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## Potential of Turmeric- Tamarind Beverage (*Curcuma domestica* Val. – *Tamarindus indica* L.) To Decrease Blood Glucose in Hyperglycemic Mice.

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### ABSTRACT

The objectives of this study were to measure the inhibition of turmeric-tamarind beverage on the activity of  $\alpha$ -glucosidase enzyme, to determine the quantity of intake capable of decreasing blood glucose level and to know the effect of turmeric-tamarind beverage on blood glucose level and superoxide dismutase (SOD) in diabetic mice. The study was conducted in 3 stage with using a complete randomized design (CRD). The first stage with five treatment of concentrations turmeric-tamarind as follows: control, (10, 20, 30, 40.50) mg/kg. The second stage with 7 treatments, namely: negative control (not given turmeric-tamarind beverage and not hyperglycemic), positive control (not given turmeric-tamarind beverage and hyperglycemic), to be given turmeric-tamarind beverage of 50, 100, 150, 200 mg/kg bw on hyperglycemic condition, and positive control of hyperglycemic with using acarbose 4.5 mg/kg bw. The third stage with 4 treatments i.e. groups of mice that are not given turmeric-tamarind beverage and not diabetes, the group of mice were given turmeric-tamarind beverage and not diabetes, group of diabetic mice not given turmeric-tamarind beverage, group of diabetic mice to be given turmeric-tamarind beverage of 100 mg/kg. The results showed that turmeric-tamarind beverages have the ability to inhibit the activity of the  $\alpha$ -glucosidase enzyme. At a concentration of 20 ppm has the highest percentage of inhibition of the enzyme activity. Provision of turmeric-tamarind beverage of 100 mg/kg bw of mice produced the lowest decrease in blood glucose levels in hyperglycemic mice. Turmeric-tamarind beverage can reduce blood glucose levels of diabetic mice. Turmeric-tamarind beverage intake of 100 mg/kg bw mice, will cause a decrease in blood glucose level of 55.83 mg/dL, whereas in mice that is not given intake, decreased blood glucose only 22.71mg/dL. Turmeric-tamarind beverage is also able to maintain the activity of SOD enzymes and the provision of this beverage can overcome the decrease of SOD in mice liver.

**Keywords:** turmeric and tamarind,  $\alpha$  - glucosidase, blood glucose, hyperglycemic, SOD enzyme

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## INTRODUCTION

One of traditional Indonesian beverages which are made from turmeric and leaves of tamarind to be called sinom beverage. This beverage has potential to develop as a functional beverage. This product is so popular that it becomes one of the leading products of the largest producers of herbal beverage in Indonesia (Anon., 2008). In the marketing, the sinom product got award as Best Product Encouragement Prize at International Conference of the 8th ASEAN Food in Vietnam (Anonymous, 2008).

Some bioactive compounds in turmeric rhizomes such as ascorbic tamarind, p-carotene, caffeine tamarind, curcumin, eugenol, cumaric (Suhaj, 2006) strongly support its benefits as a functional beverage. The yellow color of turmeric show the presence of 3 main pigments that is curcumin 1,7-bis (4- hydroxy-3-methoxyphenyl) -1,6-heptadiene-3,5-dione, demethoxy -curcumin and bis demethoxy -curcumin (Suhaj, 2006). This curcumin compound is known to have high antioxidant activity (Sharma et al, 2005 and Cousins et al., 2007), anti-inflammatory (Lin et al., 1997), anti-cancer (Huang et al., 1994; Kunchandy and Rao, 1990; Sharma et al ., 1994). Tamarind fruits show potential as anti diabetic and anti hyperlipidemic (Maiti et al., 2005; Maiti et al., 2004), antioxidants (Siddhuraju, 2007; Maisuthisakul et al., 2008 and Chanwitheesuk, 2005). According to Mulyani, et al, (2006), sinom beverages has been shown to contain bioactive components in the form of flavonoid antioxidants that can inhibit the process of fat oxidation.

In the processing of sinom beverage, heating of tamarind leaves for 2.5 minutes yields total phenols of 0.75 mg/100g, antioxidant capacity of 0.053 mg eq / 100g and vitamin C of 0.252 mg/100g, and has the highest ability in inhibiting malonaldehyde (MDA) (Mulyani, et al, 2012). Suwariani and Suhendra (2008) also reported that extracts of turmeric have the ability to inhibit the formation of malonaldehyde (MDA) in the process of fat oxidation. MDA is one of the products of fat oxidation in cell membranes in the body.

Tests of antioxidant activity of powdered turmeric-tamarind beverage (Mulyani et al. 2006) and liquid (Mulyani et al, 2011) are only done in vitro, whereas for health need testing to be done by in vivo. Antioxidant turmeric-tamarind beverage including flavonoid group that are known to reduce blood glucose or prevent diabetes mellitus (DM) disease. The initial symptoms of diabetes mellitus disease are a hyperglycemic condition resulting from the destruction of insulin-producing cells. Antioxidants in flavonoid compounds will neutralize these free radicals so that early symptoms of DM can be overcome.

According to Stumvoll et al. (2005) chronic hyperglycemic conditions will trigger diabetes mellitus disease. Currently diabetes becomes a serious threat, according to WHO (2004) diabetics in Indonesia is estimated to occupy the fourth largest in the world after India, China and America. According to Freisleben (2001) there is a close relationship between free radical compounds with the emergence of various degenerative diseases such as diabetes mellitus.

For the development of beverage functional it is necessary to test in vitro and in vivo. Testing in vitro to be done for know inhibitory power of product to enzyme  $\alpha$ -glucosidase. Testing in vivo to know the volume of intake that has ability to decrease blood glucose levels in hyperglycemic mice. The volume of intake for turmeric-tamarind beverage needs to be determined because according to Tiganis (2009) excessive consumption of antioxidant supplements actually exacerbates the risk of diabetes mellitus. Based on the problem, the purpose of this research are to measure the inhibition of turmeric-tamarind beverage on the activity of enzyme  $\alpha$ -glucosidase, to determine the intake of turmeric-tamarind beverage that able to decrease the blood glucose level of hyperglycemic rat and to know the effect of intake of turmeric-tamarind beverage to blood glucose level and SOD enzyme activity on liver of diabetic mice. With the right intake of beverages will help patients in controlling their blood glucose levels.

## MATERIALS AND METHODS

### Material

Materials research among others rhizome and turmeric hump aged  $\pm$  9 months was obtained from the village of Badung District Sulahan. The tamarind leaf that light green color obtained from the Jimbaran village of Badung-Bali, chemical reagent (pa grade) from Merck, Sigma and Brathaco Chemical, mice male of Sprague Dawley (SD), feed Mark 521, blood glucose test meter glucoDrTm

## Implementation of Research

This research was conducted in 3 stages. The first stage is the identification of tamarind turmeric inhibitory power to the activity of  $\alpha$ -glucosidase enzyme. This study used a complete randomized design (CRD) repeated 3 (three) times with a concentration treatment of turmeric-tamarind: 10, 20, 30, 40, 50 mg/kg. This treatment is applied in the manufacture of tamarind turmeric beverage. How to manufacture as follows: fresh turmeric rhizome peeled, weighed 50 g and washed. Turmeric that has been clean and to be blended for 3.5 minutes using water 700 ml then filtered. The tamarind leaf, weighed 250 g after it was washed, then the turmeric slurry and tamarind mixed then cooked until boiling and removed after 2 minutes. The mixture is cooled, filtered and used as a sample. Further tested the ability of the sample according to the treatment in inhibition of  $\alpha$ -glucosidase enzyme activity in vitro (Sutedja 2003).

The second stage is the determination of the quantity of turmeric-tamarind beverage that decreases of the blood glucose level of hyperglycemic rat. The stages of this study also used a CRD with the following treatments: negative control (not given turmeric-tamarind beverage and not hyperglycemic), positive control (hyperglycemic and not given turmeric-tamarind beverage), giving turmeric-tamarind beverage of 50, 100, 150, 200 mg/kg bw mice on hyperglycemic, and positive control hypoglycemia (hyperglycemic given acarbose 4.5 mg / kg bw orally). The study was conducted in bioassay (in vivo) using 35 male Sprague Dawley (SD) mice aged 3 months with an average weight of 150 g. The mice were then placed individually in a cage that was divided into 7 groups, so that each group had 5 tails and each was separated. The mice were fed standard 10 g each serving with beverage ad libitum (without limit) for 30 days to adapt and get a uniform condition. After the mice pass the adaptation period, then the mouse is fasted for 14 hours. In the morning at 7:00 to 8:00 am measured blood glucose. The momentary hyperglycemic condition of mice is done in a way induce 90% sucrose solution as much 1 ml/mice, given 10 min before rat was treated. After the mice treatments, was measured blood glucose level using glucoDrTm. Measurements were performed at minutes 0, 30, 60, 120, 180 and 240 after treatments. The data obtained is averaged and analyzed descriptively to determine the best quantity of intake based on the highest decrease in blood glucose.

The third stage of this research is to know the effect of turmeric-tamarind beverage on the activity of SOD enzyme and blood glucose level of diabetic mice. The study at this stage used a complete randomized design with the following treatment: the group of mice were not given turmeric-tamarind beverage and not diabetes, the group of mice were given turmeric-tamarind 100mg / kg bw and not diabetes, the group of diabetes mice was not given turmeric-tamarind and the group of diabetes mice given turmeric-tamarind 100 mg/kg bw. The treatment was repeated 5 times so that there were 20 experimental units. This research was conducted in bioassay (in vivo) using 20 mice divided into 4 treatment groups, each of which was 5 mice. This treatment was carried out for 28 days. During the treatment the mice were given standard feed and the samples were administered orally. Observations were made by measuring the blood glucose performed every day for a week. Blood glucose checking is done every 08:00 hour after being fasted for 15 hours but still given a beverage. Blood glucose levels were measured by Nesco Multi Cheek Glucose Kemel Int'l Corp. Blood samples were taken through lateral mouse tail vein. After the 28th day the mice were dissected and their hearts were taken to measure the activity of the enzyme Superoxide Dismutase (SOD) (Wijeratne et al., 2005; Prangdimurti 2007).

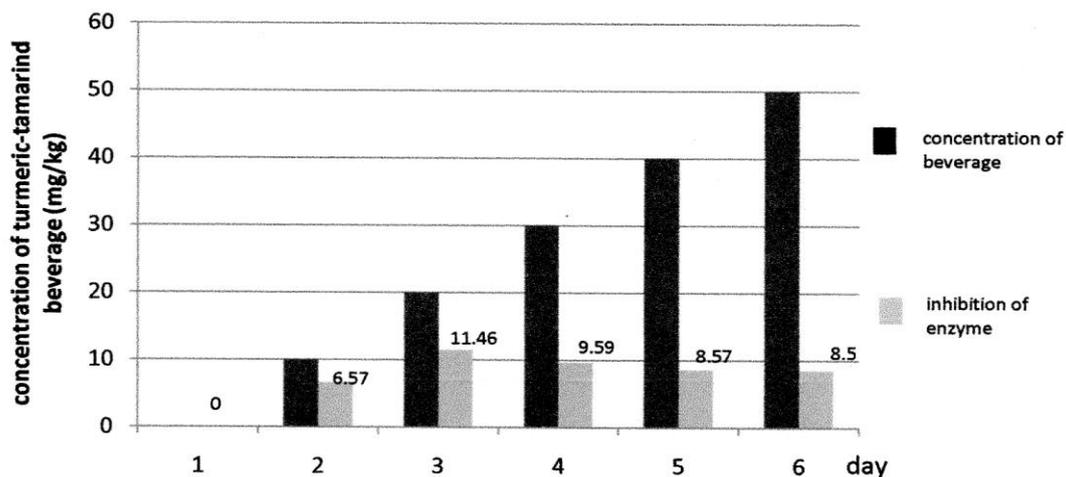
## RESULTS AND DISCUSSION

### Identification of Tamarind Turmeric Inhibitory Power on the Activity of the Enzyme $\alpha$ -Glucosidase

The results of identification of the ability of turmeric- tamarind beverage in inhibiting the activity of enzyme  $\alpha$ -glucosidase is shown in Figure 1. Figure 1 shows that at concentration of 10 mg/kg of turmeric-tamarind beverage has been able to inhibit the activity of enzyme  $\alpha$ -glucosidase. At a concentration of 20 mg/kg showed the inhibition highest, it indicates that tamarind turmeric beverage was able to delay the decomposition. oligosaccharides into monosaccharide. According to Shinde et al., In Lorenza (2012), the inhibition of the activity of the enzyme  $\alpha$ -glucosidase, it can delay the decomposition of the oligosaccharides into monosaccharide

The presence of compounds that can inhibit the activity of the  $\alpha$ -glucosidase enzyme on the turmeric-tamarind beverage, show that this product can be used as an oral drug for DM type 2 patients (Sudoyo et al.,

In Lorenza 2012). therefore this beverage can be an alternative for diabetics to lower blood glucose or hypoglycemic drugs. The working mechanism of this drink is similar to acarbose drug that inhibits the activity of  $\alpha$ -glucosidase enzymes in hydrolyzes saccharides and complex carbohydrates into glucose in the intestine This type of  $\alpha$ -glucosidase enzyme inhibitor drug does not cause hypoglycemia and has no effect on insulin levels (Sudoyo et al., In Lorenza 2012). Enzyme  $\alpha$ -glucosidase inhibitors are contraindicated in patients with short-bowel-syndrome or inflammation in the colon (Dipiro in Lorenza, 2012). The side effects of gastrointestinal  $\alpha$ -glucosidase inhibitors include, among others, bloating, nausea, diarrhea and flatulence (Suda, 2011).



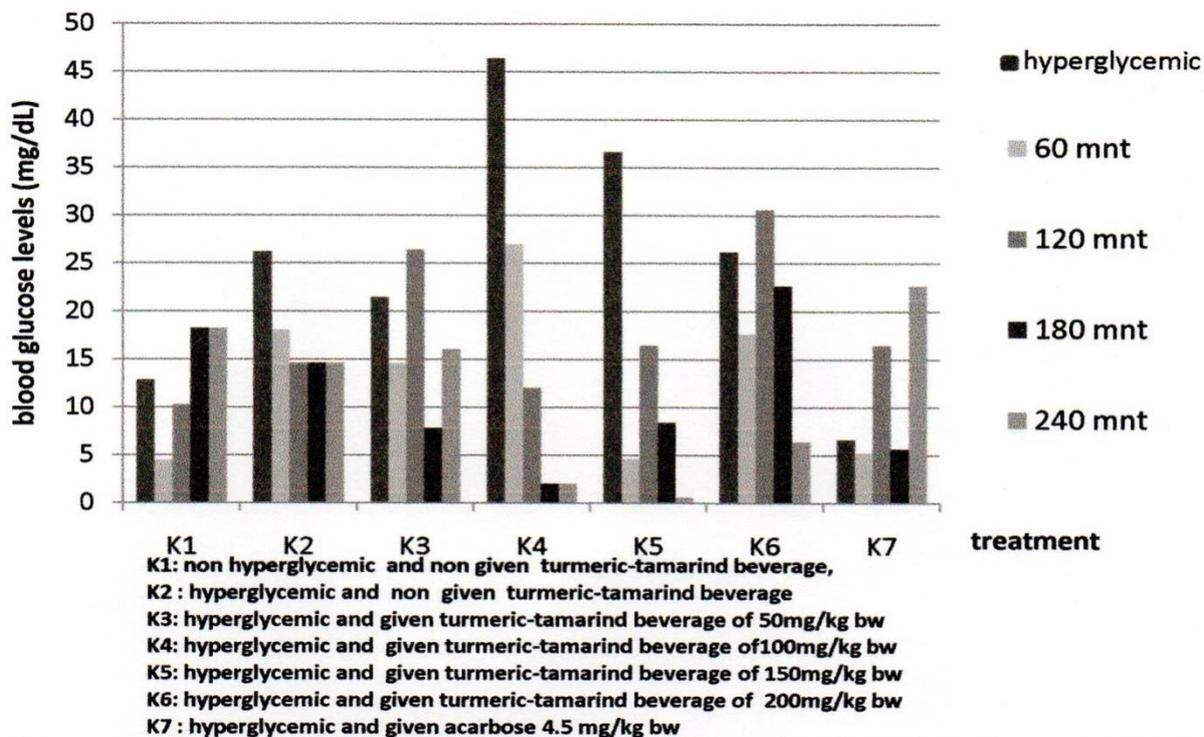
**Figure 1: Inhibition of  $\alpha$ -glucosidase enzyme activity by turmeric-tamarind beverage**

**The Effect of Quantity Intake Of Turmeric-Tamarind Beverage to The Decrease of Blood Glucose Level of Hyperglycemic Mice**

Based on the data in Figure 2 it is seen that all mice treated with turmeric-tamarind beverage showed lower blood glucose levels than control treatment. While the treatment with acarbose (blood glucose lowering substances) showed the highest decrease at minute 60, but after that, blood glucose will increase. As for other treatments the blood glucose levels trend decreased after 60 minutes.

Based on Figure 2 it appears that the treatment of not hyperglycemic and not given turmeric-tamarind beverage and treatment of hyperglycemic and is not given turmeric-tamarind beverage showed a relatively stable blood glucose decrease. While the mice treated with turmeric-tamarind beverage showed a decrease in blood glucose levels greater than the control, and the biggest decrease was on the intake treatment of 100 mg/kg bw of mice. This shows that tamarind turmeric beverage can decrease the blood glucose on a moment.

From Figure 2 it is also seen that up to 240 minutes all treatments showed a decrease in blood glucose, although all the average treatments had elevated at 120 minutes observation, but eventually decreased. Compared with other treatments, treatment on hyperglycemic and given turmeric-tamarind beverage of 100 mg/kg bw on observation from the 60th minute showed that the mice blood glucose continued to decrease until minute 240. Treatment of hyperglycemic and given turmeric-tamarind beverage also showed the lowest decrease of glucose content so that this treatment is considered as best treatment which able lowers blood glucose levels in hyperglycemic mice.



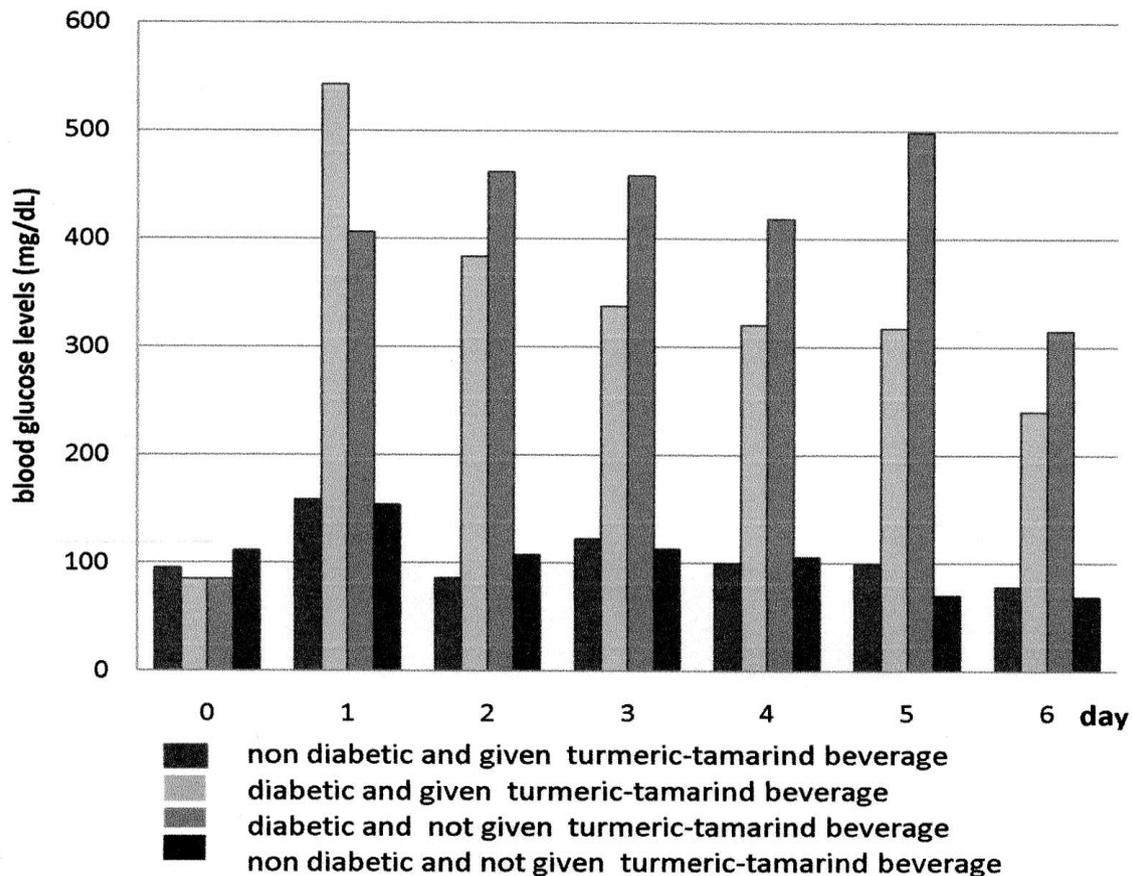
**Figure 2: The effect of turmeric-tamarind beverage intake to blood glucose levels**

The Effect of Turmeric-Tamarind Beverage Intake on Blood Glucose Level of Diabetic Mice

The effect of turmeric-tamarind beverage intake to blood glucose level of diabetic mice can be seen on Figure 3. Based on the results of blood glucose measurement showed that induction of streptozotocin of 5 mg/kg bw of intraperitoneal, significantly increased the fasting blood glucose of SD mice from the average of 84.8 mg/dL to 542.6 mg/dL and 406.2 mg/dL.

Punita in Winarsi, et al (2012) explains that enzyme activity in the glucogenesis pathway increases and simultaneously accelerates glucogenetic and lipolytic pathways. This causes the process of metabolism in diabetics affected because the enzyme activity of glycolytic pathways and phosphate pentose decreased, thereby increasing blood glucose levels. This prove that turmeric-tamarind beverage is able to reduce blood glucose levels from 542.6 to 240 mg / mL after a week of mice given the intake of 100 mg/kg bw. When compared to blood glucose levels in mice induced with streptozotocin, then decrease of blood glucose of 55.83 mg/dL occurs in mice not diabetes given turmeric-tamarind beverage of 100 mg/kg bw for one week, while the diabetic mice not given turmeric-tamarind beverage experienced a decrease in blood sugar just of 22.71 mg/dL. The turmeric-tamarind beverage in this research contains total phenol of 4.444 GAE / 100 g, vitamin C of 0.688 mg/100g. Mulyani et al (2011) states that tamarind leaves have greater antioxidant capacity than turmeric, this is due to the content of phenolic compounds and vitamin C large enough. Phenolic compounds can stimulate peripheral glucose utilization, by increasing glycolytic and glycogenic pathways, which simultaneously suppress glycogenolysis pathways and glycogeneogenesis. Through such mechanisms phenolic in turmeric-tamarind beverage can control blood glucose, so the blood glucose level of diabetic mice decreases. The condition can be seen in Figure 2. Figure 2 shows that diabetic mice which given intake of turmeric-tamarind beverage decreased blood glucose from first day to 6th day while diabetic mice who were not given turmeric-tamarind beverage showed a rise in blood glucose until day 5 and decreased on day six. This decrease in blood glucose levels in addition to phenolic compounds is also due to the content of vitamin C in beverages. Ascorbic acid / vitamin C are a non enzymatic antioxidant that plays an important role in protecting cell damage caused by free radicals. Vitamin C content in beverages also plays a role in lowering blood glucose levels of diabetic mice. Winarsi (2012) writes that the mechanism of vitamin C changes blood glucose levels is not known with certainty. However, the auto oxidation of glucose, protein glycolization, the rate of glycation product formation and the polyol pathway are involved in the formation of oxidative stress and the etiology of DM types 1 and 2. Protection against such damage is done by antioxidants as free radical

scavenging. High levels of ascorbic acid can directly inhibit erythrocyte aldose reductase, so oral administration of vitamin C is beneficial for diabetics. Vitamin C reduces glucose toxicity that contributes to prevent decreasing P-cell mass and insulin levels. Decreased of blood glucose levels occur because vitamin C plays a role in modulation of insulin in diabetics. Increased vitamin C-mediated insulin work is primarily due to increased non-oxidative glucose metabolism.



**Figure 3: Effect of turmeric-tamarind beverage intake on blood glucose level of diabetic mice**

The Effect of Turmeric-Tamarind Beverage Intake to SOD Enzyme Activity of Diabetic Mice Liver

The effect of the sample intake to the SOD enzyme activity of diabetic liver shown in Figure 3. Figure 3 shows that the activity of superoxide dismutase (SOD) in liver group of mice who were given the turmeric-tamarind beverage intake of 100 mg/kg bw had the activity of SOD the highest that is equal to 73.66U / g while the lowest activity is owned by a group of diabetic mice that are not given tamarind turmeric beverage (K +). Provision of turmeric-tamarind beverage on diabetic mice is able to maintain SOD activity is higher than the mice that are not given beverage intake. According to Valko et al., (2007) superoxide dismutase is an enzyme present in intracellular fluid, which participates in the degradation of intracellular free radical compounds. This enzyme inhibits the simultaneous presence of O<sub>2</sub> to H<sub>2</sub>O<sub>2</sub> that derived from the formation of a hydroxyl radical (\* OH). Turmeric-tamarind beverage is able to maintain the activity of SOD enzyme suspected because flavonoid compounds help the work of superoxide dismutase in eliminating free radicals. Flavonoid compounds work by donating one electron to free radical compounds so that the radical compounds are transformed into non-radical compounds, or compounds that are harmless to cells. Flavonoids help the superoxide dismutase work so that superoxide enzyme levels of dismutase in the cells are maintained. Conditions of oxidative stress such as fasting (Wresdiyati and Makita in Suarsana et al., 2013) sports (Haaji in Suarsana et al., 2013), psychic and inflammatory stress (Moller et al., Suarsana et al., 2013) and diabetes mellitus (Ahmed et al., In Suarsana et al., 2013) can increase free radicals in the body while lowering antioxidant enzymes. In relation to the potential toxicity of free radical compounds, the body has a natural defense system in the form of an endogenous antioxidant enzyme that serves to neutralize and accelerate the

degradation of free radical compounds to prevent macromolecular cell damage (Valko et al., 2007). Based on that, the provision of tamarind turmeric beverage is recommended for diabetics to help the natural defense system of endogenous antioxidant enzyme.

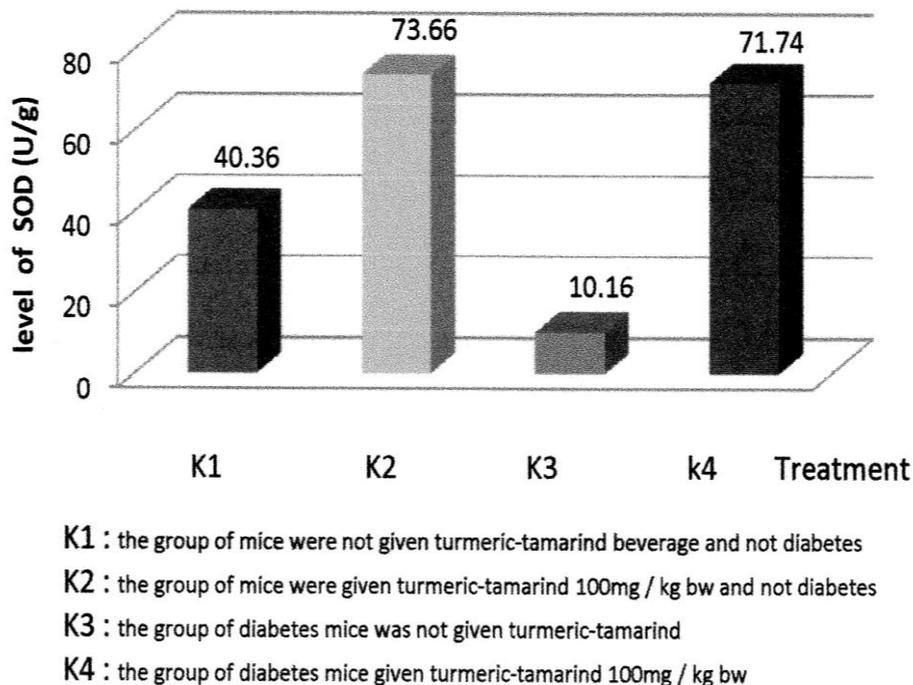


Figure 4: Effect of turmeric-tamarind beverage intake to SOD enzyme activity of diabetic mice liver

### CONCLUSIONS AND SUGGESTIONS

#### Conclusion

The results showed that turmeric-tamarind beverages have the ability to inhibit the activity of the  $\alpha$ -glucosidase enzyme. At a concentration of 20 mg/kg has the highest percentage of inhibition of the enzyme activity. Provision of turmeric-tamarind beverage of 100 mg/kg bw of mice produced the lowest decrease in blood glucose levels in hyperglycemic mice. Turmeric-tamarind beverage can reduce blood glucose levels of diabetic mice. Turmeric-tamarind beverage intake of 100 mg/kg bw mice, will cause a decrease in blood glucose level of 55.83 mg/dL whereas in mice that is not given intake, decreased blood glucose only 22.71 mg/dL. Turmeric-tamarind beverage is also able to maintain the activity of superoxide dismutase (SOD) enzymes and the provision of this beverage can overcome the decrease of SOD in mice liver.

#### Suggestions

- 1) Because it is able to lower blood glucose levels it is recommended that this turmeric-tamarind beverage is used as a functional beverage.
- 2) Need further research to be tested to humans, so the benefits of beverages can be optimized.

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