

Review

# Antimicrobial Effect of Phytochemicals from Edible Plants

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**Abstract:** Current strategies of combating bacterial infections are limited and involve the use of antibiotics and preservatives. Each of these agents has generally inadequate efficacy and a number of serious adverse effects. Thus, there is an urgent need for new antimicrobial drugs and food preservatives with higher efficacy and lower toxicity. Edible plants have been used in medicine since ancient times and are well known for their successful antimicrobial activity. Often photosensitizers are present in many edible plants; they could be a promising source for a new generation of drugs and food preservatives. The use of photodynamic therapy allows enhancement of antimicrobial properties in plant photosensitizers. The purpose of this review is to present the verified data on the antimicrobial activities of photodynamic phytochemicals in edible species of the world's flora, including the various mechanisms of their actions.

**Keywords:** antimicrobials; phytochemicals; photosensitizers; edible plants; food disinfection; food conservation



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## 1. Introduction

Although plants are able to treat many pathological conditions [1], only 15% have been investigated phytochemically, and 6% have been screened for biological activity [2]. It is widely acknowledged that many antimicrobial compounds identified and isolated from medicinal plants are very active against both Gram-positive and Gram-negative bacteria [3–7]. Between 1981 and 2019, 162 new antimicrobial drugs were approved, 94 of which were produced from plants [8].

The best-known approach to combating bacterial diseases involves the use of antibiotics. During the last decades, the overuse of antibiotics resulted in selective pressures that led to the widespread appearance of antibiotic-resistant microorganisms [9]. Each of the antibiotics in use has generally inadequate efficacy and a number of serious adverse effects [10]. It is imperative to investigate new antimicrobial agents that are more effective and less toxic than these antibiotics. From this perspective, the application of herbal compounds may potentially hold great promise. Isolation and identification of plant-based antimicrobial agents is always a challenging task, because bioactive compounds often occur as complex mixtures with other secondary metabolites. In addition, these compounds are found in such small quantities that enhancement of their antimicrobial properties is very important. The use of photodynamic therapy presents a promising possibility to improve the antimicrobial activity of phytochemicals, since many of them are photosensitizers (PSs). Although many aspects of PSs were covered by numerous reviews [11–16], edible plants and their PSs were not seriously considered as sources of new drugs and preservatives. They in fact deserve special attention, because actively cultivated edible plants are already available which are rich in useful phytochemicals. These phytochemicals are not only potential antimicrobial drugs, but are also ideal as possible preservatives for the food industry.

There is an urgent need for new natural agents that are more effective and less toxic than the currently popular compounds, such as sodium benzoate; acetic, lactic, benzoic, and sorbic acids; hydrogen peroxide, and chelators. They are used in many cases because of their ability to inhibit the activity of various microorganisms [17]. In addition, the majority of these compounds have good stability and excellent solubility in water [18]. Yet each of them has generally inadequate efficacy and a number of serious adverse effects [19]. Thus, plant-based compounds may be an alternative strategy for the food industry.

We collected and analyzed information on edible plants with antimicrobial compounds, including photodynamic phytochemicals. The aim of this review is to provide verified data on plant-based antimicrobial activities, and discuss the various mechanisms of their actions.

## 2. Antimicrobial Properties of Edible Plants

As already mentioned, many edible plants are important sources of antimicrobial compounds exhibiting high activity against both Gram-positive and Gram-negative bacteria (Table 1). Cultivated vegetables, fruits, nuts, herbs, and spices have been investigated more thoroughly than wild species; thus, they dominate the list (Table 1). Although more than 7000 species of wild edible plants are present in human nutrition [20], their antimicrobial properties are poorly investigated, and most of them still need to be studied [21,22].

A wide variety of compounds with different structures may have antimicrobial properties: polyphenols (phenolic acids, flavonoids, lignans, stilbenes, etc.); terpenoids, sulfides, coumarins, saponins, furils, alkaloids, polyines, thiophenes, different sugars, fatty oils, resins, glycosinolates, proteins, peptides, and others [23]. The quantitative distribution of the phytochemicals can vary from organ to organ or from plant to plant, depending on many factors: most notably, the plant genotype, growth conditions, developmental stage, soil, environmental conditions, agricultural practices, abiotic, and biotic stress [24].

Most edible plants are consumed after being cooked or dried. Frying, grilling, boiling, drying, and steaming are often detrimental to many phytochemicals.

Polyphenols, which occur in all plants, are the most potent antimicrobial compounds, especially phenolic acids and flavonoids. In cases where the identification and purification of active antimicrobial compounds from plants were not complete, the total phenol and flavonoid content was estimated, based on the high probability that the active phytochemicals belong to these groups.

Phenolic acids can be found in almost all edible plants. Antimicrobial properties of phenolic acids relate to the presence of double bonds and hydroxyl, methoxy, and carboxyl groups [25,26].

One phenolic acid is *p*-coumaric acid (4-hydroxycinnamic acid), which aroused interest because of contradicting reports on its antimicrobial activity. This compound exhibits antibacterial activity against three Gram-positive bacteria (*Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Bacillus subtilis*) and three Gram-negative bacteria (*Escherichia coli*, *Shigella dysenteriae*, and *Salmonella typhimurium*), eliminating bacterial cells via dual damage mechanisms: increasing the membrane permeability of the bacteria and binding to the phosphate anion of their DNA [27]. It was reported that *p*-coumaric acid demonstrated a much lower inhibitory activity against *Staphylococcus aureus*, and no inhibitory effect on *Escherichia coli*, *Listeria monocytogenes*, and *Salmonella typhimurium* [28]. In addition, it had no inhibitory effect on several Gram-positive bacteria and Gram-negative bacteria [29]. It was likewise found that *p*-coumaric acid was not effective against *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Proteus vulgaris*; but a significant antimicrobial effect was observed in combination with syringaldehyde. It is noteworthy that syringaldehyde alone did not eliminate these microorganisms [30]. Thus, antimicrobial ability can be obtained in a synergistic action between *p*-coumaric acid and certain phytochemicals whose efficacy would be very low in its absence.

Chlorogenic acid is one of the most available acids among the phenolic acid compounds. It is a well-known component in green coffee extracts [31] and many other edible

plants [32]. Its bactericidal effects against *Stenotrophomonas maltophilia* resistant to trimethoprim/sulfamethoxazole [33], *Klebsiella pneumoniae* [34], *Helicobacter pylori* [35], *Escherichia coli* [36], *Staphylococcus epidermidis* [37], and *Staphylococcus aureus* [38] were reported. In addition, chlorogenic acid had an inhibitory effect on the multidrug efflux systems of multidrug-resistant bacteria [38] and their biofilm formation [39]. On the other hand, it is not toxic against probiotic bacteria, which makes this compound suitable to use in the food industry [39].

Although caffeic acid is present in many edible plants, its antimicrobial properties were observed in propolis [40,41]. The caffeic acid enhanced the activity of several antibiotics against many bacterial strains [42–44]. The mechanism of its action is connected with the inhibition of the bacterial RNA polymerase enzyme [42]. Ferulic, *p*-coumaric, and sinapic acids of kidney beans also demonstrate antibacterial activity [42].

In many cases, there are synergistic or antagonistic reactions among phenolic acids and other compounds, which make the results from in vitro and in vivo studies variable.

Numerous antimicrobial flavonoids are present in many species of edible plants. Based on their differences in the phenyl-benzopyran core, flavonoids have been divided into several subgroups: flavanols, flavones, flavanones, anthocyanidins, and isoflavones. Several investigated mechanisms of their actions include the inhibition of nucleic acid synthesis via interference in bacterial type II topoisomerases (DNA gyrase and topoisomerase IV) activity [43]; inhibition of cytoplasmic membrane function [43]; inhibition of cell envelope synthesis [44]; inhibition of energy metabolism [43]; inhibition of cell-wall synthesis [43]; inhibition of efflux pumps in bacteria [45]; inhibition of bacterial enzyme-dependent virulence [46]; and membrane-disrupting activities [47,48]. In addition, the quorum sensing activity of flavonoids was reported [49,50]. Bacterial quorum sensing is a process of cell-to-cell communication that regulates genetic competence, bacterial colonization, biofilm formation, virulence, and other properties that make many bacteria more dangerous [3]. Although the mechanism of action of quorum-sensing flavonoids is still poorly understood, it became clear that the bacterial proteins TtgR in complex with flavonoids have properties that block the efflux pumps in bacteria [51]. In fact, epigallocatechin gallate is able to inhibit bacterial growth and suppress the expression of specific genes related to biofilm formation [52]. Remarkably, some flavonoids also inhibit bacterial toxins [53–55].

The antimicrobial activity of flavonoids is the result of a combination of several mechanisms. The flavonol morin is indicative of how many modes of actions are known, including promotion of bacterial aggregation, leakage of the cell membrane, intervention in the biofilm growth, suppression of the PBP2a-mediated resistant mechanism of action [56], and inhibition of bacterial enzyme-dependent virulence [57]. It is possible to improve antibiotic efficiency against bacteria using flavonoids as potentiators [58].

Stilbenes are nonflavonoid polyphenols found in a number of plant families, including Vitaceae. These compounds are produced in plants during the invasion of pathogens, with the most studied stilbene being resveratrol, a constitutive compound found in some foods and drinks such as red wine, of which it is a major component. Whereas resveratrol generally shows moderate antimicrobial activity, it is the precursor of more active derivatives such as pterostilbene and viniferin [59,60].

The vegetables of the Brassicaceae family are rich in glucosinolates, a group of sulfur-containing glucosides with significant antimicrobial properties [61]. At least 120 distinct glucosinolates have been identified [62]. Their modes of action include the breakdown of enzyme S-S bridges, DNA damage, and inhibition of bacterial cell growth and proliferation [63].

Terpenes are secondary metabolites (based on an isoprene structure) produced by all plants via two alternative metabolic pathways. The first is the mevalonate pathway in the cytoplasm, and the second is the methylerythritol phosphate pathway in the plastids [64]. These compounds have enormous structural diversity, with about 200,000 variants existing

in nature [65]. Indeed, the terpenes are one of the most important classes of antimicrobial phytochemicals; they are mostly found in the form of essential oils [66].

Examination of the 33 terpenes frequently reported in the secondary metabolism of plants revealed that 16 of the 33 compounds showed antimicrobial activity at the initial screening. Higher antimicrobial activity was related to the presence of hydroxyl groups (phenolic and alcohol compounds), whereas hydrocarbons reduced that activity [67]. Support of this idea is found in terpineol and eugenol, whose antimicrobial properties were demonstrated in some studies [21,68]. Moreover, these compounds are able to cause dysfunction in the bacterial membrane [67]. It was found that essential oils and their compounds are divided into two groups: slow-acting and fast-acting [68]. It was reported that terpineol, eugenol, geraniol, carveol, and citronellol were fast-acting compounds, inactivating several bacterial organisms in a two-hour period [67]. A possible mechanism of their antimicrobial action is their ability to destroy cell membrane integrity by forming a phenolic cluster that initiates lipid–protein interaction, improves the membrane’s permeability, and results in leakage of the cellular contents [69,70].

Ursolic acid is a natural terpene identified in many edible plants, such as apples, marjoram leaves, oregano leaves, rosemary leaves, sage leaves, thyme leaves, black elder leaves and bark, hawthorn leaves and flowers, coffee leaves, and the wax layer of many fruits [71,72]. A number of studies have been performed to evaluate the antibacterial properties of ursolic acid [73–75]. Its antimicrobial mode of action is connected with its ability to influence the integrity of the bacterial membrane initially, followed by inhibition of protein synthesis and the metabolic pathway [76]. It was reported that ursolic acid is able to improve antibiotic activity [77,78].

Lupeol (phytosterol and triterpene) is identified in many edible vegetables and fruits; although it exhibits significant antimicrobial activity, the mechanism of its action is not clear [79].

The saponins are a subclass of terpenoids. There are three classes of saponins (triterpenoids, steroids and glycoalkaloids) based on their different aglycone structures [22]. The triterpenoid 18- $\beta$ -glycyrrhetic acid showed an antibiotic effect on *Staphylococcus aureus* by influencing some of its important genes [22]. In addition, this compound is an immunological adjuvant [80,81].

Six saponins from *Chenopodium quinoa* Willd. were identified; these compounds destroy the bacterial biofilm system. The mechanism of their action is related to disruption of the cytoplasmic membrane and membrane proteins [82].

Both licochalcone [83] and liquiritigenin were effective against *Staphylococcus aureus* [84]. In addition, licochalcone A inhibited the formation of biofilms in many cases [85].

Although Sapindus saponins are prevalent in nonedible plants, they have such broad-spectrum antibacterial effects that it is worthwhile to pay attention to these compounds. Screening of their antibacterial activity in various combinations against seven bacteria demonstrated that only the combination of Sapindoside A and B was effective against *Micrococcus luteus*, causing damage to cell membrane proteins [86]. Sapindus saponins (Mukurozisaponin E1, Rarasaponin II, Mukurozisaponin G, and Rarasa ponin VI) inhibited *Propionibacterium acnes*; the mechanism of their action is connected with suppressing the activities of bacterial enzymes, such as lipase and tyrosinase [87].

Two lignans (sesamin and sesamol) found in *Sesamum indicum* (L.) had significant anti-quorum sensing and antibiofilm properties against *Pseudomonas aeruginosa*. The possible mechanisms of action of the lignans were investigated; they influence LasR-mediated virulence factor production [88].

A number of antimicrobial phytochemicals have not yet been identified (Table 1). Whether the antimicrobial effects of many edible plants may be a synergy of multiple phytochemicals or a single component should be a focus for future investigations. In addition, various metabolites in plant extracts have synergic or antagonistic effects on antimicrobial activity.

**Table 1.** Edible plants with antimicrobial properties.

Phytochemicals	Plant	Microorganism	References
2-vinyl-2,4-dihydro-1,3-dithiin, 3-vinyl-3,4-dihydro-1,2-dithiin, and ajoene	<i>Allium cepa</i>	<i>Bacillus subtilis</i>	[89]
Ajoene, kaempferol, and allicin	<i>Allium sativum</i>	<i>Pseudomonas aeruginosa</i> <i>Enterococcus faecalis</i> <i>Salmonella</i> , <i>Escherichia coli</i> , <i>Pseudomonas</i> , <i>Proteus</i> , <i>Staphylococcus aureus</i> , <i>Helicobacter</i>	[90–93]
Proteins	<i>Ananas comosus</i>	<i>Saccharomyces cerevisiae</i> , <i>Escherichia coli</i>	[94]
Phenolic compounds	<i>Annona squamosa</i>	<i>Staphylococcus aureus</i> , <i>Bacillus cereus</i> , <i>Staphylococcus epidermidis</i> , <i>Monilia albican</i> , <i>Escherichia coli</i> , <i>Salmonella typhimurium</i> , <i>Shigella flexneri</i> , <i>Pseudomonas aeruginosa</i>	[37]
Limonene, pinene ( $-\alpha$ , $-\beta$ ), and selinene ( $-\alpha$ , $-\beta$ )	<i>Apium graveolens</i>	<i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i>	[95]
Berberoin and lesquerellin	<i>Armoracia macrocarpa</i>	<i>Bacillus subtilis</i> , <i>Escherichia coli</i>	[96]
Iberin and some undetermined compounds 5-phenylpentyl isothiocyanate	<i>Armoracia rusticana</i>	<i>Pseudomonas aeruginosa</i> 6 strains of facultative anaerobic bacteria, <i>Streptococcus mutans</i> , <i>Streptococcus sobrinus</i> , <i>Lactobacillus casei</i> , <i>Staphylococcus aureus</i> , <i>Enterococcus faecalis</i> , and <i>Aggregatibacter actinomycetemcomitans</i> ; one strain of yeast, <i>Candida albicans</i> , and 3 strains of anaerobic bacteria, <i>Fusobacterium nucleatum</i> , <i>Prevotella nigrescens</i> , and <i>Clostridium perfringens</i> <i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Bacillus cereus</i> , <i>Proteus vulgaris</i> , <i>Escherichia coli</i> , <i>Salmonella enterica</i>	[97–99]
Phenolic compounds	<i>Aronia melanocarpa</i>	<i>Proteus mirabilis</i>	[100]
Berberine	<i>Berberis vulgaris</i>	<i>Helicobacter pylori</i>	[101]
Protein: BjCHI1	<i>Brassica juncea</i>	Several Gram-negative bacteria	[102]
Epicatechin, epicatechin gallate, epigallocatechin, and epigallocatechin gallate	<i>Camellia sinensis</i>	<i>Staphylococcus epidermidis</i> , <i>Micrococcus luteus</i> , <i>Brevibacterium linens</i> , <i>Pseudomonas fluorescens</i> , <i>Bacillus subtilis</i>	[103]
Capsaicin and dihydrocapsaicin	<i>Capsicum species</i>	<i>Bacillus cereus</i> , <i>Bacillus subtilis</i> , <i>Clostridium sporogenes</i> , <i>Clostridium tetani</i> , <i>Streptococcus pyogenes</i>	[104]
Saponins	<i>Chenopodium quinoa</i>	<i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , <i>Bacillus cereus</i> , <i>Salmonella enteritidis</i> , <i>Pseudomonas aeruginosa</i> , <i>Listeria ivanovii</i>	[82]
Kaempferol and some undetermined compounds presumably, tannins, saponins, flavonoids, alkaloids	<i>Centella asiatica</i> L.	<i>Chromobacterium violaceum</i> <i>Escherichia coli</i>	[105,106]
Oxalic, succinic, shikimic, and quinic acids	<i>Cichorium intybus</i>	<i>Streptococcus mutans</i> , <i>Actinomyces naeslundii</i>	[107]
Unknown	<i>Cinnamomum verum</i>	<i>Pseudomonas aeruginosa</i>	[108]
Unknown	<i>Citrus medica</i>	<i>Listeria monocytogenes</i>	[109]
l-limonene	<i>Citrus reticulata</i>	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i>	[110]

Table 1. Cont.

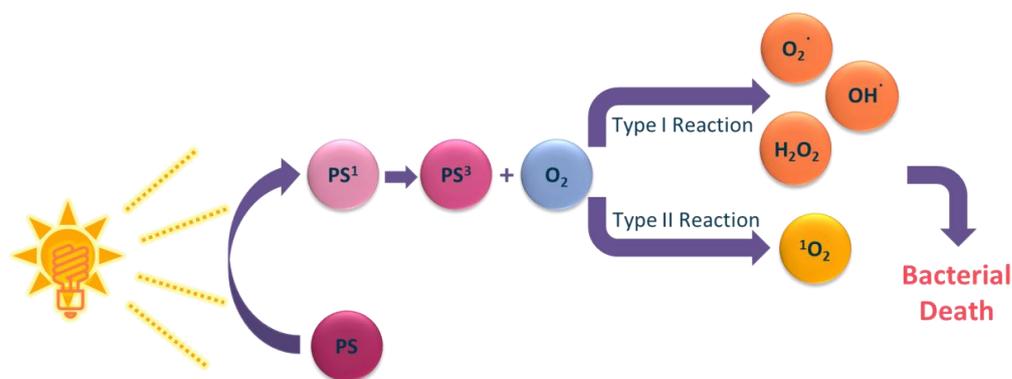
Phytochemicals	Plant	Microorganism	References
Polyphenols	<i>Citrus sinensis</i>	<i>Staphylococcus aureus</i> , <i>Enterococcus faecalis</i> , <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , and <i>Salmonella typhimurium</i>	[111]
Unknown	<i>Coffea arabica</i>	<i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i>	[112]
$\alpha$ -pinene, camphene, and linalool (2E)-dodecenal	<i>Coriandrum sativum</i> L.	<i>Listeria monocytogenes</i> , <i>Salmonella choleraesuis</i>	[113]
Protein PR-5	<i>Cucurbita moschata</i>	<i>Fusarium oxysporum</i>	[114]
Unknown	<i>Cucurbita pepo</i>	<i>Escherichia coli</i> BL21, <i>Escherichia coli</i> B-23, <i>Escherichia coli</i> BL24 JPN, <i>Shigella sonnei</i>	[115]
The octamers of epigallocatechin and its gallate Phenolic compounds	<i>Diospyros kaki</i>	<i>Salmonella enterica</i> <i>Staphylococcus aureus</i> , <i>Bacillus cereus</i> , <i>Staphylococcus epidermidis</i> , <i>Monilia albican</i> , <i>Escherichia coli</i> , <i>Salmonella typhimurium</i> , <i>Shigella</i> <i>flexneri</i> , <i>Pseudomonas aeruginosa</i>	[37,116]
Sesquiterpenoids: jambolanins	<i>Eugenia jambolana</i>	<i>Staphylococcus aureus</i>	[117]
Unknown	<i>Ficus carica</i>	<i>Streptococcus pyogenes</i> , 10 <i>Lactobacillus</i> strains	[118]
Unknown	<i>Hibiscus sabdariffa</i>	<i>Staphylococcus aureus</i> , <i>Klebsiella pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , <i>Acinetobacter baumannii</i> , <i>Streptococcus mutans</i> , <i>Campylobacter jejuni</i> , <i>Campylobacter coli</i> , <i>Campylobacter fetus</i> , <i>Pseudomonas fluorescense</i>	[119]
Kaempferol 3-O-alphaL-(2",4"-di-E-p- coumaroyl)-rhamnoside (C2), and Kaempferol 3-O-alphaL-(2"-Z -p- coumaroyl)-rhamnoside (C3)	<i>Laurus nobilis</i>	<i>Streptococcus pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , <i>Serratia marcescens</i>	[120,121]
Flavonoids	<i>Lepidium sativum</i>	<i>Proteus mirabilis</i> , <i>Staphylococcus epidermidis</i> , <i>Staphylococcus aureus</i>	[122]
Unknown	<i>Medicago truncatula</i>	<i>Chromobacterium violaceum</i> , <i>Pseudomonas putida</i> , <i>Escherichia coli</i>	[123]
L-canvanine	<i>Medigo sativa</i>	<i>Sinocrizobium melioli</i>	[124]
Unknown Peptide	<i>Momordica charantia</i>	Microorganisms of clinical interest (standard strains and multiresistant isolates) <i>Escherichia coli</i> , <i>Staphylococcus aureus</i>	[125,126]
Unknown	<i>Moringa oleifera</i>	<i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i>	[127]
Morin	<i>Morus alba</i>	<i>Staphylococcus aureus</i>	[56]
APC protein	<i>Murraya koenigii</i> L.	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Vibrio cholerae</i> , <i>Klebsiella</i> <i>pneumoniae</i> , <i>Salmonella typhi</i> , <i>Bacillus subtilis</i>	[128]
Estragol	<i>Ocimum basilicum</i>	<i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i>	[129]
Hydroxytyrosol, oleuropein	<i>Olea europaea</i>	<i>Salmonella enterica</i> , <i>Escherichia coli</i>	[130]
Unknown Thymol and carvacrol	<i>Origanum vulgare</i>	<i>Chromobacterium violaceum</i> , <i>Bacillus species</i> , <i>Salmonella enteritidis</i>	[131–133]
Anglicin and psoralen	<i>Pastinaca sativa</i>	<i>Staphylococcus aureus</i>	[134]

Table 1. Cont.

Phytochemicals	Plant	Microorganism	References
Apiol, myristicin, and b-phellandrene	<i>Petroselinum crispum</i>	<i>Staphylococcus aureus</i> , <i>Listeria monocytogenes</i> , <i>Salmonella enterica</i>	[135]
Unknown	<i>Piper longum</i> L.	<i>Chromobacterium violaceum</i>	[136]
Unknown	<i>Pistachia vera</i>	<i>Bacillus cereus</i> , <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , <i>Salmonella typhi</i> , <i>Candida albicans</i> , <i>Neurospora intermedia</i>	[137]
3-methoxy-4,5-dinitrophenol	<i>Portulaca oleracea</i>	<i>Staphylococcus aureus</i> , <i>Staphylococcus sonnei</i> , <i>Acinetobacter baumannii</i> , <i>Bacillus subtilis</i>	[138]
Phenolics, flavonoids, ortho-diphenols, and saponins.	<i>Prunus avium</i>	<i>Staphylococcus aureus</i> , <i>Escherichia coli</i>	[139]
Citric acid	<i>Prunus mume</i>	Enterobacteria	[140]
Quercetin and quercetin-3-O-arabinoside	<i>Psidium guajava</i> L.	<i>Chromobacterium violaceum</i> , <i>Pseudomonas aeruginosa</i>	[105]
$\alpha$ -amyrin and flavonoid compounds, steroidal compounds	<i>Pyrus bretschneideri</i> Rehd.	<i>Staphylococcus aureus</i> , <i>Escherichia coli</i>	[141]
Unknown	<i>Raphanus raphanistrum</i> L.	<i>Klebsiella pneumoniae</i> , <i>Pseudomonas aeruginosa</i>	[142]
Sulforaphene	<i>Raphanus sativus</i>	<i>Staphylococcus aureus</i>	[143]
Unknown	<i>Rheum officinale</i>	<i>Vibrio parahaemolyticus</i> , <i>Vibrio vulnificus</i> , <i>Vibrio alginolyticus</i> , <i>Vibrio carchariae</i> , <i>Aeromonas hydrophila</i> , <i>Edwardsiella tarda</i>	[144]
Unknown	<i>Ribes nigrum</i>	<i>Streptococcus pyogenes</i> , 10 <i>Lactobacillus</i> strains	[118]
Unknown	<i>Rosa rugosa</i>	<i>Bacillus cereus</i>	[145]
Unknown	<i>Rosmarinus officinalis</i>	<i>Streptococcus pneumoniae</i>	[146]
Unknown	<i>Solanum melongena</i>	<i>Pseudomonas aeruginosa</i>	[147]
Eugenol	<i>Syzygium aromaticum</i>	<i>Streptococcus pneumoniae</i>	[148]
Unknown Squalene, campesterol, tocopherol, isooctyl phthalate, ethyl glycopyranoside, stigmaterol, hexadecanoic acid, malvidin	<i>Syzygium cumini</i>	<i>Chromobacterium violaceum</i> , <i>Actinomyces naeslundii</i> , <i>Fusobacterium nucleatum</i> , <i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , <i>Veillonella dispar</i> , <i>Klebsiella pneumoniae</i>	[105,149,150]
Chebulic acid, combretastatin A1, corilagin, diethylstilbestrol, ellagic acid, ethyl gallate, gallic acid, piceid, resveratrol	<i>Terminalia ferdinandiana</i>	<i>Proteus mirabilis</i> , <i>Proteus vulgaris</i>	[151]
Phenolic compounds, $\gamma$ -terpinene	<i>Thymus vulgaris</i>	<i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> , <i>Salmonella typhimurium</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , <i>Enterococcus faecalis</i>	[152]
Unknown	<i>Vanilla planifolia</i> Andrews	<i>Chromobacterium violaceum</i>	[153]
Isothiocyanates	<i>Wasabia japonica</i>	<i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> , <i>Salmonella typhimurium</i> , <i>Escherichia coli</i>	[154]
Phenolic components	<i>Zingiber officinale</i> Roscoe	<i>Chromobacterium violaceum</i> , <i>Pseudomonas aeruginosa</i>	[155]

### 3. Photosensitizers from Edible Plants as a Source of New Drugs

An important group of antimicrobial agents was mentioned in our Introduction: photosensitizers. Excitation of these compounds by light leads to the generation of reactive oxygen species (ROS) that damage pathogenic cells. Light is absorbed by a photosensitizer, leading to a photodynamic process which can develop either a type I or a type II process. The former results in the formation of free radicals, such as superoxide anion ( $O_2^-$ ), hydroxyl radicals ( $OH^\cdot$ ), and hydrogen peroxide ( $H_2O_2$ ), which oxidize biomolecules. The type II process is characterized by the formation of singlet oxygen ( $^1O_2$ )—a highly reactive and strong oxidizing agent (Figure 1) [12,156,157]. ROS produced during the photodynamic process attack various targets outside of cells (for example, extracellular polysaccharides), on the surface of cells and inside them (such as proteins, lipids, and nucleic acids), and oxidize biomolecules, causing cell damage and ultimately their destruction [157–159]. The ratio between mechanisms I and II depends on the type of PS used and the microenvironment in which the photodynamic process occurs. Furthermore, an additional, oxygen-independent photoinactivation pathway has recently been proposed, a type III photochemical mechanism [160]. It includes photoinduced electron transfer, accompanied by the generation of reactive inorganic radicals which (according to the author's assumption) then attack microbial cells.



**Figure 1.** Schematic presentation of light-mediated cell damage during photodynamic treatment.

Photodynamic therapy was discovered over a century ago. It has been studied and developed for many years for the treatment of cancer [161–163]. At the beginning of the 1990s, in response to the emergence of the first drug-resistant infections, interest was renewed in studying the antibacterial properties of PSs [164,165]. Since then, many “synthetic” PSs have been shown to be effective against various types of microorganisms [165–168]. The wider spectrum of PS action compared to antibiotics, their bactericidal efficacy regardless of antibiotic resistance, as well as a lack of development of resistance to them after several sessions of therapy, emphasize the potential of using photodynamic antimicrobial chemotherapy (PACT) for the eradication of various microorganisms, such as bacteria, protozoa, and fungi [11,169,170].

Natural products from plant and animal origins contain many bioactive components that are phototoxic when activated by light [19]. The cells of microorganisms, algae, plants, and animals produce pigments for various biological purposes: photochemical reactions, antioxidant activity, defense mechanisms, attraction of pollinators, etc. Some of these pigments are photoactive and exhibit the photodynamic properties required for therapeutic use [14]. To date, more than 100 natural compounds having photodynamic activity are known [14,171]. Both pure compounds and extracts are used as PSs for PACT [13].

The main classes of natural PSs that can be found in edible plants are curcuminoids, anthraquinones, perylenequinones, furano-coumarins, alkaloids, chlorins, and flavins [13,14,171]. Table 2 presents structures of the most prospective antimicrobials from edible plants exhibiting photodynamic activity.

**Table 2.** Structures of selected photosensitizers from edible plants.

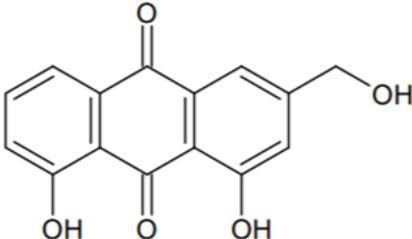
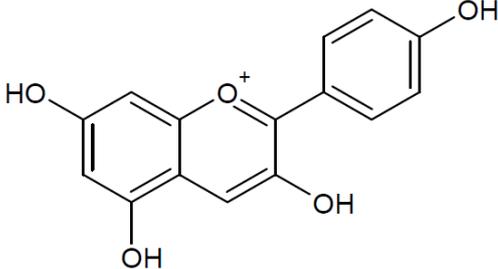
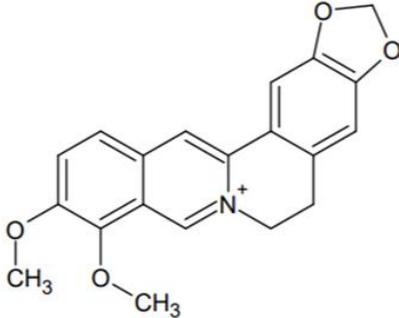
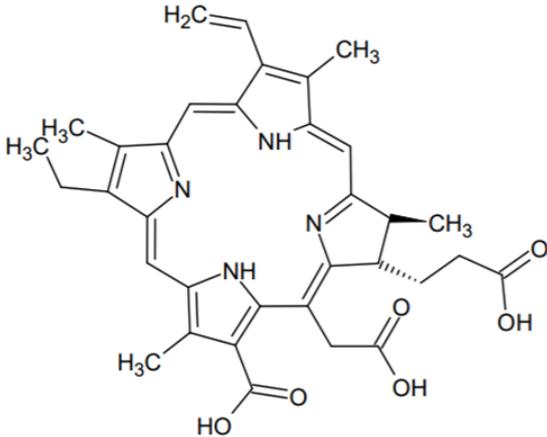
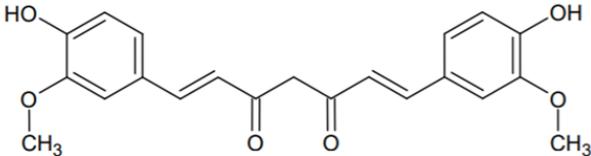
Photosensitizer	Structure
Aloe emodin	
Anthocyanidin	
Berberine	
Chlorin $e_6$	
Curcumin	

Table 2. Cont.

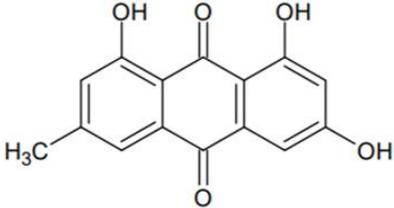
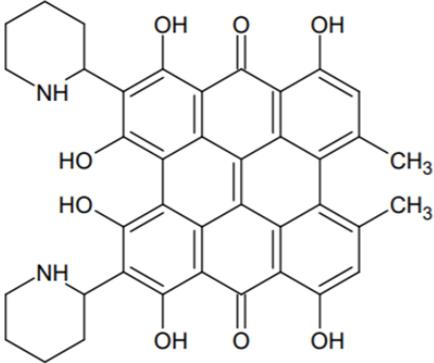
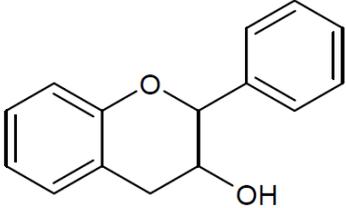
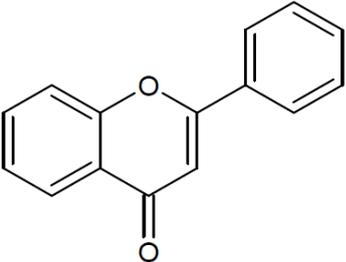
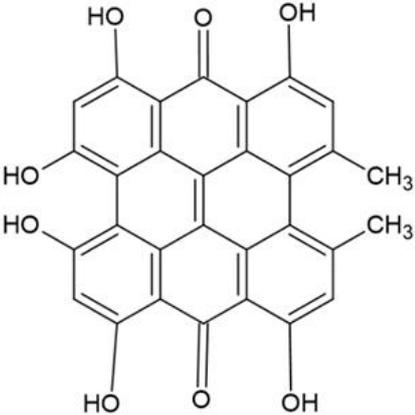
Photosensitizer	Structure
Emodin	
Fagopyrin	
Flavan-3-ol	
Flavone	
Hypericin	

Table 2. Cont.

Photosensitizer	Structure
Rhein	
Riboflavin	

The curcuminoid class consists of four linear diarylheptanoids: dicinnamoylmethane, curcumin, demethoxycurcumin, and bisdemethoxycurcumin. These compounds have a wide range of pharmacological activities, including antiviral, anti-inflammatory, anti-tumor, and antibacterial properties [172–174]. The natural yellow pigment of curcumin (diferuloylmethane) is derived from the rhizomes of turmeric (*Curcuma longa*), which for centuries was widely used for nutritional and therapeutic purposes in Asian countries [175,176]. Curcumin demonstrates photodynamic activity when irradiated with blue light, leading to an increase in  $^1\text{O}_2$  production and induction of a strong phototoxic reaction [176]. The inhibitory effect of this pigment under illumination has been demonstrated against various Gram-positive and Gram-negative bacteria (Table 3), as well as against *Candida* sp. [177–179], human norovirus on food [180], and even against mosquito larvae [181]. Curcumin is known to participate in both type I and type II reactions [182], and its antibacterial activity is associated with damaging the membranes of bacterial cells [175,183]. However, poor water solubility, relatively low bioavailability, and intense staining limit the possibilities of using curcumin as a therapeutic agent [15].

Anthraquinones (AQs) belong to a large family of compounds that are usually divided into monomeric and dimeric anthraquinones [13,15,171]. These compounds are produced by many species of flowering plants, as well as lichens and fungi. They can be found in any plant part: roots, rhizomes, leaves, flowers, and fruits [184]. Most of the studied plants containing AQ derivatives (81%) belong to the Polygonaceae, Rubiaceae, and Fabaceae families. The best known are: emodin, rhein, physcion, chrysophanol, catenarin, rubiadin, and pupurin [13,184]. AQs have a wide range of biological properties, including bactericidal, fungicidal, antioxidant, anti-inflammatory, anticancer, and many others [184]. For example, different research groups have demonstrated the photodynamic activity of aloe emodin from *Rheum palmatum* and *Aloe vera* against various bacteria [185–187] and fungi [188–190] (Table 3).

The perylenequinone (PQ) class, including hypericin, hypocrellins, elsinochromes, and others, has promising characteristics for photodynamic therapy [191]. PQs efficiently produce singlet oxygen, leading to a type II photodynamic process [171]. Their lipophilic nature helps them to penetrate cell membranes [14]. Major plant sources of PQs include herbs such as buckwheat (*Fagopyrum esculentum*) and St. John's wort (*Hypericum perforatum*) [13]. For example, hypericin isolated from the latter is known for its antibacterial and antifungal

properties (Table 3). At the same time, hypericin is poorly soluble in water; to increase efficiency of delivery, it was proposed to use liposomes or micelles [13,192]. The antimicrobial activity of some perylenequinones is summarized in Table 3, but it should be noted that a large number of PQ compounds have yet to be investigated for their photopharmaceutical properties [171].

Furanocoumarins (FCs) or psoralens are coumarins containing a furan ring, found in plants of the Rutaceae family (common rue (*Ruta graveolens*), bergamot fruits, lime, gas plant (*Dictamnus albus*), cloves (*Syzygium aromaticum*)); the Umbelliferae family (e.g., parsley (*Petroselinum crispum*), celery (*Apium graveolens*), parsnip (*Pastinaca sativa*)); the Moraceae family (figs (*Ficus carica*)); and others [14,171,193]. These compounds are phytoalexins, not normally found in uninfected tissues and appearing only when the plant is damaged by pathogens. Furthermore, the FC content is related to the growing season of the plant and can differ significantly before and after flowering [193].

FCs are incorporated into cell DNA in the dark; under the influence of UVA (ultraviolet A) or Vis illumination, a photochemical process then leads to the FC reacting with pyrimidine nucleobases. In addition, FC can react with RNA, cell membranes, and proteins; however, these reactions are less studied [171,193,194]. Moreover, under UVA illumination, psoralens can react with DNA in the absence of oxygen (type III photochemical mechanism) [160,195]. The antibacterial and antifungal activity of psoralens has been demonstrated (see Table 3), but their use for the treatment of humans is limited, due to possible toxicity [171,182].

Alkaloids, the second largest group of natural products, contain a large number of photoactive compounds. These include quinoline (chinolin) alkaloids, pterins, benzylisoquinolines, beta-carbolines, and indigo alkaloids [13,171]. Many of them exhibit antimicrobial properties when exposed to light. For example, dictamnine (4-methoxyfuro [2,3-b] quinoline), found in many Rutaceae species such as *Dictamnus albus*, has been shown to be effective in killing yeast (*Saccharomyces cerevisiae*) and bacteria (*E. coli*) [196]. Among the edible plants containing alkaloids are Berberis species containing the well-known alkaloid berberine [197]. The light-dependent antibacterial properties of this compound have been demonstrated as effective against Gram-positive *S. aureus* and Gram-negative *E. coli* [198–200] (Table 3).

Chlorins belong to the class of tetrapyrroles, macrocyclic compounds widely known for their photodynamic properties. This group also includes porphyrins and bacteriochlorins [13,14,201]. Chlorophyll, the green pigment which plays a crucial role in photosynthesis, is found in plants, cyanobacteria, and eukaryotic algae. The most studied plant sources of chlorophyll are spinach, green cabbage, and dandelion [14,15,202]. Chlorophyll derivatives, chlorins, have strong photodynamic properties and generate large amounts of singlet oxygen (type II photodynamic mechanism) which are not accompanied by the formation of toxic byproducts [203]. However, their poor solubility and low photostability limit their use [13,182].

Flavins, yellow-colored compounds with the basic structure of 7,8-dimethyl-10-alkylisoalloxazine, are widespread in nature and are involved in many biochemical reactions [204]. A well-known representative of flavins, riboflavin (vitamin B<sub>2</sub>), is synthesized by a wide range of organisms, including plants, fungi, bacteria, and animals [13,205]. When exposed to visible or ultraviolet light, riboflavin generates singlet oxygen, hydrogen peroxide, hydroxyl, and superoxide radicals exhibiting photodynamic properties (type I or type II mechanisms, depending on the oxygen concentration) [14,182,206,207]. Edible plants rich in riboflavin are green leafy vegetables (for example, spinach), dark-green vegetables (for example, asparagus), nuts (for example, almonds) and legumes (for example, soybeans) [208–210]. The antimicrobial activity of riboflavin under illumination has been demonstrated against a variety of microorganisms (Table 3).

Table 3. Photodynamic antimicrobial phytochemicals from edible plants.

Chemical Class	PS-Phytochemicals	Edible Plants Containing the PS-Phytochemicals <sup>1</sup>	Tested Microorganisms	References
Curcuminoids	Curcumin	Turmeric ( <i>Curcuma longa</i> )	<i>Acinetobacter baumannii</i>	[211]
			<i>Aggregatibacter actinomycetemcomitans</i>	[212,213]
			<i>Escherichia coli</i>	[214–220]
			<i>Enterococcus faecalis</i>	[221–227]
			<i>Helicobacter pylori</i>	[228]
			<i>Lactobacillus casei</i>	[179]
			<i>Listeria innocua</i>	[216,229]
			<i>Listeria monocytogenes</i>	[230,231]
			<i>Porphyromonas gingivalis</i>	[212]
			<i>Propionibacterium acnes</i>	[224,232]
			<i>Pseudomonas</i>	[233]
			<i>Pseudomonas aeruginosa</i>	[234]
			<i>Staphylococcus aureus</i>	[177,214,215,218,220,234–243]
			Salmonella strains	[230]
			<i>Salmonella typhimurium</i>	[239]
			<i>Streptococcus mutans</i>	[177,179,244–252]
			<i>Staphylococcus saprophyticus</i>	[253]
			<i>Vibrio parahaemolyticus</i>	[254,255]
			Oral bacteria	[202,256–261]
Bacterial Biofilms	[262]			
<i>Candida albicans</i>	[179,263,264]			
Anthraquinones	Aloe emodin	<i>Rheum palmatum</i>	<i>Acinetobacter baumannii</i>	[186,187]
			<i>Escherichia coli</i>	[218]
			<i>Enterococcus faecalis</i>	[185]
			<i>Staphylococcus aureus</i>	[185,218]
			<i>Streptococcus pneumonia</i>	[185]
	Emodin	<i>Cassia occidentalis</i>	<i>Trichophyton rubrum</i>	[190]
			<i>Candida albicans</i>	[189]
			<i>Bacillus subtilis</i>	[265]
			<i>Staphylococcus aureus</i>	[265]
			Rhein	<i>Rheum palmatum</i>
<i>Saprolegnia</i> sp.	[188]			

Table 3. Cont.

Chemical Class	PS-Phytochemicals	Edible Plants Containing the PS-Phytochemicals <sup>1</sup>	Tested Microorganisms	References
Perylenequinones	Hypericin	<i>Hypericum perforatum</i> , <i>Hypericum erectum</i> , <i>Hypericum perforatum</i> L.	<i>Bacillus cereus</i>	[267]
			<i>Escherichia coli</i>	[268–270]
			<i>Enterococcus faecalis</i>	[270]
			<i>Propionibacterium acnes</i>	[271]
			<i>Pseudomonas aeruginosa</i>	[270]
			<i>Staphylococcus aureus</i>	[268–270,272,273]
			<i>Staphylococcus saprophyticus</i> subsp. <i>bovis</i>	[274]
			<i>Candida</i> species ( <i>Candida albicans</i> , <i>Candida parapsilosis</i> , and <i>Candida krusei</i> )	[275]
			<i>Saccharomyces cerevisiae</i>	[276]
			Pathogenic fungi ( <i>Microsporum canis</i> , <i>Trichophyton rubrum</i> , <i>Fusarium oxysporum</i> ) and spoilage yeasts ( <i>Exophiala dermatitidis</i> , <i>Candida albicans</i> , <i>Kluyveromyces marxianus</i> , <i>Pichia fermentans</i> , <i>Saccharomyces cerevisiae</i> )	[277]
Fagopyrin	Fagopyrin	<i>Fagopyrum esculentum</i> Moench	Pathogenic fungi ( <i>Microsporum canis</i> , <i>Trichophyton rubrum</i> , <i>Fusarium oxysporum</i> ) and spoilage yeasts ( <i>Exophiala dermatitidis</i> , <i>Candida albicans</i> , <i>Kluyveromyces marxianus</i> , <i>Pichia fermentans</i> , <i>Saccharomyces cerevisiae</i> )	[277]
			<i>Saccharomyces cerevisiae</i>	[276]
			<i>Streptococcus mutans</i>	[278]
Furanocoumarins	8-methoxy-psoralen	Species of the genus <i>Heracleum</i> in the family Apiaceae	<i>Escherichia coli</i>	[279]
			<i>Staphylococcus aureus</i>	[279]
			<i>Salmonella typhimurium</i>	[280]
			<i>Saccharomyces cerevisiae</i>	[280]
Alkaloids	Berberine	<i>Mahonia aquifolium</i> , <i>Berberis vulgaris</i>	<i>Escherichia coli</i>	[198–200]
			<i>Staphylococcus aureus</i>	[198–200]

Table 3. Cont.

Chemical Class	PS-Phytochemicals	Edible Plants Containing the PS-Phytochemicals <sup>1</sup>	Tested Microorganisms	References
Chlorins	Chlorin <i>e</i> <sub>6</sub>	Spinach, green cabbage, dandelion	<i>Escherichia coli</i>	[281]
			<i>Propionibacterium acnes</i>	[282]
			<i>Pseudomonas aeruginosa</i>	[281]
			<i>Staphylococcus aureus</i>	[281,283]
			<i>Staphylococcus aureus</i>	[282]
			<i>Streptococcus mutans</i>	[284]
			<i>Salmonella typhimurium</i>	[281]
			Upper respiratory opportunistic pathogens ( <i>Moraxella catarrhalis</i> , <i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i> )	[285]
Flavins	Riboflavin (vitamin B2)	Spinach, asparagus	<i>Bacillus atrophaeus</i>	[286]
			<i>Escherichia coli</i>	[287,288]
			<i>Listeria monocytogenes</i>	[289,290]
			<i>Staphylococcus aureus</i>	[288]
			<i>Streptococcus mutans</i>	[291]
			<i>Streptococcus sanguinis</i>	[291]
			<i>Salmonella</i> strains ( <i>Salmonella typhimurium</i> and <i>Salmonella enteritidis</i> )	[292]
			<i>Shewanella baltica</i>	[290]
			<i>Vibrio parahaemolyticus</i>	[290]
<i>Candida albicans</i>	[293]			

<sup>1</sup> In some cases, Table 3 presents PSs found in edible plants, but for testing antimicrobial activity, PSs were either isolated from other sources or used as commercial preparations.

#### 4. Use of Natural Plant Antimicrobials for Food Disinfection

The main demands concerning food are freshness, naturalness, and minimal processing. The concept of naturalness relates to healthy and unmodified food without chemical preservatives. However, consuming raw fruits, vegetables, fruit juices, and sprouts may cause foodborne outbreaks of illness [294].

Conventional methods of microbial inactivation and food decontamination include thermal processing, sanitization, water washing, drying, freezing, refrigeration, irradiation, modified atmosphere packaging (MAP), and the addition of antimicrobial agents, disinfectants, or salts. Irradiation, heat, high pressure, magnetic or electrical fields, and ultrasound are microbial inactivation methods that do not induce microbial resistance [16,57,294,295]. Water washing and sanitization reduce bacterial load with limited success, and disinfectants might cause genotoxicity and carcinogenicity. In addition, thermal processing reduces the level of some bioactive compounds such as anthocyanin pigment, carotenoids, and vitamin C, which can be found in several fruits. Therefore, nonthermal technologies, such as dense-phase carbon dioxide (DPCD), high hydrostatic pressure (HHP), ultraviolet or ozone processing, pulsed electric fields (PEF), and ultrasound, have been studied and analyzed, with promising results.

Each technique was developed for different phases, pigments, geometries, and goals (for instance, for control of microorganisms and inactivation of pathogens on the surface of solid foods vs. the total interior volume of liquids). The DPCD technique is generally used for liquid foods, since the pressure involved damages the tissues of fruits. In PEF, high intensity and long processing affect the nutritional quality of foods. For surface decontamination of food, both UV-C and ozone treatments can be used; however, they are limited to topical applications only. Moreover, a high dosage of ozone processing alters the sensory quality of the food. Although HHP is a size- and geometry-independent treatment, it needs water or sufficient humidity content within the sample in order to avoid structural and/or textural changes. Chemical preservatives such as sugar, acids, and salts (sodium benzoate, potassium sorbate, nitrites, and nitrates) are used commercially in fruits, dairy products, confections, meats and meat products, etc. [294,295]. However, growing evidence of the harmful effects and health risks of these chemical preservatives leaves no other option but to find new methods that will reduce their amounts in foods. The optimal alternative is to substitute appropriate additives that have no adverse effects. To achieve these goals, good candidates are natural antimicrobial compounds such as bacteriocins, chitosan-fermented ingredients, and plant antimicrobials, especially plant extracts and plant-isolated compounds exhibiting a broad-spectrum activity.

The antimicrobial and antioxidant properties of plant extracts are attributed to secondary metabolites such as phenylpropanoids, terpenes, flavonoids, and anthocyanins. Since plants are easily attacked by insects, fungi, and bacteria, they develop an efficient defense system against pathogens by producing secondary metabolites, such as phenols, oxygen-substituted derivatives, terpenoids, quinines, tannins, and antimicrobial peptides (AMPs). The most promising biopreservative plant products are essential oils, plant AMPs, and plant extracts in either pure or crude form [294].

## 5. Essential Oils

Liquid essential oils can be derived from several plant parts: flowers, buds, leaves, fruits, twigs, bark, seed, wood, and roots. In the food industry, essential oils serve as flavoring agents; however, their antimicrobial and antioxidant traits make them the best candidates for food preservation. Their chemical structure and active functional groups change with the types of plants, season, harvesting time, and methods of extraction. The main active groups of essential oil compounds that are correlated with antimicrobial properties are terpenes, terpenoids, phenylpropenes, and other chemical groups [294].

To date, the mechanism of operation is not clearly defined. There is no proof of a mechanism driven by chemically active functional groups, but only a general assumption of the oil penetrating the bacterial cell membrane due to its lipophilic nature, thus disrupting cell function. It was suggested that oil compounds, possessing a phenolic functional group, change the permeability of the bacteria cell membrane and hinder the generation of ATP. Moreover, low concentrations of essential oil inhibit enzymes that are involved in energy production, and in high concentrations it precipitates the protein. Since essential oil is hydrophobic, it is more effective against Gram-positive than Gram-negative bacteria; this is probably attributable to the difference in their cell structure, especially the cell envelope [294].

Different studies have demonstrated the effectiveness of essential oils in both fresh-cut fruit and juices (Table 4). Moreover, essential oil obtained from pink pepper (native to Brazil, Paraguay, and Argentina) exhibited antimicrobial and antioxidant action in cheese, with only 2% concentration [294]. Basil essential oil added to beef burger reduced the growth of *Staphylococcus aureus* from 3 log<sub>10</sub> CFU/g to 2 log<sub>10</sub> CFU/g at 4 °C after 24 h [294]. Treatments with both clove oil and cumin oil enhanced the shelf life of red meat at 2 °C for ~15 days, and reduced the bacterial concentration by ~3.78 log<sub>10</sub>, compared to control measurements. The combination of thyme essential oil added at 0.4, 0.8, and 1.2%, and nisin at 500 or 1000 IU/g, exhibited stronger antimicrobial activity than their individual

usage, decreasing a *Listeria monocytogenes* population to below 2 log<sub>10</sub> CFU/g in minced fish during storage at 4 °C for 12 days [294].

**Table 4.** Plant antimicrobials for food disinfection and conservation.

Antimicrobial Type	Plant Antimicrobials	Plant Source <sup>1</sup>	Target Microorganism	Food	Reference
Essential oil	Bay leaf essential oil	<i>Laurus nobilis</i> , Lauraceae	Coliforms	Tuscan sausage	[296]
	Clove oil	<i>Syzygium aromaticum</i>	<i>Listeria monocytogenes</i>	Minced fish	[297]
			Native microflora	Meat	[298]
	Cuminum (cumin) seed essential oil	<i>Cuminum cyminum</i>	Spoilage moulds	Wheat and chickpea samples	[299]
	Oregano essential oil	<i>Origanum elongatum</i>	<i>Salmonella enteritidis</i>	Minced sheep meat	[300]
	<i>Origanum elongatum</i> essential oil	<i>Origanum elongatum</i>	Lactic acid bacteria, yeasts and molds	Pomegranate juice	[301]
	Thyme or marjoram essential oils	<i>Thymus vulgaris</i> and <i>Origanum majorana</i>	<i>Escherichia coli</i>	Minced pork	[302]
			<i>Escherichia coli</i>	Minced beef	[303]
	Thyme essential oil	<i>Thymus vulgaris</i>	Vancomycin-resistant <i>Enterococci</i> and <i>E. coli</i>	Feta soft cheese	[304]
			Vancomycin-resistant <i>Enterococci</i> and <i>Escherichia coli</i>	Minced beef meat	[304]
<i>Zataria multiflora</i> Boiss essential oil	<i>Zataria multiflora</i>	<i>Listeria monocytogenes</i>	Buffalo patties	[305]	
Antimicrobial peptides (AMPs)	Defensin KT43C	Cowpea seeds	<i>Fusarium culmorum</i> , <i>Penicillium expansum</i> , and <i>Aspergillus niger</i>	Dough	[306]
	Snakin	Potato tubers	<i>Listeria monocytogenes</i> and <i>Listeria ivanovii</i>	Potato	[307]
			spoilage yeast; <i>Zygosaccharomyces bailii</i>	Beverages	[308]
	Thionins	<i>Triticum aestivum</i> (wheat)	<i>Listeria monocytogenes</i> and <i>Listeria ivanovii</i>	Wheat	[309]
Plant extract	Black seed cumin	<i>Cuminum cyminum</i>	<i>Escherichia coli</i> and <i>Enterococci</i> spp.	Meat	[310]
	Clove	<i>Syzygium aromaticum</i>	<i>Escherichia coli</i> and <i>Enterococci</i> spp.	Meat	[310]
	Curcumin	Turmeric ( <i>Curcuma longa</i> L.)	<i>Aspergillus flavus</i>	Maize kernels	[311]
			<i>Escherichia coli</i> , <i>Salmonella</i> , and <i>Listeria monocytogenes</i>	Hami-melons	[312]
	Grape seeds	Grape seeds	<i>Listeria monocytogenes</i>	Buffalo patties	[305]
Raisin	Raisin (species <i>Hovenia dulcis</i> )	Mold	Wheat	[313]	

<sup>1</sup> In some cases, Table 4 presents PSs found in edible plants, but for testing antimicrobial activity, PSs were either isolated from other sources or used as commercial preparations.

Another synergetic effect was proven in the combination of *Zataria multiflora* Boiss essential oil and grapeseed extract in concentrations of 0.1% and 0.2%, respectively, which showed antioxidant activity and effective growth control of *Listeria monocytogenes* in raw buffalo patty. Another study showed that sage and thyme oils exhibited strong antimicrobial activity against vancomycin-resistant *Enterococci* and *E. coli* in minced beef meat [294].

## 6. Antimicrobial Peptides

AMPs are a part of a plant's secondary metabolite defense system. They are widely distributed in plants, plant parts, and the immune system; they participate in enzymatic networks engaged in metabolism as nutrients and storage molecules [294]. AMPs are the first

line of defense against invading pathogens, as biologically active peptides with antimicrobial, antioxidant, antithrombotic, antihypertensive, and immunomodulatory properties.

Due to their amphophilic nature and the presence of positively charged residues, they can penetrate bacterial membranes and alter their permeability. There are two types of AMPs: peptides produced without the involvement of ribosomes (bacitracins and glycopeptides), and peptides synthesized via the ribosomal pathway. The latter peptides participate in the immune defense system of the organism's body. To extract and save crucial information about AMPs, an online antimicrobial peptide database was opened in 2003, with more than 2600 different peptides identified to date. The antifungal activity of AMPs is based on their attack on the fungal cell wall, especially a chitin component that hinders its synthesis and changes the membrane permeability. AMPs also exhibit antiviral activity, in which they bind the glycosaminoglycan moiety of the cell membrane and prevent interaction between the virus and the cell. Bacterial antimicrobial peptides, such as bacteriocins, have been used in food preservation for many years [294].

## 7. Plant Extracts

Since ancient times, spices and herbs have been used not only as flavoring agents but also as preservatives. These plant extracts include leaves such as mint and rosemary, flowers such as cloves (containing eugenol, which is associated with antibacterial activity), bulbs such as garlic and onion, and fruits such as cumin and red chili.

Antimicrobial activity in plant extracts is determined by their phytochemicals. Phenolics, phenolic acids, quinones, saponins, flavonoids, tannins, coumarins, terpenoids, and alkaloids are the major classes of chemical constituents that affect the antimicrobial and antioxidant activity, as well as the flavor of the plant. The hydroxyl group of the phenolic compounds interrupts the functionality of bacterial cell membranes and shifts the electrons, reducing the proton-motive force and inhibiting ATP synthesis, causing cell death. Cinnamaldehyde inhibits bacteria cell-wall synthesis, impairing cell membrane function and affecting the synthesis of nucleic acids. The antioxidant activity of extracts from many plants, such as rosemary, oregano, thyme, sage, marjoram, basil, coriander, and pimento, is attributed to their phenolic component. Phenolic compounds of black pepper damage bacterial membranes and increase antimicrobial activity. Selection of a proper solvent for extraction from plants is crucial for preserving their antioxidant properties [294].

## 8. Limitations in Plant Antimicrobials as Food Preservatives

The US FDA and the European Commission approved some essential oils as food preservatives. The main obstacle encountered in their use is irreproducibility of a standard quality. Essential oils have different qualitative and quantitative fluctuations in their chemical composition, which influence their biological activity [294]. In addition, their strong aromas or flavors alter the organoleptic properties of foods and might reduce the appeal of some food products. Although there are several *in vitro* studies of the antimicrobial activity of plants, they are barely relevant to the application of essential oils for food preservation, since in most cases the results of *in vitro* antimicrobial activity of plant extracts differed from those observed in food. In the latter, the low activity was due to the use of crude extracts, instead of pure compounds which possess higher potency. Crude extract comprises flavonoids in a glycosidic form, which hinders their effectiveness against microorganisms. The presence of an extracting solvent also creates an obstacle for using plant extracts in food. Thus, the use of antimicrobial peptides derived from plants in food is still at its early stage. More research is needed in order to confirm their potential as food preservatives [294].

## 9. Ultrasonic Activation

Recently, new technology was proposed for control and inactivation or eradication of microorganisms. This technology, based on treatment by low-frequency, high-power

ultrasound (US), is considered to be very promising, since it is a nonthermal technology and does not induce microbial resistance.

As mentioned before, total volume depth phase performance (beyond the solid surface) is very crucial for foodborne pathogenic treatments; therefore, US is a more broad-scale method for activation of sensitizers than PDT with its very limited deep-phase penetration ability. Moreover, US may promote more uniform dispersion of a sensitizer in the growth medium. Generally, US is the transmittance of physical pressure (in longitudinal and transverse waves) through a medium at frequencies of more than 20 kHz, which is above the human hearing range [16,314]. US is already extensively applied in medicine and biology; it is now reaching the field of waterborne and foodborne disease prevention. The US technology enables deep penetration into biological tissues while retaining the treated food's nutrient quality. This is in addition to other advantages: environmentally friendly, low-energy consumption; reduced chemical and physical hazards; shorter processing time; safe and convenient operation; relatively low cost and easy focus. In liquids, its mode of action against microbes involves intracellular cavitation and microstreaming around growing and collapsing cavitation bubbles, with speeds and shear rates producing shock waves and microjets (resulting from the bubble collapse), together with ROS formation in situ during the interaction between ultrasound, sonosensitizer, and molecular oxygen; all of which results in bacterial cell death.

However, US treatment alone, without the use of a sensitizer, requires higher intensity and might be dependent on the oxygen environment. Thus, activation of a natural sensitizer by US under normal oxygen conditions seems to be the most promising solution. This technique, called sonodynamic therapy, uses low-intensity ultrasound.

The factors that affect the efficacy of US on microbial decontamination are the US amplitude, exposure duration, treatment temperature, traits of the food, and the volume being processed [16,314–316]. In a recent study by Bhavya (2019), the influence of US on 50 and 100  $\mu\text{M}$  curcumin-mediated PDT treated by blue light ( $70 \text{ J cm}^{-2}$ ) against *E. coli* and *S. aureus* in freshly squeezed orange juice was investigated and analyzed [183].

The effect of US as a pretreatment in the presence and absence of PS, and in combination of PS with blue light, was also studied. It was observed that the effect of US on the inactivation of *E. coli* was dependent on the US intensity. The *E. coli* concentration was reduced by  $3.02 \pm 0.52 \log_{10} \text{ CFU mL}^{-1}$  when treated with US alone at  $50 \text{ W cm}^{-2}$ . However, in the case of *S. aureus*, the US alone did not cause any significant inactivation of bacteria. It was suggested that these results were due to the structural difference between *E. coli* and *S. aureus* bacteria. US treatment in the presence of PS did not show any significant change in the *E. coli* concentration, but it did cause a significant decrease in the *S. aureus* concentration, compared to the US treatment alone (at  $50 \text{ W cm}^{-2}$ ). The results confirmed that the *S. aureus* bacteria were eradicated due to sonodynamic inactivation. The combined treatment of PS, US, and blue light showed a reduction in the *E. coli* concentration by  $4.26 \pm 0.32 \log_{10} \text{ CFU mL}^{-1}$ , while *S. aureus* was only reduced by  $2.35 \pm 0.16 \log_{10} \text{ CFU mL}^{-1}$ . This result showed a synergetic effect on the inactivation of the tested bacteria. Another study investigated sonodynamic action using curcumin on foodborne bacteria *B. cereus* and *E. coli* [315]. The sonodynamic antibacterial activity of curcumin on *B. cereus* was observed when the concentration of curcumin was  $0.5 \mu\text{M}$ , and a concentration of  $2.0 \mu\text{M}$  achieved a profound  $5.6 \log_{10} \text{ CFU mL}^{-1}$  reduction of bacterial concentration. However, in the case of *E. coli*, the sonodynamic action of curcumin caused an antibacterial effect at a concentration of  $20 \mu\text{M}$ , whereas when bacteria were treated by curcumin alone at  $40 \mu\text{M}$ , the cell concentration was reduced by  $2 \log_{10} \text{ CFU mL}^{-1}$  only. These results showed that curcumin at low concentrations exhibited sonodynamic antibacterial effects on *B. cereus*, while in the case of *E. coli* a higher concentration of curcumin and longer sonication time were needed to inhibit the cell growth. Gram-positive *B. cereus* was more sensitive to the curcumin sonodynamic treatment than the Gram-negative *E. coli*, probably because of a dense double outer membrane on the Gram-negative bacteria which inter-

feres with the curcumin penetration into cells and mediates higher resistance of bacteria to disinfectants.

The mechanism of ROS generation under acoustic cavitation is not fully understood. The main hypothesis suggests that the energy release is due to the collapsing microbubbles, which lead to the sonolysis of water and/or sensitizer molecules. In this way, the resulting radicals react with oxygen to form ROS [16]. As in the case of classical photodynamic therapy, sonoluminescence may cause either the type I process, leading to the formation of secondary radicals, or the type II process, in which mainly singlet oxygen eradicates the pathogenic cells. US can damage not only Gram-positive and Gram-negative bacteria, but also yeasts, fungi, algae, and even viruses.

Unfortunately, all the key factors for bacteria eradication, such as sonication frequency, intensity, and pulse cycle, might not be effective in vivo, due to the different susceptibility levels of prokaryotes and eukaryotes to ultrasonic energy. Unlike eukaryotic cells, bacteria respond to the maximum (peak) ultrasound intensity, and not to the total amount of transmitted energy (more precisely, the average cumulative ultrasound intensity). Therefore, it is necessary to choose the suitable parameters when using ultrasound energy, selecting a peak high enough and average intensity low enough to maximize bacterial damage without damaging surrounding cells and tissues [16].

The effect of ultrasound activation on foodborne pathogenic eradication still requires further in-depth study.

## 10. Conclusions

In many cases, studies on antimicrobial effects of edible plants do not focus on the identification of antimicrobial phytochemicals and their modes of action. Among these phytochemicals, polyphenols are the most potent antimicrobial compounds, especially phenolic acids and flavonoids. In some cases, various plant metabolites tend to have synergic or antagonistic effects against both Gram-positive and Gram-negative bacteria. The data presented in this review support the idea that the antimicrobial activity of the plant compounds is the result of a combination of several mechanisms.

Edible plants offer a promising therapeutic potential, especially in the case of antimicrobial compounds such as PSs. Future research priorities should include the identification of PSs and a better understanding of the mechanisms of the phytochemical activity of the plants. Being potent antimicrobial agents, PSs can serve as effective food preservatives. Further studies are necessary to improve antibiotic efficiency of PSs and other phytochemicals.

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