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# Antimicrobial Potential of Cranberry Proanthocynin in Urinary Tract Infections: A Literature Review

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***Abstract:*** ***Urinary tract infections (UTIs) are among the most prevalent bacterial infections, particularly affecting women, pregnant individuals, and children, and are often complicated by increasing antimicrobial resistance. This review evaluates the potential role of cranberry (Vaccinium macrocarpon) and its bioactive constituents, primarily A-type proanthocyanidins (PACs), in the prevention and adjunctive management of UTIs. Cranberry PACs exhibit a unique mechanism by inhibiting the adhesion of P-fimbriated Escherichia coli to uroepithelial cells, thereby reducing bacterial colonization. In addition, cranberries possess antimicrobial, antioxidant, and anti-inflammatory properties that further contribute to urinary tract health. Clinical studies show variable but promising results, especially in women with recurrent UTIs, with some trials demonstrating reduced recurrence rates when cranberry juice or extracts were consumed regularly. Pharmacokinetic studies indicate limited oral bioavailability of PACs, but their metabolites are excreted in urine where they exert local effects. Cranberry products are generally safe; however, potential drug interactions, particularly with warfarin, should be considered. This review concludes that cranberry may serve as an effective, non-antibiotic prophylactic option for recurrent UTIs, but standardized dosing, long-term safety, and high-quality clinical evidence remain areas for further research.***

***Keywords:*** ***Urinary Tract Infection (UTI), Cranberry (Vaccinium macrocarpon), Proanthocyanidins (PACs), Anti-adhesion mechanism, Recurrent UTI prevention.***

## I. INTRODUCTION

Urinary tract infection (UTI) is a common clinical problem, which can involve the urethra, bladder, and kidney.[1] UTI affects all age groups, but women are more susceptible than men, due to short urethra, absence of prostatic secretion, pregnancy and easy contamination of the urinary tract with faecal flora.[2]Additionally, the physiological increase in plasma volume during pregnancy decreases urine concentration and up to 70% pregnant women develop glucosuria, which encourages bacterial growth in the urine.[3] UTI in children is an important clinical problem. Renal scarring, which occurs in a small proportion of children (approximately 6% [4], is the most important outcome of infection as it is associated with significant future complications[5], and ultimately with end stage renal disease[6].

*Classification of UTI –*

It is understood that the infection targets the different parts of the urinary tract and as a consequence results in the contagion of the lower and the upper urinary tracts. The infection is named based on the site of infection. The infection of urethra and ureter are referred to as urethritis and ureteritis respectively where as cystitis and pyelonephritis corresponds to bladder and kidney infections.[7]. Generally UTIs are classified based on the factors that trigger the infection and the nature of occurrence. Taking these aspects in to consideration, UTIs can be classified as follows: i. Uncomplicated or complicated (based on the factor that triggers the infection) ii. Primary or recurrent (depending on the nature of occurrence)[8]. Urinary tract infections (UTIs) are common, especially in women, and frequent antibiotic use has led to rising drug resistance. First-line treatments include nitrofurantoin, trimethoprim-sulfamethoxazole, and Fosfomycin, with fluoroquinolones used for more severe cases. In pregnancy, cephalosporins and nitrofurantoin are preferred. Recurrent UTIs (rUTIs) should be managed with non-antibiotic strategies like immunostimulants (OM-89) and vaginal estrogen for postmenopausal women. Antibiotic prophylaxis is a last resort due to resistance risks. Lifestyle changes, such as increased water intake, may help, while cranberry products and probiotics show limited effectiveness. The focus is on minimizing antibiotic use and promoting safer preventive options.[9]

*Botanical description*

 

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The scientific name for cranberry plant is Vaccinium macrocarpon [10]. Cranberries, blueberries, and Concord grapes are the only 3 fruits that are native to the United States and Canada. Most commercial farms today are located in northern United States, Massachusetts, and New Jersey and the Canadian provinces of Quebec and British Columbia [11]. Commercial harvests occur in September and October. Cranberries contain 180% water and 10% carbohydrates [12]. Among other constituents are flavonoids, anthocyanins, catechin, triterpenoids, organic acids, and a small amount of ascorbic acid. The major organic acids are citric, malic, and quinic acids, with small amounts of benzoic and glucuronic acids [13]. Anthocyanin pigments obtained from cranberry pulp are used for coloring applications [14]. Cranberries can be processed into fresh fruit, concentrate, sauce products, and juice drinks [11].

## II. TAXONOMY

Family: Ericaceae (Heath family)
Genus: *Vaccinium*
Subgenus: *Oxycoccus*
Common Species:
*Vaccinium macrocarpon* (American cranberry)
*Vaccinium oxycoccos* (Northern or common cranberry)
Morphology
Growth Habit:
Low-growing, perennial, trailing vines or shrubs
Vines can extend up to 2 meters, but plants remain under 20 cm tall
Leaves:
Small, evergreen, ovate to lanceolate
5–10 mm long, with entire margins and a leathery texture
Arranged alternately on slender stems
Stems:
Thin, wiry, and woody at the base
Capable of rooting at nodes, aiding vegetative spread
Flowers
Type: Perfect (bisexual), actinomorphic
Color: Pink to reddish-purple
Structure: Four petals reflexed backward, exposing stamens and style
Pollination: Primarily by bees; buzz pollination is common Fruit
Type: True berry
Size: 9–14 mm in diameter
Color: Green when immature, ripening to deep red
Taste: Highly acidic due to organic acids (especially quinic and citric acids)
Habitat
Native Range: Temperate and boreal regions of the Northern Hemisphere
Preferred Conditions: Acidic, nutrient-poor soils in bogs and wetlands
Cultivation: Commercially grown in sandy peat soils with controlled flooding for harvest[15]

1) *Proanthocyanidins.* American cranberry has a complex and rich phytochemical composition, particularly flavan-3-ols, A type procyanidins (PACs), anthocyanins, benzoic acid, and ursolic acid. Cranberry flavan-3-ols are present as monomers, oligomers, and polymers (Table 1) [16]. These oligomers and polymers are also referred to as PACs or condensed tannins and represent w85% of the total flavan-3-ols on a weight ba sis[17,18]. PACs with at least 1 A-type linkage account for 51–91% of total PACs in cranberry[19,20]. The 11 Abbreviations used: CETP, cholesterol ester transfer protein; CHD, coronary heart disease; CRP, C-reactive protein; CVD, cardiovascular disease; DP, degree of polymerization; eNOS, endothelial NO synthase; FW, fresh weight; HDL-C, HDL cholesterol; ICAM-1, intercellular adhesion molecule 1; IMT, intima-media thickness; LDL-C, LDL cholesterol; MI, myocardial infarction; NF-kB, nuclear factor k-light-chain-enhancer of activated B cells; PAC, proanthocyanidin; PWV, pulse wave velocity; ROS, reactive oxygen species; sVCAM-1, soluble vascular cell adhesion molecule 1; UTI, urinary tract infection. distinction between A- and B-type PAC structures is of impor tance because the

difference can influence their biological properties. The A-type PACs exhibit significantly greater inhi bition of in vitro adhesion of P-fimbriated Escherichia coli bac teria to uroepithelial cells than the B-type PACs, the initial step of UTI[21].

2) *Anthocyanins.* Amounts of anthocyanins are remarkably high in cranberry, contributing to the color of the fruit and derived foodstuffs, as well as the potential effects on hu man health. American cranberry is one of the rare foods that comprise glycosides of the 6 aglycones of the anthocyanidin family: cyanidin, peonidin, malvidin, pelargonidin, delphinidin, and petunidin (Fig.1) [22]. The predominant anthocyanins are the3-O-galactosidesand3-O-arabinosides of cyanidinandpeonidin; a total of 13anthocyanins, mainly3-O-monoglycosides, have been detected [16,23]. Cranberry anthocyanin content increases with ripening and is also dependent on the cultivar and size of the fruit) [24-26].
3) *Phenolic acids.* Cranberry also contains phenolic acids, in cluding hydroxybenzoic and hydroxycinnamic acids. The former are the most abundant, with very high contents of benzoic acid at 474–557 mg/100 g FW [27-29].
4) *Terpenes.* Although much less studied than the polyphenol composition, the presence of potentially active terpenes in cranberry deserves further attention. Ursolic acid (Fig. 1) is abundant in American cranberry at 46–109 mg/100 g FW [30]. This triterpene is a constituent of numerous traditional herbal medicines and has strong anti-inflammatory effects.[31]
5) *Flavonols.* Flavonols in cranberries consist mainly in glyco sides of quercetin, myricetin, and to a lesser extent, kaemp ferol (Fig. 1). Quercetin 3-galactoside is the predominant form, but at least 11 other glycosides are present in lower concentrations [16,23].

## III. EXPERIMENTAL MODEL AND CLINICAL TRIALS

Because the pathogenesis of UTI varies depending on the patient group, the selection of study participants is especially crucial. Because bacteria can enter the bladder during sex, young, sexually active women frequently get UTIs after having sex. Structural abnormalities in the urinary system that make patients more susceptible to turbulent urine flow and the introduction of germs from the periurethral region to the bladder, renal pelvis, and/or kidney can cause UTIs in young infants. These other populations are not the same as older women who experience recurring UTIs. Thus, one needs take into account the people, product used, dosage and mode of administration, duration of exposure, adherence to the regimen, and comparator agent selection in order to properly assess the ability of cranberries to prevent or treat UTIs. The findings of individual studies and meta-analyses have been consistent, which is not surprising given these factors [32].

### *A. Clinical Trials In Adult Women And In Women With Recurrent UTIs*

The majority of research on cranberry therapies has focused on women, who are more likely than men to get UTIs, and especially on women who experience recurring UTIs. A 66-year-old woman with chronic pyelonephritis that was resistant to antibiotic treatment was the subject of an early case report [33]. Her urine (as measured by albuminuria and pyuria) improved after 8 weeks of treatment with 180 mL cranberry juice twice daily, and after 9 months, the infection was nearly totally eradicated. For two and a half years, she did not need antibiotics again. Both cross-over [34] and parallel [35–37] designs were used in placebo-controlled trials that looked at women with a history of recurrent UTIs to see if cranberry consumption can stop outbreaks. There was only one research, and several cranberry products and placebos were used in these trials. [37]

### *B. Clinical Trials in Children*

In a placebo-controlled parallel design research, Ferrara et al. [38] looked at 84 girls between the ages of 3 and 14 who had had more than one UTI in the previous 12 months. Partici pants received 100 mL of Lactobacillus GG five days a month, 50 mL of cranberry-lingonberry concentrate every day, or a 'no treatment' control for six months. The UTI rate was 48.1% for the control group, 42.3% for the Lactobacillus group, and 18.5% for the cranberry-lingonberry juice group. In a crossover trial, Foda et al. [39] recruited children with neuropathic bladders undergoing intermittent catheterisation, with an average age of 9.4 years. For six months, the children were given either water or 15 mL/(kg $ d) of cranberry juice cocktail. Asymptomatic bacteriuria and UTI recurrence did not differ between the two groups. However, the study's ability to demonstrate a statistically significant benefit was limited because 19 out of the 40 participants withdrew during the study period. Salo et al. (85) used a parallel trial strategy to examine 255 children who had previously been diagnosed with a UTI with either cranberry juice [5 mL/(kg $ d); up to 300 mL] or a placebo juice for six months.

 

## IV. DIAGNOSIS

### A. *Medical history*

The medical history is the primary basis for the clinical diagnosis of a urinary tract infection. Certain information can either raise or lower the likelihood of a urinary tract infection. Clinical research have demonstrated the following criteria [40, 41]. 1) Nycturia (↑), pollakiuria, and dysuria 2) Incontinence, either present or worsened (↑) Macrohematuria (↑) is the third 4) Suprapubic discomfort (↑) 5) Turbid urine with a "offensive" odour (↑) 6) Previous urinary tract infections (↑) 7) Vaginal discomfort and altered or fresh discharge (↓). 2) In addition, there are known risk factors that increase the chance of UTI. Among these are: 1) Sexual activity within the previous two weeks [42]. 2) Contraception using sper micide or a vaginal diaphragm [43] 3) DMPA (depot medroxypro gesterone acetate) contraception [44] 4) The use of antibiotics over the two to four weeks prior [45].

### B. *Urine testing*

#### *1)* Urine gathering

The need to clean the perineum and vulva or glans penis, as well as to collect urine midstream, has been the subject of numerous research [46,47,48].

#### *2)* Useful test techniques

A bacteriological urine culture, along with pathogen identification, quantification, and sensitivity testing, is the gold standard for a urine test. Direct techniques are frequently employed in practice to identify the bacteria or inflammation (dip sticks) in order to determine whether the patient has a UTI at all. Both immersion culture media and urine microscopy can be used to determine the bacterial count.

#### *3) Dip sticks*

One of the most common tools for diagnostic testing when there is clinical evidence of a UTI in a patient is a urine dip stick. The most often used Multistix may be able to identify leukocyte esterase, blood (as an indicator of inflammation), protein, and nitrite (a metabolic result of common urinary tract pathogens). With a likelihood ratio [LR] of 2.6 to 10.6, the presence of nitrite raises the risk of a urinary tract infection. The sensitivity is really low, though. On the other hand, leukocyte esterase detection raises the likelihood to a lower extent (LR 1.0 to 2.6). Although blood detection has a high sensitivity, its specificity is limited. Research findings regarding the usefulness of protein detection in confirming UTIs are inconsistent. [49]

#### *4) Urine Microscopy*

Gram-stained microscopy has a limited sensitivity for detecting UTIs with <105 cfu/mL because of methodological limitations. According to certain research, skilled personnel can obtain more accurate diagnoses than urine cultures. Nevertheless, the research on microscopy that is now available is diverse, and every review study comes to the conclusion that it is challenging to draw broad conclusions [50].

#### *5) Immersion culture media*

A plastic rod coated with culture medium—typically a mix of MacConkey and CLED agar—is used in these immersion assays. They need a 24-hour culture. It is impossible to replicate the laboratory-obtained sensitivity and specificity values in primary care settings (24). The results showed that the specificity was 94% (CI 88–98) and the sensitivity was 73% (95% CI 66–80) in the primary care context. The sensitivity is lowered to 65% (CI 55–74) and the specificity is almost the same (CI 90–99) if a female patient has previously had a negative nitrite test. Reliable detection of <104 cfu/ml is not possible with this method [51].

## V. TREATMENTS

### A. *Antibiotics*

Although trimethoprim/sulfamethoxazole (Bactrim, Septra) has been shown to have higher cure rates than amoxicillin, which has historically been the first-line antibiotic for UTIs, rising E. coli resistance rates have made it a less popular option. Additional options include cephalosporins like cefixime (Suprax), cefpodoxime, cefprozil (Cefzil), or cephalexin (Keflex) or amoxicillin/clavulanate (Augmentin). [52] Additionally, there was no discernible difference in the growth of resistant organisms at the end of therapy comparing treatments with short and conventional durations. [53] Therefore, in children with lower UTIs, a course of oral antibiotics lasting two to four days seems to be just as effective as a course lasting seven to fourteen days. 19.

It is not advised to take oral antibiotics in single doses or for a single day as this may be less effective than extended courses. [54, 55]. The U.S. Food and Drug Administration has approved Ciprofloxacin (Cipro) for use in treating patients aged one to seventeen who have severe UTIs and pyelonephritis caused by E. coli. [56] Commonly used antibiotics are listed in Table 1. [57]. Antibiotic therapy plays a vital role in the management of urinary tract infections (UTIs). The selection of an appropriate antibiotic depends on the type of UTI—whether uncomplicated or complicated—as well as the causative microorganism and its resistance profile. The most common pathogens include *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Enterococcus faecalis*. For uncomplicated UTIs, first-line drugs such as Nitrofurantoin, Trimethoprim-sulfamethoxazole (Co-trimoxazole), and Fosfomycin tromethamine are commonly prescribed due to their high efficacy and minimal resistance. Fluoroquinolones such as Ciprofloxacin and Levofloxacin are often used for complicated or recurrent infections, though their use should be restricted to avoid resistance development. Beta-lactam antibiotics, including Amoxicillin-clavulanate, Cefixime, Cefuroxime, and Ceftriaxone, are also effective alternatives, particularly in moderate to severe infections. In hospital-acquired or resistant infections, Aminoglycosides like Gentamicin or Amikacin may be administered parenterally. For infections caused by multidrug-resistant strains, Carbapenems such as Meropenem or Imipenem are considered last-resort options. The usual duration of therapy is 3–5 days for uncomplicated and 7–14 days for complicated UTIs. Supportive measures, including adequate hydration, proper hygiene, and regular follow-up, further enhance therapeutic success and help prevent recurrence. [56,57]

| *Antibiotic* | *Dosing* | *Common adverse effects* |
|---|---|---|
| Amoxicillin/clavulanate (Augmentin) | 25 to 45 mg per kg per day, divided every 12 hours | Diarrhea, nausea/vomiting, rash |
| Cefixime (Suprax) | 8 mg per kg every 24 hours or divided every 12 hours | Abdominal pain, diarrhea, flatulence, rash |
| Cefpodoxime | 10 mg per kg per day, divided every 12 hours | Abdominal pain, diarrhea, nausea, rash |
| Cefprozil (Cefzil) | 30 mg per kg per day, divided every 12 hours | Abdominal pain, diarrhea, elevated results on liver function tests, nausea |
| Cephalexin (Keflex) | 25 to 50 mg per kg per day, divided every 6 to 12 hours | Diarrhea, headache, nausea/vomiting, rash |
| Trimethoprim/ sulfamethoxazole (Bactrim, Septra) | 8 to 10 mg per kg per day, divided every 12 hours | Diarrhea, nausea/vomiting, photosensitivity, rash |

Table no 1. Antibiotics and their dosing for UTI in market

*B. Cranberry*

Proanthocyanidins (PACs), a class of polyphenolic chemicals that have drawn a lot of interest due to their potential to prevent urinary tract infections (UTIs), are the mainstay of cranberries' pharmacological properties. The distinctive A-type chemical structure of cranberry PACs sets them apart from the B-type connections present in other fruits' PACs. This structural difference is thought to be essential for the cranberry's ability to prevent bacteria from adhering to the bladder wall, which is a pivotal stage in the formation of UTIs [58]. Numerous phenolic acids found in cranberries, such as hydroxycinnamic acid and benzoic acid, have been investigated for their antibacterial and anti-inflammatory qualities. [59, 60]

## VI. MECHANISM OF ACTION:

*A. Proanthocynin*

| Cranberry metabolite | Mechanism of action | Clinical evidence study | Notable metabolites |
|---|---|---|---|
| Proanthocyanins-dins (PACs) | Inhibits E. coil adhesion to uroepithelial cells | Poor bioavailability, PAC metabolites, like valeric acid and valerodenedin-tected in urine | Valeric acid, Valerodone derivatives |

Table no 2. Cranberry Proanthocyanin [61]

Cranberry's ability to prevent UTIs has been explained by a number of processes, with particular emphasis on its ability to disrupt bacterial adhesion in the urinary tract [62]. After eating cranberries, urine exhibits an antiadhesion reaction that stops uropathogenic P-fimbriated E. coli from sticking to receptors on bladder cells [63]. The bacteria won't proliferate and spread infection if they can't adhere to cells. Changes in bacterial morphology [65] and/or genetically driven reductions in P-fimbrial expression [65,66] could be the cause of the decrease in adhesion forces [64]. Furthermore, it has been shown that cranberry bioactives, particularly the bigger oligomer polyphenols, have a positive impact on gut flora. [67]. These mechanisms offer a thorough understanding of how cranberry ingredients aid in the management of UTIs and are mostly based on the bioactive components of cranberries, such as proanthocyanidins (PACs), flavonoids, and phenolic acids [68,69].

*1) Anti-adhesion activity of Proanthocynin*

Cranberries' anti-adhesion qualities, which are primarily brought about by the presence of special A-type proanthocyanidins (PACs), are the main factor contributing to its efficacy against UTIs. These substances prevent P-fimbriated Escherichia coli, the most prevalent bacteria that cause UTIs, from adhering to the urinary tract's lining cells. It is thought that A-type PACs selectively connect to the P-fimbriae on the surface of E. coli, changing the bacterial cell surface and inhibiting uroepithelial cell adhesion. This process lessens the possibility of bacterial colonisation and the emergence of an illness [70,71]. Cranberry PACs dramatically reduce the adherence of P-fimbriated E. coli to uroepithelial cells in lab settings, according to research by Howell that offered preliminary support for this anti-adhesion mechanism. These results have been supported by other research, which highlights cranberry's specific effect against P-fimbriated strains of E. coli, which cause a significant percentage of UTI cases [72,73].

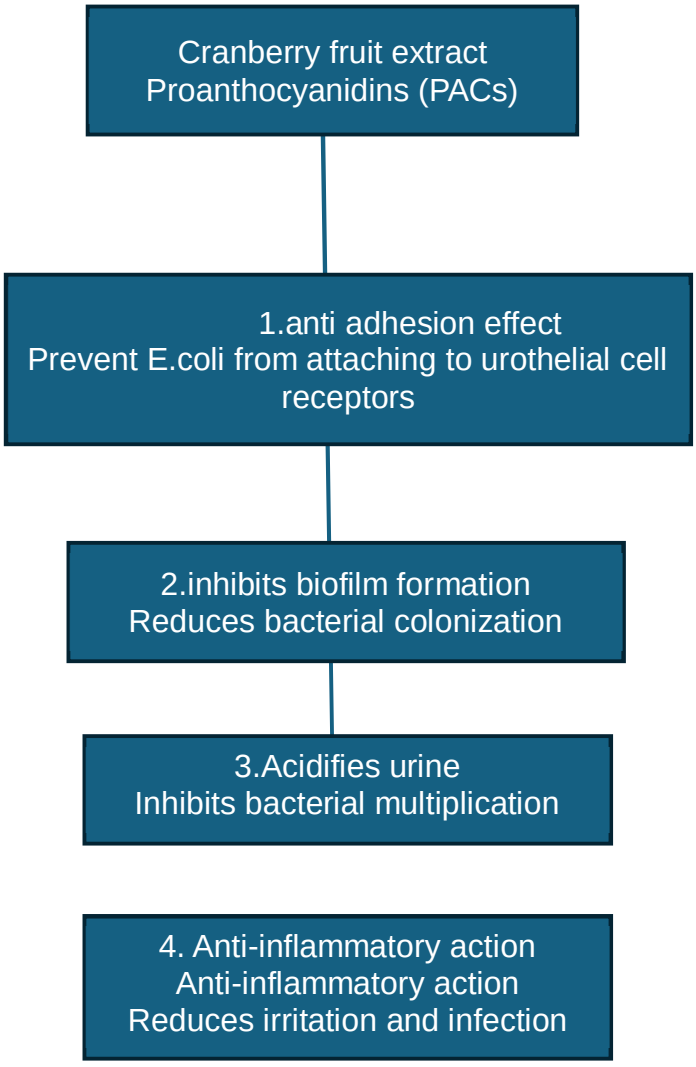


Fig no 1. MOA Of Proanthocyanin.[74]

*2) Antimicrobial characteristics*

Cranberry components provide direct antibacterial activity against a variety of uropathogens, in addition to inhibiting bacterial adhesion. The potential of cranberries' flavonoids and phenolic acids to stop bacterial growth and eradicate them has been studied [75]. These substances have the ability to damage bacterial cell walls, obstruct quorum sensing, which is a process by which bacteria communicate, and stop vital bacterial enzymes from working. For instance, studies by Côté[76] revealed that cranberry extracts have antibacterial qualities against strains of E. coli that are resistant to antibiotics, indicating that cranberries may play a part in treating the growing problem of antibiotic resistance in the treatment of UTIs[76,77].

*3) The anti-inflammatory and antioxidant properties*

The inflammation and oxidative stress associated with UTI development might exacerbate the illness and prolong the healing period. Flavonoids and other antioxidants, which are abundant in cranberries, are essential for controlling inflammation and minimising oxidative damage. By scavenging reactive oxygen species (ROS) and influencing inflammatory signalling pathways, these substances may reduce the severity of UTIs and promote healing [78]. highlighted cranberry's anti-inflammatory properties and showed how consuming it could change inflammatory biomarkers in UTI settings [79]. This implies that cranberries' anti-inflammatory and antioxidant qualities complement their antibacterial and anti-adhesion activities in the treatment of UTIs [79, 80].

*B. Pharmaco-kinetic of cranberry*

Cranberry's pharmacokinetics—the processes of absorption, distribution, metabolism, and excretion (ADME) of its active ingredients—are essential to comprehending how well it works to treat UTIs and how it interacts with medications. Proanthocyanidins (PACs), flavonoids, and phenolic acids are among the bioactive substances found in cranberries. Their distinct pharmacokinetic characteristics influence their safety and therapeutic efficacy [81].

1) *Absorption:* The chemical makeup of cranberries and the type of cranberry product (juice, extract, or capsule) that is consumed determine how well the bioactive chemicals are absorbed. According to studies, PACs have a limited oral bioavailability because of their huge molecular size and complexity. Nevertheless, systemic effects can still be produced by trace levels that are absorbed through the gastrointestinal tract. Changes from the gut microbiota can affect the bioavailability of flavonoids and phenolic acids, which are absorbed more easily. After absorption, these substances can affect a number of metabolic processes, such as those that improve antioxidant defence and prevent bacterial adhesion [70,71,81].
2) *Distribution:* After being absorbed, the bioactive ingredients in cranberries are dispersed throughout the body, with their molecular size and lipophilicity determining their particular affinity for particular tissues. The chemicals' ability to enter the urinary tract, where they can have local antibacterial and anti-adhesion actions, depends on their distribution. Research has demonstrated that metabolites from cranberry components are present in urine, suggesting that they have successfully entered the urinary system [81,82].
3) *Metabolism:* Cranberry components are mostly metabolised in the gut and liver, where they go through a lot of biotransformation. Conjugation processes that increase their water solubility and facilitate their excretion are a part of this process. Additionally, cranberry components are metabolised by the gut microbiota into a variety of metabolites that may have health benefits. Urine and plasma have been found to contain these metabolites, which include those from PACs and flavonoids, suggesting systemic exposure and biological action [83,84].
4) *Excretion:* Proanthocyanidins, hippuric acid, benzoic acid derivatives, and urinary phenolic acids are among the cranberry-derived substances whose excretion guarantees their activity in the urinary system. These metabolites enhance the antimicrobial environment, reduce bacterial adhesion, and acidify the urine, all of which contribute to the UTI-preventive benefits of cranberries. Furthermore, some substances are eliminated from the body entirely by being expelled into faeces through bile [81,85,86].

*C. Toxicity Study*

*1) Interactions*

There is a lot of curiosity and worry about how cranberries and prescriptions interact, especially when it comes to drugs like warfarin that have limited therapeutic windows. Cranberries may have an impact on the pharmacokinetics of medications taken together, either by changing how they are metabolised or by affecting how they are distributed and eliminated. Patients taking cranberry products along with warfarin have been reported to have higher international normalised ratio (INR) levels and an increased risk of bleeding.

Cranberry's effects on the cytochrome P450 enzyme system and/or platelet function are thought to be the cause of this interaction, which may prevent warfarin from being metabolised and increase its anticoagulant effects. Healthcare professionals need to be aware of the complex pharmacokinetics of cranberries and their potential to interact with drugs. In addition to being closely watched for any negative effects, patients on drugs with restricted therapeutic indices should be counselled about the possible hazards of consuming cranberries at the same time. To determine the underlying processes of these interactions and to develop recommendations for the safe co-administration of cranberry products with other drugs, more research is necessary. [87].

## VII. RECENT ADVANCEMENT

Large recent meta-analyses and systematic reviews report that regular cranberry intake—particularly products standardized for A-type PAC content—reduces recurrent UTI risk in many patient groups, though effect size varies by dose and product. The primary antimicrobial mechanism supported by in vitro and ex vivo work is anti-adhesion: A-type PACs block P-fimbriae/FimH-mediated attachment of uropathogenic E. coli to uroepithelial cells, reducing colonization. Recent randomized controlled trials and population studies (including whole-fruit powder and high-PAC capsule trials) have produced stronger clinical evidence that standardized cranberry products can lower culture-confirmed UTI incidence in selected cohorts. Researchers increasingly view PACs as an adjunct/ preventive strategy to reduce antibiotic use and the selective pressure driving resistance, rather than as a standalone treatment for acute infections [88]. Advances in formulation science — nanoencapsulation, polysaccharide/protein complexes, chitosan-based carriers and liposomal systems -are improving PAC stability, intestinal absorption and urinary excretion, addressing prior bioavailability limitations. Metabolomics work shows that gut and hepatic metabolism produce smaller PAC metabolites that are likely the bioactive urinary species, shifting focus from parent compounds to metabolite profiling in pharmacokinetic studies. Synergy studies report that PACs can potentiate efficacy of some antibiotics and urinary antiseptics in vitro, suggesting combination therapies might lower required antibiotic doses — though clinical confirmation is limited. Standardization problems persist: PAC quantification methods, A-type vs B-type proanthocyanidin reporting, and inconsistent dosing across trials make cross-study comparisons and dosing guidelines challenging. New in vitro models (organoid and flow-cell bladder epithelium systems) and better strain panels, including multidrug-resistant uropathogens, are being used to test anti-adhesive and anti-biofilm activity more rigorously. Regulatory and guideline opinions now often acknowledge cranberry's preventive potential for recurrent UTI in specific populations, but recommend standardized high-PAC preparations and call for larger, well-powered RCTs to define optimal dose and target groups [89].

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## VIII. SUMMARY

Recent advancements highlight the growing evidence supporting the antimicrobial potential of cranberry proanthocyanidins (PACs) in urinary tract infections (UTIs). Meta-analyses and systematic reviews demonstrate that cranberry products standardized for A-type PACs effectively reduce the recurrence of UTIs across various populations.

The key antimicrobial mechanism involves the inhibition of *Escherichia coli* adhesion to uroepithelial cells through the interaction of PACs with bacterial fimbriae, thereby preventing colonization. Clinical trials using whole-fruit powder and high-PAC capsules have strengthened evidence for reduced culture-confirmed UTI rates. Researchers now consider PACs as valuable preventive adjuncts that can decrease antibiotic use and mitigate antimicrobial resistance rather than as stand-alone treatments. Advances in formulation technology—such as nanoencapsulation, liposomal systems, and chitosan-based carriers—have improved PAC stability, absorption, and urinary excretion. Metabolomic studies further reveal that PAC metabolites produced by gut and hepatic metabolism are the active urinary components responsible for antibacterial effects. Additionally, synergistic effects with antibiotics have been observed, although more clinical validation is required. Despite these promising developments, challenges remain in standardizing PAC quantification methods and determining optimal dosing, emphasizing the need for larger, well-designed clinical trials to establish cranberry's therapeutic role in UTI prevention.

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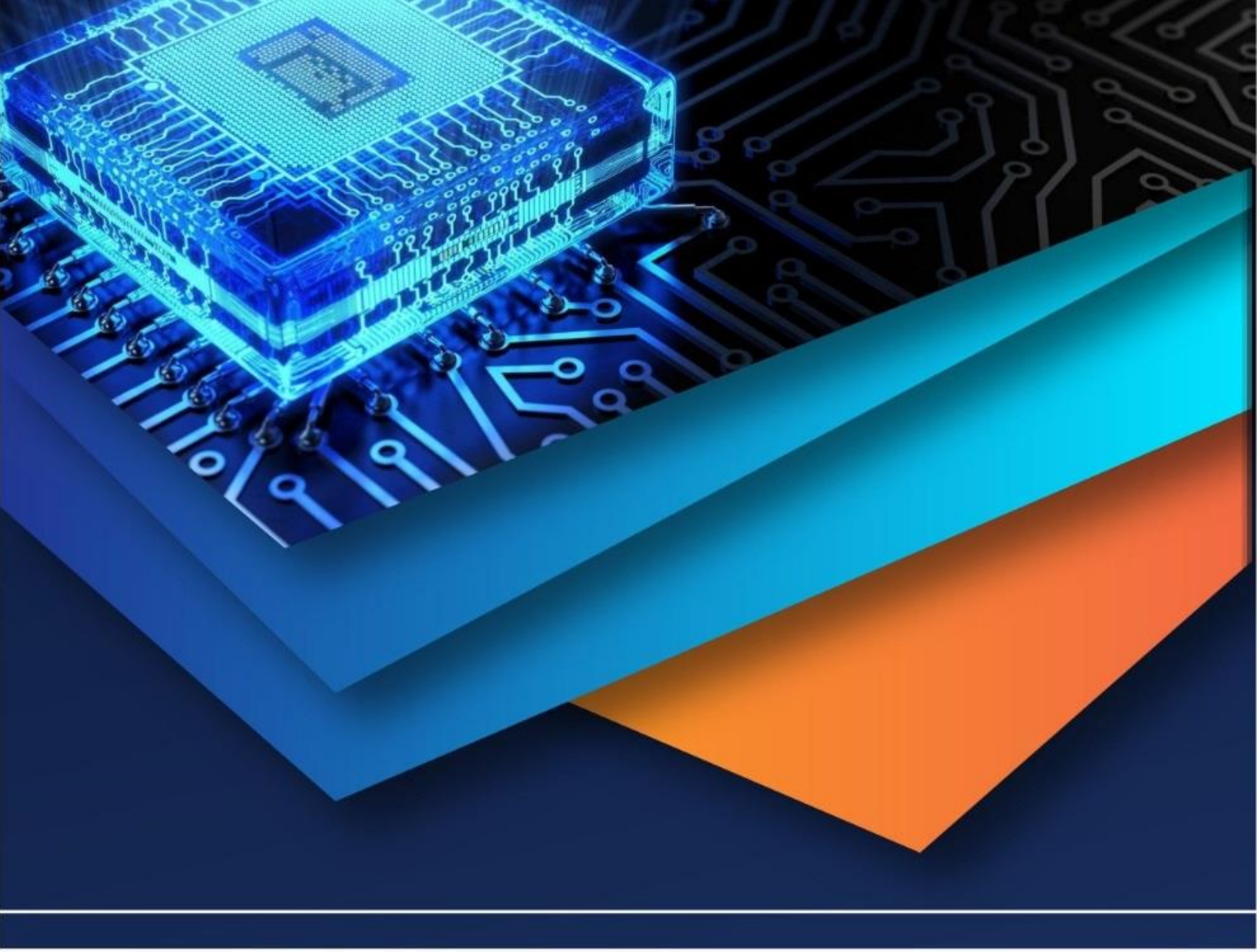

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