**Bio-guided chemical characterization and nano-formulation studies of selected edible volatile oils with potentials antibacterial and anti-SARS-CoV-2 activities**

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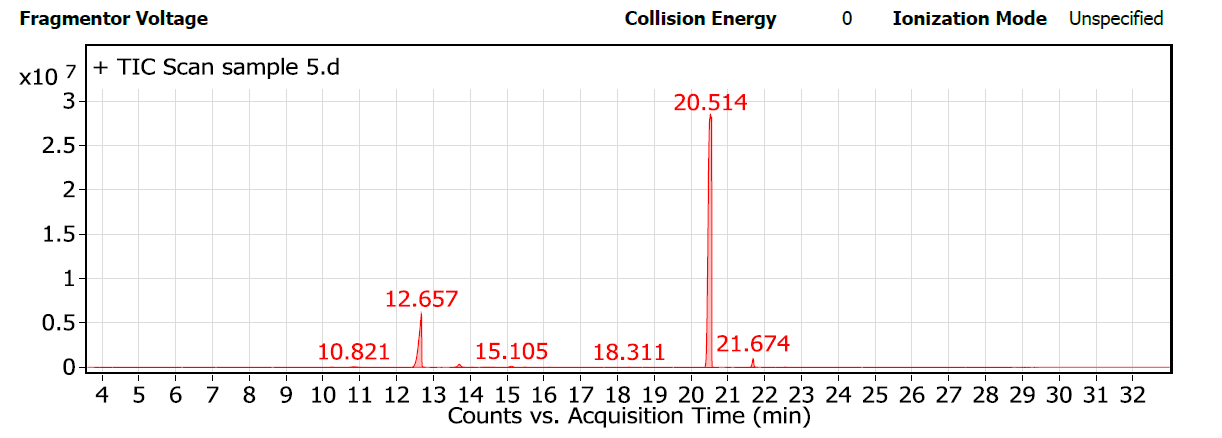
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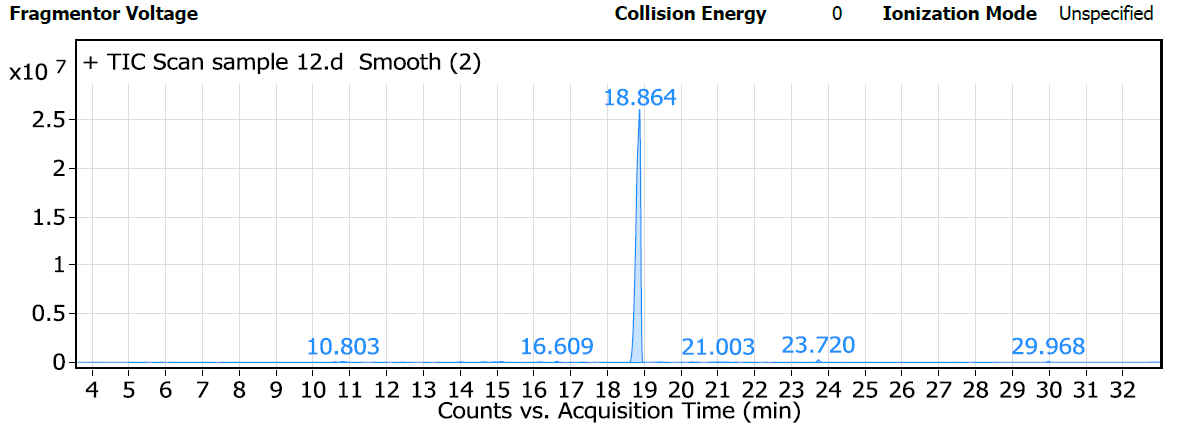
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| --- | --- | --- |
| **No.** | **Contents** | **Page** |
| **Table S1** | Traditional uses and biological activities of the selected plants used in this study. | S3 |
| **Fig. S1** | Total ion chromatograms (TIC) for gas chromatography-mass spectrometry analyses of *S. aromaticum* essential oil | S7 |
| **Fig. S2** | Total ion chromatograms (TIC) for gas chromatography-mass spectrometry analyses of *C. zeylanicum* essential oil | S7 |
|  | References | S8 |

**Table 1:** Traditional uses and biological activities of the selected plants used in this study.

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| **No.** | **Plant name** | **Traditional uses** | **Biological activities** | **Ref.** |
| 1 | *Pelargonium graveolens* | dysentery, hemorrhoids, inflammation, heavy menstrual flows, and even cancer, diabetes, diarrhea, gallbladder problems, gastric ulcers, liver problems, sterility, and urinary stones | antioxidant, anti-inflammatory, Antibacterial, Antitubercular, Bronchitis, Antifungal, Anticancer, Antiplasmodial, Insecticidal, Antihelmintic | (Amabeoku 2009, Elmann et al., 2010, Kang et al., 2010, Saraswathi et al., 2011, Ben Slima et al., 2013) |
| 2 | *Origanum majorana* | anti-cooling against allergies, fever, flu, hypertension, antipyretic, respiratory infections, antidiabetic, menstrual pain, cold in the uterus, stomach pain, cough, rheumatism, headache, insomnia, and used as an intestinal antispasmodic. | antibacterial property against different pathogenic bacteria such as *Bacillus subtilis*, *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella pneumonia*, *Salmonella choleraensius*, *Serratia* sp., antidiabetic, hepatoprotective, antimutagenic, gastrointestinal effects. | (Bouyahya et al., 2021) |
| 3 | *Syzygium aromaticum* | treatment of burns and wounds, and as a pain reliever in dental care as well as treating tooth infections and toothache, used extensively in perfumes, soaps, as a warming and stimulating agent, treatment of liver, bowel and stomach disorders; and as a stimulant for the nerves, inhibiting food-borne pathogens to treat viruses, worms. | antiviral, antimicrobial, antifungal, anticancer, antioxidant, anti-inflammatory, aphrodisiac, antipyretic, appetizer, hypnotic, anxiolytic, antiemetic, analgesic, decongestant, antimicrobial, antiepileptic, myorelaxant, and expectorant. | (Sarrami et al., 2002, Rapp and Therapy 2004, Bhowmik et al., 2012, Han and Parker 2017, Salim et al., 2017, Batiha et al., 2019) |
| 4 | *Foeniculum vulgare* | treatment of glaucoma, as a diuretic and a potential drug for the treatment of hypertension. It has been used as a galactagogue to improve the milk supply of a breastfeeding mother. | Antibacterial, antifungal, antioxidant, antithrombotic, anti-inflammatory, oestrogenic, hepatoprotective, antidiabetic, acaricidal, *in vitro* cytoprotection and antitumor activity, anti-hirsutism, and Human liver cytochrome P450 3A4 inhibitory activity. | (Albert-Puleo 1980, Javidnia et al., 2003, Özbek et al., 2003, Choi and Hwang 2004, Lee and chemistry 2004, Mohsenzadeh 2007, Tognolini et al., 2007, Zaidi et al., 2007, Agarwal et al., 2008, Faudale et al., 2008, Pradhan et al., 2008, Pai et al., 2010, Abou El-Soud et al., 2011) |
| 5 | *Carum carvi* | a spice in foods and beverages and as an alternative herbal medicine for GI ailments including dyspepsia, various spasmodic conditions, bloating, diarrhea, flatulent colic, diuretic and expectorant and used for increasing maternal milk, and dysmenorrhea. | anti-hyperglycemic, anti-hyperlipidemic, hepatoprotective, bronchopulmonary disorders as a cough remedy and demulcent, treatment of gastrointestinal disorders like Helicobacter pylori-induced gastritis, muco-protective on the duodenal peptic ulcer and gastroduodenitis and have an antiulcerogenic effect, antioxidative and antispasmodic. | (Zheng et al., 1992, Phillipson et al., 1994, Sivarajan and Balachandran 1994, Joshi and Joshi 2000, Khayyal et al., 2001, Raphael et al., 2003, Lado et al., 2004, Mahady et al., 2005, Lahlou et al., 2007, Al-Essa et al., 2010, Samojlik et al., 2010, Haidari et al., 2011, Johri 2011, Keshavarz et al., 2013) |
| 6 | *Cinnamomum zeylanicum* | indigestion, cold, cough and microbial infections, a spice in cooking to add flavor, headache, chills, abdominal pain, dysentery, vomiting, cold stomachache, chest tightness, diarrhea, frostbite, and cough, blood circulation disturbances, diabetes, dyspepsia, and gastritis, gastrointestinal neurosis, diarrhea, amenorrhea, dysmenorrhea, impotency | such as anti-inflammatory, antioxidant, and anti-proliferative properties. It is also antibacterial, antifungal, antiviral, antidote, and has properties that prevent hyperglycemia and hyperlipidemia as well as hypertension and atherosclerotic effects | (Lee et al., 2006, Liao et al., 2009, Ngoc et al., 2009, Eswaran et al., 2010, Singh and Jawaid 2012, Zhou and Technology 2016, Abeysekera et al., 2019, Zhou et al., 2019, Singh et al., 2021) |
| 7 | *Eucalyptus globulus* | upper respiratory tract infections, bronchitis symptoms, parasite infections, pruritus brought on by dermatitis, bruises, and sprains. | antibacterial effects on both Gram-positive and Gram-negative bacteria, as well as antiviral, antifungal, antioxidant, anti-inflammatory, and spasmolytic effects on human rhinoviruses, influenza viruses, and herpes simplex virus type I | (Kowalczyk et al., 2020), (Thosar et al., 2013) |
| 8 | *Laurus nobilis* | treatments for gastro-intestinal complaints including indigestion, constipation, flatulence also as carminative, diarrhea, hemorrhoids, and stomach aches treat kidney diseases, and treatment of cough, colds, influenza, and sore throat, mild sedative and against headaches | antibacterial, antifungal, antioxidant, Cytotoxic, Insecticidal, Nematicidal, inhibit nitric oxide (NO) production, and inhibit microglial activation. | (Barone 1963, Matsuda et al., 2000, Kilic et al., 2004, Ilker et al., 2009, Ivanović et al., 2010, Chen et al., 2014, Alarcόn et al., 2015, Casamassima et al., 2017, Motti et al., 2020, Nafis et al., 2020, Riabov et al., 2020, Anzano et al., 2022) |



**Fig. S1.** Total ion chromatograms (TIC) for gas chromatography-mass spectrometry analyses of *S. aromaticum* essential oil



**Fig. S2.** Total ion chromatograms (TIC) for gas chromatography-mass spectrometry analyses of *C. zeylanicum* essential oil

**References:**

Abeysekera, W. P. K. M., S. P. G. Arachchige, W. K. S. M. Abeysekera, et al., 2019. Antioxidant and glycemic regulatory properties potential of different maturity stages of leaf of Ceylon Cinnamon (Cinnamomum zeylanicum Blume) in vitro. 2019,

Abou El-Soud, N., N. El-Laithy, G. El-Saeed, et al., 2011. Antidiabetic activities of Foeniculum vulgare Mill. essential oil in streptozotocin-induced diabetic rats. 4, 139-146.

Agarwal, R., S. K. Gupta, S. S. Agrawal, et al., 2008. Oculohypotensive effects of Foeniculum vulgare in experimental models of glaucoma. 52, 77-83.

Al-Essa, M. K., Y. A. Shafagoj, F. I. Mohammed, et al., 2010. Relaxant effect of ethanol extract of Carum carvi on dispersed intestinal smooth muscle cells of the guinea pig. 48, 76-80.

Alarcόn, R., M. Pardo-de-Santayana, C. Priestley, et al., 2015. Medicinal and local food plants in the south of Alava (Basque Country, Spain). Journal of Ethnopharmacology. 176, 207-224.

Albert-Puleo, M. J. J. o. E., 1980. Fennel and anise as estrogenic agents. 2, 337-344.

Amabeoku, G. J. J. o. E., 2009. Antidiarrhoeal activity of Geranium incanum Burm. f.(Geraniaceae) leaf aqueous extract in mice. 123, 190-193.

Anzano, A., B. de Falco, L. Grauso, et al., 2022. Laurel, Laurus nobilis L.: a review of its botany, traditional uses, phytochemistry and pharmacology. Phytochemistry Reviews. 21, 565-615.

Barone, R. J. W., 1963. Le Piante Della Medicina Popolare Nel Territorio Di Falconara E San Lucido: Calabria. 17, 329-357.

Batiha, G. E.-S., A. M. Beshbishy, D. S. Tayebwa, et al., 2019. Inhibitory effects of Syzygium aromaticum and Camellia sinensis methanolic extracts on the growth of Babesia and Theileria parasites. 10, 949-958.

Ben Slima, A., M. B. Ali, M. Barkallah, et al., 2013. Antioxidant properties of Pelargonium graveolens L'Her essential oil on the reproductive damage induced by deltamethrin in mice as compared to alpha-tocopherol. Lipids Health Dis. 12, 30.

Bhowmik, D., K. S. Kumar, A. Yadav, et al., 2012. Recent trends in Indian traditional herbs Syzygium aromaticum and its health benefits. 1, 13-22.

Bouyahya, A., I. Chamkhi, T. Benali, et al., 2021. Traditional use, phytochemistry, toxicology, and pharmacology of Origanum majorana L. Journal of Ethnopharmacology. 265, 113318.

Casamassima, D., F. Chiosi, F. Vizzarri, et al., 2017. The effect of Laurus nobilis on the blood and lenses antioxidant activity in rabbit under fat-enriched diet. Physiol Res. 66, 325-333.

Chen, H., C. Xie, H. Wang, et al., 2014. Sesquiterpenes inhibiting the microglial activation from Laurus nobilis. J Agric Food Chem. 62, 4784-4788.

Choi, E.-M. and J.-K. J. F. Hwang, 2004. Antiinflammatory, analgesic and antioxidant activities of the fruit of Foeniculum vulgare. 75, 557-565.

Elmann, A., S. Mordechay, M. Rindner, et al., 2010. Anti-neuroinflammatory effects of geranium oil in microglial cells. 2, 17-22.

Eswaran, M. B., S. Surendran, M. Vijayakumar, et al., 2010. Gastroprotective activity of Cinnamomum tamala leaves on experimental gastric ulcers in rats. 128, 537-540.

Faudale, M., F. Viladomat, J. Bastida, et al., 2008. Antioxidant activity and phenolic composition of wild, edible, and medicinal fennel from different Mediterranean countries. 56, 1912-1920.

Haidari, F., N. Seyed-Sadjadi, M. Taha-Jalali, et al., 2011. The effect of oral administration of Carum carvi on weight, serum glucose, and lipid profile in streptozotocin-induced diabetic rats. 32, 695-700.

Han, X. and T. L. J. P. b. Parker, 2017. Anti-inflammatory activity of clove (Eugenia caryophyllata) essential oil in human dermal fibroblasts. 55, 1619-1622.

Ilker, U., B. Suleyman, Y. Nurettin, et al., 2009. The investigation and quantitative ethnobotanical evaluation of medicinal plants used around Izmir province, Turkey. 3, 345-367.

Ivanović, J., D. Mišić, M. Ristić, et al., 2010. Supercritical CO2 extract and essential oil of bay (Laurus nobilis L.): Chemical composition and antibacterial activity. 75, 395-404.

Javidnia, K., L. Dastgheib, S. M. Samani, et al., 2003. Antihirsutism activity of fennel (fruits of Foeniculum vulgare) extract–a double-blind placebo controlled study. 10, 455-458.

Johri, R. J. P. r., 2011. Cuminum cyminum and Carum carvi: An update. 5, 63.

Joshi, S. G. and S. G. Joshi, 2000. Medicinal plants, Oxford and IBH publishing.

Kang, H.-Y., S.-S. Na and Y.-K. J. J. o. K. A. o. N. Kim, 2010. Effects of oral care with essential oil on improvement in oral health status of hospice patients. 40, 473-481.

Keshavarz, A., M. Minaiyan, A. Ghannadi, et al., 2013. Effects of Carum carvi L. (Caraway) extract and essential oil on TNBS-induced colitis in rats. Res Pharm Sci. 8, 1-8.

Khayyal, M. T., M. A. El-Ghazaly, S. A. Kenawy, et al., 2001. Antiulcerogenic effect of some gastrointestinally acting plant extracts and their combination. 51, 545-553.

Kilic, A., H. Hafizoglu, H. Kollmannsberger, et al., 2004. Volatile constituents and key odorants in leaves, buds, flowers, and fruits of Laurus nobilis L. 52, 1601-1606.

Kowalczyk, A., M. Przychodna, S. Sopata, et al., 2020. Thymol and Thyme Essential Oil-New Insights into Selected Therapeutic Applications. Molecules. 25,

Lado, C., M. Then, I. Varga, et al., 2004. Antioxidant property of volatile oils determined by the ferric reducing ability. 59, 354-358.

Lahlou, S., A. Tahraoui, Z. Israili, et al., 2007. Diuretic activity of the aqueous extracts of Carum carvi and Tanacetum vulgare in normal rats. 110, 458-463.

Lee, H.-S. J. J. o. a. and f. chemistry, 2004. Acaricidal activity of constituents identified in Foeniculum vulgare fruit oil against Dermatophagoides spp.(Acari: Pyroglyphidae). 52, 2887-2889.

Lee, H. J., E.-A. Hyun, W. J. Yoon, et al., 2006. In vitro anti-inflammatory and anti-oxidative effects of Cinnamomum camphora extracts. 103, 208-216.

Liao, S.-G., T. Yuan, C. Zhang, et al., 2009. Cinnacassides A–E, five geranylphenylacetate glycosides from Cinnamomum cassia. 65, 883-887.

Mahady, G. B., S. L. Pendland, A. Stoia, et al., 2005. In vitro susceptibility of Helicobacter pylori to botanical extracts used traditionally for the treatment of gastrointestinal disorders. 19, 988-991.

Matsuda, H., T. Kagerura, I. Toguchida, et al., 2000. Inhibitory effects of sesquiterpenes from bay leaf on nitric oxide production in lipopolysaccharide-activated macrophages: structure requirement and role of heat shock protein induction. Life Sci. 66, 2151-2157.

Mohsenzadeh, M. J. P. J. B. S., 2007. Evaluation of antibacterial activity of selected Iranian essential oils against Staphylococcus aureus and Escherichia coli in nutrient broth medium. 10, 3693-3697.

Motti, R., G. Bonanomi, V. Lanzotti, et al., 2020. The contribution of wild edible plants to the Mediterranean Diet: An ethnobotanical case study along the coast of Campania (Southern Italy). 74, 249-272.

Nafis, A., A. Kasrati, C. A. Jamali, et al., 2020. A Comparative Study of the in Vitro Antimicrobial and Synergistic Effect of Essential Oils from Laurus nobilis L. and Prunus armeniaca L. from Morocco with Antimicrobial Drugs: New Approach for Health Promoting Products. Antibiotics (Basel). 9.

Ngoc, T. M., I. Lee, D. T. Ha, et al., 2009. Tyrosinase-inhibitory constituents from the twigs of Cinnamomum cassia. 72, 1205-1208.

Özbek, H., S. Uğraş, H. Dülger, et al., 2003. Hepatoprotective effect of Foeniculum vulgare essential oil. 74, 317-319.

Pai, M. B., G. Prashant, K. Murlikrishna, et al., 2010. Antifungal efficacy of Punica granatum, Acacia nilotica, Cuminum cyminum and Foeniculum vulgare on Candida albicans: an in vitro study. 21, 334.

Phillipson, J., F. Czygan, D. Frohne, et al., 1994. Herbal drug and phytopharmaceuticals.

Pradhan, M., S. Sribhuwaneswari, D. Karthikeyan, et al., 2008. In-vitro cytoprotection activity of Foeniculum vulgare and Helicteres isora in cultured human blood lymphocytes and antitumour activity against B16F10 melanoma cell line. 1, 450-452.

Raphael, T., G. J. I. Kuttan and immunotoxicology, 2003. Immunomodulatory activity of naturally occurring monoterpenes carvone, limonene, and perillic acid. 25, 285-294.

Rapp, R. P. J. P. T. J. o. H. P. and D. Therapy, 2004. Changing strategies for the management of invasive fungal infections. 24, 4S-28S.

Riabov, P. A., D. Micić, R. B. Božović, et al., 2020. The chemical, biological and thermal characteristics and gastronomical perspectives of Laurus nobilis essential oil from different geographical origin. Industrial Crops and Products. 151, 112498.

Salim, B., G. Said, M. Noureddine, et al., 2017. A note study on antidiabetic effect of main molecules contained in clove using molecular modeling interactions with DPP-4 enzyme. 5.

Samojlik, I., N. Lakic, N. Mimica-Dukic, et al., 2010. Antioxidant and hepatoprotective potential of essential oils of coriander (Coriandrum sativum L.) and caraway (Carum carvi L.)(Apiaceae). 58, 8848-8853.

Saraswathi, J., K. Venkatesh, B. Nirmala, et al., 2011. Phytopharmacological importance of Pelargonium species. 5, 2587-2598.

Sarrami, N., M. Pemberton, M. Thornhill, et al., 2002. Adverse reactions associated with the use of eugenol in dentistry. 193, 257-259.

Singh, N., A. S. Rao, A. Nandal, et al., 2021. Phytochemical and pharmacological review of Cinnamomum verum J. Presl-a versatile spice used in food and nutrition. Food Chemistry. 338, 127773.

Singh, R. and T. J. P. J. Jawaid, 2012. Cinnamomum camphora (Kapur). 4, 1-5.

Sivarajan, V. and I. Balachandran, 1994. Ayurvedic drugs and their plant sources, Oxford and IBH publishing.

Thosar, N., S. Basak, R. N. Bahadure, et al., 2013. Antimicrobial efficacy of five essential oils against oral pathogens: An in vitro study. 7, S071-S077.

Tognolini, M., V. Ballabeni, S. Bertoni, et al., 2007. Protective effect of Foeniculum vulgare essential oil and anethole in an experimental model of thrombosis. 56, 254-260.

Zaidi, S. F., S. Kadota, Y. J. J. o. A. Tezuka, et al., 2007. Inhibition on human liver cytochrome P450 3A4 by constituents of fennel (Foeniculum vulgare): identification and characterization of a mechanism-based inactivator. 55, 10162-10167.

Zheng, G.-q., P. M. Kenney and L. K. J. P. m. Lam, 1992. Anethofuran, carvone, and limonene: potential cancer chemoprotective agents from dill weed oil and caraway oil. 58, 338-341.

Zhou, H., Y. Guoruoluo, Y. Tuo, et al., 2019. Cassiabudanols A and B, immunostimulative diterpenoids with a Cassiabudane carbon skeleton featuring a 3-oxatetracyclo [6.6. 1.02, 6.010, 14] pentadecane scaffold from Cassia buds. 21, 549-553.

Zhou, L. J. H. U. o. S. and W. Technology, China, 2016. Studies on the Chemical Constituents and Immunomodulatory Activities of the Leaves of Cinnamomum cassia.