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Mini Review

Application of Plant Extracts in the Food and Pharmaceutical Industry

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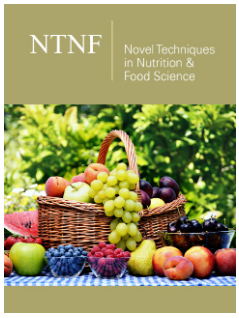

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Abstract

Plant extracts constitute an essential source of organic substances, known as plant metabolites, of immense interest to the food and pharmaceutical industries. Promising new applications of plant extracts as natural preservatives in the food industry, pharmaceutical industry, and cosmetics are under development. The main ingredient groups present in plant extracts are essential oils and polyphenols. Both have found use as food additives with divergent functions; food and feed supplements with interest in human or animal nutrition; and plant protection products. Numerous studies highlight their antimicrobial activities. Recently, there has been considerable emphasis on studies involving essential oils and extract ingredients to inhibit pathogenic microorganisms' growth. They have demonstrated that these compounds also possess potent antioxidant, anti-inflammatory, antidiabetic, and antiviral agents. Plant extracts are currently the subject of intensive scientific research and attract the cosmetics and pharmaceutical industries' attention due to their potential as pharmacologically active ingredients or natural preservatives.

Introduction

Herbal products have also been used since ancient times to flavor foods and beverages, as well as medicinal applications. An estimation indicates the existence of 250,000 to 500,000 plant species on the planet. According to World Health Organization (WHO), approximately 20,000 medicinal plants exist globally, scattered in over ninety countries. Several available plant species are widely used for human consumption, including energy drinks, capsules, health supplements, food materials, and the pharmaceutical industry to produce pharmaceutical drugs [1].

Plants contain innumerable chemical ingredients, clustered in two main groups, primary metabolites and secondary metabolites, which serve as valuable sources of biologically active molecules. Their extracts offer unlimited possibilities for controlling microbial growth, due to their chemical diversity.

Bioactive compounds are divided into two main categories as

(i) vegetable or essential oils (obtained from the olive, canola, soy, sunflower, flax seeds, avocado, grape seeds, oregano, rosemary, coriander seeds), and

(ii) plant extracts obtained from different sources such as grape seed, green tea, olive leaves, cranberry, pomegranate, broccoli, cocoa, lemon balm [2-4].

They emerge as promising sources due to their cost-effectiveness, nature-friendly, great structural diversity, and lower possibility of developing antimicrobial resistance than synthetic chemicals [5]. Also, plant extracts are rich in natural substances that function as antioxidants and agents that increase aroma and color; improve organoleptic acceptance by the consumer; extend the foods' shelf life [6].

A broad spectrum of antimicrobial activity against various bacteria, yeast, and mold, is characteristic, while changes in their bioactivity quality and quantity are critical factors in their use [7]. Growing concerns about antimicrobial resistance development have motivated the scientific community to study and explore natural antimicrobial products replacing synthetic preservatives to prevent food growth pathogens. Moreover, experts and the Federal Food, Drug, and Cosmetic Act (FFDCA) classify most plant extracts as GRAS (Generally Recognized as Safe) [8].

Inadequate and intensive use of antimicrobial agents, to mention traditional antibiotics, to treat bacterial infections in humans and animals, livestock growth, and the sub-lethal use of chemical biocides in food processing facilities disinfection have created selective pressure on microorganisms. It has promoted the survival and spread of antimicrobial-resistant pathogens [5].

Plants tissues are rich in various secondary metabolites expressing antimicrobial activity, such as saponins, tannins, alkaloids, alkenyl phenols, glycoalkaloids, flavonoids, lactones, and terpenoids [4,9]. For a broader classification, secondary metabolites classify into three main groups:

A. Phenolics derivatives: Phenols and cinnamic acid derivatives, Quinones, Flavones and flavonoids, Taninnes, Coumarins.

B. Terpenoids.

C. Alkaloids.

Different plants are documented as a significant source for discovering new pharmaceutical molecules used for severe disease treatments [10]. Species such as thyme *(Thymus vulgaris)*, saffron *(Curcuma longa)*, mustard *(Brassica juncea)*, chili *(Capsicum annuum)*, cumin *(Cuminum cyminum)*, fenugreek *(Trigonella foenumgraecum)*, coriander *(Coriandrum sativum)*, garlic *(Allium sativum)*, ginger *(Zingiber officinale)*, cloves *(Syzygium aromaticum)*, aloe vera, etc. possess several nutritional properties and compositions [1]. A unique characteristic of essential oils consists of bacteriostatic and bactericide activity on microorganisms, including *Bacillus cereus*, *Bacillus megatherium*, *Bacillus subtilis*, and Aeromonas sobria. Panax ginseng extracts are used in dietary supplements, food products, cosmetics, pharmaceuticals, and dental products. Saffron is conventionally used as a food item and in medicinal formulations. *Mentha sp*. is used in various pharmaceutical, cosmetic, and flavoring industries. *Azadirachta indica* has found applications as an insecticide, lubricant, and treatment for diabetes and tuberculosis diseases. *Ocimum sanctum* has been used in the cosmetics and pharmaceutical industries to produce medicines, tonics, and cosmetics [1].

Plant Extracts Applications in the Pharmaceutical Industry

Many natural products exist in plants with sugar moieties (called glycosides), ensuring crucial secondary metabolites, often involved in plant defense. The glycosides are not acting directly on therapeutic targets only when subjected to an enzymatic process activating the pro-drug. Plant extracts may contain bioactive NPs in the form of pro-drugs, and in some cases, these compounds can provide optimized derivatives for reaching therapeutic targets [11].

Application of plant extracts from *Vitis vinifera L*. in the cosmetic and pharmaceutical industries includes exploiting the wine industry by-products, such as grape stem and grape seeds. Microbial safety in cosmetic products has always been of particular interest to this industry branch, as microbial contamination can lead to product degradation and pose a risk to consumer health. Moreover, bacteria change the cosmetic product's chemical and physical properties and usually result in the separation of different phases, bleaching, and emission of aromatic substances. Given this high risk of pollution and, consequently, a threat to consumer health, the use of condoms is imperative.

Concerning antimicrobial activity, the extracts presented high efficacy against foot wound ulcers and Gram-positive bacteria. Furthermore, the extracts exhibited anti-inflammatory capacity by inhibiting nitric oxide production by lipopolysaccharide-stimulated macrophages, up to 35.25%. For the first time, they revealed an anti-aging effect by inhibiting anti-tyrosinase (~54%) -elastase activity (~98%). Therefore, grape curbs have demonstrated a biological potential, being of interest to the cosmetics, pharmaceutical, and food industries [12].

Various pharmaceutical industry applications involve PSO use. Reports indicate that PSO possesses antioxidant, anti-inflammatory, hepatoprotective, antidiabetic, nephroprotective, neuroprotective, and anticancer properties. It also helps improve the immune system and regulate lipid metabolism. The main functional natural product, punic acid, exhibits antioxidant, anti-obesity, anti-inflammatory, hypolipidemic, anti-nephrotoxic, and antidiabetic activity [13]. Many other examples indicate the use of plant extracts and essential oils in alternative medicine. Their application was successfully expanded during the Covid-19 pandemic [14].

Plant Extracts and Antibiotics Resistance

Recent research has shown that as bacteria become more resistant to antibiotics, traditional methods of food preservation: drying, heat treatment, and acid treatment may not be effective. The intensive use of chemical preservatives in food has significantly contributed to the increased resistance of microorganisms to antibiotics. The use of antibiotics itself aims at the effective treatment of diseases of microbial origin. Recently there has been an increase in microorganisms exhibiting resistance to common antibiotics; consequently, populations of antibiotic-resistant bacteria are emerging and spreading rapidly. A need to introduce new antimicrobials to combat them is imperative.

Plant-derived antimicrobial agents can be useful and safe alternatives to control pathogens resistant to conventional antibiotics, especially those pathogens igniting food-borne diseases, which are among the most promising microbial resistance. Plant extracts, combined with antibiotics, can be used as adjuvants to restore the drugs' efficacy toward resistant pathogens. Thymol

and carvacrol are phenol monoterpene derivatives. They are isomer constituents on thyme's essential oil *(Thymus vulgaris)*, that effectively reduce the *Salmonella typhimurium* resistance toward ampicillin, tetracycline, penicillin, bacitracin, erythromycin, and novobiocin. Similarly, carvacrol, thymol, and cinnamaldehyde are effective against *Staphylococcus aureus*. They reduced the Minimum Inhibitory Concentration (MIC) value to ampicillin, penicillin, and bacitracin.

Application of Plant Extracts in Food Products

Scientific research on plant extracts and their essential oils used as antimicrobials in the food and pharmaceutical industries has shown that these extracts have potential antimicrobial properties against food pathogens. Antimicrobial agents from plants find application in biofilm and edible coating in food systems. These biofilms and edible coatings spread slowly within the food packaging, thus prolonging antimicrobial activity duration.

Wastes from the wine industry can cause problems sustainably, thus requiring their reuse [15,16]. Therefore, new products can be generated through these wastes, giving environmental, social, and economic advantages [12]. Various cases of use as sources of plant extracts include grape seeds, whose extracts exhibit various biological activities, such as preventing harmful microorganisms from food contamination and playing a food fungicide role. Besides, Grape Seed Extracts (GSE) can supplement foods with natural antioxidants and preservatives.

GSEs are certified as G.R.A.S. supplements by the U.S. Food and Drug Administration to improve the food's overall quality and shelf life effectively. Use of grape seed extract in food preservation (Burn, 2004). Application of GSEs supplement addition to ground beef after vacuum treatment, the vegetative cells of Clostridium perfringens increased susceptibility to death as a cause of heat. These results have facilitated restaurants and catering services to accurately estimate the heating time and temperature of vacuum-cooked beef to realize food safety against pathogens [17].

Potential Mechanisms of Action as Antimicrobial of Plant Extracts in Foods

Increasing the resistance of pathogenic microorganisms to antibiotics has turned scientific research towards plant extracts as a viable alternative. Plant extracts are a promising solution for increasing antibiotic resistance and may give better results than synthetic preservatives.

The exact antimicrobial mechanisms of action of specific natural compounds against microorganisms are still unknown. Their specific plant composition may act differently for a particular group of pathogens. Gram-positive bacteria's response to plant extracts is much higher than Gram-negative bacteria's [6]. The mechanistic approach refers to lipopolysaccharides' presence in cell walls' structure of Gram-negative bacteria, capable of preventing any hydrophobic compound's diffusion process inside the cell.

Essential oils produce structural and functional damage to the bacterial cell membrane, where the optimal range of hydrophobicity is also involved in their toxicity. In summary, bacterial death can occur principally from:

1. Physical destruction of the cell membrane through the removal of cell contents or modification of active transport. Short-chain organic acids interfere with the membrane permeability process through interaction with membrane proteins.
2. Direct reduction of pH or growth medium due to increased proton concentration, suppression of intracellular pH by ionization of organic acid molecule originating from plant extracts.
3. Inhibition of enzyme activity in the cell membrane
4. Organic acids present in plant species can also inhibit NADH's oxidation, thus eliminating the supply of reducing agents in electron transport systems [18].

Conventional and Unconventional Plant Extraction Methods

Effective extraction and purification procedures are critical to the isolation and application of natural antimicrobials intended for food products. The most common extraction techniques are steam distillation and hydro-distillation. In recent decades unconventional methods such as supercritical fluid extraction has been applied, which provide improved solubility and mass transfer [2].

The usual methods of extracting essential oil from plants consume time and energy. Moreover, most extraction methods require large amounts of different solvents, and some of these solvents (hydrochloric acid, ammonium chloride, ethanol, methanol, and alcohol) are considered toxic. Conventional extraction procedures, including chemical or heat treatments, can also alter the total active ingredient content, functionality, or natural properties or produce hazardous compounds [6]. A minimal processing extraction method, such as direct mechanical extraction, seems to be more promising to avoid alteration or destruction of the active ingredients. Finally, obtained plant extracts are used directly as an antimicrobial agent against food pathogens.

Grape Seed Extracts as a Raw Material to Develop Healthy Foods

Plant extracts can serve as a critical source to meet the growing consumer demand for healthier foods. Natural phenolic compounds have improved specific functional properties of protein-based membranes and have been used as active substances in edible biofilms. Ultrafine powders from grape seeds resulted in complete absorption in the gastrointestinal tract in humans with beneficial effects and the realization of biomass use. GSEs are used as nutritional capsule products, and food additives with suitable properties increase health benefits. Due to GSE's solubility in water and ethanol, its addition to functional beverages or healthy drinks

is another alternative. They have successfully replaced sulfur dioxide (SO_2) in white wine production by avoiding the oxidation process [17].

Pomegranate Seed Oils (PSOs) constitute another important source of plant extracts. Reports give evidence that PSO improves lipid profiles and growth rate after use as feed supplements. Beneficially fatty acids will transfer to the human body by consuming these products of animal origin. Pomegranate extracts are known for their antimicrobial properties due to polyphenols such as ellagic acid and tannins. They can also increase the packaging material's antimicrobial, mechanical, and packaging properties and can be placed as a component to increase durability in edible packaging [19]. A study reports that pomegranate seed oil has antibacterial properties against *Bacillus subtilis*, *Staphylococcus aureus*, *Salmonella typhimurium*, and *Escherichia coli*.

Conclusion

Plant extracts applications are a promising trend in the bio-economy. Some plants are being used in various human health areas such as traditional medicine, functional foods, dietary supplements, and recombinant proteins. Many studies have demonstrated that some plant extracts exhibit antioxidant, antimicrobial, antidiabetic, anti-carcinogen, flavoring, beverage, and detergent properties, leading to multiple food production applicability [20]. Study reports indicate that food by-products and medicinal plants possess various nutritional, antimicrobial, and pharmacological effects and show immense potential for the food and pharmaceutical industry.

International bodies are aware of the limitations of terrestrial and marine biodiversity and suggest that the exploitation of medicinal plants and other food by-products to produce essential oil and supplements will contribute to developing a sustainable economy and improve the world population's health status.

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