Effect of corn silk powder extracts using in vivo to lipid profile and liver fat

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Abstract. This study aimed to determine the effect of corn silk powder extracts using in vivo to lipid profile and liver fat (a liver weight and adipose fat). The used experimental animals were 30 Sprague Dawley mice with 200-250 g mice weight divided into 6 groups. Each group of 5 mice was randomly determined, then the mice were caged individually. At the time of intervention for 21 days, group I received standard food, group II got hypercholesterolemia induction, group III received high-fat food induction and simvastatin drug, group IV induced hypercholesterolemia and corn silk extract dose 2.25 ml, group V induced hypercholesterolemia and extract corn silk dose 4.5 ml, and group VI got hypercholesterolemia induction of corn silk extract dose 6.75 ml. The provision of corn silk extracts is based on recommendations for consumption of vegetables per day in humans from the Food and Drug Administration (FDA) which is 30-40 g/day. Corn silk extracts were given as much as 125 ml; 250 ml; and 375 ml. The dose was then converted to mice (0.018) to obtain 2.25 ml; 4.5 ml; and 6.75 ml. Corn silk powder extracts significantly affected \((p<0.05)\) on lipid profile and liver fat (a liver weight and adipose fat). The best corn silk powder extract was at a dose of 2.25 ml with lipid profile (total cholesterol of 24.4% from 120.29±2.23 ml/dl to 90.87 ±2.01 ml/dl, HDL cholesterol of 30.35% from 56.60 ±2.81 ml/dl to 81.26±1.88 ml/dl, LDL cholesterol of 53.84% from 57.47±0.82 ml/dl to 26.53±0.77 ml/dl, triglycerides of 29.14% from 98.15±1.92 ml/dl to 69.54±6.78 ml/dl), and liver fat content in P3 treatment dose 6.75 ml with a liver weight of 7.09 g and adipose fat of 6.99 g.

Keywords: Corn silk, powder, extract, lipid profile, a liver weight, adipose fat

1. Introduction
Hypercholesterolemia is a condition characterized by an increase in fasting low density lipoprotein (LDL) levels without an increase in triglyceride levels [1]. Cholesterol is an amphipathic lipid and is an essential structural component of the membrane and in the outer layer of plasma lipoprotein. This compound is synthesized from acetyl-CoA and is a steroid precursor, sex hormone, bile acid, and vitamin D [2]. Cholesterol is very closely related to the health of the liver and blood vessels. Due to the wrong diet and lifestyle, many people face health problems due to high cholesterol levels in the blood. The body needs not too much cholesterol. An excessive amount of cholesterol will cause atherosclerosis, hardening, and narrowing of blood vessels. This is caused by excessive cholesterol that can settle and accumulate on the surface of blood vessels, commonly known as plaque [3]. LDL cholesterol is a risk factor for atherosclerosis and HDL can prevent the occurrence of this process [4]. Cholesterol...
accumulation in the coronary arteries causes narrowing of the arteries so that the blood supply containing oxygen and nutrients to the liver decreases. Lack of blood supply can cause the liver muscle to lack oxygen. This reduced oxygen supply causes pain in the left chest. Atherosclerosis is a common cause of coronary liver disease. In this situation, fibrous plaque progressively narrows the arterial lumen, which decreases the volume of blood that can flow through the lumen. This condition can lead to myocardial ischemia and eventually, death liver tissue necrosis occurs [5]. The abnormality of cholesterol metabolism is indicated by one of them with an increase in low density lipoprotein or LDL cholesterol (≥160 ml/dl). Changes in LDL cholesterol also play a role in the pathogenesis of the coronary liver disease (CHD) and are a key factor in the management of coronary liver disease (CHD) [6].

One safe alternative to reduce total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides is to consume corn silk. Corn silk is a collection of stigmas that are smooth, soft, and look like threads and yellowish hair. Corn silk comes from female flowers from corn plants [7]. Initially, the hair color of corn is usually light green, then it will turn red, yellow and light brown depending on the variety. The function of corn silk itself is to trap pollen for pollination. The hair length of corn can reach 30 cm or more and has a rather sweet taste [8]. Utilization of corn silk which is a waste from corn cultivation is still limited in its use as traditional medicine such as can be used for peluruh urine and lowering blood pressure. In addition, usually, corn silk that is still included in the skin corn is used as animal feed. There are studies that extract compounds from corn silk using various solvents such as benzene, chloroform, ethanol, ethyl acetate, methanol, and petroleum ether. The results obtained showed positive results for flavonoid, alkaloids, phenols, steroids, glycosides, carbohydrates, terpenoid and tannins [7]. Chemical content in corn hair include protein, carbohydrates, fiber several vitamins such as: vitamin B, vitamin C, vitamin K, essential oils, mineral salts such as Na, Fe, Si, Zn, K, Ca, MI and P, phytochemical compounds such as sitosterol and stigmasterol, hasperidine derivatives and quercetin [9,10], contain phenols, terpenoids, and glycosides [11]. Besides corn silk also contains maysin, β carotene, beta sitosterol, geraniol, hordenin, limonen, mentol and viteskin [12]. Corn silk is rich in phenolic compounds, especially flavonoids [13]. Corn silk extract has a diuretic effect and solubility in kidney stones [14].

2. Materials and method

2.1. Materials
The corn variety used in this study was the local variety Bisma ±70 days old from Pati Regency, Central Java. The material used for testing corn silk powder extracts against lipid and liver fat profiles is Sparque Dawley (SD) male white mice, and mice feed consisting of casein, minerals, vitamins, L-cystine, and choline bitartrate ordered directly from the manufacturer (Sigma) Mixtures of vitamins (AIN-93-VX) and minerals (AIN-93-MX) were purchased from American ICN. Mice were purchased from the Experimental Animal Development Unit, Gadjah Mada University. The size of the rat sample was determined based on the Research Guidelines for Evaluating the Safety and Efficacy of Herbal Medicines WHO, namely a minimum of 5 mice per group [15].

2.2. Method
The experimental animals used were 30 Sprague Dawley mice aged 2-3 months with a bodyweight of 200-250 g. Each group consisted of 5 mice per group. The requirements of the mice used were not malnourished, healthy, normal activities and behaviour [16], and no anatomic defects were seen and were not included in the exclusion criteria of dead mice during treatment. Exclusion criteria were mice that did not want to eat and mice that experienced a decrease in physical state or died. The solvents used were methanol and with pro analysis quality (Sigma, or E-Merck) purchased at the Santosa chemical shop, Semarang.

The provision of corn silk extract is based on recommendations for the consumption of vegetables per day in humans from the Food and Drug Administration (FDA), which is 30-40 g/day. Corn silk extract was given as much as 125 ml; 250 ml; and 375 ml. The dose is converted to mice (0.018), so that 2.25
ml is obtained; 4.5 ml; and 6.75 ml. After the adaptation period was carried out the stage of making hypercholesterolemic mice for 4 weeks by giving quail egg yolk as much as 2 ml/head/day in all treatments except normal control. Then after obtaining hypercholesterol cholesterol mice, the next treatment was predetermined treatment every day for 21 days and every week during the treatment period blood was taken through retro orbital plexus to be tested for lipid and liver fat profiles in hypercholesterolemic mice. Next, mouse blood is taken retro-orbital plexus (through the eye) using hematocrit. Then put in the Eppendorf tube. After all samples were collected, the samples were centrifuged at 4000 rpm for 15 minutes. Serum in the form of upper clear liquid was separated by blood deposits using micropipette to see body weight, feed intake, lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), adipose fat and liver weight. Measurements of total cholesterol and HDL used the enzymatic colorimetric CHOD PAP test, LDL with the Friedward method, and triglycerides by the enzymatic colorimetric test GAP PAP method. Mice are said to be in a state of hypercholesterolemia if LDL cholesterol is >27.2 ml/dl [17].

3. Results and discussion

3.1. Total Cholesterol

The mean total cholesterol among the six treatments that experienced the most significant decrease in the 21st day in treatment P1 was 4.46%, from 120.29 ml/dl to 90.87 ml/dl (table 1). The decrease in total cholesterol in the plasma will cause changes related to the potential of lovastatin, namely by increasing the speed of LDL catabolism so that it reduces plasma LDL deposits which have an effect on decreasing cholesterol total (figure 1) [19]. The content of beta sitosterol in corn silk is thought to be able to reduce cholesterol levels. Beta sitosterol in the liver will accelerate the destruction of specific enzymes needed to produce cholesterol or indirectly inhibit cholesterol formation in the liver. Beta sitosterol has a chemical structure similar to cholesterol, so it can inhibit cholesterol absorption by the blood. Cholesterol that is not absorbed by blood will be excreted out of the body [20]. The mechanism of action of beta sitosterol in reducing cholesterol in the blood is to reduce the absorption of cholesterol including triglycerides and other food fats in the digestive system. The reduction of cholesterol absorption is done by locking on binding the fat molecules from food and blocking the fat molecules from being absorbed by the intestinal mucosa cells [21].

Table 1. Cholesterol in total.

| Observation                  | Initial Research | Day 7 | Day 14 | Day 21 |
|------------------------------|------------------|-------|--------|--------|
| N Standart                   | 88.60 ± 2.62     | 87.56 ± 2.86 | 87.01 ± 2.70 | 86.41 ± 2.36 |
| K (+) Hiper → Na CMC 0.5%    | 172.04 ± 1.96    | 162.99 ± 1.76 | 118.98 ± 2.48 | 87.25 ± 3.25 |
| K (-) Hiper → Obat           | 97.35 ± 1.86     | 95.59 ± 1.90 | 94.45 ± 2.10 | 89.48 ± 1.44 |
| P1 Hiper → Extract 2.25 ml   | 120.29 ± 2.23    | 112.60 ± 7.13 | 107.74 ± 2.86 | 90.87 ± 2.01 |
| P2 Hiper → Extract 4.5 ml    | 109.25 ± 1.65    | 105.20 ± 3.55 | 102.19 ± 1.15 | 89.33 ± 3.50 |
| P3 Hiper → Extract 6.75 ml   | 99.64 ± 1.14     | 98.43 ± 1.24 | 97.08 ± 1.15 | 87.19 ± 5.47 |
3.2. LDL cholesterol
The mean LDL cholesterol level among the six treatments that experienced the most significant decrease in the 21st day at treatment P1 was 53.84%, from 67.47 ml/dl to 26.53 ml/dl (table 2). The decrease in LDL cholesterol is suspected by the presence of flavonoids and beta sitosterol in the extract of corn silk powder. Flavonoids are known to have antioxidant activity that can react with free radicals through direct capture of oxygen free radicals and inhibit enzymes that cause free radicals such as cyclooxygenase and lipoxygenase to form. In reducing LDL cholesterol levels, these antioxidant compounds are thought to work by inhibiting the HMG-CoA reductase enzyme which functions as a catalyst in the formation of cholesterol and increases the activity of Lechitin Cholesterol Acyl Transferase (LCAT). LCAT is an enzyme that can convert free cholesterol into a cholesterol ester to form a new HDL. This will increase serum HDL levels [22]. Inhibition of HMG-CoA reductase causes a decrease in cholesterol synthesis and increases the number of LDL receptors found in liver cell membranes and extrahepatic tissue so that total blood cholesterol and LDL in plasma decreases [23]. In addition, beta sitosterol can work to reduce LDL by means of a ligand for the LXR-RXR receptor (Liver X Receptor-Retinoid X Receptor). Where these receptors regulate several genes involved in the synthesis, absorption, excretion of cholesterol homeostasis and lipoprotein metabolism, including increased expression of the ABC gene (adenosine-tri-phosphate binding cassette) A1 as cholesterol transfer. High levels of phytosterol in the intracellular will also result in a reduction in the synthesis of 3-hydroxy-3-methylgluraryl Coenzyme A (HMG-CoA) reductase so that cholesterol synthesis will be inhibited so that the secretion of VLDL from liver cells will result in reduced VLDL conversion to LDL. Decreased cholesterol level was caused by inhibition of HMG-CoA by simvastatin. Simvastatin works competitively to inhibit HMG-CoA reductase which is the main enzyme of cholesterol synthesis. The inhibition of HMG-CoA reductase decreases the transformation of HMG-CoA to mevalonate which is a mechanism for cholesterol synthesis. Decreasing cholesterol levels in the liver cause stimulation of LDL receptors (up regulation) so that levels increase on the surface of the liver. LDL receptors function as LDL cholesterol clearance so that if levels increase, it will increase plasma LDL cholesterol clearance [24]. This mechanism reduces plasma LDL cholesterol. Some studies using experimental animals and humans reported carrying several components of food fiber in reducing cholesterol levels [25].

![Figure 1. Graph of cholesterol total.](image-url)
Table 2. LDL cholesterol.

| Observation          | Initial | Day 7 | Day 14 | Day 21 |
|----------------------|---------|-------|--------|--------|
| N (Standart)         | 28.01 ± 1.72 | 26.05 ± 2.44 | 26.85 ± 1.33 | 26.13 ± 1.30 |
| K (+) : Hiper → Na CMC 0.5% | 61.95 ± 1.39 | 59.36 ± 1.71 | 50.24 ± 1.44 | 26.40 ± 0.88 |
| K (-) : Hiper → Obat | 33.65 ± 1.50 | 30.18 ± 2.05 | 29.90 ± 0.90 | 26.00 ± 0.90 |
| P1 : Hiper → Extract 2.25 ml | 67.47 ± 0.82 | 53.95 ± 1.17 | 47.75 ± 1.09 | 26.53 ± 0.77 |
| P2 : Hiper → Extract 4.5 ml | 51.41 ± 1.39 | 47.83 ± 2.38 | 42.63 ± 1.67 | 24.65 ± 2.00 |
| P3 : Hiper → Extract 6.75 ml | 46.93 ± 1.84 | 43.42 ± 1.13 | 37.51 ± 1.33 | 24.92 ± 1.96 |

3.3. HDL cholesterol

The mean HDL cholesterol among the six treatments that experienced the most significant increase on day 21 in treatment P1 was 30.35%, from 56.60 ml/dl to 81.26 ml/dl (table 3).

Table 3. HDL cholesterol.

| Observation          | Initial | Day 7 | Day 14 | Day 21 |
|----------------------|---------|-------|--------|--------|
| N (Standart)         | 79.15 ± 1.91 | 79.86 ± 1.62 | 79.59 ± 1.98 | 79.05 ± 1.89 |
| K (+) : Hiper → Na CMC 0.5% | 50.64 ± 1.47 | 52.20 ± 2.15 | 56.46 ± 1.52 | 78.90 ± 4.54 |
| K (-) : Hiper → Obat | 74.75 ± 1.91 | 77.56 ± 1.56 | 75.65 ± 1.31 | 81.26 ± 2.32 |
| P1 : Hiper → Extract 2.25 ml | 56.60 ± 2.81 | 57.90 ± 2.47 | 60.95 ± 1.84 | 81.26 ± 1.88 |
| P2 : Hiper → Extract 4.5 ml | 61.56 ± 1.37 | 62.78 ± 1.63 | 65.31 ± 1.52 | 84.88 ± 3.54 |
| P3 : Hiper → Extract 6.75 ml | 68.79 ± 1.12 | 70.37 ± 1.62 | 70.34 ± 1.41 | 86.46 ± 2.45 |
3.4. Triglycerides

The results of the variance analysis showed that all treatments had a significant effect \((p<0.05)\) on triglyceride levels. The results of DMRT follow-up at the 5% level showed that there were significant differences between treatments.

The mean triglyceride levels decreased in all groups. Triglycerides are one form of fat absorbed by the intestine after experiencing hydrolysis which then enters the plasma in two forms, namely as chylomicron (which comes from intestinal absorption after consumption of fat) and as very low density lipoprotein (VLDL) formed by the liver [26]. Excessive fat consumption can increase cholesterol, LDL, and triglycerides and reduce HDL. One way to reduce cholesterol, LDL, triglycerides, and reduce HDL by consuming foods that contain antioxidants. Corn silk contains secondary metabolites such as flavonoids, saponins, tannins, alkaloids that function as antioxidants. Binjai extract \((Solanum melongena)\) which contains flavonoids can reduce triglyceride levels through a mechanism to increase lipoprotein lipase enzyme activity [27]. With the increase of the enzyme VLDL lipoprotein which transports triglycerides will undergo hydrolysis into fatty acids and glycerol. The released fatty acids are then absorbed by muscles and other tissues that are oxidized to produce energy and by adipose tissue are stored as energy reserves [28]. In addition, flavonoids can inhibit Fatty Acid Synthase (FAS), an important enzyme in fat metabolism. Obstacles to FAS directly reduce the formation of fatty acids [29]. Thus a decrease in fatty acids can cause a decrease in the formation of triglycerides.

Table 4. Triglycerides.

| Observation          | Initial Research | Day 7      | Day 14     | Day 21     |
|----------------------|------------------|------------|------------|------------|
| N (Standart)         | 69.56 ± 2.17     | 67.79 ± 1.82 | 67.67 ± 1.82 | 66.22 ± 1.60 |
| K (+) : Hiper → Na CMC 0.5% | 106.67 ± 2.30 | 102.90 ± 2.44 | 94.23 ± 1.89 | 69.71 ± 3.85 |
| K (-) : Hiper → Obat  | 77.59 ± 1.66     | 75.57 ± 1.21 | 72.57 ± 1.52 | 69.21 ± 1.62 |
| P1 : Hiper → Extract 2.25 ml | 98.15 ± 1.92 | 95.27 ± 1.66 | 86.80 ± 1.52 | 69.54 ± 6.78 |
| P2 : Hiper → Extract 4.5 ml | 93.33 ± 1.92 | 90.38 ± 2.06 | 79.37 ± 1.64 | 67.55 ± 5.65 |
| P3 : Hiper → Extract 6.75 ml | 87.07 ± 2.17 | 84.43 ± 2.20 | 75.89 ± 1.25 | 72.20 ± 2.27 |

Figure 3. Graph of HDL cholesterol.
3.5. Liver fat

3.5.1. Liver weight. The highest mean weight in the K (+) group is 15.24 g. This is directly proportional to the high total cholesterol and LDL cholesterol in K (+). It is suspected that the high total cholesterol and LDL cholesterol causes accumulation of fat so that it affects the liver weight. Fatty liver is closely related to high levels of free fatty acids, which are caused by fat mobilization from adipose tissue or from lipoprotein hydrolysis [30]. Besides fatty liver can be caused by a deficiency of saturated fatty acids and vitamins that cause infiltration of fat into liver cells. Unsaturated fatty acid deficiencies can suppress phospholipid synthesis. Therefore cholesterol can compete with essential fatty acids for esterification which results in fatty liver.

Table 5. Liver weight.

| Observation            | Liver weight (g)       |
|------------------------|------------------------|
| N (Standard)           | 6.3137 ± 0.2229        |
| K (+) : Hiper → Na CMC 0.5% | 15.2357 ± 0.4216      |
| K (-) : Hiper → Obat    | 7.2996 ± 0.3436        |
| P1 : Hiper → Extract 2.25 ml | 11.1829 ± 0.3003    |
| P2 : Hiper → Extract 4.5 ml | 9.4480 ± 0.2394      |
| P3 : Hiper → Extract 6.75 ml | 7.0944 ± 0.0845      |

Figure 4. Graph of triglycerides.

Figure 5. Graph of liver weight.
3.5.2. Adipose fat. The highest average adipose fat at K (+) is 12.10 g. The decrease in the amount of fatty tissue was more prevalent in mice given an extract of corn silk powder P3 treatment amounted to 6.99 g compared to other treatment groups, so it can be concluded that the higher the dose given, a decrease in fat occurred. The high adipose fat is also directly proportional to the high total cholesterol, LDL cholesterol, and triglycerides. This is thought to be the presence of free fatty acids in the liver. Increased transport of fat or fatty acids from the intestine to the liver because fat accumulation is sent through circulation, especially in the form of chylomicrons [18]. Lipolysis in adipose tissue releases fatty acids and then joins triglycerides in adipocytes but some fatty acids are released into the circulation and taken by the liver, the rest of the chylomicron is also sent to the liver. Giving extract of corn silk powder can reduce adipose fat in the liver. Antioxidant compounds in corn silk powder extract are thought to be a trigger for increased LPL enzyme activity by reducing lipid peroxidation. The mechanism of reducing fatty liver through endogenous pathways, namely by increasing the work of LPL enzyme activity which serves to convert VLDL to LDL so that the accumulation of VLDL in the liver can be reduced [31].

Table 6. Adipose fat.

| Observation | Adipose fat (g)     |
|-------------|---------------------|
| N (Standard)| 5.5773±0.4329       |
| K (+) : Hiper → Na CMC 0.5% | 12.0970±0.3163       |
| K (-) : Hiper → Obat  | 6.973±0.4746         |
| P1 : Hiper → Extract 2.25 ml | 9.3515±0.2695       |
| P2 : Hiper → Extract 4.5 ml | 7.8197±0.1445       |
| P3 : Hiper → Extract 6.75 ml | 6.9893±0.0976       |

Figure 6. Graph of adipose fat.

4. Conclusion
The best day 21 corn silk powder extract on P1 treatment dose 2.25 ml, with total cholesterol of 24.4% from 120.29±2.03 ml/dl to 90.87±2.01 ml/dl, cholesterol HDL was 30.35% from 56.60±2.81 ml/dl to 81.26±1.88 ml/dl, LDL cholesterol by 53.84% from 57.47±0.82 ml/dl to 26.53±0.77 ml/dl, triglycerides amounted to 29.14% from 98.15±1.92 ml/dl to 69.54±6.78 ml/dl, and liver fat levels in the P3 treatment dose 6.75 ml with a liver weight of 7.09 g and adipose fat of 6.99 g.

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