Wijayanti *et al.*
Food Production, Processing and Nutrition (2023) 5:47
https://doi.org/10.1186/s43014-023-00163-y

Food Production, Processing and Nutrition

RESEARCH

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Effect of GLITEROS specific-diabetes enteral formula modification based on tempe flour, jicama flour and sunflower seed flour on score pancreatic damage, number and diameter of the islets of langerhans of hyperglycemic rats pancreatic cells with streptozotocin induction

Lilis Wijayanti[1], Muflihatul Muniroh[2], Ahmad Ni'matullah Al-Baarri[3], Deny Yudi Fitranti[1,4], Endang Mahati[5] and Diana Nur Afifah[1,4*]

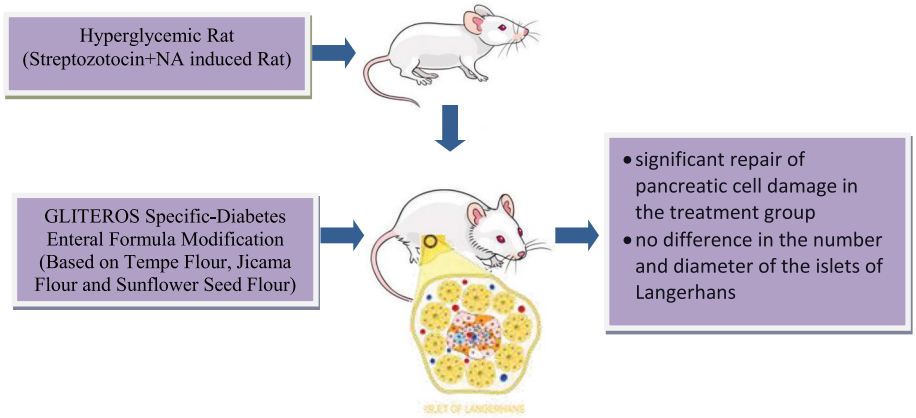
Abstract

Tempeh, yam, and sunflower's flour have been known to have antidiabetic effects, but their combined effect on the histopathology of hyperglycemic rat pancreatic cells in an enteral formula has not been proven. This study aimed to analyze the effect of GLITEROS specific-diabetes enteral formula modification based on tempeh flour, yam flour, and sunflower seed flour on the score pancreatic damage, number and diameter of the islets of langerhans of hyperglycemic rats with streptozotocin induction. The intervention was administered via an oral probe for 28 days to 30 Wistar rats, with each group consisting of 6 rats. The formula was given at a dose of 3.97 g/200 g/day (P1) and 8.75 g/200gr/day (P2) compared to standard control (K), positive control (K+), and negative control (K-). Histopathological features of the pancreas were analyzed using the hematoxylin–eosin staining method. Data were analyzed using paied t-test/Wilcoxon and ANOVA/Kruskal Wallis. The results showed a significant repair of pancreatic cell damage in the treatment group (P1 and P2) after the intervention ($p < 0.05$), but there was no difference in the number and diameter of the islets of Langerhans ($p > 0.05$). Overall, our findings suggest that the modified GLITEROS specific-diabetes enteral formula made from tempeh, yam, and sunflower seeds flour on the histopathological picture of hyperglycemia-induced rat pancreas, especially in the repair of damage to pancreatic Langerhans cells.

Keywords Enteral formula, Diabetes, Tempeh flour, Jicama flour, Sunflower seed flour, Histopathology, Pancreatic cell

*Correspondence:
Diana Nur Afifah
d.nurafifah.dna@fk.undip.ac.id
Full list of author information is available at the end of the article

Graphical Abstract



Introduction

Diabetes Mellitus (DM) is a metabolic disease with an increasing epidemic prevalence worldwide. Diabetes mellitus patients with swallowing disorders or decreased awareness will require enteral and parenteral nutritional support to meet their nutritional needs (Lewis et al. 2016). However, not only to meet dietary needs but providing nutritional support to hyperglycemic patients must also be able to control the patient's blood glucose levels. The American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines recommends enteral versus parenteral nutrition in patients with a functioning digestive tract because it reduces infection morbidity and length of hospital stay (Lewis et al. 2016; Ma et al. 2020). While the administration of standard enteral formulas has been reported to exacerbate hyperglycemia in critically ill patients with diabetes (Huhmann et al. 2018). This condition is because the standard enteral formula usually given has a composition of low fat, low fiber, and high simple carbohydrates which are quickly absorbed so that it can exacerbate hyperglycemia if given continuously (Elia et al. 2005; Mabrey et al. 2015).

GLITEROS is one of the innovations in developing an enteral formula for a particular hospital for diabetes using inexpensive local food ingredients in powder form with a low glycemic index (Sutikno et al. 2020; Wijayanti et al. 2020). Local food such as tempeh flour and yam flour were chosen as hospital enteral formula ingredients because they have anti-diabetic effects, and the prices tend to be more affordable. Tempe flour contains the amino acids leucine and isoflavones, which are known to protect pancreatic cells from apoptosis (El-kordy & Alshahrani 2015; Kridawati et al. 2019; Yang et al. 2011). Jicama extract is known to protect against pancreatic cell degeneration and prevent hypertrophy and hyperplasia in the pancreatic islets of Langerhans (Park et al. 2016; Santoso et al. 2021). Unfortunately, the fat content in the GLITEROS formula is still not up to standard, so the authors try to modify it by adding sunflower seed flour. Sunflower seed flour is rich in fat content in monounsaturated fatty acids (MUFA). It is recommended for patients with hyperglycemia because it can reduce increased oxidative stress during hyperglycemia (Patkova et al. 2017; Sutikno et al. 2020). Sunflower seed flour, apart from having an anti-diabetic effect, also contains ingredients that can help inhibit, protect, and repair damage to pancreatic cells, namely vitamin E in the form of alpha-tocopherol (92.4%), which acts as a natural antioxidant (Varsha et al. 2015; Pazdro & Burgess 2010; Anjum et al. 2012).

The contents of the three ingredients in the modified GLITEROS formula that had an effect on the pancreas prompted researchers to analyze their effect on the histopathological picture of the pancreas of streptozotocin-induced hyperglycemic rats.

Materials and methods

Study site

This study was undertaken at the Center for Food And Nutrition Studies, University of Gadjah Mada, Yogyakarta, for two months.

Enteral formula ingredients

The ingredient used in this study was 23 g of tempeh flour and 46 g of jicama flour from "Hasil Bumiku," 23 g of undried peeled sunflower seeds from "Granology," 60 g of skimmed milk from "Indoprima," 50 g of maltodextrin,

12 g of sugar from "Gulaku" and 7 g of soybean oil from "Happy."

Preparation of formula

The oven-drying method changed "Granology" undried sunflower seeds to sunflower seed flour. The undried peeled sunflower seeds are oven-dried at 100 °C for 30 min (Tenyang et al. 2022), then mashed in a food processor, and sieved using a 100 mesh sieve. Tempeh flour and jicama flour from "Hasil Bumiku" were also sieved using a 100 mesh sieve. Powdered sugar was mashed in a food processor and sieved using a 100-mesh sieve. The enteral formula was prepared by weighing the ingredients according to each ratio (Table 1). Dry ingredients, such as tempeh flour, jicama flour, sunflower seed flour, skim milk, maltodextrin, and powdered sugar, were mixed manually for three minutes. Next, soybean oil was added to the dry ingredients mixture and stirred for two minutes. All stirred ingredients are then remixed using a mixer for eight minutes to be homogeneous (Sutikno et al. 2020).

Proximate test also has been carried out to analyze enteral formulas' energy and macronutrient content, as a reference in administering enteral formulas to samples. The content of macronutrients, dietary fiber, and protein digestibility GLITEROS specific-diabetes enteral formula modification in 1000 ml formula can be seen in Table 2.

Study design

This is true experimental research experimental a post-test-only control group design randomized control group design.

Experimental groups

The intervention was given to white male rats with Wistar strain (Rattus norvegicus) aged eight weeks with a weight range of 150–200 g. All procedures were approved by the Health Research Ethics Commission, Faculty of Medicine, Diponegoro University, Semarang. The sample was 30 rats divided into five groups consisting of:

- Group K: healthy rats fed ad libitum,
- Group K-: rats with Streptozotocin 45 mg/kg body weight and Nicotinamide 110 mg/kg body weight induction without intervention with ad libitum feeding,
- Group K+: rats with Streptozotocin 45 mg/kg body weight and Nicotinamide 110 mg/kg body weight induction with commercial formula intervention,
- Group P1 : rats with Streptozotocin 45 mg/kg body weight and Nicotinamide 110 mg/kg body weight induction, and given enteral formula at a dose of 3.97 g/200g body weight,
- Group P2: rats with Streptozotocin 45 mg/kg body weight and Nicotinamide 110 mg/kg body weight induction, and given with enteral formula at a dose of 8.75g/200g body weight.

Rat with STZ induction with NA are stable in hyperglycemia if the blood glucose test results are 150–180 mg/dl (Ghasemi et al. 2014).

Determination of the dose given to rats is done by doing calculations. The calculations referred to the doses of tempeh flour, yam flour, and sunflower seed flour in previous studies, which significantly affected changes in the histopathological picture of the pancreas of rats with hyperglycemia. The first dose did not meet the amount of tempeh flour which could affect changes in the rat pancreas, so the dose was increased to 2.2 times which fulfilled the amount of tempeh flour. The Enteral Formula Nutrient Content given to the rats can be seen in Table 3 bellow.

The study was conducted for 34 days (3 days of acclimation, 3 days of STZ + NA induction, and 28 days of intervention). Histopathological analysis of rat pancreatic cells was performed after 28 days of intervention.

Table 1 GLITEROS specific-diabetes enteral formula modification composition ratio

Ingredients	GLITEROS specific-diabetes enteral formula modification
Jicama Flour(g)	23
Tempeh flour (g)	46
Sunflower seed flour (g)	23
Skimmed Milk (g)	60
Soybean oil (g)	7
Maltodextrin (g)	50
Sugar (g)	12

* For 1000 cc formula

Table 2 Table content of macronutrients, dietary fiber, and protein Digestibility GLITEROS specific-diabetes enteral formula modification in 1000 ml formula

Nutrition content /1000 mL	Formula Enteral
Energy density (kkal/mL)	1.09
Energy (kkal)	1090
Carbohydrat (%)	45.97
Protein (%)	18.45
Fat (%)	26.20
Dietary fiber (%)	25.26
Protein digestibility (%)	46.92
Water (%)	6.55
Ash (%)	2.78

Table 3 The enteral formula nutrient content given to the rats

Nutrition content	Gliteros modification	Rat dose 1 (3.97 g)	Gliteros modification (2.2x)	Rat dose 2 (8.75 g)	Commersial formula	Rat dose (4.32 g)
Energy (kkal)	1090	19.6	2398	43.16	1032	18.576
Carbohydrat (g)	501.1	9.0	1102.42	19.84	158.5	2.8512
Fat (g)	12.0	0.2	26.4	0.48	26.4	0.5184
Protein (g)	4.8	0.1	10.56	0.19	38.4	0.6912
Dietary fiber (g)	4.7	0.1	10.56	0.19	14.4	0.2592

Histological examination

The histopathological analysis of pancreatic beta cells was performed by biopsy (taking tissue from the rat's pancreas) in both the control and treatment groups. The rats from each group were euthanized on day 29 after treatment by chemical euthanasia method with chloroform. Furthermore, the rats were necropsied to take pancreatic tissue, followed by fixation of the pancreas tissue using 10% BNF solution for at least 24 h (Nowacek & Kiernan, 2010). Then the pancreas was stained with Hematoxylin Eosin. Stained pancreatic slices were evaluated using a microscope at 40× and 100× magnification in five fields of view.

The scoring system used is based on pancreatic damage, as below (Tandi et al. 2017),

Score 0: for normal cells, no change in the boundaries of the Islets of the Langerhans organ, cell number, necrotic cells, and cell shape

Score 1: for clear boundaries cell, but the number of cells begins to decrease, necrotic cells are not visible, only cell degeneration and normal cell shape

Score 2: for the cell with unclear boundaries, the number of cells is reduced, and cell degeneration and cell shape are abnormal

Score 3: the boundary is unclear, the number of cells is reduced, necrotic cells are visible, and many cell shapes are abnormal

Score 4: the cell boundaries are very unclear, the number of cells is greatly reduced, the cells are almost completely necrotic and the cell shape is abnormal.

The mean number and diameter of islets of Langerhans were calculated per slide and were averaged for each group at a magnification of 1000 X. The diameter of the islets of Langerhans is obtained by measuring the largest axis on the islets of Langerhans by image raster software. The data are then collected in an Excel sheet and submitted for statistical analysis (Tandi et al. 2017).

Statistical analysis

Quantitative data including pancreatic damage's scores, the number and diameter of the islets of Langerhans used the Kruskal Walli test, followed by the Mann Witney post hoc test ($p < 0.05$ considered as significant).

Results

Effect of enteral formula on a histopathological of rat pancreatic cells

Histopathological analysis was carried out after the intervention for 28 days in the five treatment groups. After the pancreatic tissue sample is taken, the tissue sample is processed to make preparations ready to be stained and read. Histopathological observations of the rat pancreas were carried out by observing the microanatomical structure of the islets of Langerhans in white rats in each treatment group. Furthermore, the Langerhans Island damage scoring was performed using a 0–4. The description of the damage to Langerhans Island in the five treatment groups can be seen in Fig. 1.

Effect of streptozotocin and nicotinamide induction on fasting blood glucose of rat

Fasting blood glucose levels of rats before induction of STZ + NA were taken after three days of acclimatization. Blood glucose testing after STZ + NA induction was carried out after three days of STZ + NA injection. The changes in fasting blood glucose levels in the induced and non-induced groups are presented in Table 4.

Effect of enteral formula on fasting blood glucose of rat

Fasting blood glucose levels of rats were taken after three days of STZ + NA induction and 28 days after the intervention of modified GLITEROS enteral formula and commercial formula. Changes in the average fasting blood glucose of rats in the five treatment groups before and after the intervention are presented in Table 5 below.

Effect of enteral formula on rat pancreatic cell damage score

The results of scoring damage to the islets of Langerhans are presented in Table 6. Table 6 shows that all samples in group K got a damage score of 0. On the other hand, all samples in group K(-) got the highest pancreatic cell damage category score, which was 4. While in group K(+), three samples got a score of 3 and 3 samples got a score of 4. A total of 2 samples

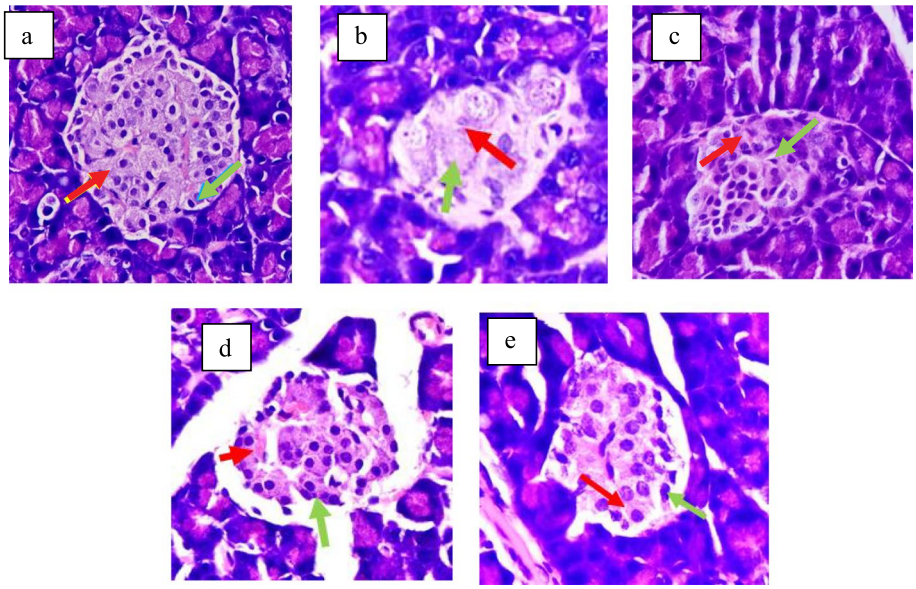


Fig. 1 Description of the damage to the islets of Langerhans in the five Wistar rat treatment groups. Note: 400× magnification, HE staining, red arrows (➡) indicate cell boundaries, and green arrows (➡) indicate cell degeneration and shape. (**a**) the control group (K) with a score of 0, (**b**) the negative control group (K-) with a score of 4, (**c**) the positive control group (K+) with a score of 3, (**d**) the treatment group 1 (P1) with a score 2, and treatment group 2 (P2) with a score of 1

Table 4 Mean of fasting blood glucose for the non-STZ group and the STZ group

FBG level (mg/dL)	Non STZ + NA induction	STZ + NA induction
Before STZ + NA induction	70.98 ± 1.47	73.00 ± 0.67
After STZ + NA induction	70.17 ± 1.47	260.45 ± 1.23
Δ	0.45 ± 0.27	187.44 ± 0.95

Table 5 Mean of fasting blood glucose for the non-STZ group and the STZ group

FBG level (mg/ dL)	Before intervention	After ntervention	Δ before and after ntervention
K	71.72 ± 1.47	73.39 ± 1.57	1.67 ± 0.33
K (-)	259.80 ± 2.85	261.30 ± 3.38	1.49 ± 0.59
K (+)	258.72 ± 2.18	99.41 ± 1.62	-159.31 ± 2.87
P1	261.55 ± 1.51	128.30 ± 2.69	-133.25 ± 2.24
P2	261.7 ± 2.55	92.41 ± 1.99	-169.31 ± 3.33

in the P1 group got a score of 2, and as many as four got a score of 3. The higher damage scores indicated the four groups that experienced cell damage. The description of pancreatic cell damage in treated rats after being given enteral formula intervention can be observed in Table 6.

The results of the One way annova test show that there are at least two groups that have different changes in GDP levels. To find out which groups had differences, a Post Hoc Games-Howell test was carried out because the variances of the five groups were different. The results of the Games-Howell Post Hoc test are presented in Table 7.

Effect of enteral formula on the area and diameter of the islets of langerhans

The results of the calculation of the number and diameter of the islets of Langerhans are presented in Table 8. The statistical analysis results showed no difference in the number and diameter of the islets of Langerhans between the five treatment groups ($p > 0.05$). Group K(-) has the least number of islands of Langerhans, while the number of Langerhans in group P2 is the highest. Groups P1, P2, and K(-) had the same diameter of islets of Langerhans, while group K had the smallest diameter of Langerhans.

Discussion

Histopathology examines the morphology of cells or tissues in microscopic preparations by staining method to diagnose degeneration, inflammation, or infection and neoplasms (Frantz et al. 2012). Histopathological analysis of the pancreas can be done either descriptively or quantitatively. Descriptive observations included observing the shape of pancreatic cells to see the presence of vacuolization, congestion, and necrosis. While the

Table 6 Langerhans island damage scoring results

Treatment Group	Pancreatic Cell Histopathology Score of Test Animals					Median	*P* value
	0	1	2	3	4	(Min–Max)	
K	6	0	0	0	0	0 (6–6)	
K (-)	0	0	0	0	6	4 (6–6)	
K (+)	0	0	0	3	3	3.5 (3–4)	0.000*
P1	0	0	2	4	0	3 (2–3)	
P2	0	2	4	0	0	2 (1–2)	

* *p* value < 0.05 = significantly different from the Kruskal Wallis test

Table 7 Post Hoc Mann Witney Langerhans Island damage scoring results

Treatment Group	Median	*P* value				
	(Min–Max)	K	K(-)	K(+)	P1	P2
K	0 (6–6)	-	0,001*	0,002*	0,002*	0,002*
K (-)	4 (6–6)		-	0,056	0,002*	0,002*
K (+)	3.5 (3–4)			-	0,030*	0,002*
P1	3 (2–3)				-	0,026*
P2	2 (1–2)					-

* *p* value < 0.05 = significantly different from the post hoc Mann Withney

Table 8 Calculation results for the number and diameter of Langerhans Islands

Treatment Group	Number of Langerhans Islands	The diameter of the islets of Langerhans (mm)
K	26 (14–32)	0.17 (0.12–0.27)
K (-)	21 (11–27)	0.22 (0.17–0.36)
K (+)	22.5 (11–41)	0.21 (0.17–0.36)
P1	24 (23–26)	0.22 (0.15–0.35)
P2	30 (21–36)	0.22 (0.18–0.25)
p	0.439	0.681

median (min–max)

quantitative analysis was carried out using morphometric methods, namely counting the number of Langerhans cells, measuring the diameter and area of the islets of Langerhans, and counting the number of pancreatic beta cells of the islets of Langerhans (El-Kordy & Alshahrani 2015; Ningrum et al. 2020).

After STZ + NA induction, the induction treatment group showed an increase of 187.44 mg/dL (Table 4). The fasting blood glucose results of STZ + NA-induced rats were above normal values and included in the hyperglycemia category. Blood glucose levels of Wistar rats will increase within 2 to 4 h after intraperitoneal induction of STZ. This increment may occur as a result of the mobilization of liver glycogen (Ghasemi et al., 2014). This increase in fasting blood glucose is related to decreased plasma insulin levels in rats due to STZ induction. Streptozotocin will interfere with glucose oxidation, reduce insulin synthesis and secretion, and interfere with glucose transport and glucokinase activity in cells (Saini & Sharma 2013). The sugar part of STZ, namely 2-deoxy-D-glucose that enters through GLUT2 into pancreatic cells will transfer the methyl group from STZ to the molecule DNA or called DNA alkylation, which causes damage resulting in DNA fragmentation and functional defects of pancreatic beta cells (Saini & Sharma 2013; Islam et al. 2017). This will inhibit the synthesis and secretion of insulin, which decreases the amount of insulin. Reduced insulin cells result in less blood glucose entering the cells, increasing fasting blood glucose levels (Bintari et al. 2015a, 2015b). Hyperglycemia will appear in rat within one hour after STZ induction and become permanent 24 h after induction (Adeghate et al. 2010). STZ induction with NA in stable rats in a hyperglycemia state of 150–180 mg/dl and glucose intolerance that does not require exogenous insulin for survival (Ghasemi et al. 2014).

Histological observation in Fig. 1 shows the description of the pancreatic rat preparations in groups K, K (-), K (+), P1, and P2, which showed different pancreatic cell structures in the five groups. The effect of giving enteral formula on the histopathological description of the pancreas of Wistar rats after STZ + NA induction generally

showed differences in the histopathology of the pancreas of Wistar rats between the control group and the treatment group. Group K (Fig. 1a) showed normal rat pancreas histology, where pancreatic cells did not undergo cell necrosis (green), had normal cell size and number, cell boundaries were still clearly visible (red), and there were no degenerated cells. Meanwhile, the group with STZ + NA induction showed histopathological changes in pancreatic cells in the form of cell necrosis, a decrease in cell number and size, and pancreatic cell degeneration compared to healthy rat in group K.

The K(-) group in Fig. 1b shows the most severe pancreatic cell damage compared to the other groups, namely cell necrosis of > 75%. Figure 1b shows very unclear cell boundaries (red), reduced cell numbers (blue), and almost all necrotic cells and abnormal cell shapes (green). While the K(+) group in Fig. 1c shows a necrosis rate of 50–75% islets of Langerhans, the boundary is not clear (red), the number of cells is reduced, necrotic cells are visible, and many cells are abnormally shaped (green). Figure 1d shows the histopathological picture of the P1 group where the islets of Langerhans have a necrosis rate of 25–50%, the cell boundaries are unclear (red), the number of cells is reduced, cell degeneration, and there are some abnormally shaped cells (green). The P2 group (Fig. 1e) showed the lightest level of damage, i.e., the necrosis rate of 1–25%. Figure 1e shows cell boundaries that are still clear (red), the number of cells begins to decrease, there is no visible necrotic cell, cell degeneration is starting to show, and the shape of the cells is still normal (green).

Furthermore, scoring was carried out on all sample preparations in the five treatment groups. The results of scoring damage to the islets of Langerhans are presented in Table 6. Table 6 shows that all samples in group K got a damage score of 0. This score indicates that the pancreatic cells in all control group samples were not damaged. On the other hand, all samples in the K(-) group got the highest pancreatic cell damage category score, 4. The K(-) group was the control group with STZ + NA induction without any treatment. The result of scoring 4 proves that STZ + NA induction can damage pancreatic cells, and there is no repair of pancreatic cells during the study.

Meanwhile, in the K(+) group, three samples got a score of 3, and 3 samples got a score of 4. A total of 2 samples in the P1 group got a score of 2, and as many as four samples got a score of 3. The higher scores indicated the four groups with cell damage. Langerhans cell damage that occurred in groups K(-), K(+), P1, and P2 was caused by STZ + NA induction. After peritoneal induction, STZ molecules enter cells via GLUT2, a low-affinity glucose transporter. Soon after, cell destruction occurs due to oxidative stress and DNA alkylation. Although most cells survive the initial effects of STZ, the pool of cells that survives mostly becomes dysfunctional and leads to elevated blood glucose levels (Hahn et al. 2020).

The results of the statistical analysis of group K(+), who received commercial enteral formula treatment, showed that there was no difference between group K(-) and group K(+) ($p > 0.05$). It shows that the damage to pancreatic cells that occurred in the K(+) group was the same as the damage to the K(-) group, and the repair of pancreatic beta cells in the K(+) group did not occur significantly. Commercial formulas are known to contain 1.7 mg of vitamin E per serving. Vitamin E helps repair pancreatic cells even though the changes that occur are not significant.

Meanwhile, groups P1 and P2, who received the intervention of enteral formula from local ingredients, showed significant differences with groups K, K(-), and K(+) ($p < 0.05$). It shows that formula administration can repair damage to pancreatic cells in groups P1 and P2, although it is not close to the condition of pancreatic cells in the control group. The P2 group who received a dose of the enteral formula 2.2 times higher also showed the lowest damage score. The statistical analysis results showed a significant difference between the P2 group and the other four groups. The P2 group experienced a greater improvement than the P1 group because the dose of the formula was 2.2 times greater than the P1 group.

The enteral formula is modified based on tempeh flour, yam flour, and sunflower seed flour which has benefits in repairing pancreatic cell damage. Tempe flour contains the amino acid arginine (21.5 mg/100 g soybean), which can repair pancreatic damage and protect pancreatic cells (Handoyo and Morita, 2006). Previous studies have shown that rats that received arginine supplementation for 30 days showed improvements in pancreatic cells, such as repairing the boundaries of most Langerhans' islets to normal and organized pancreatic acini (Hassani and Al-Mallak 2019). Tempeh flour also contains antioxidants in the form of isoflavone aglycone compounds such as genistein, daidzein, daidzin, and genistin (38.38 µg/g, 42.49 µg/g, 32.60 µg/g and 175.75 µg/g) (Kridawati et al. 2019; Kuligowski et al. 2017). Research on genistein in tempeh in vivo and in vitro with moderate to high doses showed a protective effect on pancreatic cells through the mechanism of repairing islet morphology in pancreatic cells accompanied by an increase in insulin immunoreactivity, reducing cell-pancreas damage and increased insulin levels (El-kordy & Muhammed, 2015). Isoflavone compounds in tempeh have also been investigated for their role in protecting pancreatic cells from apoptosis in the form of proliferation, increasing insulin secretion (Kridawati et al. 2019).

Jicama flour, which is rich in fiber, also indirectly protects pancreatic cells from more severe damage. Fiber can reduce the rate of gastric emptying, thereby reducing the absorption of sugar in the intestine, which can prevent damage to pancreatic cells due to high blood glucose levels (Santoso et al. 2020).

Sunflower seed flour is rich in vitamin E or tocopherol in the form of alpha-tocopherol (92.4%), which acts as a natural antioxidant (Anjum et al. 2012). STZ-induced pancreatic cell death is associated with cell apoptosis triggered by oxidative stress due to excessive intracellular ROS production (Butler et al. 2003). STZ induction also generates free radicals that directly cause oxidative damage to pancreatic beta cells (Varsha et al. 2015). Proper maintenance of antioxidant defenses may be effective in slowing the development of diabetes by maintaining the function of pancreatic cells (Pazdro & Burgess 2010). It is this vitamin E that plays a role in suppressing the increased oxidative stress and consequential apoptosis, thereby inhibiting and protecting against pancreatic cell damage (Varsha et al. 2015; Pazdro & Burgess 2010).

The results of the calculation of the number and diameter of the islets of Langerhans showed that there was no difference in the five groups. However, group P2 showed the highest number of Langerhans islands, which exceeded the number of Langerhans islands in group K. Group K(-) showed the least number of Langerhans islands. It indicates a decrease in the number of islets of Langerhans caused by the STZ effect, although the decrease experienced is not significant. The results of this decrease align with previous studies where STZ induction impacts the degeneration of islets of Langerhans cells caused by cell necrosis (El-Kordy & Alshahrani, 2015).

Conclusion

There is an effect of giving enteral formula made from tempeh, yam, and sunflower seeds flour on the histopathological picture of hyperglycemia-induced rat pancreas, especially in the repair of damage to pancreatic Langerhans cells.

Abbreviations

DM	Diabetes Mellitus
ICU	Intensive care unit
ASPEN	American Society for Parenteral and Enteral Nutrition
STZ	Streptozotocin
NA	Nicotinamide

Acknowledgements

Theis research is fully funded by the Non-Tax Revenue of the Faculty of Medicine, Universitas Diponegoro in 2021.

Authors' contributions

DNA, EM: conceptualized the study, designed experiments, supervised data collection and the study; LW: analyzed data, prepared the draft manuscript; MM, ANA, DYF: read and edited the manuscript. All authors read and approved the manuscript.

Funding

Theis research is fully funded by the Non-Tax Revenue of the Faculty of Medicine, Universitas Diponegoro in 2021.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

This research has been approved by the Health Research Ethics Committee, Faculty of Medicine, Diponegoro University (No.10/EC/H/FK-UNDIP/1/2022).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia. [2]Department of Physiology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia. [3]Department of Food Technology, Faculty of Animal and Agricultural Sciences, Universitas Diponegoro, Semarang, Indonesia. [4]Center of Nutrition Research (CENURE), Universitas Diponegoro, Semarang, Indonesia. [5]Department of Pharmacology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia.

Received: 1 February 2023 Accepted: 17 April 2023
Published online: 02 November 2023

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