



Screening of the secondary metabolites of the crude extracts of an antiviral herbal formulation using gc-ms/ms and lc-ms/ms

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Abstract

This study describes the screening of the secondary metabolites of the n-hexane, methanol, and ethanol extracts as well as the ethyl acetate layer of the medicinal herb formulation, coded BHA, using GC-MS/MS. The formulation was and is still used in the treatment of COVID-19 and other viral respiratory infectious diseases. Additionally, the methanol extract was also analysed using LC-MS/MS. Given its effectiveness and favourable results for COVID-19 patients, BHA has remained one of the most widely used herbal antiviral formulations. The choice of the herbal formulation was due to its effectiveness against COVID-19 and the fact that its constituents were listed on the container. The screening results revealed the presence of a wide range of natural products with different structural features in the herbal formulation extracts, most of which have been reported to possess significant biological and pharmacological qualities, such as anti-tumor, anti-inflammatory, antibacterial, immunomodulatory, antifibrotic, and vasorelaxation effects. A total of 75 compounds were identified, most of which resulted from the GC-MS/MS analyses, whereas the LC-MS/MS detected only 8 compounds. These included flavonoids, coumarins, alkaloids, fatty acids, terpenoids, and many other phenolic compounds. With exception of few compounds, the results revealed some discrepancies from the chemical composition reported for each individual species. These constituents exhibit antioxidant and anti-fibrotic properties, in respiratory ailments, ability to suppress lung inflammation and fibrosis, regulate blood lipid levels, and improve blood flow. The synergistic effects among the constituents of the herbal formulation may account for its efficacy. The screening results corroborate the usefulness and efficacy of the formulation and provide guidance for the safe application of the herbal antiviral formulation as well as the advancement of antiviral drugs that are successful in treating infectious respiratory diseases. Furthermore, the results confirm that herbal medicines with therapeutic capabilities can be used in the treatment of many disorders, including COVID-19.

Keywords: *Anti-inflammatory; Antiviral; Carvacrol; 6,7-Dimethylesculetin; Protobeberine alkaloid; Zanthoxylum chalybeum*

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Introduction

In an attempt to contain the virus during the COVID-19, a worldwide pandemic, communities in Tanzania and other developing countries relied primarily on herbal medicines (Anand *et*

al., 2021; Oyebo *et al.*, 2016; WHO, 2009, 2019). The reliance resulted from the fact that conventional medicines were unable to treat the pandemic (Mahomoodally, 2013; Antwi-Baffour, 2014; WHO, 2004), and the fact that medicinal

herbs are generally accessible, reasonably priced, and have the potential to be efficacious, unlike mainstream conventional pharmaceuticals that are often expensive and associated with side effects (Ekor, 2014b; Oyeboode *et al.*, 2016; WHO, 2004, 2009, 2019). These facts made plant-based drugs the most viable and promising strategy for combating the COVID-19 pandemic.

In efforts to find viable options for the fight against the virus, multiple plant-based extracts and isolated compounds have been tested as part of scientific investigations into possible COVID-19 treatments. Research has verified the protective effect of herbal medicines against respiratory viruses when used as crude extracts or as pure active components (Anand *et al.*, 2021; Khadka *et al.*, 2021; Khan *et al.*, 2021; Mani *et al.*, 2020; Sharanya *et al.*, 2021).

The search for efficacious alternative treatments for the pandemic and other respiratory infectious viral diseases was necessary due to the inability of the existing conventional medications to treat or prevent the illness. Consequently, hundreds of herbs and plant metabolites have been identified, screened, and tested for their antiviral potentials; most of which have demonstrated significant pharmacological utility in preclinical and clinical trials for the treatment or prevention of various viral infections. It has been demonstrated that several plants and isolated compounds with antiviral and immune-boosting properties can affect SARS-CoV-2, the virus that causes COVID-19 (Aini *et al.*, 2022; Ali *et al.*, 2021; Anand *et al.*, 2021; Colunga Biancatelli *et al.*, 2020; Conti *et al.*, 2020; Farmanpour-Kalalagh *et al.*, 2022; Gasmi *et al.*, 2022; Kaul *et al.*, 2021; Lima *et al.*, 2021; Pandey *et al.*, 2021). For instance, in 2020, the island nation of Madagascar announced the discovery of a tea that used traditional Malagasy botanicals, such as *Artemisia*, to treat COVID-19. This tea and pill combination was dubbed COVID-Organics, or CVO (Razanamparany, 2020).

Notwithstanding the vast increase in demand and uses of herbal medicines and the fact that herbal remedies are providing a ray of hope for human health, caution must be taken to avoid harmful side effects emanating from the use of the medicinal herbs due to the fact that some of them may be toxic to humans (Boukandou Mounanga *et al.*, 2015; Dhama *et al.*, 2018; Fatima

and Nayeem, 2016; Mensah *et al.*, 2019; Nasri and Shirzad, 2013; Subramanian *et al.*, 2018). This calls for evaluation not of the effectiveness of the therapeutic herbs but also their toxicity. As a result, hundreds of herbs and plant metabolites have been found, examined, and tested for their antiviral properties. Several of these have demonstrated notable therapeutic benefits in the treatment or prevention of different viral infectious illnesses (Dhama *et al.*, 2018).

In addition to being used against SARS-CoV, plants such as *Artemisia annua*, *Isatis indigotica*, *Lindera aggregata*, *Pelargonium sidoides*, *Glychirrhiza* spp., *Sambucus nigra*, *Caesalpinia pulcherrima*, and *Hypericum connatum*, have also been shown to have potent antiviral and immune-boosting properties against different viruses, including zika, ebola, nipah virus, and other highly pathogenic viruses (Akram *et al.*, 2018; Anand *et al.*, 2021; Khan *et al.*, 2021; Li *et al.*, 2005; Mani *et al.*, 2020; Sharanya *et al.*, 2021; Vilhelmova-Ilieva *et al.*, 2020; Wahyuni *et al.*, 2019).

Therefore, along with other drugs currently being tested against COVID-19, plant-based drugs need to be included for speedy development of COVID-19 and other viral infectious diseases treatment (Akram *et al.*, 2018; Anand *et al.*, 2021; Khan *et al.*, 2021; Sharanya *et al.*, 2021; Vilhelmova-Ilieva *et al.*, 2020).

Various studies have reported species like *Nigella sativa*, *Vernonia amygdalina*, *Azadirachta indica*, *Eurycoma longifolia*, *Ocimum sanctum*, *Withania somnifera*, *Tinospora cordifolia*, *Curcuma longa*, *Zingiber officinalis*, *Piper nigrum*, *Nigella sativa*, *Allium sativum*, *Hibiscus sabdariffa*, *Phyllanthus amarus*, *Alpinia officinarum*, *Chrysanthemum morifolium*, *Gardenia* sp. *Cinnamomum cassia*, *Vitex trifolia*, *Avicenna marina* and *Punica granatum*, to have strong antiviral properties against a variety of viruses, including the SARS-CoV-2 virus. Hence, they may be useful as COVID-19 treatment candidates (Akram *et al.*, 2018; Anand *et al.*, 2021; Patel *et al.*, 2021; Saleem *et al.*, 2018; Yashvardhini *et al.*, 2021).

Following the outbreak of COVID-19, several Tanzanian alternative medicine practitioners developed herbal medicine formulations or mixtures that they claimed were able to cure and

overall management of COVID-19 patients. One of the formulations among many, which gave positive results in the treatment and management of COVID-19 patients was BHA, which is made up of five plant species and one type of fungus. The fungus species is *Ganoderma tsugae* Murrill, whereas the plant species include *Adansonia digitata* L., *Ficus sur* Forssk, *Securidaca longipendiculata* Fresen, *Syzygium cumin* (L.) Skeels, and *Zanthoxylum chalybeum* Engl. This formulation was selected from a variety of other options based on two factors: firstly, it turned out to be among the best performing herbal formulations for the treatment and management of COVID-19 patients. Secondly, the ingredients of the combination were also clearly indicated on the container, information that allowed for more research on each individual species whereas the constituent species of the other formulations were not revealed. A thorough review covering the biological activities, ethnomedicinal applications, and secondary metabolites composition of each individual species in the formulation showed the presence of a wide range of compounds belonging to various classes of secondary metabolites with significant biological activities were present (Makangara *et al.*, 2024).

Although Tanzania like many other African countries enormously used the traditional medicines from plants sources, most of the formulations had no known phytochemical ingredients responsible for the claims. This study aimed at bridging the gap between the properties reported in literature for each individual components and those in the formulation by carrying out the screening of the secondary metabolites of three extracts and ethyl acetate layer of the medicinal herbal formulation using GC-MS/MS. In addition, LC-MS/MS analysis of the methanol extract for the formulation's non-volatile ingredients was done. Furthermore, to correlate the chemical composition identified and their corresponding biological or pharmacological properties available in the literature.

Materials and Methods

Sample collection

The light brownish powder sample of the herbal concoction was purchased in Dar es Salaam at the TANHELISO outlet store, located in SIDO House on Bibi Titi Road. The extraction was done at the Department of Chemistry laboratories, University of Dodoma whereas GC-MS/MS and LC-MS/MS analyses were done at the Government Chemist Laboratory Authority (GCLA) laboratories in Dar es Salaam.

Sample preparation

10 g of the dried and pulverized herbal formulation was sequentially soaked in 100 ml of *n*-hexane and methanol for 1 day each, filtered and dried under reduced pressure using a rotary evaporator. The extraction process yielded 0.78 g of yellowish brown and 2.52 g of light brownish oily crude extracts of hexane and methanol, respectively. The obtained 0.78 g of the hexane and 1 g of the methanol crude extracts were reconstituted in 1 ml of dichloromethane and 1 ml methanol, respectively. Furthermore, another 20 g of the sample was soaked in a mixture of ethanol/water (7:3) for 24 hours, filtered and solvent evaporated using rotary evaporator, yielding a total of 8.16 g of a dark brownish oil. The resulting ethanol crude extract was washed with ethyl acetate to give 2.45 g of the ethyl acetate layer. 1 g of each of the ethyl acetate layer and ethanol extract were reconstituted in 1 ml of dichloromethane and 1 ml methanol, respectively. 1 μ L of each of the reconstituted solutions was drawn and injected in the GC-MS/MS. Identification of the secondary metabolites was done by comparing the spectral data to Mass-hunter and NIST reference databases. Furthermore, 1 μ L of the methanol extract was drawn and injected in the LC-MS/MS. The interpretation was done by comparing the spectral data to Mass-hunter and NIST reference databases.

GC-MS/MS Analysis

An Agilent GC-MS Triple Quadrupole 7000D series with electron impact ionization was used for the chemical screening of the four crude extracts. Gas chromatography DB-17MS capillary column of length 30 m \times 0.25 mm thickness and helium (purity of 99.999%) as a carrier gas were used for the analysis of samples. 1 μ L of each

sample was injected in the GC at a constant flow rate of 1 mL/min. The temperature for ion source was 230 °C, while 280 °C temperature was for injector. The oven initial temperature was set at 65 °C, after 2 min the oven temperature raised to 290 °C at the rate of 15 °C/min. The temperature was maintained at 290 °C for 30 min, before cooling back to 65 °C at the rate of 15 °C/min. The ionization energy was 70 eV at positive electron ionization. Scan range was from m/z 50-500 range.

LC-MS/MS Analysis

A Thermo Scientific Dionex UltiMate 3000 liquid chromatography pump with OAS autosampler coupled with a Thermo Scientific Q Exactive Orbitrap mass spectrometer with a Thermo Scientific Ion Max source and a heated electrospray (HESI-II) source was used for the analysis and detection of the secondary metabolites. The mobile phases A and B were composed of acetonitrile and 1% formic acid in water, respectively. The column used was a Thermo Scientific Accucore RP-MS, 100 mm x 4.6 mm x (SN: 10508423, LOT: 14358) x 2.6 µm. To increase precursor selection and ion transmission, a single precursor ion was selected in the quadrupole as a mass filter with an isolation width of 2.0 m/z and fragmented in the HCD cell using optimized compound-specific collision energy. The resulting MS/MS product

ion spectrum was identified with a resolution of 35,000 (FWHM at 200 m/z) in the Orbitrap detector. The data was processed using Thermo Scientific TraceFinder software. Spectral matching of the spectral data from the MS/MS spectrum with those in the MassHunter and NIST databases were used to identify the secondary metabolites.

Results

This study presents the results of the GC-MS/MS analysis of the therapeutic herbal formula's hexane, ethyl acetate, methanol, and ethanol crude extracts. Additionally, LC-MS/MS analytical data for the methanol extract are also given. Furthermore, the study also reports on the biological activities of some of the identified secondary metabolites. The data from the LC-MS/MS analysis of the methanol extract is as presented in Table 2, while Table 1 displays secondary metabolites found from the GC-MS/MS studies of the medicinal herbal formulation extracts. Each of the identified secondary metabolites is listed in full in the tables along with its chemical formula, name, and measured ion mass-to-charge ratio. Additionally, each of the discovered secondary metabolites has a number, which is displayed in Tables 1 and 2.

Table 1

GC-MS/MS results of the secondary metabolites identified in the extracts of the medicinal herb formulation samples

m/z Ion	Molecular formula	Name	Structure number	Class of compound
126.1	C ₈ H ₁₄ O	(E)-2-Octenal	1	Aliphatic aldehyde
144.12	C ₈ H ₁₆ O ₂	Octanoic acid	2	Aliphatic carboxylic acid
126.1	C ₈ H ₁₄ O	Tridecanal	3	Aliphatic aldehyde
154.14	C ₁₀ H ₁₈ O	(E)-2-Decenal	4	Aliphatic aldehyde
152.12	C ₁₀ H ₁₆ O	(E,E)- 2,4-Decadienal	5	Aliphatic aldehyde
238.19	C ₁₅ H ₂₆ O ₂	Methyl 3,4-tetradecadienoate	6	Aliphatic ester
152.12	C ₁₀ H ₁₆ O	(E,Z)- 2,4-Decadienal	7	Aliphatic carboxylic acid
282.26	C ₁₈ H ₃₄ O ₂	Oleic acid	8	Aliphatic carboxylic acid

m/z Ion	Molecular formula	Name	Structure number	Class of compound
158.13	C ₉ H ₁₈ O ₂	Nonanoic acid	9	Aliphatic carboxylic acid
256.24	C ₁₆ H ₃₂ O ₂	<i>n</i> -Hexadecanoic acid	10	Aliphatic carboxylic acid
280.24	C ₁₈ H ₃₂ O ₂	(9 <i>Z</i> ,12 <i>Z</i>)-Octadeca-9,12-dienoic acid	11	Aliphatic carboxylic acid
298.25	C ₁₈ H ₃₄ O ₃	Ricinoleic acid	12	Aliphatic carboxylic acid
284.27	C ₁₈ H ₃₆ O ₂	Octadecanoic acid	13	Aliphatic carboxylic acid
198.2	C ₁₃ H ₂₆ O	2-Tridecanone	14	Aliphatic ketone
280.24	C ₁₈ H ₃₂ O ₂	13-Hexyloxacyclotridec-10-en-2-one	15	Cyclic carboxylic ester
256.17	C ₁₄ H ₂₄ O ₄	2,2-Dimethyl-6-methylene-1-[3,5-dihydroxy-1-pentenyl]cyclohexan-1-perhydrol	16	Aliphatic hydroxy peroxy compound
138.1	C ₉ H ₁₄ O	Furan, 2-pentyl-	17	Furan
98.04	C ₅ H ₆ O ₂	3-Furanmethanol	18	Furan alcohol
110.04	C ₆ H ₆ O ₂	5-Methyl furfural	19	Furan aldehyde
126.03	C ₆ H ₆ O ₃	5-Hydroxymethylfurfural	20	Furan aldehyde
208.15	C ₁₃ H ₂₀ O ₂	3-Hydroxy-3a,6-dimethyl-1,2,3,4,5,5a,6,8-octahydrocyclopenta[h]pentalen-7-one	21	Aliphatic ketone
234.16	C ₁₅ H ₂₂ O ₂	Spiro[furan-3(2H),2'-indan]-2-one, 3'a,4,4',5,5',6',7',7'a.beta.-octahydro-3'a.beta.,4'.beta.-dimethyl-4-methylene-, (2' <i>R</i>)-(1 <i>R</i> ,3 <i>E</i> ,7 <i>E</i> ,11 <i>R</i>)-1,5,5,8-	22	Sesquiterpene ester
220.18	C ₁₅ H ₂₄ O	Tetramethyl-12-oxabicyclo[9.1.0]dodeca-3,7-diene	23	Sesquiterpene epoxide
220.18	C ₁₅ H ₂₄ O	Humulenol-II	24	Oxygenated sesquiterpene
154.14	C ₁₀ H ₁₈ O	α -Terpineol	25	Monoterpenoid alcohol
220.18	C ₁₅ H ₂₄ O	2-((2 <i>R</i> ,4 <i>aR</i> ,8 <i>aS</i>)-4a-Methyl-8-methylenedecahydronaphthalen-2-yl)prop-2-en-1-ol	26	Oxygenated sesquiterpene

m/z Ion	Molecular formula	Name	Structure number	Class of compound
248.14	C ₁₅ H ₂₀ O ₃	Benzo[e]isobenzofuran-1,4-dione,1,3,4,5,5a,6,7,8,9,9a-decahydro-6,6,9a-trimethyl	27	Oxygenated sesquiterpene
220.18	C ₁₅ H ₂₄ O	Caryophyllene oxide	28	Oxygenated sesquiterpene
220.18	C ₁₅ H ₂₄ O	1,4-Methanoazulen-9-one, decahydro-1,5,5,8a-tetramethyl-, [1R-(1.alpha.,3a.beta.,4.alpha.,8a.beta.)]-	29	Oxygenated sesquiterpene
220.18	C ₁₅ H ₂₄ O	Longifolen aldehyde	30	Oxygenated sesquiterpene
220.18	C ₁₅ H ₂₄ O	Isolongifolene, 9-hydroxy-	31	Oxygenated sesquiterpene
220.2	C ₁₅ H ₂₆ O	Isolongifolol	32	Oxygenated sesquiterpene
204.19	C ₁₅ H ₂₄	Isocaryophyllene	33	Sesquiterpene
238.19	C ₁₅ H ₂₆ O ₂	(3S,3aS,6R,7R,9aS)-1,1,7-Trimethyldecahydro-3a,7-methanocyclopenta[8]annulene-3,6-diol	34	Oxygenated sesquiterpene
222.2	C ₁₅ H ₂₆ O	Drim-7-en-11-ol	35	Oxygenated sesquiterpene
150.1	C ₁₀ H ₁₄ O	<i>p</i> -Cymen-7-ol	36	Aromatic terpenoid
150.1	C ₁₀ H ₁₄ O	Carvacrol	37	Aromatic terpenoid
144.04	C ₆ H ₈ O ₄	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-	38	Pyran derivative
216.15	C ₁₅ H ₂₀ O	aR-Turmerone	39	Phenylpropanoid derivative
164.08	C ₁₀ H ₁₂ O ₂	Eugenol	40	Phenylpropanoid
178.06	C ₁₀ H ₁₀ O ₃	Coniferyl aldehyde	41	Phenylpropanoid aldehyde
180.08	C ₁₀ H ₁₂ O ₃	(<i>E</i>)-4-(3-hydroxyprop-1-en-1-yl)-2-methoxyphenol	42	Phenylpropanoid
184.07	C ₉ H ₁₂ O ₄	Phenol, 3,4,5-trimethoxy-	43	Phenolic compound
132.06	C ₉ H ₈ O	Cinnamaldehyde, (<i>E</i>)-	44	Phenylpropanoid
180.08	C ₁₀ H ₁₂ O ₃	2-Propanone, 1-(4-hydroxy-3-methoxyphenyl)	45	Phenylpropanoid ketone
164.08	C ₁₀ H ₁₂ O ₂	Phenol, 2-methoxy-4-(1-propenyl)-	46	Phenylpropanoid

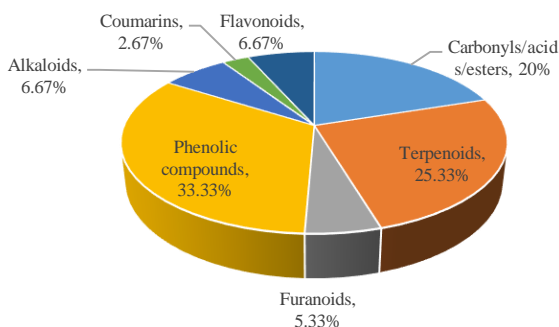
m/z Ion	Molecular formula	Name	Structure number	Class of compound
150.07	C ₉ H ₁₀ O ₂	2-Methoxy-4-vinyl-phenol	47	Phenolic compound
148.05	C ₉ H ₈ O ₂	2-Propenoic acid, 3-phenyl-	48	Phenylpropanoid
122.04	C ₇ H ₆ O ₂	Benzoic acid	49	Aromatic carboxylic acid
152.05	C ₈ H ₈ O ₃	Vanillin	50	Phenolic compound
168.04	C ₈ H ₈ O ₄	Vanillic acid	51	Aromatic carboxylic acid
276.17	C ₁₇ H ₂₄ O ₃	(E)-1-(4-Hydroxy-3-methoxyphenyl)dec-4-en-3-one (6-Shogaol)	52	Phenylpropanoid derivative
210.09	C ₁₁ H ₁₄ O ₄	<i>trans</i> -Sinapyl alcohol	53	Phenylpropanoid alcohol
180.8	C ₁₀ H ₁₂ O ₃	Phenol, 4-ethenyl-2,6-dimethoxy-	54	Phenolic compound
108.06	C ₇ H ₈ O	Benzyl alcohol	55	Aromatic alcohol
154.14	C ₁₀ H ₁₈ O	Chavicol	56	Phenylpropanoid
194.09	C ₁₁ H ₁₄ O ₃	2-Butanone, 4-(4-hydroxy-3-methoxyphenyl)- (Zingerone)	57	Phenylpropanoid
178.1	C ₁₁ H ₁₄ O ₂	Methyleugenol	58	Phenylpropanoid
132.06	C ₉ H ₈ O	3-Phenyl-2-propyn-1-ol	59	Phenylpropanoid
156.03	C ₈ H ₉ ClO	Chloroxylenol	60	Phenolic compound
346.19	C ₂₄ H ₂₆ O ₂	(+)-Sesamin	61	Lignan
316.13	C ₂₂ H ₂₀ S	Benzene, 1,1'-[2-methyl-2-(phenylthio)cyclopropylidene]bis-	62	Phenolic compound containing sulfur
332.12	C ₂₂ H ₂₀ OS	(2,3-Diphenylcyclopropyl)methyl phenyl sulfoxide, trans-	63	Phenolic compound containing sulfur
268.07	C ₁₆ H ₁₂ O ₄	5-Hydroxy-7-methoxyflavone (Techtochrysin)	64	Flavonoid
270.09	C ₁₆ H ₁₄ O ₄	(S)-4H-1-Benzopyran-4-one, 2,3-dihydro-5-hydroxy-7-methoxy-2-phenyl (Pinostrobin)	65	Flavonoid
178.06	C ₁₀ H ₁₀ O ₃	(-)-Mellein	69	Coumarin
199.06	C ₁₂ H ₉ NO ₂	Dictamnine	71	Alkaloid
259.08	C ₁₄ H ₁₃ NO ₄	Furo[2,3-b]quinoline, 4,7,8-trimethoxy- (Skimmianine)	72	Furoquinoline alkaloid

Table 2*LC-MS/MS analysis results of the methanol extract*

m/z Ion	Molecular Formula	Compound Name	Structure number	Class of compound
302.08	C ₁₆ H ₁₄ O ₆	Homoeriodictyol	66	Flavonoid
330.07	C ₁₇ H ₁₄ O ₇	3,4'-Dimethoxy-5,7,3'-trihydroxyflavone	67	Flavonoid
372.12	C ₂₀ H ₂₀ O ₇	Pentamethoxyflavone (Sinensetin)	68	Flavonoid
206.06	C ₁₁ H ₁₀ O ₄	6,7-Dimethylesculatin (Scoparone)	70	Coumarin
348.12	C ₂₁ H ₁₈ NO ₄	Chelerythrine cation	73	Benzophenanthridine alkaloid
352.15	C ₂₁ H ₂₂ NO ₄	Palmatine cation	74	Benzophenanthridine alkaloid
338.14	C ₂₀ H ₂₀ NO ₄	Jatrorrhizine cation	75	Benzophenanthridine alkaloid

The examinations of the herbal formulation's extracts yielded a total of 75 secondary metabolites, most of which were obtained from the GC-MS/MS analyses. Nine of the secondary metabolites were found by LC-MS/MS analysis; the rest were found by GC-MS/MS analysis.

Alkaloids, terpenoids, coumarins, aliphatic and aromatic carboxylic acids, phenylpropanoids, furan derivatives, and other phenolic compounds were the main types of chemicals that were found (Table 1 and 2). The distribution of the secondary metabolites identified is as presented in Figure 1 below.

Figure 1*Percentage composition of the secondary metabolites in the BHA herbal formula extracts*

Further analysis of the results revealed that only few identified secondary metabolites in the medicinal herb formulation matched with those reported in literature for the individual species (Makangara *et al.*, 2024). Compounds **61**, **70**, and **73-75** were previously reported from *Zanthoxylum* species whereas none of the detected flavonoids in formulation matched with those reported in literature. *n*-Hexadecanoic acid (**10**), α -terpineol (**25**) and caryophyllene oxide (**28**), were also reported in literature, whereas the

rest of the compounds are not reported to occur in the species, however, they have been reported to occur in other species.

Table 3 presents the biological activities that have been reported for the identified compounds, including anti-inflammatory, antiviral, antitumor, anticancer, immunomodulatory, antioxidant, vasorelaxant, cardiogenic, antihypertensive, regulation of blood lipids and many other activities.

Table 3

Biological activities reported for the observed secondary metabolites

Compound	Biological activities	References
(<i>E</i>)-2-Octenal (1)	Antifungal agent	(Luo <i>et al.</i> , 2023)
Octanoic acid (2)	Epilepsy, kidney failure, digestive disorders, antioxidant, prevention of cognitive decline	(Augustin <i>et al.</i> , 2018; Bonetti <i>et al.</i> , 2017; Mungali <i>et al.</i> , 2020)
(<i>E</i>)-2-Decenal (4)	Nematicide, alarm pheromone, mutagenic	(Kim <i>et al.</i> , 2008; Wu and Yen, 2004)
Oleic acid (8)	Antinematodal activity	(Habtemariam, 2019; Zhou <i>et al.</i> , 2012)
<i>n</i> -Hexadecanoic acid (10)	Anti-Inflammatory, and antioxidant activities	(Aparna <i>et al.</i> , 2012; Malarvizhi <i>et al.</i> , 2015)
2-Pentylfuran (17)	Anti-inflammatory, antimicrobial, insect repellent, a flavouring agent, a plant growth stimulator and a bacterial metabolite	(Alizadeh <i>et al.</i> , 2020; Cha <i>et al.</i> , 2021)
α -Terpineol (25)	Antioxidant, antimicrobial, anticancer, anticonvulsant, antiulcer, antihypertensive, antinociceptive, anticholesteremic, reliever in neuropathic pain, antidiarrheal, analgesic, and insecticidal activities	(Musterman <i>et al.</i> , 2018; Saeed <i>et al.</i> , 2023; Sales <i>et al.</i> , 2020)
Caryophyllene oxide (28)	Analgesic, anti-inflammatory and anticancer activities	(Chavan <i>et al.</i> , 2010; Fidy <i>et al.</i> , 2016; Legault and Pichette, 2010)
Longifolen aldehyde (30)	Antifungal activity	(Mukai <i>et al.</i> , 2018)

Compound	Biological activities	References
Isolongifolene, 9-hydroxy- (31)	Antioxidant activity	(Rangasamy and Namasivaya, 2013)
Isocaryophyllene (33)	Anti-inflammatory, antibiotic, antioxidant, anticarcinogenic and local anaesthetic activities	(Chavan <i>et al.</i> , 2010; Fidy <i>et al.</i> , 2016; Legault and Pichette, 2010)
<i>p</i> -Cymen-7-ol (36)	Antifungal, antibacterial, antioxidant, analgesic, antinociceptive, immunomodulatory, vasorelaxant and neuroprotective activities	(Balahbib <i>et al.</i> , 2021; Mohammed <i>et al.</i> , 2024)
Carvacrol (37)	Anti-inflammatory, antibacterial, antioxidant, anticancer, antioxidant potential in respiratory disorders, antifungal, vasorelaxant, and hepatoprotective	(Abbasloo <i>et al.</i> , 2023; Cicalău <i>et al.</i> , 2021; Imran <i>et al.</i> , 2022; Maćzka <i>et al.</i> , 2023; Magi <i>et al.</i> , 2015; Mondal <i>et al.</i> , 2021; Morais <i>et al.</i> , 2023; Sharifi-Rad <i>et al.</i> , 2018)
4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl- (38)	Antimutagenic, antimicrobial, anti-inflammatory, and antioxidant activities	(Rizvi <i>et al.</i> , 2023) (Chen <i>et al.</i> , 2021; Rizvi <i>et al.</i> , 2023; Yu <i>et al.</i> , 2013)
α -Turmerone (39)	Anti-inflammatory, antioxidant, anticancer and regulates blood sugar levels, treatment of neurodegenerative disorders	(Makaremi <i>et al.</i> , 2021; Obulesu, 2021a, 2021c; Razavi and Hosseinzadeh, 2020)
Eugenol (40)	Antidiabetic, antimicrobial, anticancer, antioxidant, anti-inflammatory, analgesic, and insecticidal activities	(Habtemariam, 2019; Mbaveng and Kuete, 2017; Nisar <i>et al.</i> , 2021; Sharma <i>et al.</i> , 2021; Sharma <i>et al.</i> , 2020; Tripathi and Mishra, 2016)
Coniferyl aldehyde (41)	Antifungal, anti-inflammatory activity	(Wang <i>et al.</i> , 2020)
Trimethoxyphenol (43)	Antioxidant activity	(Matos <i>et al.</i> , 2008)
(<i>E</i>)-1-(4-Hydroxy-3-methoxyphenyl)dec-4-en-3-one (6-Shogaol) (52)	Anticancer, anti-oxidant, antimicrobial, anti-inflammatory, immunomodulatory, anti-arthritis, antidiabetic, antifungal, and anticancer and anti-allergic to various central nervous system activities	(Arcusa <i>et al.</i> , 2022; Bischoff-Kont <i>et al.</i> , 2022; Bischoff-Kont and Fürst, 2021; Dasgupta, 2019; Inserra and Brooks, 2017; Mbaveng and Kuete, 2017; Rajini, 2023; Semwal

Compound	Biological activities	References
		<i>et al.</i> , 2015; Sheikh <i>et al.</i> , 2023; Tao <i>et al.</i> , 2023)
Phenol, 4-ethenyl-2,6-dimethoxy- (54)	Antioxidative and antimutagenic activities	(Kraljić <i>et al.</i> , 2015; Kuwahara <i>et al.</i> , 2004; Wang <i>et al.</i> , 2014)
4-(4-Hydroxy-3-methoxyphenyl)-2-butanone (Zingerone) (57)	Anti-inflammatory, antitumor, antipyretic, gastroprotective, cardiogenic, and antioxidant activities	(Ahmad <i>et al.</i> , 2015; Baptista <i>et al.</i> , 2022; Daniels <i>et al.</i> , 2022; Ekor, 2014a; Srinivasan, 2017)
Methyleugenol (58)	Immunostimulatory activity	(Nair <i>et al.</i> , 2018; Tan and Nishida, 2012; Tripathi and Mishra, 2016)
(+)-Sesamin (61)	Improve blood pressure and blood lipids, prevention of cardiovascular diseases; anti-inflammatory, anti-hypertensive activities	(Correia Alves <i>et al.</i> , 2023; Dalibalta <i>et al.</i> , 2020; Hadipour <i>et al.</i> , 2023; Huang <i>et al.</i> , 2023; Majdalawieh <i>et al.</i> , 2022; Michailidis <i>et al.</i> , 2019; Sharma <i>et al.</i> , 2023; Sun <i>et al.</i> , 2022)
<i>trans</i> - (2,3-Diphenylcyclopropyl)methyl phenyl sulfoxide (63)	Antidiabetic activity	(Deepa <i>et al.</i> , 2019)
5-Hydroxy-7-methoxyflavone (Techtochrysin) (64)	Antidiabetic, and antioxidant, induce skeletal muscle hypertrophy	(Hasan <i>et al.</i> , 2017; Ono <i>et al.</i> , 2019; Sarian <i>et al.</i> , 2017; Wieczorek <i>et al.</i> , 2022)
(S)-4H-1-Benzopyran-4-one, 2,3-dihydro-5-hydroxy-7-methoxy-2-phenyl (Pinostrobin) (65)	Anti-inflammatory, antioxidant, analgesic, antibacterial, and antitumor activities.	(González <i>et al.</i> , 2022; Kaur <i>et al.</i> , 2009; Mawa <i>et al.</i> , 2019; Raffa <i>et al.</i> , 2017; Sun <i>et al.</i> , 2020; Wieczorek <i>et al.</i> , 2022; Wu <i>et al.</i> , 2023; Zhao <i>et al.</i> , 2023)
Homoeriodictyol (66)	Improve memory impairment, antimalarial, antioxidant, anti-inflammatory, antimicrobial, and anticancer properties	(Al-Bzour <i>et al.</i> , 2024; Dunstan <i>et al.</i> , 2020; Guo <i>et al.</i> , 2022; Kuwahara <i>et al.</i> , 2004; Melo <i>et al.</i> , 2023; Saquib <i>et al.</i> , 2020)
5,6,7,3',4'-Pentamethoxyflavone (Sinensetin) (68)	Inhibition of α -glucosidase, anticancer, anti-inflammatory, antioxidant, antimicrobial, anti-obesity, anti-dementia and vasorelaxant activities	(Boniface and Ferreira, 2020; Han Jie <i>et al.</i> , 2021; Ono <i>et al.</i> , 2019; Sung <i>et al.</i> , 2012; Yuan <i>et al.</i> , 2024; Zhu <i>et al.</i> , 2024)

Compound	Biological activities	References
(-)-Mellein (69)	Phytotoxic and antifungal, anti-inflammatory and antibacterial activities	(Li <i>et al.</i> , 2021; Reveglia <i>et al.</i> , 2020; Turker and Gurel, 2005)
6,7-Dimethylesuletin (Scoparone) (70)	Anti-inflammatory, antioxidant, anti-apoptotic, anti-fibrotic and hypolipidemic activities. Treatment of hepatic dysfunction, cholestasis and jaundice	(Cai <i>et al.</i> , 2020; Ding <i>et al.</i> , 2021; Hui <i>et al.</i> , 2020; Kowalczyk <i>et al.</i> , 2022; Wang, 2021; Wirasisya and Hohmann, 2023)
Dictamnine (71)	Anti-inflammatory and insecticidal activities	(Epifano <i>et al.</i> , 2015; Lu <i>et al.</i> , 2020; Lv <i>et al.</i> , 2015; Sharma <i>et al.</i> , 2023; Yao <i>et al.</i> , 2020)
Furo[2,3-b]quinoline, 4,7,8-trimethoxy- (Skimmianine) (72)	Anticholinesterase, antiviral, antibacterial, antifungal, anti-inflammatory, antioxidant, analgesic, anticonvulsant, cardiostonic and anthelmintic activities	(Bao <i>et al.</i> , 2023; Epifano <i>et al.</i> , 2015; Mutinda <i>et al.</i> , 2023; Ombito <i>et al.</i> , 2021; Powder-George, 2023; Son, 2022; Yang <i>et al.</i> , 2012; Yao <i>et al.</i> , 2020)
Chelerythrine (73)	Anti-inflammatory, antiviral and activities, suppressing pulmonary inflammation and fibrosis, prevention of cerebral vasospasm and eryptosis reduction	(Akaberi <i>et al.</i> , 2021; Chen <i>et al.</i> , 2022; Croley <i>et al.</i> , 2023; He <i>et al.</i> , 2018; Kang <i>et al.</i> , 2022; Liu <i>et al.</i> , 2023; Valipour <i>et al.</i> , 2021)
Palmatine (74)	Anti-cancer, anti-oxidation, anti-inflammatory, neuroprotection, anti-bacterial, anti-viral and regulating blood lipids, antiseizure activity	(Bertoncello and Bonan, 2021; Grabarska <i>et al.</i> , 2021; Long <i>et al.</i> , 2019; Song <i>et al.</i> , 2018; Tarabasz and Kukula-Koch, 2020; Wu <i>et al.</i> , 2016; Yan <i>et al.</i> , 2017; Zhang <i>et al.</i> , 2012)
Jatrorrhizine (75)	Anti-inflammatory, antibacterial, antitumor, improvement of blood flow and mitotic activity	(Deng and Wan, 2021; Fu <i>et al.</i> , 2023; Long <i>et al.</i> , 2019; Rolle <i>et al.</i> , 2021; Tarabasz and Kukula-Koch, 2020; Zhong <i>et al.</i> , 2022; Zhou <i>et al.</i> , 2022)

Discussion

Among the compounds identified by the GC-MS/MS data was a series of aliphatic aldehydes, ketone, carboxylic acids and carboxylic acids esters **1-15** (Table 1; Fig. 2). *n*-Hexadecanoic acid (**10**), one of the carboxylic acids, is reported to have antioxidant and anti-inflammatory properties (Aparna *et al.*, 2012; Malarvizhi *et al.*,

2015). Generally, compounds in this group have been shown to possess antinematodal action, primarily for the fatty acids linoleic and, oleic (Habtemariam, 2019; Zhou *et al.*, 2012).

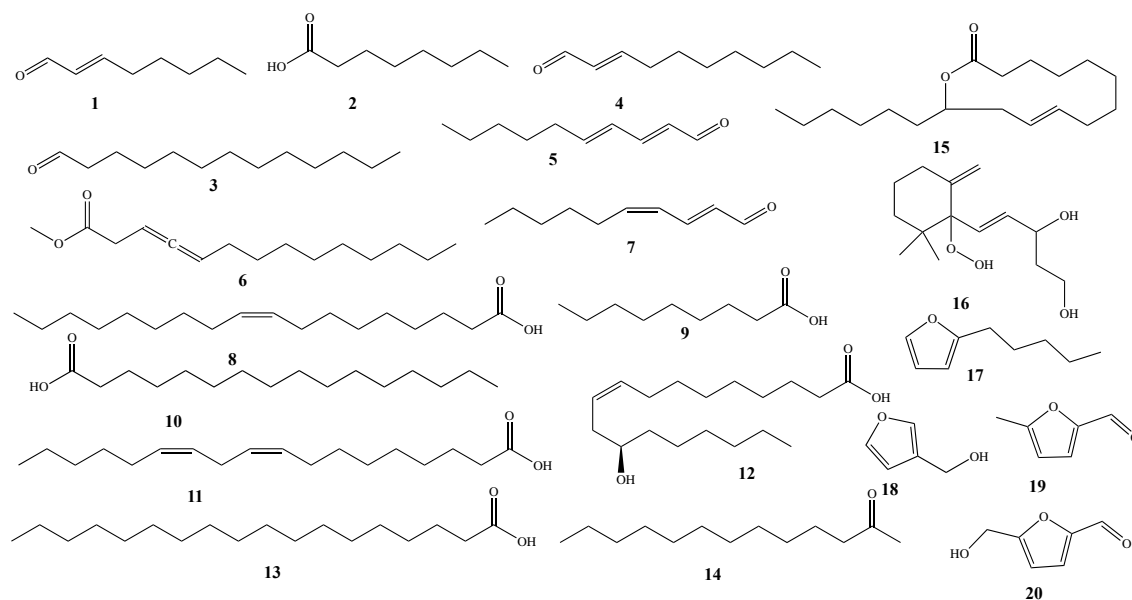
Terpenoids, primarily monoterpenes and sesquiterpenes, (**21-38**) (Table 1; Fig. 3) were another class that significantly contributed to the secondary metabolites of BHA. The biological

properties reported for the terpenoids include analgesic, anti-inflammatory, antimicrobial, antioxidant, anticarcinogenic, anticonvulsant, antiulcer, antihypertensive, anti-nociceptive, anticholesteremic, relief of neuropathic pain, antidiarrheal, analgesic, and insecticidal effects (Table 3) (Musterman *et al.*, 2018; Saeed *et al.*, 2023; Sales *et al.*, 2020). Among the terpenoids discovered are two aromatic monoterpenes, *p*-cymen-7-ol (**36**) and carvacrol (**37**). Compounds **36** and **37** have antifungal, antibacterial,

antioxidant, analgesic, antinociceptive, immunomodulatory, vasorelaxant, and neuroprotective activities. Compound **37** additionally shows antioxidant potential in respiratory illnesses and hepatoprotective properties (Balahbib *et al.*, 2021; de Carvalho *et al.*, 2020; Imran *et al.*, 2022; Maćzka *et al.*, 2023; Magi *et al.*, 2015; Mohammed *et al.*, 2024; Mondal *et al.*, 2021; Musterman *et al.*, 2018; Sharifi-Rad *et al.*, 2018; Singh *et al.*, 2021).

Figure 2

Aliphatic carboxylic acids, carbonyl compound and furan derivatives

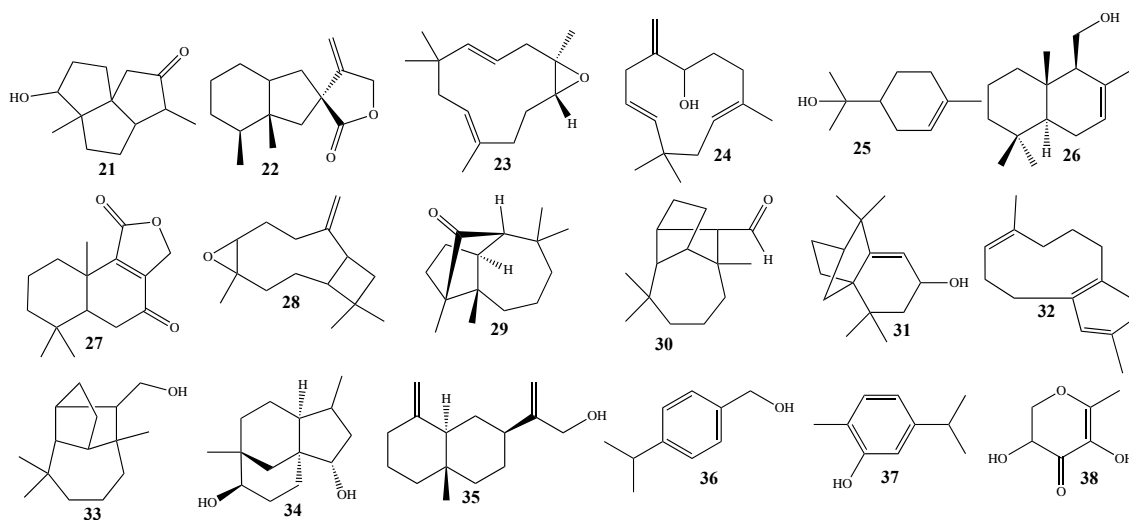


Phenylpropanoids and other phenolic compounds (**39–70**) were another class of secondary metabolites identified from the investigations of the extracts of BHA (Table 1 and 2; Fig. 4 and 5). Potential biological activities of these compounds include antidiabetic, antimicrobial, anticancer, antitumor, antioxidant, anti-inflammatory, analgesic, gastroprotective, cardiogenic, and insecticidal effects; they are also been reported to be used to treat neurodegenerative disorders and stimulate the immune system (Baptista *et al.*, 2022; Correia Alves *et al.*, 2023; Daniels *et al.*, 2022; Habtemariam, 2019; Makaremi *et al.*, 2021; Nisar

et al., 2021; Obulesu, 2021a, 2021b; Razavi and Hosseinzadeh, 2020; A. Sharma *et al.*, 2021; M. Sharma *et al.*, 2023; Sung *et al.*, 2012). Among these phenolics, *aR*-tumerone (**39**), eugenol (**40**), and its derivatives (*E*)-1-(4-hydroxy-3-methoxyphenyl)dec-4-en-3-one (6-Shogaol, **52**), 4-(4-hydroxy-3-methoxyphenyl)-2-butanone (Zingerone, **57**), and methyleugenol (**58**), which are reported to have various biological and pharmacological qualities (Baptista *et al.*, 2022; Correia Alves *et al.*, 2023; Daniels *et al.*, 2022; Habtemariam, 2019; Makaremi *et al.*, 2021; Nisar *et al.*, 2021; Obulesu, 2021a; Razavi and

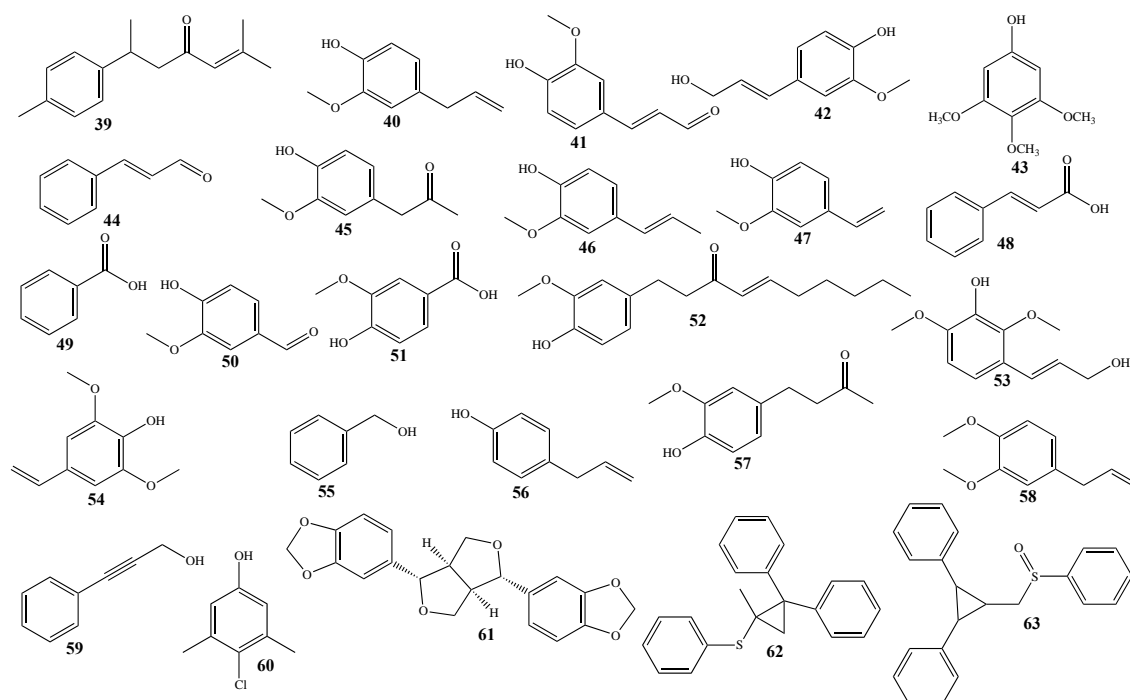
Figure 3

Terpenoids and a pyran derivative



The flavonoids, another significant group of phenolic natural products, were also found in the analyses. These include technochrysin (**64**), (S)-4H-1-benzopyran-4-one, 2,3-dihydro-5-hydroxy-7-methoxy-2-phenyl (Pinostrobin, **65**), homoeriodictyol (**66**), 3,4'-dimethoxy-5,7,3'-trihydroxyflavone (3,4'-dimethyl quercetin, **67**), and 5,6,7,3'4'-pentamethoxyflavone (Sinensetin, **68**). Pinostrobin (**65**) was the only flavonoid that was found in both studies (Table 1 and 2; Fig. 5). Compounds **66–68** were only detected in LC-MS/MS analysis, while compound **64** was detected in GC-MS/MS. Improvements in

memory impairment, antimalarial, antioxidant, anti-inflammatory, antimicrobial, and anticancer activities have been reported for the flavonoids. They have also been shown to inhibit α -glucosidase, exhibit anticancer, anti-obesity, anti-dementia, analgesic, vasorelaxant, and skeletal muscle hypertrophy activities (Table 3) (Al-Bzour *et al.*, 2024; Dunstan *et al.*, 2020; González *et al.*, 2022; Guo *et al.*, 2022; Han Jie *et al.*, 2021; Saquib *et al.*, 2020; Sun *et al.*, 2020; Wieczorek *et al.*, 2022; Wu *et al.*, 2023; Yuan *et al.*, 2024; Zhao *et al.*, 2023; Zhu *et al.*, 2024).

Figure 4*Phenylpropanoids and other phenolic derivatives*

Two coumarins, (-)-mellein (**69**) and 6,7-dimethylsculetin (Scoparone, **70**) were also among the phenolic secondary metabolites of the medicinal herb formulation that were found in this study (Tables 1 and 2). A variety of biological activities, including anti-inflammatory, antioxidant, anti-apoptotic, anti-fibrotic, and hypolipidemic, have been reported for scoparone (**70**). Scoparone (**70**) was identified in LC-MS/MS analysis of the methanol extract. The compound has also been used to treat cholestasis, jaundice, and liver dysfunction (Cai *et al.*, 2020; Hui *et al.*, 2020; Kowalczyk *et al.*, 2022; Wirasisya and Hohmann, 2023), whereas (-)-mellein is reported to have antifungal, anti-inflammatory and antibacterial activities (Table 3)(Li *et al.*, 2021; Revegla *et al.*, 2020; Turker and Gurel, 2005). Together with their well-known biological and pharmacological characteristics, the flavonoids (**66–68**) and scoparone (**70**) also have anti-fibrotic

and vasorelaxant qualities. The presence of these substances helps to maintain normal and smooth blood flow, preventing the thickening of the lung's air sac walls, and protecting the patient from thrombosis and breathing problems

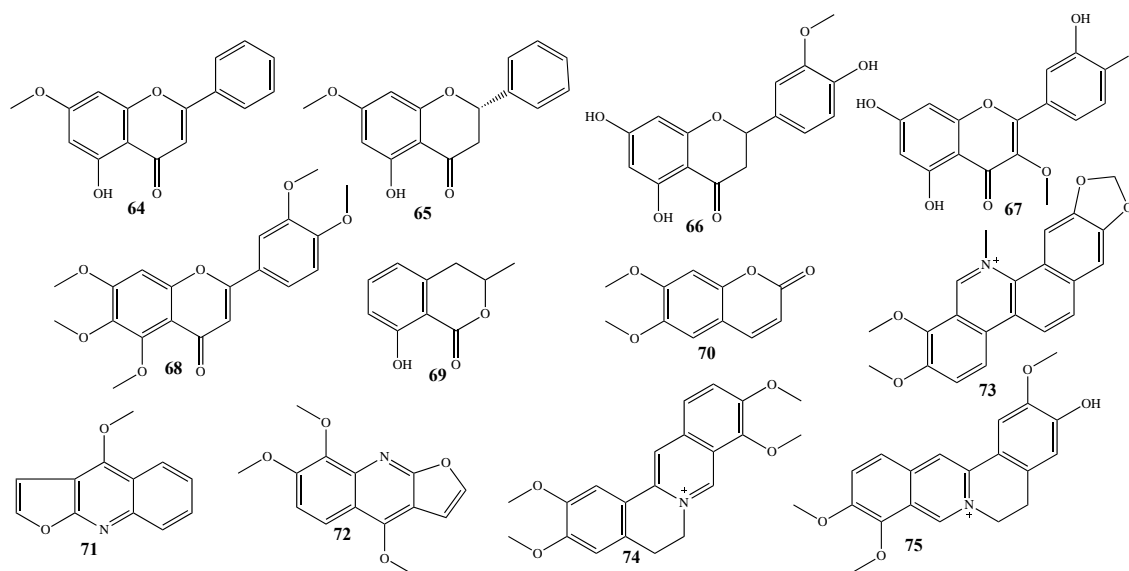
The alkaloids, dictamnine (**71**), 4,7,8-trimethoxyfuro[2,3-b]quinoline (skimmianine, **72**), and the protoberberine (benzophenanthridine) alkaloids chelerythrine (**73**), palmatine (**74**) and jatrorrhizine (**75**) were found to be among the secondary metabolites identified in the analyses. Compounds **66–69** and **73–75** were only observed in the LC-MS/MS analysis of the methanol extract (Table 2; Fig. 5). Table 3 shows the biological activities of the alkaloidal constituents of the formulation. Generally, a variety of biological activities have been reported for these compounds, for example, compound **71** is reported to have insecticidal and anti-inflammatory properties (Li *et al.*, 2024; Lu *et*

al., 2020; Lv *et al.*, 2015; Yang *et al.*, 2012), whereas compound **72**, on the other hand, has been reported to demonstrate anticholinesterase, antiviral, antibacterial, antifungal, anti-inflammatory, antioxidant, analgesic, anticonvulsant, cardiotoxic, and anthelmintic

properties (Li *et al.*, 2024; Lu *et al.*, 2020; Mutinda *et al.*, 2023; Powder-George, 2023; Yang *et al.*, 2012; Yao *et al.*, 2020). Further studies revealed compound **72** to possess *in vitro* antiviral activity against the measles virus (Anywar *et al.*, 2022).

Figure 5

Alkaloids, flavonoids and coumarins



According to reports, the protoberberine alkaloids (**73–75**) have beneficial effects on the cardiovascular system in addition to having antibacterial, antidiabetic, anti-inflammatory, antiviral, antiulcer, and antifungal qualities (Mfuh and Larionov, 2015; Mutinda *et al.*, 2023; Nyong *et al.*, 2015; Thawabteh *et al.*, 2019; Volleková *et al.*, 2003).

Chelerythrine (**73**), is reported to have anti-inflammatory and antiviral properties. Furthermore, it suppresses pulmonary inflammation and fibrosis. Additionally, it reduces eryptosis and prevents cerebral vasospasm (Chen *et al.*, 2022; He *et al.*, 2018; Kang *et al.*, 2022; Li *et al.*, 2024; Lu *et al.*, 2020; Valipour *et al.*, 2021). According to reports, palmatine (**74**) has anti-seizure, anti-cancer, anti-oxidant, anti-inflammatory, neuroprotective, anti-bacterial, and antiviral properties. It also regulates blood cholesterol levels (Grabarska *et al.*, 2021; Long *et*

al., 2019; Song *et al.*, 2018; Wu *et al.*, 2016; Yan *et al.*, 2017; Zhang *et al.*, 2012). Jatrorrhizine (**75**) on the other hand has also been shown to display similar activities to those of **73** and **74**, including anti-inflammatory, antibacterial, antitumor, blood flow enhancement, and mitotic activity (Deng and Wan, 2021; Fu *et al.*, 2023; Rolle *et al.*, 2021; Zhong *et al.*, 2022; Zhou *et al.*, 2022).

α -Terpineol (**25**), the lignan (+)-sesamin (**61**), skimmianine (**71**), and the protoberberine alkaloids **72–75**, were previously reported to be isolated from *Zanthoxylum* species, including *Z. chalybeum*, one of the species making up the herbal formulation (Adia *et al.*, 2016; Krohn *et al.*, 2011; Muganga *et al.*, 2014; Okagu *et al.*, 2021; Omosa *et al.*, 2021).

According to the results, the medicinal herb formulation contained a variety of secondary metabolites with a broad range of biological activities of pharmacological significance which

worked synergistically. The presence of these metabolites may have contributed to the effectiveness of the formulation in combating the SARS-CoV-2 virus, which is the cause of COVID-19 and other respiratory infectious viral diseases.

In addition to exhibiting anti-inflammatory, immunomodulatory, antiviral, antioxidant, antibacterial, and other biological properties which have been demonstrated by the majority of the chemicals found in the analyses, carvacrol (37) and scoparone (70) have also been shown to have anti-fibrotic and antioxidant potentials in respiratory illnesses, respectively (de Carvalho *et al.*, 2020; Hasan *et al.*, 2022; Hui *et al.*, 2020).

One major factor in the development of SARS-CoV-2, which leads to poor outcomes in COVID-19 patients, is lung fibrosis. Thus, the presence of compounds with anti-fibrotic and antioxidant potentials in respiratory illnesses, two biological processes are crucial in the fight against respiratory illnesses (de Carvalho *et al.*, 2020; Hasan *et al.*, 2022; Hui *et al.*, 2020).

Apart from the biological activities mentioned earlier, flavonoids are also known for their ability to relax blood vessels, suppress pulmonary inflammation, manage blood lipid levels and enhance blood flow. These properties are critical in the fight against respiratory infectious viral diseases like COVID-19 and the like because they avert blood thrombosis, which exacerbates patients' conditions. Vasorelaxation allows blood to pass through blood vessels more easily (de Carvalho *et al.*, 2020; Hao and Jiao, 2022; Hui *et al.*, 2020; Peng *et al.*, 2021; Wei *et al.*, 2024; Zhu *et al.*, 2022; Zuo *et al.*, 2024).

In addition to their previously listed actions, chelerythrine (73), palmatine (74), and jatrorrhizine (75), the three benzophenanthridine alkaloids, have also been shown to have the ability to suppress lung inflammation and fibrosis, regulate blood lipids, and enhance blood flow characteristics (Hao and Jiao, 2022; Hasan *et al.*, 2022; Peng *et al.*, 2021; Wei *et al.*, 2024; Zhu *et al.*, 2022; Zuo *et al.*, 2024).

Because pulmonary fibrosis and compromised immune regulation are major contributors to the pathophysiology of COVID-19 and lead to unfavourable outcomes for patients (Hasan *et al.*,

2022; Khan *et al.*, 2021; Nugraha *et al.*, 2020; Sharanya *et al.*, 2021; Zhang and Liu, 2020), the medicinal herbal formulation's efficacy in treating and managing COVID-19 patients can be attributed to the presence of secondary metabolites with antiviral, antioxidant, immunomodulatory, anti-inflammatory, and anti-fibrosis properties. The formulation may have potential applications as a preventive or curative measure for COVID-19 and other viral respiratory infections, as suggested by these data.

Conclusion

These investigations have shown that BHA extracts are rich in biologically active compounds with no mentioned toxicity. The biological characteristics of the previously described secondary metabolites have shown that the therapeutic herbal formulation contained a range of ingredients with almost similar biological effects. Due to the biological activities' synergistic combination effects of the secondary metabolites, the medicinal herb formulation demonstrated more efficacious in treating and managing COVID-19 patients and, consequently, other respiratory infectious viral diseases. The outcomes thus justify the use of the medicinal formulation because the herbal formulation's secondary metabolites in it are effective. The rationale for using the herbal mixture in the fight against respiratory viral infections is further strengthened by the reports of the safety of its constituent secondary metabolites.

Recommendations

Based on the results of this study, LC-MS/MS analyses of the hexane and ethanol extracts and the ethyl acetate layer are required to identify other secondary metabolites. A literature survey of the individual components revealed the presence of a variety of compounds, most of which were not observed in the current study, thus necessitating analyses of the other extracts. Furthermore, there is a necessity of developing the herbal formulation and other formulations with therapeutic potentials into more advanced phases of conventional medications and determining the appropriate dosages for the

herbal formulations. Lastly, using natural products that have therapeutic potential is advised; nevertheless, in order to prevent negative side effects, safety procedures must be taken.

References

- Abbasloo, E., Khaksari, M., Sanjari, M., Kobeissy, F., & Thomas, T. C. (2023). Carvacrol decreases blood-brain barrier permeability post-diffuse traumatic brain injury in rats. *Scientific Reports*, 13(1). <https://doi.org/10.1038/s41598-023-40915-x>.
- Adia, M. M., Emami, S. N., Byamukama, R., Faye, I., & Borg-Karlson, A. K. (2016). Antiplasmodial activity and phytochemical analysis of extracts from selected Ugandan medicinal plants. *Journal of Ethnopharmacology*, 186, 14–19. <https://doi.org/10.1016/j.jep.2016.03.047>.
- Ahmad, B., Rehman, M. U., Amin, I., Arif, A., Rasool, S., Bhat, S. A., Afzal, I., Hussain, I., Bilal, S., & Mir, M. U. R. (2015). A review on pharmacological properties of Zingerone (4-(4-Hydroxy-3-methoxyphenyl)-2-butanone). In *Scientific World Journal* (Vol. 2015). Hindawi Publishing Corporation. <https://doi.org/10.1155/2015/816364>.
- Aini, N. S., Kharisma, V. D., Widyananda, M. H., Murtadlo, A. A. A., Probojati, R. T., Turista, D. D. R., Tamam, M. B., Jakhmola, V., Sari, D. P., Albari, M. T., Pernamasari, D., Ghifari, M. A., Ghifari, M. R., Mandeli, R. S., Muhandi, Oktavia, B., Sari, T. K., Sriwahyuni, T., Azhari, P., ... Zainul, R. (2022). *In-silico* screening of bioactive compounds from *Syzygium cumini* L. and *Moringa oleifera* L. against SARS-CoV-2 via tetra inhibitors. *Pharmacognosy Journal*, 14(4), 267–272. <https://doi.org/10.5530/pj.2022.14.95>.
- Akaberi, T., Shourgashti, K., Emami, S. A., & Akaberi, M. (2021). Phytochemistry and pharmacology of alkaloids from *Glaucium* spp. In *Phytochemistry* (Vol. 191). Elsevier Ltd.

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<https://doi.org/10.1016/j.phytochem.2021.112923>.

- Akram, M., Tahir, I. M., Shah, S. M. A., Mahmood, Z., Altaf, A., Ahmad, K., Munir, N., Daniyal, M., Nasir, S., & Mehboob, H. (2018). Antiviral potential of medicinal plants against HIV, HSV, influenza, hepatitis, and coxsackievirus: A systematic review. *Phytotherapy Research*, 32(5), 811–822. <https://doi.org/10.1002/ptr.6024>.
- Al-Bzour, M. H., Bsieso, Y., Gammoh, O., Alqudah, M., Qnais, E. Y., Wedyan, M., & Alqudah, A. (2024). Exploring the antinociceptive potential of homoeriodictyol in nociception models. *Journal of Pharmacy and Pharmacognosy Research*, 12(4), 615–623. https://doi.org/10.56499/jppres23.1878_1_2.4.615.
- Ali, S. G., Ansari, M. A., Alzohairy, M. A., Almatroudi, A., Alomary, M. N., Alghamdi, S., Rehman, S., & Khan, H. M. (2021). Natural products and nutrients against different viral diseases: Prospects in prevention and treatment of sars-cov-2. *Medicina (Lithuania)*, 57(2), 1–12. <https://doi.org/10.3390/medicina57020169>.
- Alizadeh, M., Jalal, M., Hamed, K., Saber, A., Kheirouri, S., Fard Tabrizi, F. P., & Kamari, N. (2020). Recent updates on anti-inflammatory and antimicrobial effects of furan natural derivatives. In *Journal of Inflammation Research* (Vol. 13, pp. 451–463). Dove Medical Press Ltd. <https://doi.org/10.2147/JIR.S262132>.
- Anand, A. V., Balamuralikrishnan, B., Kaviya, M., Bharathi, K., Parithathvi, A., Arun, M., Senthilkumar, N., Velayuthaprabhu, S., Saradhadevi, M., Al-Dhabi, N. A., Arasu,

- M. V., Yattoo, M. I., Tiwari, R., & Dhama, K. (2021). Medicinal plants, phytochemicals, and herbs to combat viral pathogens including SARS-CoV-2. *Molecules*, 26(6), 1775. <https://doi.org/10.3390/molecules26061775>.
- Antwi-Baffour, S. (2014). The Place of Traditional Medicine in the African Society: The Science, Acceptance and Support. *American Journal of Health Research*, 2(2), 49. <https://doi.org/10.11648/j.ajhr.20140202.13>.
- Anywar, G. U., Kakudidi, E., Oryem-Origa, H., Schubert, A., & Jassoy, C. (2022). Cytotoxicity of medicinal plant species used by traditional healers in treating people suffering from HIV/AIDS in Uganda. *Frontiers in Toxicology*, 4. <https://doi.org/10.3389/ftox.2022.832780>.
- Aparna, V., Dileep, K. V., Mandal, P. K., Karthe, P., Sadasivan, C., & Haridas, M. (2012). Anti-inflammatory property of *n*-hexadecanoic acid: Structural evidence and kinetic assessment. *Chemical Biology and Drug Design*, 80(3), 434–439. <https://doi.org/10.1111/j.1747-0285.2012.01418.x>.
- Arcusa, R., Villaño, D., Marhuenda, J., Cano, M., Cerdà, B., & Zafrilla, P. (2022). Potential role of ginger (*Zingiber officinale* Roscoe) in the prevention of neurodegenerative diseases. In *Frontiers in Nutrition* (Vol. 9). Frontiers Media S.A. <https://doi.org/10.3389/fnut.2022.809621>.
- Augustin, K., Khabbush, A., Williams, S., Eaton, S., Orford, M., Cross, H., Heales, S. J. R., Walker, M. C., & Williams, R. S. B. (2018). Review mechanisms of action for the medium-chain triglyceride ketogenic diet in neurological and metabolic disorders (Vol. 17). www.thelancet.com/neurology.
- Balahbib, A., El Omari, N., Hachlafi, N. EL, Lakhdar, F., El Menyiy, N., Salhi, N., Mrabti, H. N., Bakrim, S., Zengin, G., & Bouyahya, A. (2021). Health beneficial and pharmacological properties of *p*-cymene. *Food and Chemical Toxicology*, 153. <https://doi.org/10.1016/j.fct.2021.112259>.
- Bao, Y., Yang, L., Fu, Q., Fu, Y., Tian, Q., Wang, C., & Huang, Q. (2023). The current situation of *Zanthoxylum bungeanum* industry and the research and application prospect. A review. In *Fitoterapia* (Vol. 164). Elsevier B.V. <https://doi.org/10.1016/j.fitote.2022.105380>.
- Baptista, B. G., Ribeiro, M., Cardozo, L. F., Leal, V. de O., Regis, B., & Mafra, D. (2022). Nutritional benefits of ginger for patients with non-communicable diseases. In *Clinical Nutrition ESPEN* (Vol. 49, pp. 1–16). Elsevier Ltd. <https://doi.org/10.1016/j.clnesp.2022.04.017>.
- Bertoncello, K. T., & Bonan, C. D. (2021). Zebrafish as a tool for the discovery of anticonvulsant compounds from botanical constituents. In *European Journal of Pharmacology* (Vol. 908). Elsevier B.V. <https://doi.org/10.1016/j.ejphar.2021.174342>.
- Bischoff-Kont, I., & Fürst, R. (2021). Benefits of ginger and its constituent 6-shogaol in inhibiting inflammatory processes. In *Pharmaceuticals* (Vol. 14, Issue 6). MDPI. <https://doi.org/10.3390/ph14060571>.
- Bischoff-Kont, I., Primke, T., Niebergall, L. S., Zech, T., & Fürst, R. (2022). Ginger constituent 6-shogaol inhibits inflammation- and angiogenesis-related cell functions in primary human endothelial cells. *Frontiers in Pharmacology*, 13. <https://doi.org/10.3389/fphar.2022.844767>.
- Bonetti, F., Brombo, G., & Zuliani, G. (2017). Nootropics, functional foods, and dietary patterns for prevention of cognitive decline. In *Nutrition and Functional Foods for Healthy Aging* (pp. 211–232). Elsevier Inc. <https://doi.org/10.1016/B978-0-12-805376-8.00019-8>.
- Boniface, P. K., & Ferreira, E. I. (2020). Opportunities and challenges for flavonoids as potential leads for the treatment of tuberculosis. In *Studies in Natural Products Chemistry* (Vol. 65, pp. 85–124). Elsevier B.V. <https://doi.org/10.1016/B978-0-12-817905-5.00003-2>.
- Boukandou Mounanga, M., Mewono, L., & Aboughe Angone, S. (2015). Toxicity studies of medicinal plants used in sub-Saharan Africa. *Journal of*

- Ethnopharmacology*, 174, 618–627. <https://doi.org/10.1016/j.jep.2015.06.005>.
- Cai, Y., Zheng, Q., Sun, R., Wu, J., Li, X., & Liu, R. (2020). Recent progress in the study of *Artemisiae scopariae* Herba (Yin Chen), a promising medicinal herb for liver diseases. In *Biomedicine and Pharmacotherapy* (Vol. 130). Elsevier Masson SAS. <https://doi.org/10.1016/j.biopha.2020.110513>.
- Cha, D. H., Roh, G. H., Hesler, S. P., Wallingford, A., Stockton, D. G., Park, S. K., & Loeb, G. M. (2021). 2-Pentylfuran: a novel repellent of *Drosophila suzukii*. *Pest Management Science*, 77(4), 1757–1764. <https://doi.org/10.1002/ps.6196>.
- Chavan, M. J., Wakte, P. S., & Shinde, D. B. (2010). Analgesic and anti-inflammatory activity of caryophyllene oxide from *Annona squamosa* L. bark. *Phytomedicine*, 17(2), 149–151. <https://doi.org/10.1016/j.phymed.2009.05.016>.
- Chen, N., Qi, Y., Ma, X., Xiao, X., Liu, Q., Xia, T., Xiang, J., Zeng, J., & Tang, J. (2022). Rediscovery of traditional plant medicine: An underestimated anticancer drug of chelerythrine. In *Frontiers in Pharmacology* (Vol. 13). Frontiers Media S.A. <https://doi.org/10.3389/fphar.2022.906301>.
- Cicalău, G. I. P., Babes, P. A., Calniceanu, H., Popa, A., Ciavoi, G., Iova, G. M., Ganea, M., & Scrobotă, I. (2021). Anti-inflammatory and antioxidant properties of carvacrol and magnolol, in periodontal disease and diabetes mellitus. In *Molecules* (Vol. 26, Issue 22). MDPI. <https://doi.org/10.3390/molecules26226899>.
- Colunga Biancatelli, R. M. L., Berrill, M., Catravas, J. D., & Marik, P. E. (2020). Quercetin and vitamin C: An Experimental, synergistic therapy for the prevention and treatment of SARS-CoV-2 related disease (COVID-19). *Frontiers in Immunology*, 11. <https://doi.org/10.3389/fimmu.2020.01451>.
- Conti, P., Gallenga, C. E., Tetè, G., Caraffa, A., Ronconi, G., Younes, A., Toniato, E., Ross, R., & Kritas, S. K. (2020). How to reduce the likelihood of coronavirus-19 (CoV-19 or SARS-CoV-2) infection and lung inflammation mediated by IL-1. *Journal of Biological Regulators and Homeostatic Agents*, 34(2), 333–338. <https://doi.org/10.23812/Editorial-Conti-2>.
- Correia Alves, E. S., Wilairatana, P., Macedo da Cruz, M. J., Campos, L. A. N. L., Lopes e Silva, M. R., Alves, D. S., Araújo, I. M., dos Santos, F. A. V., de Farias, P. A. M., Vasconcelos, E. M. G. M. de, Siyadatpanah, A., Coutinho, H. D. M., & Figueredo, F. G. (2023). Bioactivities and ethnopharmacology of *Sesamum indicum* L seed oil. *LWT*, 185. <https://doi.org/10.1016/j.lwt.2023.115120>.
- Croley, C. R., Pumarol, J., Delgadillo, B. E., Cook, A. C., Day, F., Kaceli, T., Ward, C. C., Husain, I., Husain, A., Banerjee, S., & Bishayee, A. (2023). Signaling pathways driving ocular malignancies and their targeting by bioactive phytochemicals. In *Pharmacology and Therapeutics* (Vol. 248). Elsevier Inc. <https://doi.org/10.1016/j.pharmthera.2023.108479>.
- Dalibalta, S., Majdalawieh, A. F., & Manjikian, H. (2020). Health benefits of sesamin on cardiovascular disease and its associated risk factors. In *Saudi Pharmaceutical Journal* (Vol. 28, Issue 10, pp. 1276–1289). Elsevier B.V. <https://doi.org/10.1016/j.jsps.2020.08.018>.
- Daniels, C. C., Isaacs, Z., Finelli, R., & Leisegang, K. (2022). The efficacy of *Zingiber officinale* on dyslipidaemia, blood pressure, and inflammation as cardiovascular risk factors: A systematic review. In *Clinical Nutrition ESPEN* (Vol. 51, pp. 72–82). Elsevier Ltd. <https://doi.org/10.1016/j.clnesp.2022.08.031>.
- Dasgupta, A. (2019). Anti-inflammatory Herbal Supplements. In *Translational Inflammation* (pp. 69–91). Elsevier. <https://doi.org/10.1016/B978-0-12-813832-8.00004-2>.
- de Carvalho, F. O., Silva, É. R., Gomes, I. A., Santana, H. S. R., do Nascimento Santos, D., de Oliveira Souza, G. P., de Jesus Silva, D., Monteiro, J. C. M., de Albuquerque Júnior, R. L. C., de Souza Araújo, A. A., & Nunes, P. S. (2020). Anti-inflammatory and antioxidant activity of carvacrol in the

- respiratory system: A systematic review and meta-analysis. In *Phytotherapy Research* (Vol. 34, Issue 9, pp. 2214–2229). John Wiley and Sons Ltd. <https://doi.org/10.1002/ptr.6688>.
- Deepa, S., Sujatha, K., & Velmurugan, D. (2019). The identification of bioactive compounds from *Turbinaria ornata* (Turner) J. Agaradh and computational studies. *Pharmacognosy Journal*, 11(5), 873–883. <https://doi.org/10.5530/pj.2019.11.140>.
- Deng, B., & Wan, M. (2021). Jatrorrhizine inhibits liver cancer cell growth by targeting the expressions of miR-221-3p and miR-15b-5p. *Tropical Journal of Pharmaceutical Research*, 20(8), 1573–1578. <https://doi.org/10.4314/tjpr.v20i8.4>.
- Dhama, K., Karthik, K., Khandia, R., Munjal, A., Tiwari, R., Rana, R., Khurana, S. K., Sana Ullah, Khan, R. U., Alagawany, M., Farag, M. R., Dadar, M., & Joshi, S. K. (2018). Medicinal and therapeutic potential of herbs and plant metabolites/extracts countering viral pathogens - Current knowledge and future prospects. *Current Drug Metabolism*, 19(3), 236–263. <https://doi.org/10.2174/1389200219666180129145252>.
- Ding, J., Wang, L., He, C., Zhao, J., Si, L., & Huang, H. (2021). *Artemisia scoparia*: Traditional uses, active constituents and pharmacological effects. In *Journal of Ethnopharmacology* (Vol. 273). Elsevier Ireland Ltd. <https://doi.org/10.1016/j.jep.2021.113960>.
- Dunstan, M. S., Robinson, C. J., Jervis, A. J., Yan, C., Carbonell, P., Hollywood, K. A., Currin, A., Swainston, N., Le Feuvre, R., Micklefield, J., Faulon, J. L., Breitling, R., Turner, N., Takano, E., & Scrutton, N. S. (2020). Engineering *Escherichia coli* towards de novo production of gatekeeper (2S)-flavanones: Naringenin, pinocembrin, eriodictyol and homoeriodictyol. *Synthetic Biology*, 5(1). <https://doi.org/10.1093/SYNBIO/YSA012>.
- Ekor, M. (2014a). Nephrotoxicity and nephroprotective potential of African medicinal plants. In *Toxicological Survey of African Medicinal Plants* (pp. 357–393). Elsevier Inc. <https://doi.org/10.1016/B978-0-12-800018-2.00012-1>.
- Ekor, M. (2014b). The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in Pharmacology*, 4. <https://doi.org/10.3389/fphar.2013.00177>.
- Epifano, F., Fiorito, S., Genovese, S., Granica, S., Vitalini, S., & Zidorn, C. (2015). Phytochemistry of the genus *Skimmia* (Rutaceae). In *Phytochemistry* (Vol. 115, Issue 1, pp. 27–43). Elsevier Ltd. <https://doi.org/10.1016/j.phytochem.2015.02.014>.
- Farmanpour-Kalalagh, K., Beyraghdar Kashkooli, A., Babaei, A., Rezaei, A., & van der Krol, A. R. (2022). Artemisinins in combating viral infections like SARS-CoV-2, inflammation and cancers and options to meet increased global demand. *Frontiers in Plant Science*, 13. <https://doi.org/10.3389/fpls.2022.780257>.
- Fatima, N., & Nayeem, N. (2016). Toxic effects as a result of herbal medicine intake. In *Toxicology - New Aspects to This Scientific Conundrum*. InTech. <https://doi.org/10.5772/64468>.
- Fidy, K., Fiedorowicz, A., Strzadala, L., & Szumny, A. (2016). β -caryophyllene and β -caryophyllene oxide—natural compounds of anticancer and analgesic properties. In *Cancer Medicine* (Vol. 5, Issue 10, pp. 3007–3017). Blackwell Publishing Ltd. <https://doi.org/10.1002/cam4.816>.
- Fu, M., Chen, N., Zhou, Y., Chen, S., Xu, W., Gong, S., & Geng, L. (2023). Jatrorrhizine suppresses murine-norovirus-triggered N-GSDMD-dependent pyroptosis in RAW264.7 macrophages. *Vaccines*, 11(1). <https://doi.org/10.3390/vaccines11010164>.
- Gasmi, A., Mujawdiya, P. K., Lysiuk, R., Shanaida, M., Peana, M., Gasmi Benahmed, A., Beley, N., Kovalska, N., & Björklund, G. (2022). Quercetin in the prevention and treatment of coronavirus infections: A Focus on SARS-CoV-2. *Pharmaceuticals*, 15(9), 1049. <https://doi.org/10.3390/ph15091049>.
- González, A. S., Soto Tellini, V. H., & Benjumea Gutiérrez, D. M. (2022). Study of the dermal anti-inflammatory, antioxidant, and

- analgesic activity of pinostrobin. *Heliyon*, 8(9).
<https://doi.org/10.1016/j.heliyon.2022.e10413>.
- Grabarska, A., Wróblewska-Iuczka, P., Kukula-Koch, W., Łuszczki, J. J., Kalpoutzakis, E., Adamczuk, G., Skaltsounis, A. L., & Stepulak, A. (2021). Palmatine, a bioactive protoberberine alkaloid isolated from *Berberis cretica*, inhibits the growth of human estrogen receptor-positive breast cancer cells and acts synergistically and additively with doxorubicin. *Molecules*, 26(20).
<https://doi.org/10.3390/molecules26206253>.
- Guo, P., Zeng, M., Wang, S., Cao, B., Liu, M., Zhang, Y., Jia, J., Zhang, Q., Zhang, B., Wang, R., Zheng, X., & Feng, W. (2022). Eriodictyol and homoeriodictyol improve memory impairment in A β 25-35-induced mice by inhibiting the NLRP3 inflammasome. *Molecules*, 27(8).
<https://doi.org/10.3390/molecules27082488>.
- Habtemariam, S. (2019). The chemical and pharmacological basis of cloves (*Syzygium aromaticum* (L.) Merr. and L.M.Perry) as potential therapy for type 2 diabetes and associated diseases. In *Medicinal Foods as Potential Therapies for Type-2 Diabetes and Associated Diseases* (pp. 551-578). Elsevier.
<https://doi.org/10.1016/b978-0-08-102922-0.00016-x>.
- Hadipour, E., Emami, S. A., Tayarani-Najaran, N., & Tayarani-Najaran, Z. (2023). Effects of sesame (*Sesamum indicum* L.) and bioactive compounds (sesamin and sesamol) on inflammation and atherosclerosis: A review. In *Food Science and Nutrition* (Vol. 11, Issue 7, pp. 3729-3757). John Wiley and Sons Inc.
<https://doi.org/10.1002/fsn3.3407>.
- Han Jie, L., Jantan, I., Yusoff, S. D., Jalil, J., & Husain, K. (2021). Sinensetin: An insight on its pharmacological activities, mechanisms of action and toxicity. In *Frontiers in Pharmacology* (Vol. 11). Frontiers Media S.A.
<https://doi.org/10.3389/fphar.2020.553404>.
- Hao, M., & Jiao, K. (2022). Jatrorrhizine reduces myocardial infarction-induced apoptosis and fibrosis through inhibiting p53 and TGF- β 1/Smad2/3 pathways in mice. *Acta Chirurgica Brasileira*, 37(7).
<https://doi.org/10.1590/acb370705>.
- Hasan, M. M., Ahmed, Q. U., Soad, S. Z. M., Latip, J., Taher, M., Syafiq, T. M. F., Sarian, M. N., Alhassan, A. M., & Zakaria, Z. A. (2017). Flavonoids from *Tetracera indica* Merr. induce adipogenesis and exert glucose uptake activities in 3T3-L1 adipocyte cells. *BMC Complementary and Alternative Medicine*, 17(1).
<https://doi.org/10.1186/s12906-017-1929-3>.
- Hasan, M., Paul, N. C., Paul, S. K., Saikat, A. S. M., Akter, H., Mandal, M., & Lee, S. S. (2022). Natural product-based potential therapeutic interventions of pulmonary fibrosis. In *Molecules* (Vol. 27, Issue 5). MDPI.
<https://doi.org/10.3390/molecules27051481>.
- He, N., Wang, P., Wang, P., Ma, C., & Kang, W. (2018). Antibacterial mechanism of chelerythrine isolated from root of *Toddalia asiatica* (Linn) Lam. *BMC Complementary and Alternative Medicine*, 18(1).
<https://doi.org/10.1186/s12906-018-2317-3>.
- Huang, S. M., Chuang, C. H., Rejano, C. J. F., Tayo, L. L., Hsieh, C. Y., Huang, S. K. H., & Tsai, P. W. (2023). Sesamin: A promising therapeutic agent for ameliorating symptoms of diabetes. *Molecules*, 28(21).
<https://doi.org/10.3390/molecules28217255>.
- Hui, Y., Wang, X., Yu, Z., Fan, X., Cui, B., Zhao, T., Mao, L., Feng, H., Lin, L., Yu, Q., Zhang, J., Wang, B., Chen, X., Zhao, X., & Sun, C. (2020). Scoparone as a therapeutic drug in liver diseases: Pharmacology, pharmacokinetics and molecular mechanisms of action. In *Pharmacological Research* (Vol. 160). Academic Press.
<https://doi.org/10.1016/j.phrs.2020.105170>.
- Imran, M., Aslam, M., Alsagaby, S. A., Saeed, F., Ahmad, I., Afzaal, M., Arshad, M. U., Abdelgawad, M. A., El-Ghorab, A. H., Khames, A., Shariati, M. A., Ahmad, A., Hussain, M., Imran, A., & Islam, S. (2022). Therapeutic application of carvacrol: A

- comprehensive review. In *Food Science and Nutrition* (Vol. 10, Issue 11, pp. 3544–3561). John Wiley and Sons Inc. <https://doi.org/10.1002/fsn3.2994>.
- Insera, P., & Brooks, A. (2017). Getting to the root of chronic inflammation: Ginger's anti-inflammatory properties. In *Nutritional Modulators of Pain in the Aging Population* (pp. 67–73). Elsevier Inc. <https://doi.org/10.1016/B978-0-12-805186-3.00005-9>.
- Kang, K., Jiang, H., Zhang, S., & Cheng, B. (2022). Antitumor effects of chelerythrine: A literature review. In *Natural Product Communications* (Vol. 17, Issue 6). SAGE Publications Inc. <https://doi.org/10.1177/1934578X221103028>.
- Kaul, R., Paul, P., Kumar, S., Büsselberg, D., Dwivedi, V. D., & Chaari, A. (2021). Promising antiviral activities of natural flavonoids against SARS-CoV-2 targets: Systematic review. *International Journal of Molecular Sciences*, 22(20), 11069. <https://doi.org/10.3390/ijms222011069>.
- Kaur, K., Jain, M., Kaur, T., & Jain, R. (2009). Antimalarials from nature. In *Bioorganic and Medicinal Chemistry* (Vol. 17, Issue 9, pp. 3229–3256). <https://doi.org/10.1016/j.bmc.2009.02.050>
- Khadka, D., Dhamala, M. K., Li, F., Aryal, P. C., Magar, P. R., Bhatta, S., Thakur, M. S., Basnet, A., Cui, D., & Shi, S. (2021). The use of medicinal plants to prevent COVID-19 in Nepal. *Journal of Ethnobiology and Ethnomedicine*, 17(1), 26. <https://doi.org/10.1186/s13002-021-00449-w>.
- Khan, T., Khan, M. A., Mashwani, Z. ur R., Ullah, N., & Nadhman, A. (2021). Therapeutic potential of medicinal plants against COVID-19: The role of antiviral medicinal metabolites. In *Biocatalysis and Agricultural Biotechnology* (Vol. 31). Elsevier Ltd. <https://doi.org/10.1016/j.bcab.2020.101890>.
- Kim, J., Seo, S. M., Lee, S. G., Shin, S. C., & Park, I. K. (2008). Nematicidal activity of plant essential oils and components from coriander (*Coriandrum sativum*), oriental sweetgum (*Liquidambar orientalis*), and valerian (*Valeriana wallichii*) essential oils against pine wood nematode (*Bursaphelenchus xylophilus*). *Journal of Agricultural and Food Chemistry*, 56(16), 7316–7320. <https://doi.org/10.1021/jf800780f>.
- Kowalczyk, J., Budzyńska, B., Kurach, Ł., Pellegata, D., El Sayed, N. S., Gertsch, J., & Skalicka-Woźniak, K. (2022). Neuropsychopharmacological profiling of scoparone in mice. *Scientific Reports*, 12(1). <https://doi.org/10.1038/s41598-021-04741-3>.
- Kraljić, K., Škevin, D., Barišić, L., Kovačević, M., Obranović, M., & Jurčević, I. (2015). Changes in 4-vinylsyringol and other phenolics during rapeseed oil refining. *Food Chemistry*, 187, 236–242. <https://doi.org/10.1016/j.foodchem.2015.04.039>.
- Krohn, K., Cludius-Brandt, S., Schulz, B., Sreelekha, M., & Shafi, P. M. (2011). Isolation, structure elucidation, and biological activity of a new alkaloid from *Zanthoxylum rhetsa*. *Natural Product Communications*, 6(11), 1595–1596. PMID: 22224269.
- Kushwaha, P. P., Vardhan, P. S., Kumari, P., Mtewa, A. G., & Kumar, S. (2019). Bioactive lead compounds and targets for the development of antimalarial drugs. In *Phytochemicals as Lead Compounds for New Drug Discovery* (pp. 305–316). Elsevier. <https://doi.org/10.1016/B978-0-12-817890-4.00020-2>.
- Kuwahara, H., Kanazawa, A., Wakamatu, D., Morimura, S., Kida, K., Akaike, T., & Maeda, H. (2004). Antioxidative and Antimutagenic Activities of 4-Vinyl-2,6-dimethoxyphenol (Canolol) Isolated from Canola Oil. *Journal of Agricultural and Food Chemistry*, 52(14), 4380–4387. <https://doi.org/10.1021/jf040045>.
- Legault, J., & Pichette, A. (2010). Potentiating effect of β -caryophyllene on anticancer activity of α -humulene, isocaryophyllene and paclitaxel. *Journal of Pharmacy and Pharmacology*, 59(12), 1643–1647. <https://doi.org/10.1211/jpp.59.12.0005>.
- Li, S. Y., Chen, C., Zhang, H. Q., Guo, H. Y., Wang, H., Wang, L., Zhang, X., Hua, S. N., Yu, J., Xiao, P. G., Li, R. S., & Tan, X. (2005). Identification of natural compounds with

- antiviral activities against SARS-associated coronavirus. *Antiviral Research*, 67(1), 18–23. <https://doi.org/10.1016/j.antiviral.2005.02.007>.
- Li, X., Wang, Q., Liu, L., Shi, Y., Hong, Y., Xu, W., Xu, H., Feng, J., Xie, M., Li, Y., Yang, B., & Zhang, Y. (2024). The therapeutic potential of four main compounds of *Zanthoxylum nitidum* (Roxb.) DC: A Comprehensive study on biological processes, anti-inflammatory effects, and myocardial toxicity. *Pharmaceuticals*, 17(4). <https://doi.org/10.3390/ph17040524>.
- Li, Y., Gai, Z., Wang, C., Li, P., & Li, B. (2021). Identification of mellein as a pathogenic substance of *Botryosphaeria dothidea* by UPLC-MS/MS analysis and phytotoxic bioassay. *Journal of Agricultural and Food Chemistry*, 69(30), 8471–8481. <https://doi.org/10.1021/acs.jafc.1c03249>.
- Lima, N., &rade, T., Acquah, K., Oliveira, M., Gois, K., & Medeiros, L. (2021). Phytochemicals as potential antiviral agents in SARS-CoV-2 therapy: An update. *Química Nova*. <https://doi.org/10.21577/0100-4042.20170714>.
- Liu, M., Sun, S., Meng, Y., Wang, L., Liu, H., Shi, W., Zhang, Q., Xu, W., Sun, B., & Xu, J. (2023). Benzophenanthridine alkaloid chelerythrine elicits necroptosis of gastric cancer cells via selective conjugation at the redox hyperreactive C-terminal Sec498 residue of cytosolic selenoprotein thioredoxin reductase. *Molecules*, 28(19). <https://doi.org/10.3390/molecules28196842>.
- Mensah L. K., Komlaga, M., Forkuo G., D., Firempong, A., Anning C., K., A., & A. Dickson, R. (2019). Toxicity and safety implications of herbal medicines used in Africa. In *Herbal Medicine*. IntechOpen. <https://doi.org/10.5772/intechopen.72437>
- Long, J., Song, J., Zhong, L., Liao, Y., Liu, L., & Li, X. (2019). Palmatine: A review of its pharmacology, toxicity and pharmacokinetics. In *Biochimie* (Vol. 162, pp. 176–184). Elsevier B.V. <https://doi.org/10.1016/j.biochi.2019.04.008>.
- Lu, Q., Ma, R., Yang, Y., Mo, Z., Pu, X., & Li, C. (2020). *Zanthoxylum nitidum* (Roxb.) DC: Traditional uses, phytochemistry, pharmacological activities and toxicology. In *Journal of Ethnopharmacology* (Vol. 260). Elsevier Ireland Ltd. <https://doi.org/10.1016/j.jep.2020.112946>.
- Luo, Y., Chen, X., Che, J. X., Zhang, Y., Ouyang, Q., & Tao, N. (2023). (E)-2-Octenal suppresses the growth of a prochloraz-resistant *Penicillium italicum* strain and its potential antifungal mechanisms. *Postharvest Biology and Technology*, 205. <https://doi.org/10.1016/j.postharvbio.2023.112515>.
- Lv, M., Xu, P., Tian, Y., Liang, J., Gao, Y., Xu, F., Zhang, Z., & Sun, J. (2015). Medicinal uses, phytochemistry and pharmacology of the genus *Dictamnus* (Rutaceae). In *Journal of Ethnopharmacology* (Vol. 171, pp. 247–263). Elsevier Ireland Ltd. <https://doi.org/10.1016/j.jep.2015.05.053>.
- Mączka, W., Twardawska, M., Grabarczyk, M., & Wińska, K. (2023). Carvacrol—A natural phenolic compound with antimicrobial properties. In *Antibiotics* (Vol. 12, Issue 5). MDPI. <https://doi.org/10.3390/antibiotics12050824>.
- Magi, G., Marini, E., & Facinelli, B. (2015). Antimicrobial activity of essential oils and carvacrol, and synergy of carvacrol and erythromycin, against clinical, erythromycin-resistant Group A *Streptococci*. *Frontiers in Microbiology*, 6(MAR). <https://doi.org/10.3389/fmicb.2015.00165>.
- Mahomoodally, M. F. (2013). Traditional medicines in Africa: An appraisal of ten potent African medicinal plants. In *Evidence-based Complementary and Alternative Medicine* (Vol. 2013). <https://doi.org/10.1155/2013/617459>.
- Majdalawieh, A. F., Youssef, S. M., Abu-Yousef, I. A., & Nasrallah, G. K. (2022). Immunomodulatory and anti-inflammatory effects of sesamin: mechanisms of action and future directions. In *Critical Reviews in Food Science and Nutrition* (Vol. 62, Issue 18, pp. 5081–5112). Taylor and Francis Ltd. <https://doi.org/10.1080/10408398.2021.1881438>.

- Makangara, J. J., Mshandete, A. M., Mbega, E. R., Nyika, J. R., Mbago, F., Ndilanh, E. G., Nyika, R. J., & Nyika, J. J. (2024). Review on the secondary metabolites, biological properties, and ethnomedicinal uses of the component species of the buheri wa afya formula used to treat COVID-19 in Tanzania. In *Phytomedicine Plus* (Vol. 4, Issue 1). Elsevier B.V. <https://doi.org/10.1016/j.phyplu.2023.100508>.
- Makaremi, S., Ganji, A., Ghazavi, A., & Mosayebi, G. (2021). Inhibition of tumor growth in CT-26 colorectal cancer-bearing mice with alcoholic extracts of *Curcuma longa* and *Rosmarinus officinalis*. *Gene Reports*, 22. <https://doi.org/10.1016/j.genrep.2020.101006>.
- Malarvizhi, D. A. P. M. P., Sowmya, S., Perumal, P. C., Oirere, E. K., & Gopalakrishnan, V. K. (2015). Antioxidant properties and analysis of bioactive compounds present in n-hexane root extract of *Zaleya decandra*. *International Journal of Pharmaceutical Sciences Review and Research*, 34(2), 118–123.
- Mani, J. S., Johnson, J. B., Steel, J. C., Broszczak, D. A., Neilsen, P. M., Walsh, K. B., & Naiker, M. (2020). Natural product-derived phytochemicals as potential agents against coronaviruses: A review. In *Virus Research* (Vol. 284). Elsevier B.V. <https://doi.org/10.1016/j.virusres.2020.197989>.
- Matos, M. A. R., Miranda, M. S., & Morais, V. M. F. (2008). 3,4,5-Trimethoxyphenol: A combined experimental and theoretical thermochemical investigation of its antioxidant capacity. *Journal of Chemical Thermodynamics*, 40(4), 625–631. <https://doi.org/10.1016/j.jct.2007.11.006>.
- Mawa, J., Rahman, M. A., Hashem, M. A., & Juwel Hosen, M. (2019). *Lea macrophylla* root extract upregulates the mRNA expression for antioxidative enzymes and repairs the necrosis of pancreatic β -cell and kidney tissues in fructose-fed Type 2 diabetic rats. *Biomedicine and Pharmacotherapy*, 110, 74–84. <https://doi.org/10.1016/j.biopha.2018.11.033>.
- Mbaveng, A. T., & Kuete, V. (2017). *Zingiber officinale*. In *Medicinal Spices and Vegetables from Africa: Therapeutic Potential Against Metabolic, Inflammatory, Infectious and Systemic Diseases* (pp. 627–639). Elsevier Inc. <https://doi.org/10.1016/B978-0-12-809286-6.00030-3>.
- Melo, M. N. de O., Batista, J. V. da C., Peñaloza, E. M. C., Oliveira, A. P., Garrett, R., Baumgartner, S., & Holandino, C. (2023). A scoping review of genus viscum: biological and chemical aspects of alcoholic extracts. In *Plants* (Vol. 12, Issue 9). MDPI. <https://doi.org/10.3390/plants12091811>.
- Mfuh, A. M., & Larionov, O. V. (2015). Heterocyclic N-oxides-an emerging class of therapeutic agents. *Curr Med Chem.*, 22(24), 2819–2850. <https://doi.org/10.2174/0929867322666150619104007>.
- Michailidis, D., Angelis, A., Aligiannis, N., Mitakou, S., & Skaltsounis, L. (2019). Recovery of sesamin, sesamolin, and minor lignans from sesame oil using solid support-free liquid-liquid extraction and chromatography techniques and evaluation of their enzymatic inhibition properties. *Frontiers in Pharmacology*, 10(JUN). <https://doi.org/10.3389/fphar.2019.00723>.
- Mohammed, F. S., Sevindik, M., Uysal, İ., Česko, C., & Koraqi, H. (2024). Chemical composition, biological activities, uses, nutritional and mineral contents of cumin (*Cuminum cyminum*). In *Measurement: Food* (Vol. 14). Elsevier Ltd. <https://doi.org/10.1016/j.meafoo.2024.100157>.
- Mondal, A., Bose, S., Mazumder, K., & Khanra, R. (2021). Carvacrol (*Origanum vulgare*): Therapeutic properties and molecular mechanisms. In *Advanced Structured Materials* (Vol. 140, pp. 437–462). Springer Science and Business Media Deutschland GmbH. https://doi.org/10.1007/978-3-030-54027-2_13.
- Morais, A. N. P., Lima, L. F., Silva, A. F. B., Lienou, L. L., Ferreira, A. C. A., Watanabe, Y. F., Joaquim, D. C., Alves, B. G., Pereira, A. F., Alves, D. R., Oliveira, A. C., Morais, S. M., Magalhães-Padilha, D. M., Figueiredo, J. R., & Gastal, E. L. (2023). Effect of carvacrol antioxidant capacity on oocyte maturation and embryo production in cattle. *Zygote (Cambridge, England)*, 31(2),

- 173–179.
<https://doi.org/10.1017/S0967199422000673>.
- Muganga, R., Angenot, L., Tits, M., & Frédérick, M. (2014). *In vitro* and *in vivo* antiplasmodial activity of three Rwandan medicinal plants and identification of their active compounds. *Planta Medica*, 80(6), 482–489.
<https://doi.org/10.1055/s-0034-1368322>.
- Mukai, A., Takahashi, K., & Ashitani, T. (2018). Antifungal activity of longifolene and its autoxidation products. *European Journal of Wood and Wood Products*, 76(3), 1079–1082.
<https://doi.org/10.1007/s00107-017-1281-9>.
- Mungali, M., Sharma, N., & Gauri. (2020). Caprylic/capric triglyceride. In *Naturally Occurring Chemicals against Alzheimer's Disease* (pp. 139–146). Elsevier.
<https://doi.org/10.1016/B978-0-12-819212-2.00011-6>.
- Musterman, M., Placeholder, P., Khaleel, C., Tabanca, N., & Buchbauer, G. (2018). The First Decade (1964-1972) What is so different about neuroenhancement? Was ist so anders am neuroenhancement? Pharmacological and mental self-transformation in ethic comparison Pharmakologische und mentale Selbstveränderung im ethischen Vergleich α -Terpineol, a natural monoterpene: A review of its biological properties. *Journal Xyz*, 16(2), 122–135.
<https://doi.org/10.1515/xyz-2017-0010>.
- Mutinda, E. S., Kimutai, F., Mkala, E. M., Waswa, E. N., Odago, W. O., Nanjala, C., Ndungu, C. N., Gichua, M. K., Njire, M. M., Gituru, R. W., & Hu, G. W. (2023). Ethnobotanical uses, phytochemistry and pharmacology of pantropical genus *Zanthoxylum* L. (Rutaceae): An update. In *Journal of Ethnopharmacology* (Vol. 303). Elsevier Ireland Ltd.
<https://doi.org/10.1016/j.jep.2022.115895>.
- Nair, A., Chattopadhyay, D., & Saha, B. (2018). Plant-derived immunomodulators. In *New Look to Phytomedicine: Advancements in Herbal Products as Novel Drug Leads* (pp. 435–499). Elsevier.
<https://doi.org/10.1016/B978-0-12-814619-4.00018-5>.
- Nasri, H., & Shirzad, H. (2013). Toxicity and safety of medicinal plants. In *Journal of HerbMed Pharmacology Journal homepage: J HerbMed Pharmacol* (Vol. 2, Issue 2).
<http://www.herbmedpharmacol.com>.
- Nisar, M. F., Khadim, M., Rafiq, M., Chen, J., Yang, Y., & Wan, C. C. (2021). Pharmacological properties and health benefits of eugenol: A comprehensive review. In *Oxidative Medicine and Cellular Longevity* (Vol. 2021). Hindawi Limited.
<https://doi.org/10.1155/2021/2497354>.
- Nugraha, R. V., Ridwansyah, H., Ghazali, M., Khairani, A. F., & Atik, N. (2020). Traditional herbal medicine candidates as complementary treatments for COVID-19: A review of their mechanisms, pros and cons. In *Evidence-based Complementary and Alternative Medicine* (Vol. 2020). Hindawi Limited.
<https://doi.org/10.1155/2020/2560645>.
- Nyong, E. E., Odeniyi, M. A., & Moody, J. (2015). *In vitro* and *in vivo* antimicrobial evaluation of alkaloidal extracts of *Enantia chlorantha* stem bark and their formulated ointments native and modified polymers in drug delivery View project Centre for drug discovery development and production (CDDDP) View project. *Acta Pol Pharm*, 72(1), 147–152.
<https://www.researchgate.net/publication/271447639>.
- Obulesu, M. (2021a). Health benefits of turmeric: Emphasis on anticancer activity. In *Turmeric and Curcumin for Neurodegenerative Diseases* (pp. 3–18). Elsevier.
<https://doi.org/10.1016/b978-0-12-822448-9.00006-6>.
- Obulesu, M. (2021b). Turmeric products in Parkinson's disease treatment. In *Turmeric and Curcumin for Neurodegenerative Diseases* (pp. 73–87). Elsevier.
<https://doi.org/10.1016/b978-0-12-822448-9.00002-9>.
- Okagu, I. U., Ndefo, J. C., Aham, E. C., & Udenigwe, C. C. (2021). *Zanthoxylum* species: A review of traditional uses, phytochemistry and pharmacology in relation to cancer, infectious diseases and sickle cell anemia. In *Frontiers in Pharmacology* (Vol. 12). Frontiers Media S.A.

- <https://doi.org/10.3389/fphar.2021.713090>.
- Ombito, J. O., Chi, G. F., & Wansi, J. D. (2021). Ethnomedicinal uses, phytochemistry, and pharmacology of the genus *Vepris* (Rutaceae): A review. In *Journal of Ethnopharmacology* (Vol. 267). Elsevier Ireland Ltd. <https://doi.org/10.1016/j.jep.2020.113622>.
- Omosa, L. K., Mbogo, G. M., Korir, E., Omole, R., Seo, E. J., Yenesew, A., Heydenreich, M., Midiwo, J. O., & Efferth, T. (2021). Cytotoxicity of fagaramide derivative and canthin-6-one from *Zanthoxylum* (Rutaceae) species against multidrug resistant leukemia cells. *Natural Product Research*, 35(4), 579–586. <https://doi.org/10.1080/14786419.2019.1587424>.
- Ono, S., Yoshida, N., Maekawa, D., Kitakaze, T., Kobayashi, Y., Kitano, T., Fujita, T., Okuwa-Hayashi, H., Harada, N., Nakano, Y., & Yamaji, R. (2019). 5-Hydroxy-7-methoxyflavone derivatives from *Kaempferia parviflora* induce skeletal muscle hypertrophy. *Food Science and Nutrition*, 7(1), 312–321. <https://doi.org/10.1002/fsn3.891>.
- Oyebode, O., Kandala, N.-B., Chilton, P. J., & Lilford, R. J. (2016). Use of traditional medicine in middle-income countries: a WHO-SAGE study. *Health Policy and Planning*, 31(8), 984–991. <https://doi.org/10.1093/heapol/czw022>.
- Pandey, P., Rane, J. S., Chatterjee, A., Kumar, A., Khan, R., Prakash, A., & Ray, S. (2021). Targeting SARS-CoV-2 spike protein of COVID-19 with naturally occurring phytochemicals: an *in-silico* study for drug development. *Journal of Biomolecular Structure and Dynamics*, 39(16), 6306–6316. <https://doi.org/10.1080/07391102.2020.1796811>.
- Patel, B., Sharma, S., Nair, N., Majeed, J., Goyal, R. K., & Dhobi, M. (2021). Therapeutic opportunities of edible antiviral plants for COVID-19. In *Molecular and Cellular Biochemistry* (Vol. 476, Issue 6, pp. 2345–2364). Springer. <https://doi.org/10.1007/s11010-021-04084-7>.
- Peng, L., Wen, L., Shi, Q., Gao, F., Huang, B., & Wang, C. (2021). Chelerythrine ameliorates pulmonary fibrosis via activating the Nrf2/ARE signaling pathway. *Cell Biochemistry and Biophysics*, 79(2), 337–347. <https://doi.org/10.1007/s12013-021-00967-0>.
- Powder-George, Y. L. (2023). Alkaloids. In *Pharmacognosy: Fundamentals, Applications, and Strategies, Second Edition* (pp. 167–209). Elsevier. <https://doi.org/10.1016/B978-0-443-18657-8.00005-0>.
- Raffa, D., Maggio, B., Raimondi, M. V., Plescia, F., & Daidone, G. (2017). Recent discoveries of anticancer flavonoids. In *European Journal of Medicinal Chemistry* (Vol. 142, pp. 213–228). Elsevier Masson s.r.l. <https://doi.org/10.1016/j.ejmech.2017.07.034>.
- Rajini, P. S. (2023). Indian spices and their bioactives in neurological disorders. In *Ayurvedic Herbal Preparations in Neurological Disorders* (pp. 541–575). Elsevier. <https://doi.org/10.1016/B978-0-443-19084-1.00018-1>.
- Rangasamy, K., & Namasivaya, E. (2013). *In vitro* antioxidant and free radical scavenging activity of isolongifolene. *Asian Journal of Biological Sciences*, 7(1), 13–23. <https://doi.org/10.3923/ajbs.2014.13.23>.
- Razanamparany, M. (2020). *Coronavirus: Madagascar's 'Covid-Organics' born from local tradition*. <https://www.theafricareport.com/27203/coronavirus-madagascars-covid-organics-born-from-local-tradition/>
- Razavi, B. M., & Hosseinzadeh, H. (2020). Antioxidant effects of *Curcuma longa* and its active constituent, curcumin, for the therapy of neurological disorders. In *Oxidative Stress and Dietary Antioxidants in Neurological Diseases* (pp. 249–269). Elsevier. <https://doi.org/10.1016/B978-0-12-817780-8.00017-7>.
- Reveglia, P., Masi, M., & Evidente, A. (2020). Melleins – intriguing natural compounds. *Biomolecules*, 10(5). <https://doi.org/10.3390/biom10050772>.
- Rizvi, S. N. R., Afzal, S., Khan, K. U. R., Aati, H. Y., Rao, H., Ghalloo, B. A., Shahzad, M. N., Khan, D. A., Esatbeyoglu, T., & Korma, S. A. (2023). Chemical characterisation,

- antidiabetic, antibacterial, and *in silico* studies for different extracts of *Haloxylon stocksii* (Boiss.) Benth: A Promising Halophyte. *Molecules*, 28(9). <https://doi.org/10.3390/molecules28093847>.
- Rolle, J., Asante, D. O., Kok-Fong, L. L., Boucetta, H., Seidu, T. A., Tai, L. L. K., & Alolga, R. N. (2021). Jatrorrhizine: A review of its pharmacological effects. In *Journal of Pharmacy and Pharmacology* (Vol. 73, Issue 6, pp. 709–719). Oxford University Press. <https://doi.org/10.1093/jpp/rgaa065>.
- Saeed, F., Afzaal, M., Raza, M. A., Rasheed, A., Hussain, M., Nayik, G. A., & Ansari, M. J. (2023). Lavender essential oil: Nutritional, compositional, and therapeutic insights. In *Essential Oils: Extraction, Characterization and Applications* (pp. 85–101). Elsevier. <https://doi.org/10.1016/B978-0-323-91740-7.00009-8>.
- Saleem, S., Muhammad, G., Hussain, M. A., & Bukhari, S. N. A. (2018). A comprehensive review of phytochemical profile, bioactives for pharmaceuticals, and pharmacological attributes of *Azadirachta indica*. *Phytotherapy Research*, 32(7), 1241–1272. <https://doi.org/10.1002/ptr.6076>.
- Salem, M. A., & Ezzat, S. M. (2021). The use of aromatic plants and their therapeutic potential as antiviral agents: A hope for finding anti-COVID 19 essential oils. *Journal of Essential Oil Research*, 33(2), 105–113. <https://doi.org/10.1080/10412905.2021.1886187>.
- Sales, A., Felipe, L. de O., & Bicas, J. L. (2020). Production, properties, and applications of α -terpineol. In *Food and Bioprocess Technology* (Vol. 13, Issue 8, pp. 1261–1279). Springer. <https://doi.org/10.1007/s11947-020-02461-6>.
- Saquib, Q., Ahmed, S., Ahmad, M. S., Al-Rehaily, A. J., Siddiqui, M. A., Faisal, M., Ahmad, J., Alsaleh, A. N., Alatar, A. A., & Al-Khedhairy, A. A. (2020). Anticancer efficacies of persicogenin and homoeriodictyol isolated from *Rhus retinorrhoea*. *Process Biochemistry*, 95, 186–196. <https://doi.org/10.1016/j.procbio.2020.02.008>.
- Sarian, M. N., Ahmed, Q. U., Mat So'Ad, S. Z., Alhassan, A. M., Murugesu, S., Perumal, V., Syed Mohamad, S. N. A., Khatib, A., & Latip, J. (2017). Antioxidant and antidiabetic effects of flavonoids: A structure-activity relationship-based study. *BioMed Research International*, 2017. <https://doi.org/10.1155/2017/8386065>.
- Semwal, R. B., Semwal, D. K., Combrinck, S., & Viljoen, A. M. (2015). Gingerols and shogaols: Important nutraceutical principles from ginger. In *Phytochemistry* (Vol. 117, pp. 554–568). Elsevier Ltd. <https://doi.org/10.1016/j.phytochem.2015.07.012>.
- Sharanya, C. S., Sabu, A., & Haridas, M. (2021). Potent phytochemicals against COVID-19 infection from phyto-materials used as antivirals in complementary medicines: a review. *Future Journal of Pharmaceutical Sciences*, 7(1), 113. <https://doi.org/10.1186/s43094-021-00259-7>.
- Sharifi-Rad, M., Varoni, E. M., Iriti, M., Martorell, M., Setzer, W. N., del Mar Contreras, M., Salehi, B., Soltani-Nejad, A., Rajabi, S., Tajbakhsh, M., & Sharifi-Rad, J. (2018). Carvacrol and human health: A comprehensive review. In *Phytotherapy Research* (Vol. 32, Issue 9, pp. 1675–1687). John Wiley and Sons Ltd. <https://doi.org/10.1002/ptr.6103>.
- Sharma, A., Bhardwaj, G., Sohal, H. S., & Gohain, A. (2021). Eugenol. In *Nutraceuticals and Health Care* (pp. 177–198). Elsevier. <https://doi.org/10.1016/B978-0-323-89779-2.00007-7>.
- Sharma, A., Sharma, C., Shah, O. P., Chigurupati, S., Ashokan, B., Meerasa, S. S., Rashid, S., Behl, T., & Bungau, S. G. (2023). Understanding the mechanistic potential of plant-based phytochemicals in management of postmenopausal osteoporosis. In *Biomedicine and Pharmacotherapy* (Vol. 163). Elsevier Masson s.r.l. <https://doi.org/10.1016/j.biopha.2023.114850>.
- Sharma, M., Rathi, R., Kaur, S., Singh, I., Kadir, E. A., Chahardehi, A. M., & Lim, V. (2023). Anti-inflammatory activity of herbal bioactive-based formulations for topical

- administration. In *Recent Developments in Anti-Inflammatory Therapy* (pp. 245–277). Elsevier. <https://doi.org/10.1016/B978-0-323-99988-5.00015-2>.
- Sharma, R., Oberoi, K., Sharma, K., Nagraik, R., Kumar, D., Sharma, A., & Sharma, S. (2020). "Bioactive compounds and ethnomedicinal uses of *Syzygium cumini* (L.) Skeels-A comprehensive review". *The Annals of the University Dunarea de Jos of Galati Fascicle VI – Food Technology*, 44(1), 230–254. <https://doi.org/10.35219/foodtechnology.2020.1.14>.
- Sheikh, H. I., Zakaria, N. H., Abdul Majid, F. A., Zamzuri, F., Fadhlina, A., & Hairani, M. A. S. (2023). Promising roles of *Zingiber officinale* roscoe, *Curcuma longa* L., & *Momordica charantia* L. as immunity modulators against COVID-19: A bibliometric analysis. *Journal of Agriculture and Food Research*, 14. <https://doi.org/10.1016/j.jafr.2023.100680>.
- Singh, N., Yadav, S. S., Kumar, S., & Narashiman, B. (2021). A review on traditional uses, phytochemistry, pharmacology, and clinical research of dietary spice *Cuminum cyminum* L. In *Phytotherapy Research* (Vol. 35, Issue 9, pp. 5007–5030). John Wiley and Sons Ltd. <https://doi.org/10.1002/ptr.7133>.
- Son, N. T. (2022). Skimmianine: Natural occurrence, biosynthesis, synthesis, pharmacology and pharmacokinetics. *Medicinal Chemistry*, 19(6), 556–569. <https://doi.org/10.2174/1573406419666221213124847>.
- Song, L., Zhang, H. J., Deng, A. J., Li, J., Li, X., Li, Z. H., Zhang, Z. H., Wu, L. Q., Wang, S. Q., & Qin, H. L. (2018). Syntheses and structure-activity relationships on antibacterial and anti-ulcerative colitis properties of quaternary 13-substituted palmatine and 8-oxo-13-substituted dihydropalmatines. *Bioorganic and Medicinal Chemistry*, 26(9), 2586–2598. <https://doi.org/10.1016/j.bmc.2018.04.025>.
- Srinivasan, K. (2017). Ginger rhizomes (*Zingiber officinale*): A spice with multiple health beneficial potentials. In *PharmaNutrition* (Vol. 5, Issue 1, pp. 18–28). Elsevier B.V. <https://doi.org/10.1016/j.phanu.2017.01.001>.
- Subramanian, K., Sankaramourthy, D., & Gunasekaran, M. (2018). Toxicity studies related to medicinal plants. In *Natural Products and Drug Discovery: an Integrated Approach* (pp. 491–505). Elsevier. <https://doi.org/10.1016/B978-0-08-102081-4.00018-6>.
- Sun, X., Liu, X., & Chen, S. (2020). The pharmacokinetics, tissue distribution, metabolism, and excretion of pinostrobin in rats: Ultra-high-performance liquid chromatography coupled with linear trap quadrupole orbitrap mass spectrometry studies. *Frontiers in Pharmacology*, 11. <https://doi.org/10.3389/fphar.2020.574638>.
- Sun, Y., Ren, J., Zhu, S., Zhang, Z., Guo, Z., An, J., Yin, B., & Ma, Y. (2022). The effects of sesamin supplementation on obesity, blood pressure, and lipid profile: A systematic review and meta-analysis of randomized controlled trials. In *Frontiers in Endocrinology* (Vol. 13). Frontiers Media S.A. <https://doi.org/10.3389/fendo.2022.842152>.
- Sung, B., Prasad, S., Gupta, S. C., Patchva, S., & Aggarwal, B. B. (2012). Regulation of inflammation-mediated chronic diseases by botanicals. In *Advances in Botanical Research* (Vol. 62, pp. 57–132). Academic Press Inc. <https://doi.org/10.1016/B978-0-12-394591-4.00003-9>.
- Tan, K. H., & Nishida, R. (2012). Methyl eugenol: Its occurrence, distribution, and role in nature, especially in relation to insect behavior and pollination. In *Journal of Insect Science* (Vol. 12). Library of the University of Arizona. <https://doi.org/10.1673/031.012.5601>.
- Tao, T., Zhang, P., Zeng, Z., & Wang, M. (2023). Advances in autophagy modulation of natural products in cervical cancer. In *Journal of Ethnopharmacology* (Vol. 314). Elsevier Ireland Ltd. <https://doi.org/10.1016/j.jep.2023.116575>.
- Tarabasz, D., & Kukula-Koch, W. (2020). Palmatine: A review of pharmacological properties and pharmacokinetics. In *Phytotherapy Research* (Vol. 34, Issue 1, pp.

- 33–50). John Wiley and Sons Ltd. <https://doi.org/10.1002/ptr.6504>.
- Thawabteh, A., Juma, S., Bader, M., Karaman, D., Scrano, L., Bufo, S. A., & Karaman, R. (2019). The biological activity of natural alkaloids against herbivores, cancerous cells and pathogens. In *Toxins* (Vol. 11, Issue 11). MDPI AG. <https://doi.org/10.3390/toxins11110656>.
- Tripathi, A. K., & Mishra, S. (2016). Plant monoterpenoids (prospective pesticides). In *Ecofriendly Pest Management for Food Security* (pp. 507–524). Elsevier Inc. <https://doi.org/10.1016/B978-0-12-803265-7.00016-6>.
- Turker, A. U., & Gurel, E. (2005). Common mullein (*Verbascum thapsus* L.): Recent advances in research. In *Phytotherapy Research* (Vol. 19, Issue 9, pp. 733–739). <https://doi.org/10.1002/ptr.1653>.
- Valipour, M., Zarghi, A., Ebrahimzadeh, M. A., & Irannejad, H. (2021). Therapeutic potential of chelerythrine as a multi-purpose adjuvant for the treatment of COVID-19. In *Cell Cycle* (Vol. 20, Issue 22, pp. 2321–2336). Taylor and Francis Ltd. <https://doi.org/10.1080/15384101.2021.1982509>.
- Vilhelmova-Ilieva, N., S. Galabov, A., & Mileva, M. (2020). Tannins as antiviral agents. In *Tannins - Structural Properties, Biological Properties and Current Knowledge*. IntechOpen. <https://doi.org/10.5772/intechopen.86490>.
- Vollekova, A., Košťálová, D., Kettmann, V., & Tóth, J. (2003). Antifungal activity of *Mahonia aquifolium* extract and its major protoberberine alkaloids. *Phytotherapy Research*, 17(7), 834–837. <https://doi.org/10.1002/ptr.1256>.
- Wahyuni, T. S., Azmi, D. Z., Permanasari, A., Adianti, M., Lydia, T., Widiandani, T., Aoki, U. C., Widyawaruyanti, A., Fuad, A., & Hak, H. (2019). Anti-viral activity of *Phyllanthus niruri* against hepatitis c virus. *Malays. Appl. Biol.*, 48, 105–111.
- Wang, X. Y., Yang, D., Zhang, H., Jia, C. H., Shin, J. A., Hong, S. T., Lee, Y. H., Jang, Y. S., & Lee, K. T. (2014). Antioxidant activity of soybean oil containing 4-vinylsyringol obtained from decarboxylated sinapic acid. *JAOCS, Journal of the American Oil Chemists' Society*, 91(9), 1543–1550. <https://doi.org/10.1007/s11746-014-2492-4>.
- Wang, Y., Gao, Y., Li, X., Sun, X., Wang, Z., Wang, H., Nie, R., Yu, W., & Zhou, Y. (2020). Coniferyl aldehyde inhibits the inflammatory effects of leptomenigeal cells by suppressing the JAK2 signaling. *BioMed Research International*, 2020. <https://doi.org/10.1155/2020/4616308>.
- Wang, Y. H. (2021). Traditional uses, chemical constituents, pharmacological activities, and toxicological effects of *Dendrobium* leaves: A review. In *Journal of Ethnopharmacology* (Vol. 270). Elsevier Ireland Ltd. <https://doi.org/10.1016/j.jep.2021.113851>.
- Wei, Q., Zhai, X., Song, W., Li, Z., Pan, Y., Li, B., Jiao, Z., Shi, Z., & Yu, J. (2024). Metabolomics analysis of the effects of chelerythrine on *Ustilaginoidea virens*. *Journal of Pesticide Science*, D23-065. <https://doi.org/10.1584/jpestics.D23-065>.
- WHO. (2004). *WHO Guidelines on Safety Monitoring of Herbal Medicines in Pharmacovigilance Systems*.
- WHO. (2009). *WHO monographs on selected medicinal plant*.
- WHO. (2019). *WHO strategy on Traditional Medicine 2014–2023*.
- Wieczorek, P. P., Hudz, N., Yezerska, O., Horčinová-Sedláčková, V., Shanaida, M., Korytniuk, O., & Jasicka-Misiak, I. (2022). Chemical variability and pharmacological potential of propolis as a source for the development of new pharmaceutical products. In *Molecules* (Vol. 27, Issue 5). MDPI. <https://doi.org/10.3390/molecules27051600>.
- Wirasisya, D. G., & Hohmann, J. (2023). An overview of the traditional use, phytochemistry, and biological activity of the genus *Homalanthus*. In *Fitoterapia* (Vol. 166). Elsevier B.V. <https://doi.org/10.1016/j.fitote.2023.105466>.
- Wu, I. T., Kuo, C. Y., Su, C. H., Lan, Y. H., & Hung, C. C. (2023). Pinostrobin and tectochrysin conquer multidrug-resistant cancer cells via inhibiting P-glycoprotein

- ATPase. *Pharmaceuticals*, 16(2). <https://doi.org/10.3390/ph16020205>.
- Wu, J., Xiao, Q., Zhang, N., Xue, C., Leung, A. W., Zhang, H., Tang, Q. J., & Xu, C. (2016). Palmatine hydrochloride mediated photodynamic inactivation of breast cancer MCF-7 cells: Effectiveness and mechanism of action. *Photodiagnosis and Photodynamic Therapy*, 15, 133–138. <https://doi.org/10.1016/j.pdpdt.2016.07.006>.
- Wu, S. C., & Yen, G. C. (2004). Effects of cooking oil fumes on the genotoxicity and oxidative stress in human lung carcinoma (A-549) cells. *Toxicology in Vitro*, 18(5), 571–580. <https://doi.org/10.1016/j.tiv.2004.01.004>.
- Yan, B., Wang, D., Dong, S., Cheng, Z., Na, L., Sang, M., Yang, H., Yang, Z., Zhang, S., & Yan, Z. (2017). Palmatine inhibits TRIF-dependent NF- κ B pathway against inflammation induced by LPS in goat endometrial epithelial cells. *International Immunopharmacology*, 45, 194–200. <https://doi.org/10.1016/j.intimp.2017.02.004>.
- Yang, Z. D., Zhang, D. B., Ren, J., & Yang, M. J. (2012). Skimmianine, a furoquinoline alkaloid from *Zanthoxylum nitidum* as a potential acetylcholinesterase inhibitor. *Medicinal Chemistry Research*, 21(6), 722–725. <https://doi.org/10.1007/s00044-011-9581-9>.
- Yao, Q., Gao, Y., Lai, C., Wu, C., Zhao, C. L., Wu, J. L., & Tang, D. X. (2020). The phytochemistry, pharmacology and applications of *Melicope pteleifolia*: A review. In *Journal of Ethnopharmacology* (Vol. 251). Elsevier Ireland Ltd. <https://doi.org/10.1016/j.jep.2020.112546>.
- Yashvardhini, N., Samiksha, S., & Jha, D. (2021). Pharmacological intervention of various Indian medicinal plants in combating COVID-19 infection. *Biomedical Research and Therapy*, 8(7), 4461–4475. <https://doi.org/10.15419/bmrat.v8i7.685>.
- Yuan, Z., Li, J., Xiao, F., Wu, Y., Zhang, Z., Shi, J., Qian, J., Wu, X., & Yan, F. (2024). Sinensetin protects against periodontitis through binding to Bach1 enhancing its ubiquitination degradation and improving oxidative stress. *International Journal of Oral Science*, 16(1). <https://doi.org/10.1038/s41368-024-00305-z>.
- Zhang, L., Li, J., Ma, F., Yao, S., Li, N., Wang, J., Wang, Y., Wang, X., & Yao, Q. (2012). Synthesis and cytotoxicity evaluation of 13-n-alkyl berberine and palmatine analogues as anticancer agents. *Molecules*, 17(10), 11294–11302. <https://doi.org/10.3390/molecules171011294>.
- Zhang, L., & Liu, Y. (2020). Potential interventions for novel coronavirus in China: A systematic review. In *Journal of Medical Virology* (Vol. 92, Issue 5, pp. 479–490). John Wiley and Sons Inc. <https://doi.org/10.1002/jmv.25707>.
- Zhao, L. L., Jayeoye, T. J., Ashaolu, T. J., & Olatunji, O. J. (2023). Pinostrobin, a dietary bioflavonoid exerts antioxidant, anti-inflammatory, and anti-apoptotic protective effects against methotrexate-induced ovarian toxicity in rats. *Tissue and Cell*, 85. <https://doi.org/10.1016/j.tice.2023.102254>.
- Zhong, F., Chen, Y., Chen, J., Liao, H., Li, Y., & Ma, Y. (2022). Jatrorrhizine: A review of sources, pharmacology, pharmacokinetics and toxicity. In *Frontiers in Pharmacology* (Vol. 12). Frontiers Media S.A. <https://doi.org/10.3389/fphar.2021.78312>.
- Zhou, L., Wang, J., Wang, K., Xu, J., Zhao, J., Shan, T., & Luo, C. (2012). Secondary metabolites with antinematodal activity from higher plants. In *Studies in Natural Products Chemistry* (Vol. 37, pp. 67–114). Elsevier B.V. <https://doi.org/10.1016/B978-0-444-59514-0.00003-1>.
- Zhou, Y., Wang, Y., Vong, C. T., Zhu, Y., Xu, B., Ruan, C. C., Wang, Y., & Cheang, W. S. (2022). Jatrorrhizine improves endothelial function in diabetes and obesity through suppression of endoplasmic reticulum stress. *International Journal of Molecular Sciences*, 23(20). <https://doi.org/10.3390/ijms232012064>.
- Zhu, M., Niu, J., Jiang, J., Dong, T., Chen, Y., Yang, X., & Liu, P. (2022). Chelerythrine inhibits the progression of glioblastoma by suppressing the TGFB1-ERK1/2/Smad2/3-Snail/ZEB1 signaling pathway. *Life*

Sciences, 293.

<https://doi.org/10.1016/j.lfs.2022.120358>.

Zhu, S., Meng, L., Wei, P., Gu, G., & Duan, K. (2024). Sinensetin suppresses breast cancer cell progression via Wnt/ β -catenin pathway inhibition. *Translational Cancer Research*, 13(1), 348–362. <https://doi.org/10.21037/tcr-23-1317>.

Zuo, H., Zhou, W., Chen, Y., Zhou, B., Wang, Z., Huang, S., Alinejad, T., & Chen, C. (2024). Palmatine alleviates particulate matter-induced acute lung injury by inhibiting pyroptosis via activating the Nrf2-related pathway. *Inflammation*. <https://doi.org/10.1007/s10753-024-02009-2>.