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Cranberry and its Antibacterial Activity - A Review

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The name cranberry is derived from craneberry, first named by early European settlers in America because of their resemblance to head neck and bill of crane. It is widespread throughout the cool temperate northern hemisphere, including northern Europe, northern Asia and northern North America. It is a dwarf shrub and there are four species. Cranberry is used as fresh fruit, juice, sauce and also as medicine. It contains polyphenols, vitamins, proteins, flavonoids and other rare phytochemicals. It has antimicrobial, anti inflammatory and anti tumour activities. Cranberry plantation is traditionally done in certain colder countries at high altitude. But in current global marketing strategy, cranberry products experimentally proving the benefits of cranberry will benefit the needy population. This review is made with an intension to highlight the beneficial effects of extracts of cranberry fruit.

BOTANICAL NAME:

Kingdom	: plantae
Unranked	: Angiosperms
Unranked	: Eudicots
Unranked	: Asterids
Order	: Ericales
Family	: Ericaceae
Genus	: Vaccinium
Subgenus	: Oxycoccus
Species	: Vaccinium macrocarpon

GENERAL INFORMATION:

Cranberry is one of the native fruit of North America. Cranberry can grow on wild conditions. In Eastern India cranberries were called as "sassamanesh", in South Jersey and Leni-Lenape they are referred to as "ibimi" and in Algonquins and Wisconsins they are called as "atoqua". The name cranberry was given by early German and Dutch as it's flower resembled the head and bill of the crane. In ancient times the berry was used in poultices to draw poison from arrow wounds. The red juice of cranberry was also used as dyes. Hence it was known as the "wonder fruit".

DESCRIPTION:

Cranberry is a evergreen ground cover native plant of North America. They are shrubs which grows about four metres having dark pink coloured flowers having purle spike centrally and also bears reddish black berries. The stem appears grey. Root of cranberry grows upto 4 to 6 inches below the soil and does not have rootlets and depend on mycorrhizal association to absorb its needed nutrients. They are also called as "bounceberries" as the ripe fruits have the capacity to bounce.

HABITAT:

Cranberry belongs to North America, Canada and United States. They are cultivated as commercial crops in United States, Wisconsin, New Jersey, Oregon, Washington, British Columbia, Prince Edward Island, Newfoundland etc. British Columbia and Wisconsin are the leading producers. It is also cultivated in Argentina, Netherlands and Chile. It is also cultivated in Argentina, Netherlands and Chile. They are planted during October, early November and between April to May.

CULTIVATION:

At first the berries were picked by hand. Later they found out a better technique for harvesting namely dry harvesting technique. A bit of changes was done to this method to give better results and was known as wet or water harvesting method. Most of the cranberries today are cultivated by Water Bog method or by water harvesting. Water harvesting is the process in which the cranberries are cultivated in bogs and floated in water. This is done for the convenience of the cultivator. The extent of the berries exposed to direct sunlight is directly proportional to the amount of anthocyanins present in the cranberries.

METHODS OF EXTRACTION:

- 1. Polyphenols from cranberry pomace is extracted using aqueous ethanol
- 2. By drying cranberry extract with a compound which is rich in protein like soy protein isolate. The powder contains 10% of the Polyphenols present in cranberry (23).
- 3. A concentrated juice was prepared out of the fruit. The juice is dialysed for 5 days and treated under 4 degrees against distilled water in order to obtain the Non Dialysable Compound of cranberry (14).
- 4. Spray dry method is done to get the cranberry concentrate.
- 5. Semi-preparative high-performance liquid chromatography is done to extract its essential component (10).

ESSENTIAL COMPONENTS:

- 1. Vitamin C: It helps to prevent cold ,in the production of collagen in the body, in the synthesis of norepinephrine.
- 2. Beta Carotene: Precursor of vitamin A.
- 3. Phytochemicals : Flavanols, Anthocyanins, Proanthocyanins, Catechins, Triterpenoids (4).
- 4. Phenolic acids like hydroxybenzoic acid including vanillic acid and hydroxycinnamic acid including cinnamic, coumaric, caffeic and ferocious acid

AVAILABLE FORMS:

Fresh fruits
Frozen fruit
Powders (13).
Tablets (13).
Juice (10).
Concentrate

BIOLOGICAL PROPERTIES:

BENEFICIAL:

The phenolic antioxidants present in cranberries are responsible for their antioxidant property; the antiinflammatory phytonutrients are responsible for the anti inflammatory property, Anti-inflammatory effects of cranberry is by the lipopolysaccharide induced inflammatory response inhibition; anti cariogenic (8), anti carcinogenic (4), anti fungal, anti infection (28), anti adhesion (22) and anti coaggregation effect (28).

Cranberry also helps to prevent gum disease, diabetes, stomach pain, diarrhoea, atherosclerosis, cholesterol etc. Pregnant women are more prone to urinary tract infection. Cranberry juice is most recommended and safe to use. There has been no evidence of transfer of the effects of cranberry from the mother who has consumed cranberry during her pregnancy to her foetus (12).

HARMFUL:

Cranberries have a high level of oxalates and so has a potent risk of kidney stone formation. Cranberry sometimes posses some harmful effects like blood in urine, pain when urination etc.Since cranberry juice has a high sucrose level, they can promote the plaque formation which leads to tooth decalcification. Cranberry juice when taken in large amounts or in doses more than the daily uptake level cause harmful effects like stomach upset, vomitting etc.

ANTIBACTERIAL ACTIVITY: Oral Cavity:

Streptococcus mutans kindle the genes responsible for virulence when a high level of sucrose is present in the oral environment. Major genes responsible for the virulence property of streptococcus mutans include gtfB, gtfC, gtfD which has the capacity to decode the glucosyltransferase which combines with sucrose and forms glycans (29). Sucrose from the food we intake produces glycan in the presence of glucosyltransferase which are absorbed to the surface. This results in the accumulation of bacteria like streptococcus mutans in the tooth surface and helps in forming the bulk and structure of the biofilm. Then streptococcus mutans adhered to the tooth surface produces acid which demineralises the enamel and forms dental caries. The acid produced by the streptococcus mutans in the plaque matrix resulted in the acid resistant bacteria (10). Cranberry constituent inhibited the adhesion of cariogenic bacteria on the tooth surface. This was due to the anti-adhesion activity of cranberry constituent (9). Cranberry inhibited the glucosyltransferase, F-ATPase activity and acid production and also acid tolerance (26). It does not destroy the bacteria but prevents it from adhering to the tooth structure resulting in a controlled oral flora. According to the study done by Ervin I. Weiss et al that the number of bacteria in the volunteer's saliva using mouthwash which contained cranberry extract expressed a remarkable reduction in streptococcus mutans and total bacteria than with placebo mouth wash (9). Cranberry was shown to reduce the periodontopathogens induced inflammation by reducing the inflammatory cytokines like IL-1 β , IL-6, and IL-8 and TNF- α macrophages produced by produed by lipo in polysaccharide (2).

GASTRONOMY INTESTINAL INFECTION:

Helicobacter pylori is a spiral shaped gram negative bacteria present in the duodenum and stomach. It is known to cause gastritis and stomach ulcer. It survived by releasing an enzyme called "urease" this enzyme is responsible for the production of ammonia which prevents it from acid present in the stomach by creating a neutral pH in the environment (19). An gastric infection caused by Helicobacter pylori will lead to many gastric related disease (8). A study done by Y. T. Lin et al showed that the phenolic derivatives of cranberry showed 9% inhibition of urease activity (19). Thus cranberry can also prevent infections caused by Helicobacter pylori in the gasrtointestinal tract to certain extent.

URINARY TRACT INFECTION:

Urinary tract infection is the condition in which microorganisms invade some part of the urinary tract. UTI is more common in the bladder as it is easy for the microorganisms to enter via urethra. Since the urethra of women is small in length than that of a men, women are more prone to UTI. If the infection in the bladder is left untreated, the infection progresses towards kidney and is harmful to our body. The presence of bacteria to above the threshold limit in the urine is termed as urinary tract infection (13). E. Coli is a major micro organism responsible for this infection. Some of the symptoms include urgency, frequency, dysuria, supra public pain, hematuria, cloudy urine, nausea, vomiting and delirium. . Microorganisms enter the urinary tract by adhering to the epithelial cells of the urinary tract. Many mechanisms are proposed for the anti-adhesion property of cranberry. Cranberry juice can only prevent the infection from occurring and it should not be used for treatment as it does not have any effect on the bacteria after adhesion. Recently it was proved that Proanthocyanins were responsible for the anti-adherence effect (11). There was also another mechanism proposed by Kinney that the quinic acid which is present in the cranberry juice increases the excretion of hippuric acid in the urine which is said to have antibacterial effect, thus preventing the infection (16). But this however is not accepted as it is not proved. Another mechanism is that fructose present in the

cranberry juice prevents the adhesion of fimbriated E-Coli to the uroepithelial cells (6). Another mechanism suggested is that the juice may affect the concentration of Tamn-Horsfall glycoproteins in urine which interferes with the E. coli adherence to the human kidney (7).

ADVANCEMENTS:

ANTICANCER PROPERTY:

Cranberry has the highest anti-oxidant property among all berries. It also has an anti-inflammatory property. Recent studies showed that cranberry inhibits ODC exression in Hras-transformed mouse fibroblasts induced by lipopolysaccharide (20).

These properties may result in the anti tumour activities of cranberry. Because of the antioxidant property of anthocyanins present in cranberry, the oxidative process linked to tumorigenesis is inhibited. When compared with the other components of the fruit anthocyanins have an antiproliferative or growth inhibitory properties (4). Flavonoids of cranberry are expected to have a role in the chemoprevention. Anthocyanin extracts of different berries prevented the vascular endothelial growth factor activity by tumour necrosis factor and decreased tumour growth (1). Cranberries is the main source of quercetin. Quercetin was found to inhibit tumour growth through assays and also found that it inhibited the growth of human breast adenocarcinoma, colon adenocarcinoma and chronic myelogenous leukemia cell lines (21). Quercetin have the ability to inhibit cancer cell lines proliferation of breast, colon, pancreas, leukemia(18, 5). Proanthocyanins also produces ornithine decarboxylase inhibition in the epithelial cellsby cranberry (15). Ursolic acid present in the cranberry inhibited the growth of human lung carcinoma and leukemia cell lines (27). Anti-inflammatory effects of cranberry is by the lipopolysaccharide induced inflammatory response inhibition. Many studies which were conducted in invitro conditions have been trying to find out the mechanism behind the anti-tumour activity of Phytochemicals which are taken in our diet. Tea and grape Phytochemicals are the most common in these studies (17, 24). The study about the ant carcinogenic property was started at 1996 at the university of University of Illinois (3). A study done by Seeram N. P. Et al with water soluble cranberry phenolic extracts from cranberry powder showed that they effectively inhibited the growth and multiplication of certain human cell lines(25).

CONCLUSION:

Unlike medicines or treatment, cranberry with medicinal values can be taken regularly. It is proved that it can prevent infections and it is anticarcinogic and anti-inflammatory. It can be used by terminally ill patients, old age people and in pregnancy. It helps in improving the general health and protects them from illness that are likely to occur at older ages.

REFERENCES:

- Atalay M, Gordillo G, Roy S, Rovin B, Bagchi D, Bagchi M, Sen CK. Anti-angiogenic property of edible berry in a model of hemangioma. FEBS Lett. 2003; 544: 252–257.
- Bodet C, Chandad F, Grenier D. Anti-inflammatory activity of a highmolecular weight cranberry fraction on macrophages stimulated by lipopolysaccharides from periodontopathogens. J Dent Res. 2006; 85: 235–239.
- Bomser J, Madhavi DL, Singletary K, Smith MA. In vitro anticancer activity of fruit extracts from Vaccinium species. Planta Med. 1996; 62: 212–216.
- Catherine C, Neto. Cranberry and It's Phytochemicals: A Review of In Vitro Anticancer Stiudies. The Journal Of Nutrition. 2007; 137: 186S-193S.
- Choi J, Kim J, Lee J, Kang C, Kwon H, Yoo Y, Kim T, Lee Y, Lee S. Induction of cell cycle arrest and apoptosis in human breast cancer cells by quercetin. Int J Oncol. 2001; 19: 837–844.
- Dina Zafriri, Itzhak Ofek, Rivka Adar, Marisol Pocino, Nathan Sharon. Inhibitory Activity of Cranberry Juice on Adherence of Type 1 and Type P Fimbriated Escherichia coli to Eucaryotic Cells. Antimicrobial Agents and Chemotheraphy, 1989; Jan: 92-98.
- Dulawa, J., K. Jann, M. Thomsen, M. Rambausek, and E. Ritz. 1988. Tamm-Horsfall glycoprotein interferes with bacterial adherence to human kidney cells. Eur. J. Clin. Invest. 18; 87-91.
- Dunn, B. E., H. Cohen, and M.J. Blaser. Helicobacter pylori. Clin. Microbiol. Rev. 2007; 10: 720–741.
- Ervin I. Weiss, Avital Kozlovsky, Adorno Steinberg, Ron Lev-Dor, Ronit Bar Ness Greenstein, Mark Feldman, Nathan Sharon, Itzhak Ofek. A high molecular mass cranberry constituent reduces mutans streptococci level in saliva and inhibits in vitro adhesion to hydroxyapatite. FEMS Microbiology Letters. 2004; 232: 89-92.
- Gregoire.S, A. P. Singh, N. Vorsa, and H. Koo. Influence of cranberry phenolics on glucan synthesis by glucosyl transferases and Streptococcus mutans acidogenicity. Journal of Applied Microbiology. 2007; 103: 1960–1968.
- Howell, A. B., Vorsa, N., Marderosian, A.D. and Foo, L.Y. Inhibition of the adherence of P-fimbriated Escherichia coli to uroepithelial surfaces by proanthycyanidin extracts from cranberries. NewEngland Journal of Medicine. 1998; 339: 1085±1086.
- Jean-Jacques Dugoua, Dugald Seely, Daniel Perri, Edward Mills, Gideon Koren. Safety And efficacy of cranberry (VacciniumMacrocarpon) during pregnancy and lactation. Can J Clin Pharmacol. 2008; Vol 15 (1) Winter: e80-e86. January18, 2008.
- 13. Jepson RG, Craig JC. Cranberries for preventing urinary tract infections (Review). The Cochrane Library. 2008, Issue 1.
- Julie Labrecque et al. Effects of a high-molecular-weight cranberry fraction on growth, biofilm formation and adherence of Porphyromonas gingivalis. Journal of Antimicrobial Chemotheraphy. 2006; 58: 439-443.
- Kandil FE, Smith MAL, Rogers RB, Pepin M-F, Song LL, Pezzuto JM, Seigler DS. Composition of a chemopreventive proantho-cyanidin-rich fraction from cranberry fruits responsible for the inhibition of TPA induced ODC activity. J Agric Food Chem. 2002; 50: 1063–1069.
- Kinney A B, Blount M. Effect of cranberry juice on urinary pH. Nursing Research 1979; 28(5): 287–290.
- Lambert JD, Hong J, Yang G-Y, Liao J, Yang CS. Inhibition of carcinogenesis by polyphenols: evidence from laboratory investigations. Am J Clin Nutr. 2005; 81: 284S–291S.
- Lee LT, Huang YT, Hwang JJ. Blockade of the epidermal growth factor receptor tyrosine kinase activity by quercetin and luteolin leads to growth inhibition and apoptosis of pancreatic tumorcells. Anticancer Res. 2002; 22: 1615–1627.
- Lin Y.T., Y. I. Kwon, R. G. Labbe, K. Shetty. Inhibition of Helicobacter pylori and Associated Urease by Oregano and Cranberry Phytochemical Synergies. Applied and Environmental Microbiology. Dec 2005: 8558-8569.
- Matchett M, Compton K, Kondo M, Neto CC, Hurta RAR. Lipopolysaccharide, cranberry flavonoids, and regulation of ornithine decarboxylase (ODC) and spermidine/spermine N1-acetyltransferase

(SSAT) expression in H-ras transformed cells [Abstract 507.2]. FASEB J.2005; 19(4): A825.

- Murphy BT, MacKinnon SL, Yan X, Hammond GB, Vaisberg AJ, Neto CC. Identification of triterpene hydroxycinnamates with invitro antitumor activity from whole cranberry fruit (vaccinium macrocarpon). J Agric Food Chem. 2003; 51: 3541–3545.
- R. Puupponen-Pimia, L. Nohynek, C. Meier, M. Kahkonen, M. Heinonen, A. Hopia and K.-M. Oksman-Caldentey. Antimicrobial properties of phenolic compounds from berries. Journal of Applied Microbiology. 2001; 90: 494-507.
- Roopchand DE, et al. Food-compatible method for the efficient extraction and stabilization of cranberry pomace polyphenols. Journal Food Chem. 2013; 141(4): 3664-3669.
- Sovak M. Grape extract, resveratrol, and its analogs: a review. J Med Food. 2001; 4: 93–105.
- 25. Seeram, N. P., Adams, LS, Hardy ML, Heber D. Total cranberry extract vs. its phytochemical constituents: antiproliferative and synergistic

effects against human tumor cell lines. J Agric Food Chem. 2004; 52: 2512–2517.

- Vercauteren. J. Compositions of stilbenic polyphenolic derivatives, their preparations, and their use in the treatment of disease and aging. fr. Demande 2923717 AL, 2009.
- 27. Wang M, Li J, Shao Y, Huang T-C, Huang M-T, Chin C-K, Rosen RT, Ho C-T. Antioxidative and cytotoxic components of high bush blueberry (Vaccinium corymbosum L.) in phytochemicals and phytopharmaceuticals. Champaign, IL: AOCS Press; 2000, 271–277.
- Weiss, E. I., Lev-Dor, Kashman, Y. et al. (1998). Inhibiting interspecies coaggregation of plaque bacteria with cranberry juice constituent. Journal of the American Dental Association 129: 1719-1723.
- S. Yoo, R.M. Murata, S. Duarte. Antimicrobial Traits of Tea- and Cranberry-Derived Polyphenols against Streptococcus mutans. Caries Res 2011; 45: 327–335.