IMMUNOMODULATORY EFFECTS OF SACCHAROMYCES CEREVISIAE FERMENTATE

An overview of the practical clinical applications based on the scientific literature

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Since ancient times, *Saccharomyces cerevisiae* (*S. cerevisiae*) has been used to raise bread, make wine, and brew beer. It is also referred to as brewer’s yeast, baker’s yeast, or budding yeast. In the mid-1990s *S. cerevisiae* was the first eukaryotic genome to be completely sequenced by an international consortium of researchers from 90 countries. It has since been studied extensively by geneticists, molecular biologists, computational scientists, and a variety of other researchers worldwide.

*Saccharomyces cerevisiae* fermentate is produced through a proprietary fermentation process. *S. cerevisiae* is used to create the fermentate because it is a safe, naturally-occurring microorganism that has been studied extensively and ingested by people for millennia. The branded ingredient created via the proprietary process is known as EpiCor® and is manufactured by Embria Health Sciences.

The process begins when the *S. cerevisiae* microorganisms are forced to survive while deprived of oxygen. In this anaerobic environment, the large quantities of *S. cerevisiae* produce beneficial immune-supporting compounds and metabolites such as proteins, peptides, antioxidants, polyphenols, organic acids, and nucleotides. The finished product, the fermentate, also contains beta glucans and mannans from the yeast cell wall, each of which have evidence of benefitting the immune system.

Appropriate storage and handling of the fermentate is critical. A proprietary, gentle drying process is used to kill the yeast and dehydrate the fermentate, which is then carefully packaged to protect the complex array of nutrients. The finished product is a whole food ingredient, which is much different than a simple yeast extract. As a whole food ingredient, EpiCor is minimally processed. The *S. cerevisiae* microorganisms produce beneficial metabolites during the proprietary fermentation process. During the entire process, nothing is extracted, synthesized or purified. As the branded ingredient EpiCor, *S. cerevisiae* fermentate is found in dozens of dietary supplements and functional foods. It is a vegan ingredient and does not contain wheat gluten, barley, rye, or oats. It has been certified by the Orthodox Union as Kosher, and it is NSF certified non-GMO.

*S. cerevisiae* fermentate has been the subject of several animal studies and human clinical trials. Of most interest is its ability to modulate immunity and inflammation while also supporting healthy microbial balance in the gut.

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**Immune Modulation and Inflammation**

The clinical role of *S. cerevisiae* fermentate is to strengthen the immune system, maintain optimal immunity, reduce inflammation, and positively influence the human gut microbiome. It does this by:

- Increasing secretory Immunoglobulin A antibodies
- Increasing natural killer (NK) activity
- Enhancing antioxidant potential
- Supporting microbial balance in the gut

Secretary Immunoglobulin A (sIgA) antibodies play a key role in mucosal immunity. Studies demonstrate that high intestinal sIgA is associated with lower intestinal inflammation and reduced risk of IgE-associated allergic diseases. *S. cerevisiae* fermentate has been shown to increase sIgA levels which explains, in part, its role in strengthening the immune system.

Another intriguing immune effect of *S. cerevisiae* fermentate is its ability to increase NK activity. A 2007 *in vitro* study published in *Nutrition Research* demonstrated that *S. cerevisiae* fermentate activated NK cells, as well as B cells. This same study also showed a reduction in Reactive Oxygen Species, as well as interferon gamma production. There was an overall anti-inflammatory effect illustrated by the data from this study.
Antioxidant capacity helps protect cells from oxidative damage. *S. cerevisiae* fermentate has been shown to increase antioxidant activity and reduce inflammation. Animal studies have demonstrated that *S. cerevisiae* fermentate has several acute and chronic inflammatory control mechanisms. A 2011 placebo-controlled, double-blind crossover pilot trial published in the *Journal of Medicinal Food* demonstrated that “consumption of a single 500 mg dose of EpiCor provides a rapid and transient effect on the trafficking and activation status of specific lymphocyte subsets, as well as increased antioxidant protection.” In this study, the increase in NK activity took place within two hours after consumption demonstrating a fast response rate with EpiCor.

Creating microbial balance and reducing risk of dysbiosis has far-reaching effects when it comes to enhancing immunity and controlling inflammation. *In vitro*, animal, and human clinical trials demonstrate that *S. cerevisiae* fermentate positively influences gut health on several levels. *In vitro* data confirmed that both luminal and mucosal gut microbiota is modulated to help protect against inflammation. In an animal study using a heat stress model that simulates leaky gut, *S. cerevisiae* fermentate led to a reduction in serum lipopolysaccharide endotoxins, red blood cell destruction, and white blood cell counts compared to controls, which indicates that there is a reduction in the physical damage associated with leaky gut syndrome.

Most impressive was a 2017 randomized double-blind placebo-controlled pilot trial published in *BMC Complementary and Alternative Medicine* which showed that the EpiCor intervention improved gastrointestinal discomfort and constipation by modulating the gut microbiome.

Given these significant effects on foundational aspects of health, *S. cerevisiae* fermentate can serve a diverse number of applications in clinical practice.

**Clinical Applications**

From a clinical perspective, the goal of *S. cerevisiae* fermentate treatment is not to merely reduce symptoms or provide symptom relief. The clinical objective when recommending *S. cerevisiae* fermentate is to strengthen the immune system or maintain an already healthy immune and inflammatory response on an ongoing basis to reduce risk of illness and symptoms. Maintaining and strengthening immune health was also the objective of many of the studies using *S. cerevisiae* fermentate. In particular, let’s look at the research regarding cold and flu, allergies and gut health.

**Cold and Flu**

According to the Centers for Disease Control and Prevention, each year there are millions of cases of the common cold, with adults experiencing an average of two to three colds per year and children even more frequently. While there is much controversy surrounding vaccinations, there is no question that many over-the-counter medications remain ineffective at consistently reducing the risk of developing a cold or flu. From a clinical perspective, prevention of cold and flu is where *S. cerevisiae* fermentate is evidenced to be effective.

In 2010, Moyad et al published data regarding the use of *S. cerevisiae* fermentate for cold and flu-like symptoms in *The Journal of Alternative and Complimentary Medicine*. This was a concurrent 12-week, randomized, double-blind, placebo-controlled trial that featured 116 healthy nonvaccinated individuals. The intervention was 500 mg of *S. cerevisiae* fermentate (EpiCor) daily compared to placebo. Both the incidence and duration were tracked. While there was no difference in duration or severity, those taking *S. cerevisiae* fermentate had a significant reduction in the incidence of cold or flu (*P* = 0.01).

This is similar to a previous randomized, placebo-controlled trial demonstrating that *S. cerevisiae* fermentate can help prevent cold and flu in healthy individuals who were recently vaccinated. The previous study was published by the same researchers in 2008 in the journal *Urologic Nursing*.

These studies demonstrate that regardless of vaccination history, *S. cerevisiae* fermentate may be useful for cold and flu prevention.
Allergy and Hay Fever

Hay fever, or allergic rhinitis, affects up to 30% of the population worldwide. The Centers for Disease Control and Prevention estimate that nearly 20 million American adults over age 18 were diagnosed with hay fever in 2017. Of course, this does not take into account the millions of others who did not receive a formal diagnosis that year. In addition to a high prevalence of these issues, patient surveys continue to indicate high dissatisfaction with prescription and over-the-counter (OTC) hay fever medications. A 2009 randomized, double-blind, placebo-controlled trial published in the journal Advances in Therapy demonstrated that S. cerevisiae fermentate (EpiCor) could be a safe, effective natural solution for many patients experiencing allergic rhinitis.

In this 12-week clinical trial 96 healthy individuals who tested positive for seasonal allergies and allergic rhinitis were given 500 mg of S. cerevisiae fermentate daily or placebo. Outcome measurements included in-clinic exams, validated questionnaire and standard diary, and serologic analysis at baseline, six and 12 weeks. The highest ambient pollen counts happened during the first six weeks of the study, and it was during that time that the intervention group experienced a significant reduction in nasal congestion (P = 0.04) and rhinorrhea (P = 0.005). There was a nonsignificant reduction in eye discharge.

In this study the duration of one of the most troublesome symptoms of hay fever, nasal congestion, was tracked. On average, the intervention group had 12.5 fewer days of nasal congestion compared to the placebo group (P = 0.04). In addition, the intervention group also had significantly higher salivary IgA levels (P = 0.03) compared to placebo. The researchers concluded: “This dietary supplement should be given more clinical attention as a potential immune modulating intervention for susceptible individuals with and without currently available effective OTC and prescription medications.”

Bacterial Balance

It's not surprising that S. cerevisiae fermentate's immunomodulatory effects are salutary on the gut microbiota and reduces the risk of dysbiosis. After all, the connection between the gut and the immune system has been firmly established.

To help illustrate this point, researchers conducted a randomized, double-blind, placebo-controlled pilot trial comparing S. cerevisiae fermentate to placebo that featured 80 individuals who were experiencing gastrointestinal symptoms and constipation and published their results in 2017 in BMC Complementary and Alternative Medicine. Stratified randomization created two subgroups of symptom severity: moderate (n = 25) and severe (n = 55).

Once again, the dosage used in this study was 500 mg daily of S. cerevisiae fermentate (EpiCor). Clinical outcomes included symptom improvement, stool consistency, stool frequency and perceived quality of life. In the moderate subgroup, symptoms of bloating and distension were significantly improved (P = 0.033 and P = 0.024), while stool consistency (P = 0.023) and stool frequency (P = 0.083) were improved for the total cohort. Constipation quality of life scores were also improved. The most notable improvements came within the first two weeks of the study. In the moderate intervention subgroup, there was a significant improvement in physical discomfort (P = 0.017), psychosocial discomfort (P = 0.027) and satisfaction (P = 0.013) compared to placebo.

As a secondary endpoint, qualitative changes in the gut microbiome were assayed. Interestingly, based on fecal samples collected at baseline and at three and six weeks, S. cerevisiae fermentate intake increased probiotic bacteria (Bacteroidaceae and Prevotellaceae) in the “severe” intervention group compared to placebo. These bacteria are typically deficient in people with constipation. In addition, butyrate levels were increased. Research demonstrates that butryrate plays a critical role in gut homeostasis by positively influencing the immune response. Butyrate has also been shown to feed the cells lining the colon which helps improve gut integrity.

The researchers concluded “...the reported increase in bowel movements may have altered the gut microbial community by increasing those groups of bacteria that are better adapted to a faster gastrointestinal transit time.”

The dosage used in most of the studies of S. cerevisiae fermentate was 500 mg for adults taken as one daily dose in the morning. For children, the amount is 125 mg per 40 pounds of body weight.
In total there have been eight human clinical trials demonstrating efficacy of EpiCor. It has consistently been shown to strengthen both immune and digestive health. This has broad applications in clinical practice as most patients are constantly being challenged by viruses, bacteria, environmental toxins and other pathogens. When you add increased stress, poor nutrition, lack of sleep, and other lifestyle factors that can negatively impact immunity and digestion, it makes sense to utilize a proactive prevention protocol for most patients. Because *S. cerevisiae* fermentate has also been shown to be safe, as well as effective, it is worth considering as a part of an overall integrative approach to enhancing health, especially with patients in need of additional immune and digestive support.

**Dosage and Safety Information**

To strengthen immunity and gut health, as well as control inflammation, the recommended dosage of *S. cerevisiae* fermentate is 500 mg daily for adults. This is consistent with all of the published human clinical trials. For children, the dose is 125 mg per 40 lbs of body weight. This dose can be split into several doses during the day if preferred.

Specifically regarding EpiCor, there have been many published safety and human clinical studies confirming that this substance is safe for adults and children. In addition, EpiCor meets FDA requirements to be considered Generally Recognized as Safe (GRAS). Achieving GRAS status means it has been evaluated by an independent panel of food safety experts. Based on the human clinical trials, there are no known contraindications, interactions, or adverse side effects associated with EpiCor specifically.

EpiCor is not known to upset the stomach like some other ingredients such as prebiotic fibers. It can also be taken with or without food, during any time of the day and in multiple doses. Participants in many of the studies with EpiCor in particular, took it first thing in the morning.

Given the positive safety profile and efficacy at the low dose of 500 mg daily, it makes sense to consider including *S. cerevisiae* fermentate in clinical practice as part of an integrative approach to enhancing immunity, reducing inflammation, and creating healthy bacterial balance.
Saccharomyces cerevisiae Fermentate

Selected References


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