The Effectiveness of “X” Kefir Brand Towards Glucose Level on Post Prandial Pre-Diabetes Male Mice (Mus Musculus) Swiss Webster Strains Orally

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Abstract. Pre-diabetes prevalence to diabetes is increasing every year. This pre-diabetes is based on pancreatic β cell disorder and insulin resistance causing abnormalities of body metabolism. However, in pre-diabetes this disorder has not been seen as real. The use of fermented milk in the world of health is very useful because in the milk there are many beneficial microorganisms for the body so it is expected to be an alternative ingredient in prevention earlier in pre-diabetes so as to reduce the adverse effects that occur. Research has been conducted with the aim to find out the effect of fermented milk that is kefir on post prandial blood glucose level on male mice (Mus musculus) Swiss webmaster of pre-diabetes orally. Male mice were made pre-diabetes by giving alloxan 100 mg / kg BW. The samples were 25 mice divided into 5 groups with each of 5 mice, 2 control group were negative and positive control, they left sick and given glibenclamide as much as 0.013 mg / 20 gr BB, treatment group was given various dose of kefir with various variations of 0.32 mg / 20 gr BB, 0.65 mg / 20 gr BB and 1.3 mg / 20 gr BB. The results showed a significant difference (p <0.05) on fasting glucose examination and 2 hours post prandial after administration of kefir with various doses and showed an effect of kefir for blood glucose in mice (Mus musculus) is dosis 1 of 78.28 mg/dl.

1. Introduction
Pre-diabetes is a condition of blood glucose levels in above normal but it is not Diabetes Mellitus diagnosed. The American Diabetes Association (2016) states that pre-diabetes is characterized by fasting blood glucose levels of 100-125 mg / dl and blood glucose 2 hours after eating 140-199 mg / dl. Pre-diabetes conditions can naturally develop into diabetes (Twigg & Duffield, 2009). In addition, it can increase the risk of atherosclerotic disease caused by endothelial damage on blood vessels due to increased blood glucose and can increase heart disease and other macro vascular diseases (Ciccone, et al, 2014). Diabetes also causes hyperinsulinemia which plays a role in increasing the re-absorption of uric acid in the proximal renal tubules resulting in hyperuricemia which leads to the condition of diabetes (Ellyza et al, 2012).

One of alternatives to decrease pre-diabetes in order not to lead into Diabetes is by using pro-biotic milk. Kefir is a pro-biotic milk made of fermented milk with kefir seed, which contains about 40 types of bacteria (beneficial bacteria) and yeast which is useful, where kefir is easily obtained and the
containing of microorganisms in kefir can increase the immune system so that it becomes a preventive consideration in handling diabetes.

This study aims to determine the effectiveness of kefir in reducing glucose 2 hours post prandial in male mice (Mus musculus) Swiss Webster strains pre-diabetes orally.

2. Methods
2.1. Tools and materials
Kefir, Male Mice, Aloksan, Glibenclamide, glucose strip tests

2.2. Preparation of male mice Swiss Webster
Test animals in the form of 25 male mice Swiss Webster strain which had inclusion criteria in the form of age range 2-3 months, body weight 25-30 grams, behavior and normal activity and no visible anatomical abnormalities. While the exclusion criteria included mice appearing ill, there were abnormalities of anatomy and dead mice. Then healthy mice were examined for fasting blood glucose levels (pre test).

2.3. Alloxan Induction
Alloxan was given in mice as much as 100 mg / Kg BW and gave regular food for 4 days and distilled water until it experienced pre-diabetes namely blood glucose levels of 130 - 200 mg / dl.

2.4. Treatment and dosing of test animals
Test animals that were already in pre-diabetes, they were divided into 5 groups: positive control, negative control and three treatments, namely treatment 1 with a dose of 0.32 mL / 20g BB mice, treatment II with a dose of 0.65 mL / 20g BB, and treatment III with dose of 1.3 mL / 20g BB. After being given treatment for 14 days, the blood glucose level 2 hours post prandial was examined.

3. Result and discussion
To examine the effect of kefir on post prandial blood glucose, mice were first given 100 mg / kg BB injection of alloxan monohydrate. A dose of 100 mg / kg BB (Nandhagopal, K et al, 2013) to enter the criteria for pre-diabetes. A dose of 100 mg / kg BB is chosen, because it is expected that Langerhans β cells can still produce.

Alloxan is dissolved in 0.89% NaCl. After that, the mice in negative control, positive control, and treatment control (low, medium, and high doses) were induced by alloxan intraperitoneally. Positive control in this study is glibenclamide, needed to see antidiabetic drugs that have proven its efficacy to reduce blood glucose levels. Negative control to determine blood glucose levels of pre-diabetes mice that have been induced by alloxan, and treatment control (low dose, moderate dose and high dose) to determine the effect of giving kefir in mice (pre-diabetes) during the trial period.

Induction period for 4 days where blood glucose levels are between 130-200 mg / dl. Administration of kefir and glibenclamide as pre-diabetes therapy was given to mice orally for 14 days. Glibenclamide was chosen because it can stimulate insulin secretion in the pancreatic gland (MOH, 2005). The dose of glibenclamide used was 0.013 mg / 20 g BB. The dose is used based on an effective oral dose in humans, which is 5 mg / day then converted to mouse doses. The provision of kefir preparations is given to liquid preparations without any addition. The average measurement results on the positive control showed the results of blood glucose levels under negative control, this is because in addition to be given alloxan 100 mg / kg BB also given glibenclamide as much as 0.013 mg / 20 g BW, this glibenclamide results from the conversion of human doses to mice. Where in humans is the dose of glibenclamide 5 mg / 60 mg BB (Suherman, 2007). Glibenclamide is a drug that belongs to the second type of sulfonylurea which can be used as an oral antidiabetic drug which can reduce blood glucose concentration. Glibenclamide lowers blood glucose by stimulating the body to release more insulin.
Figure 1. The effectiveness percentage of kefir on blood glucose levels in mice

Among the three groups of test doses used, the effectiveness of kefir at dose 1 resulted in an average value of fasting glucose levels of 54.55 mg/dl, and 2 hours of post prandial namely 78.28 mg/dl, then the test group dose 2 produced an average value the average fasting glucose level was 53.37 mg/dl, and 2 hours post prandial was 59.56 mg/dl, then the dose 3 group produced an average fasting glucose value of 56.36 mg/dl, and 2 hours post prandial namely 73.92 mg/dl so that the effectiveness of kefir on the blood glucose levels of the largest mice was at dose 1 of blood glucose examination 2 hours post prandial at 78.28 mg/dl. The average value of glucose level in the test group was dose 1, dose 2, and dose 3 was below the average glucose level of the negative control group. This is because in the three groups of test doses, in addition to being given alloxan induction were also given a variety of kefir preparations, but there was a decrease and increase in examination 2 hours post prandial due to the effect of activity, diet and stress levels in mice when conducting experiments.

In this study the material uses kefir because it is rich in calcium, amino acids, magnesium, various B vitamins, vitamin K, zinc, and folic acid. The benefits of consuming kefir consistently can stimulate the formation of the immune system or the immune system. Bacteria Lactic acid in kefir can be a source of pro-biotics, as pro-biotics can be useful in suppressing the population of pathogenic bacteria in the digestive tract.

4. Conclusion
Based on the results of the study it can be concluded that the effectiveness of kefir on the reduction in post prandial blood glucose levels is the largest at dose 1 of 78.28 mg/dl.

NB :
Kn : Negative control
Kf : Positive control
D1 : Dose 1
D2 : Dose 2
D3 : Dose 3
Gdp : Fasting glucose
2jpp : 2 hours post prandial
5. Reference

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Acknowledgement

This research was done at the Health Analyst Study Program of Bakti Tunas Husada STIKes and received financial assistance from P3M STIKes BTH Tasikmalaya. We also would like to thank the Chairperson of Tasikmalaya BTH STIKes who have supported us to continue working on research.