

The Preventive Effect of Curcumin Analogs (AKS-k) from Cullilawan Oil as Hepatoprotector in Rats (*Rattus Norvegicus* L.) Induced By CCl_4

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Abstract - Curcumin analogue from cullilawan oil using safrole as a precursor have the potential to cure liver function. The synthesis process method has an effect on its pharmacological effect. The effectiveness of this synthetic product as a deterrent to liver disease needs to be studied, so the aim of this study was to determine the preventive effect of curcumin analog from cullilawan oil as hepatoprotectors in rats (*Rattus norvegicus* L.) induced by CCl_4 . The method used is in vivo method using rats (*Rattus norvegicus* L.) and as a comparison material using turmeric extract (curcumin) and heap-q products. The results showed that AKS-k products had a preventive effect on liver function in male rats (*Rattus norvegicus* L.) induced by CCl_4 with an effective dosition of 52 mg / 200g bb.

Keywords - *Hepatoprotector, AKS-K, Preventive, Rattus Norvegicus L.*

I. INTRODUCTION

Curcumin analogues can be synthesized from cullilawan oil using safrol as a precursor [1, 2] and potentially as an anti-cancer [3]. The nature of the drug is due to having a functional group that can act as an antioxidant. Curcumin and curcumin analogues have similar structures and have the possibility of pharmacological properties or have better pharmacological properties [4]. Curcumin is the active ingredient of turmeric which serves to restore the carcinogenic process [5]. Curcumin is also often used as a compound that functions as a hepatoprotector that can protect and repair damage to liver cells [6]. The effectiveness of curcumin analogues synthesized from cullilawan oil as hepatoprotectors needs to be further investigated.

The liver is an organ that is very susceptible to the influence of chemical compounds and the liver is often damaged due to the entry of toxic substances. The blood supply to the liver comes from the digestive tract, so the toxic substances absorbed by the intestine will be carried to the liver through the portal vein. Toxic substances that enter

the liver can cause various toxic effects such as steatosis, necrosis, cholestasis and cirrhosis. Carbon tetrachloride (CCl_4) is a hepatotoxin that causes liver damage [7]. The purpose of this study was to determine the preventive effect of curcumin analogues (AKS-k) from cullilawan oil as hepatoprotector in rats (*Rattus norvegicus* L.) induced by CCl_4 .

II. RESEARCH METHODS

A. Materials and Tools

The materials used in this study were male rats (*Rattus norvegicus* L.) strain Sprague Dawley (SD), Curcumin analog synthesis products, methanol, turmeric, ethanol, CCl_4 , Heap-Q, neutral formalin (BNF) buffer, hematoxylin-eosin dye, Van Gieson special dye, phosphate buffer, trichloroacetic acid (TCA) 10%, 1.1.3.3-tetrametoxipropane (TMP) solution, Tris-HCl, 5% BHT, NMPI (N-methyl-2-phenyl-indole), HCl, reduced GSH, dTNB, and DiaSys® reagents. The equipment used in the study included cages, humidity gauges, thermometers, capillary pipes (mariefed),

eppendorf tubes, centrifuges, micropestles, homogenizers, vortices, incubators, glass tools.

B. Research Procedure

Mice were acclimatized for 7 days in a room with a 12-hour cycle (light / dark), humidity 70% $\pm$ 2%, and temperature 22 °C $\pm$ 2 °C. After being acclimatized, then given 0.1 ml CCl₄ / kg bb twice a week and in the following week treatment with grouping as follows; The TA1 group was given a dose of 13 mg / 200 g bb, the TA2 group was given a dose of 26 mg / 200 g bb, the TA3 group was given a dose of 52 mg / 200 g bb, the TA+1 group was given turmeric extract 130 mg / 200 g bb, the TA+2 group was given heap-Q 60 mg / 200g bb, the TA-1 group was a negative control group that was only given CCl₄ twice a week, the TAN group was a normal / untreated group. The medication is given every day for 14 days and the administration of CCl₄ is given twice a week.

Blood biochemical parameters observed were analysis of liver enzyme levels were SGOT (Serum Glutamic Oxaloacetic Transaminase) and SGPT (Serum Glutamic Pyruvate Transaminase). The blood of the model animals was taken and collected in the eppendorf tube, then centrifuged at a speed of 10000 rpm for 10 minutes at 4 °C to obtain blood serum. Biochemical measurements of blood using DiaSys® reagents and measured by UV-Vis spectrophotometer. For histopathological analysis of the liver using staining hematoxylin-eosin (H & E). Liver organ was fixed with neutral formalin (BNF) buffer solution. Before doing the staining is preceded by a deparaffinization process.

III. RESULTS AND DISCUSSION

Curcumin analogue products synthesized from cullilawan oil are used (Fig. 1a) is a product with a structural formula as in Fig. 1b in accordance with the results of the analysis using LCMS and FTIR [1].

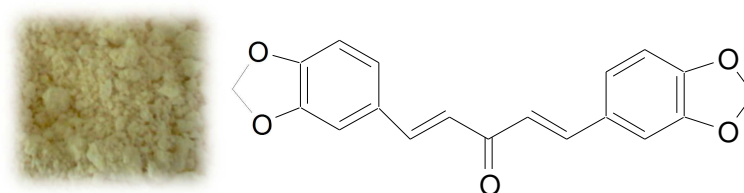


Figure 1. a) Curcumin analog products, b) Chemical structure of synthetic products analogous curcumin from cullilawan oil

Giving CCl₄ has an effect on the animal body weight, it was seen that there was a weight loss after CCl₄ (Fig. 2). Weight loss occurs due to the entry of toxic substances into the body. Giving CCl₄ continuously with administration twice a week can have an effect on liver function. The effect

of giving synthetic products has an effect on the animal's body weight, seen from the increase in body weight, although not as big as the treatment for turmeric extract curcumin and the heap-Q drug.

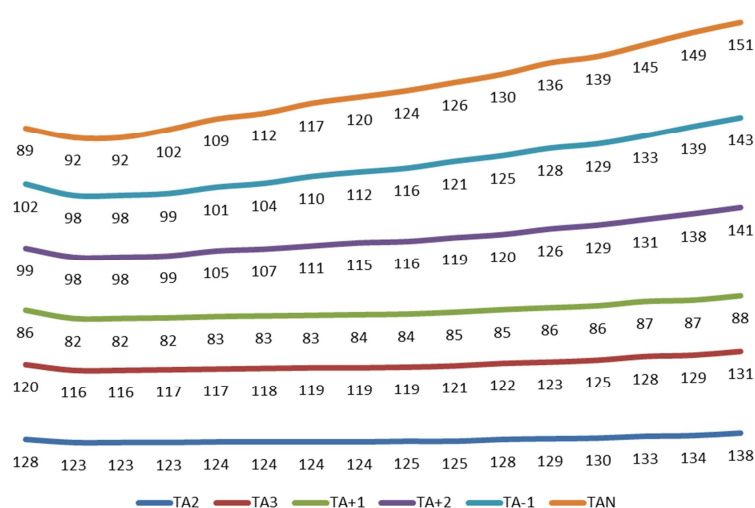


Figure 2. Graph of average body weight of model animals

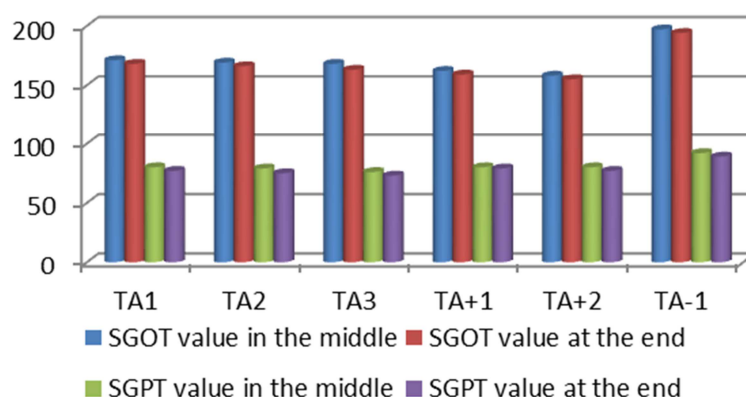


Figure 3. Results of blood biochemical analysis

Biochemical analysis of blood on the liver to determine damage from liver function is shown in Figure 3. For negative controls, it shows high SGOT values and SGPT values. This shows a damage of liver function, but in the body can regenerate so that there is a decrease in the value of SGPT and SGOT. Positive control for heap-Q products provides good value for SGOT and for curcumin (turmeric extract) gives the same results. The curcumin analog

synthetic product made gives a lower SGPT value when compared to positive controls. Products with TA3 sample code (dose 52 mg / 200g bb) give a lower value compared to other doses. The higher the dose of products curcumin analogue has a positive effect on improving liver function. To see damage from liver cells histopathological analysis was carried out for the whole treatment.

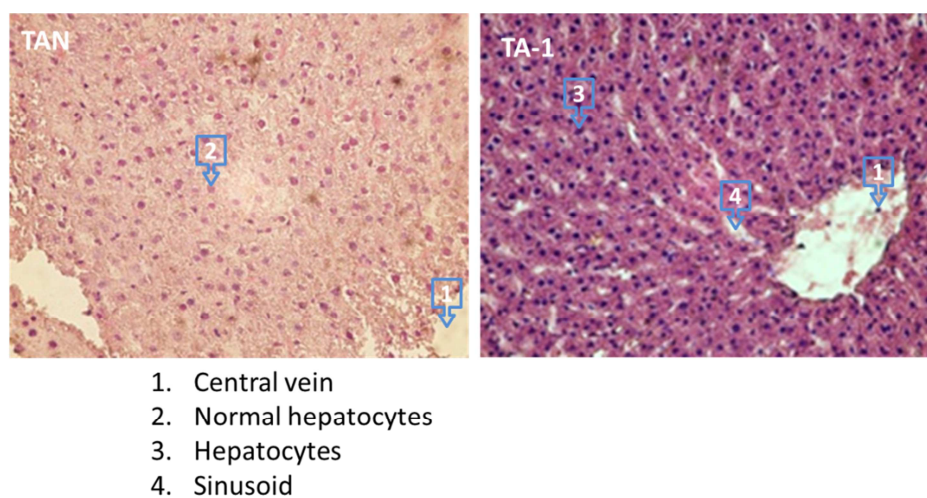


Figure 4. Microscopic images. a) normal liver structure of control mice (TAN).
b) liver structure induced by CCl₄ (TA-1).

Microscopic images for normal liver cells of mice before treatment and after induction with CCl₄ provide a description of differences in cell damage (Figure 4). Carbon tetrachloride (CCl₄) is a chemical that is toxic and can cause liver damage in the form of degeneration and necrosis. In the initial stages of liver cell damage in the form of hydropic

degeneration and continued with fat degeneration, and cell death or necrosis [8]. In normal liver cells, there is a regular arrangement of tissues because of no damage due to toxic substances. Unlike the cells that have been induced by CCl₄, there is a fatty microvascular and macrovascular appearance in the central venous area. Liver cell damage is also

characterized by the presence of vacuoles due to swollen hepatocytes and causes the sinusoid to narrow. For normal cells it is clear that hepatocytes and central veins as centers are round and empty.

The provision of curcumin analogue products made using safrol as a precursor provides a microscopic picture of liver cell structures that undergo cell degeneration. From the microscopic picture of liver cells it was shown that the dose of the curcumin analogue product which had a preventive

effect on liver function damage was a dose of 52 mg / 200g bb (Fig. 5). For lower doses, it is seen that there are hepatocytes, sinusoids and Central veins that are still clearly visible in fatty. When compared with positive control (heap-q), curcumin analog products have the potential as hepatoprotectors because they are able to provide good results even with lower doses. For curcumin alone, there is still fat in the central vein and hepatocytes despite using higher doses.

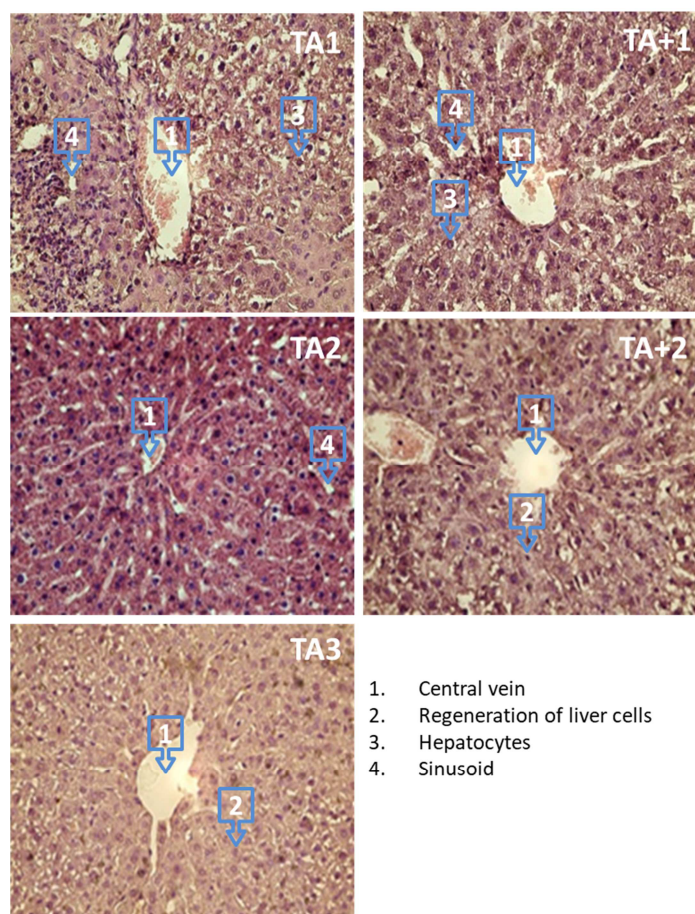


Figure 5. Microscopic images for each treatment

Effect of protecting liver function Curcumin analogues are caused by active groups in the compound. Synthetic products curcumin analogues have alkene, benzem, carbonyl and ether groups which are negatively charged, making it possible to capture free radicals so that they become neutral molecules (Fig. 1b). If free radicals in the body have been captured, then the body can automatically repair itself. This is seen from the regeneration of damaged liver cells, because it can be concluded that curcumin analog products are antioxidants and have a hepatoprotector effect [9].

IV. CONCLUSION

Curcumin analog product (AKS-k) from cullilawan oil has a preventive effect on liver function damage in male rats (*Rattus norvegicus L.*) induced CCl₄ with an effective dose is a dose of 52 mg/ 200g bb.

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