INTERNATIONAL JOURNAL OF UNANI AND INTEGRATIVE MEDICINE

E-ISSN: 2616-4558
P-ISSN: 2616-454X
IJUIM 2018; 2(2): 99-103
Received: 15-02-2018
Accepted: 16-03-2018

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Unani and contemporary perspective of *Waram al-Aalate Bawl* (Urinary tract infection)

Rushda Saeedi and Arshiya Sultana

Abstract
In Unani medicine, *Waram al-Aalate Bawl* literally means urinary tract infection. It includes *Waram al-Kulliya, Waram al-Mathana* and *Waram al-Ahleel*. Cystitis is the most common bacterial infection in young and elderly women. Recurrent UTIs (cystitis) can have a negative effect on the quality of life. Conventional management for cystitis includes antimicrobial/antibiotics. Antibiotics are the main stay treatment for acute and recurrent cystitis. Severe side effects have been reported and disturbances may require treatment to be withdrawn. Further, antibiotic resistance and previous episodes of cystitis have been positively associated with increase duration of severe symptoms of UTIs. Therefore, the need for alternative therapies for cystitis is evident. Thus, literary appraisal of classical sources was reviewed for *Waram al-Aalate Bawl* and to correlate with contemporary knowledge.
Material and Methods: The classical Unani sources viz., Al-Qanun fi'l Tibb (Canon of Medicine), Iksir-i-A'zam, Al Hawi fi'l Tibb (Continens Liber), Tarjuma Kamil al-Sana'a al-Tibbiyya, Dhakhira Khawarizm Shahi, and Tibb-i-Akbar were reviewed. Further, different search engines were also browsed on website to explore the recent studies in contemporary era
Results: The causes as per classical texts are *Waram al-Haar* and *Waram al-Barid*. *Waram al-Haar* includes *Waram al-Safrawi* and *Damavi*, *Waram al-Barid* includes *Waram al-Balghami* and *Saudawi* (*Sulb*). Recent studies also prove that short urethra,
Conclusion: Unani classical texts are very much enriched with the informative knowledge related to UTI and recent studies in contemporary proves the same. Therefore, execution of traditional system of medicines in today's era may play a very important task to restore health in a holistic way.

Keywords: Antimicrobial, anti-inflammatory, analgesics, cystitis

Introduction
In Unani medicine, *Waram al-Aalate Bawl* described as an infection that starts in the urinary system which includes *Waram al-Kulliya*, *Waram al-Mathana*, and *Waram al-Ahlil* [1] The clinical findings of *Waram al-Aalate Bawl* is similar to urinary tract infection (UTI) as described in conventional medicine. Anatomically UTIs is divided into upper (kidney-nephritis) and lower (bladder-cystitis, urethra- urethritis) UTIs [2]. Lower UTIs (cystitis) are very common and have been estimated to occur in at least 60% of women at some stage during their lives [3]. Among the 6-8 million young women estimated to have acute cystitis each year, most have only single episodes. However, some 25%-50% experience recurrent episodes [4]. Cystitis are approximately 50-fold more common in adult females than males because woman have shorter urethra that allow bacteria ascend into the bladder. Because of their high prevalence, UTIs are a public health concern, having an estimated cost of diagnosis and treatment exceeding US $25 billion over a 20 year period; it is Distressing and occasionally life threatening [3].
Cystitis is caused by microorganisms, mainly Gram negative bacteria. Indeed, E. Coli account for most cases [3]. The risk factors that predispose women to cystitis includes sexual intercourse, the use of contraception (specially spermicide based), a history of previous attack [4], menopause, genetics, bacterial virulence [3]. Treatment usually involves antibiotics, and recurrence is a major concern. Focusing on UTIs (cystitis) prevention and proper management became a major goal because of their recurrent nature, increasing antimicrobial resistance and medical costs [3]. The current management of cystitis involves course of antibiotics. Although effective, these treatments have several side effects such as urticaria, nausea, and vomiting and less serious but unpleasant side effects including oral and vaginal candidiasis and GI disturbances may require treatment to be withdrawn [5]. Treatment and prevention of urinary tract infections (UTIs) is reaching at turning point. The greater challenge presented by uncomplicated urinary tract infections is the propensity to re-occur.

Following an initial UTI, the risk of a second is 24.5% within 6 months, and up to 5% will have 3 or more episodes per year. While antibiotic therapy either daily or as post coital prophylaxis is effective at reducing recurrences, the increasing rate of antibiotic resistance among uropathogens, and concerns about the effect of antibiotic prophylaxis micro- biota, makes this strategy less desirable.

Therefore, the need for alternative therapies for UTI is evident [6]. For centuries plants have been used throughout the world as drugs and remedies for various diseases. Thus, alternative treatment is at higher priority in this era. Though, the traditional classical texts are enormously enriched with the knowledge of etiology, clinical features and treatment of various diseases, however, the traditional health care system is on the verge of annihilation. Hence, in the present era documentation and preservation of the traditional knowledge is the great challenge. Further, this immense knowledge that exists in the classical texts needs to be conserved for future research in pharmaceuticals and drug discovery. Moreover, scientific studies to test effectiveness of herbal remedies used Unani medicine and other traditional system of medicine are very scarce. Thus, literary appraisal of classical sources was reviewed for *Waram al-Aalate Bawl* (urinary tract infection) and to correlate with contemporary knowledge.

Material and Methods

The classical Unani sources viz., Al-Qanun fi'l Tibb (Canon of Medicine), Iksir-i-A'zam, Al Hawi fi'l Tibb (Continens Liber), Tarjuma Kamil al-Sana'a al-Tibbiyya, Dhakhira Khawarizm Shahi, and Tibb-i-Akbar were reviewed. Further, different search engines were also browsed on website to explore the recent studies in contemporary era.

Results and Discussion

Unani classical texts are enriched with medicines useful in *Waram al-Aalate Bawl.* The first written description of *Waram al-Aalate Bawl* was present in ancient Ebrus papyri and recommended herbal treatment to ameliorate urinary symptoms without providing insight into pathological mechanism of UTIs. Hippocrates believed that disease was caused by disharmony of four humors [7].

Ali ibn-e-Abbas Majusi in"Kamil-al- sana'a" describes *Waram al-Aalate Bawl* in detail and opined that the main cause of *Waram al-Aalate Bawl* was weakness of excretory function and inflammation of neck of urinary bladder [8]. Ibn-e-Sina gives a vivid description of *Waram al-Kulliya*, *Waram al-Mathana* in "Al Qanoon fit Tibb" [9]. Hakim Azam Khan in Aksir -i-A'zam had described *Waram al-Aalate Bawl* and classified it into *Waram al-Aalate Bawl Harr* and *Waram al-Aalate Bawl Barid* [1]. Buqrat in "Fasool- i-Buqratiya" had described that presence of cast in urine and foul smelling urine indicates that the pathology is related to the bladder [10] Razi on "Al havi fit Tib" described it under the heading of *Taqtir al -Bawl ma Hurqat* [11]. He also described the efficacy of *Mauljaban* in *Waram al-Mathana.* Similarly many Unani scholars described *Waram al -Aalate Bawl* in their famous books.

Etiopathogenesis in Unani Medicine: According to the Unani scholar's causes of *Waram al-Aalate Bawl* are disturbance in *Asbab-e-Sittah Zaruriyah* and weakening of the *Tabi'at Mudabbir al-Badan.* Alteration in *Kammiyat* and *Kafiyat* of *Akhlat* provides favourable conditions for the growth and colonization of microorganism. Hence, the cause of *Waram al-Aalate Bawl* is not the microorganism alone but disturbance in *Asbab-e-Sittah Zaruriyah* which ultimately leads to an alteration in *Akhlat.* According to Unani scholars when body is attacked by the microorganisms *Quwat Mudabbir al-Badan* is altered in various ways like *Akhlat i -Mahmooda* are eaten up by the microorganism, or their toxins are added in the akhlat [12]. Some other causes of *Waram al-Aalate Bawl* are inflammation or abscess of urinary tract, blood and pus from abscess of adjacent organs, pus contaminates the urethral and ascends and colonizes the urinary tract similarly as in conventional concept [1]. Blood and pus from abscess of adjacent organs drained into urinary tract may cause *Waram al-Aalate Bawl* [13]. Irritation due to stones and trauma leads to *Waram al-Aalate Bawl* [14]. Acute and hot humour or deranged hot temperament of bladder causes erosion of mucous membrane of urinary tract and thereby inflammation. Person having bilious temperament is more susceptible to *Hurqat al-Bawl*. Alteration in the *Mizaj* leads to disharmony of the four humours which was maintained by *Quwat i -Mudabir al –Badan* [1].

Conventional Medicine: The pathogenesis of UTI is complex and influenced by many host biological and behavioral factors and by properties of the infecting uropathogens. Gram Negative and Gram Positive bacteria and certain fungi are the causative organism. The key events in initiating each step in UTI pathogenesis are adherence and colonization of organisms. It starts with the contamination of pre-urethral area with an uropathogen. These uropathogens colonizes the urethera and than migrates into the bladder after migration there is again colonization and invasion of the bladder, mediated by pili and adhesions in turn starts inflammatory responses in the bladder, including neutrophil infiltration, begin to clear extracellular bacteria. Some bacteria evade the immune system and these bacteria undergo multiplication and biofilm formation. These bacteria produce toxins and proteases that induce host cell damage thereby releasing essential nutrients that promote bacterial survival and ascension to the kidney [15].

Classification: In Unani classical text *Waram al-Aalate Bawl* has been divided into *Waram al-Harr* and *Waram al-Barid*. *Waram al Harr* includes *Waram al-Safrawi* and *Damavi*, *Waram al- Barid* includes *Waram al-Balghami* and *Saudawi* (*Sulb*) [1].

Clinical Features: Unani scholars described that the clinical features develop according to *Ghalba i-Khilt* [1]. When the causative matter is *Damavi* then the clinical features are *Pusht Me Dard ka Ehsas* (pain in supra pubic region), *Dushwar i-Bawl* (dysuria), *Taqtir al-Bawl*(dribbling of urine) *Aur Silsile al-Bawl* (incontinence of urine), *Sauzish i-Bawl*(burning micturition) and *Tishnagi* (increased thirst), *Humma*(high grade fever), *Chehre Or Ankhon Me Surkhi*(redness of face and eyes), *Batan Me Bharipan Ka Ehsas*(heaviness in lower abdomen) etc. In case of *Safrawi* there is *Safrawi* Qai(bilious vomiting), *Thisnagi Ki Shiddat* (increased thirst), *Pusht Me Dard Ka Ehsas* (pain in supra pubic region), *Dushwarie Bawl*(dysuria), *Taqtir al -Bawl*(dribbling of urine) *Aur Silsile Bawl* (incontinence of urine), *Sauzishe -i-Bawl* (burning micturition) are more

marked. In case when the matter is *Balgham, Dushwar -i-Bawl* (dysuria), *Pusht Me Dard Ka Ehsas* (pain in supra pubic region), *Sauzish -i-Bawl* (burning micturition) are less marked and in the *Saudaw*i type the features are *Dushwar -i-Bawl* (dysuria), *Dard Or Bojh Me Kami* (less pain and heaviness in suprapubic region), *Salabat and Tamaddud* (solidification and stretching) in suprapubic region [1, 13, 16].

Factors responsible for increased incidence of UTIs in women: Short urethra (4cm), opening of the urethra is in front of the vagina (contaminated heavily with bacteria), sexual inter course, pregnancy and menopause are main factors responsible for increased incidence of UTI in women [17].

Treatment Approaches

Prevention: According to ASOG guidelines: After a bowel movement or after urinating wipe from front to back, Wash the skin around the anus and the genital area, drink plenty of fluids (including water) to flush bacteria out of your urinary system Empty your bladder as soon as you feel the urge or about every 2-3 hours, try to empty your bladder before and after sex, Wear underwear with a cotton crotch, Cranberry juice may decrease the risk of getting a UTI [17].

Antimicrobial therapy: Short course therapy: UTI respond to single dose or short course therapy. A three-day regimen of amoxicillin-clavulanate was found to be significantly less effective than a three-day regimen of ciprofloxacin in treating cystitis in women. However, resistance has increased to various antimicrobials and more than one quarter of E. coli strains causing acute cystitis are resistant to amoxicillin, sulfa drugs and cephalexin and resistance to clotrimazole is now approaching theses levels. Resistance to fluoroquinolones is also rising [2].

Seven day regimen- A longer course of therapy for cystitis should be given to patients with complicating factors that lead to lower success rates and a higher risk of relapse.[2] One of the clinical study conducted in Odisha, India by Dash M *et al*., showed antimicrobial resistance of urinary tract pathogens has increased worldwide [18].

Unani medicine: For centuries plants have been used throughout the world as drugs and remedies for various diseases. These drugs serve as pro type to develop more effective and less toxic medicine. In Unani medicine, medicinal plants such as *Khatmi, Khurfa, Haleela, Tukhme Khayarain, Raal Safed, Parsaivshaan, Khubbazi* are useful in UTI, further they action, phyto-chemical constituents and pharmacological activities are summarized Table 1. In UTI compound drugs like *Jawarish Zarooni, Jawarish i Jalinoos, Sharbat Bazoori Sharbate Zanjabeel, Safoof Mudir, Safoof Bazrulbanj, Majoon kundur, Sharbat unnab* and *Banadiqul Bazoor* [29, 30, 31] are useful in *Waram al -Aalate Bawl* are also useful. Some other formulations mentioned in classical texts are also summarized in table 2. Aforementioned medicinal plant products possess *Dafa'e Taffun* (*antiseptic*), *Musakkhin* (analgesic), *Muhallil* (anti-inflammatory) and *Mudirr-i-Bawl* (diuretice) properties. Scientifically aforementioned herbs are proven for antimicrobial, analgesics, diuretics and anti-inflammatory properties. One of the study conducted by Sharma *et al*., to evaluate antibacterial activity of some medicinal plants against major multi drug resistant UTI pathogens [28].

"In 2008, the Cochrane review supported cranberry potential use only in recurrent UTI prophylaxis for young women. Even for this indication, further clinical trials (double-blinded, randomized, placebo-controlled) displayed no differences between cranberry consumption and controls. The efficacies in other groups of subjects, such as the elderly or paediatric populations with neurogenic bladder, are even more questionable [6, 32].

Table 1: Plant products useful in UTI [19-27]

Names	Actions	Phyto- constituents	Anti-microbial action
Mako - (*Solanum nigrum*)	*Muhallil* (Anti-inflammatory), *Dafae Ta'ffun* (Antisepctic), Antioxidant, Anti fungal	Alkaloid, Glycosides, Solasonine Beta-solanigrine, Solasodine, Alpha-and beta solamargin, Steroidal Sapogenins, Diogenins, Tigogenin.	Bacteria (M. Varians, Micrococcus luteus, S. aureus S.typhi, P. maltocida, E. Coli). Fungi (A.niger, A. flavus, A. fumigates).
Kasni (*Cichorium intybus*)	*Muhallil al-Waram* (Anti-inflammatory), Anti microbial, Anti fungal	Alkaloid, Flavonoids, Sapogenins, Steroids, Sterols.	S. Aureus, E. Coli, A. niger, A. flavus
Brinjasif (*Achillea millefolum*)	*Muhallil al-Waram* (Anti-inflammatory), Anti microbial.	Alkaloid, Flavonoids, Apigenin, Salicylic acid, Chamazulene.	Candida albicans, S. Aureus, E. Coli, Streptococcus mutans.
Katan (*Linum usitatissimum*)	*Muhallil al-Waram* (Anti-inflammatory), *Dafae Ta'ffun* (Antisepctic), Antioxidant, Antimicrobial.	Palmitic, Stearic, Oleic, Linoleic acids, along with Amino acids, and Sugars, Cyanogenic Glycosides mainly Linustatin, Neolinustatin and linamarin, Lignans	S. Aureus, E. coli, Streptococcus Agalactiae, Aspergillus.
Khiyar (*Cucumis sativus*)	*Mudir-i-Bawl* (Diuretics), Antibacterial, Hypoglycemic, Hypolipidemic activity.	Rutin, Glycosides including Cucurbitaside B&C, Ferredoxin, Alpha-spinasteral, Proteolytic enzyme, ascorbic acid oxidizer and Succinic & malic dehydrogenase.	E. coli, S. typhi, E. feacalis, B. cereus.
Khubbazi (*Malva sylvestris*)-	*Muhallil* (Anti-inflammatory), *Dafae Ta'ffun* (Antisepctic), Antioxidant, Anti microbial	Sulphated flavonol glycosides, Mucilage and Tannins, Malvin(an anthocyanin), Malvin diglucoside, Carotene and ascorbic acid.	E. coli, E. feacalis, S. typhi, S. aureus, Streptococcus agalactiae.
Haleela (*Terminalia chebula*)	*Muhallil* (Anti-inflammatory), *Dafae Ta'ffun* (Antisepctic), Antioxidant, Anti- microbial	Gallic, Tricontanoic & Palmitic acids, Beta-sitosterol, Daucosterol, Tri-ethyl ester, Terchebulin along with punicalagin, Chebupentol, Arjumgenin, Phloroglucinol & Pyrogallol along	S. Aureus, E. coli, S. typhi, C. Perfringens, Helicobacter pylori, Klebsiella.

		with Ferulic, Vanillic & Caffeic acid.	
Khurfa (*Portulaca oleracea*)	*Muhallil* (Anti-inflammatory), *Dafae Ta'ffun* (Antisepctic), Antioxidant, Anti microbial, *Mudir-i-Bawl* (Diuretics).	Potassium salt, alkaloids includes I-nor-adrenaline, Dopamine, Catechol & Flavanoids includesGenistin, Querecetin	S. Aureus, E. coli, Neisseria gonorrhoea, Pseudomonas aeruginosa, Candida albicans
Kaddu (*Cucurbita maxima*)	*Mudir-i-Bawl* (Diuretics), *Muhallil* (Anti-inflammatory), *Dafae Ta'ffun* (Antisepctic), Antioxidant, Anti microbial.	Vitamin A & B, Calcium, Iron, Zinc, Cucurbitacin, Linonelic acid, Sterol glycosides & Sterol fatty acid esters & Triterpenoids.	S. Aureus, E. coli, K. Pneumonia, Pseudomonas aeruginosa.

Table 2: Some Unani formulations

1. Maghze Tukhme Khayarain (*Cucumis sativus* Linn)	17.5g
Maghze Tukhme Kaddu (*Cucurbita maxima*)	17.5g
Khurfa (*Portulaca oleracea* Linn)	14g
Tukhme Khubbazi (*Malva sylvestris*)	10.5g
Parsiaavashaan (*Adiantum capillus* Linn)	10.5g
The drugs are pounded, sieved and mixed well to make a homogenous sufuf. Orally, 3.5g powder with *sharbate banafsha* 25ml is advised twice daily for eight days [29].	
2. Maghze Tukhme Khayarain (*Cucumis sativus* Linn) *Maghze Tukhme Kaddu* *Tukhme Khitami* *Tukhme Bartang* *Isapghol* (each 28 gm) These drugs except *Isapghol* are pounded, and sieved mixed well to make a homogenous sufuf, then add *Isapghol* to form a *Binaduq,* 5 gm twice daily is administrated orally for 14 days.	
3. Tukhme Katan (Linium seeds)	9g
Nishasta	4.5g
Daily nine gram of sufuf is advised orally with water for 7days [11].	
4. Pour some *Namake Indrani* over the *Joshanda* (decoction) of *Shakhein Angoor* (stem of grapes) andadminister for 9 days [16].	
5. The douching of butter and milk cream is beneficial in case of *Waram al-Mathana* [1].	
6. Barely water is useful in *Waram al-Mathana* (cystits) [11].	
7. Camel milk is very useful in *Waram al-Aalate Bawl* [11].	
8. *Maul jaban* reduces the *Hurqat i-Bawl* [1]	

Table 3: Clinical Trials of cranberry products for UTI [33-38].

Study	n	Study design	Treatment	Results
Barbosa-cesnik 2010	319 young women with previous UTIs	Double blind, randomized, placebo-controlled	8 oz. of 27% cranberry juice	Recurrence rate of UTIs were 19.3% for cranberry treatment and 14.6% for placebo.
McMurdo *et al* 2009	137 women aged >45 years with recurrent UTIs	Double blind, randomized, placebo-controlled	500 mg of cranberry extract or 100 mg of trimethoprim	25 Um group TIs in the cranberry group and 14 in the trimethoprim group.
Ferrara *et al* 2009	84 girls with recurrent UTIs	Randomized controlled	Cranberry-lignonberry juice 50ml/day(n=27); Lactobacillus GG 100ml 5days/month(n=27)	UTIs in 18.5% of patients in the first group versus 42.3% in the second group.
Wing *et al*, 2008	188 pregnant women; gestation of <16weeks	Double- blind, randomized placebo-controlled	250 mg of cranberry juice 3 times/day (group A) or 240 mg once daily (group B) or placebo (group C).	Withdrawal rate of 38.8% (A 50.7%; B 39.7%; C 55.5%)
Stothers,2002	150 women with recurrent UTIs	Double blind, randomized, placebo-controlled	250ml pure cranberry juice or conc. Cranberry tablets	UTIs were 72% (placebo), 30% (juice; $p<0.05$) and 39% (tablets; $p<0.05$).
Walker *et al*., 1997	19 young women with recurrent UTIs	Double-blind, randomized, placebo-controlled, crossover trail	400mg of cranberry capsules	Withdrawl rate of 47.4%. UTI incidences were 2.4/subject-year-cranberry and 6.0/subject-year-placebo

Conclusion

In the present era, documentation and preservation of the traditional knowledge is the great challenge. Hence, literary appraisal of classical sources is the need of the hour. The classical Unani are enriched with etiology, clinical features and management of *Waram al-Aalate Bawl* (UTI). Further, pharmacological studies of aforementioned medicinal plant products prove that they are efficacious in UTI and correlates with contemporary knowledge. Further, randomized controlled double-blind studies are recommended to prove the efficacy of these medicinal plant products.

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