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Review Article

Recent Progress in Phytochemical-Based Interventions for Catheter-Associated Urinary Tract Infections

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ABSTRACT

UTIs are among the most common infections, and their frequent recurrent episodes, which are mostly caused by uropathogenic Escherichia coli, are making treatment more difficult. Although long-term antibiotic therapy is an effective treatment for recurrent UTIs, one of its drawbacks is the emergence of pathogenic strains resistant to the vast majority of antibiotics. Medicinal plants have great potential in the fight against catheter-associated urinary tract infections (CAUTIs) because of their antimicrobial, anti-inflammatory, and anti-adhesive qualities. Flavonoids, alkaloids, and tannins are among the many phytochemicals and plant extracts that have shown inhibitory effects against uropathogens, including Pseudomonas aeruginosa, Klebsiella pneumoniae, and Escherichia coli. These bioactive substances can stop the formation of biofilms and bacterial adhesion on catheter surfaces, two critical stages in the pathophysiology of CAUTI. This review assesses the effectiveness of different plant-derived compounds in treating CAUTIs and their mechanisms of action, as well as the possibility of creating plant-based coatings for catheters or adjuvant therapies. Given the increasing occurrence of CAUTIs, plant-based interventions may provide a practical and efficient means of prevention and treatment.

INTRODUCTION

The ancient Greek word kathiénai, which literally translates to "to thrust into" or "to send down," is where the word catheter originates. Prior to the Foley catheter's widespread use in the 1930s, male urinary retention was the primary reason for catheterization. The early catheters were usually rigid and they were designed—to the extent that they were designed at all—for intermittent catheterization. Urinary incontinence was not a medical emergency: it was left as a personal embarrassment for men and women alike, who generally adopted their own idiosyncratic methods of coping with the disability. However, the

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indwelling Foley catheter opened up a new era in the treatment of urinary retention by making both short-term and long-term catheterization possible for both males and females.(1) A catheterized patient's unusually high urine bacterial count has been described as a catheter-associated urinary tract infection (CAUTI). CAUTI happens when bacteria or other microorganisms enter the urinary tract through a urinary catheter and cause an infection. Increased morbidity, mortality, length of stay, and medical expenses have all been linked to CAUTIs. In a nutshell, it falls into two categories: CAUTI with urinary tract-related symptoms and CA-ASB (catheter-associated asymptomatic bacteriuria) without urinary tract-related expression or declaration. Up to 40% of hospital-acquired infections are device-acquired urinary tract infections, making them one of the most common healthcare-acquired illnesses.

Risk factors

Gender

Malnutrition and renal insufficiency are risk factors, and female patients and those with other active sites of infection are far more vulnerable than male patients. Both sexes are susceptible to infection. Overall, though, male infections were more prevalent than female infections. The study found evidence that refuted the idea that women's shorter urethras made them more prone to illness.

Age-related

Given that older hospital patients already have a higher number of underlying chronic conditions. In the past, though, it was not regarded as a significant risk factor. It is currently thought to be one of the risk factors for hospital-acquired UTIs, particularly in people over 70.

Period or Duration of Catheterization

Having a ureteral stent, using the catheter to measure urine output, and putting the catheter outside the operating room after hospital admission all raise the risk. The most important risk factor that can be changed, according to every study, is prolonged catheterization for more than six days; by the 30th day following catheterization, infection is practically common.

In diabetes mellitus patients

Due to severe neuropathy, impaired bladder emptying, and glucosuria, which encourages bacterial growth and compromises immune response, people with diabetes mellitus are more susceptible to catheter-associated urinary tract infections (CAUTIs). Immobility, fecal incontinence, and poor hygiene are additional risk factors. Patients who are immobilized are particularly at risk because prolonged catheter use and stagnant urine flow raise the risk of infection. The risk of CAUTIs is further increased by caregiver-related problems, such as incorrect catheter insertion and maintenance and the use of latex catheters.(2)

Pathogenesis of Infection

The primary cause of bacteriuria is the development of biofilms along the catheter surface. A complex organic material called biofilm is made up of microorganisms that grow in colonies and produce an extracellular mucopolysaccharide substance. This material contains elements found in urine, such as calcium and magnesium ions and Tamm-Horsfall protein. When organisms stick to a conditioning film of host proteins that develops along the catheter surface, biofilm formation starts as soon as the catheter is inserted. The catheter's exterior and interior surfaces are both affected. After colonizing the drainage bag, bacteria typically ascend the drainage tubing or come from the

periurethral region. Just around 5% of CA-ASB episodes occur after periurethral organisms are introduced into the bladder during catheter insertion.(3) The environment in which organisms grow in the biofilm is one in which they are comparatively shielded from host defenses and antibiotics. After an indwelling catheter is inserted, the first episode of bacteriuria is typically associated with a single species. Polymicrobial bacteriuria becomes the norm if the catheter stays in place and a mature biofilm forms. Three to five organisms are typically isolated from patients who have long-term indwelling catheters (4). As the catheter stays in place, the organisms in the biofilm continue to change, making the microbiology of the biofilm on an indwelling catheter dynamic. At a rate of roughly 3–7% per day, patients continue to pick up new organisms.(5)

Microbiology

Escherichia coli is the most prevalent pathogen. *Pseudomonas aeruginosa*, coagulase-negative *Staphylococcus, Candida spp.,* other non-fermenters, and other *Enterobacteriaceae* are also commonly isolated (6). Organisms that are resistant to antibiotics are widespread. In both acute and long-term care facilities, the urine of patients with indwelling catheters is the primary location for the isolation of resistant gram-negative organisms, such as CRE and Enterobacteriaceae that produce extended spectrum beta-lactamases (ESBL)(7). In acute care hospitals, *E. coli* is typically the most common species isolated from bacteremic CAUTI patients. For patients who have long-term indwelling catheters, Proteus mirabilis is a particularly significant organism. This species is uncommon in patients undergoing short-term catheterization because it is rarely isolated after initial colonization of the catheterized urinary tract (8). *Proteus mirabilis* is more likely to be present the longer a catheter is in place. About 40% of urine samples taken from patients who have long-term indwelling catheters contain this organism (9). Compared to other bacterial strains, *P. mirabilis* produces a greater amount of biofilm, and these strains also have a tendency to persist for longer. *P. aeruginosa, Morganella morganii, Klebsiella pneumoniae*, other Proteus species, certain *Providencia* species, and strains of *S.aureus* and coagulase-negative *staphylococci* are among the other species that produce urease. Many of these species, such as *M. morganii, K. pneumoniae*, and *P. aeruginosa*, produce urease that does not produce an alkaline urine, which is why these strains are rarely linked to significant catheter encrustation.(10)

Alternative treatments for UTI

UTIs are one of the most significant health issues at the present time due to their high frequency in community and hospitals and the economic burden they carry to both patient and government. Around the world, antibiotics such as trimethoprim, sulfamethoxazole, quinolone, and others are used as the first line of treatment. However, microbial resistance, a number of potentially fatal side effects, the need for frequent high dosages, the high expense, and the lack of effectiveness of these antibiotics encouraged researchers to look into natural treatments for urinary tract infections. Herbal remedies have a high level of effectiveness in fighting bacterial resistance, are readily available, and have few or no negative side effects.(11) The use of medicinal plants has grown in popularity and reliability because of their low or nonexistent side effects, affordability, accessibility, lack of bacterial resistance, and ability to treat urinary tract infections in patients.(12) The precise mechanism by which herbal medicines treat UTIs has not been

thoroughly understood, despite the paucity of research.(13) Research on medicinal plants, including their efficacy in treating and preventing UTIs, their mechanisms of action, and the active ingredients that give them their antibacterial qualities, has significantly increased since the turn of the twenty-first century. There are few reports on the precise action of the phytoconstituents against uropathogens, despite the fact that numerous researchers have reported the anti-uropathogenic and bactericidal activity of numerous plant extracts. These reports only include preliminary antibacterial studies using various fundamental techniques, such as disk diffusion, agar well diffusion, or minimum inhibitory concentration (MIC) of the crude plant extracts. The present review discusses about some of the medicinal plants which can be used against UTI and also some evidences to support that plant extracts can be used to coat urinary catheters to treat hospital acquired infections(14)

Plants used in treatment of UTI

***1. Arctostaphylos uva-ursi* - Bearberry**

The bearberry, or *Arctostaphylos uva-ursi*, is a low-growing evergreen shrub that belongs to the heath family, or Ericaceae. Other noteworthy plants in this family include bilberries, blueberries, and cranberries. Native to North America, as well as some parts of Europe and Asia, bearberry grows well in acidic, well-drained soils found in rocky, forest, and tundra environments.(15) Arbutin, Phenoglycosides, flavonoids, hydroxycinnamic acids, lignans, saponins, iridoids, polysaccharides, and essential oils are all found in bearberries. Keller used cerimetric titration to ascertain the total amount of hydroquinone present in bearberry leaves. Simple phenols, galloylglycosides, catechins, and flavonoids were among the compounds discovered by Olennikov and Chekhirova when they examined phenolic complexes in various *Arctostaphylos uva-ursi* parts. (16) Bearberry extracts have genitourinary system effects, which are usually manifested as nephrolytic, diuretic, and antibacterial properties and for UTIs. Arbutin is the main component to fight against UTI. After being consumed, arbutin is converted into the antimicrobial hydroquinone. Hydroquinone relieves infections like cystitis and urethritis by preventing the growth of dangerous bacteria in the urinary tract. In the form of teas, capsules, or extracts, bearberry is commonly used as a herbal remedy to treat UTIs, especially in mild cases or as a prophylactic.(17) Bearberry leaf extract's antimicrobial activity was investigated in relation to clinical isolates of urogenital pathogens that cause UTIs, including *E.coli, K.pneumoniae, P.mirabilis*, and *Enterococcus faecalis*. The active ingredients in the bearberry leaf extract, such as tannins, flavonoids, and arbutin, contributed to its strong antimicrobial activity, which was especially effective against *E.coli* and *K.pneumoniae*. Bacterial cell walls are thought to be disrupted, and bacterial growth and adhesion are inhibited as part of the antimicrobial action. Bearberry leaf extract may be a promising natural treatment for UTIs, as per the study, but more clinical research is needed to determine the right dosages and confirm its effectiveness. The zone of inhibition against *S.Enterica, S.aureus, K.Pneumonia, E.coli, P.aeruginosa* were 16.5, 30.2, 15.7, 20 and 18.6 respectively.(18)

2. Nigella sativa

Nigella sativa, also known as black seed or black cumin belongs to family Ranunculaceae (buttercup family). This plant is valued for seeds which has been used as antioxidant, antimicrobial and anti-inflammatory. So, these can be used against urinary tract pathogens. Broad-Spectrum antibacterial Activity: Both Gram-positive and Gram-negative strains of bacteria have been

shown to be vulnerable to the effects of Nigella sativa extracts. The extracts have shown efficacy against multidrug-resistant strains, including *E.coli* that produces prolonged -spectrum β-lactamase (ESBL) and methicillin-resistant *S. aureus* (MRSA).(19) Antimicrobial activities are shown by bioactive components such as nigellimine, nigellidine, and thymoquinone.It has been determined that thymoquinone, in particular, inhibits the growth of bacteria and the formation of biofilms.(20) The strength of the antimicrobial activity is affected by the extraction technique. For example, when compared to other extraction techniques, petroleum ether extracts have demonstrated better antibacterial properties. *Nigella sativa* extracts have shown the ability to inhibit biofilm formation, which is crucial since biofilms contribute to the persistence and resistance of infections, especially in catheter-associated UTIs.(21)

3. *Alhagi maurorum*

Alhagi maurorum, commonly known as camelthorn, belongs to the botanical family Fabaceae. It is a traditional plant found in middle east, including Iran. The Fabaceae family is one of the largest plant families and includes many agriculturally and medicinally important species. *Alhagi maurorum* is traditionally used in herbal medicine for its anti-inflammatory, diuretic, and antibacterial properties.(22) Numerous studies have demonstrated the therapeutic benefits and widespread use of *A. maurorum* in the treatment of gastrointestinal discomfort, liver problems, bilharziasis, and rheumatic pains. Additionally, *A. maurorum* functions as a potent diuretic and antilithiatic and may help treat UTIs.(23) The plant contains constituents like fatty acids, flavonoids, coumarins, sterols, vitamins, and alkaloids, drimenol, neophytadiene, and various hydrocarbons and terpenoids.(24) These by diuretic action stimulates urines production and flush out bacteria and toxins from the urinary tract, reducing bacterial colonization. It contains flavonoids and phenolic compounds that decrease inflammation in the urinary tract. This helps reduce pain, burning sensation, and irritation caused by UTIs. The effects of *Alhagi maurorum* extract (AME) on *P. mirabilis*, a common pathogen that causes UTIs, were examined in a study that was published in Scientific Reports. The study showed that by downregulating genes linked to virulence and quorum sensing, AME decreased the formation of biofilms. Furthermore, AME reduced calcium buildup on catheters and bacterial adherence to bladder cells, indicating that it may be useful in preventing catheter-associated UTIs. (25) *E. coli*, is a common pathogen that causes urinary tract infections, and *Alhagi maurorum* has shown antimicrobial activity against it. Research indicates that its extracts, particularly those that contain ethanol or ethyl acetate, inhibit the growth of *E. coli* in a way that is dependent on concentration. Bioactive substances such as alkaloids, tannins, and flavonoids are responsible for this effect. These substances break down the cell walls of bacteria and prevent vital biological functions.(26) A nanoemulsion was prepared by ionotropic gelation method with chitosan as nanocarrier. It exhibited enhanced antibacterial activity against *E.coli* and showed biofilm inhibition.(27) The MIC for *E. coli* was determined to be 1.75 mg/mL, indicating potent antibacterial properties.

4. *Tamarix ericoides Rottl Bark*

The tamarisk species *Tamarix ericoides Rottl*., also referred to as the Heather Tamarisk or Heather-leaved Tamarisk, is indigenous to parts of Asia and the Middle East. It is a member of the Tamaricaceae family of plants. Often found in saline and dry areas, this family of shrubs and

small trees is also referred to as the tamarisk or salt cedar family. This family's members are renowned for their resistance to high salinity and drought. (28) The GC-MS analysis identified 8 different phytochemicals involving diethyl phthalate, n-hexadecanoic acid, and 9-octadecenoic acid, known for their antimicrobial properties. With a minimum inhibitory concentration (MIC) of 1 mg/mL, the extract demonstrated inhibitory effects against *E. coli*. At concentrations of 1x, 2x, and 3x MIC, the extract treatment decreased mature *E. coli* biofilms by 81%, 85%, and 89%, respectively. Biofilm disruption and decreased bacterial adhesion on catheter surfaces were confirmed by Confocal Laser Scanning Microscopy (CLSM) and Scanning Electron Microscopy (SEM). The extract's safety for possible therapeutic uses was demonstrated by the fact that it was not toxic to healthy cells.(29) Leaf extract from *Tamarix ericoides* has demonstrated efficacy against a range of bacterial pathogens, including strains of *E.coli* that are resistant to multiple drugs and are frequently responsible for urinary tract infections. Extracts from the plant have shown promise in preventing biofilm formation, an important step in avoiding urinary tract infections (CAUTIs) linked to catheter use. Research has demonstrated that *T.ericoides* can lessen bacterial adherence on surfaces, including catheter materials, thereby reducing the risk of infection.(30) Nanoparticles of this plant were prepared that could stop the formation of biofilms. Rhizome extracts of Rhodiola rosea were used in a simple and environmentally friendly process; no extra chemicals were needed for capping, stabilizing, or reducing the nanoparticles. The resulting nanoparticles were stable, crystalline, and measured approximately 13–17 nm for gold (AuNPs) and 15–30 nm for silver (AgNPs). Their concentrations were found to be 3.3 mg/ml for AuNPs and 5.3 mg/ml for AgNPs. According to FTIR, the nanoparticles' surface contained flavonoids, terpenes, and phenols, which most likely helped with their formation and stabilization. The ability of silver nanoparticles to combat biofilms produced by *Escherichia coli* and *Pseudomonas aeruginosa* was evaluated. For *P. aeruginosa* and *E. coli*, the AgNPs showed minimum inhibitory concentrations (MICs) of 50 µg/ml and 100 µg/ml, respectively, with corresponding minimum bactericidal concentrations (MBCs) of 100 µg/ml and 200 µg/ml. The use of *R. rosea* rhizome extract as a promising natural source for the synthesis of environmentally friendly nanoparticles with strong anti-biofilm properties is supported by these findings.(31)

5. *Ampelopsis grossedentata*

The plant *Ampelopsis grossedentata* (vine tea) is the primary source of Dihydromyricetin (DHM), also referred to as ampelopsin, a naturally occurring flavonoid compound. It is recognized for its potent antioxidant, anti-inflammatory, and liver-protective qualities and is a member of the flavanonol subclass of flavonoids. DHM has drawn interest due to its neuroprotective and anti-aging properties, as well as its ability to lessen the effects of alcohol on the liver and brain. These herbal products are beneficial for cough, fever, colds, sore throat, vomiting, jaundice, nephritis, and hangovers. Dihydromyricetin has been discovered to show antioxidative, anti-inflammatory, anticancer, antimicrobial, cell death-mediating, and lipid and glucose metabolism-regulatory activities.(32) DMY displayed promise antimicrobial activity that significantly inhibits the growth of *Aspergillus flavus, Bacillus subtilis, Staphylococcus aureus, Penicillium sp*., and *Vibrio parahaemolyticus.* Nanoencapsulation of Dihydromyricetin (DMY) enhances its drug-like properties by improving solubility, stability, and sustained release. In a

study, DMY-loaded nanocapsules effectively inhibited and eradicated biofilms formed by *Pseudomonas aeruginosa* on urinary catheters. After 96 hours, the nanocapsules performed better than free DMY, making them a promising strategy for preventing and treating urinary tract infections (UTIs) associated with catheter use.They reduced 67 % of biofilm population in urinary catheter. (33)

6. *Echinochloa esculenta*-Japanese millet

The two primary species of barnyard millet that belong to the Poaceae family are *Echinochloa esculenta*, also known as Japanese barnyard millet, and *Echinochloa frumentacea*, also known as Indian barnyard millet(34). India's top producers of barnyard millet are Tamil Nadu, Bihar, Punjab, Gujarat, Orissa, Maharashtra, and Madhya Pradesh. The numerous medicinal qualities of barnyard millet, including its anticarcinogenic, anti-inflammatory, antioxidant, antimicrobial, and wound-healing capabilities, are attributed to its abundance of macronutrients, alkaloids, steroids, glycosides, and tannins, as well as its micronutrients, including iron and zinc (35) The aqueous extract of *Echinochloa esculenta* was used in a green synthesis process. The plant extract underwent a controlled reaction with zinc acetate or another zinc precursor. The generated particles were examined for their ability to combat *E. Coli, Klebsiella pneumoniae, Proteus mirabilis*, and *Pseudomonas aeruginosa*. Strong antibacterial activity was demonstrated by ZnO nanoparticles, particularly against the most prevalent UTI pathogen, E. coli. Because ZnO NPs disrupt bacterial cell membranes and produce reactive oxygen species (ROS) as an antibacterial mechanism, activity rose with increasing ZnO NP concentrations.(36)

7. *Psidium Guajava*-Guava

Guava, or *Psidium guajava*, is a tropical fruit-bearing plant that is a member of the Myrtaceae family. This family, which also includes other economically significant plants like clove and eucalyptus, is well-known for its fragrant members that are abundant in essential oils. The simple, opposite leaves of the small tree or shrub *Psidium guajava* are dotted with glands and contain aromatic oils. The plant is widely grown for its nutrient-dense fruit, which is high in dietary fiber and vitamin C, and for its white flowers, which have many stamens.(37) The flavonoidal compounds in *Psidium guajava* L. leaves were extracted, fractionated, and isolated. Five flavonoids were identified: quercetin, quercetin-3-O-α-L-arabinofuranoside, quercetin-3-O-β-D-arabinopyranoside, quercetin-3-O-β-D-glucoside, and quercetin-3-O-β-D-galactoside. For the first time, quercetin-3-O-β-D-arabinopyranoside was separated from the leaves. It should be noted that most of the flavonoidal constituents of guava leaf are quercetin derivatives, namely, quercetin, avicularin, guaijaverin, isoquercetin, hyperin, quercitrin, quercetin 3-O-gentiobioside, quercetin 4′-glucuronoide.(38) It was extracted using methanol and refrigerated until required for use and minimum inhibitory concentration determined using Mueller-Hinton agar for proving antibacterial activity and inhibition zone diameter came out to be 14-18 mm which reflects maximum inhibition against Staphylococcus aureus.(39) A study demonstrated the antimicrobial potential of *Psidium gujava* leaf extract using distilled water as the aqueous solvents . The findings showed that guava plant leaf extract's flavonoid compounds and their derivatives can stop bacteria from growing, and that uropathogenic *E. coli* is effectively inhibited by the combined action of guava leaf extract and antibiotics. Ofloxacin (100%) showed the highest antibiotic sensitivity with guava leaf extract in the investigation. As a result, guava fruit or guava juice can be

recommended to UTI patients as a supplement to antibiotic therapy. The methanol and ethanol extracts only showed inhibition against the two gram-positive bacteria, *Bacillus cereus* and *Staphylococcus aureus*, while there was no inhibition against gram-negative bacteria.(40)

8. *Anthocleista djalonensis*-Ghana bark

The Yoruba people of South West Nigeria call *Anthocleista djalonensis* A. Chev, is a member of the Gentianaceae family(41). The tree can reach a height of 15 meters, a bole that can reach a diameter of 40 cm, and twigs that occasionally have two upright spines or tiny cushions above the leaf axils . There are fourteen species in the genus *Anthocleista* (42), and the species found in West Africa are referred to by the same colloquial names (Cabbage tree) and are utilized for the same therapeutic purposes by local practitioners. A number of the genus's members serve comparable therapeutic functions. Different species' dried barks are extremely hard to distinguish from one another. The extract of *Anthocleista djalonensis* leaves, roots, and stem bark has several ethnomedical applications, including treatment of wound, constipation, diarrhoea, dysentery, abdominal pain , hepatitis, jaundice, cirrhosis, fungal skin infection, filarial worm infections, acute inflammation.(43) The outcome of the screening for phytochemicals in the *Anthocleista djalonensis* leaf extracts in methanol, petroleum ether, and hot water demonstrate the presence of cardiac glycosides, terpenoid, flavonoids, tannins, and saponins.(44) *P.aeruginosa* showed the highest zone of inhibition value of 9.67 mm when exposed to methanol extract, whereas Klebsiella pneumoniae and *E.coli* showed the lowest zone of inhibition value of 2.00 mm when exposed to hot water extract. *E.coli* was the only test organism whose growth was inhibited by petroleum ether, whereas the test organisms were inhibited by hot water at an inhibition zone that ranged from 2.00 to 4.00 mm. The outcome demonstrates that the methanol extract had stronger antibacterial properties than both the hot water and petroleum ether extracts. Prior research revealed that the methanol extract of the leaf and root had exceptional properties against certain bacterial isolates, whereas cold water and ethanol extract of the roots had high antimicrobial activity.(45)

9. *P. granatum* L-Pomegranate

The Punicacea family includes the fruit-bearing shrub known as the pomegranate (*P. granatum* L.), which was first described in the Mediterranean region but is now widely grown. Pomegranates have long been prized for their many health advantages, including their ability to biologically active compounds found in all plant parts, such as the fruit juice, peel, arils, flowers, and bark, which cause microbial activities.(46) An extraction process based on maceration with different extraction solvents (water, ethanol, methanol, ethyl acetate, etc.) has been used to extract (fruit, horns, skin, and seed). Fruit and by-product aqueous and organic extracts contain antibacterial components like hydrolyzable tannins (penicillins and punicalagin), ellagic acid, and gallic acid, which work in concert with bioactive flavonols like myricetin and quercetin and anthocyanins like cyanidin-3-glucose and pelargonidin-3-galactose.(47) The primary polyphenols in pomegranate that have been shown to have antimicrobial, antioxidant, and anti-inflammatory bioactivities are ellagitannins and anthocyanins, which are concentrated in the fruit's peel and kernels. Aqueous pomegranate peel extract's antimicrobial and antioxidant effect against uropathogenic *E. coli* has recently been reported. Rich in phenolic compounds, pomegranates are well-known for their anti-inflammatory, anti-cancer, and antioxidant

qualities. The peel (exocarp and mesocarp), which makes up around 50% of the entire fresh fruit, has the highest concentration of these substances.(48) These bioactive phytochemicals have a wide range of antimicrobial activities against fungi and both Gram-positive and Gram-negative bacteria. Seven *Punica granatum* varieties—Wonderful, Mollar de Elche, Primosole, Sassari 1, Sassari 2, Sassari 3, and Arbara Druci—grown in Sardinia, Italy, were examined for their chemical makeup and antimicrobial properties in their peels (exocarp and mesocarp). Extractions with water at 20 and 40 °C were used to measure the amounts of polar phenols, flavonoids, condensed tannins, and anthocyanins.(49) Each PPE's antimicrobial and antibiofilm properties were further examined in vitro against *Salmonella bongori, Lacticaseibacillus casei, E.coli, S.aureus, Listeria monocytogenes*, and *Limosilactobacillus reuteri*. The extracts tested had a greater effect on Gram-positive species than Gram-negative ones. The strains of *S. aureus* and *L. monocytogenes* exhibited antimicrobial activity, while the strains of *S. bongori* and *E. coli* exhibited little to no activity. At concentrations ranging from 0.19 to 1.50 mg/mL, the PPEs from Mollar de Elche, Primosole, and Sassari 3 demonstrated the strongest antimicrobial activity, reducing biofilm activity by over 70%. The extracts' punicalagin, flavonoid, and chlorogenic acid contents were positively correlated with these activities.(50) The green silver nanoparticles were synthesized by pomegranate rind extract and applied them to silicone catheter segments using *Pistacia lentiscus* mastic as a varnish. AgNPs with a primarily spherical shape and sizes ranging from 5 to 50 nm were produced using the green synthesis method. Their crystalline nature and size distribution were verified by characterization methods like transmission electron microscopy (TEM), X-ray diffraction (XRD), and UV-Vis spectroscopy. Both Gram-positive (*Staphylococcus aureus, Staphylococcus epidermidis*) and Gram-negative (*Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis*, and *Pseudomonas aeruginosa*) bacteria were significantly inhibited by the AgNP-coated catheters. Gram-negative strains were more severely inhibited. Prolonged antimicrobial action was provided by the coated catheters, which released silver ions gradually over the course of five days, with amounts ranging from 16.82 µg on day one to 4.80 µg on day five. For as long as 72 hours, the AgNP varnish successfully stopped bacterial colonization. Comparing AgNP-coated catheters to controls, scanning electron microscopy showed little to no bacterial adherence. AgNPs improved the overall antimicrobial efficacy and acted as an efficient medium for nanoparticle adhesion to the catheter surface, whereas Pistacia lentiscus mastic alone demonstrated only moderate antibacterial activity. (51)

10. *Vaccinium macrocarpon* - Cranberry

The Ericaceae family, also referred to as the heath family, includes cranberries. *Vaccinium macrocarpon*, commonly referred to as the American or large cranberry, is the main species grown for commercial use. Native to North America, this low-growing, evergreen shrub grows best in acidic, marshy soils. Other berries that have similar ecological preferences and are prized for their edible fruits, such as lingonberries, blueberries, and bilberries, are also members of the genus Vaccinium.(52) 96 Enterococcus isolates that cause urinary tract infections (UTIs) are tested for the antibacterial and antibiofilm properties of bearberry (BE), and bearberry tea (BTE). While isolates of *Enterococcus faecalis* demonstrated a moderate capacity for biofilm formation, isolates of *Enterococcus faecium* displayed multiple antibiotic resistances. These are rich in polyphenolic compounds with potent antioxidant

and antimicrobial qualities, including gallic acid, ellagic acid, catechin, quercetin, and arbutin, using UHPLC-DAD MS/MS analysis. Although they needed greater concentrations, the extracts individually demonstrated antibacterial activity. They worked in concert to greatly lower the minimum inhibitory concentrations against the bacteria. The BTE extract in particular showed the strongest individual effect on preventing the formation of biofilms and bacterial adhesion. By increasing the effectiveness of conventional antibiotics and lowering the dosages needed, such synergistic combinations may open the door for natural alternative therapies to fight antibiotic-resistant Enterococcus strains that cause UTIs. (53). A study was done to evaluate the efficacy of oral cranberry supplement on catheter-associated urinary tract infections (CAUTIs) is assessed in this six-month study. A daily oral cranberry supplement containing 36 mg of proanthocyanidin (PACs) was administered to subjects who had recurrent symptomatic CAUTIs and long-term indwelling catheters. The mean age of the 22 patients who finished the study was 77.22 years, and 77.27% of them were men. Antibiotic resistance decreased by 28% as a result of cranberry. There were 58.65% fewer major causative bacterial organisms.(54) Cranberry-containing products, particularly juice, have been shown to significantly lower the risk of urinary tract infections (UTIs) by 38% overall, 47% in women who have recurrent UTIs, and 67% in children. Greater protection was demonstrated by more frequent consumption (more than twice daily). Tablets or capsules did not work as well as cranberry juice.(55)

Table 1. Compilation of medicinal plants,Phytochemicals and Anti-UTI activities

Plant	Botanical Name	Key Phytochemicals	Activity & Mechanism	Reference Highlights
Bearberry	*Arctostaphylos uva-ursi*	Arbutin, hydroxycinnamic acids, flavonoids, tannins, poly-saccharide saponins	Anti-UTI, diuretic, nephrolytic, inhibits bacterial adhesion, hydr-oquinone active against uropathogens biofilm formation.	Effective against *K. pneumoniae*, *E. coli*, *P. mirabilis*, *E. faecalis*; inhibition zones up to 30.2 mm for *S. aureus*
Black Seed	*Nigella sativa*	Nigellidine, Nigellimine, thymoquinone	Antimicrobial against multidrug-resistant strains; Gram+/- and prevents biofilm formation	Petroleum ether extract most potent; effective against ESBL-producing MRSA and *E. coli.*
Camelthorn	*Alhagi maurorum*	Flavonoids, terpenoids, alkaloids,steroids coumarins	Anti-inflammatory, Anti-UTI; Diuretic, inhibits *P.mirabilis* bacterial adhesion; nano-formulation enhance efficacy and biofilm formation	Effective against *E. coli*, MIC 1.75 mg/mL; promising results shown by nanoemulsion.
Tamarisk	*Tamarix ericoides*	Octadecenoic acid, Diethyl phthalate, n-hexadecanoic acid	Antibiofilm and Antimicrobial and inhibits *E. coli* biofilms on catheter surfaces	Plant extract biosynthesized as Gold and silver nanoparticles showed strong anti-biofilm effects

Vine Tea	*Ampelopsis grossedentata*	DHM	Antioxidant, anti-inflammatory, anti-biofilm against catheter-associated UTIs	Nanoencapsulation improves sustained and DHM solubility action; effective against *P. aeruginosa* biofilms
Barnyard Millet	*Echinochloa esculenta*	Alkaloids, flavonoids, tannins	Anti-inflammatory,Antimicrobial green-synthesized ZnO nanoparticles show strong anti-UTI action against *P.mirabilis* and *E. coli*,	ZnO NPs produce ROS by interrupting bacterial membrane for augmented antibacterial effect
Guava	*Psidium guajava*	Quercetin-3-O-β-D-glucoside-(Quercetin derivatives)	Anti adhesive and Antibacterial against uropathogens; enhances antibiotic activity	Stronger inhibition against Gram-positive bacteria; *S.aureus* effectively inhibited by methanol extracts.
Ghana Bark	*Anthocleista djalonensis*	Terpenoids, Tannins,flavonoids	Has broad-spectrum antimicrobial; methanol extracts most effective against *E.coli*,*P. aeruginosa*	Has 9.67 mm of zone of inhibition; better than water/petroleum ether extracts
Pomegranate	*Punica granatum*	Flavonids,Ellagitanin ,anthocyanin,	Anti-inflammatory,Anti-biofilm,Anti oxidant, catheter colonization is prevented by green synthesized AgNPs.	Effective against Gram-negative & Gram-positive strains; antimicrobial action up is sustained upto 5 days by silver nanoparticles.
Cranberry	*Vaccinium macrocarpon*	Proanthocyanidin (PACs), gallic acid quercetin.	Reduces bacterial adhesion and biofilm formation; decreases antibiotic resistance	UTI incidence reduced by 38-47 %; cranberry juice more effective than tablets; most effective action against Enterococcus biofilms is shown by cranberry tea.

CONCLUSION

In spite of their effectiveness, antibiotics have several drawbacks in preventing UTIs, including the emergence of resistant strains, recurrence of infection, partial pathogen elimination, and side effects such as nausea, diarrhea, and disruption of normal microbiota. Moreover, antibiotics are often ineffective against asymptomatic bacteriuria. In contrast, plant-based alternatives offer a practical and promising approach to long-term UTI prevention. These natural remedies are generally safer, more accessible, cost-effective, and less likely to induce antimicrobial resistance. A key advantage is that bacterial resistance to herbal medicines has not been reported, likely due to the complex mix of phytochemicals contributing to their therapeutic effects. Medicinal plants such as bearberry, black seed, camel thorn, tamarisk, dihydromyricetin, barnyard millet, guava, Ghana bark, pomegranate, and cranberry have shown significant potential as anti-UTI agents. Their

integration into urinary catheter coatings also shows promise. To fully harness their potential, rigorous scientific validation and well-designed clinical trials are essential. Given the rising burden of catheter-associated urinary tract infections (CAUTIs), exploring these plant-based solutions is a critical step toward safer and more sustainable treatment options.

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