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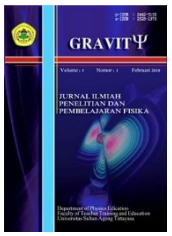

Effect of curcuma extract (*Curcuma xanthorrhiza*) on piroxicam-induced damage to the small intestine cells of mice *(Mus musculus*)

Moch. Haikal[1*], Septiana Kurniasari[2]

[1]*Biology Education Study Program, Madura Islamic University, Indonesia*

[2]*D3 Pharmacy Study Program, Madura Islamic University, Indonesia*

**E-mail: moch.haikal@fkip.uim.ac.id*

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ABSTRACT

Piroxicam is a non-steroidal anti-inflammatory drug (NSAID) widely used as an analgesic and anti-inflammatory in rheumatoid arthritis, osteoarthritis. However, Piroxicam can cause gastrointestinal side effects and peptic ulcers when given orally. Piroxicam can also cause cholestasis. Also, if Piroxicam is used continuously in high doses, it can cause damage to the small intestine. A compound can minimize small intestinal cell damage called an antioxidant. This study aims to analyze the effect of curcuma extract (Curcuma xanthorrhiza) on Piroxicam-induced damage to small intestinal cells of mice (Mus musculus). This study used 80 male mice and divided them into 3 groups, namely negative control (K-), negative Piroxicam (P-), and positive Piroxicam (P+). Giving curcuma extract given orally at a dose of 1.4 g/kgBW; 2.0 g/kgBW; 2.6 g/ kgBW; 3.2 g/kgBW and 3.8 g/kgBW, while the Piroxicam dosage used was 10 mg/kgBW and 30 mg/kgBW. The results showed that the more Piroxicam doses were given, the higher the level of small intestinal cell damage. Along with increasing the dosage of curcuma extract, the level of damage to small intestinal cells is reduced.

Keywords: curcuma, piroxicam, small intestine

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INTRODUCTION

Piroxicam is a non-steroidal anti-inflammatory drug (NSAID) widely used as an analgesic and anti-inflammatory in rheumatoid arthritis, osteoarthritis. However, Piroxicam can cause side effects in the gastrointestinal tract and peptic ulcers when given orally (Aryani, 2007). Piroxicam can also cause cholestasis. Also, if Piroxicam is used continuously in high doses, it can cause damage to small intestinal cells. Antioxidant compounds can minimize damage to the small intestine cells. One of them is curcuma (*Curcuma xanthorrhiza*). Temulawak contains main components, including curcumin, essential oils, fats, dyes, proteins, resins, cellulose, pentosan, starch, and minerals (Oktaviana, 2010).

Several research results prove that curcuma can potentially be a hepatoprotection in mice injected intraperitonally with a toxic dose of paracetamol. Also, the content of curcumin functions as an antioxidant and detoxifying

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agent from increased activity of the glutathione S-transferase (GS-t) enzyme and other glutathione (GS-x) enzymes and can protect erythrocytes and hemoglobin from oxidation caused by nitrite compounds (Sugiharto, 2004).

Curcuma xanthorrhiza has long been recognized in Asia as an antihepatotoxic. This plant is widely used to treat hepatitis C. Xanthorrhiza plants are effective in reducing hepatotoxicity levels. This is also supported by other studies showing that C. xanthorrhiza has a hepatoprotective effect that can act as an effective treatment for acute liver disease in rats (Putri, 2013).

Curcumin can also protect the liver's function, digestive tract, kidneys, reduce free radicals, and inhibit the activity of nitric oxide synthase (NOS) from macrophages (Kertia, 2011). Also, curcuma is also used to increase endurance and stamina (Dewi, et al., 2012). Temulawak can overcome liver disorders, increase bile production and secretion, anti-inflammatory, appetite enhancer, asthma medication, antioxidants, inhibit blood clotting and reduce ALT and SGOT levels (Khamidah, Antarlina & Sudaryono, 2017).

The content in curcuma contains chemical compounds that are physiologically active, for example, curcumin, starch, and essential oils. The content of curcumin in curcuma functions as antibacterial, anti-cancer, anti-tumor, and contains antioxidants. The curcuminoid content in curcuma is 1-2%, and the essential oil content in curcuma is 3-12% (Pratama, Ismail & Witjahjo, 2019).

Temulawak (*Curcuma xanthorriza* Roxb.) Is one of the many medicinal plants of the Zingiberaceae tribe that grows in Indonesia. Temulawak is known to have many benefits, including anti-hepatitis, anti-carcinogenic, antimicrobial, antioxidant, anti-hyperlipidemic, antiviral, anti-inflammatory, and detoxifying agent (Candra, 2013). Other properties of curcuma's chemical components are antibacterial, anti-fungal, neuroprotector, anti-cancer, allergy, and anti-hypercholesterolemic (Nurcholis, et al., 2012).

Previous research has proven that curcuma has fungistatic properties against several dermatophyta fungi and is bacteriostatic in the microbes such as Salmonella, Pseudomonas pyogenes, Staphylococcus aureus, and anti-fungi against Mycrosporum gypseum. The activity of 1 ml of essential oil on Pseudomonas pyogenes was comparable to 0.3 mg of tetracyclines. The action of 1 ml of essential oils on Staphylococcus aureus was equal to 29.2658 mg of tetracyclines. It is suspected that the actual oil content in the curcuma rhizome is antibacterial (Mashita, 2014).

The formulas of curcuma, turmeric, and meniran jamu can improve the tested animals' fitness as indicated by the increase in swimming endurance time of the test animals after treatment compared to the pre-treatment and control groups. The herbal formula of curcuma, turmeric, and meniran has also been proven to be safe for the liver and kidney function of test animals given doses of up to 2,160 mg/kg bodyweight for 90 consecutive days (Novianto, et al., 2020).

RESEARCH METHODS

This study used 80 male mice with an average body weight of 18-20 grams. The mice were grouped into 3 groups, namely K- (without Piroxicam and extract), P- (Piroxicam without extract) and P+ (given Piroxicam then extract). The doses of Piroxicam used were 10 mg/kgBW and 30 mg/kgBW, while temulawak extract was given in five dose variations, namely 1.4 g/kgBW; 2.0 g/kgBW; 2.6 g/kgBW; 3.2 g/kgBW and 3.8 g/kgBW.

Giving of piroxicam. Piroxicam given to mice is a finished powder that has been packaged and sold in the market, taking into account the composition contained therein. One Piroxicam capsule contains 10 mg. The dose of Piroxicam given to mice is calculated based on the bodyweight of each mouse. Piroxicam was given once a day for 7 days before the mice were given curcuma extract by force-feeding the mice using a gastric swab.

Giving of Temulawak Extract. Temulawak extract given to mice is a finished powder that has been packaged and sold in the market, taking into account the composition contained

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therein. One curcuma extract capsule contains 500 mg of curcumin. The dose of curcuma extract given to mice was calculated based on the bodyweight of each mouse. Temulawak extract was shown once a day for 7 days after the mice were given Piroxicam by feeding it to the mice using a gastric swab.

Preparation of Histology. For mice that have been operated on, their small intestine organs are taken. The small intestine of mice was dehydrated and then cut with a microtome. The pieces of the small intestine were rehydrated, and HE stained. Furthermore, it can be observed under a microscope.

RESULTS AND DISCUSSION

The data obtained in this study were the width of the villi that had broken off and indicated damage to the small intestine cells of mice under normal conditions, was induced by Piroxicam with 2 variations of doses, and induced by Piroxicam then given curcuma extract.

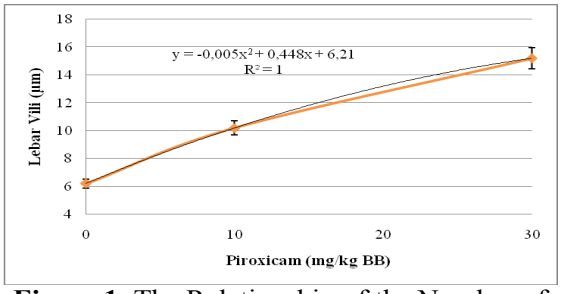

Figure 1. The Relationship of the Number of Piroxicam Doses to the Dilation of Villi in Mice Small Intestine Cells

Figure 1 shows a graph of the relationship between the number of Piroxicam doses on the enlargement of the villi in mice's small intestine cells. The amount of Piroxicam in mice with 2 dosage variations, namely 10 mg/kgBW and 30 mg/kgBW, indicates that the more Piroxicam doses are given, the greater the enlargement of the villi. This suggests that the damage to the small intestine cells of mice is getting worse. In the adverse control treatment, the width of the villi was 6.21 µm. In the Piroxicam treatment of 10 mg/kgBW and 30 mg/kgBW, the villi's widths were 10.20 µm and 15.20 µm, respectively.

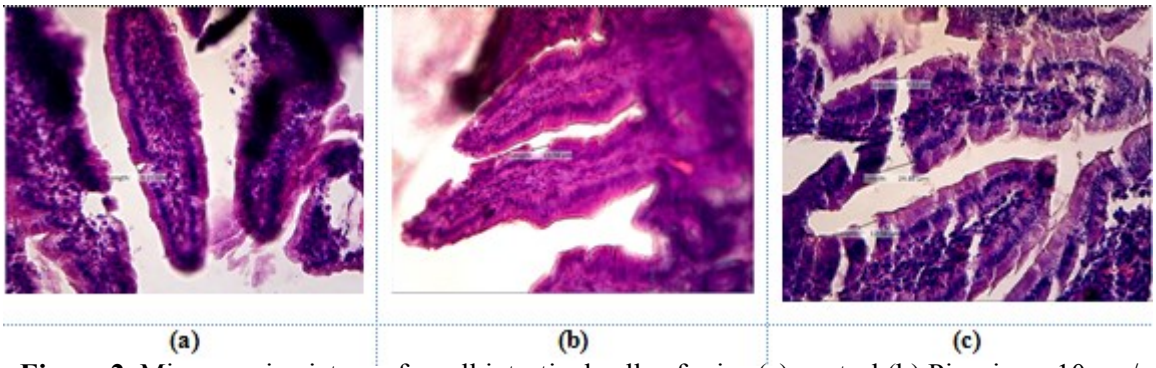

Figure 2. Microscopic picture of small intestinal cells of mice (a) control (b) Piroxicam 10 mg/kgBW (c) Piroxicam 30 mg/kgBW

Figure 2 shows a microscopic view of small intestinal cells of mice taken at 400x magnification. In control mice (standard), shown in Figure 2a, the severed villi were not very wide. However, the more doses of Piroxicam given, the greater the dilation or rupture of the villi that occurs. Giving curcuma extract also greatly affects the widening of the villi in the small intestine of mice. This is shown in Figure 3, and where there was a decrease in villi width in mice, both treated with Piroxicam dose 10 mg/kg BW and Piroxicam dose 30 mg/kg BW.

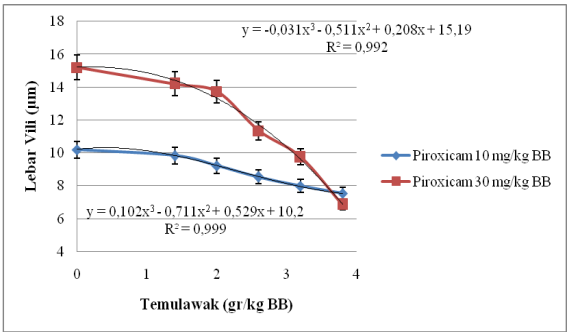

Figure 3. The Relationship of the Number of Doses of Temulawak Extract on the Dilation of Villi in Mice Small Intestine Cells

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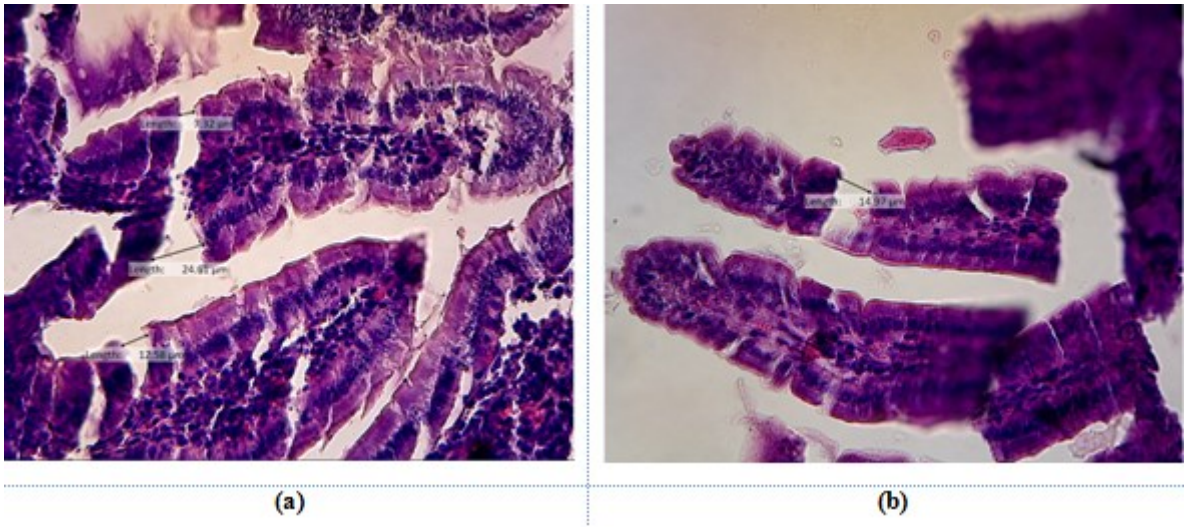

Figure 4. Microscopic picture of small intestinal cells of mice (a) Piroxicam (b) Piroxicam+ Temulawak

These results are also reinforced by the microscopic image of the mice's small intestine cells, shown in Figure 4. Giving curcuma extract can repair cell damage, such as the villi whose width begins to decrease, although the cells are not completely restored. Piroxicam is a non-steroidal anti-inflammatory drug (NSAID) with a new structure, namely oxicam, an enolic acid derivative. In general, NSAIDs have the potential to cause side effects in three organs, including the digestive tract, liver, and kidneys (Pairul, 2018). The longer the half-life of NSAIDs, such as Piroxicam, which has a half-life of 50 hours (more than 2 days 2 nights), the easier it will accumulate (buildup) in the body, which will cause toxic effects (Ramadhan, 2015). The presence of lipid peroxidation causes this toxicity. Lipid peroxidation causes necrosis of the small intestine cells. Temulawak can reduce the level of damage to the cells of the small intestine of mice, which is indicated by a decrease in the villi's width.

Figure 5 shows the chemical structure of the bioactive compounds contained in curcuma. Temulawak has many OH groups, so curcuma can capture free radicals so that these free radicals turn into stable molecules, and cells damaged by these free radicals can repair themselves (Sari, Widodo & Juswono, 2018).

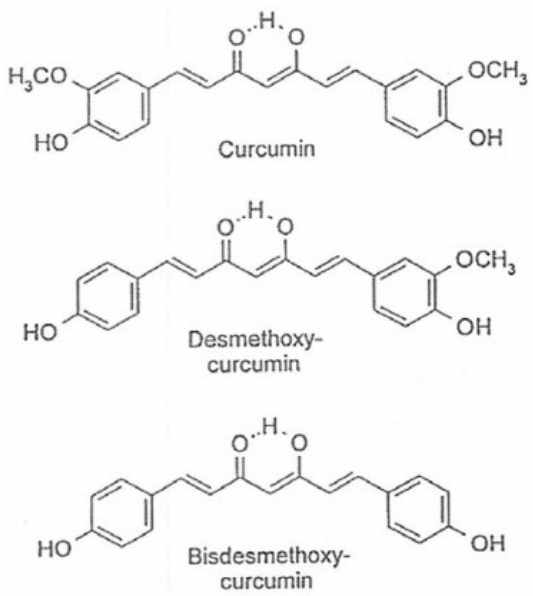

Figure 5. Chemical structure of curcuminoid compounds (Sari, Widodo & Juswono, 2018)

CONCLUSION

Piroxicam can cause gastrointestinal side effects and peptic ulcers if given orally. Temulawak extract, which is provided as a treatment for the impact of Piroxicam, can reduce the enlargement of villi in the cells of the small intestine of mice. Temulawak extract contains curcumin bioactive compounds which can minimize cell damage.

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