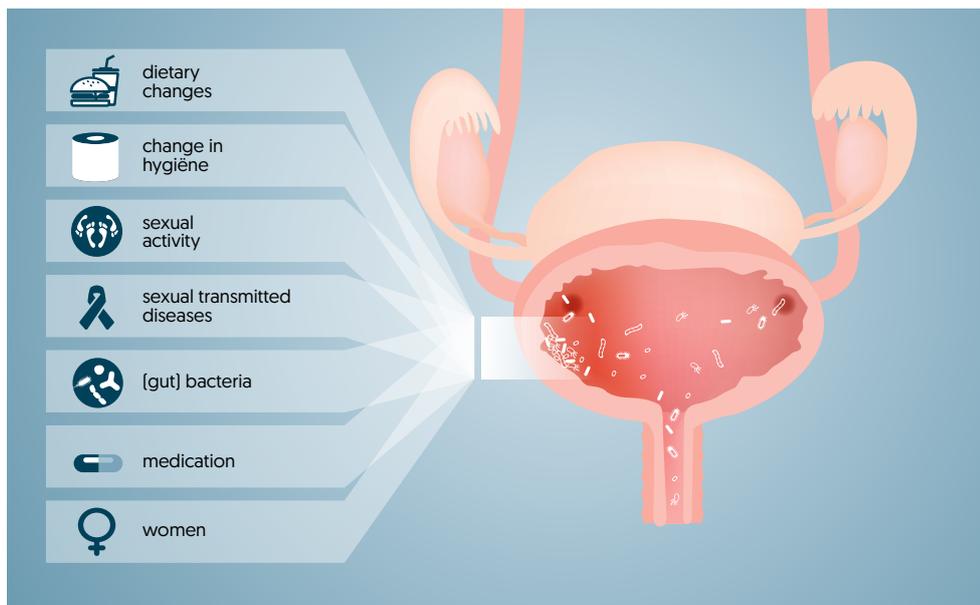


Prevention of recurrent urinary tract infections

A urinary tract infection (UTI) is a bacterial infection of the urinary tract and occurs at least once in a lifetime among one third of women^{1,2}. A recurrent UTI (rUTI) is defined as three or more UTIs per year. Between 35% to 53% of women treated for UTIs will experience an rUTI within twelve months³.

Studies have shown that the urinary tract is inhabited by micro-organisms and has its own unique microbial community^{4,5}. While it is still unknown what causes a UTI, some factors thought to disturb the urinary tract are changes in hygiene, medication, sexual activity, and diet [see figure 1]. The treatment standard for UTIs are antibiotics. Although antibiotics are very effective initially, they don't work the same way for every patient and are not ideal for long term use, as happens in preventative use for rUTIs. Also, there is no consensus on

Figure 1: Risk factors for urinary tract infections.



the ideal dose, duration, and schedule within UTIs⁶. Antibiotics cannot support the host defences and therefore don't help to resolve the risk of long-term infection recurrence⁷. Finally, antibiotics come with many negative side ef-

fects such as antibiotic resistance. These side effects have prompted researchers to look into alternatives such as probiotics to support treatment and to prevent rUTIs.

Strain selection

Winlove Clear is a multispecies probiotic food supplement developed to prevent rUTIs. The formulation consists of 7 specifically selected probiotic strains. The bacterial strains of Winlove Clear have been selected for their capacity to inhibit uropathogen growth in the vagina, bladder and gut [level 1], to strengthen the intestinal barrier [level 2], and stimulate the immune system in the gut [level 3], see figure 2. The bacterial strains have been screened for their capacity to:

- compete with uropathogens for attachment sites and nutrients⁸
- strengthen the gut barrier function
- produce antibacterial agents such as hydrogen peroxide⁸
- acidify the environment through lactic acid production
- support the host immune system.

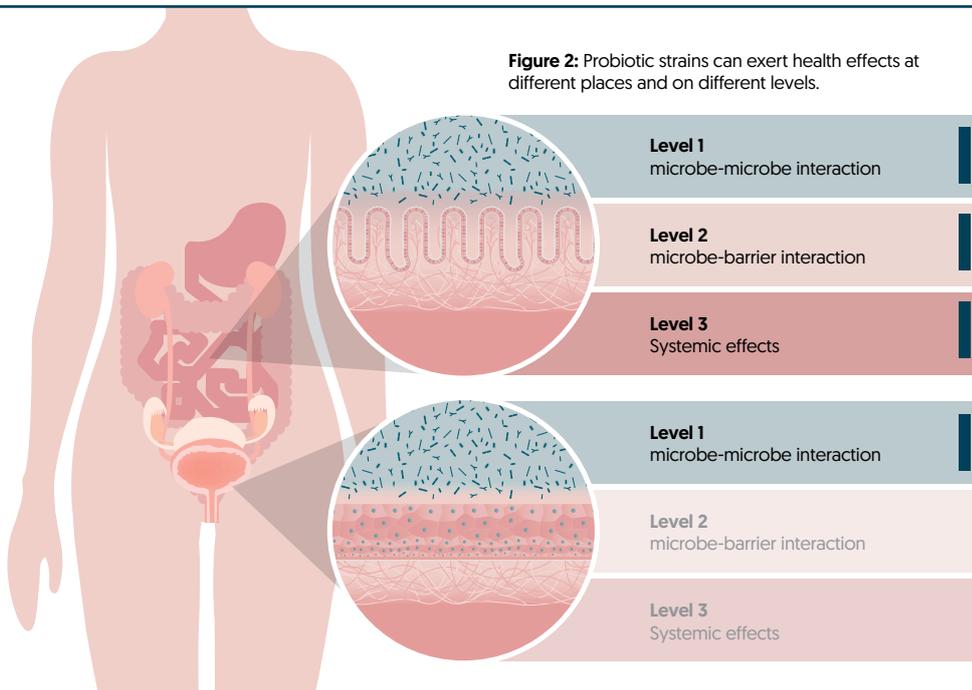


Figure 2: Probiotic strains can exert health effects at different places and on different levels.

In vitro evidence

Winlove Clear is developed to inhibit growth of uropathogens in the vagina, bladder and gut, and stimulate the immune system. The probiotic strains in Winlove Clear have been selected and tested *in vitro* for their capacity to:

- survive in the gastro-intestinal tract and in urine
- inhibit uropathogens⁹
- adhere to surface of epithelial cells
- form aggregations

- stimulate the immune system [decrease production of IL-6 and IL-8 and increase production of IL-10]
- strengthen the gut barrier function
- produce lactic acid, hydrogen peroxide and biosurfactant.

The capacity of the probiotic strains to inhibit the uropathogen *Escherichia coli* is shown in figure 3. *E.coli* often enters the bladder via the vagina from the rectum and is able to colonize

the bladder epithelium¹⁰. The graph shows that strains in Winlove Clear are able to inhibit *E.coli*. The effect of the probiotic strains to strengthen the gut epithelial barrier is shown in figure 4. For this, trans epithelial electric resistance [TEER] was measured in a transwell system with a CaCo-2 cell line. An increase in TEER indicates an improved barrier function. The graph shows that strains in Winlove Clear are capable to strengthen the barrier function.

Figure 3: Inhibition of the uropathogen *E. coli* by probiotic strains in Winlove Clear. The higher the inhibition zone, the better the inhibition.

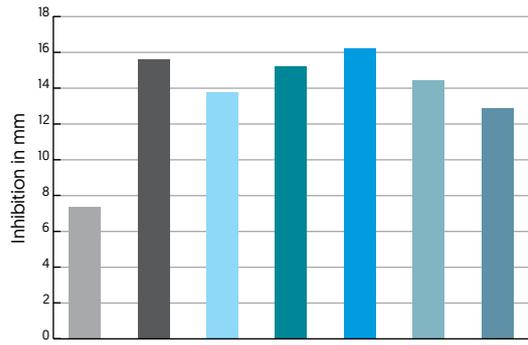
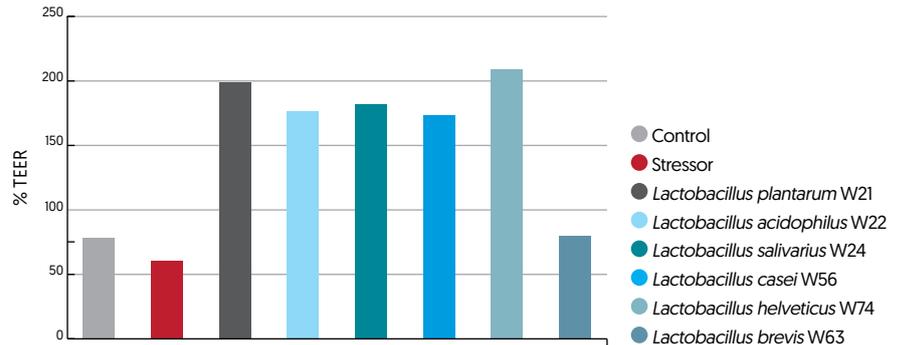


Figure 4: Effect on the epithelial barrier function by strains in Winlove Clear. An increase in % TEER indicates an improved barrier function.



Formulation details

Indication	Prevention of urinary tract infections.			
Colony forming units [CFU]	1 x 10 ⁹ CFU/gram.			
Bacterial strains	<i>L. acidophilus</i> W22 <i>L. brevis</i> W63 <i>L. casei</i> W56	<i>L. helveticus</i> W74 <i>L. pentosus</i> W2 [KCA1]	<i>L. plantarum</i> W21 <i>L. salivarius</i> W24	Possibility to add cranberry and D-mannose.
PROBIOACT® Technology	 Protective and nutritional ingredients that improve the stability of the formulation, GI survival and metabolic activity of the bacteria.			
Recommended daily dosage	3 grams.			
Treatment period	For as long as desired/needed.			
Storage and stability	Stable at room temperature, no refrigeration needed.			
Available dosage forms	Dry powder which can be supplied as bulk, sachets, capsules or fully packed [with your design].			
Safety and Quality Profile	  All probiotic strains have the Qualified Presumption of Safety [QPS] status ¹¹ . Winlove is a NSF International Certified GMP Facility for manufacturing dietary supplements and is ISO 22000:2005 certified for the development and production of pre- and probiotics.			
Marketing	Private label.			

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This information is intended for business professionals only, not for consumers. The formulations contained herein are concepts, not commercially available and not intended to diagnose, cure or prevent any diseases.

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