BLIS™

CONTAINS BLIS™ K12

BUILD IMMUNE DEFENCES AGAINST UPPER RESPIRATORY TRACT INFECTIONS

SUPPORTING IMMUNE HEALTH

Upper respiratory tract infections (URTIs) are a group of infectious diseases that affect the upper respiratory tract, including the nose, throat, sinuses, and can extend to the Eustachian tubes (in the ears). Infections can be caused by both viruses and bacteria and include the Common Cold, Influenza, and Strep Throat that lead to Sinusitis, Pharyngitis, Tonsillitis, and Otitis Media.

In general, URTIs cause inflammation in the respiratory system, which can result in symptoms such as a runny or stuffy nose, sore throat, coughing, difficulty breathing and pain. The immune system responds to the infection by releasing immune stimulating cytokines, to help prepare immune cells and epithelial cells for invasion from an enemy. This also includes production of antibodies.

HOW BLIS K12™ HELPS PREVENT URTIs

COLONISATION AND COMPETITIVE EXCLUSION

BLIS K12™ colonises in the upper respiratory tract and naturally competes with some pathogens for the same binding site, effectively crowding out bad bacteria that may cause bacterial URTIs.

ANTIMICROBIAL INHIBITION

BLIS K12™ naturally produces proteins called Bacteriocin-Like Inhibitory Substances (BLIS). These bacteriocins are antimicrobial peptides that actively target and inhibit the growth of a wide range of pathogens that can cause an upper respiratory infection.

The key bacteriocins produced by BLIS K12™ are salivaricin A2 and salivaricin B. These exhibit bactericidal effects on different respiratory pathogens. Salivaricin B specifically targets the biosynthesis of peptidoglycan in the cell wall of target pathogenic bacteria, which leads to a weakened cell wall and alteration of cytoplasmic membrane integrity. This ultimately results in the irreversible damage of the cell envelope, causing lysis of the bacterium and thus pathogen cell death [see Fig 1]. [1, 2]

ANTIMICROBIAL ACTIVITY OF BLIS K12™

Representative Pathogens:	Link to:
Streptococcus pyogenes	Acute haryngitis, rheumatic fever
Streptococcus pneumoniae	Pneumonia, ear infections
Streptococcus agalactiae	Neonatal sepsis and meningitis

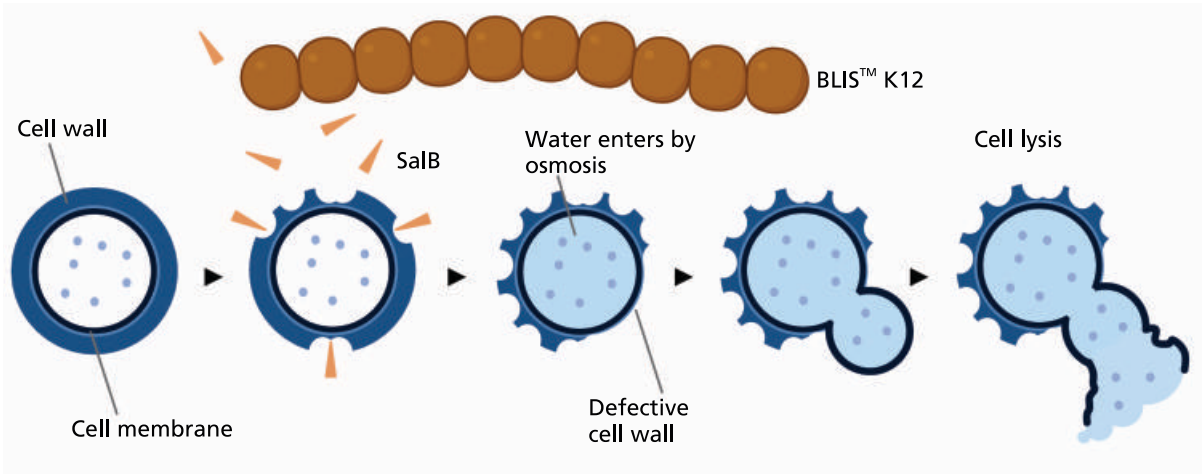


Figure 1: BLIS K12™ produced Bacteriocin Salivaricin B targeting pathogen cells.

BLIS K12™ can modulate the immune system by interfering with the signalling pathways induced by pathogens and interacting with the immune system itself. This action is mediated through multiple mechanisms including inhibition of the NF-kB pathway (inflammation/apoptosis), attenuation of IL-8 secretion induced by inflammatory molecules, upregulation of the genes responsible for activation of the interferon gamma signalling pathways with antiviral and cytokine modulation properties, alteration of the expression of genes involved in multiple innate defence pathways, epithelial layer adhesion, and homeostasis pathways. Together these actions work to stimulate an anti-inflammatory response to protect the host from inflammation and apoptosis induced by pathogens.[3]

STIMULATING IMMUNE RESPONSE

BLIS K12™ has been shown to stimulate interferon gamma (IFN-y) levels, which lead to faster immune responses and reduces likelihood to experience recurring upper respiratory tract infections. When it comes to immune response, IFN-y is a key player. This cytokine is responsible for activating macrophages, natural killer cells, and neutrophils, and plays a crucial role in both innate and adaptive immunity. Specifically, IFN-y is vital in fighting off viral upper respiratory tract infections. By activating other immune cells and boosting the overall immune response, IFN-y helps to eliminate the invading pathogen and prevent further infection.

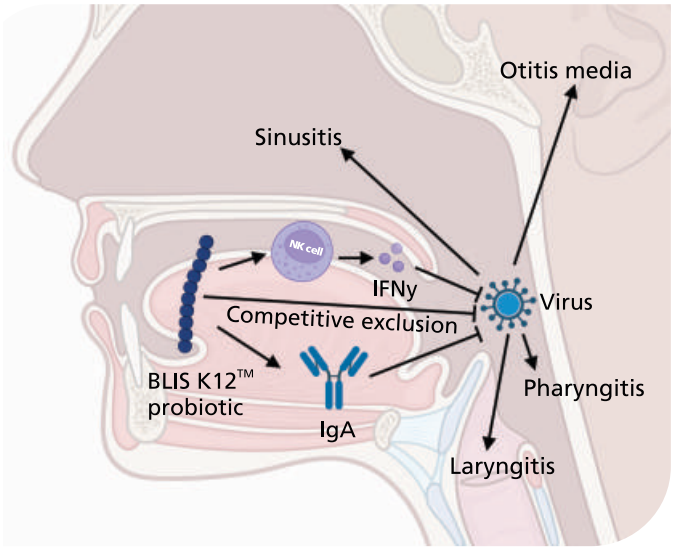


Figure 2: Shows mechanisms of actions stimulating the immune response.

Secretory immunoglobulin A (sIgA) is an antibody that is found in the mucous membranes of the body, including the mouth, nose, throat, and digestive tract. Its main function is to defend against infections by preventing pathogens from attaching to the body's mucosal surfaces and neutralizing them before they can enter the body. The study by Bertuccioli et al. has provided evidence that BLIS K12™ used for 30 days is sufficient to increase salivary IgA (increasing defence against pathogens). [4]

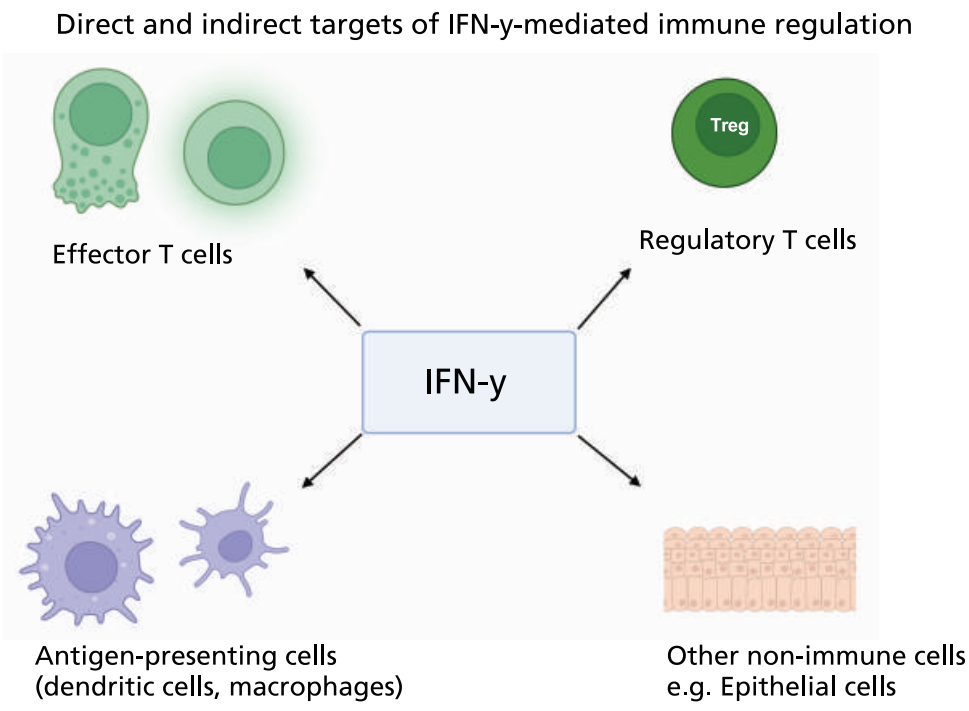


Figure 3: Direct and indirect targets of Interferon gamma (IFN-y) mediated immune regulation.

THE IMPORTANCE OF A BALANCED ORAL MICROBIOME

By establishing a more balanced homeostatic relationship between the oropharyngeal microflora and the cells of the immune system, BLIS K12™ helps to promote a symbiotic state that may provide better protection from respiratory tract infections.

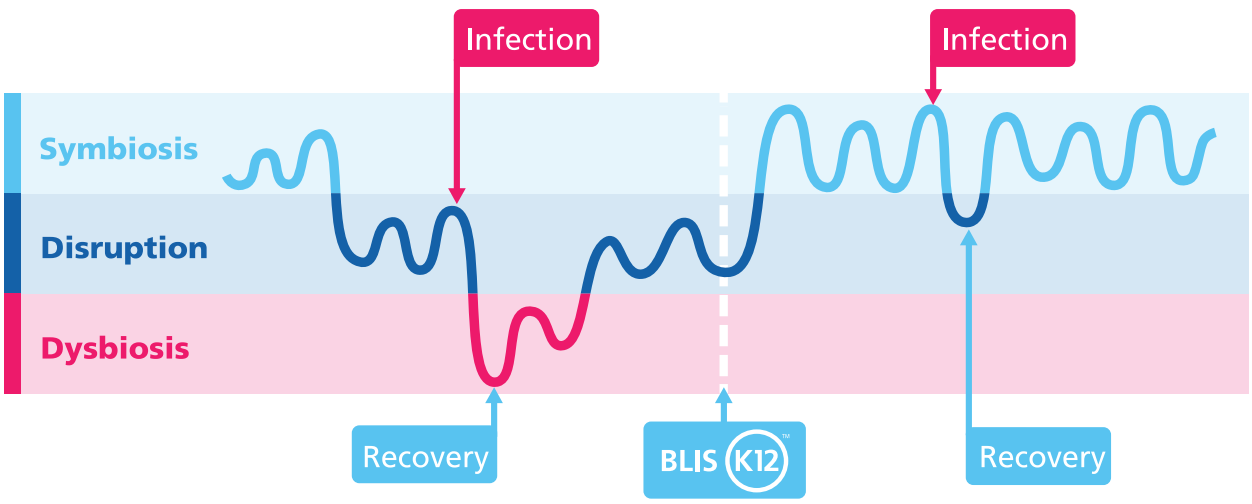
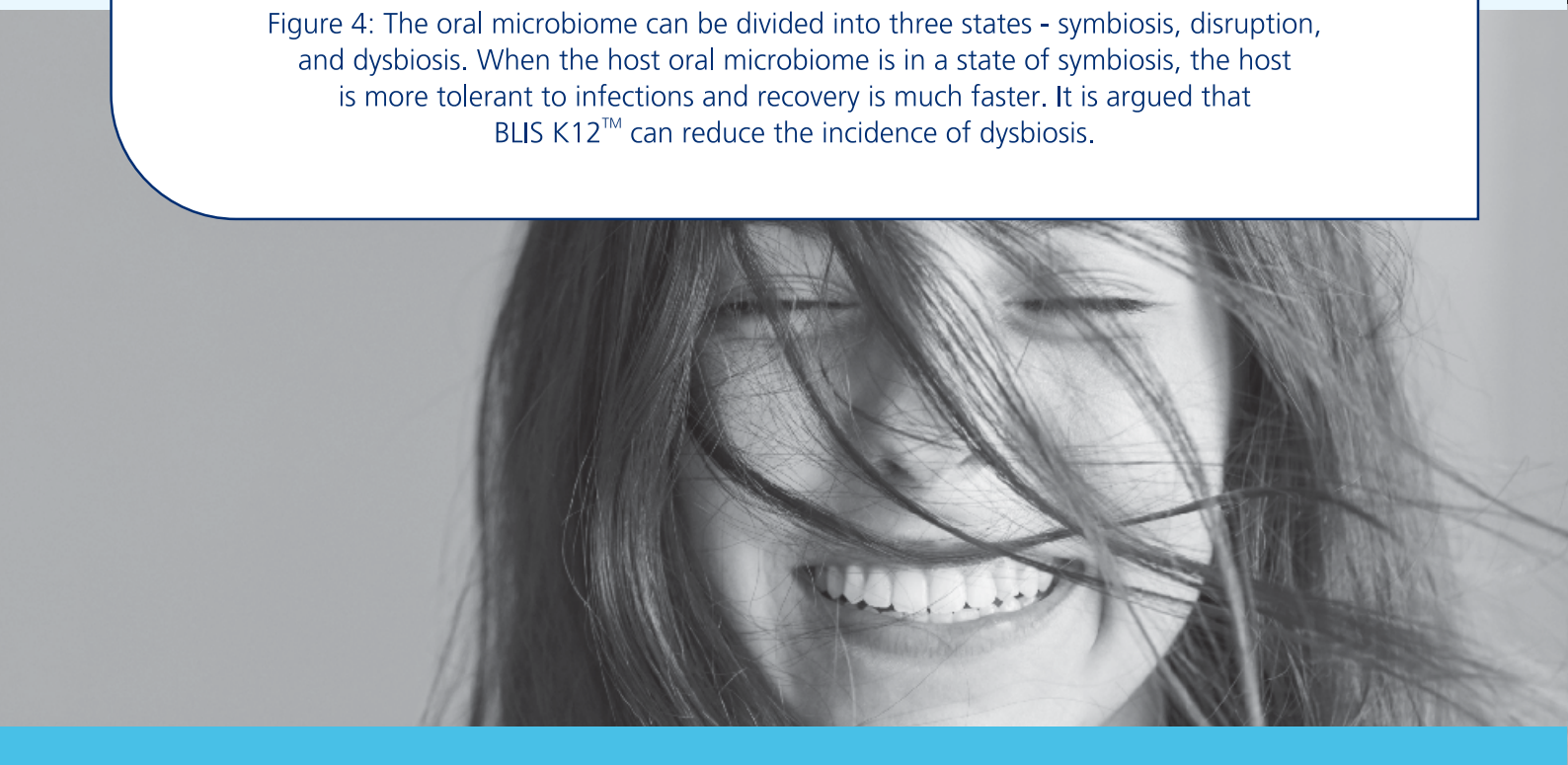


Figure 4: The oral microbiome can be divided into three states - symbiosis, disruption, and dysbiosis. When the host oral microbiome is in a state of symbiosis, the host is more tolerant to infections and recovery is much faster. It is argued that BLIS K12™ can reduce the incidence of dysbiosis.



THE RELATIONSHIP BETWEEN A HEALTHY ORAL MICROBIOME AND LUNG MICROBIOME

The microbiota in healthy lungs shares some similarities with the microbiota found in our mouth. It's interesting to note that certain bacteria, such as *Streptococcus, Prevotella,* and *Veillonella,* commonly live in both locations.

Recent studies have revealed that the microbiota present in our lungs is part of the equation to maintaining immunological homeostasis. However, when the lung microbiota becomes imbalanced due to dysbiosis, it can potentially increase vulnerability to viral infections. In the case of COVID-19, researchers have noted a significant difference in the composition of the lung microbiota between healthy individuals and those suffering from SARS-CoV-2 pneumonia. This suggests that dysbiosis may occur in the lung microbiota in patients with COVID-19.[5]

Studies have shown that when *Streptococcus salivarius* is present in the lungs, it correlates with a more stable and healthy condition.[6]

BLIS K12™ IS BACKED BY MORE THAN 20 YEARS OF RESEARCH AND CLINICAL STUDIES

20 years of studies on BLIS K12™ have shown that regular consumption of this probiotic can support immune health and reduce the recurrence and severity of viral upper respiratory tract infections.

1 STUDY

FEWER RECURRENT UPPER RESPIRATORY TRACT INFECTIONS IN CHILDREN DURING THE COLD SEASON [7]

100 children aged between 3-10 years, susceptible to upper respiratory tract infections were selected for 30 day open randomised trial. Results show children taking BLIS K12™ reduced the rate of infection from 34% to 15%. Additionally, those children showed more moderate symptoms, required less antibiotic and anti-viral treatment and had reduced absence from school.

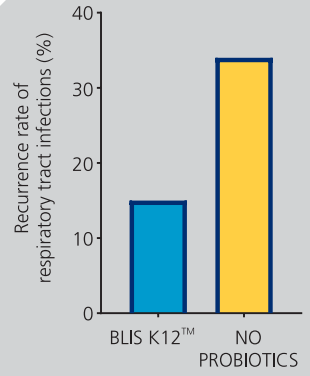


Figure 5: Reduction in the number of recurrent respiratory tract infections in the group taking BLIS K12™

2 STUDY

USE OF BLIS K12™ IN THE PREVENTION OF VIRAL PHARYNGOTONSILLITIS IN CHILDREN [8]

61 children aged between 3-13 years participated in a 90-day trial, with 31 taking BLIS K12™ containing no less than 1 billion CFU per slow-release lozenge. The treated group showed a significant decrease (80%) in viral pharyngitis and/or tonsillitis in children. The study showed a considerable reduction of episodes of both streptococcal and viral infections and reduced the number of days under antibiotic and antipyretic therapy as well as days of absence from school.

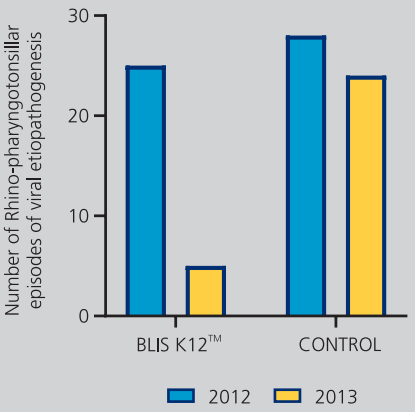


Figure 6: Shows reduction in episodes treated with BLIS K12™

3 STUDY

BLIS K12™ MAY REDUCE THE RATE OF COVID-19 INFECTION [9]

128 school aged children took part in a randomised controlled trial over the course of a 90 day period taking BLIS K12™ to combat COVID-19 infection. None of the 64 children taking BLIS K12™ tested positive for COVID-19, while 38% tested positive in the group not taking the oral probiotic. Results showed the close connection between a healthy Oral Microbiota and Lung Microbiota and that an Oral Microbiota not dominated by pathogenic species, makes the lungs less likely to develop an inflammatory response to viruses.

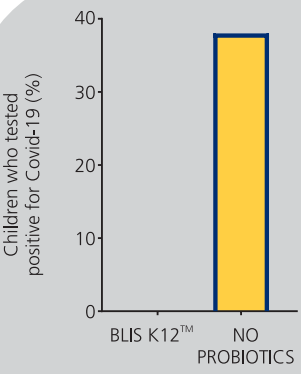


Figure 7: Number of children who tested positive for Covid-19 in each treatment group.

4 STUDY

TAKING BLIS K12™ SHOWS 95.5% IMPROVEMENT ON DAYS OFF WORK FOR FRONTLINE MEDICAL STAFF [10]

193 frontline medical staff were placed in a randomised control trial to determine the effectiveness of BLIS K12™ to minimise sick days due to viral upper respiratory infections. Participants were given 1 billion CFU of BLIS K12™ per day for 1 month. A reduced frequency of upper respiratory tract infections by 64.8%, time experiencing upper respiratory infections and oral ulcers by 78% as well as decreased number of days off work by 95.5% was observed in the group taking BLIS K12™.

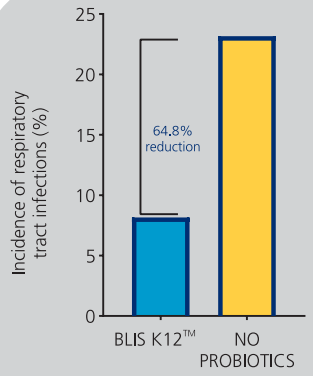


Figure 8: Reduction in the incidence of respiratory tract infections in the group taking BLIS K12™

5 STUDY

BLIS K12™ SHOWN TO HELP WITH HEALTH MARKERS AND REDUCE DEATH RATE IN HOSPITALIZED COVID-19 PATIENTS [11]

A small randomized trial of 50 patients ranging from 20-80 years (avg 48.5 years) hospitalised with COVID-19 took place over a period of 14 days. Patients taking 2 tablets of BLIS K12™ showed an improvement in blood markers, fever, oxygen saturation level, need and length of oxygen therapy and the rate of progression to ICU and death. The hypothesis that the presence of BLIS K12™ in the lungs could help reduce the lung's pro-inflammatory immune response, thus preventing excessive lung inflammation and subsequent admission to Intensive Care Unit (ICU) and even death.

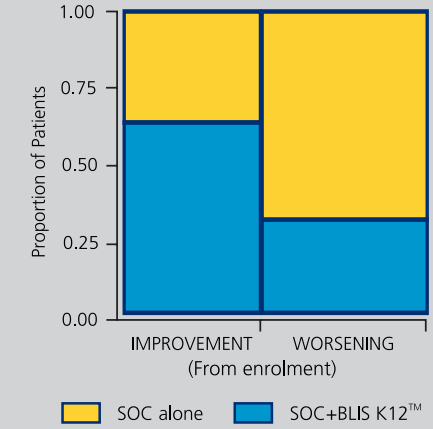


Figure 9: This mosiac plot shows improvement or worsening of supplementary oxygen need according to treatment. (SOC: Standard of Care)

REFERENCES

1. Barbour A, Tagg J, Abou-Zied OK, Philip K. New insights into the mode of action of the lantibiotic salivaricin B. Sci Rep. (2016) 6:31749. doi: 10.1038/srep31749
2. Barbour A, Wescombe P, Smith L. Evolution of lantibiotic salivaricins: new weapons to fight infectious diseases. Trends Microbiol. (2020) 28:578–93. doi: 10.1016/j.tim.2020.03.001
3. Cosseau C, Devine DA, Dullaghan E, Gardy JL, Chikatamarla A, Gellatly S, et al. The commensal Streptococcus salivarius K12 downregulates the innate immune responses of human epithelial cells and promotes host-microbe homeostasis. Infect Immun. (2008) 76:4163–75. doi: 10.1128/IAI.00188-08
4. Bertuccioli, A., Gervasi, M., Annibalini, G., Binato, B., Perroni, F., Rocchi, M. B. L., Sisti, D., & Amatori, S. (2023). Use of Streptococcus salivarius K12 in supporting the mucosal immune function of active young subjects: A randomised double-blind study. Frontiers in Immunology, 14. https://doi.org/10.3389/fimmu.2023.1129060
5. Shen Z, Xiao Y, Kang L, Ma W, Shi L, Zhang L, et al. Genomic diversity of SAR S-CoV-2 in Coronavirus Disease 2019 patients. Clin Infect Dis 2020;ciaa203.
6. Di Pierro F. A possible probiotic (S. salivarius K12) approach to improve oral and lung microbiotas and raise defenses against SAR S-CoV-2. Minerva Med. 2020 Jun;111(3):281-283. doi: 10.23736/S0026-4806.20.06570-2. Epub 2020 Apr 7. PMID: 32255312.
7. Guo, H., Xiang, X., Lin, X., Wang, Q., Qin, S., Lu, X., Xu, J., Fang, Y., Liu, Y., Cui, J., & Li, Z. (2022). Oropharyngeal Probiotic ENT-K12 as an Effective Dietary Intervention for Children With Recurrent Respiratory Tract Infections During Cold Season. Frontiers in Nutrition, 9. https://doi.org/10.3389/fnut.2022.900448
8. Di Pierro et al., Use of Streptococcus salivarius K12 in the prevention of streptococcal and viral pharyngotonsillitis in children. Drug Healthc Patient Saf. 2014, 13(6):15-20
9. Di PIERRO, F., & COLOMBO, M. (2021). The administration of S. salivarius K12 to children may reduce the rate of SARS-CoV-2 infection. Minerva Medica, 112(4). https://doi.org/10.23736/s0026-4806.21.07487-5
10. Wang, Q., Lin, X., Xiang, X., Liu, W., Fang, Y., Chen, H., Tang, F., Guo, H., Chen, D., Hu, X., Wu, Q., Zhu, B., & Xia, J. (2021). Oropharyngeal Probiotic ENT-K12 Prevents Respiratory Tract Infections Among Frontline Medical Staff Fighting Against COVID-19: A Pilot Study. Frontiers in Bioengineering and Biotechnology, 9. https://doi.org/10.3389/fbioe.2021.646184
11. Di Pierro et al (2022), Clinical Effects of Streptococcus salivarius K12 in Hospitalized COVID-19 Patients: Results of a Preliminary Study. Microorganisms, 10(10), 1926. https://doi.org/10.3390/microorganisms10101926

BLIS™

PROBIOTIC PIONEERS FOR A HEALTHIER YOU

Blis Technologies is a New Zealand-based developer and manufacturer of innovative probiotic solutions. Founded on the research of Professor John Tagg (University of Otago, New Zealand), the company was formed in 2000 to develop new bacterial species as probiotics for human health applications.

BLIS K12™ is available as raw ingredient to be formulated in finished product chewable tablet and powder formats:

- Granted FDA No-Objection GRAS status (Generally Recognized as Safe), approvals by Health Canada, FSSAI India, NPCB Malaysia and FSANZ amongst others.
- Guaranteed CFU count of >100b.

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