Original article

Evaluation subchronic toxic effect of polysaccharide peptide on lipid and hematologic profile in *Rattus norvegicus* strain Wistar

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Abstract:

Objective: There are many unknown safety for consumption in a compound of medicinal plants, one of them is polysaccharide peptide (PSP) of the extract of *Ganoderma lucidum*. Polysaccharide peptide (PSP) from *Ganoderma lucidum* mushroom extract is a bioactive substances found in the mushroom that is expected to be a drug that is safe for consumption. It is an antioxidant that has been used in the wider community as a chronic hepatopathic medicine, hypertension, and hyperglycemia. PSP cannot be circulated to the public before passing some toxicity tests to obtain information about its safety and to investigate the effect. There are many things that can be assessed from this toxicity test, some of them are lipid profile that includes (cholesterol, HDL, LDL, and TG) and blood profile (leukocytes, erythrocytes, and platelets). ***Materials and Methods***: This study used experimental post test only control group design. The sample consisted of 80 *Rattus norvegicus* Wistar strain (40 males and 40 females) were divided into normal group, the group with the administration of a dose PSP 300, 600, 1200 mg/kg/hr) for 90 days. Parameters measured were lipid and hematological profile. ***Results and Discussion***: The result of the analysis using ANOVA showed no significant effect on the administration of PSP on the level lipid and hematologic profile. The examination showed not significant at the lipid profile (cholesterol, TG, HDL, and LDL) and leukocytes. It is same as platelet and erythrocytes profile whereas there is only PCT, MCV, MCH, RBC, and RDW changed significantly, but still within normal limits. ***Conclusion***: Administration Polysaccharide peptide in subchronic study mostly showed no significant effect on the levels of lipid profiles and hematology even though there is significant effect in some parameters but it still within the normal limit. Findings from this study suggest that Polysaccharide peptide of *Ganoderma lucidum* is safe and can be exploited in healthcare delivery systems.

Key word: toxicity; polysaccharide peptide; Ganoderma lucidum; lipid profile; hematological profile; Rattus norvegicus strain wistar

Bangladesh Journal of Medical Science Vol. 15 No. 03 July'16. Page : 409-415

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Introduction:

BPPOM Indonesia (Food and Drug Administration) has received 11 276 complaints or requests for information about the drug and food since 2011. Compared to the previous year's data (2010), the number of complaints or requests for information to ULPK (Consumer Complaints Service Unit) POM increased by 10 , 48%, ie from 10 206 be 11,276. Based on the type of commodity, it can be seen that the group of complaints / requests for information that most are related to food products as much as 5,847 (51.85%), followed by successive cosmetics of 1,769 (15.69%), of traditional medicine as much as 1,598 (14.17%) and the rest is related to drugs, hazardous materials, food supplements, drugs, medical devices (medical Devices), Household Health (PKRT), and other general information.[1]

Based on these data, there are many people who use traditional medicine and medicinal plants, especially the middle to lower in an effort to preventive, promotive and rehabilitative. While many people assume that the use of medicinal plants or traditional medicines are relatively safer than synthetic drugs. However not mean herbs or traditional medicine does not have adverse side effects, if its use is less precise.[2] In addition to traditional medicine, it is also often occur on medicinal plants commonly consumed by the public, among others: supplements, vitamins, herbs and others. However there are some medicinal plants of unknown safety for consumption, one of which is a polysaccharide peptide (PSP) from Ganoderma lucidum mushroom extract.

Polysaccharide peptide (PSP) from Ganoderma lucidum mushroom extract is an agent that is expected to be a drug that is safe for public consumption. Polysaccharide peptide is a bioactive substances found in the PSP and is an antioxidant that has been used in the wider community as an agent for treatment of dizziness, insomnia, palpitations, shortness of breath, cough, and asthma.[3] Polysaccharide peptide can not be released to the public before passing some toxicity tests to obtain information about the drug's safety as well as a preliminary step before test directly to humans.[4] There are many things that can be assessed from this toxicity test, some among which is the lipid profile and hematology.

In SSR assessment lipid profile, there are several components that can be assessed that the total cholesterol, triglycerides, HDL and LDL in the blood.[5] Cholesterol is needed for the body and is used to form cell membranes, producing sex hormones and bile acids form , which is needed to digest lemak. Cholesterol is needed to obtain an optimal health. If levels of cholesterol in the blood is too high, precipitation will occur on the walls of blood vessels, and this can lead to a high risk of heart disease.[6]

While the blood profiles are profiles of erythrocytes, leukocytes and platelets.[4] Blood has an important role in the body as a component of the body's circulation which plays an important role in the transport function and hemostasis process. Disorders of the blood can occur when the number of blood components consisting of erythrocytes, leukocytes, and platelets in the blood is not normal, well below normal levels or above normal levels. This number can be affected by many factors one of which is exposure to chemicals or radiation.[7]

Materials and methods:

Study Group

The experimental animals were 80 *Rattus norvegicus* Wistar strain rats, aged 6 weeks with body weight of 100-150 g from CV. Gamma Scientific Biolab, Malang, Indonesia. Rats were divided into 8 kelompok: normal male, normal female, 3 positive control male dan 3 positive control female with administration of PSP dose: 300, 600,1200 mg/ kgBW. Administration of PSP was done with oral gavage once daily for 90 days. Maintenance *Rattus noevegicus Wistar* rats was conducted at the Laboratory of Pharmacology, Faculty of Medicine, University of Brawijaya, after we have obtained ethical clearance from the Health Research Ethics Committee by number: 400/112/K.3/302/2014. Measurement of parameters was conducted at the cental laboratory of dr. Saiful Anwar Hospital, Malang, Indonesia.

Measurement of Parameters

1. Total Cholesterol (Cobas-6000)

Cholesterol is estimated in serum by enzymatic colorimetric test on Roche automated clinical chemistry analyzersCholesterol esters are cleaved by the action of cholesterol esterase to yield free cholesterol and fatty acids. Cholesterol oxidase then catalyzes the oxidation of cholesterol to cholest-4-en-3-one and hydrogen peroxide. In the presence of peroxidase, the hydrogen peroxide formed effects the oxidative coupling of phenol and 4-aminophenazone to form a red quinone-imine dye.

Cholesterol esters + H_2O Cholesterol + RCOOH
Cholesterol + O_2 Cholest-4-en-3-one + H_2O_2

$2\ H_2O_2$ + 4-AAP + Phenol quinone-imine dye + $4\ H_2O$

The color intensity of the dye formed is directly proportional to the cholesterol concentration. It is determined by measuring the increase in absorbance.

2. LDL Cholesterol (Cobas-6000)

LDL Cholesterol is estimated in serum by homogenous enzymatic colorimetric assay on Roche automated clinical chemistry analyzers.

LDL-cholesterol esters + H_2O Cholesterol + free fatty acid

LDL-cholesterol esters are cleaved by the action of cholesterol esterase to yield free cholesterol and fatty acids. In the presence of oxygen, cholesterol is oxidized by cholesterol oxidase to Δ^4-cholestenone and hydrogen peroxide.

LDL-cholesterol + O_2 Δ^4-cholestenone + H_2O_2

In the presence of peroxidase, the hydrogen peroxide generated react with 4-amino-antipyrine and HSDA to form a purple-blue dye.

2 H2O2 + 4-aminoantipyrine + HSDA[a] + H_2O + H^+ purple-blue piqment + $5\ H_2O$

The color intensity of this dye is directly proportional to the cholesterol concentration and is measured photometrically.

3. HDL Cholesterol (Cobas-6000)

HDL Cholesterol is estimated in serum by homogenous enzymatic colorimetric assay on Roche automated clinical chemistry analyzers. In the presence of magnesium ions, dextrans sulfate selectively form water-soluble complexes with LDL, VLDL and chylomicrons which are resistant to PEG-modified enzymes. The cholesterol concentration of HDL-cholesterol is determined enzymatically by cholesterol esterase and cholesterol oxidase coupled with PEG to the amino groups (approx. 40%). Cholesterol esters are broken down quantitatively into free cholesterol and fatty acid by cholesterol esterase.in the presence of oxygen, cholesterol is oxidized by cholesterol oxidase to Δ^4-cholestenone and hydrogen peroxide. In the presence of peroxidase, the hydrogen peroxide generated react with 4-amino-antipyrine and HSDA to form a purple-blue dye. The color intensity of this dye is directly proportional to the cholesterol concentration and is measured photometrically.

4. Triglycerides (Cobas-6000)

Triglycerides in the serum were estimated by enzymatic colorimetric method on Roche automated clinical chemistry analyzers. This method is based on the work by Wahlefeld using a lipoprotein lipase from microorganisms for the rapid and complete hydrolysis of triglycerides to glycerol followed by oxidation to dihydroxyacetone phosphate and hydrogen peroxide.

Triglycerides + $3\ H_2O$ glycerol + 3 RCOOH

Glycerol + ATP glycerol-3-phosphate + ADP

Glycerol-3-phosphate + O_2 dihydroxyaceton phosphate + H_2O_2

H_2O_2 + 4-aminophenazone + 4-chlorophenol 4-(p-benzoquinone-monoimino)-phenazone + H_2O_2

The hydrogen peroxide produced then reacts with 4-aminophenazone and 4-chlorophenol under the catalytic action of peroxidase to form a red dyestuff (trinder endpoint reaction). The color intensity of the red dyestuff formed is directly proportional to the triglyceride concentration and can be measured photometrically.

Blood complete levels measurement (Sysmex XN-1000)

1. **Red blood cell (RBC)/Platelet (PLT)**

Blood is aspirated from the manual aspiraton pipette to the sample rotor valve. 4.0 μL of blood, measured by the sample rotor valve, is diluted to a ratio of 1:500 with 1.9960 mL of CELLPACK, and then sent to the RBC sample chamber as the diluted sample. The sheath injector piston sends 10.3 μL (30.9 μL in body fluid analysis mode) of diluted sample slowly to the RBC/PLT detector. The RBD detector counts the RBC and PLT via the Hydro Dynamic Focusing (DC Detection). At the same time,the hematocrit (HCT) is calculated via the RBC pulse height detection method.

2. **White blood cell (WBC)**

Blood is aspirated from the manual aspiration pipette o the sample rotor valve. 20 μL of blood, measured by the sample rotor valve, is diluted to a ratio of 1:50 with 0.980 mL of STROMATOLYSER-FB, and then sent to the reaction chamber as the diluted sample. After reacting for about 14 seconds in this condition, the red blood cells are hemolyzed. The sheath injector piston sends 40 μL of diluted sample to the optical detector block. In the optical detector block, the sample is analyzed via flow cytometry method utilizing a semiconductor laser.

Statistical Test

This study used One Way Analysis of Variance (ANOVA) to determine the effect of PSP on lipid and hematologic profile in *Rattus norvegicus* Wistar strain rats. Then Post Hoc test was performed to identify differences between groups This study used numeric data, so it concluded parametric procedures. Statistical Software Product and

Service Solutions (SPSS) software version 20 (IBM Corporation, 590 Madison Avenue, New York, USA) was utilized to obtain the data analysis.

Results and dicussion:

Results

Average level of the highest RBC found in groups of 3 male with an average grade of 8.7 RBC units per liter. While the average level of the lowest RBC found in group 1 female with an average grade of 6.7 RBC units per liter. Average level of the highest MCV found in group 1 female with an average MCV levels of 59.2 units per liter. While the average level of the lowest MCV found in group 2 males with an average grade of 49.8 MCV units per liter. It is also known that the average level of the highest MCH found in groups of 3 females with an average grade of 17.5 MCH units per liter. While the average level of the lowest MCH found in group 2 males with an average grade of 15.1 units per MCH average liter. Highest level MCHC found in groups of 3 male with an average grade of 30.9 MCHC units per liter. While the average level of the lowest MCHC found in group 1 female with an average grade of 29.2 units per MCHC average liter. Highest level of RDW found in group 2 males with an average grade of 22.4 RDW units per liter. While the average level of the lowest RDW found in normal female group with average levels of RDW at 16.1 units per liter. Average level of the highest HB found in the group of 3 males with an average grade of 13.4 units per liter HB. While the average level of the lowest HB was found in group 1 female with an average grade of 11.4 HB units per liter. Average WBC levels are highest in group 1 male with an average grade of 17.73 WBC. While the average level of the lowest WBC was found in the group of normal females with an average grade of 11.74 WBC.

In this study, obtained a change in the number of significant ($P < 0.050$) of platelets from a group of females who get exposure to the PSP than normal. In the female group exposure to 1, obtained value - average number of platelet as much as 718 ± 7:29 x 103 / uL, where the value is significantly below the control value (861.7 ± 106.11 x 103 / uL) .In female exposure group 2, the average value obtained - average number of total 919.3 ± 57.82 plateletnya x 103 / uL where the posthoc test this value can be expressed into the normal criteria or increased. Whereas in the female group exposure 3, obtained value - average number of platelet as 965 ± 104.25x 103 / uL and enter into the

Table 1. Effect of PsP on all parameters in all of dose group

Parameter	Groups														Analisis Anova (p-value)
	Jantan Normal		Betina Normal		Jantan + PsP 300mg/ KgBB		Betina + PsP 300mg/ KgBB		Jantan + PsP 600mg/ KgBB		Betina + PsP 600mg/ KgBB		Jantan + PsP 1200mg/ KgBB		Betina + PsP 1200mg/ KgBB		
		Min - Max		Min - Max		Min - Max		Min - Max		Min - Max		Min - Max		Min - Max		Min - Max	
RBC	7.6±0.5	6.82-8.4	7.2±0.5	6.53-7.91	8.3±0.6	7.76-9.18	6.7±0.56	6.03-7.34	8.1±0.4	7.42-8.5	7.2±0.7	6.21-8.09	8.7±0.3	8.4-9.21	7.1±0.6	6.08-7.84	0.452
HB	12.5±0.9	10.6-13.3	12.4±0.5	11.7-12.7	13.3±1.1	11.6-14.9	11.4±0.8	10.5-12.4	12.2±0.9	10.9-13.2	11.7-13.9	10.5-12.8	13.4±0.64	12.5-14.2	12.5±1.34	10.1-14.0	0.148
MCV	56.5±0.2	54.0-60.0	58.0±5.9	49.5-64.9	55.1±2.49	51.5-57.9	59.2±1.8	56.8-61	49.8±1.67	47.8-51.5	57.3±4.3	53.0-63.3	50.5±1.1	49.0-52.0	57.4±1.0	55.6-58.6	0.795
MCH	16.5±0.8	15.5-17.2	17.4±1.1	16.1-18.5	16.2±0.3	15.8-16.6	17.0±0.2	16.7-17.2	15.1±0.5	14.6-16	16.3±1.1	15-18.2	15.4±0.8	14.1-16.8	17.5±0.5	16.6-18.1	0.095
MCHC	29.5±1.8	27-31.8	30.5±1.2	29.0-32.2	29.5± 1	28.2-31.1	29.2±0.6	28.5-29.7	30.2±0.4	29.5-30.7	30.5±1.3	28.4-31.8	30.9±1.0	30.1-31.4	30.5±1.2	29.5-32.1	0.153
RDW	18.9±2.3	14.9-21.4	16.1±2.5	13-19.4	19.7±1.1	18.6-21.3	18.4±1.5	16.6-20.1	22.4±1.5	20.4-24.7	18.6±2.7	14.6-21.9	22.0±1.3	19.0-23.9	17.3±3.0	13.2-21.0	0.285
WBC	13.9±2.5	9.5-16.5	11.7±2.4	7.6-14.7	17.7±4.5	13.6-26.3	17±6.5	11.9-24.2	16.6±3.6	12.2-20.9	13.4±1.1	11.8-14.9	14.5±2.8	11.9-19.3	12.3±2.1	10.5-15.9	0.317
PLT	958.7±157.7	782-1232	861.7±106.1	757-1039	1092.7±72.7	888-1497	718±7.3	706-943	792.2±72.8	732-1233	919.3±57.8	839-1001	933.3±161.5	761-1067	965±104.3	784-1281	0.003
MPV	7.8±0.6	7.2-8.6	7.6±0.5	7.1-8.3	7.8±0.7	7.1-9	8±0.4	7.5-8.6	7.8±0.9	6.7-7.4	7.1±0.3	6.7-8.9	7.1±0.4	6.7-7.8	7.6±0.4	7-8.3	0.161
PCT	0.8±0.16	0.67-1.06	0.7±0.1	0.6-0.76	0.8±0.05	0.71-1.26	0.6±0.06	0.09-0.72	0.6±0.12	0.47-1.1	0.7±0.04	0.6-0.71	0.6±0.07	0.53-0.9	0.7±0.03	0.62-0.95	0.803
Kolesterol total	55.87±13.03	43-77	72.5±17.1	47-98	60.1±11.31	42-81	55.7±8.3	41-66	53.2±7.96	41-64	63.1-15.1	49-72	60.7±15.3	47-99	63.5±13.5	50-90	0.229
TG	78.85±33.05	42-126	92.8±33.03	50-158	64.1±21.7	31-102	82±30.8	44-132	53.1±17.5	22-80	69.4±16.6	53-107	67±26.5	41-127	107±72.4	52-263	0.713
HDL	40.14±10.13	30-57	52.8±13.6	35-79	45±9.09	29-55	40±6.44	31-48	34.5±4.8	27-41	42±11.7	30-65	41.5±7.5	31-54	43.4±12.3	31-57	0.152
LDL	13±4.2	7-18	12.8±4.8	5-19	13.9±4.6	7-22	10±2.44	7-14	14.44±2.3	11-17	13.3±1.49	12-16	12.7±2.8	10-17	11.62±6.7	5-25	0.489

category increase. Different with exposure group females, the male exposure group, exposure group 1 obtained value - average total number plateletnya 1092.7 ± 72.74x 103 / uL, but this value is entered in the normal range when compared with the control group (958.7 ± 157.72 x 103 / uL). While male exposure group 2 and 3 has a value - average platelet count as much as 792.2 ± 72.8x 103 / uL and 933.3 ± 161.49 x 103 / uL where post hoc deployment of the value entered a decrease category. In female exposure group, it was found that the value - average MPV groups 1,2 and 3 has a value of 8 ± 0:43 fL, 7.1 ± 0.311 fL, and 7.60 ± 0:43 fL. This value is a post hoc did not have significantly different values of the control group (7.6 ± 0.46) by ANOVA . Males group also do not have different values than the control group (7.8 ± 0:57 fl). Value - average MPV of 1.2 and 3 male group was 7.8 ± 0.70 fL, 7.8 ± 0.87 fL, and 7.1 ± 0:35 fL. This value illustrates that exposure to the PSP does not affect the volume platelet. From this experiment that the female group no significant change in the percentage platecrit happened than average - average control value is 0.7% ± 0:06. Value female groups 1,2 and 3 respectively is 0.6 ± 0.06% ± 0.7% and 0.7 ± 0:04 of 0.03% . Different of a group of females, males exposure groups 2 and 3 has an average - average value pct lower percentage significantly and post hoc differ from the control group (0.8 ± 0.16%) with a value - average percentage of PCT by 0.6 ± 0.6% and 0.6 ± 0:12 0:07%. 1 male exposure group has a value that is not different post hoc with the control group 0.8 ± 0.05% by.

Average TC levels are highest in the group of normal females with an average TC levels of 72.6 mg / dL. While the average level of the lowest TC found in the group treated males PSP dose of 600 mg / kg / hr with an average TC levels of 53.3 mg / dL. Average TG levels are highest in the group of females who received a dose of 1200 mg PSP / kg / hr with an average TG levels of 82.0 mg / dL. While the average level of the lowest TG was found in the group of males who received a dose of 600 mg PSP / kg / hr with an average TG levels of 53.1 mg / dL. Average HDL levels are highest in the group of normal females with average levels of HDL by 52.9 mg / dL. While the average level of the lowest HDL found in the male group who received a dose of 600 mg PSP / kg / hr with an average HDL levels of 34.6 mg / dL. Based on the results of measurements of LDL cholesterol chart can be seen that the average LDL levels are highest in the group of males who received a dose of 600 mg PSP / kg / hr with an average LDL levels of 14.4 mg / dL. While the average level of the lowest LDL was found in the group of females who received doses PSP 1200mg / kg / hr with an average LDL levels of 10.0 mg / dL.

Discussion:

Changes in blood and lipid profile parameters in Wistar rat species are one of the parameters that can be measured to test the effect of a chemical. Oral administration of PSP in this study makes blood parameters become important because the swallowed substance will enter the body and absorbed and transferred to the target organ throughout the blood which may affect the blood profile. In addition, blood profile is very useful to determine the metabolic disorder that occurs and as additional information to determine the body's response to injury or stress.[8]

PSP as a natural antioxidant has a wide range of pharmacological effects such as anti-inflammatory, antioxidant and immune stimulating.[9] The pharmacologic effects may have an impact to blood and lipid profile of Wistar that were given PSP orally in subchronic exposure (90 days) by using the 3-dose exposure. Subchronic testing is needed to further understand the effects of PSP on the body after repeated drug administration in order to increase knowledge about safety that is useful for drug development. Subchronic testing can also determine the use of dose regimens.[10] In the experiment, we compare the exposure group with the normal group to determine whether the effects given are toxic or not. A statistical method ANOVA and post hoc with ($P < 0.05$) were used to find a significant difference while not forgetting to compare with the existing references.

In this experiment, it was found in female rats platelet count and MPV were significantly change by ANOVA, however only platelet count that recorded to have significantly change in post hoc basis. Female rats with 1200 mg / KgBW dose were noted to have an increase of platelet count while 300 mg / KgBW dose group having their platelet number decline. The increasing of platelets is thought to occur due to the effect of the PSP as an anti-inflammatory t hat reduced the used of circulating platelets resulted in platelet count value appears relatively increased. Although the number of platelets of 1200 mg / KgBW dose female rats group in this study were noted to be significant

(965 ± 104.25 x 10^3 / uL), but this value is still in normal range if we compared it with the existence reference which is 200 x 10^3 /uL – 1500 x 10^3 / uL.[11] Decreased platelet count that occur in the PSP 300 mg / KgBW dose were suspected to happen because of the low doses of anti-inflammatory effects on the PSP has not occurred significantly and variations clump formation are not counted by the platelet counting tools that makes the calculated value decreases.[12] This wide variation of platelets in rodent is also thought to hold the key role of the different sized of platelet in MPV measurement. The platelet count value which still inside the reference range and other platelet parameters in this group are still in normal range so it is considered to have no medically significant effect. The calculation of leukocytes and platecrit in female rats were noted to be normal. This illustrates that the PSP does not affect (non-pathological) on leukocytes and platelets.

In male rats the leukocyte shown to be normal like in female rats. The platelet profiles in male rats are almost the same with the female rats. The value of platelet count, MPV and Platecrit on some PsP exposed group changed significantly in ANOVA. Among the platelet parameters that changed significantly, only the value of the platelet count in the exposure group of 600 mg / KgBW which has a value of 792.2 ± 72.8 x 10^3 / uL and platecrit the exposure group of 600 mg / KgBW and 1200 mg / KgBW which closely related with MPV and platelet count values were noted to be decreased significantly in post hoc.This decrease in platecrit are due to the reduced number of platelets in the exposure group of 600 mg / KgBW and decreased MPV exposure group 1200 mg / KgBW. However, the decrease in platelet count and platecrit were still normal when viewed from the normal range of rat platelet reference.[11] It can be concluded that the changes occurred will not giving a clinical effect and subchronic exposure of PsP will give no toxic effects on leukocytes and platelets.;

In addition to measuring leukocytes and platelets, red blood cells examined by measuring the levels of hemoglobin, RBC, MCV, MCH, MCHC and RDW. In this study subchronic administration of PSP is seen not give any effect to the group of females with no significant change in all these parameters. Male exposure group has several variants of significant changes, the parameters MCH and MCV in the exposure group 600mg / KgBW and 1200mg / KgBW showed a decline, the number of erythrocytes in the group exposure to 300 mg / kg, 600 mg / kg and 1200mg / KgBW but significant increased only group 300mg / KgBW and 1200mg / 600mg dose KgBW and RDW / KgBW and dose 1200mg / KgBW showed a decline. This illustrates that the variation in the male group decreased erythrocyte size are almost evenly which makes the capacity of each erythrocyte hemoglobin decreased. The decline of the red cells may be due to variations of mice used. However, compensation occurs with increased erythrocyte and the results showed that hemoglobin levels were normal diangka. Hemoglobin level is essential for normal oxygen distribution shows subchronic exposure PSP does not interfere with the function of eritrosti for normal hemoglobin levels in the blood. Because of all these factors are interrelated.

Examination of lipid profile to see the effects of exposure to PSP subchronically whether it will have an impact in the form of dyslipidemia or other toxic symptoms turned out to give normal result. Total cholesterol, TG, and LDL, which is the cause of the formation of plaque in blood vessels when its value above normal was not rising on PSP subchronic exposure. HDL has an important role in the stabilization and regression of plaque, thus preventing the formation of emboli, inhibits the formation of atherosclerotic plaque or regressed plaque that has been formed as well as protection against LDL oxidation was also unchanged in this study.[13] Subchronic exposure of the PSP does not reduce levels of HDL in the blood so that HDL serves to protect the vascular organ can goodly performed.This proves that PSP does not interfere lipid profile and does not cause dyslipidemia.

Conclusion:

Oral administrations of PsP subchronicaly were not proven to affect or change the lipid profile. It's proven with no increase in total cholesterol, LDL and TG followed by the HDL which had normal value in this study. Blood profiles in general did not show the abnormality, only platelets and erythrocytes in some parameters and dose groups were changed significantly. However, when compared to the reference value, this value is still within the normal threshold so that it can be said this change will not impact clinically and it can be concluded that the PSP is safe to use in the long term.

Conflict of interest: None

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