IJBPAS, June, 2020, 9(6): 1284-1290

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

HEPATOPROTECTIVE ACTIVITY OF RICE FIELD SNAIL (*Filopaludina javanica* v.d Busch 1844) IN FEMALE WISTAR RATS INDUCED HEPATOTOXICITY BY PARACETAMOL

ISTIQOMAH AN[1, 2*], SOEMARDJI AA[1] AND KUSMARDIYANI S[1]

1: School of Pharmacy, Bandung Institute of Technology, Bandung, Indonesia

2: Departement of Pharmacology, Bhakti Kencana University, Bandung, Indonesia

[*]**Corresponding Author: E Mail: aulia.nurfazri@bku.ac.id**

Received 20th July 2019; Revised 5th Oct. 2019; Accepted 5th Jan. 2020; Available online 1st June 2020

https://doi.org/10.31032/IJBPAS/2020/9.6.5072

ABSTRACT

Introduction: Rice field snail (*Filopaludina javanica* v.d Busch 1844) has been used empirically as a hepatoprotective agent. The snail is known rich of protein which is predicted to have a role in protecting the liver from damage. Its potential as a hepatoprotector still needs further proof, therefore this study was conducted to evaluate the effectiveness of the snail in preventing liver damage.

Method: The test was performed by preventive method by administering paracetamol (360 mg/kg) as inducer of liver damage for 14 days accompanied by administration of the snail and silymarin (25 mg/kg) as a comparator drug. The snails were divided into three parts of total flesh, flesh without rectum, and rectum flesh, each given in three variations of dose. Body weight monitoring was performed during the treatment and measurements of AST and ALT levels were performed on days 0, 8, and 15.

Result: This study showed that the snail inhibited liver damage caused by paracetamol toxicity. The most effective part of the snail as a hepatoprotector was the rectal flesh with the dose of 0.395 g/kg, which is equivalent to silymarin at 25 mg/kg.

Keywords: *Filopaludina javanica*, rice field snail, hepatoprotective, paracetamol

INTRODUCTION

Disorders in liver function are usually caused by viruses such as hepatitis. Besides viruses can also be caused by alcohol and drug toxicity.

More than 50% of cases of liver disease that occur are caused by drugs and have been known that more than 600 drugs associated with hepatotoxicity. The actual number may be more because not all are reported and have difficulties in detection or diagnosis **[16]**.

Paracetamol has been used since 1950 but it is known that paracetamol causes hepatotoxicity. 39% of all acute liver failure cases as due to paracetamol between 1998 and 2001, increasing to 51% in 2004 **[13]**.

Paracetamol can be absorbed rapidly in the stomach and small intestine then metabolized in the liver into a non-toxic compound. In an overdose or when use exceeds the maximum daily dose in the long term, the metabolic pathways will become saturated. Excess paracetamol will be metabolized oxidatively in the liver into a toxic compound called N-acetyl-P-benzoquinoneimine (NAPQI). Excessive NAPQI bind to vital proteins and lipid layers of hepatocyte membranes covalently and cause necrosis or liver cell death **[15]**.

Research has been conducted on the snail species *Bellamya bengalensis* and it was found that the snail of this species has a high protein content and has hepatoprotective activity because it can inhibit increased levels of GOT (glutamate oxaloacetate transaminase), GPT (glutamate pyruvate transaminase), ACP (acid phospatase), ALP (alkaline phosphatase), and bilirubin **[8]**.

The rice field snail (*Filopaludina javanica* v. d Busch 1844) is a rice pest that can be found in almost all parts of Indonesia. In West Java, aside from being used as food, rice field snail has been used empirically as a treatment for liver disease. The rice field snail belong to the same family and genus as *Bellamya bengalensis* and have very high protein content, so it can be said that the rice field snail potentially has hepatoprotector activity.

MATERIAL AND METHOD

Experimental Animals

The experimental animals were female rats Wistar strain weighing 150-200 grams.

Materials

Rice field snail, Paracetamol, Silymarin, ALT Kit, AST Kit, Aquadest, Na-CMC.

Methods

Each group of test animals, except the normal group received induction treatment and test drugs **(Table 1)**.

The female rat Wistar strain was divided into 12 groups. Each group was given treatment as shown in **Table 1** for 14 days. On days 0, 8 and 15, ALT and AST levels were measured.

Table 1: Treatment of animal Test

Group Test	Paracetamol	Total Flesh	Flesh Without Rectum	Rectum Flesh	Silymarin	Na-CMC 1%
TF1	360 mg/kg	1.655 g/kg				
TF2	360 mg/kg	3.310 g/kg				
TF3	360 mg/kg	6.620 g/kg				
WR1	360 mg/kg		1.215 g/kg			
WR2	360 mg/kg		2.430 g/kg			
WR3	360 mg/kg		4.860 g/kg			
RF1	360 mg/kg			0.395 g/kg		
RF2	360 mg/kg			0.790 g/kg		
RF3	360 mg/kg			1.580 g/kg		
CD	360 mg/kg				25 mg/kg	
PC	360 mg/kg					2ml/200g
NC						2ml/200g

Description: Negative control (NC), Positive control (PC), Comparator drug (CD), Total flesh 1 (TF1), Total flesh 2 (TF2), Total flesh 3 (TF3), Flesh without rectum 1 (WR1), Flesh without rectum 2 (WR2), Flesh without rectum (WR3), Rectum flesh 1 (RF1), Rectum flesh 2 (RF2), and Rectum flesh 3 (RF3).

RESULTS AND DISCUSSION

Paracetamol effectively used as an analgesic and antipyretic as a substitute for aspirin, but excessive use of paracetamol can cause liver damage. Liver damage is characterized by an increase in levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT).

Figure 1 shows the condition of AST levels in rats for 14 days of treatment. There was an increase in AST levels in the test group induced by paracetamol after 7 days of treatment and there was a decrease in AST levels in the test drug group after administration for more than 7 days. This means the test drug and comparator have no effect to the 7 daysadministration but show an effect when the administration is continued up to 14 days.

Figure 2 shows that the provision of rice field snail flesh for 7 days has not been able to withstand the effect of paracetamol induction, this can be seen from the increase in ALT levels in the same as the positive control group.

In the 15th day of measurement, after 14 days of treatment, there was a decrease in ALT levels in each group which given the test substance, this indicates that the administration of silymarin and rice field snail flesh can reduce ALT levels caused by administration of paracetamol.

From the results of organ histopathology, the composition of hepatocytes in the positive control group is more tenuous compared to the negative control group. There was necrosis, vacuolization, and accumulation of inflammatory cells in the positive control group. In the comparison group, the composition of hepatocytes looks denser but there are inflammatory cells. In the Total Flesh and Flesh without rectum groups, necrosis, vacuolation, and inflammation were the same as in positive control but the hepatocyte arrangement was much tighter. In the rectum flesh test group, the cell condition seemed to improve but there were still inflammatory cells. Rice field snail flesh can reduce the levels of AST and ALT but does not improbe the condition of the liver completely **(Figure 3)**.

Figure 4 shows the effect of induction and test substance on body weight changes. Bodyweight is related to the health status of the animal test. Based on the results of statistical tests there were significant differences between the percentage changes in the level of the positive control group and the negative control group ($p < 0.05$). In the positive control group, it was seen that weight loss during treatment showed that hepatotoxic induction could affect the bodyweight of the animal test.

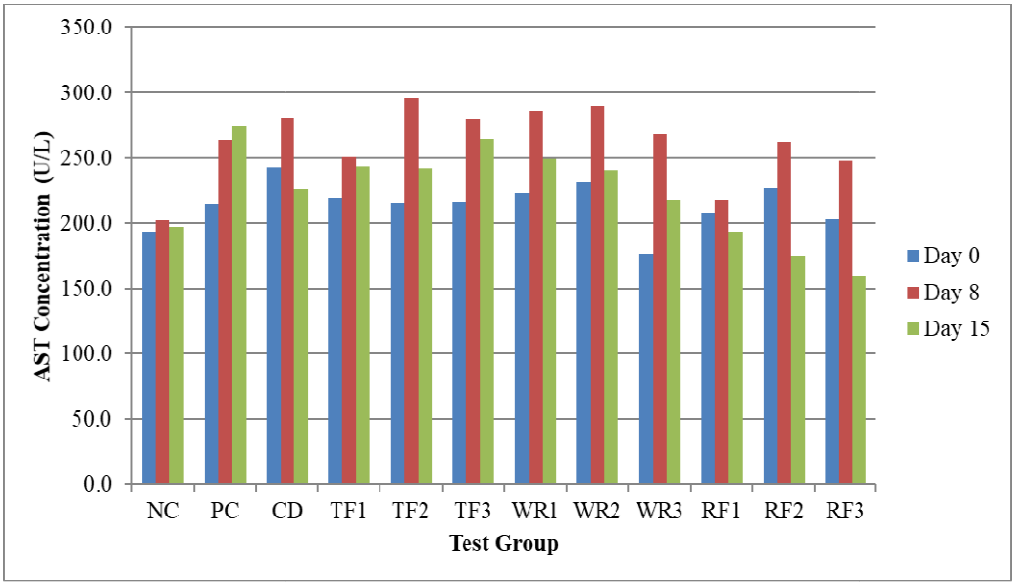

Figure 1: Average of AST levels of animal test on 0, 8, and 15 days treatment

Description : Negative control (NC), Positive control (PC), Comparator drug (CD), Total flesh 1.655 g/kg (TF1), Total flesh 3.310 g/kg (TF2), Total flesh 6.620 g/kg (TF3), Flesh without rectum 1.215 g/kg (WR1), Flesh without rectum 2.430 g/kg (WR2), Flesh without rectum 4.860 g/kg (WR3), Rectum flesh 0.395 g/kg (RF1), Rectum flesh 0.790 g/kg (RF2), and Rectum flesh 1.580 g/kg (RF3) ($p<0.05$)

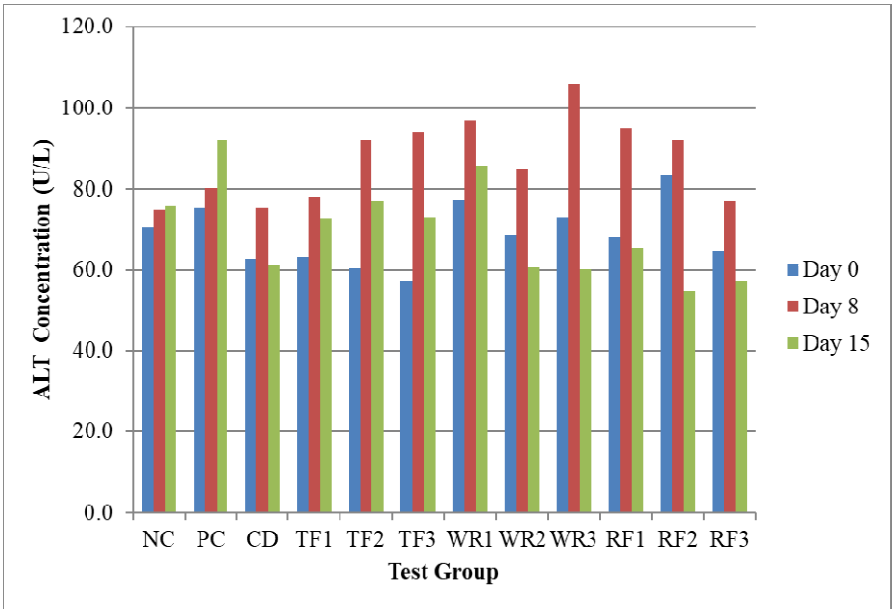

Figure 2: Average of ALT levels of animal test on 0, 8, and 15 days treatment

Description : Negative control (NC), Positive control (PC), Comparator drug (CD), Total flesh 1.655 g/kg (TF1), Total flesh 3.310 g/kg (TF2), Total flesh 6.620 g/kg (TF3), Flesh without rectum 1.215 g/kg (WR1), Flesh without rectum 2.430 g/kg (WR2), Flesh without rectum 4.860 g/kg (WR3), Rectum flesh 0.395 g/kg (RF1), Rectum flesh 0.790 g/kg (RF2), and Rectum flesh 1.580 g/kg (RF3) ($p<0.05$)

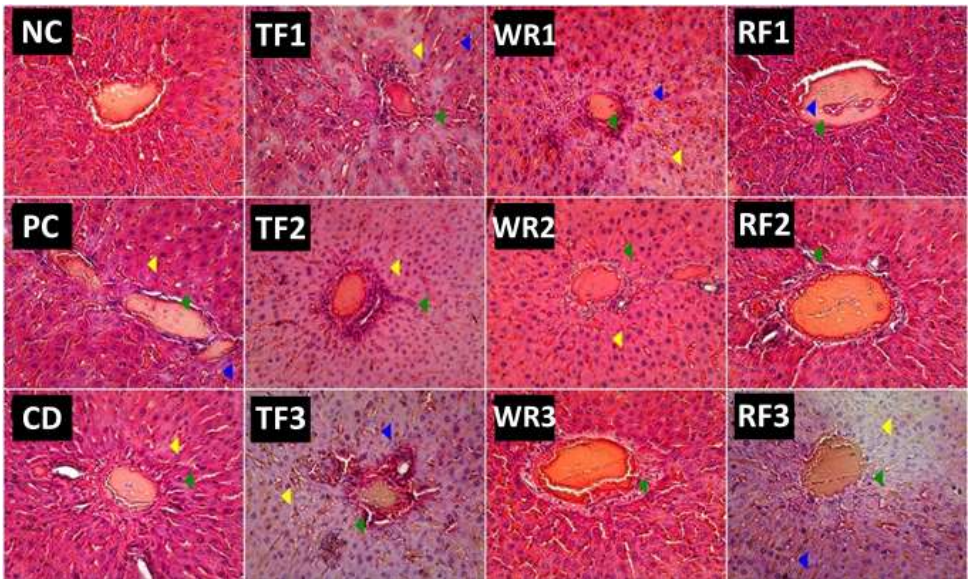

Figure 3: Liver Histopathology of animal test

Description : Negative control (NC), Positive control (PC), Comparator drug (CD), Total flesh 1.655 g/kg (TF1), Total flesh 3.310 g/kg (TF2), Total flesh 6.620 g/kg (TF3), Flesh without rectum 1.215 g/kg (WR1), Flesh without rectum 2.430 g/kg (WR2), Flesh without rectum 4.860 g/kg (WR3), Rectum flesh 0.395 g/kg (RF1), Rectum flesh 0.790 g/kg (RF2), and Rectum flesh 1.580 g/kg (RF3) ($p<0.05$), (◀) Necrosis, (◀)Vakuolization, (◀) Infiltration of inflamation cells.

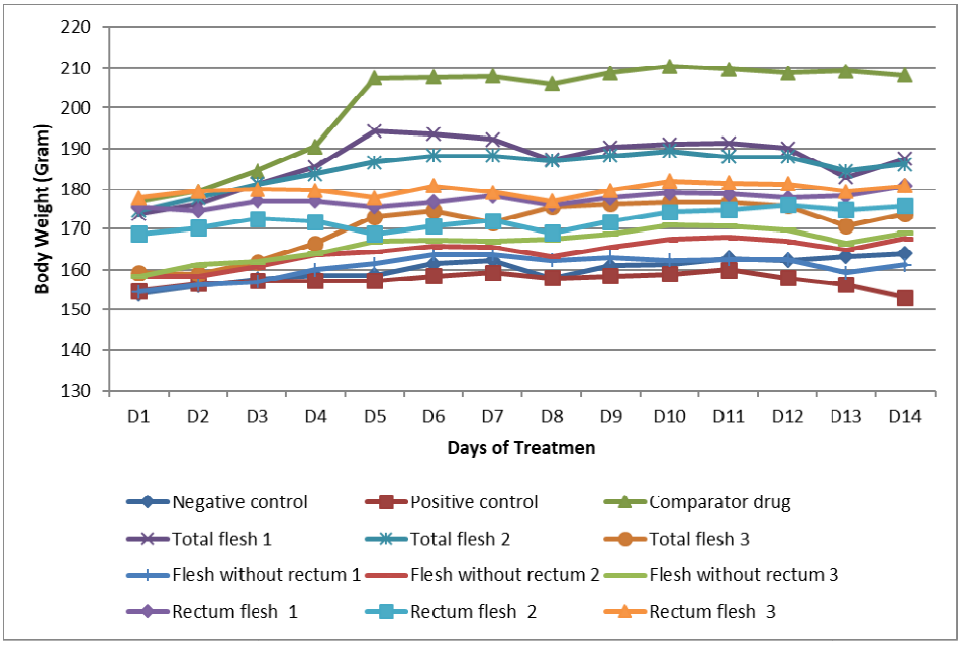

Figure 4: Body weight during treatment

Paracetamol can be fully absorbed quickly after oral administration. This shows the first major cross effect with absorption and metabolism in the liver. Paracetamol toxicity occurs associated with the production of N-acetyl-p-benzoquinoneimine (NAPQI) which is reactive by P450. When NAPQI production exceeds detoxification capacity, excess NAPQI will bind cellular components and cause hepatocyte death (necrosis). In a state of necrosis, liver cells will rupture so that the enzymes contained in liver cells will come out and enter into bloodstream **[5]**.

From the test results that the administration of rice field snail flesh can inhibit the occurrence of liver damage caused by the toxicity of paracetamol. This hepatoprotectoractivity is thought to be related to the presence of proteins and minerals contained in the flesh of rice field snails.

CONCLUSION

The results of this study indicate that rice field snail rectum meat has the potential as a hepatoprotector compared to whole meat and meat without rectum. The most effective dose of rice field snail rectum meat is at a dose of 0.395 g / kg which has the equivalent effectiveness of silymarin 25 mg / kg. The results of this study support the use of field snail as hepatoprotectors.

REFERENCES

[1] Bhattacharjee, R. danSil, P.C. (2007): Protein isolate from the herb, *Phyllanthusniruri* L. (*Euphorbiaceae*), play hepatoprotective role against carbon tetrachloride induced liver damage via its antioxidant properties,*Food and Chemical Toxicology,* **45,** 823.

[2] Brunton, L.L., Parker, K.L., Blumenthal, D.K. dan Buxton, I.L.O. (2008): Goodman & Gilman's manual of pharmacology and therapeutics, McGraw-Hill, United States of America, 445-446.

[3] Casini, A.F., Maellaro, E., Pompella, A., Ferrali, M., danComporti, M. (1987): Lipid peroxidation, protein thiols and calcium homeostasis in bromobenzene induced liver damage, Biochemical Pharmacology, 36, 3689-3694.

[4] Corwin, E.J. (2008): Handbook of pathophysiology 3rd edition, Lippincott Williams and Wilkins, 585-602.

[5] Dart, R.C., Erdman, A.R., Olson, K.R., Christianson, G., Manoguerra, A.S., Chayka, P.A., Caravati, M., Wax, P.M., Keyes, D.C., Woolf, A.D., Seharman, E.J., Booze, L.L., dan Troutman, W.G (2006) : Paracetamol poisoning : An evidence based consensus guideline for out of hospital management, Clinical Toxicology, 44, 2.

[6] Dipiro, J.T., Talbert, R.L., Yee, G.C., Matzke, G.R., Wells, B.G., dan Posey, L.M. (2011): Pharmacotherapy a pathophysiologic approach 8th edition, McGraw-Hill, New York, 1606-1608.

[7] Fraschini, F., Demartini, G, danEsposti, D. (2002): Review artticle: Pharmacology of silymarin, Clinical Drug Investigation, 22, 51.

[8] Gomes, A., Alam, M.A., Datta, P., Bhattacharya, S., dan Gomes, A. (2011): Hepatoprotective activity of the edible snail (Bellamiabengalensis) flesh extract in carbon tetrachlorideinduced hepatotoxicity in

rats,Journal of Ethnopharmacology, 138, 230.

[9] Hanje, A.J., Fortune, B., Song, M., Hill, D., dan McClain, C (2006): The use of selected nutrition supplements and complementary and alternative medicine in liver disease, Nutrition in Clinical Practice, 21, 256-263.

[10] Hodgson, E. (2004): A textbook of modern toxicology third edition, John Wiley & Sons, Inc., New Jersey, 270.

[11] Kaplowitz, N. (2004): Drug-induced liver injury, Suplement Article, 2, 44-47.

[12] Katzung., B.G., Masters, S.B., dan Trevor, A.J. (2012): Basic and clinical pharmacolgy 12th edition, McGraw-Hill Companies, New York, 1131-1132.

[13] Lee, W.M., (2012): Recent developments in acute liver failure, Best Practice and Research Clinical Gastroenterology, 26, 6.

[14] Manna, P., Sinha, M., danSil, P.C. (2007): Galactosamine-induced hepatotoxic effect and hepatoprotective role of a protein isolated from the herb CajanusindicusL. in vivo, Journal Biochem Molecular Toxicology, 21, 14.

[15] Olaleye, M. T., Akinmoladun, A. C., Ogunboye A. A., Akindahunsi, A.A. (2010); Antioxidant activity and hepatoprotective property of leaf extract of *Boerhaavia diffusa* Linn against paracetamol-induced liver damage in rats, Food and Chemical Toxicology, 48, 2200.

[16] Park, B.K., Kitteringham N.R., Maggs J.L., Pirmohamed, M., dan Williams, D., P. (2005): The role of metabolic activation in drug-induced hepatotoxicity, Annual Review Pharmacology Toxicology, 45, 177.