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MINI REVIEW

Antimicrobial activities of herbal plants from Uzbekistan against human pathogenic microbes

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Abstract

In traditional medicine of Uzbekistan, around 20% of herbal plants are used to treat various ailments, including diseases caused by pathogenic bacteria and fungi. Though conventional medicinal plants are common in Uzbekistan, many plant species potentially useful for new pharmaceuticals are less studied. They contain various biological compounds with antibacterial and antifungal activities, that could be developed into drugs. The search for novel antimicrobial compounds, especially against multidrug-resistant pathogens from aromatic and herbal plants is an essential scientific research line. However, the antimicrobial properties of several medicinally important plants from various countries are still unknown. This review aims to provide an up-to-date report on the antimicrobial activity of medicinal plants endemic to Uzbekistan widely used in traditional medicine.

Keywords Medicinal plants · Metabolites · Antibacterial activity · Antifungal activity Uzbekistan

Introduction

It is estimated that about 50,000 plant species were screened for medicinal properties and used by 80% of the world's population to treat numerous human diseases (Saslis-Lagoudakis et al. 2014; Chen et al. 2016). Uzbekistan is known for its endemism, in which 9% of 4500 species of vascular plants are considered endemic (Mamedov et al. 2004). Though traditional medicinal plants are common in Uzbekistan, many plant species potentially useful for new pharmaceuticals are less studied. The remedies derived from natural resources are widely used to treat numerous illnesses, including respiratory and urinary problems, gastrointestinal, and skin disorders as age-old tradition (McChesney et al. 2007). Since the cost of synthetic, medicinal drugs is high, the developing countries are still using herbal plants or their derivates to treat common diseases (Abu-Irmaileh and Afifi 2000). It is known that multidrug-resistant bacterial pathogens signify a growing public health threat. Therefore, there is a continuous need for effective natural therapeutic agents (Compean and Ynalvez 2014). The investigation of aromatic and herbal plants for their biologically active constituents might lead to discovery of new drugs with antimicrobial activities (Cushnie and Lamb 2005; Shrivastava et al. 2015). The medicinal plants contain various metabolites that demonstrate antimicrobial activity in vitro and vivo (Duarte et al. 2005). Many secondary metabolites derived from herbal plants from multiple countries were screened against microbes that cause various infections (Pirbalouti et al. 2010; Verma et al. 2012; Gnat et al. 2017; Egamberdieva and da Silva 2015). For example, Indian and the Middle East's medicinal plants are used for treating infectious diseases in traditional medicine (Duraipandiyan et al. 2011). Medicinal plants containing various phytochemical compounds, such as antimicrobials, essential oils, alkaloids, are also used to treat wound infections (Bahramsoltani et al. 2014). Wound healing is a critical biological process required to minimize potential infections (Gupta and Jain 2010). Finding novel biological agents for the treatment of

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wound infections generated increased interest over time. There are many reports on medicinal plants' antimicrobial properties against human pathogenic bacteria involved in skin and wound infections.

Moreover, medicinal plants associated with microbes, which play an essential role in plant health, synthesize various biologically active compounds due to the symbiosis (Egamberdieva et al. 2020; Rusatmova et al. 2020; Musa et al. 2020). It has been proven that medicinal plants with antimicrobial activity support more antagonistic endophytic bacteria against human pathogenic microbes. Many medicinal plants contain useful essential oils with antimicrobial properties (Nikolic et al. 2014). In an earlier study, the plant extracts of *Zingiber officinales* and *Thymus kotschyana* suppressed the growth of human pathogenic bacteria *Staphylococcus aureus* and *Escherichia coli* Qader et al. (2013). Similar reports demonstrated an inhibitory activity of plant extracts of *Z. officinales* and *Allium sativum* against *Staphylococcus aureus* (Betoni et al. 2006; Ushimaru et al. 2007; Sapkota et al. 2012). The plant extracts of *Boerhaavia diffusa*, *Tribulus terrestris,* and *Soymida febrifuga* inhibited *E. coli, Enterococcus faecalis, Klebsiella oxytoca* and *S. aureus* (Mishra et al. 2017). In the current era, several new infectious diseases appear worldwide. Thus, there is a great need to discover new biologically active compounds from herbal plants and develop novel drugs. Few reports are available about Uzbekistan's herbal plants and their constituents with antimicrobial activities (Kogure et al. 2004), and these endemic plants may contain pharmaceutically essential compounds. According to Gaipova and Kariyeva (2018), during the years 2015–2018, 46 natural products based on medicinal herbs were registered in Uzbekistan. Among them, *Origani vulgaris, Ziziphora pedicellata, Aerva lanata, Calendula officinalis,* and *Chamomilla officinalis K.Koch* based products are widely used.

Medicinal plants of Uzbekistan and their antimicrobial activity

In traditional medicine of Uzbekistan, around 20% of herbal plants are used for treating various ailments (Mamedov et al. 2004: Shurigin et al. 2018; Egamberdieva and Jabborova 2018). The plant species described in Avicenna's book, such as *Malva silvestris* L., *Cannabis sativa* L., *Ferula assafoetida* L., *Sesamum indicum* L., *Pyrus malus* L., *Punica granatum* L., and *Trachyspermum ammi* L. are used till today to treat various illnesses (Buranova 2015). Many of these species are used to heal wounds (Khodzhimatov 1989; Egamberdieva et al. 2017b).

The extract of *Thymus seravschanicus* is known as an antimicrobial agent for handling throat ailments (Kholmatov and Makhsumov 1993). Azizov et al. (2012) reported the commonly used plant species *Arctium lappa* in Uzbekistan, which was used to treat skin infections. *Origanum tyttanthum,* widely grown in many Uzbekistan parts, exhibited antimicrobial, hypocholesterolemic, and hypolipidemic activity (Nuraliyev and Zubaidova 1994).

The plant extract of *Hypericum perforatum* collected from the Chatkal Biosphere Reserve of Uzbekistan demonstrated antagonistic activity against *Pseudomonas aeruginosa, E. coli, E. faecalis, K. oxytoca, Klebsiella pneumoniae,* and *S. aureus* (Egamberdieva et al. 2013). Yili et al. (2009) reported the antimicrobial activity of *Anethum graveolens* against human pathogens such as *Candida albicans* and *S. aureus.* In other studies, *Silene wallichiana, Silene viridiflora*, and *Silene brahuica* inhibited several Gram-negative and Gram-positive human pathogenic bacteria (Mamadalieva et al. 2008). Moreover, the chloroform extracts of endemic plant *Ajuga turkestanica* Rgl. Brig demonstrated antimicrobial activities against *S. aureus* and *Streptococcus pyogenes* (Mamadalieva et al. 2012). The extract prepared from *Aconitum* was used in veterinary medicine for skin wounds and ulcers (Aldashev 1979). Kwon et al. (2005) found an inhibitory activity of shoot and leaves of *Agrimonia eupatoria* against hepatitis B virus in vitro experiments. Sonboli et al. (2006) reported the antibacterial and antifungal activity of *Ziziphora* species. Plant extracts of *H. perforatum* showed antagonistic properties against human pathogenic bacteria*, E. faecalis, K. oxytoca*, *K. pneumoniae, Klebsiella aerogenes, Citrobacter freundii, S. aureus, P. aeruginosa,* and *E. coli* (Egamberdieva et al. 2017b). List of some of the known medicinal plants from Uzbekistan with antimicrobial properties is presented in Table 1.

The antimicrobial activity of biologically active compounds derived from medicinal plants

The medicinal plants contain many important bioactive constituents such as terpenoids, essential oils, polyphenols, and flavonoids. These compounds demonstrated numerous biological activities; such as sedative, analgesic, antibacterial, and anti-inflammatory activities (Dall'Agnol et al. 2003). Antibacterial properties of biologically active compounds isolated from *H. perforatum* were reported by Dall'Agnol et al. (2003). The antibacterial and antifungal activities were observed in flavonoids and essential oils of *Ziziphora* species (Sonboli et al. 2006). Tada et al. (2002) isolated several biologically active compounds such as coumarins, terpenoids, and glycosides from *Prangos pabularia* roots that exhibited antibacterial activity. Phytoecdysteroids isolated from *S. wallichiana* demonstrated antimicrobial properties against various human pathogenic microbes (Mamadalieva et al. 2013). Park et al. (2000) separated the peptides shepherin from Capsella bursa's roots and observed the biologically active compound's antimicrobial activity against human pathogenic microbes. Mamadalieva et al. (2011) extracted

Table 1 The medicinal plants of Uzbekistan with antimicrobial activities

Plant species	Family	Part used	Chemical composition
Achillea millefolium L	COMPOSITAE	Steam, leaves, flowers	Volatile oils, lactons (achillicin, matricin), alkaloids, flavonoids, betains (Sezik et al. 2004)
Aconitum talassicum	RANUNCULACEAE	Aerial parts	Alkaloids (Aldashev 1979)
Acroptilon picris	ASTERACEAE	Aerial parts	Volatile (Norouzi-Arasi et al. 2006)
Agrimonia asiatica Juz	Rosaceae	Leaves, stem	Ursolic acid, tannins, flavonol glycosides, B-vitamins, saponins, trace alkaloids (Eisenman et al. 2013)
Ajuga turkestanica	LAMIACEAE	Root	20-hydroxy-esdysone,turkesterone, cyasterone
Anethum graveolens	Apiaceae	Whole plant	Essential oil (Carvone, limonene, cis-dihydrocarvone, diplaniol, 1,2-diethoxyethane) (Yili et al. 2009)
Artemisia absinthium L	COMPOSITAE	Whole plant	Volatile oils (Sezik et al. 2004)
Artemisia dracunculus	ASTERACEAE	Whole plant	(Curini et al. 2006)
Arischrada korolkowii Regel et Schmalh. Pobed	LAMIACEAE		Essential oil (Baser et al. 2002)
Asparagus persicus Baker	LILIACEAE	Leaves, root, stem	Saponin, volatile oil, flavonoids, tannins, steroidal and bitter glycosides, tyrosine, ecdysteroids (Mamedov and Craker 2001)
Astragalus sieversianus Pall	FABACEAE	Aerial part	Saponins, alkaloids, coumarins, tannins, flavonoids, vitamins C, E, and P, and carotene (Eisenman et al. 2013)
Berberis integerrima	BERBERIDACEAE	Fruit	(Khodzhimatov 1989)
Bunium persicum	APIACEAE	Whole plant	(Sardari et al. 1998)
Betula verrucosa Ehrh	BETULACEAE	Oil, bark leaves	Flavonoids, tannins, volatile oils, triterpen (Mamedov and Craker 2001)
Bidens tripartita L	COMPOSITAE	Whole plant	Flavonoids, volatile oils (Mamedov and Craker 2001)
Calendula officinalis L	COMPOSITAE	Flowers, oil	Triterpene, volatile oils, faradiol, lauric acid, carotinoids, (Mamedov and Craker 2001)
Capsella bursa	BRASSICACEAE	Roots	Peptides (Park et al. 2000)
Carum carvi	APIACEAE	Fruit	Essential oil, (Iacobellis et al. 2005)
Ceratocephala testiculata	RANUNCULACEAE	Whole plant	(Khalmatov 1964)
Centaurea belangeriana Stapt	COMPOSITAE	Flower	Glicoside, athocyane, coumarine (Sezik et al. 2004)
Dianthus tetralepis Nevski	CARYOPHYLLACEAE	Aerial part	Anthochanin, saponins, flavones, triterpene glycosides (Sezik et al. 2004)
Equisetum arvense L	EQUISETACEAE	Steam	Falvonoids, chlorogenic acid, silicis acid (Mamedov and Craker 2001)
Erodium Hoeffitianum CAM	GERANIACEAE	Aerial part	Polyphenolic compounds, phenolic acids, tannins, flavonoids (Mamedov and Craker 2001)
Ferula kuhistanica	APIACEAE	Fruit	(Tamemoto et al. 2001)
Helichrysum arenarium L	COMPOSITAE	Flowers	Flavonoids, steroids (Mamedov and Craker 2001)
Hypericum perforatum L	HUPERICACEAE	Leaves, flowers, oil	Antracene, hypericin, tannins, flavonoids, xanthone (Mamedov and Craker 2001)
Impatiens parviflora	BALSAMINACEA	Whole plant	(Khalmatov 1964)
Juniperus turkestanica	CUPRESSACEAE	Whole plant	Essential oil (Minayeva 1991)
Leonurus turkestanicus L	LABIATAE	Whole plant	Volatile oils, diterpenes, oleic acid (Mamedov and Craker 2001)

Table 1 (continued)

Plant species	Family	Part used	Chemical composition
Limonium otolepis (Srenck) Ktze	PLUMBAGINEACEAE	Aerial part	Flavonoids, tannin (Mamedov and Craker 2001)
Matricaria chamomilla L	COMPOSITAE	Flowers	Volatile oil, flavonoids, chrysospenol (Mamedov and Craker 2001)
Melissa officinalis L	LABIATAE	Whole plant	Volatile oils, eugenol, flavonoids, triterpene (Mamedov and Craker 2001)
Origanum vulgare L	LABIATAE	Leaves, flowers	Flavonoids, volatile oils, terpinene (Sezik et al. 2004)
Origanum tyttanthum Gontsch	LAMIACEAE	Aerial part	Essential oil, phenolic compounds, glucosides (Baser et al. 1997)
Padus avium	ROSACEAE	Aerial part	(Kumarasamy et al. 2002)
Peganum harmala L	ZYGOPHYLLACEAE	Seeds, roots	Alkaloids (Sezik et al. 2004)
Plantago ovata L	PLANTAGINACEAE	Leaves	Fatty oil, alkaloids (plantagonine) (Mamedov and Craker 2001)
Polygonum aviculare L	POLYGONACEAE	Roots, aerial part	Flavonoids, tannins, silicic acid (Mamedov and Craker 2001)
Prangos pabularia	APIACEAE	Leaves	Coumarins, terpenoids, and glycosides (Tada 2002)
Rosa canina	ROSACEAE	Leaves	(Khalmatov et al. 1984)
Scrophyllaria striata Boiss	SCROPHYLLARIACEAE	Aerial part	Glycoside, saponin (Mamedov and Craker 2001)
Scutellaria ramosissima (Lamiaceae)	Epilepsy, allergy, various inflammations, nervous disorders, hypertension, cytotoxic and antimicrobial activity		Flavanoids, glucosides, lipids (Yuldasheva et al. 2014)
Tanacetum vylgare L	COMPOSITAE	Whole herb	Volatile oil, flavonoids (Mamedov and Craker 2001)
Thymus vulgaris L	LABIATAE	Aerial part, oil	Volatile oil, thymol, carvacrol, terpinene, flavonoids (Mamedov and Craker 2001)
Trifolium pretense L	FABIACEAE	Flower, aerial parts	Coumarine, carotinoides (Mamedov and Craker 2001)
Tribulus terrestris	ZYGOPHYLLACEAE	Aerial parts	(Bedir et al. 2002)
Xanthium strumarium	ASTERACEAE	Aerial parts	(Murillo-Alvarez et al. 2001)
Ziziphora bungeana	LAMIACEAE	Aerial parts	Essential oil (Sonboli et al. 2006)
Zygophyllum oxianum	ZYGOPHYLLACEAE	Aerial parts	(Zaidi and Crow 2005)

flavonoids scutellarin and pinocembrin from *Scutellaria immaculata* and *Scutellaria ramosissima*, which showed antimicrobial activity against human pathogenic bacteria. In another study diterpene, methyl carnosate isolated from the *Salvia officinalis* leaves showed antimicrobial properties against *Bacillus cereus* (Climati et al. 2013). The coumarins, terpenoids, and glycosides from *P. pabularia* exhibited strong antibacterial properties (Tada et al. 2002). The phytoecdysteroids and iridoids of *A. turkestanica* demonstrated antimicrobial activities against human pathogenic microbes (Mamadalieva et al. 2013, 2018).

The human pathogens such as *C. albicans, Xanthomonas maltophilia,* and *Proteus mirabilis* were inhibited by *Artemisia dracunculus* essential oil (Curini et al. 2006). The essential oils of *Artemisia absinthium* and *Artemisia vulgaris* demonstrated a wide range of antimicrobial activity (Blagojevic et al. 2006). Norouzi-Arasi et al. (2006) reported inhibitory activity of the essential oil of *Acroptilon repens* L. against *Staphylococcus saprophyticus* and *Staphylococcus epidermidis*. The essential oil of *Cuminum cyminum* L. and *Carum carvi* L. showed antibacterial activity against various Gram-positive and Gram-negative bacteria (Iacobellis et al. 2005). *C. albicans* and *S. aureus* growth in plates were inhibited by essential oils of *A. graveolens* (Yili et al. 2009). The essential oil derived from *Pyrus salicifolia* exhibited antimicrobial activity against *S. aureus*, *Bacillus subtilis,* and *E. coli* (Mamadalieva et al. 2018). In another study, the essential oil of *Origanum vulgare* sp. *vulgare* showed antimicrobial activity against ten human pathogenic bacteria (Sahin et al. 2004).

Vanitha et al. (2020) studied the medicinal plant *Plumbago zeylanica* L. for antimicrobial activity. In their study, the new bioactive molecule, namely heneicosane, showed

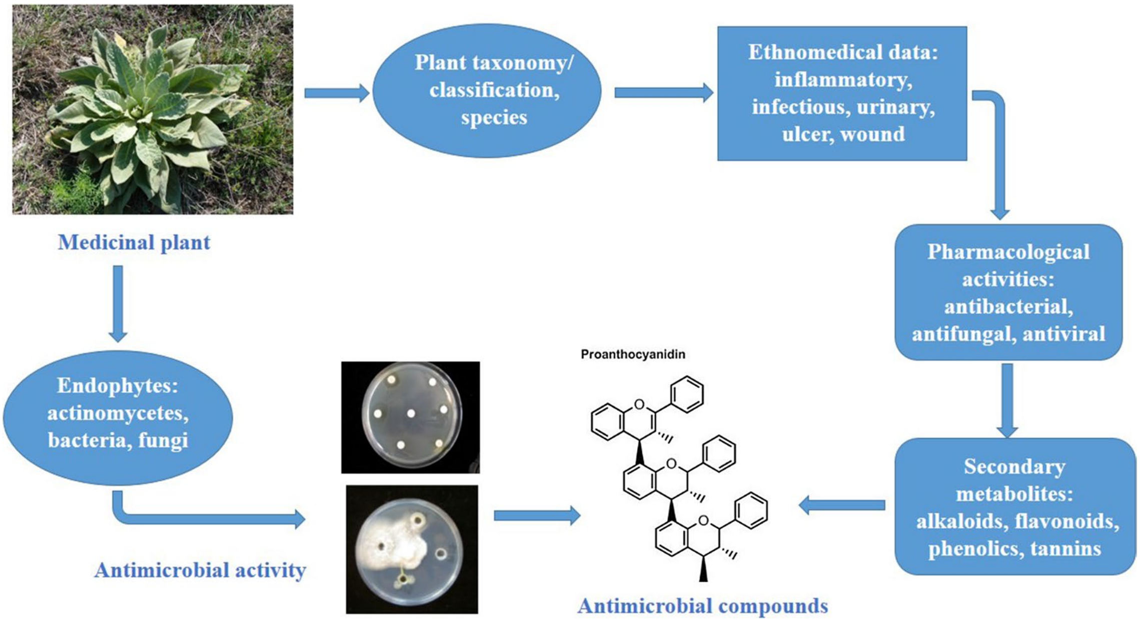

Fig. 1 The potential of medicinal plants and their associated microbes in the discovery of new antimicrobial agents

potent antimicrobial activity against *Streptococcus pneumoniae* and *Aspergillus fumigatus* at 10 µg/ml concentrations. In other studies, biologically active compounds from medicinal plants *Eurya acuminata* and *Croton caudatus* hexatriacontan-1-ol and henicosan-1-ol showed antimicrobial activity against *C. albicans* and *Mycobacterium smegmatis,* respectively (Neipihoi et al. 2020). Kianfe et al. (2020) studied the antimicrobial activity of extract and fractions of *Crinum glaucum* A. Chev. The compound ungeremine showed significant activity against *E. faecalis* and *P. aeruginosa,* while adenosine exhibited moderate activity against *P. mirabilis*. It is known that plant tissues are host for microbes that produce various secondary metabolites with biological activity, such as antimicrobial, anticancer agents, and antioxidants alongwith the plant growth regulators (Qin et al. 2011). Endophytic bacteria residing in inner parts of plant tissue produce secondary metabolites with diverse pharmacological activities, similar to their host plants (Egamberdieva et al. 2017a; Gouda et al. 2016). Therefore, they are considered a potential source of biologically active compounds with high therapeutic potential. These findings show the potential of biologically active compounds such as alkaloids, coumarins, steroids, glycosides, flavonoids, tannins, and essential oils as candidates for developing antimicrobial drugs for the prevention/treatment of infectious diseases.

Future prospects

Considering the vital role of medicinal plants in the global population's well-being, more of them should be researched as protection alternatives for synthetics. Demand for medicinal and aromatic plants in Uzbekistan and other developing countries should continue for the near future. The utilization of unique indigenous knowledge of using medicinal plants to heal human ailments has a great potential to create cost-effective solutions and to screen natural products for drug discovery. Since the medicinal plant-associated microbes also produce various biologically active compounds as their host plant, a more data-rich investigation of these extraordinary microbiome properties as a potential source for new antimicrobials is essential. Moreover, it will help in elucidating pathways and mechanisms of novel biologically active compounds from medicinal plants and their mutualistic microbes, which can be formulated as antimicrobial agents. Furthermore, plant tissue culture is a promising alternative for the production of biologically active compounds of medical importance and should be explored further.

Conclusion

The herbal plants grown in Uzbekistan are very diverse, endemic, and contain various biologically active compounds. Although many plant species are reported as sources of medicine and play a key role in human health management, their phytochemical and biological properties are less studied. They contain various biologically active compounds, which could help discover novel drugs. Therefore, there is an urgent need to continue ethnobotanical research to find and document important medicinal plants endemic to the region and investigate their potential for antimicrobial drug discovery. The present report described the current status of the medicinal plants from Uzbekistan and provided insight into herbal plants' antimicrobial properties and the justification for continuing search for novel metabolites from them. The utilization of ethnomedicinal knowledge has excellent potential to discover possible antimicrobial compounds from the medicinal plants and their associated microbes (Fig. 1).

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Compliance with ethical standards

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