



OCCURRENCE OF PHYTOCHEMICALS IN CRANBERRY (*VACCINIUM MACROCARPON* AIT.) FOR ALL-ROUND WELLNESS

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ABSTRACT

The medicinal value of cranberry has a long history of use by Americans. It has been used to cure of many diseases like Urinary Tract Infections (UTIs), used as antioxidant, anticancer, antitumor and anti-inflammatory herbal medicine. Cranberry belongs to family Ericaceae contains various types of bioactive chemicals, mostly polyphenols, including anthocyanins, flavonols, and phenolic acids which are linked to reducing incidence of certain infections, promoting heart health, protecting the urinary tract infection, decreasing inflammation associated with anti-aging property and support digestive health. In addition, laboratory studies have shown that cranberry extract reduces oxidation of LDL-cholesterol (so-called "bad" cholesterol), an effect which indicates is important in maintaining a healthy heart. Cranberries are among few foods that contain A-type proanthocyanidins. Unlike B-type proanthocyanidins, A-type proanthocyanidins have an additional ether interflavan bond between C2→O→C7. It was suggested that A-type proanthocyanidins have greater bioactivity compared to B-type. Cranberry bioactives have unique characteristics and researches are being pursued to establish correlations between cranberries' health benefits and specific compounds that contains. The most well known health benefit of cranberries is the prevention of urinary tract infections.

KEYWORDS: Cranberry, Bioactive Chemicals, UTIs, Polyphenols and Phenolic acids.

INTRODUCTION

Cranberry, originally native of America, are currently grown throughout the east and northeast parts of United States and much of Canada (Der Marderosian et al., 2008). The plant is actually a shrub or vine and bears small evergreen leaves. Cranberry (Botanical Name: *Vaccinium macrocarpon* Ait.) belongs to family Ericaceae, is loaded with vitamin C and fiber, rich in bioactive chemicals which are essential for all-round wellness (Figure 1 and 2), and also contain various chemical substances that may offer protection from tooth cavities, urinary tract infection, and inflammatory diseases. Americans used it in the preservation of meat and also as phyto-medicine (Foo et al., 2000; Guay, 2009). It contains 80 % water carbohydrate 10 % and 10 % organic chemicals like flavonoids, antho-cyanins, catechin and other organic acid (Lenter, 1991).

Emerging epidemiological evidence is increasingly pointing to the beneficial effects of fruits and vegetables in managing chronic infectious diseases. These beneficial effects are now suggested to be due to the constituent phenolic phytochemicals having antioxidant activity. Cranberry like other fruits is also rich in phenolic phytochemicals such as phenolic acids, flavonoids and ellagic acid. Reports showed that cranberries were used

to treat urinary tract infections by the Native Americans (Foo et al., 2000; Guay, 2009; Howell et al., 2010). They were consumed as a food and used for wound and blood-poisoning treatment. Research on the health benefits of cranberries started in the 1980s but intensified quickly in the last 25 years. Besides fruits, cranberry leaves were also used for urinary disorders, diarrhea and diabetes. The extract of cranberry has been used in formulation of capsules and dietary supplement (Guay, 2009; Jepson and Craig, 2007; Raz et al., 2004 and Sherwani et al., 2014).



Figure 1: Plant of cranberry.



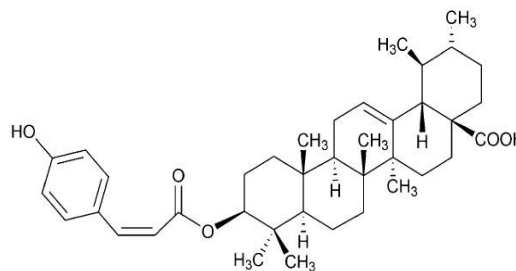
Figure 2: Fruits of cranberry.

Consumption of cranberry has been historically been linked to lower incidences of urinary tract infections and has now been shown to have a capacity to inhibit peptic ulcer-associated bacterium, *Helicobacter pylori*. Isolated compounds from cranberry have also been shown to reduce the risk of cardiovascular diseases. Recent evidence suggests the ability of phytochemical components in whole foods in being more effective in protectively supporting human health than compared to isolated individual phenolic phytochemicals. This implies that the profile of phenolic phytochemicals determines the functionality of the whole food as a result of synergistic interaction of constituent phenolic phytochemicals. Solid state bioprocessing using food grade fungi common in Asian food cultures as well as cranberry phenolic synergies through the addition of functional biphenyls such as ellagic acid and rosmarinic acid along with processed fruit extracts have helped to advance these concepts. These strategies could be further explored to enrich cranberry and cranberry products with functional phytochemicals and further improve their functionality for enhancing health benefits.

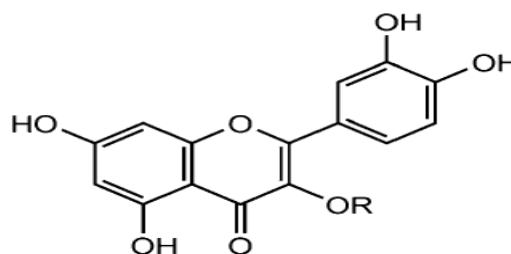
Chemical analysis

Several groups of phytochemicals have been identified in fruits of *Vaccinium* sp. That includes 3 classes of flavonoids (Flavonols, anthocyanins and proanthocyanidins), catechin's quercetin, myricetin monoglycosides, cyaniding and peonidin etc. (Neto, 2007) hydroxycinnamic acids and other phenolic acids triterpenoids the other compounds are organic acids are ascorbic acids, citric acid, malic acid, quinic acid, benzoic acid, ellagic acid and glucuronic acids (Torres et al., 1987; Bagchi et al., 2004; Neto, 2011, Blumberg et al., 2013).

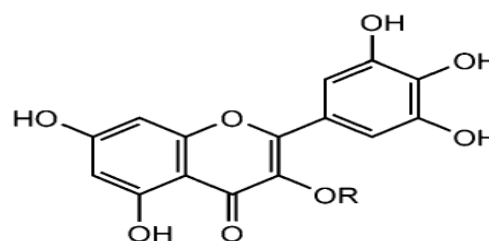
Chemical Structures of some Bioactive Compounds from Fruits of Cranberry (Neto, 2007, Blumberg et al., 2013)



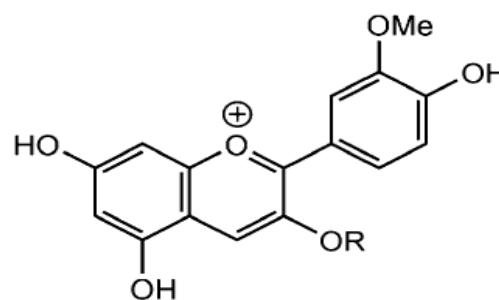
Cis-hydroxycinnamoyl ester of ursolic acid from cranberry fruit.



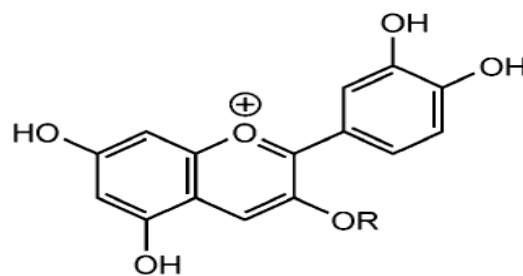
Quercetin



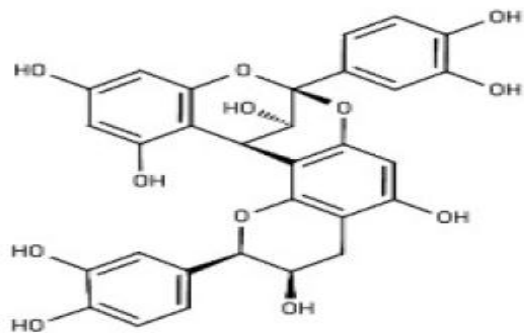
Myricetin



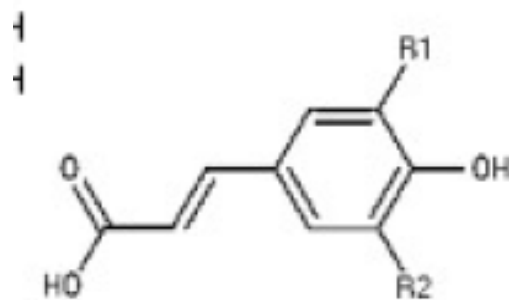
Peonidin



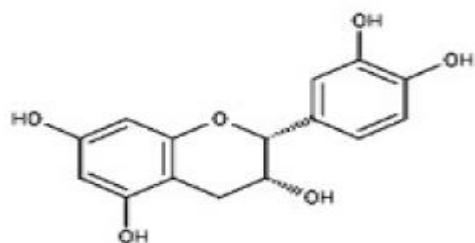
Cyanidin



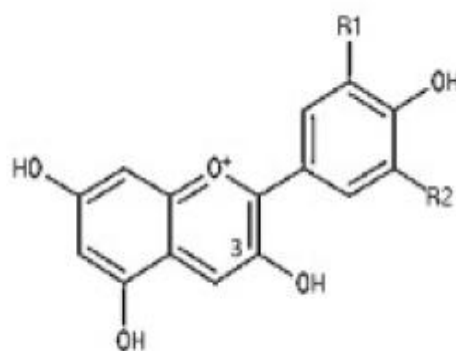
Procyanidin A2



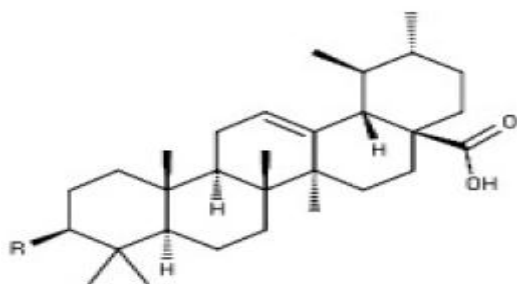
Hydroxycinnamic acids



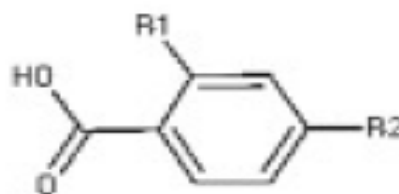
Flavan-3-ols



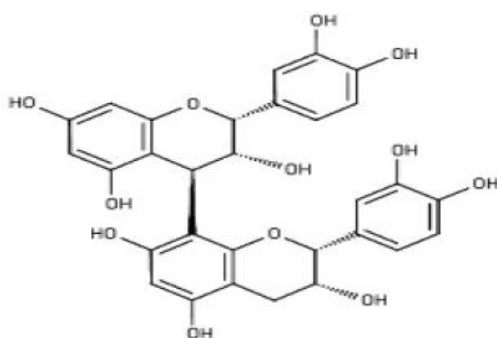
Anthocyanidins



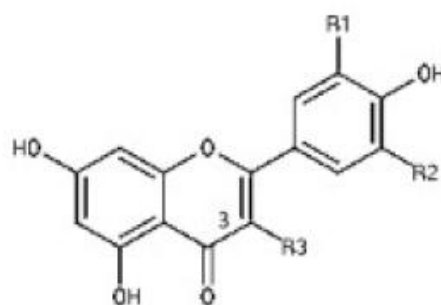
Terpenes



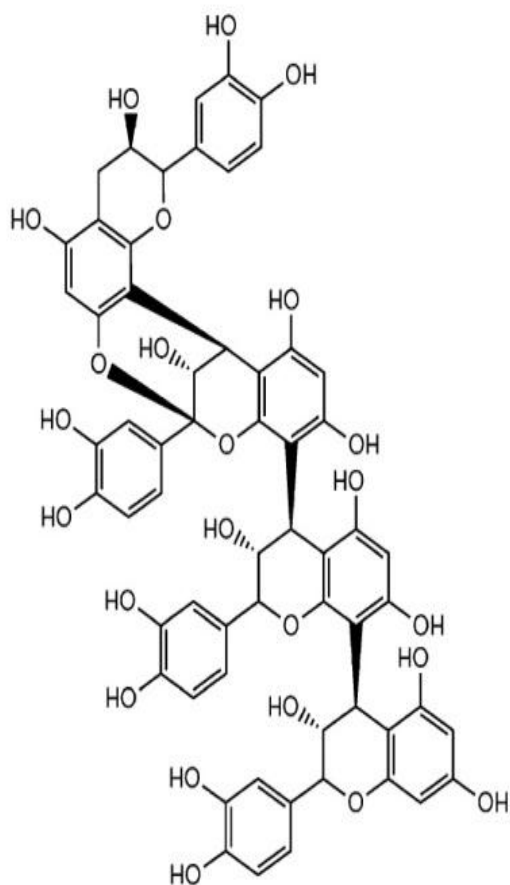
Hydroxybenzoic acids



Procyanidin B2



Flavonols



Structure of a typical cranberry proanthocyanidin tetramer composed of epicatechin units with one A-type linkage (Neto, 2007, Blumberg et al., 2013).

Health benefits

Health-promoting properties of cranberries have been based on folkloric remedies, which have existed since centuries. Cranberries contain a myriad of antioxidants in the form of polyphenolic compounds (found in abundance in most veggies and fruit, especially ones with deep red and purple hue) which, when metabolized, form new bioactive compounds that may help with gastrointestinal health and immunity overall. As a fruit, cranberries also provide prebiotic fiber, which provides fuel to body's probiotics, beneficial bacteria found in GI tract (and other tissue lining) called microbiome, the layer that serves as the first line of defense to your immune system. Additionally, cranberries may help reduce risk of chronic disease by reducing oxidative stress by way of chronic inflammation. Cranberries are high in vitamin K, a nutrient that helps regulate blood clotting. Cranberry is perhaps best known for its role in preventing UTIs. The high level of proanthocyanidins in cranberries helps lower the adhesion of certain bacteria to the urinary-tract walls, in turn fighting off infections. The antioxidant and anti-inflammatory compounds present in cranberries may improve memory and coordination. Research has shown that cranberries are beneficial in slowing tumor progression and have shown

positive effects against prostate, liver, breast, ovarian and colon cancers. The proanthocyanidins present in cranberries may benefit oral health by preventing gum disease and bacteria from binding to the teeth. The polyphenols present in cranberries may also reduce the risk of cardiovascular disease by preventing platelet build-up and reducing blood pressure.

Anti-microbial property

As the cranberry contain high amount of phenolic, essential oils, alkaloids, phenols, glycosides, coumarins and tannins, thereby it have strong antimicrobial activity against human pathogens (Eschenbecher and Josh 1977). Antimicrobial properties of cranberry are more promising due to the presence of organic compound like citric acid, quinic acid and malic acid. According to Aref et al., 1986 the prevalence of proanthocyanidins and flavonols in cranberry confirmed its major antimicrobial effect than benzoic acids. The extract of cranberry shows significant antimicrobial activity against *Saccharomyces bayanus* and *Pseudomonas fluorescen* (Aref and Nagel, 2006).

Wen et al. (2003) demonstrated that the antibacterial potential of cranberry is due to phenolic acids. The ellagitannins extracted from cranberries strongly inhibited microbes but fail to inhibit *Styphnirium* (Puupponen et al. 2005). The research of Wu et al. (2008) reported that cranberry showed significant antimicrobial power on *Styphnirium* and *E. coli*.

The extract of cranberry juice significantly effective to the strains of *Helicobacter pylori*, which is one of the contributing causes of gastric cancer and peptic ulcer disease (Gotteland et al 2008, Zhang et al 2005). The bioactive compounds of cranberry juice protect the gastric cancer and peptic ulcer by means of reducing the adhesion ability of *Helicobacter pylori* to human gastric epithelial cells (Burger et al 2002).

The oral health benefits of cranberries cannot be neglected as the extract of berries found effective against oral bacteria like *Streptococcus mutans* which is the important acidogenic bacteria in the mouth and responsible for teeth decay. Cranberry may also suggest reducing gingival or gumming tissues infections, which could protect against periodontitis (Bodet et al 2007).

In urinary tract infection

Urinary tract infections (UTIs) are most common infection in the human beings. This infection is critically occurring when bacteria are present in the urine (normally 10⁴ to 10⁵ CFU per ml) (Bacheller and Bernstein 1997). An epidemiologically survey reported that 80% of UTIs are caused by *Escherichia coli*, and in 10-15% cases it is caused by *Staphylococcus saprophyticus*. Sometime other pathogens include *Enterococci*, *Enterobacter*, *Klebsiella* and *Proteus* species are also contributing in the occurrence of infection (Kahlmeter and Brown 2002). It is more common in

adult females than male. Approximately more than One fourth of women population experiences this infection once or more in their lives, the probabilities of UTIs increases with age (Harkins, 2000; Lynch, 2004; Sherwani et al., 2014).

The juice of Cranberry has long been used for the treatment of urinary tract infections (Blatherwickz 1914). The working mechanism of cranberry is to maintain the health of Urinary tract by lowering its pH by secretion of hippuric acid, which is a bacteriostatic in nature and has the ability to acidify urine (Moen 1962). The other manner of action of cranberry extract for the prevention of urinary tract infection is a presence of important compound known as (PAC), influence the adherence ability of pathogenic *Escherichia coli* (Howell 2002, Sobota, 1984, Avon 1969, Fleet 1994, Ahuja et al 1998, Pinzon et al 2009, DI Martino 2006, Lavigne et al 2008) on the epithelium of the bladder, which thereby effect *E. coli* to infect the urinary mucous (Howell et al 2010, Howell & Foxman 2008, Jepson 2008).

As anticancer agent

Many scientists suggest that the extracts of cranberry juice have anticancer activity (Bomser et al., 1996; Kresty et al., 2011; Neto, 2007 and Blumberg et al., 2013). There are many cell culture and animal modular experiment proved anticancer effect of cranberry. In vitro studies show that cranberry extract decrease the proliferation of many forms of cancer including, breast, colon, prostate and lung (Neto 2007, 2008, Roy et al 2002; Yan et al., 2002). The Cranberry fight against cancer cell through different mechanisms, such as by retarded or inhibits the enzymes that actively take part in the tumour formation and also suppress the inflammation and cancer propagation enzyme, it's also inducing programmed apoptosis (Neto et al., 2008).

Antioxidant properties

Cranberries have a high profile of phytochemical compounds and have a highest position among all the fruit in both antioxidant quality and quantity analysis (Vinson et al 2001). It is a plentiful source of many flavonoids and phenolic acid (Yan et al. 2002), includes 3 classes of flavonoids (flavonols, proanthocyanidins and anthocyanins), hydroxycinnamic catechins, and other phenolic acids, and triterpenoids (Neto 2007). According to the study report of Yan et al. (2002) the antioxidant activity of cranberry extract was majorly associated with flavonols glycosides then the Vitamin E. This antioxidant activity devoted to the antitumor activity of cranberry (Neto 2007).

Maintain cardiovascular health

There are many reports that the consumption food containing flavonoid can lower the risk cardiovascular disease (CVD) (Erdman et al 2007, Dohadwala and Vita 2009). Investigation of many scientists reveals that the cranberries are a significant source of dietary fiber, contain flavonoids, polyphenolics and anthocyanins

(Milbury et al 2010, Vinson et al 2001, McKay and Blumberg 2013), hence its consumption are beneficial for the heart health and reduce the chances of cardiovascular disease by reducing inflammation and serum lipids (Vattem et al 2005, Ruel and Couillard 2007). Granting to the study of Krueger et al (2000), Reed (2002), Ruel et al (2008), Erlund et al (2008), T. Porari (1998) flavonoids and constituted significantly inhibit low density lipoprotein (LDL) oxidation, affect the function of platelets, increase reverse cholesterol transport and decrease total LDL-cholesterol and thereby, reduce the risk of coronary artery disease.

As Anti-inflammatory action

It is experimentally evident that cranberry possesses anti-inflammatory property due to presence of several important phytochemicals in the fruits. A study revealed anti-inflammatory action is due to the inhibition of lipopolysaccharides induced inflammatory response produced by pathogenic bacteria during infection. Evidence presented that cranberry polyphenolics inhibit expression of lipopolysaccharide induced production of inflammatory cytokines IL-1B, IL-6, IL-8 and TNF-2 (Neto, 2007).

As culinary Uses and Cosmetics benefits

Cranberries may be tangy and delicious, but don't believe they are just a pretty plant. Cranberries are loaded with health benefits that stretch through the whole human body, and researchers are certain that the extent of their benefits are growing as more and more research is conducted. Cranberries were recognized by 2013 Dietary Guidelines for Americans as a nutrient-dense fruit. Just an 8-ounce glass of cranberry juice cocktail contains 137% of the daily value of vitamin C. Perfect as a snack or a main dish, cranberries are a low-key nutrient powerhouse. A cup of this festive fruit contains just four grams of naturally occurring sugar per one whole cup of fruit.

With just 50 calories and only 4 grams of sugar per cup, these berries are low in calories *and* sugar, especially when compared to other fruits. The berry itself is tiny and very acidic in taste with a pH ranging from 3 to 5. Fresh or frozen are typically best when it comes to almost any fruit or veggie. That's because the drying process concentrates the sugar contained within the fruit or veg itself, increasing the sugar content overall while diminishing the water and fiber content. Cranberries are even more sugary than most, thanks to their naturally tart flavor — because they're often sour to taste, they're almost never dried without *any* added sugar, though one can find brands making versions with sugar substitutes. A standard serving (1/4 cup) packs about 20 grams per serving.

The processing of cranberries also reduces the antioxidant content as well as the fiber content of the fruit, so one is better off using these for flavor than for any perceived health benefit. There are a bunch of other

health benefits of eating cranberries. One cup has roughly 4 grams of fiber, loads of antioxidants (including vitamins A and E), and is a good source of vitamin C, a crucial antioxidant to protect cells from damage and to boost collagen production, helping with wound healing and skin integrity. While all foods high in antioxidants help to improve blood flow through blood vessels (therefore lowering blood pressure over time), protect cells from harmful damage (reducing risk of inflammation or from tumor growth), and reduce the risk of cholesterol buildup in arteries, they're a great choice to include as part of an overall healthful diet. Skip dried cranberries and opt for fresh or frozen to reap all the nutrition. Snack on dried cranberries daily make a person wise and healthy.

“Cranberry juice has an emulsifying effect on the fats deposited in the body which in turn help with weight loss. Since it is loaded with fiber, it also helps one stay full for longer. Cranberries help nourish the skin and make it more supple. You can blend quarter cup of honey with two tablespoons of dried cranberries and quarter tablespoon of essential oil and apply it to your skin for 10 minutes for improved results.

According to a study published in the *British Journal of Nutrition*, people who drink a glass of unsweetened cranberry juice a day have increased levels of HDL cholesterol i.e. good cholesterol by about 10%. One can reap the benefits by sneaking cranberries into oatmeal chocolate chip cookies, muffins or sprinkling a handful of cranberries on your salad or even your go-to morning cereal. The superfood also pairs beautifully with pork and chicken dishes. Current research indicates that approximately 10 ounces of cranberry juice cocktail is needed daily to achieve the bacteria-blocking benefits that ward off UTIs, ulcers and gum disease. . In addition, laboratory studies have shown that cranberry extract reduces oxidation of LDL-cholesterol (so-called “bad” cholesterol), an effect which research indicates may be important in maintaining a healthy heart. Thus, when consumed as part of a well-balanced diet containing a variety of foods, cranberries may provide positive health benefits (Blumberg et al., 2013; Zhao et al., 2018; Onyeneho and Hettiarachchy, 1993 and Kris-Etherton et al., 2002).

CONCLUSION

Cranberries are among a few foods that contain A-type proanthocyanidins. The most well known health benefit of cranberries is the prevention of urinary tract infections (UTIs). Since the turn of the century, cranberries have been used as a folk remedy for the treatment of bacterial urinary tract infections (UTIs), which cause frequent and painful urination. These condensed tannins or proanthocyanidins from the cranberry fruit prevent *Escherichia coli* (*E.coli*), the primary bacteria responsible for UTIs, from attaching to cells in the urinary tract. Thus, the bacteria are flushed from the tract

rather than being allowed to adhere, grow and lead to infection. Polyphenols of cranberries may interact with other bioactive compounds in cranberries that could protect the gut microbiota, and provide antioxidant and anti-inflammatory functions that benefit the cardiovascular system, metabolism, and immune function. This interaction may help strengthen the gut to protect against infection.

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REFERENCES

1. Sikandar Khan Sherwani, Asia Neelam, Tasveer Zahra Bokahri, Omm-e-Hany, Rana Kausar and Shanana U. Kazmi MEDICINAL VALUE OF VACCINIUM MACROCARPON (CRANBERRY): A MINI REVIEW, *World Journal of Pharmaceutical Research*, 2014; 3(6): 71-79.
2. Ahuja, S., Kaack, B. and Roberts, J. Loss of fimbrial adhesion with the addition of *Vaccinium macrocarpon* to the growth medium of P-fimbriated *Escherichia coli*. *J Urol*, 1998; 159(2): 559-62.
3. Aref, G.M. and Charles, W N. Microbial inhibitors of cranberries. *J Food Sci.* 1986; 51: 1009 -1013.
4. Aref, G.M. and Nagel, C.W. Characterization of cranberry benzoates and their antimicrobial properties. *J. Food Sci.*, 2006; 51(4): 1069-1070.
5. Avorn, J. The effect of cranberry juice on the presence of bacteria and white blood cells in the urine of elderly women. What is the role of bacterial adhesion? *Adv Exp Med Biol*, 1996; 408: 185-6.
6. Bagchi D, Sen CK, Bagchi M, Atalay M. Anti-angiogenic, antioxidant, and anti-carcinogenic properties of a novel anthocyanin-rich berry extract formula. *Biochemistry (Mosc)*, 2004; 69(1): 75-80.
7. Bacheller, C.D. and J.M. Bernstein Urinary tract infections. *Med Clin North Am*, 1997; 81(3): 719-30.
8. Blatherwick, N., The specific role of foods in relation to the composition of the urine. *Arch. Int. Med*, XIV, 1914; (3): 409-450.
9. Bodet C, Chandad F, Grenier D Cranberry components inhibit interleukin-6, interleukin-8, and prostaglandin E production by lipopolysaccharide-activated gingival fibroblasts. *Eur J Oral Sci*, 2007; 115(1): 64-70.
10. Burger O, Weiss E, Sharon N, Tabak M, Neeman I, Ofek I (2002) “Inhibition of *Helicobacter pylori* adhesion to human gastric mucus by a high-molecular-weight constituent of cranberry juice” *Crit Rev Food Sci Nutr*, 2002; 42(3): 279-84.
11. Catherine C. Neto Cranberry and Its Phytochemicals: A Review of In Vitro Anticancer Studies, *The Journal of Nutrition International Research Conference on Food, Nutrition, and Cancer*, 2007; 186S-193s.

12. Cunningham, D. G., Varmozzi, S. A., Turk, R., Roderick, R., O'Shea, E., & Brilliant, K. Cranberry phytochemicals and their beneficial health benefits. In: Shahidi, F., Weerasinghe, D.W., *Nutraceutical, Beverages, Chemistry, Nutrition, and Health Effects*. ACS, Washington, DC, 2004; 35-51.
13. DerMarderosian A, Beutler JA (2008). *The review of natural products*, 2nd ed. St. Louis: Facts and Comparisons, 2002.
14. Eschenbecher, F., & Josh, P. Research on the inhibitors in cranberries. *Acta Hort*, 1977; 61: 255.
15. Fleet JC. New support for a folk remedy: cranberry juice reduces bacteriuria and pyuria in elderly women. *Nutr Rev*, 1994; 52(5): 168-70.
16. Foo et al. (2000). A-type proanthocyanidin trimers from cranberry that inhibit adherence of uropathogenic P-fimbriated *Escherichia coli*. *American Chemical Society, J. Nat. Prod*, 2000; 63(9): 1225-1228.
17. Gotteland M, Andrews M, Toledo M, Munoz L, Caceres P, Anziani A, Wittig E, Speisky H, Salazar G. Modulation of *Helicobacter pylori* colonization with cranberry juice and *Lactobacillus johnsonii* Lal in children. *Nutrition*, 2008; 24(5): 421-426.
18. Guay, D. R. P. Cranberry and urinary tract infections. *Drugs*, 69, 775. Harkins KJ (2000) what's the use of cranberry juice? *Age and Ageing*, 2009; 29: 9- 12.
19. Howell AB, Botto H, Combescure C, Blanc-Potard A-B, Gausa L, Matsumoto T, Tenke P, Sotto A, Lavigne JP. Dosage effect on uropathogenic *Escherichia coli* anti-adhesion activity in urine following consumption of cranberry powder standardized for proanthocyanidin content: a multicentric randomized double blind study. *BMC Infect Dis*, 2010; 10: 94.
20. Howell AB. Cranberry proanthocyanidins and the maintenance of urinary tract health. *Crit Rev Food Sci Nutr* 2002; 42(3): 273-8.
21. Howell AB. Bioactive compounds in cranberries and their role in prevention of urinary tract infections. *Mol Nutr Food Res*, 2007; 51: 732-7.
22. Jepson RG, Craig JC. A systematic review of the evidence for cranberries and blue berries in UTI prevention. *Mol Nutr Food Res*, 2007; 51: 738-45.
23. Jeffrey B, Blumberg, Terri A, Camesano, Aedin Cassidy, Penny Kris-Etherton, Amy Howell, Claudine Manach, Luisa M. Ostertag, Helmut Sies, Ann Skulas-Ray, and Joseph A. Vita (2013). Cranberries and Their Bioactive Constituents in Human Health, *Adv Nutr*, 2013; 4(6): 618-632, doi: 10.3945/an.113.004473
24. Jepson RG, Craig JC. Cranberries for preventing urinary tract infections. *Cochrane Database Syst Rev*, 2008; (1): CD001321.
25. Kahlmeter, G. and D.F. Brown, Resistance surveillance studies--comparability of results and quality assurance of methods. *J Antimicrob Chemother*, 2002; 50(6): 775-7.
26. Krenn L, Steitz M, Schlicht C, Kurth H, Gaedcke F Anthocyanin- and proanthocyanidin-rich extracts of berries in food supplements - analysis with problems. *Pharmazie*, 2007; 62: 803-12.
27. Lavigne JP, Bourg G, Combescure C, Botto H, Sotto A. In-vitro and in-vivo evidence of dose-dependent decrease of uropathogenic *Escherichia coli* virulence after consumption of commercial *Vaccinium macrocarpon* (cranberry) capsules. *Clin Microbiol Infect*, 2008; 14(4): 350-355.
28. Lenter C Geigy scientific tables. 8th ed. West Caldwell, NJ: CIBA Geigy, 1991.
29. Lynch DM Cranberry for prevention of urinary tract infections. *Am. Fam. Phys*, 2004; 70: 2175-2177.
30. Moen DV. Observations on the effectiveness of cranberry juice in urinary infections. *Wisconsin Med J*, 1962; 61: 282-3
31. Neto, C. C. Cranberry and its phytochemicals: A review of in vitro anticancer studies. *J Nutr*, 2007; 137: 186-193.
32. Papas PN, Brusca CA, Ceresia GC. Cranberry juice in the treatment of urinary tract infections. *Southwest Med*, 1966; 47: 17-20.
33. Pinzon-Arango PA, Liu Y, Camesano TA. Role of cranberry on bacterial adhesion force and implications for *Escherichia coli*-uroepithelial cell attachment. *J Med Food*, 2009; 12(2): 259-270.
34. Puupponen-Pimia, R., Nohynek, L., Meier, C., Kahkonen, M., Heinonen, M., Hopia, A., & Oksman Candente, K. M. Antimicrobial properties of phenolic compounds from berries. *J Appl. Microbiol*, 2001; 90: 494-507.
35. Raz R, Chazan B, Dan M Cranberry Juice and Urinary infections. *Clin. Inf. Dis*, 2004; 38: 1413-1419.
36. Sobota, A.E. Inhibition of bacterial adherence by cranberry juice: potential use for the treatment of urinary tract infection. *J Urol*, 1984; 131(5): 1013-6.
37. Vatter, D.A., Ghaedian, R. and Shetty, K. Enhancing health benefits of berries through phenolic antioxidant enrichment: focus on cranberry. *Asia Pac J Clin Nutr*, 2005; 14: 120-30.
38. Vatter, D.A. and Shetty, K. Functional phytochemicals from cranberries: Their mechanism of action and strategies to improve functionality. In: *Food biotechnology*, 2nd Edition [Shetty, K., Paliyath, G., Pometto, A.L. III and Levin, R.E. (eds)]. Boca Raton, FA: CRC Press, 2005; 789-823.
39. Wen, A., Pasacal, D., Stanich, K. and Toivonen, P. Antilisterial activity of selected phenolic acids. *Food Microbiol*, 2003; 20: 305-311.
40. Wu, V.C.H., Qiu, X., Reyes, B.G., Lin, Y. and Pan, Y. Application of cranberry concentrate (*Vaccinium macrocarpon*) to control *Escherichia coli* O157: H7 in ground beef and its antimicrobial mechanism related to the down regulated sip, hde A and cfa. *Food Microbiol*, 2009; 1-7. doi: 10.1016/j.fm.2008
41. Zhang, L., Ma, J., Pan, K., Go, V.L., Chen, J. and You, W.C. Efficacy of cranberry juice on *Helicobacter pylori* infection: a double-blind,

- randomized placebo-controlled trial. *Helicobacter*, 2005; 10(2): 139-45.
42. Onyeneho, S.N. and Hettiarachchy, N.S. Antioxidant activity, fatty acids and phenolic acids compositions of potato peels. *J Sci Food Agric*; 1993; 62: 345-50.
 43. Kris-Etherton, P.M., Hecker, K.D., Bonanome, A., Coval, S.M., Binkoski, A.E., Hilpert, K.F., Griel, A.E. and Etherton, T.D. Bioactive compounds in foods: their role in the prevention of cardiovascular disease and cancer. *Am J Med*, 2002; 30: 113 9B: 71S-88S.
 44. Shaomin Zhao, Haiyan Liu and Liwei Gu American Cranberries and Health Benefits - an Evolving Story of 25 years, 2018 *Journal of the Science of Food and Agriculture*, 2018. DOI: 10.1002/jsfa.8882
 45. Bomser, J., Madhavi, D.L., Singletary, K. and Smith, M.A. In vitro anticancer activity of fruit extracts from *Vaccinium* species. *Planta Med*, 1996; 62: 212-6.
 46. Dohadwala, M.M. and Vita, J.A. Grapes and cardiovascular disease. *J Nutr*, 2009; 139: 1788S-93S.
 47. Erdman, J.W. Jr, Balentine, D., Arab, L., et al. Flavonoids and heart health: Proceedings of the ILSI North America Flavonoids Workshop, May31-June 1, 2005, Washington, DC. *J Nutr*, 2007; 137: 718S-37S.
 48. Erlund, I., Koli, R., et al. Favorable effects of berry consumption on platelet function, blood pressure, and HDL Cholesterol. *Am J Clin Nutr*, 2008; 87: 323-31.
 49. Harkins, K.J. What's the use of cranberry juice? Age and Ageing, 2000; 29: 9- 12.
 50. Kresty, L.A., Howell, A.B. and Baird, M. Cranberry proanthocyanidins mediate growth arrest of lung cancer cells through modulation of gene expression and rapid induction of apoptosis. *Molecules*, 2011; 16: 2375-90.
 51. Krueger, C.G., Porter, M.L., Weibe, D.A., Cunningham, D.G. and Reed, J.D. Potential of cranberry flavonoids in the prevention of copper-induced LDL oxidation. *Polyphenols Communications*, 2000; 447-448.
 52. Milbury PE, Vita JA, Blumberg JB. Anthocyanins are bioavailable in humans following an acute dose of cranberry juice. *J Nutr*, 2010; 140: 1099-104.
 53. Reed, J. Cranberry flavonoids, atherosclerosis, and cardiovascular health. *Crit Rev Food Sci Nutr*, 2002; 42: 301-316.
 54. Roy, S., Khanna, S., Alessio, H.M., Vider, J., Bagchi, D., Bagchi, M. and Sen, C.K. Anti-angiogenic property of edible berries. *Free Radic Res*, 2002; 36(9): 1023-31.
 55. Ruel, G. and Couillard, C. Evidences of the cardioprotective potential of fruits: the case of cranberries. *Mol Nutr Food Res*, 2007; 51: 692-701.
 56. Ruel, G., Pomerleau, S., et al. Low-calorie cranberry juice supplementation reduces plasma oxidized LDL and cell adhesion molecule concentrations in men. *British Journal of Nutrition*, 2008; 99(2): 352-359.
 57. Porcari, T., J.P. and Harbin, D. Cranberry extract inhibits low-density lipoprotein oxidation. *Life Sciences*, 1998; 62(24): 381-386.
 58. Torres AM, Mau-Lastovicka T, Rezaaiyan R. Total phenolics and high-performance liquid chromatography of phenolic acids of avocado. *J Agric Food Chem*, 1987; 35: 921-925.
 59. Vinson, J.A., Su, X., Zubik, L. and Bose, P. Phenol antioxidant quantity and quality in foods: *Fruits. J. Agric. Food Chem*, 2001; 49: 5315-21.
 60. Yan, X., Murphy, B.T., Hammond, G.B., Vinson, J.A. and Neto, C.C. Antioxidant activities and antitumor screening of extracts from cranberry fruit (*Vaccinium macrocarpon*). *J Agric. Food Chem*, 2002; 50: 5844-5849.