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FRUCTOSE EFFECTS ON BLOOD GLUCOSE AND URIC ACID LEVELS

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Abstract – This study aims to show the effects of fructose on human health with approach animal sample research. Interest is based on the due to problems of excess sugar consumption, especially the type of fructose that many peoples don't know realize it. This objective is supported by the data world sugar consumption is constantly increasing. Consumption of fructose over the normal limit will increase the risk of disease. The focus of this research parameter are the blood glucose levels and uric acid. This study design was Randomized Post Test Control Group Design uses the subject of male white rats *Rattus norvegicus* (n = 39). The research subjects were then divided into three groups. The control group K (n = 13) was administered 1 cc of distilled water, the low dose group P1 (n = 13) was given a solution of fructose 1 cc at a dose of 450 mg/150grBW/day and the high dose group of P2 (n = 13) was given a solution of fructose 1.5 cc at a dose of 1350 mg/ 150grBW/day. Treatment of the subjects during for 30 days. Test results on blood glucose levels an increase of 46% ($P < 0.05$) in the high-dose nor in uric acid levels also increased 48% in the high dose ($P < 0.05$). Observation on fructose-containing food products have not been found labels to the inclusion of fructose contained heavy detail. The conclusion from this research that consumption of fructose at high levels can harm health risk giving. To anticipate the necessary arrangements total amount of consumption of sugar, especially fructose and regulations in order to do innovation will labeling fructose in food and beverage products. Labeling would be beneficial for consumers because they can regulate the amount of sugar consumed fructose safe day.

INTRODUCTION

Fructose is a natural substance found in many fruits (fruits). Technological innovation foodstuffs allows the conversion of starch to fructose compound derived from corn, known as high fructose corn syrup (HFCS) (Marshall and Koii, 1957). The use of fructose in Indonesia in packaging products is increasing. The use of fructose has increased significantly due to growing food and beverage industry, followed by a shift in lifestyle of the people, especially the urban areas to the consumption of food and beverage packaging is characterized by the increase of data monthly expenditure / capita as much as four times in the span of 2002 to 2011 (BPS, 2014). As it is known today has many food and beverage products that use fructose as a sweetener to replace glucose or sucrose on the grounds of efficiency, such as the use of HFCS to food and soft drinks (Beverage Institute Indonesia, 2014). Increased fructose consumption in the United States based on data from the USDA

currently is above about 100g/day (Tappy and Le, 2010). Previous research proves that a smaller dose of 100g/day can lead to decreased insulin sensitivity of cells to insulin sensitivity (Livesey, 2009). The hormone insulin helps maintain the entry of glucose into cells so the decline of this hormone will increase the risk of type 2 diabetes mellitus (DM type 2). Statement by Livesey reinforced by research LeCoultre *et al*., (2013) which concluded that the consumption of 3 or 4 g fructose/kg/day in humans can decrease hepatic insulin sensitivity index (HISI) of approximately 20% and 19% which is accompanied by an increase intrahepatocellular lipids (IHCL) were respectively 113% and 102%. Besides, the use labels more detail (detail Identitiy label) is important because with this community is more concerned about his health (Kempen *et al*., 2012) as to determine the number of calories you have consumed and is expected to be a correlation between the detail label and enhancements to community understanding to health but to see it required direct observation of the product.

Fructose and Toxicity

Chemical formula fructose is $C_6H_{12}O_6$ one group with glucose and can form a heterocyclic structure (Slavin, 2014). Fructose can be consumed by a variety of food, but the fructose is consumed in high doses in a short period of time (6-7 days) have shown adverse health effects (Le Coultre *et al*., 2013). Research in Brazil stated that the provision of a solution of 10% fructose and 20% were able to lead to a state of hyperinsulinemia and hyperglycemia (Livesey, 2009). One of the factors that play a role, resulting in a person at great risk to fructose is still a lack of supervision of food and beverage products on the market. This is in accordance with the NA-DFC statement that "the capacity and ability of POM limited laboratory provides an opportunity not controlled products risk to health" (NA-DFC, 2013). Many of the food products that added fructose or HFCS that does not include fructose or only lists a net weight of net carbohydrates alone and some have only included net product alone, more worrying many parents who do not control the consumption of foods and beverages containing sugar at son. For example, in the Jakarta area of data in 1993 showed that 96.7% of parents give to their children sugary snacks (Yuyus, 2002). Ignorance of how much total sugar was consumed mainly fructose per day increase the risk of someone suffering from non-communicable diseases or Non Communicabel Disease (NCD), especially type 2 diabetes mellitus (DM type 2). DM a major concern because it has a further manifestation of the poor is an increased risk of cardiovascular disease (CVD), damage to the kidneys, eyes and nerves (Holt, 2010).

DM status overview of the clinical condition a person can be easily seen from the plasma glucose levels primarily fasting glucose (fasting glucose) because the change is relatively smaller (Holt, 2010). Besides the addition of glucose levels in the form of variable inspection uric acid levels are also important. It is based on the metabolism of fructose is dangerous at high levels because it uses ATP energy in each of the initial phosphorylation resulting intracellular phosphate depletion so as adenosine diphosphate (ADP) generated in the cell will be broken down into adenosine monophosphate (AMP). Furthermore AMP compounds are metabolized to uric acid (Moriwaki, 2014; Khitan and Dong, 2013). This is dangerous because increased uric acid above the normal range would increase the risk of hypertension (Hwang *et al*., 1987) and CVD (White, 2012) is due to uric acid can result in decreased levels of nitric oxide, or NO plasma directly in endothelial cells and vessels blood in the muscle cells (Kang *et al*., 2005). NO compound was instrumental in vasodilatation (Witte and Adrian, 2002). The mechanism of the increased risk of incident DM caused by the decrease of NO is the effect of increased rigidity of blood vessels (vasoconstriction). Stiffness in the vascular endothelium system resulting in receptor sensitivity was decreased (Khosla *et al*., 2005) and an increase of uric acid levels will increase the risk of kidney stones (Chol *et al*., 2005). In Indonesia country risk of death from the disease is still high can be seen from the graph the percentage of mortality. Diabetes mellitus ranks 3rd leading cause of death in Indonesia, hypertension positioned to-5 (Figure 1b) and the heart of the first position (MoH, 2012).

Consumption

Indonesia country at great risk going against the excessive consumption of fructose compounds found in food and beverage packaging is due to the increase in the consumption behavior of Indonesian society towards food products and beverage packaging. This increase can be seen from the costs incurred by public Indonesia's monthly per capita consumption of food and drink that has increased four-fold in just over nine years (2002-2011) (CBS,

2014). Average expenditure per capita per month based on reports NA-DFC 2011 for processed food and beverages also increased from 50.62% in 2009 to 51.43% in 2010 (NA-DFC, 2011). In addition the data increased consumption of foods and beverages supported also by data reports industry sales, which increased by almost 2-fold, in just a span of 6 (Figure 1a) year (2007- 2012) with sales of 402 trillion to 700 trillion (GAPMMI, 2014). High risk is also experienced by the Indonesian state is shifting lifestyles with increased consumption of food products and beverages. This risk can be seen clearly from the BPS (Figure 1a), which showed an increase in spending a month on food products and beverages expenditure so much as 4-fold (CBS, 2014).

Increased Cases of Disease

Increased disease due to a shift in the pattern of life have built relationships with the large number of deaths by non-communicable diseases in Indonesia, such as diabetes, hypertension and heart (Ministry of Health, 2012) and he also said explicitly in the annual report 2013 NA-DFC that non-communicable diseases are becoming a problem in Indonesia such as heart disease, stroke and obesity has attacked a young age (NA-DFC, 2013). More specifically in the CDC report NCHS (Centers for Disease Control and Prevention National Center for Health Statistics) of 2013 states that the increase in the consumption of added sugars has been associated with weight gain over weight (Ervin and Cynthia, 2013) is more specific in a study concludes that soft drinks containing HFCS can increase body weight significantly (Tordoff and Alleva, 1990).

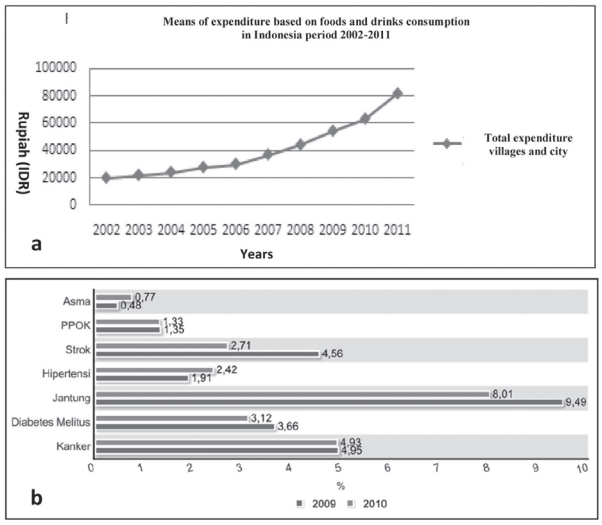

Fig. 1. a) Graph increased consumption of food products and beverages (bottled). Source of data: The Central Bureau of Statistics (BPS), Indonesia. b) The percentage of non-communicable disease deaths in hospital Indonesia in 2009-2010. Source: Ministry of Health of the Republic of Indonesia (Ministry of Health), 2012.

MATERIALS AND METHODS

The subjects in this study using experimental animals in the form of white male rats (*Rattus norvegicus*), which previously had met the inclusion criteria such as: weight subjects ranging from 150-200 grams, the subjects did not have diabetes (blood glucose screening beginning using test strips Brand GE 100 Lot 113610C) and there is no physical defects. Fructose used are standardized fructose ($C_6H_{12}O_6$) were obtained from Sigma-Aldrich Ltd. No. 104007. The subjects were divided into 3 groups: control group K, P1, P2 (n = 13). Fructose is given in the form of a solution. P1 group given fructose solution as much as 1 cc / day at a dose of 450 mg/150grBW/day for the low dose group, while for the high dose given fructose solution, 1.5 cc at a dose of 1350 mg/150grBW/day. The control group was given distilled water as much as 1 cc / day. Treatment of the subjects carried out for 30 days. All actions of treatment in experimental animals has been approved by the ethical committee of the Faculty of Veterinary Medicine Airlangga University with number 407-KE. For observation, made directly to products containing fructose to know in detail the labels listed.

Statistic analysis

The statistical analysis used in this study including normality test, homogeneity test, One Way Anova and *LSD Post Hoc test* with a level of significance (P = 0.05).

RESULTS AND DISCUSSION

The results of the study showed that the mean glucose levels of blood glucose levels in the control group was (141 ± 24) mg / dl. Provision of fructose in the lower levels (P1) did not show a significant difference to an average value that is (177 ± 29) mg / dl. The significant differences are in the delivery of high doses of fructose in which the mean glucose levels significantly different from the mean value is (206 ± 37) mg / dl compared to the group K as well as the P1 group (P <0.05). The results of the study showed that uric acid levels of uric acid in the

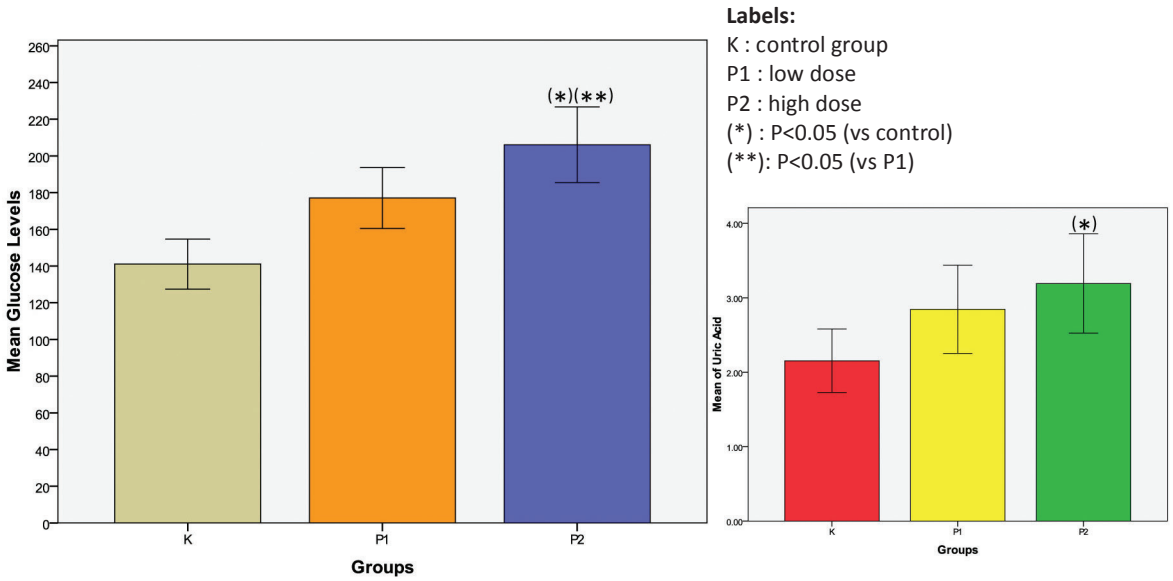

Fig. 2. Diagram effect of fructose on blood glucose levels (blue) and uric acid levels (green) Mean ± SD. *) Significant P <0.05 vs control, **) significant P <0.05 vs P1.

control group was (2.1 ± 0.7) mg / dl. In the administration of low doses of fructose does not occur a significant increase in group P1 with a mean value of uric acid levels are (2.8 ± 0.9) mg / dl.

Significant differences occurred in the group P2 where the mean uric acid levels are (3.1 ± 1.1) mg / dl compared with control group (P <0.05) (Figure 2).

The research result is in line with penlitian by Livesey, (2009) which states that fructose can induce a state of hyperglycemic (blood glucose above normal). Increased uric acid levels (hyperuricemia) in this study are consistent with studies by (Hallfrisch, 1990). Uric acid rises have negative effects on the endothelium of blood vessels such as the rigidity. Stiffness of the system resulted in the vascular endothelium such as insulin receptor sensitivity was decreased (Khosla *et al.*, 2005) and an increase of uric acid levels will increase the risk of kidney stones (Chol *et al.*, 2005).

Fructose Food Products

The use of labels in detail on the product can increase consumer awareness on health (Kempen *et al.*, 2012; Samson G, 2012). The results of observations performed directly on food products and beverages containing fructose undiscovered labeling their total levels of fructose contained in the packaging products (Figures 3a and 3b). In figure 3a product has a weakness for heavy detail every ingredient is not listed when the material contained therein fructose. In the Figure 3b products already listed sugar fructose but for this type of material has not been specified.

Fig. 3. a) The product solids weight of fructose without detail. b) liquid food products without detail heavy fructose fructose.

The negative impact of the absence of labeling detail total levels of fructose in pengan material above resulted in consumers do not know how much you've consumed in a day thus increasing the risk of NCD diseases such as diabetes and hypertension.

CONCLUSIONS

Fructose is shown to have a negative effect on health in large doses are characterized by increased levels of uric acid and blood glucose. Test results on blood glucose levels an increase of 46% ($P < 0.05$ vs. control) at high doses while in uric acid levels also increased 48% in the high dose ($P < 0.05$ vs. control). Observation on fructose-containing food products did not reveal any detail inclusion weight of fructose contained. For Indonesia, the regulation of the use of fructose in food and beverage packaging has set firmly and clearly it is that then increases the risk of the Indonesian people to suffer from NCDs such as diabetes, gout, hypertension and heart. To anticipate this will require innovation to the labels of food products and beverages one is labeling the total fructose as part of education on health.

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