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Unlocking Therapeutic Potential of Bengkoang (*Pachyrhizus erosus*) Inulin and *Lactobacillus* Synergies in Synbiotics for Immunomodulatory Interventions in Indonesia: A Review

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Abstract

BACKGROUND: Indonesia's vision for 2045 encapsulates a grand aspiration for global competitiveness and resilience, with an emphasis on cultivating robust and skilled human capital. This study delves into the pivotal role of health-centric food and beverages as a fundamental component aligned with the Sustainable Development Goals 2030. The objective is to confront non-communicable diseases and preempt the anticipated surge in malnutrition-related fatalities projected for Indonesia's population of 340 million by 2045. The findings illuminate the potential of synbiotics, specifically highlighting the synergistic relationship between Bengkoang inulin and *Lactobacillus*.

METHODS: Conducted through a narrative literature review method, this research meticulously synthesized articles drawn from national and international journals published within the past decade. The rigorous selection criteria honed in on themes surrounding synbiotics, *Pachyrhizus erosus*, immunomodulators, inulin, and *Lactobacillus*. The chosen articles underwent comprehensive analysis and synthesis.

RESULTS: Synbiotics exhibited promising enzymatic activities, growth enhancements, and significant immune modulation. These outcomes signal substantive implications for disease prevention and overall health enhancement. The discussion emphasizes the potential application of synbiotics as a promising therapeutic intervention for malnutrition. It is underscored by its multifaceted impact on gut health, nutrient absorption, immune modulation, and its potential therapeutic applications across diverse health domains – the pivotal role of synbiotics in averting health disparities and augmenting overall well-being. The discussion delves into the immunomodulatory potential of synbiotics, elucidating their ability to fine-tune immune responses, mitigate inflammation, and potentially enhance vaccine efficacy.

CONCLUSION: This comprehensive analysis underscores the far-reaching implications of synbiotic therapy, positioning it as a promising avenue for therapeutic innovation and holistic health interventions.

Introduction

Indonesia Gold 2045 envisions global competitiveness, emphasizing human resources as the cornerstone. Projected 2045 demographics peak with a majority in the productive age bracket of 15–64, highlighting a demographic bonus [1]. Consequently, Indonesia needs to engage in endeavors aligning with the tenets of 4.0 industrial revolution principles to actualize this demographic bonus [2].

Indonesia, following the making Indonesia 4.0 blueprint, prioritizes five key sectors, including health-centric food and beverages. Technological advancements, diverse products, and improved distribution are crucial for industrial growth, aligning with the sustainable development goals (SDGs) to ensure better health and well-being by 2030 [3], [4], [5], [6].

According to the World Health Organization (WHO), over 50% of infant and child deaths are linked to inadequate or poor nutrition [7]. Data from basic health research and the pocketbook of nutrition status monitoring in 2016 reported that the proportion of undernourished toddlers aged 0–59 months in 2013 was 19.6%. This figure escalated from 17.9% in 2010. Nutrition-related concerns require swift and precise interventions, in line with the WHO's vision and mission in 2016 as an embodiment of the SDGs labeled #WORKFORCE2030, encompassing various policies to attain SDG objectives by advocating for research and implementable innovations [8], [9].

While the period of malnutrition may be brief, its consequences can be lifelong. Recent estimates suggest that 30% of global child deaths are directly or indirectly associated with malnutrition [10]. Malnutrition predisposes individuals to infections, while infections exacerbate malnutrition, creating a hazardous cycle, particularly during growth periods [11]. This failure can permanently limit a child's physical and cognitive capacities, resulting in long-term damage [12].

Inadequate food intake leads to weight loss, diminished immunity, pathogen invasions, and growth and developmental hindrances in children [7]. They become more susceptible to disorders such as diarrhea, malabsorption, loss of appetite, nutritional diversions for immune responses, and nitrogen loss in urine, all contributing to a chain reaction of nutritional deficiencies that undermine the body's defense mechanisms [13]. These events lead to reduced food intake and can exacerbate an individual's health conditions, potentially leading to other complications, including chronic degenerative diseases and decreased intelligence [14].

Numerous efforts have been undertaken by the government and stakeholders, ranging from providing supplementary foods to direct interventions targeting the root causes [15]. However, a series of breakthrough studies suggest that there might be one overlooked potential solution: The tens of trillions of beneficial bacteria residing in the digestive tract, known as gut microbiota. Hence, critical is this microbiota that scientists often refer to as a separate organ [13], [16].

It has been observed that healthy gut microbiota develops over time, while undernourished gut microbiota appears to remain immature, lacking diversity and the ability to produce and absorb required nutrients at each growth stage. Moreover, standard therapeutic foods for malnutrition fail to rectify the imbalance in the long term. Consequently, developmental issues affecting their microbial organs persist [13], [17].

In this context, synbiotic therapy emerges as a compelling option. Synbiotics are products containing two components: Probiotics and prebiotics, working synergistically to enhance bacterial resilience in the gut [18]. In this study, the chosen source of synbiotics is Bengkoang inulin isolate, serving as the prebiotic. Bengkoang, also known as yam bean jicama or Mexican turnip *(Pachyrhizus erosus)*. The selection of Bengkoang is based on its abundant availability, particularly in tropical regions like Indonesia [19]. This extract is added to the *Lactobacillus* bacteria medium, showing a positive impact on growth, and used as a sample probiotic agent. It is found that this combination could potentially serve as a supportive therapy for enhancing systemic health in the future [20].

Materials and Methods

This review employed a narrative literature review method, meticulously selecting articles sourced from a spectrum of national and international journals published within the past decade. The chosen publications, comprising original research and systematic reviews, were extensively screened based on stringent criteria and keyword searches. The focus primarily encompassed studies available in both English and Indonesian languages, specifically targeting synbiotics, *P. erosus*, immunomodulators, inulin, and *Lactobacillus* as key themes for investigation.

The selection process emphasized the articles' relevance and alignment with the research objectives. Rigorous inclusion and exclusion criteria were applied to ensure a comprehensive yet focused pool of literature. The chosen articles underwent scrutiny to extract pertinent information. Following this, a meticulous synthesis and analysis of these articles were conducted, enabling the compilation and summarization of their collective findings. This meticulous approach facilitated the amalgamation of diverse insights and perspectives from the identified articles. It allowed for the creation of a comprehensive narrative that represents a holistic view of the subject matter. Moreover, this methodology ensured that the resultant synthesis represents a coherent and informed narrative.

The inclusion criteria of this study were primary literature or journals (original research), full text, in English and Indonesian, time period 2013–2023, researching the role and mechanism of synbiotics as immunomodulatory interventions which focused on studies related to utilization of Bengkoang (*P. erosus*) and *Lactobacillus*. The exclusion criteria are if the research group is mixed with other compounds, does not have a control group, the discussion about the mechanism is not explained, and the journal is not indexed.

Results and Discussion

Inulin from Bengkoang (P. erosus) extract as a promising prebiotic and Lactobacillus as an effective probiotic agent

Bengkoang, also known as yam bean jicama or Mexican turnip, has garnered attention due to its high prebiotic content [21]. Its inulin content, a type of oligosaccharide fructan, has been the focus of research due to its potential as a prebiotic. Inulin can be fermented by specific gut microbes, particularly Bifidobacterium and *Lactobacillus* bacteria, leading to the desired synbiotic effects [19]. Studies have demonstrated that inulin exhibits significant prebiotic properties, enhancing the growth of beneficial bacteria in the digestive tract and supporting a healthy gut microbiota balance [22].

The research from Bhanja *et al*. extracted inulin from jicama or Bengkoang *(P. erosus)* through microwave heating and conducted a thorough characterization employing diverse analytical methods. The derived inulin exhibited comparable prebiotic attributes to commercially accessible counterparts. Notably, it facilitated the growth of beneficial probiotics and displayed notable antioxidant capabilities. These

findings strongly advocate for the prospective utilization of this isolated inulin as a potent prebiotic in forthcoming applications [23].

Lactobacillus bacteria, a common group of probiotics found in fermented products, have shown significant potential as probiotic agents. Various *Lactobacillus* strains have been studied for their ability to modulate the gut microbiota, enhance the immune system, and improve digestive conditions [24]. Some studies have highlighted the critical role of *Lactobacillus* bacteria in stimulating the production of beneficial compounds such as lactic acid, creating an environment less favorable for pathogenic bacteria and promoting the growth of beneficial bacteria [25], [26].

Studies demonstrating the synergistic effect of Bengkoang (P. erosus) extract and Lactobacillus

Recent studies have delved deeper into elucidating the synergistic potential between Bengkoang (*P. erosus*) extract and various strains of *Lactobacillus*. A study by Pulbutr *et al*. (2021) investigated the specific enzymatic reactions catalyzed by *Lactobacillus* in the presence of bengkoang (*P. erosus*) extract. The findings unveiled a significant increase in the enzymatic activity of key digestive enzymes when Bengkoang (*P. erosus*) extract was introduced, suggesting a potential role in improving nutrient absorption and overall digestive health. The impact of the Bengkoang (*P. erosus*) tuber extract on bacterial growth and acid production mirrored the effects observed with commercial inulin at equivalent concentrations tested. These findings underscore the prebiotic characteristics of the Bengkoang (*P. erosus*) tuber extract, particularly in specific probiotics like *Lactobacillus plantarum* [27].

Moreover, Santoso *et al*. expanded on this research area, emphasizing the beneficial impact of the Bengkoang (*P. erosus*) extract and *Lactobacillus* combination on the gut microbiota composition. Their investigation revealed a noteworthy shift toward a more beneficial microbial profile within the gut, indicating a potential role in modulating gut dysbiosis and promoting overall gut health [28]. In a different context, a study by Oladejo *et al*. focused on the immunomodulatory effects of the Bengkoang (*P. erosus*) extract and *Lactobacillus* co-culture. Their research demonstrated a significant increase in mucosal immunity markers and anti-inflammatory responses, suggesting a potential application in immune system modulation and disease prevention [29].

Some findings from various studies explore the synergistic effect of Bengkoang (*P. erosus*) extract and *Lactobacillus* on overall health outcomes. Their comprehensive review supported the notion that this combination exhibits a multifaceted positive impact on gut health, nutrient absorption, immune modulation, and metabolic functions. These studies collectively underline the promising synergistic effects of Bengkoang (*P. erosus*) extract and *Lactobacillus*, providing a robust foundation for further exploration into novel therapeutic interventions and functional food development. Understanding these implications is crucial in comprehending the benefits of synbiotics in gut health and their potential to improve overall health [28], [30], [31].

Immunomodulatory role of synbiotic: A synergistic approach of Bengkoang (P. erosus) inulin and Lactobacillus

Probiotics trigger mucosal immune responses, producing sIgA that plays a role in local humoral immunity in the intestinal mucosa and mucosa-mediated cell immunity [32]. Administering probiotics can enhance digestive enzyme activity, optimizing nutrient absorption by influencing the anatomy of intestinal villi to be higher and denser [33]. These probiotics, when provided with specific substrates, can generate active anti-tumor agents and produce various vitamins such as thiamine (B1), riboflavin (B2), pyridoxine (B6), cyanocobalamin (B12), and folic acid. *Lactobacillus* probiotics can also generate several antibiotics such as acidolin, acidophilin, and lactocidin [34].

Beneficial bacterial species like *Lactobacillus* reduce inflammation and fortify intestinal walls. They also aid in breaking down complex carbohydrates and proteins, assisting in the production and absorption of essential amino acids for growth [35]. Given that a growing brain is one of the body's most voracious organs, this benefit is particularly crucial for healthy nervous system development [36]. More importantly, gut microbiota diversity can shield the body from harmful bacterial infections, such as *Shigella*, *Listeria*, or *Salmonella*, through competitive mechanisms. A well-established bacterial community makes it difficult for pathogens to find niches and proliferate [37].

Meanwhile, prebiotics serve as nutritional substrates for bacterial metabolism and probiotic growth [38], [39]. Inulin extract, regarded as a prebiotic, acts as a source of nutrition and boosts *Lactobacillus* bacteria growth through anaerobic facultative fermentation. Consequently, these bacteria undergo fermentation to obtain energy [39], [40]. While in the large intestine, almost all inulin is fermented into short-chain fatty acids [28]. Certain specific microflora produce lactic acid and antimicrobial compounds that impede pathogen growth, enhance intestinal motility, convert bile and bile acids, and aid in nutrient absorption. This event results in a lowered large intestine pH, hindering pathogen growth, and thus boosting an individual's immunity [34].

Regarding its utilization as a soluble dietary fiber in the body, inulin prebiotics are physically soluble in water but are not digestible by digestive enzymes. They reach the intestines intact and are fermented by

specific microflora. The more inulin added to the liquid medium, the greater the number of growing cells, primarily due to the increased availability of substrates for fermentation processes and energy production utilized by bacteria in their growth. This combined process forms the basis of the product [18], [36].

The prebiotic inulin substrate is utilized in facultative anaerobic fermentation by *Lactobacillus* probiotics as an energy source. During this fermentation process, a molecule transforms without any oxidation. Parts of the inulin molecule lose hydrogen atoms while other segments gain additional hydrogen atoms [41]. This fermentation process yields a certain amount of energy and lactic acid as a byproduct. The energy is utilized for bacterial activities, while the lactic acid produced within a specific concentration range does not negatively affect the growth of *Lactobacillus* bacteria due to its tolerance to acid. If the accumulation of lactic acid remains dissociated within that concentration range, inhibition of *Lactobacillus* bacteria by lactic acid does not occur. Lactic acid prevents the growth of pathogenic bacteria in the digestive tract [42].

Previous research has shown that the optimal colony growth exists at a concentration of 0.5%, with an average colony count of 206 for *Lactobacillus acidophilus* and 200 for *Lactobacillus bulgaricus*. Meanwhile, the colony count in media without the addition of inulin compound from onion extract, at a concentration of 0%, showed an average colony count of 10 for *L. acidophilus* and 8 for *L. bulgaricus*. Colony counts from testing indicate that adding inulin compound from onion extract in the range of 0.25–0.5% can enhance the growth rate of *L. acidophilus* and *L. bulgaricus*, with optimal growth observed at a concentration of 0.5% inulin compound from onion extract addition using the aseptic agar pouring method [20], [21], [22].

The immune system plays a crucial role in maintaining health. Synbiotics, particularly the combination of Bengkoang *(P. erosus)* extract and *Lactobacillus* bacteria, have shown potential in stimulating immune responses. Synbiotics can provide positive signals to immune cells and enhance the production of molecules that regulate immune responses, such as cytokines and interferon-gamma, which are essential in balancing the immune system [43].

Synbiotics play a role in optimizing specific and non-specific immunity. By boosting antibody production, synbiotics can help fight infections, reduce the risk of allergies, and strengthen the immune response to pathogens [44]. In addition, synbiotics can stimulate macrophages and other phagocytic cells that aid in capturing and destroying bacteria and viruses [45], [46].

The role of synbiotics in regulating inflammatory responses in the body is an intriguing research focus. Studies suggest that synbiotics can alleviate excessive inflammation associated with certain autoimmune diseases such as rheumatoid arthritis and lupus. This modulatory effect is believed to arise from the synergistic interaction between active compounds from Bengkoang *(P. erosus)* extract and the regular effects of *Lactobacillus* bacteria on the immune system [46], [47].

The sugar hydrolysis by lactic acid bacteria results in the release of more phenolic compounds, thereby increasing antioxidant activity. The increased release of phenols from hydrolysis leads to heightened phenol activity that enters the bacterial cell and traverses the cell wall and cytoplasmic membrane. Active antibacterial and antioxidant activities occur within the bacterial cell due to the phenolic compounds, causing the denaturation of cytoplasmic protein components, rendering the metabolism inactive, hindering bacterial growth, or causing death [48].

Recent studies have emphasized the crucial role of synbiotics in improving the gut microbiota composition, which, in turn, influences various aspects of human health. The synergistic combination of bengkoang (*P. erosus*) extract and *Lactobacillus* has been shown to positively impact the balance of gut microbiota, enhancing the presence of beneficial bacteria while suppressing harmful pathogens. These findings align with research demonstrating the capacity of synbiotics to restore microbial dysbiosis, promoting a healthier gut environment [49]. Such a balanced gut microbiota composition is associated with improved metabolic functions, strengthened immune responses, and reduced inflammation within the gastrointestinal tract [50], [51].

Furthermore, the immunomodulatory effects of synbiotics extend beyond the gut, demonstrating systemic implications. Studies have revealed that the modulation of gut microbiota through synbiotic intervention contributes to the regulation of immune responses outside the gastrointestinal system. The enhancement of the gut barrier function by synbiotics can play a crucial role in averting systemic inflammation and maintaining overall immune homeostasis [52]. This effect is particularly promising in preventing the onset of inflammatory diseases and autoimmune conditions by regulating immune responses at mucosal sites [53].

The synergy between Bengkoang (*P. erosus*) extract and *Lactobacillus* in synbiotics has shown promise in modulating cytokine profiles. Synbiotic administration has been observed to regulate the production of various cytokines, such as interleukins and tumor necrosis factor, which are vital in shaping immune responses [46]. This modulation indicates the potential of synbiotics in fine-tuning immune reactions, thereby contributing to a balanced immune system. Such immunomodulation is pivotal in mitigating exaggerated immune responses linked to allergies, asthma, and certain autoimmune disorders [54], [55].

Moreover, synbiotic-mediated immunomodulation has exhibited a promising role in enhancing vaccine responses. Research suggests that synbiotic

supplementation could augment the efficacy of vaccinations by strengthening the immune system's ability to mount robust responses against antigens. By potentiating the adaptive immune system, synbiotics hold the potential as supportive agents to optimize vaccine outcomes [56]. Simultaneous supplementation of prebiotics or probiotics alongside influenza vaccination shows significant potential in enhancing the effectiveness of the vaccine [57].

The application of synbiotics also appears to have the potential in supporting the treatment of chronic diseases [58], [59]. Some studies indicate that synbiotics can contribute positively to managing conditions such as diabetes, heart disease, and even oncological conditions. Potential mechanisms include the modulatory effects provided on immune components that play a crucial role in controlling these chronic conditions [45], [60], [61].

The cumulative evidence from these studies underscores the multifaceted immunomodulatory potential of synbiotics derived from Bengkoang (*P. erosus*) extract and *Lactobacillus*. These findings present a compelling argument for further exploration of synbiotic interventions as a means to bolster immune function, not only within the gut but also systemically, opening avenues for therapeutic applications.

Conclusion

The study sheds light on the potential of synbiotics, specifically the synergistic relationship between Bengkoang (*P. erosus*) inulin and *Lactobacillus*. Through a narrative literature review, it reveals significant outcomes in enzymatic activities, growth enhancements, and immune modulation. The implications suggest the promising role of synbiotics as a therapeutic intervention for disease prevention and health improvement. Its multifaceted impact spans gut health, nutrient absorption, immune modulation, and potential therapeutic applications across various health domains. The discussion emphasizes its potential application in malnutrition therapy, its role in immune response modulation, inflammation mitigation, and potential enhancement of vaccine efficacy. This comprehensive analysis positions synbiotic therapy as a promising avenue for therapeutic innovation and holistic health interventions.

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