Nutraceutical properties of unripe banana flour resistant starch: A review

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ABSTRACT

The present review provides a comprehensive discussion of the prebiotic, anti-diabetic, anti-colorectal cancer, and anti-cardiovascular disease effects of unripe banana flour resistant starch (BFRS). Unripe banana flour is considered a useful ingredient in the food industry due to its high resistant starch content (up to 68% w/w %). The beneficial effects of BFRS against the non-communicable diseases of diabetes, obesity, cardiovascular disease, and colorectal cancer emanates from its resistance to hydrolysis and escape of upper-gastrointestinal tract digestion, which results in delayed glucose absorption, and colonic fermentation modulation with increased colonic short-chain fatty acids (acetate, propionate, and butyrate) concentrations. Therefore, unripe banana flour resistant starch can be recommended as an alternative functional ingredient in food products. However, more *in vivo* studies with should be conducted to further ascertain the mechanisms underlying its beneficial effects and the associated changes in the microbiome. The influence of other food product ingredients and processes on its efficacy, and targeted production of specific SCFAs in the colon, needs to be researched to optimize its application.

KEYWORDS: Unripe banana flour; Diabetes; Resistant starch; Prebiotics; Obesity; Cardiovascular disease; Non-communicable diseases.

INTRODUCTION

Bananas are the most widely produced tropical fruit [1], accounting for over 50% of tropical fruits produced worldwide [2] and more than 70% of the global trade in horticultural crops. The production of bananas increased from 67 million in 2002 to 114 million in 2017 - 2019 and is projected to increase to 128 million tons in 2028 [2]. Nevertheless, roughly 20% of banana fruits are not marketed due to defects, with a considerable proportion of such fruits disposed of as waste [3]. It suggested that the production of unripe banana flour can reduce the wastage of bananas caused by improper post-harvest handling and thereby extend their shelf life for further usage [4, 5]. Due to its health-promoting properties, unripe banana flour has been used in developing products such as pasta [6-12], bread [13], and cookies/biscuits [14-18]. Unripe banana flour can be used as a raw (uncooked) additive in food products such as ice cream [19], beverages [20-22] and dietary interventions/supplementation [23-25].

Unripe banana flour contains bioactive compounds such as phenolics [26, 27]; flavonoids [15, 26-28]; carotenoids [26, 27, 29]; and phytosterols [30, 31]. Phenolic compounds protect against cancer, while flavonoids provide protective effects against oxidation-derived free radicals and reactive oxygen species (ROS) [32, 33]. Phytosterols (β-sitosterol, campesterol, and stigmasterol) compete with cholesterol for absorption in the small intestine and offer protection against breast, colon, and prostate cancers [33]. Beta-carotene, a vitamin A precursor present in bananas, provides protection against vitamin A deficiency and reduces the risk of diseases such as type II diabetes, cancer, and cardiovascular disease [32]. Resistant starch and the bioactive compounds present in unripe banana flour can modulate metabolic activities to provide protective and preventative effects on non-communicable diseases such as colorectal cancer, cardiovascular diseases, diabetes, and obesity [13, 32-35].

Despite the beneficial health effects derived from unripe banana flour-resistant starch (BFRS), there are limitations in the integration of information regarding its nutraceutical properties. Previous reviews have focused on physico-chemical characteristics and digestibility[36], and beneficial effects of banana-flour-only systems [37], properties, and applications [38, 39]. Hence, this review provides a detailed description of the prebiotic, hypoglycemic, and anti-diabetic effects of unripe banana flour resistant starch.

Prebiotic effects of unripe banana flour

Studies reported on the prebiotic effects of banana flour are summarized in Table 1. The resistant starch present in unripe banana flour and its derived products is classified as a prebiotic because it resists gastrointestinal digestion and facilitates the proliferation of beneficial microbiota growth in the colon [40].

Effect on gut microbiota population

Based on both *in vitro* and *in vivo* studies, unripe BFRS has been shown to have the potential to increase the population of beneficial microbiota in the gut (Table 1). The firmicutes/bacteriodetes (F/B) ratio plays a role in maintaining healthy and normal intestinal homeostasis and has recently been shown to correlate with probiotic effects [41, 42]. It has been suggested that bacteroidetes can improve obesity, glucose homeostasis, and prevent inflammatory-related diseases [43-45]. Rosado, Rosa, Martins, Soares, Almo, Monteiro, Mulder, Moura-Nunes and Daleprane [46] demonstrated that the population of bacteroidetes (22 - 29%) was greater than that of firmicutes (22 - 23%) in the gut of mice on an unripe banana flour-enriched diet. Unripe banana flour has been reported it to modulate the firmicutes/ bacteroidetes (F/B) ratio in the intestines [47] and increase the population of bacteroidetes relative to firmicutes [46, 48]. Unripe banana flour is suggested to produce a higher proportion of bacteroidetes compared to firmicutes due to its resistant starch [46]. The higher levels of bacteroidetes and their associated effects may be related to their higher carbohydrate encoding enzymes compared to firmicutes, which facilitate increased SCFA concentrations [49]. Though BFRS can lead to higher levels of bacteroidetes, firmicutes are still important gut microbiota due to their ability to produce butyrate, whilst bacteroidetes produce acetate and propionate [50-52].

The effect of unripe banana flour on F/B ratio may however be modulated by the BMI (Body Mass Index) status of the individuals. There have been diverse findings reported regarding the relationship between the F/B ratio and obesity [46]. Differences in SCFA profiles between healthy and obese individuals are due to changes in the microbiome of obese individual. The significance of the microbiome to obesity was demonstrated by the fact the obesity can be transferred from healthy individuals from obese individuals by transferring the GIT microbiome of obese individuals [53, 54]. Changes do not only occur at phylum level (F/B ratio); but also occur at genera and species level [55]. Unripe banana flour has been shown to modulate the microbiome by facilitating recovery form dysbiosis by enhancing the proliferation of *Bacteroidaceae*, *Porphyromonadaceae* and, *Lachnospiraceae* genera [56]. Unripe banana flour was also associated with the proliferation of *Verrucomicrobiaceae*, and *Coprococcus-2* in addition to *Lachnospiraceae* [57]. The changes in microbial populations associated with obesity include decreased diversity in microbiota, decreases in *Escherichia coli, Bifidobacterium*, and increases in *methanobacteria smithii*, *Lactobacillus*, and the F/B ratio [58]. These changes are associated with increased energy sequestration from the food by the bacteria and increased transmembrane transport [59], increased cellular deposition of triglycerides by increased uptake of fatty acids by adipose tissues due to a decrease in the activity of the fasting-induced adipose factor [41], in addition to the breakdown of otherwise unavailable carbohydrates [60]. The dysbiosis is has been correlated with the occurrence of disorders in the intestines and the metabolic syndromes

Studies suggest that bacteroidetes are generally more abundant in obese individuals compared to normal BMI individuals [61], while other studies have reported higher number of firmicutes than bacteroidetes in obese individuals [62-67]. Additionally, several other studies have shown that there is no difference in the F/B ratio between obese and non-obese individuals [61, 68-70]. This discrepancy in the reported results probably results from unspecified underlying factors such the presence of other food ingredients/diets [59, 71, 72], and host-specific characteristics such as age [72-75] and life style [75] which are have generally not been taken into consideration in most studies. This is coupled with methodological limitations in most studies, such as insufficient sample sizes (number of individuals studied) given the FB ratio is greatly influenced by died, food additives, physical activity, antibiotics use, and geography [75]. It is also suggested that changes at species, genus, and family level may be more important than the F/B ratio [41]. Other phyla such as *Proteobacteria* probably may also play a modulating or complementary role to the FB ratio, and that the microbiome changes are not limited to the changes in F/B ratio [76, 77]. The role of the characteristics of the unripe banana flour used has not been put into consideration in most studies [37]. However, unripe banana flour-resistant starch content and physicochemical properties can vary significantly even for cultivars grown under the same agronomic conditions [78]. Additionally, the type of resistant starch that results in a given unripe banana flour containing product can affect the SCFAs profile, given different resistant starch types may lead to different SCFA profiles [79, 80]. Therefore, there is need for research to further establish the causes of the discrepancies in the F/B ratio responses to unripe banana flour in obese individuals. This would facilitate better and targeted usage of the prebiotic effect of unripe banana flour.

Unripe banana flour-resistant starch can maintain these beneficial microbiota populations above recommended minimum levels (6 log CFU/ml) [81]. An *in vitro* study by Suryaatmadja Jenie, Saputra and Widaningrum [82] demonstrated that modified unripe banana flour yogurt maintained the viability of *Bifidobacterium bifidum* and *Lactobacillus plantarum* (8.08 - 9.24 log CFU/ml). Similarly, Batista, Silva, Cappato, Ferreira, Nascimento, Schmiele, Esmerino, Balthazar, Silva, Moraes, Pimentel, Freitas, Raices, Silva and Cruz [83] found that unripe banana flour in fermented milk maintained the viability of *Streptococcus thermophilus, Lactobacillus acidophilus,* and *Bifidobacterium lactis* at 7.02 - 8.78 log CFU/ml.

Lactobacillus, Bifidobacterium, and Streptococcus thermophilus are vital microbes in the gut because they lead to increased acetate, propionate, and butyrate levels [48, 84-87]. *Lactobacillus plantarum BSL* has been suggested to reduce liver damage by producing cytokines and antagonistic compounds, reducing the secretion of pro-inflammatory interleukin and protecting against pathogens [88, 89]. *Bifidobacterium* may contribute to the maintenance of gastrointestinal health, enhancement of barrier function, and immunomodulation [90, 91]. Furthermore, *S. thermophilus* prevents inflammatory bowel disease through increased production of anti-inflammatory (IL-4, IL-5, IL-10) cytokines and reduced secretion of pro-inflammatory IL-1β and IFN-γ [92]. *Lactobacillus acidophilus* creates a conducive environment for developing of *Akkermanisa muciniphila* (an organism that increases intestinal mucin thickness and attenuates gut leakages) [93]. Therefore, it maybe concluded that unripe banana flour and its resistant starch can be applied as a prebiotic from maintaining beneficial bacteria populations at optimal levels.

Effect on short-chain fatty acids (SCFAs) production

There is a dose-response effect of unripe banana flour-resistant starch on the concentrations of SCFAs [94-96]. High RS diets are suggested to result in higher levels of butyrate and other SCFAs compared to low RS diets due to enhanced colonic fermentation [94, 96]. However, the reported proportions of acetate, propionate, and butyrate with consumption of unripe banana flour have varied between studies (Table 1). A global average of the glucose concentrations reported from the different studies (Table 1, only studies result with blood concentrations used), indicated that the average concentrations were 32.3, 12.1 and 10.4 mmol/L for acetate, propionate and butyrate, respectively. This is in agreement with reports that indicated that acetate accounts for 50 – 70% of all SCFAs and reaches systematic circulation in significant amounts as it has a negligible effect on colonocytes compared to other propionate and butyrate [96-99]. Acetate is important as it supplies energy to the muscles and expedites the rate at which glucose is drawn from the portal blood through the reduction of free fatty acids due to its non-insulinogenic nature [97].

The effect of unripe banana flour on SCFA has also been shown to lead to higher relative proportions on propionate compared to acetate and butyrate in some studies [21, 100]. Propionate suppresses total cholesterol by reducing the synthesis of cholesterol production enzymes and increasing the synthesis of bile salts to improve the removal of cholesterol [101, 102]. It also reduces circulating insulin and curtails hepatic triglyceride levels and glucose homeostasis [103]. Hence, an unripe banana flour-containing diet can modulate the propionate levels and provide the associated benefits.

Although there is an increase in the butyrate concentration on the consumption of a diet with unripe banana flour, the amounts reported, relative to acetate and propionate have varied (Table 1). Some studies have demonstrated a relatively higher increase in the concentration of butyrate relative to acetate and propionate, on the consumption of an unripe banana flour-containing diet [25], while others have reported lower amounts [95]. The possible explanation is that butyrate tends to be in lower concentrations compared to other SCFAs because most of the absorbed butyrate is metabolized by colonic epithelium [104, 105]. Butyrate is important due to its role in the maintenance of a healthy colon and the prevention of colorectal cancer [24, 99, 100, 106]. Butyrate plays a significant role in colon epithelial health through enhanced cell proliferation and reduced paracellular permeability [104, 105, 107, 108]. Delivery of adequate amounts of butyrate to appropriate sites, protects against early tumorigenic events [109]. The contribution to the prevention of colorectal cancer is through improved differentiation of cancer cells and reduction of tumor growth [96, 110-112]. It is a more effective anti-colorectal cancer agent than acetate and propionate due to the cell cycle arrest and apoptosis mechanisms it sets off [113].

Variations in the relative concentrations of various SCFAs could be attributed to the source of unripe BFRS and the health and lifestyle conditions of the subjects [75, 99]. The type of banana resistant starch between R1 to R5, can influence the type of SCFA that dominates, for example acetate was shown to be produced more by R2, while propionate resulted most when R3 was used [99]. Despite variations in the relative increases in the concentration of SCFAs, RS found in unripe banana flour can be classified as a prebiotic as it is fermented selectively and leads to specific changes in gastrointestinal microbiota activity/composition leading to the host obtaining benefits from it [48, 89, 94, 95, 100, 114, 115]. However, although unripe banana flour leads to an increase in SCFAs, the mechanisms underlying the variations in their relative proportions need to be further elucidated. This will facilitate the application of unripe banana flour under particular conditions, for example, enhanced butyrate proportions for colorectal cancer alleviation.

Hypoglycemic effects of unripe banana flour

Unripe banana flour has been demonstrated to have *in vitro* (Table 2) and *in vivo* (Table 3) hypoglycemic effects. Increased digesta bulk reduces the time required for hydrolysis by facilitating faster movement of material through the gastrointestinal tract [96, 116-121]. Furthermore, the unripe banana flour induces a reduction in the rate of gastric emptying[122] and resists hydrolysis due to granular and molecular level mechanisms in addition to presence of other non-starch carbohydrates, as summarized by Zhang and Hamaker [123]. These mechanisms lead to a reduced rate of postprandial glucose release, hence a lower insulin requirement, and beneficial colonic fermentation of upper-GIT-escaped starch.

In vitro studies

In vitro studies have involved the assessment of glycemic (GI) and hydrolysis (HI) indices. The GI measures the rate at which starchy foods are converted to glucose after consumption and is categorized into low (<55%), medium (56 – 69%), and high (≥70%) [124]. The hydrolysis index is the percentage of glucose released from food samples compared to the amount of glucose released from a standard sample (e.g. white bread) in 180 min [125]. The HI is obtained by dividing the area under the hydrolysis curve of a given sample relative to the corresponding area of a reference sample [126, 127].

Several in vitro studies on different unripe banana flour containing products have been carried out (Table 2). An increase in resistant starch content, decrease in hydrolysis index and GI, relative to control samples was reported in products such as cookies [14, 16], pasta [7, 128-130], spaghetti [130, 131], deep-fried snacks [132], Tortillas [133] and bread [13] (Table 2). The *in vitro* studies done so far have mainly involved addition levels ≤50% addition (Table 2), probably due to product failure at higher levels of addition resulting from lack of appropriate hydrocolloidal properties (absence of gluten) compared to wheat flour. It is evident from the studies (Table 2) that the incorporation of unripe banana flour into food products leads to low GI and HI levels. The efficacy of the unripe banana flour was demonstrated by relatively small amounts of resistant starch such as 2.84[7] and 3.15% w/w [130] leading to substantially low HIs of 50 and 55%, respectively. Even a small amount of resistant starch is reported to be sufficient in attenuating postprandial hyperglycemia [134].

In the reported studies (Table 2), it was also notable that some products developed such as cookies and bread, involved heat treatment, which would ideally disrupt the intragranular crystallinity by gelatinization, thereby reducing native crystallinity-based resistance to enzymatic hydrolysis. This implied greater significance of starch-molecular-level mechanisms such as retrogradation and amylopectin structural properties [123]; and amylose-lipid complexation [135] compared to granule level mechanisms.

The amount of resistant starch induced by the presence of unripe banana flour depended on the type of product and processing conditions, given the resistant starch in the products at 50% unripe banana flour addition (Table 2) showed values that increased from 3.27% [132], to 8.5% [14], 19.09 [131] and to 23.3% [128] in the different studies, some of which had the same product type (Table 2). A similar trend was also observed for the hydrolysis index, whose values ranged from 40%-90% with an average value of 58%, and the GI index whose values ranged between 57-115% with an average of 75% (Table 2). The differences probably resulted from different molecular level and granular level modifications of the starch during the processing of the products, which leads to different levels of susceptibility to hydrolysis. The type of resistant starch in a given food significantly affects the extent to which postprandial hyperglycemia is suppressed [136]. It is therefore essential that the effect of processing conditions and unripe banana flour characteristics are assessed for specific products to optimize the hypoglycemic effects of added unripe banana flour.

In vivo (animal and human) studies

In vivo studies have demonstrated in both animal and human subjects, that the incorporation of unripe banana flour in foods leads to reduced GI and postprandial glucose (Tables 3). Low GI foods control postprandial glucose peaks by inducing prolonged glucose absorption, which leads to the suppression of postprandial hyperglycemia, reduced free fatty acid synthesis, and lower counter-regulatory responses caused by abrupt swings in blood glucose [137, 138]. The inhibition of free fatty acid synthesis enables quicker removal of glucose from blood circulation and maintains glucose above baseline levels [138, 139]. Furthermore, reduced postprandial hyperglycemia enables the accommodation of the less-than-optimum insulin responses that are enlisted in diabetics [140].

Studies reported have shown *in vivo*, that the incorporation of unripe banana flour leads to a low GI (<55%) (Table 3). However, postprandial glucose results, relative to control samples, have apparently shown some discrepancies in studies involving rats, albeit with most decreasing with the presence of unripe banana flour in the diet (Table 3). The desirable/normal postprandial glucose levels for rats ranges between 80 - 150 mg/dl, with 200 - 250 mg/dl being considered a prediabetic phase [141]. Rats with glucose levels above 250 mg/dl are considered to be diabetic. Studies by Silva, Cerdeira, Brito, Salles, Ravazi, Moraes, Rufino, Oliveira and Santos [10], Ademosun, Odanye and Oboh [142] showed significant decreases in postprandial glucose with unripe banana flour incorporated feed compared with controls (without banana flour) in diabetic rats. However, for normal non-diabetic rats, the effect of unripe banana flour addition has been reported to be less pronounced relative to control samples [143, 144]. These results suggest that the postprandial hypoglycemic effect of unripe banana flour is more pronounced in individuals with diabetes compared to non-diabetic individuals.

Woerle and Gerich [145] stated that blood glucose in humans should not exceed 160 mg/dl, with 200 mg/dl being considered the threshold. Several studies have shown that the presence of unripe banana flour in the diet leads to postprandial glucose levels within the desirable range relative to control samples without unripe banana flour (Table 3). The reduced postprandial hyperglycemia results in reduced insulin secretion upon the incorporation of unripe banana flour relative to control samples in both rats [144, 146] and humans [22]. It has been concluded that unripe banana flour modulation of postprandial glucose peaks leads to lower insulin secretion and improves insulin sensitivity and glucose tolerance [22, 147, 148].

A comparison of the different *in vivo* studies showed a dose-dependent response for both the *in vivo* glycemic index and postprandial glucose (Table 3). A plot of the maximum and minimum glycemic index (Figure 1a) and postprandial glucose (Figure 1b) from the different studies showed a clear dose-response effect (Figures 1a and b respectively). However, the dose-dependent response changes to become less pronounced at higher levels of unripe banana flour addition beyond 60% addition (Figures 1 a and b). It followed a second order polynomial equation with R^2 values of 0.52 and 0.57 (Figures 1a and b). It is hence recommended that banana flour may be added only up to 60% in different products, beyond which the additional *in vivo* effect is less pronounced.

Obesity

Unripe Banana Flour-Resistant Starch (BFRS) and Satiety

Several studies have shown a positive effect of unripe banana flour consumption on obesity. Escobar, Rocha-Gomes, Reis, Herrera, Guedes, Silva, Lessa, Dessimoni-Pinto and Riul [149] reported that unripe banana flour can be used for weight control. They found, like Rech, Freygang and de Azevedo [150], that male Wistar rats on <20% of BFRS diet had higher weight losses compared to those on the control and commercial resistant starch diets. Similarly, Alvarado-Jasso, Camacho-Díaz, Arenas Ocampo, Jiménez-Ferrer, Mora-Escobedo and Osorio-Díaz [25] showed that *ad libitum* supplementation of a high-fat diet with agavins and banana flour (62%) significantly reduced the body weight of mice. Hoffmann Sardá, Giuntini, Gomez, Lui, Negrini, Tadini, Lajolo and Menezes [22] demonstrated that daily energy intake by healthy volunteers was reduced by 7.27 and 14% after the consumption of unripe banana flour-containing food, with no changes observed in the daily energy intake for healthy volunteers who consumed the control diet. Unripe banana flour and its food products were suggested to modulate obesity, by improving satiety and reducing hunger [147].

However, optimum levels of unripe banana flour probably have to be found for each application given at higher levels of unripe banana flour addition an increase in triglycerides was observed in rats [149].

A recent study observed that the anti-obesity properties of unripe BFRS are associated with the regulation of gut microbiota [47]. Unripe banana flour reduced the relative abundance of *Romboutsia* and *Oligella* (positively correlated with glucolipid metabolism, total cholesterol, and triacylglycerol) and increased the relative abundance of bacteroidetes in the gut of obese rats [47]. Furthermore, unripe BFRS was reported to increase the relative abundance of gram-positive bacteria such as *Lactobacillus* and *Lactobacillus acidophilus*, and *Lactobacillus plantarum* [82, 83, 89]. *Lactobacillus plantarum* HAC01 contributes to obesity reduction by interacting with other microbes to regulate the expression of a gene that is related to lipid metabolism [151]. *L. plantarum FRT10* alleviates obesity by decreasing the F/B ratio, activation of the PPARα/CPT1α pathway, and regulating TG-synthesizing enzymes in the liver [152]. It has also been suggested that *L. plantarum LMT1-48* inhibits fat through the regulation of lipogenic genes and the production of SCFAs in HFD-induced mice [153]. The effects of *L. plantarum* on obesity were strain-specific and therefore warrant further research. The proliferation of *L. acidophilus* that results from the consumption of unripe banana flour reduces the accumulation of fat through a gut dysbiosis mechanism (*Akkermanisa muciniphila*) and a lowered F/B ratio [93, 154].

Unripe banana flour enhancement of SCFAs production has been suggested to contribute to obesity reduction [155]. Butyrate (SCFAs) is hypothesized to play a role in the reduction of obesity by activating G-protein coupled receptors and enhancing the secretion of satiety hormones [156]. It has been proposed that changes in blood glucose concentration increase satiety by stimulating the 'satiety center' in the ventromedial hypothalamus (VMH) and inhibiting the feeding center (glucostatic mechanism) [157]. Gut hormones (cholecystokinin, glucagon-like-peptide-1, oxyntomodulin, peptide YY, and pancreatic polypeptide) transmit satiety hormones to the brain and causes ghrelin to delay hunger [157, 158]. Propionate has also been hypothesized to lead to increased satiety and reduced gastric emptying through its influence on free fatty acid receptor which leads to increased secretion of PYY and GLP1 [159].

Unripe Banana Flour and Lipoproteins

Cholesterol exists as low-density lipoprotein (LDL-c) and high-density lipoprotein (HDL-c). Low-density protein causes a build of cholesterol in the arteries. However, high-density lipoprotein, rich in protein is desirable because it contributes to the removal of cholesterol from the bloodstream and its transport to the liver. Rech, Freygang and de Azevedo [150] reported that HDL-c (high-density lipoprotein) levels (53.40 mg/dl) were three times higher than LDL-c (low-density lipoprotein) levels (15.88 mg/dl) on consuming a diet with unripe banana flour. Similar results were demonstrated by Escobar, Rocha-Gomes, Reis, Herrera, Guedes, Silva, Lessa, Dessimoni-Pinto and Riul [149], Agustin, Febriyatna, Damayati, Hermawan, Faiziah, Santoso and Wulandari [23], and dos Santos Bueno, Guiguer, dos Santos Bueno and de Souza [160]. This result demonstrated that unripe banana flour favors the development of high-density lipoprotein, hence the removal of cholesterol from the bloodstream and therefore can be recommended for preventing of cardiovascular diseases.

Conclusion

Unripe banana flour-resistant starch is a promising functional ingredient as it enhances the anti-diabetic, prebiotic, anti-cardiovascular disease, and anti-obesity properties of food products. The mechanism of unripe banana flour's beneficial effects is associated with its starch resistance to enzymatic hydrolysis, thereby by-passing intestinal digestion (Figure 2). The by-passed starch leads to the proliferation of beneficial microbiota which increases the production of SCFAs (acetate, propionate, and butyrate). Although these beneficial effects have been demonstrated through in vivo studies in both animal and human models, more research must determine the relative importance of the different mechanisms (molecular, supramolecular, granular, and food matrix levels) through which unripe banana flour induces these desirable effects. The role in influencing the F/B ratio and the entire GIT microbiome and the relative influences between obese and normal BMI individuals need to be assessed. An elucidation of the difference in responses between diabetics and non-diabetes should be done to further unravel the mechanisms by which unripe banana flour imparts its nutraceutical properties. The influence of processing conditions and ingredients on the resultant microbiome needs to be determined, in addition to the influence of the unripe banana flour characteristics at molecular, supra-molecular and granular level on the resultant microbiome and SCFAs. These studies will facilitate the application of unripe banana flour to target specific ailments such as diabetes, obesity, hypercholesteremia, and irritable bowel syndrome among others. Results from these studies will contribute for increased utilization of unripe banana flour thereby enhancing human health in general.

AUTHORSHIP CONTRIBUTION STATEMENT

Siphosethu Dibakoane: Literature Review, Writing – review & editing. **Tonna Anyasi:** Supervision, Writing –review & editing. **Belinda Du Plessis:** Writing – review & editing. **Laura Suzzanne Da Silva:** Writing – review & editing. **Mohammad Emmambux**: Writing – review & editing**. Victor Mlambo:** Supervision, Writing – review & editing. **Obiro Cuthbert Wokadala:** Conceptualization, Supervision, Writing – review & editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

Table 1. Effect of Banana Flour Resistant Starch (BFRS) on the Microbiota Population and Production of Short Chain Fatty Acids (SCFA)

Sample/Experiment formulation	Percentage of unripe banana flour	Subject details	Duration	Microbiota population	Acetate	Propionate	Butyrate	References
Feces enriched with banana powder	1	6 donors, Age (24 – 28 years). Body Mass Index (BMI) (18.5 - 25	2 days	*Bacteroidetes* (37.71 - 43.38). *Bacteriodetes* (26.31 - 31.26). *Firmicutes* (34.65 - 37.71)	1.67 – 22.76 mmol/L	0.56 – 6.94 mmol/L	0.61 – 3.33 mmol/L	[48]

		kg/m^2)						
Banana flour in fermented milk	5 - 10			*Streptococcus thermophilus* (8.53 - 8.78 log CFU/mL). *Lactobacillus acidophilus* (8.77 - 7.14 log CFU/mL). *Bifidobacterium lactis* (7.34 - 7.02 log CFU/mL)	15.43 – 16.48 mmol/L	29.69 – 33.97 mmol/L	7.27 – 9.88 mmol/L	[83]
Unripe peeled and unpeeled powder	100		48 h	*Lactobacillus* (9.3 - 9.7 CFU/ml). *Escherichia coli (E. coli)* (0.9 - 1.1 CFU/ml). *Salmonella*				[89]

				typhi (1.0 - 1.05 CFU/ml)				
Modified unripe banana flour yogurt	40 -70		4 weeks	*Bifidobacterium bifidum* (8.08 - 9.24 CFU/ml). *Lactobacillus plantarum* BSL. (8.06 - 9.21 CFU/ml)				[82]
Low and high RS diet with wheat seed, cornbread, and banana flour	11.2	11 volunteers, 5 males, and 6 females, Age (22 - 54), BMI (17.9 - 31.5	8 weeks	-	79 - 99.5 mmol/L	18.0 - 20.5 mmol/L	19.0 - 26.2 mmol/L	[96]

		kg/m^2)						
Low and high RS diet	3.1 – 51.6	8 participants, 2 males, and 6 females Age (32.9), BMI (18.9 - 24.9 kg/m^2)	-	-	0.12 – 0.17 mmol/L	0.023 – 0.31 mmol/L	0.036 – 0.056 mmol/L	[94]
Low and high RS diet	11.3 – 14.4	Six subjects, 1 male and 5 females Age (39 - 59)	7 days		44.1 mmol/L	11.8 mmol/L	11.1 mmol/L	[95]
A high-fat diet with agavins and banana	-	6 male mice, Age (5	-	-	17 mmol/L	1 mmol/L	0.5 mmol/L	[25]

flour		weeks)						
Banana flour enriched banana diet	5 – 10	28 Male Wistar rats, Age (3 weeks)	36 days		6.94 mmol /L	5.83 – 6.16 mmol/L	2.76 – 3.38 mmol /L	[24]
Raw banana flour diet Cooked banana flour diet	4.1 – 54.2	10 participants, (5 men and 5 women) Age (28 - 70), Weight (19 - 35 kg/m^2)	-	-	62.3 mmol /L 54 mmol /L	17 mmol/L 18.3 mmol/L	34.8 mmol /L 27 mmol /L	[98]
Banana flour enriched diet	15	Mice	4 weeks	*Firmicutes* (-22-(-23%) *Bacteroidetes* (22- 29%)				[46]

Standard and high-fat diet enriched with banana flour	15	6 male mice, Age (3 months)	14 weeks		0.2 - 22.4 µmol/g	3.8 - 5.0 µmol/g	4.1 - 4.7 µmol/g	[114]
Unripe banana flour in cocoa beverage	65	60 obese females, Age (20 - 50) Weight (25 - 35 kg/m2)	6 weeks		6.76 µmol/g	7.15 umol/g	4.88 umol/g	[21]
Green banana flour resistant starch	4	Mice, Age (7 months) Weight (19 g)			9 – 60 µg/g	10 – 61 µg/g	5 – 17 µg/g	[100]
Diet supplemented with RS enriched biscuits	30.86	12 participants, aged (22- 43) BMI (18.6-	15-day interval	-	59.4 %	15.0%	16%	[99]

	28.4)				
Unripe banana starch and mass flour	100	57.4 - 68.3	14.4 - 23.0	17.3 - 19.6	[40]

Table 2. *In vitro* hypoglycemic effects of banana flour resistant starch

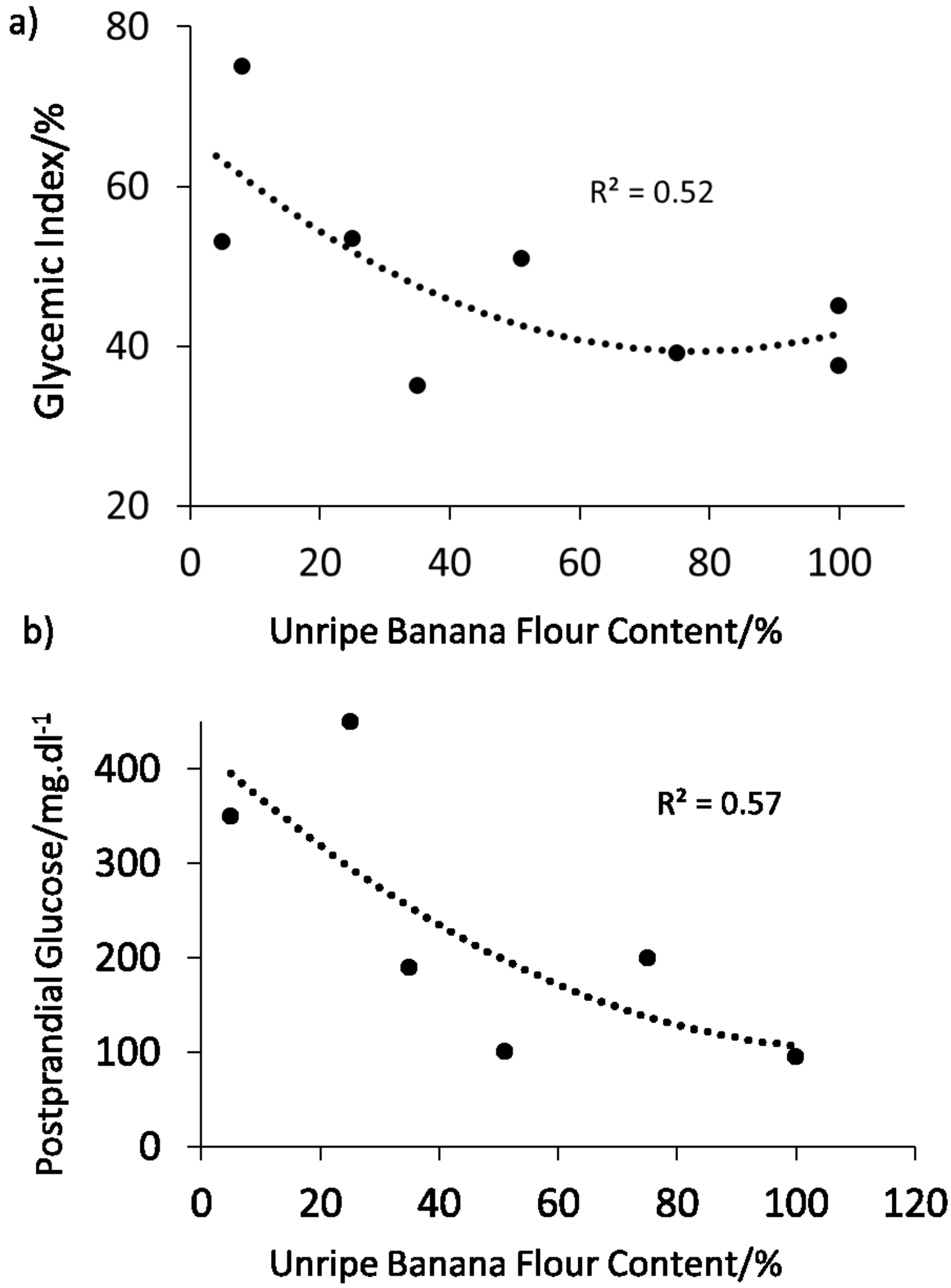
% Banana flour	Products	Resistant Starch (%)	Hydrolysis Index (%)	Glycemic Index (%)	Reference
15 - 50	Cookies	3.1 - 8.37	61 – 90	98.6 - 115.2	[14]
15	Cookies	8.42	60.71	60.53	[16]
10 - 50	Noodles	9.54 - 23.31	41.72 - 60.15	62.61 - 72.73	[128]
15 - 45	Spaghetti	2.84 - 12.42	32 – 55	-	[7]
30 and ß- glucan	Noodles	12.3 – 14.4	59.5 - 65	31 – 39.7	[129]
15- 100	Spaghetti	3.15 – 6.95	40 – 50	70.00 – 76.9	[130]
50	Spaghetti	12.27- 19.09	23 – 35		[131]
38	Bread	6.7	65.1	64.3	[13]
10-50+ corn peak and maize flour	Snacks	1.92 - 3.27	23.32 - 31.17	28.30 - 35.07	[132]
60 corn flour: 40 banana flour	Tortilla	26.0 - 29.0	60 – 80	96.46 - 106.31	[133]

Table 3. *In vivo* hypoglycemic effect of banana flour resistant starch

Diet formulation	Percentage of unripe banana flour (%)	Subject/age/weight or body mass index (BMI)	Glycemic index (GI) (%)	Postprandial Glucose	Reference
Cookies	25 - 75	Male Wistar rats, Age (8 - 12 weeks). Weight (200 g) -	39.15 – 53.43		[18]
Green (unripe) banana pasta	25 - 75	60 male Wistar rats, Age (6-8 weeks). Weight (180 - 300 g),		200 - 450 mg/dl	[10]
Orange peel flavored unripe plantain noodles	5 - 35	Diabetic rats	35.03 - 53.09	190 - 350 mg/dl	[142]
Plantain, tiger nut, and soybean flour	51.07 - 100	40 white albino rats, Weight (180 - 200 g)	45 – 51	95 - 101 mg/dl	[143]

meals					
Raw banana powder	0.2 – 0.6	50 Sprague-Dawley male rats. Age (4 weeks).		144 – 180 mg/dl	[144]
Plantain, soy cake, and cassava flour dough meals	8- 100	60 Male Wistar rats, 5 weeks Age (4 weeks)	37.5 – 75	55 - 70%	[146]
Banana fruit and peel powder	5 – 10	36 adult male rats, 4 weeks		150.34 - 155.57 mg/dl	[161]
Unripe banana flour supplemented diet	80	22 human volunteers, Age = (27.6), BMI (22.8 kg/m^2)		87.3 mg/dl	[22]

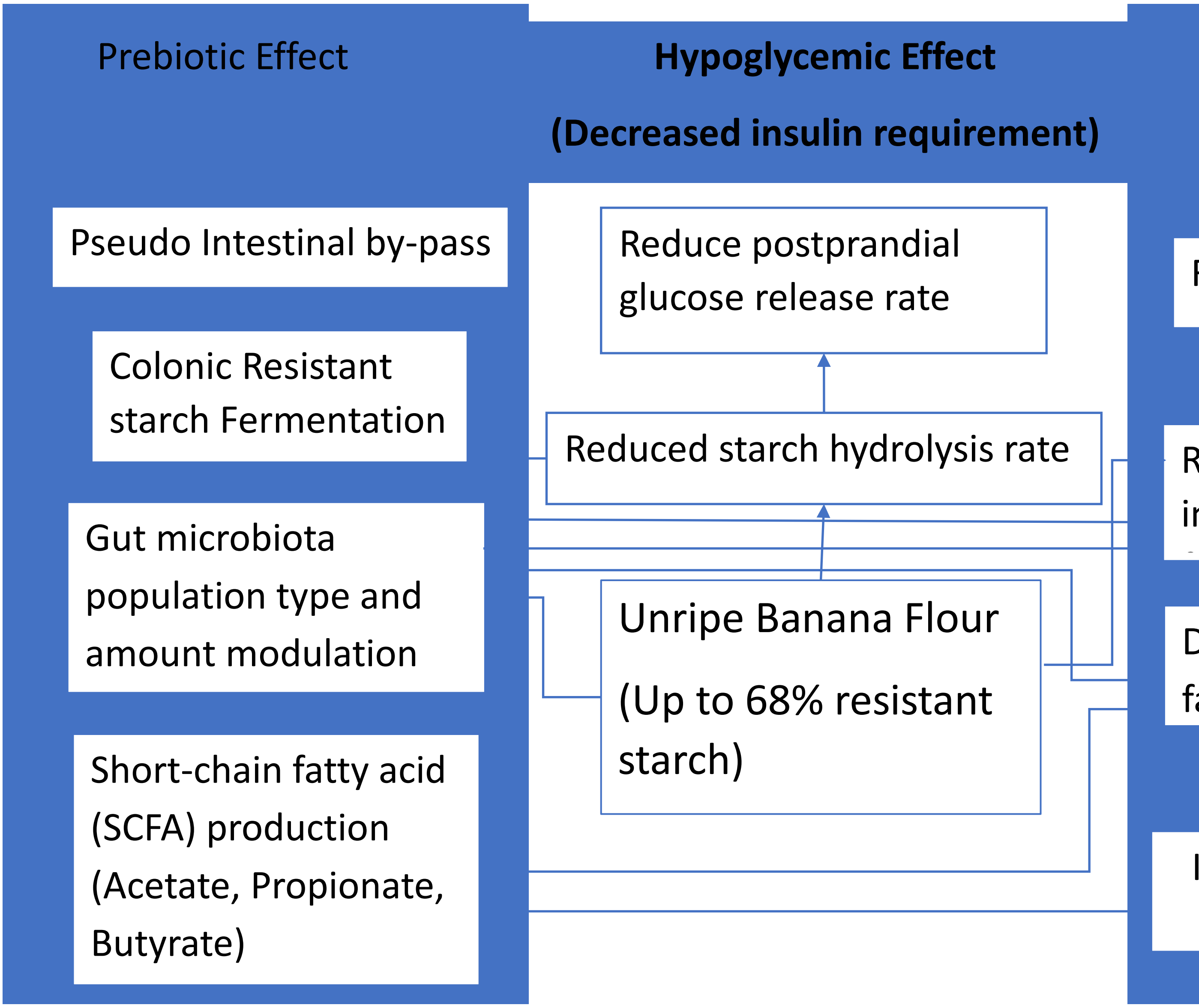
Figure 1. *In vivo* hypoglycemic effect of unripe banana flour showing changes in glycemic index and postprandial glucose with unripe banana flour-containing food consumption



Value plotted were obtained from literature as attached in table 2.

The minimum and maximum values of unripe banana flour content and their corresponding dependent variable s (a and b) were plotted.

Figure 2. Prebiotic, hypoglycemic, and anti-obesity mechanisms of unripe banana flour



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Unripe banana flour nutraceutical effects resulting from starch resistance to enzymatic hydrolysis in the upper gastro-intestinal tract leading to reduced rate of postprandial glucose release hence a lower insulin requirement, and bypass of starch into the colon thereby modulating colonic bacterial populations leading to higher production of short-chain fatty acids.

Figure 2. Prebiotic, hypoglycemic, and anti-obesity mechanisms of unripe banana flour