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SUBCRONIC TOXICITY AND HEPATOPROTECTOR POTENTIAL OF MIANA LEAF EXTRACT ON WHITE RAT WHICH INDICATED BY ANTI TUBERCULOSIS DRUGS Sesilia Rante Pakadang1, Santi Sinala1*, Sisilia Teresia Rosmala Dewi1, Heri Soemantoro2, Maria Hilaria3 1. Lecturer at Department of Pharmacy, Poltekkes Kemenkes Makassar, Makassar, Indonesia 2. Researcher at Medical Faculty, Airlangga University, Surabaya, Indonesia 3.

Lecturer at Department of Pharmacy, Poltekkes Kemenkes Kupang, Kupang, Indonesia * Corresponding Author Santi Sinala, Department of Pharmacy, Poltekkes Kemenkes Makassar, Baji Gau No.10, Mamajang, Makassar, Indonesia. Telp. +6285255918123. Email : santisinala@poltekkes-mks.ac.id ABSTRACT Damage to liver function is the most common cause of patients or doctors stopping treatment.

Anti-tuberculosis (OAT) drug-induced hepatotoxicity is mainly caused by oxidative stress caused by drugs and metabolites. Subchronic toxicity is one of the conditions for testing long-term used drugs such as OAT. The research aims to determine the potential of miana leaf extract (EDM) as a hepatoprotector and prevent toxicity due to OAT administration.

The study used 5 groups of Wistar rat test animals namely K1 (normal mice given placebo); K2 (OAT-induced mice given placebo); K3 (OAT-induced mice given Makassar EDM); K4 (OAT-induced mice given EDM Kupang); K5 (OAT-induced mice given Silymarin). Tests on mice were carried out after 30 days of treatment with parameters SGOT, SGPT, total bilirubin, creatinine and liver histopathology.

The results showed that EDM has the potential as a hepatoprotector by preventing an

increase in SGOT, SGPT and total bilirubin so as to avoid liver damage due to OAT induction. EDM has the potential to prevent toxicity due to the administration of OAT with creatinine parameters. Keywords: miana leaf extract, OAT, hepatoprotector, toxicity

INTRODUCTION The first-line treatment of tuberculosis according to tuberculosis prevention guidelines (9) is the use of anti-tuberculosis (OAT) drugs such as isoniazid, rifampicin, pyrazinamide, streptomycin and ethambutol.

The most common factor in the treatment of tuberculosis is the side effects of OAT against damage to liver function such as hepatitis, hypersensitivity reactions, nausea, and vomiting (Gautam, 2012). Drug-induced hepatotoxicity and metabolites such as OAT are mainly caused by oxidative stress (18). Prevention of drug induced liver injury (DILI) has been carried out using chemical compounds or natural ingredients.

The effect of n-acetylsysteine ??hepatoprotector in preventing damage to liver function due to administration of OAT (4). Singh (18) have compared the effects of hepatoprotector n-acetylsysteine, silymarin and curcumin. The results can reduce hepotoxic HepG2 cells during OAT administration with parameters of survival, morphology, mitochondrial respiration and cell cycle.

Krisnansari (11) proved the hepatoprotective potential of propolis against white mice induced by CCl4 (carbon tetra chloride). Propolis is proven to provide a significant difference in IL-6, superoxide dismutase, body weight and histopathology of rat liver. Huda proved the formulation of polyberbal sharbat chylosin as a hepatoprotector against total bilirubin, ALT, AST, ALP and rat liver histopathology (8).

Research assumes that the hepatoprotective effect is related to the antioxidant properties of plant extracts. Shehab investigated the antioxidant capacity of Fagonia indica Burn extract, Calotropis procera RBr and Salsola imbricate Forssk as potential hepatoprotectors for CCl4-induced mice, because they can reduce ALT, AST and serum bilirubin levels (17).

Phenolic compounds from plants such as quercetine and rosmarinic acid have the potential as antioxidants that can counteract oxidative stress as a pathophysiological mechanism of DILI (21). Plants that have potential as antioxidants and hepatoprotectors become therapeutic mechanisms so that it is important to be given as a complementary in the treatment of tuberculosis such as: meniran, miana, mangosteen, temulawak, rosella, kencur, kedondong forest, garlic, brotowali (13,14).

Al-Snafi has identified 45 medicinal plants in Iraq that contain secondary metabolites that are antioxidants (3). In India found 4167 species of medicinal plants that have been used for the treatment of liver disorders, filariasis and diabetes mellitus (16). Verma has reviewed 15 plants as hepatoprotective in Iranian folk medicine (19).

Kumar identified the antioxidant properties of herbs as a hepatoprotector with oxidative mechanisms against toxic chemicals (10). The use of plants even as hepatoprotectors need to consider the subchronic toxicity caused. Especially for long-term use such as complementary tuberculosis treatment. Rachmawati and Ulfa examined the toxicity of yellow wood extract to the liver and kidneys with parameters of SGOT, SGPT, histopathology of the liver and kidney (15).

This study aims to determine the toxicity and hepatoprotective potential of EDM in OAT-induced white rats. The hepatoprotector function was tested based on the parameters AST / SGOT, ALT / SGPT, histopathological features of white rat liver. Toxicity prevention function based on white rat bilirubin and creatinine..

MATERIAL AND METHODS Test material are EDM originating from Makassar City and Kupang City, OAT, Sylimarin and Sodium CMC as placebo. The extract was prepared based on maceration method. The dosage of the test material consisted of Rifampicin 25mg / kg BW rat / day; INH 25mg / kg BW rat / day; Placebo Na CMC 1%; EDM from Makassar 250 mg / kg rat / day; EDM from Kupang 250 mg / kg body weight / day; Sylimarin 25 mg / kg BW rat / day.

Test sample is white rat (Rattus norvegicus) Wistar strain; male, healthy, 2-3 months old, body weight 150-200g. Procedure for testing. White rats were grouped in 5 groups with 7 rats for each treatment group. Every day the rats were fed and drank ad libitum. Every day rats get different treatment for each group. K1 (control group animals were given placebo (sodium CMC) orally once a day for 30 days).

K2 (negative control group was given OAT and Placebo orally once a day for 30 days). K3 (treatment group given OAT and EDM from Makassar orally once a day for 30 days). K4 (treatment group given OAT and EDM from Kupang orally once a day for 30 days). K5 (positive control group given OAT and silymarin orally once a day for 30 days). OAT given is a combination drug of rifampicin and INH.

Administration of OAT and EDM or Silymarin is done 1 hour apart to prevent drug interactions). After the end of treatment the dieuthanasia rats were then dissected to take specimens for testing. Specimens taken were rat blood for AST / SGOT, ALT / SGPT testing, total bilirubin, creatinine and complete blood.

Mouse liver organ specimens for histopathological testing of the liver. Maintenance and treatment of samples was carried out in the animal laboratory of the Faculty of Medicine, Airlangga University (FKUA). Blood sample testing is carried out in the Dr. Chemistry clinical laboratory laboratory. Soetomo Surabaya.

Histopathological testing was performed with HE staining preparations in the anatomic pathology laboratory FKUA Surabaya. FINDING AND DISCUSSION Finding The potential of EDM as a hepatoprotector for tuberculosis treatment is based on the results of rat blood sample testing according to the following table Table 1.

Test results on the number of SGPT, SGOT, Bilirubin and Creatinine in white rat test animals after OAT induction and treated with test material Treatment Group _n _ Results of rat blood measurements _ _ _ _SGOT _SGPT _Bilirubin _Kreatinin _ _K1 _7 _118.28 _22.85 _0.056 _0.457 _ _K2 _7 _144.4 _52.14 _0.081 _0.571 _ _K3 _7 _115 _32.42 _0.071 _0.507 _ _K4 _5 _112 _42.8 _0.076 _0.468 _ _K5 _5 _98 _42.8 _0.07 _0.434 _ _ White rat test liver was prepared until histopathological preparations were made.

After staining hematosycline eosin (HE) and observed with a microscope with the results according to figure 1. PREPARAT OF RAT LIVER _VENA CENTRALIS _PORTAL TRIAD _NEKROSIS _ _K 1 _ _Congestion looks _Lymphocyte infiltration forms bridging and bleeding _There is no necrosis _ _K 2 _ _Congestion and hyalinization appear _Lymphocyte infiltration, bleeding and hyalinization _Necrosis occurs (picnosis, karyorrhexis, karyolysis) _ _K 3 _ _Some congestions appear _Lymphocyte infiltration and some bleeding _There is no necrosis _ _K 4 _ _Some congestions appear _Lymphocyte infiltration forms bridging _There is no necrosis _ _K 5 _ _Some congestions appear _Multiple lymphocyte infiltration and bleeding _There is no necrosis _ _Information : K1 (normal rat given a placebo); K2 (OAT-induced rat given placebo); K3 (OAT-induced rat given Miana Makassar); K4 (OAT-induced rat given Miana Kupang); K5 (OAT-induced rat given Silymarin) Discussion The results of phytochemical screening from EDM and antioxidant testing proved that EDM contains flavonoid compounds that have potential as antioxidants (13).

Liver damage is also caused by free radicals released by cells that are induced by OAT so that the antioxidant function of EDM in this case can prevent malfunctioning and liver damage. In this case Airaodion have proven the hepatoprotective effect of Parkia biglobosa in rats induced by oxidative stress with parameters AST, ALT, LDH, LPO, CAT, SOD and GSH. Then it can be stated that EDM which contains antioxidants has the potential to be a hepatoprotector with its antioxidant mechanism(2).

In accordance with research Shehab which shows the relationship of phenolic content in several herbal medicines as antioxidants and hepatoprotectors with the parameters of reducing the amount of ALT, AST, CAT, GSH, SOD and TBARS and proving that the flavonol content of quercitrin and rosmarinic acid play a role in reducing DPPH free radicals (17). Airaodion have proven the hepatoprotective effect of Parkia biglobosa in

rats induced by oxidative stress with the same parameters(2).

Symptoms of hepatotoxicity in patients receiving tuberculosis treatment are based on an increase in serum alanine aminotransaminase in both ALT / SGPT and AST / SGOT amounts that appear after OAT administration such as rifampicin and INH. Increased serum 3-5 times the normal value accompanied by symptoms of hepatitis (5). Grouping of test animals was done to compare the effect of Na CMC (K2) test material; EDM from Makassar (K3); EDM from Kupang (K4) and silymarin (K5).

The hepatotoxic parameters tested after administration of OAT are: an increase in the normal value of AST and / or ALT; an increase in total serum bilirubin and an improvement in liver function after stopping OAT. While creatinine testing is done to prevent toxicity. The parameters tested are in line with studies that test kidney toxicity including creatinine and BUN, while liver function includes SGOT, SGPT, HDL, LDL, total cholesterol, total protein, albumin, and triglycerides (5,7). The test results showed an increase in SGOT and SGPT in K2 compared to K1 by (22%) and (128%).

Based on the analysis there was a decrease in the number of SGOT and SGPT towards K2, namely in K3 (25%) and (86%); K4 (27%) and (41%): K5 (39%) and (41%). The Mann Whitney test showed that K3 and K4 were not significantly different from K1 for the SGOT and K3 parameters because they gave the largest and significant decrease in SGPT with other treatments for the SGPT parameter.

Based on the results of research on the effect of giving EDM as a hepatoprotector with parameters of the amount of SGOT, SGPT, total bilirubin and histopathological features of the liver, the relationship between these variables is the mechanism of hepatoprotector that occurs in OAT induced rats. In the study, it was proven that mice induced by OAT on K2 showed an increase in the amount of SGOT, SGPT and total bilirubin compared to K1, which means that there has been impaired liver function due to OAT administration. Other studies have shown an increase in SGPT due to 7.5-fold OAT-induced hepatotoxicity in patients with HIV / AIDS and 100% of subjects given 600mg rifampicin experienced hepatotoxicity due to increased SGOT and SGPT (12).

The test results showed an increase in total bilirubin and creatinine from K2 to K1 (31.57%) and (24.94%). However, there was a decrease in K2 from K3 (17.56%) and (11.2%); K4 (6.63%) and (22.53%); K5 (14%) and (29.97%). Mann Whitney analysis shows the amount of creatinine K3, K4 and K5 is not significantly different from one another.

Total bilirubin can be used to detect hepatobilers, hepatitis, cirrhosis and other liver diseases. Likewise, Huda and Mosaddik have proven the hepatoprotector effect of

herbal medicine formulas by comparing silymarin based on decreasing the amount of ALT / SGPT, AST / SGOT, ALP and total bilirubin(8).

Histopathological picture of liver showed damage occurred in K2 rat's liver compared to other groups, because necrosis had occurred with the characteristics of the discovery of picnosis, karyoreksis and karyolisis. Although in general in all samples congestion occurs in the central vein but in K2 congestion is accompanied by hyalinization.

Whereas in K3, K4 and K5 only found a few congestions in the observation of the entire microscopic field of view. In the triad portal lymphocyte infiltration and bleeding occurred in all treatment groups. But in K2 it turns out to be hyalinized, so it can be stated that K3 and K4 have potential as hepatoprotectors based on the rat liver damage picture.

According to Zachary and McGavin in the case of acute cell damage, the process is that at first the cell nucleus undergoes picnosis (damage to the cell nucleus so that the cell contents thicken) and then chromatin in the cell nucleus will dissolve (karyolysis) followed by a breakdown of the cell nucleus (karyoreksis)(21). The hepatoprotective function of herbal medicines such as propolis, yellow wood and 15 other types of herbs has been proven based on histopathological features (11,15,19).

In line with the results of the study of the potential of EDM as a hepatoprotector Ahsan also proved the potential of herbs as hepatoprotector with the results of reducing SGOT, SGPT and total bilirubin and showing differences in the histopathological picture of CCl4 induced rat liver(1). Yani and Singh also reported the hepatoprotective effect of N-Acetylcysteine ??in preventing DILI due to OAT so it was recommended to use hepatoprotector in OAT treatment to avoid the occurrence of hepatotoxic in patients who were given rifampicin and INH treatment(20).

The results of this study support the function of EDM not only as a preventive, complementary curative tuberculosis (14) but also functions as a hepatoprotector and prevents toxicity due to treatment. CONCLUSION EDM has potential as a hepatoprotector by reducing the number of AST / SGOT and ALT / SGPT OAT induced white mice EDM has the potential to prevent OAT toxicity based on improved histopathology of the liver and is able to maintain the amount of OAT induced white rat bilirubin and creatinine .

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V / 2019 from the Ethics Commission of the Polytechnic of the Ministry of Health Makassar (Politeknik Kesehatan Makassar Kementerian Kesehatan Republik Indonesia) CONFLICT OF INTEREST There are not a conflict of interest with another REFERENCES Ahsan MR,et all: Hepatoprotective Activity of Methanol Extract of Some Medicinal Plants Against Carbon Tetrachloride Induced Hepatotoxicity in Rats.

European Journal of Scientific Research vol.37 No.2.2009.Pp.302-310. Airaodion AI, et all, Hepatoprotective Effect of parkia biglobosa on Acute Ethanol-induced Oxidative Stress in Wistar Rats, International Research Journal of Gastroenterology and Hepatology.2(1):1-11, 2019 Al-Snafi AE. Theraupetic Properties of medicinal Plants: A review of plants with antioxidant activity (Part 1).

International Journal of Pharmacy and Therapeutics, 6(3).2015. Baniasadi S, Protective effect of N-acetylcysteine on antituberculosis drug induced hepatotoxixity. Randomized controlled trial. Eur. J. Gastroenterol Hepatol 2011. Feb; 23: 193 Bihar S. Gangguan Hati pada Pengobatan Tuberkulosis, RS. Siloam Dhirga Surya, Medan,2015 Gautam : Review on Herbal Plants Useful in Tuberculosis. International Research Journal of Pharmacy, 2012, 64-67. Hendriani R.,

Uji toksisitas subkronis kombinasi ekstrak etanol buah mengkudu (Morinda citrifolia Linn.) dan rimpang jahe gajah (Zingiber officinale R.) pada tikus wistar. karya ilmiah. Univ Padjadjaran Fak Farmasi Jatinangor, 2017 Huda MN, Mosaddik MA. Hepatoprotective activity of sharbat chylosin a polyherbal formulation against carbon tetrachloride induces hepatotoxicity in rats.

Word Journal of Pharmacy and Pharmaceutical Sciences. 2018, Vol. 7, Issue 9, 73-79. Kemenkes RI: Pedoman Nasional Penanggulangan Tuberkulosis. Kementerian Kesehatan RI Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan, Jakarta.2011 Kumar CH, et all, A Review on hepatoprotective activity of medicinal plants. International Journal of Pharmaceutical Sciences and Research. 2011; vol.

2(3): 501-515 Krisnansari D, et all, Potensi hepatoprotektor propolis terhadap hepar tikus putih (Rattus norvegicus) yang diinduksi karbon tetrakhlorida. Jurnal Ners vol. 9, no. 2, Oktober 2014: 270-278 Luthariana L, et all. Faktor risiko terjadinya hepatotoksisitas imbas obat antituberkulosis pada pasien HIV/AIDS. Jurnal Penyakit Dalam Indonesia, vol.

4, no 1, Maret 2017 Pakadang SR, Wahjuni CU, Notobroto HB, Winarni, Dwiyanti R, Yadi, Sabir M, Hatta M, Immunomodulator Potential of Miana Leaves (Coleus scutellarioides (L) Benth) in Prevention of Tuberculosis Infection American Journal of Microbiological Research, 2015, Vol. 3, No. 4, 129-134 Available online at

http://pubs.sciepub.com/ajmr/3/4/2 © Science and Education Publishing Pakadang SR, Wahjuni CU, Notobroto HB, Winarn.

Miana Leaves (Coleus scutellarioides (L) Benth) as the Complement at Tuberculosis Treatment. Proceeding, International Conference 1 st Health Technology Department, Ministry of Health, Makasssar, 2016 Rachmawati E and Ulfa EU, Uji toksisitas subkronik ekstrak kayu kuning (Arcangelisia flava Merr) terhadap hepar dan ginjal. Global Medical and Health Communication, 2018. vol. 6. No.

1 Satyapal NT, Yadav S, Contributions of Indian Council of Medical Research (ICMR) in the area of Medicinal plants/ Traditional medicine. Journal of Ethnopharmacology volume 197. 2 february 2017, p39-45. Shehab NG, et all, Impact of phenolic composition on hepatoprotective and antioxidant effects of four desert medicinal plants.

BioMed Central Complementary and Alternative Medicine 2015. 15:401. Singh M, et all, Protective effect of curcumin, silymarin and N-acetylcysteine on antitubercular drug-induced hepatotoxicity assessed in an in vitro model Research article 2012 Verma R, A review on hepatoprotective activity of medicinal plants. Journal of Medicinal Plant Studies. 2018: 6(1):188-190 Yani MS, Singh G,.

Efek hepatoprotektif N-asetilsistein dalam mencegah drug-induced-liver-injury akibat obat antituberkulosis: laporan kasus berbasis bukti. Indonesian Journal of CHEST (Critical and Emergency Medicine.) Vol 2, no. 2, Apr-Jun 2015. Zachary, et all. Pathologic Basis of Veterinary Disease, Fifth Edition . Missouri: Elsevier, Inc, 2012

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