

Novel Phytomedicine Approaches for the Management of Urinary Tract Infections: A Review of Plant-Derived Antimicrobial Agents and Clinical Applications

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Abstract

Urinary tract infection (UTI) is one of the prime diseases affecting urinary tract, which is principally caused by bacteria. The management of UTI is mainly done by antibiotics. Continued allopathic treatment with various antibiotics may cause side effects, furthermore it is also known that bacteria causing infection can develop resistance to the existing antibiotics that have been prescribed, if the medication is used for a long time. Considering this situation, it is relevant to search for an alternative management, which is effective, safe and economical. Various medicinal plants and herbs are described in Ayurveda for the treatment of UTI. As medicinal plants have a long history and are proven to be very effective in preventing and treating infections, present investigation was taken up using a medicinal plant *Inula racemosa* Hook. F. for the management of UTIs. The present study investigated the antimicrobial potential of medicinal plants against two most resistant gram negative urinary tract pathogens; *Pseudomonas aeruginosa* and *Enterococcus faecalis*. Methanolic as well as chloroform crude plant extracts were examined for their antimicrobial activity and results showed high antimicrobial potential. Anti-bacterial response was observed in dose-dependent manner in both the extracts used i.e., with increasing dosage antibacterial response increased. This study indicates that this crude plant extracts can be a good source of antimicrobial compounds and can lead to the development of novel broad spectrum antibiotics in future.

Keywords:

Urinary tract infection, Medicinal plants, *Inula racemosa* Hook. F., Antimicrobial activity

Introduction

A urinary tract infection is an infection that begins in the urinary system. It is the second most common after respiratory infection accounting for nearly 25% of all infections. UTI's results in 3.6 million hospital visit each year and greater than 100,000 hospital admissions annually (Khannal, 2014). UTIs affect both the genders but women are more likely to be vulnerable by it and up to 50% of women suffer from UTIs at some point of their life. Women of the reproductive age group are the most susceptible, may be due to their short urethra, and certain behavioural factor which include delay in micturition, sexual activity and the use of contraceptives which promotes colonization of the peri-urethral area with coliform bacteria. The prevalence of UTI in women is about 3% at the age of 20, increasingly by about 1% in each subsequent decade (Pushpalatha, 2008). In males, UTI is uncommon (in comparison to females), except in the first year of life and in men over 60, in whom urinary tract obstruction due to prostatic hypertrophy may occur. UTI causes morbidity and in a small minority of cases, renal damage and chronic renal failure (Anderson; 1983; Litza and Brill, 2010).

Urinary tract infection is a collective term that describes any infection or presence of microbial pathogen in the urinary tract namely the kidneys, ureters, bladder and urethra. The urinary tract infection can be divided into upper urinary tract infection encompassing kidneys and ureters and lower urinary tract infecting bladder and urethra (Tan and Chlebickci, 2016).

UTI's can be classified as uncomplicated or complicated (based on the factor that triggers the infection) and primary or recurrent (depending on the nature of occurrence). Uncomplicated UTIs typically affect individuals who are otherwise healthy and have no structural or neurological urinary tract abnormalities (Vasudevan, 2014; Adhikari and Dhakal, 2015). Complicated UTIs are associated with factors that compromise the urinary tract or host defence, including urinary obstruction, urinary retention caused by neurological disease, immunosuppression, renal failure, renal transplantation, pregnancy and the presence of foreign bodies such as calculi, indwelling catheters or other

drainage devices (Levison and Kaye ,2013; Lichtenberger and Hooton, 2008). Recurrent UTI is a common phenomenon that is observed among women who have experienced uncomplicated UTIs and they are classified as reinfection and relapse (Vasudevan, 2014).

Causative agent of UTIs

UTIs mostly caused by both Gram-negative and Gram-positive bacteria, as well as by certain fungi. The most common agent of UTIs (about 80%) is uropathogenic *Escherichia coli*, bacterial strain that usually inhabit the colon. However, many other bacteria can also cause an infection for example, *Enterococcus*, *Klebsiella*, *Pseudomonas*, *Enterobacter*, *Proteus*, *Staphylococcus*, *Mycoplasma*, *Chlamydia*, *Serratia* and *Neisseria* spp. but are far less frequent than *E. coli*. In addition, fungi (*Candidia* and *Cryptococcus* spp.) and some parasites (*Trichomonas*, *Schistosoma*) also may cause UTIs (Cheesbrough, 1998; Kasper, 2005; Strohl, 2007).

Symptoms of UTI

The common symptoms of UTIs are frequent urge to urinate, inflammations in both men and women, painful feeling in the area of the bladder or urethra during urination, milky, cloudy or reddish urine, foul-smelling urine and fever , which means that the infection has reached the kidneys (Cattell, 1996).

A lot of researches were carried out for the prevention, treatment and management of UTIs. Patients suffering from UTI are commonly treated with antibiotics, even though they are useful, they involve considerable amount of risk. Use of antibiotics can result in long-term alteration of the normal micro-biota of the urinary and gastrointestinal tract and in the development of multi-drug resistant uropathogens (Kostakioti, 2012). It is also recognized that using antibiotics frequently may contribute to recurring UTIs and increase dependency on antibiotic use which may further weaken the immune system. Importantly, the “golden era” of antibiotics is also waning with the increasing use of its (Bose, 2014).Hence, there is a need of rationally designed and alternative line of management which is both effective and safe. After the careful review of the literature available no reference was found in which *Inula racemosa* Hook. F. is used in any form for the treatment and management of UTIs. In this regard, the study was undertaken to evaluate the effect of *Inula racemosa* Hook. F. in the management of urinary tract infection (Boon, 2006).

Herbal therapy in Urinary tract infection

Use of herbal plants for the prevention, treatment and management is as old as the disease is. Initially ojhas, village healers and Ayurvedic doctors were using either single or mixture of herbal plants extracts or paste for the treatment of UTIs. The most common was medicinal waist-bath, washing with medicinal water and ointments. Herbs are generally a safe way to strengthen and tone the body’s systems. Herbal remedies may relieve urinary tract infections by combating the bacteria, decreasing irritation and healing urinary tract tissues. Some herbs also help to prevent future occurrences. Natural remedies can provide effective alternative prescription medications and their side effects (Cunningham, 2003; Foster and Duke, 2014).

Inula racemosa Hook. F.:

Inula racemosa Hook. F. is a tropical herb belonging to Asteraceae family useful to pacify Kapha (water), Vata (air) and Doshas (humors) in body. It is widely used in Ayurveda because of its beneficial therapeutic uses: like Aruchi, Adhyaman (gas), Hikka (hiccups), Jvara (fever), Kasa (Cough), Svasa (asthma), Parsvasula (chest pain), Sosh (edema), Ardit (facial paralysis) and Pandu (low haemoglobin level) (Jadavji and Acharya, 2007).

Objective of the study:

To evaluate the effect of *Inula racemosa* Hook. F. extracts in the management of urinary tract infections.

Material and methods

Roots of plant *I. racemosa* were shade dried and extracted with respective solvents of Methanol and Chloroform.

- 1. Preparation of Extract:** The crude extract was obtained by macerating 30 g of dried plant powder in 95% in respective solvents and kept on a rotary shaker for 24 h. The extract was then filtered, centrifuged at 5000 g for 15 min and was dried under reduced pressure. The extract was stored at 4°C in airtight bottles.
- 2. Isolation of microbial strains:** Microorganisms used in this study was *Pseudomonas aeruginosa* and *Enterococcus faecalis*. For isolation of these pathogenic microorganisms, mid-stream urine specimens were collected from patients of urinary tract infection (UTI) of Dr. B. Lal Clinical Laboratory Pvt. Ltd., Jaipur. Samples were taken before any antibiotic administration. Antimicrobial susceptibility patterns of the isolates

were determined using CLSI 2013 guidelines by agar well diffusion method and most resistance strains were selected.

- Diffusion method:** The microbial growth inhibitory potential of the plant extracts was determined by using agar well diffusion method (Hagerman, 1988). One microorganism of each strain was selected to determine the antimicrobial activity of plant extracts. Inocula were prepared by mixing few microbial colonies in sterile nutrient broth and comparing the turbidity with the standard 0.5 McFarland solution (McFarland, 1907) which is equivalent to 10^6 – 10^8 CFU/ml. 100 μ l of standard suspension of all selected isolate was inoculated by spreading on the surface of Mueller Hinton agar (Oxoid). Plants extracts were mixed with diluted concentrations (30 μ l, 60 μ l and 90 μ l) and poured into inoculated plates by making wells in it. Plates were incubated at 37°C overnight for determination of IZ.

Result and discussion

Different bacterial species were isolated from mid-stream urine specimens collected from patients of UTI of Dr. B. Lal Clinical Laboratory Pvt. Ltd., Jaipur. Antimicrobial susceptibility patterns of the isolates were determined using CLSI 2013 guidelines by agar well diffusion method and most resistance strains were selected. The microbial growth inhibitory potential of the plant extracts was determined by using agar well diffusion method. Plants extracts were mixed with diluted and poured into inoculated plates by making wells in it. Plates were incubated at 37°C overnight for determination of IZ. The present study investigated the antimicrobial potential of medicinal plants against common gram negative urinary tract pathogens. Most resistant strains *Pseudomonas aeruginosa* and *Enterococcus faecalis* were selected for the present investigation. Methanolic as well as chloroform crude plant extracts were examined for their antimicrobial activity against the two selected pathogenic microorganisms, and showed high antimicrobial potential (**Table-1 and 2, Figure-1,2,3 and 4**). Anti-bacterial response was observed in dose-dependent manner in both the extracts used i.e., with increasing dosage antibacterial response increased.

Table 1: Anti-bacterial activities of various extracts of *I. racemosa* against multi drug resistant pathogen (*Pseudomonas aeruginosa*) isolated from UTI patients

S. No.	Plant extracts (in μ l)	Zone of Inhibition (IZ in mm) from roots	
		Chloroform extract	Methanolic extract
1.	30	8	9
2.	60	10	11
3.	90	13	16

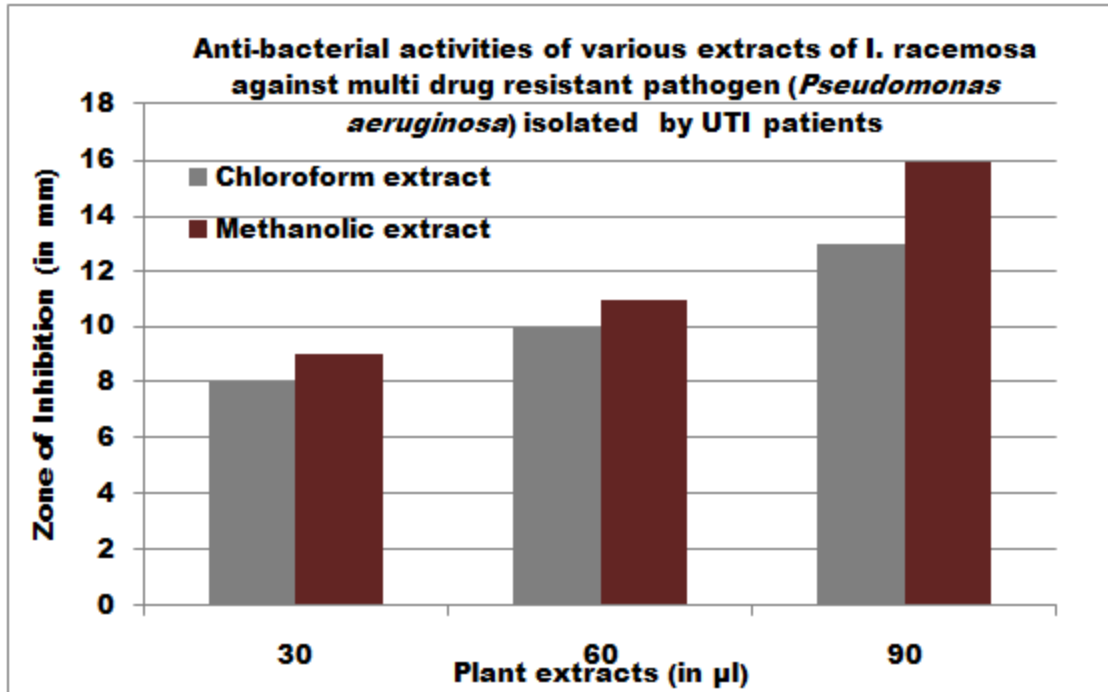
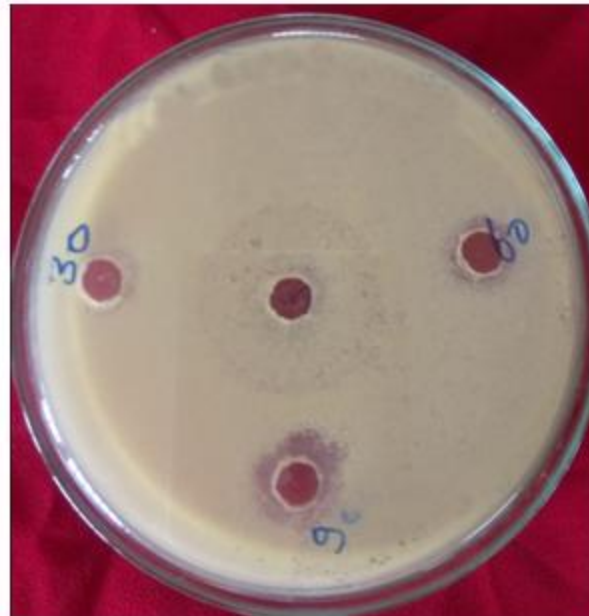
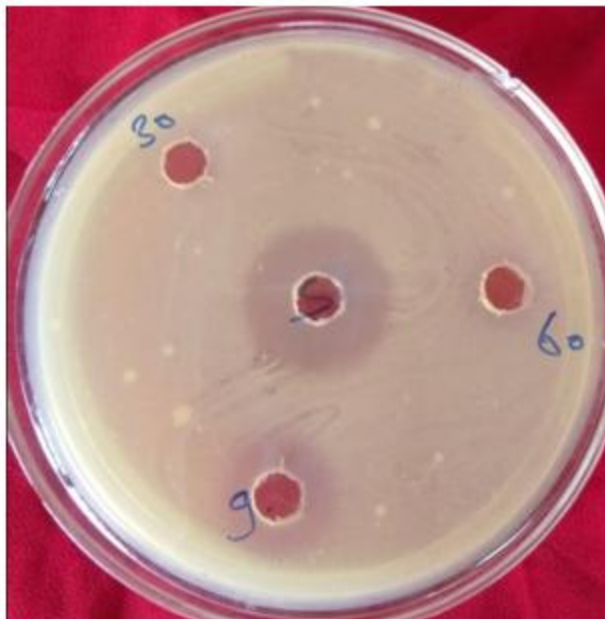


Figure-1 Graph showing anti-bacterial activities of various extracts of *I. racemosa* against multi drug resistant pathogen (*Pseudomonas aeruginosa*) isolated from UTI patients



Chloroform extract



Methanol extract

Figure-2 Disk diffusion plates showing anti-bacterial activities of various extracts of *I. racemosa* against multi drug resistant pathogen (*Pseudomonas aeruginosa*) isolated from UTI patients.

Table 2: Anti-bacterial activities of various extracts of *I. racemosa* against multi drug resistant pathogen (*Enterococcus faecalis*) isolated from UTI patients

S. No.	Plant extracts (in μ l)	Zone of Inhibition (IZ in mm) from roots	
		Chloroform extract	Methanolic extract
1	30	0	11
2	60	8	16
3	90	11	13

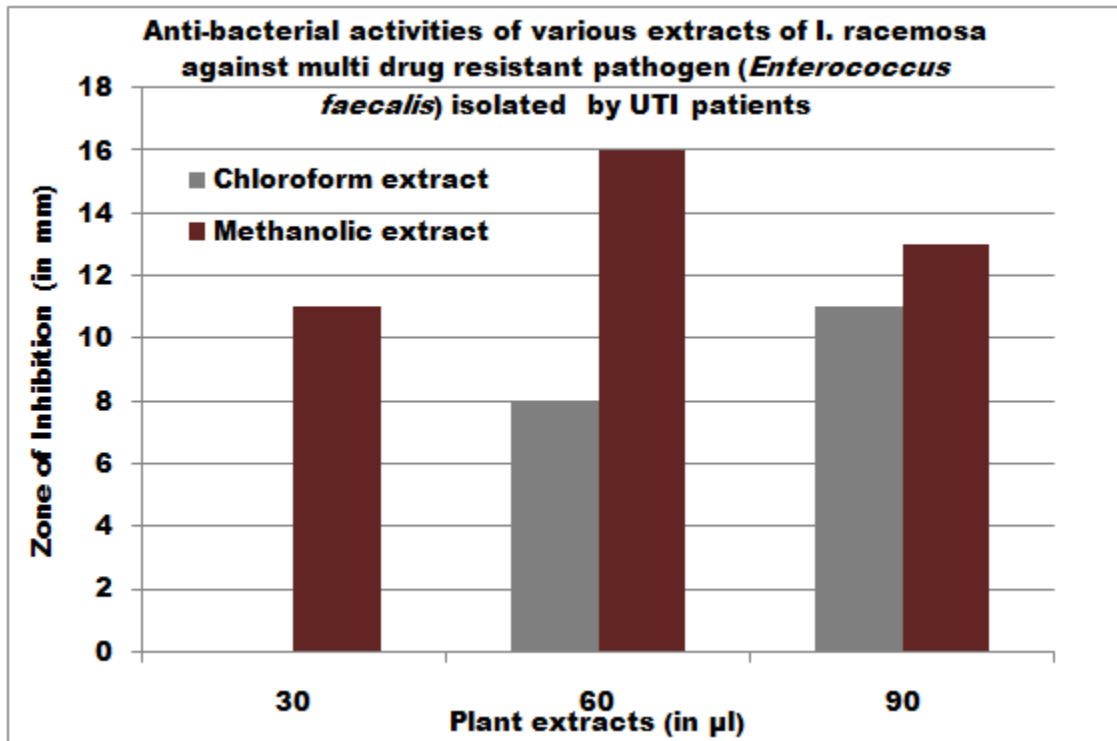
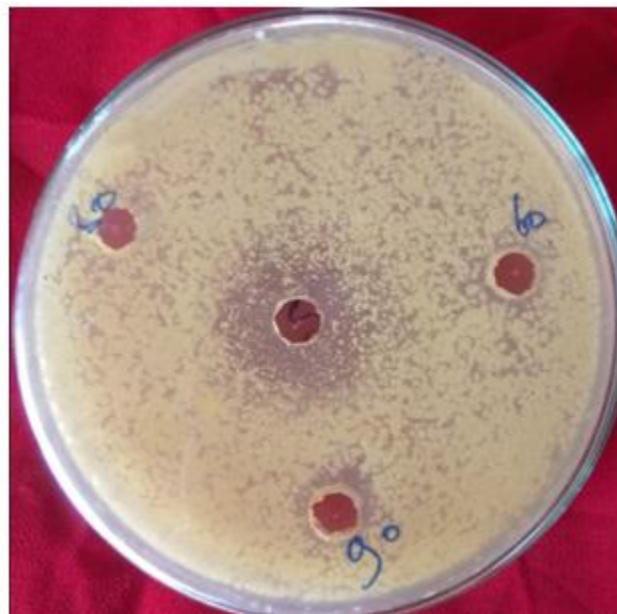
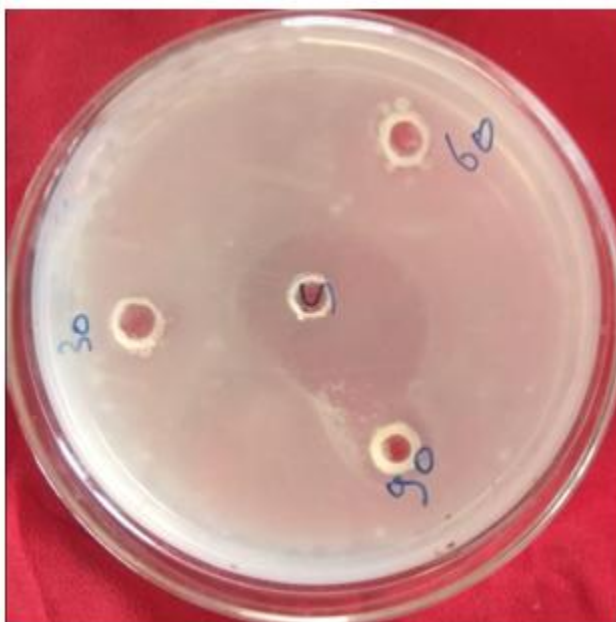


Figure-3 Graph showing anti-bacterial activities of various extracts of *I. racemosa* against multi drug resistant pathogen (*Enterococcus faecalis*) isolated from UTI patients



Chloroform extract



Methanol extract

Figure-4 Disk diffusion plates showing anti-bacterial activities of various extracts of *I. racemosa* against multi drug resistant pathogen (*Enterococcus faecalis*) isolated from UTI patients

After determining the antimicrobial activity of plant extracts. This study indicates that this crude plant extracts can be a good source of antimicrobial compounds and can lead to the development of novel broad spectrum antibiotics in future.

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