

## Quality of Live Improvement Antituberculosis Consumer

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### Abstract

Antituberculosis is the most liver damage causes. Rifampicin and Isoniazide, in combination, are toxic compounds. Isoniazide and rifampicin metabolites causes lipid peroxidation. The hepatoprotective effect of rosella calyx water extract on liver damage induced with Isoniazide-rifampicin evaluated by examination of malondialdehyd levels in the liver organ. 25 male wistar rats divided into 5 groups, ie group I (INH-rifampicin + rosella water extract 250 mg/kgBW), group II (INH-rifampicin + rosella water extract 125 mg/kgBW), group III (INH-rifampicin + rosella water extract 62.5 mg/kgBW), group IV (healthy control) and group V (Isoniazide-rifampicin). MDA liver levels were analyzed after 35 days of treatments. The test results of each group are, group I has mean MDA levels  $0.023912 \pm 0.011$  mg/ml, group II  $0.023526 \pm 0.009$  mg/ml, group III  $0.027168 \pm 0.007$  mg/ml group IV  $0.03437 \pm 0.009$  mg/ml and group V  $0.236846 \pm 0.118$  mg/ml. The kruskal-wallis test showed significantly value 0.008 ( $p < 0.05$ ) and Post hoc Mann U whitney test showed that group V was significantly different to group I, II, III, and IV ( $p = 0.008$ ) respectively, roselle extract can be used as a hepatoprotector antioxidant to improve the tuberculosis drug consumer quality of life through improved health by lowering lipid peroxidation that causes liver damage.

**Keywords:** *Rosella Extrac; Hepatoprotective; Rifampicin-Isoniazide; MDA Levels*



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### INTRODUCTION

Epidemiological studies in China in 2013, antituberculosis is the leading cause of liver damage (Devarbhavi, 2012; Kim *et al.*, 2017). Rifampicin, Isoniazide, pyrazinamide, and their active metabolites are the most potential hepatotoxic compounds (Pandit *et al.*, 2012; Enriquez-Cortina *et al.*, 2013). Isoniazide toxicity mechanisms through the reactive metabolites formations, Isoniazide was metabolized and eliminated mainly in the liver. Isoniazide was metabolized become a non toxic agent by acetylation reaction to N-acetyl Isoniazide was hydrolyzed to acetylhydrazine and isonothinic acid. However, when acetylhydrazine was metabolized by NAT-2 and CYP2E1 enzymes, reactive metabolites are formed and can bind to the liver cell component causing hepatotoxicity. in fact, use in combined, it will increase the risk of hepatotoxicity (An and Wu, 2010; Leung *et al.*, 2012; Pandit *et al.*, 2012). Liver damage is closely related to the occurrence of oxidative stress. One of the oxidative stress markers is elevated MDA levels and decreased antioxidant activity that can cause various tissue damage (Del Rio *et al.*, 2005; Pandit *et al.*, 2012).

Rosella (*Hibiscus sabdariffa* L.) is alternative traditional medicine that has antioxidant activity, antihypotention, antiurolitiatik, hepatoprotective, antihiperlipidemic, imunomodulator, antidiabetic, anticancer, and diuretic (Patel, 2014; Hopkins *et al.*, 2013). The main components of roselle are organic acids, malic and citric acids, fiber, flavanoid, glycosides, polyphenols, catechins, galocatechins, caffeine and anthocyanin acids (delphinidin-3-sambubioside and cyanidin-3-sambubioside) was found in water extracts (Hopkins *et al.*, 2013).

## MATERIAL AND METHOD

### Importance of Economic Geography

The research at the Laboratory of Biopharmaca and Pharmacy Clinic Faculty of Pharmacy Hasanuddin University. Samples are simplicia rosella calyx. Infus water 25% was prepared, then filtered was added with 2.5 grams of maltodextrin and then dried by using freeze dryer to become rosella powder encapsulated maltodextrin. The dose of encapsulated rosella water extract of maltodextrin to be used is 250 mg/kgBW/day, 125 mg/KgBW day and 62,5 mg/kgBW/day.

### Animal Handling

Animals used were rats (*Rattus norvegicus*) wistar males can be observed from their physical condition, with an average weight of 150-250 grams. Twenty 25 male wistar rats were divided into 5 treatment groups, ie group I (healthy control), group II (isoniazid-rifampicin), group III (isoniazid-rifampicin + rosella water extract 62.5 mg/kgBW), group IV (isoniazid-rifampicin + rosella water extract 125 mg/kgBW) and group V (isoniazid-rifampicin + rosella water extract 250 mg/kgBW) treated for 35 days.

### MDA Levels

- a. Measurement of raw curves.

The standard solution used to measuring lipid peroxidation level is a standard MDA diagnostic of 1,1,3,3-tetramethoxypropane (TMP). The standard solution was prepared using 1 ml TMP stock solution dissolved in 10 ml PBS (Phosphate buffer saline). 6 variations of dilution are 0,05; 0.1; 0.15; 0.2; 0.25 and 0.3 ppm. Then measured the absorbance at 532 nm wavelength.

- b. Examination of MDA level in the liver

The liver was crushed and weighed 400 mg, 2 ml PBS (pH 7.4) was added into the mortal and mixed until homogeneous, then centrifuged 20 minutes at 3000 rpm. 0,5 ml supernatant was added 1 ml of 1% TBA mixture and 1% TCA into the tube and heated in the water bath at 95 ° C for 50 min and cooled in room temperature. Centrifuged again and then measured MDA level with UV-Vis spectrophotometer at 532 nm wavelength.

## DATA ANALYSIS

Data analysis of MDA liver organ levels obtained abnormal data distribution analyzed with Kruskal-Wallis and continued with Mann U Whitney to see significant differences between groups.

## RESULT AND DISCUSSION

The test results of measurements MDA levels in liver organ showed that rosella water extract could decrease lipid peroksidasi to improve liver function. The result of Kruskal-Wallis test showed that MDA concentration in group II liver was significantly different with treatment group given rosella water extract with 0.008 value ( $p < 0.05$ ).

Table 1. Rat liver MDA level induced isoniazide-rifmpicin

| Group | Absorbantion | MDA level            |
|-------|--------------|----------------------|
| I     | 0.125094     | 0.023912+0.011723279 |
| II    | 0.125002     | 0.023526+0.00939977  |
| III   | 0.131502     | 0.027168+0.007081308 |
| IV    | 0.144362     | 0.03437+0.00991199   |
| V     | 0.48578      | 0.236846+0.11863038  |

**Note:** Mean  $\pm$ SD; ie group I (INH-rifampicin + rosella water extract 250 mg/kgBW), group II (INH -rifampicin + rosella water extract 125 mg/kgBW), group III (INH -rifampicin + rosella water extract 62.5 mg/kgBW), group IV (healthy control) and group V (INH-rifampicin)

The rosella flower extract has strong antioxidant activity to reduce reactive oxygen and free radicals, inhibits xanthine oxidase activity, protects cell damage from lipid peroxidation, inhibits Cu<sup>2+</sup> mediating reactive thiobarbituric acid substances formation, enhances superoxid dismutase, catalase and glutathione activity and inhibits formation of malondialdehyde (MDA) at 100-300 mg/kgBW (Da-Costa-Rocha et al., 2014).

Rosella flowers were studied as hepatoprotectors based on previous studies that infusion of rosella flowers with concentrations of 25% and 40% could decrease SGOT and SGPT against anti-TB drug-induced (Serang, 2016). In fact, rosella water extract (300, 200 and 100 mg/kgBW) showed hepatoprotective activity in mice by increasing glutathione levels, catalase and decreasing lipid oxidation levels (Patel, 2014, Da-Costa-Rocha et al., 2014).

In this study, Isoniazide-rifampicin is used as an inducer of hepatotoxicity, because of Isoniazide-rifampicin metabolites cause of liver damage in clinical cases (Devarbhavi, 2012; Chang et al., 2014; Kim et al., 2017). Isoniazide was metabolized to acetylhydrazine and isonothinic acid that are non-toxic compound, while rifampicin acts on the enzyme cytochrome P450 increase Isoniazide metabolism to acetylhydration and acetylhydracin (Achz) are rapidly converted into their active metabolites and increases oxidative elimination from asetilhydrazine, liver necrosis caused by Isoniazide and rifampicin in combination (An and Wu, 2010; Leung et al., 2012; Pandit et al., 2012; Kim et al., 2017).

## CONCLUSION

Roselle water extract can be used as a hepatoprotector antioxidant to improve the tuberculosis drug consumer quality of life through improved health by lowering oxidative stress that causes liver damage.

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