REVIEW PAPER

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A Review of Medicinal Plants for the Treatment of Earache and Tinnitus in Iran

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Abstract

Background and purpose: Despite numerous trials, there has not yet been any definite strategy to reduce replicable long-term tinnitus and earache. Complementary and alternative medical approaches have been used to decrease the symptoms of tinnitus and earache. This study was conducted to report medicinal plants that are used to treat ear disorders, especially earache and tinnitus in different regions of Iran. **Evidence Acquisitions:** Directory of Open Access Journals (DOAJ), Google Scholar, PubMed, LISTA (EBSCO), Embase, and Web of Science were searched using relevant search terms to retrieve eligible publications. **Results:** Twenty-three species from sixteen families were used for the treatment of earache and tinnitus in Iran. Plants from families Asteraceae and Lamiaceae were the most commonly used plants for the treatment of earache. *Ginkgo biloba* was frequently reported for the treatment of tinnitus. **Conclusion:** This study shows the important role of medicinal plants in the treatment of earache and tinnitus in some regions of Iran. The medicinal plants reported in this review can be considered in treatments for earache and tinnitus if examined more extensively in clinical trials.

Keywords: herb, tinnitus, Iran, earache, drug discovery.

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INTRODUCTION

Hearing disorders are associated with certain changes in the physical functioning of the hearing system and affect one's ability to process sounds. These disorders cause difficulty establishing communication with others. Hearing losses are divided into three types, namely conductive, sensorineural, and mixed[1,2], and may cause other disorders such as earache and tinnitus and therefore exacerbate the associated problems of the patients.

Earache

Earache is one of the most common ear disorders[3-5]. If ear anatomy is pathologically involved, earache is referred to as primary, and if the surrounding organs are pathologically involved, it is referred to as referred earache. In children, primary earache is more common while adults are more likely to develop referred earache[6]. In differential diagnosis between primary and referred earache, description and physical examination play a determinative role. Primary earache can be due to acute or chronic otitis media, external otitis, mastoid diseases, Eustachian tube dysfunction, cerumen impaction, ear inflammation, trauma to the ear, or tumoral lesions[7-9] that are easily diagnosed by clinical symptoms. In some cases, however, para-clinical tests such as radiography and audiogram tests are required[3,5,10-12]. Although the causes of primary earache can be benign and self-limiting, ear tumors, metastatic tumors, or primary tumors in the surrounding organs can present with earache[13-15]

Tinnitus

Tinnitus is one of the most common ear, nose, and throat disorders with an estimated 14.2% prevalence in adults. Tinnitus is considered irritating and a serious issue in 3-5% of the patients[16]. Tinnitus is a complicated and multifactorial disorder; although certain factors such as stress and anxiety, exposure to loud noises, anti-inflammatory drugs, antibiotics, and sedatives are definite causes of tinnitus in some cases, the definite cause of this disease cannot be detected in other cases[17]. Holistic and novel approaches and therapies to treat tinnitus, which cause few side effects, are constantly being sought out. In many cases, there is no standard treatment for tinnitus. Anti-depressants seem to reduce tinnitus yet with numerous side effects. Current treatments for tinnitus include the use of hearing aids, voice therapy, environmental sound enrichment, adjuvant therapies, vasodilators using corticosteroids, anticonvulsants, antispasmodics, lidocaine, and benzodiazepines[18]. Cinnarizine is an anti-histamine used to treat tinnitus, however, the use of high doses of cinnarizine causes vasodilation. In addition to pharmacological treatments, phytotherapy may be used to treat tinnitus.

Despite recent developments in modern medicine, there are still no standard treatments for hearing loss. These disorders have fueled research to discover new therapeutic approaches. In this regard, there has been a renewed interest in the approaches of traditional medicine and phytotherapy. Medicinal plants and their derivatives have been studied using scientific approaches *in vitro, in vivo,* and ultimately in clinical trials so that more efficient therapeutic approaches and drugs can be discovered[19-26]. Indeed, in any region across the world, local people use different medicinal plants and approaches to treat diseases, most of which have not yet been scientifically investigated and confirmed[27-39]. Because ethnobotanical evidence is mostly unwritten or has been reported in textbooks only in the language of a specific country, researchers abroad do not have access to such information and cannot be aware of newly identified drugs. It is important to publicize this valuable information to identify and review the traditional uses of medicinal plants in different regions of the world to prevent and treat several diseases. This can help researchers discover new therapeutic approaches and develop more effective drugs. This review was conducted to report medicinal plants occurring in different regions of Iran and used for ear disorders (especially earache and tinnitus) in this country with reference to articles on ethnobotany and textbooks on Iranian traditional medicine and herbal drugs.

MATERIAL AND METHODS

Scientific databases Directory of Open Access Journals (DOAJ), Google Scholar, PubMed, LISTA (EBSCO), Embase, and Web of Science were searched using relevant search terms to retrieve eligible publications on traditional medicine and medicinal plants to treat ear diseases. In addition, a library search was conducted to examine less widely accessible textbooks on Iranian traditional medicine and medicinal plants to collect relevant evidence.

RESULTS AND DISCUSSION

According to this review, it was established that the people in Khorasan, Kerman, Hormozgan, Fars, Kohghiluyeh va BoyerAhmad, Kermanshah, West Azerbaijan, Semnan, Khuzestan, and Isfahan provinces regularly used medicinal plants to treatment earache and tinnitus in Iran. The study revealed that species belonging to sixteen families were used for the treatment of earache and tinnitus in Iran by the people of these provinces (Tables 1 and 2). The data also showed that the members of families Asteraceae and Lamiaceae were the most commonly used plants to treat earache. Four medical plants consisting of Panax ginseng, Melissa officinalis, Allium cepa, and Ginkgo biloba (Table 2) were frequently reported to be used for the treatment of tinnitus by the people of different regions of Iran. Leaves were the most frequently used parts of the plants, including herbal preparations, followed by the flower and roots, fruits, and seeds. Boiling the plant was the most commonly used method of preparation to use these plants to treat earache and tinnitus[40-50].

Our library search showed that Iranian's use certain plants, according to traditional medicine, to treat earache

and tinnitus. For example, *Calendula officinalis* or *Calendula persica* is used as an independent preparation to treat earache in Iran. *Origanum majorana* is dissolved in olive oil and *Carum carvi* juice and the resulting solution is used to treat earache. Pulverized olive leaf is mixed with honey and is applied into the ear, as an ointment, to treat ear infection[51,52]. *Allium sativum* can exert therapeutic effects on otitis media. To achieve this purpose, *Allium sativum* wrapped up in a small piece of clean cloth is applied into the ear to relieve otitis media. To reduce tinnitus, *Amygdalus communis* oil is dropped, alongside *Matricaria recutita* juice, into the ear. To reduce tinnitus, first, *Origanum majorana* is boiled and then its juice is mixed with olive oil; the resulting solution is poured into the ear. *Allium cepa* juice is dropped into the ear to reduce tinnitus[51-53].

In Iran, people use various medicinal plants for the prevention and treatment of earache and tinnitus. However, the effects of most of these plants have not been investigated and confirmed in animal models and clinical trials. In other regions of the world, especially in East Asia, some medicinal plants are used for the treatment of hearing disorders and their effects have been investigated. For example, *Gushen Pianas* a Chinese medicinal herb is effective in the treatment of sensorineural deafness and tinnitus. Zhai et al. indicated that the effect of Gushen Pianis is due to splenonephric hypofunction and phlegm-accumulation stasis[54]*. Radix astragali* has been used for the treatment of deafness for hundreds of years in Chinese medicine history. The investigators have shown that *R. astragali* can effectively reduce cisplatin ototoxicity through inhibiting apoptosis of hair cells[55]. In addition, *R. astralgi* reduces the acoustic trauma by inhibiting the down-regulation of cx26, and Potassium Voltage-Gated Channel Subfamily Q Member 1 (KCNQ1) through inhibiting ROS production[56]. Reactive oxygen species (ROS) are produced when the ear is under pathological condition. ROS are negative regulators of

Table 1. The list of medicinal plants used to treat earache in Iran.

Family	Scientific name	Local names	Part used	Medicinal uses	Geographical regions	Ref
Lamiaceae	*Teucrium polium L*	Kalpooreh	Flower	Ear infections and earache	Khorasan razavi province	40
Cannabinaceae	*Cannabis sativa L.*	Shahdaneh	Seed	Earache	Khorasan razavi province	40
Cannabinaceae	*Cannabis sativa*	Shahdoneh	Seeds, Leaves	Earache	Isfahan province	41
Euphorbiaceae	*Ricinus communis*	karchak	Seeds	Earache	Isfahan province	41
Lamiaceae	*Mentha spicata*	Nana	Apical parts	Strengthen the hear	Isfahan province	41
Myrtaceae	*Eucalyptus camaldulensis Dehnh*	Barge bid	Leaves	Earache	Isfahan province	41
Asteraceae	*Artemisia santolina Schrenk*	Dermaneh	Flower, Leaves, Stem	Ear lesion	Kerman province	42
Apiaceae	*Bunium persicum (Boiss.)*	Zireh	Seed	Children earache	Hormozgan province	43
Cupressaceae	*Juniperus excelsa M.B.*	Ouras, abras, aras,hooras, andgazk	Leaves,fruit	Earache	Hormozgan province	43
Asteraceae	*Sonchus asper (L.)Hill*	Shirtighak	Leaves, root, stem, flower, fruit	Earache	Hormozgan province	43
Euphorbiaceae	*Chrozophora tinctoria*	Chabla	Leaves,fruit	Earache	Fars province	44
Asteraceae	*Lactuca sativa*	Aghja ghoyogh	Leaves	Earache	Fars province	44
Malvaceae	*Malva parviflora*	Toola	Leaves,fruit	Earache	Fars province	44
Alliaceae	*Allium rubellum M.Bieb.*	Sir-ezangulei, Ajujeh	Bulb	Ear infections	Kohghiluyeh va Boyer Ahmad Province	45
Lamiaceae	*Origanum vulgare*	Marjoram	Leaves	Earache	Kohghiluyeh va Boyer Ahmad Province	45
Pteridaceae	*Adiantum capillus-veneris*	Parsiavashoon	Leaves	Earache	Fars Province	46
Caprifoliaceae	*Lonicera caprifolium*	Picheaminod oleh	Leaves and flowers	Earache	In the temperate and cold temperate regions	47, 48
Adoxaceae	*Sambucus nigra*	Aghtisiyah	flowers	Ear infections	Kermanshah and West Azerbaijan province	49
Combretaceae	*Terminalia arjuna*	Arjon	Latex	Earache	Khuzestan province	48
Asteraceae	*Artemisia scoparia*	Dermaneh sharghi	Shoot	Earache	Khorasan razavi, Isfahan, Semnan and Tehran province	50

Table 2. The list of medicinal plants used to treat tinnitus in Iran.

Family	Scientific name	Local name	Part used	Geographical regions, Iran	Ref.
Araliaceae	*Panax ginseng*	Jinseng	Root	This plant is imported to and cultivated in Iran	51
Lamiaceae	*Melissa officinalis*	Varangbo	Shoot	Gorgan, Mazandaran, Kurdistan, and Ilam provinces	51
Amaryllidaceae	*Allium cepa*	Piaz Khoraki	Bulb	In different regions of Iran	52
Ginkgoaceae	*Ginkgo biloba*	Jinko	Leaves	This plant is imported to and cultivated in Iran	53

gap-junction channels such as cx26, reducing intercellular coupling in many systems. Noise-induced hearing loss was reported to be associated with inhibition of cx26 and KCNQ1 by increasing ROS production. *R. astralgi* can also effectively reduce cisplatin ototoxicity through the inhibition of apoptosis of hair cells[56,57]. In addition, the potential protective effects of astragalosides have been demonstrated against cisplatin-induced oxidative stress in the guinea pig cochlea. Astragaloside IV inhibited the activity of inducible nitric oxide synthase (iNOS) and nitrotyrosine in the cochlea exposed to impulse noise, leading to decrease in outer hair cells (OHCs) with stereocilia loss and minor auditory brainstem response (ABR) threshold shifts[58]. Astragaloside IV can inhibit iNOS to protect the ear from the impulse noise. Another possible mechanism is that astragaloside IV directly scavenges ROS[59]. In addition, astragaloside IV can decrease noise induced hearing loss (NIHL) by inhibiting the apoptosis of cochlear cells through the suppression of ROS[58]. It was also reported that carboxy alkyl esters of *Uncaria tomentosa* can induce otoprotection by increasing potential antioxidant activities[60]. A study indicated that Korean red ginseng (KRG) ameliorated acute 3-nitropropionic acid-induced cochlear damage in mice. In an animal model of acute cochlear dysfunction induced by intratympanic administration of 3-NP, the hearing impairment was found to be dose-dependent, and that functional changes were well matched with the histological changes. KRG ameliorates the cochlear damage induced by 3-NP in the acute stage through suppression of degeneration of fibrocytes in lateral walls and spiral ganglion cells[61]. A clinical trial in Japan indicated that Wu-Ling-Sanas, a popular anti-lithic chinese herbal formula, in combination with an oral steroid was significantly more effective than the diuretic alone, Wu-Lin-San alone, or the steroid-diuretic combination[62].

CONCLUSION

In Iran, medicinal plants and herbal drugs are more popular among people because they are cheap with fewer side effects compared with synthesis drugs, but when the patients go to clinics for their diseases, physicians prescribe the synthesis drugs for the diseases such as earache and tinnitus because their effects have been confirmed scientifically and their therapeutic responses work quickly. This study has shown the important role of Iranian medicinal plants in the treatment of earache and tinnitus in some regions of Iran. Phytochemical and pharmacological studies with such plants are needed to confirm their anti-earache and tinnitus activities. The use of medicinal plants and their derivatives results in reduction in the overall prevalence of earache probably due to inhibition of ROS production, and iNOS and anti-inflammatory activities. Thus, the extract of the above mentioned plants, or their purified derivatives, are valuable extracts to be considered in the treatment of earache and tinnitus, and should be investigated more extensively in clinical trials.

Conflict of interest

We declare that there is no any conflict of interests for this publication.

Ethical consideration

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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