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Research article

# Longan syrup with lingzhi mushroom extract: Evaluation of safety and efficacy on immune and inflammatory modulation in healthy adults

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## **Abstract**

A longan (Dimocarpus longan Lour) syrup with lingzhi mushroom (Ganoderma lingzhi) extract was developed as a sweetener rich in bioactive constituents because of their excellent bioactivities. First, a single-dose, crossover experiment was conducted in healthy adults (n =20) to determine postprandial glucose excursion over 2 hr following consumption of the syrup. Second, a 12 wk prospective, single-group study was used to preliminarily evaluate the effects on glycemic control, hepatic and renal functions and immune and inflammatory responses to the syrup in healthy persons (n = 8). Fasting plasma glucose, glycated hemoglobin, hepatic enzymes, blood urea nitrogen, creatinine, immunoglobulins (Igs) and C-reactive protein (CRP) were measured at baseline and weeks 4, 8 and 12. The syrup increased postprandial glucose to a lesser extent than 50 g glucose solution, with the incremental area under the curve (iAUC) of blood glucose of  $327.83 \pm 19.81$  mg/dL.hr versus  $384.08 \pm 28.28$  mg/dL.hr, respectively (p < 0.05). Although the syrup was classified as a high-glycemic index food (glycemic index = 85.35), daily consumption of the syrup had no significant effect on blood glucose. Hepatic and renal functions did not change significantly throughout the study. No significant alterations in Igs and CRP were observed. However, the individual-level analysis identified strong indications of improvement in immunoglobulin G and CRP at the end of the study. The results showed the beneficial effects on immune and inflammatory responses of longan syrup with lingzhi mushroom extract without adverse effects on the glycemic profile nor on the hepatic or renal functions, suggesting the health-promoting potential of this novel syrup.

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## Introduction

Environmental factors confronting humans in their everyday lives, for example, air pollution, smoking, poor nutrition, and stress, weaken the immune system immensely and deteriorate the body's anti-inflammatory response, contributing to many irreversible and incurable health conditions and diseases (Ter Horst et al., 2016). Therapeutic approaches that are capable of strengthening immune function and reducing inflammation are the key to disease prevention (Chaplin, 2010; Furman et al., 2019). Nowadays, nutraceuticals and functional foods have received much attention globally to promote health and wellness (Barnes et al., 2016; Cong et al., 2020). Therefore, scientific data are needed to ensure the safety and proper use of such products.

Longan (Dimocarpus longan Lour; family Sapindaceae) is a popular edible fruit widely cultivated in tropical countries such as China, Vietnam and Thailand (Zhang et al., 2020). As it is the major exported fruit of Thailand, longan is considered an important economic fruit crop (Office of Agricultural Economics, 2012). The fruit has also been used as a traditional medicine for modulating metabolic function, facilitating sleep and relieving anxiety (Bai et al., 2020; Zhang et al., 2020). Research suggests that a cluster of nutrients and bioactive constituents in longan fruit pulp exhibits immunomodulatory (Meng et al., 2014; Rong et al., 2019; Yi et al., 2015), anti-inflammatory (Huang et al., 2012), antioxidative (He et al., 2009; Yang et al., 2014) and antitumor (Jiang et al., 2014) properties. Due to the sweet delicious taste and nutritional values of the longan pulp, longan has the potential to be a natural sweetener with many health benefits. Lingzhi (Ganoderma lucidum; family Ganodermataceae) is a medicinal mushroom that has been used in traditional Chinese practice for decades (Pan and Lin, 2019). It is believed that lingzhi mushroom can improve health, delay aging and extend life expectancy by modulating defense mechanisms against invading pathogens, inflammation and oxidative stress (Lin and Deng, 2019; Pan and Lin, 2019; Wang and Lin, 2019). The combination of longan and lingzhi mushroom could provide a positive combined effect on health.

Longan syrup with lingzhi mushroom extract is a new food product, which is categorized as a carbohydrate-containing food. Little is known about the safety and efficacy of the syrup. Thus, the objectives of the current study were to evaluate any adverse effects of longan syrup combined with lingzhi mushroom extract on the glycemic profile, including postprandial blood glucose excursion and glycemic control,

as well as hepatic and renal functions. The glycemic index (GI) value of longan syrup combined with lingzhi mushroom extract was also investigated along with determining the effects of the syrup on immune and inflammatory responses in healthy Thai adults.

#### Materials and Methods

Materials

Longan pulp was used for extraction. Briefly, the longan pulp was blended into small size and then boiled at 100°C for 1 hour. After squeezing, the extract was boiled for another hour at 100°C before filtering. The filtrate was then boiled again at 100°C for 2 more hours until the concentrated extract has 70°Brix. Lingzhi extract was a gift from Khao Yai Panorama Farm (Nakhon Ratchasima, Thailand). Lingzhi extract was added into Longan extract and the final concentration was 0.5%.

This work was divided into two studies.

Single-dose, crossover experiment

Ethics statements

The protocol of this crossover study was reviewed and approved by the Mae Fah Luang University Ethics Committee on Human Research (Approval No. EC 19306-20), and the study was registered on March 17, 2020 (NCT04313543).

**Participants** 

The inclusion criteria were nondiabetic, healthy Thai persons at Mae Fah Luang and Chulalongkorn Universities aged 18–60 yr who had a body mass index (BMI) in the range 18.5–24.9 kg/m² (n = 20). The exclusion criteria were: (i) fasting plasma glucose (FPG) > 100 mg/dL, (ii) thyroid disease, (iii) self-reported uncontrollable illnesses and life-threatening diseases, (iv) allergy to longan and lingzhi products, (v) use of medications, herbs and diet supplements affecting blood glucose level a month before study enrollment and (vi) pregnancy or breastfeeding.

Study procedure and ethical approval

Determination of the GI value of the syrup was carried out in accordance with the World Health Organization protocol (Food and Agriculture Organization of the United Nations, 1998). The experiments were set up on two occasions with a 7 d washout period. After a 10 hr overnight fast, participants were assigned to consume either 64.94 g of longan syrup with lingzhi mushroom extract (equivalent to 50 g of glucose) or 50 g of glucose powder as the tested food and the reference food, respectively. Both foods were served in 250 mL of water in random order on separate occasions at 0700 hours. Participants were requested to consume the entire portion of food within 5 min. Finger-prick capillary blood was collected serially 5 min before and 15 min, 30 min, 45 min, 60 min, 90 min and 120 min after food consumption using an Accu-chek® Performa (Roche, Germany) glucometer for blood glucose concentration measurement. The GI value was determined from the incremental area under the curve (iAUC) of blood glucose in response to the syrup divided by the iAUC of blood glucose in response to 50 g of glucose solution. The iAUC of blood glucose was calculated using the trapezoidal method by integrating the area from the baseline glucose level and incremental postprandial blood glucose.

Prospective, single-group study

## Ethics statements

The study protocol was reviewed and approved by the Mae Fah Luang University Ethics Committee on Human Research (REH-62320), and the study was registered on January 25, 2021 (NCT04728009).

## **Participants**

Apparently healthy adults at Mae Fah Luang and Chulalongkorn Universities aged 18–60 yr who had glycated hemoglobin (HbA1c) < 7% (n = 8) were enrolled in the study. Persons were excluded if they had the following conditions: (i) self-reported immunodeficiency diseases, autoimmune diseases, infectious diseases, diabetes, thyroid diseases, cancer, hepatic or renal dysfunction or both, uncontrollable illnesses and life-threatening diseases, (ii) allergy to longan and lingzhi products, (iii) use of medications, herbs and diet supplements affecting immune system, inflammatory response and blood glucose a month before study enrollment and (iv) pregnancy or breastfeeding. Participant recruitment was performed after ethical approval had been obtained. Persons who satisfied the eligibility criteria were asked to sign an informed consent form before participating in the experimental period.

Study procedure

All participants were assigned to consume 5 mL of longan and lingzhi mushroom syrup as a sweetener, daily in the morning for 12 wk. Overnight fasting blood samples were collected at baseline (week 0) and weeks 4, 8 and 12, for measurements of the following outcomes.

Glycemic profile based on fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c);

Hepatic function, based on aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP);

Renal function, based on blood urea nitrogen (BUN) and creatinine (Cr);

 $Immune\ response,\ based\ on\ immunoglobulin\ (Ig),\ including\ IgG,\ IgM,\ IgA,\ and\ IgE$ 

Inflammatory response based on C-reactive protein (CRP).

Study intervention

Longan syrup with lingzhi mushroom extract was formulated and provided by the sponsor company, PC Innova, Inc. The product was registered as a food product under the Food and Drug Administration, Ministry of Public Health, Thailand with registration number 10-1-04741-5-0003. In brief, fresh fruit pulp of longan was stewed in hot water until it softened. No sugar or other additives were added. The pulp was removed using filtration to obtain the concentrated longan juice. Subsequently, spray-dried powder of lingzhi mushroom extract was dissolved in water (50% weight per weight). To obtain the finished product, 99 g of longan juice was mixed with 1 g of the lingzhi extract in water. The sugar content of the syrup was 77 degrees Brix. The product was intended to be used in place of sugar as a beverage sweetener.

## Statistical analysis

Data analysis was performed using the SPSS Statistics, Version 22.0 software package (SPSS. Co., Ltd; Bangkok Thailand). Changes in postprandial glucose excursion in response to the study interventions and changes in the clinical outcomes after daily administration of the syrup throughout the study were analyzed using repeated-measures analysis of variance. Time was considered a factor for the analyses. A *p*-value < 0.05 was considered to indicate statistical significance.

## Results

Participants' demographic data and baseline values of clinical outcomes

Single-dose, crossover experiment

In the single-dose, crossover experiment, 20 nondiabetic, healthy adults with an average age of  $22.45 \pm 1.54$  yr were recruited of whom 60% (n = 12) were female. The average BMI of the study group was  $21.71 \pm 1.59$  kg/m<sup>2</sup>.

A prospective, single-group study

Eight participants were recruited, consisting of seven females (87.5%) and one male (12.5%). Their average age was  $35.19 \pm 5.57$  yr. Table 1 describes the participants' demographic data and baseline values of their clinical outcomes.

Effect on glycemic control

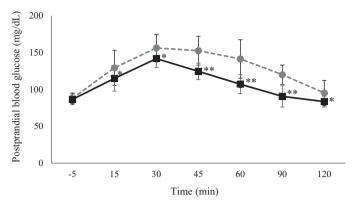
Effect on postprandial glucose excursion and determination of glycemic index

First, postprandial glycemic responses to longan and lingzhi mushroom syrup and 50 g of glucose solution were determined by observing the pattern of blood glucose excursion, as demonstrated in Fig. 1. After consumption of the glucose solution, the blood glucose concentration increased sharply in the early period and reached its maximum level after 30 min. Then, the postprandial blood glucose concentration declined continuously and returned to the baseline level within 120 min. The tested syrup and glucose solution elicited similar postprandial glycemic responses. However, the tested syrup resulted in relatively low postprandial blood glucose elevation at every time point (p < 0.05 at 15 min, 30 min and 120 min and p < 0.001 at 45 min, 60 min and 90 min versus the glucose solution). Restoration of blood glucose to the baseline level was seen at 90 min. In addition, the iAUC  $_{0-120 \text{ min}}$  of

**Table 1** Demographic data of participants and baseline values of clinical outcomes (n = 8)

Demographic data	Number (%)
Underlying diseases	
Hypertension	1(12.5)
None	7(87.5)
Current medications, herbs and diet supplements	
Vitamin B complex	2(25.0)
Astaxanthin	1(12.5)
None	4(50.0)
Currently smoking	0(0)
Currently drinking alcohol	0(0)
Clinical outcome	$Mean \pm SD$
BMI (kg/m²)	24.36 ± 3.99
FPG (mg/dL)	$101.43 \pm 6.19$
HbA1c (%)	$5.16 \pm 0.22$
AST (U/L)	$18.88 \pm 6.62$
ALT (U/L)	$22.63 \pm 7.29$
ALP (U/L)	$65.63 \pm 14.67$
BUN (mg/dL)	$11.13 \pm 1.55$
Cr (mg/dL)	$0.67 \pm 0.08$
IgG (mg/dL)	$1,460.00 \pm 271.82$
IgM (mg/dL)	$200.11 \pm 84.96$
IgA (mg/dL)	$229.25 \pm 35.68$
IgE (IU/mL)	$28.22 \pm 16.95$
CRP (mg/L)	$2.25 \pm 1.63$

BMI: body mass index; FPG: fasting plasma glucose; HbA1c: glycated hemoglobin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; BUN: blood urea nitrogen; Cr. creatinine; Ig. immunoglobulin; CRP: C-reactive protein



**Fig. 1** Blood glucose excursion following consumption of longan and lingzhi mushroom syrup (■) and 50 g of glucose solution (●), where for each time, error bars indicate  $\pm$  SD, \* = significant difference at p < 0.05 and \*\* = significant difference at p < 0.001 vs. the glucose solution

blood glucose following consumption of the tested syrup was significantly lower versus the glucose solution ( $327.83 \pm 19.81$  mg/dL.hr versus  $384.08 \pm 28.28$  mg/dL.hr for syrup and glucose solution, respectively). Second, the GI value of the tested syrup was identified. Compared to the reference glucose solution (GI = 100), the GI value of the longan and lingzhi mushroom syrup was 85.35.

Effect on fasting plasma glucose and glycated hemoglobin Measurements of FPG and HbA1c were performed to determine the long-term effects of the syrup on the glycemic profile. The mean concentrations of FPG and HbA1c did not differ significantly from the baseline as shown in Table 2.

## Effect on hepatic and renal function

No changes in the mean concentrations of AST, ALT, ALP, BUN and Cr were found, with the values of all parameters being in normal ranges throughout the study, as reported in Table 2.

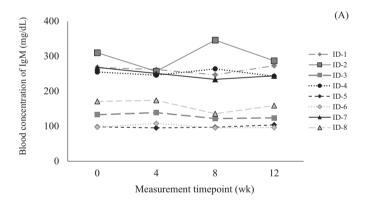
# Effect on the immune response

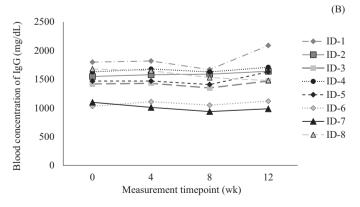
Blood concentrations of the immunoglobulins IgG, IgM, IgA and IgE were measured to evaluate the effect of longan syrup with lingzhi mushroom extract on the immune system. At baseline, the mean values of all immunoglobulins, except IgM, were within the normal ranges. Table 2 shows that compared to the baseline, there were no variations in the levels of IgG, IgM, IgA and IgE throughout the 12 wk study period. Nonetheless, a significant decrease in IgG was observed at week 8 compared with week 4 (-72.63 mg/dL; 95% confidence

intervals of -133.977 mg/dL to -11.273 mg/dL and p = 0.021). The mean level of IgG was subsequently restored at the end of the study. The increase in IgG was seen in six of the eight (75%) participants (Fig. 2A). However, there was no change in the mean IgM concentration after receiving the intervention. Interestingly, the level of IgM tended to decrease, specifically in four of the five (80%) participants whose IgM values were outside the normal reference range at the beginning of the study (Fig. 2B).

## Effect on inflammatory response

CRP was evaluated as an indicator of the inflammatory response. No significant change in CRP was found at any measurement time, as shown in Table 2. Interestingly, there was one participant who presented with a moderately high CRP at baseline for whom a decreasing trend in CRP was observed (6.23 mg/L versus 5.42 mg/L at week 0 and week 12, respectively) after daily consumption of the tested syrup for 12 wk.





**Fig. 2** Spaghetti plots of individual changes in blood concentrations of: (A) IgG; (B) IgM throughout the study, where each line (ID-1 to ID-8) represents one participant (total n = 8)

**Table 2** Mean concentrations ( $\pm$  SD) of blood glucose, parameters related to hepatic and renal functions, immunoglobulins and inflammatory marker after syrup consumption (n = 8)

Outcome	$Mean \pm SD$	Mean change (95% confidence intervals)	<i>p</i> -value
Blood glucose			
FPG (mg/dL)			
Week 0	$101.43 \pm 6.19$	-	-
Week 4	$101.86 \pm 2.97$	0.43 (-8.29, 9.14)	1.000
Week 8	$102.29 \pm 2.87$	0.86 (-8.32, 10.03)	1.000
Week 12	$102.71 \pm 2.06$	1.29 (-6.43, 9.00)	1.000
HbA1c (%)			
Week 0	$5.16 \pm 0.22$	-	-
Week 4	$5.17 \pm 0.11$	0.01 (-0.32, 0.35)	1.000
Week 8	$5.19 \pm 0.11$	0.03 (-0.31, 0.36)	1.000
Week 12	$5.20 \pm 0.82$	0.04 (-0.22, 0.31)	1.000
Hepatic function			
AST (U/L)			
Week 0	$18.88 \pm 6.62$	-	-
Week 4	$18.13 \pm 6.90$	-0.75 (-4.92, 3.42)	1.000
Week 8	$19.25 \pm 6.78$	0.38 (-2.37, 3.12)	1.000
Week 12	$17.38 \pm 5.97$	-1.50 (-4.80, 1.80)	0.851
ALT (U/L)			
Week 0	$22.63 \pm 7.29$	-	-
Week 4	$22.00 \pm 9.00$	-0.63 (-4.69, 3.44)	1.000
Week 8	$23.88 \pm 9.39$	1.25 (-3.69, 6.19)	1.000
Week 12	$21.25 \pm 5.36$	-1.38 (-8.48, 5.73)	1.000
ALP (U/L)			
Week 0	$65.63 \pm 14.67$	-	-
Week 4	$62.25 \pm 15.52$	-3.38 (-10.31, 3.56)	0.721
Week 8	$64.00 \pm 15.55$	-1.63 (-5.86, 2.61)	1.000
Week 12	$62.63 \pm 13.71$	-3.00 (-9.66, 3.66)	0.873
Renal function			
BUN (mg/dL)			
Week 0	$11.13 \pm 1.55$	-	-
Week 4	$10.81 \pm 1.77$	-0.31 (-1.46, 0.84)	1.000
Week 8	$11.13 \pm 1.91$	0.00 (-1.26, 1.26)	1.000
Week 12	$11.18 \pm 2.34$	0.05 (-2.46, 2.56)	1.000
Cr (mg/dL)			
Week 0	$0.67 \pm 0.08$	-	-
Week 4	$0.71 \pm 0.08$	0.04 (-0.01, 0.10)	0.157
Week 8	$0.70 \pm 0.10$	0.02 (-0.03, 0.08)	1.000
Week 12	$0.67 \pm 0.09$	-0.01 (-0.05, 0.03)	1.000

Table 2 Continued

Outcome	$Mean \pm SD$	Mean change (95% confidence intervals)	<i>p</i> -value
Immune response			
IgG (mg/dL)			
Week 0	$1,\!460.00 \pm 271.82$	-	-
Week 4	$1,468.75 \pm 281.30$	8.75 (-57.67, 75.17)	1.000
Week 8	$1,396.13 \pm 271.58$	-63.88 (-164.84, 37.09)	0.330
Week 12	$1,515.75 \pm 345.71$	55.75 (-140.36, 251.86)	1.000
IgM (mg/dL)			
Week 0	$200.11 \pm 84.96$	-	-
Week 4	$191.54 \pm 70.77$	-8.56 (-34.25, 17.10)	1.000
Week 8	$192.74 \pm 92.57$	-7.38 (-37.68, 22.93)	1.000
Week 12	$191.31 \pm 78.80$	-8.80 (-23.47, 5.87)	0.393
IgA (mg/dL)			
Week 0	$229.25 \pm 35.68$	-	-
Week 4	$231.00 \pm 39.01$	1.75 (-9.64, 13.14)	1.000
Week 8	$218.50 \pm 30.07$	-10.75 (-28.65, 7.15)	0.392
Week 12	$234.38 \pm 42.71$	5.13 (-19.04, 29.29)	1.000
IgE (IU/mL)			
Week 0	$28.22 \pm 16.95$	-	
Week 4	$30.04 \pm 18.02$	1.83 (-6.21, 9.86)	1.000
Week 8	$30.47 \pm 19.41$	2.25 (-7.94, 12.44)	1.000
Week 12	$31.21 \pm 19.55$	2.99 (-6.67, 12.65)	1.000
Inflammatory response			
CRP (mg/L)			
Week 0	$2.25 \pm 1.63$	-	-
Week 4	$2.78 \pm 1.51$	0.53 (-0.32, 1.38)	0.346
Week 8	$2.43 \pm 1.98$	0.18 (-0.72, 1.07)	1.000
Week 12	$2.53 \pm 1.37$	0.28 (-0.77, 1.33)	1.000

FPG: fasting plasma glucose; HbA1c: glycated hemoglobin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; BUN: blood urea nitrogen; Cr: creatinine; Ig: immunoglobulin; CRP: C-reactive protein

## Discussion

The safety of longan syrup with lingzhi mushroom extract was evaluated by testing for the presence of adverse effects on the glycemic profile and hepatic and renal functions. Longan syrup with lingzhi mushroom extract is categorized as a carbohydrate-containing food. Hence, determining the effect of the syrup on the glycemic profile is critical to ensure that the syrup does not induce the development of diabetes and can be consumed safely by healthy persons as well as diabetic patients. The current study evaluated the acute and long-term effects of the syrup on blood glucose and the GI value of

the syrup was determined, indicating longan syrup with lingzhi mushroom extract is a high-GI food (GI = 85.35) so that it can rapidly raise postprandial blood glucose and aggravate insulin secretion. Nonetheless, the pattern of postprandial glycemic response to a single-dose administration of the syrup appeared better than that of the glucose solution because the syrup increased the blood glucose concentration to a relatively low level. Furthermore, the elevation in blood glucose was mollified (by insulin-stimulated glucose disposal) sooner after bolus administration of syrup versus the glucose solution. The pharmacokinetic profile of fructose, which is the fundamental element of the syrup, provides

a plausible explanation for these findings. In comparison with other monosaccharides, fructose molecules are digested and absorbed into the blood circulation at a slower rate, while they are quickly absorbed into peripheral cells during the glucose uptake process (Chen et al., 2011). In addition, the GI value of fructose at 15 is considerably lower than that of glucose at 100 (Chen et al., 2011). The daily administration of the syrup had no significant effect on FPG, HbA1c or any parameters related to hepatic and renal functions. The results indicated that moderate consumption of longan syrup with lingzhi mushroom extract was neither related to induction of diabetes nor implicated in hepatic or renal impairment.

The current study also determined the preliminary effect of longan syrup with lingzhi mushroom extract on immune and anti-inflammatory responses in healthy persons. No significant alterations were observed in the mean blood concentrations of immunoglobulins and CRP. However, the individuallevel analysis identified favorable trends of improvement in immune and inflammatory responses. First, the syrup restored the decreased level of IgG in 75% of participants. The mild reduction in IgG during the first 8 wk of the syrup supplementation was unclear. No evidence demonstrated the reduction in immunoglobulins following longan and lingzhi mushroom consumption. It was assumed that the decreased IgG, at least, might not be likely to be clinically significant as there were no reports of any signs and symptoms that related to IgG deficiency. Second, following syrup administration, the blood IgM concentration tended to decrease in any person who had an elevated IgM level at baseline. The decrease in IgM could suggest the alleviation of pathogenic triggers. The IgG and IgM antibodies play a pivotal role in humoral immunity against invading pathogens and IgG is the most abundant immunoglobulin found in blood and body fluids (Schroeder and Cavacini, 2010). Insufficient IgG increases susceptibility to infection and illnesses (Fried and Bonilla, 2009). IgM is considered an indicator of acute exposure to pathogens, since it is involved in the primary immune response (Schroeder and Cavacini, 2010). Therefore, the observed changes in the IgG and IgM levels suggested a promising modulatory effect of the syrup on immune function.

A decrease in CRP was observed (as a marker for inflammation) in a participant who had abnormally high CRP at the end of the study, although there was no significant effect on the mean CRP level. These results indicated that daily administration of the syrup may also alleviate inflammation. The slight change in immune status could be explained by

the nature of the immune-defense mechanism in a normal person. The immune system is generally in surveillance mode. Immune cells can eliminate foreign substances without presenting symptoms in individuals who have healthy immune function. Massive responses to invading substances, including elevation in immune cell proliferation and cytokine secretion, can be detected when the levels of pathogens increase substantially in the body (Percival, 2016).

Many studies agree that longan has potential as a nutraceutical and functional food. For example, longan stimulated systemic immunity by activating macrophage phagocytosis (Yi et al., 2015) and lymphocyte proliferation (Meng et al., 2014; Yi et al., 2012). Furthermore, it strengthened intestinal mucosal immunity by increasing the secretion of mucosal antibodies (Bai et al., 2020) and stimulated the growth of probiotic bacteria, including Streptococcus thermophiles, Lactobacillus acidophilus, and Lactobacillus delbrueckii in the gastrointestinal tract (Cheng et al., 2018). Polysaccharides are known as the dominant compound responsible for the immunomodulatory properties of longan fruit pulp and in addition, water extract of longan reduced inflammation in a preclinical study, where the proposed mechanisms of action were suppression of lipopolysaccharideinduced nitric oxide (NO) and tumor necrosis factor-α production in macrophages (Huang et al., 2012). For its part, lingzhi mushroom has an immunomodulating effect through various pathways in *in vitro* and *in vivo* experiments. For example, its polysaccharides promoted the functional maturation of dendritic cells, the important antigen-presenting cells that serve as the initiator of immune response (Chan et al., 2007). In addition, the fruiting body extract of lingzhi mushroom increased the phagocytic activity of immune cells (Wang and Lin, 2019). A proteoglycan derived from the fruiting body was capable of enhancing macrophage proliferation and modulating cytokine response (Ji et al., 2007). Similarly, lingzhi polysaccharides stimulated cytokine production and secretion (K. I. Lin et al., 2006).

The limitations of the present work included the study design and sample size. A randomized controlled trial with a larger sample size of healthy volunteers should be conducted. The relatively low proportion of male participants should be addressed in future work and the effect of gender differences on clinical outcomes should be carefully considered. Diabetic patients and immunocompromised hosts should also be included as participants in future research studies to determine whether the syrup is safe and effective in specific populations.

The preliminary findings of the current study demonstrated that daily administration of 5 mL of longan syrup with lingzhi mushroom extract was safe and was not associated with any significant adverse events. The syrup also showed promising effects on immune and anti-inflammatory responses.

#### **Conflict of Interest**

The authors declare that there are no conflicts of interest.

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