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# The Preventive and Curative Effects of Gotu Kola and Turmeric Extracts on Liver Function Damage Induced by Paracetamol in Rats

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***Abstract:*** The preventive and curative effects of gotu kola and turmeric extracts on the damage of rat liver induced by paracetamol were studied by using 68 male rats (*Sprague dawley*). The experiment was conducted in a Completely Randomized Design with 5 treatments of combination of gotu kola and turmeric extracts. Parameters measured were the activity of aspartate transaminase (AST), alanine aminotransferase (ALT) and glutathione peroxidase (GSH-Px) and histopathology examination of the liver. The result showed that administration of gotu kola and turmeric extracts either during preventive or curative treatment decreased the levels of AST and ALT. The result showed that the extracts of gotu kola and turmeric could inhibit the decrease in GSH-Px enzyme activity (preventive effect) and stimulated the increase in GSH-Px enzyme activity (curative) and regenerate the damaged liver cells caused by paracetamol induction (curative). Combination of 18.75 mg gotu kola extract and 336 mg turmeric extract gave the best result in preventive and curative effects. It was concluded that gotu kola and turmeric extracts could be used to prevent and to cure the liver damage due to the excessive consumption of paracetamol.

***Keywords*** *- gotu kola (Centella asiatica), turmeric (Curcuma longa), glutathione peroxidase, AST/ALT, liver*

## I. INTRODUCTION

Paracetamol, which serves as an analgesic and antipyretic, when it is consumed in an excessive dose will deplete the glutathione content (GSH) and form an electrophile metabolite as a free radical such as N-asetyl-p-benzoquinonimine (NAPQI). The free radical of NAPQI will bind covalently with the protein macromolecules of liver cells, which lead to the damage of liver cells due to the paracetamol induction [1, 2]. The liver damage induced by free radicals will decrease glutathione peroxidase (GSH-Px) activities in the liver and increase the blood concentrations of aspartate transaminase (AST) and alanine aminotransferase (ALT).

Some plants have been used to treat the disorder of the liver, including cirrhosis [3, 4]. The turmeric (*Curcuma longa*) is known to have antioxidant [5], anti-tumor [6], anti-microbial [7], anti-inflammation [8], wound healing [9], and gastric protector [10] activities. Turmeric extract has an activity as hepatoprotector against the toxicity induced by carbon tetrachloride [11]. The gotu kola (*Centella asiatica*) also contains natural antioxidants [12, 13] such as terpenoid, flavonoid and glycoside that can protect the brain damages caused by the increased free radical production due to aging [14]. The present experiment was designed to study the preventive and curative effects of combination of gotu kola and turmeric extracts on prevention and cure of liver damaged induced by paracetamol.

## II. MATERIALS AND METHODS

### 2.1 Location

This study was conducted in the Faculty of Veterinary Medicine, Bogor Agricultural University. Preparations of dry extracts of gotu kola and turmeric were conducted in the Laboratory of Medicinal Plants and Spices Research Center, Bogor Agricultural University. Histopathological preparations were conducted in the Laboratory of Pathology, Faculty of Veterinary Medicine, Bogor Agricultural University, and for the histopathological observation and evaluation was conducted in the Laboratory of Pathology, Veterinary Research Institute, Bogor, Indonesia.

### 2.2 Experimental design

The experiment used *Spraque dawley* rats. Before treatment, the experimental rats were adapted to the experimental cage and management for 7 days. The experiment consisted of 2 parts i.e., preventive and curative. In preventive experiment, the experimental rats were treated with gotu kola and turmeric extracts for

11 days then followed by paracetamol induction of liver damage (180 mg/200 g body weight) for 3 days (days 12 to14). In curative experiment, the experimental rats were induced liver damage by paracetamol (180 mg/200 g body weight) for days 1 to 3 then followed by treatment with gotu kola and turmeric extracts for 11 days, but the experimental rats were continued to be administered paracetamol for induction of liver damage on days 5, 7, 9 and 11. In each experimental group (Preventive and Curative Experiments), the experimental rats were divided into 5 groups based on the dosage of gotu kola and turmeric extract administration i.e., I, Rats administered 18.75 mg gotu kola extract without turmeric extract; II, Rats administered 336 mg turmeric extract without gotu kola extract, III, Rats administered 18.75 mg gotu kola extract and 112 mg turmeric extract; IV, Rats administered 18.75 mg gotu kola extract and 224 mg turmeric extract; and V, Rats administered 18.75 mg gotu kola extract and 336 mg turmeric extract. A group of rats without gotu kola and turmeric extract administration and without paracetamol treatment were used as a negative control group. A group of rats treated with paracetamol (180 mg/200 g body weight) for 7 days without gotu kola and turmeric extracts administrations were used as a positive control group.

**2.3 The experimental protocol**

The experiment was conducted for 14 days. Blood samples were collected on days 1, 3, 5, 9, 11 and 14 for measurement of plasma aspartate transaminase (AST) and alanine aminotransferase (ALT) concentrations. Plasma concentrations of AST and ALT enzymes were measured by using International Federation of Clinical Chemistry (IFCC) reference procedures [15]. One hundred microliters of plasma was mixed with the 1000µL working solution and maintained at 30°C for 1 minute. The absorbance was read with spectrophotometer at λ 340 nm and 1745 factor. The absorbance was read again after 1, 2, and 3 minutes. The activities of GSH-Px enzymes in the liver were measured by following method described by Fohle and Gunzler [16].

**2.4 Histopathological examination**

The observation of liver histopathological changes in the experimental *Spraque dawley* rats were conducted for 14 days of experiment. The liver samples were washed with 0.9% physiological saline solution, fixed in Bouin solution for 12 to 24 hours. Then the tissues were blocked with paraffin, after being dehydrated in serial alcohol (70, 80, 90, and 100%) and clearing with xylol (I, II, III). Paraffin block was cut with a microtome thickness of 5 microns and stained with hematoxylin eosin staining (HE). Histological observation of the liver included hepatocytes (liver cells), and central venous sinusoid. The examination of liver histological preparation was done under microscope with magnification of 200x. The histological changes observed were congestion, infiltration of inflammatory cells, hemorrhage, and necrosis. The lesions were congestion, inflammation, hemorrhage, and necrosis.

**2.5 Data analysis**

The data obtained were then analyzed statistically using one-way Anova test. For the test group that had significant difference, it followed by the Duncan test. The significance limit used was $p<0.05$. For the histological observation, the data were present descriptively.

## III. RESULTS AND DISCUSSION

**3.1 AST and ALT concentrations in negative and positive control groups**

The AST and ALT concentrations in negative and positive control group rats are presented in Table 1. The negative control group rats had AST and ALT concentrations of 7.17±0.03 U/L and 6.36±0.01U/L, respectively. In the positive control group, administration of 360 mg paracetamol for 10 days increased the AST concentrations 6 times (43.68±31.57 U/L) as compared to negative control group (7.17±0.03 U/L). It was reported that AST and ALT levels could increase up to 10-500 times as compared to normal level after paracetamol induction of liver damage [17].

**3.2 AST and ALT concentrations in preventive group rats**

Average concentrations of AST and ALT in the preventive group rats (rats given gotu kola and turmeric extracts from day 1 to 11, followed by induction of liver damage by paracetamol) are presented in Table 1. In rats administered 18.75 mg gotu kola extract without turmeric administration (Group I), the concentrations of AST and ALT enzymes were 7.22±0.03 U/L and 6.40±0.04 U/L, respectively. In rats administered 336 mg turmeric extract without gotu kola extract (Group II), the concentrations of AST and ALT were 7.18±0.05 U/L and 6.37±0.01 U/L, respectively. The concentrations of AST and ALT in Group I and II, respectively, were similar (only higher by 0.4% and 0.2%, respectively) as compared to those of normal or negative control group.

Table 1. AST and ALT concentrations in the plasma and GSH-Px concentrations in the liver of experimental rats treated with combination of gotu kola and turmeric extracts prior to (preventive) and after (curative) stimulation of liver damage by paracetamol.

| Group | AST concentration (U/L) | ALT concentration (U/L) | GSH-Px concentration (mU/min/mg protein) |
|---|---|---|---|
| **Negative control** | 7.17±0.03[b] | 6.36±0.01[b] | 204.27±13.29[c] |
| **Positive control** | 43.68±31.57[a] | 42.41±31.64[a] | 123.21±2.93[d] |
| **Preventive group** | | | |
| **I** | 7.22±0.03[b] | 6.40±0.04[b] | 265.41±13.35[b] |
| **II** | 7.18±0.05[b] | 6.37±0.01[b] | 274.67±9.00[b] |
| **III** | 7.20±0.03[b] | 6.28±0.02[b] | 198.73±1.90[c] |
| **IV** | 7.16±0.03[b] | 6.28±0.03[b] | 217.66±14.82[c] |
| **V** | 7.19±0.02[b] | 6.37±0.01[b] | 301.91±17.68[a] |
| **Curative group** | | | |
| **I** | 7.39±0.41[b] | 6.52±0.07[b] | 244.01±11.50[b] |
| **II** | 7.35±0.37[b] | 6.57±0.04[b] | 263.63±16.07[b] |
| **III** | 7.49±0.45[b] | 6.37±0.06[b] | 241.60±32.18[b] |
| **IV** | 7.41±0.32[b] | 6.38±0.04[b] | 245.74±15.82[b] |
| **V** | 7.52±0.42[b] | 6.42±0.05[b] | 275.40±5.13[b] |

[a,b,c,d]Different superscripts in the same column indicate significant different ($p<0.05$). Negative Control Group consisted of rats without gotu kola and turmeric extract administration and without paracetamol treatment. Positive Control Group consisted of rats treated with paracetamol for 7 days without gotu kola and turmeric extract administration. Preventive group, rats administered with combination of gotu kola and turmeric extracts prior to induction of liver damage by paracetamol. Curative group, rats administered with combination of gotu kola and turmeric extracts after induction of liver damage by paracetamol. I, Rats administered 18.75 mg gotu kola extract without turmeric extract; II, Rats administered 336 mg turmeric extract without gotu kola extract, III, Rats administered 18.75 mg gotu kola extract and 112 mg turmeric extract; IV, Rats administered 18.75 mg gotu kola extract and 224 mg turmeric extract; and V, Rats administered 18.75 mg gotu kola extract and 336 mg turmeric extract.

In Groups III rats administered 18.75 mg gotu kola and 112 mg turmeric extracts, the concentrations of AST and ALT were 7.20±0.03 U/L and 6.28±0.02 U/L, respectively. In Group IV rats administered 18.75 mg gotu kola and 224 mg turmeric extracts, the AST and ALT concentrations were 7.16±0.03 U/L and 6.28±0.03 U/L, respectively. In Group V rats given 18.75 mg gotu kola and 336 mg turmeric extracts, the concentrations of AST and ALT were 7.19±0.02 U/L and 6.37±0.01 U/L, respectively. In groups of rats administered a combination of gotu kola and turmeric extracts, the concentrations of AST and ALT only changed by around 0.02 and 0.2%, respectively, as compared with the negative control group.

These results were consistent with the previous results that the normal level of AST in mice was 141±67.4 IU/I and the normal level of ALT was 12.6±4.40 IU/I [18]. The levels of AST and ALT found in this study were categorized below the normal value. The decreased AST and ALT concentrations were related to the paracetamol induction of liver damage on days 11, 12, and 13, after the administrations of gotu kola and turmeric extracts. There were increases in AST and ALT enzyme concentrations due to paracetamol induction. However, administration of gotu kola and turmeric extracts prior to induction of liver damage by paracetamol inhibited the increase in AST and ALT concentrations that could decrease the damage of rat liver.

**3.3 AST and ALT concentrations in curative group rats**

Concentrations of AST and ALT in the curative group rats (rats induced liver damage with paracetamol from days 1 to 3, followed by gotu kola and turmeric extracts administration from days 4 to 14, but paracetamol administration was still given on days 5, 7, 9, and 11) are presented in Table 1. In rats induced with paracetamol followed by administration of 18.75 mg gotu kola extract without turmeric extract administration, the average concentrations of AST and ALT were 7.39±0.41 U/L and 6.52±0.07 U/L, respectively. In rats induced with paracetamol followed by administration of 336 mg turmeric extract without gotu kola extract administration, the average concentrations of AST and ALT were 7.35±0.37 U/L and 6.57±0.04 U/L, respectively. These levels were decrease compared to those found in positive control group.

In rats induced with paracetamol followed by administration of 18.75 mg gotu kola and 112 mg turmeric extracts, the concentrations of AST and ALT were 7.49±0.45 U/L and 6.37±0.06 U/L, respectively. In rats induced with paracetamol followed by administration of 18.75 mg gotu kola and 224 mg turmeric extracts, the concentrations of AST and ALT were 7.41±0.32 U/L and 6.38±0.04 U/L, respectively. In rats induced with paracetamol followed by administration of 18.75 mg gotu kola and 336 mg turmeric extracts, the concentrations of AST and ALT were 7.52±0.42 U/L and 6.42±0.05 U/L, respectively. In curative group rats, it was appeared that the concentrations of AST and ALT decreased after the administration of gotu kola and turmeric extracts. The results indicated that gotu kola and turmeric extracts had potentials to be used as curative agents for liver damage caused by paracetamol induction.

**3.4 Glutathione peroxidase activities in the livers of the experimental rats**

The activities of GSH-Px in the liver of experimental rats are presented in Table 1. In negative or normal control group rats, glutathione peroxidase activity was 204.27±13.29 mU/minute/mg protein. In positive control group rats, there was a dramatic decrease ($p<0.05$) in glutathione peroxidase activity (123.21±2.93 mU/minute/mg protein) caused by the liver cells damage due to the induction with a toxic dose of paracetamol. The activity of glutathione peroxidase enzyme decreased by 39.68% as compared to that of normal (negative) control group rats ($p<0.05$). A toxic dose of paracetamol causes the depletion of glutathione in the liver because it can no longer compensate especially for the massive production of NAPQI, reduction of mitochondrial glutathione (GSH) which lead to the toxicity in liver [19]. Paracetamol generates the free radical of NAPQI, which can bind the protein [20], and oxidize the protein of sulfhydryl [21].

In the preventive group, rats induced with paracetamol after administration of 18.75 mg gotu kola extract without turmeric administration (Group I), there was an increase in glutathione peroxidase activity by 29.93% to 265.41±13.35 mU/minute/mg protein ($p<0.05$), as compared to negative control group and increased more than twice (115.41%) as compared to positive control rats. This result clearly showed the significant effect of gotu kola extract for binding the free radicals produced by paracetamol oxidation. The gotu kola extract can improve the activities of antioxidant enzymes such as superoxide dismutase (SOD), catalase and glutathione peroxidase (GSH-Px), and the antioxidants such as glutathione (GSH) [22].

In the rats induced with paracetamol after administration of 336 mg turmeric extract without gotu kola extract administration (Group II), the glutathione peroxidase enzyme activity (274.67±9 mU/minute/mg protein) increased by 34.46% ($p<0.05$) as compared to negative control group and increased by more than twice (122.93%) as compared to positive control group rats. It was reported that curcumin not only played a role as an antioxidant and bound the free radicals, but also increased the activity of antioxidant enzyme such as superoxide dismutase (SOD), catalase and glutathione peroxidase (GSH-Px) [23]. High dose of curcumin can act as a hydroxyl radical scavenger [24].

In the rats induced with paracetamol after administration of 18.75 mg gotu kola extract and 112 mg turmeric extract (Group III), the activity of GSH-Px enzyme was 198.73±1.9 mU/minute/mg protein similar to (decreased slightly by 2.71%) as compared to negative control group rats, but increased by 61.29% as compared to the decreased activity of GSH-Px in positive control rats. This low activity of GSH-Px enzyme was due to the dosage of gotu kola and turmeric extracts were not able to bind and neutralize the free radicals produced by paracetamol induction of liver damage. However, in rats induced by paracetamol after administration of 18.75 mg gotu kola extract and 224 mg turmeric extract (Group IV), there was no significant increase in GSH-Px enzyme activity (217.66±14.82 mU/minute/mg protein) (increased slightly by 6.56%) as compared to negative control group, but increased by 76.66% as compared to positive control rats. In rats induced by paracetamol after administration of 18.75 mg gotu kola extract and 336 mg turmeric extract (Group V), GSH-Px enzyme activity was 301.91±17.68 mU/minute/mg protein and increased by 47.80% as compared to negative control group rats and increased by 145.04% as compared to the decreased GSH-Px activities in the positive control group rats. Administration of a combination of gotu kola and turmeric extracts could protect and prevent liver from damage caused by paracetamol induction ($p<0.05$).

In curative group, rats induced with paracetamol followed by administration of 18.75 mg gotu kola extract without turmeric extract administration (Group I), glutathione peroxidase activity was 244.01±11.5

mU/minute/mg protein, 98.04% higher than in positive control rats and increased by 19.45% as compared to negative control rats. The result indicated that administration of gotu kola extract after paracetamol induction of liver damage could bind free radicals produced by toxic paracetamol. Rats induced with paracetamol followed by administration of 336 mg turmeric acid without gotu kola extract administration (Group II) had about 113.97% higher glutathione peroxidase enzyme (263.63±16.07 mU/minute/mg protein) as compared to positive control rats and increased by 29.06% as compared to negative control rats. The result indicated that 336 mg turmeric extract administration could act as an antioxidant against toxic paracetamol. In rats induced with paracetamol followed by administration of 17.87 mg gotu kola extract and 112 mg turmeric acid (Group III), GSH-Px enzyme activity increased to 241.60±32.18 mU/minute/mg protein and increased by 96.09% as compared to positive control group and increased by 18.29% as compared to negative control group rats. In rats induced with paracetamol followed by administration of 17.87 mg gotu kola extract and 224 mg turmeric acid (Group IV), the GSH-Px enzyme activity was 245.74±15.82 mU/minute/mg protein (increased 99.45% as compared to positive control group) and increased by 20.30% as compared to negative control group rats. In rats induced with paracetamol followed by administration of 17.87 mg gotu kola extract and 336 mg turmeric acid (Group V) the activity of GSH-Px enzyme was 275.40±5.13 mU/minute/mg protein (increased by 123.52% as compared to positive control group and increased by 34.82% as compared to negative control group rats). It was concluded that administration of gotu kola and turmeric extracts could cure and improve the activity of glutathione peroxidase enzyme ($p<0.05$) that was decrease due to paracetamol induction.

**3.5 Histopathological appearance of normal or negative control and positive control groups**

Histology of liver from normal (negative) control rats is presented in Figure 1. There was no pathological abnormality found. In the positive control group administered 180 mg/200 g rat body weight for 7 days, the necrosis of liver tissue was found (Figure 2).

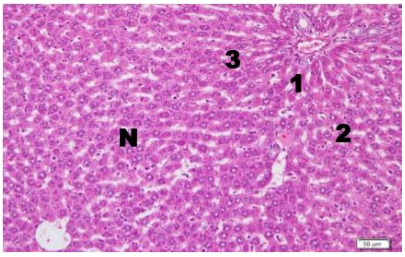


Figure 1. Liver tissue of normal control group, there was no pathological abnormality. (1) Vena centralis, (2) Liver epithelial cells, and (3) Sinusoid. HE. x200.

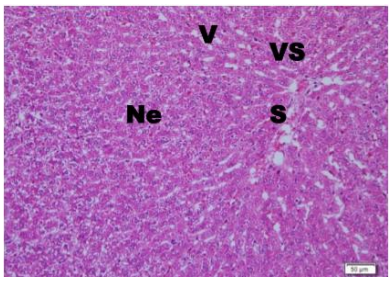


Figure 2. Liver tissue of positive control group with paracetamol induction (N: Normal; V: Cells with vacuole; Ne: Necrosis; VS: Vena centralis; S: Sinusoid). HE.x200.

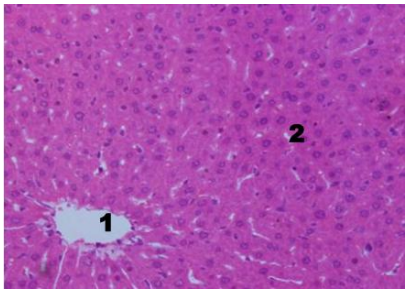


Figure 3. Liver tissue of rats administered 17.85mg gotu kola extract without turmeric administration prior to paracetamol induction did not show any specific abnormality except polymorphonuclear. (1) Vena centralis and (2) Liver cells appeared to form polymorphonuclear and some of them were in basophilic color. HE. x200.

The necrosis of the liver cells was also related to the microsomal enzymes, because some medicines could increase the activity of these enzymes. Paracetamol is a toxic compound that when enters the body will be induced by the microsomal enzymes (microsomal cytochrome P-450) in the liver. This process will increase the production of free radicals that can result in the damage of hepatocytes. In necrosis condition, the liver cells rupture so the amino transferase enzyme, namely glutamic oxaloacetic transaminase (GOT) and glutamic pyruvate transaminase (GPT) in the liver cells, enter and exit the bloodstream, resulting in the increase of AST and ALT activities exceeding the normal level [25].

The level of AST and ALT in the paracetamol induced rats in this experiment increased more than 6 times as compared to the normal level in the negative control group (Table 1). The increased the activities of these enzymes caused the decrease of the activity of glutathione peroxidase enzyme, approximately 40% as compared to normal control. The dose of toxic paracetamol used in this experiment caused a depletion of glutathione in the liver because it could no longer compensate the massive production of NAPQI, especially the depletion of mitochondrial gluthatione (GSH) that resulted in the toxicity of the liver [19].

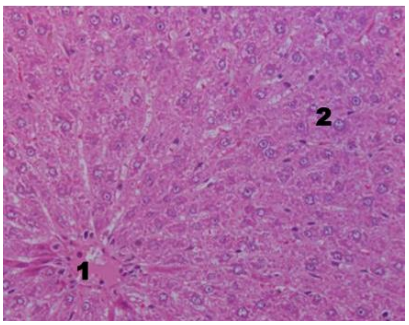


Figure 4. Liver tissue of rats administered 336 mg turmeric extract without gotu kola extract administration prior to paracetamol induction did not show any specific abnormality. Vena centralis (1) and liver epithelial cells (2) had polymorphonuclear. HE. x200.

**3.6 Histopathological appearance of liver of rats administered of gotu kola and turmeric extract as preventive treatment**

Administration of 17.85 mg gotu kola extract without turmeric extract administration prior to paracetamol induction (Group I) did not change the liver tissue as compared to control (Figure 3). This data indicated that administration of gotu kola without administration of turmeric extracts could protect the liver from the damage induced by paracetamol. Administration of 336 mg turmeric extract without gotu kola extract administration prior to paracetamol induction did not change the liver tissue as compared to control (Figure 4). Administration of 17.85 mg gotu kola extract and 112 mg turmeric extract prior to paracetamol induction damaged the liver tissue (Figure 5). This combination of gotu kola and turmeric extracts could not protect the liver cells from damage induced by paracetamol. Rats administered 17.85 mg gotu kola extract and 224 mg turmeric extract and rats administered 17.85 mg gotu kola extract and 336 mg turmeric extract prior to paracetamol induction showed a light regeneration of the liver cells (Figure 6, Figure 7), probably there was a little damage of the liver cells with the average of the enzyme level only increased slightly (AST by 0.02% and ALT by 0.2%). The increase of GSH-Px at this dose was about 23-26%. This combination dose could protect the tissue liver by regenerating cells ($p<0.05$).

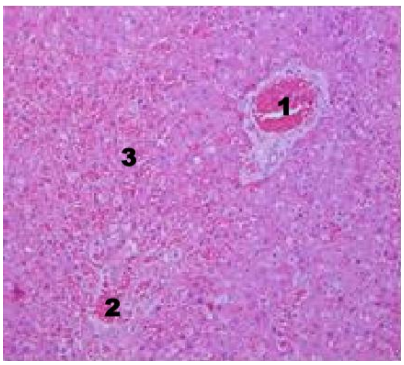


Figure 5. Liver tissue of rats administered 18.75 mg gotu kola and 112 mg turmeric extracts prior to paracetamol induction had mid-zonal hepatic necrosis. (1). Portal tract had congestion in vena portalis and necrosis, (2).

Vena centralis had congestion, and (3) Midzonal part of liver that had necrosis and liver cells vacuolization, congestion in sinusoid and also haemorrhage. HE. x200.

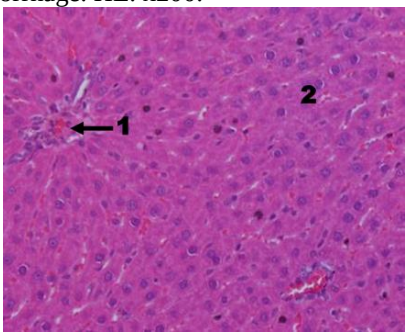


Figure 6. Liver tissue of rats administered 18.75 mg gotu kola and 224 mg turmeric extracts prior to paracetamol induction showed a regeneration of liver cells. (1) Portal tract and (2) regeneration of liver cells in midzonal part showed that liver cells were basophilic colored and polymorphonuclear. HE. x200.

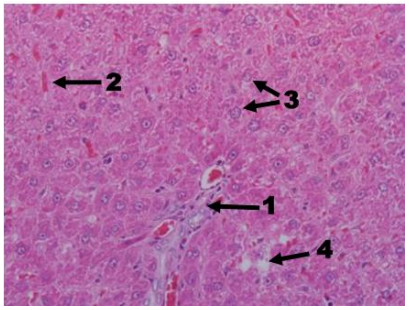


Figure 7. Liver tissue of rats administered 18.75 mg gotu kola and 336 mg turmeric extracts prior to paracetamol induction had light degeneration of liver cells (1). Portal tract had congestion in blood vessels, (2). Sinusoid congestion, (3). Polymorphonuclear of liver cells, and (4). Vacuolization in epithelial cells of liver. HE. x200.

**3.7 Histopathological appearance of liver of rats administered of gotu kola and turmeric extract as preventive treatment**

Administration of 17.85 mg gotu kola extract without turmeric extract administration after paracetamol induction of liver damage (Group I) did not change the liver tissue (Figure 8). This result was expected since the extract could protect the liver from the damage due to paracetamol induction. In rats administered 336 mg turmeric extract without gotu kola extract (group II), liver tissues showed regenerations (Figure 9). At the combination of 17.85 mg gotu kola and 112 mg turmeric extracts (Group III), 17.85 mg gotu kola and 224 mg turmeric extracts (Group IV), and 17.85 mg gotu kola and 336 mg turmeric extracts (Group V), liver tissues showed cells regeneration (Figure 10, Figure 11, Figure 12). There was a little damage of the liver cells since the average of enzyme levels slightly increased for AST by 0.02% and ALT by 0.2%. The increases in GSH-Px at these doses were about 23 to 26%. The combination of gotu kola and turmeric extracts administration could cure the liver damage induced by paracetamol by regenerating cells ($p<0.05$).

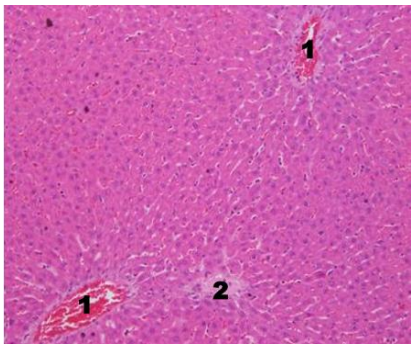


Figure 8. Liver tissue of rats administered 18.75 mg gotu kola without turmeric extracts administration after paracetamol induction did not show any specific abnormality. (1). Portal tract and (2) Vena centralis. HE. x200.

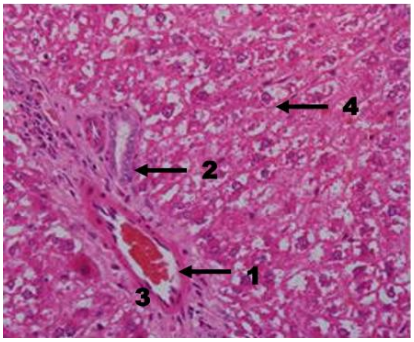


Figure 9. Liver tissue of rats administered 336 mg turmeric extracts without gotu kola extract administration after paracetamol induction showed a liver regeneration. (1) Portal tract (Tractus portalis), (2) Ductus choleductus, (3) Vena portalis, and (4) Vacuolization in liver epithelial cells. HE. x200.

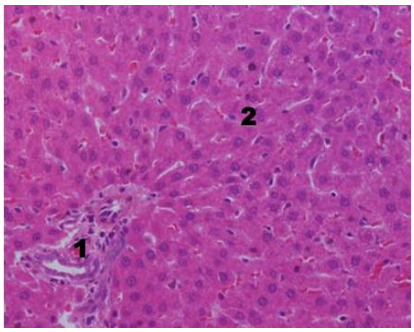


Figure 10. Liver tissue of rats administered 18.75 mg gotu kola and 112 mg turmeric extracts after paracetamol induction showed a regeneration of liver cells. (1) Portal tract and (2). Regeneration of liver cells that were basophilic color. HE. x200.

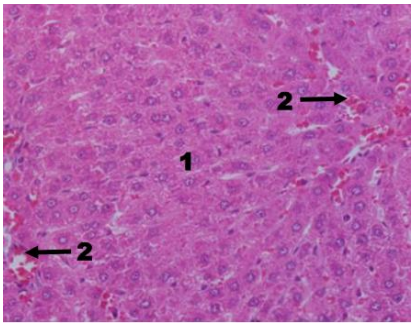


Figure 11. Liver tissue of rats administered 18.75 mg gotu kola and 224 mg turmeric extracts after paracetamol induction showed a regeneration of liver cells. (1). Liver cells had a regeneration with basophilic color and polymorphonuclear, and (2). Congestion of sinusoid. HE. x200.

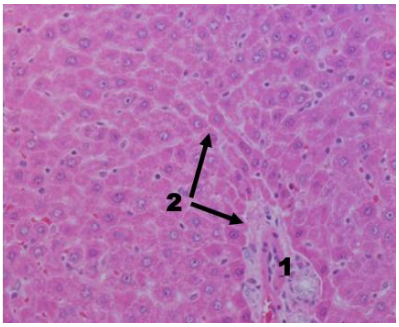


Figure 12. Liver tissue of rats administered 18.75 mg gotu kola and 336 mg turmeric extracts after paracetamol induction showed a regeneration of liver cells. (1). Portal tract and (2). Liver cells had regeneration with basophilic color. HE. x200.

## IV. CONCLUSION

The extract of gotu kola, turmeric, and a combination of both these extracts can prevent the damage of the liver and increase the activity of glutathione peroxidase enzyme at a dose of 17.85 mg gotu kola and 336 mg turmeric extracts. On the histopathological observation, a dose of 17.85 mg gotu kola and 336 mg turmeric extracts both preventive and curative showed a regeneration of liver cells.

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