1. *Lactobacillus acidophilus* (L. acidophilus) and *Bifidobacterium lactis* (B. lactis) are live microbial supplements that improve the flora in the intestinal tract.
2. Special strains were selected based on the high adherence rate in the intestinal lumen.
3. Unique delivery system releases probiotics at the site of delivery, increasing the probability of colonization in the small and large intestines.

**Serving Size:** One Capsule  
**Capsule Size:** Size 3 hard gelatin capsule  
**Suggested Use:** Take one to three capsules daily, preferably before meals.  
**Ingredients per Capsule:**
- *Lactobacillus acidophilus* (at inception): approximately 500 million cells
- *Bifidobacterium lactis* (at inception): approximately 500 million cells
- Total live bacterial count (at inception): 1 billion cells
- Total live bacterial count (at expiration): 500 million cells

**Other Ingredients:** Dextrose, potato starch, cellulose, magnesium stearate (vegetable source), titanium dioxide.

**General Description:** A nonrefrigerated advanced probiotic formula that provides beneficial bacteria for both the upper and lower gastrointestinal. This product has a two-year expiration date.

**Background Science About the Product†**
This product was developed to provide a live probiotic formula that addresses the flora needs of both the upper and lower gastrointestinal (GI) tract while requiring no refrigeration and a two-year expiration date.

**Bifidobacteria and gastrointestinal health**
*Lactobacillus acidophilus* and *Bifidobacterium lactis* are two strains of bacteria that belong to a class of lactic acid producing bacteria called bifidobacteria. *L. acidophilus* is a beneficial bacterium that primarily resides in the small intestine. Small amounts of *L. acidophilus* occur in cultured foods such as yogurt and kefir. Cultured milks are more easily digested by human beings than the milk from which they are produced. It has been reported that cultures of *L. acidophilus* may be beneficial as dietary adjuncts, especially after antibiotic therapy. These organisms do not replace the intestinal bacteria, but help to keep the microflora in the proper balance. Consuming fermented products containing these organisms allows the continuous passage of these organisms through the gut. By doing so, they compete for essential nutrients and for attachment sites on the epithelium thus minimizing or inhibiting colonization of the intestinal tract by invading pathogens.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.  
† See Glossary of Terms section for explanation of technical terms.
**Scientific Summary**

*L. acidophilus* and *B. lactis* are two strains of bifidobacteria that are referred to as LA-5 and BB-12, respectively. All bifidobacteria have several general characteristics in common: anaerobic, nonmotile, gram-positive, curved rods often occurring as bifurcated Y-forms. They are non-sporulating organisms and catalase-negative. They ferment sugars with lactic acid as major end products.

The colonization and benefits of bifidobacteria can only be realized if the bifidobacteria are able to adhere to the intestinal mucus, which is why choosing probiotic supplements with specific strains that have been determined to adhere to the intestinal mucus is so important.

**How and Why it Works**

The intestinal bacterial flora consists of many types of bacteria. The normal human intestinal bacterial flora is important for more reasons; they are involved in proteolysis, i.e. they break down the proteins into smaller units and into amino acids so that they can be absorbed. They are also important to the synthesis of some vitamins and they have an effect on the function of the intestine since they improve peristalsis.5

The mucus covering the epithelial cells is the initial surface that ingested micro-organisms confront in the human gut and is considered an important site for bacterial adhesion and colonization.6 Mucus is continually subjected to degradation, conversely new mucin glycoproteins (the major components of mucus) are constantly secreted. Thus, bacteria able to adhere to mucus but unable to reach the epithelial cells might be dislodged from the mucosal surface.7

Many strains of bifidobacteria may not be able to adhere properly to the small and large intestine because they do not survive passage through the high acidity of the stomach. However, special manufacturing processes and specific strain selection (selected for high adherence properties), in combination with sufficient numbers of live bacterial cells supports colonization in the gastrointestinal tract. Using a special matrix comprised of polysaccharides, the freeze-dried, live bacteria in Dual Action Acidophilus & Bifidus™ are released in the duodenum at pH 6.5, where they can be the most biologically effective.

Colonization of beneficial bacteria in the gastrointestinal tract has been well researched for a many health conditions including constipation, diarrhea, inhibiting pathogenic microflora, supporting the immune response, reducing the risk of breast and colon cancer, decreasing cholesterol, and prevention of gastrointestinal disturbance from antibiotic treatment.

The antagonistic activity of lactic acid producing bifidobacteria is due to the production of organic acids (lactic acid, acetic acid, formic acid) causing a decrease in pH and also due to the removal of carbohydrates as nutrient sources. In addition, the lactobacilli produce various antimicrobial substances such as hydrogen peroxide and bacteriocins, alone or in combination.8

**Clinical Support and Trials**

The majority of studies on probiotics focus on the benefits to gastrointestinal health and immune modulation response. The primary therapeutic use of probiotics focuses on the benefits resulting from adequate numbers of beneficial bacteria colonizing in the gastrointestinal tract and producing lactic acid.

**Infant and Child Nutrition**

Hatakka, et al,9 reported in 2001, the results of a 7-month long double blind, placebo controlled study with 571 healthy children aged 1-6 years. The children were administered a standard milk or a *Lactobacillus* fortified milk. The results demonstrated that children in the *Lactobacillus* group had fewer days of absence from day care because of illness, reduced...
incidences of suffering from respiratory infections, and reduction in antibiotic treatments for respiratory infection.

Langhendries, et al,\textsuperscript{10} in 1995, assessed the growth, tolerance, acceptability and fecal flora composition of 20 healthy full-term infants fed with a fermented whey formula containing viable bifidobacteria during the first two months of life in a double-blind, randomized controlled study. The results were compared to a control group of fully breast-fed infants. Results indicated that the bifidobacteria fortified formula induced similar beneficial bacteria colonization at one month of age as the breast-fed infants.

In 1998, Haschke, et al\textsuperscript{11} reported meta-analysis results of double-blind, randomized, controlled feeding studies conducted on healthy children between the ages of 4 and 36 months of age in the U.S., China, and Thailand. Results demonstrated that colonization of Bifidobacterium lactis (BB-12) was confirmed when supplemented with milk-based formulas, but not soy-based formulas. Feeding the milk-based formula with probiotic supplementation resulted in protection from rotavirus infection, fewer periods with hard bowel movements and a lower incidence of diaper rash.

Another double-blind, randomized study in 1998 by Saavedra, et al\textsuperscript{12} was conducted on 119 infants for 24,845 subject days. Results demonstrated that regular consumption of live probiotics resulted in a more desirable bowel habit characterized by higher prevalence of soft bowel movements and decreased prevalence of diaper rash.

Fukushima, et al,\textsuperscript{13} in 1998, reported results of supplementing a bifidobacteria supplemented formula to seven healthy Japanese children (15-31 months old) for 21 days. During the period of formula intake, the administered strain (BB-12) was detected in the feces. Fecal levels of total IgA and anti-poliovirus IgA during intake of the formula were significantly higher than those before intake. The results suggest that the increase in local IgA levels resulting from ingestion of the probiotic formula may contribute to the enhancement of the mucosal resistance against gastrointestinal infections.

**Immune Health**

In 2001, Elmer reported in a summary that the putative mechanisms of action of probiotics in protecting the immune system include production of pathogen-inhibitory substances, inhibition of pathogen attachment, inhibition of the action of microbial toxins, stimulation of immunoglobulin A, and trophic effects on intestinal mucosa.\textsuperscript{14}

Link-Amster, et al,\textsuperscript{15} in 1994, healthy adult volunteers were evaluated in a double-blind, randomized study. Volunteers consumed a fermented milk containing \textit{L. acidophilus} and BB-12 over a period of 3 weeks during which Salmonella typhi (a pathogenic bacteria) was administered. A control group ate no fermented foods and also received the \textit{S. typhi}. Fecal flora analyses showed an increase in \textit{L. acidophilus} and BB-12 counts during fermented milk intake. The specific serum IgA titer rise to \textit{S. typhi} in the test group was significantly higher than in the control group. These results indicate that lactic acid bacteria which can persist in the gastrointestinal tract can act as adjuvants to the humoral immune response.

Hatcher, et al,\textsuperscript{16} in 1993, reported results from an \textit{in vitro} study evaluating the macrophage activity of \textit{L. acidophilus} and \textit{Bifidobacterium longum}. The study determined that lactic acid producing bacteria are capable of altering macrophage function and significantly phagocytosis of inert particles or viable \textit{S. typhi}.

**Gastrointestinal Health**

In 1998, Kirjavainen, et al,\textsuperscript{7} isolated human mucus from fecal samples of newborns, two and six-month olds, and adults. The adherence to this mucus by the bacteria (BB-12, among others) was assessed \textit{in vitro}. BB-12 demonstrated a 9-14% adherence rate. All the strains
adhered better to the mucus of adults than to that of infants. BB-12 adhered significantly better to any infant mucus than the rest of the strains.

Shu, et al,\(^\text{17}\) reported in a 2001 controlled study of weanling piglets that probiotic treatment using BB12 resulted in reduced severity of weanling diarrhea and maintained a greater feed conversion efficiency during weaning. The protective effect of probiotic feeding was associated with lower concentrations of fecal rotavirus and \(E. \text{ coli}\) via a mechanism of enhanced immune-mediated protection. The results of this study suggest that probiotic treatment may be an effective dietary means of preventing or limiting diarrhea in human infants.

In 1992, Alm, et al\(^\text{18}\) presented results of \(L. \text{ acidophilus}\) and \(B. \text{ bifidum}\) use in 24 randomly selected geriatric patients aged from 68 to 99 years in a geriatric care hospital. Each suffered from constipation over a period of several years. Bowel movements and administration of laxatives were registered continuously by medical personal for the duration of the study. It was determined that the need for laxatives was diminished during periods of probiotic consumption and the defecation rate was significantly improved.

Jiang, et al,\(^\text{19}\) in 1995, reported results from a controlled in vitro model, which mimics colonic fermentation. Preliminary studies demonstrated that bacterial populations stabilized within 2 days. Control culture samples without the addition of \(L. \text{ acidophilus}\) was fermented simultaneously. The study determined that probiotic supplementation increased acetate and propionate production by colonic bacteria and suggests that supplementation with lactic acid bacteria may modify colonic fermentation in patients with intestinal disturbances, such as antibiotic-associated diarrhea.

**Lactose Intolerance**

Driessen, et al\(^\text{20}\), reported results from a 1989 review of clinical research that for the effective utilization of lactose, people are dependent on the enzyme \(\beta\)-galactosidase. Due to a shortage of intestinal \(\beta\)-galactosidase, lactose is not hydrolysed and, consequently not absorbed. Lactose arrives at the distal intestine (colon) where it is fermented by the microbial flora, which leads to the formation of hydrogen. This may cause flatulence, diarrhea and stomachache. Lactose-intolerant people digest fermented milk better than normal milk. This is partially attributed to the fermentation of lactose by the lactic acid bacteria and, consequently, a lower lactose concentration in fermented food products.

In 1992, Jiang et,\(^\text{21}\) reported that consumption of \(L. \text{ acidophilus}\) is considered beneficial in improving lactose digestion. \(L. \text{ acidophilus}\) may temporarily supplement the intestine with exogenous \(\beta\)-galactosidase. In vitro testing demonstrated that supplementation with LA-1 resulted in a rapid decrease of lactose concentration within one day. In the control group, lactose concentration decreased a fraction of then LA-1 supplemented group. The data suggest that \(L. \text{ acidophilus}\) supplements could enhance colonic fermentation of lactose. Further, the study also demonstrated that persistent exposure to lactose could lead to colonic bacterial adaptation to digest lactose due to inducible bacterial lactase.

**Cholesterol**

In 1993 Klaver and Meer\(^\text{22}\) studied the mechanism of the proposed assimilation of cholesterol by \(L. \text{ acidophilus}\) and \(B. \text{ bifidobacterium}\) in the presence of cholesterol and oxgall. In vitro control experiments demonstrated that cophrecipitation of cholesterol during culturing was a result of formation of deconjugated bile salts, and cophrecipitation of cholesterol during culturing was a result of formation of deconjugated bile salts. It was concluded that the removal of cholesterol from the test sample was not due to bacterial uptake of cholesterol, but resulted from bacterial bile salt-conjugating activity.
Tumors and Cancer

In 1997, Biffi, et al\textsuperscript{23} studied the direct effect of probiotic-fermented milk on breast cancer cells (\textit{in vitro}). Results showed cellular growth inhibition induced by the fermented milk. Findings suggested the presence of an \textit{ex novo} compound produced from the lactic acid bacteria during fermentation provided antiproliferative activity useful in the prevention and therapy of solid tumors like breast cancer.

Miettinen, et al.\textsuperscript{24} investigated in a 1996 study the role of cytokines interactions between lactic acid bacteria and the immune system. Production of tumor necrosis factor (TNF), interleukin-6 (IL-6), and interleukin-10 (IL-10) from human peripheral cells after stimulation with live bacteria. Production of TNF, IL-6, and IL-10 was induced in amounts even greater than those obtained with lipopolysaccharide as a stimulant. Their results suggest that lactic acid bacteria can stimulate nonspecific immunity.

A 1997 study conducted by Rangavajhyala, et al\textsuperscript{25} suggested that \textit{L. acidophilus} has a suppressive effect on chemically induced tumors in experimental animals. LA-1 induced the production of higher levels of IL-1 and TNF than other lactobacilli. The results of the experiment revealed that the nonlipopolysaccharide components of LA-1 stimulate the production of IL-1 and TNF by macrophages, indication that this organism stimulated the production of immunologic factors.

\textbf{Table 1. Brief Summary of Research using \textit{L. acidophilus} (LA-5) and \textit{L. bifidus} (BB-12)}

<table>
<thead>
<tr>
<th>Researcher</th>
<th>Date</th>
<th>Model</th>
<th>Research Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fukushima\textsuperscript{13}</td>
<td>1998</td>
<td>Children</td>
<td>Probiotic formula containing BB-12 was able to contribute to resistance against gastrointestinal infections.</td>
</tr>
<tr>
<td>Saavedra\textsuperscript{12}</td>
<td>1998</td>
<td>Infants</td>
<td>Regular consumption of live probiotics resulted in more desirable bowel movements and decreased prevalence of diaper rash.</td>
</tr>
<tr>
<td>Haschke\textsuperscript{11}</td>
<td>1998</td>
<td>Infants</td>
<td>Feeding milk-based formula with BB-12 provided protection from rotavirus infection, fewer hard bowel movements, and lower incidence of diaper rash.</td>
</tr>
<tr>
<td>Kirjavainen\textsuperscript{7}</td>
<td>1998</td>
<td>Infants and Adults</td>
<td>Bacterial strain BB-12, among others, had between a 23-29.9% adherence rate to the intestinal mucus, with the best adherence occurring in infants.</td>
</tr>
<tr>
<td>Vanderhoof\textsuperscript{26}</td>
<td>1998</td>
<td>Review</td>
<td>Results of human and animal studies suggest that patients with inflammatory diseases may benefit from probiotics.</td>
</tr>
<tr>
<td>Fukushima\textsuperscript{28}</td>
<td>1997</td>
<td>Children</td>
<td>BB-12 in a follow-up formula reached the intestines of healthy children and proliferated.</td>
</tr>
<tr>
<td>Plockova\textsuperscript{27}</td>
<td>1997</td>
<td>In vitro</td>
<td>LA-5 was found to have antifungal activity.</td>
</tr>
<tr>
<td>Miettinen\textsuperscript{24}</td>
<td>1996</td>
<td>In vitro</td>
<td>Lactic acid producing bacteria have been shown to induce proliferation of immune cells and enhance synthesis of antibodies to microbial pathways.</td>
</tr>
<tr>
<td>Langhendries\textsuperscript{10}</td>
<td>1995</td>
<td>Infants</td>
<td>Probiotic fortified formula induced a prevalence of colonization similar to that of breast-fed infants.</td>
</tr>
<tr>
<td>Jiang\textsuperscript{19}</td>
<td>1993</td>
<td>In vitro</td>
<td>\textit{L. acidophilus} supplements could have an affect on enhancing colonic fermentation of lactose.</td>
</tr>
<tr>
<td>Black\textsuperscript{29}</td>
<td>1991</td>
<td>Adults</td>
<td>Volunteers receiving lactic acid bacteria producing bacteria were recolonized faster than those receiving a placebo.</td>
</tr>
</tbody>
</table>
**Safety**

This product is safe for men and women of all ages.

**Interactions**

Garlic: Acidophilus may decrease the absorption of garlic. If taken concurrently, separate dosages by three hours.\(^{30}\)

**Key Scientific Points to Remember**

1. *Lactobacillus* and *Bifidus* are part of the normal flora living in the gastrointestinal tract.
2. They act by competing for nutrients with other organisms such as *Candida*, thus preventing the other organism from reproducing and flourishing to infection.
3. Beneficial bacteria are responsible for assisting in the digestion and absorption of several vitamins, including the fat-soluble vitamins.
4. It appears that *Lactobacillus* may decrease cholesterol by assimilating it.
5. Probiotic supplements have demonstrated improved symptoms in supporting gastrointestinal health, including diarrhea.
6. *Lactobacillus* has been shown to increase production of tumor necrosis factor, inducing non-specific immune benefits.
7. Some research shows that the consumption of probiotics has been suggested to be involved in decreasing enzymes in the colon that play a role in causing cancer.

**Who Would or Should Use the Product**

1. People who want to consume probiotics.
2. Lactose-intolerant individuals who need probiotics but can’t tolerate dairy products.
3. People who have recently been prescribed antibiotics.

**Who Should Not Use the Product**

No exceptions.

**Objections and Common Questions**

1. *What is the difference between this product and our regular Acidophilus Capsules?*

   PROBIOTIC COMPLETE™ is a formula containing two strains of beneficial bacteria including *Lactobacillus acidophilus* (LA-5) and *bifidobacterium lactis* (BB-12). Our existing Acidophilus contains one strain of *Lactobacillus acidophilus*. In addition, the new formula has special processing that eliminates the need for refrigeration and maintains a two year expiration date.

2. *Why does this product contain dextrose and what is it?*

   Dextrose is used in the processing of the protective matrix to help the bacteria survive the acidity of the stomach, and reach the areas of the gastrointestinal tract where they can be of most benefit.

   **NOTE:** Please see attached information sheet called “Dextrose and Your Health” for more details on dextrose.
3. **Does this need to be refrigerated?**

No, in fact it is not recommended to refrigerate this product (after opening) as the additional condensation from refrigeration will result in increased moisture content, possibly reducing the shelf life of this product.

4. **What is the difference between LA-1 and LA-5?**

LA-1 and LA-5 are synonymous terms for a specific strain of *Lactobacillus acidophilus.*

**Glossary of Terms**

- **Bacteriocins**: toxins produced by bacteria.
- **Bifurcated**: to divide or be divided into two parts or branches.
- **Catalase**: an enzyme in the blood and in most living cells that catalyzes the decomposition of the hydrogen peroxide into water and oxygen.
- **Epithelium**: membranous tissue composed of one or more compact layers of cells that cover most internal and external surfaces of the body and its organs.
- **In Vitro**: in an artificial environment outside the living organism.
- **In Vivo**: within a living organism.
- **Macrophage**: any of the large phagocytic cells of the reticuloendothelial system.
- **Pathogenic**: capable of causing disease, originating or producing disease.
- **Phagocytosis**: the engulfing and ingestion of bacteria or other foreign bodies by phagocytes (cells).
- **Probiotic**: meaning “for life”, microbial food supplements which beneficially affect the host's health.
- **Reticuloendothelial**: of, or relating to, or being the widely diffused bodily system constituting all phagocytic cells except certain white blood cells.
- **Trophic**: of or relating to nutrition.

**References**


