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Probiotic (protexin) modulates glucose level in sucrose-induced hyperglycaemia in Harwich strain *Drosophila melanogaster*

Jimoh Abdulazeez^{1*}, Muhammad Zainab^{1*} and Aliyu Muhammad²

Abstract

Background: Probiotics are beneficial microorganisms that alter microbial flora to promote human and animal health by ameliorating the physiological and psychological hitches and distress. The aim of the study was to investigate the protective effect of probiotic (protexin) in sucrose induced hyperglycaemia in Harwich strain *Drosophila melanogaster*.

Methods: For lethal concentration, different concentrations of probiotic were fed on fresh breaded *D. melanogaster* for two weeks in two phases. The concentrations varied from 10 to 1000 mg. For increment in haemolymph glucose level, Insta-larva of 540 *D. melanogaster* was divided into six groups of thirty larva ($n = 30$) each in triplicate. Baseline glucose level was determined by administering group normal diet, while group 2–6 were fed with a normal diet containing 30% sucrose. For body weight, Eppendorf microtubes were weighed and anaesthetised flies were transferred into the tubes which were, re-weigh to get the actual weight of the flies before and after sucrose intake. Treatment supplement was introduced after flies emerged to be three days old. Group I: (Normal Control) received a normal cornmeal diet 30 g. Group II: (positive control) received normal diet + 30% sucrose only. Group III; received 10 mg of metformin/30 g diet. Group IV received 250 mg of probiotic/30 g of normal diet. Group V received 500 mg of probiotic/30 g normal diet. Group VI received 1000 mg of probiotic/30 g normal diet. All treatments lasted for 7 days. At the end of the treatment period, flies were immobilized and anaesthetised in ice and homogenised vigorously in 0.1 M phosphate buffer, pH 7.4. Eppendorf microtubes were weighed and anesthetized flies were transferred into them, and re-weighed with appropriate micro-litre of phosphate buffered saline (PBS) added and the flies were squashed to get the supernatant. The resulting homogenates were centrifuged at $10,000 \times g$, 4 °C for 10 min. The supernatant was separated from the pellets into labelled tubes and used for the various biochemical assays. Data were expressed as mean \pm standard error of mean (SEM) and subjected one-way analysis of variance (ANOVA), followed by Tukey post-hoc test for multiple comparisons between groups. Statistical package Graph Pad Prism version 8.1 was used for statistical analysis and values of $p < 0.05$ were considered significant. Lethal concentration, logic probit test software was used.

Results: The dosage of probiotic ranging from 10 to 1000 mg were not toxic to the fruit-fly. The LC_{50} of protexin after seven days was found to be greater than 1000 mg. Significantly ($p < 0.05$) decreased in hemolymph glucose concentration was recorded for the base-line (phase one) in the normal control group, compared to diabetic-induced groups.

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There was a significant ($p < 0.05$) decline in body weight and blood glucose level in all the treatment groups, when compared to the diabetic untreated group.

Conclusions: Administration of sucrose diet increased the blood glucose level and body weight in diabetic *D. melanogaster* flies, mitigated by administration of probiotics (protexins).

Keywords: *Drosophila melanogaster*, Probiotic, Hyperglycemia, Diabetes mellitus, Body weight

Background

Diabetes mellitus (DM) is a chronic endocrine disease with metabolic disorders and multiple etiologies. It is initially characterized by glucose impairment, leading to high blood glucose levels with carbohydrate, lipid and protein disorders as a result of insufficiency in insulin function (WHO 1999; Leslie et al. 2016). Type 1 diabetes occurred either due to autoimmune disease characterized by T-cell mediated destruction of beta-pancreatic cells that leads to metabolic disturbances or insensitivity of receptor to insulin action known as type 2 diabetes (Ozougwu et al. 2013). Elevation of blood glucose caused by disruption of carbohydrate, protein and fat metabolism leads to diabetic complications in several organs and tissues, including eyes, kidneys, nerves and blood vessels (Schlienger 2013). The most severe clinical manifestations are ketoacidosis or a non-ketotic hyperosmolar state that may lead to dehydration, coma and, in the absence of effective treatment, death (Leslie et al. 2016). Over the past decades, DM is becoming a serious international public health problem and very predominant disease, affecting people of different classes and races worldwide (Kavishankar et al. 2011). Report from International Diabetes Federation (IDF 2021) revealed that the menace presently affects well over 425 million people globally and, by 2045 the figure may reach 629 (IDF 2021).

D. melanogaster, known colloquially as the fruit fly, is common pest in homes, restaurants and places where food is served or rotten fruits are found. Their small size (2–3 mm), short generation time, the easy and inexpensive way to culture them in the laboratory, and their powerful genetic tools have established the *Drosophila* fly as one of the leading animal models for education and biomedical research (Millburn et al. 2016). The fly, *D. melanogaster* remains advantageous alternative organism to mammalian models for exploring different human pathologies, including metabolism-related disorders such as obesity and DM (Morris et al. 2012). *Drosophila* is an excellent model for investigating DM because approximately 74% of human disease-causing genes are conserved in this species, and more importantly, the mechanisms of glucose homeostasis are highly conserved between mammals and *Drosophila* (Graham and Pick, 2016). Many researchers have demonstrated that a high

sugar diet elicits insulin-resistant phenotypes in *Drosophila* that represents the pathophysiology of T2DM in humans. The phenotypes are observed by increase in fat deposition and circulating glucose level and shortened life-span in adult flies (Pasco and Leopold, 2012). The *Drosophila* genome codes for seven several insulin-like peptides, which are secreted from the insulin-producing cells (IPC) of the brain. There are eight *Drosophila* insulin-like peptide (DILP8) which act as a relaxin homolog, binding to a different type of receptor, and controlling corporal symmetry (Colombani et al. 2015). According to Food and Agriculture Organization of the United Nations (FAO 2002) and World Health Organization (WHO 2016) working group experts, probiotics are “live strains of strictly selected microorganisms that, when consumed in sufficient amounts, confer a health benefit to humans (Hill et al. 2014). They are prepared in the form of yogurt, fermented foods and capsule supplements such as pills, powders, and liquid drops, and in functional foods (soy-based products, cabbage, maize) (Senok et al. 2005; Sivamaruthi et al. 2019). The widest strains of probiotics *Bifidobacterium* and *Lactobacilli* have been thought to pretense efficacy for the management of hyperglycemia in diabetes mellitus (Kohnert et al. 2015). *Bifidobacterium* genus is a Gram-positive, rod shape, non-motile, non-spore-forming and anaerobic organism. Interestingly, protexin contain both strains of these active probiotics. In many animal species, various types of *bifidobacteria* colonize the intestinal tract (Zhang et al. 2003).

Protexin is a multi-strains probiotic that contain different types of strains which include *Lactobacillus plantarum*, *Lactobacillus delbrueckii subsp. bulgaricus*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Bifidobacterium bifidum*, *Streptococcus salvarius subsp. thermophilus*, *Enterococcus faecium*. Probiotics are of different strains and two strains widely used in functional foods and dietary supplements are *Lactobacillus* and *Bifidobacterium*. The other strains are *Bacillus*, *Streptococcus*, *Escherichia coli* strain, yeasts and *Saccharomyces* (Gomes et al. 2014). They are present in natural products, but they may also be added to food. Probiotics alter the composition of the gut microbiome, which enhances the attainment microbial balance. The change in the gut microbiome and its fermentation may

favour the pathologic conditions associated with type 2 DM (Everard and Cani 2014), and subsequently beneficial in prophylactic and therapeutic intervention in T2DM. Combining the gut microbiota with appropriate medication, has emerged as a promising and novel intervention to fight the looming worldwide diabetes epidemic (Cardinali et al. 2020). In recent decades, several trials have been conducted to evaluate the antidiabetic nature of probiotic preparations (Sivamaruthi et al. 2019). Therefore, the aim of the study was to investigate the modulatory effect of Probiotic (Protexin) in Sucrose Induced Hyperglycaemia in Harwich strain *Drosophila melanogaster*.

Methods

Reagents

Multi-strains Probiotic (Reg. No. G1265 Act 36/1947, Benrose, South Africa), Agar-agar, Nipagin, Cornmeal, Sucrose, baker's yeast, Phosphate buffered saline, ethanol, water, normal saline, *Drosophila* INSL3 Elisa kit 48 tests (CK-bio-20744, Shanghai Coon Koon Biotech Co., Ltd).

Instruments

Hand lens, spectrophotometer (Beuckman DU640 UV/VIS), forceps, vials, foam plug, Eppendorf tubes, panit brush, Petri-dish, weighing machine, centrifuge machine (KJLC-I centrifuge Model KX3400C) (KENXIN Intl. Co., Hong Kong).

Experimental flies

Drosophila melanogaster (Harwich strain) was obtained from the Department of Biological Sciences, Faculty of Life Sciences, Ahmadu Belo University, Zaria, Nigeria. The flies were maintained and reared on normal diet made up of cornmeal medium, containing 1% w/v brewer's yeast, 0.08% v/w nipagin and agar-agar at constant temperature and relative humidity (25 ± 1 °C; 60%, respectively) under 12 h dark/light cycle conditions.

Techniques

The LC_{50} of probiotic (Protexin) in *Drosophila melanogaster* was determined using different concentrations of probiotic on fresh-breaded *Drosophila melanogaster* for a period of two weeks in two phases following the procedure of Bele and Khale (2014), with some modifications. Percentage inclusion of probiotic was selected at levels at which it did not show significant toxicity to the flies by estimating the lethal concentration (LC_{50}) Table 1.

The methodology used in induction (diet containing 30% sucrose and 30 g cornmeal diet) and treatment (diet containing 30% sucrose, 30 g cornmeal and

Table 1 Phases of the LC_{50} in determining the dose of Probiotic to administered to *Drosophila melanogaster*

Groupings	Concentrations
Phase I	
Group I	10 mg of probiotic per 10 g fly diet
Group II	20 mg of probiotic per 10 g fly diet
Group III	30 mg of probiotic per 10 g fly diet
Group IV	40 mg of probiotic per 10 g fly diet
Group V	60 mg of probiotic per 10 g fly diet
Group VI	70 mg of probiotic per 10 g fly diet
Phase II	
Group I	100 mg of probiotic per 10 g fly diet
Group II	200 mg of probiotic per 10 g fly diet
Group III	250 mg of probiotic per 10 g fly diet
Group IV	500 mg of probiotic per 10 g fly diet
Group V	750 mg of probiotic per 10 g fly diet
Group VI	1000 mg of probiotic per 10 g fly diet

probiotic 250 mg, 500 mg and 1000 mg) was adopted from Omale et al. (2020), with some modification. Briefly, flies of both sexes were mixed and kept in a humidified (60%), temperature-controlled incubator with 12 h on/ off light cycle at 24 degrees/C in 2.5×6.5 cm bottles containing 30 mL standard cornmeal medium. Experiments commenced on the 2nd day after fertilization because the fly offspring were in the second instar lava stage. Larval period was chosen for the ingestion period because the larvae presented higher feed rate, rapid growing and sexual immaturity compared to adults.

For collection of larvae, approximately 10 female flies were allowed to lay eggs in different valves containing a medium enriched with yeast to oviposition during a period of 6 h. After 24 h, 50 first instar larvae (L1) were rinsed in 0.5% (v/w) sodium hypochlorite solution and 1% phosphate buffer saline (PBS), and then transferred to the culture medium from each treatment with a paint brush. This asepsis method was performed to reduce the number of microorganisms that could proliferate in adherent culture medium and interfere in the larval growth and survival. After 48 h, the second instar larva (both genders, 2–3 days old) was divided into six groups containing 50 larva each (three replicates per group) (Table 2). The induction lasted till flies emerged to three days of age and intervention was carried out for a period of 7 days.

Before intervention, 20 lavas (already adult flies) were picked at random from each valve and were homogenized, squash in an Eppendorf tube, containing PBS and the supernatant was used to access base-line glucose level.

Table 2 Experimental animal grouping of sucrose diet induced *Drosophila melanogaster* administered with Probiotic (protexin)

Grouping	Induction	Treatment
Group I	Control (place on normal diet)	No treatment
Group II	Experimental control group (diet + 30% sucrose)	No treatment
Group III	Experimental group (diet + 30% sucrose)	10 mg of metformin per 10 g fly diet
Group IV	Experimental group (diet + 30% sucrose)	250 mg of probiotic per 10 g fly diet
Group V	Experimental group (diet + 30% sucrose)	500 mg probiotic per 10 g fly diet
Group VI	Experimental group (diet + 30% sucrose)	1000 mg of probiotic per 10 g fly diet

Measurement of body weight

The flies were placed in Eppendorf microtubes. The initial weight of the tube was subtracted from the weight after introduction of flies to get the initial weight (before induction). Weight was also obtained after administration of sucrose diet by subtracting it from the initial weight of Eppendorf microtubes (after induction) and probiotics (after treatment).

Estimation of lymph glucose level

Estimation of lymph glucose level was done using the procedure and calculation of spectrum diagnostics liquizyme. Glucose reagent was determined after enzymatic oxidation in the presence of glucose oxidase. The formed hydrogen peroxide reacted under catalysis of peroxidase with phenol and 4-nitrogen phyline forming a red violet dye. It was then mixed and incubated for 10 min at 37 °C for 20 min at 15–25 °C. The absorbance of the specimen was measured and standard against reagent of ink within 30 min.

$$\text{Glucose concentration (mg/dL)} = \frac{\text{absorbance of specimen}}{\text{Absorbance of standard}} \times 100$$

Statistical analyses

Data were expressed as mean ± standard error of mean (SEM) using one-way analysis of variance (ANOVA), followed by *Tukey* post-hoc test for multiple comparisons between groups. Statistical package, GraphPad Prism version 8.1 was used for the analyses. Values of $p < 0.05$ was considered statistically significant, and lethal concentration, logic probit test software was used.

Results

Figure 1 shows the Lethal concentration of multi-strain probiotic (protexin), in two phases (lesser dose and higher dose). There was no significant difference in mortality in the first phase and higher concentrations (100 mg/30 g diet–1000 mg/30 g diet) of the second phase.

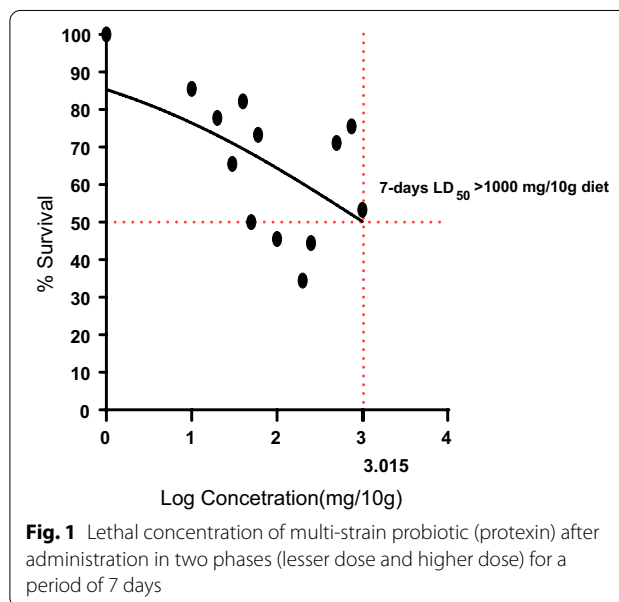


Fig. 1 Lethal concentration of multi-strain probiotic (protexin) after administration in two phases (lesser dose and higher dose) for a period of 7 days

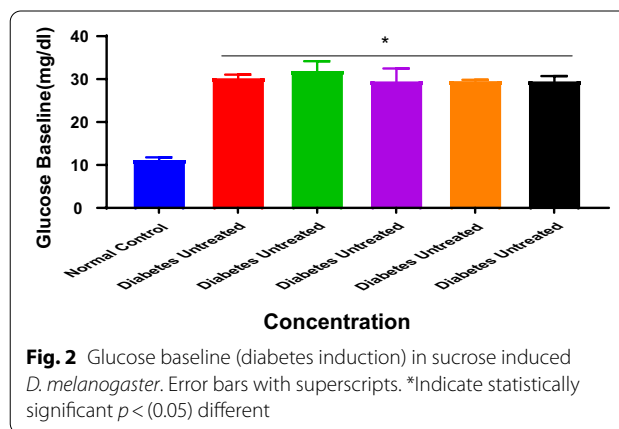


Fig. 2 Glucose baseline (diabetes induction) in sucrose induced *D. melanogaster*. Error bars with superscripts. *Indicate statistically significant $p < (0.05)$ different

Figure 2 glucose concentration measured after the induction of diabetes significantly ($p < 0.05$) increased to 30.07 ± 0.977 mg/dL, 31.77 ± 2.417 mg/dL, 29.37 ± 3.121 mg/dL, 29.4 ± 0.4359 mg/dL and 29.33 ± 1.391 mg/dL in all the diabetes groups

compared to normal control group 11.03 ± 0.7424 mg/dL.

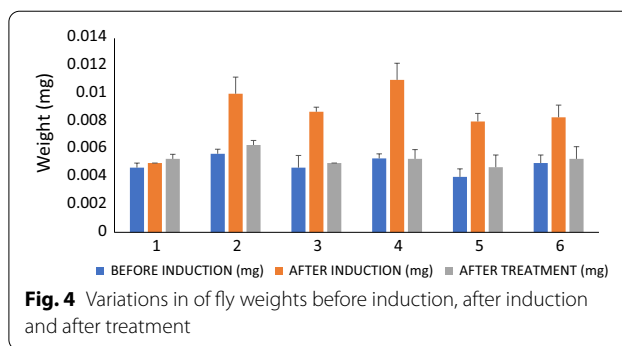
Figure 3 glucose concentration significantly ($p < 0.05$) elevated 30.07 ± 0.977 mg/dL in diabetes untreated group compared to normal control 11.03 ± 0.7424 mg/dL. Significant decrease was also found in metformin 11.4 ± 0.6245 mg/dL and probiotic 250 mg (11.37 ± 0.8373 mg/dL) 500 mg (12.23 ± 0.636 mg/dL) and 1000 mg (11.2 ± 0.3606 mg/dL) when compare with diabetic untreated group. Diabetes show ($p > 0.05$) when compared to the control.

Figure 4 shows that weight significantly ($p < 0.05$) elevated in the groups after induction group compared to before induction and after receiving treatment in the groups.

Figure 5 shows significant increase in size of the diabetic fly at the top with consumptions of sucrose diet, compared with the normal fly of the same age.

Discussion

Scores of researchers have attempted to control hyperglycemia in DMT2 and if the absorption of glucose in the intestines is limited, then hyperglycemia could manage the body system (Kohnert et al. 2015; Tahrani et al. 2013). To limit the absorption of glucose in the intestine, an attempt to change the microflora of the intestine can be done with those which utilize glucose only. Regular intake of probiotics before meals can increase the population of microbes that can use only glucose as their sole source of energy. Microbes such as probiotics can oxidize glucose through anaerobic glycolysis to lactic acid, which can be absorbed into the blood and move to the muscles, brain, liver, and kidneys for energy production and utilization (Nieuw-dorp et al. 2014). The results obtained from the study showed no significant difference in mortality among the concentrations and control in the first phase of this study. At higher concentrations (100 mg/30 g diet–1000 mg/30 g diet) of the second phase, there was also



no significant mortality, indicating the supplement was not toxic to *D. melanogaster*. The results obtained from the first and second phase of mortality study shows that probiotics exhibited no toxicity and was not toxic to *D. melanogaster*.

From the result the obtained, increase in glucose concentration in the groups fed with sucrose diet compared to normal diet group indicate that diabetes has been induced. The result of this present study also supports the previous findings of Omale et al. (2020), who demonstrated an increase in hemolymph glucose level in groups fed with high sucrose content for ten days to induce type 2 diabetes in the *D. melanogaster* flies.

Although after the administration of probiotic supplement, the glucose concentration significantly decreased in treatment groups compared to hyperglycemia untreated group, the potential mechanisms underlying the effects of probiotics on glycaemia-related parameters have not been fully understood. The decrease in haemolymph glucose level after administration of probiotic may be due the action of the gut microbiota, which plays a key role in maintaining the intestinal homeostasis. According to Yadav et al. (2008), a probiotic-supplemented fermented milk product called Dahi (yogurt) dramatically suppressed diet-induced insulin resistance and protected from streptozotocin-induced diabetes in animal models. It was also observed that

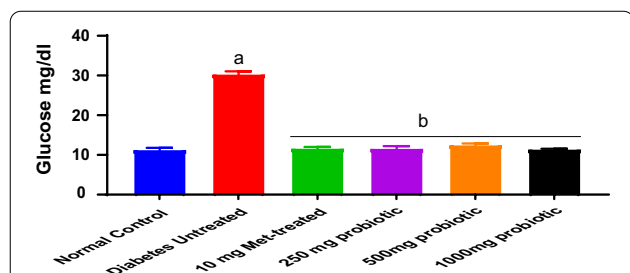


Fig. 3 Haemolymph glucose level after treatment with probiotic. Error bars having different superscript letters ^{a,b} Indicate statistically significant $p < (0.05)$ different

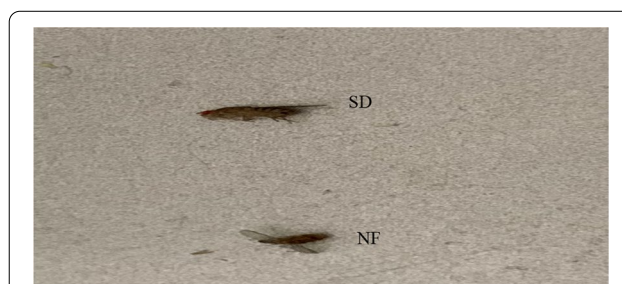


Fig. 5 Male *Drosophila* fly fed with sucrose diet (SD) at the top versus normal fly fed with standard feed below (NF)

probiotic Dahi suppressed the diabetes progression and its complication by enhancing the antioxidant system.

The gut microbiota is composed mainly of bacteria of the *Firmicutes* phylum (the dominant genus *Lactobacillus*) and smaller portions of Proteobacteria (*Acetobacter* is the dominant genus) also exist in its microbiota composition (Softic et al. 2017). *Firmicutes* are the main "good" bacteria that reside in the microbiota, and their increased in numbers provide notable benefits, including protection against chronic inflammatory diseases, such as diabetes. It is postulated that endogenous intake of probiotic (good bacteria) leads to increase in Firmicutes in the gut microbiota, which decreases the haemolymph glucose level in groups administered with probiotics (Rutter et al. 2015).

The effect of probiotic bacteria on glucose metabolism is probably due to their immune-modulating properties and probiotic bacteria strains which enhance the composition and function of the intestinal microflora (Softic et al. 2017). The probiotic bacteria stimulate the bacterial endotoxin transport into the bloodstream, and increase the circulation of lipopolysaccharide and proinflammatory cytokines, which decreases inflammation (Rezaei et al. 2017). Therefore, probiotic bacteria decrease insulin resistance (Rutter et al. 2015). Studies also revealed that mechanisms associated with gut flora-mediated pathology of diabetes is through: increased energy harvest, increased blood LPS levels (endotoxemia) and low-grade inflammation (Delzenne et al. 2011). These make modulation of gut flora considered as a potential target to treat diabetes. Probiotics are novel gut flora modulators, and their role in the prevention of and diabetes treatment has been implicated in the recent past. Metformin is a standard drug for diabetes and it reduces the amount of sugar released by the liver into the blood (hepatic gluconeogenesis). It also enhances intestinal glucose uptake from the circulated glucose in the blood by accumulating it into the mucosa of the small intestine. Probiotics have a similar mechanism of action in terms of absorption of glucose in the intestine, which may be the reason why it is able to reduce haemolymph glucose level. The result of the study agrees with that of Adefegha et al. (2020), who demonstrated that feeding *Drosophila melanogaster* with high sucrose diet increases in haemolymph glucose level, when compared with flies fed with normal cornmeal diet. The findings of Omale et al. (2020) also demonstrated an increase in haemolymph glucose level in groups fed with high sucrose content for 10 days to induce T2DM in *D. melanogaster* flies. Also in consonant with our findings is the work of Sambo (2019), who investigated the potential anti-diabetic activities of probiotic strains, *L. acidophilus* and *L. bulgaricus*

against fructose-fed hyperglycemic rats. The result of the present study further demonstrated that probiotic does not exert hypoglycaemic effect as the glucose level did not go below normal control value. This finding further shows that probiotic could be safe to use in normoglycaemic subjects.

It has been known that patients with T2DM have long-term obesity, followed by the gradual onset of fat metabolic abnormalities. In this study, similar symptoms were observed in high sucrose diet-fed *Drosophila* flies, that recorded a slight increase in body fat storage, compared to the normal diet fed flies. The fat accumulation may be the reason for the increase in the body weight.

Conclusions

Our findings reveal that probiotics is non-lethal and safe to use. Administration of multi-strain probiotic (Pro-texin) mitigates hyperglycaemia and increased body weight induced by sucrose sugar diet in *D. melanogaster*.

Abbreviations

T2DM: Type-2 diabetes mellitus; LC₅₀: Lethal concentration; DM: *Drosophila melanogaster*; DILP8: *Drosophila* insulin-like peptide.

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Author contributions

All authors read, approved the final manuscript and contributed equally in this research. The final manuscript was reviewed and approved by all the authors. MZ and JA carried out the laboratory work. AL analysed and interpreted the data on the blood glucose level, body weight and median lethal concentration.

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Availability of data and materials

Relevant data are included within the paper. Corresponding author has possession of all the raw data available for assessment by interested researchers.

Declarations

Ethical approval and consent to participate

Study was approved by the ethical committee of Ahmadu Bello University, Zaria, Nigeria in accordance with the principles guiding the use and handling of experimental animals.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

- Adefegha SA, Opeyemi BO, Oboh G (2020) Purple onion in combination with garlic exerts better ameliorative effects on selected biomarkers in high-sucrose diet-fed fruit fly (*Drosophila melanogaster*). *Comp Clin Pathol* 20:03117–03119
- Bele A, Khale A (2014) Phytochemical screening of aloe vera; An overview. *Int J Adv Pharm Res* 5(8):363–367
- Cardinali N, Bauman C, Ayala FR, Roberto G (2020) Two cases of type 2 diabetes mellitus successfully treated with probiotics. *Clin Rep* 4:1–6
- Colombani J, Andersen DS, Boulan L (2015) *Drosophila* Lgr3 couples organ growth with maturation and ensures developmental stability. *Curr Biol* 25(20):2723–2729
- Delzenne NM, Neyrinck AM, Backhed F, Cani PD (2011) Targeting gut microbiota in obesity: effects of prebiotics and probiotics. *Nat Rev Endocrinol* 7:639–646
- Everard A, Cani PD (2014) Gut microbiota and GLP-1. *Rev Endocr Metab Disord* 15:189–196
- Food and Agriculture Organization (FAO) (2002) Guidelines for the Evaluation of Probiotics in Food; Report of a Joint FAO/WHO Working Group on Drafting Guidelines for the Evaluation of Probiotics in Food; FAO: London, ON, Canada
- Gomes AC, Bueno AA, de Souza RG, Mota JF (2014) Gut microbiota, probiotics and diabetes. *Nutr J* 13:60
- Graham P, Pick L (2016) *Drosophila* as a model for diabetes and diseases of insulin resistance. *Curr Top Dev Biol* 121:397–419
- Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B (2014) Expert consensus document: the international scientific association for probiotics and prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol* 11(8):506–514
- International Diabetes Federation (2021) Diabetes Atlas. 10th Edition
- Kavishankar GB, Lakshmi Devi N, Mahadeva MS (2011) Diabetes and medicinal plants review. *Int J Pharm Biomed Sci* 2(3):65–80
- Kohnert KD, Heinke P, Vogt L, Salzsieder E (2015) Utility of different glycemic control metrics for optimizing management of diabetes. *World J Diabetes* 6:17–29
- Leslie RD, Palmer J, Schloot NC, Lernmark A (2016) Diabetes at the crossroads: relevance of disease classification to pathophysiology and treatment. *Diabetologia* 59:13–20
- Millburn GH, Crosby MA, Gramates LS, Tweedie S, FlyBase C (2016) FlyBase portals to human disease research using *Drosophila* models. *Dis Model Mech* 9(3):245–252
- Morris SNS, Coogan C, Chamseddin K, Fernandez-Kim SO, Kolli S, Keller JN (2012) Development of diet-induced insulin resistance in adult *Drosophila melanogaster*. *Biochim Biophys Acta* 1822:1230–1237
- Nieuwdorp M, Gijljamse PW, Pai N, Kaplan LM (2014) Role of the microbiome in energy regulation and metabolism. *Gastroenterology* 146:1525–1533
- Omale S, Aguiyi JC, Bukar BB, Ede SO, Amagon KI, Amagon L, Usman O, Chinello V, Oshibanjo DO (2020) Fruiting body of *pleurotus ostreatus* reduces serum glucose and modifies oxidative stress in type 2 diabetic: *Drosophila melanogaster* (Fruit-Fly). *Adv Pharmacol Pharm* 8(3):41–50
- Ozougwu JC, Obimba KC, Belonwu CD, Unakalamba CB (2013) The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. *J Physiol Pathophysiol* 4(4):46–57
- Pasco MY, Leopold P (2012) High sugar-induced insulin resistance in *Drosophila* relies on the lipocalin neural lazarlillo. *PLoS ONE* 7:365–383
- Rezaei M, Sanagoo A, Jouybari L, Behnampoo N, Kavosi A (2017) The effect of probiotic Yogurt on Blood glucose and cardiovascular Biomarkers in patients with type II diabetes. *A Randomized Control Trial* 6(4):25–35
- Rutter GA, Pullen TJ, Hodson DJ, Martinez-Sanchez A (2015) Pancreatic beta- cell identity, glucose sensing and the control of insulin secretion. *Biochem J* 466(2):203–218
- Sambo RS (2019) The effect of probiotic bacteria on high sugar diet induced diabetes Type-2 symptoms in fruit fly with focus on lipid metabolism. Bachelor Degree Project in Biomedicine, University of Skovde.
- Schlienger JL (2013) Type 2 diabetes complications. *La Presse Med* 42(5):839–848
- Senok AC, Ismaeel AY, Botta GA (2005) Probiotics: facts and myths. *Clinical Microbiology Infection* 11(12):958–966
- Sivamaruthi BS, Prasanth MI, Kesika P, Chaiyasut C (2019) Role of probiotics in human mental health and diseases-a mini review. *Trop J Pharm Res* 7:167–178
- Softic S, Gupta MK, Wang GX, Fujisaka S, O'Neil, I B. T. and Rao, T. N. (2017) Divergent effects of glucose and fructose on hepatic lipogenesis and insulin signaling. *J Clin Invest* 127:4059–4074
- Tahrani AA, Barnett AH, Bailey CJ (2013) SGLT inhibitors in management of diabetes. *Lancet Diabetes Endocrinol* 1:140–151
- World Health Organization (1999) Definition, Diagnosis and Classification on Diabetes Mellitus and its Complications. World Health Organization Department on Non-Communicable Disease Surveillance, Geneva
- World Health Organization (2016) Diabetes Mellitus and its Complications. World Health Organization Department on Non-Communicable Disease Surveillance, Geneva
- Yadav H, Jain S, Sinha PR (2008) Oral administration of dahi containing probiotic *Lactobacillus acidophilus* and *Lactobacillus casei* ameliorated the Streptozotocin-induced oxidative stress and dyslipidemia in rats. *J Dairy Res* 75:189–195
- Zhang F, Ye C, Li G, Ding W, Zhou W, Zhu H (2003) The rat model of Type 2 diabetic mellitus and its glycometabolism characters. *Exp Anim* 52:401–407

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