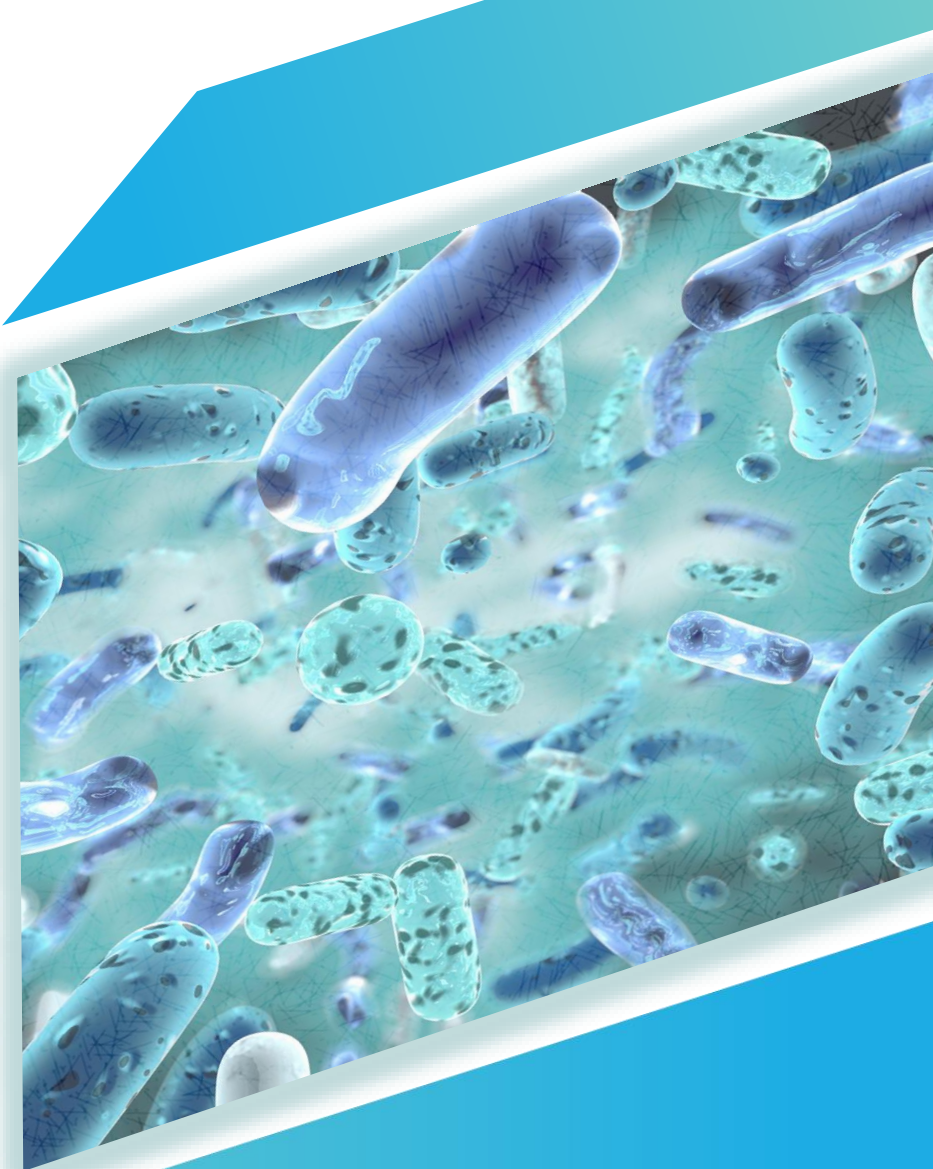


Role Of Probiotics In Treatment Of Urinary Tract Infections

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Introduction:

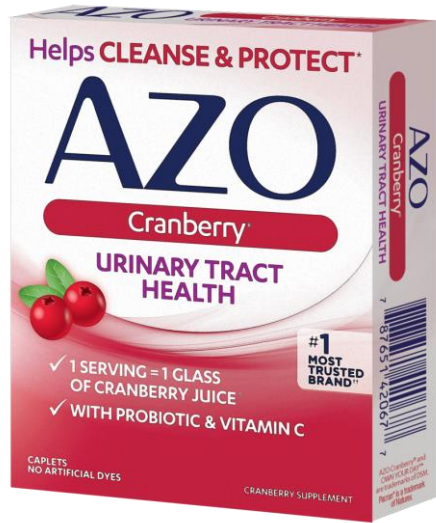
- Urinary tract infection (UTI) is one of the most common diseases of childhood
- UTI affects about 2% of boys and 8% of girls by the age of 7 years
- A significant proportion of the children (10–30%) have a recurrence of UTI following the initial episode.
- UTI leads to serious morbidities :kidney scars, ESRD, hypertension
- Antibiotics are the cornerstone of UTI management

Cont.

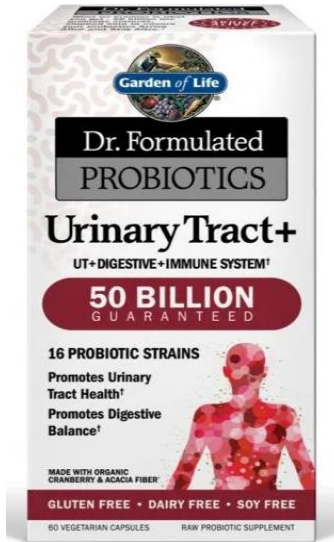
- Low-dose long-term antibiotic prophylaxis is used to prevent UTI
- **Adverse effects of long term antibiotic therapy:**
 - Dysbiosis of vaginal and intestinal normal flora
 - Antibiotic resistance
- **Non-antibiotic therapies** may be beneficial to accentuate the efficacy of antibiotic therapy and prevent the long term side effects of antibiotics



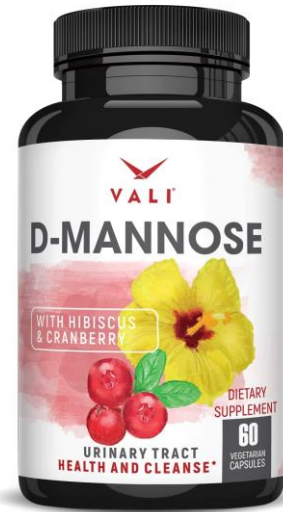
Non-antibiotic therapies to prevent recurrent UTI



Cranberry
juice



probiotics



D-mannose



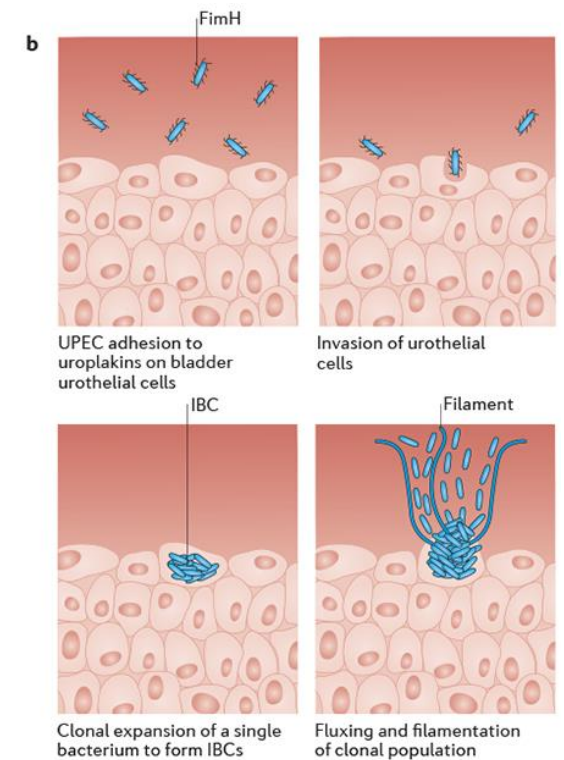
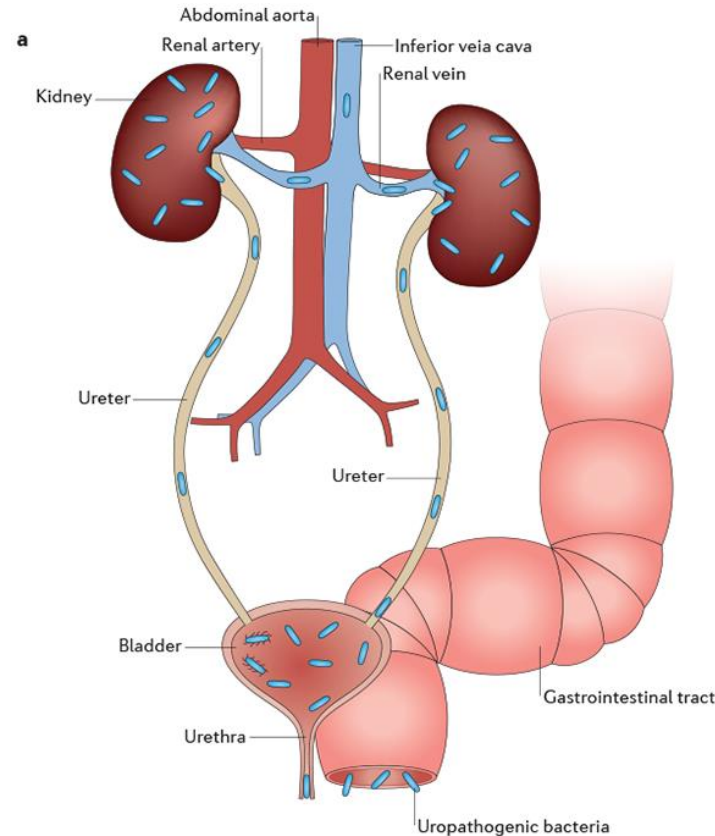
vitamins



Vaccine

Two most crucial steps in the pathogenesis of UTI

- **Urogenital colonization with uropathogens**
 - **Probiotics** and **Vitamin C** prevent UTI by **inhibiting colonization** of uropathogens
- **Adherence of bacteria to uroepithelium**
 - **Cranberry** and **D-mannose** inhibit their **adherence to uroepithelium**



These non-antibiotic interventions have shown promising results in adults but in children, the trials were of smaller size and demonstrated conflicting efficacy.



Probiotics:

- Live micro-organisms that can elevate the host's health level
- The mechanism of action of probiotics:
 - Maintenance of the mucosal barrier
 - Resistance to colonization
 - Inactivating bacterial toxins and virulence factors
 - competition with uropathogens for iron
 - Maintaining a normal bladder PH



Probiotics:

- Human breast milk, known as natural probiotics, was proven to prevent UTI in infants.
- Commercially available probiotic products decreased the incidence of UTI in preterm infants

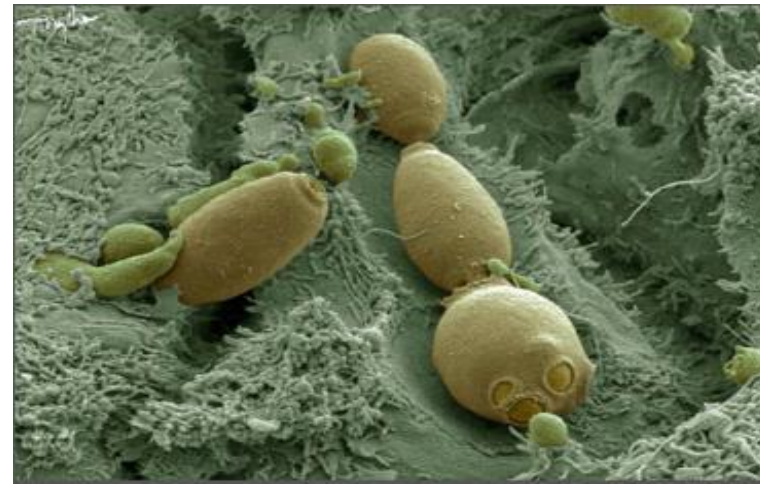


Most common used probiotics in prevention of recurrent UTI

- *Lactobacillus acidophilus*



- *Saccharomyces boulardii*



Probiotics Vs Placebo :



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- Two studies compared probiotics with placebo in children at risk of recurrence of UTI (but no structural anomaly or obstruction)

Probiotic therapy was effective in reducing UTI recurrence



Probiotics Vs antibiotics in primary VUR:



- Two trials compared probiotics against antibiotic prophylaxis in patients with primary VUR

Probiotics have similar efficacy as antibiotic prophylaxis in preventing UTI but with a significantly lower risk of antimicrobial resistance

No significant difference in risk of new kidney scarring between probiotic and antibiotic groups



Probiotics +Antibiotics Vs antibiotics



- 2 Studies compared probiotic plus antibiotic prophylaxis combination with antibiotic alone

Probiotics + antibiotics are slightly better in preventing UTI recurrence

Probiotics + antibiotics lowers the incidence of antibiotic resistance

No significant difference in the risk for new kidney scarring



Efficacy of Probiotic Prophylaxis After The First Febrile Urinary Tract Infection in Children With Normal Urinary Tract

- 181 children, aged 4 months to 5 years, with a normal urinary tract after recovery from their first febrile UTI were randomly divided in 2 groups (probiotic mixture of *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Bifidobacterium bifidum*, and *Bifidobacterium lactis* (n = 91)) and placebo (n = 90) for a total of 18 months
- ✓ (AAP recommended that antimicrobial prophylaxis not be given to children aged 2 to 24 months after their first febrile UTI if the results of renal and bladder ultrasonography are normal but as there is always concern about the high recurrence of UTI in the infants, non antibiotic measures are of interest.)

Results:

- *At 18 months, composite cure was observed in 96.7% (3 of 91 patients) of the patients in the probiotic group and 83.3% (15 of 90) of the patients in the placebo group (difference, -13.3 percentage points [95% confidence interval, -8.9 to 4.1]; P = .02)*
- *Compared with placebo, probiotic prophylaxis reduced the incidence of UTI recurrence significantly in children after a febrile UTI.*
- *This efficacy was more pronounced in girls than in boys*


prebiotics

Prebiotics are the substrate for probiotics production.

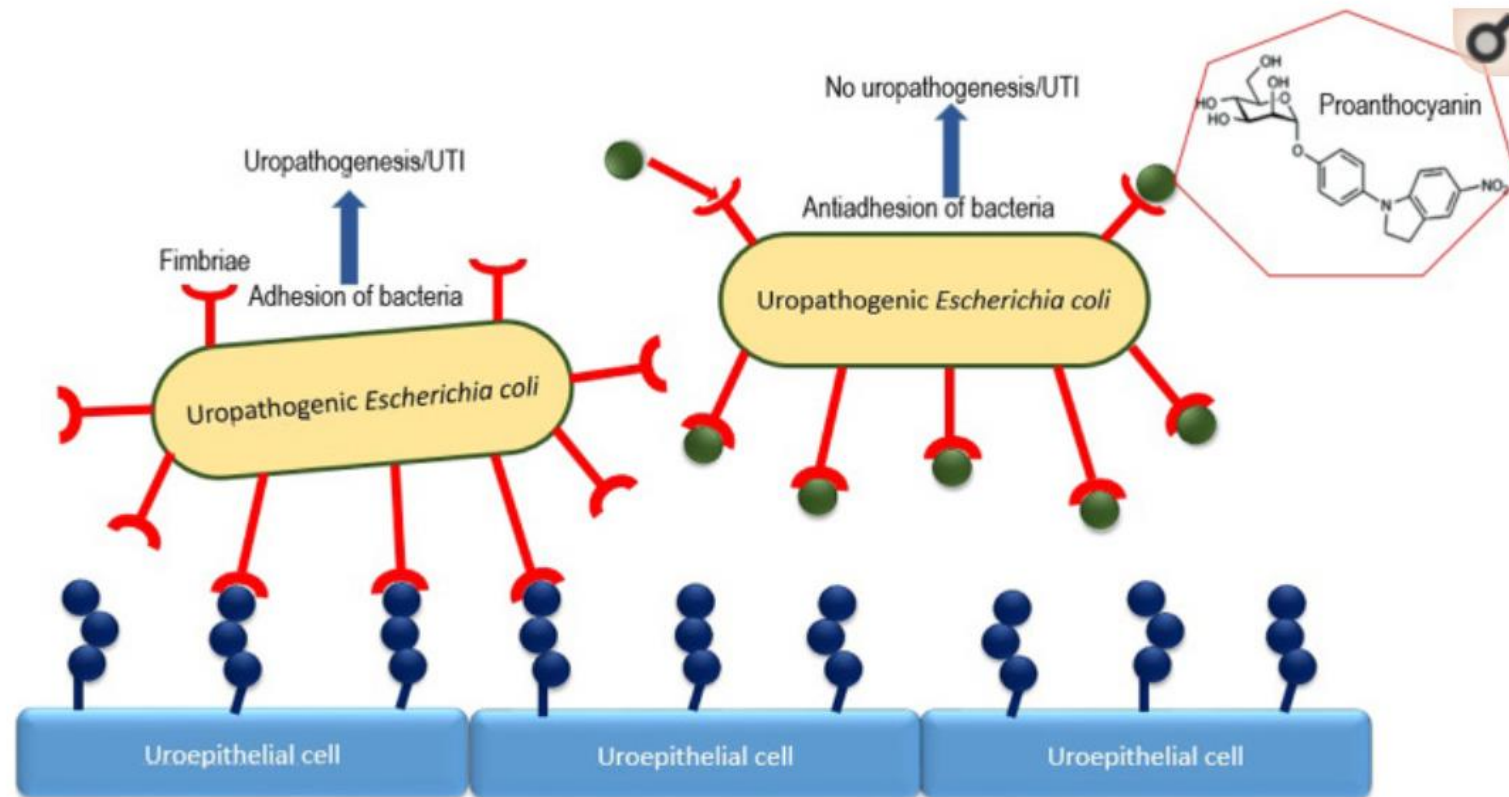
- Recently, oligosaccharides have been found to play a significant role in the modulation of microbiota.
- **Hemicellulose-Derived Oligosaccharides:**
- xylan → Xylooligosaccharides (XOS)
- Mannan → Mannooligosaccharides (MOS)
- arabino-xylan → Arabino-xylooligosaccharides (AXOS)

Benefits of the oligosaccharides:

- (1) Their consumption does not increase the blood glucose level or spike the secretion of insulin because of the formation of a gel in the gut through which it dissolves
- (2) Their nature is non-cariogenic and low calorific (0–3 kcal/g of sugar)
- (3) They stimulate the growth of specific microorganisms that enrich the gut environment by decreasing PH.
- (4) They ameliorate the absorption of the minerals (mainly calcium) through the intestinal cells.

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- Among all the HDOs, **arabinoxylglucan oligosaccharides** have been found to be effective in the prevention of UTIs.
 - **Cranberry** (*Vaccinium macrocarpon*) juice containing arabino-xyloglucan oligosaccharides showed an anti-adhesion effect against P-fimbriated *E. coli* in swine.
 - **High mannose-containing glycoprotein** oligosaccharides attached to the pathogenic fimbriated *E. coli* were found to be the reason for mannose-inhibited hemagglutination

Proanthocyanidins, a substance present in cranberries directly inhibit fimbriae-mediated adhesion of *E. coli* to uroepithelium



Cranberry Vs placebo:



- Five clinical trials compared cranberry products with placebo in children with the structurally normal urinary tract

Cranberry products significantly reduced the incidence of recurrent UTI over a period of 6–12 months when compared to placebo or no therapy in children with normal urinary tract

Cranberry Vs antibiotics:



- One trial compared cranberry products with antibiotic prophylaxis in children with recurrent UTI

No significant difference in recurrence of UTI

No data regarding the antimicrobial resistance is reported.

Cranberry products in neuropathic bladder:



- Four trials assessed the efficacy of cranberry products in patients with neurogenic bladder who were either catheterized or were on CIC.

Three trials did not find any significant effect of cranberry over placebo in terms of bacteriuria, symptomatic UTI, or pyuria

**One study found significantly lower UTI rates per year during cranberry use compared to the placebo;
This positive effect was seen only in girls and in patients without VUR.**

No data is revealed on the effect of cranberry on kidney scars



Pooled estimates from the meta-analyses showed that the ingestion of cranberry products reduces UTI recurrence by 52% in children with the normal urinary tract.

Unresolved questions :


what are the most effective strains?

What is the ideal combination of strains?

What is the effective doses?

Is long-term use safe?

What is the side- effect in children?

A photograph of a residential street in winter. The ground is covered in a thick layer of snow. Bare trees line the street, their branches dusted with snow. In the background, houses are visible, some with snow on their roofs. A small car is parked further down the road. The overall atmosphere is quiet and cold.

Thanks for your attention