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BOTANY, PHYTOCHEMISTRY, PHARMACOLOGICAL ACTIVITY AND BIOTECHNOLOGICAL DEVELOPMENT OF OCIMUM BASILLICUM L.

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ABSTRACT

An urgent demand for natural compound alternatives to conventional medications has arisen due to global health challenges, such as drug resistance and the adverse effects associated with synthetic drugs. Plant extracts are considered an alternative due to their favorable safety profiles and potential for reducing side effects. Sweet basil (Ocimum basilicum L.) is a valuable plant resource and a potential candidate for the development of pharmaceutical medications. A single pure compound or a combination of compounds exhibits exceptional medicinal properties, including antiviral activity against both DNA and RNA viruses, antibacterial effects against both Gram-positive and Gram-negative bacteria, antifungal properties, antioxidant activity, antidiabetic potential, neuroprotective qualities, and anticancer properties. The plant contains various phytochemical constituents, which mostly consist of linalool, eucalyptol, estragole, and eugenol. For centuries, community and traditional healers across the globe have employed O. basilicum L. to treat a wide range of ailments, including flu, fever, colds, as well as issues pertaining to digestion, reproduction, and respiration. In addition, the current research presented underscores the significant potential of O. basilicum-related nanotechnology applications in addressing diverse challenges and advancing numerous fields. This promising avenue of exploration holds great potential for future scientific and technological advancements, promising improved utilization of medicinal products derived from O. basilicum L.

KEYWORDS: Ocimum basilicum L., antiviral, antifungal, anticancer, nanotechnology, biotechnology.

INTRODUCTION

In recent years, natural plant-based products have emerged as a valuable global resource for the development and innovation of novel drugs.[1] Hence, exploring bioactive compounds from various sources, including plants, might be an excellent method for discovering new potential drugs. This is because the current availability of raw materials for drug discovery and development, pharmacophores, and a framework for effective medications for a wide range of clinical indications is notably limited.[2] Hence, ethnopharmacological studies are of great significance, as they harness traditional knowledge to effectively screen and improve the chances of discovering novel drugs.[3]

Basil (Ocimum basilicum L.) is one of the species in the Lamiaceae family, which is well known for having a wide variety of medicinal properties. The plant is traditionally recognized for its utilization for both culinary and perfumery purposes.[4] For example, in the province of East Nusa Tenggara, Indonesia, the Tetun people frequently consume fresh, raw O. basilicum L. leaves in order to treat malaria. In addition, it is also used for treating rheumatism, high cholesterol, hypertension, headaches, and stroke in the Indonesian province of North Sumatra by the Batak Karo people.[5] O. basilicum L. leaves also find application as an anti-helminthic remedy among the Muna Tribe in the province of Southeast Sulawesi, Indonesia.[6]

Some of the uses stated are associated with the main constituents found in O. basilicum L. plant parts, which include linalool, eugenol, geranial, methyl eugenol, 1,8-cineole, and other compounds.[7] These compounds were found to play important roles as antimicrobials, antioxidants, anticancer agents, and antidiabetics.[8] Certain chemical compounds, specifically linalool and eugenol, are in great demand at present. This urgency arises from the resistance exhibited by Staphylococcus aureus, which is known for its ability to create biofilms.[9]

This article aims to present a comprehensive overview of the current and ongoing progress in the use of O. basilicum L. for medical purposes in human and animal healthcare, with the aim of serving as a guide, which traces the historical uses of Ocimum basilicum L. from ethnopharmacology to biotechnological development.[10] Additionally, this article aims to promote further clinical research efforts and the development of pharmaceutical formulations using Ocimum basilicum L. as a valuable resource.[11]

The investigation commences by examining the morphological and chemical compositions of Ocimum basilicum L. Subsequently, we proceed to gather empirical evidence derived from ethnomedicinal data originating from diverse regions and continents around the world.[12] Moreover, there are substantial data supporting the therapeutic benefits of this plant species from the perspectives of microbiology and biomedicine. Finally, we will explore the future prospects of nanotechnology in this field and investigate the strategies to enhance its metabolite production.[13]


- Macroscopic characteristics
  - Leaves:-opposite, ovate, smooth, bright green with characteristic aromatic odour and slightly pungent taste.
  - Stem:-Square-shaped (typical of Lamiaceae), soft, green or purplish.
  - Flowers:- Small, white to purplish, arranged in terminal racemes.
  - Seeds:- Small, black, oval, swell in water forming a mucilaginous coat.
  - Chemical constituents :- Linalool, Estragole (methyl chavicol),1,8-cineole, eugenol
  - Family :- Lamiaceae
  - Part used :- Leaves, flowering tops, seeds, essential oil.[14]

Biotechnological Development in *Ocimum basilicum* L. Research

The field of biotechnology involves the utilization of scientific methodologies to alter and enhance the characteristics of plants, animals, and micro-organisms in order to increase their overall value. The demand for herbal medicine on a global scale is substantial and exhibits a consistent growth rate.[15] Various technologies have been implemented to facilitate the promotion of bioactive compounds in medicinal plants. Secondary metabolites, which are considered vital constituents of the plants, hold significant economic value due to their applications as pharmaceutical products, perfumes, pigments, and food additive products.[16]

1) Green Nanotechnology Production in Ocimum basilicum L. for Medical Application

Previously, we discussed the antibacterial and antifungal properties of O. basilicum L., which were extensively explored from 2010 to 2018, revealing its potential for combating various bacterial and fungal infections.[17] Over the last five years, numerous studies on nanotechnology have demonstrated the ways of enhancing the antimicrobial properties of this plant. One notable advantage of using plant extracts for synthesizing nanoparticles is their ability to generate a larger zone of inhibition compared to chemical synthesis methods.[18]

The essential oil of Ocimum basilicum L. had moderate antibacterial activity against Gram-negative bacteria. However, combining and formulating the essential oil into chitosan nanocarriers with nanoencapsulation technology exhibited strong antibacterial and antibiofilm properties against E. coli and S. aureus, resulting in inhibitory zones measuring 15.3 mm and 21 mm, respectively.[19] This combination damages the cell membrane, and therefore, it causes the leakage of biological macromolecules. Therefore, the combination has good potential for overcoming Gram-negative resistance against antibiotics. ZnO NP is one of the nanoparticles, which showed great antibacterial activity against Pseudomonas aeruginosa, with 20 mm inhibitory zone diameter.[20]

ZnO NP synthesized with the Ocimum basilicum L. extract was tested against other bacteria species and exhibited a great inhibitory zone diameter for S. aureus (19.3 mm), E. coli (13.2 mm), S. typhimurium (8.2 mm), L. monocytogenes (11.4 mm), B. subtilis (9.3 mm), and P. aeruginosa (12.4 mm). It also showed great MIC for antibacterial activity, ranging from 0.78 µg/mL, 1.56 µg/mL, 3.12 µg/mL to 6.25 µg/mL [136].[21] Along with ZnO NP, copper oxide nanoparticles (CuO NPs) enhance the antibacterial activity against S. aureus and E. coli more than the extract itself. In addition to the monometallic synthesized nanoparticle, there are bimetallic synthesized nanoparticles. This is a combination of two different types of metallic nanoparticles in one particle, which work synergistically.[22] In this study, a combination of silver and platinum nanoparticles (AgPt NP) exhibited a significant inhibitory effect on S. aureus, E. faecalis, E. coli, and K. pneumoniae rather than the monometallic nanoparticle. The bimetallic particle showed an inhibitory diameter of 9–25 mm, whereas the monometallic particle of each nanoparticle only showed an inhibitory diameter under 10 mm.[23]

Another study demonstrated the green synthesis of reduced graphene oxide (RGO)-zinc oxide (ZnO) nanocomposite, or RGO-ZnO NCs. It was shown that at a concentration of 30 µg/mL, an inhibition zone was observed for the Cocci strain and E. coli at 20 mm and 10 mm, respectively. RGO-ZnO NCs had antibacterial activity at a small concentration, whereas the essential oil or extract of Ocimum basilicum L. itself needed higher concentrations to achieve the same results.[24] This study will also become the basis for the next development and investigation of RGO-ZnO NCs as potential antioxidant candidates and diabetes treatments. Another potential diabetic therapy based on a synthesized silver nanoparticle was found in O. basilicum L. leaf extract. The result demonstrated inhibitory activity against α-amylase—which was higher than antidiabetic medicine acarbose—and high inhibitory activity against α-glucosidase, higher than acarbose and crude extract. This finding suggests the need for alternative therapies for diabetic treatment.[25]

A recent study demonstrated that O. basilicum L. chemical constituents were responsible for the green biosynthesis of ZnO NPs. In combination with bacterial phages, ZnO NPs demonstrated antibacterial activity against Salmonella enterica and deformation on biofilm, which were caused by Staphylococcus sciuri. Another study demonstrated the green synthesis of silver nanoparticles (Ag NPs) in combination with phage ZCSE6 for antibacterial activity against Salmonella enterica.[26] The O. basilicum L. extract works as a bio-reducing agent in order to create Ag NPs effectively. It was shown that the Ag NPs exhibited antibacterial activity; the minimum concentration to inhibit growth was 6.25 µg/mL, and the minimum bactericidal concentration was 12.5 µg/mL. Surprisingly, the Ag NPs in combination with phage ZCSE6 had great bactericidal activity, with a lower concentration than the MIC, which suppressed the growth of S. enterica 24 h after treatment.[27]

In addition to utilization of the Ocimum basilicum L. extract for synthesizing nanoparticles, the mucilage from the seed in combination with nanoparticles can create a novel natural wound dressing.[28] Basil seed mucilage (BSM) was dried and then combined with ZnO NP to create a hydrogel sponge. As the weight percent (wt%) of ZnO NP increased, the antibacterial activity of the BSM hydrogel sponge was enhanced. It exhibited great antibacterial activity at 50 wt% ZnO NP against E. coli and S. aureus, with an inhibitory zone at 15.9 mm and 16.7 mm, respectively.[29] The increasing ZnO NP wt% content on the hydrogel sponge also resulted in a slight decrease in thickness, porosity, degree of swelling, and a slight increase in the water holding capacity.[30] The BSM with ZnO NP is considered non-toxic to human

keratinocyte (HaCat) cells. This hydrogel sponge could have the potential to be commercialized as a natural healthcare product.[31]

In addition to antibacterial functions against human pathogens, the synthesis of silver nanoparticles (Ag NPs) can also work as a control agent for the management of plant viral infections. This study tested Ag NPs against cucumber mosaic virus (CMV), which infects squash.[32] Spraying the foliar containing Ag NPs at a concentration of 100 µg/mL resulted in enhanced growth, delayed indication of disease symptoms, and a significant reduction of up to 92% in CMV accumulation levels as compared to the non-treated plants. It also increased the soluble carbohydrate, free radical scavenging activity, antioxidant enzymes, and total phenolic and flavonoid contents.[33] This finding could be an alternative for treating plant viral disease instead of using chemical biocides. There is a substantial opportunity in developing a green synthesis of nanoparticles within the O. basilicum L. extracts, which could be a potential therapy and alternative treatment in many cases of human diseases.[34]

Biotechnological Techniques for Improving the Metabolite Production of O.basilicum L.

It is known that the medicinal plant O. basilicum L. is a rich source of valuable phytoconstituents. The diversity of chemical compounds in O. basilicum L., alone or in synergy, exhibits some medicinal properties. The current production of horticulture crops is centered on improving the quality, quantity, and safety of products, as well as yield, in order to meet the demands of the food and health industries, which have a strong reliance on chemical compounds.[35] The advancement of O. basilicum L. production is influenced by various aspects, including environmental parameters (light, soil nutrients, temperature, water, CO2 levels), cultivars, and cultivation methods. Several studies have demonstrated various experiments on how to improve the chemical compounds derived from the plant Ocimum basilicum L.[36]

One study showed that narrow-bandwidth light treatments of basil seeds were observed to have relative effects on volatile oils. Light conditions may increase the value and quality of this herb, which is appreciated for human wellness.[37] Light treatments could induce the three main compounds in Ocimum basilicum L., which are eugenol, linalool, and 1,8-cineol (eucalyptol). Eugenol and linalool are induced by blue-red-green (BRG) light, and 1,8-cineole is induced by BRG, blue-red-yellow (BRY), and blue-red-far-red (BRFr) light. These compounds mainly play a role as antimicrobial and antioxidant agents. The blue and red LED

treatments can potentially improve O. basilicum L. growth and increase the phenolic content of the plants; thus, the different cultivars can also have a different result. The green cultivar in this study was mostly stimulated by the red light, and the red cultivar was stimulated by the blue light.[38]

In addition to the light treatments, the abiotic (CdCl2 and AgNO3) and biotic (YE) yeast extract elicitors were found to increase the total amount of phenolic and flavonoid contents.[39] Chicoric and rosmarinic acid increased with the treatment of CdCl2 and AgNO3 at 5 µM. Rutin and isoquercetin also increased with the YE treatment, up to 1.6 times and 1.9 times. Meanwhile, the highest amounts of linalool and estragole were observed in the treatment with AgNO3, up to 2.8 times and 0.5 times. Arbuscular mycorrhizal fungi (AMF), which are another type of biotic elicitors, showed a promising capacity in increasing the production of essential oil, with eugenol and γ-cadinene being the compounds with the highest ratios, which composed the essential oil.[40] Various methods of enhancing the chemical compounds of O. basilicum L. were discussed above to emphasize the importance of naturally synthesized compounds. One such approach involves improving the growth factors through light treatments and optimizing the formulation of biotic or abiotic elicitors.[41]

Herbal therapeutic potency of Ocimum basilicum (Basil or Tulsi)

Ocimum basilicum (Basil or Tulsi) were found to contain rich concentration of phytochemicals including essential oils (eugenol, linalool, and methyl chavicol), phenolic compounds and alkaloids that contribute to its diverse medicinal properties and biological activities. Minimal boiling, stir-frying, steaming, oven-baking and microwaving can intact the bio accessibility of vitamins content, minerals content and pigments volume concentration, phenolic components like rutin, rosmarinic acid, and quercetin of basil (Ocimum basilicum L.) leaves.[42] Eugenol and linalool are major basil essential oils that showed broad-spectrum antimicrobial properties in previous findings. Methyl chavicol (estragole) of basil leaves was found to showed significant anti-inflammatory and analgesic properties. Basil's antioxidant properties are explored for high concentrations of polyphenols present in its extracts like flavonoids, phenolic acid and tannins.[43] The mode of action of antiradical/antioxidant activity involves scavenging of Reactive Oxygen Species (ROS) by flavonoids such as quercetin and kaempferol and phenolic acids such as rosmarinic acid and caffeic acid. It is resulted in reducing oxidative stress and contribute to the overall health benefits of basil

extracts. Basil was also studied for terpenes and terpenoids which found to have potent analgesic and anti- inflammatory effects.[44]

Ocimum basilicum (Basil or Tulsi) has been exploited from ancient times for its potent antimicrobial properties due to containing essential oils and phenolic compounds. Eugenol shows great antibacterial properties not only against gram-positive but also gram-negative bacteria. Similarly, linalool has been shown to possess potent antifungal properties, making it effective against fungal infections.[45] Basil leaves are found to have methyl chavicol, also known as estragole that exhibits antimicrobial activity against various pathogenic microbes and fungi. In addition to essential oils, basil are explored for high concentration of quercetin and kaempferol, rosmarinic acid and caffeic acid that exhibit potent antimicrobial activities. Eugenol present in basil extracts are found to exhibit strong antiradical activity and anti-apoptotic potential to protect protecting cells from oxidative stress-induced damage.[46]

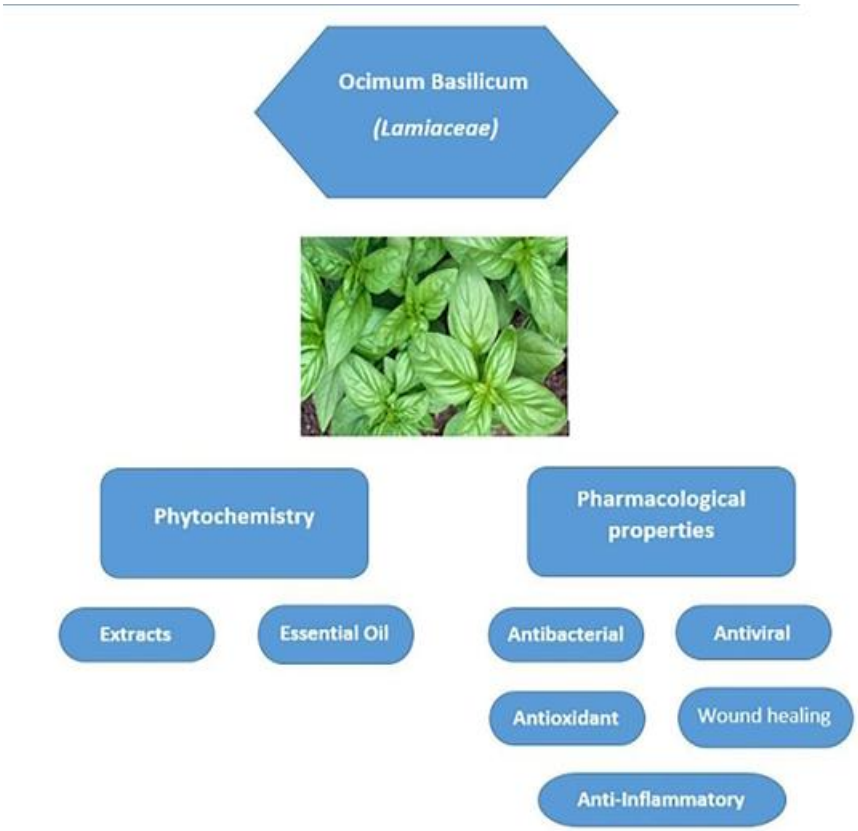
Linalool (floral and spicy terpene alcohol) present in Ocimum basilicum (Basil or Tulsi) is found to possess notable antimicrobial and antifungal properties against wide range of bacteria, including Gram-positive and Gram-negative strains.[47] Hence, linalool used in preparation of topical cream, ointment and oral formulation to teat microbial infections that found to exhibit anti-inflammatory properties to aid in symptoms of swelling and inflammation at the wound site.[48] It is also observed further to facilitate the healing process by stimulating cellular proliferation, collagen synthesis and alleviating symptoms associated with acne, eczema, and dermatitis.[49]

Future outlook of clinical implications of Ocimum basilicum (Basil or Tulsi)

Hence, vegetative parts of Ocimum basilicum (Basil or Tulsi) were found to have excellent concentration of essential oils which proved its clinical and medical implications. In addition, it proved more sustainable holistic approach into safe and cost-effective synthesis of herbal therapeutic preparations for maintaining well-being of human health in their daily lives as religious based health remedies.[50] Furthermore, future outlook for basil in healthcare is found to appear more promising with continued research endeavours and innovative approaches that emerge as non-toxic and cost- effective alternatives in promoting health and mental wellness. Researchers have found plaque inhibitory effect of holy basil based mouth wash that can be likely to have ability to kill dental plaque periodonto pathogens P. intermedia and F. nucleatum in vitro study.[51] Many previous preclinical studies have also observed that Basil or Tulsi possess notable concentration of phytochemicals like eugenol,

rosmarinic acid, apigenin, myretenal, luteolin, β-sitosterol, and carnosic acid.[52] Therefore, Basil or Tulsi based herbal preparations can be safe and helpful in preventing chemical-induced DNA damage causing skin cancer, liver cancer, oral cancer and lung cancer due to its high antioxidant activity by altering gene expressions, inhibiting angiogenesis and metastasis as potent anti- apoptotic agent due to having various phytochemicals like eugenol, rosmarinic acid, apigenin, and carnosic acid.[53] The aqueous extract of Basil or Tulsi and its flavanoids, orintin, and vicenin are found to protect mice model against γ-radiation-induced sickness and mortality by selectively protecting the normal tissues against the tumoricidal effects of radiation.[54]

Uses



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