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Antibacterial and Pharmacological Properties of *Ephedra foliata*: A Comprehensive Review

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Abstract: A member of the *Ephedraceae* family, *Ephedra foliata* Boiss. Ex C.A. Mey is a shrub found in arid and semi-arid regions of the world, and has gained recognition for its various pharmacological characteristics and possible medical uses. The main aim of this review is to provide a thorough examination of *E.foliata*'s antibacterial and pharmacological properties, emphasizing its importance in both conventional and contemporary medicine. The plant carries antibacterial properties as it exhibit secondary metabolites like flavonoids, tannins, saponins, alkaloids and phenolic compounds. In addition to its antibacterial qualities, *E.foliata* has a variety of pharmacological activity, such as antioxidant, metabolic regulating effects and anti-inflammatory effects. These properties play a crucial role in managing certain health conditions like respiratory disorders (asthma, cold, fever, cough), metabolic imbalances, diabetic conditions (Anti-diabetic) and manage weight related issues. Various genus of *Ephedra* has been studied so far yet *E.foliata* need to be highlighted. This paper compiles information regarding its antibacterial, ethnobotanical, pharmacological properties and in order to encourage precise avenues for further investigation.

Keywords: Pharmacological, Ethnobotany, *Ephedra*, Antibacterial

I. INTRODUCTION

A. Botanical Characteristics

Ephedra is a genus of Gymnosperm belonging to family *Ephedraceae* and order Gnetales of the Indian Thar Desert. It is related to the conifers and Gnetophyta division (1). *E.intermedia*, *E.alata*, *E. campylopodia*, and other are common *Ephedra* species. *E.foliata* commonly known as *Mauhang* is a shrub found in arid and semi-arid climates across the world. It typically grows in dry and rocky environment where it reclines, woody stem with small scale-like leaves. Because of transformation to dry season condition, it lacks large leaves. The plant produces small cone like construction rather than flowers making it particular within variety as shown in Fig.1 This plant has photosynthetic stems conserving water and reduced transpiration. These characteristics are important for understanding the survival of this plant in this extreme condition, affecting its restorative and biological properties, especially with regards to its secondary metabolites. (2)



Fig.1 *Ephedra foliata*: A herbaceous plant.

B. Taxonomic classification

Kingdom: Plantae; Phylum: Tracheophyta; Division: Gnetophyta; Class: Gnetopsida; Order: Ephedrales; Family: Ephedraceae; Genus: Ephedra; Species: Ephedra foliata.

Common name- Shrubby horsetail in English, *Unt Phog* in Rajasthani, *Alanda warakia*, *feder waraki* in Arabic.

Distribution- It is flourishing in Southwest Asia, and North Africa (3, 4)

C. Ethnobotany

Traditionally *E.foliata* has been used in folk medicine for centuries, particularly in districts where it develops naturally. Its significance in the local cultures, where it is frequently used in health benefits, no matter what it is raw and dealt with kinds, is made clear by its utilization for customary behaviors. This herb has long been used to treat asthma, liver diseases, etc. It has been utilized as an energizer to help energy and relieve weariness as well as diuretic. It has been used to treat improper digestion and even guide in weight reduction. This plant show unique success in handling of Covid-19 infection. (3)

The World Health Organisation appraises that 4 billion individuals, 80% of the total populace, by and by use home grown medication for some part of essential well being care. Plant showed extensive variety of pharmacological exercises including antimicrobial, cell reinforcement, hypolipidemic, anti-asthma, anti-diabetes, anticancer, respiratory cardiovascular, focal anxious, immunological against proactive, pain relieving antipyretic, anti-rheumatoid arthritis & numerous other pharmacological impacts as shown in Fig.2. (4)

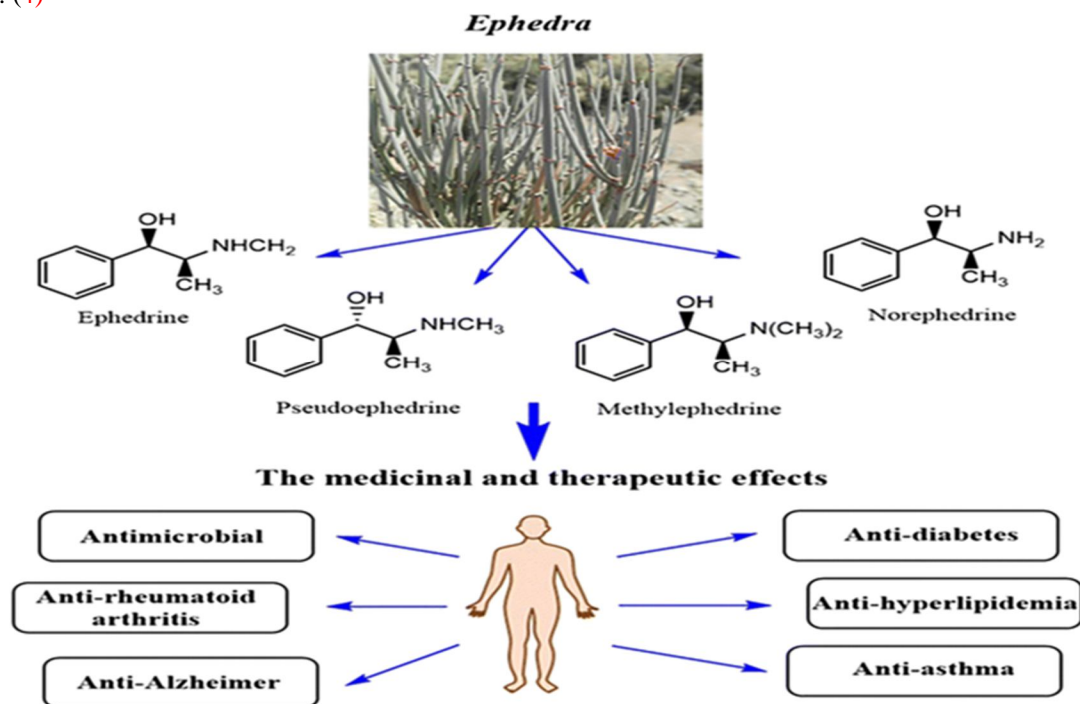


Fig.2 Chemical constituent and its pharmacological effects.

The classical traditional Chinese medicine prescription Ge-Gen decoction, which comprises 7 herbs, composed of a species of *Ephedra* is referred in the ancient Chinese Medical book, “The Treatise on Febrile disease”, worldwide. *Ephedra* species are used to treat typical cold, cough, symptoms as well as serious illness in humans including diabetes, cancer, and microbial infection (5) Recently, consideration is being devoted to the significance of several species as possible cash crops in the US & India. (6). In India, *Ephedra foliata* has the potential to be a profitable crop since it grows well in dry and semi-arid areas. Its importance stems from the plants’s rich alkaloids, particularly ephedrine, which is highly sought after for medicinal uses such as stimulant, weight management, and respiratory problem treatments. Farmers in areas prone to drought may gain financially support from growing *Ephedra foliata* since it is a crop that requires fewer resources. *Ephedra foliata*, a plant that has garnered attention due to its potential antibacterial capabilities is part belonging to the Ephedraceae family. It has been used to treat various respiratory diseases due to its bronchodilator properties allocated to bioactive alkaloids such as ephedrine. (7)

II. CHEMICAL COMPOSITION AND ITS ANTIBACTERIAL PROPERTIES

Plants create a greater variety of chemicals that are crucial for environmental adaptation and defense. These compounds comprises phenolics, alkaloids, steroids, terpenes & have a high degree of biocompatibility and are useful as agrochemicals, flavorings, pharmaceuticals and good colorants. The production of metabolites is frequently limited to a concrete species or genus at a given growth or development cycle depending on particular conditions. It may be impacted by various stresses, both abiotic and biotic. (8)

Having been used by the Chinese for well over five thousand years, *Ephedra* constitutes one among the oldest identified medications (9). Plant life is considered to contain about 2 lakh metabolites including both primary and secondary both (10-14). Because of the ephedrine type alkaloids they contain and their therapeutic benefits, the chemistry of the herb forms have drawn interest. *Ephedra* genus is one of the first genera of medicinal plants known to science which has 69 species primarily found in semi-arid regions(15). Numerous biological actions of *Ephedra*, both refined substances, and raw extract, have been mentioned, including painkiller, antioxidant, and antiphlogistic. (16)

First of all, ephedrine-type alkaloids, which are found in the aerial portions of many plant species, typically include between 0.02% and 3.4% of six optically active alkaloids as shown in Fig.3. (-)Ephedrine (EPH) is the primary one, accounting for 30–90% of all alkaloids. (+)PSE, or pseudoephedrine, is the diastereomer of (+)-N-Methylpseudoephedrine, (+)-N-Methylpseudoephedrine, (-)-EPH, (-)-N-Methylephedrine, and (-)-Norephedrine (17). Second, *Ephedra* species include amino acids and nonephedrine alkaloids. Ephedroxane (18), Ephedradine A (19), 6-hydroxykynurenic acid (20), cyclopropyl- α -amino acid (20), maokonine (21) and 6-methylkynurenic acid (22), N-methylbenzylamine (23), and Tertmethylpyrazine (24). Thirdly, a variety of non-alkaloidal natural constituents of *Ephedra* include kaempferol 3-O-rhamnoside, trans-cinnamic acid, catechin, syringin, epicatechin, and symplocoside. Herbacetin 7-O-glucoside, isovitexin 2-O-rhamnoside, pollenitin B, and herbacetin 7-O-neohesperidoside (25)

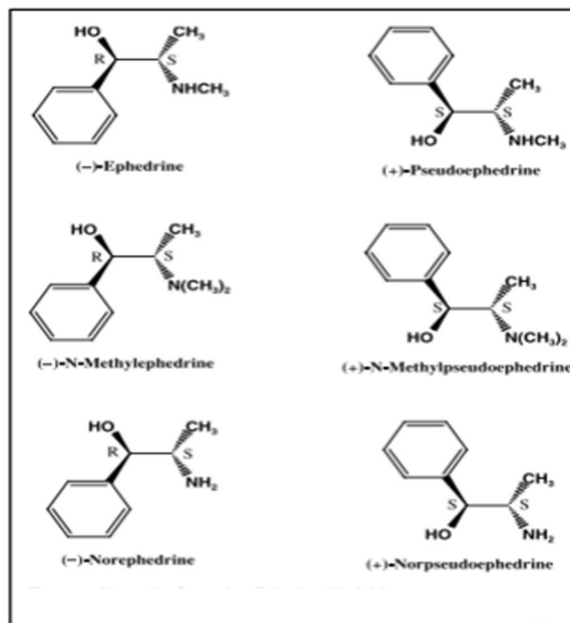


Fig 3. Ephedrine type alkaloids.

A study reveals that both pseudoephedrine and ephedrine were produced by *Ephedra foliata* (26, 27). These two alkaloids found in this were formed in amounts of 0.04-0.2% (28). In an attempt to stimulate *E. foliata* callus to produce higher amounts of ephedrine and pseudoephedrine, it appeared that culture tissues exposed to blue or red light increased the production threefolds. (29)

The other most varied class of specialized metabolites generated found in the *Ephedra* genus are flavonoids, & phenolic compounds. Herbacetin 8-methyl ether 3-O-glucoside-7-O-rutinoside and herbacetin 7-O-(6''-quinyglucoside) are two flavanoids that were identified from *E.alata* Decne. (30). Numerous flavones, flavanols, & analogues of phenolic compounds, notably apigenin that lucenin 1 as well as lucenin 3 are being isolated from *E. antisiphilitica* Berland. ex C.A. Mey.(31). Firmicutes, Actinobacteria, and Proteobacteria were the most common endophytic bacterial species in *E. foliate*. Bioactive substances with notable antibacterial, antioxidant, and anticancer capabilities are produced by the strains F5, A1, and A3 respectively. (32).

Studies show that the antibacterial properties of *Ephedra* species are mediated by alkaloids, which include compounds, phenolics, pseudoephedrine in addition to ephedrine. *E.foliata* has been shown through multiple investigations to exhibit strong antimicrobial action against a variety of bacterial strains, such as either Gram+ and Gram- ones. The fluid concentrate of *E. foliate* showed promising antibacterial movement against both *Escherichia coli* and *Staphylococcus aureus*. Riaz et al. (33) Around 12 mixtures as orsellinic and isocoumarins corrosive subordinates are considered in the synthetic arrangements of endophytic parasite species realted to *Ephedra* species. (34, 35, 36). The inhibitory effect of *E.foliata* phyto-complex extracts on the bacterial growth in numerous human pathogens suggests antibacterial potential values. 37(a),(b). A study reveals antimicrobial properties of extract of the different parts of the plant like leaves, stem of *Ephedra foliata* against human pathogenic, (*S. typhi*, *Enterobacter aerogenes*, *E.coli*, *K. pneumonia*) and plant pathogen like *Agrobacterium tumifaciens*. (38). Thus studies show that *Ephedra foliata* could be a great source of antibacterial agents.

III. PHARMACOLOGICAL EFFECTS OF EPHEDRA FOLIATA

According to earlier pharmacological research, *Ephedra* species have cardiovascular, hepatoprotective, antioxidant, anti-diabetic and antibacterial properties. *Ephedra* is believed in Chinese medicine to enhance warmth, maintain *qi* and reduce coughing. An experiment done by Mei et al shows the anti-asthmatic property of *Ephedra*(39). The Mahaung decoction prevents the asthmatic elevation property which indicates that its decoction can be used as medication used to treat people with allergic asthma (40). *Ephedra*-dervied phenolic compounds exhibit exceptional antibacterial activity versus both Gram+ and Gram- fungus and bacteria. Its stems and seeds are rich in antimicrobial substances and has distinct methods and prohibitory effects on various bacterial species. Phenolic substances derived from *Ephedra* exhibit exceptional antibacterial activity against Gram-positive and Gram-negative bacteria and fungi. (41)

Ephedra studies depicts that it mostly cure the various types of cancer like lung cancer, thyroid cancer, breast cancer, etc. The aforementioned results suggests that *Ephedra* might be utilized to treat clinical cancer, however, more investigations into cellular mechanisms underlying *Ephedra*'s efficacy in treating many kinds of cancer has not been carried out, which could have an impact on *Ephedra*'s future clinical use. Herbacetin containing a type of flavanoid aglycone 7-O-neohesperidin has anticancer properties (42-43). The potential use of *Ephedra* to treat COVID-19 infection was shown by a fairly recent investigations, which found the fact that the quinoline-2-carboxylic acid which could efficiently disrupt the chemicals that are active that result from the link within ACE2, or angiotensin-converting enzyme 2, and the spike protein of SARS-Cov2 beneficiary binds subject (the SARS-Co RBD) prohibit viral infection.(44)

Ephedra foliata's hepatoprotective properties were investigated in Wistar albino rats. In rats, ccl4 was used to cause liver damage. The liver status was assessed using the following parameters: Alkaline phosphatase (ALP), total bilirubin, serum s glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT). At 500mg/kg doses, crude extract of *Ephedra foliata* (whole plant) having hepatoprotective effect shown to be substantial in all parameters examined, with SGPT, ALP, SGOT, bilirubin decreasing by 21.2, 46.2, 39.5,42.6%, respectively. The extract significantly decreased SGOT, ALP, and bilirubin at the lower doses (250mg/kg) (P<0.05)(45)

Ephedrine's pharmacology- Both α and β receptors were activated by ephedrine. Noradrenaline was released from the tissue that had an indirect effect in addition to a direct effect on the receptors. ephedrine's effects on different organs and systems were comparable to those of adrenaline. Additionally, it is a modest CNS stimulant. Generally it produces effects, some are listed here like cardiovascular, bronchiodilation, nasal congestion, mydriasis, weight loss, cytotoxic effects of ephedrine and pseudoephedrine, spinal anesthesia, etc (46). A study reveals the presence of various type of phytochemicals like 6-hydroxykynurenic acid, vicenin 2, ephedrine, & 3-sophoroside 7-rhamnoside. These chemicals play a crucial role in pharmacological properties of *Ephedra foliate*. (47, 48)

IV. CONCLUSION AND FUTURE PERSPECTIVES

We analysed the botanical characteristics, taxonomical details, chemical composition, ethnobotany, pharmacological properties of *Ephedra foliata*. More than 60 species of *Ephedra* have been identified which constitutes more than 100 compounds including flavonoids, sugars, organic phenolic acids, alkaloids, etc. According to manuscript's background, the inhibitory effect of *E.foliata* phyto-complex extracts on the bacterial growth of many human diseases demonstrates their high antibacterial potential. The pharmacological effects have been identified include antiasthmatic, antipyretic, among others. Although its toxicity cannot be ignored but its clinical applications are of large scale too, as it can be used to treat skin disease, helpful in weight loss, liver diseases, and COVID-19 infection.

Because the continuous threat of bacteria resistance to traditional antibiotics, the antimicrobial qualities of *E.foliata* preparations are of particular interest. Over 20 *Ephedra* plant species have had the pharmacological characteristics studied, but still plenty of other *Ephedra* plant's chemical makeup and pharmacological properties have not and *Ephedra foliate* is one of them. In this study we thoroughly summarized the clinical use of *Ephedra* for the first time after reviewing numerous publications.

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