BLUESTONE PHARMA®

LEADERS IN MEDICAL PROBIOTICS

Bactoblis®

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PRODUCT OF THE YEAR

CLINICAL PORTFOLIO

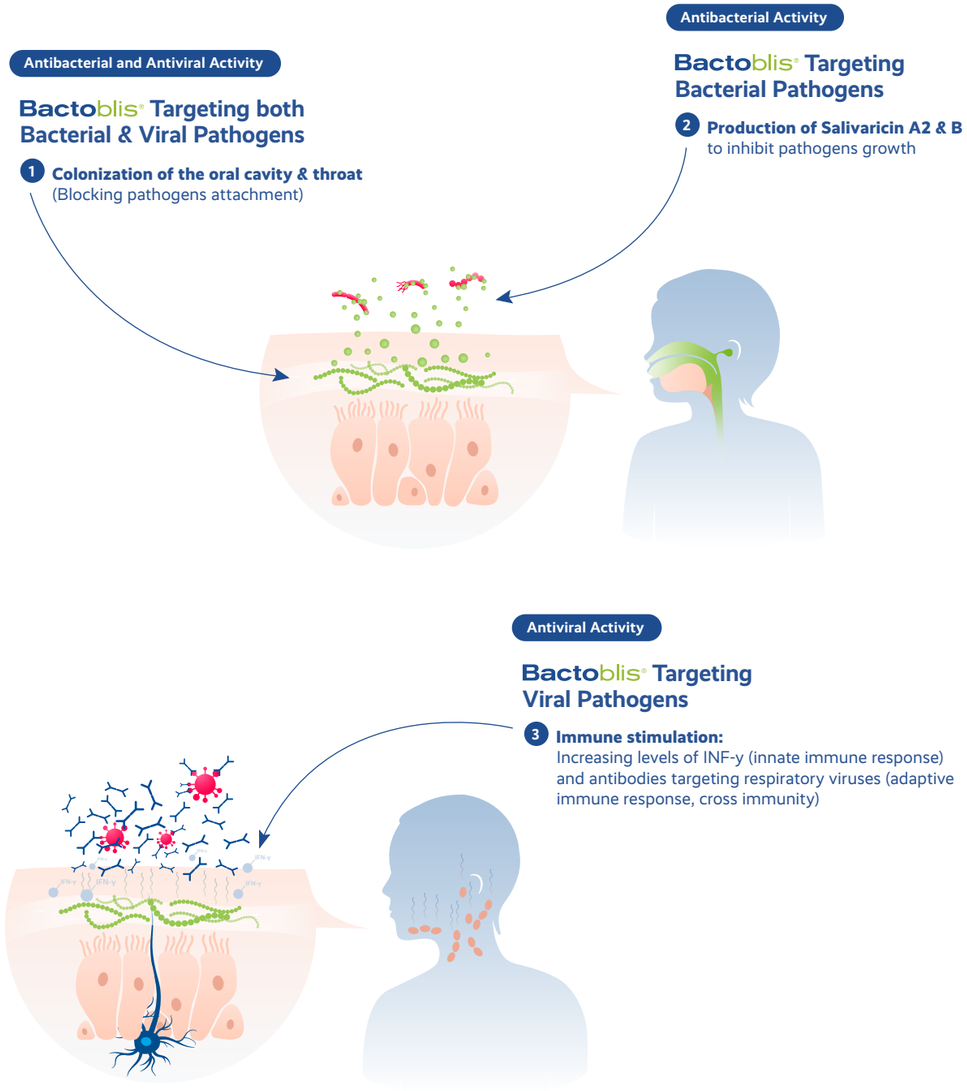
No.1 Pediatrician Brand for Respiratory Infections

> 30 Clinical Studies

Bactoblis®

Index of Studies

Mode of Action



SACHET

Bactoblis®: Impacting the Nasopharyngeal and Saliva Microbiome

Acute otitis media (AOM) is a prevalent cause of antibiotic prescriptions in young children. Hoewever, conventional probiotics have proven insufficient evidence in preventing AOM, increasing the need for a superior solution. Recent research has highlighted the potential of **Bactoblis®** in preventing respiratory infections.

In this study, we investigate the influence of **Bactoblis®** on the nasopharyngeal and saliva microbiome, examining the presence of otopathogens in the nasopharynx and assessing **Bactoblis®** colonization in both the nasopharynx and saliva.

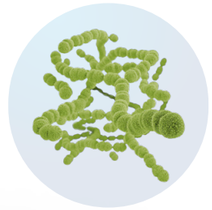
Material and Methods

Aim of the study:	Assess the impact of **Bactoblis®** on the nasopharynx and saliva microbiome in children attending daycare.
Study type:	Randomized, controlled clinical study. Was approved by the Ethical Committee of Oulu University Hospital and the Finnish Medicines Agency. (Finland)
Patients:	121 Children (**Bactoblis® group:** 81 and **Control group:** 40)
Subject description:	› Children below 3 years old › Children attending daycare, known as a risk factor for AOM › Children with a history of recurrent otitis media or otorrhea, and children with present or earlier tympanostomy tubes
Method:	**Microbiologic samples:** A nasopharyngeal bacterial swab sample was obtained using a sterile flocked swab and transferred immediately into a sterile tube containing 1 mL liquid Amies solution. Saliva samples were collected using saliva collection sponge spears. All samples were cooled and delivered on wet ice for processing and storage. The saliva tubes were centrifuged for 17 minutes at 1500 rpm. The saliva collection sponge spears were then discarded, and the saliva was stored as such. All samples were stored at -20°C until DNA extraction and next-generation sequencing. **Microbiome analysis of nasopharyngeal and saliva samples:** Extracted DNA from nasopharyngeal and saliva samples using the QIAamp PowerFecal DNA kit. After making necessary modifications to the manufacturer's protocol, the temperature was increased to 95°C and eluted the final DNA product to 50 mL to enhance DNA yield. Amplification of bacterial hypervariable regions V4-V5 of the 16S rRNA gene and conducted PCR with specific primers, followed by purification. DNA concentration was measured with a bioanalyzer DNA chip, and sequencing was performed using Ion torrent PGM. The data was analyzed using QIIME2, and microbiome information was deposited in the NCBI BioProject database. **Otorrhea or middle ear effusion:** A clinical ear examination with otoscope was performed upon study entry to reveal its current presence. **Patient background information:** Including previous antibiotic history from electronic medical records and the national electronic prescription registry were collected.
Treatment:	1 **Bactoblis®** sachet per day for 30 days

Reference: Sarlin 2020. The Pediatric Infectious Disease Journal

Results

- **Bactoblis®** proves to increase the relative abundance of *S. salivarius* in the nasopharynx and saliva microbiome compared to before. (Figure 1 and 2)
- **Bactoblis®** leads to a notable decrease in the relative abundance of otopathogens within the nasopharyngeal microbiome.
- **Bactoblis®** results in a successful local colonization of *S. salivarius* in the oral cavity.



Clinical Evidence

Figure 1

Nasopharynx

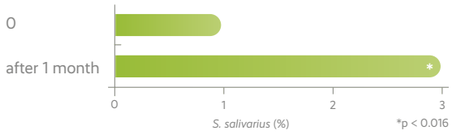
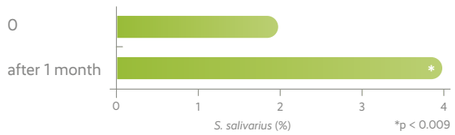


Figure 2

Saliva



Conclusion

Bactoblis® showcases its multifaceted effectiveness by enhancing the relative abundance of *S. salivarius* in the saliva microbiome, diminishing the prevalence of pathogens in the nasopharyngeal microbiome, and establishing successful local colonization of *S. salivarius* in the oral cavity. A significant impact for addressing AOM in children.

Bactoblis®: Your Shield Against Throat Infections

Bactoblis® plays a preventive role in reducing the incidence of streptococcal pharyngitis and/or tonsillitis, revealing a promising alternative to fight against these type of infection in children.

Methods and Materials

Aim of the study:	To determine the efficacy of **Bactoblis®** in reducing the incidence of streptococcal pharyngitis and/or tonsillitis in patients with a previous history of these infections.
Study type:	Independent clinical study. This study was conducted during routine outpatient work following international guidelines and in line with the principles outlined in the Declaration of Helsinki. (Turkey)
Patients:	44 children and adults. (**Bactoblis® group:** 20 and **Control group:** 14 and **Before group:** 10)
Subject description:	› Children and adults aged 12-45 years old. › Children and adults with total absence of symptoms of infective disease at the time of enrollment and recurrent streptococcal pharyngitis and/or tonsillitis in the previous year.
Method:	**Recurrent pharyngitis and/or tonsillitis:** confirmed by throat swab (positive for group A hemolytic Streptococcus).
Treatment:	1 **Bactoblis®** lozenge per day for 90 days.

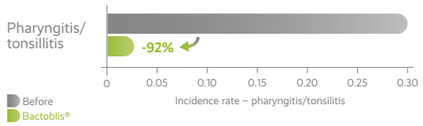
Results

- **Bactoblis®** results in a significant 92% reduction of pharyngo-tonsillar infections compared to the previous year when children did not received treatment. Control group shows no improvement. (Figure 1)
- **Bactoblis®** demonstrates an impressive 80% reduction in the incidence of pharyngo-tonsillar infections over the 3-month follow-up period.
- **Bactoblis®** exhibits no adverse effects or intolerability, resulting in no dropouts.

Clinical Evidence

Figure 1

Less Recurrent Throat Infections



Bactoblis® inhibits group A *streptococcus* acquisition and the prevalence of sore throat

Conclusion

- **Bactoblis®** reduces the incidence of pharyngo-tonsillar infections, emphasizing its potential in combating these type of diseases.
- **Bactoblis®** contributes to improved health outcomes and a better quality of life for individuals susceptible to suffer from pharyngo-tonsillar infections.

Reference: Gun et al 2017. Indian Journal Research

Bactoblis®: The Game Changer for Children Suffering from Recurrent Streptococcal Infections

Streptococcus pyogenes is the leading cause of pharyngitis, tonsillitis, and acute otitis media in children worldwide. To date, the use of an oral probiotic to counteract these diseases is well known, such is the case of our formula **Bactoblis®**, containing a K12 probiotic strain that releases two lantibiotics bacteriocins named salivaricin A2 and salivaricin B, highly effective to fight with *Streptococcus pyogenes* and reduce the incidence of such infections in a significant percentage.

Materials and Methods

Aim of the study:	Preventive role of **Bactoblis®** in reducing the number of episodes of streptococcal infections and acute otitis media.
Study type:	Multicenter, randomized clinical study, following international guidelines and in line with the principles outlined in the Declaration of Helsinki. No ethical approval was needed. (Italy)
Patients:	82 Children. (**Bactoblis® group:** 45 and **Control group:** 37)
Subject description:	› Children aged 3-12 years old. › Total absence of symptoms of infective disease at the time of enrollment; and diagnosis of recurrent streptococcal (group A hemolytic Streptococcus) pharyngitis and/or tonsillitis in the previous year.
Method:	Recurrent pharyngitis and/or tonsillitis in the previous year confirmed by throat swab (positive for group A hemolytic Streptococcus)
Treatment:	1 **Bactoblis®** lozenge per day for 90 days.

Results

- **Bactoblis®** shows a remarkable 92% reduction in the episodes of streptococcal pharyngeal infection and a significant 40% decrease in acute otitis media episodes. (Figure 1 and 2)
- **Bactoblis®** reduces the incidence of pharyngeal and ear infections by 66% over a 6-month follow up period.
- **Bactoblis®** demonstrates excellent acceptance among children, with no reported adverse effects or dropouts during the study.

Clinical Evidence

Figure 1

Reduction in the Episodes of Streptococcal Pharyngeal Infection

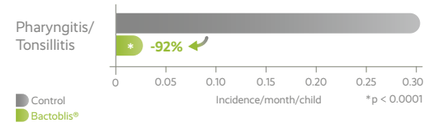
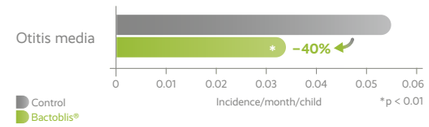


Figure 2

Decreased Incidence of Acute Otitis Media Episodes



Conclusion

- **Bactoblis®** has the potential to significantly reduce the occurrence of streptococcal pharyngeal infection and acute otitis media in children, and its effects seems to persist even after the treatment period.
- **Bactoblis®** is safe and well tolerated by children.

Reference: Di Pierro et al 2012. Int J Gen Med

LOZENGE

Bactoblis®: Prevents Recurrent Throat Infections in Children

With the increase of antibiotic resistance, lantibiotics have become an interesting alternative. **Bactoblis®** shows strong abiities to prevent pathogens from causing recurrent throat infections in children. It offers a safer and effective way to fight against antibiotic resistance.

Methods and Materials

Aim of the study:	› To evaluate the recurrence rate of infection associated with BHSGA before and after **Bactoblis®** › To evaluate the presence of episodes of respiratory infections before and after **Bactoblis®**
Study type:	Open, non-randomized clinical study. The study was performed with the consent of the local ethics committee. (Ukraine)
Patients:	66 children (**Bactoblis® group:** 42 and **Control group:** 24)
Subject description:	› Children aged 3-10 years old. › Children diagnosed with recurrent respiratory diseases such as throat infections.
Method:	› **Pharyngo-tonsillar infection**: was diagnosed according to the Mclsaac clinical scale: with ≥ 2 points (adenopathy, fever 38°C, lack of cough, tonsillo-pharyngitis exudate, age, season) + confirmation of pharyngo-tonsillar infections using a quick streptococcal test (Streptatest) or Mclsaac score= 5. › **Recurrent Respiratory Infections**: was defined as three or more episodes of tonsillopharyngitis for 6 months or four or more episodes for 12 months.
Treatment:	1 **Bactoblis®** lozenge per day for 30 days.

Clinical Evidence

Figure 1

Decreased Throat Infection Episodes

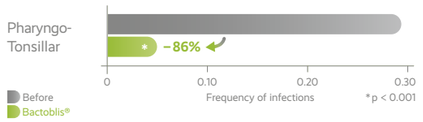
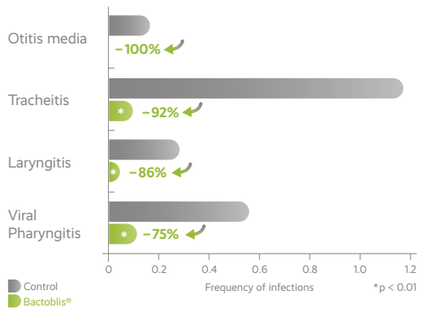


Figure 2

Less Respiratory Infections



Results

- **Bactoblis®** results in a significant 86% reduction in throat infections episodes, after 6 months of treatment. (Figure 1)
- **Bactoblis®** reduces various respiratory infections, such as: viral pharyngitis, tracheitis, laryngitis and acute otitis media. (Figure 2)
- **Bactoblis®** demonstrates a significant decrease in symptoms among patients when used as an add-on to standard treatment.
- **Bactoblis®** reveals a notable reduction in the colonization of *H. bacillus*, *S. aureus*, and *S. pneumococcus* in the oropharyngeal mucosa.
- **Bactoblis®** reports no side effects.

Conclusion

- **Bactoblis®** prevents the relapse of throat infections, indicating its role as an add-on to standard treatment for these types of infections.
- **Bactoblis®** exhibits positive outcomes for children with pharyngeal tonsil hypertrophy, suggesting its efficacy in managing the condition and potentially reducing associated complications.
- **Bactoblis®** demonstrates significant results in preventing episodes of respiratory infections, including viral pharyngitis, tracheitis, laryngitis and acute otitis media, highlighting its broad-spectrum benefits for respiratory health.

Reference: Kryuchko and Tkachenko 2017. Child's health

LOZENGE

Bactoblis®: Putting an End to Recurrent Respiratory Infections in Kids on Antibiotics

The rising incidence of recurrent respiratory infections in children is a significant concern for healthcare professionals. Despite antibiotics being commonly used, their effectiveness is limited against multi-microbial causes and high antibiotic resistance. Luckely, **Bactoblis®**, emerges as a promising alternative. With its inhibitory effects against respiratory pathogens, **Bactoblis®** demonstrates a positive impact in preventing pharyngotonsillitis, otitis media and others.

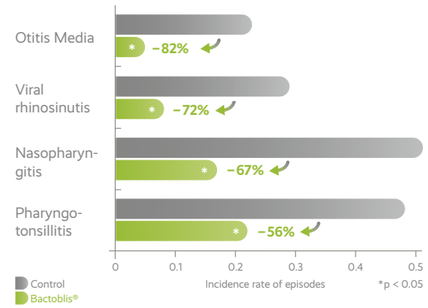
Methods and Materials

Aim of the study:	Evaluate the efficacy of the use of **Bactoblis®** in children as a preventive measure against recurrent respiratory infections.
Study type:	Controlled prospective, open-Label, randomized, computerized, single-center clinical study. (Ukraine)
Patients:	57 children (**Bactoblis® group:** 36 and **Control group:** 21)
Subject description:	› Children aged 6-10 years old › Children with recurrent pharyngeal disease
Method:	› **Recurrent respiratory disease diagnosis:** performed on the Mclsaac clinical scale: with ≥ 2 points (lumphadenopathy, 38°C fever, no cough, casepurulent exudate in the tonsils, patients age) + confirmation of BHSA with Streptatest. › **Recurrent respiratory disease:** defined as three or more exacerbations of the process over 6 months or more than four episodes over 12 months. › All suvereyed children were monitored dynamically by a pediatric otolaryngologist and pediatrician with local status evaluation
Treatment:	1 **Bactoblis®** lozenge per day for 30 days.

Clinical Evidence

Figure 1

Less Recurrent Respiratory Infections



Results

- **Bactoblis®** demonstrates a significant positive impact in reducing the frequency of recurrent respiratory infections. (Figure 1)
- **Bactoblis®** shows a significant reduction in HPT's clinical inflammation index from 45% to 10%.
- **Bactoblis®** significantly reduces *S. aureus* and *S. pneumoniae* incidence in children with pharyngo-tonsillar infections.
- **Bactoblis®** shows significantly less episodes of recurrent infections (RI) during the 6-month follow-up period
- **Bactoblis®** reports no side effects.

Conclusion

- **Bactoblis®** treatment delivers significant benefits in children with recurrent respiratory diseases: reduced infections, less antibiotic use, and enhanced pharyngeal tonsil microbiocenosis.
- **Bactoblis®** demonstrates a significant improvement in clinical symptoms of pharyngeal tonsil hypertrophy.
- **Bactoblis®** treatment can be repeated 2-3 courses per year for optimal therapeutic benefits, given its good tolerability and absence of side effects.

Reference: Gavrilenko 2018. Child's health

Bactoblis®: Helps Stop Chronic Tonsillitis in Kids

Chronic Tonsillitis is a prevalent allergic infection impacting 10-15% of children, involving persistent palatine tonsil inflammation. Key responsible is group A beta-hemolytic streptococcus. **Bactoblis®** have shown promise in enhancing well-being, reducing hypertrophy and fever, and normalizing blood counts in affected children. This localized colonization also reduces *S. aureus* and group A streptococcus isolations and lowers acute respiratory viral infection rates.

Methods and Materials

Aim of the study:	To prove **Bactoblis®** as an alternative to prevent and treat chronic tonsillitis in children
Study type:	Open-label clinical study. (Ukraine)
Patients:	54 children (**Bactoblis® group:** 33 and **Control group:** 21)
Subject description:	Children aged 9-14 years old Children diagnosed with chronic tonsillitis
Method:	**Chronic tonsillitis:** Diagnosed through the following diagnostic criteria: Availability of clinical and epidemiological data indicating the streptococcal etiology of tonsillitis Negative microbiological tests between episodes of the disease An increase in the titers of antistreptococcal antibodies after each case of tonsillitis
Treatment:	1 **Bactoblis®** lozenge per day for 30 days.

Results

- **Bactoblis®** demonstrates a significantly lower chronic tonsillitis incidence rate of 11.1 ± 4.3%, compared to the higher rate of 28.6% ± 9.9% in the control group. (Figure 1)
- **Bactoblis®** significantly enhances the overall well-being of children with chronic tonsillitis by alleviating clinical symptoms and improving key biomarkers. (Figure 2)
- **Bactoblis®** reduces tonsil hypertrophy, alleviating swallowing, breathing, and throat discomfort in children.
- **Bactoblis®** leads to a reduction in mild fever-like symptoms, characterized by a slight increase in children's body temperature.
- **Bactoblis®** decreases the incidence of regional lymphadenitis.
- **Bactoblis®** proves a 52.9% reduction in ASL-O (strep. biomarker) levels in children's blood.

Clinical Evidence

Figure 1

Reduced Chronic Tonsillitis Incidence

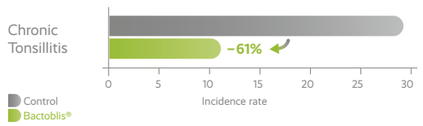
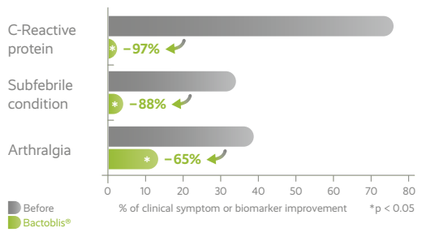


Figure 2

Alleviation of Chronic Tonsillitis Symptoms + Key Biomarkers Improvement



Conclusion

- **Bactoblis®** proves to be an effective treatment for children with chronic tonsillitis, enhancing their overall health by reducing the frequency of tonsillitis episodes, alleviating disease-like symptoms, and improving key health indicators.
- **Bactoblis®** significantly reduces the presence of *S. aureus* and group A streptococcus in the oropharynx, showcasing an effective and safe treatment to prevent colonization by respiratory pathogens.

Reference: Marushko et al 2018. Clinical Pediatrics

Bactoblis®: Shows a High Protection Against Recurrent Respiratory Infections

Group A beta-hemolytic streptococci (GABHS) are a frequent cause of recurrent respiratory infections in young children. The high prevalence of these infections contributes substantially to the total current antibiotic prescribing. **Bactoblis®** interferes with the growth of GABHS and also leads to reduced antibiotic consumption.

Materials and Methods

Aim of the study:	Efficacy of **Bactoblis®** in reducing Group A Beta-hemolytic Streptococcus (GABHS) during the treatment period and throughout the follow up period.
Study type:	Independent research, retrospective observational clinical study. This study was performed according to the criteria contained in the Declaration of Helsinki and was approved by the Ethics Committee of the Local Health Authority of Piacenza. (Italy)
Patients:	130 children (**Bactoblis® group:** 76 and **Control group:** 54)
Subject description:	› Children aged 3-7 years old. › Children with a diagnosis of GABHS RPTIs during a certain period (January 2011-December 2013)
Method:	› **GABHS infections:** diagnosed using standardized clinical and microbiological criteria, based on the McIsaac clinical score and the rapid throat swab (RAD). McIsaac score with clinical score >2 (adenopathy, fever 38°C, absence of cough, pharyngo-tonsillar exudate, age, season) + confirmation of GABHS presence with RAD method or McIsaac score =5. › **RPTI:** defined as ≥3 episodes of pharyngotonsillitis over a period of 6 months, or ≥4 episodes over a period of 12 months.
Treatment:	1 **Bactoblis®** lozenge per day for 90 days.

Results

- **Bactoblis®** results in an impressive 84% reduction of pharyngo-tonsillar infections. (Figure 1)
- **Bactoblis®** shows a significant decrease in pharyngo-tonsillar infections during the 9-month follow-up period. (Figure 2)
- **Bactoblis®** demonstrates an impressive efficacy, with 88% of treated children remaining free from infections throughout the treatment course.
- **Bactoblis®** exhibits no reported side effects.

Clinical Evidence

Figure 1

Less Pharyngotonsillar Infections

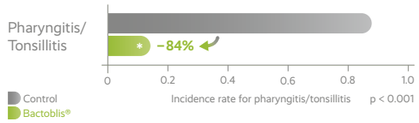


Figure 2

Reduction of Pharyngotonsillar Infections During Follow-Up Period

4x less likely the need for antibiotic therapy in children suffering from recurrent respiratory infections

Conclusion

- **Bactoblis®** reduces the incidence of pharyngotonsillar infections in children.
- **Bactoblis®** shows a remarkable reduction in the incidence of pharyngo-tonsillar infections during the 9-month follow-up period. Highlighting the effectiveness of **Bactoblis®** in preventing such infections and reducing the need of antibiotic therapy.

Reference: Gregori et al. 2016, There Clin Manag

Bactoblis®: Tonsillitis Management in Kids

Recurrent Tonsillitis (RT), a common condition in children, is characterized by persistent or frequently recurring inflammation of the palatine tonsils or adenoids. *Streptococcus pyogenes* is a primary bacterial culprit. Traditional treatment includes the use of antibiotics, but increasing antibiotic resistance is a significant concern. To address this challenge, emerging management options include the use of oral probiotics, particularly **Bactoblis®**, which naturally inhibits *S. pyogenes*.

Material and Methods

Aim of the study:	Evaluate the efficacy and safety of **Bactoblis®** in preventing acute respiratory infections in young children who had just started attending kindergarten.
Study type:	Open-label, single-centre, randomized, controlled clinical study. The study was conducted in Poltava Regional Children's Clinical Hospital and in compliance with the Declaration of Helsinki. The Local Ethics Committee approved the protocol. (Ukraine)
Patients:	58 Children (**Bactoblis® group:** 28 and **Control group:** 30)
Subject description:	› Children aged 2-4 years old. › Children attending kindergarten (without any clinical background such as autoimmune diseases)
Method:	Parents were told to bring the kids to the clinic if they noticed symptoms of oropharyngeal infection. A medical examination and pharyngel swab test were perfomed, and if positive antibiotics were administered. After the antibiotic therapy, **Bactoblis®** treatment continued for 90 days. In cases of viral infection with pharyngolaryngeal pain or fever, acetaminophen or ibuprofen was prescribed. Other conditions were treated according to local pediatric guidelines.
Treatment:	1 **Bactoblis®** sachet per day for 90 days.

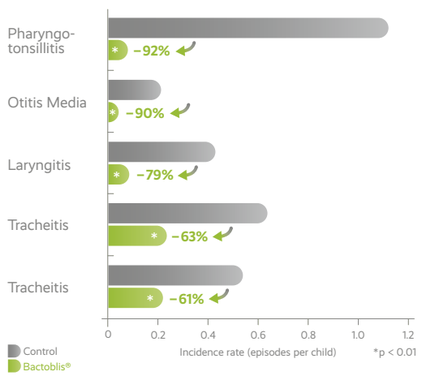
Results

- **Bactoblis®** leads to a significant reduction in the incidence of acute respiratory infections, with the greatest efficacy in reducing the incidence of pharyngotonsillitis and otitis media. (Figure 1)
- **Bactoblis®** reduces the use of antipyretics and shortens the duration of antibiotic treatment.
- **Bactoblis®** results in a reduction in days of preschool absence.
- **Bactoblis®** shows an excellent tolerability, no side effects or dropouts.

Clinical Evidence

Figure 1

Reduction of Acute Respiratory Infections



Conclusion

- **Bactoblis®** is an effective preventive solution for reducing common respiratory tract infections in healthy young children attending kindergarten. It's safety and acceptability make it a valuable addition to preventive healthcare.
- **Bactoblis®** not only reduces the use of antipyretics and antibiotics, but also minimizes kindergarten absence. This underscores the potential of **Bactoblis®** to promote the overall well-being of children in this age group.

Reference: Kryuchko and Tkachenko 2021a. Nutrafoods

Bactoblis®: Defense Against Infant Respiratory Infections

Pediatric sore throat, produced by both bacterial and viral infections, represents a prevalent healthcare challenge. The prevalence of Group A-beta-haemolytic Streptococcus (GABHS) contributes to the economic burden and raises concerns about antibiotic over-use. Although the majority of cases originate from viruses, antibiotics are frequently prescribed for children. Probiotics, particularly **Bactoblis®**, emerge as a promising substitute. With proven effectiveness in preventing recurrent streptococcal infections, **Bactoblis®** stands out as a superior choice to enhance children's respiratory health.

Methods and Materials

Aim of the study:	Evaluate the efficacy and safety of **Bactoblis®** powder for the prevention of respiratory diseases in young children.
Study type:	Open-label, single-centre, randomized, controlled clinical study. This study was conducted following the principles laid down by the Declaration of Helsinki. (Ukraine)
Patients:	62 Children (**Bactoblis® group:** 32 and **Control group:** 30)
Subject description:	› Children aged 6 months - 2 years old
Method:	› **Health assessment:** Performed by an otorhinolaryngologist. › **Oropharyngeal symptoms:** underwent a medical examination and a rapid pharyngeal swab test. This test detects streptococcal antigens qualitatively, supporting the diagnosis of group A streptococcal infection. Upon a positive test result, antibiotics or ibuprofen were prescribed, depending on the disease's origin.
Treatment:	1 **Bactoblis®** sachet per day for 30 days.

Results

- **Bactoblis®** demonstrates a 63% reduction in the incidence of viral infections. (Figure 1)
- **Bactoblis®** proves an impressive 87% reduction in antibiotic use and a 52% decrease in antipyretic use. (Figure 2)
- **Bactoblis®** reduces the need for visiting ENT specialists.
- **Bactoblis®** supports a reduction in bacterial complications and the need for antibacterial agents.
- **Bactoblis®** shows no side effects or dropouts.

Clinical Evidence

Figure 1

Reduction of Bacterial Infections Incidence

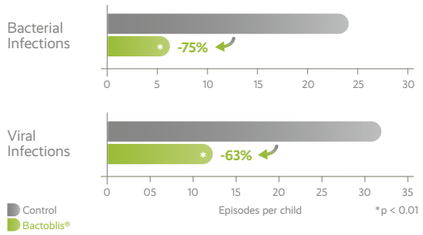
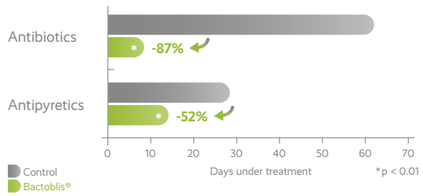


Figure 2

Less Antibiotic and Antipyretic Use



Conclusion

- **Bactoblis®** is a superior probiotic that helps to prevent viral respiratory infections in children. It helps to restore the natural microbiome after antibiotic therapy and prevent bacterial complications.
- **Bactoblis®** creates resistance to viral infections, making it particularly beneficial during seasonal diseases and in high-risk environments for children. Becoming a solution for promoting pediatric health.

Reference: Kryuchko and Tkachenko 2021b. Nutrafoods

Bactoblis®: Shows Protection From Respiratory Infections in Healthy Children Attending Kindergarten

LOZENGE

Kindergarten is a crucial period for children, who are more vulnerable to respiratory infections. **Bactoblis®** offers protection for children attending kindergarten without a history of recurrent streptococcal pharyngotonsillitis or acute otitis media.

Materials and Methods

Aim of the study:	To evaluate the role of **Bactoblis®** in the control of streptococcal disease and acute otitis media in children attending the first year of kindergarten.
Study type:	Multicentre, open-label, randomized, controlled clinical study. The study was conducted according to the criteria set by the Declaration of Helsinki and with the approval of the local Ethics Committee. (Italy)
Subjects:	222 healthy children. (**Bactoblis® group:** 111 and **Control group:** 111)
Subject description:	› Children aged 3 years old › Children soon to attend kindergarten and free of a streptococcal disease.
Method:	**Streptococcal disease:** Absence confirmed by a rapid throat swab test for group A streptococcus.
Treatment:	1 **Bactoblis®** lozenge per day for 180 days.

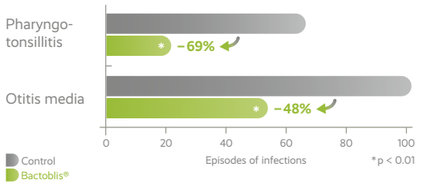
Results

- **Bactoblis®** achieves a 69% reduction of recurrent pharyngotonsillitis episodes and a 48% decrease in otitis media episodes. (Figure 1)
- **Bactoblis®** leads to a significant reduction of 67% in the episodes of otitis media during the 3-month follow up period.
- **Bactoblis®** has no adverse effects reported, and none of the children dropped out the treatment.

Clinical Evidence

Figure 1

Less Respiratory Infections in Healthy Children



During the 3-month follow-up period, none of the children in the **Bactoblis®** group exhibited any cases of scarlet fever.

Conclusion

- **Bactoblis®** dramatically reduces the incidence of pharyngotonsillitis episodes and middle ear infections in healthy children.

Reference: Di Pierro et al 2016b. Eur Rev

Bactoblis®: Effective Treatment to Optimize Pediatric ENT Care

SACHET

Childhood is marked by a high prevalence of Acute Respiratory Infections (ARIs), driving intensive research into innovative treatment options. Bacteriocins have emerged as a key focus, with particular interest in the effectiveness of *S. salivarius* K12. This strain produces class I bacteriocins that target major ARI pathogens such as *S. pyogenes*, *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*. These findings set up **Bactoblis®** as a good alternative to standard treatments for enhancing pediatric respiratory health.

Material and Methods

Aim of the study:	Evaluate the efficacy and safety of **Bactoblis®** in the complex treatment of acute tonsillitis, rhinosinusitis, stomatitis and otitis media in children.
Study type:	Open-label, non-randomized clinical study. (Ukraine)
Patients:	55 Children (**Bactoblis® group:** 35 and **Control group:** 20)
Subject description:	› Children aged 3-7 years old. › Children with ARI of the upper respiratory tract (rhinosinusitis, tonsillitis), inflammation of the oral mucosa and middle ear.
Method:	Evaluation of the effectiveness of **Bactoblis®** was conducted based on a study of the dynamics of regression of clinical symptoms during the course of treatment.
Treatment:	1 **Bactoblis®** sachet per day for 10 days.

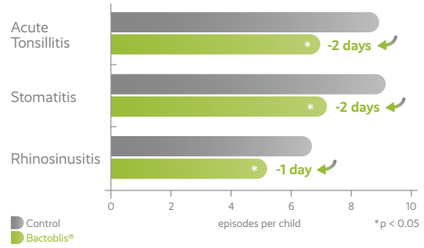
Results

- **Bactoblis®** demonstrates a significant improvement in acute tonsillitis, rhinosinusitis, and stomatitis, leading to faster relief from symptoms. It also reduces respiratoy illness duration by 2 days. (Figure 1)
- **Bactoblis®** shows a 1.5-2 times lower likelihood of requiring antibiotics or antipyretics as a standard therapy of the disease.

Clinical Evidence

Figure 1

Less Days Sick



Conclusion

- **Bactoblis®** significantly shortens the duration of respiratory ENT diseases in children, reducing the need for antibiotics or antipyretics.
- **Bactoblis®** proves to be highly effective as an oral probiotic for treating acute respiratory ENT diseases in children.

Reference: Kryuchko and Tkachenko 2021c. Pediatrics

LOZENGE

Bactoblis®: A Triple Defense Against Streptococcal, Viral Pharyngotonsillitis and AOM

Bactoblis® efficacy extends beyond bacterial infections and acute otitis media (AOM) episodes, as K12 exhibits potential in preventing viral pharyngotonsillitis infections by modulating salivary cytokines. This includes the ability to elevate γ-interferon (wihout modifying either IL- 1β or TNF-α levels) levels and reduce IL-8 release.

Methods and Materials

Aim of the study:	To evaluate the role of **Bactoblis®** in reducing the incidence of streptococcal, viral pharyngotonsillitis and acute otitis media (AOM) in subjects with non-recurrent streptococcal infection.
Study type:	Retrospective clinical study in accordance with the Declaration of Helsinki and approved by local ethics committee. (Italy)
Patients:	133 children (**Before** and **after** treatment with **Bactoblis®**)
Subject description:	› Children aged 3-14 years old. › Children diagnosed at least once with pharyngo-tonsillar infection and/or AOM in the previous year.
Method:	› **Streptococcal pharyngo-tonsillar infection:** confirmed by a rapid swab positive for group A streptococcus. › **Viral infection:** diagnosed according to the following criteria: negative rapid swab for streptococcal disease, absence of petechiae on the palate, absence of submandibular lymphadenopathy, mild dysphagia and absence of headache, abdominal pain or hyperpyrexia. › **AOM:** diagnosed by pneumatic otoscopy and clinical signs.
Treatment:	1 **Bactoblis®** lozenge per day for 180 days.

Results

- **Bactoblis®** leads to a significant reduction of viral pharyngotonsillitis, streptococcal, and acute otitis media episodes, compared to the previous year. (Figure 1)
- **Bactoblis®** results in a decrease in the number of absentee days from school for children and from work for parents. (Figure 2)
- **Bactoblis®** proves a remarkable decrease of 88% in antibiotic use and an 85% reduction in the need for antipyretics.
- **Bactoblis®** shows no dependency on sex or age.

Clinical Evidence

Figure 1

Reduction in Respiratory Infections

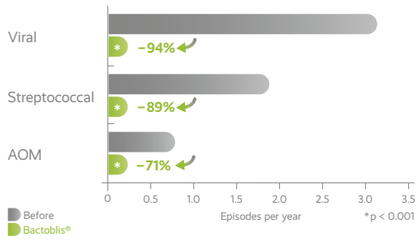
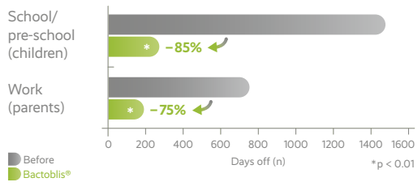


Figure 2

Less Absences from School and Work



Conclusion

- **Bactoblis®** proves to be highly effective in reducing the incidence of both bacterial and viral pharyngotonsillitis and acute otitis media (AOM).
- **Bactoblis®** leads to a significant decrease in the use of antibiotics and antipyretics. Offering a safer alternative to manage non-recurrent infections.
- **Bactoblis®** results in a noteworthy reduction in the frequency of missed pre-school, school, and work days, contributing to enhanced attendance and productivity in the society.

Reference: Di Pierro et al 2018. Minerva Pediatrica

LOZENGE

Bactoblis®: Protecting Children Against Pharyngotonsillitis and Respiratory Infections

Bactoblis® is known to inhibit the growth of *Streptococcus pyogenes*, a major contributor to pharyngotonsillitis, as well as other respiratory pathogens, like *H. influenzae*, *S. pneumoniae*, and *M. catarrhalis*, to a lesser degree.

Methods and Materials

Aim of the study:	Evaluate the effectiveness of preventive use of two courses of **Bactoblis®** treatment in children with viral and bacterial diseases of the respiratory tract, and to assess side effects and safety of its use.
Study type:	Open-label, non-randomized clinical study. The study was conducted with the consent of the local ethics committee. (Ukraine)
Patients:	48 Children (**Before** and **after** treatment with **Bactoblis®**)
Subject description:	› Children aged 3-14 years old. › Children experiencing pharyngotonsillitis and/or viral disease in the respiratory tract
Method:	› **Clinical evaluation:** Performed based on the anamnesis data on episodes of pharyngotonsillitis and viral diseases of the respiratory tract, the peculiarities of their course, the rate of achievement of the therapeutic effect when using a symptomatic therapy. All children were examined by an otolaryngologist as appropriate to assess the local status. › Differences in infections episodes, days lost, and medication were determined using the Wilcoxon signed-rank test, and the non-parametric Mann-Whitney U-test was used to analyze ordinal variables.
Treatment:	1 **Bactoblis®** lozenge per day for 30 days.

Results

- **Bactoblis®** presents up to 91% reduction in the incidence of both viral and bacterial pharyngotonsillitis. (Figure 1)
- **Bactoblis®** demonstrates a positive effect of its preventive use in reducing episodes of upper respiratory tract infections. (Figure 2)
- **Bactoblis®** proves a 70% improvement in acute otitis media episodes.
- **Bactoblis®** results in a remarkable reduction of over 80% of antibiotics and antipyretics use in children's therapy.
- **Bactoblis®** reduces the frequency of absences from preschool by 81%, and a school attendance absence by 77%.
- **Bactoblis®** shows no side effects.

Reference: Kryuchko and Tkachenko 2018. Child's health

Clinical Evidence

Figure 1

Reduction of Pharyngotonsillitis Episodes in Children

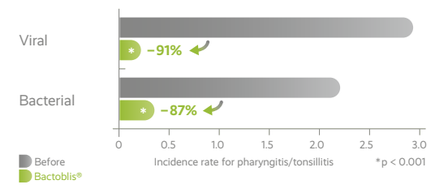
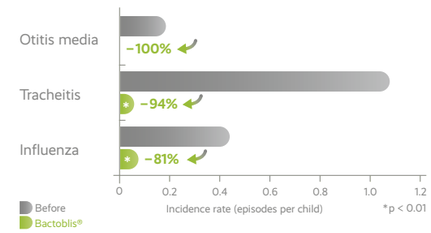


Figure 2

Less Respiratory Infections Episodes



Conclusion

- **Bactoblis®** proves to be highly effective in preventing bacterial and viral respiratory tract infections in children. These positive results highlight **Bactoblis®** as a promising alternative for enhancing children's respiratory health.
- **Bactoblis®** exhibits a remarkable safety profile and excellent children acceptance, indicating the feasibility of 2 courses for 30 days over the course of a year.

LOZENGE

Bactoblis®: Guardian of Children's Ears Against Otitis Media

Otitis media is a common issue among pediatric patients with a high incidence in both acute otitis media (AOM) and secretory otitis media (SOM) in children. Bacterial pathogens such as *S. pneumoniae*, *H. influenzae*, *M. catarrhalis* and *S. pyogenes* cause AOM by ascending from the nasopharynx to the middle ear. **Bactoblis®** proves to inhibit the growth of these pathogens and reduce bacterial pharyngotonsillitis in children.

Methods and Materials

Aim of the study:	1. To evaluate the safety and tolerability of **Bactoblis®** in children with middle ear exudate. 2. To investigate **Bactoblis®** potential protective effect in reducing AOM recurrences. 3. To monitor SOM progression through tone audiometry, tympanometry, endonasal endoscopy, otoscopy, and tonsillar examination.
Study type:	Pilot, uncontrolled clinical study. The study was conducted in agreement with the criteria set by the Declaration of Helsinki. The approval from the ethical board was not required. (Italy)
Patients:	22 children (**Before** and **after** treatment with **Bactoblis®**)
Subject description:	› Children aged 3-9 years old. › Children with a recent history of recurrent AOM and with unilateral or bilateral fluid in the middle ear for at least 2 months.
Method:	› **AOM incidence**: Has been calculated as episodes of AOM per month per child. › **Audiometry**: The study utilized AM13 FreeQuency audiometer, TDH 39 headphones, and a Mitaso soundproof booth. Pure tone audiometry tested frequencies from 250 to 8,000 Hz for hearing threshold, with the bone route used as needed (250 to 4,000 Hz). The technique used was sound-to-silence, and the threshold was considered to be the lowest intensity at which the child responded 100% of the times to the presence of sound. Hearing degree classification followed Northern and Downs values: normal (score =0; up to 15 dB), mild transmissive hypoacusis (score= 1;16 to 70 dB), and severe transmissive hypoacusis (score= 2; over 71 dB). › **Tympanometry**: A Zodiac 901 tympanometer was used to assess the condition of the middle ear. The tympanogram was evaluated according to three types of conditions: type A (normal); type B (presence of middle ear exudate); type C (tubaric dysfunction). › **Otoscopy**: The data obtained from otoscopy were categorized into four grades of classification: normal tympanic membrane (score =0); matt-like tympanic membrane (score =1); matt-like and retracted tympanic membrane (score =2); and adherent (glue-ear) tympanic membrane (score =3). › **Endonasal endoscopy**: Examination was done using Olympus pediatric fiberscope with a 2.2 mm flexible nasal endoscope. The other equipment used for assessing slow movements were video camera attached to endoscope, a colored television, and a image recorder. Data have been evaluated as percentage of obstruction. › **Tonsillar examination**: Tonsil volume was classified according to validated criteria as follows: tonsils in the tonsillar fossa barely been behind the anterior pillar (score=0); tonsils visible behind the anterior pillar (score=1); hypertrophic tonsils extended three-quarters of the way to middle line (score=2); and tonsils completely obstructing the airway, known as kissing tonsils (score=3).
Treatment:	1 **Bactoblis®** lozenge per day for 90 days.

Results

- **Bactoblis®** demonstrates a 43% reduction in AOM incidence compared to the previous year. (Figure 1)
- **Bactoblis®** proves up to 66% improvement in bilateral tone audiometry. (Figure 2)
- **Bactoblis®** exhibits a significant improvement in bilateral tympanometry, particularly regarding the presence of middle ear exudate.
- **Bactoblis®** shows a notable improvement of approximately 40% in bilateral otoscopy results.
- **Bactoblis®** reveals a 30% reduction in Eustachian tube obstructions and a 40% decrease in the size of palatine tonsils.
- **Bactoblis®** indicates no side effects or dropouts reported.

Bactoblis® confirms to have a safe and effective profile for children suffering from AOM.

Clinical Evidence

Figure 1

Reduction of AOM Incidence

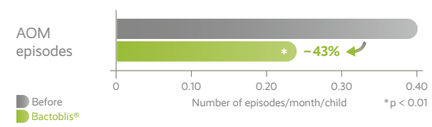
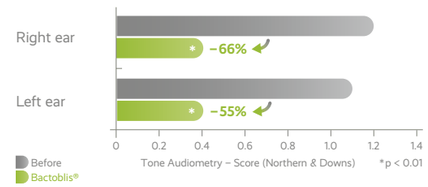


Figure 2

Bilateral Tone Audiometry



Conclusion

- **Bactoblis®** intervention in children suffering from asymptomatic secretory otitis media (SOM), demonstrates a favorable safety profile and an excellent tolerability.
- **Bactoblis®** exhibits a protective effect against acute otitis media (AOM) incidence, offering a preventive measure to reduce the recurrence in children suffering from this condition.
- **Bactoblis®** demonstrates impressive results in specific clinical outcomes and relevant features in children with secretory otitis media (SOM), particularly in terms of bilateral tone audiometry improvement.

Reference: Di Pierro et al 2015. Int J Gen Med

SACHET

Bactoblis®: A breath of Relief for Kids with Secretory Otitis Media

Secretory otitis media (SOM) is a common ENT condition in children, often linked to unresolved acute otitis media, post-viral rhinosinusitis, or adenoid hypertrophy. It results in persistent middle ear fluid, reduced auditory function, and various ear-related complaints.

The use of **Bactoblis®** plays a role in reducing the incidence and severity of SOM, which improves patient's quality of life.

Aim of the study:	To evaluate **Bactoblis®** effectiveness, safety, and tolerance in children with SOM, as well as its potential to prevent recurrent AOM and determine SOM regression using key indicators performance.
Study type:	Uncontrolled clinical study. The study was conducted on the basis of the Department of children's orohinolaryngology, audiology and phoniatrics of the Skupyk National Medical Academy of Postgraduate Education. (Ukraine)
Patients:	22 Children (**Before** and **after** treatment with **Bactoblis®**)
Subject description:	› Children aged 2-6 years old. › Children diagnosed with recurrent SOM, with an exudation in the middle ear for at least 3 months.
Method:	› **Pure-Tone Audiometry:** Using the MA-13 audiometer to analyze hearing thresholds from 250 to 8000 Hz, employing the bone path when necessary. The method was silent, and the threshold was defined as the lowest intensity where a child consistently responded to the sound. Average tonal thresholds at 250-2000 Hz for children were classified as normal (score=1; 16 to 70 dB), and decrease in diminishing hearing due to impaired sound transmission (score=2, over 71 dB). › **Tympanometry:** An otometrics tympanometer was used to assess the condition of the middle ear. The tympanogram was evaluated under three types of conditions: type A (normal condition); type B (presence of exudation in middle ear and type C (auditory tube dysfunction. › **Microostoscopy:** The data were classified according to four stages: normal eardrum (score=0); opaque eardrum (score=1); opaque and retracted eardrum (score=2); thickened eardrum with a fluid level (score=3). › **Endonasal endoscopy:** Performed using a straight or angular Karl Storz endoscope with inspection of the intra-nasal structures, the arch of the nasal part of the pharynx, the pharyngeal opening of auditory tube with eustachian cushions. › **Examination of palatine tonsils:** The volume of PT was classified according to the approved criteria as follows: PT are barely visible behind the anterior brace in the tonsil fossa (score=0); PT are visible on the front bracket (score=1); hypertrophied PT are located three-quarters of the way to the midline (score=2); PT totally complicate clear airway (score=3).
Treatment:	1 **Bactoblis®** sachet per day for 30 days.

Results

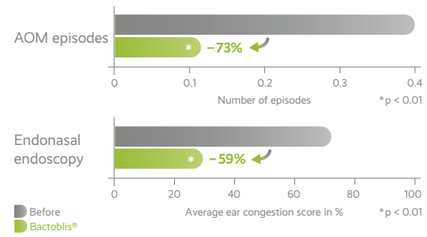
- **Bactoblis®** demonstrates a 73% reduction in AOM cases and a 59% decrease in endonasal endoscopies when compared to the previous year. (Figure 1)
- **Bactoblis®** proves a 65% improvement in otoscopic data of the eardrum and 60% decrease in ear congestion.
- **Bactoblis®** performs a significant improvement in tympanometry. Particularly, the presence of exudation in the middle ear, as indicated by T=30, only observed in only two cases on both sides. However, there were no significant differences regarding the impairment of auditory tube function.
- **Bactoblis®** shows exceptional tolerability with no side effects or patient dropout.

Bactoblis® is the leading oral probiotic for addressing recurrent respiratory infections and improving auditory function in children with Secretory Otitis Media resulting from middle ear exudation.

Clinical Evidence

Figure 1

Effective Reduction of AOM Episodes and Endonasal Endoscopy



Havrylenko 2019. Child's health

Conclusion

- **Bactoblis®** shows a protective effect by stimulating antibacterial immune mechanisms, leading to a reduction in AOM recurrence.
- **Bactoblis®** demonstrates a significant improvement in clinical symptoms in children suffering from SOM.
- **Bactoblis®** mantains a remarkable safety profile when addressing asymptomatic SOM.

Reference: Havrylenko 2019. Child's health

Bactoblis®: Efficacy and Tolerability in Acute Tonsillopharyngitis in Children

Acute tonsillopharyngitis (ATP) is a common infectious disease in children, comprising around 15% of acute respiratory illnesses. The excessive and irrational use of antibiotics has led to antibiotic resistance and associated complications. Consequently, there is a growing interest in exploring alternative medicines, such as bacteriocins, probiotic bacteria, and bacteriophages, as potential substitutes for antibiotics in ATP treatment. These alternatives offer promising solutions to combat antibiotic resistance while providing effective therapeutic options, such is the case of **Bactoblis®**.

Methods and Materials

Aim of the study:	To study the efficacy and tolerability of **Bactoblis®** in the treatment of acute tonsillopharyngitis in children.
Study type:	Open, randomized, controlled, post-registration clinical study conducted at the children infectious diseases hospital of Bogomolets National Medical University of children infectious diseases hospital. (Ukraine)
Patients:	50 children. (**Bactoblis® group:** 25 and **Control group:** 25)
Subject description:	› Children and teenagers aged 2-18 years old. › Children with acute streptoccocal tonsillopharyngitis
Method:	**Acute streptococcal tonsillopharyngitis:** Confirmed by rapid test for the detection of beta hemolytitic strep. of group A and the results of bacteriological seeding of a smear from the nasopharynx.
Treatment:	1 **Bactoblis®** lozenge per day for 10 days.

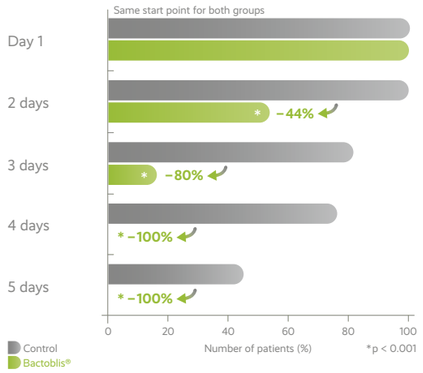
Results

- **Bactoblis®** shows a significant reduction in the average duration of sore throat (1.91 ± 0.65 days) in children suffering from acute tonsillopharyngitis, compared to the control group (4.21 ± 1.13 days). (Figure 1)
- **Bactoblis®** shows no adverse effects.

Clinical Evidence

Figure 1

Reducing Sore Throat Duration



Conclusion

- **Bactoblis®** is effective in the treatment of acute tonsillopharyngitis in children besides the well documented benefits in preventing the incidence of respiratory infections.
- **Bactoblis®** is safe and effective as a co-therapy with common antibiotics in children suffering from acute tonsillopharyngitis

Bactoblis® is effective in the treatment of acute tonsillopharyngitis in children

Reference: Kramarev et al 2020. Actual Infectology

Bactoblis®: Tonsillitis Management in Kids

Recurrent Tonsillitis (RT), a common condition in children, is characterized by persistent or frequently recurring inflammation of the palatine tonsils or adenoids. *Streptococcus pyogenes* is a primary bacterial culprit. Traditional treatment includes the use of antibiotics, but increasing antibiotic resistance is a significant concern. To address this challenge, emerging management options include the use of oral probiotics, particularly **Bactoblis®**, which naturally inhibits *S. pyogenes*.

Material and Methods

Aim of the study:	Evaluate the effectiveness of **Bactoblis®** in the complex treatment of children with Recurrent Tonsillitis.
Study type:	Open- label clinical study
Patients:	35 Children (**Bactoblis® group:** 20 and **Control group:** 15)
Subject description:	› Children aged 5-15 years old. › Children diagnosed with Recurrent Tonsillitis.
Method:	› **Streptococcal infections**: Using a "Streptatest", an immunochromatographic rapid test designed to detect group A beta-hemolytic Streptococcus antigens in throat swabs. › **Bacterial analysis of oropharyngeal biomaterial**: Testing conducted on all children, including species identification and antibiotic sensitivity. Microorganism significance determined by growth grades III (> 10^4 CFU/ml) or IV (10^5 CFU/ml) › The study includes data collection, medical history, exams, and lab tests (blood, urine, throat swab for diphtheria)
Treatment:	1 **Bactoblis®** lozenge per day for 90 days.

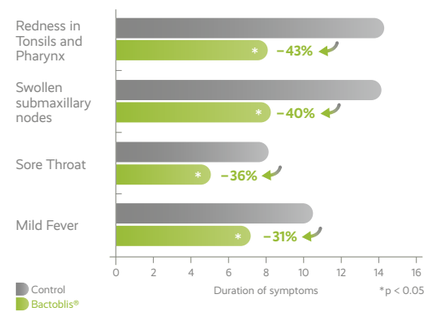
Results

- **Bactoblis®** effectively mitigates recurrent tonsillitis symptoms, addressing both local (tonsil swelling and redness) and general (subfrebrile condition, submandibular cervical lymph node enlargement, and tenderness). (Figure 1)
- In children with recurrent tonsillitis (RT), *S. pyogenes* was present in all cases, and *S. aureus* in 60%.
- Sensitivity tests found both *S. pyogenes* and *S. aureus* to be highly resistant to penicillin (100% and 61%, respectively) and oxacillin (66% and 57%, respectively).
- **Bactoblis®** significantly improve the upper respiratory microbiome, reducing colonization by *S. pyogenes* and *S. aureus* within the first 7-days, which persisted for the entire month.

Clinical Evidence

Figure 1

Reduction of Recurrent Tonsillitis Symptoms



Conclusion

- **Bactoblis®**, when used as an add-on therapy to standard treatment for recurrent tonsillitis, leads to a significantly reduction in both the duration and severity of symptoms, along with objective changes in the mucous membranes of the respiratory tract and regional lymph nodes.
- **Bactoblis®** improves the respiratory tract microbiome and reduces the need of antibiotics, thus preventing antibiotic resistance.
- **Bactoblis®** is safe and effective for recurrent tonsillitis treatment in children.

Reference: Ilchenko et al 2020. Actual Infectology

LOZENGE

Bactoblis®: Prevents ENT Infections and Shortens Antibiotic Use

Pharyngo-tonsillitis is commonly diagnosed in children, and a significant number of cases are attributed to both bacterial and viral infections. **Bactoblis®** colonizes the oral cavity & the throat, releases salivaricins to combat pathogens, and demonstrates modulations that decrease IL-8 levels while boosting salivery interferon–γ. These actions indicate possible antiviral and antibacterial properties.

Material and Methods

Aim of the study:	**Bactoblis®** prevention of bacterial and viral pharyngo-tonsillar infections.
Study type:	Multicenter, open, randomized, controlled clinical study. Conducted according to the criteria set by the Declaration of Helsinki and with the approval of the local ethics committee. (Italy)
Patients:	61 Children. (**Bactoblis® group:** 31 and **Control group:** 30)
Subject description:	› Children aged 3-13 years old. › Children who had experienced recurrent pharyngotonsillitis with an average of at least three episodes during the corresponding quarter of the previous year.
Method:	**Bacterial infections:** were diagnosed through a positive rapid swab test for group A and group B streptococci. **Viral infections**: were determined based on the following criteria: negative rapid swab for streptococci, no submandibular lymphadenopathy, no petechiae on the palate, mild dysphagia, no headache, no abdominal pain, and no hyperpyrexia.
Treatment:	1 **Bactoblis®** lozenge per day for 90 days.

Results

- **Bactoblis®** achieves an outstanding 97% reduction in bacterial infections, surpassing the infection rates observed in the previous year. (Figure 1)
- **Bactoblis®** demonstrates an impressive 80% decrease in the incidence of viral infections. (Figure 2)
- **Bactoblis®** exhibits a significant reduction in the use of antibiotics and antipyretics. (Figure 3)
- **Bactoblis®** results in a noteworthy decrease in absences from both school and work.

Clinical Evidence

Figure 1

Less Bacterial Infections

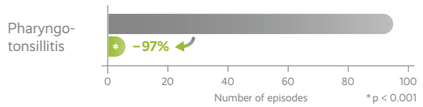


Figure 2

Less Viral Infections

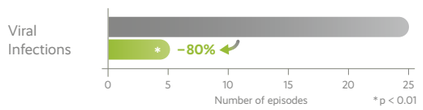
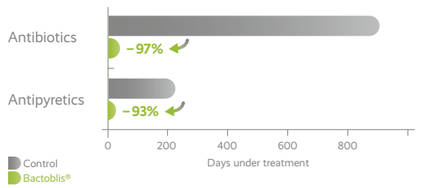


Figure 3

Reduction in the Use of Antibiotics and Antipyretics



Conclusion

- **Bactoblis®** demonstrates a significant reduction in the frequency of both bacterial and viral infections. Highlighting its potential as an effective preventive measure against both types of infections.
- **Bactoblis®** leads to a decreased dependency on antibiotic and antipyretic therapies. Serving as an alternative or add-on to standard therapy and reducing the risk associated with antibiotic overuse.
- **Bactoblis®** results in less absences both from school and work.

Reference: Di Pierro et al 2014. Drug, healthc and patient saf

LOZENGE

Bactoblis®: Protecting Kids During Cold Season

Oropharyngel microbiome is a protective environment against respiratory infections, and it is essential for the overall health. Oral colonization by pathogens contributes to recurrent respiratory infections, especially in children, who have still an immature immune system. Factors like asthma, allergies, and early antibiotic use increase the risk of suffering from these types of infections. **Bactoblis®** shows a significant role against respiratory infections, both from bacterial and viral origin.

Material and Methods

Aim of the study:	Prove **Bactoblis®** clinical efficacy and safety as an alternative during acute respiratory infections among children with a history of recurrent respiratory infections during cold season.
Study type:	Single-center, open, randomized and controlled clinical study. The study was conducted according to the criteria set by the Declaration of Helsinki and with the approval of the local ethics committee. (China)
Patients:	100 children (**Bactoblis® group:** 47 and **Control group:** 50) 3 patients drop the study before it ended.
Subject description:	› Children aged 3-10 years old › Children attending to school › Children who experienced 3 or more episodes of respiratory infections in the previous year
Method:	During the entire study period if any symptoms or respiratory infections were present, the children must be taken to the hospital for further examination and medical treatment prescribed if needed; if there was evidence of respiratory infections, the children in both groups were asked to record the variety and duration of drug treatment and continue complementarily taking **Bactoblis®** throught the study period.
Treatment:	1 **Bactoblis®** lozenge per 30 days.

Results

- **Bactoblis®** proves a 56% reduction in respiratory symptoms. (Figure 1)
- **Bactoblis®** shortens the days of antibiotic use by 97% and antipyretics by 100%. (Figure 2)
- **Bactoblis®** reduces by 68% the onset duration of respiratory symptoms.
- **Bactoblis®** as an add on therapy to standard medication demonstrates a 27% reduction in the average duration of each respiratory episode.
- **Bactoblis®** lowers the absent days from school by 80% and from work by 97%

Reference: Guo et al 2022. Frontiers

Clinical Evidence

Figure 1

Reduction of Respiratory Infections

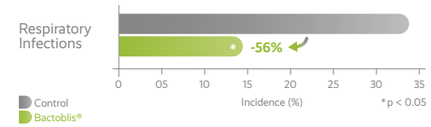
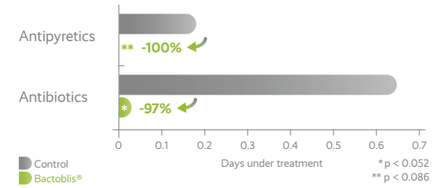


Figure 2

Less Absence From School



Conclusion

- **Bactoblis®** reduces recurrent respiratory infections in children attending school, particularly during the cold season. As an add-on therapy to standard treatments, it shortens symptoms severity and duration, decreases the use of antibiotics and antipyretics, and absence from school.
- **Bactoblis®** is a good alternative to standard therapy, promoting the increase of protective microbiome and preventing the intrusion of respiratory pathogens into children's body.

LOZENGE

Bactoblis®: A Powerful Defense Against Adeno-Tonsillectomies

Acute pharyngo-tonsillitis is a common condition in children, often treated with antibiotics. However, when traditional treatment fails, surgery becomes necessary. Research has revealed the efficacy of **Bactoblis®**, in preventing such infections. This alternative therapy reduces antibiotic use, improves quality of life, lowers school absences, and minimizes the need for surgery.

Methods and Materials

Aim of the study:	› Evaluate the preventive role of **Bactoblis®** in reducing the recurrence rate of pharyngo-tonsillar episodes and the concomitant use of other drugs. › Evaluate the tolerability of **Bactoblis®**, the effectiveness in terms of clinical improvement, days of absence from school, reduction of the use of standard therapies, and cancellation from the surgical planning list.
Study type:	Prospective, randomized, open, and monocentric clinical study. (Italy)
Patients:	100 children. (**Bactoblis® group:** 50 and **Control group:** 50)
Subject description:	› Children aged 5-10 years old. › Children diagnosed with chronic tonsillitis › Children enrolled in the surgical planning list for adenotonsillectomy since 2014
Method:	**Chronic tonsillitis:** Diagnosed by GAS and confirmed by clinical exam by one of the study authors.
Treatment:	1 **Bactoblis®** lozenge per day for 90 days.

Results

- **Bactoblis®** results in a 64% reduction of pharyngo-tonsillar infections. (Figure 1)
- **Bactoblis®** leads to a significant decrease of 82% in antibiotic use and a 54% reduction in the use of antipyretics. (Figure 2)
- **Bactoblis®** shows a 72% decrease in the number of children requiring surgery. (Figure 3)
- **Bactoblis®** exhibits a notable decrease of 54% in the number of absence days from school per child.

Clinical Evidence

Figure 1

Reduction in Pharyngo-Tonsillar Infections

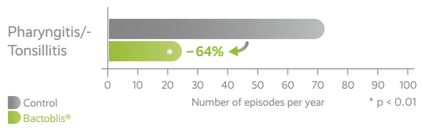


Figure 2

Decrease in Antibiotic and Antipyretic Consumption

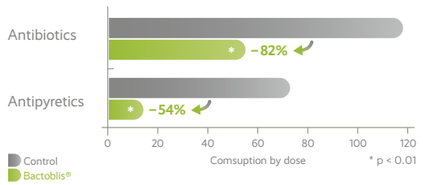
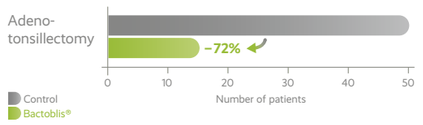


Figure 3

An Alternative to Surgical Intervention



Conclusion

- **Bactoblis®** is efficacious to protect against chronic tonsillitis caused by group A streptococcal (GAS) infections.
- **Bactoblis®** shows a significant decline in antibiotic and antipyretic use, showing important benefits as a preventive treatment.
- **Bactoblis®** significantly reduces the number of children requiring adeno-tonsillectomy, highlighting its potential in minimizing the need for surgical interventions.

Reference: Marini et al 2019. Int J Gen Med

LOZENGE

Bactoblis®: Reveals Protection Against Throat Infections

In the majority of the cases, acute otitis media is attributed to the growth of *Streptococcus pyogenes*; however, it can also be associated with viral pathogens. In such cases, **Bactoblis®** demonstrates potential efectiveness in preventing such infections and acute otitis media episodes.

Materials and Methods

Aim of the study:	Evaluate the role of **Bactoblis®** in the control of pediatric streptococcal disease and its potential to help against viral infections.
Study type:	Multicenter, open, nonrandomized, controlled clinical study. The study was conducted according to the criteria set by the Declaration of Helsinki and with the approval of the Local Ethics Committee. (Italy)
Patients:	124 children (**Bactoblis® group:** 48 and **Control group:** 76).
Subject description:	› Children aged 3-10 years old. › Children attending preschool or school. › Children with a history of recurrent streptococcal pharyngotonsillitis with an average of >3 episodes in the previous year (2013).
Method:	› **Recurrent streptococcal pharyngotonsillitis:** confirmed by a rapid swab positive for Group A streptococcus. › **Streptococcal throat infections:** confirmed by standardized clinical & microbiological assessment, acute otitis media confirmed by pneumatic otoscopy and viral infections confirmed by standardized clinical assessment.
Treatment:	1 **Bactoblis®** lozenge per day for 90 days.

Results

- **Bactoblis®** shows a remarkable 90% reduction in recurrent throat infections. (Figure 1)
- **Bactoblis®** demonstrates a significant reduction in common viral infections such as viral pharyngitis, rhinitis, and the flu. (Figure 2)
- **Bactoblis®** shows a reduction in the incidence of acute otitis media episodes.
- **Bactoblis®** is highly accepted by children, with no dropouts reported.

Clinical Evidence

Figure 1

Less Recurrent Throat Infections

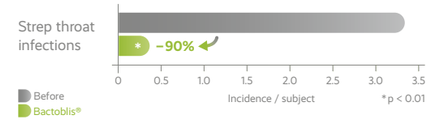
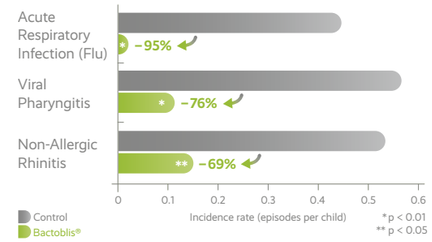


Figure 2

Reduction of Viral Infections



Conclusion

- **Bactoblis®** demonstrates protection from recurrent throat infections and acute otitis media.
- **Bactoblis®** exhibits a reduction in the incidence of common viral infections.

Bactoblis® is safe and effective for recurrent respiratory infections and microbial dysequilibria.

Reference: Di Pierro et al 2016a. Drug, Healthc, Patient Saf

Bactoblis®: Reduces SARS-CoV-2 Infections in Children Attending School

LOZENGE

The prevalence of SARS-CoV-2 and the associated disease COVID-19, stands as a notable challenge to public health. The oral cavity serves as the virus's primary entry point, and research highlights the vital role of oral and lung microbiome in SARS-CoV-2 infections.

COVID-19 patients display distinct oral bacteria and inflammatory profiles. Moreover, the oral cavity appears to be the primary source of lung microbiome community, acquired via aspiration and inhalation. Alterations in lung microbiome have been noted between SARS-CoV-2 patients and healthy subjects. This connection emphasizes the link between oral health and susceptibility to respiratory infections, offering insights for improved COVID-19 prevention and management.

Methods and Materials

Aim of the study:	To investigate the efficacy of **Bactoblis®** in reducing the risk of SARS-CoV-2 Infections and COVID-19.
Study type:	Randomized, controlled clinical study. (Italy)
Patients:	128 Children (**Bactoblis® group:** 64, **Control group:** 64)
Subject description:	› Children aged 7-8 years old. › Children attending to school experiencing COVID-19 symptoms and/or in contact with COVID-19 positive family members or classmates.
Method:	**SARS-CoV-2:** confirmed by specific antigen nasal swab.
Treatment:	1 **Bactoblis®** lozenge per day for 90 days

Results

- **Bactoblis®** leads to a full reduction of positive SARS-CoV-2 antigen tests. (Figure 1)
- **Bactoblis®** proves a significant decrease in COVID-19 symptoms (e.g. fever, headache and coughing). (Figure 2)
- **Bactoblis®** demonstrates an exceptional acceptance and tolerability.

Clinical Evidence

Figure 1

Reduction of SARS-CoV-2 Infections

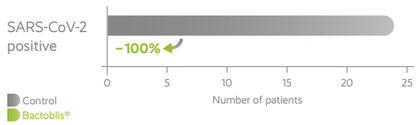
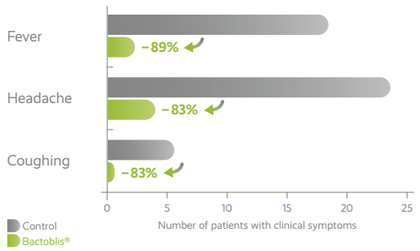


Figure 2

Alleviation of COVID-19 Symptoms



Conclusion

- **Bactoblis®** proves to effectively reduce SARS-CoV-2 infections in children.
- **Bactoblis®** could potentially provide protection against COVID-19 for children returning to school or daycare and those in high-risk environments such as traveling.

Reference: Di Pierro et al 2021. Minerva Med

Bactoblis®: Safety and Efficacy in Children with PFAPA Syndrome

PFAPA syndrome, characterized by periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis, predominantly affects young children. The recurrent flares of symptoms, occurring every 2-8 weeks, have a significant impact on children's quality of life, including lower physical, emotional, and psychosocial functioning, as well as compromised school performance. While current treatment involves glucocorticoids, there is increasing interest in exploring the potential of prophylactic **Bactoblis®** administration to counteract oral cavity-related pathogenesis associated with PFAPA syndrome.

Methods and Materials

Aim of the study:	To evaluate **Bactoblis®** efficacy on the recurrence of PFAPA febrile flares assessing any statistically signficant difference between the number of PFAPA flares in the 12-months before treatment and the last follow-up visit.
Study type:	Multicenter clinical study approved by the ethics committee of Siena University. Retrospective and prospective examination of medical records (Italy).
Patients:	85 Children with PFAPA syndrome. (**Before** and **after** treatment with **Bactoblis®**)
Subject description:	› Children median age 4.58 years old. › Children with PFAPA condition listed on the AIDA International registry.
Method:	**PFAPA syndrome:** Diagnosed according to Marshall criteria.
Treatment:	1 **Bactoblis®** lozenge per day for 90 days

Results

- **Bactoblis®** performs an 85% reduction in the total number of flares observed in the patients. (Figure 1)
- **Bactoblis®** shows a significant decrease in the number of patients experiencing PFAPA symptoms. (Figure 2)
- **Bactoblis®** leads to a significant decrease in the annual number of febrile flares, reducing it from a median of 13.0 in the 12 months prior treatment to 5.5 during the subsequent 12 months after.
- **Bactoblis®** results in a significant decrease in the duration of fever episodes during flares, reducing it from a median of 4 days to 2 days.
- **Bactoblis®** reports no side effects.

Clinical Evidence

Figure 1

Significant Decrease in Total Number of Febrile Flares

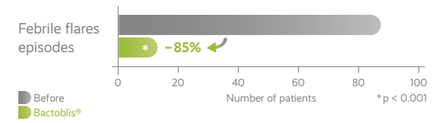
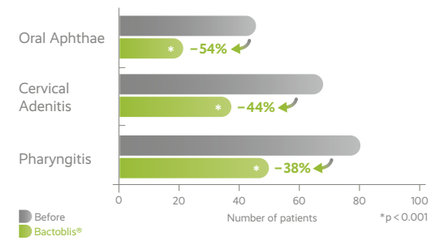


Figure 2

Reduction of PFAPA Symptoms in Affected Patients



Conclusion

- **Bactoblis®** proves to be a safe and effective solution for managing PFAPA syndrome.
- **Bactoblis®** reduces not only the number of PFAPA flares, but also the duration and accompanying symptoms

Reference: La Torre et al 2023. Frontiers in Medicine

SACHET

Bactoblis®: Potential in Children with Microaspiration Syndrome

The mucous membrane in the upper respiratory airway plays a vital role as the body's frontline defense against pathogens and environmental threats. Its defense mechanisms include colonization resistance, where indigenous microorganisms prevent pathogen adhesion, and the synthesis of protective substances. Changes in microbial communities within the respiratory tract can significantly affect children's overall health. Children with microaspiration syndrome are frequently linked to central nervous system issues and face an increased risk of recurrent respiratory infections. **Bactoblis®** has the potential to prevent these infections by outcompeting pathogens and producing antibacterial compounds.

Methods and Materials

Aim of the study:	Investigate the efficacy of **Bactoblis®** for prevention of recurrent respiratory infections in children with microaspiration syndrome.
Study type:	Open-label clinical study
Patients:	46 Children (**Before** and **after** treatment with **Bactoblis®**)
Subject description:	› Children aged 6 months - 7 years old › Children with recurrent respiratory issues due to microaspiration syndrome › Children aged over 6-months who have a medical history of regurgitation syndrome or are currently experiencing it
Method:	**Rumination syndrome:** Diagnosed using a five-point scale recommended by ESPGHAN experts. **Microaspiration:** Diagnosed by using clinical and anamnestic criteria, as well as lab-based instrumental methods (including sputum cytology, fibroesophagealgastroscopy) **Streptococcal infection:** Diagnosed by using the rapid test Streptatest and immunochromatographic analysis.
Treatment:	1 **Bactoblis®** sachet per day for 30 days (2 courses)

Results

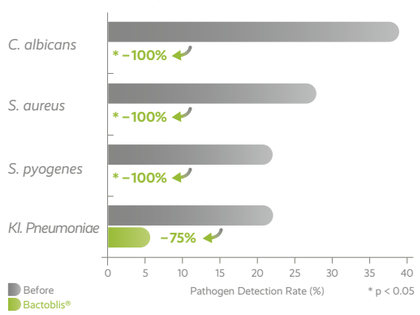
- **Bactoblis®** has a positive effect on the oral microbiome and eliminates colonization of harmful bacteria in children experiencing microaspiration syndrome, such as *C. albicans*, *S.aureus* and *S. pyogenes*, and also reduces the tendency of Kl. pneumoniae. (Figure 1)
- **Bactoblis®** reduces recurrent respiratory infections incidence by 1.6 times (from 3.9 ±1.2 to 2.4±1.1 episodes per year), and illness duration by 1.5 times (from 1.5±0.1 months to 1.0±0.5 months) in children.
- **Bactoblis®** reports no side effects.

Reference: Ilchenko 2019. Pediatrics

Clinical Evidence

Figure 1

Eradication of Key Pathogens in Microaspiration Syndrome



Conclusion

- **Bactoblis®** proves to be a highly efficacious treatment in children with clinically confirmed microaspiration syndrome, by preventing recurrent respiratory infections and reducing antibiotic use, offering potential benefits in managing these specific patients.
- **Bactoblis®** may also benefit young children with rumination syndrome, who are at risk for microaspiration syndrome and recurrent respiratory infections, given its long-lasting presence after oral administration. This approach is rational and justified for maintaining a healthy microbiome in the URA (upper respiratory airway) mucous membranes.

Other Benefits from Bactoblis®

Oral Colonization

The effect of oral probiotics (streptococcus salivarius K12) on the salivary level of secretory immunoglobulin A, salivation rate and oral biofilm: A pilot randomized clinical trial. Babina et al 2022.

Respiratory Infections in Adults

Clinical evaluation of the oral probiotic *Streptococcus salivarius* K12 in the prevention of recurrent pharyngitis and/or tonsillitis caused by streptococcus pyogenes in adults. Di Pierro et al 2013.

Optional location therapy of chronic tonsillopharyngitis to achieve long-term remission. Bezshapochny et al 2020.

Experience with the use of oral probiotic streptococcus salivarius K12 for the prevention of recurrence of pharyngotonsillar episodes. Puhlik et al 2021.

Oropharyngeal probiotic prevents respiratory tract infections among frontline medical staff fighting against covid-19: A pilot study. Wang et al 2021.

Possibilities of probiotic therapy in chronic inflammatory diseases of oropharynx. Ovchinnikov et al 2022.

Clinical effects of streptococcus salivarius K12 in hospitalized COVID-19 patients: results of preliminary study. Di Pierro et al 2022./

Use of streptococcus salivarius K12 in supporting the mucosal immune function of active young subjects: A randomised double blind study. Bertuccioli et al 2023.

Oral Cavity Dysbiosis

Criteria for choosing the method of correction of disbacteriosis of authorities oral cavity. Karakov et al 2020.

Halitosis

Correction of Halitosis in chronic inflammatory diseases of the oropharynx in adult. Saulevich et al 2021.

Psoriasis

Improvement of Psoriasis using oral probiotic streptococcus salivarius K12: a case-control 24-month longitudinal study. Zangrilli et al 2022.

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