Development of functional foods based on anthocyanin-rich riceberry rice extract (*Oryza sativa* L.) and its effects on postprandial biochemical parameters in human.

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A Dissertation Submitted in Partial Fulfillment of the Requirements
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การพัฒนาอาหารฟังก์ชันจากสารสกัดข้าวไรซ์เบอร์รี่ที่อุดมไปด้วยสารแอนโทไซยานินและผลกระทบต่อตัวชี้วัดทางชีวเคมีหลังรับประทานอาหารในคน

น.ส.ธนิสา อนุญาหงษ์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
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Field of Study	Food and Nutrition
Thesis Advisor	Associate Professor SIRICHAI ADISAKWATTANA, Ph.D.
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ธนิสา อนุญาหงษ์ : การพัฒนาอาหารฟังก์ชันจากสารสกัดข้าวไรซ์เบอร์รี่ที่อุดมไปด้วยสารแอนโทไซยานินและผลกระทบต่อตัวชี้วัดทางชีวเคมีหลังรับประทานอาหารในคน. (Development of functional foods based on anthocyanin-rich riceberry rice extract (*Oryza sativa* L.) and its effects on postprandial biochemical parameters in human.) อ.ที่ปรึกษาหลัก : รศ. ดร.สิริชัย อดิศักดิ์วัฒนา, อ.ที่ปรึกษาร่วม : ดร.จรูญศรี ชูศักดิ์

ข้าวไรซ์เบอร์รี่เป็นการผสมข้ามพันธุ์ของข้าวหอมนิลที่มีสีม่วงกับข้าวดอกมะลิ 105 เม็ดสีของข้าวไรซ์เบอร์รี่มีสารต้านอนุมูลอิสระสูงโดยเฉพาะสารแอนโทไซยานิน จากการศึกษาก่อนหน้าพบว่า การประยุกต์ใช้ข้าวไรซ์เบอร์รี่ในผลิตภัณฑ์อาหารสามารถเพิ่มฤทธิ์การต้านอนุมูลอิสระได้ อย่างไรก็ตาม ศักยภาพในการประยุกต์ในอาหารของสารสกัดข้าวไรซ์เบอร์รี่ในโยเกิร์ตและผลิตภัณฑ์เครื่องดื่ม รวมทั้งผลกระทบภายหลังรับประทานผลิตภัณฑ์เหล่านี้ในคนยังไม่มีการศึกษา โดยการศึกษานี้ สารสกัดข้าวไรซ์เบอร์รี่เตรียมจากการผสมของข้าวไรซ์เบอร์รี่กับน้ำในอัตราส่วน 1:2 โดยน้ำหนักต่อปริมาตร ตามด้วยขั้นตอนการทำแห้งเยือกแข็ง ผลการศึกษาพบว่า สารสกัดข้าวไรซ์เบอร์รี่อุดมไปด้วยสารประกอบฟีโนลิคและสารแอนโทไซยานิน ที่เป็นสารพฤกษเคมีหลัก คือ สารไซยานิดิน-3 กลูโคไซด์ และพีโอนิดิน-3-กลูโคไซด์ การเสริมสารสกัดข้าวไรซ์เบอร์รี่ลงในโยเกิร์ต ช่วยเพิ่มปริมาณสารฟีโนลิค สารแอนโทไซยานินและฤทธิ์การต้านอนุมูลอิสระอย่างมีนัยสำคัญทางสถิติ นอกจากนี้ สารสกัดข้าวไรซ์เบอร์รี่ยังมีผลทำให้ค่าซีเนอเรซีสและค่าความแข็งตัวของโยเกิร์ตลดลง เมื่อผ่านระบบการย่อยอาหารจำลอง พบว่าโยเกิร์ตที่เสริมด้วยสารสกัดข้าวไรซ์เบอร์รี่ มีปริมาณสารโพลีฟีนอล สารแอนโทไซยานิน และฤทธิ์การต้านอนุมูลอิสระสูงกว่าโยเกิร์ตสูตรควบคุม การเติมสารสกัดข้าวไรซ์เบอร์รี่ร้อยละ 0.125 และ 0.25 โดยน้ำหนักต่อน้ำหนักในโยเกิร์ตไม่พบผลกระทบทางลบของการยอมรับโดยรวมของผู้บริโภค เมื่อเทียบกับโยเกิร์ตสูตรควบคุม เมื่อเก็บรักษาในตู้เย็นเป็นเวลา 21 วัน โยเกิร์ตที่เติมสารสกัดข้าวไรซ์เบอร์รี่ยังคงมีปริมาณสารโพลีฟีนอลและฤทธิ์การต้านอนุมูลอิสระ การบริโภคโยเกิร์ตที่เติมสารสกัดข้าวไรซ์เบอร์รี่ร้อยละ 0.25 ช่วยชะลอการเพิ่มขึ้นของระดับน้ำตาลในเลือดและเพิ่มการต้านอนุมูลอิสระในเลือดภายหลังรับประทานอาหารในกลุ่มตัวอย่างสุขภาพดีอย่างมีนัยสำคัญทางสถิติ โดยคะแนนความหิว ความอิ่ม ความอยากรับประทานอาหารและความเต็มอิ่ม ให้ผลเหมือนกันในทุกประเภทของโยเกิร์ต ผลการศึกษาที่น่าสนใจ เมื่อบริโภคอาหารที่มีคาร์โบไฮเดรตสูงไขมันปานกลางร่วมกับเครื่องดื่มสารสกัดข้าวไรซ์เบอร์รี่ (ร้อยละ 0.5 โดยน้ำหนักต่อปริมาตร) ช่วยลดระดับน้ำตาล ฮอร์โมนอินซูลิน ไตรกลีเซอร์ไรด์ กรดไขมันอิสระ และระดับมาลอนไดอัลดีไฮด์ในเลือดภายหลังรับประทานอาหารในคนน้ำหนักเกินและอ้วนอย่างมีนัยสำคัญทางสถิติ นอกจากนี้เครื่องดื่มจากสารสกัดข้าวไรซ์เบอร์รี่ยังช่วยลดสารตัวบ่งชี้การอักเสบ ได้แก่ IL-1β , IL-6 และ TNF-α ภายหลังรับประทานอาหารมีคาร์โบไฮเดรตสูงไขมันปานกลางที่เวลา 3 และ 6 ชั่วโมง แต่อย่างไรก็ตาม ไม่พบความแตกต่างของคะแนนความหิว ความอิ่ม ความอยากรับประทานอาหารและความเต็มอิ่มในอาหารทดสอบทั้งหมด การศึกษานี้แนะนำว่า สารสกัดข้าวไรซ์เบอร์รี่สามารถเป็นส่วนประกอบจากธรรมชาติในการผลิตโยเกิร์ตและเครื่องดื่มเพื่อสุขภาพชนิดใหม่ ซึ่งช่วยลดการตอบสนองของน้ำตาลในเลือด เพิ่มความสามารถในการต้านอนุมูลอิสระ และลดสารเกิดการอักเสบในคนได้

สาขาวิชา อาหารและโภชนาการ ลายมือชื่อนิสิต .....

ปีการศึกษา 2562 ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

ลายมือชื่อ อ.ที่ปรึกษาร่วม .....

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KEYWORD: Riceberry rice, functional food, anthocyanin, postprandial biochemical parameters.

Tanisa Anuyahong : Development of functional foods based on anthocyanin-rich riceberry rice extract (*Oryza sativa* L.) and its effects on postprandial biochemical parameters in human.. Advisor: Assoc. Prof. SIRICHAI ADISAKWATTANA, Ph.D. Co-advisor: Charoonsri Chusak, Ph.D.

Riceberry rice *(Oryza sativa L.)*, is a crossbreed of Kao Hom Nin, a local non-glutinous purple rice and Khoa Dawk Mali 105. Its pigment contains high amount of antioxidant compounds, especially anthocyanins. Previously, riceberry rice exhibited its food application with high antioxidant activity. However, the potential of food application of riceberry rice extract (RBE) in yogurt and beverage products and its postprandial effect on humans remains unknown. In this study, RBE was prepared from a mixture of riceberry rice and distilled water in 1:2 w/v ratio following the freeze-drying process. The results showed that RBE contained phenolic compounds and anthocyanins mainly cyanidin-3-glucoside and peonidin-3-glucoside. The supplementation of RBE to yogurt significantly increased total phenolic (TPC) content, anthocyanin content and antioxidant activity. Furthermore, yogurt representing a reduction of syneresis and firmness can be achieved by RBE. In gastrointestinal digestion, yogurt supplemented with RBE resulted in higher level of TPC, anthocyanin content and antioxidant activity than the control yogurt. The addition of 0.125-0.25% (w/w) RBE into yogurt did not negatively influence the overall acceptability, compared to the control yogurt. The higher TPC and antioxidant activity of yogurt supplemented with 0.125-0.25% (w/w) RBE was observed during 21 days of refrigerated storage. Moreover, acute consumption of yogurt enriched with 0. 25% RBE significantly suppressed postprandial plasma glucose and improved postprandial antioxidant status in healthy subjects. The rating scores of hunger, fullness, desire to eat, and satiety were similarity in all types of yogurts. Interestingly, consumption of high-carbohydrate, moderate-fat (HCMF) meal with RBE beverage (0.5% w/v) significantly attenuated postprandial glucose, insulin, triglyceride, free fatty acid and MDA level in overweight and obese subjects. In addition, it significantly reduced inflammatory cytokines (IL-1β, IL-6 and TNF-α) after 3 and 6 h of HCMF-meal consumption. However, there were no significant differences in the rating scores of hunger, fullness, desire to eat, and satiety among tested meals. This study suggests that RBE offers a promising natural ingredient to produce novel yogurt and functional drink in order to reduce glycemic response, improve antioxidant capacity and reduce inflammatory cytokine in humans.

Field of Study:	Food and Nutrition	Student's Signature .....
Academic Year:	2019	Advisor's Signature .....
		Co-advisor's Signature .....

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CHAPTER I

INTRODUCTION

1.1 Background and significant of the study

Functional foods are defined as foods that they beneficially affect one or more target functions in the body, beyond basic nutrition (Ozen, Pons, & Tur, 2012). The concept of functional foods is not only essential for living but also as a source of mental and physical well-being. Functional foods may prevent and reduce the risk factors for several diseases and enhance physiological function (Howlett, 2008). In recent years, the global market for functional foods has been growing rapidly worldwide. Especially, the main market is Asia Pacific, account for 34% of total revenue worldwide market (Vicentini, Liberatore, & Mastrocola, 2016). It has been shown that several reasons for increasing use of functional foods include personal health awareness, increased incidence of self-medication, increased level of information from health authorities, and desire to good quality of life and scientific developments in nutrition research (Granato et al., 2020). For instance, probiotic yogurt and fermented milk are particularly fashionable gut health products in Japan (Granato et al., 2020), whereas fortification with fiber, calcium, and vitamins are popular in the United States (Siro, Kápolna, Kápolna, & Lugasi, 2008). Typically, plant-based foods such as fruit, vegetable and whole grains are recognized as functional food due to phytochemicals contents and their bioactivities (Shahidi, 2009). Previous reviews stated that bioactive

of functional foods have been promoted as optimal defensive antioxidants by reducing oxidative stress. Antioxidants are commonly found in the plant-based foods such as vitamin C, vitamin E, carotenoids, flavonoid, phenolic acid, and anthocyanins. They have high potential for regulation of metabolic balance and therapeutic options for metabolic syndromes (Brown, Poudyal, & Panchal, 2015; Howlett, 2008).

Today, it has been clearly demonstrated that dietary and lifestyle modification, especially the use of functional food could produce a credibly decreased risks in metabolic syndromes, resulting in decreased comorbidities (Brown et al., 2015). Previous cohort studies revealed that regular consumption of polyphenol; flavone, flavonol and catechin decreased in percentage of body fat, wait-to-hip ratio and lower body mass index (BMI) in Chinese and Netherland people (Chiva-Blanch & Badimon, 2017; Hughes et al., 2008). The positive effects of polyphenols on body fat are due to enhancing thermogenesis, increasing fat oxidation, increasing energy expenditure (Dulloo, Seydoux, Girardier, Chantre, & Vandermander, 2000), enhancing noradrenaline-induced lipolysis in adipose tissue and inhibition of pancreatic lipase activity leading to the favorable changes of abdominal fat distribution (Han et al., 2001). Interestingly, plant bioactive compounds especially polyphenol and anthocyanins have been shown to inhibit pancreatic **α**-amylase and **α**-glucosidase activity consequently to reduce postprandial hyperglycemia (Adisakwattana et al., 2010; McDougall et al., 2005). For example, consumption of *Clitoria ternatea* flower extract with high content of anthocyanins suppressed peak postprandial glucose and insulin concentration (Chusak,

Thilavech, Henry, & Adisakwattana, 2018). Furthermore, consumption of plant-based antioxidant improved plasma antioxidant capacity in human subjects (Scalbert, Manach, Morand, Rémésy, & Jiménez, 2005). It has been investigated that consumption of blueberry, *Clitoria ternatea*, chokeberry or mixed grapes were associated with increased postprandial plasma antioxidants such as ferric reducing ability of plasma (FRAP), oxygen radical absorbance capacity (ORAC) and trolox equivalent antioxidant capacity (TEAC) (Chusak et al., 2018; Nälsén, Basu, Wolk, & Vessby, 2006; Oszmiański & Lachowicz, 2016; Prior et al., 2007). In addition, consumption of strawberry rich anthocyanins significantly attenuated postprandial inflammatory response as measured by high-sensitivity C-reactive protein (hs-CRP) and IL-6 in overweight subjects (Edirisinghe et al., 2011). Likewise, short-term consumption of anthocyanins rich blackcurrant extract significantly lowered the level of TNF-α and IL-6 (Lyall et al., 2009). It has been demonstrated that plant-based anthocyanins may inhibit the activation of NF-kB, resulting in a suppression of TNF-α and IL-6 secretion (Karlsen et al., 2010; Karlsen et al., 2007). Therefore, plant-based anthocyanins may be considered as a functional ingredient for develop functional foods by reduction of postprandial glucose, improvement of plasma antioxidant capacity and lowering of pro-inflammatory cytokines.

Anthocyanins are the group of naturally occurring pigments belonging to the family of polyphenols. They are responsible for red, purple, and blue colors presented

in plants such as blackberries, blueberries, bilberries, grape, strawberries and black rice (Tian et al., 2019). Recent evidences reveal that anthocyanins exert their biological effects including antioxidant activity, anti-hyperglycemia, anti-hyperlipidemia, anti-inflammation, and improvement of gut microbiota (Krga & Milenkovic, 2019; Tian et al., 2019). In current food processing and manufacturing, anthocyanins are often used as a natural food additive and colorant in milk, ice cream and yogurt (Morata, López, Tesfaye, González, & Escott, 2019). Scientists discovered that incorporation of anthocyanins to yogurt improves antioxidant activity (Jaster et al., 2018; Trigueros, Wojdyło, & Sendra, 2014) and promotes the growth of lactic acid bacteria during refrigerated storage (D. Liu & Lv, 2019).

Riceberry rice (*Oryza sativa* L.), a dark purple rice variety from Thailand, is originated from a crossbreed between Hom Nil rice and Jasmine rice. This specific rice cultivar was reported to contain a large amount of cyanidin-3-glucoside (C3G) and peonidin-3-glucoside (P3G), the glycoside form of anthocyanins (Leardkamolkarn et al., 2011). Previous studies have been reported the biological properties of riceberry rice including antioxidant, anti-cancer, anti-hyperglycemic, anti-hyperlipidemic and anti-inflammatory activity (Arjinajarn et al., 2017; Leardkamolkarn et al., 2011). As strategies to prevent diet-related non-communicable diseases (NCDs), riceberry rice has been made to produce commercial rice flour and promote its application in bread with medium glycemic index (GI) and high antioxidant activity (Thiranusornkij, Thamnarathip, Chandrachai, Kuakpetoon, & Adisakwattana, 2019). Furthermore, riceberry rice could

be successfully applied for the formulation of dysphagia diet, a special eating plan for people who have moderately to severely trouble swallowing (Suttireung et al., 2019). Although riceberry rice seems to be a promising functional ingredient, its potential food application in yogurt products and functional beverage has yet to be discovered in this context. Therefore, the objectives of this study were develop the functional food products from anthocyanins-rich riceberry rice extract and assess its influence on postprandial biochemical parameters in human.

1.2 The objectives of the study

 To investigate the effects of probiotics yogurt enriched with riceberry rice extract (*Oryza Sativa* L.) on physicochemical properties, functional properties, probiotic viability and sensory acceptability.

 To determine the effects of probiotic yogurt enriched with riceberry rice extract (*Oryza Sativa* L.) on postprandial glycemic response and antioxidant status in healthy subjects.

 To study the effect of riceberry rice (*Oryza Sativa* L.) beverage with high-carbohydrate, moderate-fat meal on postprandial glycemic response, antioxidant status, lipidemic response, and inflammatory markers in overweight and obese subjects.

1.3 Hypotheses in the study

 Riceberry rice extract maintains physicochemical properties of probiotic yogurt, improve functional properties of probiotic yogurt, increases probiotic viability, and improve sensory acceptability.

 Consumption of probiotic yogurt enriched with riceberry rice extract may decrease postprandial glucose level and increase antioxidant status in healthy subjects.

 Consumption of riceberry rice beverage with high-carbohydrate, moderate-fat meal may decrease postprandial glucose level, increase antioxidant status, decrease lipidemic response and decrease inflammatory markers in overweight and obese subjects.

CHAPTER II

REVIEW OF LITERATURE

2.1 Non-communicable diseases (NCDs)

Non-communicable diseases (NCDs) are globally the leading causes of morbidity and mortality worldwide. According to World Health Organization (WHO), NCDs are defined as the diseases of long duration and with generally slow in progression which are not passable from one person to another (Alwan, 2011). The major four group of NCDs is diabetes, cardiovascular diseases, chronic respiratory diseases and cancers. Interestingly, unhealthy diets are a significantly key modifiable behavioral risk factor for NCDs which contributes to the occurrence of a cluster of disorders known as metabolic syndrome which are abdominal obesity, hypertension, dyslipidemia, and disturbed metabolism of glucose or insulin (Alberti, Zimmet, & Shaw, 2005). Recently, the change in dietary pattern of Asian population has been reported the relationship between the increase in consumption of refined carbohydrates, sugar and saturated fat and the prevalence of metabolic syndromes (Hristova et al., 2014).

2.1.1 Dietary carbohydrate

Carbohydrate, as the major source of dietary energy, provides approximately 45-70% of total energy in the human diet. However, excessive consumption of both naturally and added ingredients from carbohydrate are particularly concerned harmful

health effects such as weight gain, obesity and type 2 diabetes (Wali, Raubenheimer, Senior, Le Couteur, & Simpson, 2020).

2.1.2 Dietary fat

The consumption of high fat diet has been increasing in all populations worldwide. However, the recommendation of total fat intake in adults is reported to be only 20-35% of total energy intake (Lupton et al., 2002). The intake of high amount of saturated fats and trans fatty acids alters postprandial blood lipid level, causing insulin sensitivity. These abnormal functions may lead to development of type 2 diabetes and cardiovascular diseases (Lupton et al., 2002).

2.1.3 Appetite

Appetite referred to as a sensation related to food intake. It is an important factor for influence of eating behavior and energy intake. Satiety defines as the state of inhibition of eating. Hunger defines as a nagging, irritating feeling signifies food deprivation of a degree that the further eating episode should take place. Fullness defines as a sensation of the degree of stomach filling, and prospective food consumption describes as an indicator of the supposing amount of forthcoming food intake (Sørensen, Møller, Flint, Martens, & Raben, 2003) In appetite study, visual analogue scales (VAS) are the most commonly rating methods used in the form of horizontal lines of varying length, with words anchored at each end describing the extremes of a unipolar question (Rogers, Carlyle, Hill, & Blundell, 1988). Therefore, the

subjects are asked about their appetite following a meal including hunger, desire to eat, satiety and fullness and prospective food intake.

2.2 Strategies to control hyperglycemia and hyperlipidemia

2.2.1 Carbohydrate digestion

The digestion of carbohydrate begins in the mount by the action of salivary α-amylase that hydrolyzes α-1,4 linkage of starch granules to maltose. After that, pancreatic α-amylase digests approximately 60% of starch in the small intestine. Then, α-glucosidases including lactase, galactose, and maltase catalyze the hydrolysis of disaccharides to absorbable monosaccharides in the surface of intestinal epithelial cells (Dashty, 2013). The monosaccharides are absorbed into the blood circulation via passive and active transport systems. The glucose is uptake to different cells in order to maintain blood sugar in the hypoglycemic state and energy supply to the peripheral tissues such as the liver, skeletal muscle and adipose tissue (Dashty, 2013; FAIRCHILD et al., 2003).

2.2.2 Fat digestion

In the process of fat digestion and absorption, dietary fat, an energy-dense nutrient, provides essential fatty acids (FAs), enhancing absorption of fat-soluble vitamin such as vitamin E and D (Carreiro & Buhman, 2019). The majority of dietary fat is present in the form of triacylglycerol (TAG) which consists of three fatty acid

molecules connected to a 3-carbon glycerol backbone. The digestion of dietary fat initiates at the small intestine by the action of pancreatic lipase through hydrolysis of TAG to two free fatty acids (FFAs) and 2-monoacylglycerol (MAG). The digestive products are formed to cholesterol micellization by incorporation with bile acid and free cholesterols. After FFAs and MAG have been taken up by enterocytes, they are resynthesized into TAG at the endoplasmic reticulum membrane and can be incorporated into chylomicrons (CMs) transported by lymph and then blood circulation to tissues (Carreiro & Buhman, 2019).

Consumption of high-carbohydrate or high-fat meal often results in postprandial hyperglycemia and/or hypertriglyceridemia (Lacroix, Des Rosiers, Tardif, & Nigam, 2012) that may influence the postprandial pro-oxidative status (Gregersen, Samocha-Bonet, Heilbronn, & Campbell, 2012) Hyperglycemia or high blood glucose is a main effect on oxidative stress in which imbalances between free radical and antioxidant defense. In mitochondria, the high concentration of glucose induces the formation of reactive oxygen species (ROS) include superoxide (O^{-}_{2}), hydrogen peroxide (H_2O_2) and reduced the power of antioxidant enzymes (Lacroix et al., 2012) Moreover, an exaggerated rise in postprandial hyperglycemia markedly induces endothelial dysfunction, consequently increases circulating levels of intracellular adhesion molecule 1 (ICAM 1), and the production of inflammatory cytokines including IL-6, TNF-

α and IL-18 (A Ceriello et al., 1998). The elevation of this cytokines has been reported to interfere the insulin signaling and impairment of β-cell function (C. Liu et al., 2016).

2.2.3 Diets related to digestive enzyme inhibition

2.2.3.1 Carbohydrate digestive enzyme inhibition

In order to control blood glucose, the inhibition of carbohydrate digestive enzymes such as pancreatic α-amylase and intestinal α-glucosidase is one of the therapeutic approaches for suppression of postprandial hyperglycemia (Adisakwattana, Ruengsamran, Kampa, & Sompong, 2012). Several natural plants have demonstrated the inhibitory effect against intestinal α glucosidase and pancreatic α-amylase activities (Adisakwattana, Ruengsamran, et al. , 2012; Akkarachiyasit, Charoenlertkul, Yibchok- anun, & Adisakwattana, 2010; Poosri, Thilavech, Pasukamonset, Suparpprom, & Adisakwattana, 2019). Many studies investigates the potential of plant or plant extract such as seaweed, *criteria ternatea*, berry, and riceberry rice to inhibit carbohydrate digestive enzymes (Boath, Grussu, Stewart, & McDougall, 2012; Chusak et al., 2018; Pantidos, Boath, Lund, Conner, & McDougall, 2014; Poosri et al., 2019). Figure 1 shows the purposed mechanisms of plant diets for inhibiting carbohydrate digestion and absorption.

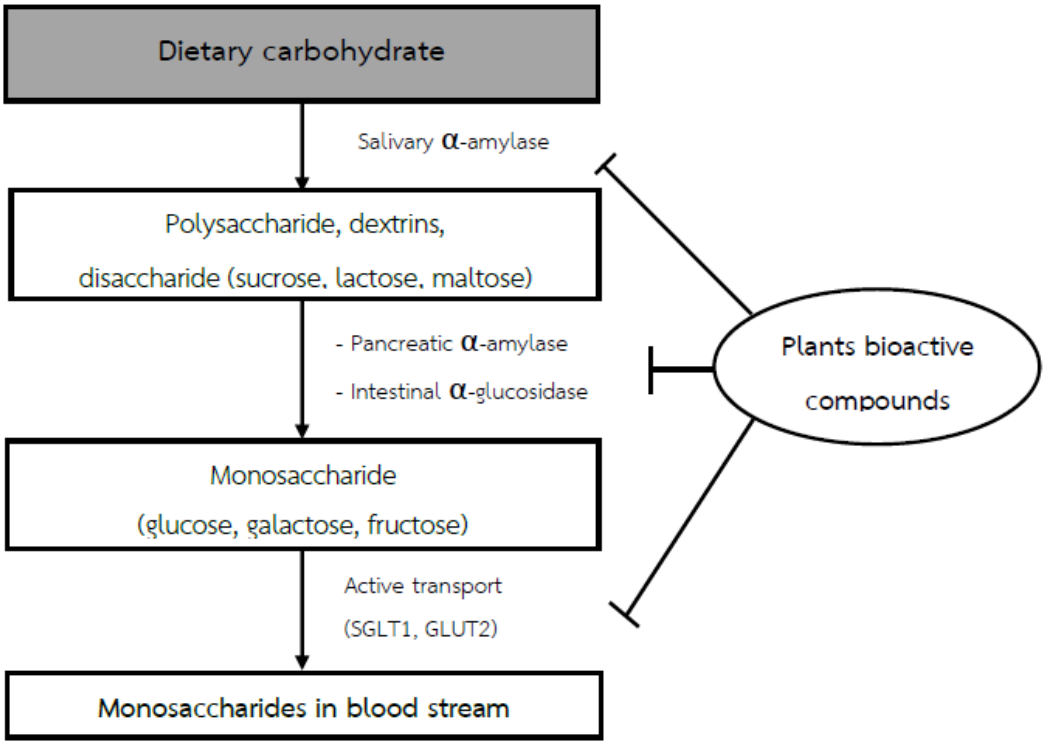


Figure 1 The purposed mechanisms of plant diets for inhibiting carbohydrate digestion and absorption.

2.2.3.2 Fat digestive enzyme inhibition

Inhibition of fat digestion and absorption is an alternative approach of controlling postprandial hyperlipidemic response (Adisakwattana, Intrawangso, Hemrid, Chanathong, & Mäkynen, 2012). Pancreatic lipase is known as a key enzyme in dietary triglycerides and fatty acids (de la Garza, Milagro, Boque, Campión, & Martínez, 2011). Several plant extract have been investigated the inhibitory effect on pancreatic lipase, cholesterol micellization, bile acid binding which may lead to delay postprandial hypertriacylglycerolaemia and hypercholesteroleamia (Adisakwattana, Intrawangso, et

al., 2012; Poosri et al., 2019). Figure 2 illustrates the purposed mechanisms for inhibiting fat digestion and absorption modified from de la Garza et al. (2011).

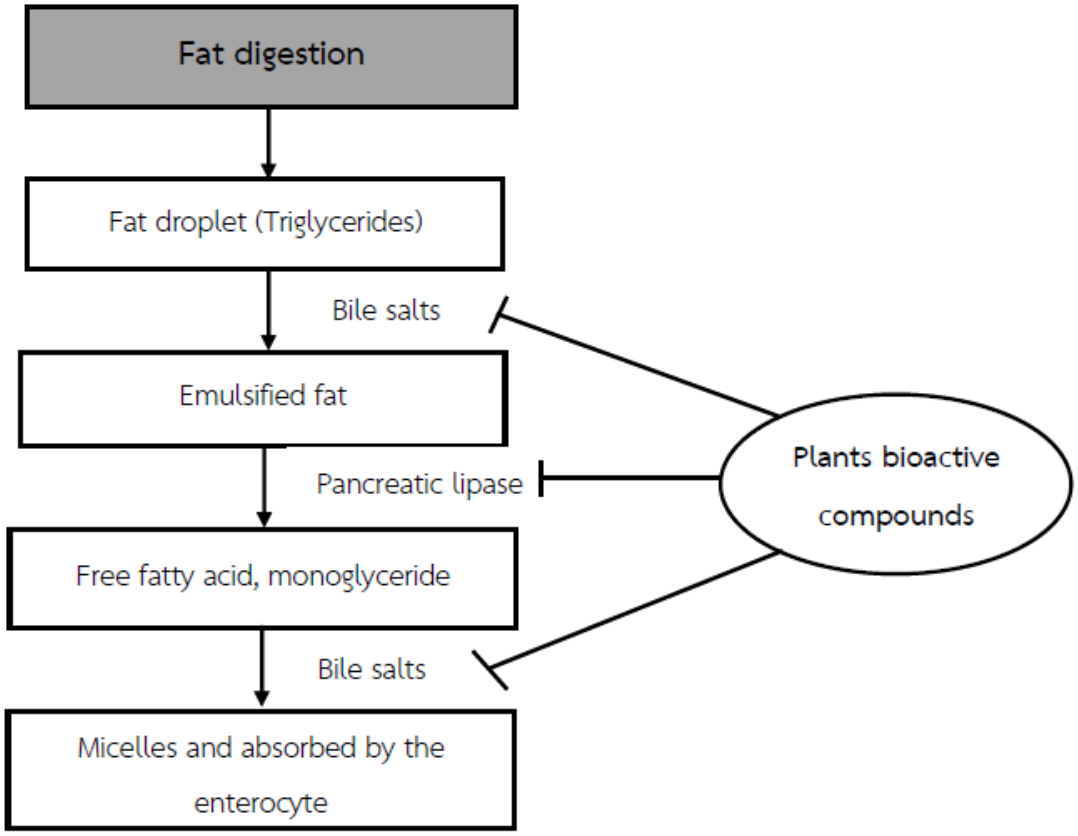


Figure 2 The purposed mechanisms for inhibiting fat digestion and absorption

2.2.4 Diets related to nutrient absorption

2.2.4.1 Carbohydrate absorption

The monosaccharides (glucose, galactose and fructose) were absorbed in the brush border of the mature enterocytes. The glucose and galactose are actively transported into the enterocyte through Na^+-glucose cotransporter SGLT1 and across the basolateral membrane by the glucose transporter GLUT2. Many researchers found

that plant extracts rich in polyphenols and flavonoid improved hyperglycemia by inhibiting digestive enzyme activities, decreasing the activity of SGLT1- mediated transporter (Garza et al., 2013; Z. Wang, Clifford, & Sharp, 2008). The purposed mechanisms of plant diets for inhibiting carbohydrate digestion are shown in Figure 1.

2.2.4.2 Fat absorption

Pancreatic cholesterol esterase is an enzyme to hydrolyze dietary cholesterol esters to free cholesterol (Myers-Payne, Hui, Brockman, & Schroeder, 1995). The inhibition of pancreatic cholesterol esterase leads to a limit the absorption of dietary cholesterol, resulting in delayed cholesterol absorption (Heidrich, Contos, Hunsaker, Deck, & Vander Jagt, 2004). Interestingly, previous studies reported that the extracts of edible plants can inhibit cholesterol esterase and down-regulate NPC1L1 mRNA expression, a cholesterol transport protein, leading to reduced fat absorption (Adisakwattana, Intrawangso, et al., 2012; Poosri et al., 2019). Figure 3 shows the purposed mechanisms of plant diets for inhibiting fat absorption, modified from Leifert and Abeywardena (2007).

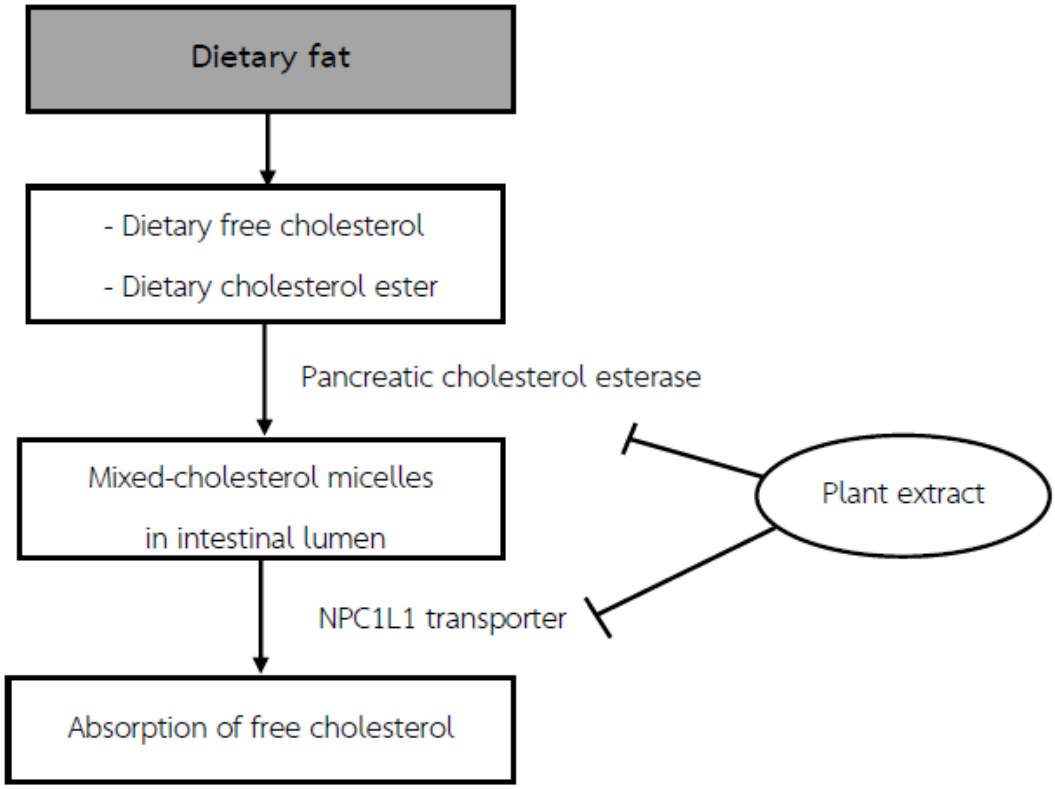


Figure 3 The purposed mechanisms of plant diets for inhibiting fat absorption

2.2.5 Diets related to control appetite

Diet composition is an important factor influencing on the amount of food intake. A previous work has been shown that high protein (25- 30%) intake improvements in appetite control and satiety compared to high fat and /or high carbohydrate diet (Neacsu, Fyfe, Horgan, & Johnstone, 2014). Yogurt is one type of food that contains protein between 8 and 14 g of protein/serving. A previous study found that the consumption of high protein yogurt (24 g protein) as afternoon snack led to reduce hunger, increased fullness and delay subsequent eating in healthy women (Douglas, Ortinau, Hoertel, & Leidy, 2013). The potential to yogurt contribute

to satiety and reduced appetite due to its increased gastric emptying (Fernandez, Panahi, Daniel, Tremblay, & Marette, 2017). Moreover, whey protein and casein can suppress shot-term food intake led to metabolic regulation through the stimulation of hormones regulating food intake and glucose utilization include insulin, glucagon-like peptide, peptide tyrosine tyrosine, and cholecystokinin and inhibition of ghrelin (Fernandez et al., 2017; Panahi & Tremblay, 2016). Recently, a randomized controlled trial found that consumption of plant polyphenol modulated appetite biomarkers, including glucagon-like peptide-1, ghrelin, leptin, and resistin, and also improved the appetite score (hunger, satiety, fullness and prospective food consumption) compare to the placebo group in overweight subjects throughout eight weeks (Boix-Castejón et al., 2018). Figure 4 illustrates the possible mechanisms of plant polyphenols on regulation of appetite, modified from (Boix-Castejón et al., 2018).

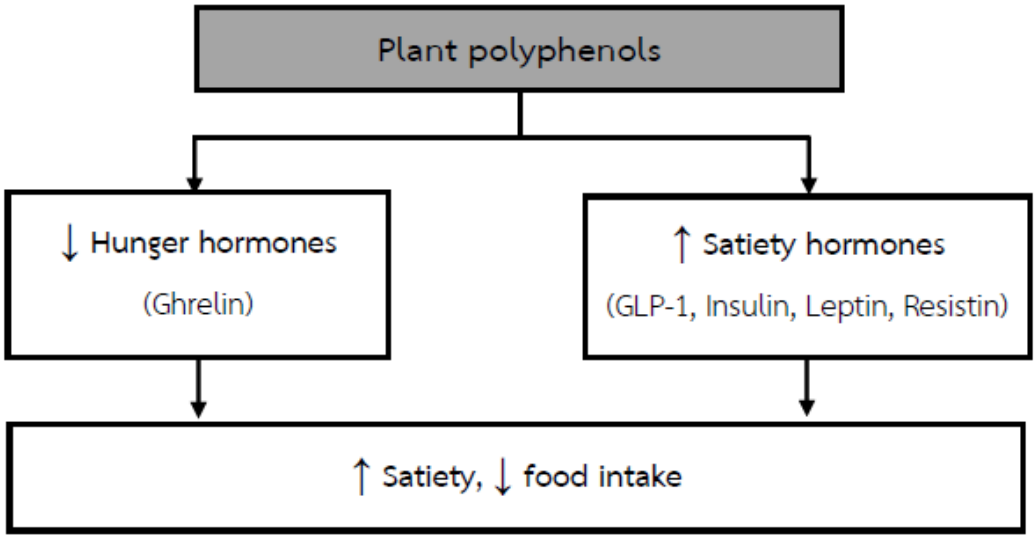


Figure 4 Possible mechanisms of plant polyphenols on regulation of appetite

2.3 Functional food

Functional foods provide a beneficial effect on one or more target functions in the body (Ozen et al., 2012). The concept of functional foods is not only essential for living but also as a source of mental and physical well-being. Functional foods may prevent and reduce the risk factors for several diseases and enhance physiological function (Howlett, 2008). To classify the functional foods, they must be consumed as foods not as a pill or capsules (Howlett, 2008). The most popular functional food products on the market are yogurt, cereals, margarines/butters, and energy/proteins bars and drinks (Granato et al., 2020). In general, the functional ingredients are dietary fibers, vitamins, minerals, oligosaccharides, essential fatty acids (omega-3), lactic acid bacteria cultures, lignin and antioxidant substances (Lobo, Patil, Phatak, & Chandra, 2010).

2.3.1 Effect of functional ingredients on postprandial hyperglycemia

Antioxidant substances are the most popular ingredients in functional food found in edible plants. They have shown to possess antioxidant, anti-inflammatory, anti-hyperglycemic, anti-hyperlipidemic activities (Basu, Nguyen, Betts, & Lyons, 2014; Granato et al., 2020). For example, strawberry, a rich source of phytochemical compounds such as ellagic acid, anthocyanins, quercetin, and catechin has been shown to increase plasma antioxidant, to decrease total cholesterol and LDL-C and lipid peroxidation, and to attenuate postprandial glucose (Basu et al., 2014). In clinical

trials, consumption of strawberry and blueberry rich in anthocyanin also attenuated postprandial glucose and insulin concentration (L. Bell, Lamport, Butler, & Williams, 2017; Edirisinghe et al., 2011). Moreover, consumption of *Clitoria ternatea* flower beverage rich in anthocyanin without sucrose significantly increased postprandial plasma antioxidant capacity. It also improved postprandial glucose, insulin and antioxidant status when consumed with sucrose (Chusak et al., 2018).

2.3.2 Effect of functional ingredients on reduction of postprandial hyperlipidemia

Abnormal postprandial hyperlipidemia with increasing triglyceride, chylomicron remnants, and free fatty acids induces oxidative stress and inflammation in human body. A previous report that functional ingredients from edible plants suppressed postprandial triglycerides and free fatty acid (Brown et al., 2015). In clinical trials, ingestion of diets rich in polyphenols improved fasting and postprandial dyslipidemia and reduced oxidative stress in overweight and obese subjects (Annuzzi et al., 2014). Consistent with a study of black soybean extract rich in polyphenols and anthocyanin reported that the intake of black soybean attenuated postprandial hyperlipidemia include serum triglycerides and LDL-cholesterol in type 2 diabetic patients (Kusunoki et al., 2015).

2.3.3 Effect of functional ingredients on postprandial antioxidant capacity

The functional ingredients act as antioxidants which help delay, inhibit or prevent the oxidative processes related to chronic diseases (Granato et al., 2020). The mechanisms of functional ingredients on preventing oxidative stress are demonstrated in Figure 5. Previous studies showed that consumption of functional food rich in phytochemicals such as *Clitoria ternatea* flower beverage, bread made from anthocyanin-rich riceberry rice, and wild blueberry extract powder supplement with high-fat meal (Chusak, Pasukamonset, Chantarasinlapin, & Adisakwattana, 2020; Chusak et al. , 2018; Kay & Holub, 2002) significantly increased in postprandial plasma antioxidant capacity measure by ORAC, FRAP, TAC, and TEAC assays.

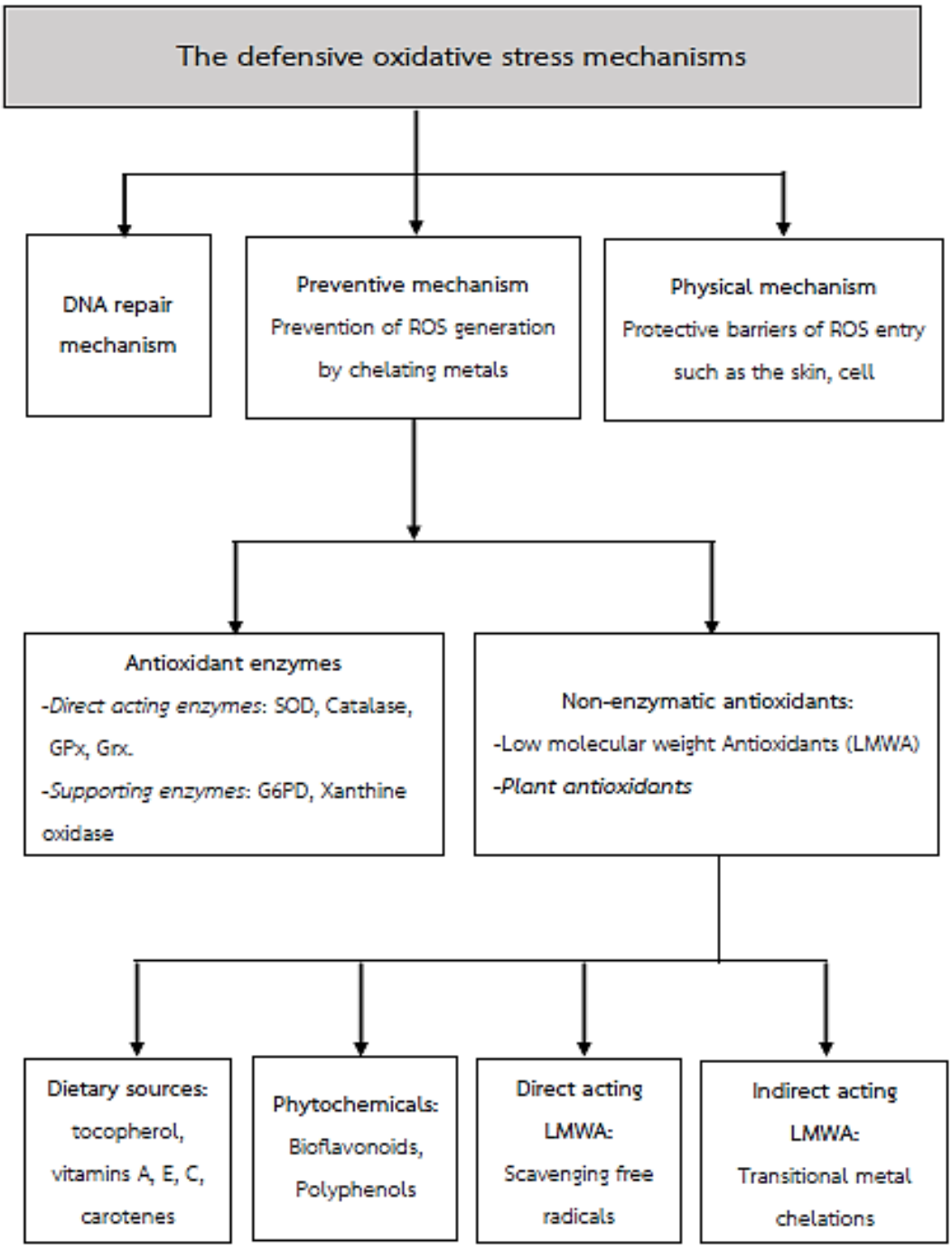


Figure 5 The defensive oxidative stress mechanisms , modified from Engwa (2018).

2.3.4 Anti-inflammation activity

The low-grade inflammation has been linked between adiposity and the risk of chronic metabolic disorder. An increase in inflammatory markers such as interleukins (IL-1, IL-6) and tumor necrosis factor alpha (TNF-α) have been found in overweight and obese individuals (Coelho, Hermsdorff, & Bressan, 2013). Interesting, phytochemicals in functional foods have been shown to modulate the inflammatory biomarkers. For example, consumption of orange juice or plant sterol-rich orange juice for eight weeks significantly reduced inflammatory biomarkers including IL-1β and IL-6 in healthy subjects (Devaraj, Jialal, Rockwood, & Zak, 2011). In overweight subjects, the consumption of high-carbohydrate or moderate-fat meal with strawberry beverage significantly reduced the postprandial inflammatory response measured by high-sensitivity C-reactive protein and IL-6 (Edirisinghe et al., 2011).

2.3.5 Yogurt

Yogurt, one of well-known fermented dairy product, has been popularly consumed worldwide because it is recognized as an excellent source of calcium and relatively low-fat content in combination with high protein constituents (Mckinley, 2005). There have been many studies reporting that consumption of yogurt containing lactic acid bacteria reduces the absorption of cholesterol, improves immune system, enhances bowel function and prevents colon cancer and the infection of *Helicobacter pylori* (Gahruie, Eskandari, Mesbahi, & Hanifpour, 2015; Aryana & Olson, 2017). Lactic

acid bacteria such as *Streptococcus thermophilus* and *Lactobacillus bulgaricus*, is commonly used as a starter culture of yogurt. Today, lactic acid bacteria have a number of well- established literatures regarding health benefits through various mechanisms of action (Aryana et al., 2017).

2.3.5.1 Characteristics of yogurt

In the food industry, yogurt is mainly classified as set-yogurt and stirred yogurt. A set-yogurt is prepared in retail containers, giving a continuous undisturbed gel structure in the final product, whereas a stirred yogurt has a delicate protein gel structure developed by fermentation, resulting in a smooth and viscous texture (Tamime & Robinson, 1999) . The standard composition of yogurt for human consumption following the CODEX is shown in Table 1.

Table 1 The composition of yogurt and fermented milk (Commission, 2003)

Composition	**Yogurt, Alternate culture yogurt and acidophius milk**
Milk protein	Min 2.7%
Milk fat	Less than 15%
Titrable acidity, (express as % lactic acid)	Min 0.6%
Sum of microorganisms constituting the starter culture (cfu/g, total)	Min 10^7
Labelled microorganisms (cfu/g, total)	10^6

The characters of set-type yogurt are shown in Table 2.

Table 2 The important characteristics of set-type yogurt

Characters	Definitions	Range	Ref.
pH	The amount of acid in yogurt	4.5-4.8	(Chandan & O'Rell, 2013); Marchiani et al. (2016)
Titratable acidity	Used as a measure of quality in yogurt	0.6-0.9%	(Aryana & Olson, 2017); Commission (2003)
Syneresis	Presence of superficial liquid	<20%	Öztürk et al. (2018)
Firmness/gel strength	The force necessary to attain a given deformation.	65.6-310.4 g	(Pan, Liu, Luo, & Luo, 2019)
Adhesiveness	The force necessary to remove the material that adheres to the mouth during eating	150-550 g.s.	Akalın, Unal, Dinkci, and Hayaloglu (2012)

2.3.5.2 Yogurt culture

According to the Codex alimentarious commission 2010 (Commission, 2003), yogurt is fermented milk made from symbiotic culture including *Streptococcus thermophiles and Lactobacillus delbrueckii* subsp*. bulgaricus.* To reach the optimum of health benefits, lactic acid bacteria must be ingested in sufficient quantities to remain their viability after gastrointestinal tract digestion. Recently, the number of viable bacteria is recommended to have at least 10^6 CFU/g of viable cell at the time of yogurt consumption (Terpou, Papadaki, Lappa, Kachrimanidou, Bosnea, & Kopsahelis, 2019). However, there are several factors affecting the loss of bacterial viability in yogurt such as the decrease in pH of medium during the storage, the accumulation of other organic acids from growth and fermentation (Michael, Phebus, & Schmidt, 2010) and the dissolved oxygen concentration, moisture content, packaging and the storage condition of yogurt (Tripathi & Giri, 2014). Many studies have attempt to investigate the effect of plant extracts in order to improve the quality of yogurt such as increasing antioxidant activity and the viability of lactic acid bacteria in yogurt during refrigerated storage (Oh et al., 2016). For example, the addition of mandarin melonberry (*Cudrania tricuspidata*) and *Morus alba* L. leaf extracts could increase the lactic acid bacteria count of set-type yogurt during refrigerated storage (Oh et al, 2016). The examples of plant extracts fortified to yogurt are shown in Table 4.

2.3.5.3 Yogurt consumption and health benefits

Previous studies have shown that yogurt product with lactobacilli and other probiotic bacteria enhance the nutritional value by increasing the availability and digestibility. Yogurt contains higher levels of free amino acids due to the proteolysis by the yogurt cultures. Moreover, the consumption of yogurt would provide health benefits, mainly normal intestinal microflora, protecting against gastrointestinal pathogens, improved immune system (Gahruie, Eskandari, Mesbahi, & Hanifpour, 2015; Tripathi & Giri, 2014). Figure 6 demonstrates the health benefits of yogurt consumption. The positive health effect of yogurt consumption was express in Table 3.

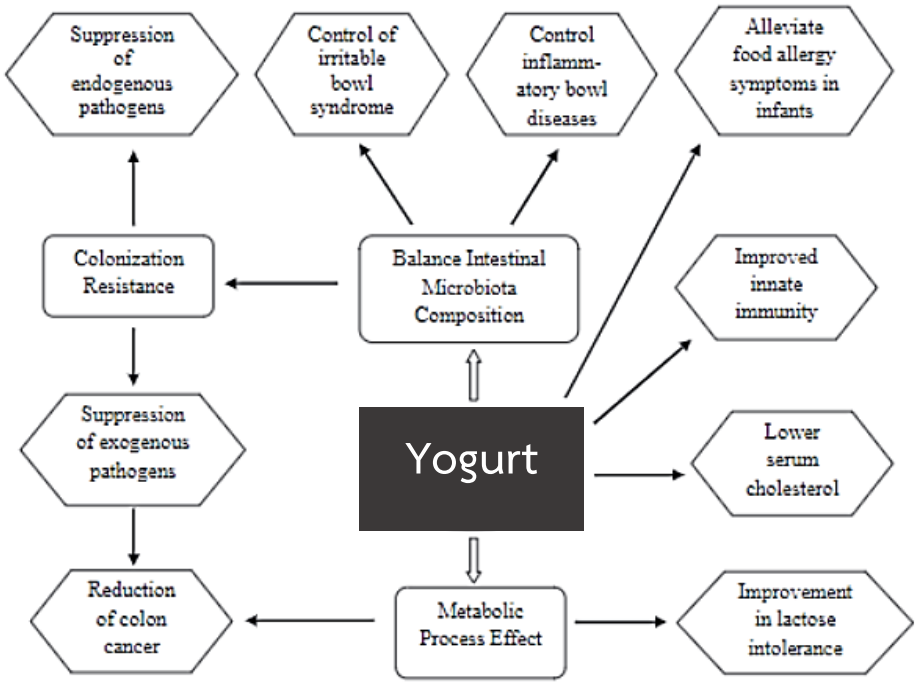


Figure 6 The health benefits of yogurt (Adapted from (Tripathi & Giri, 2014)

Table 3 Clinical studies of yogurt on biomarkers and appetite.

Category	Subjects	Treatment	Outcome	References
Glycemic response	Healthy subjects	Acute yogurt intake (200 g of yogurt with steamed rice)	↓ postprandial glucose	Yagi, Kishimura et al. (2018)
	Healthy males	Acute yogurt intake (250 g of yogurt)	↓ postprandial glucose ↓ postprandial insulin	El Khoury, Brown et al. (2014)
Lipid profiles	Hypercholesterolemic female	300 g/d for six months	↑ HDL	Kiessling, Schneider et al. (2002)
	Healthy females	100 g/d for two weeks and then 200 g/d for further two weeks.	↓LDL/HDL ratio	Fabian and Elmadfa (2006)
	Healthy females	300 g/d for six weeks	↓ total cholesterol and HDL	Sadrzadeh-Yeganeh, Elmadfa et al. (2010)

Abbreviations: ↓, decrease; ↑, increase

Table 3 (Continued)

Category	Subjects	Treatment	Outcome	References
Inflammation	Elderly	180 g/d for eight weeks	↓ *H. pyrori*-induced gastric mucosal inflammation	Sakamoto, Igarashi et al. (2001)
	Children	400 ml/d for four weeks	↓ serum IL-6	Yang and Sheu (2012)
Appetite	Healthy females	8-days	↓appetite	Heap, Ingram et al. (2016)
	Healthy females	Acute yogurt intake (180 g of yogurt with meal)	↑satiety score	Ayaz, Akyol et al. (2017)
	Overweight men	Acute yogurt intake (278 g of yogurt)	↓appetite, ↓subsequent energy intake	Dougkas, Minihane et al. (2012)

Abbreviations: ↓, decrease; ↑, increase

2.3.5.4 Effect of storage time on stability and physicochemical properties of yogurt

Based on the information, the storage time had a significant effect on the stability and physicochemical properties of yogurt such as pH, acidity, syneresis, texture, appearance, color, and the growth of yogurt culture or probiotic bacteria. These parameters influence the sensory property of yogurt. Nowaday, the incorporation of plants or plant extracts into yogurt has been interest due to the potential of bioactive compounds on enhancing living probiotic bacteria and improvement of physicochemical properties during refrigerated storage. The examples of plants fortified yogurt are illustrated in Table 4.

2.3.5.5 Development of yogurt

The incorporation of plant or fruits into yogurt may enhance the physicochemical properties and functional properties of yogurt such as improve phenolic content of yogurt and enhance growth and stability of lactic acid bacteria (Caleja et al., 2016; Gahruie et al., 2015; Jaster et al., 2018). Many studies have attempted to investigate the effect of plant extracts in order to improve the quality of yogurt such as increasing antioxidant activity and the viability of lactic acid bacteria during refrigerated storage (Oh et al., 2016). For example, the addition of mandarin melonberry (*Cudrania tricuspidata*) and *Morus alba* L. leaf extracts could increase the probiotic count of the set-type yogurt during refrigerated storage (Oh et al., 2016).

Moreover, the pulp of blueberry flower containing polyphenols and anthocyanins can improve the viscosity, the rate of syneresis, sensory acceptability and the stability and antioxidant activity of yogurt during refrigerated storage (D. Liu & Lv, 2019). However, the addition of plant extract may influence on physicochemical properties of yogurt. Previous studies found that fortification of yogurt with plant extract such as grape extract, green tea, thyme and mint extract modified the acidification together with reduction of starter culture activity and extension of the fermentation time (Alwazeer, Bulut, & Tunçtürk, 2020; Da Silva et al., 2017). Table 4 showed the plant extract and their effect on antioxidant properties, physicochemical, and microbiological during storage period.

Table 4 Example of plant fortified yogurt with enriched of bioactive phytochemical components

Type of yogurt	Plant source	Active compounds	Antioxidant activity	Physicochemical properties	Microbiological properties (end of storage)	Storage time (Days)	References
Set yogurt	Pomegranate	Flavonoid, Anthocyanin	↑DPPH, FRAP	-	-	28	Trigueros, Wojdyło et al. (2014)
Stirred yogurt	Strawberry	Anthocyanin	↑DPPH, ABTS	↓pH, ↑TA ↓VISC	NS	7	Jaster, Arend et al. (2018)
Set yogurt	Blueberry flower pulp	Phenolic compounds	↑DPPH, ABTS, OH radical scavenging activities	↓pH, ↑TA ↓Syneresis ↑ VISC, Firmness	↑ LAB	29	Liu and Lv (2019)
Set yogurt	*Cudrania tricuspidata* leaf extracts	Phenolic compounds	↑DPPH, ABTS, FRAP	↓Fermentation time ↓pH, ↑TA	↑ LAB	28	Oh, Lee et al. (2016)
Set yogurt	*Morus alba* leaf extracts	Phenolic compounds	↑DPPH, ABTS, FRAP	↓Fermentation time ↓pH, ↑TA	↑ LAB	28	Oh, Lee et al. (2016)
Set yogurt	Grape extract	Phenolic compounds, proanthocyanidins	-	↑Fermentation time ↑Syneresis ↓Gel strength	↑ LAB	12	Da Silva, Junior et al. (2017), (Carreiro and Buhman 2019)
Set yogurt	Green tea	Catechins	-	↑pH ↓Syneresis ↑ VISC	-	14	Dönmez, Mogol et al. (2017)

Abbreviations: TA, titratable acidity; LAB, lactic acid bacteria; VISC, viscosity; NS, not significant when compared to the control

Table 4 (Continued)

Type of yogurt	Plant source	Active compounds	Antioxidant activity	Physicochemical properties	Microbiological properties (end of storage)	Storage time (Days)	References
Set yogurt	Green coffee	Chlorogenic acid	-	↑pH ↓Syneresis ↑ VISC	-	14	Dönmez, Mogol et al. (2017)
Stirred- yogurt	Grape pomace	Phenolic compounds	↑DPPH	↓pH, ↑TA ↑Syneresis	NS	21	Marchiani, Bertolino et al. (2016)
Set yogurt	Plant extracts (Olive, garlic, onion, citrus)	-Bioactive compounds	-	↑Fermentation time ↑pH, ↑TA ↑Syneresis ↓Firmness	NS	50	Michael, Phebus et al. (2010)
Stirred- yogurt	Broccoli Carrot Pumpkin Red sweet pepper	flavonoids Carotenoids, lutein, ascorbic acid, phenolic, capsaicinoids	↑DPPH, FRAP	-	-	14	Najgebauer-Lejko, Grega et al. (2014)
Set yogurt	Pomegranate juice powder	Phenolics	↑DPPH, FRAP	↑ Firmness, consistency, cohesivness	-	21	Pan, Liu et al. (2019)
Stirred-yogurt	Zeaxanthin extract from Goji berry	Zeaxanthin	-	↓pH, ↑TA ↑Syneresis ↓Firmness, Consistency VISC	-	28	de Campo, Assis et al. (2019)

Abbreviation: TA, titratable acidity; LAB, lactic acid bacteria; VISC, viscosity; NS, not significant when compared to the control.

The researchers discovered that incorporation of anthocyanins to yogurt improves antioxidant activity, enhance texture of yogurt, and increased total solids of yogurt (Trigueros, Wojdyło, & Sendra, 2014; Jaster, Arend, Rezzadori, Chaves, Reginatto, & Petrus, 2018) and promotes the growth of lactic acid bacteria during refrigerated storage (Liu et al., 2019).

2.3.6 Functional beverage

Functional beverage is a non-alcoholic drink containing non-traditional constituents such as beverage fortified with vitamin A, C, E and other functional ingredients like phytochemicals in its formulation. Phytochemicals especially phenolics can be used as a functional ingredient (Ahmad, Butt, Huma, & Sultan, 2013). The potential of bioactive compound in the plant or plant extract are recognized as a functional ingredient due to health benefits such as antioxidant, anti-inflammatory, anti-diabetic and lowering of total triglyceride and cholesterols (Granato et al., 2020; Siro et al., 2008).

2.3.6.1 Characteristics of functional beverage

In general, functional beverage is a beverage fortified with functional ingredients. The functional beverage is designed for reducing the health risk problem such as high cholesterol or high blood pressure, reduced negative effect for health such as lactose-free milk, and product improved health such as eye health drink with lutein or a bone health drink with calcium and other health benefits (Siro et al., 2008).

2.3.6.2 Health benefits

A previous study found that consumption of high-carbohydrate and moderate- fat meal supplement with freeze- dried strawberry beverage that high content of polyphenols and anthocyanin resulted a reduction in the levels of IL-6 and hs-CRP over the 6 h postprandial period (Edirisinghe et al., 2011). In a study in healthy subjects, ingestion of *Clitoria ternatea* flower beverage with and without sucrose significantly increases postprandial plasma antioxidant capacity without hypoglycemia in the fasting stage. It also improved postprandial glucose, insulin and antioxidant status when consumed with sucrose (Chusak et al., 2018). In an animal study with rats fed a fructose-rich diet, ingestion of chokeberry extract added to the drinking water significantly reduced gene expression of inflammatory cytokines including IL-1β, IL-6 and TNF-α (Qin & Anderson, 2012). However, the study of riceberry rice beverage on postprandial status and biochemical parameters in the clinical trial was not found.

The functional ingredients such as probiotics/prebiotic/synbiotics, polyunsaturated fatty acids (PUFAs), and antioxidants substance are often used for fortified beverage. Table 5 shows the bioactive compounds and health benefits, modified from Granato et al. (2020).

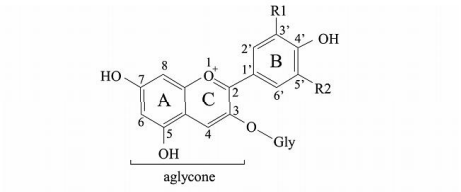
Table 5 The bioactive compounds and health benefits

Bioactive compounds	Source	Health benefits
β-Carotene	Yellow, orange, and green leafy vegetables and fruits	Antioxidant, provitamin A, prevent eye diseases, radioprotective and antimutagenic
Lutein	Green leafy vegetables	Antioxidant, anti-inflammatory, antiatherogenic, antihypertensive, antidiabetic, antiulcer, ↓cancer risk, prevents eye diseases.
Lycopene	Tomato, melon, peach, etc.	Antioxidant, ↓ cardiovascular disease, ↓cancer risk
Inulin	Asparagus, garlic, chicory, onion, etc	Prebiotic effect, ↓atherosclerosis, ↑satiety
Resveratrol	Red grape, blueberries, blackberries, cocoa	↓ Cardiovascular disease, ↓LDL-cholesterol
Isoflavones	Soy-based foods, flaxseeds	↓ Cardiovascular disease, ↓LDL-cholesterol, osteoporosis, ↓ diabetes mellitus risk, and liver disease
Anthocyanins, proanthocyanidins	Grape, blueberries, grapeberries	Antioxidant, prevent and treat hyperuricemia/or gout, ↓ cardiovascular disease

Abbreviations: ↓, decrease; ↑, increase

2.4 Anthocyanins

Anthocyanins are water-soluble pigments belonging to the family of polyphenols. Most of them are red, purple, and blue colors presented in plants such as blackberries, blueberries, bilberries, grape, strawberries and black rice (Tian et al., 2019). There are at least six main types of anthocyanins in nature, including pelargonidin, cyanidin, peonidin, delphinidin, petunidin and malvidin (Morata et al., 2019). The basic structure of anthocyanin is illustrated in Figure 7. Anthocyanins are not essential nutrients; no toxicity and deficiency disorder has been reported. The pharmacological properties are antioxidant activity, anti- cancer, anti- hyperglycemia, anti- hyperlipidemia and anti-inflammation (Miguel, 2011; Pojer, Mattivi, Johnson, & Stockley, 2013; Takikawa, Inoue, Horio, & Tsuda, 2010). As for the amount of daily intake, China has been defined a specific proposed level of 50 mg per day for anthocyanins (He & Giusti, 2010), whereas the joint FAO/WHO Expert Committee on Food Additive has established an acceptable daily intake of 2.5 mg per kg per day (Wallace & Giusti, 2015).



Anthocyanidin (aglycone)	R groups	Approximate distribution in fruits and vegetables
Pelargonidin	R1=R2=H	~ 12%
Cyanidin	R1=OH, R2=H	~ 50%
Delphinidin	R1=R2=OH	~ 12%
Peonidin	R1=OCH_3, R2=H	~ 12%
Petundidin	R1=OH, R2=OCH_3	~ 7%
Malvidin	R1=R2=OCH_3	~ 7%

Figure 7 The basic structure of anthocyanins (Krga & Milenkovic, 2019).

Over the past decades, anthocyanin have been stated in antioxidant effects (Miguel, 2011; Pojer et al., 2013). The antioxidant capacity of anthocyanins is able to donate the hydrogen (electron) to free radicals and even reactive oxygen species (Pojer et al., 2013). Moreover, anthocyanins improved glycemic control by inhibiting α-glucosidase and α-amylase activity, leading to decrease carbohydrate digestion and absorption (Mirmiran, Bahadoran, & Azizi, 2014). Furthermore, anthocyanins had the ability to inhibit the activity of pancreatic lipase leading to the reduction of intestinal absorption of dietary fat (Fabroni, Ballistreri, Amenta, Romeo, & Rapisarda, 2016). In addition, anthocyanin also reported the potential for anti-inflammatory activity by inhibiting the expression and biological activity of some pro-inflammatory cytokines by suppressing NF-kB; a transcriptional regulator that consists of homo-and heterodimer of proteins. The translocation of NF-kB results in the transcription of several pro-inflammatory genes, such as cytokines include TNF-α, IL-1β and IL-6 and inducible enzymes (Miguel, 2011).

2.4.1 Cyanidin

The most common types of anthocyanin are cyanidin, delphinidin, pelargonidin, peonidin, petunidin and malvidin. Anthocyanins are widely distributed in fruits and vegetables (Khoo, Azlan, Tang, & Lim, 2017; Krga & Milenkovic, 2019). Cyanidin-3-glucoside (C3G) is known as the largest group of pigments in berries, dark grapes, cabbages and black rice etc. (He & Giusti, 2010; Miguel, 2011). The potential of

C3G includes antioxidant, anticancer and anti-inflammatory activities (Ding et al., 2006; Duymuş, Göger, & Başer, 2014). A previous study found that C3G extracted from blackberry was able to scavenge free radical, down regulated the expression of COX-2 and TNF-α (Ding et al., 2006). Similar to the study in animal model, administration of C3G reduced COX-2 activity and increased the defensive antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (Šarić et al., 2009). Another study also found that C3G potentially reduce blood glucose, total triglyceride and total cholesterol in diabetic rats (Li et al., 2018). In addition, C3G decreased the level of TNF-α and IL-6 and improved antioxidant status via reduction of the MDA level and increase SOD level (Li et al., 2018). In addition, the consumption of black currant extract that high amount of cyanidin have been shown to reduce postprandial glycemia by inhibiting α-amylase and inhibiting the breakdown of carbohydrate in the intestine by the inhibiting α-glucosidase activity (Barik et al., 2020).

2.4.2 Peonidin

Peonidin, a type of anthocyanin found in nature, is mainly in the form of peonidin-3-glucoside (P3G) (Khoo et al., 2017). Normally, P3G has been found in plants such as berries, grapes, and red wines etc. (B¹kowska-Barczak, 2005). Previous studies demonstrated that P3G is also found in black rice and riceberry rice with high potential of antioxidant activity, anti-cancer activity, and anti-glycation activity (Leardkamolkarn et al., 2011; Zhang et al., 2019).

2.5 Riceberry rice

2.5.1 Characteristics

Riceberry rice (*Oryza sativa L.),* a kind of color rice with dark purple pigment, this cultivar was developed from cross-breed between Hom Nin rice, a Thai non glutinous purple rice, and Jasmine rice or Khoa Dawk Mali 105 (Figure 8) (Arjinajarn et al., 2017). This variety was developed by the Rice Science Center, Kasetsart university, Thailand. The characteristics of this rice were 105-110 cm in height, 130 days to maturity, pericarp and kernel color was deep purple, amylose content was 15.6% and gel temperature less than 70 °C.

Figure 8 Riceberry rice (*Oryza sativa* L.)

This specific rice cultivar was reported to contain a large amount of cyaniding-3-glucoside (C3G) and peonidin-3-glucoside (P3G), the glycoside form of anthocyanins

(Leardkamolkarn et al., 2011). Table 6 is shown the nutrition compositions of riceberry rice (Prangthip et al., 2013).

Table 6 The nutrition compositions of riceberry rice

	Values (per 100 gram)
Energy (kcal)	366.2
Protein (g)	8.9
Fat (g)	8.2
Carbohydrate (g)	64.2
Insoluble fiber (g)	8.37
Soluble fiber (g)	4.47
Calcium (mg)	123
Magnesium (mg)	393
Sodium (mg)	307
Potassium (mg)	726
	Values (per gram dry matter)
α-tocopherol (μg)	11.61 ± 0.50
γ-oryzanol (mg)	1.80 ± 0.20
Ferulic acid (μg)	176.80 ± 5.56
Cyaniding-3-glucoside (μg)	431.50 ± 11.10
Peonidin-3-glucoside (μg)	141.90 ± 5.50
Catechin (mg)	4.39 ± 0.10
CoQ10 (μg)	2.33 ± 0.10
Polyphenol (mg GAE)	12.37 ± 1.99
Total flavonoids (mg CE)	8.26 ± 0.31
Total ORAC (μmol TE)	317.64 ± 14.07

2.5.2 Biological properties of riceberry rice

2.5.2.1 In vitro study

Various studies have demonstrated biological and pharmacological properties of riceberry rice extract such as anti-cancer activity, antioxidant activity, and antiglycation activity (Daiponmak, Senakun, & Siriamornpun, 2014; Leardkamolkarn et al., 2011; Somintara, Leardkamolkarn, Suttiarporn, & Mahatheeranont, 2016). Interestingly, Poosri et al. (2019) revealed that anthocyanin-rich extract of riceberry rice was capable in inhibiting carbohydrate and lipid digestion and absorption as shown in Figure.9 and 10. Anthocyanin rich extract of riceberry rice inhibited the key steps of carbohydrate digestion and absorption such as intestinal α- glucosidase and suppressed mRNA expression of SGLT1. As for lipid digestion and absorption, riceberry rice extract had the ability to inhibit the activity of pancreatic lipase, decrease cholesterol micellization, bind to bile acid and down- regulated NPC1L1 mRNA expression (Poosri et al., 2019). Moreover, supplementation of riceberry for 12 weeks significantly improved hyperglycemia (blood glucose, insulin and GLUT-4 levels), hyperlipidemia, oxidative stress (MDA), antioxidant status (ORAC) and pro-inflammatory state (TNF-α and IL-6) in streptozotocin (STZ)-induced diabetic rats (Prangthip et al., 2013). Similarly, supplementation of riceberry oil for 12-week significantly improved hyperglycemia and hyperlipidemia in STZ- induced diabetic diabetes rats

(Kongkachuichai et al., 2013). Besides, anthocyanin- rich riceberry bran extract decreased oxidative stress, inflammation and apoptosis in rats (Arjinajarn et al., 2017).

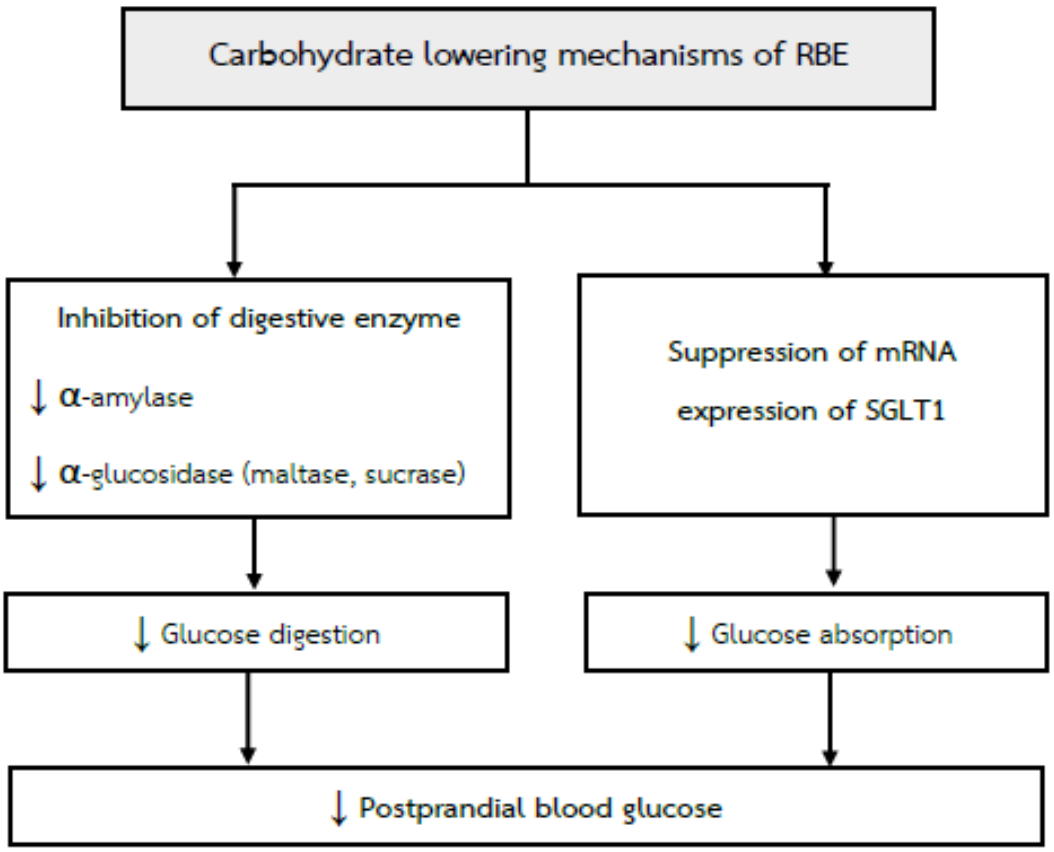


Figure 9 The possible mechanism of RBE for inhibiting carbohydrate digestion and absorption , modified from Poosri et al. (2019).

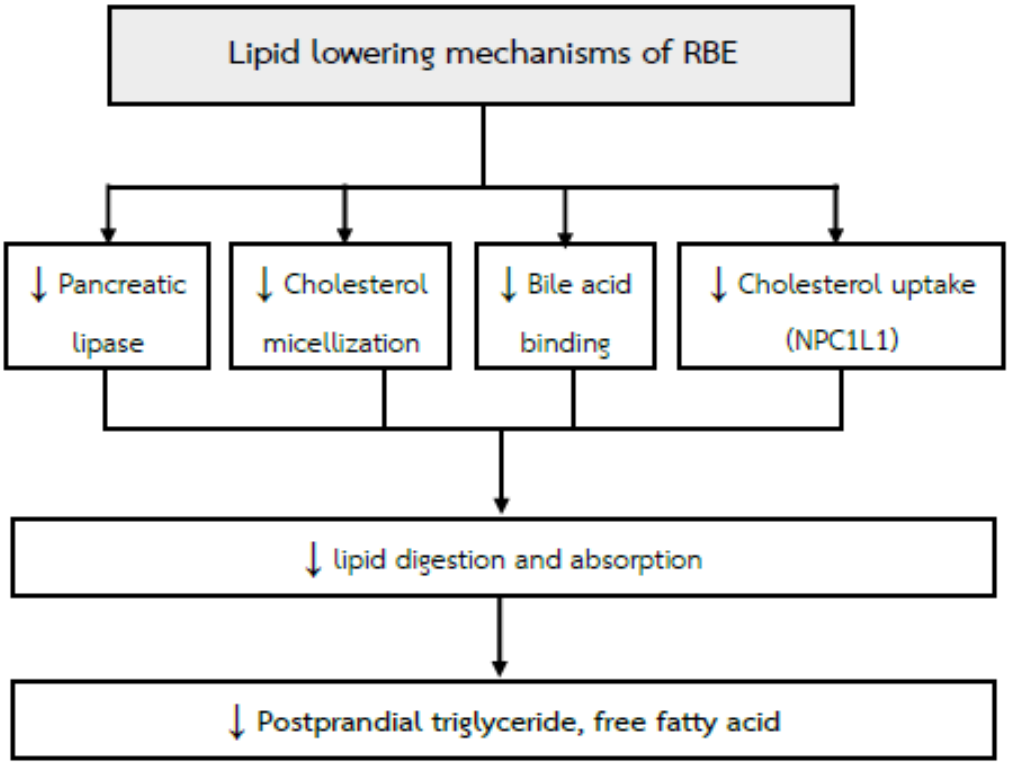


Figure 10 The possible mechanism of RBE for inhibiting lipid digestion and absorption , modified from Poosri et al. (2019).

2.5.2.2 Clinical study

A previous study of Chusak et al. (2020) found that the consumption of bread made from anthocyanin- rich riceberry rice improved postprandial plasma glucose, insulin and antioxidant status in healthy subjects (Chusak et al., 2020). Another study stated that ingestion of riceberry rice puddings, the formulation of dysphagia diet lowered postprandial plasma glucose when compared to white bread (Suttireung et al., 2019).

CHAPTER III

MATERIALS AND METHODS

Chemicals

1,1-diphenyl 2-picrylhydrazyl (DPPH)	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
2,2'-Azino-bis-(3-ethylbenzothiazoline -6-sulphonic acid) (ABTS)	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
2,2′-Azobis(2-methylpropionamidine) Dihydrochloride (AAPH)	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
2,4,6-tri(2-pyridyl)-1,3,5-triazine (TPTZ)	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
2,6-di-tert-butyl-4-methylphenol (BHT)	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
5,5′-dithiobis-(2-nitrobenzoic acid) (DTNB)	Calbiochem (Darmstadt, Germany)
6-hydroxyl-2,5,7,8-tetramethyl Chhromane-2-carboxylic acid (Trolox)	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
Amyloglucosidase solution	Megazyme (Illinois, USA)

Acetic acid	Merck (Darmstadt, Germany)
Acetonitrile	Merck (Darmstadt, Germany)
Bile extracts porcine	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
Cyanidin-3-glucoside chloride	Phytolab (GmbH & Co. KG, Germany).
Ethanol	Merck (Darmstadt, Germany)
Fluorescein sodium salt	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
Folin-Ciocalteu's reagent	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
Glucose oxidase kit (Glucose LiquiColor®)	HUMAN GmbH (GmbH, Germany)
Hydrocholic acid (HCl)	Merck (Darmstadt, Germany)
Iron (II) sulfate	Ajax finechem (Auckland, New Zealand)

Iron (III) chloride hexahydrate	Ajax finechem (Auckland, New Zealand)
Potassium sodium tartrate	Ajax finechem (Auckland, New Zealand)
L-cysteine	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
Maleic acid	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
Malondialdehyde (MDA)	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
Methanol	Merck (Darmstadt, Germany)
Monosodium phosphate (NaH_2PO_4)	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
Pancreatin from porcine pancreas	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
Peonidin-3--glucoside chloride	Phytolab (GmbH & Co. KG, Germany).
Pepsin from porcine gastric mucosa powder	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)

Porcine pancreatic α-amylase	Sigma-Aldrich Chemical Co. Ltd (St. Louis, MO, USA)
Sodium acetate anhydrate	Ajax finechem (Auckland, New Zealand)
Sodium chloride (NaCl)	Ajax finechem (Auckland, New Zealand)

Laboratory equipment

Colorimeter	Hunter Associates laboratory Inc. (USA)
Freezer -20°C	Sanyo (Osaka, Japan)
Freeze dryer machine	GRT., Grisrianthong. Co., Ltd, (Samutsakorn, Thailand)
High speed refrigerated micro-centrifuge	Hettich (Tuttlingen, Germany)
High speed universal centrifuge (HERMLE Z 383 K)	Hermle Labor technik (GmbH, Germany).
Homogenizer (Polytron PT 3100 D)	Kinematica AG (Luzern, Switzerland
Hot air oven	Conthem Scientific (New Zealand)
Microplate reader Infinite® 200 PRO	Tecan Trading (AG,Switzerland)
pH meter	Thermo Scientific, Inc. (Waltham, MA, USA)
pH meter	METTLER TOLEDO® (OH, USA)

Pipette	Thermo Scientific, Inc. (Waltham, MA, USA)
Precision Weighing Balances	Sartorius Corporation (New York, USA)
Refrigerator 4°C	Sharp (Kyoto, Japan)
Texture analyzer (TA.XT-Plus Texture analyzer)	Technologies Corp. and Stable Micro Systems Ltd. (MA, USA)
Vortex	Gemmy industrial corp. (Taipei, Taiwan)

3.1 Part I: Incorporation of anthocyanin-rich riceberry rice in yogurts: Effect on physicochemical properties, antioxidant activity and *in vitro* gastrointestinal digestion

3.1.1 Preparation of riceberry rice extract (RBE)

The aqueous extract of riceberry rice was prepared by a mixture of riceberry rice and distilled water in 1:2 w/v ratio. The mixture was heated at 45 °C for 40 min with continuous stirring, then the supernatant was collected and filtered with Whatman No. 1 filter paper. In our preliminary experiment, the highest amount of polyphenol content was obtained by this condition. The sample was frozen at -18 °C for 48 h. After that, the sample was placed in a freeze dryer GFD-30S (GRT., Grisrianthong. Co., Ltd, Thailand) and dried at -30 °C, at pressure of 0.15 mbar for 27 h and 30 min. The riceberry rice extract (RBE) powder was kept in the laminated aluminum foil vacuum bags at -20 °C until used.

3.1.2 Preparation of set-type yogurt

The set-type yogurt procedure was adapted from a previous report (Chandan & O'Rell, 2006). In brief, whole milk was heated to 50 °C and skimmed milk powder (3% w/w) for the adjusted dry matter content to 14% and sucrose (5% w/w) were added, then homogenized at 7000 rpm, 65 °C for 5 min followed by the addition of 0.125, 0.25 and 0.5 % (w/w) RBE. After heating at 90 °C for 10 min, the standardized milk was cooled to 43 °C and inoculated with 0.02 % w/v of a mixed yogurt freeze-dried culture

containing *Streptococcus thermophilus*, *Lactobacillus delbrueckii* subsp. *bulgaricus*, *Lactobacillus acidophilus* LA-5 and *Bifidobacterium animalis* subsp. *lactis* BB-12. The inoculated milk was incubated for 5 h at 43 ℃. When the pH of yogurt reached to 4.6, the yogurt samples were cooled at 4 ℃ to stop the fermentation and kept at 4 ℃ and analyzed at 1, 7, 14 and 21 days of refrigerated storage.

Figure 11 The control yogurt and yogurt with RBE

3.1.3 Physicochemical properties of yogurt

3.1.3.1 Kinetic parameters

The kinetic parameters were measured using the changes in pH values of yogurt during fermentation until the pH 4.6 (Zhang et al., 2019). V_{max}, maximum acidification rate, defined as the maximum slope of the pH curve, was calculated from the change in pH over time (dpH/dt) and expressed as pH units*10^{-3}/min. T_{max}(h) and $T_{pH\ 5.0}$ (h) were calculated from the time at the reach to V_{max} and the time required to

reach a pH 5.0, respectively. Finally, T_f (h) was calculated from the time required to complete the fermentation at pH 4.6. The parameters were calculated using Sigma Plot 13, Systat Software, San Jose, CA). The change in pH values of yogurt samples was measured using a pH-meter (Mettler Toledo S.A.E., Barcelona Co., Ltd, Spain).

3.1.3.2 Titratable acidity

The titratable acidity (TA) of yogurt samples was determined by the titration method adapted from a previous study (da Silva, Junior, Gomes, dos Santos Pozza, Britten, & Matumoto-Pintro, 2017). Briefly, the yogurt samples were diluted with distilled water at the ratio 1:9. After that, 0.1% phenolphthalein as an indicator were added into the mixture. The yogurt mixture was then titrated with 0.01 N NaOH under continuous stirring until the development of a stable faint pink color for 1 min. The amount of acid produced from the yogurt was expressed as g lactic acid /100g of yogurt.

3.1.3.3 Syneresis

The syneresis of yogurt was determined by a centrifugation procedure according to a previous study (Mani-López, Palou, & López-Malo, 2014). Initially, 20 g of sample was weighed and then centrifuged at 6600*g* at 4 ℃ for 30 min using a HERMLE Z 383 K centrifuge (Hemle Labortechnik GmbH, Germany). The syneresis value was reported as the volume of separated liquid per 100 g of yogurt.

3.1.3.4 Color

The color of yogurt samples was evaluated using a Colorimeter (Color flex, Hunter Associates laboratory, Inc, USA). The instrument was calibrated with a white tile calibration plate (L* = 93.45; a* = -1.00; b* = 2.15). The results were expressed as the CIE L*, a* and b* color values, where L*was represent lightness, a* represent redness (+) to greenness (-) and b* represent yellowness (+) to blueness (-) of yogurt.

3.1.3.5 Texture analysis

The texture of yogurt was performed using TA-XT2 texture analyzer (Stable Micro Systems, Godaming, UK) equipped with a software. The testing probe and conditions were cylinder probe diameter 25 mm (P25/L), pre-test speed = 5 mm/s, test speed 3.0 mm/s, target mode = strain, time 3 s and trigger force = 0.5 g with 2000 g of calibration weight. The test was carried out directly in a 40 g sample cup, performed in triplicate. All experiments were performed at 5 °C. The major textural of set-yogurt characteristics, including firmness or gel strength (the peak of compression force during the penetration) and adhesiveness (negative force area) were tested.

3.1.4 Microbiological analysis

The total *lactobacillus* count (TLC) of yogurt samples was performed at day 1, 7, 14 and 21. The samples were conducted according to the methodology with the reference method ISO 15214 (1998). The de Man, Rogosa, and Sharpe (MRS) agar was used for quantifying viable cell of lactic acid bacteria during refrigerated storage. After

inoculation, the plates were inverted and incubated in anaerobic jars containing gas-pack (Oxoid, ThermoFisher Scientific, UK) at 30 ℃ for 72 h. In this study, the pour plate method gives an estimate of the viable bacterial count. After specifying the period of time, count the colonies in each dish. The results were expressed as colony forming unit per gram yogurt (CFU/g yogurt).

3.1.5 Total phenolic content and antioxidant activity of yogurt

The preparation of yogurt samples was done according to a previous study with minor modifications (Marchiani et al., 2016). Briefly, 10 g of each yogurt sample was diluted with 10 mL of distilled water at 25 ℃. The mixture was continuous stirred in a shaker at 100 rpm for 30 min, then centrifuged at 2000*g* at 4 ℃ for 30 min. The supernatant was collected and filtrated through Whatman No.1 paper and the extracts were stored at -20 ℃ until analysis. The total phenolic content (TPC) was determined using Folin-Ciocalteu assay as reported by Chayaratanasin, Barbieri, Suanpairintr and Adisakwattana (2015). In brief, the extract (50 µL) was mixed with 50 µL of Folin-Ciocalteu reagent (diluted 1:10-fold). After 5 min of incubation, 50 µL of 10% (w/v) Na_2CO_3 was added. The mixture was mixed and incubated at room temperature in the dark for 30 min. The absorbance was read at 760 nm. Total phenolic content was expressed as mg gallic acid equivalent (GAE) per 100 g yogurt.

The DPPH radical scavenging activity was measured using the stable radical DPPH (1,1-diphenyl 2-picrylhydrazyl) (Chayaratanasin et al., 2015). The absorbance was measured at 515 nm. The result was expressed as mg ascorbic acid equivalents per 100 g yogurt. Ferric reducing antioxidant power (FRAP) was measured according to a previously published method (Chayaratanasin et al., 2015). The absorbance was measured at 595 nm. The FRAP value was calculated using the standard curve of $FeSO_4.7H_2O$ solution. The result was expressed as mmol $FeSO_4$ per 100 g yogurt.

3.1.6 Identification and quantification of anthocyanins

Identification and quantification of anthocyanin was performed by high performance liquid chromatography (HPLC). The extraction of yogurt sample was done following the previously published report with minor modification (Trigueros et al., 2014). In brief, yogurt (5 g) was mixed with 15 ml of 2% acidified methanol, then the solution was mixed for 5 min. After centrifugation at 3500 rpm at 4°C for 15 min, the supernatant was collected and store at -20 C until future used. The HPLC condition for this experiment was modified from a previous study (Ścibisz, Ziarno, Mitek, & Zarębа, 2012). The sample extract was diluted three times with 2% acidified methanol before injected into HPLC system model SPD-10A (Shimadzu, Kyoto, Japan) with a UV-detector, the column was C_{18} (250x4.6 mm, VertiSep™ AQS-Vertical Chromatography CO., LTD), the mobile phase was composed of solvent A (10% formic acid) and solvent B (10% formic acid, 22.5% acetonitrile and 22.5% methanol). Twenty microliters of

sample were run at 0.6 mL/min flow on a column and monitored for absorbance at 515 nm. The identification of anthocyanins in RBE was performed by comparing their retention times and spiking the samples with cyanidin-3-glucoside and peonidin-3-glucoside. The standard curve was prepared using cyanidin-3-glucoside (C3G) and peonidin-3-glucoside (P3G) with the concentration of 0.5 to 8 µg/ml. The values were reported as mg cyanidin-3-glucoside equivalent and mg peonidin-3-glucoside equivalent per 100 g yogurt.

3.1.7 *In vitro* gastrointestinal digestion of yogurt

All yogurt samples were subjected to *in vitro* digestion in order to investigate the release of glucose, TPC, anthocyanins, and antioxidant activity. The simulating oral, gastric and intestinal phase was performed according to the previously described method (Oliveira & Pintado, 2015) with minor modification. The yogurt sample (2 g) was mixed with 3200 U/ml porcine α-amylase in 0.2 M carbonate buffer at pH 7. After the oral phase for 20 second, the gastric phase was started by the addition of 3200 U/ml porcine pepsin in 0.02 M HCl, pH 2 at 37°C for 1 h. In the intestinal phase, 28 U/ml amyloglucosidase (3 mg/ml), pancreatin (2 mg/ml) in 0.2 M sodium acetate buffer pH 6 and bile salts (12 mg/ml) was added into the digesta and incubated at 37 °C. The sample was collected at the baseline, after gastric and intestinal phase (0, 30, 60, 120 and 180 min) with continuous stirring. The samples were cooled in an ice bath to stop the enzyme activity and centrifuged at 12000 rpm at 4 °C for 15 min. The

supernatants were collected and stored at - 20 ℃ until further analysis. The concentration of glucose was measured using the glucose oxidase kit. The concentration of glucose was expressed as mg/ dL. The TPC and ferric reducing antioxidant power (FRAP) assay was performed according to a previously published method (Chayaratanasin et al., 2015). The results of TPC and FRAP were expressed as mg GAE per 100 g yogurt and mmol $FeSO_4$ per 100 g yogurt, respectively. The content of anthocyanin was determined using HPLC. The results were expressed as µg cyanidin-3-glucoside equivalent and µg peonidin-3-glucoside equivalent per 100 g yogurt.

3.1.8 Sensory analysis

The sensory acceptability of yogurt samples after 1 day of refrigerated storage was evaluated by 42 untrained panelists, the participants were 18- 50 years old, ever to consumed yogurt. Participants were required to be non-smokers, not pregnant and lactation, free from food allergies, and no evidence of dietary intolerances, restrictions or adverse reactions to dairy products. The sensory attributes including color, odor, taste, flavor, texture and overall acceptance of each yogurt. Each panelist was received 4 cups of yogurt samples which code with a random three-digit number. The affective dimension of the consumer perception of the samples was qualified by the sensory evaluation form as 10 cm visual analog scale (VAS) (unacceptable, acceptable and no criticism) (Soukoulis, Panagiotidis, Koureli, & Tzia, 2007).

3.1.9 Statistical analysis

Data were reported as mean ± S.E.M (*n*=3). Statistical analyses were performed using one-way ANOVA followed by Duncan's multiple range test (P <0.05). In simulated digestion and refrigerated storage, Two-way analysis of variance (ANOVA) was used for the comparisons between the effect of treatment and time followed by Duncan's multiple range test (P <0.05).

3.2 Part II: The effect of rice-berry yogurt on postprandial glycemic response and antioxidant status in healthy subjects.

3.2.1 Preparation of probiotic yogurt with or without RBE

The set-type yogurt procedure was adapted from a previous report (Chandan & O'Rell, 2006). In brief, whole milk was heated to 50 ℃ and milk powder (3% w/v) and sucrose (5% w/v) were added, then homogenized at 7000 rpm, 65 ℃ for 5 min followed by the addition of RBE at 0.25% (w/v). After heating at 90 ℃ for 10 min, the standardized milk was cooled to 43 ℃ and inoculated with 0.02% of a mixed yogurt freeze-dried culture containing *Streptococcus thermophilus*, *Lactobacillus delbrueckii* supsp. *bulgaricus*, *Lactobacillus acidophilus* LA-5 and *Bifidobacterium animalis* subsp. *lactis* BB-12. The inoculated milk was incubated for 5 h at 43 ℃. When the pH of yogurt reached to 4.6, the yogurt samples were cooled at 4 ℃ to stop the fermentation and kept at 4 ℃ until further used. All the probiotic yogurt (Figure 3.1) was prepared by a researcher at the Department of Nutrition and Dietetics, Faculty of Allied Health Sciences, Chulalongkorn university.

Figure 12 The probiotic yogurt with or without RBE for participants

3.2.2 Sample size calculation

The sample size was calculated from the formula for crossover study design by setting 95% confidence level and 80% power of test to detect the difference on area under the curve (AUC) for plasma insulin from the previous study (Törrönen, McDougall et al. 2012). The sample size was calculated using the following equation:

$$n = \frac{(Z_{\alpha/2}+Z\beta)^2\ \boldsymbol{\sigma}^2}{\Delta^2}$$

where n = participants in each group, $Z_{1-\alpha/2}$ = confidence interval at 95% is 1.96 (Type I error), $Z\beta$ = power of test (80%) is 0.84 (Type II error), $\boldsymbol{\sigma}$ = standard deviation, Δ = change in the two group of the considered parameter.

$$n = \frac{(1.96+0.84)^2(3677.7)^2}{(2502)^2}$$

n = 16.9 ~ 17 participants

After 30% dropout rate, a total of 23 participants was recruited for the study.

3.2.3 Participants' criteria

Inclusion criteria

- Age 18-40 years old men and women
- BMI 18.5-22.9 kg/m^2
- Fasting blood glucose < 100 mg/dl
- Fasting total cholesterol < 200 mg/dl
- Fasting triglyceride < 150 mg/dl
- No evidence of dietary intolerances, restrictions or adverse reactions to dairy products

Exclusion criteria

- Diagnose as diabetic glucose intolerance or insulin resistance
- Use of medication known to interfere with glucose homeostasis or intestinal absorption
- Pregnancy and lactation
- Allergy to the study product
- Moderate or intense physical activity (exceeding 6 h/week)
- Use of nutritional supplements
- Regularly Smoking

3.2.4 Ethic approval

The study protocol was approved by the office of Ethics Review Committee for Research Involving Human Research Subjects, Human Science Group, Chulalongkorn University (COA No. 241/2018). All subjects gave their written informed consent to participate. All information of participants was kept confidential. There were no major changes in the study protocol after initiation of the study.

3.2.5 Study design and intervention

Design of the study was a randomized-controlled, crossover trial with a 1-week washout periods. The procedure of the study was shown in figure 3.2. The participants were randomly assigned to the sequence of the probiotic yogurt with or without RBE by using computer sampling. Prior to each study period, the participants instructed to avoid intake of phytochemical-rich foods such as berries, tea, soy, strawberry, citrus fruits, red grape, black rice etc. Moreover, the participants were asked to fast for 10-12 h overnight for each study period. On the test day, they arrived at the Department of Nutrition and Dietetics, Faculty of Allied Health Sciences, Chulalongkorn university and were weighted upon arrival. After 10 min rest, an intravenous catheter was inserted into a peripheral arm vein for repeated blood collection by a registered nurse and the subjects' appetite sensation was assessed with a visual analogue scale (VAS) (at 0 min). After that, all participants were introduced to consume the 350 g probiotic yogurt with or without RBE within 10 min. During this study, drinking-water was limited not more

than 1,000 ml. In addition, participants were also introduced to maintain their usual diet and physical activity until the end of the study.

The subjects' appetite sensation VAS were 100 mm in length with words anchored at each end, expressing the most positive and the most negative rating. VAS were evaluated for hunger, fullness, desire to eat and satiety at before (0 min) and after consumption of a test yogurt at 30, 60, 90, 120, 150, and 180 min.

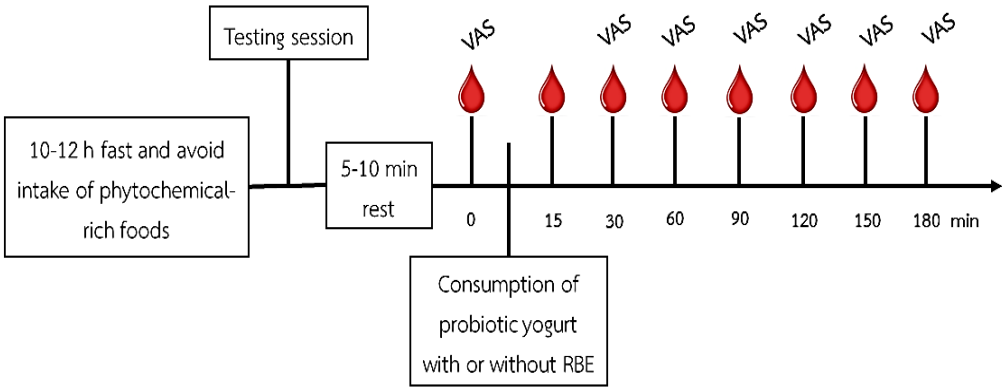


Figure 13 Study session protocol

3.2.6 Blood collection and analysis

Venous blood samples were collected through an intravenous (I.V.) catheter inserted into a forearm vein by registered nurses. Blood samples was collected before (0 min) and after consumption of a test yogurt at 15, 30, 60, 90, 120, 150, and 180 min. At all-time points, blood samples were collected into NaF and EDTA tubes for analysis of plasma glucose, plasma insulin, and antioxidant status. The blood samples were centrifuged at 3000 rpm for 15 min at 4 °C to recover plasma. After centrifugation, plasma was kept in Eppendorf tubes and stored at – 80 °C until analysis.

3.2.7 Measurement of plasma glucose

Plasma glucose was measured by using a glucose oxidase method (HUMAN GmbH, Germany).

3.2.8 Measurement of plasma antioxidant capacities

Ferric Reducing Antioxidant Power (FRAP) assay in a redox-linked colorimetric reaction using methods modified from Benzie and Strain (107). Plasma sample (10 µL) was incubated with FRAP reagent (90 µL) containing 0.3 M sodium acetate buffer (pH 3.6), 10 mM TPTZ in 40 mM HCl and 20 mM FeCl3. After incubation at room temperature for 30 min, the reaction was read at the absorbance at 595 nm. The result was interpreted the EC (Equivalence concentration) value from a standard curve of $FeSO_4$.

Trolox Equivalent Antioxidant Capacity (TEAC) assay was measured based on the inhibition of the scavenging of 2,2'-azinobis (3-ethyl benzothiazoline-6-sulfonic acid) diamonium salt radical ($ABTS^{\cdot+}$) (96). The $ABTS^{+}$ reagent was prepared by the mixture of 7 mM ABTS in 0.1 M PBS (pH 7.4) and 2.45 mM K2S2O8 in distilled water (1:1, v/v). After incubation for 16 h at room temperature, $ABTS^{+}$ solution was diluted with 0.1 M PBS (pH 7.4) to adjust the absorbance between 0.900 and 1.000 at 734 nm. The adjusted $ABTS^{+}$ solution was added into the plasma. After incubation for 6 min. The reaction was measured at 734 nm and plasma TEAC was expressed as mM Trolox equivalents.

3.2.9 Measurement of plasma oxidant

Malondialdehyde (MDA) assay was indicated as an end products of lipid peroxidation by using a method based on the formation of thiobarbituric acid (TBA) method under acidic conditions to produce a pink-colored product. Plasma was mixed with 10% trichloroacetic acid (TCA) and 50 mM 2,6-Di-tert-bytyl-4-methylphenol (BHT). After that, the mixture was centrifuged at 12,000 rpm for 10 min. then, 0.67% TBA was added to the supernatant and then the mixture was incubated at 100 ℃ for 10 min. The pink-colored of reaction was measured at 532 nm. Plasma MDA concentration was calculated from the calibration curve of MDA and expressed as μmol/L MDA (Wolff and Dean 1987).

3.2.10 Statistical analysis

The data were reported as mean ± SEM. The statistical analyses were performed using SPSS version 22 (Chicago, IL). The Shapiro-Wilk test was used to test normality of the data. In human study, postprandial Incremental Area Under the Curve (IAUC) for glucose, insulin, antioxidant status and lipid peroxidation (MDA) was calculated using the Trapezoidal rule. Statistical analysis was determined by using repeated measure ANOVA and followed by Post hoc test by Duncan's multiple comparison. Paired t-test was used for comparison between treatment. P-value < 0.05 was considered statistically significances.

3.3 Part III: The consumption of riceberry rice beverage with high-carbohydrate, moderate- fat meal on postprandial glycemic response, antioxidant status, lipidemic response, and inflammatory markers in overweight and obese subjects.

3.3.1 RBE powder preparation

The aqueous extract of riceberry rice was prepared by a mixture of riceberry rice and distilled water in 1:2 w/w ratio. The mixture was heated at 45 ℃ for 40 min with continuous stirring, then the supernatant was collected and filtered with Whatman No. 1 filter paper. In our preliminary experiment, the highest amount of polyphenol content was obtained by this condition. The sample was frozen at -18 ℃ for 48 h. After that, the sample was placed in a freeze dryer GFD-30S (GRT., Grisrianthong. Co., Ltd, Thailand) and dried at -30 ℃, at pressure of 0.15 mbar for 27 h and 30 min. The riceberry rice extract (RBE) powder was kept in the laminated aluminum foil vacuum bags at -20 ℃ until used.

3.3.2 Sample size calculation

The sample size was calculated from the formula for crossover study design by setting 95% confidence level and 80% power of test to detect the difference of least-square means for plasma insulin from the previous study (Edirisinghe, Banaszewski et al. 2011). The sample size was calculated using the following equation:

$$n = \frac{(Z_{\alpha/2}+Z_{\beta})^2\,\sigma^2}{\Delta^2}$$

where n = participants in each group, $Z_{1-\alpha/2}$ = confidence interval at 95% is 1.96 (Type I error), $Z\beta$ = power of test (80%) is 0.84 (Type II error), σ = standard deviation, Δ = change in the two group of the considered parameter.

$$n = \frac{(1.96+0.84)^2(68.1)^2}{(55.6)^2}$$

$$n = 11.76 \sim 12 \text{ participants}$$

After 30% dropout rate, a number of participants in this study was 16.

3.3.3 Participants' criteria

Inclusion criteria

- 18-40 years old men
- BMI 23.0-29.9 kg/m^2
- Fasting blood glucose < 100 mg/dl

Exclusion criteria

- Diagnose as diabetic glucose intolerance or insulin resistance
- Use of medication known to interfere with glucose homeostasis or intestinal absorption
- Use of medication known to interfere with cholesterol or triglyceride and inflammatory level
- Allergy to the study product
- Moderate or intense physical activity (exceeding 6 h/week)

- Use of nutritional supplements
- Regularly Smoking

3.3.4 Ethic approval

The study protocol was approved by the office of Ethics Review Committee for Research Involving Human Research Subjects, Human Science Group, Chulalongkorn University (COA No. 241/2018). All subjects gave their written informed consent to participate. All information of participants was kept confidential. There were no major changes in the study protocol after initiation of the study.

3.3.5 Study design and intervention

This study design was carried out using a randomized-controlled, crossover trial with a 1-week. Participants were randomly assigned to consume a high-carbohydrate, moderate-fat meal (HCMF) or a high-carbohydrate, moderate-fat meal with 2 g RBE powder beverage (HCMF+RBE) as shown in Table 7 and Figure 14. The freeze-dried riceberry powder was prepared by mixing 400 ml of water and 10 g of sucrose.

Figure 14 The study meal

Table 7 Nutritional information about the testing meal

Compositions	HCMF	HCMF + RBE
RBE extract (g)	-	2
White breads (slices)	4	4
Condensed-milk (g)	10	10
Butter (g)	15	15
Sugar (g)	10	10
Total calories (kcal)	535	535
CHO : Fat : Protein ratio	68.8 : 25.2 : 6.0	68.8 : 25.2 : 6.0

Adapted from Chusak et al. (2014).

The procedure in this study was shown in figure 6. All testing meals were prepared freshly by a researcher. On the test day, they arrived at the Department of Nutrition and Dietetics, Faculty of Allied Health Sciences, Chulalongkorn university and were weighted upon arrival after a 10-12 h overnight fast. After 10 min rest, an intravenous catheter was inserted into a peripheral arm vein for repeated blood collection by a registered nurse and the subjects' appetite sensation was assessed with a visual analogue scale (VAS) (at 0 min). Then, they were introduced to consume a test meal within 10 min. During this study, drinking-water was limited not more than 1,000 ml. They were instructed to avoid intake of phytochemical-rich foods such as berries, tea, soy, strawberry, citrus fruits, red grape, black rice etc. until completed the study. The subjects' appetite sensation VAS were 100 mm in length with words anchored at each end, expressing the most positive and the most negative rating. VAS were evaluated for hunger, fullness, desire to eat and satiety at before (0 min) and after consumption of a test yogurt at 30, 60, 90, 120, 180, 240, 300 and 360 min.

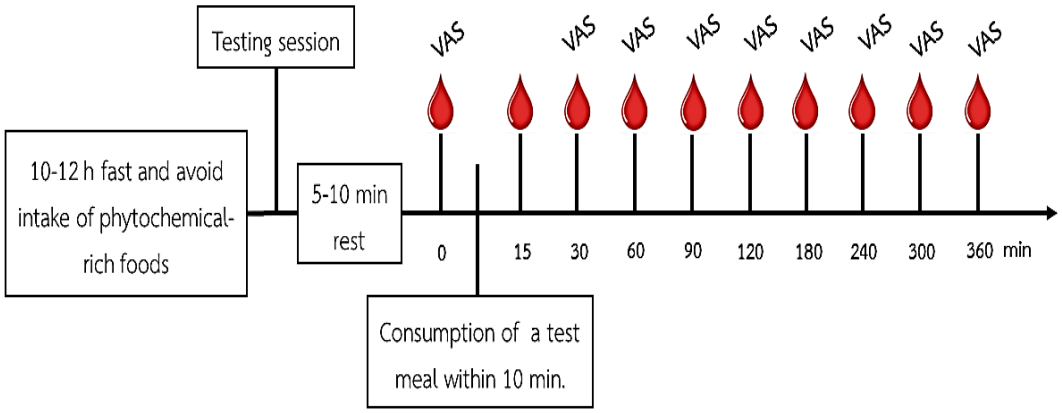


Figure 15 The study protocol

3.3.6 Blood collection and analysis

The blood samples were collected through an intravenous catheter inserted into a forearm vein by registered nurses and remained into a subject's forearm for collecting blood samples until 6 hours. Blood samples were collected before and 15, 30, 60, 90, 120, 180, 240, 300, and 360 min after consumption of the study meal. At all-time points, blood was collected into NaF and EDTA tubes for analysis of plasma glucose, insulin, triglyceride, antioxidant, and inflammatory markers. The samples were centrifuged at 3000 rpm for 15 min at 4 °C to recover plasma. After centrifugation, plasma was kept in Eppendorf tubes and stored at –80 °C until analysis.

3.3.7 Measurement of plasma glucose, insulin and triglyceride

Plasma glucose by using a glucose oxidase method (HUMAN GmbH, Germany). As for plasma triglyceride was measured using a triglyceride enzymatic Colorimetric method (HUMAN GmbH, Germany). Plasma insulin was measured by an insulin ELISA kit (Thermo Fisher Scientific Inc., USA).

3.3.8 Measurement of plasma antioxidant capacities

Ferric Reducing Antioxidant Power (FRAP) assay in a redox-linked colorimetric reaction using methods modified from Benzie and Strain (1996). Plasma sample (10 µL) was incubated with FRAP reagent (90 µL) containing 0.3 M sodium acetate buffer (pH 3.6), 10 mM TPTZ in 40 mM HCl and 20 mM FeCl3. After incubation at room temperature for 30 min, the reaction was read at the absorbance at 595 nm. The

result was interpreted the EC (Equivalence concentration) value from a standard curve of $FeSO_4$.

Trolox Equivalent Antioxidant Capacity (TEAC) assay was measured based on the inhibition of the scavenging of 2,2'-azinobis (3-ethyl benzothiazoline-6-sulfonic acid) diamonium salt radical ($ABTS^{\cdot+}$) (96). The $ABTS^{+}$ reagent was prepared by the mixture of 7 mM ABTS in 0.1 M PBS (pH 7.4) and 2.45 mM K2S2O8 in distilled water (1:1, v/v). After incubation for 16 h at room temperature, $ABTS^{+}$ solution was diluted with 0.1 M PBS (pH 7.4) to adjust the absorbance between 0.900 and 1.000 at 734 nm. The adjusted $ABTS^{+}$ solution was added into the plasma. After incubation for 6 min. The reaction was measured at 734 nm and plasma TEAC was expressed as mM Trolox equivalents.

3.3.9 Measurement of plasma oxidant

Malondialdehyde (MDA) assay was indicated as an end products of lipid peroxidation by using a method based on the formation of thiobarbituric acid (TBA) method under acidic conditions to produce a pink-colored product. Plasma was mixed with 10% trichloroacetic acid (TCA) and 50 mM 2,6-Di-tert-bytyl-4-methylphenol (BHT). After that, the mixture was centrifuged at 12,000 rpm for 10 min. then, 0.67% TBA was added to the supernatant and then the mixture was incubated at 100 ℃ for 10 min. The pink-colored of reaction was measured at 532 nm. Plasma MDA concentration was

calculated from the calibration curve of MDA and expressed as μmol/L MDA (Wolff and Dean 1987).

3.3.10 Measurement of plasma free fatty acid and inflammation

The plasma concentration of free fatty acid, IL-1β, IL-6, and TNF-α was performed by using commercially available high-sensitivity enzyme-linked immunosorbent assay kits (R&D System Inc., Minneapolis, MN) according to the manufacture' instructions.

3.3.11 Statistical analysis

The data was reported as mean ± SEM. Postprandial Incremental Area Under the Curve (iAUC) for plasma glucose, insulin, triglyceride, antioxidant status, MDA, free fatty acid, IL-1β, IL-6, and TNF-α were calculated using the Trapezoidal rule. The Shapiro-Wilk test was used to test normality of the data. Statistical analysis was determined by using repeated measure ANOVA and followed by Post hoc test by Duncan's multiple comparison. P-value < 0.05 was considered statistically significances.

CHAPTER IV

RESULTS

4.1 Part I: Incorporation of anthocyanin-rich riceberry rice in yogurts: Effect on physicochemical properties, antioxidant activity and *in vitro* gastrointestinal digestion

4.1.1 Characteristic of riceberry rice extract (RBE)

The photographs of riceberry rice and its powder extract (RBE) are shown in Figure 4.1. The results found that the TPC, DPPH radical scavenging activity and FRAP of RBE were 69.95±5.78 mg gallic acid equivalent/g extract, 93.57±7.7 mg ascorbic acid equivalent/g extract and 592.12±55.3 mmol $FeSO_4$/g extract, respectively. From the HPLC analysis, C3G (2.05±0.04 mg/g extract) and P3G (0.78±0.01 mg/g extract) were identified in RBE.

Figure 16 Riceberry rice and its powder extract (RBE)

4.1.2. Kinetic parameters

Figure 17 represents the pH change of yogurt supplemented with RBE during the fermentation time. The addition of RBE did not reduce the initial pH of the milk, whereas it significantly increased pH of the mixture after 2 h of fermentation. However, the time taken for yogurt supplemented with RBE to reach pH 4.6 was similar to that of the control. The acidification kinetic parameters of yogurt supplemented with RBE are shown in Table 8. The maximum acidification rates (V_{max}) were between 8.78 and 12.77 10^{-3} pH units per min. The addition of RBE (0.125-0.5%) to yogurt resulted in a significant decrease in V_{max}. The time to reach a maximum acidification rate (T_{max}) was increased when yogurts were supplemented with RBE 0.25% and 0.5%. Moreover, RBE did not change the fermentation time (T_f) when compared to the control.

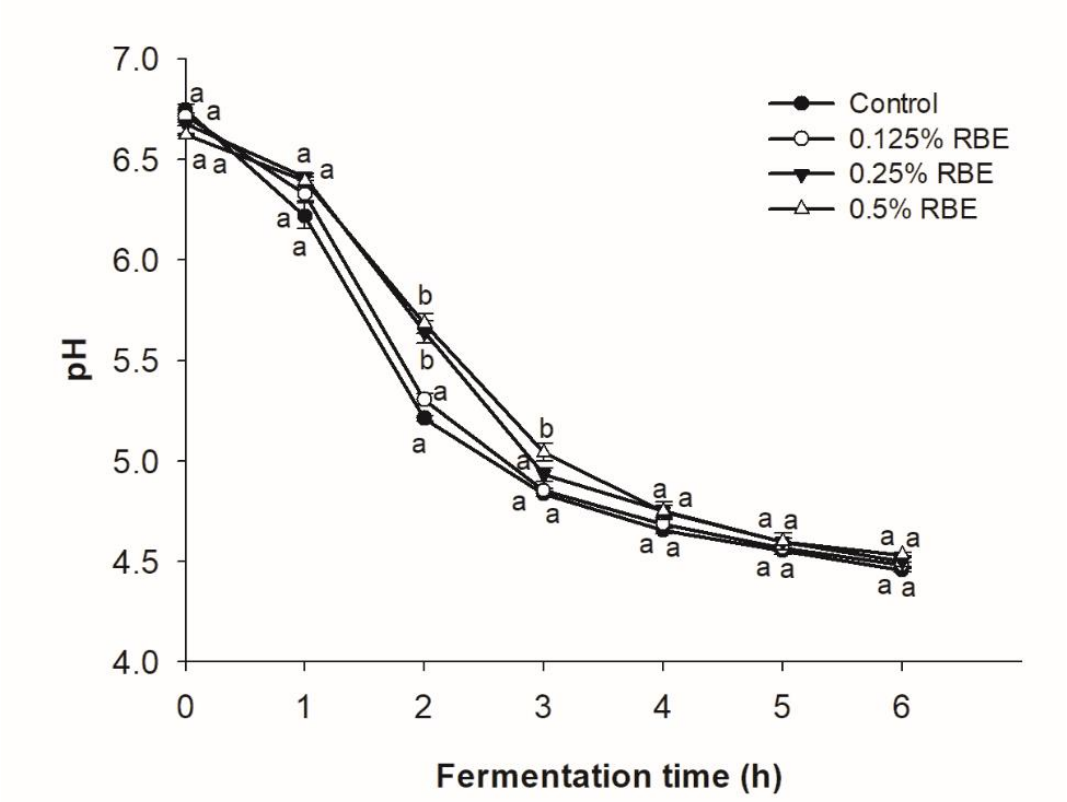


Figure 17 pH values of yogurt samples during fermentation time. The results are expressed as mean ± S.E.M (n=3). Means with different letters are significant different (P<0.05).

Table 8 Acidification kinetic parameters of yogurt supplemented with RBE during fermentation.

Samples	V_{max} (10^{-3}pH units/min)	T_{max} (h)	$T_{pH\ 5.0}$ (h)	T_f (h)
Control	12.77±0.34[a]	2.00±0.05[a]	3.62±0.03[a]	4.66±0.03[a]
RBE 0.125%	11.75±0.20[b]	2.00±0.03[a]	3.70±0.03[a]	4.73±0.03[a]
RBE 0.25%	9.69±0.24[c]	3.00±0.07[b]	3.65±0.27[a]	4.75±0.04[a]
RBE 0.5%	8.78±0.26[d]	3.00±0.09[b]	3.75±0.23[a]	4.78±0.08[a]

V_{max} = maximum acidification rate (10^{-3}pH units/min); T_{max} = time at which V_{max} was reached; $T_{pH5.0}$ = time to reached pH 5.0; T_f = time to complete the fermentation at pH 4.6. The results are expressed as mean ± SEM (n= 3). Means with difference superscripts are significantly different (P<0.05). RBE concentration is reported on a weight/weight basis (w/w).

4.1.3. Physicochemical properties, microbiological analysis, total phenolic content and antioxidant activity of yogurt

Table 9 shows the results of pH, titratable acidity, syneresis, texture profiles, TLC, TPC, anthocyanins and antioxidant activity of yogurt supplemented with RBE at day 1 of refrigerated storage. The addition of RBE into yogurt had no effect on changes in pH and titratable acidity when compared to the control yogurt. As for the result of syneresis, an important index for evaluating quality of set-type yogurt, indicates a balance between attraction and repulsion forces within the casein network and the rearrangement capacity of the network bond (Matumoto-Pintro, Rabiey, Robitaille, & Britten, 2011). In this study, the addition of RBE (0.125-0.5%) caused a significant reduction in syneresis of yogurt. For the firmness, an important parameter to measure the quality of set yogurt, indicate force necessary to attain a given deformation. In this study, RBE at concentration of 0.5% produced a significant decrease firmness of yogurt. As shown in Table 9, the addition of RBE did not affect the number of viable lactobacilli count in yogurt. As for the results of total phenolic content and antioxidant activity of yogurt showed that yogurt supplemented with RBE had significantly higher TPC, C3G, P3G, DPPH radical scavenging activity and FRAP when compared to the control.

Table 9 Physicochemical properties, total lactobacillus count (TLC), total phenolic content (TPC), cyanidin-3-glucoside (C3G), peonidin-3-glucoside (P3G), and antioxidant activity of yogurt supplemented with RBE at day 1 of refrigerated storage.

Experiments	pH	Titratable acidity (%)	Syneresis (%)	Firmness (g)	Adhesiveness (g.s)	TLC (CFU/g yogurt)	TPC (mg GAE /100 g yogurt)	C3G (mg/ 100 g yogurt)	P3G (mg/ 100 g yogurt)	DPPH (mg Ascobic acid/100 g yogurt)	FRAP (mmol trolox /100 g yogurt)
Control	4.69±0.01^{a}	0.60±0.03^{a}	14.13±0.32^{a}	268.11±20.35^{a}	393.92±20.53^{a}	2.07x10^{9}±0.03^{a}	4.58±0.35^{a}	N.D.	N.D.	2.19±0.06^{a}	5.26±0.52^{a}
0.125%RBE	4.67±0.03^{a}	0.64±0.02^{a}	12.05±0.58^{b}	258.57±13.23^{a}	372.99±20.42^{a}	2.00x10^{9}±0.21^{a}	6.50±0.27^{b}	2.88±0.12^{a}	1.31±0.06^{a}	3.96±0.10^{b}	17.42±0.43^{b}
0.25%RBE	4.66±0.02^{a}	0.71±0.04^{a}	8.45±0.49^{c}	239.71±14.94^{a}	366.61±15.82^{a}	2.10x10^{9}±0.10^{a}	8.04±0.26^{c}	4.97±0.20^{b}	2.25±0.10^{b}	5.83±0.18^{c}	25.64±0.96^{c}
0.5%RBE	4.63±0.06^{a}	0.66±0.04^{a}	8.14±0.53^{c}	224.07±11.26^{b}	388.74±42.07^{a}	2.07x10^{9}±0.19^{a}	11.65±0.2^{d}	9.38±0.06^{c}	4.13±0.17^{c}	10.69±0.36^{d}	41.06±2.60^{d}

The results are expressed as mean ± SEM (n = 3). Means with difference superscripts are significantly different (p<0.05). N.D. not detection. RBE concentration is reported on a weight/weight basis (w/w).

4.1.4 *In vitro* gastrointestinal digestion

The effects of RBE on the release of glucose from yogurts are shown in Figure 18. In gastric phase, there was no significant difference in the release of glucose between the control and yogurt supplemented with RBE. After yogurts were digested at the intestinal phase, the significant increase in glucose release from yogurts was perceived. Interestingly, RBE (0.25% and 0.5%) slightly reduced the glucose release from yogurt at the beginning of intestinal phase. However, RBE did not show a significant difference in the glucose release between the control and yogurt supplemented with RBE during 60-180 min.

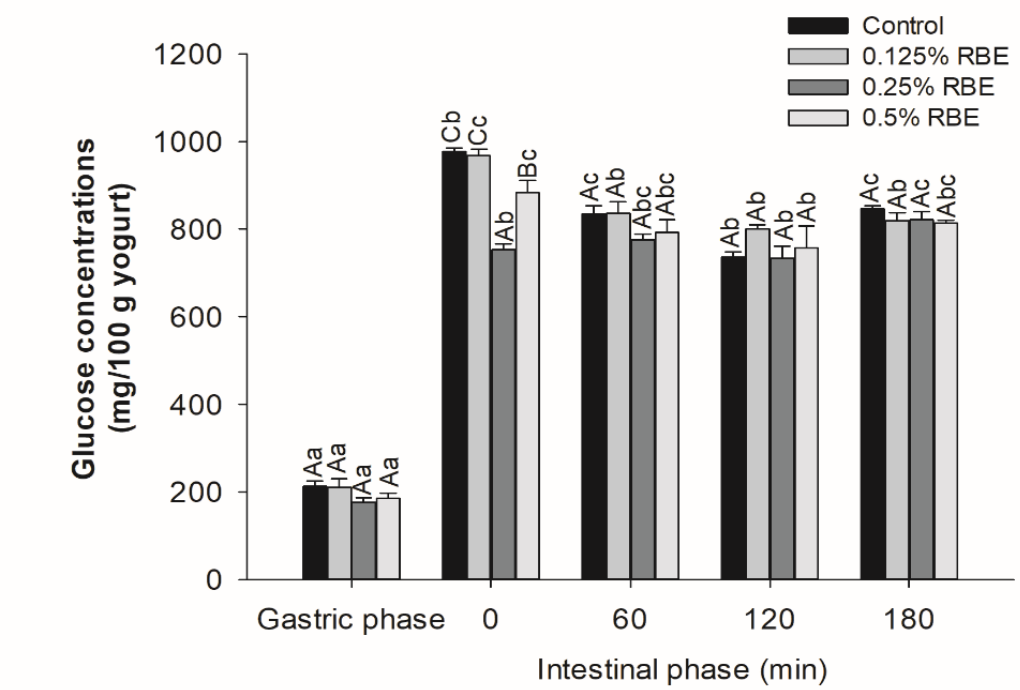


Figure 18 The release of glucose of yogurts supplemented with 0.125, 0.25, and 0.5 % (w/w) riceberry rice extract (RBE) during *in vitro* gastrointestinal digestion. The results are expressed as mean ± S.E.M (n=3). Means with different lowercase letters (a-c: time effects) at the same treatment are significant different (P<0.05). Means with different uppercase letters at the same time (A-D: treatment effects) are significant different (P<0.05).

Figure 19 shows the level of TPC in all yogurts during *in vitro* gastrointestinal digestion, respectively. In the gastric phase, a significant higher level of TPC in yogurt supplemented with RBE was observed at the beginning of intestinal phase. The gradual increase in the release of the TPC from yogurt supplemented with RBE was markedly noticed after the intestinal phase when compared to control.

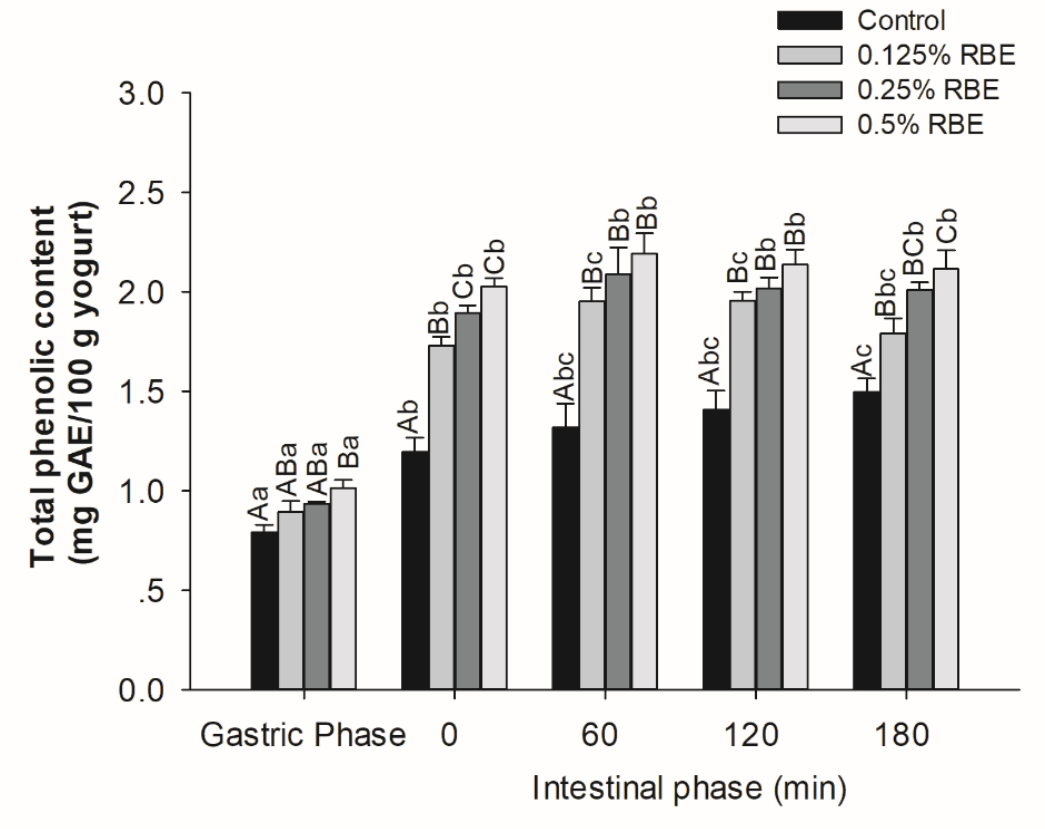


Figure 19 The level of TPC of yogurts supplemented with 0.125, 0.25, and 0.5 % (w/w) riceberry rice extract (RBE) during *in vitro* gastrointestinal digestion. The results are expressed as mean ± S.E.M (n= 3). Means with different lowercase letters (a-c: time effects) at the same treatment are significant different (P<0.05). Means with different uppercase letters at the same time (A-C: treatment effects) are significant different (P<0.05).

Figure 20 and 21 demonstrate the level of C3G and P3G in yogurts supplemented with RBE during *in vitro* gastrointestinal digestion. The results found that the level of C3G and P3G in yogurts supplemented with RBE increased at the gastric phase, whereas they decreased at the beginning of intestinal digestion. As the intestinal digestion proceeded, the level of C3G and P3G in yogurts supplemented with RBE remain unchanged. The gradual decrease in the level of anthocyanins in yogurt from gastric to intestinal digestion, as was observed

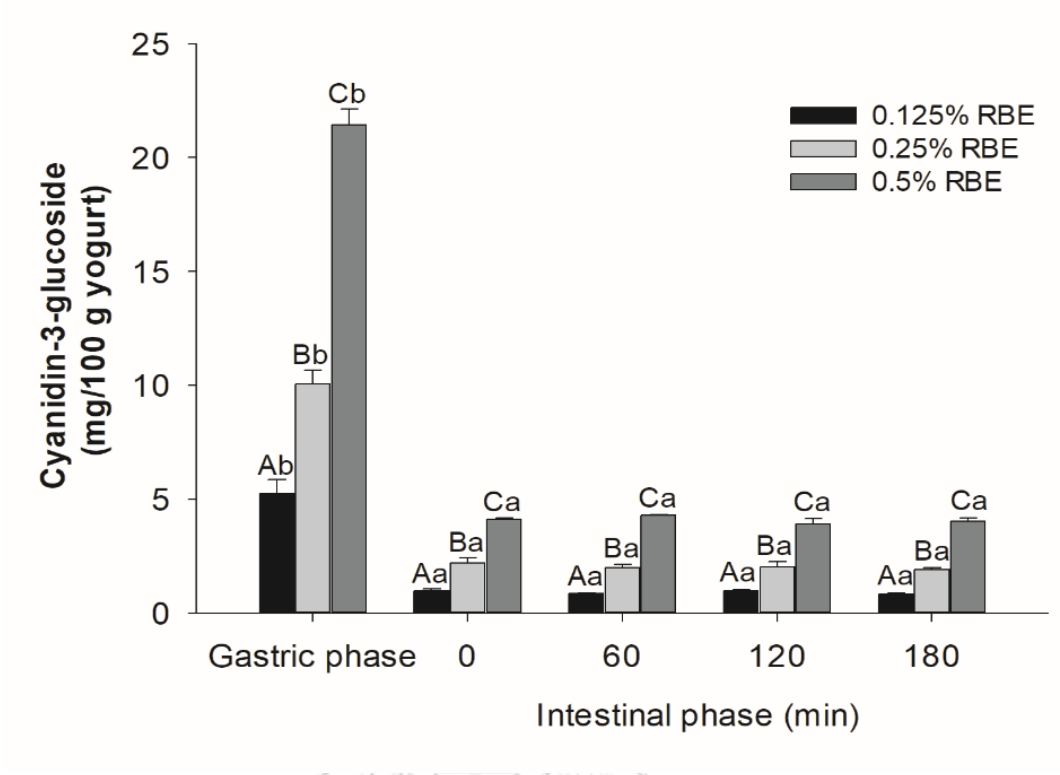


Figure 20 The level of C3G of yogurts supplemented with 0.125, 0.25, and 0.5 % (w/w) riceberry rice extract (RBE) during *in vitro* gastrointestinal digestion. The results are expressed as mean ± S.E.M (n=3). Means with different lowercase letters (a-b: time effects) at the same treatment are significant different (P<0.05). Means with different uppercase letters at the same time (A-C: treatment effects) are significant different (P<0.05).

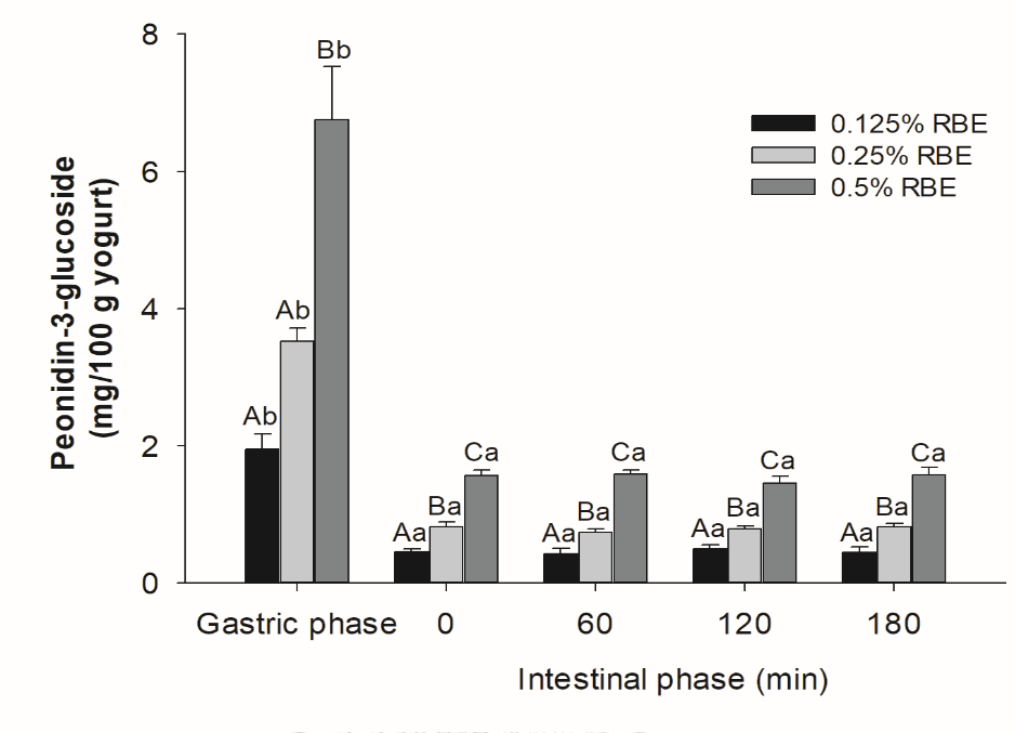


Figure 21 The level of P3G of yogurts supplemented with 0.125, 0.25, and 0.5 % (w/w) riceberry rice extract (RBE) during *in vitro* gastrointestinal digestion. The results are expressed as mean ± S.E.M (n=3). Means with different lowercase letters (a-b: time effects) at the same treatment are significant different (P<0.05). Means with different uppercase letters at the same time (A-C: treatment effects) are significant different (P<0.05).

The results for antioxidant activity of yogurt supplemented with RBE subjected to the simulated gastrointestinal environment are presented in Figure 22. When comparing with gastric digestion, the FRAP value of the control yogurt significantly increased at 0, 60 and 120 min after intestinal digestion.

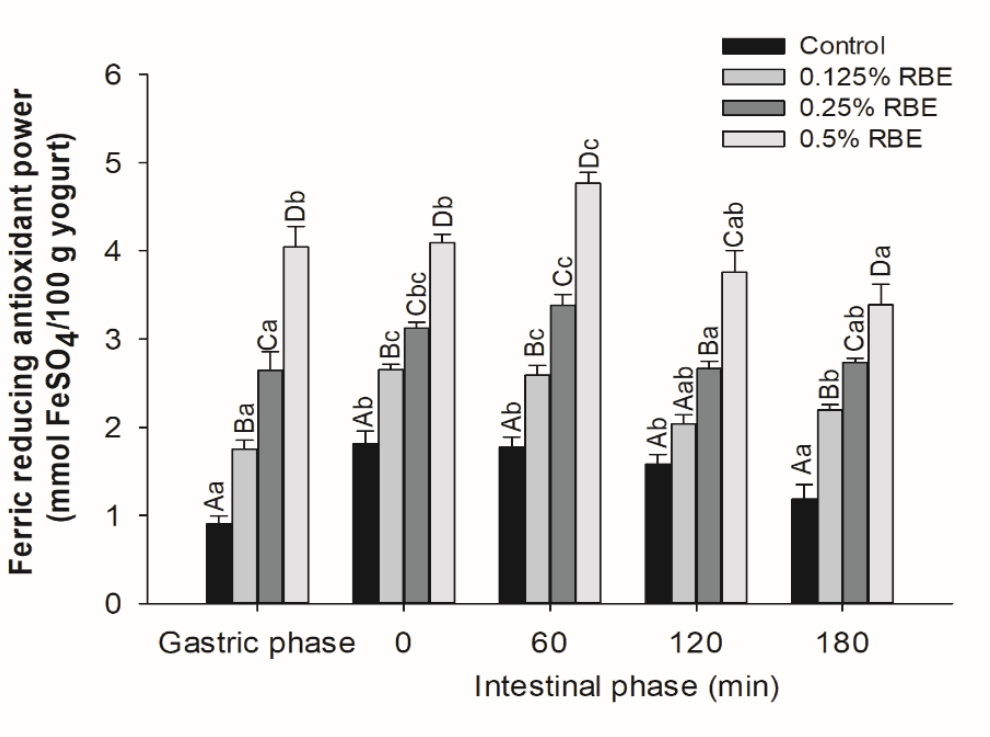


Figure 22 The FRAP values of yogurts supplemented with 0.125, 0.25, and 0.5% (w/w) riceberry rice extract (RBE) during *in vitro* gastrointestinal digestion. The results are expressed as mean ± S.E.M (n=3). Means with different lowercase letters (a-c: time effects) at the same treatment are significant different (P<0.05). Means with different uppercase letters at the same time (A-D: treatment effects) are significant different (P<0.05).

4.1.5. Sensory evaluation

The results describing the effect of RBE on sensory attributes of yogurt at day 1 of refrigerated storage are reported in Table 10. The results indicated that addition of RBE into yogurt caused a slight decrease in the score of parameters including color, odor and appearance. In particular, 0.125% and 0.25% RBE did not change the score of flavors and demonstrated a good overall acceptability of consumer.

Table 10 Sensory evaluation of yogurts supplemented with RBE at day 1.

Experiments	Characteristics					
	Color	Odor	Flavor	Texture	Appearance	Acceptability
Control	8.06±0.27^{a}	7.92±0.30^{a}	8.02±0.25^{a}	8.25±0.23^{a}	8.09±0.23^{a}	8.43±0.20^{a}
0.125%RBE	6.53±0.38^{b}	6.70±0.32^{b}	7.45±0.23^{a}	7.47±0.20^{b}	7.16±0.29^{b}	7.87±0.17^{a}
0.25%RBE	6.72±0.33^{b}	6.73±0.32^{b}	7.36±0.30^{a}	7.83±0.19^{ab}	7.31±0.25^{b}	8.10±0.18^{a}
0.5%RBE	5.54±0.38^{c}	5.15±0.38^{c}	5.88±0.37^{b}	6.76±0.33^{c}	6.30±0.33^{c}	6.37±0.32^{b}

The results are expressed as mean ± SEM (n = 42). Means with difference superscripts are significantly different (P<0.05). RBE concentration is reported on a weight/weight basis (w/w).

4.1.6 Physicochemical, phytochemical, microbiological and antioxidant changes in yogurt during refrigerated storage

Table 11 shows the results for physicochemical properties, microbiological analysis, phytochemical compounds and the antioxidant activity of yogurt supplemented with 0.125% and 0.25% RBE during 21 days of refrigerated storage. It can be observed that the acidity and the pH values of yogurt supplemented with RBE did not differ significantly when compared to the control at the same day of storage. However, all formulated yogurts significantly decreased the number of LAB at 14 days and 21 days of refrigerated storage. For the syneresis of all formulated yogurts gradually decreased throughout 21 days of refrigerated storage. Yogurts supplemented with RBE showed lower syneresis than the control at 1, 7 and 14 days of storage, except for the end of storage. As for the results of color, the changes in the color profiles of yogurt supplemented with RBE during 21 days of storage. It is clear that the lower value of L* (lightness) and b* (yellowness) together with the higher value of a* (redness) was identified in yogurt supplemented with RBE, as compared to the control. The color profiles of yogurts supplemented with RBE remained constant until the end of the storage, except value of a*. Throughout 21 days of refrigerated storage, the TPC, C3G and P3G of yogurts supplemented with RBE remained constant. However, RBE-supplemented yogurt exhibited significantly higher TPC, C3G and P3G than the control throughout the study. As expected, the addition of RBE into yogurt produced significantly higher DPPH and FRAP value than the control throughout 21 days of

refrigerated storage. However, the DPPH and FRAP values of yogurts supplemented with RBE gradually decreased at day 21 when compared to day 1.

Table 11 Physicochemical properties, total lactobacillus count (TLC), total phenolic content (TPC), cyanidin- 3- glucoside (C3G), peonidin- 3- glucoside (P3G) and antioxidant activity of yogurt supplemented with RBE during 21 days of refrigerated storage.

Characteristics	Experiments	Day 1	Day 7	Day 14	Day 21
pH	Control	4.69 ± 0.02^{Ab}	4.75 ± 0.01^{Bc}	4.66 ± 0.01^{Aab}	4.65 ± 0.00^{Aa}
	0.125% RBE	4.67 ± 0.03^{Aa}	4.71 ± 0.04^{ABa}	4.62 ± 0.05^{Aa}	4.63 ± 0.03^{Aa}
	0.25% RBE	4.66 ± 0.02^{Aa}	4.64 ± 0.01^{Aa}	4.62 ± 0.02^{Aa}	4.63 ± 0.01^{Aa}
Titratable acidity (%)	Control	0.60 ± 0.03^{Aa}	0.58 ± 0.01^{Aa}	0.59 ± 0.00^{Aa}	0.58 ± 0.01^{Aa}
	0.125% RBE	0.64 ± 0.02^{ABa}	0.60 ± 0.02^{Aa}	0.61 ± 0.01^{Aa}	0.60 ± 0.00^{Aa}
	0.25% RBE	0.71 ± 0.04^{Bb}	0.63 ± 0.03^{Aab}	0.66 ± 0.01^{Bab}	0.61 ± 0.02^{Aa}
TLC (CFU/g yogurt)	Control	$2.07\times10^{9}\pm0.03^{Aa}$	$1.78\times10^{9}\pm0.41^{Aa}$	$7.03\times10^{8}\pm0.24^{Ab}$	$4.30\times10^{8}\pm0.67^{Ab}$
	0.125% RBE	$2.00\times10^{9}\pm0.21^{Aa}$	$1.82\times10^{9}\pm0.23^{Aa}$	$8.14\times10^{9}\pm0.32^{Ab}$	$5.13\times10^{8}\pm0.50^{Ab}$
	0.25% RBE	$2.10\times10^{9}\pm0.10^{Aa}$	$1.81\times10^{9}\pm0.45^{Aa}$	$8.43\times10^{9}\pm0.41^{Ab}$	$5.97\times10^{8}\pm1.40^{Ab}$
Syneresis (%)	Control	14.13 ± 0.32^{Aa}	12.94 ± 0.03^{Ab}	12.35 ± 0.06^{Ab}	8.36 ± 0.22^{Ac}
	0.125% RBE	12.05 ± 0.58^{Ba}	11.47 ± 0.08^{Ba}	11.87 ± 0.16^{Aa}	8.75 ± 0.47^{Ab}
	0.25% RBE	8.45 ± 0.49^{Ca}	6.69 ± 0.33^{Ca}	7.92 ± 0.80^{Ba}	6.44 ± 0.31^{Ba}
L*	Control	44.01 ± 0.43^{Aa}	42.82 ± 0.14^{Aa}	43.20 ± 0.14^{Aa}	43.34 ± 0.12^{Aa}
	0.125% RBE	24.64 ± 0.58^{Ba}	24.74 ± 0.11^{Ba}	24.78 ± 0.08^{Ba}	24.84 ± 0.13^{Ba}
	0.25% RBE	18.98 ± 0.29^{Ca}	19.08 ± 0.11^{Ca}	18.87 ± 0.03^{Ca}	19.06 ± 0.01^{Ca}
a*	Control	-1.09 ± 0.05^{Aa}	-1.21 ± 0.14^{Aa}	-1.26 ± 0.01^{Aa}	-1.24 ± 0.06^{Aa}
	0.125% RBE	8.96 ± 0.13^{Bb}	8.70 ± 0.04^{Bab}	8.69 ± 0.10^{Bab}	8.55 ± 0.15^{Ba}
	0.25% RBE	10.13 ± 0.07^{Cb}	10.02 ± 0.05^{Cb}	10.02 ± 0.02^{Cb}	9.86 ± 0.01^{Ca}
b*	Control	8.30 ± 0.23^{Aab}	7.86 ± 0.16^{Aa}	8.41 ± 0.15^{Aab}	8.65 ± 0.17^{Ab}
	0.125% RBE	4.67 ± 0.02^{Ba}	4.65 ± 0.08^{Ba}	4.82 ± 0.13^{Ba}	4.66 ± 0.03^{Ba}
	0.25% RBE	4.63 ± 0.05^{Ba}	4.47 ± 0.07^{Ba}	4.63 ± 0.16^{Ba}	4.72 ± 0.03^{Ba}

The results are expressed as mean ± SEM (n=3). Means with different lowercase letters (a-e: time effects) at the same treatment are significant different ($P<0.05$). Means with different uppercase letters at the same day (A-D: treatment effects) are significant different ($P<0.05$). N.D., not detected. RBE concentration is reported on a weight/weight basis (w/w).

Table 11. (continued)

Characteristics	Experiments	Day 1	Day 7	Day 14	Day 21
TPC (mg GAE **/**100g yogurt**)**	Control	4.58±0.35^{Aa}	5.14±0.32^{Aa}	5.52±0.26^{Aa}	4.58±0.30^{Aa}
	0.125% RBE	6.50±0.27^{Ba}	7.16±0.67^{Ba}	7.56±0.53^{Ba}	6.50±0.14^{Ba}
	0.25% RBE	8.04±0.26^{Ca}	8.80±0.47^{Bab}	9.41±0.45^{Cb}	8.14±0.35^{Cab}
C3G (mg**/**100g yogurt**)**	Control	N.D.	N.D.	N.D.	N.D.
	0.125% RBE	2.88±0.12^{Aa}	2.42±0.18^{Aa}	2.67±0.06^{Aab}	2.45±0.05^{Aa}
	0.25% RBE	4.97±0.20^{Ba}	4.88±0.16^{Ba}	5.02±0.12^{Ba}	4.32±0.09^{Bb}
P3G (mg/100g yogurt**)**	Control	N.D.	N.D.	N.D.	N.D.
	0.125% RBE	1.31±0.06^{Aa}	1.31±1.21^{Aa}	1.17±0.03^{Aa}	1.13±0.05^{Aa}
	0.25% RBE	2.25±0.10^{Ba}	2.00±0.09^{Bb}	2.02±0.05^{Bb}	2.01±0.02^{Bb}
DPPH (mg ascorbic acid	Control	2.19±0.06^{Abc}	2.38±0.16^{Ac}	1.98±0.02^{Ab}	1.65±0.09^{Aa}
equivalents **/**100 g	0.125% RBE	3.96±0.10^{Ba}	4.07±0.33^{Ba}	3.22±0.21^{Bb}	2.62±0.15^{Bb}
yogurt**)**	0.25% RBE	5.83±0.18^{Cab}	6.00±0.54^{Cb}	4.89±0.12^{Ccb}	3.89±0.26^{Cc}
FRAP (mmol trolox	Control	4.98±0.20^{Aa}	4.82±0.26^{Aa}	4.54±0.25^{Aa}	4.23±0.12^{Aa}
/100 g yogurt**)**	0.125% RBE	17.79±0.18^{Bd}	16.90±0.12^{Bc}	15.11±0.26^{Bb}	12.61±0.25^{Ba}
	0.25% RBE	25.64±0.96^{Cb}	24.04±1.05^{Cab}	21.44±1.95^{Ca}	20.05±0.50^{Ca}

The results are expressed as mean ± SEM (n=3). Means with different lowercase letters (a-e: time effects) at the same treatment are significant different (P<0.05). Means with different uppercase letters at the same day (A-D: treatment effects) are significant different (P<0.05). N.D., not detected. RBE concentration is reported on a weight/weight basis (w/w).

4.2 Part II: The effect of riceberry rice yogurt on postprandial glycemic response and antioxidant status in healthy subjects.

Twenty-three subjects were recruited for this study according to Consolidated Standards of Reporting Trials (CONSORT) flow diagram (Figure 23). All participants were randomly assigned into two group. Four subjects withdrew during the study due to the reasons unrelated to the study. Nineteen participants finally completed the study. The baseline characteristics of nineteen participants are shown in Table 12.

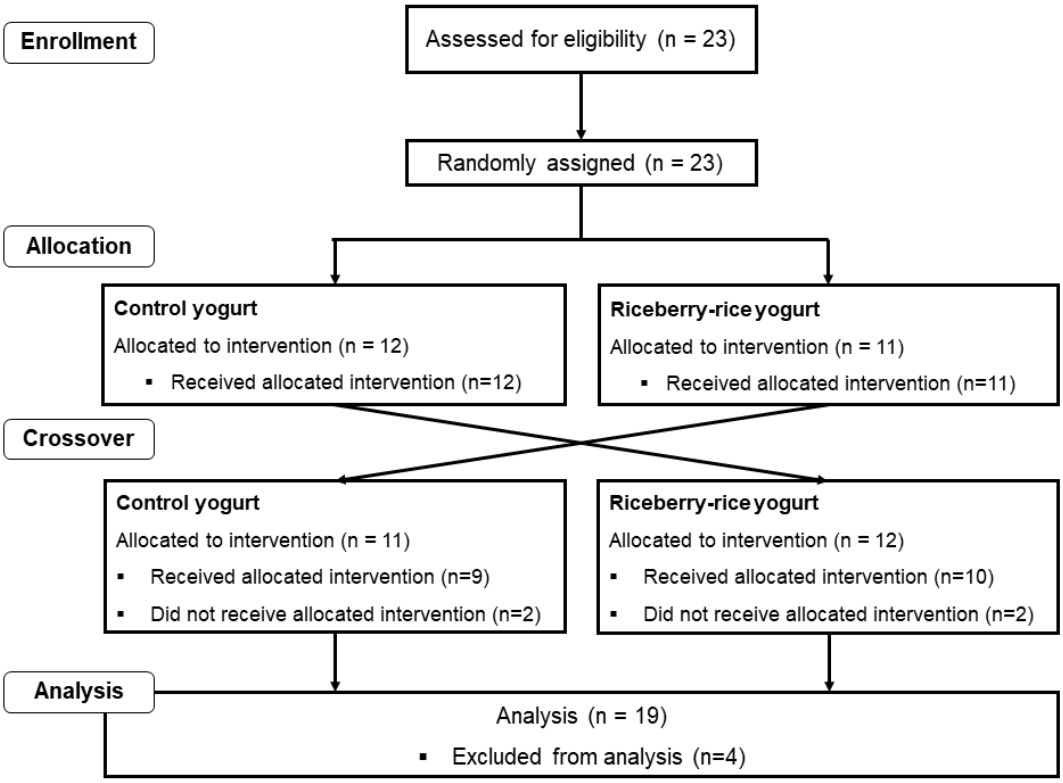


Figure 23 The Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

Table 12 Baseline characteristics of the study participants

	Mean ± SEM
Age (years)	28.05 ± 2.98
Height (cm)	21.24 ± 0.38
Weight (Kg)	58.33 ± 2.19
BMI (Kg/m^2)	21.24 ± 0.38
Fasting plasma glucose (mg/dL)	83.63 ± 1.00
Total cholesterol (mg/dL	167.32 ± 8.12
Serum triglyceride (mg/dL)	52.95 ± 3.79
LDL-C (mg/dL)	113.53 ± 6.62
HDL-C (mg/dL)	43.20 ± 3.53
Creatinine (mg/dL)	0.72 ± 0.04
BUN (mg/dL)	11.58 ± 0.54

All values are mean ± SEM, n=19

4.2.1 Nutritional profile of yogurt

The nutrient composition of yogurt is shown in Table 13. All yogurts had similar energy content approximately 349.06-349.62 kcal/350 g yogurt. The macronutrient distribution of yogurt was 48.85-50.22 % carbohydrate, 15.76-15.82% protein, and 34.38-33.97% fat, respectively.

Table 13 Nutrient composition of yogurt for 1 serving size (350 g).

Composition	Control yogurt	Riceberry rice yogurt
Energy (kcal)	349.06	349.62
Carbohydrate (g)	43.51	43.89
Protein (g)	13.76	13.83
Fat (g)	13.34	13.20
Moisture (g)	275.87	275.52
Ash (g)	3.54	3.57
% Carbohydrate	49.85	50.22
% Protein	15.76	15.82
% Fat	34.38	33.97

4.2.2 Postprandial plasma glucose concentration

Figure 24A. shows plasma glucose concentrations of in the subject during the postprandial period after intake of yogurts. Plasma glucose increased significantly at 15 and 30 min ($P<0.05$) then returned to the baseline level within 60 min. Consumption of riceberry yogurt resulted in a significantly lower postprandial plasma glucose concentration at 30 and 120 min when compared to the control. A 25% reduction in iAUC of glucose for riceberry yogurt in relative to the control was observed (Figure 24B).

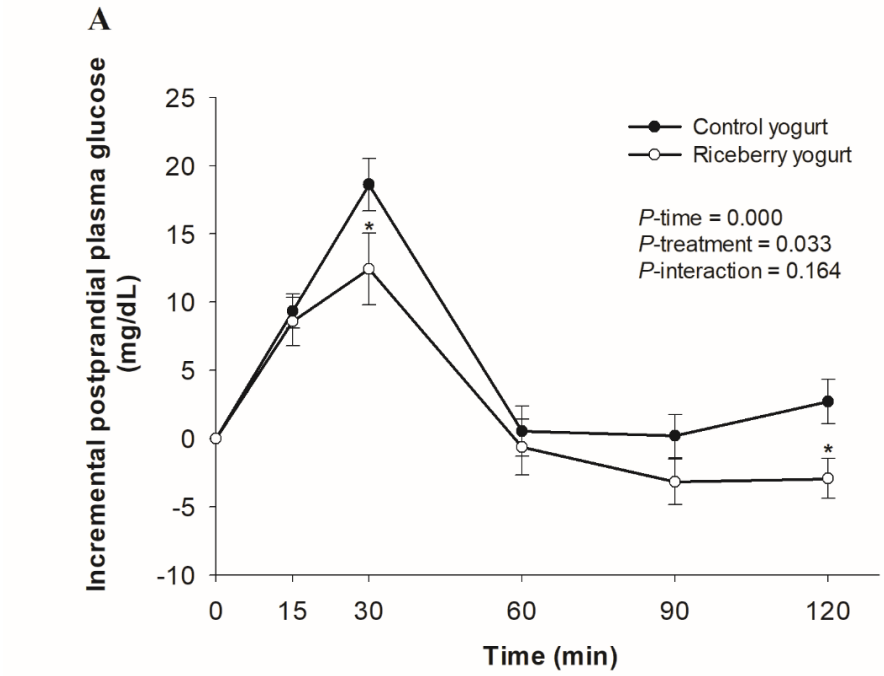


Figure 24 Effect of riceberry yogurt on postprandial plasma glucose in the subjects. (A) Changes in plasma glucose concentration during 120 min and (B) incremental area under the curves (iAUCs) of plasma glucose. Baseline of plasma glucose level in the group consumed a control yogurt and a riceberry yogurt were 78.5±1.4 mg/dL and 82.1±3.5 mg/dL, respectively. Data are presented as mean ± SEM, n= 19. * P<0.05 compared to the control yogurt.

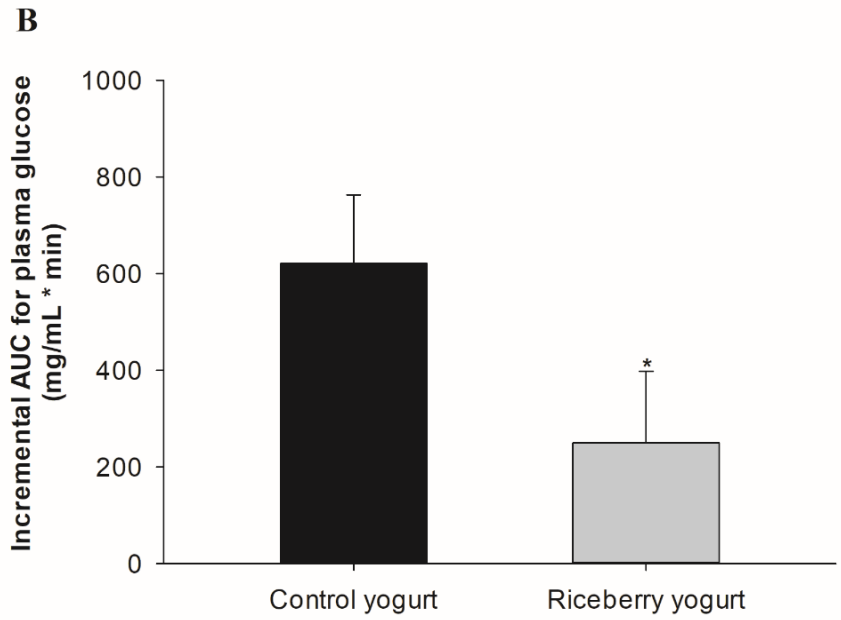


Figure 24 Incremental area under the curves (iAUCs) for postprandial plasma glucose.

Data are presented as mean ± SEM, n=19. * $P<0.05$ compared to the control yogurt.

4.2.3 Plasma antioxidant status

Plasma FRAP

A significant increase in FRAP level was found at 30 min after the consumption of yogurts (Figure 25A). Compared to the control, the postprandial plasma FRAP level of riceberry rice yogurt was higher at 60, 90, and 120 min. The iAUC of plasma FRAP level was significantly higher after consumption of riceberry yogurt compared with the control (Figure 25B).

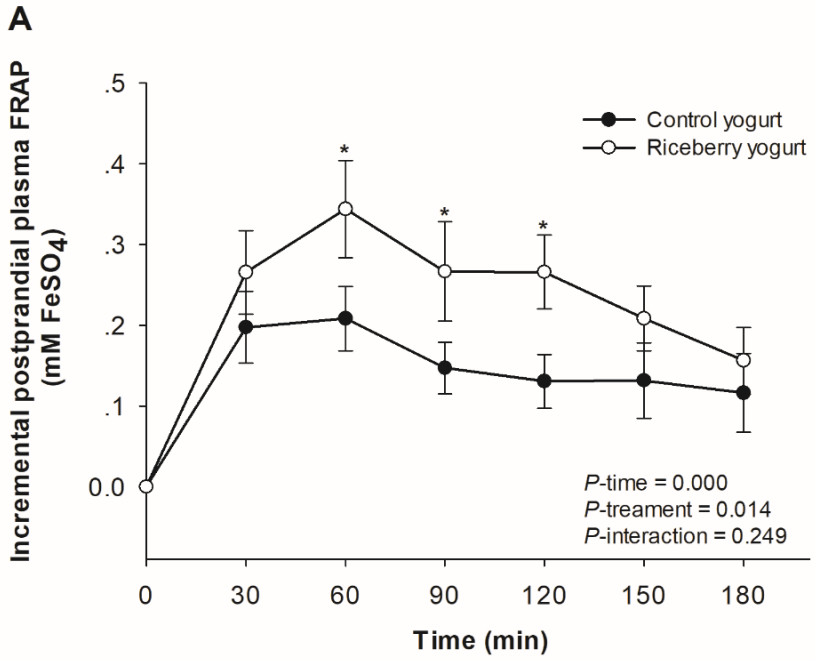


Figure 25 Effect of riceberry yogurt on postprandial plasma FRAP in the subjects. (A) Changes in plasma FRAP during 180 min and (B) incremental area under the curves (iAUCs) of plasma FRAP. Baseline of plasma FRAP level in the group consumed a control yogurt and a riceberry yogurt were 0.20±0.04 mM $FeSO_4$ and 0.17±0.03 mM $FeSO_4$, respectively. Data are presented as mean ± SEM, n=19. * P<0.05 compared to the control yogurt.

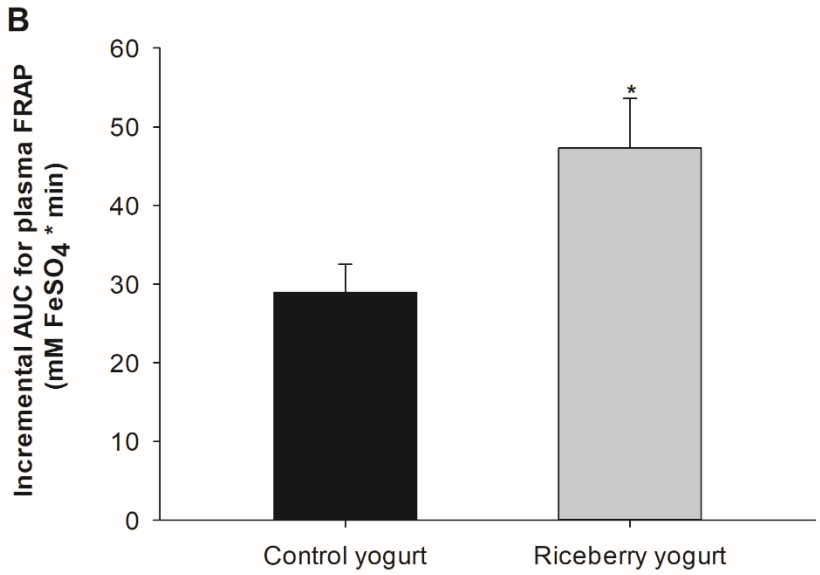


Figure 25 Incremental area under the curves (iAUCs) for postprandial plasma FRAP.

Data are presented as mean ± SEM, *n*=19. * *P*<0.05 compared to the control yogurt.

 Plasma TEAC

Consumption of all yogurts caused a significant increase in TEAC level above baseline for all time points. Plasma TEAC levels at 30, 90, 120, and 150 min were significantly higher in participants who received riceberry yogurt than in those who consumed the control yogurt. Interestingly, riceberry yogurt demonstrated higher levels of plasma TEAC than the control (Figure 26A). The iAUC of plasma TEAC was significantly higher following riceberry rice yogurt compared with the control (Figure 26B).

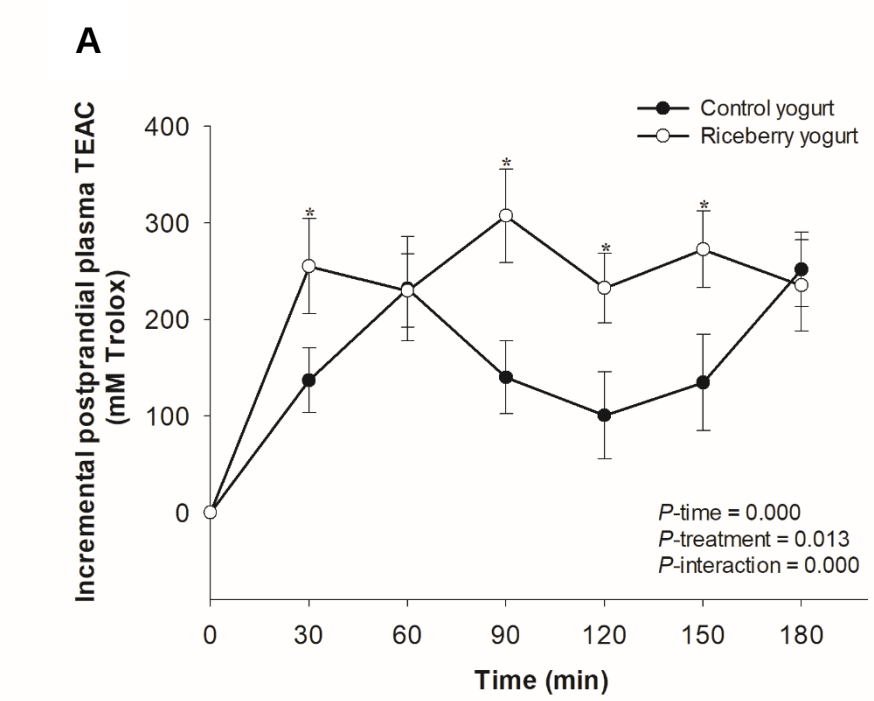


Figure 26 Effect of riceberry yogurt on postprandial plasma TEAC in the subjects. (A) Changes in plasma TEAC during 180 min and (B)) incremental area under the curves (iAUCs) of plasma TEAC. Baseline of plasma TEAC level in the group consumed a control yogurt and a riceberry yogurt were 1800. 87±218. 00 mM Trolox and 1647.84±144.39 mM Trolox, respectively. Data are presented as mean ± SEM, n=19. * P<0.05 compared to the control yogurt.

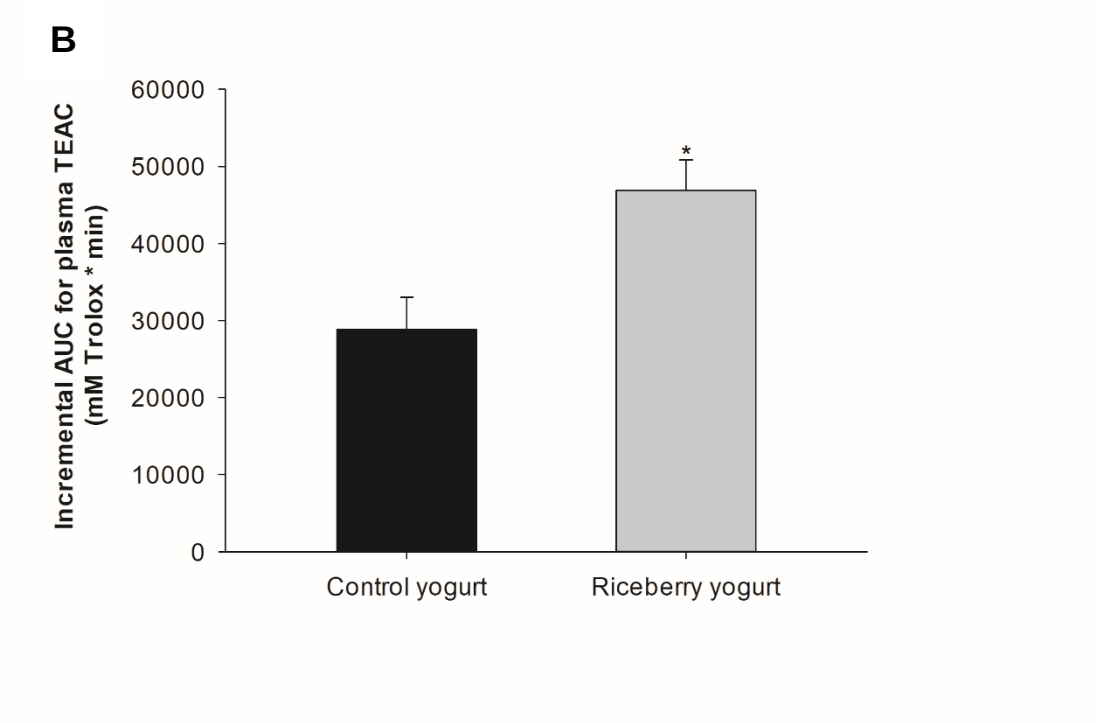


Figure 26 Incremental area under the curves (iAUCs) for postprandial plasma TEAC.

Data are presented as mean ± SEM, n=19. * P<0.05 compared to the control yogurt.

Plasma ORAC

As shown in Figure 27A, the postprandial plasma ORAC level appeared immediately following intake of all yogurts and returned to the baseline level at 180 min. The plasma ORAC level at 30, 60, 90, and 120 min were significantly higher in riceberry rice yogurt than those in the control. The iAUC of plasma ORAC was 2.91-fold greater in the subjects who consumed riceberry yogurt, as compared to the control (Figure 27B).

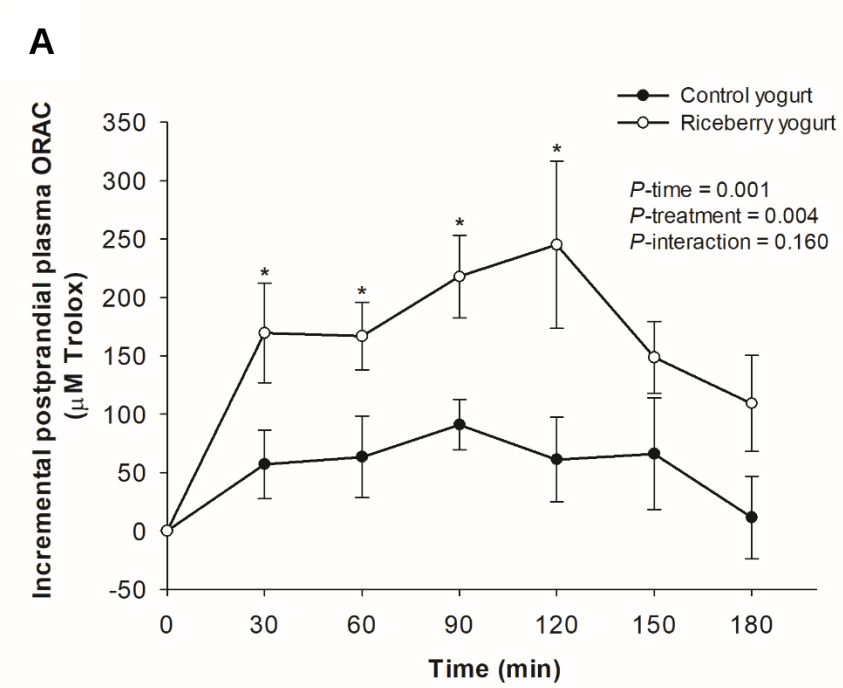


Figure 27 Effect of riceberry yogurt on postprandial plasma ORAC in the subjects. (A) Changes in plasma ORAC during 180 min and (B)) incremental area under the curves (iAUCs) of plasma ORAC. Baseline of plasma ORAC level in the group consumed a control yogurt and a riceberry yogurt were 1429. 01±44. 35 μM Trolox and 1431. 27±47. 42 μM Trolox, respectively. Data are presented as mean ± SEM, n= 19. * P<0.05 compared to the control yogurt.

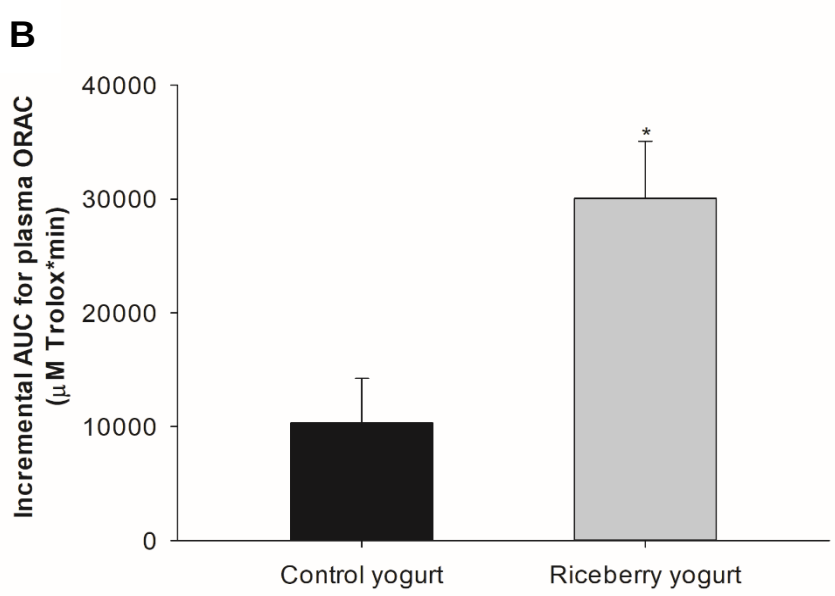


Figure 27 Incremental area under the curves (iAUCs) for postprandial plasma ORAC.

Data are presented as mean ± SEM, *n*=19. * *P*<0.05 compared to the control yogurt.

Plasma Thiol

As shown in Figure 28A, the postprandial plasma thiol level was elevated after consumption of all yogurts when compared to the baseline level. Nevertheless, postprandial plasma thiol did not differ between riceberry yogurt and the control yogurt. In comparison to the control riceberry yogurt caused a 1.79-fold increase iAUCs of plasma thiol (Figure 28B).

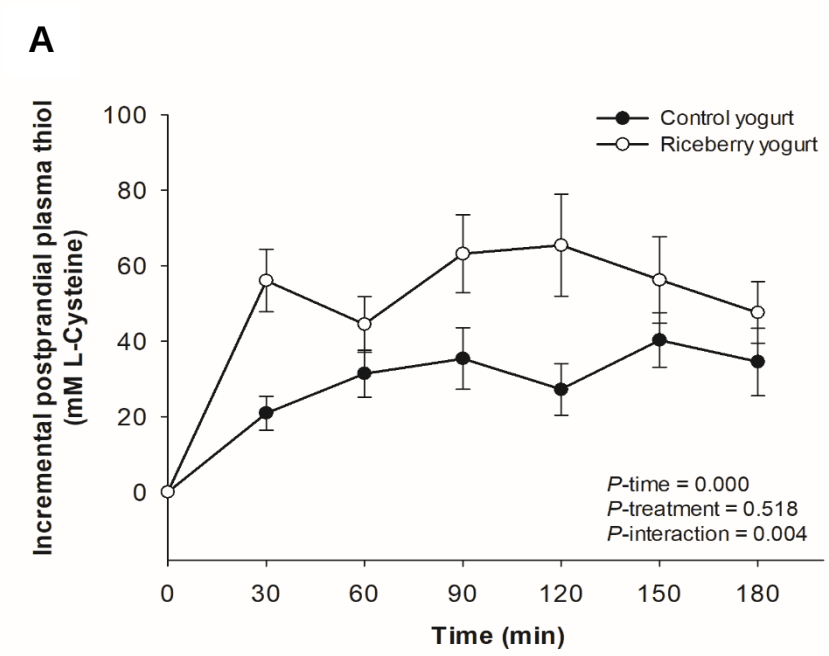


Figure 28 Effect of riceberry yogurt on postprandial plasma thiol in the subjects. (A) Changes in plasma thiol during 180 min and (B)) incremental area under the curves (iAUCs) of plasma thiol. Baseline of plasma thiol level in the group consumed a control yogurt and a riceberry yogurt were 616.76±61.71 mM L-Cysteine and 653.98±61.21 mM L-Cysteine, respectively. Data are presented as mean ± SEM, n=19. * P<0.05 compared to the control yogurt.

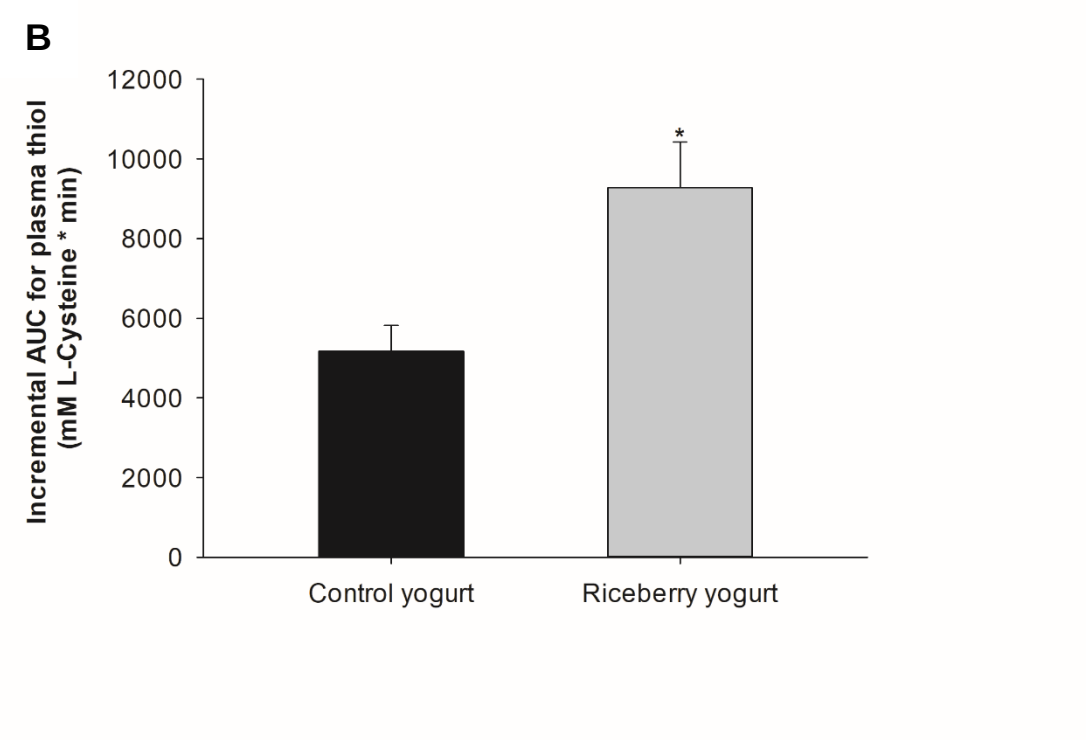


Figure 28 Incremental area under the curves (iAUCs) for postprandial plasma thiol.

Data are presented as mean ± SEM, *n*=19. * *P*<0.05 compared to the control yogurt.

Lipid peroxidation

The results of postprandial plasma MDA concentration after consumption of yogurts are presented in Figure 29A. Plasma MDA concentration increased significantly from baseline following the control yogurt markedly increased the level of MDA. No significant change in the level of MDA was detected after consumption of riceberry yogurt. A 33 % reduction in iAUC of postprandial plasma MDA was observed following consumption of riceberry yogurt (Figure 29B).

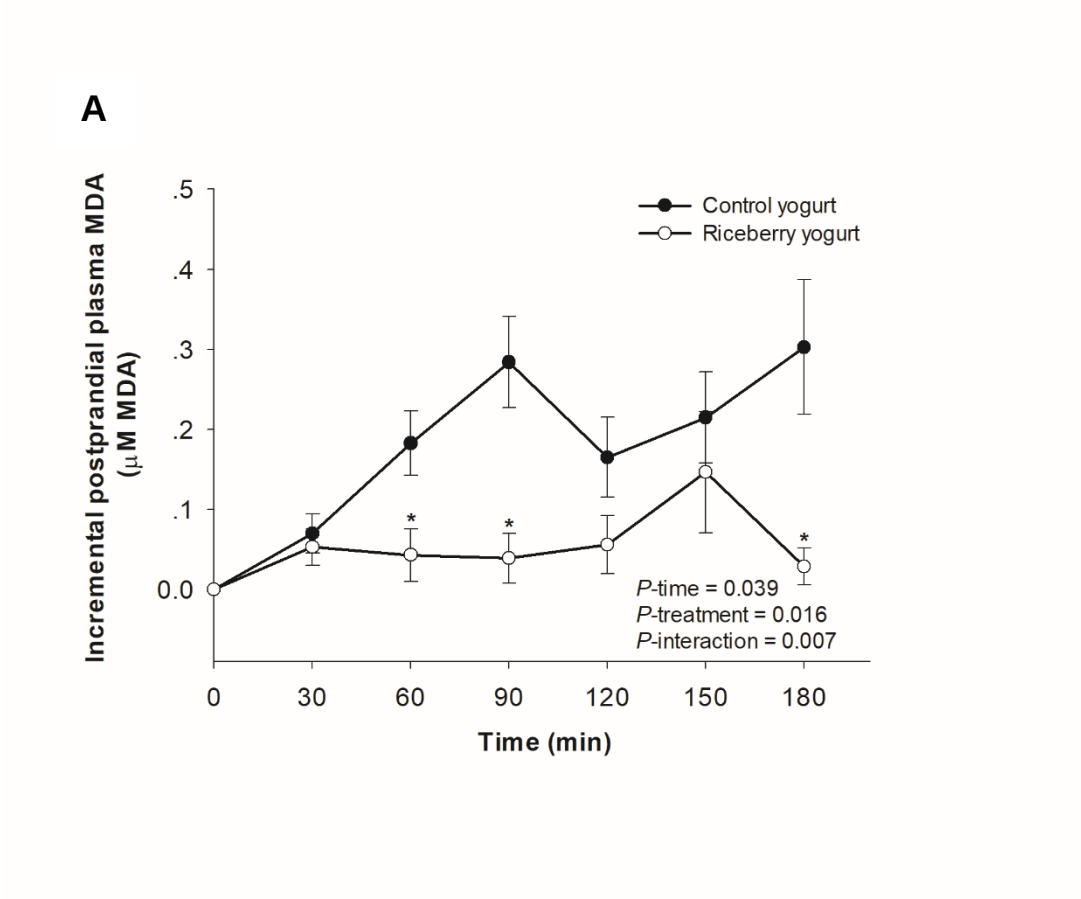


Figure 29 Effect of riceberry yogurt on postprandial plasma MDA in the subjects. (A) Changes in plasma MDA during 180 min and (B)) incremental area under the curves (iAUCs) of plasma MDA. Baseline of plasma MDA level in the group consumed a control yogurt and a riceberry yogurt were 0.30±0.04 μM MDA and 0.30±0.04 μM MDA, respectively. Data are presented as mean ± SEM, n= 19. * P<0.05 compared to the control yogurt.

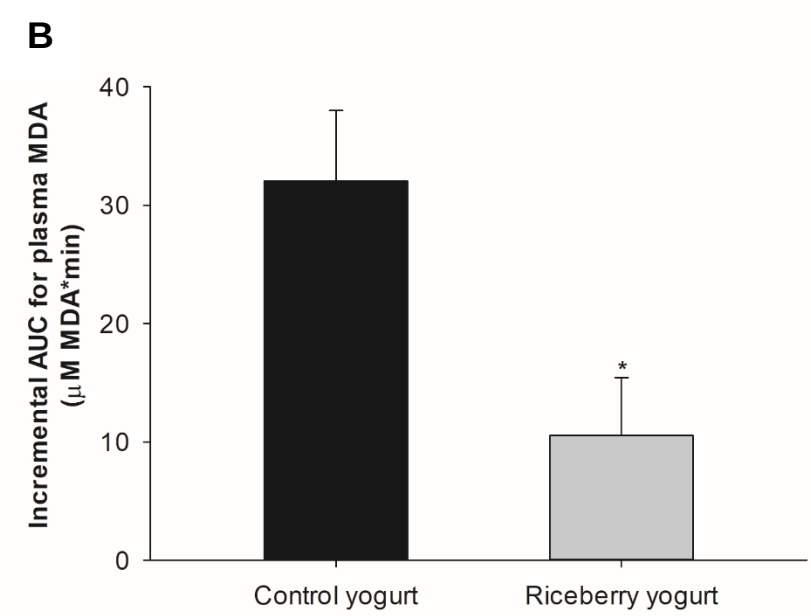


Figure 29 Incremental area under the curves (iAUCs) for postprandial plasma MDA.

Data are presented as mean ± SEM, *n*=19. * *P*<0.05 compared to the control yogurt.

4.2.4 Subjective rating of hunger, fullness, desire to eat, and satiety

The results of satiety after consumption of yogurts are illustrated in Figure 30A-D. Ingestion of all yogurts markedly altered the hunger, fullness, desire to eat, and satiety rating, as compared to baseline. However, there were no significant differences in the rating score of hunger, fullness, desire to eat, and satiety among all yogurts.

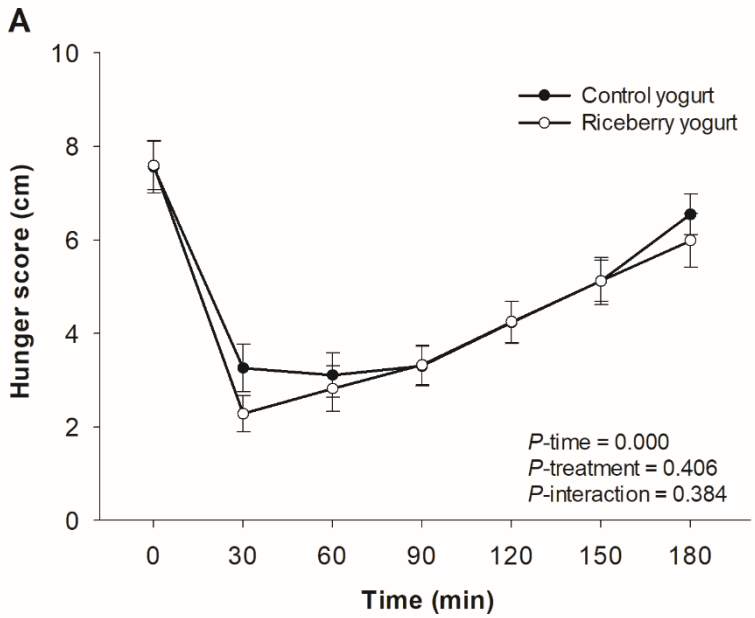


Figure 30 Changes in appetite, hunger (A), fullness (B), desire to eat (C), and satiety (D) in healthy participants after consuming either the control yogurt or riceberry yogurt. Data are presented as mean ± SEM, n=19. * $P<0.05$ compared to the control yogurt.

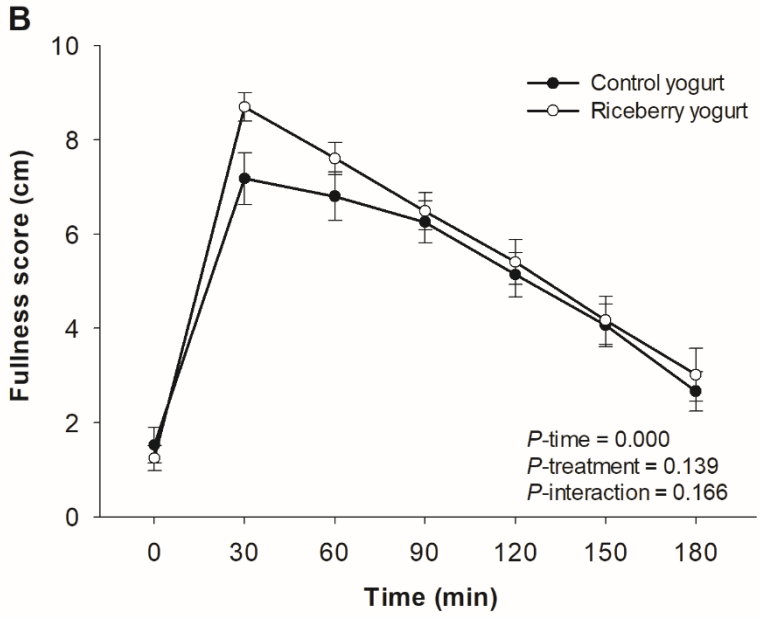


Figure 30 Changes in fullness score after the consuming either the control yogurt or riceberry yogurt. Data are presented as mean ± SEM, n=19. * *P*<0.05 compared to the control yogurt.

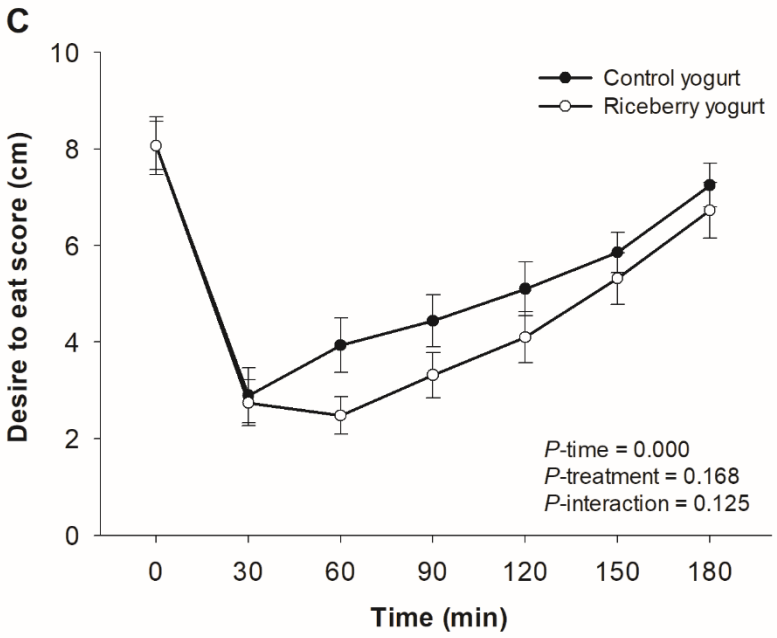


Figure 30 Changes in desire to eat score after the consuming either the control yogurt or riceberry yogurt. Data are presented as mean ± SEM, n=19. * $P<0.05$ compared to the control yogurt.

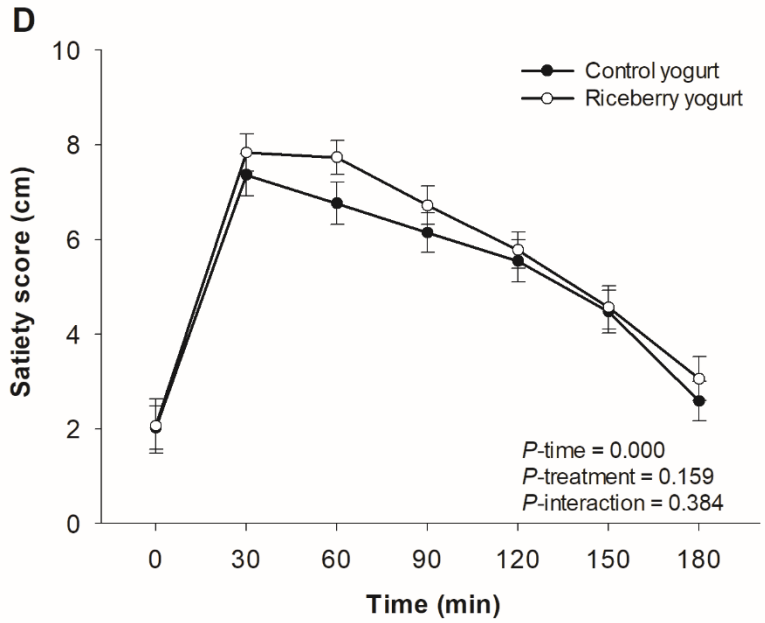


Figure 30 Changes in satiety score after the consuming either the control yogurt or riceberry yogurt. Data are presented as mean ± SEM, n=19. * *P*<0.05 compared to the control yogurt.

4.2.4 The maximum plasma concentration (C_{max}) and the peak plasma concentration (T_{max})

The maximum plasma concentration (C_{max}) and the peak plasma concentration (T_{max}) after ingestion of all yogurts are presented in Table 14. Consumption of riceberry yogurt caused a higher C_{max} of plasma glucose than that of the control. However, it slightly delayed the peak plasma glucose when compared to the control. In addition, the group who consumed riceberry rice yogurt had higher value of Cmax of postprandial plasma FRAP than that of the control, with the similar value of T_{max}. Additionally, there were no changes in C_{max} and T_{max} of postprandial plasma TEAC, Thiol, ORAC, and MDA between riceberry yogurt and the control.

Table 14 The maximum plasma concentration (C_{max}) and the peak plasma concentration (T_{max}) of postprandial plasma glucose, FRAP, TEAC, Thiol, ORAC, and MDA after ingestion of riceberry rice yogurt.

Parameters	Control yogurt	Riceberry rice yogurt
Glucose		
$Cmax_{0-180}$ (mg/dL)	93.46 ± 2.45	102.18 ± 4.89*
$Tmax_{0-180}$ (min)	26.05 ± 1.56	38.68 ± 9.41
FRAP		
$Cmax_{0-180}$ (mM $FeSO_4$)	0.55 ± 0.03	0.64 ± 0.04*
$Tmax_{0-180}$ (min)	88.42 ± 12.24	88.42 ± 10.38
TEAC		
$Cmax_{0-180}$ (mg Trolox equivalent)	2,194.83 ± 243.95	2,118.94 ± 174.08
$Tmax_{0-180}$ (min)	121.58 ± 12.24	113.68 ± 11.38
ORAC		
$Cmax_{0-180}$ (μM Trolox)	1,644.65 ± 45.51	1,797.13 ± 78.49
$Tmax_{0-180}$ (min)	96.32 ± 13.29	113.68 ± 11.14
Thiol		
$Cmax_{0-180}$ (mM L-Cysteine)	686.68 ± 63.93	756.74 ± 65.65
$Tmax_{0-180}$ (min)	120.00 ± 9.73	99.47 ± 11.01
MDA		
$Cmax_{0-180}$ (μM MDA)	0.73 ± 0.10	0.51 ± 0.08
$Tmax_{0-180}$ (min)	120.00 ± 10.76	97.89 ± 12.74

The results are expressed as mean ± SEM (*n*=19). Means with superscripts * are significantly different compare to the control yogurt ($P<0.05$).

4.3 Part III: The consumption of riceberry rice beverage with high-carbohydrate, moderate-fat (HCMF) meal on postprandial glycemic response, antioxidant status, lipidemic response, and inflammatory markers in overweight and obese subjects

Seventeen men were recruited for the study. One subject was excluded due to not meeting the inclusion criteria. Three subjects withdrew during the study with the reasons unrelated to the study. Therefore, the total number of participants in this study was thirteen (Figure 31). Baseline characteristics of subjects are shown in Table 15.

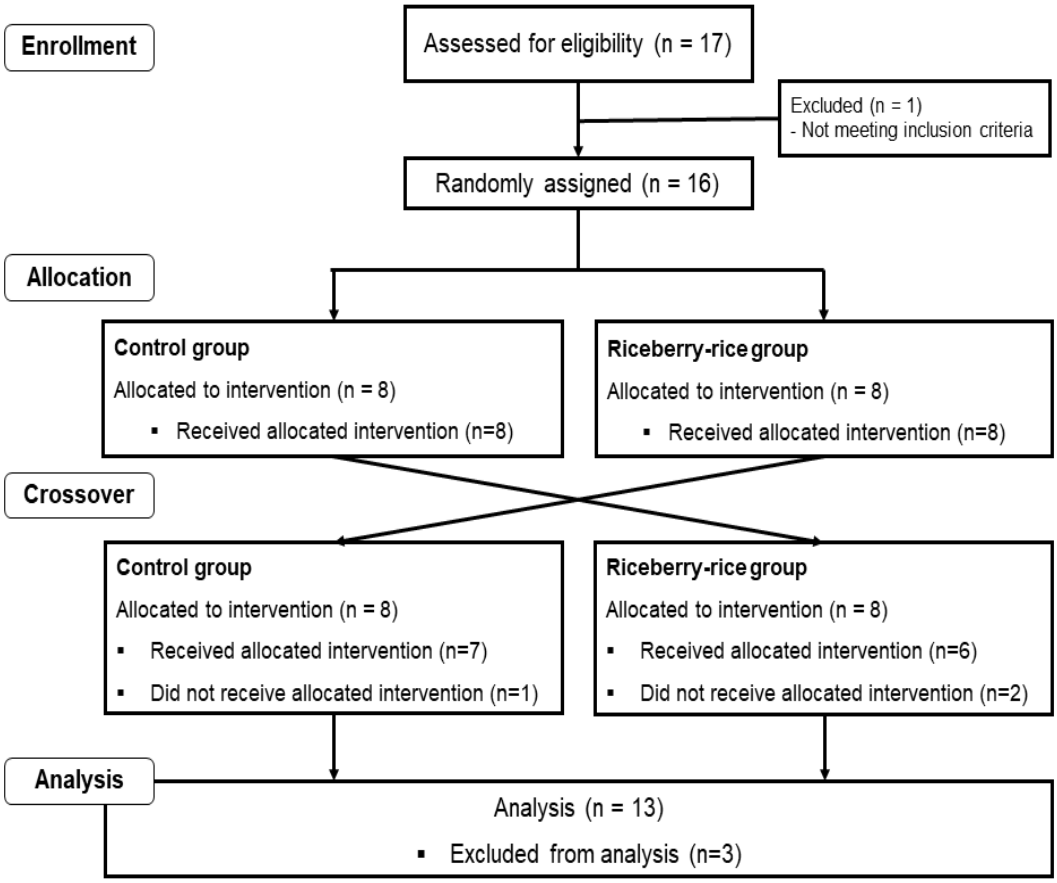


Figure 31 The CONSORT flow diagram

Table 15 Baseline characteristics of participants (n=13).

	Mean ± SEM
Age (years)	24.46±0.90
Height (cm)	173.00±0.01
Weight (Kg)	77.23±2.28
BMI (Kg/m^2)	25.92±0.69
Fasting plasma glucose (mg/dL)	92.62±2.00
Total cholesterol (mg/dL	189.92±6.57
Serum triglyceride (mg/dL)	118.00±8.78
LDL-C (mg/dL)	122.54±6.54
HDL-C (mg/dL)	43.78±5.10
Creatinine (mg/dL)	0.88±0.03
BUN (mg/dL)	13.23±0.56

All values are mean ± SEM, n=13

4.3.1 Plasma glucose concentration

As presented in Figure 32A, consumption of high fat meal significantly increased postprandial plasma glucose from the baseline level, with the peak concentration at 30 min. Then, it returned the baseline after 180 min of HCMF intake. riceberry rice beverage suppressed HCMF meal induced increase in postprandial plasma glucose concentration at 30, 60, 90, and 120 min. In addition, 60% reduction of iAUC for postprandial plasma glucose was seen after consumption of HCMF meal with riceberry rice beverage (Figure 32B).

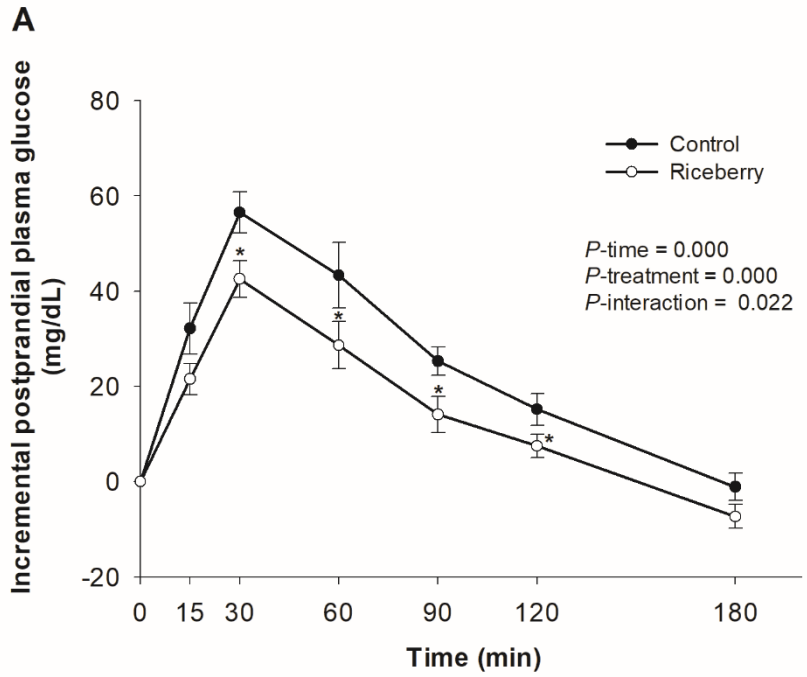


Figure 32 Postprandial plasma glucose responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage. (A) Changes in plasma glucose concentration during 180 min and (B) incremental area under the curves (iAUCs) of plasma glucose. The baseline of plasma glucose level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 78.01±2.94 mg/dL and 82.09±2.10 mg/dL, respectively. Data are presented as means± SEM, n= 13: * $P< 0.05$ compared with a high carbohydrate-moderate fat meal.

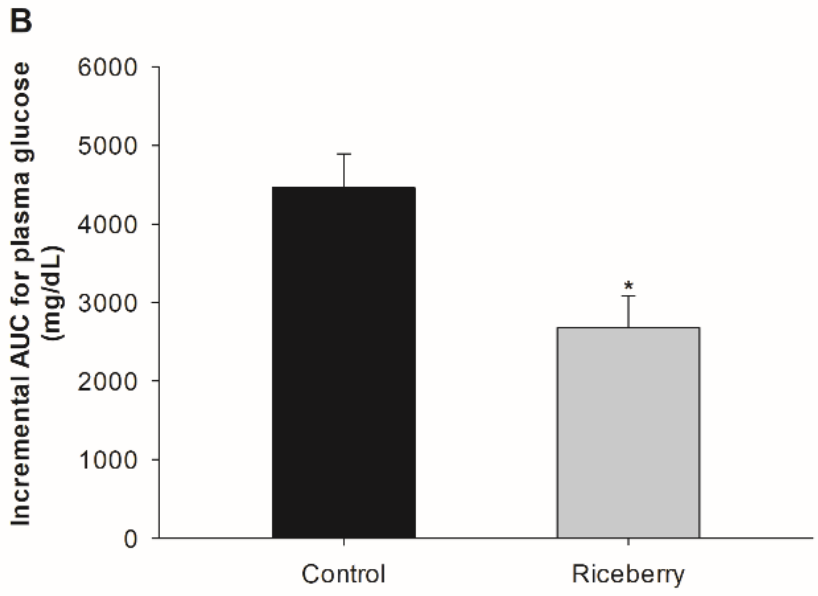


Figure 32 Incremental area under the curves (iAUCs) of plasma glucose. Data are presented as means± SEM, n=13: * *P*< 0.05 compared to the control.

4.3.2 Plasma insulin concentration

Changes in postprandial plasma insulin response after ingestion of HCMF meal are illustrated in Figure 33A. HCMF meal caused a rise in postprandial plasma insulin after 15 min of intake. Comparing at individual time point, the subjects who consumed HCMF meal together with riceberry rice beverage showed significantly lower level of postprandial plasma insulin at 60 and 90 min, compared those in the control group. Additionally, HCMF meal plus riceberry rice beverage was 2.38-fold lower insulin iAUC than the control (Figure 33B).

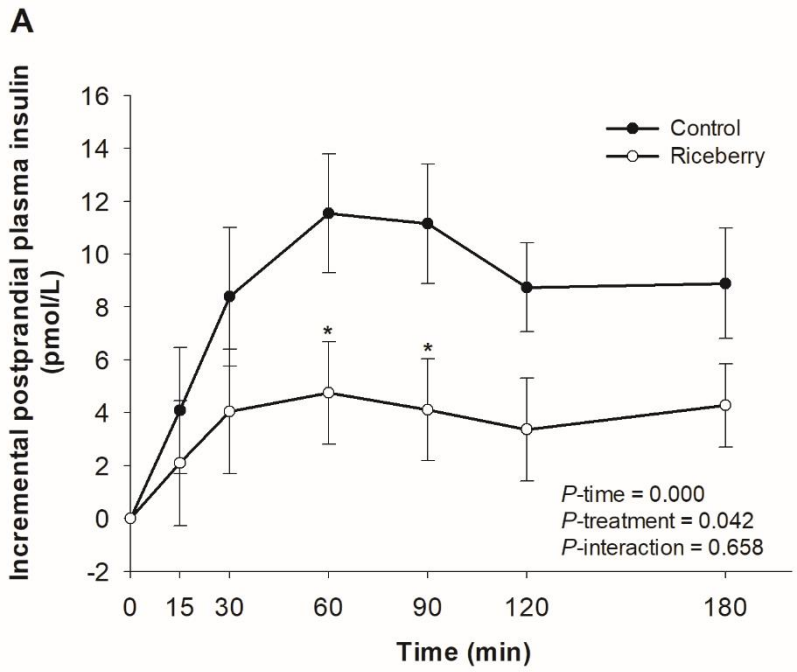


Figure 33 Postprandial plasma insulin responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage. (A) Changes in plasma insulin concentration during 180 min and (B) incremental area under the curves (iAUCs) of plasma insulin. The baseline of plasma insulin level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 144.76±5.21 pmol/L and 151.47±7.25 pmol/L, respectively. Data are presented as means± SEM, n= 13: * $P< 0.05$ compared with a high carbohydrate-moderate fat meal.

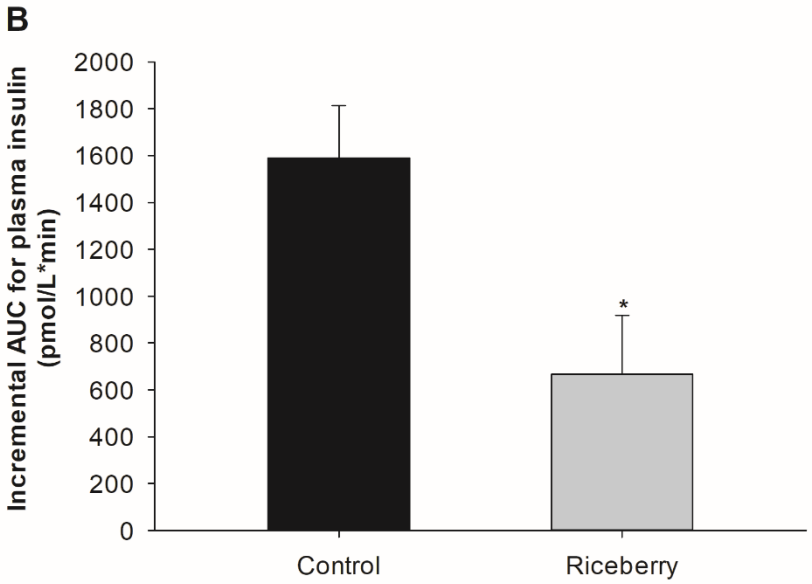


Figure 33 Incremental area under the curves (iAUCs) of plasma insulin. Values are means ± SEM, n=13: * *P*< 0.05 compared to the control.

4.3.3 Plasma antioxidant status

Plasma FRAP

When compared to the baseline level, postprandial plasma FRAP was slightly increased after ingestion of all tested meal (Figure 34A). Interestingly, HCMF meal with riceberry rice beverage resulted in an increase postprandial plasma FRAP level at 120, 180, 240, and 360 min, as compared to the control. A 3.7-fold higher iAUC of postprandial plasma FRAP was observed according to the consumption of HCMF meal with riceberry rice beverage (Figure 34B)

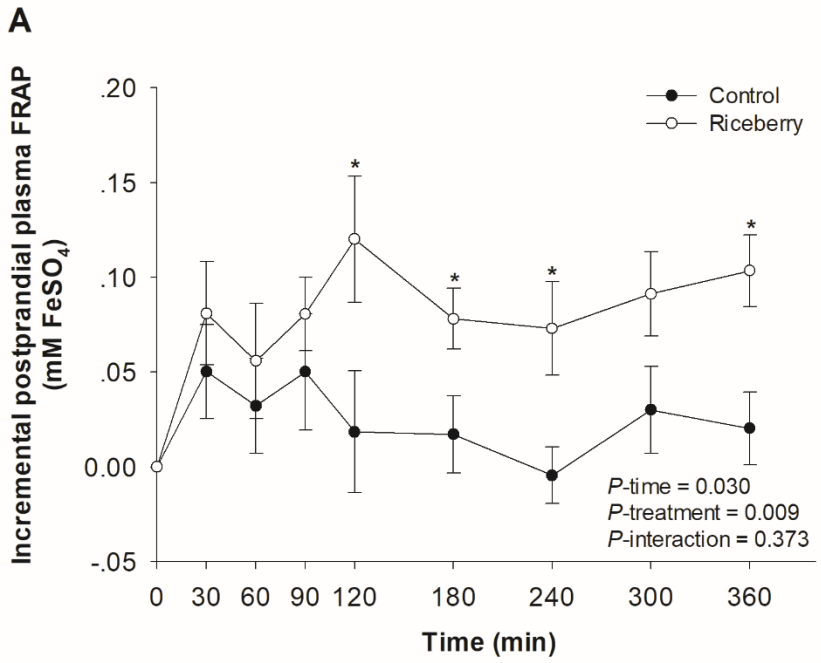


Figure 34 Postprandial plasma FRAP responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage. (A) Changes in plasma FRAP concentration during 360 min and (B) incremental area under the curves (iAUCs) of plasma FRAP. The baseline of plasma FRAP level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 0.13±0.02 mM $FeSO_4$ and 0.12±0.02 mM $FeSO_4$, respectively. Data are presented as means± SEM, n= 13: * $P< 0.05$ compared with a high carbohydrate-moderate fat meal.

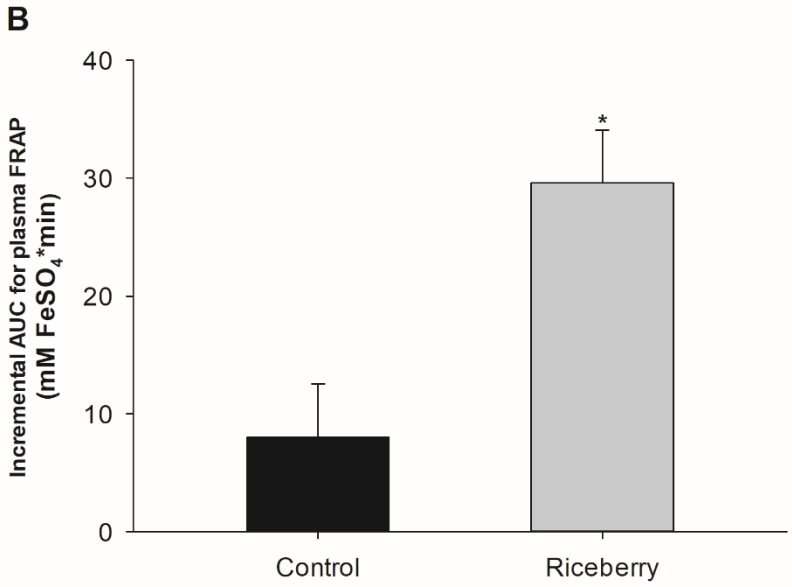


Figure 34 Incremental area under the curves (iAUCs) of plasma FRAP. Values are means ± SEM, n=13: * *P*< 0.05 compared to the control.

Plasma TEAC

HCMF did not alter postprandial plasma TEAC level throughout 360 min, whereas riceberry rice beverage was able to increase postprandial plasma TEAC level when consumption with HCMF (Figure 35A). In addition, the significant plasma TEAC level was observed at 30, 90,240, and 300 min. Additionally, HCMF meals with riceberry rice beverage produced 6.47-fold higher iAUC for plasma TEAC than the control group (Figure 35B).

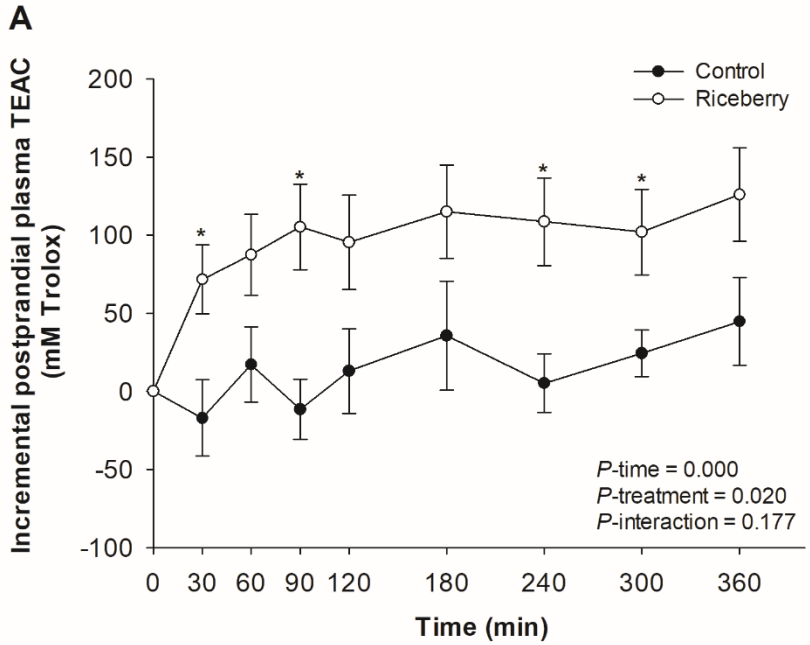


Figure 35 Postprandial plasma TEAC responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage. (A) Changes in plasma TEAC concentration during 360 min and (B) incremental area under the curves (iAUCs) of plasma TEAC. The baseline of plasma TEAC level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 1438.74±43.04 mM Trolox and 1616.63±72.38 mM Trolox, respectively. Data are presented as means± SEM, n= 13: * $P< 0.05$ compared with a high carbohydrate-moderate fat meal.

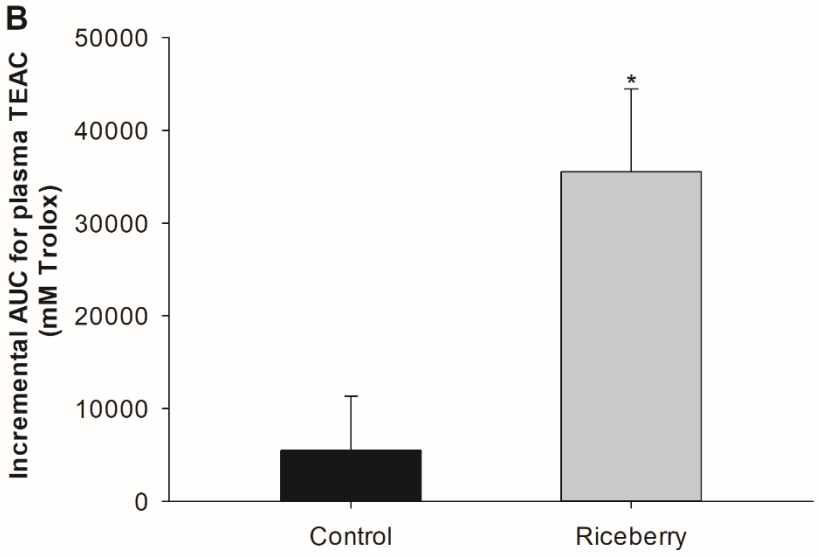


Figure 35 Incremental area under the curves (iAUCs) of plasma TEAC. Values are means ± SEM, n=13: * *P*< 0.05 compared to the control.

Plasma Thiol

In comparison to the baseline level, a rise in postprandial plasma thiol was markedly seen in the HCMF meal but not in the control (Figure 36A). Postprandial plasma thiol of riceberry beverage intervention was found to be significantly higher at 60, 90, 180, 240, 300, and 360 min when compared to the control. The iAUC of postprandial plasma thiol responses of riceberry beverage was lower than that of the control (Figure 36B).

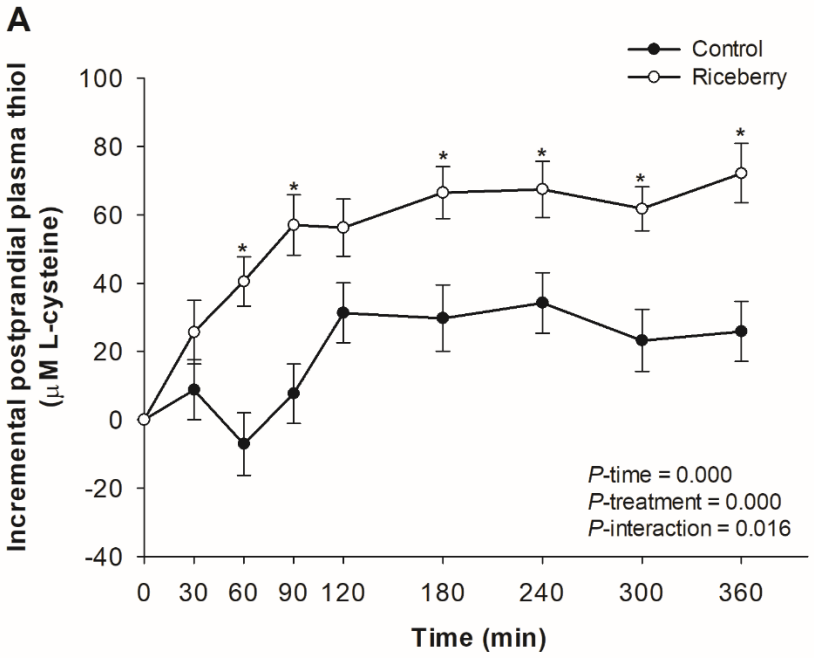


Figure 36 Postprandial plasma thiol responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage. (A) Changes in plasma thiol concentration during 360 min and (B) incremental area under the curves (iAUCs) of plasma thiol. The baseline of plasma thiol level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 555.71±36.33 μM L-cysteine and 510.73±37.43 μM L-cysteine, respectively. Data are presented as means± SEM, n= 13: * $P< 0.05$ compared with a high carbohydrate-moderate fat meal.

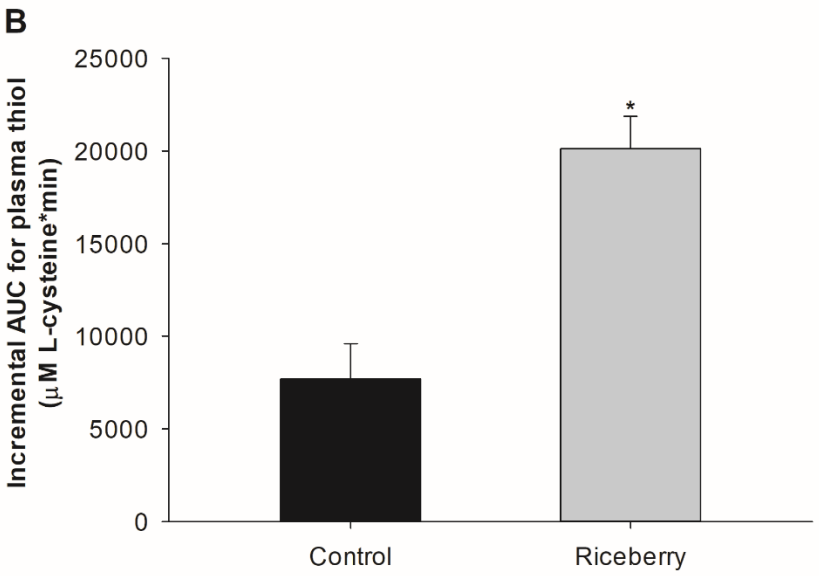


Figure 36 Incremental area under the curves (iAUCs) of plasma thiol. Values are means ± SEM, n=13: * *P*< 0.05 compared to the control.

Lipid peroxidation

The results of postprandial plasma MDA concentration after consumption of all tested meal are presented in Figure 37A. In comparison to the baseline level, consumption of HCMF meal markedly increased the MDA level at 30 min, whereas ingestion of HCMF meal together with riceberry rice beverage led to suppress postprandial plasma MDA at 30-120 min. As shown in Figure 37B, there was significantly lower in iAUC of plasma MDA in the subjects who consumed HCMF meal together with riceberry rice beverage, as compared to the control.

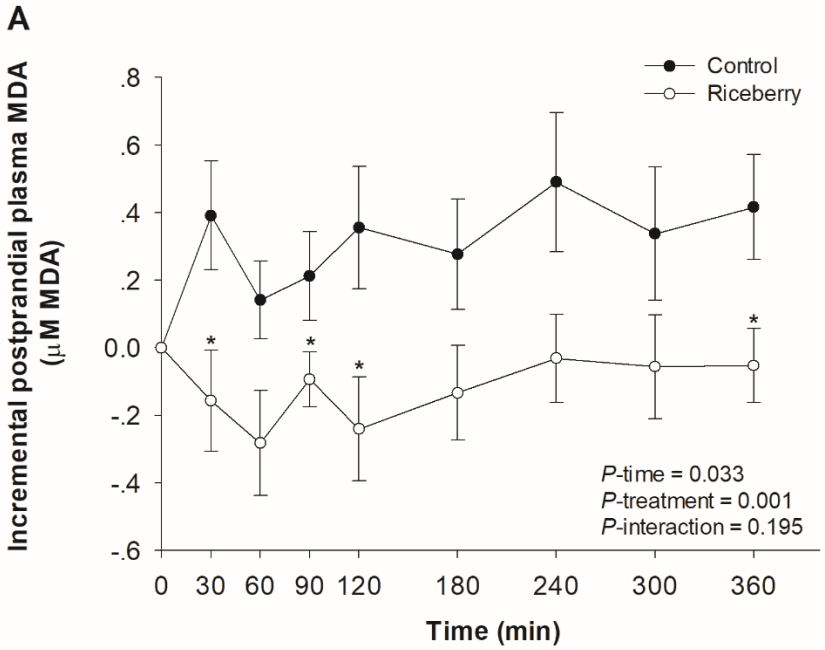


Figure 37 Postprandial plasma MDA responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage. (A) Changes in plasma MDA concentration during 360 min and (B) incremental area under the curves (iAUCs) of plasma MDA. The baseline of plasma MDA level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 0.97±0.19 μM MDA and 1.35±0.18 μM MDA, respectively. Data are presented as means± SEM, n=13: * *P*< 0.05 compared with a high carbohydrate-moderate fat meal.

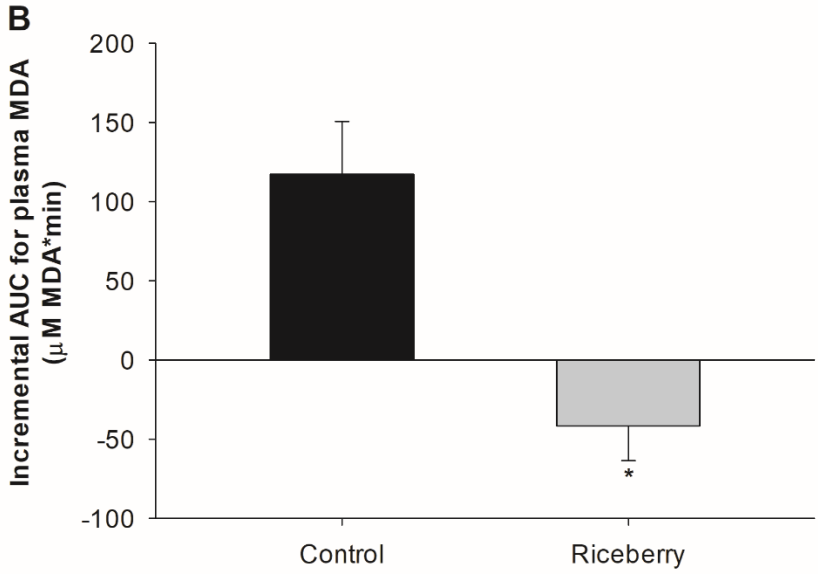


Figure 37 Incremental area under the curves (iAUCs) of plasma MDA. Values are means ± SEM, n=13: * *P*< 0.05 compared to the control.

4.3.4 Serum triglyceride and free fatty acid

Serum Triglyceride

Ingestion of HCMF meal significantly increased serum triglyceride at 180 and 240 min (Figure 38A). The serum triglyceride level increased significantly after consumption of HCMF meal Additionally, the iAUC for postprandial serum triglyceride after consumption of HCMF meal with riceberry rice beverage was significantly lower than that of the control group (Figure 38B).

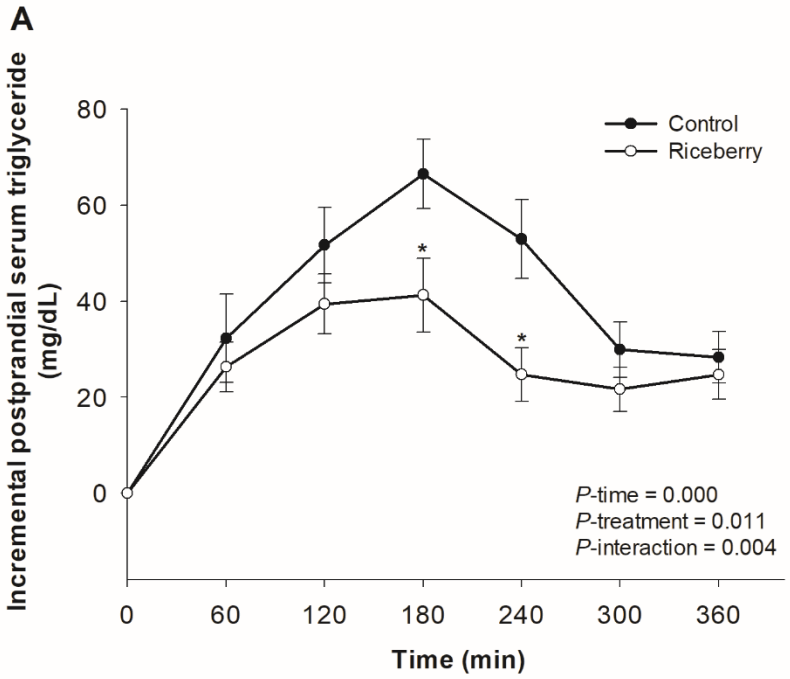


Figure 38 Postprandial serum triglyceride responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage. (A) Changes in serum triglyceride concentration during 360 min and (B) incremental area under the curves (iAUCs) of serum triglyceride. The baseline of serum triglyceride level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 175.13±40.61 mg/dL and 169.49±32.13 mg/dL, respectively. Data are presented as means± SEM, n= 13: * $P< 0.05$ compared with a high carbohydrate-moderate fat meal.

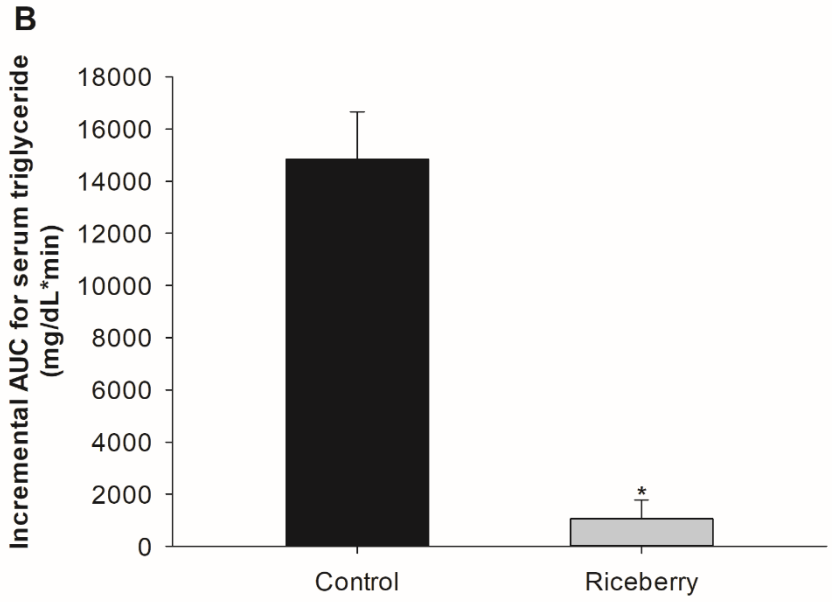


Figure 38 Incremental area under the curves (iAUCs) of serum triglyceride. Values are means ± SEM, n=13: * *P*< 0.05 compared to the control.

Serum free fatty acid (FFA)

The results of postprandial serum FFA after consumption of HCMF with and without riceberry rice beverage are presented in Figure 39. When comparing with the baseline level, the consumption of HCMF meal caused a significant rise in serum FFA, whereas ingestion of HCMF with riceberry rice beverage could attenuate this level at 180 min (*P*-time = 0.001).

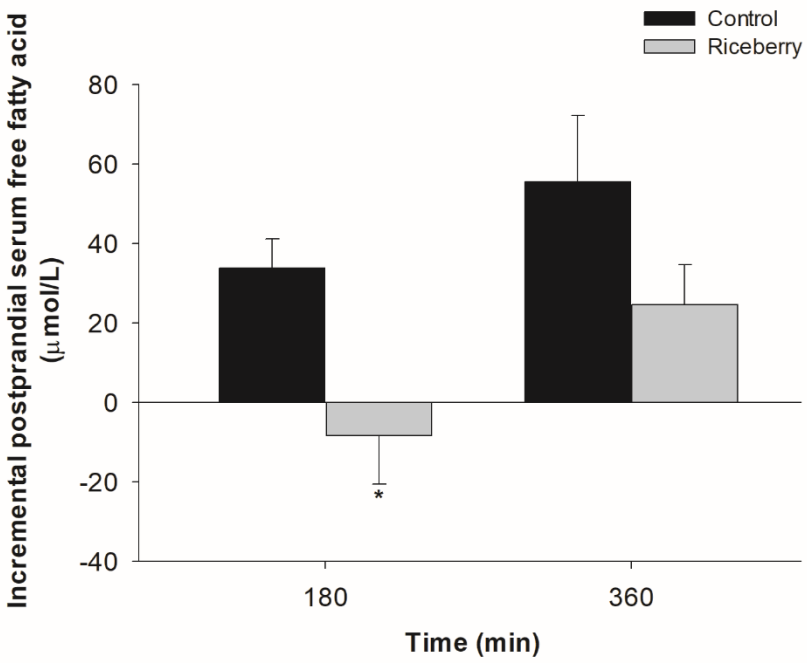


Figure 39 Incremental postprandial serum free fatty acid responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage during 360 min. The baseline of serum free fatty acid level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 401.38±36.06 μmol/L and 400.61±31.06 μmol/L, respectively. Data are presented as means± SEM, n= 13: * $P< 0.05$ compared with a high carbohydrate-moderate fat meal.

4.3.4 Serum inflammatory markers

Serum IL-1β

Ingestion of HCMF meal resulted in a slight decrease the level of serum IL-1β (*P*-time= 0.004). Interestingly, riceberry rice beverage demonstrated the effect on decreased postprandial serum IL-1β at 180 and 360 min (*P*-treatment=0.024) in the subjects who received HCMF meal (Figure 40).

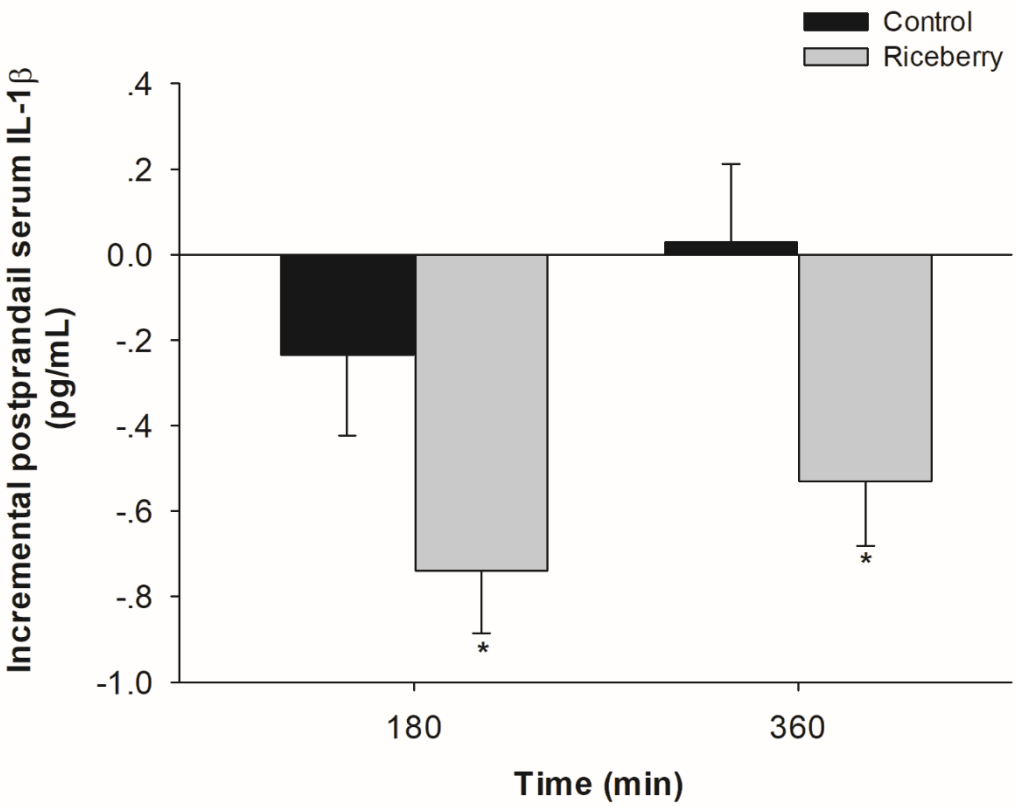


Figure 40 Incremental postprandial serum IL-1β responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage during 360 min. The baseline of serum IL-1β level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 34.99±1.66 pg/mL and 36.59±1.31 pg/mL, respectively. Data are presented as means± SEM, n=13: * *P*< 0.05 compared with a high carbohydrate-moderate fat meal.

Serum IL-6

Postprandial serum IL-6 responses after consumption of tested meal are illustrated in Figure 41. The intake of all testing meal did not postprandial serum IL-6 when compared to the baseline level (*P*-time= 0.313). However, HCMF with riceberry rice beverage showed a significantly lower serum IL-6 than the control at 180 and 360 min (*P*-treatment=0.000).

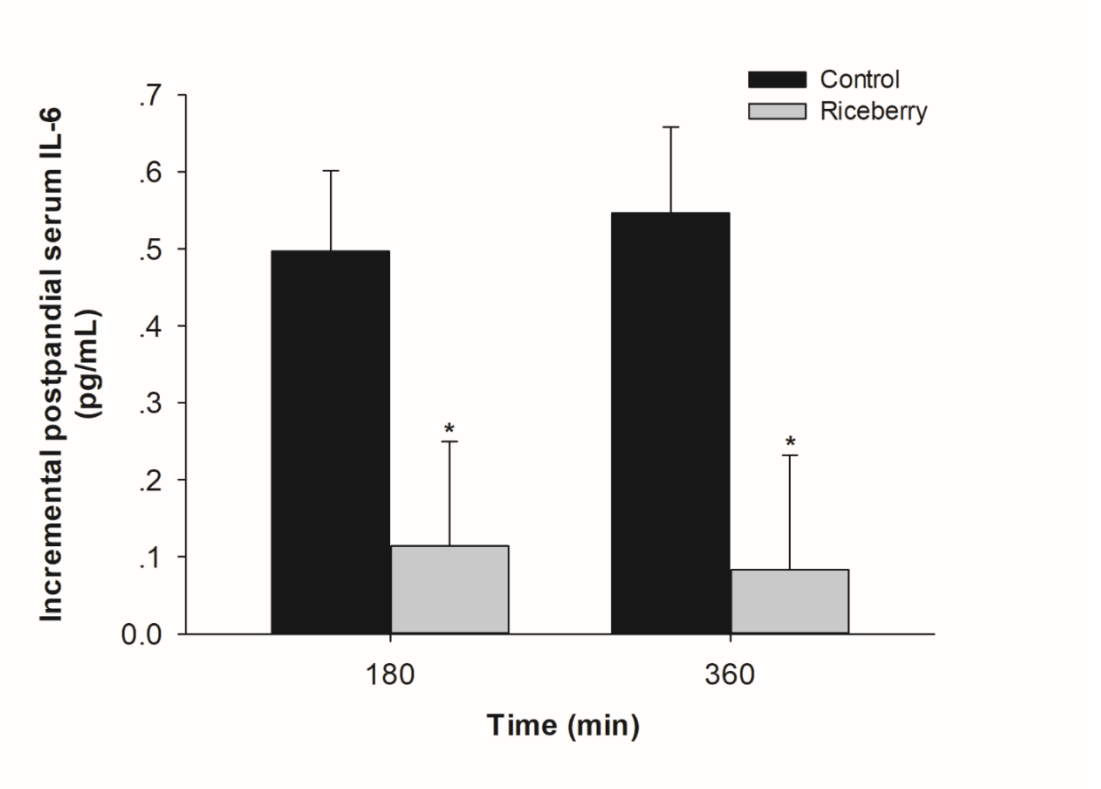


Figure 41 Incremental postprandial serum IL-6 responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage during 360 min. The baseline of serum IL-6 level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 25.02±0.86 pg/mL and 26.83±0.89 pg/mL, respectively. Data are presented as means± SEM, n=13: * $P< 0.05$ compared with a high carbohydrate-moderate fat meal.

Serum TNF-α

The results of postprandial serum TNF-α after consumption of HCMF meal with and without riceberry rice beverage are expressd in Figure 42. In comparison to the baseline level, ingestion of HCMF meal altered the change in postprandial serum TNF-α at 180 and 360 min (*P*-time=0.008). Drinking riceberry rice beverage could suppress postprandial serum TNF-α at 360 min when consumed with HCMF meal (*P*-treatment=0.008).

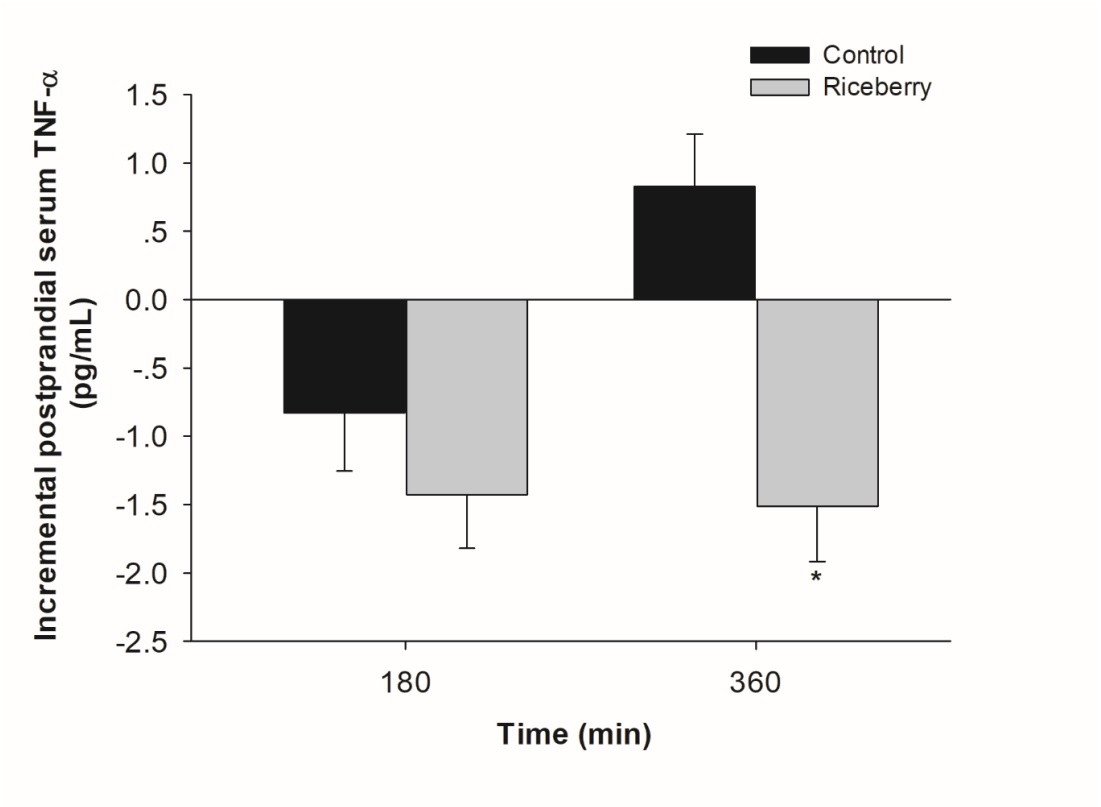


Figure 42 Incremental postprandial serum TNF-α responses to high carbohydrate-moderate fat meal consumed with riceberry rice beverage during 360 min. The baseline of serum TNF-α level in the group administered a high carbohydrate-moderate fat meal and a high carbohydrate-moderate fat meal plus 2 g of the extract were 53.07±1.77 pg/mL and 56.27±1.78 pg/mL, respectively. Data are presented as means± SEM, n=13: * *P*< 0.05 compared with a high carbohydrate-moderate fat meal.

4.3.6. Subjective rating of hunger, fullness, desire to eat, and satiety

The results of subjective rating score of hunger, fullness, desire to eat, and satiety are represented in Figure 43A-D. The rating scores of hunger, fullness, desire to eat, and satiety were altered when consumption of HCMF meal and it returned the baseline level after 360 min. However, there were no significant differences in the rating scores of hunger, fullness, desire to eat, and satiety among tested meals.

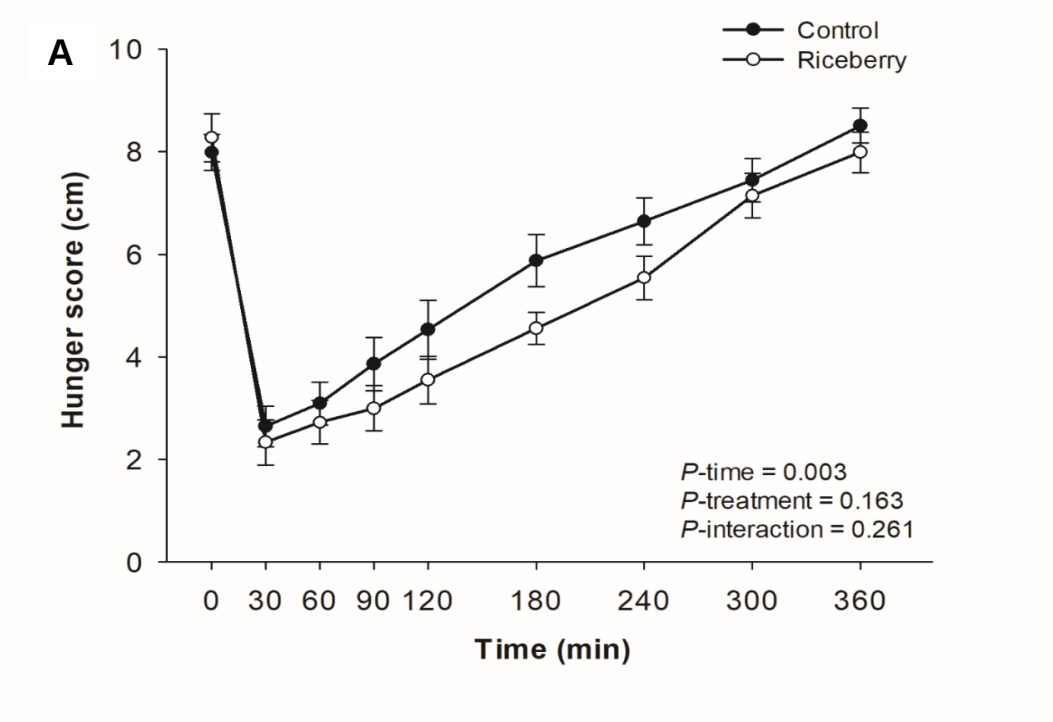


Figure 43 Changes in appetite , hunger (A), fullness (B), desire to eat (C), and satiety (D) after the consumption of HCMF meal and HCMF meal with riceberry rice beverage. Values are mean ± SEM, n=13: * $P < 0.05$ compared to the control.

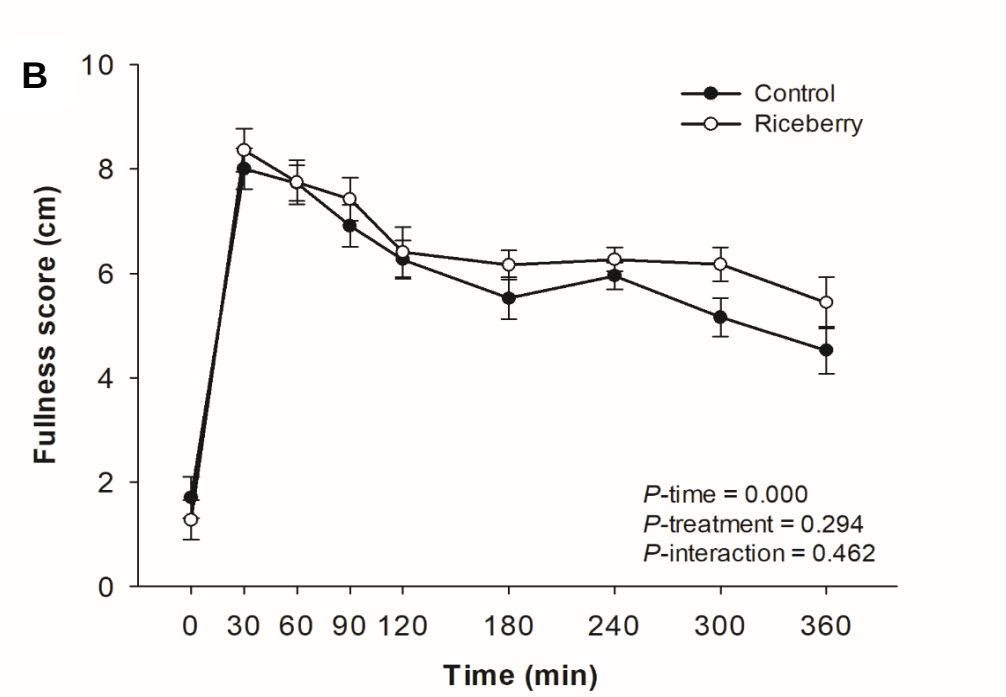


Figure 43 Changes in fullness score after the consumption of HCMF meal and HCMF meal with riceberry rice beverage. Values are mean ± SEM, n=13: * *P*< 0.05 compared to the control.

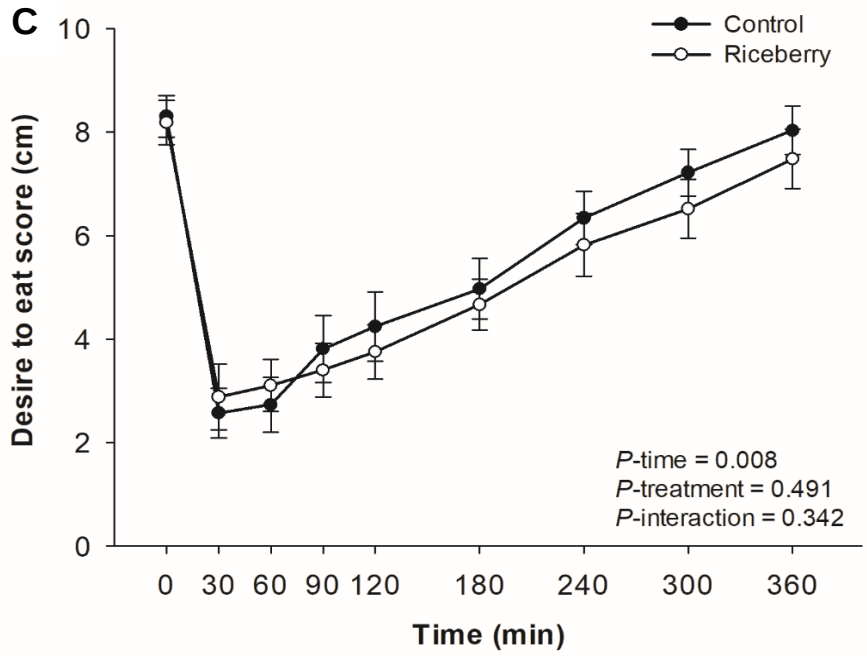


Figure 43 Changes in desire to eat score after the consumption of HCMF meal and HCMF meal with riceberry rice beverage. Values are mean ± SEM, n= 13: * $P < 0.05$ compared to the control.

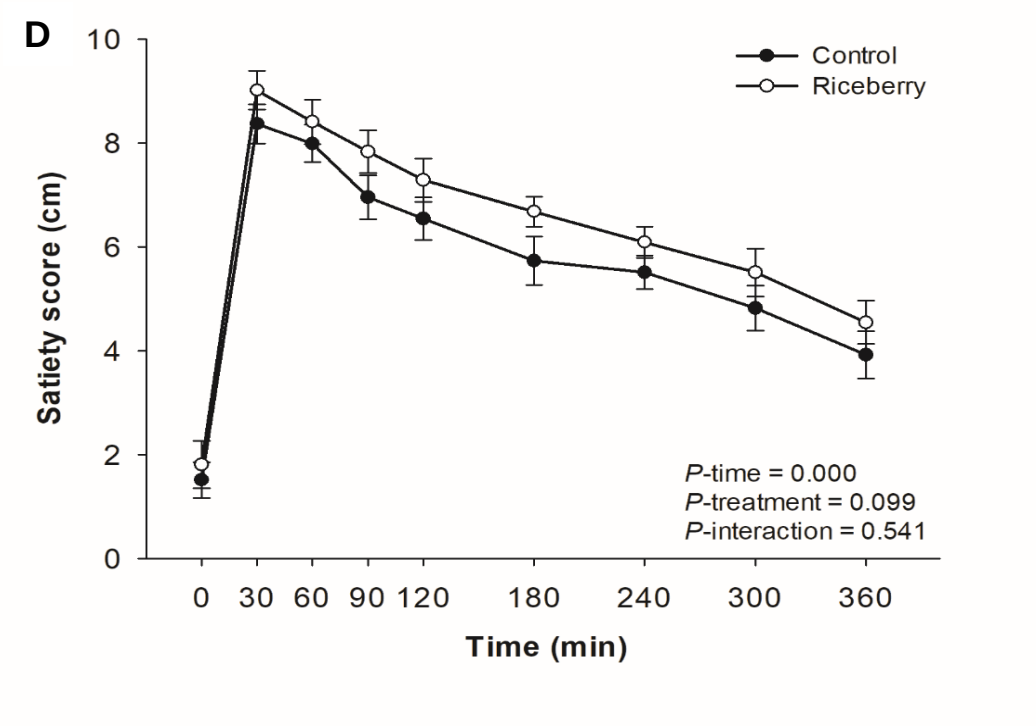


Figure 43 Changes in satiety score after the consumption of HCMF meal and HCMF meal with riceberry rice beverage. Values are mean ± SEM, n=13: * *P*< 0.05 compared to the control.

4.3.7. The maximum plasma concentration (C_{max}) and the peak plasma concentration (T_{max})

As shown in Table 16, the C_{max} of postprandial plasma glucose was lower in HCMF with riceberry rice beverage. The peak of postprandial plasma glucose (T_{max}) of HCMF meal with and without riceberry rice beverage at 31.15 min and 39.23 min, respectively. However, there were no differences in C_{max} and T_{max} of postprandial plasma insulin, FRAP, TEAC, Thiol, MDA, and triglyceride.

Table **16** The maximum plasma concentration (C_{max}) and the peak plasma concentration (T_{max}) of postprandial plasma glucose, insulin, FRAP, TEAC, Thiol, MDA and triglyceride after ingestion of HCMF meal with riceberry rice beverage**.**

Parameters	HCMF meal	HCMF with Riceberry
Glucose		
$Cmax_{0-360}$ (mg/dL)	138.53 ± 6.06	127.10 ± 4.77*
$Tmax_{0-360}$ (min)	39.23 ± 3.99	31 15 ± 2.66*
Insulin		
$Cmax_{0-360}$ (pmol/L)	162.56 ± 6.67	162. 10 ± 7.56
$Tmax_{0-360}$ (min)	66.92 ± 13.11	66.92 ± 17.62
FRAP		
$Cmax_{0-360}$ (mM $FeSO_4$)	0.23 ± 0.04	0.33 ± 0.04
$Tmax_{0-360}$ (min)	193.85 ± 33.22	133.85 ± 31.06
TEAC		
$Cmax_{0-360}$ (mg Trolox equivalent)	1,557.06 ± 54.26	1,792.95 ± 77.17
$Tmax_{0-360}$ (min)	244.62 ± 29.97	226.15 ± 36.05
Thiol		
$Cmax_{0-360}$ (mM L-Cysteine)	610. 49 ± 36.66	609.04 ± 38.54
$Tmax_{0-360}$ (min)	200.77 ± 23.87	226.15 ± 29.14
MDA		
$Cmax_{0-360}$ (μM MDA)	1.94 ± 0.39	226.15 ± 33.56
$Tmax_{0-360}$ (min)	1.84 ± 0.26	170.77 ± 27.88
Triglyceride		
$Cmax_{0-360}$ (mg/dL)	248.05 ± 42.07	223.49 ± 34.93
$Tmax_{0-360}$ (min)	175.38 ± 15.88	189.23 ± 23.38

The results are expressed as mean ± SEM (n = 13). Means with superscripts are significantly different (P<0.05) compared to the control.

CHAPTER V

DISCUSSION

5.1 Part I: Incorporation of anthocyanin-rich riceberry rice in yogurts: Effect on physicochemical properties, antioxidant activity and *in vitro* gastrointestinal digestion

Riceberry rice a group of polyphenols that recognizes as antioxidant especially anthocyanin. The current findings are consistent with previous studies indicating that C3G and P3G are the most abundant anthocyanins in riceberry rice (Arjinajarn et al., 2017; Leardkamolkarn et al., 2011). However, RBE, in the present study, had lower total phenolic compounds than other studies which may be due to the different method and solvent used for extraction (Arjinajarn et al., 2017; Leardkamolkarn et al., 2011).

Several studies found that fortification of yogurt with plant extract such as grape extract, green tea and rheum ribe extract modified the acidification together with reduction of starter culture activity and extension of the fermentation time (da Silva et al., 2017; Alwazeer, Bulut, & Tunçtürk, 2019). However, another report has shown that addition of chia seed water extract or chia seed ethanol extract at 0.05 or 0.1% significantly increased the fermentation rate in yogurt (Kwon, Bae, Seo, & Han, 2019). In this study, no change in the fermentation time of yogurt supplemented with RBE

was observed, suggesting that RBE can be a most suitable for development of functional yogurt without increasing fermentation time.

The addition of RBE into yogurt had no effect on changes in pH and titratable acidity when compared to the control yogurt. The similar results were also found in other reports of yogurt supplemented with grape, green coffee powder and blueberry flower pulp (da Silva et al., 2017; Dönmez, Mogol, & Gökmen, 2017; Liu et al., 2019). The level of titratable acidity of yogurt supplemented with RBE also meets the requirement criteria established by the Codex Alimentarius (2010), which defines that the titratable acidity (express as % lactic acid) of yogurt should not be less than 0.6 %. As for the syneresis, an important index for evaluating quality of set-type yogurt, indicates a balance between attraction and repulsion forces within the casein network and the rearrangement capacity of the network bond (Matumoto-Pintro, Rabiey, Robitaille, & Britten, 2011). Our findings are in agreement with other studies demonstrating that the fortification of blueberry flower pulp into yogurt resulted in a decrease in syneresis (Liu et al., 2019). A decrease in syneresis by RBE contributes to increase the entrapment of water within the gel network, resulting in reduction of serum release from yogurt (Dönmez et al., 2017). This effect might be related to the presence of polyphenols in RBE (Mahdian & Tehrani, 2007). It has been shown that polyphenols have a high affinity for casein, leading to formation of soluble complexes, which create in size and even form sediments. Its interaction promotes the weak strength of the casein network (hydrophobic interaction) together with complementary

formation of hydrogen bonding. This phenomenon stabilizes the complexes, leading to maintaining water in the network and limitation of the serum release from the gel network (Charlton et al., 2002; Oliveira, Alexandre, Coelho, Lopes, Almeida, & Pintado, 2015). This interaction of protein and polyphenol may be the reason for the explanation of reduced syneresis of yogurt (Charlton et al., 2002; Oliveira et al., 2015). Firmness, an important parameter to measure the quality of set yogurt, indicate force necessary to attain a given deformation. In this study, the similar results of unchanged firmness were also provided in the studies of incorporating green tea, moringa leave, sacha inchi extracts into yogurt (Shokery, El-Ziney, Yossef, & Mashaly, 2017; Vanegas-Azuero & Gutiérrez, 2018). However, inconsistent results of decreased firmness were obtained when studying the effect of grape extract and zeaxanthin nanoparticle addition on yogurt (da Silva et al., 2017; de Campo et al., 2019). It has been shown that the increase in total solids by polyphenol-rich natural products influences the strength of the three-dimensional network of milk protein (Lee & Lucey, 2010; Liu, Zhang, Wang, Luo, Guo, & Ren, 2014; Vital, Goto, Hanai, Gomes-da-Costa, de Abreu Filho, Nakamura, & Matumoto-Pintro, 2015).Pelaes Vital et al. suggest that interaction of polyphenols and casein could be attributed to higher amount of water in the gel, the increase softness of yogurt due to the decreased syneresis. Adhesivenesss is the force necessary to remove the material that adheres to the mouth during eating. The results demonstrated no significant change in adhesivenesss between the control and yogurt supplemented with RBE. Moreover, the addition of RBE did not affect the

number of viable lactobacilli count in yogurt, suggesting that RBE did not influence the development of the starter microorganisms. Our results are in accordance with previous studies indicating that fortified grape pomace and concentrated strawberry pulp had no effect on the number of lactic acid bacteria when compared to the control yogurt (Marchiani et al., 2016; Jaster et al., 2018). Furthermore, the lactic acid bacteria count of yogurt with RBE are within the acceptable range (>10^9 cfu/g yogurt) of Codex Alimentarius (2010). This observed range might play the potential to achieve the beneficial effect on the human organism, including a balance of normal intestinal microflora, protection against gastrointestinal pathogen, reduced risk of colon cancer and intestinal inflammation, improvement of lactose intolerance and (Tripathi et al., 2014; Jaster et al., 2018). In addition, previous studies indicate that addition of plant extracts such as cinnamon, strawberry, and blueberry flower pulp could increase the antioxidant activity of yogurt (Helal & Tagliazucchi, 2018; Jaster et al., 2018; Liu et al., 2019). This antioxidant activity has been associated with the presence of polyphenols (Jaster et al., 2018). Our reports found that C3G and P3G are the major bioactive anthocyanin found in RBE. These compounds are recognized as a potent antioxidant, especially antiradical and reducing capacities (Ryu, Han, Park, & Kim, 2000). Therefore, the results of higher antioxidant activity of yogurt are mostly due to the presence of polyphenol and anthocyanin constituent in RBE.

According to the results from *In vitro* gastrointestinal digestion, the findings suggest that the increase in the release of TPC from yogurt at intestinal phase may be

attributed to stirring or the intestinal enzymatic reaction (Carbonell- Capella, Buniowska, Esteve, & Frígola, 2015). The gradual decrease in the level of anthocyanins in yogurt from gastric to intestinal digestion, as was observed in this present study, is in agreement with previous studies. Oliveira et al (2015) described that the transition of strawberry enriched yogurt from the acidic gastric to mild alkaline intestinal condition resulted in a decrease in the amount of anthocyanin content. A great decline in the content of C3G and P3G in yogurt occurring after the gastric digestion is related to the chemical structure of anthocyanins. It has been shown that anthocyanins are highly stable under an acidic or neutral environment and easily degraded at higher pH of solution (Oliveira et al., 2015; Krga et al., 2019). Interestingly, the increase in FRAP value may be attributed to the release of the antioxidant free amino acid and peptide from the milk protein sequences (Rutella, Tagliazucchi, & Solieri, 2016; Pan, Liu, Luo, & Luo, 2019). The addition of RBE into yogurt demonstrated higher FRAP value than the control during gastric and intestinal digestion. Especially, a significant increase in FRAP of yogurts supplemented with RBE was observed at 60 min when compared to the beginning of intestinal digestion. This result may have occurred because of the increase in release of polyphenolic compounds from yogurts by stirring or the enzymatic activity during simulated gastrointestinal digestion (Carbonell- Capella, Buniowska, Esteve, & Frígola, 2015). This process may facilitate the breakdown of molecules from the interaction of polyphenols with hydrophobic sites of proteins. However, a considerable loss of anthocyanins (C3G and P3G) with concomitant increase

in TPC of yogurt supplemented with RBE was obtained in this study. This suggests that C3G and P3G in RBE may not play a role in the increased FRAP value during intestinal digestion. Lafarga et al. (2019) supported that TPC positively correlated with the FRAP value during *in vitro* intestinal digestion of food containing polyphenolic compounds. In addition, other polyphenolic compounds were identified in riceberry rice including protocatechuic acid, vanillic acid, *p*-coumaric acid, ferulic acid, and sinapic acid, rutin, myricetin, and quercetin 3- glucuronide (Peanparkdee, Yamauchi, & Iwamoto, 2017). These compounds act as antioxidant which markedly exhibited the FRAP values. Thus, the observed increase in FRAP value of yogurt supplemented with RBE during intestinal digestion could be attributed to the release of other polyphenolic compounds.

As for the effect of RBE on sensory attributes of yogurt, our results are consistent with previous studies that the scores of textural attributes were altered after addition of polyphenol-rich grape pomace and olive leaf extract into yogurts (Soukoulis et al., 2007; Marchiani et al., 2016; Tavakoli, Hosseini, Jafari, & Katouzian, 2018). The alteration of sensory characteristics of food products by the polyphenolic compounds was partly involved color, odor and astringency. Based on the data obtained in this study, supplementation of RBE (0.125% and 0.25%) could be suitable for the development of functional yogurt because these concentrations improved antioxidant activity without generating significant negative fermentation time, the number of LAB, physiochemical and sensory properties. Therefore, yogurt supplemented with 0.125% and 0.25% RBE was selected for a further experiment.

During the refrigerated storage period, it is well documented in the literature that the reduction of LAB in yogurt during refrigerated storage resulted from many factors such as food ingredient and additives, oxygen content and redox potential, moisture content/ water activity, storage temperature, pH and titratable acidity, and packaging aspects (Tripathi et al., 2014). Surprisingly, RBE did not improve the number of LAB in yogurt during 7-21 days of refrigerated storage when compared to the control. The obtained result is similar to other studies that addition of strawberry pulp into yogurts could not improve the number of LAB during refrigerated storage (Jaster et al., 2018; Tseng & Zhao, 2013). However, the number of LAB in yogurts supplemented with RBE maintained above the recommended counting by Codex Alimentarius (2010). According to the results of syneresis, the similar results are obtained from the study of Liu et al (2019), who report that blueberry flower pulp decreased syneresis of yogurt. Although the reduced syneresis of yogurts supplemented with RBE was apparently detected, but these values were within an acceptable range as compared to the previous study (Aportela-Palacios, Sosa-Morales, & Vélez-Ruiz, 2005). If syneresis was lower than 39%, indicating that yogurt had a desirable property of consumer acceptability. Additionally, the TPC, C3G and P3G of yogurts supplemented with RBE remained constant. However, RBE-supplemented yogurt exhibited significantly higher TPC, C3G and P3G than the control. These findings were consisted with a report of Trigueros et al (2014) who found no significant change in the concentration of anthocyanin in yogurt fortified with pomegranate during refrigerated storage. The

maintaining content of anthocyanins (C3G and P3G) is also supported by the color analyses, where no reduction in the parameter of red color (a*) was seen at day 1, 7 and 14. Our study also found that the DPPH and FRAP values were increased, this result is in agreement with previous studies that adding natural plant extracts increased the DPPH and FRAP values of yogurt, whereas the decreased antioxidant activity of yogurt was observed during the storage period of 14 days (Najgebauer-Lejko, Grega, & Tabaszewska, 2014).

5.2 Part II: Postprandial effect of yogurt enriched with anthocyanin from riceberry rice on glycemic response and antioxidant capacity in healthy adults: A cross-over randomized study

Yogurt has received considerable attention as a potential approach to reducing the risks of weight gain, obesity, type 2 diabetes and cardiovascular diseases (Crichton & Alkerwi, 2014; Possa, Corrente, & Fisberg, 2017). Especially, several studies have reported the successful fortification of yogurt with bioactive compounds from edible plants such as green tea, black tea, white tea (Muniandy, Shori, & Baba, 2016), chamomile (Caleja et al., 2016), strawberry pulp (Jaster et al., 2018) and aronia juice (Nguyen & Hwang, 2016). In our previous study, riceberry rice extract supplementation to yogurt significantly increased total phenolic content (TPC), cyanidin-3-glucoside (C3G), peonidin-3-glucoside (P3G) with a concomitant increase in DPPH radical scavenging activity and ferric reducing antioxidant power (FRAP). In addition, this yogurt produced higher release of TP and FRAP than the control under gastrointestinal digestion (Anuyahong, Chusak, & Adisakwattana, 2020). It is the first study to investigate whether riceberry rice yogurt decreases postprandial glycemic response and improves antioxidant capacity in healthy adults. A reduction in the postprandial glucose excursion (40.23%), after consumption of riceberry rice yogurt, was observed in healthy subjects. Cross-over studies have explored acute effects riceberry rice bread (50 g) on postprandial glucose and insulin concentration in healthy volunteers (Chusak et al., 2020). After riceberry rice bread intakes, the AUC was 60% lower in comparison to

jasmine rice bread. Furthermore, riceberry rice bread significantly attenuated the elevation of postprandial insulin concentration after 15 min consumption. The main reason to explain these effects is the ability of phytochemical compounds on the inhibition of carbohydrate digestive enzymes (Adisakwattana, Ruengsamran, et al., 2012; Chusak et al., 2020; Törrönen et al., 2010). A previous study reported that the anthocyanin-rich extract of riceberry rice was capable in inhibiting intestinal α-glucosidase such as maltase and sucrase (Poosri et al., 2019). Especially, the main anthocyanin identified in riceberry rice extract, cyanidin-3-glucoside and peonidin-3-glucoside, was proved to be effective pancreatic α-amylase and α-glucosidase inhibitors (Akkarachiyasit et al., 2010; Poosri et al., 2019; Sui, Zhang, & Zhou, 2016).

Post-meal hyperglycemia and glycemic fluctuations induces excessive production of reactive oxygen species (ROS). The excessive formation of ROS may be a contributing factor for induction of pathological changes related to the development of cardiovascular diseases (O'Keefe & Bell, 2007). Interestingly, dietary antioxidants help scavenge and neutralize excessive and inappropriate reactive oxygen species, sequencing to balance against oxidant condition (Stephens, Khanolkar, & Bain, 2009). Scientific evidence suggest that consumption of phytochemical-rich plants improves plasma antioxidant capacity and reduces lipid peroxidation in humans (Einbond, Reynertson, Luo, Basile, & Kennelly, 2004; Mertens-Talcott et al., 2008; Rizvi, Jha, & Pandey, 2010). The different assays have been developed to measure plasma

antioxidant capacity such as ORAC, TEAC and FRAP. The ORAC assay refers the ability of antioxidant molecules to inhibit peroxyl radical induced oxidation (Cao, Alessio, & Cutler, 1993), whereas the TEAC assay indicates the ability of hydrogen-donating antioxidants to neutralize a radical cation in both lipophilic and hydrophilic environments (Mira, Silva, Rocha, & Manso, 1999). Furthermore, FRAP assay could reflect the ability of antioxidants to reduce the reaction of Fe^{3+}/Fe^{2+}couple. Compared to fasting, the yogurt control significantly increased plasma antioxidant capacity (FRAP, TEAC and ORAC). Remarkably, plasma FRAP, TEAC and ORAC was high by 163.69%, 162.52% and 291.18% after 180 min of riceberry rice yogurt, in comparison with the yogurt control. In the support of this, yogurt supplemented with riceberry rice extract (0.25%) produced 4.8-and 1.75-fold higher FRAP and total polyphenolic content than the control yogurt, respectively (Anuyahong et al., 2020). The observed effect on increased postprandial antioxidant capacity is consistent with a previous study of the subjects following riceberry rice bread (Chusak et al., 2020). The plasma FRAP level after riceberry rice bread consumption was greater than that of jasmine rice and wheat bread. Another notable result from our study showed that consumption of control yogurt led to an increase in plasma MDA above the baseline level. This alteration was markedly attenuated by riceberry rice yogurt consumption. However, this pattern was not seen in the subjects who consumed riceberry rice bread (Chusak et al., 2020). The dissimilar outcomes of these studies might be due to the low amount of fat composition in bread.

Other clinical studies have also shown improvement in plasma antioxidant capacity following consumption of anthocyanin-rich plants such as butterfly pea flower (Chusak et al., 2018), chilean berry (Urquiaga et al., 2017), and açai berry (Mertens-Talcott et al., 2008). It is suggested that the increased plasma antioxidant capacity may be partly attributed to the antioxidant activity of polyphenols (Chusak et al., 2018). In this context, cyanidin-3-glucoside and peonidin-3-glucoside, an active ingredient identified in riceberry rice yogurt, are recognized as free radical scavenging activity. Previous studies revealed that these compounds have antioxidant activity as measured by FRAP, TEAC, and ORAC assays (Stintzing, Stintzing, Carle, Frei, & Wrolstad, 2002; Y. Wang et al., 2016). In addition, cyanidin-3-glucoside and peonidin-3-glucoside had the ability to reduce the formation of lipid peroxidation in UVB irradiation model and vitamin E-depleted rat (Ramirez-Tortosa et al., 2001; Tsuda, Shiga, Ohshima, Kawakishi, & Osawa, 1996). Interestingly, consumption of anthocyanin-rich strawberries and chokeberries, mainly cyanidin-3-glucoside reduced human plasma MDA levels by 31.4% and 46% respectively (Alvarez-Suarez et al., 2014; Kardum et al., 2014). Through these actions, we suggest that cyanidin-3-glucoside and peonidin-3-glucoside in riceberry rice yogurt may play a role in an increase in plasma antioxidant capacity leading to decrease in lipid peroxidation. However, other phytochemical compounds may have influenced on postprandial antioxidant capacity. Therefore, the further study is required to quantify the postprandial concentration of individual polyphenol after riceberry yogurt consumption.

Visual analog scales (VAS) are relievable tools for the evaluation of subjective appetite sensation about hunger, fullness, desire to eat, and satiety (Mortensen et al., 2018). In our study, the scores of all parameters did not show any significant differences between riceberry rice yogurt and the control yogurt. This finding is in agreement with the earlier study that bread made from riceberry rice did not alter subjective rating scores of hunger, fullness, desire to eat, and satiety in healthy adults. In addition, the change in postprandial level of glucagon-like peptide-1 (GLP-1), a type of incretin hormone was not detected following consumption of riceberry rice bread (Chusak et al., 2020). This hormone enhances glucose-stimulated insulin secretion, inhibits glucagon secretion and gastric emptying and regulates appetite and satiety (Tsuda, 2015). It has been shown that anthocyanins stimulated the secretion of GLP-1 in Murine GLUTag Cell Line (Kato, Tani, Terahara, & Tsuda, 2015). It has been hypothesized that consumption of riceberry rice yogurt could not module satiety and appetite through the stimulation of GLP-1, possibly as a result from a small amount of anthocyanin and its bioavailability. We acknowledge some potential limitations to the current study. First, we did not introduce a full meal to consume with riceberry yogurt. Other macro- and micronutrients may interfere the postprandial effect of riceberry rice yogurt on plasma glucose and antioxidant capacity. Moreover, this study was only a relatively young and healthy population, older age subjects were not included to increase the homogeneity of postprandial response.

5.3 Part III: The consumption of riceberry rice beverage with high-carbohydrate, moderate- fat meal on postprandial glycemic response, antioxidant status, lipidemic response and inflammatory markers in overweight and obese subjects.

High carbohydrate diets rich in saturated fat promote postprandial dysmetabolism by the impairment of postprandial blood glucose, free fatty acids, and triglycerides (O' Keefe & Bell, 2007). Postprandial hyperglycemia accompanied by excessive hyperlipidemia has been reported to significantly increase the risk of development and progression of metabolic disorders such as metabolic syndrome, diabetes mellitus, hypertension, and cardiovascular diseases, consequently induced the formation of endothelial dysfunction, oxidative stress, and inflammation (D. Bell, O'Keefe, & Jellinger, 2008; Antonio Ceriello, 2005). Moreover, long-term intake of high carbohydrate meals also induce abnormal insulin secretion, resulting in hyperinsulinemia (Ludwig, 2002). The present study found that riceberry rice beverage significantly decreased postprandial plasma glucose and insulin response in overweight to obese subjects following high carbohydrate moderate fat (HCMF) meal. In agreement with other studies, anthocyanins- rich plants together with high carbohydrate meal could suppress postprandial glucose meal in the human study. For example, Castro-Acosta et al. (2016) revealed that a drink containing low sugar and anthocyanin-rich blackcurrant extract reduced postprandial glycemia response in the subjects after consumption of a high carbohydrate meal (Castro-Acosta et al., 2016). In overweight adults, a recent study was carried out by Edirisinghe et al. who found that

postprandial plasma insulin response was reduced after consumption of HCMF with strawberry anthocyanin beverage (Edirisinghe et al., 2011). Furthermore, the bilberry extract exhibited a reduction in postprandial plasma glucose concentration after OGTT challenge in overweight subjects. This effect was probably due to the ability of anthocyanin-enriched bilberry extract to reduce the activity of α-amylase activity, α-glucosidase (Alnajjar et al., 2020).

As a result of high content of bioactive compounds, riceberry rice is an interesting source of incorporating polyphenols and anthocyanins, especially cyanidin-3-glucoside and peonidin-3-glucoside. The main hypothesis to explain the reduced postprandial glucose and insulin response by riceberry beverage action is the inhibition of the digestive tract carbohydrate-hydrolyzing enzymes, including α-amylase and α-glucosidase (Poosri et al., 2019). Several studies reported that cyanidin-3-glucoside and peonidin-3-glucoside are capable of interfering with maltase and sucrase (Akkarachiyasit et al., 2010; Nile & Park, 2014).

There are increasing evidence demonstrating that the postprandial oxidative stress is related to the formation of reactive oxygen species (ROS) which is a contributing factor to development of non-communicable chronic diseases (NCDs) (Burton-Freeman, 2010). The postprandial oxidative stress response after meal consumption depends on various factors including the chemical nature of macronutrient intake, the unsaturation degree of dietary fatty acids, the amount of

lipids intake, phytonutrient quantity, among others (Bloomer, Kabir, Marshall, Canale, & Farney, 2010; Khor et al., 2014). It has been documented that plasma oxidative stress could arise as readily from the hydroperoxides associated with an intake of high fat and carbohydrate diets. This leads to a reduction in postprandial antioxidant capacity, thiol level as well as an increase in the end products of lipid peroxidation (MDA). Consumption of diets rich in bioactive compounds produced greater potential to modulate cellular reductive-oxidative (redox) balance and even promoted plasma antioxidant capacity (Burton-Freeman, 2010). Interestingly, Burton-Freeman et al. suggested that ingestion of flavonoid-rich strawberry beverage significantly decreased postprandial insulin and triglyceride concentration with a concomitant reduction in oxidative stress in overweight adults (Burton-Freeman, Linares, Hyson, & Kappagoda, 2010). A study of Mazza et al. described that freeze-dried blueberry powder along with high fat meal increased serum antioxidant capacity in the appearance of serum total anthocyanins in male subjects (Mazza, Kay, Cottrell, & Holub, 2002). Besides, an increase in plasma thiol after consumption of beverage increased protein thiol, a physiological mechanism of endogenous antioxidant response (Chusak et al., 2018). The oxidation of protein can be relieved by a non-enzymatic reaction with sulfhydryl groups as found in cysteine and glutathione (Urquiaga et al., 2017). In healthy male volunteers, consumption of anthocyanin-rich berry beverage had significantly effect on increasing postprandial antioxidant capacity with decreasing oxidation of lipid and protein, indicating by lowering plasma MDA and protein carbonyls (Urquiaga et al.,

2017). The current study found that consumption of riceberry rice beverage increased plasma FRAP, TEAC, thiol level and decreased plasma MDA level in subjects after consumption of HCMF, suggesting that riceberry rice beverage could improve postprandial antioxidant status. The current study is consistent with a previous study that consumption of bread made from 100% riceberry rice had higher postprandial level of plasma FRAP, TEAC and thiol than that of wheat and rice bread (Chusak et al., 2020). It is most likely due to the presence of anthocyanins in riceberry rice extract responsible for antioxidant effect. Anthocyanins may act as a free radical scavenger by donating the hydrogen atoms, transferring electrons to free radicals or removing the molecular species of active oxygen generated from lipid peroxidation (Naseri et al., 2018). In addition, anthocyanins may help protect the thiol group depletion of endogenous antioxidant enzymes. This suggests that this effect anthocyanins contribute increase in plasma total antioxidant potential after consumption of antioxidant-plant based food (Serafini et al., 2002).

Moreover, consumption of dietary fat is absorbed into lymphatic circulation and then entered to the liver when they are hydrolyzed by hepatic triglyceride lipase. A previous report suggested that intake of fat-containing meal significantly elevated plasma triglyceride and free fatty acid concentrations (Tamburrelli et al., 2012). The elevation of triglyceride and FFAs induces lipid peroxidation which may produce cell injury and low-grade inflammatory responses to injury that indirectly promote oxidation in target tissues such as skeletal muscle, the liver, and adipocytes that may

contribute to insulin resistance, obesity, metabolic syndrome, and cardiovascular diseases (Boden, 2008). During inflammatory state, pro-inflammatory cytokines are secreted from the mature adipocytes such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-1 beta (IL-1β), adiponectin and leptin etc. (Teng, Chang, Chang, & Nesaretnam, 2014). TNF-α is the first cytokine to be defined as a common influencer associated with obesity, inflammation, diabetes, and cardiovascular diseases (Divella, De Luca, Abbate, Naglieri, & Daniele, 2016). Besides, IL-1β and IL-6 involve in the inflammatory process, cell proliferation, differentiation and apoptosis (Lagathu et al., 2006). Normally, IL-6 is responsible for the acute phase response in the liver and further promotes the progression of acute to chronic inflammation by activating monocyte recruitment (Gabay, 2006). In postprandial lipidemic response, consumption of the meal containing moderate to high fat produced the peak of triglyceride level at 3-4 h which returned to baseline at 6-8 h (Nakamura, Miyoshi, Yunoki, & Ito, 2016). In the present study consistent with another trial in overweight and obese subjects who consumed high fat meal, the peak triglyceride level was also detected at 3 h in the present study (Beals et al., 2019). In addition, postprandial FFAs and pro-inflammatory cytokines including TNF-α, IL-1β and IL-6 responses was increased after HCMF meal challenge around 6 h when compared to the baseline level. Several reports have shown that consumption of a large lipid content caused an increase in postprandial pro-inflammatory cytokines in healthy, overweight, and obesity (Demmer et al., 2016;

Masson & Mensink, 2011; Poppitt et al., 2008). A study of Demmer et al. demonstrated that levels of plasma TNF-α and IL-6 were increased from baseline and peaked at 6 h in response to high fat meal in overweight and obese adults (Demmer et al., 2016). An increase in cytokines IL-6, IL-1 and TNF-α has been linked to inflammatory degenerative diseases (Divella et al., 2016). It is proposed that increase in cytokines may involve in 1) reduction and block of capillaries lipoprotein lipase synthesis; 2) blocking of insulin receptors of adipocytes; 3) activation of lipoprotein lipase sensitive hormone in adipocytes; 4) induction of endothelial inflammation; 5) reduction in insulin signaling; 6) promotion in pro-atherosclerotic effect; 7) stimulation of the oxidation of fatty acids and gluconeogenesis; and 8) inhibition of adiponectin secretion (Divella et al., 2016).

Recently, anthocyanins had the ability to reduce intestinal absorption of dietary fat by inhibiting the activity of pancreatic lipase (Fabroni et al., 2016; Sergent, Vanderstraeten, Winand, Beguin, & Schneider, 2012). The present study found that consumption of riceberry rice beverage with HCMF meal results in a reduction of postprandial plasma triglyceride and free fatty acids. These results are in agreement with a study of Polley et al. that consumption of tart cherry rich in anthocyanins decreased postprandial triglyceride levels in men following a high fat meal (Polley, Oswell, Pegg, & Cooper, 2019). The current study suggests that the reduction of postprandial plasma triglyceride and free fatty acids is due to the effect of riceberry

rice on inhibition of pancreatic lipase, binding bile acid disrupting cholesterol micelle formation (Poosri et al., 2019). Previous research has also shown that anthocyanins in riceberry rice extract such as C3G and P3G act this manner (Yao, Xu, Zhang, & Lu, 2013). It is possible that suppression of postprandial lipid response leads to the reduction of postprandial pro-inflammatory cytokine release. A study performed with twenty-three adults demonstrated a reduction in postprandial free fatty acids with concomitant decrease in the level of cytokines including IL-1β and IL-6 following a moderately high fat meal with blueberry yogurt (Ono-Moore et al., 2016). In this study, the levels of IL-1β, IL-6, and TNF-α were significantly suppressed after consumption of riceberry rice beverage with HCMF meal. These findings are similar to other reports of anthocyanin intervention. For example, acute supplementation of raspberry significantly lowered postprandial biomarkers of inflammation including IL-6 and TNF-α in adult with type 2 diabetes (Schell, Betts, Lyons, & Basu, 2019). A previous study in overweight subjects given a high-carbohydrate and moderate-fat meal supplemented with freeze-dried strawberry beverage resulted a reduction in the levels of IL-6 and hs-CRP over the 6 h postprandial period (Edirisinghe et al., 2011). In a study with rats fed a fructose-rich diet, ingestion of chokeberry extract significantly reduced gene expression of inflammatory cytokines including IL-1β, IL-6, and TNF-α (Qin & Anderson, 2012).

Visual analogue scales (VAS) are usually applied in clinical study to record subjective sensations such as hunger, fullness and desire to eat (Sepple & Read, 1989).

In regard to the present study, no differences in subjective ratings of hunger, fullness, desire to eat, and satiety were observed between riceberry rice beverage with HCMF meal and the control. These results was similar to a study of Chusak et al., who suggested that consumption of bread made from 100% riceberry rice did not show any difference in hunger, fullness, desire to eat, and satiety (Chusak et al., 2020).

The current study presents several limitations that needed to be discussed. For example, the study was the lack of data on dietary fat record during the study that may result in the different effect on appetite and energy metabolism (Flint, Helt, Raben, Toubro, & Astrup, 2003). Second, there was the lack of plasma individual anthocyanin and their metabolites after intake of riceberry rice beverage. This may help evaluate its correlation with plasma antioxidant capacity.

CHAPTER VI

CONCLUSION

The results from this study indicated that the addition of riceberry rice extract (RBE) to yogurt decreased the syneresis of yogurt and increased the content of polyphenol, anthocyanins and antioxidant activity without the effect of viable lactobacilli. According to the results of this study, during refrigerated storage antioxidant activity decreased, and TPC and anthocyanins were constant. Also, anthocyanin content decreased at the end of the simulated gastrointestinal conditions. In addition to this, antioxidant activity measured by FRAP test showed fluctuation during gastrointestinal digestion. The findings suggest that RBE at 0.125% and 0.25% (w/w) can be used as a natural source to improve the content of phytochemical compounds and antioxidant activity of yogurt without a significant sacrifice of sensory acceptability.

In healthy volunteers, consumption of yogurt enriched with 0.25% RBE led to a reduction of postprandial plasma glucose and a lower glucose peak was observed at 30 min after ingestion. Moreover, consumption of riceberry rice yogurt improved postprandial increased plasma FRAP, TEAC, ORAC, thiol level. In addition, the postprandial plasma MDA level was reduced in healthy subjects which received riceberry rice yogurt. Furthermore, consumption of riceberry rice yogurt had similar rating scores of hunger, fullness, desire to eat, and satiety as compared to control.

Interestingly, consumption of riceberry rice beverage (0.5 % w/v) with HCMF meal significantly decreased postprandial plasma glucose and insulin concentration in overweight and obese subjects. Moreover, ingestion of riceberry rice beverage increased postprandial antioxidant capacity including plasma FRAP, TEAC, and thiol level. In addition, consumption of HCMF meal together with riceberry rice beverage led to suppress postprandial plasma MDA at 30-120 min. Finally, ingestion of HCMF with riceberry rice beverage could attenuate postprandial serum triglyceride and FFA and improves postprandial inflammatory cytokine include IL-1β, IL-6, and TNF-α. However, there were no significant differences in the rating scores of hunger, fullness, desire to eat, and satiety among tested meals. Futures studies are needed to determine the effect of riceberry rice yogurt and beverage consumption with the meal on postprandial response in diabetic patients and hyperlipidemic subjects.

In conclusion, our findings suggest that the riceberry rice extract can be offered as a promising natural ingredient for development of novel yogurt and functional drink in order to reduce glycemic response and inflammatory cytokine as well as improve plasma antioxidant capacity in humans.

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Table A Incremental change in postprandial plasma glucose, ferric reducing ability of plasma (FRAP), trolox equivalent antioxidant capacity (TEAC), oxygen radical absorbance capacity (ORAC), thiol, and malondialdehyde (MDA).

Time (min)	Glucose (mg/dL)		FRAP (mM $FeSO_4$)		TEAC (mM Trolox)	
	Control yogurt	Riceberry yogurt	Control yogurt	Riceberry yogurt	Control yogurt	Riceberry yogurt
0	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}
15	9.35 ± 1.25^{Ab}	8.59 ± 1.78^{Ab}	-	-	-	-
30	18.62 ± 1.92^{Ac}	12.43 ± 2.62^{Bb}	0.20 ± 0.04^{Ab}	0.27 ± 0.05^{Abc}	137.16 ± 33.54^{Abc}	254.91 ± 49.15^{Bb}
60	0.54 ± 1.81^{Aa}	-0.64 ± 2.05^{Aa}	0.21 ± 0.04^{Ab}	0.34 ± 0.06^{Bc}	231.93 ± 54.03^{Acd}	229.58 ± 37.94^{Ab}
90	0.18 ± 1.58^{Aa}	-3.18 ± 1.68^{Aa}	0.15 ± 0.03^{Ab}	0.27 ± 0.06^{Bbc}	140.12 ± 37.87^{Ab}	307.23 ± 48.20^{Bb}
120	2.70 ± 1.63^{Aa}	-2.95 ± 1.45^{Ba}	0.13 ± 0.03^{Ab}	0.27 ± 0.05^{Bbc}	100.56 ± 45.14^{Ab}	232.42 ± 35.76^{Bb}
150	-	-	0.13 ± 0.05^{Ab}	0.21 ± 0.04^{Ab}	134.69 ± 49.82^{Abc}	272.61 ± 39.72^{Bb}
180	-	-	0.12 ± 0.05^{Ab}	0.16 ± 0.04^{Ab}	251.68 ± 38.60^{Ad}	235.28 ± 47.20^{Ab}

Data are presented as mean ± SEM, n=19. Means with different lowercase letters (a-d: time effects) at the same treatment are significant different ($P<0.05$). Means with different uppercase letters at the same day (A-B: treatment effects) are significant different ($P<0.05$) compared to the control.

Table A (Continued)

Time (min)	ORAC (μM Trolox)		Thiol (mM L-Cysteine)		MDA (μM MDA)	
	Control yogurt	Riceberry yogurt	Control yogurt	Riceberry yogurt	Control yogurt	Riceberry yogurt
0	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}
15	-	-	-	-	-	-
30	57.08 ± 29.21^{Aa}	169.55 ± 42.82^{Bbc}	20.93 ± 4.50^{Ab}	56.10 ± 8.24^{Bb}	0.07 ± 0.02^{Aab}	0.05 ± 0.02^{Aab}
60	63.44 ± 35.02^{Aa}	166.83 ± 28.93^{Bbc}	31.37 ± 6.19^{Ab}	44.49 ± 7.38^{Ab}	0.18 ± 0.04^{Abc}	0.04 ± 0.03^{Bab}
90	90.93 ± 21.55^{Aa}	217.88 ± 35.21^{Bbc}	35.43 ± 8.17^{Ab}	63.18 ± 10.32^{Bb}	0.28 ± 0.06^{Ac}	0.04 ± 0.03^{Bab}
120	61.12 ± 36.18^{Aa}	245.04 ± 71.59^{Bc}	27.21 ± 6.83^{Ab}	65.46 ± 13.56^{Bb}	0.17 ± 0.05^{Abc}	0.06 ± 0.04^{Aab}
150	66.04 ± 47.68^{Aa}	148.74 ± 30.70^{Abc}	40.33 ± 7.24^{Ab}	56.25 ± 11.49^{Ab}	0.21 ± 0.06^{Abc}	0.15 ± 0.08^{Ab}
180	11.47 ± 35.49^{Aa}	109.19 ± 41.11^{Aab}	34.49 ± 8.93^{Ab}	47.59 ± 8.15^{Ab}	0.30 ± 0.08^{Ac}	0.03 ± 0.02^{Bab}

Data are presented as mean ± SEM, n=19. Means with different lowercase letters (a-c: time effects) at the same treatment are significant different ($P<0.05$). Means with different uppercase letters at the same day (A-B: treatment effects) are significant different ($P<0.05$) compared to the control.

Table B Incremental postprandial plasma glucose, insulin, ferric reducing ability of plasma (FRAP), trolox equivalent antioxidant capacity (TEAC), thiol, malondialdehyde (MDA), serum triglyceride, free fatty acid, IL-1β, IL-6, and TNF-α.

Time (min)	Glucose (mg/dL)		Insulin (pmol/L)		FRAP (mM $FeSO_4$)	
	Control	Riceberry	Control	Riceberry	Control	Riceberry
0	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aab}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}
15	32.19 ± 5.38^{Acd}	21.51 ± 3.25^{Ade}	4.08 ± 2.40^{Aab}	2.09 ± 2.37^{Aa}	-	-
30	56.49 ± 4.34^{Ae}	42.56 ± 3.86^{Bf}	8.39 ± 2.63^{Abc}	4.05 ± 2.36^{Aa}	0.05 ± 0.02^{Aa}	0.08 ± 0.03^{Ab}
60	43.31 ± 6.89^{Ad}	28.66 ± 4.96^{Be}	11.54 ± 2.25^{Ac}	4.74 ± 1.94^{Ba}	0.03 ± 0.03^{Aa}	0.06 ± 0.03^{Aab}
90	25.31 ± 2.97^{Abc}	14.08 ± 3.79^{Bcd}	11.15 ± 2.26^{Ac}	4.10 ± 1.93^{Ba}	0.05 ± 0.03^{Aa}	0.08 ± 0.02^{Ab}
120	15.16 ± 3.34^{Ab}	7.49 ± 2.41^{Bbc}	8.74 ± 1.67^{Abc}	3.37 ± 1.95^{Aa}	0.02 ± 0.03^{Aa}	0.12 ± 0.03^{Bb}
180	-1.11 ± 2.89^{Aa}	-7.34 ± 2.51^{Aa}	8.89 ± 2.09^{Abc}	4.28 ± 1.57^{Aa}	0.02 ± 0.02^{Aa}	0.08 ± 0.02^{Bb}
240	-	-	-	-	0.00 ± 0.01^{Aa}	0.07 ± 0.02^{Bb}
300	-	-	-	-	0.03 ± 0.02^{Aa}	0.09 ± 0.02^{Ab}
360	-	-	-	-	0.02 ± 0.02^{Aa}	0.10 ± 0.02^{Bb}

Data are presented as mean ± SEM, n=13. Means with different lowercase letters (a-d: time effects) at the same treatment are significant different ($P<0.05$). Means with different uppercase letters at the same day (A-B: treatment effects) are significant different ($P<0.05$) compared to the control.

Table B (Continued)

Time (min)	TEAC (mM Trolox)		Thiol (mM L-Cysteine)		MDA (μM MDA)	
	Control	Riceberry	Control	Riceberry	Control	Riceberry
0	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aab}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}
30	-17.11 ± 24.38^{Aa}	71.60 ± 22.02^{Bab}	8.75 ± 8.76^{Aabc}	25.60 ± 9.34^{Ab}	0.39 ± 0.16^{Aa}	-0.16 ± 0.15^{Ba}
60	17.11 ± 24.08^{Aa}	87.46 ± 25.98^{Ab}	-7.10 ± 9.15^{Aa}	40.48 ± 7.28^{Bbc}	0.14 ± 0.11^{Aa}	-0.28 ± 0.15^{Aa}
90	-11.57 ± 19.33^{Aa}	105.19 ± 27.26^{Bb}	7.63 ± 8.72^{Aabc}	56.96 ± 8.88^{Bcd}	0.21 ± 0.13^{Aa}	-0.09 ± 0.08^{Ba}
120	12.92 ± 27.18^{Aa}	95.31 ± 30.28^{Ab}	31.29 ± 8.85^{Ac}	56.22 ± 8.36^{Acd}	0.36 ± 0.18^{Aa}	-0.24 ± 0.15^{Ba}
180	35.71 ± 34.90^{Aa}	115.04 ± 29.84^{Ab}	29.74 ± 9.76^{Ac}	66.48 ± 7.68^{Bd}	0.28 ± 0.16^{Aa}	-0.13 ± 0.14^{Aa}
240	5.24 ± 18.70^{Aa}	108.56 ± 28.00^{Bb}	34.23 ± 8.84^{Ac}	67.41 ± 8.28^{Bd}	0.49 ± 0.21^{Aa}	-0.03 ± 0.13^{Aa}
300	24.28 ± 14.90^{Aa}	101.91 ± 27.39^{Bb}	23.21 ± 9.12^{Abc}	61.72 ± 6.40^{Bcd}	0.34 ± 0.20^{Aa}	-0.06 ± 0.15^{Aa}
360	44.77 ± 28.19^{Aa}	125.89 ± 29.78^{Ab}	25.86 ± 8.75^{Abc}	72.13 ± 8.68^{Bd}	0.42 ± 0.15^{Aa}	-0.05 ± 0.11^{Ba}

Data are presented as mean ± SEM, n=13. Means with different lowercase letters (a-d: time effects) at the same treatment are significant different ($P<0.05$). Means with different uppercase letters at the same day (A-B: treatment effects) are significant different ($P<0.05$) compared to the control.

Table B (Continued)

Time (min)	Triglyceride (mg/dL)		Free fatty acid (μmol/L)		IL-1β (pg/mL)	
	Control	Riceberry	Control	Riceberry	Control	Riceberry
0	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}
60	32.31 ± 9.19^{Ab}	26.29 ± 5.24^{Abc}	-	-	-	-
120	51.66 ± 7.81^{Ac}	39.45 ± 6.21^{Ac}	-	-	-	-
180	66.53 ± 7.22^{Ac}	41.28 ± 7.68^{Bc}	33.91 ± 7.35^{Aa}	-8.31 ± 12.24^{Ba}	-0.24 ± 0.19^{Aa}	-0.74 ± 0.15^{Ba}
240	52.92 ± 8.19^{Ac}	24.74 ± 5.63^{Bbc}	-	-	-	-
300	29.91 ± 5.75^{Ab}	21.64 ± 4.57^{Ab}	-	-	-	-
360	28.36 ± 5.35^{Ab}	24.73 ± 5.22^{Abc}	55.54 ± 16.74^{Aa}	24.75 ± 10.03^{Aa}	0.03 ± 0.18^{Aa}	-0.53 ± 0.15^{Ba}

Data are presented as mean ± SEM, n=13. Means with different lowercase letters (a-d: time effects) at the same treatment are significant different ($P<0.05$). Means with different uppercase letters at the same day (A-B: treatment effects) are significant different ($P<0.05$) compared to the control.

Table B (Continued)

Time (min)	IL-6 (pg/mL)		TNF-α (pg/mL)	
	Control	Riceberry	Control	Riceberry
0	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}	0.00 ± 0.00^{Aa}
180	0.50 ± 0.10^{Aa}	0.11 ± 0.14^{Ba}	-0.83 ± 0.43^{Aa}	-1.43 ± 0.39^{Aa}
360	0.55 ± 0.11^{Aa}	0.08 ± 0.15^{Ba}	0.83 ± 0.38^{Aa}	-1.51 ± 0.40^{Ba}

Data are presented as mean ± SEM, n=13. Means with different lowercase letters (a-d: time effects) at the same treatment are significant different ($P<0.05$). Means with different uppercase letters at the same day (A-B: treatment effects) are significant different ($P<0.05$) compared to the control.

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