RMMG
Revista Médica de Minas Gerais

REVIEW ARTICLE

Evidence on the use of beta-glucans in the prevention and reduction of respiratory infections in the pediatric population: a systematic review

Evidências sobre o uso de beta-glucanas na prevenção e redução de infecções respiratórias na população pediátrica: uma revisão sistemática

Caroline Nunes dos Santos[1], Kevin Gustavo dos Santos Silva[1], Maria Ilisi Monteiro[1], Daniela de Melo Amaral[2], Vitoria Monteiro da Luz Camargo[2], Gabriela Tassara Rodrigues Correia[2], Maria Olívia Stanislau Affonso de Araújo[1,2], Carlos Rocha Oliveira[1]

ABSTRACT

Introduction: Acute respiratory infections are among the leading causes of childhood morbidity and mortality, imposing economic and social burdens. Beta-glucans, natural polysaccharides, have shown immunomodulatory properties, potentially beneficial in pediatric populations. **Objective:** To assess the efficacy of beta-glucans in preventing and reducing upper respiratory tract infections in the pediatric population. **Methods:** A systematic review and meta-analysis was carried out using data from the PubMed, Google Scholar, SciELO, Embase, and Cochrane Library databases with descriptors defined in the Medical Subject Headings (MeSH). No language or publication date restrictions were applied, provided that the studies fulfilled the predefined eligibility criteria. A random-effects model meta-analysis was applied to assess heterogeneity and pooled effects. IgA, IgG, IgM, and other biological markers were used as treatment indicators. **Results and Discussion:** Seven studies met eligibility criteria, showing a potential reduction in infection incidence, symptom duration, and medication use in beta-glucan-supplemented groups. However, the meta-analysis revealed high heterogeneity (I^2 = 99.59%), complicating definitive conclusions. Despite these limitations, significant differences were noted (p<0.001), favoring the intervention group. The findings underscore the need for well-designed, large-scale trials to elucidate the benefits of beta-glucans, particularly regarding biological markers like IgA and IgG. **Conclusions:** Due to high heterogeneity, the meta-analysis did not establish conclusive efficacy. Although a potential benefit is suggested, current evidence does not support widespread clinical use. Further standardized clinical trials are necessary to confirm the findings and determine optimal use.

Keywords: Beta-glucans; Children; Respiratory infections; Imunomodulation; Prevention.

[1] Universidade Anhembi Morumbi, Faculdade de Medicina, São José dos Campos, São Paulo, Brazil.

[2] Hospital Municipal Dr. José de Carvalho Florence, Departamento de Pediatria, São José dos Campos, São Paulo, Brazil.

Associate Editor Responsible:
Gabriela Araujo Costa
Faculdade de Medicina da Pontifícia Universidade Católica de Minas Gerais.
Belo Horizonte/MG, Brazil.

Corresponding author:
Carlos Rocha Oliveira
Universidade Anhembi Morumbi, Faculdade de Medicina, São Paulo, Brazil.
Email: carlos.rocha@unifesp.br

Supporting sources:
None.

Conflicts of interest:
None.

Received on: May 16, 2025.
Approved on: March 22, 2026.
Publication Date: June 29, 2026.

DOI: 10.5935/2238-3182.2025e36206-en

RESUMO

Introdução: As infecções respiratórias agudas são uma das principais causas de morbidade e mortalidade infantil, com impactos econômicos e sociais significativos. As beta-glucanas, polissacarídeos naturais, têm demonstrado propriedades imunomoduladoras, sendo possivelmente benéficas na população pediátrica. **Objetivo:** Avaliar a eficácia das beta-glucanas na prevenção e redução de infecções respiratórias de vias aéreas superiores em crianças. **Métodos:** Foi realizada uma revisão sistemática e meta-análise utilizando dados das bases PubMed, Google Scholar, SciELO, Embase e Cochrane Library com descritores definidos no *Medical Subject Headings* (MeSH). Como critérios de inclusão, não houve restrição de idioma ou de data de publicação, desde que o estudo atendesse aos critérios de elegibilidade descritos. Aplicou-se um modelo de efeitos aleatórios para avaliar a heterogeneidade e os efeitos combinados. Marcadores biológicos, como IgA, IgG e IgM, foram considerados indicadores do tratamento. **Resultados e Discussão:** Sete estudos atenderam aos critérios de elegibilidade, demonstrando possível redução na incidência de infecções, duração dos sintomas e uso de medicamentos nos grupos suplementados com beta-glucanas. Contudo, a meta-análise revelou alta heterogeneidade (I^2 = 99,59%), dificultando conclusões definitivas. Apesar disso, observaram-se diferenças significativas (p<0,001) a favor do grupo intervenção. Os achados reforçam a necessidade de ensaios bem delineados e de maior escala para elucidar os benefícios das beta-glucanas, principalmente em relação a marcadores biológicos como IgA e IgG. **Conclusões:** Devido à alta heterogeneidade, a meta-análise não estabeleceu eficácia conclusiva. Embora um benefício em potencial seja sugerido, a evidência atual não apoia o uso clínico generalizado. Estudos clínicos padronizados adicionais são necessários para confirmar os achados e determinar o uso ideal.

Palavras-chave: Beta-glucans; Children; Respiratory infections; Immunomodulation; Prevention.

Introduction

Acute respiratory infections (ARIs) are common childhood illnesses and represent the leading cause of morbidity, hospitalization, and death in children, in addition to causing economic losses for families and society[1-3]. ARIs are also among the most common reasons for medical office visits[4]. Studies show that, with increasing age, the incidence of respiratory infections decreases; however, at specific ages, such as preschool years, or in certain groups, such as patients with chronic diseases, those undergoing immunosuppressive therapy, and athletes, their frequency increases[5].

Viruses are the main infectious agents of ARIs[6], including respiratory syncytial virus (RSV), rhinovirus, metapneumovirus, parainfluenza virus, enterovirus, influenza virus (FLU), coronavirus, adenovirus (ADV), and human bocavirus, accounting for approximately 70% of ARI cases[2]. Conventional treatment includes supportive care to improve airway patency, oxygen supplementation, and adequate hydration[7]. Several studies have investigated neuraminidase inhibitors and newer antiviral agents, including polymerase inhibitors, demonstrating promising outcomes in the treatment of these infections among adults, children, and high-risk populations[8].

Recurrent respiratory infections (RRIs), in turn, are defined as at least six to eight episodes per year, affecting 15% to 20% of children under five years of age[9]. The incidence of RRIs has increased in recent years due to deterioration caused by environmental pollution and lifestyle changes, such as early socialization of children[10]. An alternative approach has been investigated for the prevention and treatment of RRIs, one of which is the use of beta-glucans,

biologically active polysaccharides. Beta-glucans, found in various natural sources, have immune properties and effects influenced by their origin.

Yeast-derived beta-glucans, especially β-1,3/1,6-glucans, have been extensively investigated for their immunomodulatory potential[11]. These polysaccharides primarily exert their effects through the activation of neutrophils and macrophages, thereby promoting a more robust and effective immune response[12]. Several beta-glucans from different origins have demonstrated interesting biological activities, including anti-inflammatory and immunomodulatory properties13. Its immunomodulatory mechanism of action is mainly linked to the interaction with specific receptors on innate immune system cells, such as Dectin-1 receptors on macrophages and neutrophils, promoting phagocytosis, the modulation of cytokine release, and a more efficient immune response. Given the scarcity of studies on the topic, this study aimed to conduct a systematic review to assess the effect of beta-glucan on viral upper respiratory tract infections in the pediatric population.

Methods

The protocol for this systematic review was prospectively registered in the international database PROSPERO under the registration number CRD4202341176090. The search strategy was developed by a specialized librarian (or by the researchers) using the PICO framework. The complete example of the strategy for PubMed/MEDLINE is presented below, using Boolean operators (AND, OR) and truncation (*): ("Beta-Glucans"[MeSH Terms] OR "beta-glucan"[Title/Abstract]) AND ("Respiratory Tract Infections"[MeSH Terms] OR "Upper Respiratory Tract Infections"[MeSH Terms] OR "respiratory infection"[Title/Abstract] OR "URTI"[Title/Abstract]) AND ("Child"[MeSH Terms] OR "pediatric"[Title/Abstract] OR "child"[Title/Abstract] OR "infant"[Title/Abstract]) AND ("Clinical Trial"[Publication Type] OR "randomized controlled trial"[Publication Type] OR "RCT"[Title/Abstract]).

Similar strategies, adapted to the syntax of each database, were applied to the other sources (Embase, Cochrane etc.). No date or language filters were applied in the initial search to maximize the retrieval of relevant studies. An additional search was performed using Google Scholar, along with manual screening of the reference lists of the studies included, to identify potentially relevant publications.

Assessment of Risk of Bias in the Studies Included

The methodological quality and risk of bias of the studies included were independently assessed by two reviewers, using tools appropriate for each study design. For randomized controlled trials, the Cochrane RoB 2 tool was used. For prospective observational studies, the ROBINS-I (Risk Of Bias In Non-randomized Studies - of Interventions) tool was employed. Disagreements were resolved by consensus or by a third reviewer. The results of this assessment are summarized narratively in the discussion. The research question was formulated based on the PICO strategy, which encompasses Population, Intervention, Comparison, and Outcome. The structure of the question was as follows: P (pediatric population), I (use of beta-glucan during episodes of upper respiratory tract infections), C (control group using other therapies or placebo), and O (outcomes related to clinical response).

Inclusion criteria comprised published clinical trials with no restriction on language or publication date, evaluating the efficacy of beta-glucan in the treatment of viral upper respiratory tract infections in children under 12 years of age. The outcomes analyzed included: shorter symptom duration, decreased frequency of infections, and reduction of complications and hospitalizations.

The initial search yielded 320 articles. Studies including newborns, patients with comorbidities or previous immunocompromise, non-viral infections, or those not meeting the inclusion criteria were excluded. After this screening, 10 relevant articles remained. Of these, 7 were selected for data extraction, but 2 were excluded for addressing only laboratory criteria and 1 for being a duplicate of another study already included. The methodological quality, specifically the risk of bias, of the randomized clinical trials included in the review was assessed using the JADAD scale. As this was a systematic review, submission to and approval by a Research Ethics Committee was not required. To identify studies in the databases and registries, the PRISMA (2020) methodology was used, as shown in Figure 1.

For the meta-analysis, a random-effects model was used to account for heterogeneity among the different clinical trials. The analysis was stratified based on group type (test and control). The effects of treatment progression were analyzed using a forest plot, stratified by each clinical trial, to better visualize the variation among studies. As treatment markers, the quantifications of Immunoglobulin A (IgA), Immunoglobulin G (IgG), Immunoglobulin M (IgM) and other biological parameters were observed. Statistical inferences were evaluated using a two-tailed Z-test, with degrees of freedom of k-1 (where k is the number of studies), to test the null hypothesis that the summary effect equals zero. Additionally, a correlation map was generated between the effects evaluated at baseline and final points for the test and control groups. Analyses were conducted using the Python language, employing the scipy and statsmodels libraries for statistical analysis and seaborn for graphical construction.

Results

The studies included were conducted in Italy (n = 1), Poland (n = 2), Canada (n = 1), China (n = 1), Spain (n = 1), and Slovakia (n = 1). Six studies were published in English and one in Spanish. The analyzed articles highlighted the action of beta-glucan in the treatment of upper respiratory tract infections in children under 12 years old, starting from 2012. However, the highest concentration of articles was between 2012 and 2016.

In the randomized placebo-controlled trials, a statistically significant reduction in the incidence of respiratory infections was observed in the beta-glucan-supplemented groups compared with placebo (p<0.05). In one of the trials, the frequency of upper respiratory tract infections was significantly lower in the intervention group (0.20 ± 0.55 *vs.* 0.42 ± 0.78; p<0.05). Significant reductions were also reported for specific symptoms, such as sore throat and myalgia (p<0.05), as well as decreased use of β2-agonists, inhaled corticosteroids, and antibiotics (p<0.05).

In the prospective studies, when comparing the supplementation period with the same period of the previous year, a significant reduction was observed in the number of respiratory infections (7.07 ± 2.89 *vs.* 3.87 ± 3.19; p<0.001), emergency department visits (48.6% *vs.* 71.1%; p<0.001), and school absenteeism (19.3 *vs.* 31.8 days; p<0.01).

The main methodological characteristics and evaluated outcomes of the included studies are detailed in Table 1.

It was observed that most studies involved children up to 12 years old, with age, sex, and health condition being specified. The studies assessed children with a history of recurrent respiratory infections, with the lower and upper age limits varying across studies. There were no populations under 1 year old or over 12 years old.

Regarding the incidence of respiratory infections, it was noted that in the placebo-controlled studies, there was a significant decrease in these infections in the control groups (which received beta-glucan) compared to the placebo groups. In the prospective studies, a positive effect of beta-glucan was also observed, as there was a decrease in respiratory infections during the supplementation period when compared to the same period in the previous year, when the populations did not receive the supplement. In three studies, which analyzed the use of medications such as beta-2 agonists, antibiotics, and symptomatic treatments, there was a reduction in the use of these medications in the beta-glucan-supplemented groups compared to the non-supplemented groups. In two studies, a reduction in the duration of respiratory infection symptoms was observed in the supplemented groups. In one of the studies, it was noted, regarding the frequency of specific types of respiratory tract infections, that there was a reduction in otitis media, laryngitis, bronchitis, and the common cold during the supplementation period with beta-glucan, compared to the same period in the previous year when no supplementation was administered. In this same study, no significant reduction in the incidence of pneumonia and tonsillitis was observed.

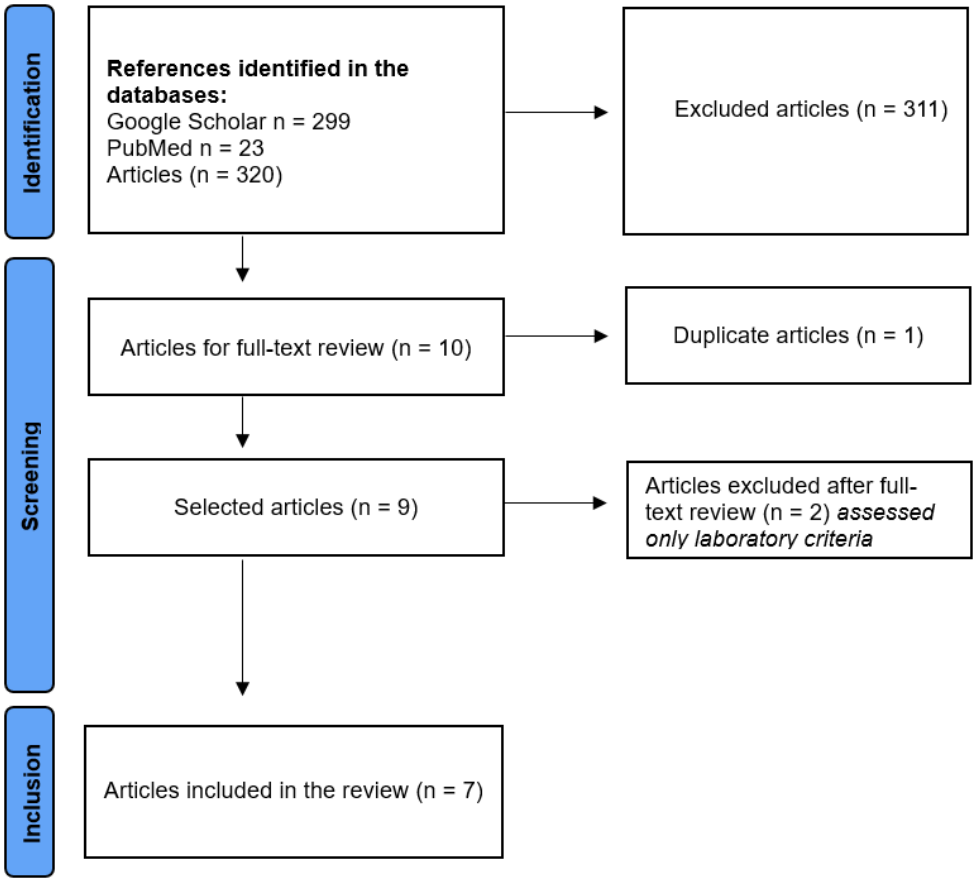

Figure 1. Flowchart of the search process.

Source: Elaborated by authors.

The meta-analysis produced inconclusive statistical evaluations concerning the study's objectives, highlighting the difficulty in interpreting the results based on these approaches. No significant effects were identified based on the I^2 analysis. To assess the heterogeneity among the studies, Cochran's Q test was performed. The result indicated a Q statistic value of 1961.494, and the I^2 index was calculated to be 99.59%. These values demonstrate a high heterogeneity among the studies included in the meta-analysis, suggesting significant variations between individual study results and reinforcing the need to interpret the findings with caution, as well as highlighting the need for greater uniformity in future studies.

Finally, the subgroup analysis indicated that children aged 1 to 4 years, supplemented with beta-glucans of fungal origin, showed greater consistency in the outcomes of reduced respiratory infections (I^2 = 75%). These results suggest that the heterogeneity may be partially explained by the diversity in study methods.

Discussion

Upper respiratory tract infections are one of the leading causes of pediatric visits worldwide. These infections generate significant morbidity, especially among vulnerable populations, such as young children. These infections are primarily managed symptomatically, with antibiotics reserved for bacterial complications. However, the high rate of antimicrobial use in children is concerning, given its potential impact on bacterial resistance and infant microbiota. In this context, finding alternatives that strengthen the immune system and reduce the frequency and severity of respiratory infections is a priority in pediatric medicine.

Beta-glucans, natural substances found in fungi, yeasts, and cereals, have gained attention due to their potential immunomodulatory properties. Studies included in this systematic review provide evidence that beta-glucan supplementation may contribute to reducing the frequency and severity of respiratory infections in children. The reduction in symptoms and infection duration observed in groups that used beta-glucan suggests a potential role in modulating the innate immune response, which may prevent the viral infections from progressing to bacterial complications (Figure 2).

Despite the promising results, this review has important limitations that must be considered. The number of included studies is small, and the methodological heterogeneity among them, especially regarding the source and dose of beta-glucans, outcomes definitions, and the populations studied, was extremely high (I^2=99.59%), which prevents definitive and generalizable conclusions. Additionally, some studies may present a risk of bias, particularly those with open-label prospective designs, and the potential for conflict of interest due to industry funding in part of the literature cannot be ruled out. Therefore, the interpretation of the findings must be made with caution.

Table 1. Characteristics of the studies included in the review

Author (Year)	Study design	Population	Intervention	Main outcomes
Singh et al. (2024)[17]	Double-blind randomized placebo-controlled trial	Children aged 4–12 years	2 gummies/day for 98 days	Reduction in sore throat and myalgia
Tosca et al. (2024)[18]	Randomized controlled trial	Children aged 2–6 years with recurrent RTIs	Nasal spray, twice daily for 3 months	Reduction in RTIs and wheezing; decreased use of β2-agonists and antibiotics
Rennerova et al. (2022)[19]	Multicenter prospective open-label study	Children aged 1–12 years with recurrent RTIs	Liquid beta-glucan (1 mL/5 kg) for 3 months	Reduction in upper RTIs
Jesenak et al. (2013)[20]	Double-blind randomized placebo-controlled trial	Children aged 2–10 years with history of RTIs	1 mL/5 kg daily for 6 months	Reduction in upper RTIs and influenza-like illness
Meng et al. (2016)[21]	Prospective observational study	Children aged 1–12 years with RTIs	Beta-glucan + vitamin C for 3 months	Reduction in emergency department visits and school absenteeism
Grau et al. (2015)[22]	Prospective open-label study	Children aged 3–7 years with recurrent RTIs	Syrup containing Pleuran® + vitamin C for 3 months	Reduced incidence of RTIs and school absenteeism
Pasnik et al. (2017)[23]	Double-blind randomized placebo-controlled trial	Children aged 1–4 years with ≥2 recent URTIs	Daily supplementation for 12 weeks	Reduction in number and duration of URTIs

Abbreviations: RTIs = respiratory tract infections; URTIs = upper respiratory tract infections.
Source: the authors.

The Canadian study, for example, demonstrated a significant reduction in symptoms such as sore throat and muscle aches in the group that received beta-glucan, highlighting its effectiveness in alleviating common cold symptoms. This finding is reinforced by the Italian study, which reported improvements in sleep quality and reduced nasal congestion, symptoms often associated with upper airway inflammation. These results suggest that the use of beta-glucans not only prevents infections but also improves the quality of life during infectious episodes, an important aspect of pediatric care.

Another relevant finding was the decrease in the need for symptomatic medications and emergency visits, as evidenced by studies conducted in Spain and Slovakia. These findings suggest a potential reduction in the healthcare system burden, as well as benefits for families, such as fewer school absences and reduced parental work absences. The consistency of results observed across different age groups and countries reinforces the global relevance of beta-glucan as a preventive strategy.

However, the quantitative analysis faced significant challenges due to the high heterogeneity (I^2 = 99.59%) among the included studies, which limited the possibility of conducting a conclusive meta-analysis. The observed heterogeneity can be attributed to the variability in the types of beta-glucans used (Table 1), which varied between beta-glucans derived from yeast and those from the fungal source *Pleurotus ostreatus*, each with potential differences in structure, molecular weight, and, consequently, immunological activity. There was also significant variation in the form of administration (gummies, nasal spray, syrup), as well as in dosage and treatment duration, which impacted outcome assessment criteria and reflected differences in methodological designs and study populations. Given this limitation, the study adopted a hybrid approach, combining a narrative review and subgroup analysis to better contextualize the findings. The subgroup analysis highlighted specific benefits of beta-glucans in children with a history of recurrent respiratory infections, suggesting that these compounds may be more effective in specific contexts.

Despite the limitations, the review demonstrated that beta-glucans have the potential to reduce the incidence and severity of respiratory infections in children, as well as decrease the need for symptomatic medications. The narrative review, complemented by subgroup analysis, emphasized the relevance of future studies to standardize dosages, types of beta-glucans, and biological markers, such as IgA, IgG, and IgM, which are important to elucidate the immunological mechanisms underlying the observed responses.

The consolidated analysis reinforces that beta-glucans may be a promising addition to preventive strategies for respiratory infections in childhood. However, further well-designed and large-scale clinical trials are needed to consolidate these findings and guide their safe and effective use in clinical practice.

Finally, although not the focus of this review, the observed reduction in the use of medication and visits to health services raises the hypothesis that beta-glucan supplementation may be a cost-effective intervention in contexts of high incidence of respiratory infections. Future economic analyses are justified to explore this question.

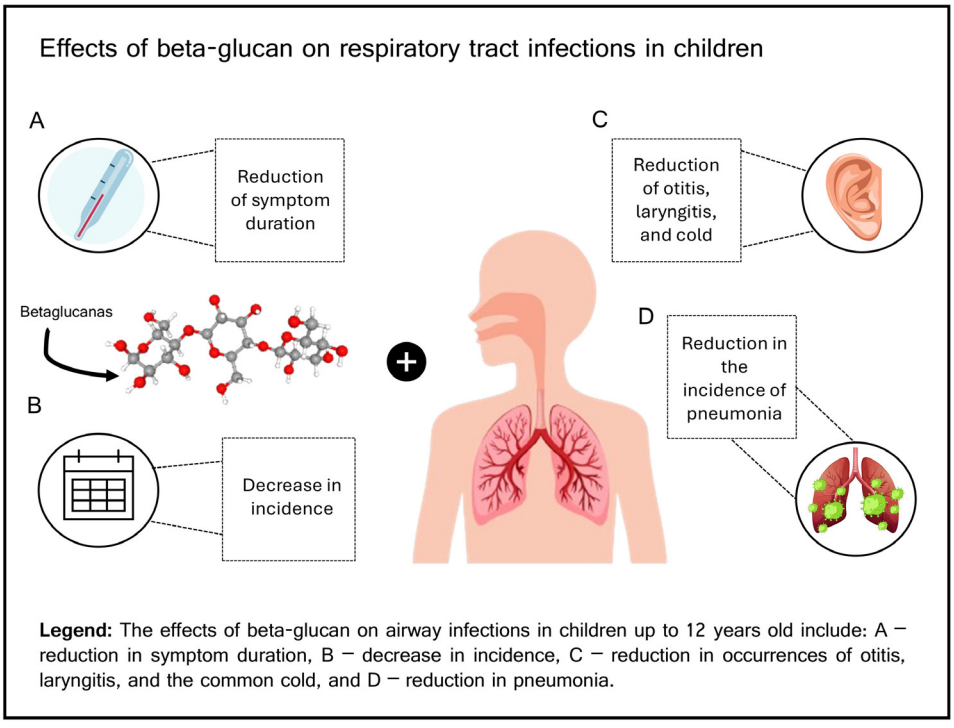

Figure 2. Potential effects of beta-glucan on respiratory tract infections in children.

Source: Elaborated by authors.

Conclusion

There is preliminary evidence suggesting a potential benefit of beta-glucans in reducing respiratory infections in children, but current data are insufficient to support widespread clinical use. Larger, standardized, and better methodologically reported randomized controlled trials are necessary to confirm this efficacy, elucidate the immunological mechanisms involved, and establish optimal doses and formulations.

Author's contributions

We describe contributions to the papers using the taxanomy (CRediT) provided above:

Conceptualization, Investigation, Methodology, Visualization & Writing – review & editing: CR Oliveira; MOSA de Araújo. *Project administration, Supervision & Writing – original draft*: CR Oliveira; CN dos Santos; KGS Silva; MI Monteiro. *Validation & Software*: GTR Correia; DM Amaral; VML Camargo . *Data curation & Formal Analysis*: MOSA de Araújo, CR Oliveira.

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