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Effect Investigation of Aqueous Cranberry (*Vaccinium arctostaphylos* L.) Extract in Accompanied with Antibiotics on Urinary Tract Infections (UTI) Created by *Escherichia coli in Vitro*

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1. Introduction

The bladder wall is coated with various mannosylated proteins which interfere with the binding of bacteria to the uroepithelium. As binding is an important factor in establishing pathogenicity for these organisms, its disruption results in reduced capacity for invasion of the tissues.[1a,b] Moreover, the unbound bacteria are more easily removed when voiding. The use of urinary catheters (or other physical trauma) may physically disturb this protective lining, thereby allowing bacteria to invade the exposed epithelium.[1a,b]Over ninety percent of all UTIs are ascending and starting with colonization of periuretheral area.[1c-d] The most common organism implicated in Urinary tract infections UTIs (80–85%) is *E. coli*,[1a,b] while *Staphylococcus saprophyticus* is the cause in 5–10%. [1a,b] The genus *Escherichia coli* (*E.coli*) with five species is a member of Entrobacteriaceae family. This gram negative bacilli is associated with a variety of diseases, such as urinary tract nfections(UTIs), meningitis and so on. *E.coli* can produce adhesins (P pili, AAF/I,AAF/III,..) which bind to cells lining the bladder and upper urinary tract.[1c-d] During cystitis, uropathogenic *Escherichia coli* (UPEC) subvert innate defenses by invading superficial umbrella cells and rapidly increasing in numbers to form intracellular bacterial communities (IBCs).[1,2] By working together, bacteria in biofilms build themselves into structures that are more firmly anchored in infected cells and are more resistant to immune-system assaults and antibiotic treatments.[2a,b] This is often the cause of chronic urinary tract infections.

Bacteruria can be symptomatic or asymptomatic. There are no signs in asymptomatic Bacteruria but bacteria are isolated; in these cases treatment is necessary for pregnant women and patients who have instrument in genitourinary tract. Therefore, infection is defined by clinical parameters and special situations, no by identification of microbe solely.[1c-d] In complicated or questionable cases, confirmation via urinalysis, looking for the presence of nitrites, leukocytes, or leukocyte esterase, or via urine microscopy, looking

for the presence of red blood cells, white blood cells, and bacteria, may be useful.[1a,b] Urine culture shows a quantitative count of greater than or equal to 10^3 colony-forming units (CFU) per mL of a typical urinary tract organism along with antibiotic sensitivity is useful to select appropriate antibiotic .[1a,b] On the whole, diagnosis is based on symptoms and urine culture.[1c-d]

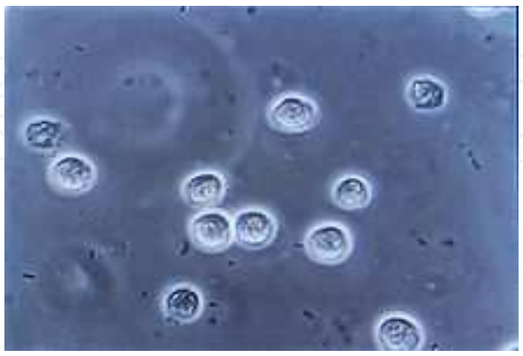


Fig. 1. Multiple bacilli (rod-shaped bacteria have shown as black and bean-shaped) shown between white cells at urinary microscopy. This is called bacteriuria and pyuria, respectively. These changes are indicative of a UTI. See [1a,b]

Accurately, estimate of its incidence is difficult because many cases have not been reported. According to the 1997 National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, urinary tract infection accounted for nearly 7 million office visits and 1 million emergency department visits, resulting in 100,000 hospitalizations.[1,3] The other investigate reported over 1.7 million emergency department visits and more than 8.8 million office visits between 1999 and 2000.[1d]

UTIs are frequently seen among women than men. Assessments show 50 percent of all women have an episode of UTI during their lifetime. Others are at risk for UTIs due to elderly, pregnancy, catheters, genitourinary tract abnormalities, underlying diseases (i.e. diabetes), renal stones and so on. Uncomplicated UTIs occur in young women in sexually active age, but complicated UTIs occur in individuals who have one or more structural abnormalities in genitourinary tract or have catheters indwelling. .[1a-d,4] Some of agents (abnormalities in urinary tract, renal stones, diabetes, genetic factors like receptors for bacterial pili, spinal cord injuries and etc.) which promote women for UTIs, also are common in men, and could add prostatitis and spermicides agents as other promoting factors in men. Albeit, the incidence of UTIs in men <65 year old is very low; but incidence of UTIs in men older than 65 increases dramatically, as UTIs ratio in female-to- male declines.[1a-d]

Pediatrics UTIs create great morbidity and long standing problems, including impaired renal function and hypertension. Bacteria have been seen in approximately 1% of all babies' and more in boys' bladder, and bacteremia often is present. Risk of UTIs in non-circumcised males younger than 6 months is 12 times more than circumcised control group. According to statistics from 1990, the prevalence of urinary tract infections in pre-school and school girls was 1% to 3%, nearly 30-fold higher than that in boys.[1a,4] Also, the statistics from the same year show that approximately 5% of girls will develop at least one urinary tract infection in their school years.[1a] Children with recurrent UTIs may be treated with preventative antibiotics that decrease the rate of microbiological recurrence but not

symptomatic recurrence.[1a,5] These infections are often asymptomatic and it can be cause of most renal damages.[1a-d]

Cranberries have enormous medical value. This was known to man from a very long time ago. The name cranberry derives from "craneberry", first named by early European settlers in America who felt the expanding flower, stem, calyx, and petals resembled the neck, head, and bill of a crane. Another name used in northeastern Canada is mossberry. The traditional English name for Vaccinium oxycoccos, fenberry, originated from plants found growing in fen (marsh) lands. In 17th century New England cranberries were sometimes called "bearberries" as bears were often seen feeding on them.[6]

In North America, Native Americans were the first to use cranberries as food. Native Americans used cranberries in a variety of foods, especially for pemmican, wound medicine and dye. Calling the red berries Sassamanash, natives may have introduced cranberries to starving English settlers in Massachusetts who incorporated the berries into traditional Thanksgiving feasts. In the 1820s cranberries were shipped to Europe.[6,7] Cranberries became popular for wild harvesting in the Nordic countries and Russia. In Scotland, the berries were originally wild-harvested but with the loss of suitable habitat, the plants have become so scarce that this is no longer done. Cranberries are a group of evergreen dwarf shrubs or trailing vines in the genus *Vaccinium* subgenus *Oxycoccos*, or in some treatments, in the distinct genus *Oxycoccos*. They can be found in acidic bogs throughout the cooler regions of the Northern Hemisphere.[6]

Vaccinium arctostaphylos L. genus that is relevant to the *Ericaceae* family has over 450 species which are found mostly in the cooler areas. A deciduous shrub grows to 3m by 2m. It is in flower from May to July, and the seeds ripen in September. The flowers are hermaphrodite (have both male and female organs) and are pollinated by Insects.[8,9] The plant prefers light (sandy) and medium (loamy) soils and requires well-drained soil. The plant prefers acid soils and can grow in very acid soil (pH 4-5). It can grow in semi-shade (light woodland) or no shade. It requires moist soil.[8,9] This kind of Cranberry (*Vaccinium arctostaphylos L.*) is growing in north and the parts of west of Iran. The local name of this herb is Qare-Qat (QΛre-QΛt).[8,9]

Historically, cranberry beds were constructed in wetlands. Currently cranberry beds are constructed in upland areas that have a shallow water table. The topsoil is scraped off to form dykes around the bed perimeter.[6a] Clean sand is hauled in to a depth of four to eight inches. The surface is laser leveled flat to provide even drainage. Beds are frequently drained with socked tile in addition to the perimeter ditch. In addition to making it possible to hold water, the dykes allow equipment to service the beds without driving on the vines. Irrigation equipment is installed in the bed to provide irrigation for vine growth and for spring and autumn frost protection.[6a]

Cranberries are related to bilberries, blueberries, and huckleberries, all in *Vaccinium* subgenus *Vaccinium*. These differ in having stouter, woodier stems forming taller shrubs, and in the bell-shaped flowers, the petals not being reflexed. Cranberries are susceptible to false blossom, a harmful but controllable phytoplasma disease common in the eastern production areas of Massachusetts and New Jersey. [6a]

2. Urinary tract infections (UTI)

UTIs are a serious health problem affecting millions of people each year. Infections of the urinary tract are the second most common type of infection in the body. The urinary tract

includes the kidneys, ureters, bladder and urethra. Any part of the urinary tract can become infected, but bladder and urethra infections are the most common. Women are especially prone to UTIs for reasons that are not yet well understood. One woman in five develops a UTI during her lifetime. A UTI is a bacterial infection that affects any part of the urinary tract.[10] The main causal agent is *Escherichia coli*. When bacteria get into the bladder or kidney and multiply in the urine, they may cause a UTI. The most common type of UTI is acute cystitis often referred to as a bladder infection. An infection of the upper urinary tract or kidney is known as pyelonephritis, and is potentially more serious. Although, they cause discomfort, urinary tract infections can usually be easily treated with a short course of antibiotics with all no significant difference between the classes of antibiotics commonly used.[10] UTIs are common in women and children and it causes some permanent side effect on kidneys. Since many years, peoples to treatment UTI utilize this herb and sometimes with appropriate antibiotics.[10]

3. Chemistry of cranberry

The chemical compositions of the different genius of *Cranberry* were studied widely. In the most genius of *Cranberry* some chemical compounds such as flavonoids, sugar, protein, total fat and some important fatty acids were identified. Raw cranberries have moderate levels of dietary fiber, Ca, Mg, Mn, P, K, Na, Vitamins C, A, K, Carotene, Lutein, Zeaxanthin and the essential dietary mineral, manganese, as well as a balanced profile of other essential micronutrients.[8] Cranberries also contain malic acid. By measure of the Oxygen Radical Absorbance Capacity with an ORAC score of 9,584 units per 100 g, cranberry ranks near the top of 277 commonly consumed foods.[6a,11,12] Raw cranberries are a source of polyphenol antioxidants, phytochemicals under active research for possible benefits to the cardiovascular system and immune system, and as anti-cancer agents.[6a,13,14]

Cranberry juice contains a chemical component, a high molecular weight non-dialyzable material (NDM), as noted above, that is able to inhibit and even reverse the formation of plaque by *Streptococcus mutans* pathogens that cause tooth decay.[6a,15,16] Cranberry juice components also show efficacy against formation of kidney stones.[6a,17,18] Raw cranberries and cranberry juice are abundant food sources of flavonoids such as proanthocyanidins, flavonols and anthocyanidins (cyanidin, peonidin and quercetin). [6a,19,20] These compounds have shown promise as anti-cancer agents in in vitro studies. However, their effectiveness in humans has not been established, and may be limited by poor absorption into cells and rapid elimination from the blood.[6a] Since 2002, there has been an increasing focus on the potential role of cranberry polyphenolic constituents in preventing several types of cancer.[6a,21-26] In a 2001 University of Maine study that compared cranberries with twenty other fruits demonstrated that cranberries had the largest amount of both free and total phenols, with red grapes at a distant second place. [6a-27] Cranberry tannins have anti-clotting properties and may reduce urinary tract infections [6a-28] and the amount of dental plaque-causing oral bacteria, thus being a prophylaxis for gingivitis.[6a-29]

The main chemical compositions that extracted from *Cranberry* contain mineral compounds, flavonoids, benzoic acid, triterpenoids, anthocyanins, catechin, β-hydroxybutiric acid, citric acid, glucuronic acid, quinic acids, ellagic acid, sugar(fructose, *D*-mannose), protein, total fat and some important fatty acids. In one study, the chemical composition of *Vaccinium arctostaphylos L.* essential oil were determined by utilize GC and GC/MS methods.[9,30] The

major determined volatiles in this type of Cranberry, are: hexadecanoic acid(27%), vitispirane(6.5%), β-ionone(5.9%) and sandaracopimaradiene(4.8%).[9,30] L. Y. Foo et al. in 2000 reported the proanthocyanidin fraction of Cranberry, isolated from the ethyl acetate extract that was investigated for ability to prevent adherence of *E. coli* to mannose-resistance adhesion by determining the ability to prevent agglutination of both isolated P-receptor resin-coated beads and human erythrocytes.[9,31] The characterization of Flavonols in Cranberry (*Vaccinium macrocarpon*) were investigated by N. Vorsa et al.[4]. In this report, the main Flavonols were extracted by acetone and ethylacetate and identified in this herb, such as: myricetin-3-β-xylopyranoside, quercetin-3-β-galactoside, quercetin-3-β-glucoside, quercetin-3-α-arabinopyranoside, quercetin-3-α-arabinofuranoside, 3′-methoxyquercetin-3-α-xylopyranoside, quercetin-3-O-(6′′-p-coumaroyl)β-galactoside and quercetin-3-O-(6′′-benzoyl)β-galactoside.[9,32]

In 2004, two species, *Vaccinium membranaceum* and *Vaccinium ovatum*, native to Pacific Northwestern North America, were evaluated for their total, and individual, anthocyanin and polyphenolic compositions by Lee et al..[33,34] *Vaccinium ovatum* had greater total anthocyanin (ACY), total phenolics (TP), oxygen radical absorbing capacity (ORAC), and ferric reducing antioxidant potential (FRAP) than did *V. membranaceum*. The pH were also higher in *V. ovatum*. Berry extracts from each species were separated into three different fractions anthocyanin, polyphenolic, and sugar/ acids by solid-phase extraction.[33] The anthocyanin fractions of each species had the highest amount of ACY, TP, and antioxidant activity. Each species contained 15 anthocyanins (galactoside, glucoside, and arabinoside of delphinidin, cyanidin, petunidin, peonidin, and malvidin) but in different proportions. Their anthocyanin profiles were similar by high-performance liquid chromatography (HPLC) with photodiode array detection (LC-DAD) and high-performance liquid chromatography with photodiode array and mass spectrometry detections (LC-DAD-MS).[33] Each species had a different polyphenolic profile. The polyphenolics of both species were mainly composed of cinnamic acid derivatives and flavonol glycosides. The major polyphenolic compound in *V. membranaceum* was neochlorogenic acid, and in *V. ovatum*, chlorogenic acid.[33] Some of the main compounds achieved, are: gallic acid, protocatechuic acid; neochlorogenic acid; cinnamic acid dervatives; catechin; chlorogenic acid; vanillic acid; caffeic acid; epicatechin; flavonol glycosides; delphinidin 3-galactoside; delphinidin 3-glucoside; delphinidin 3-arabinoside; cyanidin 3-galactoside; cyanidin 3-glucoside; petunidin 3-galactoside; cyanidin 3-arabinoside; petunidin 3-glucoside; peonidin 3-galactoside; petunidin 3-arabinoside; malvidin 3-galactoside; peonidin 3-glucoside; peonidin 3-arabinoside; malvidin 3-glucoside; malvidin 3-arabinoside.[33,34]

In 2006, the chemical composition of the *Qare-Qat* or Iranian *Vaccinium (V.arctostaphylos L.)* had been investigated by Sedaghathoor etal.[30] It is a shrub that grows in the north of Iran. The fruits of *Qare-Qat* were collected from natural habitats and examined for chemical composition such as minerals. The results showed that the ripe fruit of *V.arctostaphylos L.* had 30.6% sugars, 15.5% protein, 1.5% total fat and 2% soluble solids. Dry matter, nitrogen and calcium contents of fruits were 22.3%, 2.5% and 1.4%, respectively.[30] Furthermore, about twelve compounds were identified as essential oil components of shoots of this plant. The major volatiles present in *Vaccinium arctostaphylos L.* shoots were hexadecanoic acid (27.0%), vitispirane (6.5%), *Beta*-ionone (5.9%) and sandaracopimaradiene (4.8%). Some of the essential oil components of this type of cranberry are: 2-Cyclopenten-1-one, 4-acetyl -2,3,5,5-pentamethyl; Acetic acid 1-hydroxy-3,7-dimethyl-oct-6-enyl ester; Delta-3-Carene; Vitispirane; Naphthalene-1,2-dihydro-5,8-trimethyl; 1,3-Diacetylbenzene; *β*-Ionone; 2-

Pentadecanone; Sandaracopimaradiene; Hexadecanoic acid; Eicosane-2,6,10,14,18-pentamethyl and Isopimaradiene.[30]

Some of the physicochemical properties, like the logarithm of calculated Octanol-Water partitioning coefficients ($logK_{ow}$), total biodegradation and (TB_d in mol/h) and median lethal concentration 50 (LC_{50}) were calculated for some of the chemicals of the cranberry speciesby the EPI-suit v4.00 package.[35] See Table 1.

The octanol-water partition coefficient (K_{ow}) is a measure of the equilibrium concentration of a compound between octanol and water that indicates the potential for partitioning in to soil organic matter (i.e., a high K_{ow} indicates a compound which will preferentially partition into soil organic matter rather than water). This coefficient is inversely related to the solubility of a compound in water. The $logK_{ow}$ is used in models to estimate plant and soil invertebrate bioaccumulation factors. This parameter is also used in many environmental studies to help determine the environmental fate of chemicals.[9,35-38]

Biodegradation is usually quantified by incubating a chemical compound in presence of a degrader, and measuring some factors like oxygen or production of CO_2. The biodegradation studies demonstrate that microbial biosensors are a viable alternative means of reporting on potential biotransformation. However, a few chemicals are tested and large data sets for different chemicals need for quantitative structural relationship studies.[9,39]

An LC_{50} value is the concentration of a material in air that will kill 50% of the test subjects (animals, typically mice or rats) when administered as a single exposure (typically 1 or 4 hours). Also called the median lethal concentration and lethal concentration 50, this value gives an idea of the relative acute toxicity of an inhalant material. Typical units for LC_{50} values are parts per million (ppm) of material in air, micrograms (10^{-6} = 0.000001 g) per liter of air and milligrams (10^{-3} = 0.001 gr) per cubic meter of air.[9,40]

In accordance with the calculated data of the components 1-21 in cranberries, by EPI-suit v4.00 package (see Table-1), hexadecanoic acid (6.962), sandaracopimaradiene, isopimaradiene (6.445), 2-pentadecanone (5.658), δ-3-carene (4.611), β-ionone (4,424), naphthalene-1,2-dihydro-5,8-trimethyl (3.303) and acetic acid 1-hydroxy-3,7-dimethyl-oct-6-enyl ester (3.023) have the highest logarithm of octanol-water partition coefficient ($logK_{ow}$), respectively. Accordingly, the compounds have the lowest water solubility (S_w, mg.L^{-1}/25^{o}C). Neochlorogenic acid and Chlorogenic acid with -1.014 have the lowest amount of $logK_{ow}$. The compound with the highest lethal concentration (LC_{50}, mg/L) was gallic acid. Meanwhile, sandaracopimaradiene, isopimaradiene had the lowest LC_{50} (0.04). The total biodegradation (TB_d) of naphthalene-1,2-dihydro-5,8-trimethyl among and δ-3-carene among 1-21 were the highest and for β-ionone was the lowest (in mol/h×10^{-5}).

5. Urinary tract infections (UTI) and cranberry

As discussed Cranberries have enormous medicinal value. These berries are not just good to eat; they also contain different kinds of chemicals that are nutritious. While the people in the 17th century and there about knew generally the basic medicinal values of cranberries (the East Europeans even believed it to have the ability to cure cancer), research today has discovered other medicinal benefits that we can derive from cranberries.[41a-c] Cranberries have been found to be effective in battling urinary tract inflammation, oral disease, as well as even heart ailments. Here we will see how cranberries help prevent Urinary Tract Infection (UTI).[41a-c] While different food products or plants work in different ways, cranberries have their own way of reducing the risk of illness in the human body.[41a-c]

No.	Compounds in Cranberries	Calculated concerns		
		$logK_{ow}$	LC_{50} [b] (in mg/L or ppm)	Total Biodegradation (in mol/h $\times 10^{-5}$)
1	2-Cyclopenten-1-one, 4-acetyl -2,3,5,5-pentamethyl	1.531	344.87	5.2
2	Acetic acid 1-hydroxy-3,7-dimethyl-oct-6-enyl ester	3.023	22.52	5.8
3	δ-3-Carene	4.611	0.53	7.9
5	Naphthalene-1,2-dihydro-5,8-trimethyl	3.303	11.44	8.1
6	1,3-Diacetylbenzene	1.354	462.55	5.7
7	β-Ionone	4.424	1.32	1.3
8	2-Pentadecanone	5.658	0.11	3.1
9	Sandaracopimaradiene	6.445	0.04	2.6
10	Hexadecanoic acid	6.962	0.09	3.0
12	Isopimaradiene	6.445	0.04	2.6
13	Gallic acid	0.855	1218.82	5.4
14	Protocatechuic acid	0.914	985.24	6.0
15	Neochlorogenic acid	-1.014	272.80	2.6
16	Cinnamic acid	2.071	989.53	6.5
17	Catechin	1.175	1115.68	3.2
18	Chlorogenic acid	-1.014	272.80	2.6
19	Vanillic acid	1.219	593.19	5.5
20	Caffeic acid	1.110	785.65	5.1
21	Epicatechin	1.175	1115.68	3.2

[a]The values were calculated by EPI-suit v4.00 package.[35] [b] Asterisk designates, Chemical may not be soluble.

Table 1. The calculated logarithm of calculated Octanol-Water partitioning coefficients ($logK_{ow}$), water solubility at 25°C (mg/L), median lethal concentration 50 (LC_{50}) and total biodegradation and (TB_d in mol/h) of some of the chemical components of some species of Cranberries.[35]

One of the biggest and most widely health benefits of eating cranberries, in whatever form, either as whole fruit or juice or cocktail, is that it helps prevent urinary tract infection (UTI). While this was what our elders passed on to us as traditional oral medicinal knowledge, it is now recognized as official medical fact.[41a-c]

Kidney stones are most often caused by high levels of ionized calcium (as in calcium salts) in the urine. Cranberries can help prevent this condition because they are rich in quinic acid, which increases the acidity of the urine. As a result, the levels of ionized calcium in the urine are lowered. The infection is basically caused by bacteria.[41a-c, 42] The bacteria latch on to the surface or lining of the cells of different body parts. Once they are attached to the lining of the specific body part in question, they feed off the cells or the surface or the lining they are attached to, and increase their numbers by reproducing, and in the process cause infections. In the case of UTI, this process happens in the lining of the urinary tract.[41a-c,

42] Initially, researchers went off-track when they figured that the cranberries' ability to prevent UTI was because of its acidity. It has reported that cranberries prevent UTI by preventing the bacteria causing UTI from attaching itself to the surface of the urinary tract lining. Amy Howell published this discovery in the New England Journal of Medicine in 1998.[41a-c-50] The research shows that cranberries are basically rich in proanthocyanidins. Proanthocyanidins are tannins, a type of organic chemical compound, that have been condensed. This is how it works. The proanthocyanidins have their own specific way of functioning – they are blockers that block the bacteria from attaching themselves to the surface of the lining of the specific body part in question. In the case of UTI, the proanthocyanidins prevent the bacteria from getting glued to the lining of the urinary tract.[42-50] The most common side effects associated with excessive cranberry consumption are diarrhea and an increased risk of developing kidney stones. Regular cranberry consumption by women trying to prevent UTIs may result in *vulvovaginal candidiasis*. Alterations in the normal vaginal bacteria may lead to increased *fungal* growth.[42]
In 1984 was surveyed the anti adhering of Cranberry on 77 strains of *E. coli* that in 75% samples it was verified.[38] In 1994, was examined the extraction of this herb for treating 153 persons who involved to UTI.[39] In 1995, was showed that UTI in women is decreased for 52% by Craberry extract prophylaxy.[9,40,51] In 2006, was investigated the effect of Cranberry in prevention on urinary tract infection in children, and prevention of nonspecific bacterial cell adhesion in immunoassays by use of Cranberry juice.[9,52,53] Sometimes peoples to treatment UTIs, utilize this herb with appropriate antibiotics.

6. Experimental section

In this study, were examined 61 isolated *E. coli* from urine sample of the patients that they had referred to the hospitals and laboratories of Sanandaj city. Dried fruit of Cranberry (*Vaccinium arctostaphylos L.*) was altered to powder and then was acquired aqueous extraction (1%) from it. This concentration was based on Boland's study.[9] The most concentration of Cranberry in media was selected that had not any effect on bacteria on the media than media without plant extract. One control plate (Mueller-Hilton agar without Cranberry) was chosen for each strain.

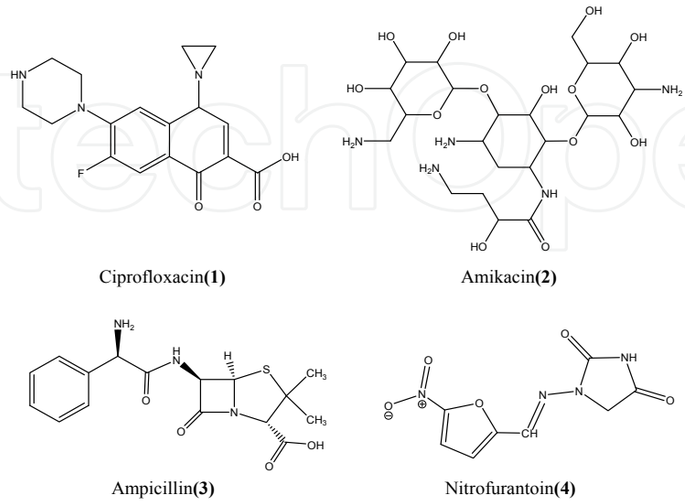


Fig. 2. The chemical structures of Ciprofloxacin-1, Amikacin-2, Ampicillin-3 and Nitrofurantoin-4.

The other plate contained Mueller-Hilton agar accompanied Cranberry 1% extraction. A certain number of bacterias ($1.5x10^8$ CFU/ml) based on 0.5 Macfarland scale was cultured on the media. After this stage, the antibiotic disks (Ciprofloxacin-1, Amikacin-2, Ampicillin-3, Tetracyclin, Co-trimoxazole, Nalidixic acid, Ceftazidime and Nitrofurantoin-4) were cultured. After 24 hours incubation in 37°C was measured the zone around of the each disks and compared with standard schedule.[9,54]

6.1 Results and discussions

The results of the investigation were demonstrated in Table-1. The results were analyzed based on Ki test. The most susceptibility belonged to Amikacin-2 in frequency of the control group with 93.45%. The lowest frequency was 9.8% for Ampicillin-3. The other type of antibiotics the susceptibilities in control group were: Co-trimoxazol 39.34%, Ceftazidime 51%, Nalidixic acid 54.1%, Nitrofurantoin 62.3%, Tetracyclin 72.13% and Ciprofloxacin-1 73.8%. In test group, Nitrofurantoin-4 shows the most susceptibility (72.13%) and the lowest belongs to Ampicilline(18%). In addition, percentage of susceptibility for other antibiotics as Amikacin, Co-trimoxazole, Nalidix acid, Ceftazidime and Tetracyclin were: 28.87%, 34.42%, 52.48%, 55% and 70.5%, respectively.[9] In accordance with the results, not only aqueous extract of Cranberry did not show any synergistic effect with any antibiotics, but also it showed sever antagonistic effect against Ciprofloxacine-1 and Amikacine-2 (P=0.00). See Table-2. However, in acidic pH Ampicillin-3 and Nitrofurantoin-4 had 10% increased in function, but in the whole statistical computation did not show any significant difference (see Table-2). Nitrofurantoin-4 shows better function in acidic pH. Ampicillin and Amoxicillin are resistant and absorbed much better in acidic pH. On the contrary, Co-trimoxazole is more effective in alkaline pH.[9] In neutral or acidic media it is changed to crystal form and precipitate.[9,54] In spite of the fact that there are no significant statistical difference between two plates (test plate and control plate), It was found that antagonistic effect between Cranberry and two antibiotic disks i.e. Ciprofloxacin-1 and Amikacin-2 (P=0.00). The results show that use Cranberry with some antibiotics that explained here can diminish the medicinal effects of the antibiotics in UTIs treatments. The awareness about interfere and the suppression of the appropriate medicinal effect of antibiotics by *Vaccinium arctostaphylos L.* can be useful for treating UTIs.[9]

Some of the physicochemical properties like: the logarithm of calculated Octanol-Water partitioning coefficients ($logK_{ow}$), total biodegradation and (TB_d in mol/h and gr./h), water solubility (S_w, $mg.L^{-1}/25^oC$) and median lethal concentration 50 (LC_{50}) were calculated for the antibiotics (Ciprofloxacin, Amikacin, Ampicillin and Nitrofurantoin). The octanol-water partition coefficient (K_{ow}) is a measure of the equilibrium concentration of a compound between octanol and water that indicates the potential for partitioning in to soil organic matter (i.e., a high K_{ow} indicates a compound which will preferentially partition into soil organic matter rather than water).[35-40] The TB_d is another useful and important factors in chemical and biochemical studies. It needs to use the effective and useful mathematical methods for making good concern between several data in chemistry and biochemistry. An LC_{50} value is the concentration of a material in air that will kill 50% of the test subjects (animals, typically mice or rats) when administered as a single exposure (typically 1 or 4 hours). One of the other important physicochemical factors of compounds is water solubility (S_w, $mg.L^{-1}/25^oC$). Some of the other calculated physicochemical properties of the antibiotics (Ciprofloxacin, Amikacin, Ampicillin and Nitrofurantoin) on UTIs that is created by *Escherichia coli* in Vitro and some of the chemical components of *Cranberry* were calculated.

Concerns		Ciprofloxacin(1)			Amikacin(2)			Ampicillin(3)			Nitrofurantoin(4)		
		Blank	Cranberry	Total	Blank	Cranberry	Total	Blank	Cranberry	Total	Blank	Cranberry	Total
Susceptibility	No.	45	11	56	57	17	74	6	11	17	38	44	82
	%	73.8	18	-	93.45	28.87	-	9.8	18	-	62.3	72.13	-
Stability	No	16	50	66	4	44	48	55	50	105	23	17	40
	%	26.2	82	-	6.55	72.13	-	90.2	82	-	73.7	27.87	-

*The P-value for the samples was 0.00.

Table 2. The comparison of the sensitivity of *Escherichia coli* to the antibiotics (1-4).[9]

Antibiotics 1-4	Calculated concerns			
	$logK_{ow}$ [a]	Water Solubility at 25°C (mg/L)	LC_{50} [b] (in mg/L or ppm)	Total Biodegradation (in mol/h ×10^{-5})
Ciprofloxacin(1)	-8×10^{-4}	11480	9303.95	2.8
Amikacin(2)	-8.7807	1×10^{6}	3.15×10^{8}	1.6
Ampicillin(3)	1.4538	439.3	780.24	2.7
Nitrofurantoin(4)	-0.1675	1382.0	12523.00	3.9

[a]The values were calculated by EPI-suit v4.00 package.[35] [b] Asterisk designates, Chemical may not be soluble.

Table 3. The calculated logarithm of calculated Octanol-Water partitioning coefficients ($logK_{ow}$), water solubility at 25°C (mg/L), median lethal concentration 50 (LC_{50}) and total biodegradation and (TB_d in mol/h) of the antibiotics Ciprofloxacin(1), Amikacin(2), Ampicillin(3) and Nitrofurantoin(4).[9,35]

[35-40] See Table-3. In accordance with the calculated data of the antibiotics (ciprofloxacin-1, Amikacin-2, Ampicillin-3 and Nitrofurantoin-4), by EPI-suit v4.00 package (see Table-3), ampicillin-3 (1.4538) has the highest logarithm of octanol-water partition coefficient ($logK_{ow}$). Accordingly, the compound has the lowest water solubility (S_w, mg.L^{-1}/25°C). Amikacin-2 with -8.7807 has the lowest amount of $logK_{ow}$ among selected antibiotics 1-4. The calculations show that the antibiotic with the highest lethal concentration (LC_{50}, mg/L) was amikacin-2. Meanwhile, ampicillin-3 had the lowest LC_{50}. The total biodegradation (TB_d) of Nitrofurantoin-4 among the selected antibiotics 1-4 was the highest and for amikacin-2 was the lowest (in mol/h×10^{-5}).

7. Conclusion

The chemical compositions of the different types of Craberry were investigated. It was determined that this type of medicinal herb was utilized for UTI treatments. *Vaccinium arctostaphylos L.* genus was used to investigate the synergistic effect of aqueous Cranberry (*Vaccinium arctostaphylos L.*) extract in accompanied with antibiotics (Ciprofloxacin-1, Amikacin-2, Ampicillin-3 and Nitrofurantoin-4) on UTIs created by *Escherichia coli* in Vitro. The results show that use Cranberry with some antibiotics that explained here can show some interference effects with the antibiotics and diminish the medicinal effects of the antibiotics (antagonist effect) in Urinary tract infections (UTI) treatments.[9] Some of the physicochemical properties, like the logarithm of calculated Octanol-Water partitioning coefficients ($logK_{ow}$), total biodegradation and (TB_d in mol/h) and median lethal concentration 50 (LC_{50}) were calculated for some of the chemicals of the cranberry species and antibiotics (Ciprofloxacin-1, Amikacin-2, Ampicillin-3 and Nitrofurantoin-4).[9,35-40]

8. References

[1] a)Urinary tract infection ,Wikipedia:
http://en.wikipedia.org/wiki/Urinary_tract_infection.

b) Nicolle LE (February 2008). "Uncomplicated urinary tract infection in adults including uncomplicated pyelonephritis". *Urol. Clin. North Am.* 35 (1): 1–12.
c) Murray P., Rsental K., Pfaller M."Medical Microbiology", 2005, ; ElSEVIER MOSBY; 5th ed.
d) Mahon C., Lehman D.,Manuselis G. "Text Book of Diagnostic Microbiology"; 2007; ; ElSEVIER; 3rd ed.
e) "Bacteriology- TOPLEY and WILSON'S Microbiology and Microbial I nfections", 2005, , Edward Arnold, volume 2, Edward Arnold publisher,10th ed.

[2] a) Justice S, Hunstad D, Seed P, Hultgren S (2006). Filamentation by *Escherichia coli* subverts innate defenses during urinary tract infection. *Proc Natl Acad Sci USA* 103 (52): 19884–9.
b) http://www.biofilmsonline.com/cgi-bin/biofilmsonline/00448.html.

[3] Foxman, B (2003). "Epidemiology of urinary tract infections: incidence, morbidity, and economic costs.". *Disease-a-month* 49 (2): 53–70.

[4] Hooton, T. M. (1990). "The epidemiology of urinary tract infection and the concept of significant bacteriuria". *Infection* 18: S40–3.

[5] Dai, B; Liu, Y; Jia, J; Mei, C (2010). "Long-term antibiotics for the prevention of recurrent urinary tract infection in children: a systematic review and meta-analysis.". *Archives of disease in childhood* 95 (7): 499–508.

[6] a) http://en.wikipedia.org/wiki/Cranberry.
b) http://www.cranberryinstitute.org/about_cranberry.htm.
c) http://www.tcpalm.com/news/2009/nov/19/give-thanks-for-cranberries-grown-with-a-taste.
d) http://www.hortresearch.co.nz/index/news/493.

[7] http://www.cranberries.org/cranberries/history.html.

[8] a) Schonbeck-Temesy E., Wien, K. H. Rechinger K. H.(1992) *Flora Iranica*, Graz. b) Huxley A., (1992) *The New RHS Dictionary of Gardening,* MacMillan Press, New York. c)http://en.wikipedia.org/wiki/Vaccinium;http://www.ibiblio.org/pfaf/cgibin/arr_html?Vaccinium+arctostaphylos&CAN=LATIND .

[9] Taherpour A., Noorabadi P., Abedii F. and Taherpour A. A., (2008) Effect of Aqueous Cranberry(*Vaccinium arctostaphylos L.*)Extract Accompanied with Antibiotics on UTIs caused by Escherichia coli in vitro, *J. Pur. & Appl. Micro.,* 2(1), 135-138.

[10] a) http://kidney.niddk.nih.gov/kudiseases/pubs/utiadult/
b) http://familydoctor.org/online/famdocen/home/women/gen-health/190.html.
c) http://www.wrongdiagnosis.com/u/urinary_tract_infections/intro.htm.
d) http://www.patient.co.uk/doctor/Urinary-Tract-Infection-in-Adults.htm.

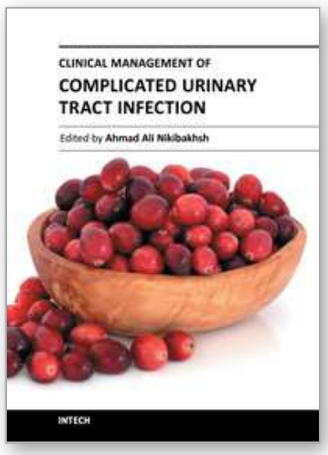
[11] Oxygen Radical Absorbance Capacity (ORAC) of Selected Foods (2007). Prepared by Nutrient Data Laboratory Beltsville Human Nutrition Research Center (BHNRC) Agricultural Research Service (ARS) U.S. Department of Agriculture (USDA). http://www.ars.usda.gov/nutrientdata.

[12] http://www.nal.usda.gov/fnic/foodcomp/search/.

[13] Seifried H.E., Anderson D.E., Fisher E.I., Milner J.A. (2007). A review of the interaction among dietary antioxidants and reactive oxygen species. *J Nutr Biochem.* 18 (9): 567–79.

[14] Halliwell B. (2007). Dietary polyphenols: good, bad, or indifferent for your health?. *Cardiovasc Res.* 73(2) 341–7.
[15] http://www.cranberryinstitute.org/health/dental.htm.
[16] http://www.webmd.com/food-recipes/news/20051123/cranberry-juice-cuts-cavities.
[17] McHarg T., Rodgers A., Charlton K. (2003) Influence of cranberry juice on the urinary risk factors for calcium oxalate kidney stone formation. *BJU Int.* 92(7) 765–8.
[18] Kessler T., Jansen B., Hesse A. (2002). Effect of blackcurrant-, cranberry- and plum juice consumption on risk factors associated with kidney stone formation. *Eur J Clin Nutr*, 56(10) 1020–3.
[19] Duthie S.J., Jenkinson A.M., Crozier A., *et al.* (2006) The effects of cranberry juice consumption on antioxidant status and biomarkers relating to heart disease and cancer in healthy human volunteers. *Eur J Nutr* 45 (2): 113–22.
[20] Zheng W., Wang S.Y. (2003) Oxygen radical absorbing capacity of phenolics in blueberries, cranberries, chokeberries, and lingonberries. *J Agric Food Chem.* 51 (2) 502-9.
[21] I.O. Vvedenskaya & N. Vorsa, Flavonoid composition over fruit development and maturation in American cranberry, Vaccinium macrocarpon *Ait. Plant Science,* 167(5), 2004, 1043-1054.
[22] http://newsletter.cancerresearchsociety.ca/bulletin/omni/articles/4190.aspx.
[23] Neto C.C. (2007). "Cranberry and blueberry: evidence for protective effects against cancer and vascular diseases". *Mol Nutr Food Res* 51 (6): 652–64.
[24] Ferguson P.J., Kurowska E.M., Freeman D.J., Chambers A.F., Koropatnick J. (2006). "In vivo inhibition of growth of human tumor lines by flavonoid fractions from cranberry extract". *Nutr Cancer* 56 (1): 86–94.
[25] Seeram N.P., Adams L.S., Zhang Y., *et al.* (December 2006). "Blackberry, black raspberry, blueberry, cranberry, red raspberry, and strawberry extracts inhibit growth and stimulate apoptosis of human cancer cells in vitro". *J Agric Food Chem.* 54 (25): 9329–39.
[26] Sun J., Chu Y.F., Wu X., Liu R.H. (2002). Antioxidant and antiproliferative activities of common fruits. *J Agric Food Chem.* 50 (25): 7449–54.
[27] Vinson J.A., Su X., Zubik L., Bose P. (2001). Phenol antioxidant quantity and quality in foods: fruits. *J Agric Food Chem.* 49 (11): 5315–21.
[28] Efros M., Bromberg W., Cossu L., Nakeleski E., Katz A.E. (2010), Novel concentrated cranberry liquid blend, UTI-STAT with Proantinox, might help prevent recurrent urinary tract infections in women. *Urology*. 76(4) 841-5.
[29] http://www.eurekalert.org/pub_releases/2008-07/wpi-cjc072108.php.
[30] Sedaghathoor S., Kashi A. K., Talaei A. R., Khalighi A. (2006), *In. J. Agr. Bio.,* 8(1), 45-46.
[31] Foo L. Y., Lu Y., Howell A. B. and Vorsa N. (2000) *Phytochemistry,* 54, 173-181.
[32] Vvedenskaya I. O., Rosen R. T., Guido J. E., Russell D. J., Mills K. A. and Vorsa N. (2004) *J. Agri. Food Chem.,* 52(2), 188-195.
[33] Lee J., Finn C. E. and Wrolstad R. E. (2004) *J. Agric. Food Chem.,* 2004, 52, 7039-7044.
[34] Lee, J.; Finn, C. E.; Wrolstad, R. E. (2003) Anthocyanin pigment and total phenolic content of three *Vaccinium* species native to the Pacific Northwest of North America. *HortScience*, *5*, 959-964.
[35] Foo L. Y., Lu Y., Howell A. B. and Vorsa N. (2000),, *Phytochemistry,* 54, 173-181.

[36] Vvedenskaya I. O., Rosen R. T., Guido J. E., Russell D. J., Mills K. A. and Vorsa N. (2004) *J. Agri. Food Chem.,* 52(2), 188-195.
[37] Sobota A. (1984) *J. Urol.,* 131(5), 1013-1016.
[38] Ofek I., Goldhar G., Zafriri D., N. (1991) *Engl. J. Med.*, 324, 1599.
[39] Foxman B., Geiger A. M., Palin K. (1995) *Epidemiology*, 6(2), 162-168.
[40] a) http://www.furtherhealth.com/article/54_1_The-Cranberry/.
b) http://www.furtherhealth.com/article/54_2_Cranberry-Facts/.
c) http://www.furtherhealth.com/article/54_3_Benefits-of-Cranberries/.
[41] http://www.altmd.com/Articles/Cranberry--Encyclopedia-of-Alternative-Medicine
[42] Davies J.R. (2000), *Healing Herbs-In a Nutshell: CRAN BERRY*.Boston:Element Books, Inc.
[43] Fetrow C. W. and Juan R. A. (2000) *The Complete Guide to Herbal Medicines*. Springhouse, PA: Springhouse Corporation.
[44] McCaleb R., Evelyn L. and Krista M. (2000) *The Encyclopedia of Popular Herbs: Your Complete Guide to the Leading Medicinal Plants*. Rocklin, CA: Prima Health.
[45] Murray M. and Joseph P. (1998) *Encyclopedia of Natural Medicine*. Rocklin, CA: Prima Health.
[46] Avorn J., Monane M., Gurwitz J.H., et al. (1994) Reduction of Bacteriuria and Pyuria after Ingestion of Cranberry Juice. *J. of the American Medical Association,* 271, 751-4.
[47] Jepson R., Mihaljevic L. and Craig J.,(2004) Cranberries for preventing urinary tract infection. *Cochrane Database Syst Rev*.
[48] Patel, D.A., B. Gillespie, J.D. Sobel, et al. (2004) Risk factors for recurrent vulvovaginal candidiasis in women receiving maintenance antifungal therapy: Results of a prospective cohort study,*American Journal of Obstetrics and Gynecology*, 644–53.
[49] Weiss, E.I., A. Kozlovsky, D. Steinberg, R., et al. (2004) A high molecular mass cranberry constituent reduces mutans streptococci level in saliva and inhibits in vitro adhesion to hydroxyapatite. *FEMS Microbiol Lett*, 89–92.
[50] Schlager T. A., Anderson S., Trudell J. K. (1999) *J. Pediatric*, 135(6), 698-702.
[51] Fanos V., Atzei A., Zaffanello M., Piras A. and Cataldi L. (2006) *J. Chemoth.,*18(3), 21-24.
[52] Johnson-White B., Buquo L., Zeinali M., Ligler F. S. (2006) *Analy. Chem.,* 78(3), 853-857.
[53] Bertran G. (2001) *Basic & Clinical Pharmacology,* 8th Ed., pp. 771, 757, 765, 796, 798, 800, 808, 810 and 846.



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Complicated urinary tract infections (cUTIs) are a major cause of hospital admissions and are associated with significant morbidity and health care costs. Knowledge of baseline risk of urinary tract infection can help clinicians make informed diagnostic and therapeutic decisions. Prevalence rates of UTI vary by age, gender, race, and other predisposing risk factors. In this regard, this book provides comprehensive information on etiology, epidemiology, immunology, pathology, pathogenic mechanisms, symptomatology, investigation and management of urinary tract infection. Chapters cover common problems in urinary tract infection and put emphasis on the importance of making a correct clinical decision and choosing the appropriate therapeutic approach. Topics are organized to address all of the major complicated conditions frequently seen in urinary tract infection. The authors have paid particular attention to urological problems like the outcome of patients with vesicoureteric reflux, the factors affecting renal scarring, obstructive uropathy, voiding dysfunction and catheter associated problems. This book will be indispensable for all professionals involved in the medical care of patients with urinary tract infection.

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