




# The Effect of Gembili Tuber (*Dioscorea esculenta* L.) Analog Rice on Body Weight Changes, Lactic Acid Bacteria Profile, Short Chain Fatty Acid Levels, and Fasting Blood Glucose Levels in Rats Model of Type 2 Diabetes Mellitus

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**Abstract:** Type 2 Diabetes Mellitus (T2DM) is characterized by insulin resistance and elevated blood glucose levels. This study aims to investigate the effects of gembili tuber analog rice (GTAR) on body weight, lactic acid bacteria (LAB) profile, short-chain fatty acids (SCFA) levels, and fasting blood glucose in a T2DM rat model. Male Albino Wistar rats were assigned to four groups: normal control (NG), diabetic control (DG), GTAR1 (4.16 g/rat/day dose), and GTAR2 treatment (6.17 g/rat/day dose). The interventions lasted for 14 days. Data analysis included appropriate statistical tests. GTAR dosage and duration significantly influenced body weight, SCFA levels, and fasting blood glucose levels in the T2DM rat model. Moreover, the LAB profile in the GTAR1 and GTAR2 groups exceeded that of the NG and DG groups. Further investigation is necessary to determine the specific soluble fiber responsible for the observed blood glucose reduction in rats. The findings indicate the potential of GTAR as an alternative therapy or dietary substitute for staple rice in managing T2DM. These findings contribute to the growing body of evidence on dietary interventions for T2DM management.

**Keywords:** fasting blood glucose; gembili tuber analog rice; lactic acid bacteria; short chain fatty acids; type 2 diabetes mellitus.

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## 1. Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterized by decreased insulin sensitivity, leading to reduced insulin production and impaired glucose transport to the liver, muscle cells, and fat cells, resulting in elevated blood glucose levels (hyperglycemia) [1]. Type 2 diabetes, which makes up the bulk of diabetes cases, is largely preventable and, in some cases, potentially reversible if identified and managed early in the disease course. However, all

evidence indicates that diabetes prevalence is increasing worldwide [2]. The International Diabetes Federation (IDF) reported that the global number of diabetes mellitus cases among individuals aged 20 to 79 years reached 463 million in 2019, and it is projected to increase to 537 million in 2021, with an estimated increase of 46% by 2045 [3,4]. The International Diabetes Federation also stated that 90% of diabetes cases worldwide are T2DM. Indonesia, in particular, ranks 9th with the largest number of diabetes cases, exceeding 10 million people, and this number continues to rise each year [3]. The Consensus of the Indonesian Endocrinology Association (Perkeni) in 2011 showed that the prevalence of Diabetes Mellitus among individuals aged over 15 years increased by 2% from 2013 to 2018 [5].

Type 2 Diabetes Mellitus patients are more susceptible to complications such as macrovascular diseases (hypertension, hyperlipidemia, heart attacks, coronary artery disease, stroke, cerebral and peripheral vascular diseases), microvascular diseases (retinopathy, nephropathy, and neuropathy), and cancer [6]. These accompanying complications not only impact the quality of life of individuals with diabetes but also increase the healthcare costs borne by the patients and healthcare departments. This theory is supported by research presented by the American Diabetes Association (ADA), stating that the estimated total cost of managing diabetes increased by 26%, from \$245 billion in 2012 to \$327 billion in 2017 [7]. Therefore, appropriate intervention management for individuals with diabetes is crucial for preventing complications that negatively affect quality of life and result in increased healthcare costs. Inadequate diagnosis and treatment of diabetes are likely to be major contributors to these early deaths, highlighting the urgent need to provide better access to insulin and basic diabetes education and care [8].

One pharmacological therapy that can be given to patients with T2DM is the use of Dipeptidyl Peptidase-4 (DPP-4) inhibitors. Sitagliptin is an antidiabetic medication that can be used by T2DM patients with low insulin secretion capacity [6]. Based on a study [9], treatment with sitagliptin had mild to moderate side effects, such as a potential increased risk of pancreatitis and pancreatic cancer, which led some T2DM patients to discontinue the treatment. Therefore, there is a need for non-pharmacological alternative therapies for T2DM to prevent these side effects. Dietary management, including consuming various high-fiber foods, is a recommended dietary intervention for individuals with diabetes [10]. Based on the American Diet Association's recommendation of consuming 24 grams of fiber per day (8 grams of soluble fiber and 16 grams of insoluble fiber) can reduce plasma glucose levels by up to 10%, insulin concentration by up to 12%, and plasma cholesterol and triglyceride levels by up to 12% in T2DM patients. The gembili tuber has high fiber content, with 1.1 g/100g, which is five times higher than rice (0.2 g/100g) [11], and it increases to 10.8 g/100g after being processed into analog rice products [12]. The high dietary fiber content in gembili tuber analog rice has great potential to be used as an alternative therapy for T2DM, offering a viable option to substitute or replace traditional staple rice. The administration of insulin, which is a soluble fiber derived from *Dioscorea esculenta* tuber, at a dose of 180mg per rat per day for 14 days, had hypoglycemic properties and reduced creatinine and urea levels in streptozotocin-induced diabetic rats compared to the control group [13].

Short-chain fatty acids are derived from the fermentation of dietary fiber and resistant starch in the gut. They modulate several metabolic pathways and are involved in obesity, insulin resistance, and T2DM [14]. Soluble fiber and insoluble fiber are almost entirely metabolized by colonic bacteria [15]. Review studies have shown that high fiber consumption can increase gut microbiota such as fecal *Bifidobacterium* sp. and *Lactobacillus* sp., further

increasing SCFAs such as lactate, acetate, propionate, and butyrate, which help stabilize blood glucose by increasing insulin levels through the Glucagon-Like Peptide-1 (GLP-1) hormone [16-18]. Based on the study [19], T2DM patients with fiber intake  $\geq 10$  g/day for 8 weeks had lower insulin reductions compared to those with fiber intake  $< 10$  g/day. Other studies have shown that increased SCFA levels can reduce 2-hour postprandial blood glucose levels, total cholesterol, and LDL and slow gastric emptying, resulting in a longer-lasting feeling of fullness [20].

Based on the study by Kisnawaty *et al.* [21], there was a significant increase ( $p < 0.001$ ) in the levels of High-Density Lipoprotein (HDL) in T2DM rats with the treatment of providing gembili tuber analog rice diet at 4.16 g/rat/day (increased by 32.09 mg/dL) and 6.17 g/rat/day (increased by 44.36 mg/dL). When transformed into analog rice, the increase in the dietary fiber content of gembili tuber has the potential to be a treatment diet for individuals with diabetes mellitus (DM). Therefore, this *in vivo* study was conducted to prove the hypoglycemic properties of gembili tuber analog rice through the enhancement of lactic acid bacteria (LAB) and short-chain fatty acids (SCFA) profiles in DMT2 rats.

## 2. Materials and Methods

This research was classified as laboratory experimental research. The process of producing gembili tuber analog rice was conducted in the Food Technology Laboratory of Muhammadiyah Surakarta University. The experimental animal testing and examination of lactic acid bacteria profiles, blood glucose levels, and rats' weight were carried out in the Food and Nutrition Center Laboratory, Gadjah Mada University, Yogyakarta, Indonesia. This study has obtained ethical approval from the Health Research Ethics Commission of the Medicine Faculty, Muhammadiyah University of Surakarta, with the code 4247/A.2/KEPK-FKUMS/IV/2022.

### 2.1. Material and dosage information.

The gembili tuber was obtained from Boyolali Regency. The process of making gembili tuber flour and gembili tuber analog rice refers to Wardani *et al.* [12]. Based on the research, the production of gembili tuber analog rice with a drying temperature of 70°C has higher dietary fiber content and antioxidant activity compared to heating temperatures of 80° and 90°C. In this study, a drying temperature of 70°C is used to obtain gembili tuber analog rice with higher dietary fiber content and antioxidant activity [12].

### 2.2. Examination of soluble fiber, insoluble fiber, and resistant starch.

The samples examined were gembili tuber flour and gembili tuber analog rice. The method of examination for soluble fiber content, insoluble fiber content, and resistant starch used a multi-enzyme method based on AOAC (1990) [22]. Each sample was examined twice.

### 2.3. Animals and experimental design.

The research samples were male Albino Wistar rats weighing between 150-200 grams, aged 8 weeks, physically active, and without any anatomical abnormalities. The treatment of rats in this study was the same as that in the study by Kisnawaty *et al.* [21]. Each treatment group consisted of 7 rats, resulting in a total of 28 samples across the 4 treatment groups. All groups were given standard laboratory feed (comfeed) and had *ad libitum* access to drinking

water. After a 7-day adaptation period, all rats received a single injection of nicotinamide adenine dinucleotide (NAD) at a dose of 230 mg/kg body weight and streptozotocin (STZ) at a dose of 65 mg/kg body weight. After 3 days, blood glucose levels exceeding 150 mg/dL indicated the onset of hyperglycemia [23]. The rats were divided into 4 groups [21]: NG (Normal Group), DG (Diabetes Group), GTAR1 (diabetes group receiving gembili tuber analog rice at a dose of 4.16 g/rat/day), and GTAR2 (diabetes group receiving gembili tuber analog rice at a dose of 6.17 g/rat/day). The amount of gembili tuber analog rice given was calculated based on the conversion of daily staple food requirements for adult individuals in Indonesia, as referenced from the Health Ministry of the Indonesian Republic in 2014 [24].

#### *2.4. Weight measurement in T2DM mice.*

The rat's weight was measured using a digital weighing scale with a precision of 0.01 grams. The measurement unit of the rat's weight was grams. Rats were weighed 5 times: before adaptation (BW1), after adaptation/before given STZ and NAD induction (BW2), before treatment on day 0 (BW3), on day 7 after treatment (BWD7), and on day 14 after treatment (BWD14).

#### *2.5. Lactic acid bacteria profile test.*

The tools and materials used for examining the lactic acid bacteria included pipettes, Petri dishes, an incubator, a colony counter, PGY media, and CaCO<sub>3</sub>. The procedure involved diluting the homogenate (microbiological test sample preparation) to certain levels (10<sup>-2</sup>, 10<sup>-3</sup>, 10<sup>-4</sup>, etc.) by transferring 1 ml of homogenate into 9 ml of diluent using a sterile pipette (1 ml volume). Homogenization was performed with a vortex during dilution. Then, 0.1 ml from each dilution was transferred into sterile Petri dishes (in duplicates). Approximately 12-15 ml of PGY media with CaCO<sub>3</sub> (in a sterile and warm condition) was added to each dish containing the diluted homogenate. The mixture was immediately swirled in a circular motion (clockwise and counterclockwise) on the table to ensure thorough mixing between the diluted homogenate and the agar media. The Petri dishes were incubated at 30°C for 48 hours. After incubation, typical colonies, surrounded by a clear zone, were observed. The colony count (cfu/ml) for each gram or milliliter of the test sample was calculated as the average of duplicate colony counts.

#### *2.6. Short-chain fatty acid levels test.*

The examination of SCFA levels in this study was conducted using the GC-FID (Gas Chromatography-Flame Ionization Detector) method. The specimens used for analysis were the digesta samples obtained from the rat's cecum at the end of the research. The levels of short-chain fatty acid types, such as acetate, propionate, and butyrate acid, were determined. The optimization conditions for the GC-FID analysis in the rat's cecum can be found in Table 1.

**Table 1.** Optimization analysis conditions of GC-FID in the rat's cecum.

Parameter condition	
Brand	: Shimadzu
Detector	: FID
Temperature	: 240°C
Injector temperature	: 240°C
Column	: RTX-Wax (Length 30-meters, diameter 0.255 mm)
Column temperature	: 145°C
Carrier gas	: Helium
Column flow rate	: 0,80 ml/minute
Split ratio	: 50
Injection volume	: 1 ul

*2.7. Blood glucose level test.*

In this research, the fasting blood glucose levels were measured on day 0 and day 14. The fasting blood glucose levels test uses the enzymatic colorimetric method. Rats' blood samples were collected after a fasting period of 6-8 hours. A total of 1000 µl of standard sugar reagent was mixed with 10 µl of serum from the rat's blood. The solution was incubated at 37°C for 10 minutes. Subsequently, it was read using a spectrophotometer (model of the equipment, brand, city, and country of the equipment) at a wavelength of 510 nm.

*2.8. Statistical analysis.*

The results were reported as the mean ± standard deviation. The statistical analysis was performed using IBM SPSS Statistics 25, including testing for normality and homogeneity, independent sample t-tests, One-Way ANOVA/Kruskal-Wallis test, Two-Way ANOVA, and Tukey Test.

**3. Results and Discussion**

Table 2 presents the content of soluble fiber, insoluble fiber, and resistant starch in gembili tuber flour and gembili tuber analog rice, highlighting their respective nutritional compositions.

**Table 2.** The soluble fiber, insoluble fiber, and resistance starch in gembili tuber flour and gembili tuber analog rice.

Examination	Gembili tuber flour (mean±SD)	Gembili tuber analog rice (mean±SD)	p-value
Soluble Fiber (%)	0.25±0.02	0.34±0.03	0.014*
Insoluble Fiber (%)	4.71±0.10	8.58±0.04	<0.001*
Resistance Starch (%)	4.21±0.01	6.26±0.01	<0.001*

Descriptions: \*There is a difference in the soluble fiber/insoluble fiber/resistant starch content between the processing of gembili tuber flour and gembili tuber analog rice (Independent t-test)

Table 3 presents data on weight change, lactic acid bacteria profile, short-chain fatty acids, and fasting blood glucose levels in T2DM rats, providing insights into the physiological and metabolic responses observed in the study.

**Table 3.** Data of weight change, lactic acid bacteria profile, short chain fatty acid, and fasting blood glucose levels in T2DM rats.

Duration	Doses				p-value <sup>c, a</sup>	
	NG	DG	GTAR1	GTAR2		
Mean±SD						
Body weight (grams)						
BW1	184.57±3.69	186.57±4.65	186.57±3.10	186.71±3.68	0.683	<0.001 <sup>a</sup>
BW2	189.57±3.82	191.57±4.43	191.86±2.97	191.86±3.89	0.630	
BW3	194.71±3.50	185.86±4.88	186.14±3.29	186.00±4.12	0.001 <sup>*c</sup>	
BWD7	202.14±3.80	183.43±6.19	189.71±3.25	191.14±3.98	<0.001 <sup>*c</sup>	
BWD14	209.00±4.08	172.57±4.12	194.43±2.99	198.43±3.87	<0.001 <sup>*c</sup>	
p-value <sup>b</sup>	<0.001 <sup>*</sup>	<0.001 <sup>*</sup>	<0.001 <sup>*</sup>	<0.001 <sup>*</sup>		
Lactat acid bacteria (cfu/ml)						
D14	1.15x10 <sup>5</sup>	1.77 x 10 <sup>7</sup>	2.31 x 10 <sup>7</sup>	2.53 x 10 <sup>8</sup>	0.249 <sup>c</sup>	
Short-chain fatty acid level (µg/g)						
Acetic acid (D14)	153.12±8.50	33.98±3.75	94.20±5.30	135.52±8.30	<0.001 <sup>*c</sup>	
Propionat acid (D14)	53.80±6.24	14.11±4.50	35.01±3.30	40.55±5.60	<0.001 <sup>*c</sup>	
Butirat acid (D14)	23.75±2.82	5.60±1.22	12.84±1.83	15.50±1.85	<0.001 <sup>*c</sup>	
Fasting blood glucose level (mg/dl)						
D0	71.82±1.18	269.63±2.33	268.84±1.89	269.91±2.31	<0.001 <sup>*c</sup>	<0.001 <sup>a</sup>
D14	71.97±1.40	270.82±2.12	117.69±3.17	103.84±1.26	<0.001 <sup>*c</sup>	
p value <sup>d</sup>	0.124	0.337	<0.001 <sup>*</sup>	<0.001 <sup>*</sup>		

BW1: Rat's weight before adaptation; BW2: After adaptation/before induction using STZ and NAD; BW3: After STZ and NAD induction (day 0 before treatment); BWD7: Day 7 after treatment; BWD14: Day 14 after treatment; D0: Fasting blood glucose level at 0 days; D14: Fasting blood glucose level at 14 days; <sup>a</sup>The doses and durations effect of gembili tuber analog rice administration on BW/short-chain fatty acid level/fasting blood glucose levels in rats (Two Way Anova test); <sup>b</sup>The durations effect of gembili tuber analog rice administration on rat's BW (One Way Anova Test); <sup>c</sup>The doses effect of gembili tuber analog rice administration on lactic acid bacteria profile in T2DM rat's feces (Kruskal Wallis Test); <sup>d</sup>The durations effect of gembili tuber analog rice administration on fasting blood glucose levels (independent sample T Test).

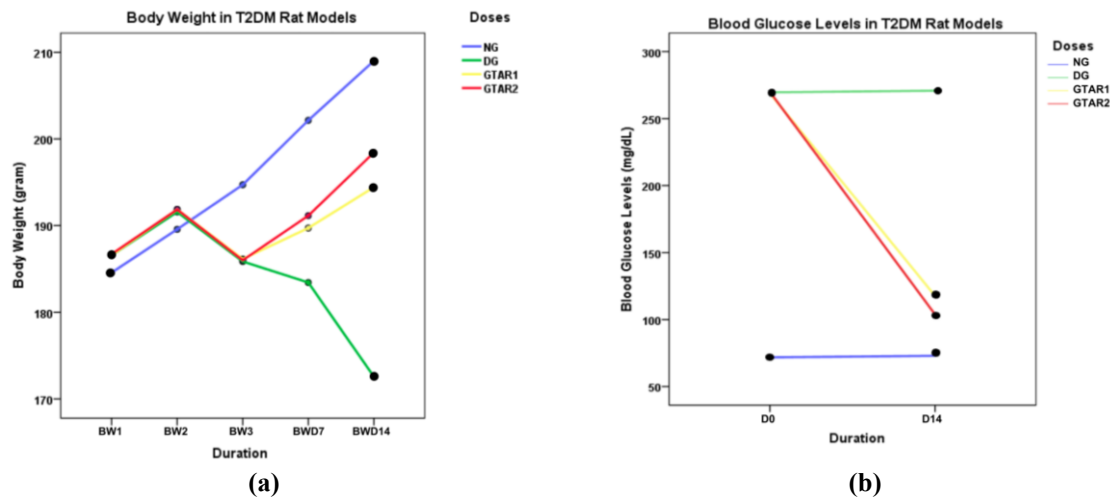
The effect of gembili tuber analog rice was analyzed by comparing one group with another, as presented in Table 4.

**Table 4.** The Effect of gembili tuber analog rice on one group with another.

Doses/Duration		p-value <sup>c</sup>
Body weight		
Duration		
BW1	BW2	<0.001 <sup>*</sup>
	BW3	0.299
	BWD7S	<0.001 <sup>*</sup>
	BWD14	<0.001 <sup>*</sup>
BW2	BW1	<0.001 <sup>*</sup>
	BW3	0.040 <sup>*</sup>
	BWD7	0.996
	BWD14	0.169
BW3	BW1	0.299
	BW2	0.040 <sup>*</sup>
	BWD7	0.014 <sup>*</sup>
	BWD14	<0.001 <sup>*</sup>
BWD7	BW1	<0.001 <sup>*</sup>
	BW2	0.996
	BW3	0.014 <sup>*</sup>
	BWD14	0.334
BWD14	BW1	<0.001 <sup>*</sup>
	BW2	0.169
	BW3	<0.001 <sup>*</sup>
	BWD7	0.334
Doses		
NG	DG	<0.001 <sup>*</sup>
	GTAR1	<0.001 <sup>*</sup>
	GTAR2	<0.001 <sup>*</sup>

Doses/Duration		p-value <sup>e</sup>
DG	NG	<0.001*
	GTAR1	<0.001*
	GTAR2	<0.001*
GTAR1	NG	<0.001*
	DG	<0.001*
	GTAR2	0.665
GTAR2	NG	<0.001*
	DG	<0.001*
	GTAR1	0.665
Short-chain fatty acid level (µg/g)		
Doses		
NG	DG	<0.001*
	GTAR1	<0.001*
	GTAR2	<0.001*
DG	NG	<0.001*
	GTAR1	<0.001*
	GTAR2	<0.001*
GTAR1	NG	<0.001*
	DG	<0.001*
	GTAR2	<0.001*
GTAR2	NG	<0.001*
	DG	<0.001*
	GTAR1	<0.001*
Fasting blood glucose level		
Doses		
NG	DG	<0.001*
	GTAR1	<0.001*
	GTAR2	<0.001*
DG	NG	<0.001*
	GTAR1	<0.001*
	GTAR2	<0.001*
GTAR1	NG	<0.001*
	DG	<0.001*
	GTAR2	<0.001*
GTAR2	NG	<0.001*
	DG	<0.001*
	GTAR1	<0.001*

<sup>e</sup>The effect of gembili tuber analog rice on one group with another (Tukey Test).



**Figure 1. (a) Body weight in T2DM rat models; (b) Blood glucose levels in T2DM rat models.**

Table 2 shows a significant difference in the levels of soluble fiber, insoluble fiber, and resistant starch between the processing of gembili tuber flour and gembili tuber analog rice. The processing of gembili tuber into gembili tuber analog rice resulted in an increase of 0.9% in soluble fiber content. The gembili tuber flour processed into gembili tuber analog rice had a higher insoluble fiber content, increasing by 3.87%. Additionally, the gembili tuber flour processed into gembili tuber analog rice had a higher level of resistant starch, increasing by

2.05%. A total of sixty-four bioactive compounds were detected across the insoluble fiber sources that appeared in the research. They fell into three categories: phenolic acids, flavonoids, and non-flavonoid compounds. The non-flavonoid compounds included tannins, tocopherols, tocotrienols, vitamin C, retinol equivalents, carotenoids, chlorophylls, and betalains [25]. The insoluble fiber and bioactive-rich plant sources were associated with the management of blood glucose [26]. Insoluble fiber has benefits such as shortening bowel transit time, improving laxation due to its bulking capacity, and supporting intestinal microflora growth (esp. probiotic species) due to its fermentation in the large intestine [27]. The chemical constituents from plant cell walls are non-cellulose polysaccharide oligosaccharides, pectins,  $\beta$ -glucans, and gums [27]. Soluble dietary fiber can be easily accessed and metabolized by fiber-degrading microorganisms in the intestine, producing a series of beneficial and functional metabolites [28]. Postpone gastric emptying, direct blood glucose levels, and lower serum cholesterol levels, due mainly to its effects of increasing the viscosity of gut content and colonic fermentation [27]. This research shows that gembili tuber analog rice has a higher resistant starch content (6.26%) than gembili tuber flour (4.21%). The results of other studies are the same as this study [29]. Dinamo is a starch potato cultivar that is grown in a field in the southern part of Sweden, and the mature tuber was harvested and stored at 6°C for two weeks. It has 4.4 to 6.7 % of dry matter. Resistant starches are components of dietary fiber, which are included in the analogous carbohydrate [27]. Resistant starch is the portion of starch that is not digested in the small intestine and is fermented in the colon by microorganisms, resulting in the formation of short-chain fatty acids, which may be associated with some metabolic effects and beneficial effects on health. An improvement in glucose tolerance, greater cellular sensitivity to insulin, and increased post-meal satiety are other potential benefits of resistant starch in the diet [30].

According to Table 3, during the course of the study, the DG group showed a decrease in BW from 186.57±4.65 grams (before adaptation) to 172.57±4.12 grams (after 14 days of treatment). Meanwhile, rats in the NG, GTAR1, and GTAR2 groups showed a tendency to increase in BW during the study. Based on the statistical test results, the p-value was <0.001, and the calculated F-value was 21.539, greater than the tabled F-value of 1.67. This indicates that the dosage and duration of administration of gembili analog rice influence the weight change of T2DM rats. Based on Table 3, there is a significant difference between the NG and DG groups and the other groups. Additionally, there is a significant difference between BW1, BWD7, and BWD14. In Figure 1, it can be observed that the weight of rats in the DG group exhibited a decrease. Conversely, in the NG, GTAR1, and GTAR2 groups, a weight increase was noted from the time the rats received STZ and NAD induction until day 14 of the study.

This study is consistent with the findings of Pournaghi *et al.* [31]. The study showed a significant decrease in average body weight between the control group and the STZ-induced diabetic group or the STZ-induced diabetic group treated with metformin (p-value <0.05). In this study, diabetes condition was induced in the rat by a single intraperitoneal injection of STZ at a dose of 45 mg/kg body weight in a fasting rat. The diabetes condition was confirmed 48 hours after STZ administration. In another study [32], diabetes was induced in mice using a single dose of STZ (160 to 240 mg/kg), a compound known for its toxicity to pancreatic beta cells. Diabetes was induced in male mice (weighing approximately 30 g) from Taconic Farms (TAC), Jackson Laboratories (JAX), and Charles River Laboratories (CRL). The mice were monitored for 30 days to observe adverse effects such as blood glucose levels and insulin requirements. In CRL mice given 240 mg/kg STZ, more than 95% developed diabetes within

4 to 5 days, with a relatively low decrease in body weight (average of 0.4 g). On the other hand, TAC and JAX mice were more sensitive to STZ, as evidenced by faster onset of diabetes (even at lower doses of STZ), higher insulin requirements after STZ administration, a greater decrease in body weight (average: TAC 3.5 g; JAX 3.7 g), and higher mortality rate.

In this study, the weight of rats in the GTAR1 and GTAR2 groups after being given gembili tuber analog rice on days 7 and 14 showed a significant increment ( $p$ -value  $<0.001$ ). The explanation for the rat's weight change could be related to the nutritional content of the gembili tuber. The inulin content of gembili tuber is 1.53 g/mg of gembili flour [33]. Another study [34] found a higher inulin content in gembili tuber (26.22%) than in wheat (only 0.5-1%) [35]. Another study [36] revealed that feeding chickens a diet substituted with gembili tuber flour at a level of 0.5%, 1%, or 1.5% can increase carcass weight. This can be attributed to the presence of inulin content in gembili tuber flour. Beneficial gut bacteria can utilize the prebiotic properties of inulin to stimulate growth, thereby enhancing optimal and efficient nutrient absorption. As a result, there is an increase in growth and carcass weight. Obesity and markers of inflammation, such as white blood cell count (WBC), were identified as potential risk factors for T2DM. This research provides the foundation for implementing dietary and exercise interventions aimed at promoting weight loss and reducing white blood cell count as part of a program designed for the prevention and management of T2DM [37].

Inulin functions as a storage polysaccharide composed of D-fructose units linked together by  $\beta$  bonds, which remain unaffected by enzymatic breakdown within the digestive system. This particular polysaccharide can be metabolized by beneficial bacteria residing in the colon, serving as a prebiotic fiber with selective properties [38]. Inulin is thought to share many of the properties of soluble dietary fibers [39,40], such as the ability to lower blood lipids and stabilize blood glucose [39]. The content of dietary fiber in analog taro rice cooked at 70°C is 10.8/100g [12], which is ten times higher than regular rice (1.1 g/100g) [11]. Dietary fiber promotes the growth and activity of beneficial bacteria in the human digestive system by serving as food for beneficial gut microflora. This activity of dietary fiber is known as prebiotic activity, and fibers that exhibit this activity are known as prebiotics. Prebiotics are generally defined as non-digestible food components that beneficially affect the host by stimulating the growth and activity of beneficial bacteria (such as Lactobacilli and Bifidobacteria) in the human digestive system, resulting in improved health of the host [41].

Based on the results in Table 3, the highest population of lactic acid bacteria in rats was observed in the GTAR2 group ( $2.53 \times 10^8$ ), followed by the GTAR1 group ( $2.31 \times 10^7$ ). Statistical analysis showed no significant effect of gembili tuber analog rice consumption on the profile of lactic acid bacteria ( $p$ -value=0.249). However, the high population of lactic acid bacteria in the GTAR2 and GTAR1 groups indicates prebiotic properties that contribute to weight gain in rats.

Another relevant study on this topic was conducted by Pramono *et al.* [42] demonstrated that the addition of gembili tuber flour at different concentrations had a significant effect ( $p < 0.05$ ) on total LAB count, reduction of sugar, crude fiber, viscosity, and organoleptic properties in yogurt. The ideal treatment involved the addition of 2% gembili tuber flour, resulting in a total LAB count of  $9.2 \times 10^9$ , sugar reduction of 0.653 mg/mL, crude fiber content of 1.3%, viscosity of 82.25 cPs, and organoleptic properties with a moderately acidic taste and preferred viscosity. The total LAB count in the T1 group (2% gembili tuber flour added to the amount of milk) was higher than in the T0 group (without the addition of gembili tuber flour) [42]. This can be attributed to the inulin content in gembili tuber flour,

which supports the optimal growth of lactic acid bacteria through symbiosis. Inulin is soluble in water and is not digested by human digestive enzymes. Furthermore, inulin is converted into short-chain fatty acids (SCFA) such as acetate, propionate, and butyrate, as well as lactate and gas [40,43].

Lactic acid bacteria are not only involved in weight gain in experimental animals. They also offer other benefits such as modulation of inflammation, interaction with dietary components, influence on gut permeability, involvement in glucose and lipid metabolism, insulin sensitivity, and energy homeostasis in mammals [44]. When anaerobic gut commensal bacteria, such as Clostridia species, ferment indigestible carbohydrates, short-chain fatty acids (SCFA) such as butyrate, propionate, and acetate are produced [45].

Information related to LAB in producing SCFA is explained by Kang *et al.* [46]. SCFAs, including acetic acid, propionic acid, and butyric acid, are produced by four bacterial strains. *B. bifidum* MG731 showed the highest total SCFA production (4998.6  $\mu\text{g/g}$ ), followed by *B. lactis* MG741 (2613.9  $\mu\text{g/g}$ ), *L. salivarius* MG242 (1456.1  $\mu\text{g/g}$ ), and *L. plantarum* MG989 (630.2  $\mu\text{g/g}$ ). These results indicate that the selected strains have potential anti-inflammatory effects and provide a molecular basis for the development of functional probiotics.

This study also examined the SCFA levels in rat feces. On day 14, the concentrations of acetic acid (153.12 $\pm$ 8.50  $\mu\text{g/g}$ ), propionic acid (53.80 $\pm$ 6.24  $\mu\text{g/g}$ ), and butyric acid (23.75 $\pm$ 2.82  $\mu\text{g/g}$ ) were highest in the feces of the normal group (NG) of rats compared to other groups (Table 3). The diabetes group (DG) had the lowest concentrations of acetic acid (33.98 $\pm$ 3.75  $\mu\text{g/g}$ ), propionic acid (14.11 $\pm$ 4.50  $\mu\text{g/g}$ ), and butyric acid (5.60 $\pm$ 1.22  $\mu\text{g/g}$ ) compared to the other groups. Additionally, the concentrations of acetic acid, propionic acid, and butyric acid increased with increasing doses of gembili tuber analog rice. The high levels of SCFA in the NG, GTAR1, and GTAR2 groups were consistent with the high profile of LAB in these groups.

Butyric acid is the most significant acid that influences the conditions in the large intestine. Butyric acid is a preferred nutrient for cells lining the epithelium of the large intestine, especially in the distal colon and rectum. Butyric acid positively influences the growth of the large intestine's mucosa, proliferation of crypt cells, and gene expression in the initial response. Acetic acid serves as fuel for skeletal and cardiac muscles, kidneys, and the brain, as well as a substrate for the synthesis of fatty acids and cholesterol. Propionic acid is metabolized by the liver. Only SCFA can be the primary source of glucose after metabolism and is used for energy production. The level of propionic acid can lower blood cholesterol levels [40]. It has been shown that administration of butyrate, acetate, and propionate in rats can increase the expression of regulatory T cells that produce anti-inflammatory interleukin 10 (IL-10) through the inhibition of histone deacetylase (HDAC) [47]. Butyric acid increases the expression of interleukin 18 (IL-18) in epithelial cells, enhances the expression of IL-10 in dendritic and macrophage cells, and induces the differentiation of regulatory T cells, thereby providing protection against colitis [48]. According to a study, propionate given as a diet to rats for 4 weeks had shown a reduction in fasting blood glucose levels and inhibit gluconeogenesis in isolated hepatocytes, possibly through its conversion to methylmalonyl-CoA and succinyl-CoA, both of which are specific inhibitors of pyruvate carboxylase. Moreover, propionate can indirectly affect liver glucose metabolism by reducing the concentration of fatty acids in the plasma [49].

Soluble fiber (inulin) in gembili tuber analog rice acts as a prebiotic, producing SCFAs (acetate, propionate, and butyrate) through the fermentation of lactic acid bacteria in the large intestine. This resulted in an increase in the butyrate absorption by the intestinal epithelium, serving as the main energy source for the phosphorylation of adenosine monophosphate-activated protein kinase (AMPK) and the release of glucagon-like peptide-1 (GLP-1) [14]. Acetate and propionate bind to G-protein-coupled receptors (GPR41 or 43) in the intestinal epithelium to carry out their functions. Activation of GPR41 promotes the secretion of peptide YY (PYY), controls the feeling of satiety (slowing down gastric emptying), and shortens intestinal transit time. Additionally, GPR43 inhibits proinflammatory production and increases GLP-1, which contributes to the production and induction of pancreatic  $\beta$ -cell proliferation, enhancing insulin sensitivity and reducing blood glucose levels [50].

The Two-Way ANOVA test yielded a calculated F value of 21.539, which is greater than the critical F value of 2.21, with a p-value of  $<0.001$  (listed in Table 3). Therefore, it can be stated that the dosage and duration of administration of the gembili tuber analog rice influence fasting blood glucose levels in rats. Rats in the GTAR1 and GTAR2 groups experienced a significant decrease in fasting blood glucose levels over 14 days. Both groups of rats had fasting blood glucose levels below the normal range, with the GTAR1 group at  $117.69 \pm 3.17$  mg/dL and the GTAR2 group at  $103.84 \pm 1.26$  mg/dL. Based on Table 3, the blood glucose levels of the rats in each group differ significantly. Figure 1b shows that the NG and DG groups did not experience changes in blood glucose levels during the study. In contrast, the GTAR1 and GTAR2 groups had a significant decrease in blood glucose levels on day 14. Increasing the dosage and duration (up to 14 days) of gembili tuber analog rice administration has been proven to significantly reduce fasting blood glucose levels. This may be attributed to the presence of soluble fiber, such as inulin, in the gembili tuber. Thus, it affects the absorption of macronutrients, especially carbohydrates, by slowing gastric emptying and shortening the transit time in the small intestine [51]. Furthermore, it leads to a decrease in gluconeogenesis in the liver, mediated by short-chain carboxylic acids, especially propionic acid [44].

During the 14-day study, rats in the NG group had normal blood glucose levels ( $\leq 150$  mg/dL) on days 0 and 14, with  $71.82 \pm 1.18$  and  $71.97 \pm 1.40$  mg/dL readings, respectively. The NG group of rats did not receive any treatment and had normal body conditions, thus not affecting fasting blood glucose levels. Rats in the NG, GTAR1, and GTAR2 groups on day 0 experienced hyperglycemia due to fasting blood glucose levels exceeding 150 mg/dL because they were induced with STZ and NAD.

A study reported that a single injection of 230 mg/kg BW of NAD and 65 mg/kg BW of STZ resulted in blood glucose levels reaching  $>150$  mg/dL after 3 days, indicating hyperglycemia in rats [23]. STZ administration can be used to induce type 2 diabetes. STZ has a selective toxic effect on  $\beta$  cells due to its high affinity for  $\beta$ -cell membranes. The genotoxic effect of STZ in animals occurs through the reduction of NAD in pancreatic  $\beta$  cells via GLUT2 (Glucose transporter 2), which can cause cellular damage through DNA strand breakage, leading to cell death. NA is a biochemical precursor of NAD and is an inhibitor of poly-ADP-ribose polymerase-1 (PARP-1) [52]. NAD is a derivative of vitamin B3 (niacin) with antioxidant capacity that can reduce the cytotoxic action of STZ. Extreme DNA damage contributes to the hyperactivation of PARP-1, depletion of cellular resources, and necrotic cell death. Several studies have shown that NA can protect pancreatic  $\beta$  cells from severe STZ-induced cytotoxicity. NA protects  $\beta$  cells against STZ through various mechanisms. NA acts as a scavenger of oxygen free radicals and NO, inhibits PARP with an IC<sub>50</sub> value of  $210 \pm 2.9$

$\mu\text{M}$ , suppresses cytokine-induced MHC class II expression, and provides  $\text{NAD}^+$ . NA also enhances  $\beta$ -cell regeneration and islet cell growth while inhibiting apoptosis. Additionally, NA can act as a methyl group acceptor, reducing DNA methylation. NA is a cytoprotective agent that inhibits apoptosis through the prevention of phosphatidylserine externalization and DNA degradation [23].

#### **4. Conclusions**

The dosage and duration of administering gembili tuber analog rice significantly influence weight gain, SCFA (acetate, propionate, and butyrate) levels, and fasting blood glucose levels in the DMT2 rat model. Additionally, the lactic acid bacteria profile in the GTAR1 and GTAR2 groups was higher than in the NG and DG groups. However, further research is needed to investigate the soluble dietary fiber content in gembili tuber analog rice to determine the specific type of soluble fiber that predominantly contributes to the reduction in blood glucose levels in rats.

#### **Author Contributions**

All authors have read and agreed to the published version of the manuscript.

#### **Institutional Review Board Statement**

This study has obtained ethical approval from the Health Research Ethics Commission of the Medicine Faculty, Muhammadiyah University of Surakarta, with the code 4247/A.2/KEPK-FKUMS/IV/2022.

#### **Informed Consent Statement**

Not applicable.

#### **Data Availability Statement**

Data supporting the findings of this study are available upon reasonable request from the corresponding author.

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#### **Conflicts of Interest**

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.

## References

1. Olokoba, A.B.; Obateru, O.A.; Olokoba, L.B. Type 2 Diabetes Mellitus: A Review of Current Trends. *Oman Medical Journal* **2012**, *27*, 269–273, <https://doi.org/10.5001/omj.2012.68>.
2. Ong, K.L.; Stafford, L.K.; McLaughlin, S.A.; Boyko, E.J.; Vollset, S.E.; Smith, A.E.; Dalton, B.E.; Duprey, J.; Cruz, J.A.; Hagins, H.; *et al.* Global, Regional, and National Burden of Diabetes from 1990 to 2021, with Projections of Prevalence to 2050: A Systematic Analysis for the Global Burden of Disease Study 2021. *The Lancet* **2023**, *402*, 203–234, [https://doi.org/10.1016/S0140-6736\(23\)01301-6](https://doi.org/10.1016/S0140-6736(23)01301-6).
3. International Diabetes Federation IDF Diabetes Atlas Ninth Edition 2019; International Diabetes Federation, **2019**.
4. International Diabetes Federation IDF Diabetes Atlas 10th Edition 2021; International Diabetes Federation, **2021**.
5. Kementerian Kesehatan RI Hasil Riset Kesehatan Dasar Tahun 2018; Lembaga Penerbit Badan Penelitian dan Pengembangan Kesehatan, **2019**.
6. Wu, Y.; Ding, Y.; Tanaka, Y.; Zhang, W. Risk Factors Contributing to Type 2 Diabetes and Recent Advances in the Treatment and Prevention. *Int. J. Med. Sci.* **2014**, *11*, 1185–1200, <https://doi.org/10.7150/ijms.10001>.
7. American Diabetes Association Economic Costs of Diabetes in the U.S. in 2017. *Diabetes Care* **2018**, *41*, 917–928, <https://doi.org/10.2337/dci18-0007>.
8. Cousin, E.; Duncan, B.B.; Stein, C.; Ong, K.L.; Vos, T.; Abbafati, C.; Abbasi-Kangevari, M.; Abdelmasseh, M.; Abdoli, A.; Abd-Rabu, R.; *et al.* Diabetes Mortality and Trends before 25 Years of Age: An Analysis of the Global Burden of Disease Study 2019. *The Lancet Diabetes & Endocrinology* **2022**, *10*, 177–192, [https://doi.org/10.1016/S2213-8587\(21\)00349-1](https://doi.org/10.1016/S2213-8587(21)00349-1).
9. Scott, L.J. Sitagliptin: A Review in Type 2 Diabetes. *Drugs* **2017**, *77*, 209–224, <https://doi.org/10.1007/s40265-016-0686-9>.
10. Chandalia, M.; Garg, A.; Lutjohann, D.; Von Bergmann, K.; Grundy, S.M.; Brinkley, L.J. Beneficial Effects of High Dietary Fiber Intake in Patients with Type 2 Diabetes Mellitus. *N Engl J Med* **2000**, *342*, 1392–1398, <https://doi.org/10.1056/NEJM200005113421903>.
11. Indonesia, P.A.G. Tabel komposisi pangan Indonesia; Elex Media Komputindo: **2013**.
12. Wardani, R.K.; Subariyatun, S.; Azhari, S.W.; Sofyan, A. Functional Properties of Instant Yellow Rice of Gembili Tubers (*Dioscorea Esculenta*) to Improve Food Security. *International Summit on Science Technology and Humanity (ISETH)* **2021**, *2021*, 25–33.
13. Soetoko, A.S.; Safitri, A.H.; Isradji, I.; Wibowo, K.A.T.; Nandira, A.; Rafiq, D.Z.A.; Savita, S.; Al-Baari, A.N.; Budi, Y.; Fatmawati, D. Antidiabetic Effect of Inulin from *Dioscorea esculenta* in Streptozotocin-Induced Diabetic Rats. *International Journal of Health Medicine and Current Research*, **2018**, *3*(03), 953–957.
14. Portincasa, P.; Bonfrate, L.; Vacca, M.; De Angelis, M.; Farella, I.; Lanza, E.; Khalil, M.; Wang, D.Q.-H.; Sperandio, M.; Di Ciaula, A. Gut Microbiota and Short Chain Fatty Acids: Implications in Glucose Homeostasis. *Int J Mol Sci* **2022**, *23*, 1105, <https://doi.org/10.3390/ijms23031105>.
15. Dhingra, D.; Michael, M.; Rajput, H.; Patil, R.T. Dietary Fibre in Foods: A Review. *J Food Sci Technol* **2012**, *49*, 255–266, <https://doi.org/10.1007/s13197-011-0365-5>.
16. Byrne, C.S.; Chambers, E.S.; Morrison, D.J.; Frost, G. The Role of Short Chain Fatty Acids in Appetite Regulation and Energy Homeostasis. *Int J Obes (Lond)* **2015**, *39*, 1331–1338, <https://doi.org/10.1038/ijo.2015.84>.
17. Cani, P.D.; Geurts, L.; Matamoros, S.; Plovier, H.; Duparc, T. Glucose Metabolism: Focus on Gut Microbiota, the Endocannabinoid System and Beyond. *Diabetes & Metabolism* **2014**, *40*, 246–257, <https://doi.org/10.1016/j.diabet.2014.02.004>.
18. Zhang, X.; Gregg, E.W.; Williamson, D.F.; Barker, L.E.; Thomas, W.; Bullard, K.M.; Imperatore, G.; Williams, D.E.; Albright, A.L. A1C Level and Future Risk of Diabetes: A Systematic Review. *Diabetes Care* **2010**, *33*, 1665–1673, <https://doi.org/10.2337/dc09-1939>.
19. Mao, T.; Huang, F.; Zhu, X.; Wei, D.; Chen, L. Effects of Dietary Fiber on Glycemic Control and Insulin Sensitivity in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis. *Journal of Functional Foods* **2021**, *82*, 104500, <https://doi.org/10.1016/j.jff.2021.104500>.
20. Raninen, K.; Lappi, J.; Mykkänen, H.; Poutanen, K. Dietary Fiber Type Reflects Physiological Functionality: Comparison of Grain Fiber, Inulin, and Polydextrose. *Nutr. Rev.* **2011**, *69*, 9–21, <https://doi.org/10.1111/j.1753-4887.2010.00358.x>.
21. Kisnawaty, S.W.; Wulandari, A.; Sofyan, A.; Mustikaningrum, F.; Jusoh, T.F.I.C.K. Peningkatan Kadar High Density Lipoprotein (HDL) pada Tikus Diabetes Melitus Tipe 2 Efek dari Pemberian Beras Analog Umbi Gembili. *Jurnal Kesehatan* **2023**, *16*, 194–203.
22. Association of Official Analytical, C.; Helrich, K. Official methods of analysis of the Association of Official Analytical Chemists, 15<sup>th</sup> edition, 1990 edition; The Association: Arlington, VA, **1990**.
23. Ghasemi, A.; Khalifi, S.; Jedi, S. Streptozotocin-Nicotinamide-Induced Rat Model of Type 2 Diabetes (Review). *Acta Physiologica Hungarica* **2014**, *101*, 408–420, <https://doi.org/10.1556/APhysiol.101.2014.4.2>.

24. Kemenkes RI Peraturan Menteri Kesehatan Republik Indonesia Nomor 41 Tahun 2014 Tentang Pedoman Gizi Seimbang; Kementerian Kesehatan RI, **2014**.
25. Timm, M.; Offringa, L.C.; Van Klinken, B.J.-W.; Slavin, J. Beyond Insoluble Dietary Fiber: Bioactive Compounds in Plant Foods. *Nutrients* **2023**, *15*, 4138, <https://doi.org/10.3390/nu15194138>.
26. Krawęcka, A.; Sobota, A.; Pankiewicz, U.; Zielińska, E.; Zarzycki, P. Stinging Nettle (*Urtica Dioica* L.) as a Functional Component in Durum Wheat Pasta Production: Impact on Chemical Composition, In Vitro Glycemic Index, and Quality Properties. *Molecules* **2021**, *26*, 6909, <https://doi.org/10.3390/molecules26226909>.
27. Bhide Kshirsagar, S.; Takarkhede, S.; Govind Jha, A.; Pradeep Jain, R.; Sunil Jadhav, V.; Dharmendra Jadhav, D. A Comprehensive Review on Dietary Fiber and Their Functional Properties in Human Body. *World J. Bio. Pharm. Health Sci.* **2020**, *04*, 059–076, <https://doi.org/10.30574/wjbpshs.2020.4.3.0104>.
28. Guan, Z.-W.; Yu, E.-Z.; Feng, Q. Soluble Dietary Fiber, One of the Most Important Nutrients for the Gut Microbiota. *Molecules* **2021**, *26*, 6802, <https://doi.org/10.3390/molecules26226802>.
29. Zhao, X.; Andersson, M.; Andersson, R. Resistant Starch and Other Dietary Fiber Components in Tubers from a High-Amylose Potato. *Food Chemistry* **2018**, *251*, 58–63, <https://doi.org/10.1016/j.foodchem.2018.01.028>.
30. Bojarczuk, A.; Skąpska, S.; Mousavi Khaneghah, A.; Marszałek, K. Health Benefits of Resistant Starch: A Review of the Literature. *Journal of Functional Foods* **2022**, *93*, 105094, <https://doi.org/10.1016/j.jff.2022.105094>.
31. Pournaghi, P.; Sadrkhanlou, R.-A.; Hasanzadeh, S.; Foroughi, A. An Investigation on Body Weights, Blood Glucose Levels and Pituitary-Gonadal Axis Hormones in Diabetic and Metformin-Treated Diabetic Female Rats. *Vet Res Forum* **2012**, *3*, 79–84.
32. Graham, M.L.; Janecek, J.L.; Kittredge, J.A.; Hering, B.J.; Schuurman, H.-J. The Streptozotocin-Induced Diabetic Nude Mouse Model: Differences between Animals from Different Sources. *Comp Med* **2011**, *61*, 356–360.
33. Yuniastuti, A.; Iswari, R.S. Isolation and Identification of Inulin and Fos from *Dioscorea Esculenta*. *KSS* **2019**, <https://doi.org/10.18502/kss.v3i18.4696>.
34. Fera, M.; Masrikhiyah, R. Retensi Kadar Inulin Dari Umbi Gembili (*Dioscorea Esculenta* L) Pada Produk Cookies Sebagai Alternatif Produk Pangan Tinggi Serat. *Jurnal Teknologi Pangan dan Gizi* **2021**, *19*, 101–108.
35. Moshfegh, A.J.; Friday, J.E.; Goldman, J.P.; Ahuja, J.K. Presence of Inulin and Oligofructose in the Diets of Americans. *J Nutr* **1999**, *129*, 1407S–11S, <https://doi.org/10.1093/jn/129.7.1407S>.
36. Fajrih, N.; Khoiruddin, M. Penggunaan Umbi Gembili Sebagai Prebiotik Alami Terhadap Persentase Karkas Dan Lemak Abdominal Pada Broiler. *JURNAL TERNAK* **2020**, *11*, 13, <https://doi.org/10.30736/jtk.v11i1.62>.
37. Park, S.-H.; Lee, H. Obesity, Leukocytes, and High-Sensitivity C-Reactive Protein Biomarkers Associated with Type 2 Diabetes Mellitus in South Korean Adults. *Iran J Public Health* **2022**, *51*, 1827–1835, <https://doi.org/10.18502/ijph.v51i8.10268>.
38. Meyer, D.; Blaauwhoed, J.P. 30 - Inulin. In *Handbook of Hydrocolloids (Second Edition)*, Phillips, G.O., Williams, P.A., Eds.; Woodhead Publishing: **2009**; pp. 829–848, <https://doi.org/10.1533/9781845695873.829>.
39. Ilievska, N.; Pavlova, V.; Kirovska, V.; Ilievska, J.; Pavlovska, M. Nutritional and health benefits of inulin as functional food and prebiotic. *Journal of Hygienic Engineering and Design* **2019**, *27*, 45–48.
40. Slavin, J.L.; Savarino, V.; Paredes-Diaz, A.; Fotopoulos, G. A Review of the Role of Soluble Fiber in Health with Specific Reference to Wheat Dextrin. *J Int Med Res* **2009**, *37*, 1–17, <https://doi.org/10.1177/147323000903700101>.
41. Slavin, J. Fiber and Prebiotics: Mechanisms and Health Benefits. *Nutrients* **2013**, *5*, 1417–1435, <https://doi.org/10.3390/nu5041417>.
42. Pramono, Y.B.; Dwiloka, N.B.; Mulyani, S.; Setiani, B.E.; Rochmayani, M.; Bahtiar, D.E. Utilization of Lesser Yam (*Dioscorea Esculenta* L.) Flour as Prebiotic in Yogurt to Total Lactic Acid Bacteria (LAB), Sugar Reduction, and Organoleptic Properties. *Digital Press Life Sciences* **2020**, *2*, 00011, <https://doi.org/10.29037/digitalpress.22325>.
43. Nyman, M. Fermentation and Bulking Capacity of Indigestible Carbohydrates: The Case of Inulin and Oligofructose. *Br J Nutr* **2002**, *87*, S163–S168, <https://doi.org/10.1079/BJN/2002533>.
44. Aw, W.; Fukuda, S. Understanding the Role of the Gut Ecosystem in Diabetes Mellitus. *J of Diabetes Invest* **2018**, *9*, 5–12, <https://doi.org/10.1111/jdi.12673>.
45. Koh, A.; De Vadder, F.; Kovatcheva-Datchary, P.; Bäckhed, F. From Dietary Fiber to Host Physiology: Short-Chain Fatty Acids as Key Bacterial Metabolites. *Cell* **2016**, *165*, 1332–1345, <https://doi.org/10.1016/j.cell.2016.05.041>.
46. Kang, C.-H.; Kim, J.-S.; Park, H.M.; Kim, S.; Paek, N.-S. Antioxidant Activity and Short-Chain Fatty Acid Production of Lactic Acid Bacteria Isolated from Korean Individuals and Fermented Foods. *3 Biotech* **2021**, *11*, 217, <https://doi.org/10.1007/s13205-021-02767-y>.

47. Smith, P.M.; Howitt, M.R.; Panikov, N.; Michaud, M.; Gallini, C.A.; Bohlooly-Y, M.; Glickman, J.N.; Garrett, W.S. The Microbial Metabolites, Short-Chain Fatty Acids, Regulate Colonic T<sub>reg</sub> Cell Homeostasis. *Science* **2013**, *341*, 569–573, <https://doi.org/10.1126/science.1241165>.
48. Singh, N.; Gurav, A.; Sivaprakasam, S.; Brady, E.; Padia, R.; Shi, H.; Thangaraju, M.; Prasad, P.D.; Manicassamy, S.; Munn, D.H.; *et al.* Activation of Gpr109a, Receptor for Niacin and the Commensal Metabolite Butyrate, Suppresses Colonic Inflammation and Carcinogenesis. *Immunity* **2014**, *40*, 128–139, <https://doi.org/10.1016/j.immuni.2013.12.007>.
49. Lee, Y.-K.; Salminen, S. The Coming of Age of Probiotics. *Trends in Food Science & Technology* **1995**, *6*, 241–245, [https://doi.org/10.1016/S0924-2244\(00\)89085-8](https://doi.org/10.1016/S0924-2244(00)89085-8).
50. Everard, A.; Cani, P.D. Gut Microbiota and GLP-1. *Rev Endocr Metab Disord* **2014**, *15*, 189–196, <https://doi.org/10.1007/s11154-014-9288-6>.
51. Tsuneyuki, O.; Takahisa, T.; Norimasa, H. Nondigestibility of a New Sweetener, “Neosugar,” in the Rat. *The Journal of Nutrition* **1984**, *114*, 1574–1581, <https://doi.org/10.1093/jn/114.9.1574>.
52. Rais, N.; Ved, A.; Ahmad, R.; Parveen, K.; Gautam, G.K.; Bari, D.G.; Shukla, K.S.; Gaur, R.; Singh, A.P. Model of Streptozotocin-Nicotinamide Induced Type 2 Diabetes: A Comparative Review. *CDR* **2022**, *18*, e171121198001, <https://doi.org/10.2174/1573399818666211117123358>.

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