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Haematological and Biochemical Serum Profiles of Experimental Rats Fed with GMO and Non-GMO Soybean

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ABSTRACT

The imbalance between the consumption and production causes the Indonesian government to import soybean from various countries. The United States, where 94% of its soybean products are transgenic, acts as the main exporter. Currently, the consumption of Genetically Modified Organism (GMO) soybeans causes a controversy regarding of its safety for consumers. This study is aimed to compare the haematological and biochemical serum profiles of experimental rats which were fed with imported GMO and non-GMO soybeans (imported and local Grobogan soybeans). This study was conducted by exercising a subchronic toxicity test for 90 days with 10 and 20% protein ration levels. GMO soybean had a significant ($p<0.05$) effect in lowering platelets, albumin, and ureum value, as well as increasing the uric acid values. However, the decrease was still within the normal reference value. In addition, there was not any evidence of adverse effects that was observed in the blood composition, liver, and kidney of the rats which were fed with GMO soybean, even though the protein content for their ration had been increased from 10 to 20%. To conclude, the haematological and biochemical profiles of GMO soybean were equivalent to the non-GMO soybean.

Keywords: biochemical profiles, genetically modified organism, haematological, soybean.

INTRODUCTION

Soybean is mostly utilised as a source of vegetable protein as compared to other agricultural commodities. In Indonesia, soybean is mainly processed into tempe, tofu, tauco, and other products. This resulted in soybean becoming the most important agricultural commodity after rice and corn. Soybean has several benefits compared to other *Leguminosae* and *Cerealia* groups, which are high in its protein content (40–44% dw), higher content of and more complete essential amino acids, and rich in isoflavones.

Each year, the average national soybean consumption increases by 2.4% (Aldillah 2015). However, the increase in the level of consumption is not on par with local soybean productivity. To fulfill the demand of national soybean stock, the government imports soybean from various countries, especially from USA, Brazil, and Argentina. In 2019, Indonesia imported 2.67 million tons of soybean to fulfill the demand of 3.1 million tons (BPS 2020). Meanwhile, 94% of soybean grown in America are soybean produced through GMO cultivaton or Genetically Modified Organism (GMO) (USDA 2020).

The genetic engineering enables the soybean plant to express 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase that is isolated from *Agrobacterium tumefaciens* CP4 strain (CP4 EPSPS). This gen encodes an enzyme that is tolerant to glyophosate herbicide. This results in soybean plants which are able to withstand diseases and pests, more tolerant against herbicides, and resulting in bigger bean sizes. Nevertheless, GMO plants are still causing controversies and concerns in society, especially regarding to its safety and toxicity due to the inserted foreign genes.

Indonesia regulates GMO in food safety assessment, which is the Head of Indonesian Food and Drug Agency's (Indonesian FDA) Act Number 6 Year 2018. Indonesia Biosafety Clearing House (IBCH) also releases nine types of GMO proteins that had already own safety certificates and distribution licenses. Several

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studies showed that there was an equivalence between local soybean with GMO and non-GMO soybean. Astawan *et al.* (2019) reported that local Grobogan soybean flour had equivalent physicochemical properties with imported GMO and non-GMO soybean. Even, it had a higher protein content and antioxidant capacity. Tempe that was produced from imported soybean (GMO and non-GMO) did not have any significant differences in protein quality, MDA level, and SOD when it was compared to local Grobogan soybean. The consumption of tempe that was made from GMO and non-GMO soybean for 90 days did not cause any abnormalities in the reproductive organs of male rats (Maskar *et al.* 2015).

Until now, World Health Organization (WHO) stated that there were not any specific reports regarding of the health side effects caused by GMO food consumption (WHO 2014). Nonetheless, the cautionary in GMO food safety must still be implemented. One of the ways to evaluate GMO food safety is through in vivo subcronic toxicity test. This study is aimed to observed the comparability of GMO soybean with non-GMO soybean (local Grobogan and imported soybean) on haematological and biochemical serum profiles of experimental rats by conducting a subchronic toxicity test for 90 days. The use of local soybean in this study was due to the perception that local soybean is safer for consumption than the imported non-GMO soybean.

METHODS

Design, location, and time

This experimental study used a Completely Randomized Design (CRD). The research activities included producing the soybean flour, preparing the ration and experimental rats, and the haematological and biochemical profiles analysis. Research activities were carried out in the *Rumah Tempe Indonesia* (RTI) Cilendek, Bogor; Animal Laboratory SEAFAST Center, IPB University; and Regional Health Laboratory; from January–June 2019.

Materials and tools

The main materials that were examined were the local Grobogan soybean (obtained from Grobogan Region, Central Java, Indonesia), the imported GMO Event GTS 40-3-2, and the non-GMO soybean (US Origin). The experimental rats that were used in this study were 35 male *Sprague Dawley* strain (5 rats/group) aged 6–8 weeks, which were obtained from the Indonesian Food and Drugs Agency of Republic Indonesia. The equipments that were used for the haematological and biochemical profile analysis consisted of blood tube with Ethylene Diamine Tetraacetic Acid (EDTA), blood tube for serum collection, automatic haematology analyser (Medonic M-series Haematology Analyzer, Boule Medical, Stockholm, Sweden), and chemistry analyser (Vital Scientific Selectra Junior Clinical Chemistry Analyzer, Dieren, The Netherlands).

Procedures

Production of the soybean flour and ration formulation. To produce the flour, the soybean had to be sorted, washed, soaked for 6 hours, cooked at 100°C for 30 minutes, removed from the husks, washed and drained, dryed using tray dryer at 60°C for 6 hours, milled using disc mill, and sieved using 60 mesh siever (Astawan *et al.* 2015; Astawan *et al.* 2019). For the ration formulation, the proximate analysis was conducted in all types of soybean flour and casein (control). The ration formulations of each group of rats were differentiated based on the type of soybean flour (GMO, non-GMO, and local soybean) and its protein content (10 and 20%). For control group, the rats were fed with casein ration that contained 10% protein content.

Experimental rats. The experimental rats were initially adapted for seven days to the standard ration (casein) feeding for envirnonmental adjustment and weight selection. The rats were housed individually in plastic cages. The selected rats for the experiment had the differences in weight of no more than 10 grams between the treatment groups and not more than 5 grams in same treatment group (Astawan *et al.* 2015). The feed and water were given ad libitum for 90 days according to the protocol of GMO food testing by the European Food Safety Authority (EFSA 2011).

Haematological and biochemical profiles serum analysis. After 90 days, rats were anesthetized with ketamine-xylazine solution (7:2) (Wresdiyati *et al.* 2018). 3 ml of blood samples were drawn from the heart and were divided into 2 tubes. ±0.5 ml of blood was required for the haematological analysis while the remaining blood was used for serum analysis. The haematological analysis consisted of erythrocyte content, haemoglobin, haematochrite percentage, total of leucocyte, and platelets quantity. Meanwhile, the biochemical serum profile consisted of; 1) Serum lipid profile: cholesterol, triglycerides, High Density Lipoprotein (HDL), and Low Density Lipoprotein (LDL); 2) Serum protein profile: ureum, creatinine, total protein and albumin,; 3) Other analysis: uric acid content, blood glucose,= Aspartate Aminotransferase (AST), and Alanine Aminotransferase (ALT) enzymes.

Data analysis

The data were processed using Microsoft Excel 2010 and SPSS 26.0 (IBM for Windows). The quantitative data were tested using Analysis of Variance (ANOVA) at a confidence interval of 95%, continued with Duncan test to determine the significant differences between the treatments.

RESULTS AND DISCUSSION

Proximate analysis

The result of proximate analysis on the three types of soybean flour and casein is shown in Table 1. The quality of the soybean flour could be observed on its protein content. The analysis of variance result showed that protein content from the three types of soybean flour were insignificant ($p>0.05$), but it was significantly lower than casein ($p<0.05$). This was because the casein in form of concentrate had a protein content of 65–<90%.

The result of protein source proximate analysis would be used as a reference in formulating the ration (Table 2). In the soybean flour with 20% protein content, the addition of corn oil was not needed. For all rats' soybean flour rations, the addition of fiber source (CMC) was not needed. These was due to the fat and fiber content within the soybean flour had already fulfilled the ration composition requirements for experimental rats (8 and 1 %, respectively).

Haematological profile

The main function of erythrocite or red blood cell is to distribute oxygen from the lungs to the whole body. The percentage amount of erythrocyte in blood volume counts as haematochrite value. The increased of haematochrite value indicates increased blood viscosity. In erythrocyte component, there is haemoglobin, a protein that contains iron which binds the oxygen.

The analysis of variance result showed that all treatments did not have any significant differences in erythrocyte, haemoglobin, and haematocrit levels ($p>0.05$) (Table 3). All groups of experimental rats had erythrocyte, haemoglobin, and haematocrit levels in accordance with the reference values 6.35–8.05x10^6/mm^3, 13.10–16.10 g/dl, and 33.00–50.00%, respectively (Booth *et al.* 2010; He *et al.* 2017).

This showed that GMO soybean and Non-GMO soybean (local and imported) were capable in providing nutrients intake for erythrocyte synthesis. Soybean is a source of vitamin B, contains a relatively high level of Fe, and non-essential nutrients. There are several precursors

Table 1. Proximate analysis of soy flour and casein

Parameter	Types of flour			
	GMO soybean	Non-GMO soybean	Grobogan soybean	Casein
Water (% wb)	3.45±0.44	4.25±0.42	4.03±0.01	4.21±0.16
Ash (% db)	3.58±0.03^b	3.70±0.04^c	3.17±0.01^a	4.16±0.06^d
Crude protein (% db)	48.45±1.82^a	43.80±7.26^a	49.69±1.06^a	79.22±0.31^b
Fat (% db)	31.13±0.27^d	29.85±0.14^c	26.43±0.43^b	0.24±0.01^a
Carbohydrate (% db)	16.84±1.57	22.65±7.08	20.72±0.63	12.18±0.20
Crude fiber (% db)	7.78±0.35^b	7.83±0.85^b	7.65±0.32^b	0.43±0.31^a

The numbers on the same line with different letters showed significantly different results ($p<0.05$) based on Duncan's test; db: Dry base; wb: Wet base; GMO: Genetically modified organism

Table 2. Ration composition (g/kg)

Types of flour	Protein	Corn oil	Mineral	Vitamin	Water	CMC[1]	Corn starch
GMO20	413	0	35	10	36	0	506
GMO10	206	16	43	10	43	0	682
Non-GMO20	457	0	33	10	31	0	470
Non-GMO10	228	12	42	10	40	0	668
Local20	402	0	37	10	34	0	516
Local10	201	27	44	10	42	0	676
Casein	126	80	45	10	45	9	685

GMO20: GMO soy flour 20% protein content; GMO10: GMO soy flour 10% protein content; Non-GMO20: Non-GMO soy flour 20% protein content; Non-GMO10: Non-GMO soy flour 10% protein content; Local20: Local grobogan soy flour 20% protein content; Local10: Local Grobogan soy flour 10% protein content; [1]Carboxymethyllcellulose

which affect the formation and maturation of erythrocyte and haemoglobin, namely Fe, B9 and B12 vitamins, and amino acids. Deficiency from one of those nutrients will result in the disturbance of erythrocyte and haemoglobin synthesis, which resulting in anaemia.

The functions of white blood cell or leucocyte are to fight infections, protect the body against foreign organism through phagocytosis, and the synthesis and distribution of antibodies. The increase in total leucocytes can be caused by the body's response to infection, inflammation, stress, and certain diseases. The analysis of variance result showed that there were not any significant differences in leucocyte levels ($p>0.05$). Table 3 showed that all types of soybean flour and its protein concentration resulted in leucocyte level within the normal range in experimental rats, which was 3.00–11.13x10^3/mm^3 (He *et al.* 2017). Several health concerns have been associated with GM food that are caused by inserted foreign gene, like allergenicity, toxicity or genetic hazards. The results of this study could indicate that rats which

Table 3. Haematological profiles of rats after 90 days of trial

Types of flour	Haematology profile				
	Erythrocytes (x10^6/mm^3)	Haemoglobin (g/dl)	Haematocrit (%)	Leucocytes (x10^3/mm^3)	Platelets (x10^3/mm^3)
GMO20	7.81±0.36	13.68±1.09	36.26±1.95	7.74±2.11	618.40±42.47bc
GMO10	7.72±0.24	13.18±0.37	34.54±2.39	5.60±1.26	564.80±33.54[ab]
Non-GMO20	7.45±0.15	13.26±0.73	34.64±1.44	7.68±1.04	697.40±53.81[d]
Non-GMO10	7.45±0.15	13.06±0.40	34.76±1.58	7.60±1.04	676.00±74.71[cd]
Local20	7.92±0.25	13.82±0.58	35.66±1.36	7.5±1.08	666.00±66.35cd
Local10	7.61±0.45	13.10±0.60	33.88±1.78	7.62±1.57	524.00±63.65[a]
Casein	7.92±0.47	13.84±0.76	36.56±1.50	7.36±2.82	614.60±30.70[bc]
Reference value	6.35–8.05	13.10–16.10	33.00–50.00	3.00–11.13	370–1383

GMO20: GMO soy flour 20% protein content; GMO10: GMO soy flour 10% protein content; Non-GMO20: Non-GMO soy flour 20% protein content; Non-GMO10: Non-GMO soy flour 10% protein content; Local20: Local grobogan soy flour 20% protein content; Local10: Local Grobogan soy flour 10% protein content; The numbers in the same column with different letters showed significantly different results ($p<0.05$) based on Duncan's test

were fed with GMO soybean did not develop any inflammation even when the protein consumption was increased to 20%.

The platelets are synthesised inside the bone marrow and contribute to blood clotting and homeostasis. The analysis of variance result showed that the treatments had a very significant effect on platelets level in blood ($p<0.05$). The 10% local soybean treatment had the lowest platelet levels. Low platelet levels could indicate that an inflammation was occurring. However the platelet levels were still within the normal range for the experimental rats, which was 370–1383x10^3/mm^3 (Petterino & Argentino-Storino 2006). So it can be inferred that the inflammation did not occur in all treatments.

The consumption of local Grobogan soybean, imported GMO, and non-GMO soybean along with the increase of protein level in experimental rats for 90 days had some effects in the haematological profile. Even though there were some effects, all haematological profiles were still within the reference range level. Therefore, imported GMO are just as safe as non-GMO soybean (local Grobogan and imported). This result was in accordance with Qi *et al.* (2012), who stated there were not any haematological abnormalities observed in Sprague-Dawley rats for 90 days when its fed with GMO soybean that express cp4 epsps, even when the protein consumption is 30%.

Blood glucose

Glucose is a result of carbohydrate metabolism and glycogen conversion in the liver. Blood glucose testing is a screening protocol to show the inability of pancreatic cells to produce insulin, the inability of small intestine to absorb glucose, the inability of cells to utilise glucose efficiently, and the inability of liver to store and catabolise glycogen.

The analysis of blood glucose in experimental rats which were fed with ration from different types of protein source and level is shown in Figure 1. The analysis of variance result showed that the treatments did not have any significant effects in blood glucose of the experimental rats ($p>0.05$). The blood glucose levels in all groups after 90 days of treatment remained below the reference value to be categorised as diabetic, specifically 250 mg/dl to indicate that the rats suffered from diabetes mellitus (Fathiazad *et al.* 2013).

Soybeans have non-nutritional compounds that has the ability to maintain blood glucose levels such as isoflavones, saponins, tannins and oligosaccharides by inhibiting α-amylase and α-glucosidase activity. Oligosaccharides in soybean were classified as Soluble Dietary Fiber (SDF) which could not be digested by digestive enzymes and were able to be fermented by the intestinal bacteria.

Serum lipid profile

The recommended lipid profiles which need to be routinely checked are total cholesterol, Low Density Lipoprotein (LDL) cholesterol, High Density Lipoprotein (HDL) cholesterol, and Triglyceride (TG). Cholesterol is a lipid compound that is needed by the body to synthesise

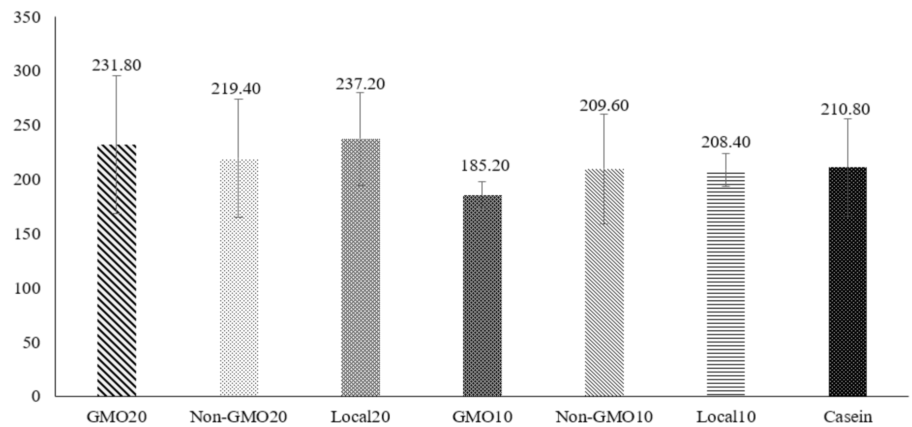

Figure 1. Rats blood glucose profile after 90 days of trial for each types of flour

important substances such as cell membrance, hormones, vitamin D, and bile acid. However, the excessive consumption of cholesterol could cause hypercholesterolaemia. There were two types of cholesterols which were observed in this study, namely LDL and HDL. LDL is known as “the bad cholesterol” which can cause the constriction of blood vessel which is known as atherogenic effect. Meanwhile, HDL is known as “the good cholesterol” due to its anti-atherogenic effect.

Daleprane *et al.* (2010) showed that the consumption of GMO and non-GMO soy can reduce the value of triglycerides and total cholesterol compared to consuming an animal protein source. However, this study did not show a significant difference ($p>0.05$) between plant protein (soybean) and animal protein (casein).

The analysis of variance result showed that all experimental groups treatments did not have any significant effects in cholesterol, triglycerides, HDL, and LDL levels ($p>0.05$) (Table 4). All parameter levels were within the normal range, which were 24.36–78.50 mg/dl for cholesterol, 20.37–117.80 mg/dl for triglyceride (He *et al.* 2017), 35.00–66.70 mg/dl for HDL, and 20.28–81.55 mg/dl for LDL (Ihedioha *et al.* 2013). The level of HDL in experimental rats were higher compared to its LDL level.

Serum protein profile

The analysed serum protein profile in this study consisted of total protein, albumin, ureum and creatinine (Table 5). The serum protein profile can be used to evaluate the condition of the liver and kidneys. Albumin is a main protein in blood which is synthesised by the liver to maintain the balance of water distribution in the body. Ureum or urea content in the blood (Blood Urea Nitrogen (BUN)) is a metabolised protein stored in the liver and acts as the indicator of kidney function. Creatinine is a by-product which is resulted from the break down of creatine muscle and phosphocreatine produced during skeletal muscle contraction.

The result of variance analysis (Table 6) showed that GMO soybean that was given to rats did not have any significant effect in the total protein value and creatinine ($p>0.05$). However, GMO soybean 10% protein had a significant effect ($p<0.05$) in lowering the albumin and ureum value ($p<0.05$). The increased in albumin and ureum values in rats fed 20% protein were due to the influence of higher protein concentrations than rats fed 10% protein. Although there are significant differences in some values of serum protein profile, these values are still within the reference value.

Table 4. Profiles of rat lipid serum after 90 days of trial

Types of flour	Serum lipid profile			
	Total cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
GMO20	49.80±8.70	39.80±5.93	45.00±5.15	37.00±15.36
GMO10	54.60±10.38	45.50±12.26	49.60±11.06	45.20±18.43
Non-GMO20	44.60±11.08	47.80±16.10	44.60±5.46	28.80±5.97
Non-GMO10	47.20±9.36	50.40±15.98	46.20±4.92	31.40±2.41
Local20	48.00±2.55	38.60±5.90	47.20±2.17	32.20±4.76
Local10	58.60±7.27	49.20±6.91	52.60±6.46	36.00±6.67
Casein	59.2±11.39	55.80±14.62	54.80±12.76	32.40±2.07
Reference value	24.36–78.50	20.37–117.80	35.00–66.70	20.28–81.55

GMO20: GMO soy flour 20% protein content; GMO10: GMO soy flour 10% protein content; Non-GMO20: Non-GMO soy flour 20% protein content; Non-GMO10: Non-GMO soy flour 10% protein content; Local20: Local grobogan soy flour 20% protein content; Local10: Local Grobogan soy flour 10% protein content; The numbers in the same column with different letters showed significantly different results ($p<0.05$) based on Duncan's test
HDL: High density lipoprotein ; LDL: Low density lipoprotein

Table 5. Profiles of rat serum protein after 90 days of trial

Types of flour	Serum protein profile			
	Total cholesterol (mg/dl)	Albumin (mg/dl)	Ureum (mg/dl)	Creatinine (mg/dl)
GMO20	6.46±0.61	3.30±0.21b	31.62±6.14[ab]	0.63±0.05
GMO10	5.61±0.20	2.92±0.11[a]	25.14±2.29[a]	0.69±0.16
Non-GMO20	6.82±1.00	3.35±0.30[b]	38.16±5.26[bc]	0.63±0.10
Non-GMO10	6.73±1.04	3.31±0.29[b]	38.54±5.05[bc]	0.64±0.10
Local20	6.50±0.40	3.43±0.14[b]	54.60±8.34[d]	0.70±0.06
Local10	6.08±0.31	3.12±0.16[ab]	42.86±2.75[c]	0.70±0.15
Casein	6.60±0.48	3.41±0.33[b]	31.76±4.92[ab]	0.84±0.14
Reference value	5.80–8.10	2.40–4.10	18.50–96.35	0.29–0.90

GMO20: GMO soy flour 20% protein content; GMO10: GMO soy flour 10% protein content; Non-GMO20: Non-GMO soy flour 20% protein content; Non-GMO10: Non-GMO soy flour 10% protein content; Local20: Local grobogan soy flour 20% protein content; Local10: Local Grobogan soy flour 10% protein content; The numbers in the same column with different letters showed significantly different results ($p<0.05$) based on Duncan's test

The reference value of the total protein, albumin, ureum, and creatinine were 5.80–8.10 g/dl for the total protein, 2.40–4.10 g/dl for the albumin, 18.50–96.35 mg/dl for the ureum, and 0.29–0.90 mg/dl for the creatinine (Petterino and Argentino-Storino 2006). These indicated that the livers and kidneys of experimental rats which were fed with local, imported GMO, and non-GMO soybean for 90 days remained in good condition.

Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT)

Liver cells produce two types of enzyme that are used for liver function indicator, namely the Aspartate Aminotransferase (AST) and the Alanine Aminotransferase (ALT). ALT is commonly found in liver and less in the heart, kidney, and skeletal muscle. Therefore, ALT level is more specific to liver function than AST.

AST enzyme, on the other hand, is commonly found in lungs, cardiac muscle, skletal muscle, pancreas, bone, and brain. In normal condition, AST and ALT are present inside the liver cell. If the liver cell is damaged and cannot maintain the integrity of its cell membranes, both enzymes will be released into the blood circulation. The higher the level of AST and ALT in blood, the more severe the liver damage. The increase of AST and ALT occur during the oxidative stress, obesity, liver cirrhosis, and hepatitis.

The analysis of variance result showed that there was a significant effect ($p<0.05$) from the treatments in experimental rats' AST and ALT level (Table 6). However, Duncan's further test showed that in AST value, GMO soybean were not significantly different from non-GMO soybeans (local Grobogan and imported), but it had a significant effect in increasing the ALT value. Although there were significant differences between the treatment groups, the AST and ALT levels were still in accordance with the reference levels 59.00–139.00 U/L and 19.00–56.00 U/L, respectively (He *et al.* 2017).

Results showed that soybean protein and its non-protein nutrients were capable in maintaining the cell integrity. Zhang *et al.* (2015) reported that the oligosaccharides in soybean was capable to decrease the AST and ALT levels. It also provided protective effects from oxidative stress in heart cells. In this study, the levels of AST and ALT did not indicate the liver damage occurrence in the experimental rats. In addition, the relative weight of liver organ to body weight (Table 6) levels were still within the normal range

Table 6 . Profiles of AST, ALT, liver weight and uric acid of rats after 90 days of trial

Types of flour	AST (U/L)	ALT (U/L)	% The relative weight of the liver	Uric acid (mg/dl)
GMO20	78.20±11.05[ab]	48.20±15.80[abc]	2.58±0.23	0.72±0.22[b]
GMO10	80.20±8.81[abc]	50.20±7.66[bc]	2.62±0.23	0.38±0.23[a]
Non-GMO20	65.60±12.97[a]	35.80±5.17[a]	2.67±0.22	0.40±0.25[a]
Non-GMO10	67.20±15.19[a]	37.20±6.38[ab]	2.54±0.16	0.32±0.13[a]
Local20	81.60±13.87[abc]	47.40±3.85[abc]	2.70±0.36	0.36±0.11[a]
Local10	99.60±18.53[c]	55.60±13.87[c]	2.75±0.20	0.36±0.19[a]
Casein	80.34±16.98[bc]	37.60±6.65[ab]	2.55±0.18	0.62±0.28[ab]
Reference value	60.00–139.00	19.00–56.00	2.30–3.10	1.50–3.00

GMO20: GMO soy flour 20% protein content; GMO10: GMO soy flour 10% protein content; Non-GMO20: Non-GMO soy flour 20% protein content; Non-GMO10: Non-GMO soy flour 10% protein content; Local20: Local grobogan soy flour 20% protein content; Local10: Local Grobogan soy flour 10% protein content; The numbers in the same column with different letters showed significantly different results ($p<0.05$) based on Duncan's test

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase

of 2.3–3.10%. Organ to body weight could be used as the most sensitive indicator to evaluate the treatment effect in toxicology studies (Piao *et al.* 2013). The results showed that GMO soybean administration for 90 days did not show any toxic effects on the liver. It means, GMO soybean is as safe as non-GMO soybean (local Grobogan and imported) in terms of toxicity effects on the liver.

Uric acid

Uric acid is a final product of the catabolism of nucleic acid in which 90% of it were the product of purine catabolism aided by guanase and xanthine oxidase enzymes. The analysis of uric acid profile in rats serum is shown in Table 6. The analysis of variance results showed that the treatment had a significant effect on the level of uric acid in experimental rats ($p<0.05$). The normal level of uric acid for rats ranged between 1.50–3.00 mg/dl. The analysis result showed that the uric acid levels were lower than its normal level. According to the Indonesian Ministry of Health (2011), the level of uric acid was not clinically significant if the level was below its normal range.

This study showed that the consumption of soybean did not increase the uric acid level in experimental rats, even though the consumption was increased to 20%. Therefore, the perception in society regarding the consumption of soybean can increase the level of uric acid is not scientifically proven. This statement is supported by a study done by Messina *et al.* (2011) which stated that soybean consumption and soybean raw material did not increase the level of uric acid in serum. This result was suspected due to the presence of isoflavones in which could prevent the xanthine oxidase in oxidating nucleic acid (Li *et al.* 2013).

CONCLUSION

Subchronic toxicity testing for 90 days on experimental rats showed that the imported GMO soybean had the same or equivalent haematological and biochemical serum value as the non-GMO soybean (local Grobogan and imported). Although there were significant differences in several parameters, all treatment groups had haematological and biochemical serum profiles that were within the normal reference value range. These results indicated that the imported GMO is as good as the non-GMO soybean (local Grobogan and imported).

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AUTHOR DISCLOSURES

The authors do not have any conflict of interest.

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