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A Study of Most Widely Used Herbal Medicines in Iranian Traditional Medicine for Treatment of Urinary Incontinence

Sousan Hafizi[1·], Alireza Abbasian [2*], Maliheh Tabarraei [2]

[1]PhD Candidate of Traditional Medicine, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran
[2] Department of Traditional Medicine, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

Urinary incontinence (UI) is a common and costly disease that, though not fatal, significantly affects social, economic, and psychological well-being. Although there are several treatments for the disease, none is still suitable and without complication; therefore, in this study, we used methods of Iranian traditional medicine and its thousands of years' experience. To find a proper definition for UI in T.M., we studied bladder diseases in five reference books (The Canon of Medicine by Avicenna, the Exir-e-Azam by Hakim Azam Khan, Zakhireye Khwarazmshahi by Zayn al-Din Gorgani, Makhzan ul Advia by Hakim Gilani, and Teb Al-Akbar by Hakim Muhammad Arzani) and selected post-void dribbling and urinary incontinence (both means involuntary leakage of urine). After examining the causes and symptoms of the disease, we collected some of treatments provided by the Iranian traditional medicine (since from the perspective of Iranian medicine, treatment is first done by changes in diet and lifestyle, then medications and finally by practical methods). Then, we found different treatments, among which we examined the most common herbs in hope of introducing a new treatment for the disease relying on the traditional medicine. Involuntary leakage of urine and urinary incontinence were used interchangeably in old medical books, in which overactive bladder followed by uninhibited contractions of the detrusor muscle was the main cause. In the present study, causes, symptoms, and diagnosis of the disease were thoroughly investigated.

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KEYWORDS

Urinary incontinence, Selselolbol, Taghtirolbol.

INTRODUCTION

Urinary incontinence (UI) is a common and costly disease that, though not fatal, significantly affects social, economic, and psychological well-being. According to the International Continence Society (ICS), urinary incontinence is the result of uncontrolled urination (1). This problem is more prevalent in women than men and has a direct relationship with age (1, 2). The prevalence of UI in middle age in women and men is approximately 30-60% and 14-31%, respectively (1). According to a study in the United States, 25% of people over 20 years of age suffer from UI, and economic burden of the disease is estimated to be $82 million by 2020 (3). Apart from the economic burden, UI leads to other issues including social and occupational conflicts and sexual problems (4). According to Urology Foundation, UI is divided into three types: 1) Stress UI; 2) Urge UI; and 3) Mixed UI.

Stress UI: In this type of the disease, a person experiences an involuntary leakage of urine because of increasing intra-abdominal pressure followed by cough, sneeze, or increased physical activity.

Urge UI: It is a condition in which a person is unable to hold his/her urine when he/she has strong urge to urinate.

· **Contact**: Sousan Hafizi, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran
abbasian@sina.tums.ac.ir Tel: 00989125049346

Mixed UI: In this type of the disease, a person experiences both types of urinary incontinence (1, 3, 5-7). Apart from gender, factors such as obesity, hormonal disorders and type of delivery play an important role in this type of the disease (1, 4, 6). In addition, history of hysterectomy, diabetes, inadequate physical activity, frequent urinary tract infections, depression, menopause, smoking, special diets, certain medications, and heart problems can all contribute to this complication (1). The prevalence of urinary incontinence in the United states was reported to be 25.7 million and 26 million in Taiwan in 2020 (8). In a study in Brazil in 2019, 35% of women developed urinary incontinence during menopause (9).

The economic burden of the UI In the UK is approximately €1 billion a year (10). Yoshitaka et al (2018) reported that in 2010, the prevalence of urinary incontinence among women in the United States is approximately 18 million, which would reach 28 million by 2050 (6). Researchers believe that the prevalence of urinary incontinence is higher than this because social taboos sometimes prevent people from reporting the problem (2). A study in Iran shows that, the prevalence of UI seems to be approximately 23.5% (2, 11). Despite the high number of patients with urinary incontinence, several treatments have been proposed for the problem, though none is still suitable and without complication (12, 13); therefore, the present study aimed to investigate the treatments for the UI provided by the Iranian traditional medicine. The study focused on the commonly used herbs in the treatment of the disease in hope of introducing a new treatment for the disease relying on the traditional medicine.

Method

This review article investigated the symptoms, diagnosis, and treatments for the bladder diseases provided by the Iranian traditional medicine in five reference books: The Canon of Medicine by Avicenna (5th century), the Exir-e-Azam by Hakim Azam Khan (14th century), Zakhireye Khwarazmshahi by Zayn al-Din Gorgani (6th century), Makhzan ul Advia by Hakim Gilani, and Teb Al-Akbar by Hakim Muhammad Arzani (12th century). In these five books, 95 medicinal plants were mentioned, among which the most frequent were selected. Then, the related papers were searched in PubMed, Google Scholar, and SID databases.

Results

Historically, unlike common diseases such as bladder stones and urinary retention, there is rarely a description of urinary incontinence and related therapies in medical history except for limited reports on overflow incontinence because of urinary tract obstruction and extra-urethral incontinence due to rupture of pelvic floor during childbirth. In these cases, abnormal ducts are formed between the bladder and vagina (vesicovaginal fistula), which leads to leakage of urine from the vagina. The vesicovaginal fistula has been found in mummified bodies from 2150 BC. After reviewing papers on classical medicine, several treatments for the disease were found.

The first line therapy is lifestyle change; for example, a 3-5% decrease in baseline weight leads to a 47% reduction in stress urinary incontinence. Strengthening pelvic floor muscle is one of the first line treatments (6). In fact, myogenic and neurogenic causes are important in creating this problem (12).

Medication is the second choice, often with less invasive drugs and then surgical treatments; for example, skin patches and vaginal creams containing estrogen are prescribed in the early stages of drug treatment. Vaginal treatments are effective in women with hormonal problems and vaginal dryness to improve blood flow. The next step in treatment is anticholinergic and beta-agonist drugs (4-6).

Anticholinergic drugs affect the detrusor muscle and reduce urinary incontinence. They block the muscarinic receptors in the detrusor muscle and reduce the contraction (6, 12). Among these drugs are: Oxybutynin, tolterodine, solifenacin, trozepium, and darifenacin. Anticholinergic drugs have many side effects, including dry mouth, dry eyes and skin, abdominal pain, upset stomach, fatigue and constipation.

The next class of drugs are the beta-3 adrenoceptor agonists. One example is mirabegron, which increases bladder capacity. In other words, the detrusor muscle relaxes and increases urine volume. One of the important side effects of the drug is hypertension, dry mouth, and constipation (6).

Another group is antidepressants that prevent serotonin-norepinephrine reuptake, reduce parasympathetic activity, and increase the sympathetic effects leading to the closure of the urinary tract, thus treating incontinence. Duloxetine is an example of these drugs and its side effect is nausea. Though common in European countries, it is not prescribed in the United States.

Surgical treatment is another choice, which is mainly recommended for people with mixed UI. This method is costly, with complications including bleeding, infection, and urinary retention. Another invasive method is the injection of botulinum toxin into the detrusor muscle, which allows the bladder muscle to retain more urine. This method is associated with complications such as urinary retention and urinary tract infection (6).

According to studies, the main treatments were medication and surgery; however, these methods were associated with many complications and incomplete response to therapy (3, 14).

Scientists believed that bladder wall acts as a barrier, though recent studies has confirmed other roles, including secretion and nervous stimulation. Although information on this matter is not yet complete, it is necessary to know that the secretions of the urothelium wall and the nervous stimulation in this area are very important in bladder function. There are several receptors and channels in the bladder wall that play an essential role in the bladder function. By bladder filling and developing urine pressure on the bladder wall, ATP is released from these cells, stimulating the parasympathetic nerve, leads to a contraction in the detrusor muscle, which causes urination to occurs. During storage phase when bladder is relaxed, the sympathetic nerve is stimulated, not only prevents the detrusor muscle from contraction but also stops urethral sphincter from opening to prevent urination (15).

Since the treatment of urinary incontinence by mentioned methods were costly, with many complications, and there were incomplete responses to therapy, it is necessary to seek another method, namely herbal medicine. In this regard, five most important reference books of Iranian traditional medicine were used, including the Canon of Medicine by Avicenna, the Exir-e-Azam by Hakim Azam Khan, Zakhireye Khwarazmshahi by Zayn al-Din Gorgani, Makhzan ul Advia by Hakim Gilani, and Teb Al-Akbar by Hakim Muhammad Arzani.

First, for equivalence, we examined bladder diseases in these books. Then we found post-void dribbling and urinary incontinence equivalent. Urinary incontinence is the involuntary leakage of urine while post-void dribbling occurs when urine remaining in the urethra after voiding the bladder slowly leaks out after urination (13, 16-18). The different causes of the disease were discussed below.

Taghtirolbol causes	Exir-e-Azam	Teb Al-Akbar	Zakhireye Khwarazmshahi	the Canon of Medicine
Urinary irritation due to food, fatigue and sexual intercourse	×	×	×	×
Cold temperament	×		×	×
Increased urination due to fluids consumption	×		×	×
Weakness of bladder muscle		×	×	×
Inflammation around the bladder muscle	×	×	×	×
Cold dystemperament of external muscle	×	×	×	×
Dystemperament of bladder and weak urinary continence	×	×	×	×
Involvement of organs above bladder	×	×	×	×
Bladder wounds and injuries	×	×	×	×
Central insensitivity	×			×
Hot temperament		×		
Simple hot Dystemperament of bladder				×

Urinary incontinence(salesolbol)	Exir-e-Azam	Teb Al-Akbar	Zakhireye Khwarazmshahi	the Canon of Medicine
Cold bladder	×	×	×	×
Bladder moisture or wetness	×	×		×

Overuse of diuretics and fruits	×	×	×	×
Bladder heat	×	×		×
Pressure around/ the bladder and spine problems	×	×	×	×
weakness and paralysis in the bladder		×	×	×

According to the five reference books, the most common causes of post-void dribbling includes:
Muscle weakness around the bladder (13, 16-18)
Cold temperament of bladder (13, 16-18)
Wounds/temperament of food consumed (13, 16-18)
Involvement of organs around the bladder due to pressure from adjacent viscera (13, 16-18)
And the causes mentioned in the three books include:
Cold temperament of the kidneys and liver (13, 16, 18)
Consumption of fluids. (13, 16, 18)
Common causes of urinary incontinence (Salesolbol) in the books mentioned books (13, 16-18) also include:
Cold temperament of bladder (which is very important)
Consumption of Diuretics
Pressure to the bladder and spinal cord problems (13, 16-18).

Other causes include:
Heat and humidity of bladder (16-18)
Relaxation of bladder muscles (13, 17, 18)
After studying the causes, the treatment of the diseases was investigated and the herbal medicines (95 plants) used in the books were collected. The plants provided by Makhzan ul Advia are as follows (13, 16-18):
Quercus Ilex
Cyperus Langus
Boswellia Certeria
Nigella sativa
Elettaria cardamomum
Myrtus Communis
Punica Granatum
Costus Speciosus
Ficus Carica
Ceracus Mahaleb

Name	Family	Parts used	Temperament
Quercus ilex	Fagaceae	Fruit, husk	Cold and dry
Cyperus langus	Cyperacea	Root	Hot and dry
Boswellia certeria	Burseraceaeh	Resin	Hot and dry
Myrtus communis	Myrtaceae	Fruit, leaf, flower, kernel, stem	Cold and dry
Punica granatum	Punicaceae	Fruit, husk, flower, leaf	Cold and wet
Costus specious	Zingiberaceae	Root	Hot and dry
Ficus carica	Moraceae	Fruit, extract, leaf	Hot and wet
Cerasus mahlab	Rusaceae	Fruit, husk, leaf	Hot and dry
Ellataria cardamomum	Zingiberaceae	Seed, husk	Hot and dry
Nigella sativa	Ranunculaceae	Seed	Hot and dry

DISCUSSION

Quercus ilex: It is found in abundance in Iran and has long been used to treat stomach ulcers, dysentery, intestinal inflammation and laryngitis. Its important compounds are tannins and polyphenols with anti-inflammatory and anti-prostaglandin properties (19). In a study in Tunisia (2017), effects of the flavonoids, which have anti-

acetylcholine function and reduce muscle contraction have been investigated (20).

Cyperus langus: This plant is perennial, has creeping rhizomes, and grows in tropical regions of Iran. The root of this plant is used as an astringent, appetizing, and anti-diarrhea in traditional medicine. Its anti-diarrheal properties affect the Na+/K+-ATPase (21).

The presence of flavonoids, alkaloids, tannins and polyphenols makes this plant analgesic and anti-diarrheal. A study by Indian researchers published in 2012 showed that the sedative effect of this plant was due to isocurcumenol in essential oil. In this paper, an inhibiting effect of the plant has been reported on Na+/K+-ATPase pump, which causes muscle relaxation (22).

Boswellia certeria: It is the gum of a tropical tree that has been used for many years in China, India, and the Middle East. It is used in India as an anti-inflammatory drug and analgesic and in China for blood circulation and analgesia. Its active

compound, boswellic acid is analgesic and quasi-steroidal. In one study, the substance had a dramatic effect on the condition of brain cells and improved memory in mice (23). Oleogome extract has anti-inflammatory effect and is used in arthritis (24). In another study in Iran (2016), the high antioxidant of this gum were proven effective in inflammatory diseases, cancer, Crohn's disease, and Colite. It also improves memory due to the protective effect of boswellic acid on the nervous system (25).

Myrtus communis: In traditional treatments, this plant is used as an antispasmodic and anti-diarrhea (by reducing bowel movements) (26). Its active compounds include cineole, myrtenol, pinene and Comphen and strong tannins (27). In a study (2017), the effectiveness of tannins and phenols in improving blood circulation was investigated (26). Another property of the plant is antispasmodic effect on bronchial pressure and muscle relaxation (28).

Punica granatum: The tree grows in Asia, America, Africa, and Australia. Its various parts are used for the treatment of digestive problems, abdominal pain, and bacterial infections. Its active compound are flavonoids, anthocyanins, tannins and fatty acids (29). With astringent properties, it decreases diarrhea by affecting bowel movements. The plant contains polyphenolic compounds with estrogenic properties (30), and its tannins and flavonoids improve vascular blood flow (31). Other properties include the urinary tract and bile duct relaxation (32, 33).

Costus speciosus: In Arab countries, the plant is used for food and as a medication. In a study in Saudi Arabia (2018), it was found that the plant prevents the proliferation of cancer cells and is very effective in prostate cancer. Also, the alkaloids in this plant are muscle relaxants and have antispasmodic effect (34).

In a study in Iran, the effectiveness of this plant in the treatment of urinary incontinence was examined and it was found that people who used the costus speciosus oil under umbilicus twice a day had an 87% reduction in symptoms of urinary incontinence (11).

Ficus carica: This plant is native to the Mediterranean and its fruit contains vitamins, minerals, organic acids, phenols, phytosterols, anthocyanins, trepenoids and coumarin. It is used as a treatment to relieve constipation, cough and to reduce blood lipids. The fruit is rich in antioxidants and is effective in cardiovascular, inflammatory diseases, and gastrointestinal ulcers (35).

This plant has been used to treat seizure. Quarastine and luteolin are two important flavonoids in this plant that have antispasmodic, sedative, analgesic, and anticonvulsant effects by regulating epinephrine light and 5-hydroxytryptamine in the brain (36).

Ceracus mahaleb: The fruit of this plant has antioxidant and anti-inflammatory properties and is effective in improving the function of mitochondria (37).

In this plant, there is a high amount of anthocyanin and its important compound include malic acid, citric acid, and hydroxycinnamic acid (38). Hydroxynamic acid with muscarinic effect and inhibiting parasympathetic function may considerably reduce muscle spasm (39).

Nigella sativa: The oily part of this plant has active compounds called ThymoquIinone and dithymoqiunone. It is also a good source for minerals such as iron, copper, phosphorus and zinc. With its protective effects on the nerves, nigella sativa improves memory and reduces epilepsy (40, 41). In a study in Mashhad and Isfahan (2015-2016), it was found that the active compounds of this plant are effective in urinary problems such as cystitis (42). In 2014, its anti-asthmatic effect was also proven (43).

Elettaria cardamomum: This fragrant seed is widely used in Arab countries for food and medication. It has been used in the treatment of gastrointestinal, respiratory and anticonvulsant diseases. The active metabolites of this plant are Chanel alfapenine, betapenine, sabonin, limonene, cineole, etc. Its flavonoids and alkaloids improve cardiovascular, gastrointestinal, and pulmonary problems. These tannins and sterols are calcium channel blockers with antispasmodic properties (44).

In this plant, cineol prevents the nerves from degeneration and improves the blood flow, thus effective in the treatment of Alzheimer's disease (45).

CONCLUSION

Anticholinergic drugs are a common treatment for urinary incontinence, though they are associated with a number of complications, including palpitations, tachycardia, confusion, nausea, and urinary retention (11).

Beta-adrenergic drugs are another group of treatment that may cause headaches, confusion, and hypertension (6, 11). Since the treatment of urinary incontinence by mentioned methods were costly, with many complications, and there were incomplete responses to therapy, it is necessary to seek another method, namely herbal medicine. In this regard, five most important reference books of Iranian traditional medicine were used, including the Canon of Medicine by Avicenna, the Exir-e-Azam by Hakim Azam Khan, Zakhireye Khwarazmshahi by Zayn al-Din Gorgani, Makhzan ul Advia by Hakim Gilani, and Teb Al-Akbar by Hakim Muhammad Arzani. After examining 10 widely used plants in

treatment of urinary incontinence, it was found that the main therapeutic effects include relief from muscle spasm, neuroprotection, and increased blood flow. In other words, herbal medicines are as effective as chemical treatments except that the former have fewer side effects and are low-cost.

Costus speciosus: Its effect on the bladder area has been proven in reference books of Iranian traditional medicine (11).
Quercus ilex: One of the most widely used plants to relieve muscle spasm by inhibiting acetylcholine (20). Due to the effectiveness of this plant in creating proper vaginal tonicity, it may help to better close the urethra (21).
Boswellia certeria: With active compounds such as boswellic acid, the plant is effective in improving blood circulation in the brain, thus improving the activity of the nervous system (23).
Myrtus communis: With its high tannins and flavonoids, it is highly effective in increasing blood flow, reducing spasm, and improving urinary incontinence (26).
Ficus carica: With its active compounds of Quarastine and luteolin, the plant has anti-inflammatory properties and is a good treatment for asthma because of its antispasmodic function (36).
Punica granatum: This plant is abundant in Asian countries and with its tannins and flavonoids improves blood flow; on the other hand, with its estrogenic properties, may improve urinary incontinence (29-31).
Elettaria cardamomum: In this plant, tannins and sterols in the calcium channel block can improve spasm and muscle relaxation, which seems to help improve urinary incontinence (44).
Nigella sativa: In spite of thymoquinone and dithymoquinone compounds and other minerals, it seems to be effective in urinary problems and cystitis (40, 42).
Cyperus langus: This plant has a sedative and relaxing effect by inhibiting sodium and potassium pumps, which seems to be effective in urinary incontinen (22).
Ceracus mahaleb: This plant has antioxidant and anti-inflammatory effects. Its hydroxynamic acid with muscarinic effect and inhibiting parasympathetic function may considerably reduce muscle spasm (39).
Due to the fact that medicinal plants play an important role in improving nervous system and blood flow as well as relaxing muscles relaxation, they could be effective in treatment of urinary incontinence; however, further clinical trials are recommended to shed more light on how these plants affect urinary problems.
In short, according to ancient medical texts, urinary continence is the result of complete function of the bladder and bladder-neck (external sphincter) during the reserve phase. Urinary continence is the ability to keep from accidentally leaking urine from one's bladder. Cold temperament and sphincter protrusion are the leading causes of urinary incontinence. Today, the correct function of bladder is considered to depend on the health of the complex neural pathway of sphincter. Sphincter protrusion has its own treatment strategies, by which it is likely to take important steps in treatment of urinary incontinence.

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