No. 11862/2566). The authors gratefully acknowledge Taratera Corporation Co., Ltd. for providing the cannabis leaves used in this study. We also express our sincere appreciation to the Department of Thai Traditional and Alternative Medicine, Ministry of Public Health, for their essential support in compiling and translating classical medicinal manuscripts.

References

1. Yongram C, Meeboonya R, Chokchaisiri S, Wonganan O, Sansila W, Kaewudom S, Kakatum N, Kanjanakaroon A, Kamoltham T, Roongpisuthipong C, Sripan P. A qualitative ethnopharmacological analysis of cannabis-based formulations for insomnia in Thai traditional medicine recipes. Trop J Nat Prod Res. 2025; 6(6):43. https://doi.org/10.26538/tjnpr/v9i6.43
2. Chokevivat V. The role of Thai traditional medicine in health promotion. In: The 6th Global Conference on Health Promotion; 2005; Bangkok, Thailand. p.1–25.
3. Laohavanich M. Political economy of cannabis in Thailand. Chulalongkorn Med J. 2022; 66(1):11. https://doi.org/10.58837/CHULA.CMJ.66.1.11
4. Al Naqbi K, Manoharan R, Nair CS, Kandhan K, Alyafei MS, Jaleel A. Exploring the antioxidant potential of medicinal plants in the United Arab Emirates (UAE): Emphasizing their significance in novel drug development. Pharm Pract. 2025; 23(1):3113. https://doi.org/10.18549/PharmPract.2025.1.3113
5. Wang Y, Cao X, Ma J, Liu S, Jin X, Liu B. Unveiling the longevity potential of natural phytochemicals: A comprehensive review of active ingredients in dietary plants and herbs. J Agric Food Chem. 2024; 72(45):24908–24927. https://doi.org/10.1021/acs.jafc.4c07756
6. Nutmakul T, Chewchinda S. Synergistic effect of Trikatuk, a traditional Thai formulation, on antioxidant and alpha-glucosidase inhibitory activities. Heliyon. 2023; 9(1):e13063. https://doi.org/10.1016/j.heliyon.2023.e13063
7. Promchiang J, Aukkanimart R, Sriraj P. Anti-hepatocellular carcinoma and antioxidant activities of a Thai traditional liver disease formulation: GC-MS and FTIR profiling. J Appl Pharm Sci. 2025; 15(08):135–146. https://doi.org/10.7324/JAPS.2025.219038
8. Masraksa W, Daodee S, Monthakantirat O, Boonyarat C, Khamphukdee C, Kwankhao P, Mading A, Muenhong P,

Maneenet J, Awale S, Matsumoto K, Chulikhit Y. Suk-SaiYasna remedy, a traditional Thai medicine, mitigates stress-induced cognitive impairment via Keap1-Nrf2 pathway. Int J Mol Sci. 2025; 26(11):5388. https://doi.org/10.3390/ijms26115388
9. Department of Thai Traditional and Alternative Medicine, Ministry of Public Health. Collection of conserved Thai traditional medicine wisdom: National Thai medicine formulas incorporating cannabis. Nonthaburi: Ministry of Public Health; 2021.
10. Verma P, Singh B, Sharma P, Tukra S, Ait Kaddour A, Bhat Z. Mechanistic advances and therapeutic applications of *Zingiber officinale* Roscoe. Food Chem Adv. 2025; 8:101060. https://doi.org/10.1016/j.focha.2025.101060
11. Valarezo E, Ledesma-Monteros G, Jaramillo-Fierro X, Radice M, Meneses MA. Antioxidant application of clove (*Syzygium aromaticum*) essential oil in meat and meat products: A systematic review. Plants. 2025; 14(13):1958. https://doi.org/10.3390/plants14131958
12. Priyanjani HA, Senarath RM, Senarath WTPSK, Munasinghe M. Propagation, phytochemistry and pharmacology of *Plumbago indica*: A review. J Pharm Res Int. 2021; 33:188–202.
13. Luca SV, Gaweł-Bęben K, Strzępek-Gomółka M, Czech K, Trifan A, Zengin G, Korona-Glowniak I, Minceva M, Gertsch J, Skalicka-Woźniak K. Insights into the phytochemical and multifunctional biological profile of spices from the genus *Piper*. Antioxidants (Basel). 2021; 10(10):1642. https://doi.org/10.3390/antiox10101642
14. Ministry of Public Health. The announcement to define the Thailand national traditional medicine textbook and Thailand national traditional pharmacopoeia. Bangkok: Department for Development of Thai Traditional and Alternative Medicine, Royal Thai Government Gazette; 2016.
15. Yongram C, Panyatip P, Siriparu P, Ratha J, Sungthong B, Tadtong S, Puthongking P. Influence of maturity stage on tryptophan, phenolic, flavonoid, and anthocyanin content, and antioxidant activity of *Morus alba* L. fruit. Rasayan J Chem. 2022; 15(3):1693–701. http://doi.org/10.31788/ RJC.2022.1536958
16. Maroof K, Chen KF, Lee RFS, Goh BH, Mahendra CK, Siow LF, Gan SH. A preliminary study on phenolics, antioxidant and antibacterial activities of *Acacia mangium* and *Garcinia mangostana* propolis collected by *Geniotrigona thoracica*. Food Chem Adv. 2023; 2:100255. https://doi.org/10.1016/j.focha.2023.100255
17. Rumpf J, Burger R, Schulze M. Statistical evaluation of DPPH, ABTS, FRAP, and Folin-Ciocalteu assays to assess the antioxidant capacity of lignins. Int J Biol Macromol. 2023; 233:123470. https://doi.org/10.1016/j.ijbiomac.2023.123470
18. Siriparu P, Panyatip P, Pota T, Ratha J, Yongram C, Srisongkram T, Sungthong B, Puthongking, P. Effect of germination and illumination on melatonin and its metabolites, phenolic content, and antioxidant activity in mung bean sprouts. Plants. 2022; 11:2990. https://doi.org/10.3390/plants11212990
19. Čopra-Janićijević A, Culum D, Vidic D, Tahirović A, Klepo L, Bašić N. Chemical composition and antioxidant activity of the endemic *Crataegus microphylla* Koch subsp. *malyana* KI Chr. & Janjić from Bosnia. Ind Crops Prod. 2018; 113:75–79. https://doi.org/10.1016/j.indcrop.2018.01.016
20. Chen X, Deng H, Heise JA, Puthoff DP, Bou-Abboud N, Yu H, Peng J. Contents of cannabinoids in hemp varieties grown in Maryland. ACS Omega. 2021; 6(47):32186–32197. https://doi.org/10.1021/acsomega.1c04992
21. Palmieri S, Maggio F, Pellegrini M, Ricci A, Serio A, Paparella A, Lo Sterzo C. Effect of the distillation time on the chemical composition, antioxidant potential and antimicrobial activity of essential oils from different *Cannabis sativa* L. cultivars. Molecules. 2021; 26(16):4770. https://doi.org/10.3390/molecules26164770
22. Sukweenadhi J, Yunita O, Setiawan F, Kartini K, Siagian MT, Danduru N, Avanti C. Antioxidant activity screening of seven Indonesian herbal extract. Biodiversitas. 2020; 21(5):2062–2067. https://doi.org/10.13057/biodiv/d210532
23. Xiao F, Xu T, Lu B, Liu R. Guidelines for antioxidant assays for food components. Food Front. 2020; 1:60–69. https://doi.org/10.1002/fft2.10
24. Rufino MSM, Alves RE, Brito ES, Jiménez JP, Saura-Calixto F, Mancini-Filho J. Bioactive compounds and antioxidant capacities of 18 non-traditional tropical fruits from Brazil. Food Chem. 2010; 121(4):996–1002. https://doi.org/10.1016/j.foodchem.2010.01.037
25. Phuyal N, Jha PK, Raturi PPR, Rajbhandary S. Total phenolic, flavonoid contents, and antioxidant activities of fruit, seed, and bark extracts of *Zanthoxylum armatum* DC. Sci World J. 2020; 2020:8780704. https://doi.org/10.1155/2020/8780704
26. Nurcholis W, Putri DNS, Husnawati H, Aisyah SI, Priosoeryanto BP. Total flavonoid content and antioxidant activity of ethanol and ethyl acetate extracts from accessions of *Amomum compactum* fruits. Ann Agric Sci. 2021; 66:58–62. https://doi.org/10.1016/j.aoas.2021.04.001
27. Kiokias S, Proestos C, Oreopoulou V. Phenolic acids of plant origin: A review on their antioxidant activity in vitro (o/w emulsion systems) along with their in vivo health biochemical properties. Foods. 2020; 9(4):534. https://doi.org/10.3390/foods9040534
28. Michalak M, Zagórska-Dziok M, Klimek-Szczykutowicz M, Szopa A. Phenolic profile and comparison of the antioxidant, anti-ageing, anti-inflammatory, and protective activities of *Borago officinalis* extracts on skin cells. Molecules. 2023; 28(2):868. https://doi.org/10.3390/molecules28020868
29. Puthongking P, Ratha J, Panyatip P, Datham S, Siriparu P, Yongram C. The effect of extraction solvent on the phytochemical contents and antioxidant and acetylcholinesterase inhibitory activities of extracts from the leaves, bark and twig of *Dipterocarpus alatus*. Trop J Nat Prod Res. 2023; 7(12):5595–5600. https://tjnpr.org/index.php/home/article/view/3202
30. Dawidowicz AL, Olszowy-Tomczyk M, Typek R. CBG, CBD, Δ9-THC, CBN, CBGA, CBDA and Δ9-THCA as antioxidant agents and their intervention abilities in antioxidant action. Fitoterapia. 2021; 152:104915. https://doi.org/10.1016/j.fitote.2021.104915
31. Barboza JN, da Silva Maia Bezerra Filho C, Silva RO, Medeiros JVR, de Sousa DP. An overview on the anti-inflammatory potential and antioxidant profile of eugenol. Oxid Med Cell Longev. 2018; 2018:3957262. https://doi.org/10.1155/2018/3957262
32. Keramat M, Golmakani MT, Durand E, Villeneuve P, Hosseini SMH. A comparison of antioxidant activities by eugenyl acetate and eugenyl butyrate at frying temperature. J Food Process Preserv. 2021; 45(4):e15320. https://doi.org/10.1111/jfpp.15320
33. Qin B, Yang K, Cao R. Synthesis and antioxidative activity of piperine derivatives containing phenolic hydroxyl. J Chem. 2020; 2020:2786359. https://doi.org/10.1155/2020/2786359
34. Bolouri-Moghaddam MR, Le Roy K, Xiang L, Rolland F, Van den Ende W. Sugar signalling and antioxidant network connections in plant cells. FEBS J. 2010; 277(9):2022–2037. https://doi.org/10.1111/j.1742-4658.2010.07633.x
35. Sundarraj S, Thangam R, Sreevani V, Kaveri K, Gunasekaran P, Achiraman S, Kannan S. γ-Sitosterol from *Acacia nilotica* L. induces G2/M cell cycle arrest and apoptosis through c-Myc suppression in MCF-7 and A549 cells. J Ethnopharmacol. 2012; 141(3):803–809. https://doi.org/10.1016/j.jep.2012.03.014
36. Yazici ZMC, Bilge B, Bolkent S. Anti-inflammatory potential of delta-9-tetrahydrocannabinol in hyperinsulinemia: An experimental study. Mol Biol Rep. 2022; 49(12):11891–11899. https://doi.org/10.1007/s11033-022-07996-9
37. Shabana SM, Gad NS, Othman AI, Mohamed AF, El-Missiry MA. β-caryophyllene oxide induces apoptosis and inhibits proliferation of A549 lung cancer cells. Med Oncol. 2023; 40(7):189. https://doi.org/10.1007/s12032-023-02022-9

38. Gushiken LFS, Beserra FP, Hussni MF, Gonzaga MT, Ribeiro VP, de Souza PF, Campos JCL, Massaro TNC, Hussni CA, Takahira RK, Marcato PD, Bastos JK, Pellizzon CH. Beta-caryophyllene as an antioxidant, anti-inflammatory and re-epithelialization agent in a rat skin wound excision model. Oxid Med Cell Longev. 2022; 2022:9004014. https://doi.org/10.1155/2022/9004014
39. Türkez H, Celik K, Toğar B. Effects of copaene, a tricyclic sesquiterpene, on human lymphocyte cells in vitro. Cytotechnology. 2014; 66(4):597–603. https://doi.org/10.1007/s10616-013-9611-1
40. Rodriguez S, Sueiro RA, Murray AP, Leiro JM. Bioactive sesquiterpene obtained from *Schinus areira* L. (Anacardiaceae) essential oil. Proceedings. 2019; 41(1):85. https://doi.org/10.3390/ecsoc-23-06649
41. Bansod S, Chilvery S, Saifi MA, Das TJ, Tag H, Godugu C. Borneol protects against cerulein-induced oxidative stress and inflammation in acute pancreatitis mice model. Environ Toxicol. 2021; 36(4):530–539. https://doi.org/10.1002/tox.23058
42. Rychter AMR, Hryhorowicz S, Słomski R, Dobrowolska A, Krela-Kaźmierczak I. Antioxidant effects of vitamin E and risk of cardiovascular disease in women with obesity: A narrative review. Clin Nutr. 2022; 41(7):1557–1565. https://doi.org/10.1016/j.clnu.2022.04.032
43. Ali L, Khan S, Nazir M, Raiz N, Naz S, Zengin G, Mukhtar M, Parveen S, Shazmeen N, Saleem M, Tareen RB. Chemical profiling, in vitro biological activities and Pearson correlation between phenolic contents and antioxidant activities of *Caragana brachyantha* Rech.f. S. Afr J Bot. 2021; 140:189–193. https://doi.org/10.1016/j.sajb.2021.04.009
44. Liguori I, Russo G, Curcio F, Bulli G, Aran L, Della-Morte D, Gargiulo G, Testa G, Cacciatore F, Bonaduce D, Abete P. Oxidative stress, aging, and diseases. Clin Interv Aging. 2018; 13:757–772. https://doi.org/10.2147/CIA.S158513