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# Phytochemical Compounds as Antibacterial Agents: A Mini Review

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**Abstract**

Phytochemicals are secondary metabolites mostly produced by higher plants to enable them to survive under various biotic and abiotic stresses. Scientific reports exhibited that these natural compounds have direct and indirect effects on human, animal, fungal and bacterial physiology. Among them, the ability of some phytochemical compounds to suppress or eradicate the pathogenic bacteria with various mode of actions such as phenolic compounds, alkaloids, terpenoids, carotenoids, and some sulfur-containing phytochemicals. Such phytochemical molecules are suggested to meet the urgent need for new antibacterial drugs to overcome the growing phenomenon of the emergence of multi-drug resistant bacterial pathogens. This mini review aimed to demonstrate the recent reports on some phytochemical molecules which showed potent antibacterial activity and may help future researchers working on innovation of new antibacterial drugs with a different mode of action to control the crisis of antibiotics resistant pathogens.

**Keywords:** Phytochemical; Secondary metabolites; Antibacterial; Antibiotics; Medicinal plants

## Introduction

Ancient humans have used plants as a medicine since antiquity, this assumption was built upon interesting fossil records discovered dates to 60000 years ago in Iraq (Mesopotamia) [1,2]. Therefore, plants considered as the main source for medications against various diseases including bacterial infections since the appearance of man on Earth. Accordingly, herbal products were the cornerstone for both of ancient and modern medicine. Recently, in some developed countries such as the United States, pharmaceutical drugs derived from herbs represent about 25%, whereas, in some fast-developing countries of large populations and great cultural heritage such as China and India, it comprises about 80% of the total pharmaceuticals [3].

The secret lies behind the continued use of medicinal plants as a remedy to its amazing ability of producing various and renewable bioactive secondary metabolites known as phytochemical compounds. In recent years, despite huge advances in antibiotic therapies and sophisticated infection strategies, the overuse and improper consumption and wrong implementation of antibiotics to treat pathogenic infections, have led to emergence of multi-drug resistant bacteria which recorded resistance against almost all known antibiotics, this crisis could lead to a disaster threaten the Human existence on Earth in the near future unless new alternatives to the regular antibiotics innovated [4-6]. In scientific literature, Massive researches suggest that some phytochemical compounds extracted from medicinal plants showed effective antibacterial potential against multi-drug-resistant pathogens and these compounds could be exploited as antibacterial drugs [7]. In view of the potential of some phytochemicals as promising antibacterial drugs soon, the current mini review is aimed at briefly reviewing the scientific reports that exhibited the in vitro antibacterial activity of some major classes of phytochemical agents.

## Production of Plant Bioactive Compounds

Recent advances in analytical chemistry revealed that plants produce a vast array of metabolites, it is estimated that each single plant species produce between five thousand to tens of thousands of these bioactive metabolites which enables the plant to adapt and survive under various biotic and abiotic stresses in the environment [8].

Two main types of metabolites are produced by plants, primary and secondary metabolites. Primary metabolites are a kind of metabolites that are directly involved in the plant growth, increasing and proliferation. They usually pull off some basic physiological functions in the plant cells. Some common examples of primary metabolites include Carbohydrates, lipids, proteins, nucleic acids, and vitamins. Whereas, secondary

metabolites are a kind of metabolites that are produced for special functions required for the plant to survive in its environment and these compounds have no role in the growth or the development of the plant (Figure 1).

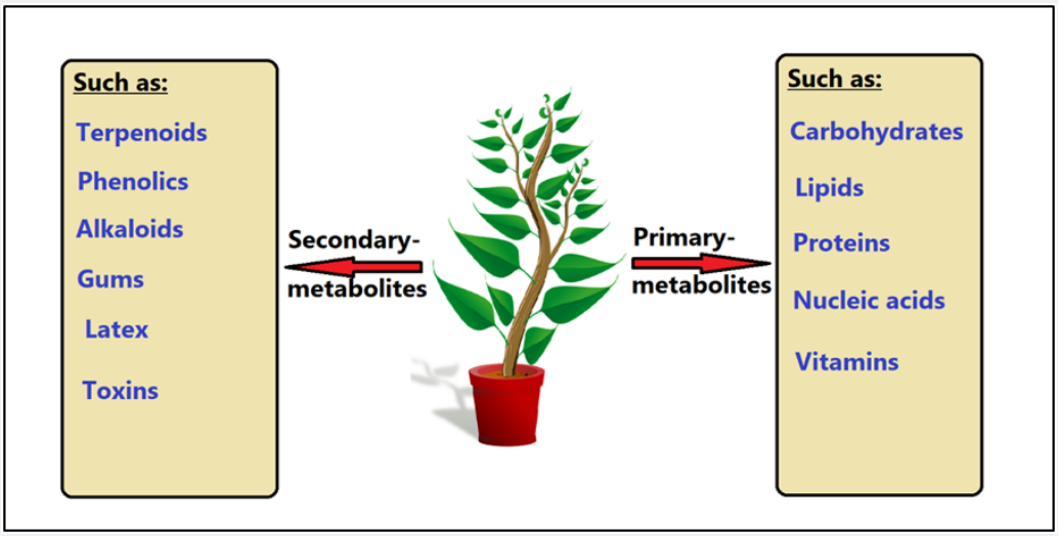


**Figure 1:** Primary and secondary metabolites of plants.

Plant secondary metabolites can be classified into four main categories;

(i) Phenolic compounds such as flavonoids, tannins, chalcones, coumarins and phenolic acids.,

(ii) terpenes such as hemiterpenes, monoterpenes, sesquiterpenes, diterpenes, sesterpenes, triterpenes, tetraterpenes and polyterpenes,

(iii) Nitrogen-containing compounds such as non-protein amino acids, cyanogenic glucosides and alkaloids, and

(iv) Sulphur-containing compounds such as glucosinolates, alliinins, phytoalexins, thionins, defensins and lectins [9-11]. Plant secondary metabolites are known also as phytochemical compounds, these phytochemicals were reported having direct or indirect effects on the human, animal, fungal and bacterial cells; Some phytochemical compounds showed bioactive effects such as stimulation of the immune system, modulation of enzyme actions, modulation of hormone metabolism, pain-relieving properties, anti-oxidant, anti-inflammatory, anti-cancer, anti-bacterial and antiviral activity [12].

## Phytochemical Compounds as Antibacterial Agents

**Table 1:** Few examples of major phytochemical compounds extracted from plants and showed potent antibacterial activity.

| Plant Name | Scientific Name | Part Used | Phytochemical Category | Susceptible Bacteria | Ref. |
|---|---|---|---|---|---|
| Pomegranate | *Punica granatum* | Peels of the fruit | Phenolic compounds | *Staphylococcus aureus, Enterobacter aerogenes, Salmonella typhi and Klebsiella pneumoniae* | [17] |
| Rue | *Ruta graveolens* | Leaves | | *Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa* | [18] |
| Nutmeg | *Myristica fragrans* | seed kernel inside the fruit | | *Providencia stuartii* ATCC299645 and 28 other Gram-negative strains | [19] |
| Mango | *Mangifera indica* | kernel | | *Propionibacterium acnes, Staphylococcus aureus, Staphylococcus epidermidis.* | [20] |


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| | | | | | |
|---|---|---|---|---|---|
| common red, crimson or lemon bottlebrush, | *Callistemon citrinus* | Leaves | Alkaloids | *Staphylococcus aureus* (ATCC 9144), *Pseudomonas aeruginosa* (ATCC 27853) | [22] |
| Trailing Eclipta Plant | *Eclipta alba* | Leaves | | *Staphylococcus aureus Escherichia coli* | [23] |
| Twin-apple | *Ochrosia oppositifolia* | leaves, stembark and roots. | | *Staphylococcus aureus,* MRSA*, Bacillus subtilis, Salmonella thyphimurium, Serratia marcescens* and *Vibrio fluvialis* | [24] |
| Mesquite | *Prosopis juliflora* | leaf, pod and flowers | | *Escherichia coli, Staphylococcus aureus, Bacillus cereus, Psuedomonas putida, Klebsiella sp., Salmonella sp., Acinetobacter sp,* and *Alcaligen* sp. | [25] |
| Guaitecas Cypress | *Pilgerodendron uviferum* | Wood and bark | Terpenoids | Twelve different microorganisms including Gram-positive, Gram-negative bacteria and fungal strains. | [27] |
| Shining poverty bush | *Eremophila lucida* | Leaves | | *Staphylococcus aureus* ATCC 29213, *Staphylococcus aureus* ATCC 25923 | [28] |
| Sarang semut | *Myrmecodia pendans* | Areal parts | | *Streptococcus mutans* | [29] |
| Guiera | *Guiera senegalensis* | Galls | Carotenoids | *Escherichia coli* ATCC 25922; *Salmonella typhimurium* ATCC 13311; *Staphylococus aureus* ATCC 6538, *Bacillus cereus* ATCC 13061 | [31] |
| Annatto | *Bixa orellana* | Fruits | | *Staphylococcus aureus* | [32] |

In recent years, the phenomenon of antibiotic-resistant bacteria has grown dramatically, which considered as a major global health threat. Chemically synthetic antibiotics are failed to keep pace with the bacterial mutations machine which can neutralize the effects of most known antibiotics. Regretfully, antibiotics are not consumed as a human drug only, but they are also consumed in large amounts for farm animals and fish in aquaculture Which doubled the crisis of antibiotics misuse to become a health and environmental problem [13,14]. The reason behind this amazing resistance to antibiotics is related to the fact that the pathogenic bacterial cell has a sophisticated mechanism of mutation enables them to survive inside the host effectively with various strategies. Among these strategies; The ability of bacteria to modify the target sites to avoid the action of antibiotics, decrease the antibiotic penetration and efflux, and make some chemical alternation on the antibiotic molecule to neutralize its effect [15]. Accordingly, introducing some antibacterial phytochemical molecules as drugs which act on bacterial cells with a different mode of action could help in combat this antibacterial crisis. Scientific reports cited that many phytochemical molecules have effective antibacterial activities, such as phenolic compounds, alkaloids, terpenoids, carotenoid and some sulfur-containing phytochemicals. In this mini review, we will mention only a few examples (only 2 to 4 previous studies) to explain the efficacy of these phytochemical categories as antibacterial agents (Table 1).

## Phenolic Compounds

Phenolic compounds are well known bioactive phytochemical molecules, scientific reports evaluated up-to-date about 8000 phenolic compounds, halve of them are flavonoids; Phenolic compounds have versatile benefits for human health, for example, but not limited, antioxidants, anti-inflammatory, anti-cancer, antibacterial, immune system promoting, cardio-protective agents, and skin protection from UV radiation, [16]. With regard to antibacterial activity, hundreds of plants showed antibacterial phenolic compounds extracted from different plant parts, such as Pomegranate peels the methanol, ethanol and aqueous extracts showed high content of phenolic compounds and exhibited remarkable antibacterial activities against *Staphylococcus aureus*, *Enterobacter aerogenes*, *Klebsiella pneumoniae* and *Salmonella typhi* [17]. The leaves


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extracts using deep eutectic solvents of Rue (*Ruta graveolens*) revealed the highest antibacterial activity against gram-negative *Pseudomonas aeruginosa*, and it was also active but with lesser degrees against *Bacillus subtilis, Staphylococcus aureus* and *Escherichia coli* [18]. The crude extract and isolated phytochemical compounds of the seed kernel inside the Nutmeg fruit (*Myristica fragrans*) were tested against 29 tested Gram-negative bacterial strains, the best antibacterial activity recorded with *Providencia stuartii* ATCC299645, while the other strains recorded varying degrees of susceptibility towards these extracts [19]. The kernel of mango fruit (Mangifera indica) exhibited noticeable antibacterial activity against some acne-causing bacteria such as *Propionibacterium acne*, *Staphylococcus aureus*, and Staphylococcus epidermidis [20].

## Alkaloids

Alkaloids are one of the largest and diverse phytochemical group, there are about 12000 alkaloids extracted from various plants and extensively studied; Alkaloids have many benefits for human health, for example, but not limited, muscle relaxant, narcotic analgesics, anti-cancer and antimicrobial agents, also some drugs were derived from alkaloids such as morphine, apomorphine and codeine [21]. The following are few examples of plants rich in alkaloids and showed effective antibacterial properties; The alkaloids extracted from leaves of Callistemon citrinus exhibited highest antibacterial activity against *Staphylococcus aureus* (ATCC 9144) and good activity against *Pseudomonas aeruginosa* (ATCC 27853) the mode of action of the extracted alkaloids showed that these molecules inhibiting ATP-dependent transport of compounds across the bacterial cell membrane [22]. Alkaloids from leaf extract of Eclipta alba was tested against some human pathogenic bacteria, *Staphylococcus aureus* and *Escherichia coli* were among the most susceptible bacteria and it was found that the inhibitory action of the alkaloid increased with the increase in concentration against all tested pathogens [23]. A plant growing in Southeast Asia known as Twin-apple (Ochrosia oppositifolia) was investigated for its antibacterial potential, all plant parts (Leaves, stem-bark and roots) reported different degrees of antibacterial activities; However, leaves and stem bark showed the highest inhibitory effect against *Staphylococcus aureus* followed by *Bacillus subtilis* Salmonella thyphimurium and Serratia marcescens, where the highest inhibitory effect of roots was against MRSA (Methicillin Resistant *Staphylococcus aureus*) and Vibrio fluvialis [24]. The alkaloid rich fraction extracted from a small shrub known as Mesquite (*Prosopis juliflora*) recorded high antibacterial activity against *Staphylococcus aureus*, Bacillus cereus, *Escherichia coli, Psuedomonas putida, Klebsiella sp., Salmonella sp., Acinetobacter sp.* and *Alcaligen sp*. [25].

## Terpenoids

Terpenoids are an important diverse class of phytochemical compounds. Based on scientific literature, it has been confined about 40 000 compounds belonging to terpenoids which makes it one of the largest classes of phytochemicals. Terpenoids are widely used as flavors, fragrances, insecticides, pharmaceutical and industrial compounds [26]. A lot of studies claimed that many terpenoid compounds have potent antibacterial activity. Twelve pure terpenoid compounds extracted from the wood and bark of an aromatic cypress tree (Pilgerodendron uviferum) exhibited varied degrees of remarkable antibacterial activities against twelve different microorganisms including *Staphylococcus aureus, Bacillus subtilis, Streptococcus pyogenes, Escherichia coli, Pseudomonas aureginosa, Fusarium graminearum, Ophiostoma piliferum, Rhizoctonia solani, Phragmidium violaceum, Schizophyllum commune, Pythium irregulare and Botrytis cinerea* [27]. Terpenoids extracted from leaves of *Eremophila lucida* possess good antimicrobial activity against Gram-positive bacteria (*Staphylococcus aureus* ATCC 29213 and *Staphylococcus aureus* ATCC 25923) but did not show activity against the Gram-negative bacteria (*Escherichia coli* ATCC 25922) [28]. Terpenoids isolated from an Indonesian plant known as Sarang Semut (*Myrmecodia pendans*) revealed significant antibacterial activity against *Streptococcus mutans*, the main causative agent of Caries in Human [29].

## Carotenoids

Carotenoids are lipid phytochemical metabolites; they are an important phytochemical class of bioactive diverse properties and till now there are up to 600 carotenoids have been identified and isolated from plants. One of its main roles in the plant is the production of pigments for coloring fruits and vegetables; Scientific studies showed that they possess many protective roles against some diseases and disorders such as cancer, aging-associated diseases, cardiovascular diseases, antioxidant properties and many more [30]. Unfortunately, investigations on the antibacterial potential of carotenoids from plants are little and many studies focusing on carotenoids of some fungal species and Streptomyces. Although, some interesting investigations stated that carotenoids exhibited a remarkable antibacterial activity; Galls of Guiera plant (Guiera senegalensis) from Burkina Faso showed good contents of carotenoids which recorded significant antibacterial activities against *Staphylococus aureus ATCC 6538, Bacillus cereus 13061, Escherichia coli ATCC 25922, Salmonella typhimurium ATCC 13311, and no effect with Proteus mirabilis ATCC 35659* [31]. Carotenoids extracted from fruits of Annato (Bixa orellana L., growing in Philippine, revealed high antibacterial activity against *Staphylococus aureus* [32].

## Other Phytochemical compounds

Plentiful phytochemicals not mentioned above have been found to exhibit antibacterial properties such as sulfur-containing phytochemicals and many more. However, this mini-review has attempted to focus only on the limited number of reports on some phytochemical molecules which showed potent antibacterial activity. Surprisingly, in nature, sometimes


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different categories of phytochemical compounds may act synergistically all together effectively on microbes than if separated into pure compounds. To better illustrate the image, we will give an example on a virus known as Herpes simplex (HSV), it was found that some phytochemical constituents of latex and propolis are more effective as an antiviral agent than if separated to individual compounds Cowan [2]. Accordingly, it would be advantageous to Establishing scientific programs and international research groups supported by governments, Scientific Associations and pharmaceutical companies for more investigations in that worthy field.

## Conclusion and Future Perspectives

No doubt that numerous studies in the past few decades have shown that plants are a good potential source for new antibacterial drugs. Accordingly, there is a promising future for the antibacterial medicinal plants as there are tremendous and diverse numbers of plants on Earth and most of them are not investigated well yet. Moreover, herbal medicine is gaining popularity day by day and subsequently launching new natural antibacterial drugs in the pharmaceutical markets will gain wide acceptance. However, more comprehensive studies related to the isolation of antibacterial phytochemical compounds from medicinal plants much work must still be carried out, to ensure the selection of bioactive and non-toxic or possible side effects of the nominated antibacterial phytochemicals. On the other side, financial support is crucial to push the scientific efforts forward which rely on the interest of pharmaceutical companies to invest in that promising field.

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