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LITERATURE REVIEW

Harnessing the Potential of Synbiotic Therapy for Childhood Malnutrition: A Narrative Review of Onion Inulin Extracts and Probiotic-Rich Dadih

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Abstrak

Malnutrisi dan kekurangan gizi pada anak-anak sebagian besar disebabkan oleh kurangnya asupan makanan dan penyakit, sehingga menimbulkan risiko besar jika tidak dilakukan intervensi tepat waktu. Munculnya bidang sinbiotik, kombinasi simbiosis probiotik dan prebiotik, memberikan jalan yang menjanjikan dalam terapi nutrisi. Ini secara efektif memodulasi komposisi dan aktivitas metabolisme mikrobiota usus. Pendekatan ini selaras dengan Tujuan Pembangunan Berkelanjutan tahun 2030, yang menawarkan strategi hemat biaya untuk profilaksis dan imunomodulasi. Studi ini menggali tinjauan literatur naratif, mengkaji potensi penerapan ekstrak inulin yang berasal dari bawang merah (Allium cepa Linn.), ditambah dengan manfaat dari dadih tradisional Sumatera yang kaya probiotik, sebagai terapi suportif. Penekanannya terletak pada manipulasi mikrobiota usus dan modulasi sistem kekebalan tubuh, yang bertujuan untuk meringankan keparahan komplikasi terkait malnutrisi pada anak-anak. Namun, mencapai kemanjuran dan keamanan optimal dengan sinbiotik memerlukan uji coba lebih lanjut yang ketat. Uji coba ini harus secara khusus menargetkan penyempurnaan rejimen dosis dan formulasi komposisi yang kondusif untuk memperoleh respons aman yang diinginkan dalam kondisi klinis. Kesimpulannya, eksplorasi inulin yang bersumber dari ekstrak bawang merah, dipadukan dengan terapi suportif yang berfokus pada manipulasi mikrobiota usus dan modulasi kekebalan tubuh serta dadih kaya probiotik, menunjukkan potensi langsung untuk penerapan praktis dalam mengatasi kekurangan gizi pada masa kanak-kanak. Melakukan uji coba tambahan sangat penting untuk menyempurnakan dosis dan formulasi, sehingga memungkinkan sinbiotik menawarkan solusi yang aman, efektif, dan terukur dalam memerangi malnutrisi pada anak-anak di seluruh dunia.

Kata kunci: gizi buruk, sinbiotik, inulin, dadih, anak

Abstract

Malnutrition and undernutrition in children are predominantly attributed to insufficient dietary intake and diseases, posing substantial risks without timely intervention. The emerging field of synbiotics, a symbiotic combination of probiotics and prebiotics, presents a promising avenue in nutritional therapy. It effectively modulates the composition and metabolic activities of the intestinal microbiota. This approach aligns seamlessly with the Sustainable Development Goals for 2030,

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offering a cost-effective strategy for both prophylaxis and immunomodulation. This study delves into a narrative literature review, examining the potential application of an extract derived from onion (Allium cepa Linn.) inulin, coupled with the beneficial attributes of the probiotic-rich traditional Sumatran dadih, as a supportive therapy. The emphasis lies in manipulating the intestinal microbiota and modulating the immune system, aiming to alleviate the severity of malnutrition-related complications in children. However, achieving optimal efficacy and safety with synbiotics necessitates further rigorous trials. These trials should specifically target refining dosage regimens and formulating compositions conducive to eliciting the desired, safe responses in clinical settings. In conclusion, the exploration of inulin sourced from onion extracts, integrated with supportive therapy focusing on gut microbiota manipulation and immune modulation alongside probiotic-rich dadih, shows immediate potential for practical application in addressing childhood malnutrition. Conducting additional trials is paramount to fine-tuning dosages and formulations, enabling synbiotics to offer safe, effective, and scalable solutions in combating malnutrition among children worldwide.

Keywords: malnutrition, synbiotics, inulin, dadih, children

INTRODUCTION

The prevalent and immediate causes of malnutrition and undernutrition in children, as per the UNICEF conceptual framework, are insufficient dietary intake and diseases like diarrhea, leading to deficient growth and development [1]. According to WHO, more than 50% of infant and child deaths are related to malnutrition and malnutrition [2]. In Indonesia, based on Basic Health Research (Riskesdas) data and the 2016 Nutritional Status Monitoring Results (PSG) pocketbook, the proportion of toddlers aged 0 to 59 months with malnutrition and malnutrition in 2013 reached 19.6 percent. This figure increased from 17.9 percent in 2010 [3].

Therefore, nutritional problems need to be addressed quickly and precisely at the root. This is in line with WHO's vision and mission in 2016 as a driver of the SDGs called #WORKFORCE2030 which contains various joint policies to achieve the SDGs goals by encouraging implementation research and innovation [4].

While inadequate access to nutrition remains the primary cause, the role of gut microbiota in this condition is increasingly recognized [5]. Understanding these causes and devising strategies to combat malnutrition is of paramount public health interest. Manipulating gut microbiota offers a potential avenue for alleviating malnutrition, with synbiotics, a combination of probiotics and prebiotics, emerging as a promising investigation [6].

Synbiotics, functioning synergistically as nutritional therapy and promoting host health benefits, offer a gentle yet potent approach to modulating intestinal microbiota composition and metabolic functions [7]. The gut microbiota plays a pivotal role in fermenting non-digestible substrates like dietary fiber and endogenous intestinal mucus, fostering the growth of specific microbes that produce gas and short-chain fatty acids (SCFA) [8]. Probiotics trigger a mucosal immune response which will produce sIgA which plays a very important role in local humoral mucosal immunity and mucosal cell mediated immunity. Meanwhile, prebiotics are needed as nutritional substances needed for bacterial metabolism and fertile growth of probiotic bacteria [9,10].

In line with achieving the Sustainable Development Goals 2030, synbiotics stand as cost-effective prophylactic measures against various human ailments. They maintain commensal microbial communities and metabolic networks essential for human health while serving as immunomodulators, particularly beneficial for malnourished individuals with weakened immunity [6,11].

We aim to assess the potential of a synbiotic approach therapy utilizing Lactobacillus bacteria as a probiotic and extracting Inulin from onions as a prebiotic. This research endeavors to restore intestinal homeostasis, enhance children's immunity, and evaluate its effects to contribute toward sustainable

development across pertinent sectors. The objective is to analyze the efficacy of this synbiotic intervention, offering insights that can advance research in life sciences and medical fields. This innovation strives to provide integrative studies and recommendations, aiming for an improved state of health and well-being.

METHOD

This paper conducts a narrative literature review on prebiotics, probiotics, synbiotics, inulin, intestinal microbiota, onion, infection complications, immunity, and chronic malnutrition. Data from scientific sources underwent rigorous analysis to compose this comprehensive review, enabling a detailed examination of diverse scholarly works and proposing future pathways for medical literature advancement.

Articles chosen were primarily original research from national and international journals published within the last 10 years. Inclusion criteria encompassed both English and Indonesian articles, broadening perspectives on the specified keywords and ensuring a comprehensive scope of literature. Each article underwent strict scrutiny for originality, relevance, and credibility. The synthesized analysis aimed to extract pivotal insights, contributing to a comprehensive narrative review aiming to guide future medical research and practice.

RESULTS AND DISCUSSION

Immunomodulatory Role of Inulin and Dadih Synbiotics: Understanding Antimicrobial Actions and Immune Enhancement

Probiotics can increase the activity of digestive enzymes so that the absorption of nutrients becomes more optimal with the wider absorption area because probiotics can affect the intestinal anatomy (the intestinal villi) and become higher and denser. This probiotic, if it obtains a specific substrate will produce some antibiotics that are easily absorbed by the body [10,12].

Probiotics can produce anti-tumor active ingredients, produce various vitamins, such as thiamin (B1), riboflavin (B2), pyridoxine (B6), cyanocobalamin (B12), folic acid which is easily absorbed by the body [13]. Dadih is a fermented product from buffalo milk which is one of the traditional food products from West Sumatra. Dadih is rich in good bacteria, especially the *Lactobacillus sp* and *Bifidobacterium sp.* Therefore, it can be regarded as a food source rich in probiotics [14]. *Lactobacillus acidophillus* probiotics can also produce several antibiotics such as acidolin, acidophilin, and lactocidin [15].

Species of good bacteria such as *Lactobacillus* and *Bifidobacterium* can reduce inflammation and strengthen the intestinal wall. They can also help break

down complex carbohydrates and proteins [16]. Importantly, these good bacteria also aid in the production and absorption of amino acids that are essential for the growth and regeneration of damaged cells [17].

Microbiomes reduce inflammation and strengthen the intestinal wall and help break down complex carbohydrates and proteins. And importantly, these good bacteria also help the production and absorption of amino acids that are essential for growth, the diversity of intestinal microbiota can protect the body from bad bacterial infections through competition. Manni et al links microbiota to inflammation that hyper-inflammation (HYPi) in individuals with a pre-existing chronic inflammation (CHRi) can exacerbate acute inflammation (ACUi), leading to heightened susceptibility to severe viral diseases like Covid-19 [18,19].

Based on Surono et al, that identified candidate probiotic lactic bacteria among indigenous dadih lactic, reported that milk cultured with Enterococcus faecium IS-27526 significantly lowered fecal mutagenicity of rats as compared to the control group, skim milk, and milk cultured with L. plantarum IS-20506. These results suggest that Enterococcus faecium IS-27526 may serve as a potential probiotic strain with its antimutagenicity [14].

On the other hand, Harahap et al reported that the fermentation process of traditional Sumatran dadih leads to the proliferation of Lactic Acid Bacteria (LAB), potentially serving as probiotics with immunomodulatory capabilities. This study aimed to isolate LAB strains from dadih, identifying specific strains with antagonistic properties against pathogenic bacteria. Among these, DA01 exhibited the highest phagocytic activity in macrophages when combined with inulin, emphasizing the potential of dadih-derived LAB as effective probiotics with immunomodulatory functions [20].

All prebiotic compounds that enter the human digestive tract will be fermented by bacteria in the large intestine through several metabolic pathways for inulin fermentation [10]. The main products of inulin fermentation are butyrate, while the main products of fructooligosaccharide (FOS) fermentation are acetic acid and lactic acid. The results of studies on inulin metabolism to produce butyric acid via the butyl-CoA and acetate transferase CoA pathways show a high diversity among microorganisms in the digestive tract regarding their ability to utilize external acetate as acosubstrate. So, it also restores the intestinal homeostasis [21].

Inulin is a polymer of fructose units. Inulin is soluble in water, cannot be digested by digestive enzymes but is fermented by the colonic microflora. Inulin is also one of the components of foodstuffs with a very high content of dietary fiber so that it can be used as a functional food [22]. Besides being

used as a functional food, Inulin also used as a substitute for fat and sugar in low-calorie food products and as a raw material for fructose syrup. Inulin has a taste that tends to be sweet and can be combined with specific probiotics in product form, such as yogurt, kefir, and curd [23,24].

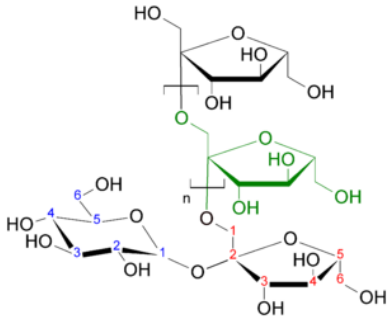

Fig 1. Molecular structure of Inulin [25].

Synergistic Effects of Inulin-Dadih Synbiotics: Antimicrobial Mechanisms and Immune Modulation

Inulin compound obtained from a series of previous extraction processes can be said to be prebiotic because it can be a nutrient and increase the growth of the *Lactobacillus* bacteria through a facultative anaerobic respiration fermentation process. While in the large intestine, almost all of the inulin is fermented into short-chain acids and some specific microflora produce lactic acid. Events like this cause the pH in the large intestine to decrease so that the growth of pathogenic bacteria is inhibited. Changes in pH to acid will cause antimicrobial effects for pathogenic microbes [26,27].

Another mechanism of this antimicrobial property is that lactic acid bacteria also produce antimicrobial peptides such as bacteriocins which have inhibitory properties, so that the cell membrane cannot function properly in terms of selecting molecules in and out of cells. This mechanism causes a person's immune system to increase. Synbiotics have also been suggested to alter the composition of the colonic microbiota, reduce inflammatory processes in the gut mucosa, and have the ability to induce remission in inflammatory bowel disease as well as prevent travelers' diarrhea, and improve the overall quality of life in patients [28].

While in the large intestine, almost all inulin undergoes fermentation into short-chain acids, with specific microflora producing lactic acid [21]. This leads to the creation of antimicrobial compounds, impeding the growth of pathogenic bacteria, enhancing bowel movements to relieve constipation, converting bile pigments and acids, and aiding nutrient absorption. This event decreases the pH in the large intestine, inhibiting the

proliferation of pathogenic bacteria and consequently boosting an individual's immune response [29,30]. This mechanism presents promising prospects for supportive therapy in children with chronic malnutrition, reducing the likelihood of infection complications through enhanced immune function [21,31]. The role of probiotics and prebiotics from onion and dadih is illustrated in the following image.

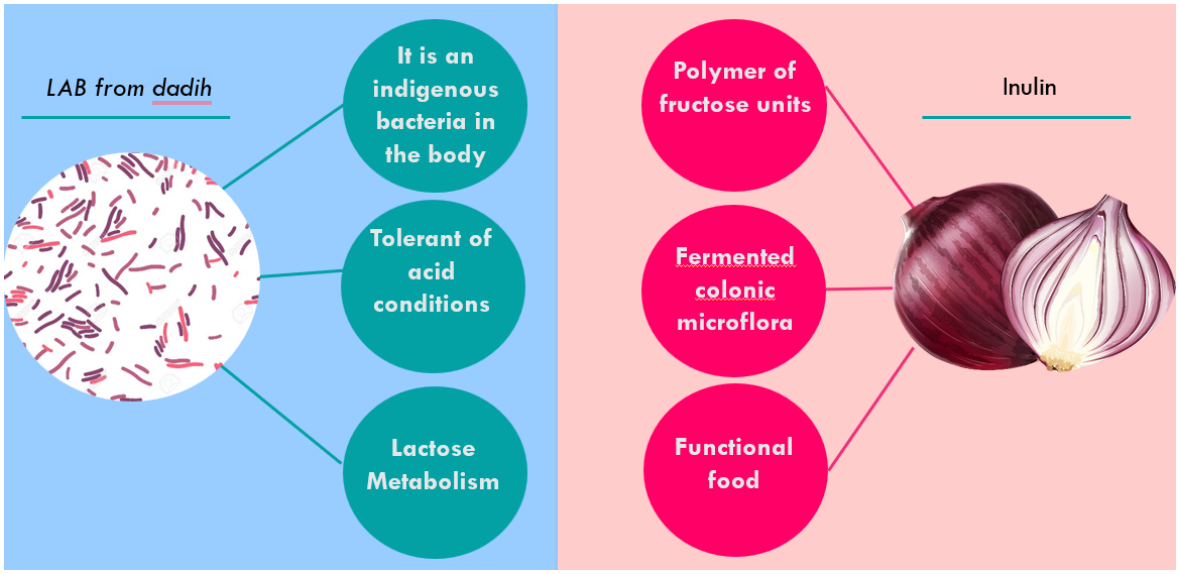

Figure 2. The illustration roles of probiotics and prebiotics from inulin and dadih sources.

Regarding its utilization as a soluble dietary fiber in mammalian bodies, inulin acts as a prebiotic known for its solubility in water but resistance to digestion by digestive enzymes (non-digestible), thus reaching the intestines intact and being fermented by specific microflora [32]. The supplementation of more inulin (prebiotic) into a liquid medium corresponds to a higher cell count growth within that medium. This occurrence is due to the increased availability of substrates for the fermentation process, generating energy utilized by test bacteria for their growth activities [23,33].

The therapeutic mechanism of synbiotics derived from Inulin and Dadih from West Sumatra revolves around their combined action as potent immunomodulators. Research conducted by Arnold elucidates that Inulin, a prebiotic compound, serves as a substrate for beneficial bacteria, promoting the growth and activity of Lactic Acid Bacteria (LAB) found in Dadih, a traditional fermented product. This synergy between Inulin and LAB enhances their probiotic properties, facilitating an improved immune response. Studies have highlighted that LAB strains isolated from Dadih possess antagonistic qualities against pathogenic bacteria, showcasing their potential as probiotic agents [34]. When combined with Inulin, these LAB strains from Dadih exhibit heightened

macrophage phagocytic activity, indicating their ability to enhance immune function through synbiotic intervention [35].

Moreover, the immunomodulatory effects of these synbiotics sourced from Inulin and Dadih are underscored by their influence on phagocytic activity in macrophages. The specific LAB strains isolated from Dadih, particularly strain DA01, exhibit substantial phagocytic activity when combined with Inulin. This heightened activity in macrophages suggests a robust immune response mediated by synbiotics. The findings shed light on the potential therapeutic application of Dadih-derived LAB strains when coupled with Inulin as a promising approach to boost immune function and establish a balanced gut microbiota [20,36,37]. Summary of the mechanism of action of inulin from shallots as a prebiotic and LAB from dadih as a probiotic.

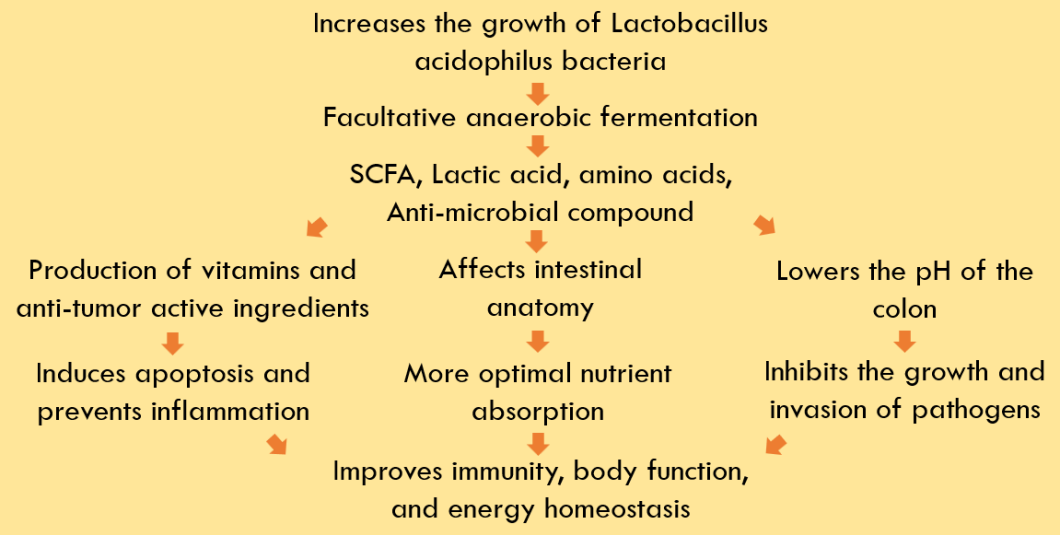

Figure 3. The summary elucidates inulin's shallot and dadih in synbiotic mechanism of action.

Supportive therapy with the principle of synbiotics using the probiotic agent *Lactobacillus acidophilus* and inulin isolates from onion sources has great potential to be developed as palliative care for malnourished patients [38]. This is because of the relatively easy breeding process and the abundant number of prebiotic source plants that spread throughout the world, especially in Indonesia and other tropical countries [20].

CONCLUSION

From the analysis and synthesis results, it is evident that extracting inulin from onion (Allium cepa linn.) and dadih as probiotics coupled with a supportive therapy approach based on the intestinal microbiota shows promising potential for immediate and easy application. This is primarily due to the ready availability of raw materials and relatively

uncomplicated breeding processes. A series of studies is needed to build a scientific foundation before it is applied to better health conditions.

Starting with the concept of preliminary studies, in-vitro, in-vivo testing, drug formulations, and 4-generation clinical trials to ensure the efficacy of these agents in collaboration with pharmaceutical companies and health food-beverage products.

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CONFLICT OF INTEREST

No potential conflicts of interest were reported by the authors.

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