

Review Article

Unlocking the potential: Exploring antimicrobial properties in Asteraceae, Apiaceae, and Rosaceae plant species from Kazakhstan

Baikin Baimakhanova, Amankeldi Sadanov, Irina Ratnikova, Gul Baimakhanova, Erik Shorabaev, Zere Turlybaeva, Assya Balgimbaeva, Zhanar Nurgaliyeva, Roza Seisebayeva, Kulniyazova Gulshat, Kapassov Sarzhan, Aknur Turgumbayeva, Gulnaz Seitimova, and Zhanserik Shynykul

Received (first version): 11-March-2025,

Accepted: 01-May-2025,

Published online: 30-Oct-2025

Abstract

Kazakhstan's rich botanical landscape harbors a treasure trove of medicinal knowledge and practices, deeply rooted in its terrain and cultural heritage. This review explores the diverse flora of Kazakhstan, highlighting the country's vibrant phytobiota and the significant role of traditional healing methods within Kazakh society. Despite the abundant botanical resources, there remains a lack of comprehensive understanding regarding the biochemical composition of most plants, as well as a scarcity of information about the synthesis regulation of biologically active compounds. Moreover, the absence of sufficient pharmaceutical infrastructures exacerbates the underutilization of Kazakhstan's diverse plant life as a source of valuable bioactive compounds. Among the various plant families, Asteraceae, Apiaceae and Rosaceae are extensively studied, with research focusing on the antimicrobial and phytochemical properties of select species. This exploration underscores the potential of these plant families in medicine and phytochemistry, highlighting the need for further research to unlock their therapeutic treasures. Overall, this review emphasizes the importance of bridging traditional knowledge with contemporary scientific research to fully utilize Kazakhstan's botanical resources for medicinal purposes and beyond.

Keywords: Medicinal plants, stress factors, conservation, sustainability, aquaponics, drug development

Baikin Baimakhanova. Research and Production Center for Microbiology and Virology LLC, Almaty, Kazakhstan, bbbayken@mail.ru

Amankeldi Sadanov. Research and Production Center for Microbiology and Virology LLC, Almaty, Kazakhstan, a.sadanov1951@gmail.com

Irina Ratnikova. Research and Production Center for Microbiology and Virology LLC, Almaty, Kazakhstan; iratnikova@list.ru

Gul Baimakhanova. Research and Production Center for Microbiology and Virology LLC, Almaty, Kazakhstan; bgulb@mail.ru

Erik Shorabaev. Research and Production Center for Microbiology and Virology LLC, Almaty, Kazakhstan. eshorabaev@mail.ru

Zere Turlybaeva. Research and Production Center for Microbiology and Virology LLC, Almaty, Kazakhstan. tzj2009@yandex.kz

Assya Balgimbaeva. Research and Production Center for Microbiology and Virology LLC, Almaty, Kazakhstan. imv_rk@list.ru

Zhanar Nurgaliyeva. S.D. Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan, nurgaliyeva.z@kaznmu.kz

Roza Seisebayeva. S.D. Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan, , seisebaeva_68@nail.ru

Kulniyazova Gulshat. Higher School of Medicine, Al-Farabi Kazakh National University, Almaty 050040, Kazakhstan, k_gulshat@mail.ru

Kapassov Sarzhan. Astana Medical University, Astana

00001, Kazakhstan kapasov1959@gmail.com

Aknur Turgumbayeva*. Higher School of Medicine, Al-Farabi Kazakh National University, Almaty 050040, Kazakhstan, turgumbayeva.aknur@med-kaznu.com

Gulnaz Seitimova. Al-Farabi Kazakh National University, Faculty of Chemistry and Chemical Technology, Almaty, Kazakhstan; gulnaz.seitimova@gmail.com

Zhanserik Shynykul. Higher School of Medicine, Al-Farabi Kazakh National University, Almaty 050040, Kazakhstan, shynykul.zhanserik@med-kaznu.com

INTRODUCTION

Research on Kazakhstan's available resources unveils a treasure trove of diverse medicinal knowledge and practices deeply embedded within the Kazakh terrain¹. This repository encompasses a broad spectrum of medical expertise and ideologies that have flourished and evolved within the Kazakh society across centuries, representing an intricate mosaic of traditional healing methods. Passed down through successive generations, these healing practices have been meticulously preserved, serving as an integral component of Kazakh folk medicine, thus safeguarding age-old wisdom for the enlightenment of future generations².

In recent years, there has been a notable surge in the use and exploration of drugs and dietary supplements derived from plants. Ethnopharmacologists, botanists, microbiologists, and natural-products chemists are actively searching the globe



for phytochemicals and potential drug candidates to combat infectious diseases. While a significant portion of existing pharmaceuticals, ranging from 25% to 50%, are plant-derived, none are currently utilized as antimicrobials³. Traditional healers have historically relied on plants for preventing or treating infectious ailments, prompting Western medicine to seek to replicate their successes. Plants contain a diverse array of secondary metabolites, including tannins, terpenoids, alkaloids, and flavonoids, which laboratory studies have shown to possess antimicrobial properties⁴.

In the realm of flora, Kazakhstan's botanical landscape stands as a testament to remarkable diversity, housing an impressive array of approximately 6,400 higher vascular plant species, alongside around 5,000 fungi, 486 lichens, over 2,000 algae, and roughly 500 bryophytes. This botanical opulence, estimated at 14,500 to 15,500 taxa, vividly underscores the country's vibrant phytobiota. This rich botanical tapestry, however, transcends mere biodiversity; it harbors practical significance, with over 1,000 plant species identified by Aralbai possessing medicinal properties⁵. While more than 500 introduced, cultivated, and imported plant species contribute to Kazakhstan's botanical wealth, historical practices—especially during the Soviet era—have significantly depleted this resource, notably affecting medicinal plants, with an estimated 80% of plant resources extensively harvested⁶. The botanical landscape of Kazakhstan unfolds a rich tapestry of plant species, with distinct families playing a pivotal role in contributing to the country's floral diversity. Among these families, Asteraceae takes the lead with an impressive array of 196 species, followed closely by Apiaceae, boasting 89 unique species⁷. Despite the prominence of these families in medicinal contexts, it is intriguing to note that research focusing on the resource potential of medicinal species within Asteraceae and Apiaceae has been limited. This underscores the untapped reservoir of knowledge regarding the therapeutic properties and applications of numerous plant species within these families.

Within the broader spectrum of medicinal herbs, a staggering 648 species contribute to the rich herbal heritage of Kazakhstan. However, the knowledge about their resource potential remains largely unexplored. A mere 88 out of the 648 medicinal herb species have undergone the meticulous process of raw material inventory, representing a mere 3.6% of the plants within the seven leading families. This disparity highlights a significant gap in understanding the full scope of medicinal properties present in these diverse plant species⁶. Further exploration of a subset of widely distributed plant species in Kazakhstan has revealed that some species are not only recognized for their medicinal potential but have also found applications in official medicine^{6,7}. These species, belonging to the Asteraceae, Rosaceae, Lamiaceae, Fabaceae, Ranunculaceae, Apiaceae, and Brassicaceae families, provide a glimpse into the therapeutic richness of Kazakhstan's natural flora⁸. The pharmacological applications of these family species highlight the valuable contributions of these families to the field of medicine, laying a foundation for potential therapeutic interventions and drug discovery⁹. Kazakhstan's botanical wealth, as represented by these families, is not

only vast in terms of species diversity but also holds immense potential for medicinal applications. The limited exploration of the resource potential within these families emphasizes the need for more extensive and focused research efforts to unveil the therapeutic treasures hidden within Kazakhstan's botanical landscape.

Despite the abundance of botanical resources, there is still a lack of comprehensive understanding regarding the biochemical composition of most plants, along with a scarcity of information about the synthesis regulation of biologically active compounds¹⁰. Additionally, the absence of sufficient pharmaceutical infrastructures designed to harness these biologically active substances worsens the situation. Consequently, the vast potential of Kazakhstan's diverse plant life as a source of valuable bioactive compounds remains largely untapped due to these knowledge gaps and inadequate pharmaceutical development frameworks¹¹.

Among the various plant families, Asteraceae and Apiaceae are extensively studied. In Kazakhstan, as in many other countries, research on plant species belonging to these families is more prevalent compared to other plant families. For instance, the species in genera such as *Artemisia*, *Echinacea*, *Centaurea*, *Baccharis*, and *Calendula* (belonging to the Asteraceae family) have shown antimicrobial activity¹². These species are often used in ethnomedicine to treat infections, inflammation, and parasites. The essential oils and crude extracts from these plants have been identified as the effective parts or components with antimicrobial properties, with a particular focus on essential oils. Similarly, the species in genera such as *Aegopodium*, *Ferula*, and *Ledebouria* (belonging to Apiaceae) are also known for their antimicrobial properties¹³⁻¹⁵. Studies have shown that these plants have the potential to be used as natural alternatives to synthetic antimicrobial agents. Further research is ongoing to explore the full range of therapeutic benefits and potential applications of these plant species in the field of medicine.

In this review, we focused on antimicrobial and phytochemical studies conducted on plant species belonging to the Asteraceae, Apiaceae and Rosaceae families. This exploration sheds light on the intricate relationship between these plant families, emphasizing their potential in the realms of both medicine and phytochemistry. As we delve deeper into the findings of these studies, a compelling narrative emerges, underscoring the multifaceted nature of these plants and their significant contributions to antimicrobial research. Furthermore, the aim was to examine antibiotic resistance historically and gather contemporary insights from scientific literature on the potential of medicinal plants as an alternative strategy. The antimicrobial studies conducted on the selected plant species have unraveled a diverse array of properties, showcasing their efficacy against various pathogens. The nuanced interactions between these plants and microorganisms provide valuable insights into potential therapeutic applications. Notably, the outcomes of these studies contribute to the ongoing efforts to combat microbial infections, especially in the context of the rising challenges posed by antibiotic resistance. Moreover,



complementing the antimicrobial investigations, our focus extended to the phytochemical composition of these plant species. By scrutinizing the intricate chemical profiles of Asteraceae, Apiaceae and Rosaceae members, we aimed to unravel the compounds responsible for their antimicrobial efficacy. Phytochemical analyses reveal a rich tapestry of secondary metabolites, including phenolic compounds, alkaloids, flavonoids, and terpenoids, each playing a unique role in enhancing the plants' antimicrobial properties.

Furthermore, our review emphasizes the need for a holistic understanding of these plant families, encompassing not only their antimicrobial potential but also their broader applications in traditional medicine, agriculture, and biodiversity conservation. By bridging the gap between traditional knowledge and contemporary scientific research, we pave the way for a more comprehensive utilization of these botanical resources. Moving forward, this review sets the stage for future research endeavors. It prompts the exploration of lesser-known plant species within Asteraceae and Apiaceae encouraging researchers to uncover hidden antimicrobial treasures. Additionally, the integration of advanced analytical techniques, such as metabolomics and bioinformatics, promises to unveil novel bioactive compounds and intricate biochemical pathways, further enhancing our understanding of these plants' antimicrobial prowess.

METHODS

Ethnobotanical, phytochemical, pharmacological, and clinical information spanning from 2000 to 2023 was gathered from a variety of sources, including online journals, magazines, and books published in English, Arabic, and Persian. To compile this data, electronic databases such as Google, Google Scholar, PubMed, Science Direct, Researchgate, and other online collections were extensively utilized. For efficient retrieval, specific keywords like MIC, antimicrobial, Asteraceae, Apiaceae, and Rosaceae plant extract were employed on the aforementioned search engines. The manuscript comprehensively discusses the utilization of these keywords in exploring pharmacological and ethnomedicinal aspects, providing a holistic overview of the gathered information.

A brief history of the application of plant species in central Asia

The evolution of Kazakh Folk Medicine showcases a dynamic journey marked by transitions and flourishing advancements across successive centuries (Figure 1). Kazakh traditional medicine boasts a rich heritage of employing medicinal plants to combat infectious diseases¹⁶. Throughout history, Kazakh healers have relied on a diverse array of indigenous flora known for their antimicrobial properties. Plants like *Artemisia* spp., thyme, and sage have been traditionally used to address infections due to their potent antimicrobial and antiseptic qualities. With a profound understanding of these botanical remedies, passed down through generations, Kazakh traditional medicine continues to harness the healing power of these medicinal plants in treating various infectious diseases,

contributing to a holistic approach to health and wellness deeply rooted in nature's remedies^{6,17}.

Abu Raihan al-Biruni (973-1048) and Abu Ali ibn Sina, also known as Avicenna (980-1037), were renowned polymaths whose work greatly influenced the development of medical knowledge during the Islamic Golden Age^{18,19}. Both scholars extensively studied traditional medicinal practices and documented their findings, which laid the groundwork for integrating empirical observations and scientific principles into medicine. Their seminal works, such as al-Biruni's "Kitab al-Saydah" ("Book of Medicaments") and Avicenna's "The Canon of Medicine," meticulously recorded medicinal plants and investigated their potential antimicrobial properties, recognizing their effectiveness in treating various illnesses. Through their meticulous observations and writings, al-Biruni and Avicenna provided valuable insights into the antimicrobial properties of numerous plant species, significantly advancing the early understanding and use of natural remedies in disease management. For example, Avicenna's "The Canon of Medicine" includes a dedicated volume on medicinal plants, detailing around 1500 therapeutic remedies and cataloging almost 800 distinct varieties of medicinal vascular plants¹⁹.

During the 15th century AD, Oteyboydak Tleukabyl, a prominent Kazakh healer, authored the manuscript "*Shipagerlik Bayan*", often translated as "*The Healer's Testament*". This seminal work outlines the core principles of Traditional Kazakh Medicine (TKM), combining empirical knowledge with cultural and spiritual healing practices. The text includes detailed descriptions of medicinal herbs, anatomy, pathology, immune responses, and dietary recommendations. Recognized as a foundational document, *Shipagerlik Bayan* reflects the holistic approach to health and disease in Kazakh medical tradition. Through practical experimentation and research conducted in the steppe laboratory, he developed a total of 1108 different types of remedies, including 858 from medicinal plants, 318 from animal organs, and approximately 60 from metallic sources. As a medical practitioner, his contributions were crucial in shaping ancient Kazakh folk medicine, which relied on collective knowledge acquired over generations. His profound understanding led to the categorization of Kazakh medicinal plants into distinct groups—fortifying, refreshing, warming, and laxative—each tailored for specific medical purposes. These systematic classifications formed the foundation of Kazakh traditional medicine, with plant species methodically utilized to treat a wide array of health conditions prevalent in Kazakh society. For example, fortifying plants were used to enhance vitality and strengthen the body, while refreshing plants invigorated and rejuvenated. Warming plants alleviated symptoms of cold-related illnesses, and laxative plants addressed gastrointestinal issues and facilitated digestion. Tleukabyl's meticulous understanding of these plant species and their therapeutic properties allowed for their targeted application in treating various ailments, including respiratory conditions like bronchitis and bronchial asthma, chronic rheumatoid arthritis, stomach-related discomforts such as high acidity and diarrhea, as well as more critical conditions like hemostasis, metrorrhagia, and venomous snake bites. His



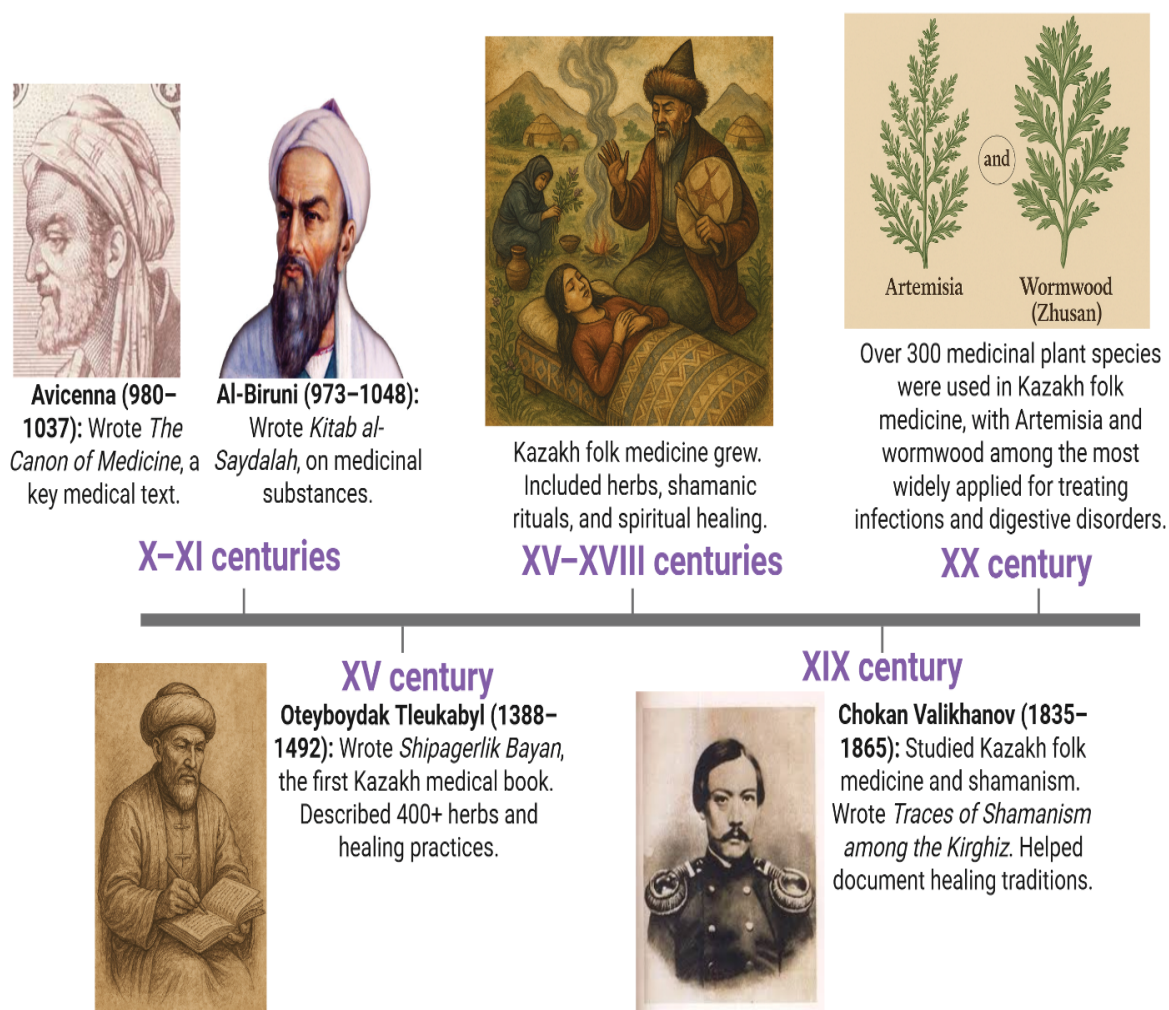


Figure 1. Evolution of Kazakh Folk Medicine: transition and flourishing across centuries^{6,17,18,19}.

contributions highlighted the effective use of natural resources in managing diverse health conditions, demonstrating the potency and versatility of Kazakh medicinal flora¹⁶. During the XV–XVIII centuries, Kazakh folk medicine experienced a vibrant evolution, embracing shamanistic elements deeply ingrained in healing practices. References to this period are found in historical records and explorations by scholars like Chokan Valikhanov (“Traces of shamanism among the Kirghiz”). Shamanistic rituals, spirit communication, and herbal remedies became integral to Kazakh healing traditions, emphasizing holistic approaches to ailments. This fusion, documented in Kazakh oral history, demonstrates the synergy between spiritual beliefs and pragmatic health remedies. The enduring influence of shamanism in Kazakh folk medicine during this era reflects a profound connection between spiritualism and healing practices²⁰.

In contrast to other medical systems within Central Asia, such as the Persian-influenced traditions observed in Uzbekistan or the Tibetan-rooted practices prevalent in the Kyrgyz and Tajik regions, Kazakh traditional medicine is distinguished

by its synthesis of nomadic lifestyles, steppe ecology, and shamanistic practices. Whereas systems like Unani-Tibb prioritized the establishment of written pharmacopoeias and urban clinical environments, the evolution of Kazakh healing occurred within mobile contexts, emphasizing the importance of oral knowledge transmission, indigenous flora, and spiritual healing facilitated by baksys (shamans). The categorization of plants based on their therapeutic properties (e.g., fortifying, warming) and the employment of steppe-specific herbs such as *zhusan* (*Artemisia*) illustrate a distinctive, environmentally adapted approach to medicinal practices^{14,16,20}.

In the early 20th century, the field of botany focused on the practical applications of plants, their compounds, and derived products was termed “economic botany”. In the Soviet Union, this practical aspect of botany underwent analysis, systematization, and the setting of future research goals. During the 1930s to 1950s, efforts were made to search for and identify plants with useful characteristics in Kazakhstan. Kazakhstan boasts a natural flora exceeding 6,000 plant species. The exact count of medicinal plant species in Kazakhstan remains fluid,

with the list growing annually. Over 150 plant species have been utilized in both official and traditional medicine to treat a variety of ailments²¹.

Impact of Pathogens on Human History and the Ongoing Battle Against Antibiotic Resistance

Pathogenic bacteria have had a profound impact on human demography and culture through various illnesses, epidemics, and pandemics. Despite the documentation of numerous historical outbreaks, many of the agents responsible for these events remain unknown. It is crucial to recognize the collaborative role of both viral and bacterial pathogens in causing these occurrences, a fact that is frequently overlooked. For instance, during the 1918 influenza pandemic (Spanish flu), initial reports attributed fatalities to viral pneumonia. However, further investigation revealed that most victims died from subsequent bacterial pneumonia^{22,23}.

Major civilizations throughout history, such as ancient Egypt, Mesopotamia, Rome, China, India, and Islamic civilizations, have all faced large-scale epidemics. However, identifying the precise microorganism responsible for these ancient outbreaks poses a significant challenge²⁴⁻²⁷. One of the most infamous pandemics in history, the bubonic plague or Black Death, was caused by the bacterium *Yersinia pestis* and transmitted by fleas. This devastating plague swept through Europe between 1346 and 1353, leading to the deaths of an estimated 40% of the continent's population²⁸. Globally, fatalities from the Black Death are estimated to have ranged from 50 million to 200 million people²⁹. Another significant disease, syphilis, caused by the bacterium *Treponema pallidum*, emerged in Europe around 1494 and led to approximately 5 million deaths³⁰. Furthermore, the cholera pandemic that began in 1817 resulted in hundreds of thousands of deaths across Asia, Africa, and Europe before subsiding in 1823³¹.

Antibiotics, hailed as the "magic bullets" against bacterial infections, represent one of the most transformative medical breakthroughs of the twentieth century. Their introduction revolutionized the treatment of bacterial diseases, saving millions of lives and significantly reducing the morbidity and mortality associated with bacterial infections. Before the discovery of antibiotics, bacterial infections such as pneumonia, tuberculosis, and sepsis were often fatal³². The first antibiotic, penicillin, was discovered by Alexander Fleming in 1928, and its widespread use during World War II marked the beginning of the antibiotic era³³. Since then, numerous antibiotics have been developed, each with its own spectrum of activity and mechanism of action. However, the misuse and overuse of antibiotics have led to the emergence of antibiotic-resistant bacteria, posing a significant threat to global public health. The rise of antibiotic resistance highlights the importance of judicious antibiotic use, antimicrobial stewardship programs, and the development of new antibiotics to combat the evolving threat of bacterial infections³⁴. Despite these challenges, antibiotics remain indispensable tools in modern medicine, continuing to play a vital role in the fight against bacterial diseases.

Consequently, plant species are increasingly recognized as promising sources of antibiotics, offering a natural alternative to synthetic drugs. Many plant-derived compounds have shown antibacterial properties, making them potential candidates for the development of new antibiotics³⁵. Traditional medicine systems, such as Ayurveda, Traditional Chinese Medicine, and Indigenous medicinal practices, have long relied on plant-based remedies for treating bacterial infections^{36,37}. These natural remedies often contain bioactive compounds that can inhibit the growth of bacteria or disrupt their cellular processes. Harnessing the antibiotic potential of plant species not only offers a sustainable approach to combating bacterial infections but also highlights the importance of preserving biodiversity for medicinal purposes. Continued research into plant-derived antibiotics could lead to the discovery of novel drugs that are effective against antibiotic-resistant bacteria, helping to address the growing threat of antimicrobial resistance.

Understanding antibiotic resistance: mechanisms, challenges, and solutions

In the early stages, many antimicrobial medications, such as penicillin, were derived from natural sources like fungi or bacteria³⁸. For example, vancomycin, teicoplanin, and daptomycin, which impede cell wall formation, originate from *Amycolatopsis orientalis*, *Actinoplanes teichomyceticus*, and *Streptomyces roseosporus*, respectively³⁹⁻⁴¹. Other drugs, like streptomycin, erythromycin, and gentamicin, which inhibit protein synthesis, are sourced from microorganisms such as *Streptomyces griseus*, *Streptomyces erythreus*, and *Micromonospora sp*^{42,43}. Colistin and polymyxin B, which disrupt cytoplasmic membrane permeability, are isolated from *Bacillus colistin* and *Bacillus polymyxa*⁴⁴. Lastly, carbapenem and cephalosporin drugs, which inhibit cell wall synthesis, are derived from *Streptomyces cattleya* and *Cephalosporium acremonium*, respectively^{45,46}. The excessive use of synthetic antibiotics has been linked to significant side effects and poses risks to microorganisms involved in biogeochemical cycling. Furthermore, the potential lethality associated with antibiotic-resistant bacteria is comparable to that of viral epidemics or pandemics⁴⁷. For example, the COVID-19 pandemic was reported to pose a significant risk to hospitalized patients and immunocompromised individuals, leading to a higher incidence of secondary infections, often caused by antibiotic-resistant bacteria⁴⁸.

Antibiotic resistance is driven by two main factors: bacterial adaptability and human influence. Bacteria, being among the most successful microorganisms on Earth, have demonstrated remarkable adaptability over billions of years. Recently, bacterial cells have shown the ability to develop various resistance mechanisms, leading to the emergence of multidrug-resistant pathogens or superbugs. These mechanisms include mutation, plasmid-mediated resistance, biofilm formation, quorum-sensing, outer membrane permeability modification, efflux pumps, reduced uptake, inactivation of antibiotics by bacterial enzymes, and alteration of the antibiotic target. On the human side, antibiotic consumption patterns, misuse, overuse, patient demands, and behaviors regarding antibiotics



contribute significantly to the issue of antibiotic resistance. Understanding these molecular mechanisms of antibiotic resistance is crucial for discovering new antibacterial drugs and developing effective approaches^{28,49}.

Bacteria, among the most successful microorganisms on Earth, exhibit remarkable adaptability and resilience in diverse environments, a trait that has enabled their persistence on the Earth's surface for over 2 billion years⁵⁰. To combat the rising threat of multidrug-resistant pathogens or superbugs, understanding the molecular mechanisms of antibiotic resistance is essential for discovering novel antibacterial drugs and developing effective treatment approaches. Recent studies have highlighted the ability of bacterial cells to develop a range of resistance mechanisms. The convergence of these mechanisms can lead to the emergence of multidrug-resistant pathogens, posing significant challenges to healthcare systems worldwide. Addressing this challenge requires a comprehensive understanding of the mechanisms underlying antibiotic resistance. Mutation, for example, can lead to spontaneous alterations in the DNA sequence of a gene, affecting the trait it codes for. Even a single base-pair change can alter the expression of one or more amino acids, modifying the enzyme or cell structure and resulting in resistance to the targeted antibiotic⁵¹.

Additionally, plasmid-mediated resistance plays a crucial role in the spread of antibiotic resistance genes. Plasmids, capable of being transferred between bacteria of the same or different species via conjugation, often carry numerous antibiotic resistance genes. This phenomenon, known as multidrug-resistant plasmids, severely limits treatment options for infections caused by Gram-negative bacteria. Moreover, biofilm formation represents another significant mechanism of antibiotic resistance. Bacteria that adhere to damaged tissue or medical devices often encase themselves in a matrix of polysaccharides and peptides, forming a slimy coating known as a biofilm. The resistance of biofilms to antibiotics is attributed to complex multicellular mechanisms. Lastly, quorum sensing, a bacterial communication strategy dependent on population density, regulates various activities, including antibiotic resistance. This process has been observed in the development of resistance in *Pseudomonas aeruginosa* when it moves to a new niche and is exposed to antibiotics^{28,46}.

Bacteria can develop resistance to antibacterial medication through various mechanisms. Changes in the DNA sequence of a gene can occur spontaneously, affecting the expression of amino acids and altering the enzyme or cell structure, leading to resistance. Antibiotic resistance genes carried on plasmids can spread among bacteria through conjugation, contributing to the dissemination of multidrug-resistant bacteria⁵². Bacteria can also create biofilms, protective layers that provide resistance to antibiotics through complex multicellular mechanisms. Another mechanism is quorum sensing, a bacterial communication strategy based on population density, which regulates the expression of genes involved in antibiotic resistance. The outer membrane of Gram-negative bacteria

acts as a barrier to antibiotics, which can modify their outer membrane to enhance resistance. Bacteria use efflux pumps to remove antibiotics from the cell, reducing membrane permeability. They also produce enzymes that deactivate antibiotics, rendering them ineffective. Additionally, bacteria can alter the antibiotic's target site, evading its effects by preventing the antibiotic from binding to its receptor or inducing mutation-induced changes to the target site, resulting in reduced sensitivity to the drug^{28,46,49}.

Patterns of antibiotic consumption, along with the misuse and overuse of antibiotics, patient demands, and human behaviors related to antibiotics, are widely recognized as major contributors to the problem of antibiotic misuse and overuse. Self-medication is the most common cause of human pathogen resistance to antibiotics, with 20% of human antibiotic usage occurring in hospitals and 80% in communities. Up to 50% of community usage is considered unnecessary and unjustified. The prevalence of nosocomial infections and antibiotic misuse are significant public health concerns, as antibiotics are frequently used in hospitals for surgical procedures and nosocomial infections, which affect approximately 15–20% of hospitalized patients⁵³.

Unfortunately, humans extensively use antibiotics in food animals to promote growth and prevent illness. Multiple studies have shown that antibiotic resistance resulting from antibiotic use in food animals has a negative impact on human health and the development of resistant bacteria⁵⁴. A similar situation occurs in aquaculture, where the widespread use of antibiotics in large quantities in fish food raises concerns about the presence of residual antibiotics in fish flesh and fish products. Furthermore, antibiotic residues from pharmaceutical companies and the accumulation of large amounts of discarded antibiotics in the environment pose serious environmental risks, as the global antibiotic market consumes between 100,000 and 200,000 tons annually^{55,56}. Antibiotic residues in the environment can have various negative ecological consequences. Climate change may also contribute to the risk of pathogen spread, as changing climatic conditions can alter the distribution and density of organisms, leading to new interactions and increased chances of emerging infectious diseases⁵⁷. Therefore, human behavior in the mass production of antibiotics, the deposition of residues in nature, and the misuse of antibiotics in medicine, veterinary medicine, and agriculture have all significantly contributed to the emergence of antibiotic-resistant bacteria.

Harnessing the therapeutic potential of medicinal plants

Traditional medicinal plants have been used for treatments long before the establishment of Western medicine and the emergence of modern science and technology⁵⁸. Compounds derived from plants were the basis of antimicrobial drugs before the antibiotic era. There are believed to be between 250,000 and 500,000 plant species (Angiosperms) on Earth, with only a small fraction (less than 10%) being consumed by humans and other animals, while many are used for medicinal purposes^{59,60}.



Despite a temporary decline during the Industrial Revolution, popular interest in medicinal plants persists globally. The World Health Organization (WHO) reports a significant and increasing global trend in the use of herbal medicines and phytonutrients to address various health concerns within different national healthcare systems. While plants remain the primary source of healthcare for 80% of individuals in developing countries, herbal remedies have gained acceptance in developed nations, where complementary and alternative medicines have become mainstream^{60,61}. In response to the widespread emergence of antibiotic-resistant bacteria, there has been a growing focus on investigating and applying naturally derived compounds from medicinal plants. This has garnered substantial attention among researchers.

Plant-derived antibacterial agents and unraveling their mechanisms of action

Following the confirmation of the antibacterial efficacy of numerous medicinal plants through scientific studies, the subsequent stage in utilizing these plant compounds as natural antibacterial agents involves understanding their mechanisms of action. Generally, the antibacterial attributes of medicinal plants are believed to stem from two primary mechanisms: chemically interfering with the synthesis or function of crucial bacterial components, and/or circumventing typical antibacterial resistance mechanisms. This mechanism is consistent with well-established antibacterial medicinal plants. Plants may restore the body's physiological balance to enhance resistance to pathogens, a concept absent in antibiotic treatment. In contrast to modern medicine, which often modifies and synthesizes drugs as single bioactive compounds to target specific disorders or infections, traditional medicine typically involves synergism, offering multiple targets against specific diseases. Medicinal plants such as garlic (*Allium sativum*), ginger (*Zingiber officinale*), green tea (*Camellia sinensis*), St. John's wort (*Hypericum perforatum*), black cumin (*Nigella sativa*), licorice (*Glycyrrhiza glabra*), Mongolian milkvetch (*Astragalus membranaceus*), and purple coneflower (*Echinacea spp.*) have a long history of efficacy against microbial diseases. These plants also possess immune-boosting properties and can potentially combat bacterial pathogens if thoroughly researched and effectively utilized^{62,63}.

Antimicrobial activities of Asteraceae, Apiaceae, and Rosaceae species

Kazakhstan's geographical location, situated between Siberia and the Central Asian deserts, and bordered by the Caspian Sea and the towering peaks of the Tien-Shan mountains, gives the country a diverse range of natural landscapes. These include forest-steppes, steppes, arid foothills, small hills, high mountain ranges, deserts' plateaus, salt marshes, sand massifs, lakes, rivers, streams, and wetlands, primarily found in lowland areas. This variety supports a rich biological diversity and various ecosystems. Kazakhstan's territory was divided into 29 main floristic provinces and several subprovinces with distinct flora. Despite mountain ecosystems covering only 7% of the country, each mountain system (such as the Altai, Tarbagatai, Dzhungar Alatau, Northern and Western Tien-Shan, Chu-Ili mountains,

Zailiyski Alatau, and Karatau) represents a separate floristic province. This is due to their location, development character, geo-botanical integrity, and the presence of different natural zones based on altitude, known as "belt-forming" groups of vegetation types specific to certain altitudinal strips on mountain profiles. For example, the Altai region is characterized by a flora typically found in Siberia and not elsewhere in Central Asia⁸. Nonetheless, certain plant species are present in all seven mountain systems of Kazakhstan and are commonly found across a wide range of floristic provinces. For instance, 11 plant species from the Asteraceae family, 16 plant species of Apiaceae, and 11 Rosaceae species have been reported to be distributed in all seven mountain systems of Kazakhstan^{1,6,7,8}. Certain plant species have shown a wide-ranging antibacterial activity against human pathogens.

Antimicrobial activities of Asteraceae

The Asteraceae family, commonly known as the aster, daisy, or sunflower family, comprises a vast array of plant species with diverse biological activities. Among these, the investigation of antibacterial properties and Minimum Inhibitory Concentrations (MIC) has gained significant attention. This essay aims to provide a comprehensive exploration of the antibacterial activity of various Asteraceae plant species against different microorganisms, focusing on their MIC values. Asteraceae is one of the largest and most diverse plant families, encompassing a wide range of genera and species⁶⁴. Many members of this family have been traditionally used for medicinal purposes due to their rich phytochemical content. The antibacterial properties of Asteraceae plants have become a subject of scientific interest, driven by the urgent need for novel and effective antimicrobial agents. For instance, *Achillea millefolium* L., commonly known as yarrow, is a well-known member of the Asteraceae family and the antibacterial activity of *Achillea millefolium* L. has been investigated against various microorganisms, including *S. epidermidis*, *S. aureus*, *B. cereus*, *E. faecalis*, and *E. coli*. The MIC values reported for this plant against these strains demonstrate its potential as an antimicrobial agent. The efficacy of *Achillea millefolium* L. against both gram-positive and gram-negative bacteria suggests a broad-spectrum antibacterial activity⁶⁵.

Achillea asiatica Sergo and *Achillea setacea* are additional members of the Asteraceae family that have exhibited antibacterial properties^{66,67}. The former demonstrated activity against *S. Aureus*, *C. Albicans*, and *P. aeruginosa*, with MIC values ranging from 27 to 29.1, 15.7 to 34.8, and 0.05, respectively⁶⁶. On the other hand, *Achillea setacea* displayed antibacterial activity against *E. faecalis* with an MIC of 62.5⁶⁷.

Antennaria dioica, a member of the Asteraceae family, exhibited antibacterial activity against various fungal strains, including *Aspergillus flavus*, *Aspergillus niger*, *Candida albicans*, *Candida parapsilosis*, and *Penicillium fumiculosum*, with MIC values ranging from 31.25 to 62.5. Similarly, *Artemisia annua* demonstrated antibacterial activity against *S. Aureus* with an MIC of 0.125. Moreover, *Artemisia vulgaris* L., commonly known as mugwort, has been studied for its antibacterial activity against *S. aureus*, *B. subtilis*, and *E. coli*. The MIC



values reported for different strains indicate varying degrees of effectiveness, showcasing the complexity of the interactions between plant compounds and microbial species. These findings underscore the need for further research to elucidate the mechanisms behind the antibacterial effects of *Asteraceae* plants⁶⁹.

Artemisia sieversiana displayed antibacterial activity against *Erwinia carotovora*, *Pseudomonas corrugate*, *Pseudomonas syringae*, and *Xanthomonas vesicatoria*, with MIC values ranging from 5.31 to >42.5⁷². Additionally, *Artemisia santolinifolia* exhibited antibacterial activity against *S. aethiopsis*, *S. aureus*,

and *S. epidermidis* strains, with MIC values ranging from 5.0 to 216.59. These results highlight *Asteraceae* plants' potential in combating gram-negative and gram-positive bacterial strains⁷³.

Overall, the *Asteraceae* family presents a rich source of plant species with diverse antibacterial activities against various microorganisms. The reported MIC values indicate the potency of these plants in inhibiting the growth of bacterial and fungal strains (Table 1). The wide spectrum of activity observed in different *Asteraceae* species underscores the potential for developing novel antibacterial agents. However, further research is essential to identify and isolate the active compounds

Table 1. Antibacterial activity and minimum inhibitory concentrations (MIC) of various plant species of Asteraceae against different microorganisms

Extracted plant species	Microorganism	The value of activity, MIC (µg/ml)	Main antimicrobial compounds	Reference(s)
Achillea millefolium L.	Staphylococcus epidermicis	12.6	casticin, apigenin, thymol, carvacrol	[65]
	Staphylococcus aureus	15.4		
	Bacillus cereus	29.2		
	Enterococcus faecalis	63.8		
	Escherichia coli	22.8		
Achillea asiatica Sergo	Staphylococcus aureus	27 to 29.1	camphor, caryophyllene oxide, 1,8-cineole, camphene, β-pinene, germacrene	[66]
	Candida albicans	15.7 to 34.8		
	Pseudomonas aeruginosa	0.05		
Achillea setacea	Enterococcus faecalis	62.5	camphor, 1,8-cineole, α-terpineol	[67]
Ajania fruticulosa	Candida albicans	20	myrcene, 1,8-cineole, and pinene	[68]
Antennaria dioica	Aspergillus flavus	62.5	luteolin, kaempferol, apigenin	[69]
	Aspergillus niger	62.5		
	Candida albicans	31.25		
	Candida parapsilosis	31.25		
	Penicillium fusiculosum			
Artemisia annua L.	Staphylococcus aureus	0.125	camphor, β-caryophyllene	[70]
Artemisia vulgaris L.	Staphylococcus aureus	6.568 ± 1.033,	eucalyptol , sabinene , endo-Borneol , 2,7-Dimethyl-2,6-octadien-4-ol , and 10-epi-γ-Eudesmol .	[71]
	Bacillus subtilis,	5.971 ± 1.033,		
	Escherichia coli 97	7.164 ± 0.0		
	Escherichia coli 57	5.375 ± 0.0		
Artemisia sieversiana	Erwinia carotovora	21.2	absinthin, epiashantin, triclin	[72]
Willd.	Pseudomonas corrugate	21.2		
	Pseudomonas syringae	5.31		
	Xanthomonas vesicatoria	> 42.5		
Artemisia santolinifolia	Salvia aethiopsis	216.59	-	[73]
	Staphylococcus aureus	10		
	Staphylococcus epidermicis	5		
Artemisia pauciflora	Streptococcus pneumoniae	64	-	[74]
	Klebsiella pneumoniae	72		
	Streptococcus pyogenes	98		
	Bacillus subtilis	50		
	Staphylococcus aureus	25		
	Pseudomonas aeruginosa	10		
Artemisia juncea	Staphylococcus aureus	285.694 ± 0.002	-	[75]



responsible for these effects and understand the underlying mechanisms. The findings discussed in this essay contribute to the growing body of knowledge on the antibacterial properties of Asteraceae plants, paving the way for future applications in the field of antimicrobial drug discovery.

The main antimicrobial compounds found in selected species of Asteraceae, such as casticin, apigenin, thymol, carvacrol, camphor, caryophyllene oxide, 1,8-cineole, camphene, β -pinene, germacrene, α -terpineol, myrcene, luteolin, kaempferol, eucalyptol, sabinene, endo-borneol, 2,7-dimethyl-2,6-octadien-4-ol, 10-epi- γ -eudesmol, absinthin, epiashantin, and triclin, have been reported to exhibit antimicrobial activity against a variety of human pathogens. These pathogens include *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus cereus*, *Enterococcus faecalis*, *Escherichia coli*, *Candida albicans*, *Pseudomonas aeruginosa*, *Aspergillus flavus*, *Aspergillus niger*, *Candida parapsilosis*, *Penicillium fumiculosum*, *Bacillus subtilis*, *Erwinia carotovora*, *Pseudomonas corrugate*, *Pseudomonas syringae*, and *Xanthomonas vesicatoria*. These compounds may act synergistically to combat microorganisms by targeting different aspects of microbial growth and survival, such as cell wall synthesis, membrane integrity, protein synthesis, and enzyme activity, leading to more effective antimicrobial activity compared to individual compounds.

Antimicrobial activities of Apiaceae

The Apiaceae family, also known as the carrot or parsley family, encompasses a diverse group of plants with notable culinary and medicinal significance. Recent scientific interest has focused on unraveling the antimicrobial properties of various Apiaceae species, recognizing their potential in combating microbial infections. In this essay, we delve into the antimicrobial activity of selected Apiaceae plant species, shedding light on their individual properties and highlighting their promising roles in the realm of medicine⁷⁶. For example, *Aegopodium alpestre* has been investigated for its antimicrobial activity. Studies indicate inhibitory effects against *Escherichia coli*, with reported MIC values of 3,100 and 3,200 $\mu\text{g/ml}$. While the potency of *Aegopodium alpestre* is moderate, further research is needed to identify specific bioactive compounds responsible for these effects and to explore potential applications in microbial control⁷⁷. Moreover, *Aegopodium podagraria*, or ground elder, stands out for its antimicrobial activity against *Bacillus subtilis*. The reported MIC values range from 1,250 to 5,000 $\mu\text{g/ml}$, suggesting variability in the inhibitory potential. Unravelling the compounds responsible for this variability and understanding their mechanisms of action could provide valuable insights into harnessing the full antimicrobial potential of *Aegopodium podagraria*⁷⁸.

Angelica decurrens, a member of the Apiaceae family, exhibits antimicrobial activity against both *Escherichia coli* and *Bacillus subtilis*, with MIC values of 14.9 and 14.0 $\mu\text{g/ml}$, respectively. This dual effectiveness against Gram-negative and Gram-positive bacteria positions *Angelica decurrens* as a potential candidate for further exploration in developing broad-spectrum antimicrobial agents. *Angelica palustris*, or marsh angelica, displays antimicrobial activity against *Staphylococcus aureus*,

Escherichia coli, and *Pseudomonas aeruginosa*. The reported MIC values range from 1.24 to 2.04 $\mu\text{g/ml}$, highlighting its potential against both Gram-positive and Gram-negative bacteria⁷⁹. Moreover, *Angelica sylvestris* demonstrates antimicrobial activity against a spectrum of bacterial strains, including *Enterobacteria aerogenes*, *Enterococcus species*, *Escherichia coli*, *Citrobacter freundii*, and *Lactobacillus plantarum*. The consistent MIC values of 1.80 and 6.30 $\mu\text{g/ml}$ suggest potential therapeutic applications against a diverse range of bacteria, showcasing its broad-spectrum antimicrobial potential^{81,82}. Other plant species provide evidence of their wide-ranging antibacterial activity against human pathogens (Table 2)⁸³⁻⁹⁶.

Antimicrobial activities of Rosaceae species

The Rosaceae family comprises numerous plant species that are widely distributed and have economic and medicinal significance. Phytochemical analysis has revealed that the effective and nutritional components of these plants mainly include 61 flavonoids, 83 triterpenes, 75 tannins, 10 phenolic acids, 10 polysaccharides, eight fatty acids, eight organic acids, 15 carotenes, and two vitamins. As such, flavonoids, triterpenes, and tannins are identified as the principal active components of this genus. Modern pharmacological studies have further validated that the Rosaceae genus exhibits a diverse range of bioactivities and nutritional benefits, including antineoplastic and anti-cancer properties, anti-inflammatory effects, liver protection, antioxidant properties, blood sugar regulation, nervous system protection, and cardiovascular protection⁹⁷. Besides their diverse uses, many plants belonging to the Rosaceae family have been found to possess antimicrobial properties. This essay will provide an overview of the antimicrobial activities of Rosaceae species, focusing on their therapeutic potential against various microorganisms⁹⁸. Several studies have reported the antibacterial activities of various selected Rosaceae species against both Gram-positive and Gram-negative bacteria (Table 3)⁹⁹⁻¹¹¹.

Strong Antimicrobial Phytoconstituents of Asteraceae, Apiaceae, and Rosaceae species

Although synthetic antimicrobial agents are widely approved in many countries, researchers continue to be drawn to the potential of medicinal plant-derived natural compounds. These compounds offer a vast resource for discovering new bioactive substances that can combat resistant microorganisms. Chemicals derived from medicinal plants represent a diverse group of compounds naturally found in plants. They have the ability to enhance the clinical efficacy of older antibiotics, potentially overcoming issues of resistance. Therefore, it is important to consider plant species from families such as Asteraceae, Apiaceae, and Rosaceae, among others, when searching for new antimicrobial agents. These plant families have been historically rich sources of bioactive compounds with antimicrobial properties. Their exploration could lead to the discovery of novel antimicrobial agents to address the challenges posed by resistant microorganisms¹¹².

Bioactive plant extracts often consist of complex mixtures



Table 2. Antibacterial activity and minimum inhibitory concentrations (MIC) of various plant species of Apiaceae against different microorganisms				
Name of plant species	Antibacterial	MIC (µg/ml)	main antimicrobial	Reference(s)
			compounds	
Aegopodium alpestre	Escherichia coli	3.1	β-caryophyllene	[77]
	Aerogenic bacterium	3.2		
Aegopodium podagraria	Bacillus subtilis	1.25 – 5.00	quercetin, kaempferol, apigenin, caffeic acid, chlorogenic acid,	[78]
Angelica decurrens	Escherichia coli	14.9	ligustilide, ferulic acid, coumarins	[79]
	Bacillus subtilis	14		
Angelica palustris	Staphylococcus aureus	1.24	–	[80]
	Escherichia coli	1.75		
	Pseudomonas aeruginosa	2.04		
Angelica sylvestris	Enterobacteria aerogenes	1.8	–	[81,82]
	Enterococcus durans	1.8		
	Enterococcus faecalis	1.8		
	Enterococcus faecium	1.8		
	Escherichia coli	6.3		
	Citrobacter freundii	6.3		
Bulpeurum bicuale Helm	Iron bacteria	275.2	–	[83]
	Purple sulfur bacteria	296.9		
	Methanobacteriae	118.7		
Bulpeurum longifolium L subsp aureum	Escherichia coli	>256.00	–	[84]
	Aerogenic bacterium	5		
Bulpeurum multinerve	Staphylococcus aureus	15.9	limonene	[85]
	Fusarium oxysporum	16.9		
	Aspergillus niger	13.4		
Carun carvi	Genera Clavibacter	10.33	carvone, limonene, carvacrol, thymol	[86]
	Curtobacterium	11.23		
	Rhodococcus	9.83		
	Erwinia	7.32		
	Xanthomonas	11.03		
	Ralstonia	0.83		
Agrobacterium	0.76			
Cenolophium denudatum	Staphylococcus aureus	27.5 – 265.00	apiole, β-phellandrene, γ-terpinene:	[87]
	Enterococcus faecalis			
	Acinetobacter boumannii			
	Serratiamarcescens			
	Klebsiella pneumoniae			
Pseudomonas aeruginosa				
Conioselinum tataricum	Staphylococcus aureus	26.50 – 30.10	γ-terpinene, β-phellandrene, apiole	[88]
	Escherichia coli			
	Aspergillus niger			
	Candida albicans			

Eryngium planum L.	Escherichia coli	22.5	γ-terpinene, β-phellandrene, apiole	[89,90]
	Staphylococcus aureus	27.5		
	Candida albicans	17.8		
Ferula foetida Bunge	Staphylococcus aureus	175	-	[91,92]
	Staphylococcus epidermidis	125		
	Bacillus subtilis	100		
	Escherichia coli	100		
	Klebsiella pneumoniae	105		
	Pseudomonas aeruginosa	100		
Heracleum dissectum	Staphylococcus aureus	27.7	-	[93,94]
	Staphylococcus epidermidis	27.5		
Heracleum sibiricum	Candida albicans	0.50 – 16.00	bergapten, pimpinellin, isopimpinellin, xanthotoxin and imperatorin	[95]
Peucedanum morisonii	Pseudomonas aeruginosa	12.7	peucedanin	[96]
	Staphylococcus aureus	12.9		
	Salmonella typhimurium	11.6		

Table 3. Antibacterial activity and minimum inhibitory concentrations (MIC) of various plant species of Rosaceae against different microorganisms

Extracted plant species	Microorganism	The value of activity, MIC (μg/ml)	Solvent/fraction	Reference(s)
Agrimonia pilosa	Staphylococcus aureus	62.5	limonene	[99-101]
	Bacillus subtilis	0.625		
	Klebsiella pneumoniae,	175		
	Pseudomonas aeruginosa,	175		
	Ralstonia solanacearum	175		
Comarum palustre L.	Staphylococcus aureus	1.56	-	[102]
	Bacillus subtilis	1.56		
	Pseudomonas aeruginosa	1.56		
Crataegus chlorocarpa	Staphylococcus aureus	1.25	-	[103]
Cotoneaster melanocarpus	Staphylococcus aureus,	0.195	-	[104]
	Candida albicans	0.391		
Crataegus sanguine	Bacillus cereus	100	-	[105]
Filipendula ulmaria	Escherichia coli,	156	-	[106]
	Enterococcus faecalis,	156		
	P. cyclopium,	250		
	F. oxysporum,	500		
Geum rivale L.	Staphylococcus aureus,	15.6	ellagic acid, caffeoyl-hexoside malate, ellagic acid pentoside	[107]
	Escherichia coli,	31.2		
	Staphylococcus aureus	27.17		
Rubus caesius L.	Clostridium bifermentans	1.61	quercetin, apigenin, kaempferol, rutin	[108]
	Clostridium sporogenes	1.62		
	Enterococcus faecalis	1.61		
P. chrysantha	S. epidermidis	48	-	[109]
	Bacillus cereus	14		
	Bacillus subtilis	55		
	Escherichia coli	60		

	Shigella flexaneriae	64		
	Shigella boydii	25		
		28		
Silaum silaus	Staphylococcus aureus	100	-	[110]
	Staphylococcus epidermidis	200		
	Escherichia coli	150		
	Enterobacter cloacae	200		
	Klebsiella pneumoniae	300		
	Pseudomonas aeruginosa	230		
	Candida albicans	350		
	Candida tropicalis	600		
	Candida glabrata	600		
Spiraea chamaedryfolia	Helicobacter pylori	100	-	[111]

of ingredients, and their combined action can produce a more potent effect. These compounds can impact microbial cells in various ways, with their primary target often being the cytoplasmic membrane. They can alter the membrane's structure, integrity, permeability, or functionality, leading to disruptions in essential cellular processes¹¹³. Additionally, plant extracts have been proposed to contain inhibitors of efflux pumps (EP), which are protein complexes responsible for removing toxic substances from microbial cells. By inhibiting EP, plant extracts may prevent the removal of antimicrobial compounds from the cell, leading to increased effectiveness against microbes. This synergistic action and multi-target effects make plant extracts attractive candidates for combating microbial infections, especially in the context of increasing antibiotic resistance. Understanding the mechanisms by which these plant compounds act on microbial cells is crucial for developing new strategies to combat resistant pathogens. Further research is needed to elucidate the specific compounds responsible for these effects and to optimize their use in antimicrobial therapy. Additionally, exploring the potential interactions between different compounds within plant extracts could provide valuable insights into their synergistic effects and enhance their therapeutic potential¹¹⁴.

Despite the wide variety of these compounds, they can be categorized into several main groups based on their chemical structures, composition, biosynthetic pathway, or solubility. These groups include alkaloids, terpenoids, and polyphenols. The mechanisms of action and antimicrobial activity of the most significant compounds from these chemical groups are discussed below and summarized in the following sections [Table 4].

Numerous herbal remedies emphasized within Kazakh traditional medicine are concurrently acknowledged in formal pharmacopoeias and international herbal databases, thereby affirming their substantiated therapeutic efficacy. For example, *A. millefolium* is incorporated in the European Pharmacopoeia for its application in alleviating minor spasms and treating superficial injuries¹³³. *Artemisia annua*, recognized

for its highly effective antimalarial constituent artemisinin, is cited in the WHO Monographs as well as the Chinese Pharmacopoeia¹³⁴. Similarly, *Filipendula ulmaria* is recorded for its anti-inflammatory attributes and is officially endorsed in European herbal medicinal practices¹³⁵. In the realm of cardiovascular treatment, various species of *Crataegus* are acknowledged in the European Pharmacopoeia for their therapeutic applications concerning cardiac conditions¹³⁶. These recognitions illustrate the correspondence between traditional Kazakh methodologies and universally accepted medicinal criteria, thereby accentuating the pharmacological significance of the region's ethnobotanical legacy.

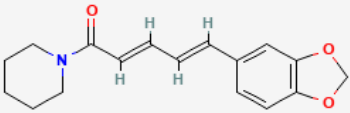
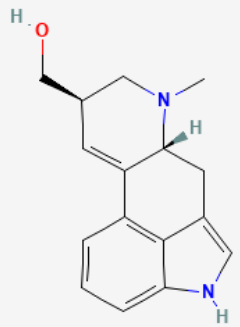
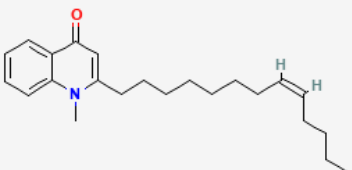
Exploring the Antibacterial Potential of Asteraceae, Apiaceae, and Rosaceae Plant Species: Importance and Challenges

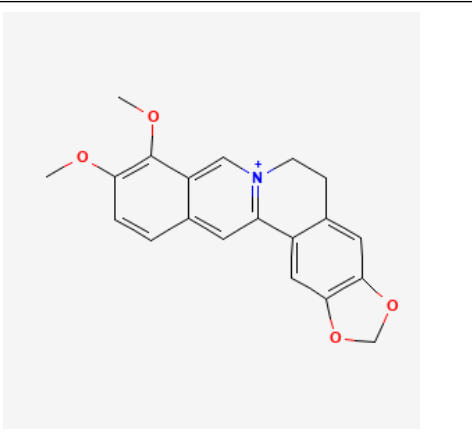
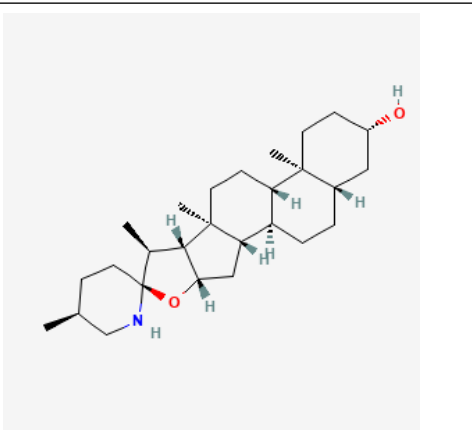
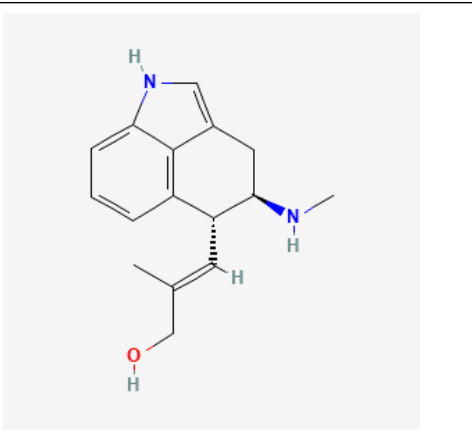
The exploration of antibacterial properties in plant species from the Asteraceae, Apiaceae, and Rosaceae families is of significant importance due to their rich medicinal potential. These plant families have been historically renowned for their diverse array of bioactive compounds, making them promising sources for the development of new antimicrobials. However, the complexity and variability of plant extracts present several challenges in this endeavor¹¹².

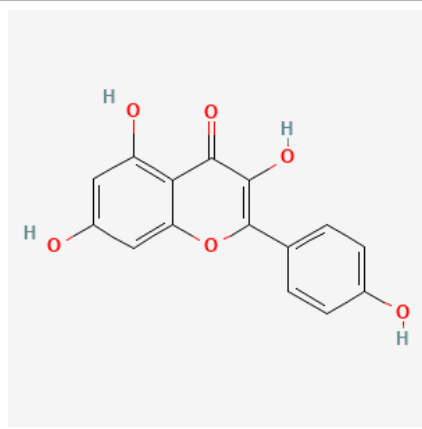
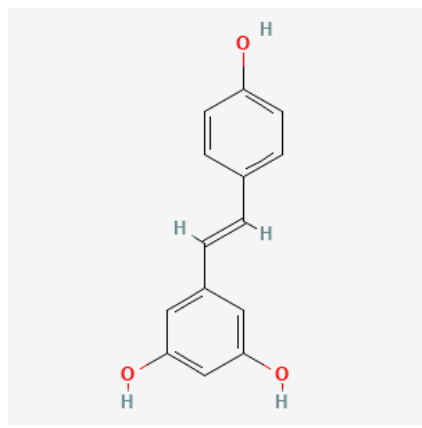
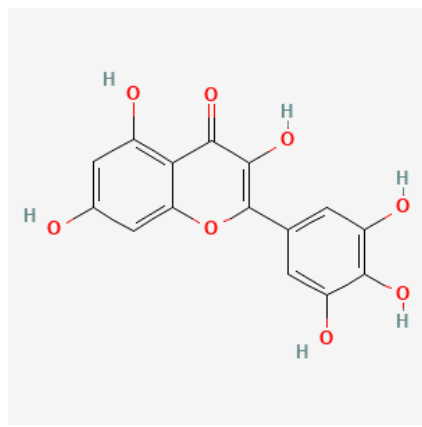
One of the major challenges is the translation of in vitro studies to in vivo experiments and human clinical trials. While in vitro studies provide initial insights into the antimicrobial potential of plant extracts, further research is essential to understand their exact mechanisms and potential as alternative or supplementary treatments for microbial diseases. Additionally, only plant extracts with low or moderate Minimum Inhibitory Concentration (MIC) values should be prioritized for further investigation, ensuring their efficacy against microbes¹²³.

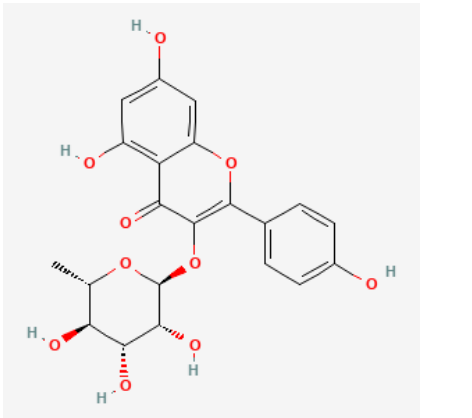
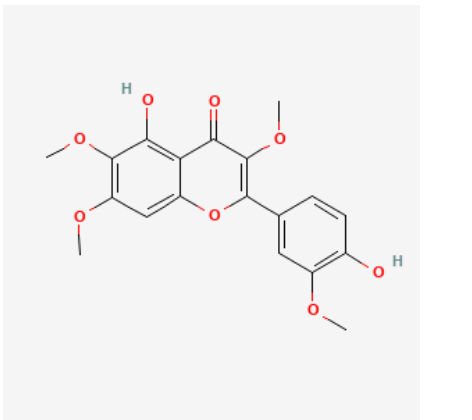
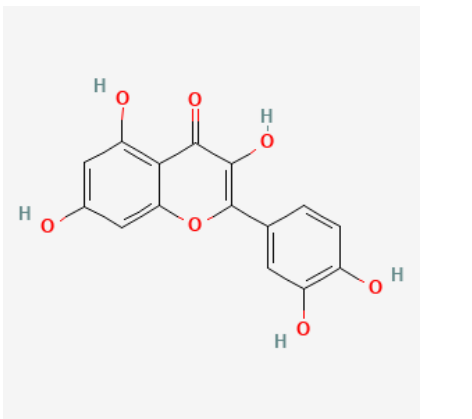
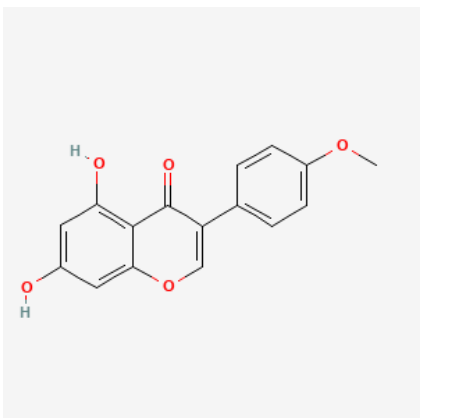
Another challenge lies in the standardized extraction methods and in vitro testing procedures. Standardization is crucial to ensure systematic research and proper interpretation of results. Furthermore, the identification of bioactive compounds within complex plant extracts and their synergistic effects poses a significant challenge. Plant compounds often require complex

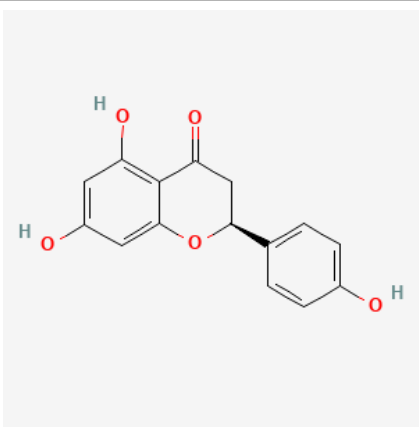
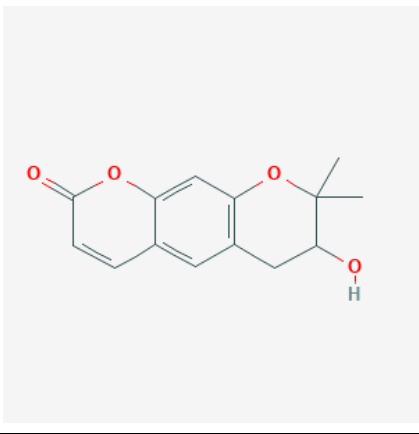
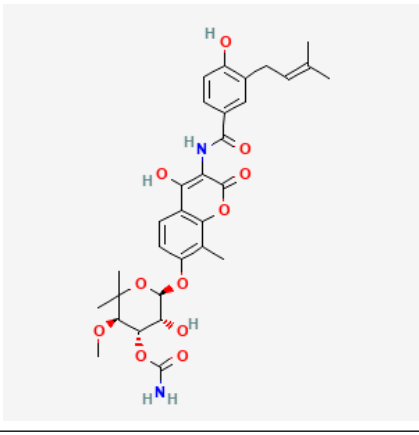


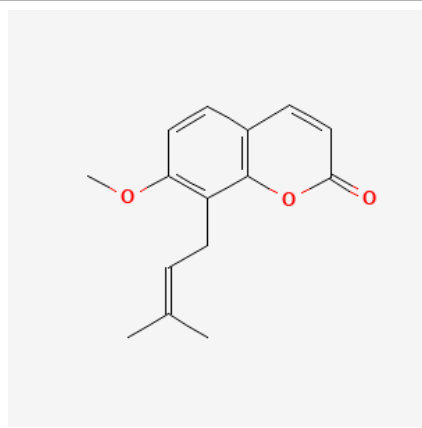
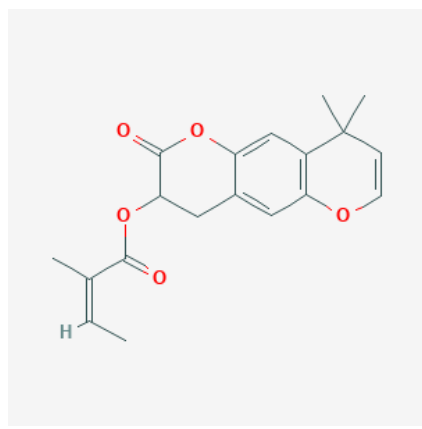
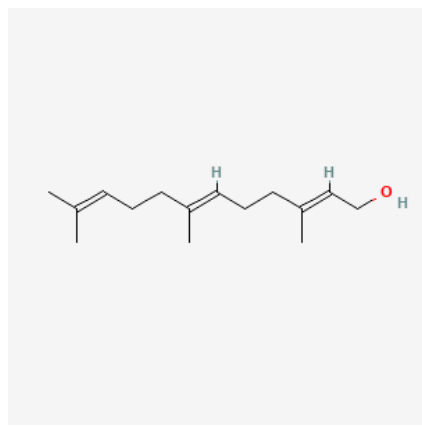
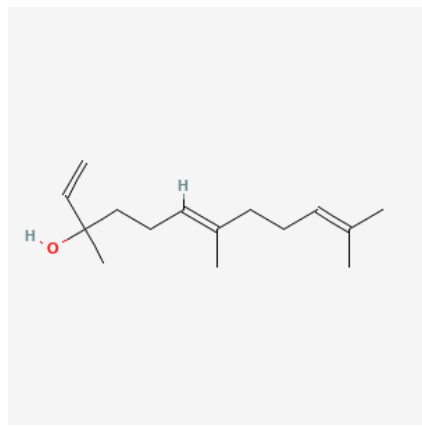
Table 4. Potent Antimicrobial Compounds from Asteraceae, Apiaceae, and Rosaceae Plant Species: Recent Findings					
Chemical class of plant-based compounds	Compound	Chemical structure	Active against	Concentration	Mechanism of action
Alkaloids	Piperine		<i>Staphylococcus aureus</i>	100 µg/mL	Inhibits efflux pumps [115]
	Lysergol		<i>Escherichia coli</i>	–	Inhibits efflux pumps [116]
	Evocarpine		<i>Mycobacterium tuberculosis</i>	5 µg/mL	Inhibits efflux pumps [117]

Berberine	 <p>The image shows the chemical structure of Berberine, a quaternary alkaloid. It features a complex polycyclic ring system consisting of a benzene ring fused to a pyridine ring, which is further fused to a decalin system. The structure includes several methoxy groups and a quaternary nitrogen atom.</p>	Escherichia coli Candida albicans	4 mM	Inhibitor of cell division, Inhibitor of protein and DNA synthesis [118]
Tomatidine	 <p>The image shows the chemical structure of Tomatidine, a pentacyclic alkaloid. It consists of a decalin core with a piperidine ring fused to one of the decalin rings. The structure includes several stereocenters and a hydroxyl group.</p>	Listeria, Bacillus and Staphylococcus spp	-	ATP synthase inhibitor [119, 120]
Chanoclavine	 <p>The image shows the chemical structure of Chanoclavine, a tetracyclic alkaloid. It features a benzene ring fused to a pyridine ring, which is further fused to a decalin system. The structure includes a hydroxyl group and a methyl group.</p>	Escherichia coli	-	Inhibits efflux pumps [121]

Phenolic substances	Kaempferol		<i>Candida albicans</i>	125 µg/mL	Inhibits efflux pumps [122]
	Resveratrol		<i>Mycobacterium smegmatis</i> , <i>Campylobacter jejuni</i>	0.064, 0.313 mg/mL	Inhibits efflux pumps [123, 124]
	Myricetin		<i>Mycobacterium smegmatis</i>	32 µg/mL	Inhibits efflux pumps [125]

<p>Kaempferol rhamnoside</p>		<p><i>Staphylococcus aureus</i></p>	<p>1.56 µg/mL</p>	<p>Inhibits efflux pumps [126]</p>
<p>Chryso-splen-tin</p>		<p><i>Staphylococcus aureus</i></p>	<p>6.25 µg/mL</p>	<p>Inhibits efflux pumps [127]</p>
<p>Quercetin</p>		<p><i>Staphylococcus aureus</i></p>	<p>75 µg/mL</p>	<p>Inhibits efflux pumps [128]</p>
<p>Biochanin A</p>		<p><i>Staphylococcus aureus</i></p>	<p>10 µg/mL</p>	<p>Inhibits efflux pumps [129]</p>

	Naringenin		<i>Enterococcus faecalis</i>	256 µg/mL	Inhibits efflux pumps [130]
Coumarins	Aegelinol		<i>Salmonella enterica</i> serovar Typhi, <i>Enterobacter aerogenes</i> , <i>Enterobacter cloacae</i> , <i>Staphylococcus aureus</i>	16 µg/mL	Inhibitor of DNA gyrase [131]
	Novobiocin		<i>Salmonella enterica</i> serovar Typhi, <i>Enterobacter aerogenes</i> , <i>Enterobacter cloacae</i> , <i>Staphylococcus aureus</i>	—	Inhibitor of DNA gyrase [132]

	Osthole		Salmonella enterica serovar Typhi, Enterobacter aerogenes, Enterobacter cloacae, Staphylococcus aureus	32 µg/mL	Inhibitor of DNA gyrase [132]
	Agasyllin		Salmonella enterica serovar Typhi, Enterobacter aerogenes, Enterobacter cloacae, Staphylococcus aureus	155 µg/mL	Inhibitor of DNA gyrase [132]
Terpenes	Farnesol		Staphylococcus aureus	20 µg/mL	Disruption of cell membrane [132]
	Nerolidol		Staphylococcus aureus	40 µg/mL	Disruption of cell membrane [132]

combinations to enhance their activity, and identifying these synergistic or antagonistic effects is critical for the development of effective antimicrobials¹¹².

To address these challenges, advanced analytical techniques such as metabolomics are being increasingly utilized to identify and characterize bioactive compounds in plant extracts. These techniques can help predict and correlate the metabolomic profile of extracts with their bioactivity, aiding in the development of new antimicrobials. Additionally, emerging technologies like nanotechnology and bio-adhesive materials show promise in enhancing the effectiveness of plant antimicrobial compounds¹¹⁴.

Despite these challenges, the demand for new antimicrobials from traditional medicinal plants remains high. With the rising threat of antimicrobial resistance, the development of effective, affordable, and safe antimicrobials from plant sources is crucial. Overcoming the challenges associated with exploring the antibacterial potential of plant species from the Asteraceae, Apiaceae, and Rosaceae families could lead to the discovery of novel antimicrobials, addressing the urgent need for new therapeutic options.

CONCLUSION

The prominence of families like *Asteraceae*, *Rosaceae*, *Lamiaceae*, *Fabaceae*, *Ranunculaceae*, *Apiaceae*, and *Brassicaceae* in medicinal contexts highlights their potential contributions to official medicine. Despite their significance, research focusing on the resource potential of medicinal species within these families is limited, indicating an untapped reservoir of therapeutic knowledge. While 648 medicinal herb species contribute to Kazakhstan's herbal heritage, only a fraction has undergone rigorous investigation, emphasizing a critical gap in understanding the full scope of their medicinal properties.

The review's focus on antimicrobial and phytochemical studies involving some plant species from *Asteraceae*, *Apiaceae*, and *Rosaceae* families unravels a diverse array

of properties, showcasing their efficacy against various pathogens. The nuanced interactions between these plants and microorganisms provide valuable insights into potential therapeutic applications, especially in the context of combating antibiotic resistance. Phytochemical analyses reveal a rich tapestry of secondary metabolites, each playing a unique role in enhancing antimicrobial properties.

The review concludes by emphasizing the need for a holistic understanding of these plant families, encompassing not only their antimicrobial potential but also broader applications in traditional medicine, agriculture, and biodiversity conservation. Bridging the gap between traditional knowledge and contemporary research sets the stage for comprehensive utilization of botanical resources. The integration of advanced analytical techniques promises to unveil novel bioactive compounds, enhancing our understanding of these plants' antimicrobial prowess and contributing to ongoing research in natural product discovery. As we navigate the complexities of plant-microbe interactions, this review serves as a catalyst for future investigations, contributing to the evolving landscape of antimicrobial research and the discovery of natural products.

AUTHOR CONTRIBUTIONS

Conceptualization, B.B., A.S., I.R., S.O., E.S., G.B., A.A.; writing—original draft preparation, A.B., A.S., Z.T. A.T., Z.S.; writing—review and editing, A.B., G.S., A.T., Z.T., G.K.; visualization, G.S., Zh.N., R.S., K.S.; supervision, B.B.; project administration, B.B., A.S.; funding acquisition, E.Sh., G.S., All authors have read and agreed to the published version of the manuscript.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

FUNDING

This work was funded by Ministry of Science and Higher Education, Republic of Kazakhstan. BR28713215 New domestic biological preparations based on microorganisms for agriculture and organization of their production.

References

1. Berganayeva, G.; Kudaibergenova, B.; Litvinenko, Y.; Nazarova, I.; Sydykbayeva, S.; Vassilina, G.; Izdik, N.; Dyusebaeva, M. Medicinal Plants of the Flora of Kazakhstan Used in the Treatment of Skin Diseases. *Molecules* 2023, 28, 4192. doi.org/10.3390/molecules28104192
2. Jumagaliyeva, K.V.; Sarmurzina, N.; Kairgalieva, G.K. History of traditional medicine of the Kazakh people. *J. Samara Sci. Cent. RAS Hist. Sci.* 2020, 1, 117–126. (In Russian) [[Google Scholar](#)] [[CrossRef](#)]
3. Cowan, M.M. Plant products as antimicrobial agents. *Clin Microbiol Rev.* 1999, 12(4), 564–582. doi:10.1128/CMR.12.4.564.
4. Vaou, N.; Stavropoulou, E.; Voidarou, C.; Tsigalou, C.; Bezirtzoglou, E. Towards Advances in Medicinal Plant Antimicrobial Activity: A Review Study on Challenges and Future Perspectives. *Microorganisms*. 2021, 9(10), 2041. doi:10.3390/microorganisms9102041.
5. Sarsenbayev, K.N. Medicinally Important Plants of Kazakhstan. In *Vegetation of Central Asia and Environs*, 1st ed.; Egamberdieva, D.; Öztürk, M.; Springer: 2018, 263–289. doi:10.1007/978-3-319-99728-5_10.
6. Grudzinskaya, L.; Gemejiyeva, N.; Karzhaubekova, Z. The Kazakhstan medicinal flora survey in a leading families volume. *Bulletin of the Karaganda University. Biology, Medicine, Geography Series*, 2020, 100(4), 39–51. doi.org/10.31489/2020bmg4/39-51.
7. Grudzinskaya, L.; Gemejiyeva, N.; Karzhaubekova, Z.; Nelina, N. Botanical coverage of the leading families of medicinal flora of Kazakhstan. *BIO Web of Conferences*, 2021, 31, 00007. doi.org/10.1051/bioconf/20213100007.
8. Kotukhov, Y. A. Supplement to the "Flora of Kazakhstan". *Grasses of East Kazakhstan*. Turczaninowia, 2021, 24(2), 156–169. [doi](#).



[org/10.14258/turczaninowia.24.2.15](https://doi.org/10.14258/turczaninowia.24.2.15)

9. Atanasov, A. G.; Zotchev, S. B.; Dirsch, V. M.; Supuran, C. T. Natural products in drug discovery: advances and opportunities. *Nature Reviews Drug Discovery*, 2021, 20(3), 200–216. doi.org/10.1038/s41573-020-00114-z.
10. Sheth, B. P.; Thaker, V. S. Plant systems biology: insights, advances and challenges. *Planta*, 2014, 240(1), 33–54. doi.org/10.1007/s00425-014-2059-5.
11. Berganayeva, G.; Kudaibergenova, B.; Litvinenko, Y.; Nazarova, I.; Sydykbayeva, S.; Vassilina, G.; Izdik, N.; Dyusebaeva, M. Medicinal Plants of the Flora of Kazakhstan Used in the Treatment of Skin Diseases. *Molecules*. 2023, 28(10), 4192. doi: 10.3390/molecules28104192.
12. Gou, J.; Lu, Y.; Xie, M, et al. Antimicrobial activity in Asterceae: The selected genera characterization and against multidrug resistance bacteria. *Heliyon*. 2023, 9(4), e14985. doi:10.1016/j.heliyon.2023.e14985.
13. Stefanovic, O.; Comic, L.; Stanojevic, D.; Sukdolak, S. S. Antibacterial Activity of *Aegopodium podagraria* L. Extracts and Interaction Between Extracts and Antibiotics. *Turkish Journal of Biology*. 2009, 33(2),145-150 doi.org/10.3906/biy-0810-21
14. Boghrati, Z.; Iranshahi, M. *Ferula* species: a rich source of antimicrobial compounds. *Journal of Herbal Medicine* 2019, 16, 100244. doi.org/10.1016/j.hermed.2018.10.009.
15. Proença, A. C.; Luís, Â.; Duarte, A. P. The Role of Herbal Medicine in the Treatment of Acne Vulgaris: A Systematic Review of Clinical Trials. *Evid Based Complement Alternat Med*. 2022, 2022, 2011945. doi:10.1155/2022/2011945.
16. Jumagaliyeva, K.V.; Sarmurzina, N.; Kairgalieva, G.K. History of traditional medicine of the Kazakh people. *J. Samara Sci. Cent. RAS Hist. Sci*. 2020, 1, 117–126. (In Russian) [[Google Scholar](#)] [[CrossRef](#)]
17. Gubanov, I.A.; Kiseleva, K.V.; Novikov, V.S.; Tikhomirov, V.N. Illustrated determinant of plants of Central Russia. *Mosc. Assoc. Sci. Publ. CMC Inst. Technol. Res*. 2004, 3, 11. (In Russian) [[Google Scholar](#)]
18. Samsó, J. The First Golden Age of Islamic Science. *International Review of Science*, 2018, 4(1).4033, doi.org/10.37282/991819.18.2.
19. Mahdizadeh, S.; Khaleghi, G. M.; Gorji, A. Avicenna's Canon of Medicine: a review of analgesics and anti-inflammatory substances. *Avicenna J Phytomed*. 2015, 5(3), 182-202.
20. McKenzie, K. E. Chokan Valikhanov: Kazakh Princeling and scholar. *Central Asian Survey*, 1989, 8(3), 1–30. doi. org/10.1080/02634938908400671.
21. Ryabushkina, Nat;alja, et al. Brief review of Kazakhstan flora and use of its wild species. *Asian and Australasian Journal of Plant Science and Biotechnology*, 2008, 2.2, 64-71.
22. Morens, D. M.; Anthony, S. F. The 1918 influenza pandemic: insights for the 21st century. *The Journal of infectious diseases* 2007, 195.7, 1018-1028.
23. Short, K.R.; Kedzierska, K.; van de Sandt C. E. Back to the Future: Lessons Learned From the 1918 Influenza Pandemic. *Front Cell Infect Microbiol*. 2018, 8, 343. doi: 10.3389/fcimb.2018.00343.
24. Andrades, V. A.; Mitnik, A.; Key, F.M.; Haak, W.; Allmäe, R.; Belinskij, A.; Daubaras, M.; Feldman, M.; Jankauskas, R.; Janković, I.; et al. The Stone Age Plague and Its Persistence in Eurasia. *Curr. Biol*. 2017, 27, 3683–3691.e8. [[Google Scholar](#)] [[CrossRef](#)] [[Green Version](#)]
25. Susat, J.; Lübke, H.; Immel, A.; Brinker, U.; Macăne, A.; Meadows, J.; Steer, B.; Tholey, A.; Zagorska, I.; Gerhards, G.; et al. A 5,000-year-old hunter-gatherer already plagued by *Yersinia pestis*. *Cell Rep*. 2021, 35, 109278. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
26. Rasmussen, S.; Allentoft, M.E.; Nielsen, K.; Orlando, L.; Sikora, M.; Sjögren, K.G.; Pedersen, A.G.; Schubert, M.; Van Dam, A.; Kapel, C.M.O.; et al. Early Divergent Strains of *Yersinia pestis* in Eurasia 5000 Years Ago. *Cell*. 2015, 163, 571–582. [[Google Scholar](#)] [[CrossRef](#)] [[Green Version](#)]
27. Taubenberger, J.K.; Reid, A.H.; Lourens, R.M.; Wang, R.; Jin, G.; Fanning, T.G. Characterization of the 1918 influenza virus polymerase genes. *Nature*. 2005, 437, 889–893. [[Google Scholar](#)] [[CrossRef](#)]
28. Abdallah, E.M.; Alhatlani, B.Y.; de Paula, M. R.; Martins, C.H.G. Back to Nature: Medicinal Plants as Promising Sources for Antibacterial Drugs in the Post-Antibiotic Era. *Plants (Basel)*. 2023,12(17),3077. Published 2023 Aug 28. doi:10.3390/plants12173077
29. Mathers, C. D.; Boerma, T.; Ma Fat, D.; Global and regional causes of death. *British Medical Bulletin*, 2009, 92(1), 7–32. <https://doi.org/10.1093/bmb/ldp028>
30. Tampa, M.; Sarbu, I.; Matei, C.; Benea, V.; Georgescu, S.R. Brief history of syphilis. *J Med Life*. 2014,7(1),4-10.
31. Hu, D.; Liu, B.; Feng, L.; Ding, P.; Guo, X.; Wang, M.; Wang, L. Origins of the current seventh cholera pandemic. *Proceedings of the National Academy of Sciences*, 2016, 113(48), E7730-E7739. doi.org/10.1073/pnas.160873211
32. Salam, M.A.; Al-Amin, M.Y.; Salam, M.T.; et al. Antimicrobial Resistance: A Growing Serious Threat for Global Public Health. *Healthcare (Basel)*. 2023,11(13), 1946. doi:10.3390/healthcare11131946
33. Adedeji, W.A. The treasure called antibiotics. *Ann Ib Postgrad Med*. 2016,14(2), 56-57.
34. Llor, C.; Bjerrum, L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. *Ther Adv Drug Saf*. 2014,5(6), 229-241. doi:10.1177/2042098614554919
35. Cowan, M.M. Plant products as antimicrobial agents. *Clin Microbiol Rev*. 1999, 12(4),564-582. doi:10.1128/CMR.12.4.564
36. Chassagne, F.; Samarakoon, T.; Porras, G.; et al. A Systematic Review of Plants With Antibacterial Activities: A Taxonomic and Phylogenetic Perspective. *Front Pharmacol*. 2021, 11, 586548. doi:10.3389/fphar.2020.586548.



37. Wu, X.; Li, W.; Qin, Z.; et al. Traditional Chinese medicine as an adjunctive therapy for mild and common COVID-19: A systematic review and network meta-analysis. *Medicine (Baltimore)*. 2021, 100(40), e27372. doi:10.1097/MD.00000000000027372
38. Lobanovska, M.; Pilla, G. Penicillin's Discovery and Antibiotic Resistance: Lessons for the Future?. *Yale J Biol Med*. 2017, 90(1), 135-145.
39. Ogawara, H.; Comparison of Antibiotic Resistance Mechanisms in Antibiotic-Producing and Pathogenic Bacteria. *Molecules*. 2019, 24(19), 3430. doi:10.3390/molecules24193430
40. Hsieh, Y.C.; Lin, Y.C.; Huang, Y.C. Vancomycin, teicoplanin, daptomycin, and linezolid MIC creep in methicillin-resistant *Staphylococcus aureus* is associated with clonality. *Medicine (Baltimore)*. 2016, 95(41), e5060. doi:10.1097/MD.0000000000005060
41. Kılınç S, Tunç T, Pazarıcı Ö, Sümer Z. Research into biocompatibility and cytotoxicity of daptomycin, gentamicin, vancomycin and teicoplanin antibiotics at common doses added to bone cement. *Jt Dis Relat Surg*. 2020;31(2):328-334. doi:10.5606/ehc.2020.74943
42. Bennett, J.E.; Dolin, R.; Blaser, M.J. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases E-book; Elsevier Health Sciences: Amsterdam, The Netherlands, 2019.
43. Kzhyshkowska, J.; De Berardinis, P.; Bettencourt, P. Research and Development: The Past, Present and Future, Including Novel Therapeutic Strategies. In *Fighting an Elusive Enemy: Staphylococcus aureus and Its Antibiotic Resistance, Immune-Evasion and Toxic Mechanisms*; Frontiers: Lausanne, Switzerland, 2022
44. Michalopoulos, A.; Falagas, M. E. Colistin and Polymyxin B in Critical Care. *Critical Care Clinics*. 2008, 24(2), 377–391. <https://doi.org/10.1016/j.ccc.2007.12.003>
45. Lin, X.; Kück, U. Cephalosporins as key lead generation beta-lactam antibiotics. *Appl Microbiol Biotechnol*. 2022, 106(24), 8007-8020. doi:10.1007/s00253-022-12272-8
46. Mousavifar, L.; Roy, R. Alternative therapeutic strategies to fight bacterial infections. *Innate Immun*. 2018, 13, 25.
47. Akram, F.; Imtiaz, M.; Haq, I. U. Emergent crisis of antibiotic resistance: A silent pandemic threat to 21st century. *Microbial Pathogenesis*. 2023, 174, 105923. <https://doi.org/10.1016/j.micpath.2022.105923>
48. Catalano, A.; Iacopetta, D.; Ceramella, J.; et al. Antibiotic-Resistant ESKAPE Pathogens and COVID-19: The Pandemic beyond the Pandemic. *Viruses*. 2023,15(9),1843. doi:10.3390/v15091843
49. Boyd, N.K.; Teng, C.; Frei, C.R. Brief overview of approaches and challenges in new antibiotic development: A focus on drug repurposing. *Front. Cell. Infect. Microbiol*. 2021, 11, 684515.
50. Nguyen, J.; Lara-Gutiérrez, J.; Stocker, R. Environmental fluctuations and their effects on microbial communities, populations and individuals. *FEMS Microbiol Rev*. 2021,45(4),fuaa068. doi:10.1093/femsre/fuaa068
51. Krzemiński P., Markiewicz Z., Popowska M. Entry Routes of Antibiotics and Antimicrobial Resistance in the Environment. In: Hashmi M.Z., editor. *Antibiotics and Antimicrobial Resistance Genes: Environmental Occurrence and Treatment Technologies*. Springer International Publishing; Cham, Germany: 2020. pp. 1–26.
52. Coculescu, B.I. Antimicrobial resistance induced by genetic changes. *J Med Life*. 2009, 2(2), 114-123.
53. Alsayed, A.R.; Darwish, E.I.; Hajji, F.; Al-Najjar, M.A.A.; Abazid, H.; Al-Dulaimi, A. Patterns of antibiotic use, knowledge, and perceptions among different population categories: A comprehensive study based in Arabic countries. *Saudi Pharm J*. 2022, 30(3), 317-328. doi:10.1016/j.jsps.2022.01.013
54. Rather, I.A.; Kim, B.C.; Bajpai, V.K.; Park, Y.H. Self-medication and antibiotic resistance: Crisis, current challenges, and prevention. *Saudi J Biol Sci*. 2017, 24(4), 808-812. doi:10.1016/j.sjbs.2017.01.004
55. Cabello, F.C. Heavy use of prophylactic antibiotics in aquaculture: A growing problem for human and animal health and for the environment. *Environ. Microbiol*. 2006, 8, 1137–1144.
56. Polianciuc, S.I.; Gurzău, A.E.; Kiss, B.; Ștefan, M.G.; Loghin, F. Antibiotics in the environment: causes and consequences. *Med Pharm Rep*. 2020, 93(3), 231-240. doi:10.15386/mpr-1742
57. Baker, R.E.; Mahmud, A.S.; Miller, I.F.; Rajeev, M.; Rasambainarivo, F.; Rice, B.L.; Takahashi, S.; Tatem, A.J.; Wagner, C.E.; Wang, L.-F. Infectious disease in an era of global change. *Nat. Rev. Microbiol*. 2021, 20, 193–205.
58. Short, E.E.; Caminade, C.; Thomas, B.N. Climate Change Contribution to the Emergence or Re-Emergence of Parasitic Diseases. *Infect Dis (Auckl)*. 2017, 10, 1178633617732296. doi:10.1177/1178633617732296
59. Borris, R. P. Natural products research: perspectives from a major pharmaceutical company. *J Ethnopharmacol*. 1996, 51, 29–38.
60. Emeka, P.; Badger-Emeka, L.; Fateru, F. In vitro antimicrobial activities of *Acalypha ornata* leaf extracts on bacterial and fungal clinical isolates. *J. Herb. Med*. 2012, 2, 136–142.
61. World Health Organization. *WHO Guidelines on Safety Monitoring of Herbal Medicines in Pharmacovigilance Systems*; World Health Organization: Geneva, Switzerland, 2004.
62. Bennett, J.E.; Dolin, R.; Blaser, M.J. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases E-book; Elsevier Health Sciences: Amsterdam, The Netherlands, 2019.
63. Tortora, G.J.; Case, C.L.; Funke, B.R. *Microbiologia*, 12th ed.; Artmed Editora: Floresta, Brazil, 2016.
64. Rolnik A, Olas B. The Plants of the Asteraceae Family as Agents in the Protection of Human Health. *Int J Mol Sci*. 2021, 22(6), 3009. Published 2021 Mar 16. doi:10.3390/ijms22063009



65. Mazandarani M.; Mirdeilami S. Z.; Pessarakli M. Essential oil composition and antibacterial activity of *Achillea millefolium* L. from different regions in North east of Iran. *Journal of Medicinal Plants Research*. 2013, 7(16), 1063-1069.
66. Marcelina, Strzpek-Gomółka; Katarzyna Gawel-Bęben; Wirginia Kukula-Koch. "Achillea Species as Sources of Active Phytochemicals for Dermatological and Cosmetic Applications". *Oxidative Medicine and Cellular Longevity*. 2021, Article ID 6643827, 14 pages, 2021. <https://doi.org/10.1155/2021/6643827>
67. Canan, K.; Ayse, N.Y.; N. Ulku, K.Y. Evaluation of antimicrobial properties of *Achillea* L. flower head extracts. *Pharmaceutical Biology*. 2009,47(1), 86-91, DOI: 10.1080/13880200802448682
68. Meng, J.C.; Hu,Y.F.; Chen, J.H.; Tan,R.X. Antifungal highly oxygenated guaianolides and other constituents from *Ajania fruticulosa*.*Phytochemistry*.2001,1141-1145,ISSN 0031-9422,[https://doi.org/10.1016/S0031-9422\(01\)00389-2](https://doi.org/10.1016/S0031-9422(01)00389-2).
69. Babotă, M.; Mocan, A.; Vlase, L.; Crişan, O.; Ielciu, I.; Gheldiu, A.M.; Vodnar, D.C.; Crişan, G.; Păltinean, R. Phytochemical Analysis, Antioxidant and Antimicrobial Activities of *Helichrysum arenarium* (L.) Moench. and *Antennaria dioica* (L.) Gaertn. Flowers. *Molecules*. 2018, 23(2),409. doi: 10.3390/molecules23020409.
70. Prakash, C.; Gupta, B.; Dutta, D.; Pant, P.; Joshi, D. R. L. in vitro antibacterial activity of *artemisia annua* linn. growing in india. 2009, Retrieved from: <https://www.greenpharmacy.info/index.php/ijgp/article/view/96>
71. Chebbac, K.; Ghneim, H.K.; El Moussaoui, A.; Bourhia, M.; El Barnossi, A.; Benziane, O. Z.; Salamatullah, A.M.;Alzahrani, A.; Aboul-Soud, M.A.M.; Giesy, J.P.; Guemmouh, R.; Antioxidant and Antimicrobial Activities of Chemically-Characterized Essential Oil from *Artemisia aragonensis* Lam. against Drug-Resistant Microbes. *Molecules*. 2022,27(3),1136. doi: 10.3390/molecules27031136.
72. Ivănescu, B.; Burlec, A.F.; Crivoi, F.; Roşu, C.; Corciovă, A.; Secondary Metabolites from *Artemisia* Genus as Biopesticides and Innovative Nano-Based Application Strategies. *Molecules*. 2021, 26(10),3061. doi: 10.3390/molecules26103061. PMID: 34065533; PMCID: PMC8160890.
73. Ūrgeovă, E.; Uváčková, L.; Vaneková, M.; Maliar, T. Antibacterial Potential of Microwave-Assisted Extraction Prepared Hydrolates from Different *Salvia* Species. *Plants (Basel)*. 2023, 12(6), 1325. doi: 10.3390/plants12061325.
74. Umam, K.; Feng, C.S.; Yang, G.; Tu, P.C.; Lin, C.Y.; Yang, M.T.; Kuo, T.F.; Yang, W.C.; Tran, N. M. H. *Phytochemistry, Pharmacology and Mode of Action of the Anti-Bacterial Artemisia Plants*. *Bioengineering (Basel)*. 2023, 10(6), 633. doi: 10.3390/bioengineering10060633. PMID: 37370564; PMCID: PMC10295440.
75. Abioye, O.E.; Akinpelu, D.A.; Okoh, A.I. Synergistic Effects of n-Hexane Fraction of *Parkia biglobosa* (Jacq.) Bark Extract and Selected Antibiotics on Bacterial Isolates. *Sustainability* 2017, 9, 228. <https://doi.org/10.3390/su9020228>
76. Wang, X.J.; Luo, Q.; Li, T.; et al. Origin, evolution, breeding, and omics of Apiaceae: a family of vegetables and medicinal plants. *Hortic Res*. 2022, 9. doi:10.1093/hr/uhac076
77. Zhong, A.; Shen, P.; Sun, Y.; Feng, J.; Zhu, J.; Li, L.; Wu, Z.; Zang, H. Chemical composition and biological evaluation of the essential oil of the flowering aerial parts of *Aegopodium alpestre* Ledeb. *Nat Prod Res*. 2023, 1-6. doi:10.1080/14786419.2023.2286605.
78. Stefanovic, O.; Comic, I.; Stanojevic, D.; Sukdolak, S.S. "Antibacterial Activity of *Aegopodium podagraria* L. Extracts and Interaction Between Extracts and Antibiotics". *Turkish Journal of Biology*.2009, 33(2),<https://doi.org/10.3906/biy-0810-21>
79. Nurzyńska-Wierdak, R. Chemical Diversity, Yield, and Quality of Aromatic Plants. *Agronomy*. 2023, 13(6), 1614. <https://doi.org/10.3390/agronomy13061614>
80. Zabka, M. Antifungal Efficacy and Convenience of *Krameria lappacea* for the Development of Botanical Fungicides and New Alternatives of Antifungal Treatment. *Agronomy*. 2022, 12(11), 2599. <https://doi.org/10.3390/agronomy12112599>
81. Abbasi, A.M.; Khan, M.A.; Ahmad, M.; Jahan, S.; Sultana, S. Ethnopharmacological application of medicinal plants to cure skin diseases and in folk cosmetics among the tribal communities of North-West Frontier Province. *J Ethnopharmacol*. 2010, 128, 322–335.
82. Altuner, E.M.; Çetin, B.; Çökmüş, C. Antimicrobial activity of *Tortella tortulosa* (Hedw.) Limpr. Extracts. *Kastamonu University Journal of Forestry Faculty*. 2010, 10, 111-116.
83. Hocine, L.; Yasmina, H.; Soizic, P.; Nacira, B.; Salah, A.; Gurdip, S.; Pratibha, S.; Valery, A.; Lech, S. Chemical composition and antimicrobial activity of essential oil of *Bupleurum montanum* and *B. plantagineum*. *Natural Product Communications*. 2009, 4, 1605–1610.
84. Zhong, A.; Shen, P.; Sun, Y.; Feng, J.; Zhu, J.; Li, L.; Wu, Z.; Zang, H. Chemical composition and biological evaluation of the essential oil of the flowering aerial parts of *Aegopodium alpestre* Ledeb. *Nat Prod Res*. 2023, 1-6, doi: 10.1080/14786419.2023.2286605.
85. *Bupleurum* Species Scientific Evaluation and Clinical Application. Taylor & Francis Group Boca Raton, London, New York, 2012
86. Iacobellis, N.S.; Lo Cantore, P.; Capasso, F.; Senatore, F. Antibacterial activity of *Cuminum cyminum* L. and *Carum carvi* L. essential oils. *J Agric Food Chem*. 2005, 53(1), 57-61. doi: 10.1021/jf0487351. PMID: 15631509.
87. Miloud, M.; Senussi, N. Evaluation of antibacterial activity of ethanolic leaf extracts of three medicinal plants against pathogenic bacterial species. *Scientific Journal of Applied Sciences of Sabratha University*, 2023, 38-49. <https://doi.org/10.47891/sabujas.v0i0.38-49>
88. Ali, A.; Alqaseer, K.; Fatlawi, D.; Shehab, S.; Falah, M.; Hassan, M.; Shnain, W.; Radhi, O. *Saussurea lappa*: An Important Medicinal Plant for Treatment Different Diseases: A review. *Kufa Journal for Nursing Sciences*, 2011, 11(1), 1–19. <https://doi.org/10.36321/kjns.vi20211.427>.



89. Gemejiyeva, N. G.; Grudzinskaya, L. M. Current State and Prospects for Studies on the Diversity of Medicinal flora in kazakhstan. *Vegetation of Central Asia and Environs*. 2018, 239–26. [[Google Scholar](#)]
90. Chen, S. L.; Yu, H.; Luo, H. M.; Wu, Q.; Li, C. F.; Steinmetz, A. "Conservation and sustainable use of medicinal plants: Problems, Progress, and Prospects". *Chinese Medicine*. 2016, 11, 1–10. [[Google Scholar](#)]
91. Shiva, K.; Roya, M.; Atousa, A. [Chemical Composition and Antibacterial Activity of the *Leutea elbursensis* Mozaff. Essential Oil from Dried Aerial Parts and Rhizome](#). *Journal of Essential Oil Bearing Plants*. 2022, 25(5), 1054-1061.
92. Riza, B.; Gun, B.; Ilkay, G.; Ersan, T.; Ummuhan, S.; Ebru, K.; Aylin, D.; Hakan, Arslan. [Chemical Composition and Antimicrobial Activity of Essential Oil and Various Extracts of *Onosma sieheana* Hayek Roots](#). *Journal of Essential Oil Bearing Plants*. 2019, 22(1), 94-104.
93. Pimenov, M. G.; Leonov, M. V. The Asian Umbelliferae Biodiversity Database (ASIUM) with Particular Reference to South-West Asian Taxa. *Turk J Bot*. 2004, 28, 139–145. [[Google Scholar](#)]
94. Mozaffarian, V. A. *Dictionary of Iranian Plant Names (In Persian)* 6th ed. Tehran, Iran: Farhang Moaser Press; 2010. [[Google Scholar](#)]
95. Burt, S. Essential oils: Their antibacterial properties and potential applications in foods - A review. *International Journal of Food Microbiolog*. 2004, 94, 223–253.
96. Mbah, J. A.; Gatsing, D.; Efang, S. M. N. Antibacterial agents from the seeds of *Peucedanum zenkeri* L. (Umbelliferae). *Pak J Med Sci*, 2010, 26(2), 314-318.
97. Wang, Y.; Zhao, Y.; Liu, X.; Li, J.; Zhang, J.; Liu, D. Chemical constituents and pharmacological activities of medicinal plants from *Rosa* genus. *Chin Herb Med*. 2022, 14(2), 187-209. doi:10.1016/j.chmed.2022.01.005
- 98.
99. He, L.; Cheng, H.; Chen, F.; Song, S.; Zhang, H.; Sun, W.; Bao, X.; Zhang, H.; He, C. Oxidative Stress-Mediated Antibacterial Activity of the Total Flavonoid Extracted from the *Agrimonia pilosa* Ledeb. in Methicillin- Resistant *Staphylococcus aureus* (MRSA). 2022, 9(2), 71. doi: 10.3390/vetsci9020071.
100. Choi, H.; Yu, E. A.; Lee, S. G. Antibacterial Activities Effect by Methanol Extracts from *Agrimonia pilosa*. *Journal of Agriculture and Life Science*. 50(3), 165-171.
101. Dhami, D. S.; Shah, G. C.; Kumar, V.; Joshi, Y.; Tripathi, M.; Bisht, M. Essential oil composition and antibacterial activity of *Agrimonia Pilosa* Ledeb (Rosaceae). *Chemical Science*. 2018, 7(3), 499-505.
102. Borawska, M. H.; Czechowska, S. K.; Markiewicz, R.; Socha, K.; Nazaruk, J.; Pałka, J.; Isidorov, V. A. Enhancement of antibacterial effects of extracts from *Cirsium* species using sodium picolinate and estimation of their toxicity. *Natural product research*. 2010, 24(6), 554–561. <https://doi.org/10.1080/14786410902770728>.
103. Zhang, L. L.; Zhang, L. F.; Xu, J. G. Chemical composition, antibacterial activity and action mechanism of different extracts from hawthorn (*Crataegus pinnatifida* Bge.). *Scientific reports*. 2020, 10(1), 8876. <https://doi.org/10.1038/s41598-020-65802-7>.
104. Kicel, A. An overview of the genus *Cotoneaster* (Rosaceae): phytochemistry, biological activity, and toxicology. *Antioxidants*. 2020, 9(10), 1002.
105. Behta, E.; Burduniuc, P. O.; Bucov, V.; Craciun, O.; Bivol, M.; Burduniuc, A.; Balan, G. Antimicrobial discovery—impact of the natural sources. *Studia Universitatis Moldaviae (Seria Științe Reale și ale Naturii)*. 2020, 136(6), 39-48.
106. Katanić, J.; Boroja, T.; Stanković, N.; Mihailović, V.; Mladenović, M.; Kreft, S.; Vrvić, M. M. Bioactivity, stability and phenolic characterization of *Filipendula ulmaria* (L.) Maxim. *Food & Function*. 2015, 6(4), 1164-1175.
107. Orlova, A.; Kysil, E.; Tsvetkova, E.; Meshalkina, D.; Whaley, A.; Whaley, A. O.; Laub, A.; Francioso, A.; Babich, O.; Wessjohann, L. A.; Mosca, L.; Frolov, A.; Povydysh, M. Phytochemical Characterization of Water Avens (*Padus avium rivale* L.) Extracts: Structure Assignment and Biological Activity of the Major Phenolic Constituents. *Plants (Basel, Switzerland)*. 2022, 11(21), 2859. <https://doi.org/10.3390/plants11212859>
108. Hering, A.; Stefanowicz-Hajduk, J.; Hałasa, R.; Olech, M.; Nowak, R.; Kosiński, P.; Ochocka, J. R. Polyphenolic Characterization, Antioxidant, Antihyaluronidase and Antimicrobial Activity of Young Leaves and Stem Extracts from *Rubus caesius* L. *Molecules (Basel, Switzerland)*. 2022, 27(19), 6181. <https://doi.org/10.3390/molecules27196181>
109. Zhang, H.; Ruan, C.; Bai, X.; Chen, J.; Wang, H. Heterocyclic alkaloids as antimicrobial agents of *Aspergillus fumigatus* D endophytic on *Edgeworthia chrysantha*. *Chemistry of Natural Compounds*. 2018, 54, 411-414.
110. Widelski, J.; Graikou, K.; Ganos, C.; Skalicka-Wozniak, K.; Chinou, I. Volatiles from Selected Apiaceae Species Cultivated in Poland—Antimicrobial Activities. *Processes* 2021, 9, 695. <https://doi.org/10.3390/pr9040695>
111. Shen, Y.; Liang, W. J.; Shi, Y. N.; Kennelly, E. J.; Zhao, D. K. Structural diversity, bioactivities, and biosynthesis of natural diterpenoid alkaloids. *Natural Product Reports*. 2020, 37(6), 763-796.
112. Sartelli, M.; Labricciosa, F. M.; Barbadoro, P.; Pagani, L.; Ansaloni, L.; Brink, A. J.; Carlet, J.; Khanna, A.; Chichom-Mefire, A.; Coccolini, F. The Global Alliance for Infections in Surgery: Defining a model for antimicrobial stewardship—Results from an international cross-sectional survey. *World J. Emerg. Surg*. 2017, 12, 34.
113. Karp, B. E.; Engberg, J. Comment on: Does the use of antibiotics in food animals pose a risk to human health? A critical review of published data. *J. Antimicrob. Chemother*. 2004, 54, 273–274. [[Google Scholar](#)]
114. Larsson, D. J. Antibiotics in the environment. *Upsala J. Med. Sci*. 2014, 119, 108–112.
115. Khameneh, B.; Iranshahi, M.; Ghandadi, M.; Ghoochi Atashbeyk, D.; Fazly Bazzaz, B. S.; Iranshahi, M. Investigation of the



- antibacterial activity and efflux pump inhibitory effect of co-loaded piperine and gentamicin nanoliposomes in methicillin-resistant *Staphylococcus aureus*. *Drug Dev Ind Pharm*. 2015, 41(6), 989–94.
116. Maurya, A.; Dwivedi, G.R.; Darokar, M.P.; Srivastava, S.K. Antibacterial and synergy of clavine alkaloid lysergol and its derivatives against nalidixic acid-resistant *Escherichia coli*. *Chem Biol Drug Des*. 2013, 81(4), 484–90.
117. Hochfellner, C.; Evangelopoulos, D.; Zloh, M.; Wube, A.; Guzman, J.D.; McHugh, T.D.; et al. Antagonistic effects of indoloquinazoline alkaloids on antimycobacterial activity of evocarpine. *J Appl Microbiol*. 2015, 118(4), 864–72.
118. Zoric, N.; Kosalec, I.; Tomic, S.; Bobnjarić, I.; Jug, M.; Vlajnić, T.; et al. Membrane of *Candida albicans* as a target of berberine. *BMC Complement Altern Med*. 2017, 17(1), 268.
119. Lamontagne.; Boulet, M.; Isabelle, C.; Guay, I.; Brouillette, E.; Langlois, J.P.; Jacques, P.E.; et al. Tomatidine Is a Lead Antibiotic Molecule That Targets *Staphylococcus aureus* ATP Synthase Subunit C. *Antimicrob Agents Chemother*. 2018, 62(6).
120. Guay, I.; Boulanger, S.; Isabelle, C.; Brouillette, E.; Chagnon, F.; Bouarab, K.; et al. Tomatidine and analog FC04-100 possess bactericidal activities against *Listeria*, *Bacillus* and *Staphylococcus* spp. *BMC Pharmacol Toxicol*. 2018, 19(1), 7.
121. Dwivedi, G.R.; Maurya, A.; Yadav, D.K.; Singh, V.; Khan, F.; Gupta, M.K.; et al. Synergy of clavine alkaloid ‘chanoclavine’ with tetracycline against multi-drug-resistant *E. coli*. *J Biomol Struct Dyn*. 2019, 37(5), 1307–25.
122. Randhawa, H.K.; Hundal, K.K.; Ahirrao, P.N.; Jachak, S.M.; Nandanwar, H.S. Efflux pump inhibitory activity of flavonoids isolated from *Alpinia calcarata* against methicillin-resistant *Staphylococcus aureus*. *Biologia*. 2016, 71(5), 484–93.
123. Lechner, D.; Gibbons, S.; Bucar, F. Plant phenolic compounds as ethidium bromide efflux inhibitors in *Mycobacterium smegmatis*. *J Antimicrob Chemother*. 2008, 62(2), 345–8.
124. Ferreira, S.; Silva, F.; Queiroz, J.A.; Oleastro, M.; Domingues, F.C. Resveratrol against *Arcobacter butzleri* and *Arcobacter cryaerophilus*: activity and effect on cellular functions. *Int J Food Microbiol*. 2014;180, 62–8.
125. Jin, J.; Zhang, J.Y.; Guo, N.; Sheng, H.; Li, L.; Liang, J.C.; Wang, X.L.; Li, Y.; Liu, M.Y.; Wu, X.P.; et al. Farnesol, a Potential Efflux Pump Inhibitor in *Mycobacterium smegmatis*. *Molecules*. 2010, 15, 7750–7762. <https://doi.org/10.3390/molecules15117750>
126. Holler, J.G.; Christensen, S.B.; Slotved, H.C.; Rasmussen, H.B.; Gúzman, A.; Olsen, C.E.; et al. Novel inhibitory activity of the *Staphylococcus aureus* NorA efflux pump by a kaempferol rhamnoside isolated from *Persea lingue* Nees. *J Antimicrob Chemother*. 2012, 67(5), 1138–44.
127. Stermitz, F.R.; Cashman, K.K.; Halligan, K.M.; Morel, C.; Tegos, G.P.; Lewis, K. Polyacylated neohesperidosides from *Geranium caespitosum*: bacterial multidrug resistance pump inhibitors. *Bioorg Med Chem Lett*. 2003, 13(11), 1915–8.
128. Veiko, A.G.; Olchowik-Grabarek, E.; Sekowski, S.; et al. Antimicrobial Activity of Quercetin, Naringenin and Catechin: Flavonoids Inhibit *Staphylococcus aureus*-Induced Hemolysis and Modify Membranes of Bacteria and Erythrocytes. *Molecules*. 2023, 28(3), 1252. doi:10.3390/molecules28031252
129. Morel, C.; Stermitz, F.R.; Tegos, G.; Lewis, K. Isoflavones as potentiators of antibacterial activity. *J Agric Food Chem*. 2003, 51(19), 5677–9.
130. Pacyga, K.; Pacyga, P.; Topola, E.; Viscardi, S.; Duda-Madej, A. Bioactive Compounds from Plant Origin as Natural Antimicrobial Agents for the Treatment of Wound Infections. *Int J Mol Sci*. 2024, 25(4), 2100. doi:10.3390/ijms25042100
131. Waites, K.B.; Duffy, L.B.; Dowzicky, M.J. Antimicrobial susceptibility among pathogens collected from hospitalized patients in the United States and in vitro activity of tigecycline, a new glycolcycline antimicrobial. *Antimicrob Agents Chemother*. 2006, 50(10), 3479–3484. doi:10.1128/AAC.00210-06
132. Maxwell, A. The interaction between coumarin drugs and DNA gyrase. *Mol Microbiol*. 1993, 9(4), 681–6.
133. European Medicines Agency (EMA). Community Herbal Monograph on *Achillea millefolium* L., Herba; EMA: London, UK, 2010. Available online: https://www.ema.europa.eu/en/documents/herbal-monograph/final-community-herbal-monograph-achillea-millefolium-l-herba_en.pdf (accessed on 24 May 2025).
134. World Health Organization. WHO Monograph on Selected Medicinal Plants, Volume 4; WHO Press: Geneva, Switzerland, 2009; pp. 5–15. (*Artemisia annua* L.).
135. European Medicines Agency (EMA). Assessment Report on *Filipendula ulmaria* (L.) Maxim., Herba; EMA: London, UK, 2011. Available online: https://www.ema.europa.eu/en/documents/herbal-report/assessment-report-filipendula-ulmaria-l-maxim-herba_en.pdf (accessed on 24 May 2025).
136. European Pharmacopoeia Commission. European Pharmacopoeia, 10th ed.; Council of Europe: Strasbourg, France, 2020; Volume 1, Monograph No. 0722. (*Crataegus* spp.).



