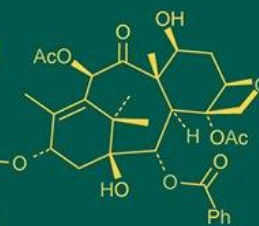
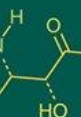
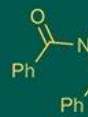


## International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693  
 ISSN Online: 2617-4707  
 NAAS Rating (2026): 5.29  
 IJABR 2026; 10(2): 95-101  
[www.biochemjournal.com](http://www.biochemjournal.com)  
 Received: 07-11-2025  
 Accepted: 28-12-2025

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## Phytochemical diversity and antibacterial mechanisms of medicinal plants native to Iraq: A comprehensive review

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DOI: <https://www.doi.org/10.33545/26174693.2026.v10.i2b.7335>

### Abstract

**Background:** The growing worldwide epidemic of antibiotic resistance accelerated by the rapid development of multidrug-resistant (MDR) pathogens requires the study of new therapeutic approaches to be explored urgently. Medicinal plants are an important critical and well-proven source of diverse bioactive secondary metabolites.

**Objectives:** The comprehensive review aims at providing a systematic description of the high levels of phytochemical diversities of the Iraqi indigenous medicinal plants and to critically explain the complex molecular pathways by which the natural compounds exert strong antibacterial effects.

**Methodology:** Over 60 publications were under rigorous and purposeful examination. This encompassed the data obtained through large-scale ethnobotanical surveys, sophisticated phytochemical screenings (e.g., HPLC, GC-MS) as well as detailed mechanistic studies of Iraqi flora.

**Results:** The results support the evidence of an important and ubiquitous presence of the most important secondary metabolites: potent alkaloids, flavonoid, phenolic acid, and terpenes in the most prevalent families (Asteraceae, Lamiaceae, and Rosaceae). All these compounds share the property of broad-spectrum antibacterial effects to Gram-positive and Gram-negative pathogens, integrating clinically relevant MDRs.

**Conclusions:** It is possible to attribute the above-stated amazing antibacterial activity of the Iraqi medicinal plants to the element of multi-targeted effects composed of direct cell membrane disruption, inhibition of key metabolic enzymes, and advanced interference with bacterial virulence factors. This compilation highlights the fact that Iraq has a rare botanical history that remains a priceless but underutilized source of finding and developing next-generation antibiotic agents.

**Keywords:** Phytochemical, antibacterial, Iraqi medicinal plants, Multidrug-Resistant (MDR)

### Introduction

The application of botanical resources in therapy is as old as the beginning of the history of human civilization, as the principle underlining traditional medicine in every part of the world. The birthplace of civilisation in the Middle East, and more specifically in the present-day territory of Iraq, the ethnobotanical expertise of the Sumerian and Babylonian eras gave life to an extremely powerful and deep ethnobotanical memory in current times. The heterogeneous geography of Iraq-which stretches over mountainous Kurdistan in the north, to alluvial plains and marshlands of the south-provides a distinctive ecological niche to a large diversity of medicinal plants. These are not merely cultural artifacts, but complex biochemical factories with the ability to produce a myriad of secondary metabolites that are specially adapted to protect against microbial predation <sup>[1]</sup>. Since the effectiveness of traditional antibiotics continuously declines due to an active development of multi-drug-resistant (MDR) bacteria, the scientific community started coming back to nature. The so-called post-antibiotic era is no longer an event of the distant future but a present-day reality, according to which such usual infections as before could take deadly proportions <sup>[2]</sup>. In this situation, the medicinal plants of Iraq are an opportune horizon to the discovery of drugs. In contrast to synthetic antibiotics which most often hit one metabolic pathway, plant-based extracts are often an amalgamation of compounds which can offensively attack a number of bacterial targets concurrently, thus reducing the chances of resistance emergence <sup>[3]</sup>. This review summarises the level of information on the phytochemical components of extraction and the antibacterial action of Iraqi medicinal plants.

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It is our aim by filling the gap between the traditional ethnobotanical knowledge and the current pharmacological research to highlight the importance of botanical diversity of Iraq in the global quest to control the infectious diseases. The following parts will outline phytochemical profiles of the major native species and discuss the advanced molecular mechanisms used by the natural agents to counteract the threats of bacteria [4].

### Phytochemical diversity of Iraqi flora

The phytochemical situation in Iraq is characterized by an unprecedented amount of secondary metabolites that play the key role in the expression of the medicinal properties that can be found in the native plants. Such constituents are conventionally divided into a number of major groups, in particular, alkaloids, flavonoids, phenolic acids, tannins, terpenes, and saponins. Every type of class is characterized by unique chemical structures and biological functions part of which form the antibacterial profile of the plant [5]. In particular, alkaloids can be considered one of the strongest classes of phytochemicals in the Iraqi medicinal plants. Some species native to the area (such as the common Syrian Rue, also known as *Peganum harmala*) are particularly are rich sources of beta-carboline alkaloids, such as harmine and harmaline, among others [6]. These nitrogenous compounds have been reported to be intercalative with bacterial DNA as well as block the functioning of key

enzymes hence interfering with cell replication [7]. In the same manner, alkaloid composition of the *T. foenum-graecum* (fenugreek) was likewise associated with high activity to suppress either *Staphylococcus aureus* or *Escherichia coli* [8].

Flavonoids/phenolic compounds are common all over the botanical spectrum of Iraq and they serve as potent antioxidants and antimicrobial agents. In the Asteraceae family, e.g., *Achillea santolina*, flavonoids and terpenes have been shown to be highly concentrated and are involved in its action against *Pseudomonas aeruginosa* [9, 10]. These polyphenolic compounds have been reported to impair the integrity of bacterial membranes in addition to preventing the activity of cytoplasmic enzymes [11]. The Kurdistan region has been noted to harbor plants like *Teucrium parviflorum* and the plants are also a good source of iridoids and flavonoids, which are utilized in local medicine as antimicrobial and anti-inflammatory agents [12].

The richness of these phytochemicals can also be demonstrated in (Table 1), the overview of the main bioactive compounds and antimicrobial properties of the selected Iraqi medicinal plants. These different classes of compounds often interact synergistically to produce both a wider range of activity than can be produced by isolated constituents, which is the basis of the effectiveness of traditional herbal preparations [13].

**Table 1:** Phytochemical Diversity of Selected Medicinal Plants Native to Iraq

| Botanical Name                   | Family       | Key Phytochemicals      | Antibacterial Activity                    | Ref.    |
|----------------------------------|--------------|-------------------------|-------------------------------------------|---------|
| <i>Achillea santolina</i>        | Asteraceae   | Flavonoids, Terpenes    | <i>S. aureus</i> , <i>P. aeruginosa</i>   | [9, 10] |
| <i>Adiantum capillus-veneris</i> | Pteridaceae  | Flavonoids, Phenols     | <i>E. coli</i> , <i>Bacillus subtilis</i> | [1, 14] |
| <i>Agrimonia eupatoria</i>       | Rosaceae     | Tannins, Coumarins      | <i>S. aureus</i> , <i>E. coli</i>         | [1, 15] |
| <i>Camellia sinensis</i>         | Theaceae     | Polyphenols, Catechins  | Broad spectrum                            | [16]    |
| <i>Dodonaea viscosa</i>          | Sapindaceae  | Saponins, Steroids      | <i>S. aureus</i> , <i>K. pneumoniae</i>   | [6]     |
| <i>Myrtus communis</i>           | Myrtaceae    | Essential oils, Phenols | <i>S. aureus</i> , <i>P. aeruginosa</i>   | [6, 17] |
| <i>Peganum harmala</i>           | Nitrariaceae | Alkaloids (Harmine)     | <i>S. aureus</i> , <i>E. coli</i>         | [6]     |
| <i>Teucrium parviflorum</i>      | Lamiaceae    | Iridoids, Flavonoids    | <i>S. aureus</i>                          | [12]    |
| <i>Thymus vulgaris</i>           | Lamiaceae    | Thymol, Carvacrol       | Broad spectrum                            | [6, 17] |
| <i>Trigonella foenum-graecum</i> | Fabaceae     | Saponins, Alkaloids     | <i>S. aureus</i> , <i>E. coli</i>         | [8]     |

### Antibacterial mechanisms of action

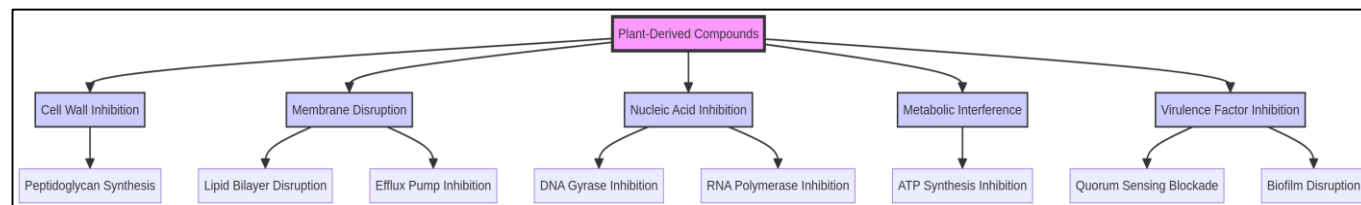
The antimicrobial action of plant-based compounds is not the effect of one particular action but a complex of molecular mechanisms that target diverse processes of bacterial physiology. Such mechanisms can be classified into groups like cell-wall/membrane disruption, protein and nucleic-acid synthesis inhibition, and termination of bacteria virulence and signaling pathways [18]. Bacterial cell membrane disruption is one of the most common mechanisms that have been recorded in plants in Iraq used in medicine. The terpenes and essential oils, including the ones, extracted from *Thymus vulgaris* and *Myrtus communis*, have very strong lipophilic properties that allow them to incorporate into the lipid bilayer of the bacterial cytoplasmic membrane [6, 17]. This improves membrane permeability, causes the leakage of vital intracellular contents including ATP and ions and eventually results in cell death. This effect is also caused by phenolic compounds that denature membrane proteins and cause a change in the physical properties of the cell envelope [1, 11]. Beyond membrane disruption, many phytochemicals prevent the production of necessary macromolecules.

Alkaloids, such as can suppress the work of DNA gyrase and topoisomerase, which are important during the process of DNA replication and transcription [7, 18]. Flavonoids were found to disrupt the translation process by binding bacterial ribosomes as well as block the RNA polymerase activity [19]. These measures are effective to prevent the increase and spread of the pathogen, which has a bacteriostatic or bactericidal effect and varies depending on the concentration and type of compound.

Moreover, in a more recent study attention has been paid to the ability of plant extracts to disrupt bacterial virulence factors yet not necessarily causing cell death. Such an anti-virulence approach encompasses the prevention of quorum sensing (QS), a system of bacterial communication that helps them to coordinate virulence gene expression and biofilm formation. Iraqi derivatives like the use of *Agrimonia eupatoria* and *Adiantum capillus-veneris* have been shown to inhibit QS messages and prevent the formation of protective biofilms, exposing the bacteria to the host immune response and traditional antibiotic activity [1, 15]. (Table 2) shall summarise the major antibacterial mechanisms and shall be illustrated in the (Figure 1).

**Table 2:** Antibacterial Mechanisms of Major Phytochemical Classes

| Phytochemical Class | Specific Mechanism of Action                                   | Target Site          | Ref.     |
|---------------------|----------------------------------------------------------------|----------------------|----------|
| Alkaloids           | Intercalation into DNA, inhibition of nucleic acid synthesis   | DNA/RNA              | [7, 18]  |
| Flavonoids          | Inhibition of cytoplasmic membrane function, enzyme inhibition | Membrane/Enzymes     | [18, 19] |
| Phenols             | Protein denaturation, disruption of cell wall/membrane         | Cell Wall/Membrane   | [1, 11]  |
| Terpenes            | Disruption of the lipid bilayer, increased permeability        | Cytoplasmic Membrane | [1, 18]  |
| Tannins             | Complexation with proteins, inactivation of microbial enzymes  | Enzymes/Proteins     | [1, 17]  |
| Saponins            | Formation of pores in the membrane, leakage of cell contents   | Cell Membrane        | [6, 18]  |

**Fig 1:** Schematic representation of the multi-targeted antibacterial strategies employed by phytochemicals native to Iraqi flora

### Ethnobotanical significance and modern pharmacology

The shift of the tradition of ethnobotanical use into the new pharmacological use presents a strategic channel through which the new antibacterial treatment method can be developed. A rich collection of empirical observations which have long been preserved in Iraq through the continuing dependency on medicinal flora is now being sought to be proved by modern science. Ethnobotanical directories made in places like Sulaymaniyah and Erbil have registered a great deal of botanical taxa actively utilized by local apothecaries to treat a scale of infections [20, 21]. An example of this practice is the application of the traditionally Iraqi praxis of amelioration of cutaneous injuries and skin infections with *Staphylococcus aureus* using a rare and exotic plant, *Achillea santolina*, which is now supported by laboratory evidence of its potency against the bacterium [9]. Similarly, the use of an analogous approach in explanation of the traditional use of the gastrointestinal and respiratory diseases treating agent-*Peganum harmala* by the results of a high level of antibacterial alkaloids concentration in its seeds [6]. This agreement between indigenous knowledge and the empirical observation stresses the need to preserve and question indigenous botanical expertise.

However, the pathway of a crude phytochemical extract to a clinical useful medication is full of challenges. Its chemical complexity concerning the chemical is a tapestry of complex chemicals, which is beneficial to synergistic interactions, but poses significant challenges to standardisation and quality assurance. Moreover, the cytotoxicity of certain phytoconstituents has a potential risk, and therefore, it requires a careful consideration. Modern pharmacological research in Iraq is increasingly focusing on the separation of individual active compounds and the use of state of the art techniques like nanotechnology to increase the transport and efficacy of the antimicrobials naturally found in plants [22, 23]. Fusing ancient wisdom with modern technology, Iraqi experts are opening new ways of creating the future generation of natural antibiotics [24].

### Taxonomic distribution and phytochemical profiles of Iraqi medicinal plants

Medicinal flora of Iraq is characterized by a high level of taxonomic diversity, as various botanical families are able to provide a significant number of phytochemical signatures to the natural pharmacopeia of the country. The Asteraceae

family is one of the most represented families in the Iraqi environment and it comprises species such as *Achillea santolina*, *Artemisia herba alba*, and *Carthamus tinctorius*, all of which have been recognised as having potential in terms of their therapeutic activities. The *Artemisia herba alba*, which is quite prevalent in the desert regions is especially abundant in the sesquiterpene lactones and essential oils; these compounds have proven to be very inhibitory to the Gram-positive bacteria [21, 25]. The severe desert climatic conditions cause the generation of secondary metabolites to develop a survival strategy in the desert, hence defining the phytochemical composition of such plants [26].

The Lamiaceae family is also dominant when it comes to the Iraqi traditional medicine. Some of these foods include *Thymus vulgaris*, *Rosmarinus officinalis* and *Mentha longifolia* which are commonly used as staple foods in local markets and are often used due to their antimicrobial effects. They are typified by large amounts of volatile oils, specifically monoterpenes like thymol and carvacrol that in addition to giving them a characteristic smell have been shown to be potent destabilisers of bacterial cell membranes [6, 17, 27].

The genus *Teucrium* is more diverse especially in the mountainous areas of Kurdistan where some of the species like *Teucrium parviflorum* and *Teucrium polium* have been used as sources of their iridoid and flavonoids. The specialised metabolites are reported to have broad spectrum antibacterial properties, which makes them promising targets in the context of pharmacological studies [12, 28]. The other important family is the complex of Rosaceae, which includes *Agrimonia eupatoria* and some species of *Prunus*. The *Agrimonia eupatoria* is a good source of tannins and coumarins and has been discovered in the more temperate northern parts of Iraq. These compounds are characterized by their capability to bind with bacterial proteins and enzymes, and this causes the inactivation of key metabolic developmental pathways [1, 15]. The occurrence of the above phytochemicals in Iraqi Rosaceae highlights the wide array of chemical response mechanisms used by indigenous plants to deal with the threatening microbes.

The Fabaceae family is rich in *Trigonella foenum-graecum* and *Glycyrrhiza glabra* (licorice) which have saponins and alkaloids of various types and were traditionally used as a remedy to respiratory and skin infections [8, 29]. It is also used in traditional Iraqi medicine with *Luffa cylindrica*

having been recorded, and more recently, the phytochemical profile has been confirmed by this method with triterpenoids and saponins as its components [30]. Antidermatogenic and antibacterial effects of the local landraces of *Lawsonia inermis* (henna) have also been explored, pointing out the significance of henna in dermatology [31, 32].

Another group of sources of bioactive compounds is the Iridaceae family, including *Iris* spp. which are isoflavonoid-producing biomolecules that have been in the spotlight of phytochemistry and biological activity research in the area [33]. An investigation in to some of the Iraqi medicinal plants of the Basrah area established their roles as spasmolytic plants and antibacterials plants which presents a scientific explanation to their usage in the traditional aspect [34]. Phytochemical and morphological variations of different species provide basic background information in conservation and utilisation processes [35]. Other *in vitro* studies on antioxidant and antimicrobial activity of various Iraqi medicinal plants also support the traditional use [36]. Two plants of the Mustansiriyah family have also been described as having antibacterial activity in Iraq, and this adds to the corpus of evidence [37].

Antibacterial activity screening of a total of twenty-two Iraqi wild plants has reported a number of promising ones that should be investigated further [38]. Iraq is also the site of an extensive taxonomic foundation of medicinal flora, comprising of *Cordia myxa* and *Ferulago* spp., which remains a target of intensive phytochemical and biological diversity studies [39, 40].

#### Advanced phytochemical analysis and standardization

With the scientific world moving toward inclusion of herbal medicines in mainstream medicine, the need to perform sophisticated phytochemical analyses and extensive standardization is becoming more and more apparent. To determine and to quantify the bioactive constituents of native flora [6], in Iraq, there is the use of a variety of modalities analytical modalities such as High-Performance Liquid Chromatography (HPLC), Gas Chromatography-Mass Spectrometry (GC-MS), and Nuclear Magnetic Resonance (NMR) spectroscopy [36, 41]. The methods offer overall profiles of phytochemicals that are imperative in ensuring the quality, safety, and therapeutic effect of products derived out of plants. Indicatively, the standardization of the extracts of *Achillea santolina* involves the determination of individual flavonoids and terpenes on which the antibacterial function of the extract is based. Similarly, the concentration of beta-carboline alkaloids is studied in the analysis of seeds of a plant, which displays a rather high level of variability with regard to the geographic provenance and harvesting time [6, 9]. These studies are essential in production of uniform herbal preparations that can be put through clinical trials and ultimately regulatory approval. Furthermore, heavy metal research in Iraqi medicinal vegetation is an essential aspect of safety evaluation because plants might absorb materials from the soil and become dangerous to human wellbeing [8, 36].

Another frontier that is emerging in the research on the Iraqi medicinal plants is the usage of nanotechnology. Scientists are investigating green synthesis of nanoparticles with additional plant extracts as reducing as well as stabilizing agents. These gold or silver nanoparticles have proved to be their best in terms of antibacterial application as opposed to the crude extracts themselves. As an example, silver

nanoparticles made using the extracts of *Camellia sinensis* or *Thymus vulgaris* have been demonstrated to possess strong antibacterial effects against multi-drug resistant organisms [16, 23]. This ground-breaking method increases the effectiveness of plant-based antibacterials in addition to providing a more sustainable and eco-friendly way of developing nanoparticles.

#### Synergistic effects and combination therapies

Another feature of medicinal flora that is especially notable is its ability to produce synergies with the effect of a group working outweighing the action of individual components in se. Implementing this synergy is an essential concept of traditional phytotherapy and thus is an ever-growing way to overcome antimicrobial resistance. The synergistic interactions between different phytochemical classes in the same species or the one between various species extracts of a taxa can occur in the repertoire of the Iraqi medicinal plants [42, 43].

An example is that, concomitant use of aqueous and alcoholic extracts prepared of *Laurus nobilis* and the *Rosmarinus officinalis* has shown a synergistic antibacterial effect on a variety of pathogenic microorganisms, such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* [43, 44]. This synergism is explained by the presence of the wide variety of compounds, focusing at the same time on a wide variety of loci in the cells, including the peptidoglycan layer, cytoplasmic membrane and key metabolic enzymes. These combination therapies eliminate the bacteria by attacking the pathogen through a number of mechanistic pathways and reduce the likelihood of resistance developing.

Moreover, the combination of plant extracts and traditional antibiotics is also an interesting research line. Some phytochemicals are commonly known as resistance modifiers and enhance the action of antibiotics by inhibiting bacterial efflux systems or inactivating resistance determinants such as beta-lactamases. Some studies done on Iraqi endemic species such as *Agrimonia eupatoria* have shown that its extracts have the ability to culminate insensitivity, to regular antibiotics on resistant strains [1, 15]. Such an approach is not only going to increase the usefulness of the existing antimicrobial agents but also will also provide a new set of tools to combat infections caused by multi-drug resistant microorganisms. This systematic study of these synergistic interactions, therefore, is one of the areas of emphasis of modern pharmacological research in Iraq [37, 42, 45].

#### Molecular targets of Iraqi phytochemicals

The subtle interaction of the plant-based secondary metabolites with bacterial targets is a complex process which involves a range of chemical and physical reactions. It is essential that a comprehensive insight on these interactions at the molecular stratum should be understood in order to rationalize the development of new antibacterial therapeutics. A family of key molecular targets has been outlined in the specific environment of the Iraqi phytomedicines, which comprises the cell wall, enzymes of metabolism and genetic material [1, 11, 17]. Most of the phytochemicals occur at the bacterial cell envelope; this is a combination of the peptidoglycan-laden cell wall and the cytoplasmic membrane. Phenolic compounds and terpenoids, which are common in the Iraqi flora, e.g.,

*Myrtus communis* [10], and terpenoids, e.g., *Thymus vulgaris* [12], modify the lipid bilayer of the membrane and change its structure to result in an increased permeability [6, 17]. This is often characterized by the incorporation of lipophilic molecules into the membrane matrix and therefore disrupts the packing of phospholipids as well as the activity of the membrane-bound proteins. This leads to leakage of ions and small metabolites such as potassium and ATP that subsequently causes dissipation of the proton gradients, a process that eventually causes cell death [18, 46].

The other salient target is the bacterial cell wall which in this case is the peptidoglycan synthetic apparatus. Some plant extracts have also shown inhibitory effects on the enzymes that coordinate the chain of cross-linking of the peptidoglycans, just as beta-lactam antibiotics do. As an example, extracts of the plant, *Dodonaea viscosa* have demonstrated the ability to disrupt the integrity of cell walls in Gram-positive organisms, triggering lysis [6, 47]. The latter mechanism of action is particularly effective against the common Iraqi pathogen *Staphylococcus aureus* that is increasingly becoming resistant to other traditional cell-wall types of inhibitors.

Outside of the cell envelope, there is an abundance of phytochemicals that attack intracellular machineries. Alkaloids obtained with extracts of *Peganum harmala* and *Trigonella foenum-graecum* have been known to penetrate the cell of bacteria and interact with the nucleic acids. These agents have the capability to intercalate between the base pairs and cause structural deformations that suppress the catalytic functions of the DNA polymerase and the RNA polymerase [6, 7, 8]. This kind of interference will successfully block the bacterial genome replication and transcription, which inhibits the growth of pathogens. Moreover, the different flavonoids have been reported to have inhibition of the activity of key metabolic enzymes, such as those involved in fatty acid synthesis and respiratory cascade. Plant-derived compounds will disrupt these essential processes and thus may have formidable bacteriostatic or bactericidal effect [18, 19, 48].

### **Inhibition of bacterial virulence and biofilm formation**

Over the past few years, antibacterial studies have been shifted from only having a goal of elimination of bacterial pathogens but to counteracting the virulence tips. This paradigm is often referred to as anti-virulence therapy and aims to reduce the microbial pathogenicity but not to subject the microbes to the high selective pressure, which often promotes the development of resistance. The Iraqi medicinal flora is an excellent source of these anti-virulence agents, especially the agents that affect quorum sensing (QS) and biofilm formation. Quorum sensing is an advanced cellular communication network, which bacteria use to coordinate behaviors relative to population density. It regulates the expression of diverse virulence factors, among which are toxins, motility apparatuses and biofilm matrices. Interestingly, there are a number of Iraqi plant groups of taxa that have been reported to contain compounds that are capable of interfering with QS signalling, and these include: *Agrimonia eupatoria* and *Adiantum capillus-veneris* [1, 14, 15]. Such quorum quenchers can either enzymatically break down signalling molecules, use receptor sites or block synthesis of the signalling itself. Plant extracts are essentially breaking down this intercellular communication so that pathogenic bacteria are essentially silenced by the

extract, hampering their ability to produce an organized attack on the host.

Another key virulence determinant that forms the basis of chronic bacterial processes is biofilm formation. Biofilms consist of complex consortia of microbes embedded into a self-produced extracellular matrix which protects individual cells of the biofilm against the host immune system and other classical antibiotics. The Iraqi medicinal botanicals have proven to be effective in the inhibition of sulphur biofilm formation or subversion of existing ones. As an example, extracts of: *Camellia sinensis* and *Thymus vulgaris* have been reported to inhibit the bacterial adherence to abiotic surfaces and to inhibit the production of the matrix [49, 50]. These phytochemicals therefore make bacteria more vulnerable to therapeutic interventions thus making it easier to cure persistent infections that would be resistant to eradication. The fact that the Iraqi phytochemicals have the ability to intercept the elaborative bacterial mechanisms highlights their potential as an upcoming group of anti-infective agents [51-53].

### **Challenges and future perspectives in Iraqi phytomedicine**

Although the Iraqi medicinal plants have huge potential, there are a number of challenges that need to be overcome to maximize the therapeutic value of the plant. One of the main hindrances is a lack of detailed clinical information. Although encouraging results were demonstrated on many species *in vitro* and in animal models, a properly designed clinical trial would need to be carried out to determine the safety and effectiveness of these species when used in humans. This will require an integrated collaboration between the researchers, clinicians and regulatory bodies in Iraq to ensure that there is a strong framework of clinical testing of herbal products [37, 54]. The other issue that is of high concern is the issue of sustainable management of the botanical resources of Iraq. Excessive exploitation of wild medicinal plants, habitat degradation and climate change have all become a great menace to the biodiversity of the country. There is a pressing need to protect the environment through conservation techniques, such as establishing conservation areas and inventing sustainable cultures of cultivation of important medicinal plants. With the encouragement of the field of such crops, Iraq would have a steady source of quality raw production of pharmaceutical plants and preserve its natural heritage [21, 55].

Moreover, the need to combine the traditional information with modern science requires the multidisciplinary approach. This project has botanists, pharmacologists, ethnobotanists, chemists and even social scientists. The cooperation of these specialists can be more effective to record the traditional knowledge, find bioactive compounds and create new therapeutic agents. The use of the high-tech technologies, including genomics, proteomics, and metabolomics will become instrumental in the clarifications of the intricate interactions of the plant metabolites and the bacterial targets [23, 56]. The future of the Iraqi phytomedicine is hopeful. The discovery of new antibacterial drugs has a strong basis in the country due to the diverse botanical resources available in the country coupled with the long tradition of herbal medicine and the development of a strong scientific community. With an opportunity to tackle the issue of standardization, clinical validation, and conservation, Iraq can be on the forefront of the rest of the

world to create sustainable and effective treatments of infectious diseases. Further discoveries of the Iraqi green gold would continue to bring much discovery that has a direct positive impact on the area and the world general [57, 58].

## Conclusion

The native medicinal flora found in Iraq is a vast unexploited source of phytochemical diversity with significant antibacterial properties. This review has outlined the review the prolific repertoire of secondary metabolites in Iraqi botanicals, namely; alkaloids, flavonoids, and terpenes, as well as faceted molecular pathways through which the agents counteract bacterial pathogens. Starting with disrupting the cellular membranes up to the prevention of proliferation of quorum-sensing pathways, biofilm formation, etc., these natural products offer a multi-targeted approach that gains steadily in relevance in the context of increasing antibiotic resistance. The intersection of ancient ethnobotanical knowledge with the modern pharmacological research is absolutely essential in discovery and cultivation of new therapy agents. In spite of all the challenges that still exist in terms of standardization and clinical validation, the above evidence confirms the importance of the Iraqi botanical heritage as a source of inspiration to be used in the process of pharmacotherapeutics development in the future. Further funding of the research on the Iraqi medicinal plants will both increase the international campaign against infectious diseases, in addition to protecting a critical cultural and biological heritage of future generations.

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