# POTENTIAL SOYBEAN (Glycine max) (L.) merr) ON HISTOPATHOLOGY OF LIVER AND PANCREAS IN TYPE 2 DIABETIC MICE

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# POTENTIAL SOYBEAN (Glycine max) (L.) merr) ON HISTOPATHOLOGY OF LIVER AND PANCREAS IN TYPE 2 DIABETIC MICE

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## ABSTRACT

**Background** Various diabetic complications caused by poor control of the disease, such as vascular disease systemic (accelerated atherosclerosis), heart disease, microvascular disease of the eye as a cause of blindness and retinal degeneration (diabetic retinopathy), cataracts, kidney damage as a cause of kidney failure and damage to the peripheral nerves (neuropathy diabetic).
**Method** This research was the experimental study and it was *randomized pretest posttest control group design*. The number of experimental animals in each group were four tails, and total sample were 28 tail, divided into 7 groups .
**Results** The results showed that the average number of cells in the islets of Langerhans of the pancreas third lowest for the group DM mice, while the highest was found in the treatment group DM + extract of soybean variety Wilis, it indicates that the Streptozotocin effective to make the animal into diabetic mice. The percentage of liver cells were dying in preparations painted with Hematoxylin eosin, at least found in diabetic treatment group with the extract of soybean varieties Gema.
**Conclusion** Giving soy extracts on diabetic mice can inhibit damage to the pancreas Langerhans and soy extracts Gema types can minimize the number of liver cell death is lowest. It is advisable to use soybean varieties Gema as an alternative to research on herbal therapy for patients with type 2 diabetes.

**Keywords**: DM, Soybean varieties Gema and Wilis, histopathological liver and pancreas

## INTRODUCTION

In 2013, the proportion of the Indonesian population aged ≥15 years with diabetes was 6.9 percent. The prevalence of diagnosed diabetes was highest in doctors DI Yogyakarta (2.6%), Jakarta (2.5%), North Sulawesi (2.4%), and East Kalimantan (2.3%). The prevalence of diabetes is diagnosed based on symptoms or a doctor, is highest in Central Sulawesi (3.7%), North Sulawesi (3.6%), South Sulawesi (3.4%) and East Nusa Tenggara (3.3%) (MoH , 2013). the prevalence of DM in Indonesia rising from year to year. Patients affected not only the age of retirement, but many were of childbearing age.

The extent of the complications of diabetes seem to be correlated with high blood glucose concentration so that excess glucose is thought to be a major cause of tissue damage (Rahbani, 1999). This phenomenon is caused by the ability of hyperglycemia in vivo in the oxidative modification of various substrates, in addition, hyperglycemia is also involved in the formation of free radicals (Droge, 2002). Hyperglycemia causes auto oxydation glucose, protein glycation, and activation of the metabolic pathway of polyol which further accelerates the formation of reactive oxygen species (Ueno, 2002).

HbA1c is formed from glucose bond with the amide groups on the amino acid valine at the end of the beta chain of globulin in haemoglobin normal adult which occurs in two stages. The first phase occurred aldimin form covalent Schiff base which is stable and the second stage occurs as Amadori products rearrangement to form a stable ketamine. In the hyperglycemic state will increase Schiff base formation between the aldehyde group of glucose with lysine residues, arginine and

histidine. In addition, collagen glycosylation products and other long-lived proteins in the interstitial and blood vessel walls undergo a series rearrange to form *irreversible advanced glycosylation end products* (AGEs), which continue to accumulate in the walls of blood vessels. These AGEs have a number of chemical and biological properties of potentially pathogenic and is thought to contribute underlying diabetic complications (Basta, 2004)

One effort in the management of Diabetes Mellitus is a change of diet. From the point of diet, soy products can help because they contain fiber that lowers the rate of absorption of glucose into the bloodstream. Soybean classified as a material with a low *index glicaemix* and helps normalize blood glucose levels. Soy Protein contains many amino acids glycine and arginine. Replacement of animal protein with soy protein can be a means of prevention and effective treatment for Diabetes (eBookPangan.com, 2006).

Soybean is crops with the content of polyphenol compounds are reported to have various biological activities, which are beneficial to health, including preventing oxidative stress (Prakash *et al.,* 2007). Intake of foods made of soy beans has been found to lower the risk factors for chronic diseases. Specific component in soybean seed particularly isoflavones, saponins, vitamin C, tocopherols attributed to the protective effects of oxidative stress (Dajanta, *et a* l., 2013). Survey epidemiological and animal studies show that the content of isoflavones in soy have a protective effect against menopausal syndrome, and a variety of diseases, including cardiovascular disease, cancer, hyperlipidemia, osteoporosis and other chronic diseases (Clarke, *et al.,* 2013).

Research conducted by Yulia, *et al.,* 2014 [a] proving that soybean varieties Anjasmoro extract can reduce levels of pollutants trigger free radicals in the blood. Further research conducted by Yulia, *et al.,* 2014 [b] using other soybean varieties show varying biological activity in lowering lipid peroxidation activity, potentially as an antioxidant. Further research conducted by Yulia, *et al.,* 2014 [a] prove of some varieties of soybean seed, variety Argomulyo provides the highest antioxidant effect. High content of isoflavones in soybeans are also shown to be significantly beneficial for menopausal women in terms of increasing the levels of collagen, elasticity and thickness of the skin epithelium (Accorsi-Neto, *et al.,* 2009). Besides isoflavones, soy bean varieties detam 2 proved to have an active compound content of other antioxidants that *hexadecanoic acid* methyl ester and *hexadecanoic acid, ethyl ester*. Isoflavones in soy also been shown to inhibit bone resorption and stimulates bone formation in postmenopausal women (Ma, *et.al.,* 2008).

Based on the biological activity possessed soybean mentioned above, then the soybean potential to be developed in the form of herbal preparations that act as antioxidants and protection of Diabetes Mellitus with the taste acceptable to consumers.

## RESEARCH METHOD

This research had the experimental study and this design was *randomized pretest posttest control group*

The population in experimental research were male mice strain Balb / C 10 weeks old weighing 25 to 30 g, healthy physical characteristics of clear-eyed, shiny fur, active motion, obtained from the Laboratory of Biochemistry, University of Airlangga. The use of experimental animals would receive certificates of airworthiness of conduct by the Research Ethics Committee from Health Polytechnic, Health Ministry of Surabaya, Indonesia.

*Mus musculus* were strain BALB / C, male, adult, aged 10 weeks, weight 25-30 grams number 28, taken with random allocation. They injected with streptozotocin so that they becomes animal models of diabetes mellitus type 2. Animal experiments acclimatized to environment experimental cages for approximately two weeks, then grouped into seven treatment groups and each treatment group consisted of 4 mice, were given drinking water ad libitum. Giving Streptozotocin with a single dose of 55 mg / kg intraperitoneally to create an animal model of diabetic.

The chemicals used in the study: 10% formalin, *Hematoxylin eosin, pellet* feed starter and distilled water. The tools used in this study

include: balance sheet, cages of mice, weighing animals, sonde *oral,* microtome, *object glass,* paraffin, microscope, like coloring, *Cambridge Pad, syringes* 1 and 3 ml, a set of tools minor surgery (for harvesting the organs of mice).

Soybean extract dissolved in CMC Na mucilago equivalent to a dose of 1 g soybean (Wilis / Gema / Argomulyo varieties) / 20 g BB mg / kg / oral / day / mouse, given at noon, with the sonde (Evennia, 2012)

Liver tissue was taken, soaked in 10% formalin and then made preparations with paraffin. A layer of tissue slices with a microtome results, followed by *Hematoxylin eosin* staining. Observations tissue necrosis as a% using a microscope.

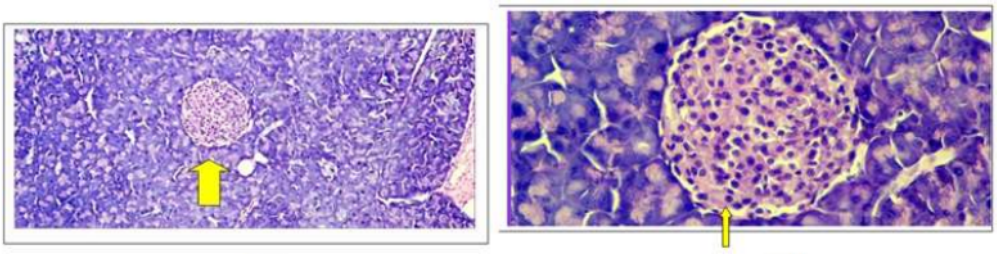
**RESULTS**

Calculation the numbe of cells in pancreatic of Langerhans, painted with Hematoxylin Eosin. The number of cells in the pancreatic of Langerhans can be shown in the table below:

Table 1. Average number of cells in the pancreatic of Langerhans with Hematoxylin Eosin

| Group | The mean number of cells in the islets of Langerhans Pancreas 3 |
|---|---|
| The negative control (Normal + soybean extract) | 141.6 |
| Pre Test (DM) | 66.8 |
| Placebo control (DM + CMC) | 84.3 |
| DM + Metformin | 94.2 |
| DM + extract of soybean variety Wilis | 102.7 |
| DM + extract of soybean varieties Gema | 96.8 |
| DM + extract of soybean varieties Argomulyo | 90.3 |

From Table 1 shows that the average number of cells in the islets of Langerhans third lowest for the DM group, this indicates that Streptozotocin effective to make the animal into a DM.Microscopic picture of the islets of Langerhans can be seen below



(A) (B)

Fig 1. Microscopic cells in the islets of Langerhans in the enlargement (A) 100x and (B) 400x

There is no significant difference pancreatic islets of Langerhans cell numbers in groups of mice were exposed to soy, but the result is higher when compared to other diabetic group. This shows that the soybean extract protects Langerhans network conditions.

2.Calculation percentage amount cell dead of hepatic with hematoxylin eosin.
The number of cell death in liver which can be shown as follows:

Table 2. The number of cell death (%) in liver with Hematoxylin Eosin

| Group | The mean percentage number of liver cell death |
|---|---|
| The negative control (Normal + soybean extract) | 9.8 |
| Pre Test (DM) | 75 |
| Placebo control (DM + CMC) | 50 |
| DM + Metformin | 21 |
| DM + extract of soybean variety Wilis | 32.5 |
| DM + extract of soybean varieties Gema | 18.8 |
| DM + extract of soybean varieties Argomulyo | 31.7 |

While the picture of liver tissue can be seen below.

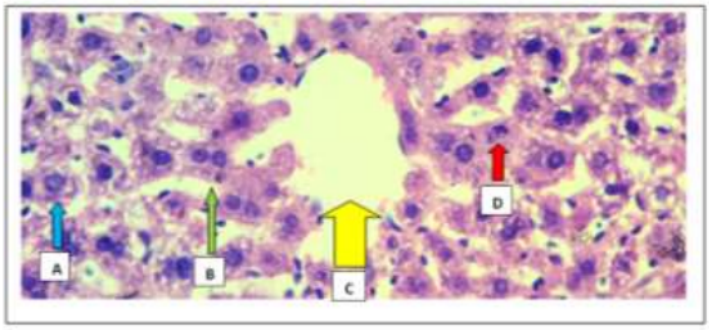



Fig 2. Microscopic description hepatic 400x magnification,
A: Hepatocyte cells degenerate hydropic
B: Sinusoid widened
C: Vena centralis,
D: Hepatocyte cells experiencing Karyorrhexis

From table 2 shows that the soybean varieties Gema effectively acts as a hepatoprotective compared with other soybean varieties. This was evident by the number of dead liver cells smaller than other varieties

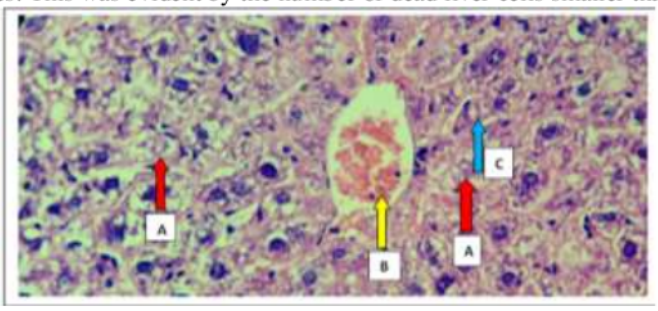



Fig 3. Overview of microscopic hepatic 400x magnification
A: Hepatocyte cells experiencing kariolisis
B: Vena centralis experiencing congestion
C: Hepatocyte cells degenerate Hydropic

## DISCUSSION

Necrotic cell death, occurs when a stimulus that causes injury to the cell is too strong or prolonged. Cell necrosis is characterized by swelling and internal rupture that most of the mitochondria, and he explained the stimulation of the inflammatory response (Corwin, 2009). Necrosis is recognizable as a cell or tissue showed certain changes both macroscopically and microscopically. Grossly necrotic tissue will appear turbid *(opaque),* no longer bright, white and gray color, while microscopically, entirely reddish necrotic tissue, do not take the dye eosin hematoxylin, often pale (Pringgoutomo, 2002). In this study, administration of streptozotocin with intraperitoneally in mice damaging the pancreas so that it looks the number of cells in the islets of Langerhans decreased in diabetic mice.

Morphologic necrosis was the result of enzymatic digestion and protein denaturation occurring simultaneously. Enzymatic digestion by hydrolytic enzymes can be derived from the cell itself (autolysis) may also originate from inflammatory cell lysosomes (Kumar; Cotran & Robbins, 2007). In necrosis, changes mainly located in the nucleus and has three patterns, namely ( Lestari, 2011):

1. Psycosis, the core experience crenation, the homogenization of cytoplasm and increased eosinophils, DNA condenses into a solid mass melisut.
2. Karyorrhexis, namely core fragmented (divided by fragment) which pyknotik.
3. Karyolysis, which occurred fading due to the activity of chromatin basophil cell DNA

Cell death and tissue unnatural / necrosis has stages that occur include: swelling of cells, digestion of chromatin, membrane rupture (plasma and organelles), the hydrolysis of DNA, vacuolation by reticulum endoplasmic, destruction of organelles, cell lysis and the release of the contents of intra cells after damage the plasma membrane is the cause of the inflammation / inflammation in necrosis.

Number of high liver cell death in mice exposed group streptozotocin because these chemicals undergo xenobiotic metabolism and turns out to be toxic to the liver tissue. The content of phytochemicals in soy extracts such as acidic phenols, flavonoids and isoflavones (phytochemical polyphenols and phytoestrogens) are insulin mimetic and acts as an inhibitor of α-glycosidase will slow the absorption of polysaccharides, dextrin and disaccharide in the intestine, thus preventing an increase in glucose (Silva, 2013) (Djamil, 2009). The existence of phytochemicals in soy extracts can control hyperglycemia conditions so that the process of the liver and pancreas tissue damage can be inhibited.

## CONCLUSION AND RECOMMENDATION

### Conclusion

Soy extract in patients with diabetes can reduce the damage to Langerhans of the pancreas and liver tissue.

### Recommendation

Soybean is good food for people with diabetes because it is insulin mimetic and researchers can then use soy as an alternative herbal therapy for patients with type 2 diabetes.

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