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Cranberry Bioactive Compounds and Health Benefits: An Integrative Review of Chemistry, Mechanisms, and Clinical Applications

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ABSTRACT: The perennial tree known as cranberries *Vaccinium macrocarpon* belongs to the family Vaccinium, which lies in the family Ericaceae and is frequently used as a functional food. The northern United States, particularly Massachusetts, Wisconsin, and Maine; Quebec, France; the Commonwealth of Georgia; Santiago throughout South Americas; and northeastern Europe are the main locations for cranberries. Then may also be found in the cities of Fuyuan City, Jiamusi, which is in Heilongjiang Province, and within the wider Khingan Range in China. The plants are highly adaptable to soil conditions and like acidic soils, and they flourish in chilly locations. Most biologically active substances, including polyphenols (like proanthocyanidins, chlorogenic acid, for example, flavonols and anthocyanins, and coffee extract, etc.), triterpenoids and other nutrients, are abundant in cranberries. Research has demonstrated the pharmacological effects of chemical substances extracted from cranberry fruit, including anti-inflammatory, antioxidant, cancer fighting, and urinary tract infection treatment properties. These chemical components are frequently used in clinical settings to treat heart failure, prevent urinary tract infections, lower blood pressure, and combat Helicobacter pylori infection, including other illnesses. Cranberries, which are called for their abundance in a range of mineral constituents, trace elements, and vitamins, also play a significant part in daily nutrition. The Pubmed, the Web of Nature, Scopus, CNKI (China's National Intellectual Infrastructure), and comparable works are used in this work. This study provides a thorough analysis of the pharmacological system of action, plant-based composition.

Keywords: Cranberry, Anthocyanin, Polymeric color, Proanthocyanidin, Precipitate.

INTRODUCTION

The cranberries fruit (*Vaccinium macrocarpon* Ait.) is an animal of the flowering plant order and species *Vaccinium*. It is an annual shrub with purplish-red berries, white or reddish camping blooms, and rounded or oval leaves Cranberries were extensively planted in natural biological grounds primarily in North Europe and North America, as well as within ecological planting bases in China's Ding-a-lings valley region and Fuyuan County City in Heilongjiang Province. Cranberries are primarily grown in the chilly, acidic earth of the northern hemisphere. Concord grapes, blueberries, and cranberries are viewed as the three classical fruits of North America. According to the Manual of Traditional Chinese Medicine, rheumatism and gout are frequently treated with cranberry leaves, which are purifying and diuretic; dysentery can be treated with the fruit (Alifakı *et al.*, 2022). Because the anthocyanins define juice colour quality, a crucial factor in consumer appeal, and as anthocyanins are vital to human health, it is critical to comprehend the anthocyanin content of juices made from fruit and the way anthocyanins are what fluctuate throughout the course of the juice's shelf life. Consuming anthocyanin-rich juices in particular has been proven to be beneficial for chronic inflammation, in addition to the advantages of regular polyphenol consumption, such as decreased risk of dying from all causes, cardiovascular disease mortality, various types of cancer, diabetes, and Parkinson disease. Because fruit juice has less fiber and more sugar than whole fruit, there has been discussion among dieticians and public health experts about whether or not it should be consumed. However, new research suggests that consuming 100% fruit juice is a good way of boosting the amount of fruit eaten as part of a nutritious meal plan (Anitha *et al.*, 2024). A high concentration of health-promoting oxidants is specifically crucial for fruit juice quality because the macronutrients in fruit juice appear to be less advantageous for individuals than whole fruit. Fruit juice's polyphenols do not have the same antioxidant capacity hence comprehension of the poly composition of fruit juices is important (Arvinte & Amariei 2022).

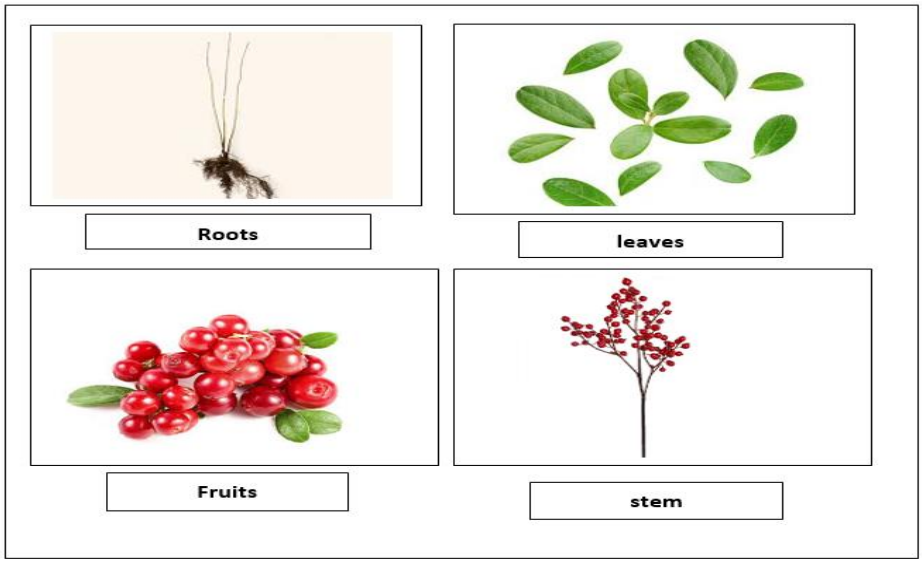

Fig. 1. Botanical parts of cranberry.

METHODOLOGY

In the first stage of our investigation, we methodically evaluated every study that was found using Cranberry-related keyword searches. After eliminating duplicate entries, we first reviewed titles as well as abstracts to assess their applicability in light of the predetermined inclusion criteria. A careful analysis of the whole text and a thorough evaluation of the bibliography were conducted for studies that met these criteria in order to guarantee a thorough comprehension of the pertinent literature.

BOTANICAL DESCRIPTION

The cranberry (*Vaccinium macrocarpon)*, a tiny, perennially evergreen woody plant that covers the ground in dense mats, is a member of the Ericaceae family. Its prostrate, trailing stems have nodes that give rise to shallow, fibrous, adventitious roots. Short, upright blooming branches are produced by the thin, woody stems. The leaves of this plant are small, simple, alternating, evergreen, oblong to elliptic, leathery, and have full margins; the lower surface is pale because of a waxy covering, while the top surface is glossy and dark green. amorphous, feminine and bisexual, the petals are produced individually or in small pods on short stalks. Every flower has four reflexed sepals and four tenacious sepals. with eight stamens bearing elongated anthers and an inferior, four-celled ovary with a single style. The fruit is a many-seeded, globose red berry with a spongy pericarp that enables it to float, and the seeds are small and numerous, embedded in the fleshy pulp.

A. Taxonomy classification

Taxonomic Rank	Classification
Kingdom	Plantae
Division	Angiosperms
Class	Eudicots
Order	Ericales
Family	Ericaceae
Genus	*Vaccinium*
Species	*Vaccinium macrocarpon* Aiton

B. Geographical description

Native to North America, the cranberry (*Vaccinium macrocarpon*) thrives best in cool temperate climates, especially in acidic bogs, swamps, and wetlands. It is extensively found in sections of Canada as well as the northeast and north-central regions of the United States. The plant grows best in regions with cool temperatures, lots of fresh water, and acidic, sandy soils. Beyond its natural habitat, cranberries are now grown in nearly every region of the globe include Americas, Europe, and Asia, particularly in areas with comparable climates. The United States (particularly Illinois, Rhode Island, and the state of Jersey), the Canada, and Chile account for the majority of commercial production.

C. Morphological description

The cranberry (*Vaccinium* spp.) is a small, evergreen, perennial shrub with thin, trailing stems that cover the ground in dense mats. Short, erect branches with leaves and flowers are generated by the wiry, crawling stems. The leaves of the plant are small, simple, oblong to ovate in arrangement, with straight edges and a leathery feel; the underside is lighter than the topmost part, which is dark green and glossy. The flowers are usually pink to pale deep purple, with four sharply folded petals that reveal distinct stigma and the central pistil. They are carried single or in tiny clusters on thin pedicels and have a bobbing habit. The strawberry has an even outer layer and is round to oval in shape.When fully grown, the smooth, glossy skin of the circular to ovoid berry changes from green to a dark crimson. Numerous tiny seeds are contained in the delicious, acidic flesh of each berry.

D. Cultivation

Cranberries are primarily grown in cool, temperate climates with ideal soil and climate. The crop grows best in sandy, acidic soils that are high in nutrients, have a pH between 4.0 and 5.5, and have good drainage. A plentiful supply of clean water is necessary for cranberries' irrigation because of annual floods, which serve the purpose for harvesting, pest control, and safeguarding against frost. Vine cuttings are

typically sown in prepared beds for root propagation. The plants grow best in temperatures that are modest, and they prefer full sun and cool growing seasons. Blasting to promote new upright growth, trimming, eliminating weeds, and infection and pest protection are examples of routine management techniques. Ripening berries are often harvested in the autumn months, either by wet harvesting for processing— in which floods in the fields allow mature fruit floating around as easy collection—or dry harvest for market purchase of fresh berries.

E. Collection

Cranberries are commonly collected in late autumn, during the harvest season. These tiny, spherical, red berries are often picked by hand or with specialised harvesting tools. They grow on low-lying plants in marshy locations. Cranberries are occasionally picked in huge quantities and placed in baskets or pots to create a colourful show of red fruit. Cranberries are even inundated in shallow water in certain industrial settings, which makes it easier to pick the berries as they float to the top. In order to ensure that none of the nutrient-dense fruit is wasted, this collection of apples can be categorized, cleaned, and subsequently utilised for a variety of purposes, including producing liquid desserts, jams, or dried snacks.

F. Synonyms

Source	Names
English	Cranberry
Botanical	Vaccinium macrocarpon
Hindi	kraenberi
Sankrit	Karanda, Shukla Phal
Tamil	Kārantā
Ayurveda	Kashaya (astringent)
Others	Mossberry, Fenberry

PHYTOCHEMISTRY OF CRANBERRY

Flavonoids, anthocyanins, phenolic acids, and triterpenoids are only a few of the distinctive chemical components found in cranberry fruit (Bai *et al.,* 2021) Cranberry fruit is high in dietary fibre, nutrients (calcium, potassium, with magnesium), vitamin C, plus the antioxidant vitamin E in addition to being a significant source of biologically active ingredients (Balawejder *et al.,* 2023). Researchers from both domestic and international countries have employed a range of scientific techniques to obtain the chemical makeup of cranberries and discovered that the berries also contain soluble compounds like pectin and dietary fibre (Bansal *et al.,* 2024). Polyphenolic substances, such as the flavonols (Barbosa *et al.,* 2024). proanthocyanidins, tannins phenolic acids, and anthocyanins, are especially abundant in cranberries. A class of naturally occurring chemical substances known as polyphenols has many phenolic hydroxyl groups.Researchers from both domestic and international countries have employed a range of scientific techniques to obtain the chemical makeup of cranberries and discovered that the berries also contain soluble compounds like pectin and dietary fibre. Polyphenolic substances, such as the flavonols substance (Blumberg *et al.,* 2013) proanthocyanidins, tannins (Castellanos *et al.,* 2024), phenolic acids, and anthocyanins, are especially abundant in cranberries. A class of naturally occurring organic substances having many kinds of phenolic hydroxyl groups is known as polyphenols. Researchers have mostly used experimental methods like spectrophotometry, the use of liquid and advanced liquid chromatography to carry out in-depth studies in the chemical makeup of cranberry fruits, but the results of these studies are currently dispersed (Chang *et al.,* 2022). The article provides an overview of the several categories of chemical elements that can be extracted from cranberries

A. Anthocyanin

In addition to giving cranberries and its processed counterparts their vibrant colour, the anthocyanin chemicals found in large quantities in cranberries may also be beneficial to human health. In the kingdom of plants, anthocyanins are soluble in water natural pigments that hydrolyse to produce coloured glycosides. Anthocyanins are crucial elements of the secondary metabolites of plants that are significant for human nutrition and the food industry. Cranberries have six primary anthocyanins: geranium pigment, cornflower pigments, delphinium pigment, peony tint, petunia pigments, and mallow pigment (Chatterjee *et al.,* 2012). Pigment-3-O-galactoside and pigment-3-O-arabinopyranoside were the main anthocyanin components in mature cranberries, and the amount of anthocyanin of cranberry skin was found to be substantially higher than that of fruit pulp discovered that in Canadian wild cranberries. (Davidson *et al.,* 2014; Debnath and An 2019). anthocyanins were primarily detected in paeonidin-3-O-arabinoside and paeonidin-3-O-galactoside. Cranberries from different regions have diverse anthocyanin compositions, but in Euro pean locales, the primary anthocyanin components were cornflowerin-3-O-galactoside, paeoniflorin-3-O-galactoside, and a compound called paeoniflorin-3-O- and 3-O-arabinopyranoside cornflower in (Denis *et al.,* 2015 ; Déziel *et al.,* 2012). These results imply that fruit ripening stage, provenance, and varietal variations affect the amount of flavonoid active components in cranberries. The potential advantages of anthocyanins and associated anthocyanin-rich foods in avoiding the development of cancer, diabetes, and other cardiovascular, and neurological illnesses, as well as the general interest in the battle against oxidative stress, have also been demonstrated by a number of both in vitro as well as vivo studies. Fig. 4 summarises and classifies the anthocyanin components found in cranberries.

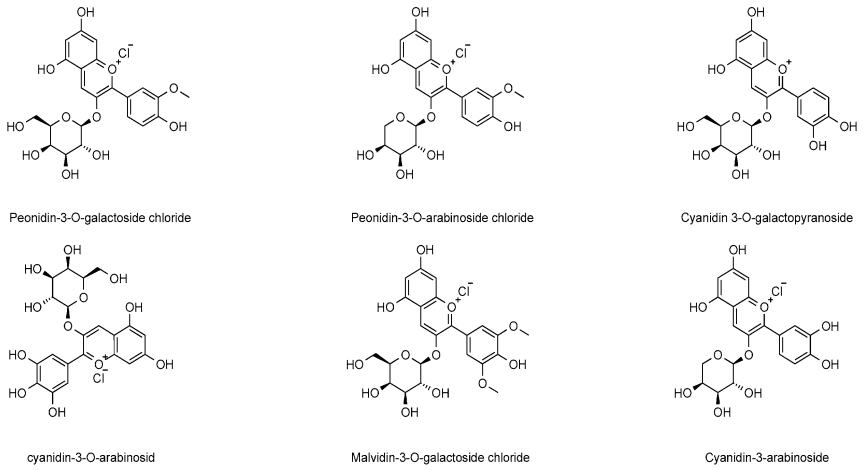

Fig. 2. Major anthocyanin-like chemical constituents in cranberries (Diepeveen *et al.,* 2022).

B. Proanthocyanidins

A large class of polyphenolic chemicals found across the kingdom of plants is called proanthocyanidins. Heating these substances in an acidic environment can convert them into anthocyanins. A-type bonds make up the majority of proanthocyanidins in cranberries, while B-type bonds predominate in proanthocyanidins found from other plant sources (Dubey *et al.,* 2025). Cranberries are known for their proanthocyanidins, which are oligomers or polymers comprised up of varying concentrations of catechins and epicatechins, and are connected by C4-C8 or C4-C6 bonds. Cranberries can successfully prevent Escherichia coli from adhering to uroepithelial cells because of their high content of type A these substances (El-Saadony *et al.,* 2024). The distinctive elements of cranberries that set them apart from other berries are type A proanthocyanidins.have demonstrated their unique ability to prevent UTIs. In order to extract polyphenols and oils sequentially, employed a ternary mix solvent (CO_2 + alcohol + water) between 25 to 50 MPa and 40–60 °C. High-purity proanthocyanidins were recovered from cranberry pomace with an 88% reduction in ethanol consumption when compared to the conventional solvent approach. With the right columns and mobile phases, HPLC, or high-performance liquid chromatography, can efficiently separate the synthetic chemical components in cranberries. Özlem and associates. With the right columns and mobile phases, high-performance liquid chromatography, or HPLC, can efficiently separate the polyphenolic chemical substances in cranberries extracted phenolic substances from cranberries using microwave, ultrasound, and mixed ultrasound and microwave techniques. The experiments' findings covered total monomer anthocyanin content, polymer colour, vitamin C content, and other percentages of phenolic compounds in the extracts. One of the main active chemicals in cranberries.

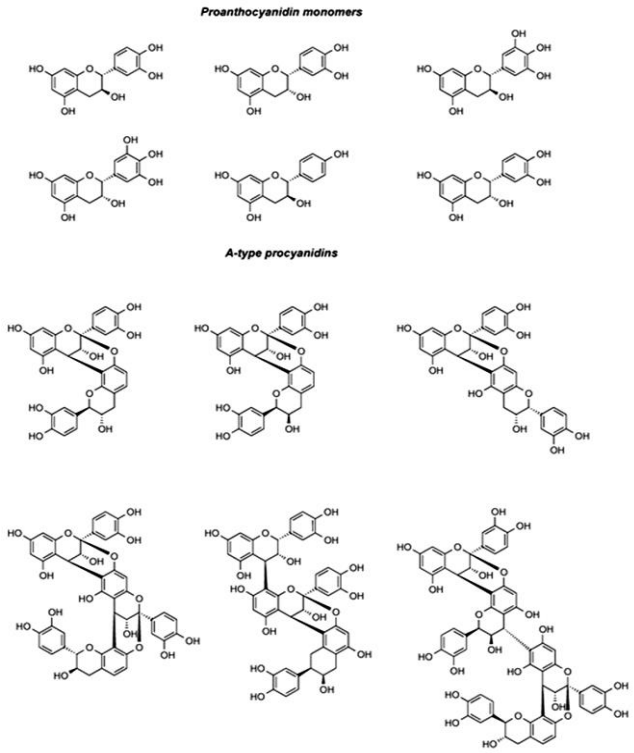

Fig. 3. Major Proanthocyanidin-like chemical constituents in cranberries (Febriza *et al.,* 2024).

C. Flavonol

A group of secondary metabolic products found across the kingdom of plants, Flavonol are essential for cultivation, development, and defence mechanisms. Quercetin, also called kaempferol populin, isorhamnetin, myricetin, as well as 3- O-galactoside, hyperpside isoquercitrin, and quercetin 3-O- L-arabinoside are the principal nutritional components found in cranberries. These compounds have important physiological functions and biological benefits. Researchers have discovered that European strawberry pomace extracts contain 8.4 mg of populin per 100 g and are higher in organic acids, flavonols, and stilbenes than other fruits (Febvey *et al.*, 2023). Additionally, researchers found 2.1 mg/g of isorhamnetin in cranberries using analytical methods such LC-MS/MS. Cranberries are the primary source of isorhamnetin in the form of glycosides like isorhamnetin-3-O-glucoside. acrylamide and caffeine-laden glycoside derivatives of Cranberries' physiological activity may be impacted by these compounds. Caffeoyl groups improve molecules' ability to transport electrons, making them more effective at scavenger radicals that are unstable like DPPH & ABTS. Furthermore, these derivatives have better inhibitory impacts on lipid peroxidation than unacylated isorhamnetin glycosides. These compounds are better able to protect cellular proteins and DNA from oxidative stress-induced damage. They exhibit more noticeable inhibition on oxidative stress-related apoptosis, particularly in trials that mimic intestinal or vascular settings (Gbinigie *et al.*, 2020). Cranberry flavonol components frequently work in concert alongside different polyphenolic components to improve the therapeutic impact of preventing UTIs.

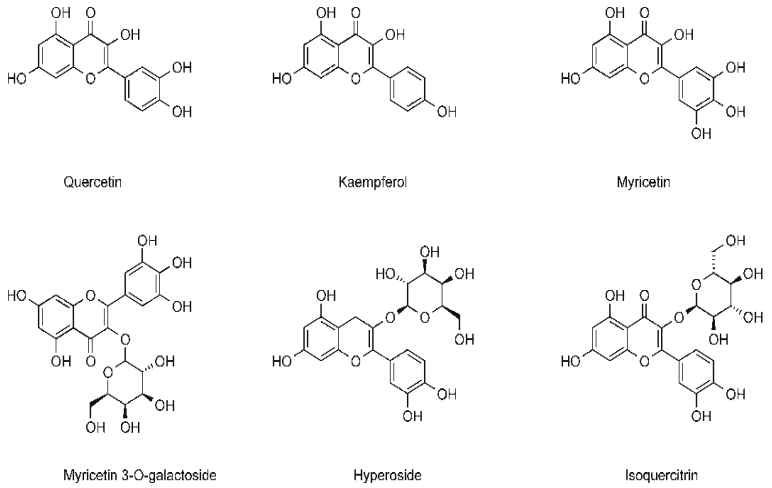

Fig. 4. Major flavonol compounds in cranberries and their content across different varieties (González *et al.*, 2024).

CLINICAL APPLICATIONS

Cranberries, a type of berry rich in various bioactive components like proanthocyanidins, anthocyanidins and terpenoids that give them significant medicinal and antimicrobial pharmacological properties, have attracted a lot of interest in a variety of clinical applications. Cranberries' latent value has been demonstrated by clinical use in a number of areas, most notably oral and urinary health. Cranberries have also shown promise in preventing cancer and cardiovascular illnesses. However, to ensure the safety and effectiveness of cranberries, individual variations and the combinations of these items with other medications or treatments must be considered during clinical application.

A. Urinary Health

Cranberries have important clinical uses in the avoidance and treatment of urologic illnesses, particularly in the avoided UTIs and adjuvant therapy of UTIs. A-type proanthocyanidins, which are abundant in cranberries, significantly inhibit urinary tract pathogen bacterium *E. coli* and successfully lessen bacterial adhesion to the cell membrane . Research indicates that the presence of two chemicals with anti-adhesion capabilities in cranberry juice prevents fimbriae-expressing E. coli from adhering to urinary canal epithelial cells, hence reducing urinary tract infections. By preventing the inflammation that leads to infections in the bladder, cranberry consumption also lessens symptoms like urgency, frequency, purulent exudate, and foul odor. Furthermore, By preventing an inflammatory reaction to infections in the urinary tract, cranberry consumption also lessens indications like urgency, frequency, purulent exudate, and strange odor. Cranberries also aid in maintaining the equilibrium of the urethral flora, controlling the pH of the urinary environment, preventing the growth of pathogenic bacteria, and encouraging the growth of beneficial bacteria, all of which strengthen the urethra's natural defenses against infections. By virtue of its lower pH, cranberries and their extracted form can directly buffer urine, enhance the urethral milieu, and prevent the growth of urethral infectious bacteria (Gu *et al.*, 2003). In intestinal epithelial cells, proanthocyanidins and their microorganism component 3, 4 dihydroxyphenylacetic acid obtained from cranberries partially corrected the beneficial microRNA response.

B. Oral Health

As a vital component of human health, oral health is intimately related to overall health and life satisfaction. By avoiding and treating dental caries, reducing dentin erosion, and encouraging enamel remineralization,

cranberries, a fruit rich in a range of bioactive compounds like proanthocyanidins and anthocyanins, have a good impact on oral health. Cranberries' chemical makeup of proanthocyanidins demonstrates potent pharmacological activities, including antibacterial and antioxidant properties, with notable antimicrobial effects on infectious infectious illnesses of the mouth like periodontitis and dental caries and significant protective effects from the growth of bacteria additional to pulpal infections (Hotchkiss *et al*., 2022). It was mentioned that a prevalence of caries experiment involving sixty preschoolers revealed that daily consumption of probiotic and cranberry extract tablets decreased the rate of cavities in preschoolers. Additionally, cherries and their juices can reduce dentin degradation by inhibiting matrix metal metalloproteinases, or MMPs, which are present in saliva and dentin for maintain (Howell, 2007). Cranberry extract has anticariogenic qualities and enhances enamel and dentin revitalization by decreasing the biomass and increasing the pH level of biofilm from teeth. Cranberries also enhance oral health in several ways, such as by reducing mouth odor and plaque development. Cranberries are useful in preventing and treating oral diseases due to their antimicrobial, biofilm-preventing, and microecological stabilization-regulating qualities. Current experimental studies have only partially proven the curative effects of cherries on dental caries, tooth decay, and a number of other oral infectious diseases; it is currently unknown that cranberries have substantial healing effects on clinical treatment.

C. Nutritional Significance

In addition to its many bioactive elements, cranberries are high in minerals like calcium, magnesium, and potassium and also contain vitamins like C, E, and other antioxidants and the B vitamins .These elements work together to efficiently eliminate harmful free radicals from the human body and shield tissues from oxidative damage, this is crucial for treating neurological disorders, cancer, and cardiovascular disease. Cranberries' high dietary fiber content also supports intestinal peristalsis and preserves the intestinal tract function. Ascorbic acid, the primary form of vitamin C, is one of the several soluble in fat and water-soluble vitamins that give cranberries their antioxidant qualities (Katsargyris *et al.*, 2012). Cranberries also have a variety of roles in preventing oral health issues, delaying the aging process, and boosting immunity. According to studies, consuming a cranberry beverage for six weeks dramatically enhanced the suppleness and smoothness of skin on the face and arms, particularly in women over 40, and significantly decreased UV-induced skin erythema .Through multi-component synergistic effects, the anti-aging impact of cranberry extracts combined with additional extracts from plants can be strengthened. It was discovered that the oxidation process of chilled fresh meat was slowed down when cranberries and rosemary were combined, indicating that cranberry complexes had a great deal of potential in the reactive (Kocabas and Sanlier 2024). To sum up, cranberries are rich in nutritional content.

PHARAMCOTHERAPEUTIC APPLICATION OF CRANBERRY

Anthocyanins, antioxidants, volatile oils, and other bioactive compounds are abundant in cranberries, a herb that belongs within the genus Vaccinium, which is found in the genus Ericaceae. These ingredients have proven to be remarkably effective in pharmacological effects like antioxidant, anti-inflammatory, antibacterial, and anticancer activities. They have also showed promise for use in research areas like skin health and metabolic control Numerous research have examined the chemical makeup of cranberries thus far, confirming their pharmacological effects (Kristensen *et al.*, 2019). Nevertheless, more thorough research on the pharmacological effects and mechanism of action of cranberries is desperately needed, as the existing investigation of these effects is still superficial. Cranberry PACs have limited systemic absorption; instead, their metabolites are excreted in urine where they exert their anti-adhesion activity, typically within hours of ingestion. Clinically effective dosing often targets 36 mg of type A PACs daily, found in many standardized extracts, though cranberry juice can also be used. Cranberry is generally well tolerated, but gastrointestinal upset may occur, and its high oxalate content may increase kidney stone risk in susceptible individuals. The most significant drug interaction is with warfarin, as cranberry may elevate INR and increase bleeding risk, necessitating caution or close monitoring. Overall, cranberry functions as a non-antibiotic preventive agent for UTIs, with strong safety but notable interaction considerations.

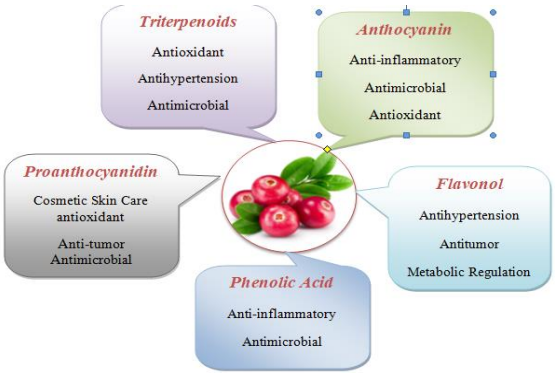

Fig. 5. Main active ingredients and pharmacological effects in cranberries.

A. Antioxidant Activity

Antioxidant compounds such as anthocyanins, these phenolic acids, ascorbic acid, and triterpenoids are among the chemical components found in cranberry fruits, which constitute a substantial source of antioxidants. By scavenging excessive radicals throughout the body, such as hydroxyl and superoxide anion radicals, these chemical parts demonstrate their potent antioxidant properties Excessive levels of free radicals, which are unstable chemicals created by the body's metabolism, can damage intracellular proteins, lipids, and DNA, resulting in cellular senescence and death Once the physique endures a pathological condition like hyperlipidemia, ischemia-reperfusion, or inflammation, The production of NO becomes abnormal. Cranberries include flavonoids (anthocyanins, etc.) that have been shown to have important cardioprotective and cognitive benefits, suppress oxidative stress, and modulate NO levels (Lessard-Lord *et al.,* 2024). Research has shown that elements like delphinidin, and cornflower pigments taken from blueberries have antioxidant qualities that lower levels of ROS within cells and ease ciliary muscle tension According to additional research, cranberry extracts can dramatically boost the body's antioxidant enzyme activity, fortify the antioxidant defense system, lessen the harm that oxidative stress does to the body, and both prevent and postpone the onset of diseases.

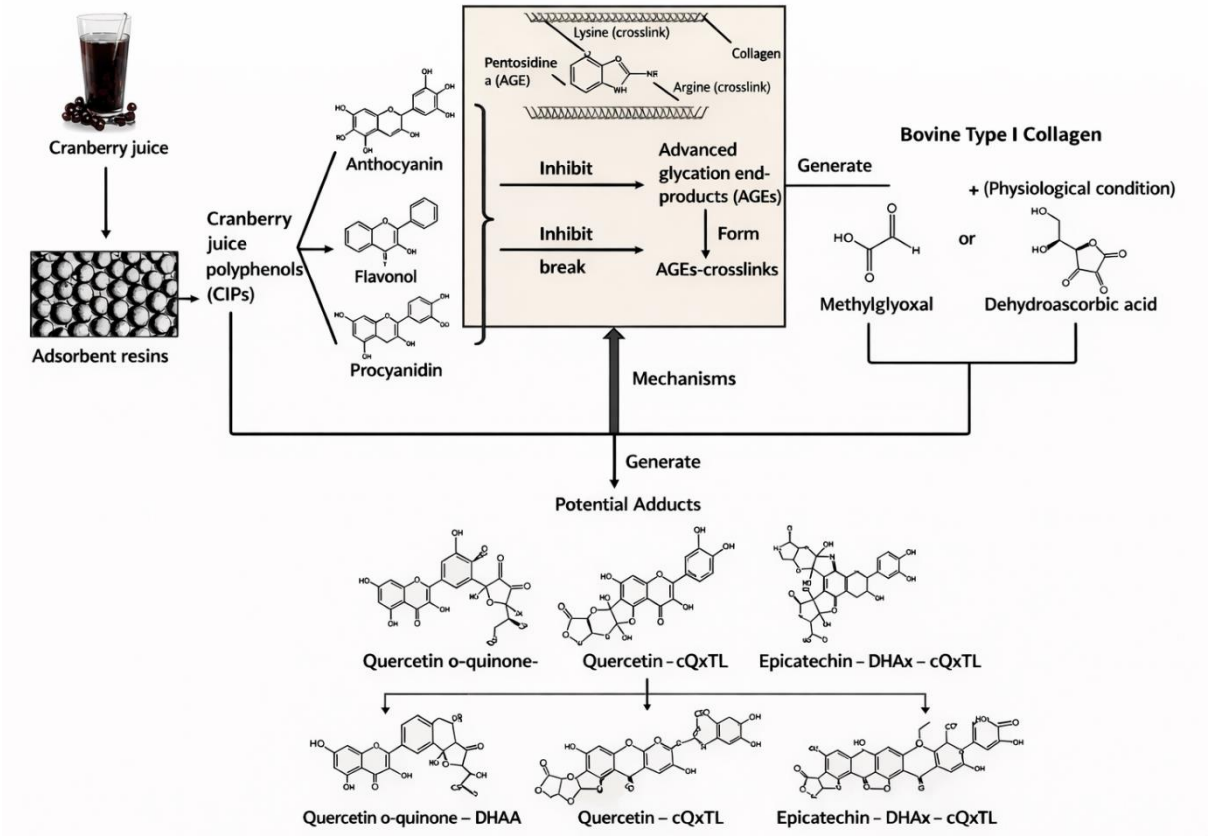

Fig. 6. Mechanism of action of major antioxidant components in cranberry (Mizutani *et al.,* 2021).

B. Antimicrobial Activity

Significant antibacterial action is demonstrated by cranberries, particularly in the inhibition of prevalent pathogenic microbes in the urinary system. Its distinct antimicrobial mechanism is useful in the adjuvant treatment and prevention of associated disorders. Proanthocyanidins, cyanide triterpenoids and other active ingredients found in cranberries reduce bacterial adherence and damage the cell wall or structure to produce their antibacterial actions Oral health is greatly impacted by one of the primary pathogenic microorganisms in the oral cavity. Streptococcus pyogenes growth is inhibited by bioactive substances such type A proanthocyanidins that exist in cranberry extracts. Inhibit glycan-mediated protein attachment, bonding, and aggregation in Streptococcus pyogenes, as well as the production of intractable polysaccharides in the matrix of cells Additionally, cranberries reduce the inflammatory response brought on by the introduction of bacteria of gingival tissue by preventing Porphyromonas gingivalis, and Fusobacterium nucleatum from attaching to gingival epithelial cells. Numerous chemical components in the berry isolates have demonstrated significant inhibiting effects on a variety of harmful bacteria in in-vitro experiments, indicating that they may be a substantial source of preventative foods (Narwojsz *ey al.,* 2019). Herapies with cranberry polyphenol derivatives 3, 4-dihydroxyphenylacetic acid and phenylacetic acid demonstrated positive effects in a urinary barrier model using T24 cells cultured in Trans well inserts as well as either uninfected or UPEC-infected.

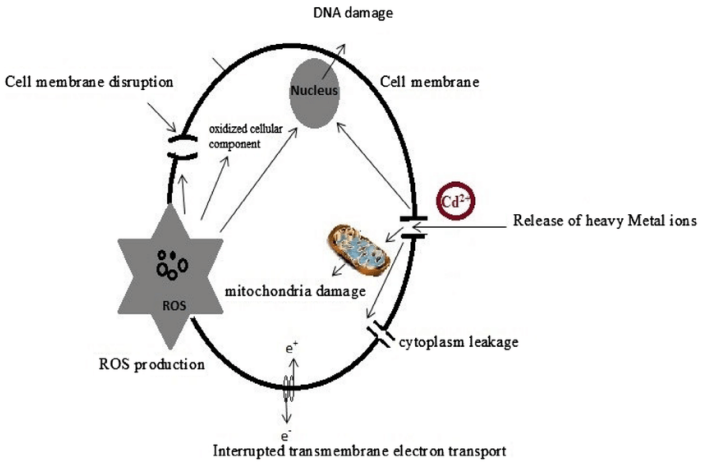

Fig. 7. Schematic diagram of inhibition of bacterial protein synthesis by |Proanthocyanidin components in cranberries (Nemzer *et al.*, 2022).

C. Anti-Inflammatory Activity

The anti-inflammatory benefits of cranberries are linked to the modification of pro-inflammatory cell signaling pathways, which are made possible by their abundance of biologically active substances. Inflammatory factors are released when the NF-κB pathway, a crucial regulator during inflammation, is cherries' polyphenolic components have strong anti-inflammatory properties, as may be linked to the suppression of the generation of ROS, also known as reactive oxygen species, and disruption of cellular signaling pathways (Nussbaumer *et al.*, 2025). It has been demonstrated that terpenoids in cranberries considerably reduce the level of production of inflammatory cytokines that promote inflammation (IL-6, tumor necrosis factor-, and TNF-α) in THP-1 cells**.** Blocking biological pathways for anti-inflammatory actions in a human monocyte cell line. Numerous studies have assessed the anti-inflammatory properties of cranberries and their capacity to improve immune system regulation in periodontitis and implant therapy. The findings indicate that the antimicrobial properties of cranberries may be connected to the removal of inflammatory factors by phagocytes (Quan *et al.*, 2023 ; Rana *et al.*, 2022). Furthermore, cranberry juice reversed oxidative stress caused by rotenone (ROT) in a number of tissues, with the brain showing the most negative impact. Therefore, cranberries' anti-inflammatory properties stem from their polyphenolic chemistry, which directly inhibits oxidative stress, interferes with certain signalling pathways, and indirectly controls the metabolism of gut flora.

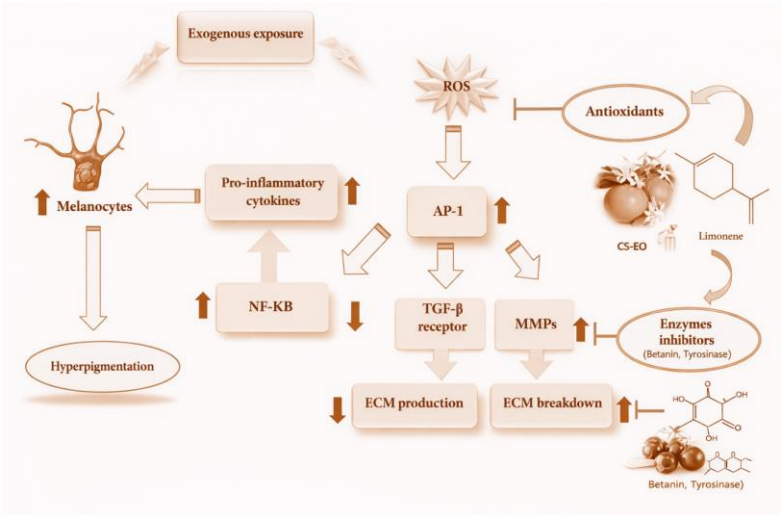

Fig. 8. Schematic diagram of anti-inflammatory activity from cranberry (Sedbare *et al.*, 2022).

D. Anti-Tumour Activity

Proanthocyanidins, also called anthocyanidins, and triterpenoids are among the many bioactive substances found in cranberries that may have anticancer effects. Finding new anticancer medications is particularly crucial because cancer is a complicated disease that affects many organs and systems across the body and is characterized by aberrant cell growth and metastasis. The number if cancer patients worldwide is still rising Human prostate carcinoma cells treated with varying quantity of berries extract for six hours showed a significant decrease in cancer cell viability, as well as a decrease in the G2-M phase of the life cycle and an increase in the G1 phase. These findings could potentially be related to the detrimental effect of its supplementation on cell cycle protein regulation (Urbstaite *et al.*, 2022). This was associated with the cranberry extract's suppression of the proliferation-promoting molecules such as cytokinin E, which inhibits cytokinin-dependent phosphatase 2, and cytokinin- dependent kinase - 4. In pediatric glioblastoma cell lines, discovered that using cranberry

extract alone had minimal effect on U87 cells; however, adding cranberry extract to radiation treatment dramatically reduced U87 cell growth and increased These results imply that cranberries and their extracts may be exploited as natural anticancer medicines, particularly for adjuvant therapy and tumor prevention Nevertheless, the majority of experimental research is still in the animal testing phase, and more validation is required for clinical research. This was linked to the reduction of proliferation-promoting chemicals by the cranberry extract, including cytokinin E, and inhibits cytokinin-dependent kinase 2 and cytokinin-dependent kinase found that cranberry extract itself had little effect on U87 cells in adolescent glioblastoma cell lines; however, cranberry extract added to radiation treatment significantly decreased U87 cell number and enhanced cell (Williams *et al.*, 2023). These findings suggest that blackberries and their extracts could be used as natural anticancer medications, especially for tumor prevention and adjuvant therapy.

E. Other Pharmacological Effects of Cranberry

Cranberries have shown other possible pharmacological properties besides to these effects. Additionally, cranberries have demonstrated benefits in the management of neurological and cardiovascular conditions. Cranberry extract injections have been demonstrated to dramatically improve cardiac injury-related serum markers, increase the oxidation of low-density lipoprotein, and improve the function of high-density lipoprotein (HDL), all of which lower the risk of developing atherosclerosis. Additionally, cranberries' anti-inflammatory and antioxidant qualities have a preventative and ameliorative effect on neurodegenerative illnesses including Parkinson's syndrome and Alzheimer's disease by reducing reactive oxygen species and inflammatory injury in the brain.

CLINICAL TRIALS

Papas *et al.* (1966) reported the first clinical, albeit uncontrolled, trial on the effectiveness of cherries in treating UTIs in According the study authors, out of 60 patients with symptoms from the lower urinary tract and bacterial infections who were given 480 mL of cranberry drink every day for three weeks, 38 (63%) showed signs of persistent bacterial infections, and 4 (7%) showed no signs of bacterial infection. Thirty-two (53%) of the patients showed improvement in their symptoms, but six weeks after the treatment ended, we looked at the rate of relapse as a variable index in UTI patients who experienced numerous relapses after consuming cranberry juice (UR65). From the end of 2007 to September 2009, a double-blind, randomized, controlled placebo study was carried out in Japan. Outpatients between the ages of 20 and 79 made comprised the subjects, who had been divided into two distinct sets at random. Group A of participants was given cranberry juice, while Group P was given a placebo. The beverages' colour and flavour were changed to keep people blind. For 24 weeks, the participants consumed one glass (125 millilitre) of cranberry extract or a placebo once a day before bed. UTI recurrence was the main outcome. Within the 50-year-old female group the risk of UTI relapse differed significantly among groups A as well as P (log-ranked analysis; p = 0.0425 for each group). In this group's analysis, 31 out of 63 patients (49.2%) in group P and 16 out of 55 individuals (29.1%) in group A experienced a UTI relapse. In this study, a 24-week ritual of drinking cranberry juice avoided the return of UTI in a small group of female participants.

A. Clinical trial data

Study / Trial	Design / Population	Key Outcome	Reference
Prevention of symptomatic UTIs in women, children, and susceptible groups	Meta-analysis of ~50 RCTs with ~8,857 participants	Cranberry products probably **reduce risk of symptomatic culture-verified UTIs** in women with recurrent UTIs, children and susceptible individuals, but not clearly in all populations	(Wituckii *et al.*, 2022)
Proanthocyanidin standardized cranberry powder trial	90-day randomized, dose-dependent study (UTI subjects, female adults)	High and low doses of cranberry powder **reduced *E. coli* positive cultures** and symptoms vs control	(Wu and Prior, 2005)
Cranberry extract UTI prevention in women (clinicaltrials.gov NCT02572895)	Trial among sexually active women with recurrent UTIs	Designed to test optimal cranberry extract dose effectiveness (results summary not publicly detailed)	(Xia *et al.*, 2021)
Clinical trials listing Vaccinium macrocarpon supplementation	Single-blind RCT with polyphenol cranberry supplementation	Evaluated effect of daily cranberry polyphenol on outcomes (full data not in public summary)	(Xue *et al.*, 2024)
Clinical trials in pregnant women (systematic review context)	RCTs in pregnant women with cranberry supplementation	Mixed compliance and tolerability; some tendency to reduce UTI incidence	(Yang *et al.*, 2022)

FUTURE SCOPE

Numerous bioactive components can be found in cranberries. Since the 20th century, researchers have been examining the advantages of cranberry for urinary system health. Researchers have focused more on cranberry Phytochemicals' ability to prevent cancer and vascular illnesses in the 21st century. Cranberries' Anthocyanin, procyanidins and Flavonol have all been shown to have potential benefits for stopping cancer. Numerous clinical studies have looked into the cardiometabolic adverse effects of cranberries. Cranberries were found to lower a number of cardiometabolic risk variables and to have a favorable impact on inflammatory cholesterol profiles. These

days, there is increasingly proof that cranberries play new significant functions in keeping intestinal health. It has been demonstrated that cranberries or cranberry juice can prevent intestinal irritation and prevent H. pylori from colonizing the gastrointestinal tract. Clinical trials with better study designs are desperately needed in future research to show the benefits of cranberries for cardiac, metabolic, and urinary tract health. To clarify the mechanisms of cranberry' impact on digestive health, hypothesis-driven experimentation employing dogs or cell culture is required. Copyright 2018 Chemical Pharmaceutical Society.

CONCLUSIONS

In the fields of pharmaceuticals, clinical medicine, and nutrition, cranberries have produced noteworthy scientific findings. Cranberries' bioactivity is based on a variety of Phytochemical substances, including Proanthocyanidin and anthocyanidins, triterpenoids, and minerals like vitamins and trace elements. Cranberries have a variety of pharmacological effects, including as antibacterial, antioxidant, anti- cancer, and anti-inflammatory drugs, and they are useful in preventing urinary tract and cardiovascular disorders due to their high level of bioactive chemicals. Cranberries have been shown in clinical applications to be remarkably effective in preventing and treating diseases of the urinary system, preserving digestive tract health, and aiding in cardiovascular diseases, offering new choices for pertinent preventative and curative measures. Cranberries are nutrient-dense, versatile, age-appropriate, and frequently utilized in diets. However, there are limitations to current cranberry studies. Although the various effects of cranberry are widely known, the precise method of action is still unknown. The reliability and generalization of experimental investigations are limited by certain studies' small sample sizes and brief research periods. Direct comparison and analysis of results is challenging due to varying experimental circumstances and procedures. In order to understand how cranberries treat illnesses, future study should concentrate on the underlying mechanisms of their pharmacological actions. In order to increase the validity and dependability of experimental research, long-term, comprehensive clinical studies should be carried out concurrently. Predicted that as research advances, cranberries will play an important part in a wider variety of sectors and significantly improve human health.

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