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PREFACE

Praise and gratitude that the Jurnal Ilmiah kedokteran Wijaya Kusuma (JIKW) Vol. 11, No. 2, September 2022 edition published. This issue contains articles that discuss aspects of Surgery, Pediatric, Neurology, Physiology, Biochemistry, Biomedical Sciences, Pharmacology, and Public Health Sciences, from Original research, Case Reports, as well as literature review.

Jurnal Ilmiah Kedokteran Wijaya Kusuma (JIKW) receive scientific articles from original research, reports or case studies, studies or literature reviews, as well as medical science, which are oriented to updating information in medical science and technology. It expected be the sources of scientific information and contributing in overcoming medical problems.

The editors invite various scientists from various higher education and research institutions to provide scientific contributions, both in the form of research results and scientific studies on various topics of Health and Medical Science. We welcoming for critics, inputs from readers, medical professionals, or those related to publishing, for the sake of increasing the quality of the journal as we all hope.

The editor hopes that the scientific articles published in the Jurnal Ilmiah Kedokteran Wijaya Kusuma (JIKW) will be useful for academics, researchers and professionals working in the medical world and network building for researchers.

Editor in Chief

Jurnal Ilmiah Kedokteran

Wijaya Kusuma

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Review Article

Karakter Positif Sagu: Sebuah Tinjauan Literatur

Abstrak

Sagu adalah makanan kaya karbohidrat yang mengandung pati resisten. Di beberapa daerah di negara-negara seperti Indonesia, Malaysia, dan Papua Nugini, sagu adalah makanan pokok yang

A Sago Positive Character: A Literature Review

Budhi Setiawan^{1*}, Fetriyuna Fetriyuna^{2,3}, Sri Murniani Angelina Letsoin^{4,5}, Ratna Chrismiari Purwestri^{3,6}, Ignasius Radix A.P. Jati⁷

Abstract

Sago is a carbohydrate-rich food that contains resistant starch. In some parts of Indonesia, Malaysia, and Papua New Guinea, sago is a common staple food. Studies have been performed to elucidate the physicochemical and structural properties of sago starches. The paper's objective is to review potential positive physiological responses to sago-based product consumption from previous records. This study is a literature review of preceding published articles related to sago intake in human subjects' research. The literature search was performed through databases with assigned keywords combination and then selection of the articles based on the criteria. The outcomes of this review concluded that sago had a lower glycemic index with immediate intestinal absorption. Sago-based products could provide a suitable energy source for sustaining physical performance and promoting faster recovery after exercise. It can be an appropriate alternative as an energy source for active healthy individuals.

Keywords: Sago; glycemic index; physiological response; resistant starch; carbohydrate; supplement.

umum dikonsumsi. Telah dilakukan penelitian untuk menjelaskan sifat fisikokimia dan struktur pati sagu. Tujuan tinjauan ini adalah untuk meninjau potensi positif respon fisiologis terhadap konsumsi produk berbahan dasar sagu dari penelitian dengan subyek manusia yang dilakukan sebelumnya. Penelitian ini berupa tinjauan literatur dari artikel-artikel yang telah dipublikasi sebelumnya. Pencarian literatur dilakukan pada beberapa basis data dengan

menggunakan kombinasi kata kunci yang telah ditetapkan dan kemudian seleksi artikel didasarkan pada kriteria. Hasil tinjauan ini menyimpulkan bahwa sago memiliki indeks glikemik yang rendah dengan penyerapan di usus yang cepat. Produk berbasis sago menyediakan sumber energi yang dapat mempertahankan

kinerja fisik dan mempercepat pemulihan setelah berolahraga. Sago dapat menjadi sebuah alternatif yang tepat sebagai sumber energi untuk individu sehat yang aktif.

Kata Kunci: *Sago; indeks glikemik; respon fisiologis; pati resisten; karbohidrat; suplemen.*

INTRODUCTION

The Sago palm (*Metroxylon sago*) grows naturally in tropical forests that can produce sago starch extracted from the pith or medulla of the plant's stem (Karim et al., 2008). In Papua New Guinea and Indonesia, sago starch is a staple food that is traditionally prepared by heating stones or by mixing it with hot water (sago porridge, so-called *papeda*) (Metaragakusuma et al., 2016). The significance of sago in the typical diet and as a staple food in the domestic is crucial since it is a food with a high carbohydrate content that is advised to be consumed as a substitute for staple foods. Sago starch usage can aid in a wider variety of foods (Burlingame & Dernini, 2012).

The development of numerous bakery products over the past few decades, including bread, cake, croissants, cookies, and crackers, has raised a demand for wheat flour (Enghiad et al., 2017). Due to increasing consumer awareness of the harmful effects of consuming wheat gluten on health such as wheat allergy, coeliac disease, and non-coeliac gluten sensitivity (Balakireva & Zamyatnin Jr, 2016; Czaja-Bulsa, 2015), it opens up an opportunity for sago utilization. Sago flour and sago starch can be applied as components in bread products, primarily as a partial substitution for wheat flour because of their physicochemical characteristics (Konuma et al., 2012). Sago can be used in bakery goods like cake, bread, and brownies in place of wheat flour because it is gluten-free and a rich source of starch (Kumari, 2019).

Sago starch contains approximately 90 percent carbohydrate per 100 grams, which is about similar to tapioca (89 percent) and sweet potato (86 percent), but significantly higher than white rice (34 percent) or wheat (59 to 71 percent). Furthermore, Sago starch comprises a small proportion of protein and very low-fat content per 100 grams, which are 0.1 percent and 0.01 percent, respectively (Escarnot et al., 2012; Grace & Henry, 2020; Sonia et al., 2015). In order

to increase the protein and micronutrient content of a sago-based cuisine, it was later combined with food sources of both animal and plant protein, such as mung beans, soybeans, mushrooms, and fish as the source of fat and minerals (Azkia et al., 2021; Litaay et al., 2021; Mogra & Midha, 2013; Tjokrokusumo et al., 2019).

In Asian diets, carbohydrates are the main source of energy. However, the quantity and quality of carbohydrates are crucial in the management and prevention of diabetes. Foods with a high glycemic index raise blood sugar and insulin levels, which in turn encourage insulin resistance and type 2 diabetes (T2D) through depleting pancreatic β cells (Mohan et al., 2018). The inquiry of whether high carbohydrate proportion in diets has a beneficial or unfavorable effect on cardiometabolic risk factors has sparked interest, especially for T2D. However, the amount of carbohydrates in high carbohydrate diets has no universal definition among researchers, and studies use different standards. Because the definition of high carbohydrate or low carbohydrate diet can be subjective, the labels "higher carbohydrate diet" or "lower carbohydrate diet" seem to be more accurate (Accurso et al., 2008; Feinman et al., 2015; Kodama et al., 2009; Liebman, 2014; Naude et al., 2014). Conversely, the more common staple foods such as white rice and wheat, have more protein (3.9 percent and 10 to 16 percent, respectively) and fat (2.9 percent and 1.1 to 37 percent, respectively) content (Escarnot et al., 2012; Sonia et al., 2015).

Due to the possibility that carbohydrates may have negative effects on postprandial hyperglycemia and aberrant plasma lipid levels, including an increase in triglyceride levels and a decrease in levels of high-density lipoprotein cholesterol (Hyde et al., 2019; Park et al., 2017), the argument over the benefits and drawbacks of a high carbohydrate diet has grown more heated in recent years. However, current findings indicate

also that a high good carbohydrate diet does not worsen lipid profiles, notably triglyceride and high-density lipoprotein cholesterol, or glycemic management (Mohan et al., 2018). When made up of high-fiber, low-glycemic index/low-glycemic load foods rather than refined carbohydrates or high-glycemic index foods, a high carbohydrate diet has similar effects to a low carbohydrate diet (Jung & Choi, 2017; Mohan et al., 2018; Schwingshackl & Hoffmann, 2013). Since sago composition is mainly carbohydrate and it has been popular as a staple food as well as an alternative of various flours, thus, the main objective of this paper was to review possible physiological responses of sago-based food consumption in humans. The focus of this study was on the beneficial effects of sago on human health, which were supported by both *in vitro* and *in vivo* studies that may shed additional insight on the underlying mechanisms.

METHODS

In order to comprehend the possible impact of sago-based products on physiological responses from human research, a literature review methodology was applied. The literature search used keyword combinations like "sago" AND "supplementation," "sago" AND "glycemic," and "sago" AND "physiologic." The documents were chosen in accordance with the following inclusion criteria: (1) full-text articles from journals that have been published online; (2) publications in English or Indonesian; (3) the articles' relevance to the study's aims; and (4) human subject research. Using the selected keywords, a literature search was conducted from July to August 2022 on Science Direct, PubMed, and Google Scholar databases, and the paper search was limited from 2002 to 2022. All articles obtained from literature search and meeting the criteria were summarized in a table and then discussed using the outcomes of relevant studies.

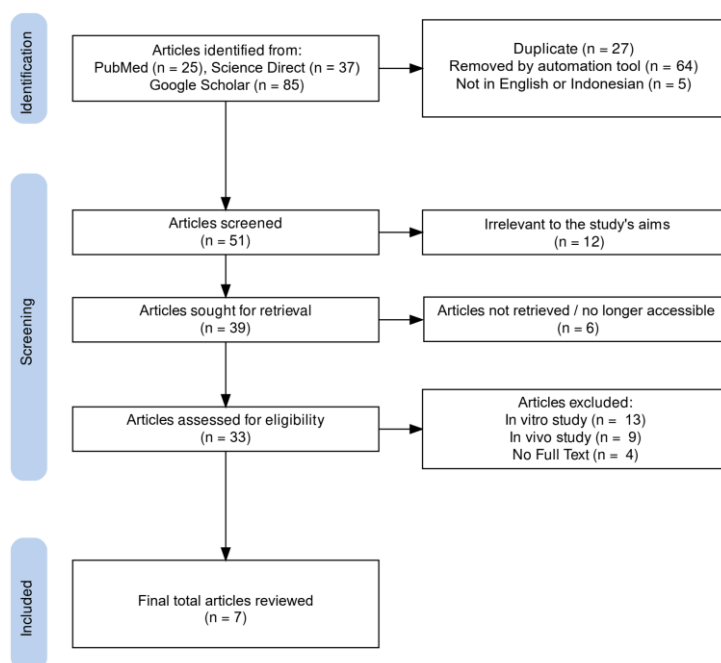


Figure 1. Literature searching strategy and identification via databases using keywords

RESULT

The literature search resulted in 147 papers, where most of the papers from the databases were excluded (Figure 1.). Based on the more advanced search (i.e., the combination of keywords and accessibility) and thorough checking of the relevancy of the studies, the

research objectives, and methodologies for all selected articles, 7 papers in total were included in the review. Four of them were included concerning sago-based product supplementation in exercise and performance, while three articles were reviewed about glycemic index tests (Table 1.).

Table 1. Summary of the physiological effects of sago-based foods consumption

No.	Methods	General outcomes	References
1.	Seven healthy volunteers (males and females) contributed to the glycemic index test using a post-test design. The glycemic indexes of sago noodles and wheat noodles were 26 and 47, respectively, with glucose as the standard. In four different types of sago noodles, the resistance starch composition ranged from 7.55 to 9.45 mg/g, and wheat resistance starch content was 2.44 mg/g.	Different types of Sago noodles had 3.09 to 3.87 times higher resistant starch composition than wheat noodles. Wheat noodles showed 1.81 times higher glycemic index in comparison with sago noodles.	(Haliza et. al., 2006)
2.	Five clinically healthy individuals participated in the post-test designed glycemic index test. The Glycemic Bread Equivalent (GBE) of foods serves as a representation of a food's relative glycemic potency (RGP). Sago khichdi and potatoes had lower glycemic reactions than bread ($p < 0.05$). The potato had an RGP of 52 while sago khichdi had an RGP of 33 per 100 g. Sago khichdi and potatoes had lower overall AUC insulin responses than bread ($p < 0.05$).	Sago khichdi had faster absorption and lower area under the curve (AUC) of glycemic and insulin responses compared to white bread.	(Singhania & Senray, 2012)
3.	Sago glycemic index test with a post-test-controlled design consisted of two groups with 10 healthy volunteers in each group. The glycemic index of pure sago analog rice, sago analog rice with the addition of 5%, and 10% red bean were 40.7, 48.3, and 50.4, respectively.	Pure sago analog rice and analog sago rice with red bean flour have shown a low glycemic index.	(Wahjuningsih et al. 2016)
4.	Prospective experimental post-test design with twelve healthy male subjects. The plasma glucose area under the curve (AUC) of sago gel was higher than white bread. The plasma insulin AUC of sago gel was higher than white bread and sago porridge. Sago gel, sago porridge, and sago paste showed comparable glycemic responses. However, the insulin response of sago porridge was higher than sago paste and sago gel.	Supplementation of Sago paste and sago porridge is useful in pre and during exercise to improve performance. Sago gel intake during recovery can be effective during a subsequent endurance activity.	(Ahmad et al., 2009)
5.	A randomized, double-blind placebo-controlled crossover design study with 8 recreational male cyclists as participants. Times to exhaustion after placebo, sago, and sago-soy consumption were 4.09 +/- 1.28, 5.49 +/- 1.20, and 7.53 +/- 2.02 min, respectively. Sago-soy supplementation improved endurance during high-intensity cycling by 84% (44–140%; $p < 0.001$) and by 37% (15–63%; $p < 0.05$) compared to placebo and sago, respectively.	A combination of sago and soy protein consumption could delay fatigue in high-intensity cycling.	(Ghosh et al., 2010)
6.	Eight trained male cyclists participated in a crossover design. Dur-plasma Sago's glucose increased during exercise more than the control did ($p < 0.05$). Substrate oxidation rates, however, remained constant ($p > 0.05$). Higher plasma sodium levels (2 ± 2 mmol/liter) with Dur-Sago were observed, together with lower whole-body sweat loss (544 ± 636 g) and decreased plasma volume contraction (all $p < 0.05$). Dur-Sago caused an increase in heart rate	Sago feeding during exercise with heat stress resulted in some "beneficial" physiological reactions, but the post-prandial performance was unaffected.	(Jusoh et al., 2016a)

<p>(5 ± 13 beats/min), but the performance was comparable to control (+0.9 ± 2.3%, p > 0.05).</p>	
<p>7. Crossover design and the subject included 8 trained male cyclists. Average power output was not different between trials during the first exercise (286 ± 67 vs. 281 ± 59 W), however in the second exercise, the sago group was higher than the control (283 ± 60 vs. 274 ± 61 W, p < 0.05)</p>	<p>Sago consumption during recovery from exercise in a warm, humid environment enhances recovery of performance in the following exercise when compared to a water-only control. (Jusoh et al., 2016b)</p>

DISCUSSION

In 1981, the glycemic index (GI) was introduced for the first time (Jenkins et al., 1981). Groups of 5 to 10 healthy fasting participants were given particular food individually to see how it affected their blood glucose levels. Blood glucose levels were assessed over a period of two hours and expressed as a proportion of the area under the glucose response curve for a given amount of the carbohydrate (Jenkins et al., 1981). It refers to the degree and duration of blood glucose elevation that occurs after a 12-hour fast in response to a particular carbohydrate intake ratio to a standard carbohydrate, typically glucose or white bread. The Glycemic index is divided into three categories: Low GI (below 56), Medium GI (between 56 and 69), and High GI (beyond 69) on a scale from 0 to 100 (Augustin et al., 2015). It has been shown that sago had a lower glycemic index value (40.7, low level) (Wahjuningsih et al., 2016) compared to the other staple foods, for instance, white rice (61–87, medium to high level) and sweet potato (77, medium) (Osman et al., 2021). Other studies reported the values of sago glycemic index using different settings were 27 (Haliza et al., 2006) and 33 bread equivalent per 100 g (Singhania & Senray, 2012). However, the three commonly used glycemic index categories may be incorrectly assigned to foods due to variations in GI methodologies. It could be related to variations in baseline HbA1c and insulin index, indicating that even in people with normoglycemia, longer-term glycemic control and insulin responsiveness have an impact on the GI score (Matthan et al., 2016).

In human studies, sago has shown preliminary evidence for a beneficial effect on exercise performance (Table 2.). Despite sago having a lower glycemic index, sago-based products provide a higher glycemic response that can improve physical performance during exercise (Ghosh et al., 2010; Matthan et al., 2016; Wahjuningsih et al., 2016). Sago-based meals have demonstrated higher glycemic and insulinemic

responses when compared to white bread, and therefore, their intake may improve performance in prolonged exercise (Ahmad et al., 2009). Hence, sago could be an option as a food or supplement for athletes or people in physical exercise to maintain performance and accelerate recovery. It could be due to starch-based foods that are high amylopectin content (e.g., sago and potatoes) speeding up the absorption of sugar, supplying the cells' need for energy immediately (Singhania & Senray, 2012).

Sago is more likely to be suitable as a supplement before and during exercise because of its physical and chemical characteristics. For example, sago consumption during exercise showed a beneficial physiologic response (Jusoh et al., 2016a). Also, sago consumption in a recovery time could improve performance during a subsequent exercise period compared to a water-only control. It was because of blood glucose levels following recovery from sago consumption were also greater (Jusoh et al., 2016b). Nevertheless, further study is required to compare the findings to other known carbohydrate sources. Meanwhile, research was also performed by combining sago with soy protein to improve the protein content of the sago-based product and its functionality. Sago and soy protein consumed after moderately strenuous cycling exercise improved subsequent high-intensity endurance capacity when compared to sago alone and a placebo (Ghosh et al., 2010).

Resistant starch (RS) refers to all types of starch that are digested in the colon to produce short chain fatty acids but are inaccessible to human digestive enzymes (Ashwar et al., 2016). Table 2. describes that RS can be divided into five types (RS1–RS5), some of which are created or altered commercially and added to food as functional ingredients (types 2, 3, and 4), while others occur naturally in foods (types 1, 2, 3, and 5) (Lockyer & Nugent, 2017; Patterson et al., 2020; Tian & Sun, 2020). On the other hand, prebiotics

are known as nutrients or food elements that resist digestion in the upper gastrointestinal tract, fermented by the intestinal microbiota, and on a selective basis, stimulating the growth and/or activity of the beneficial intestinal bacteria. An essential component of the concept is that it must improve host health (Zaman & Sarbini, 2016). Resistant starch type 3 (RS3) can be produced from different parts (top and bottom) of *Metroxylon sagu* with different growth stages (Abd Rashid et al., 2020). Produced from

Metroxylon sagu starch, sago resistant starch type III (RS3) has been shown resistant to digestion by stomach acids and enzymes. Additionally, sago RS3 displayed prebiotic properties such as inducing beneficial gut bacteria (e.g., *Bifidobacterium sp.*, *Lactobacillus bulgaricus*, *Clostridium butyricum*, *Eubacterium rectale*) growth with short-chain fatty acid released even on par with those of commercial prebiotics (Purwani et al., 2012; Zi-Ni et al., 2015; Zi-Ni & Rosma, 2020).

Table 2. Classification of types of resistant starch (RS), characteristics, and food sources (Ashwar et al., 2016; Lockyer & Nugent, 2017; Raigond et al., 2015)

RS types	Characteristics	Food sources
RS1	Because of the physical defense provided by protein matrices and cell walls, which thwart digesting enzymes.	Whole or partly milled grains, legumes, and seeds.
RS2	Starches are resistant to enzymatic hydrolysis because of their crystalline structure.	Green bananas, raw potatoes, high-amylose maize, and ginkgo starch.
RS3	When starchy foods are cooked and chilled, retrograded starch is created. The establishment of hydrogen bonds during retrogradation allows the polymer chains to reassociate and form double helices.	Potatoes that have been cooked and then allowed to cool, crusty bread, pasta, rice, cornflakes, and food items that have undergone repeated moist heat treatment.
RS4	Modified starch that has undergone chemical alterations, such as esterification, etherification, or cross-linking. Starch cannot be digested due to chemical changes that limit enzyme access and create atypical links.	Foods that have chemically modified starches (e.g., bread and cakes).
RS5	The foods contain amylose-lipid complexes, which can be produced artificially and added to foods or develop naturally during processing and reform after cooking.	Foods with high amylose-lipid complex content.

Besides sago RS3, sago fronds can be enzymatically hydrolyzed to produce sago frond sugar (SFS), which contains 16 to 18 percent cellobiose, known as a type of prebiotic sugar (Dyg Salwani et al., 2018). The sago starch oligosaccharides have been used to enhance the growth of lactic acid bacteria (*Lactobacillus bulgaricus* and *Streptococcus thermophilus*) in homemade yogurt, with the potential to be developed as prebiotic food (Shima et al., 2012). Traditionally processed sago starch (*Lemantak*) had resistant starch content at 62.61 percent and could be used as fermentation substrate for *Lactobacillus acidophilus* and *Bifidobacterium animalis* at 37°C for 24 hours in anaerobic conditions (Arshad et al., 2018). Hence, these abovementioned in vitro study outcomes confirmed the prebiotic properties of sago.

Resistant starch is well known for its role in regulating obesity and T2D through the modification of gut microbiota composition.

Starch-degrading enzymes and intestinal metabolites are produced as a result of the change of a specific microbial composition, which enhances the function of the healthy gut barrier (Liu et al., 2020). Gut microbial fermentation of resistant starch in the large bowel increases the short-chain fatty acids (SCFA) composition such as acetate, propionate, and butyrate (Liu et al., 2020; Topping & Clifton, 2001). By controlling luminal pH and mucus production, short-chain fatty acids are crucial for maintaining the integrity of the gut. Additionally, they fuel epithelial cells and control mucosal immune response (Blaak et al., 2020). It has been shown that resistant starch might reduce hyperglycemia, hyperinsulinemia, and hyperlipidemia. This can be due to restricting gluconeogenesis, increasing glycogenesis, maintaining glucose and lipid homeostasis, and ameliorating pancreatic dysfunction (Meenu & Xu, 2019). In addition, studies have shown that resistant starch intervention may improve the

serum level of inflammatory biomarkers such as interleukin-6 and tumor necrosis factor-alpha (Vahdat et al., 2020), thus it is suggested that resistant starch can reduce inflammatory incidence.

In animal model studies, sago-based product interventions have demonstrated potential beneficial effects on metabolic indices. Sago-resistant starch has shown potential as a strategy for obesity and overweight control in obese rats. Sago-resistant starch promoted satiety, lowered visceral adipose tissue, and improved hepatic lipid content (Thompson et al., 2021). The anti-obesity effect could be due to the prebiotic properties of sago starch which had resulted in higher *Bifidobacterium spp.* and *Lactobacillus spp.* growth, the significant increase in the total concentration of fecal and caecum short-chain fatty acids, and lower fat accumulation in the liver (Laang, 2018). In line with the aforementioned outcomes, sago consumption has played a significant role in diabetic animal models. For example, sago-based product intervention has improved insulin sensitivity and lipid profile (Wahjuningsih et al., 2018) as well as stimulated better pancreatic Langerhans β - cell function. The mechanisms involved are absorption reduction, insulin expression of pancreatic β -cell elevation, and the total amount of short-chain fatty acids rise (Wahjuningsih et al., 2020). Furthermore, modified sago-resistant starches (RS2 and RS3 types) intake could down/upregulate genes that are related to the regulation and enzymatic pathway of glucose and glycogen metabolism in the liver which has an important role in diabetes management (Lokman et al., 2021). Additionally, besides metabolic benefits, sago supplementation has been shown advantageous effects on antioxidant activity indices such as liver superoxide dismutase, catalase, and liver α -tocopherol (Hirao & Igarashi, 2003).

This paper was constrained by limited amount of published human subjects research on Sago. Furthermore, the number of participants were also small and most of the studies were conducted in Asia. Discussion part utilized pertinent *in vitro* and *in vivo* studies for possible explanations and may produce different outcomes in human. Similarly, consumption of Sago-based products using different food combinations and

heat treatments as well methodology settings could reflect a range of values.

CONCLUSION

This review revealed possible influences of sago starch consumption on human health, which can be further study direction. Sago-resistant starch provides favorable physiological responses that can be due to its lower glycemic index and faster absorption. Furthermore, prebiotic properties of Sago resistant starch induce beneficial intestinal microbiota composition that results in increased SCFA levels and better intestinal epithelium protection. Consumption of sago starches has a favorable impact on metabolic parameters like improved pancreatic β -cells and insulin functions as well as lipid panels. Sago-based foods make a good source of supplements for sustaining physical performance and hastening recovery in a period of peri-exercise. The physical and chemical properties of sago, which is frequently grown and consumed in warm, humid climates, make it suitable as a supplement for physical work out. Sago can be a suitable alternative as an energy source for active healthy people as well as disorders like obesity and diabetes because of its beneficial physiological benefits. More multicentered human studies are needed to provide in depth understanding. Sago-based food supplements, together with balanced macronutrient composition and micronutrient fortification on people, may lead to an improvement in value.

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