

## Effect of Kenikir Leaves Extract on Gastric Histology Description of Male White Rats Induced By Aspirin

Nurri Yusriyyah JS<sup>1\*</sup>, Husnarika Febriani<sup>2</sup>, Syukriah<sup>3</sup>

<sup>1,2,3</sup> Department of Biology Faculty of Science and Technology, Universitas Islam Negeri Sumatera Utara

### Abstract

Using aspirin for long time can make ulcer. Using traditional medicinal plants is alternative in treating gastric ulcers. This experiment aims to determine effect of kenikir leaves extract (*Cosmos caudatus* Kunth.) on gastric morphology and histology decription of male white rats (*Rattus norvegicus*) induced by aspirin. 25 rats were divided into 5 groups, KN (control), KP (aspirin 200 mg/kgBW for 10 days), P1 (aspirin 200 mg/kgBW for 10 days + kenikir leaves extract 700 mg/kgBW for 14 days), P2 (aspirin 200 mg/kgBW for 10 days + kenikir leaves extract 800 mg/kgBW for 14 days), P3(aspirin 200 mg/kgBW for 10 days+kenikir leaves extract 900 mg/kgBW for 14 days). Parameters observed were morphological and histological of the gastric. Data were analyzed by oneway ANOVA test and continued with Duncan's test. The results kenikir leaves did not have a significant effect on the morphology but histologically, kenikir leaves extract had a significant effect by improving the thickness of gastric layer. It can be concluded that kenikir leaves extract can be used as an alternative to treat gastric ulcers because it can improve the thickness of gastric layer

**Keywords:** *Cosmos caudatus* K., Gastric, Aspirin

### Introduction

The digestive system is one of the organ systems that have an important role in processing and digesting food and substances that enter the body. The stomach is a digestive organ that has a protective layer in the form of a mucous layer which has the main function to protect it from damage caused by exposure to food and foreign substances that enter the stomach, including drugs. One of the damage that occurs in the gastric mucosa is the erosion of the gastric mucosal layer which will make wounds on the stomach or also known as gastric ulcers (Szabo et al., 2012).

Gastric ulcers are caused by several factors, including unhealthy lifestyles, alcohol consumption, smoking and consuming excessive amounts of acidic and spicy foods. Other causes that cause gastric ulcers include infection by the bacterium *Helicobacter pylori* and the use of non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs are a class of drugs that are usually used to obtain anti-inflammatory, analgesic, and antipyretic effects. One of the drugs belonging to the NSAID group is aspirin (Mustaba et al., 2012).

Aspirin is a type of drug that is often used in the world. This is because aspirin is sold

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\*Corresponding Author: Nurri Yusriyyah JS, email: [nurrijs14@gmail.com](mailto:nurrijs14@gmail.com), Fakultas Sains dan Teknologi Universitas Islam Negeri Sumatera Utara, Jl. Lapangan Golf, Kec. Pancur Batu, Kabupaten Deli Serdang, Sumatera Utara  
First Author, Second Author, Third Autor, full affiliation address.

freely and is widespread in the community. Consumption of aspirin in long time have side effects including damage to the stomach. The effect of the use of aspirin is to inhibit the action of the cyclooxygenase enzyme. With the inhibition of the action of the cyclooxygenase enzyme, the process of prostaglandin synthesis also obstacles. Prostaglandins an important role in the production of mucus in the stomach which is a defensive factor (protection) of the gastric mucosal layer from aggressive (damaging) factors in the gastric mucosal layer (Wijaya, 2017).

Efforts that can be made to treat and reduce gastric ulcers are by consuming synthetic drugs such as ranitidine, omeprazole, antacids, sucralfate and misoprostol. However, these drugs can certainly cause other side effects if taken for a long time (Putri et al., 2019).

Due to these unavoidable side effects, the use of traditional medicinal plants is also a solution that is used by the community because it is considered to have a milder effect when compared to using synthetic drugs or also known as chemical drugs. One type of plant that has many benefits is kenikir (*Cosmos caudatus* Kunth.). Kenikir is one type of plant that is often found in the neighborhood and its young leaves are often used as vegetables or fresh vegetables consumed by the community. Kenikir leaves have antioxidant and anti-inflammatory pharmacological effects. The leaves of this plant contain various active compounds such as flavonoids, poniphenols, saponins, tannins, alkaloids and essential oils. The content of derivatives of flavonoid compounds in the form of quercetin and kaempferol contained in kenikir leaves is high, ranging from 0.3-143 mg/100g wet weight of kenikir leaves. anti-inflammatory

can repair the damage that occurs to the organs in the body (Andarwulan, 2010).

Based on these injuries, this study was conducted to determine the effectiveness of giving kenikir leaf extract (*Cosmos caudatus* K.) on tissue repair in the stomach after being induced by aspirin.

## Research Methods

### Kenikir Leaves Extract

Kenikir leaves obtained from Binjai City are cleaned of dirt and then dried in a place that is not exposed to direct sunlight for 14 days. Then the dried kenikir leaves are mashed using a blender and sieved using a sieve to obtain a fine powder (simplicia). The extract was continued by maceration process using 96% ethanol for 3 days. The process of making kenikir extract is followed by a filtration process. The filtrate obtained was then concentrated using a vacuum rotary evaporator at a temperature of 60 C.

### Experiment Animal and Treatment

A total of 25 male white rats (*Rattus norvegicus*) aged 3-4 months with a body weight of 150-200 grams. Then divided into 5 treatment groups. KN (without treatment (control)), KP (aspirin 200 mg/kgBW for 10 days), P1 (aspirin 200 mg/kgBW for 10 days + kenikir leaf extract 700 mg/kgBW for 14 days), P2 (aspirin 200 mg/kgBW for 10 days) 10 days + kenikir leaf extract 800 mg/kgBW for 14 days), P3 (aspirin 200 mg/kgBW for 10 days + kenikir leaf extract 900 mg/kgBW for 14 days). All treatments were administered by the oral method.

### Gastric Morphology Observetion

After the treatment was given to the rats, surgery was carried out which had previously been euthanized using chloroform. Then the gastric organ was

removed by cutting the oesophagus and the other end in the duodenum. After cleaning, the stomach was then observed for changes in color and changes in the surface of the stomach in each treatment.

### Gastric Histology Observation

Observation of histology preparations on gastric organs was carried out under a trinocular microscope with 400x and

### Result and Discussion

#### Morphological

Observation of gastric morphology was carried out macroscopically by observing changes in color and

100x magnification. Observations were made in five fields of view on various changes that occurred, then scored based on tissue changes

#### Data Analysis

All data obtained using the One-Way ANOVA test and continued with Duncan's test. All data obtained will be tested using SPSS Release 26.

consistency in the stomach of rats. The morphological description of the stomach after being given kenikir leaf extract (*Cosmos caudatus* K.) and aspirin induction is presented in the table and figure below:

**Table 1**

*Gastric Morphology*

| Group | Colour | Cosistency |
|-------|--------|------------|
| KN    | Pink   | Soft       |
| KP    | Pink   | Soft       |
| P1    | Pink   | Soft       |
| P2    | Pink   | Soft       |
| P3    | Pink   | Soft       |

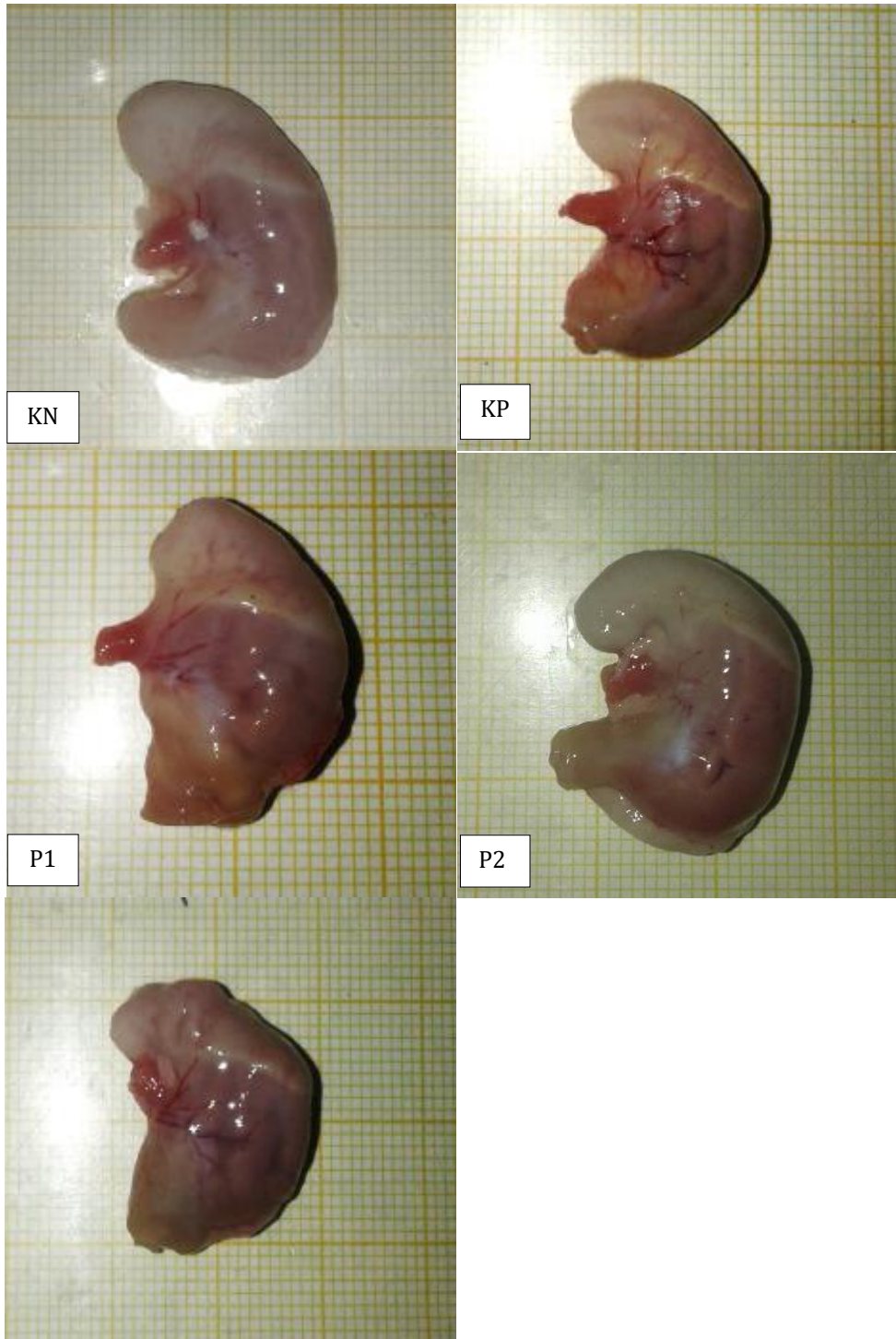
Tables and figures show the color of the stomach in each treatment group, which is pink with a soft consistency and smooth surface. According to Lintong et.al, 2013 a normal stomach is a pink stomach with a chewy or soft consistency. The normal condition of the stomach showed that the administration of aspirin and kenikir extract did not change the morphology of the stomach. This is because the stomach has a protective layer that protects the stomach from various aggressive factors that can damage the stomach.

The normal condition of the stomach showed that the administration of aspirin

and kenikir extract did not change the morphology of the stomach. This is because the stomach has a protective layer that protects the stomach from various aggressive factors that can damage the stomach. And aspirin only damages at the cellular and tissue levels so that aspirin-induced gastric morphological changes are not seen. The same thing also happened to the administration of kenikir extract which only improved at the cellular and tissue level so that no visible changes in gastric morphology induced by kenikir extract

**Figure 1**

*Gastric Morphology. KN= With Treatment, KP=Aspirin 200mg, P1= Aspirin 200mg+Kenikir Leaves Extract 700mg, P2= Aspirin 200mg+Kenikir Leaves Extract 800mg, P3= Aspirin 200mg+Kenikir Leaves Extract 900mg*



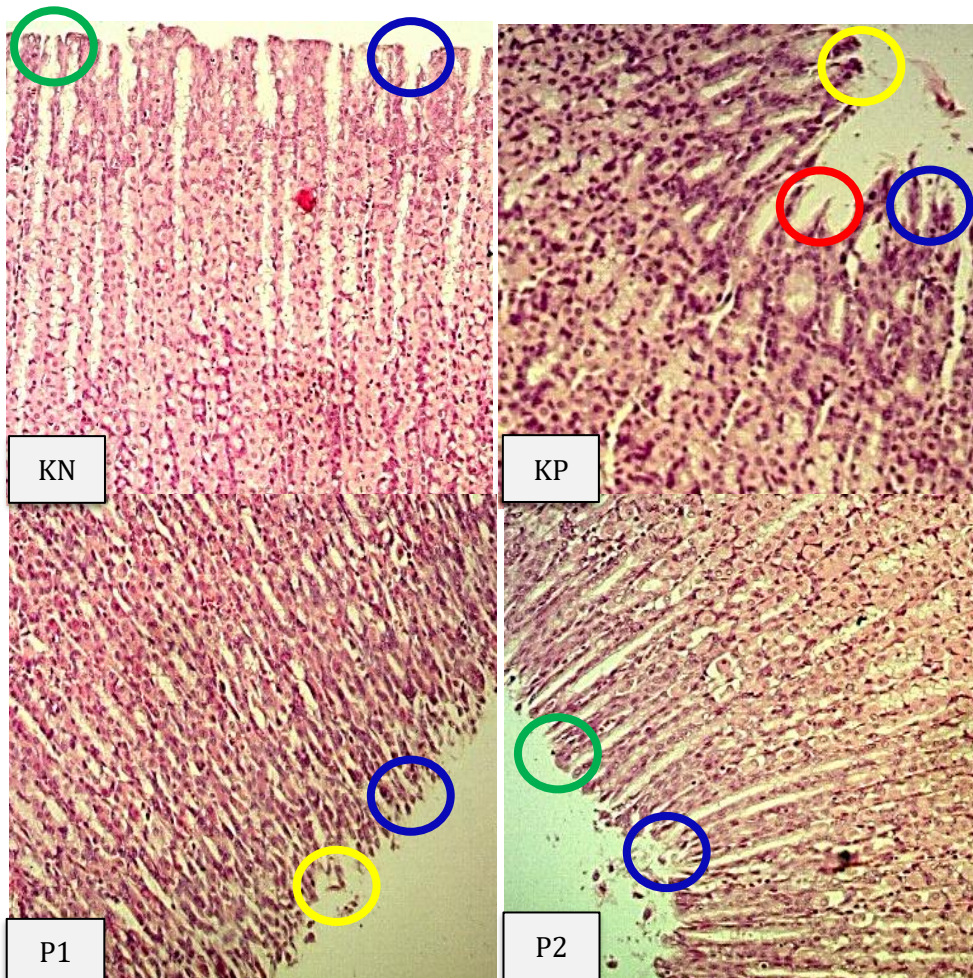


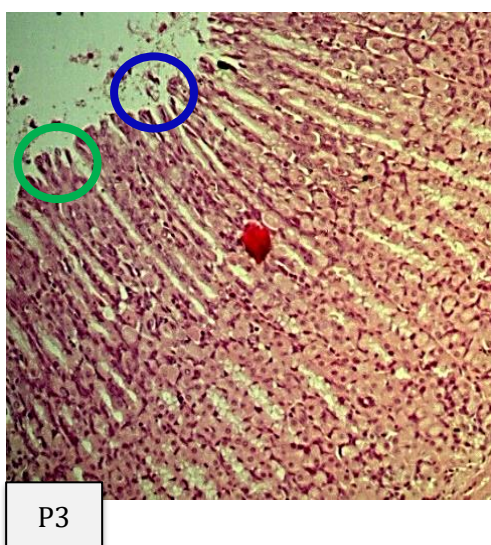
## Histological

Histological observations were carried out by observing gastric tissue preparations using a trinocular microscope

### Figure 2

*Histology of Epithelial Damage in Gastric Mucosa of Aspirin Induced Rat (Rattus norvegicus) and Kenikir Leaf Extract (Cosmos caudatus Kunth.) With HE Staining at 400 x magnification. KN=without treatment, KP=Aspirin 200mg, P1=Aspirin 200mg+ Kenikir Leaf Extract 700mg, P2= Aspirin 200mg+Kenikir Leaf Extract 800mg, P3= Aspirin 200mg+Kenikir Leaf Extract 900mg. Description: Green Circle: Normal Epithelium, Blue Circle: Epithelial Cell Desquamation, Yellow Circle: Epithelial Cell Erosion, Red Circle: Ulceration.*





**Tabel 2**

*Average Epithelial Cell Damage in Gastric Mucosa SD Standard Deviation. KN=without treatment, KP=Aspirin 200mg, P1=Aspirin 200mg+ Kenikir Leaf Extract 700mg, P2= Aspirin 200mg+ Kenikir Leaf Extract 800mg, P3= Aspirin 200mg+ Kenikir Leaf Extract 900mg. abc numbers followed by different letters in the column show a significant difference ( $p < 0.05$ ).*

| Group | Gastric Mucosal Epithelial Cell Damage Average Score $\pm$ SD |
|-------|---|
| KN    | 0,36 $\pm$ 0,29 <sup>a</sup>                                  |
| KP    | 1,52 $\pm$ 0,64 <sup>b</sup>                                  |
| P1    | 0,84 $\pm$ 0,51 <sup>a</sup>                                  |
| P2    | 0,88 $\pm$ 0,30 <sup>a</sup>                                  |
| P3    | 0,60 $\pm$ 0,40 <sup>a</sup>                                  |

In addition to histological observations using the scoring method, data collection was carried out using the scoring method which was then analyzed by one-way ANOVA testing. Based on the table and figure data above, it is known that the KP group or the group induced with aspirin 200mg/KgBW were significantly different from other groups, this indicates that the KP group is the group with severe damage. This is caused by the use of aspirin which can damage the epithelial cells in the gastric mucosal layer. Based on the scoring results,

at a dose of 700 mg/kg BW has an average of 0.84 and at a dose of 800 mg/kg BW it has an average of 0.88 and at a dose of 900 mg/kg BW has an average value of 0.60. With a value of 0.60, it can be said that the use of kenikir leaf extract at a dose of 900mg/kgBW is the best dose that can improve the gastric mucosa after the use of aspirin.

In the KN (Negative Control) group or the untreated group, there were normal epithelial cells and also desquamated epithelial cells. Desquamation is the occurrence of detachment of epithelial cells

from the tissue surface. Desquamation that occurs in gastric epithelial cells is a defense response to friction that occurs in the stomach. Under normal circumstances, epithelial cells on the surface of the digestive tract regenerate with desquamation that occurs every 1-3 days. Desquamation that occurs in the KN group is a physiological response that occurs due to the regeneration of epithelial cells in the gastric mucosa. However, the desquamation that occurred in the KP, P1, P2, and P3 groups was strongly suspected to be related to the administration of aspirin which irritates the gastric mucosal layer, resulting in desquamation of epithelial cells in the stomach.

In the KP group (positive control) which was the aspirin-induced group, there were epithelial cells that experienced desquamation, erosion and ulceration. Erosion itself is characterized by the loss of 1-10 mucosal epithelial cells. Ulceration is generally characterized by the loss of more than 10 epithelial cells (Barthel, 2003). The damage that occurs to the epithelial cells is caused by the administration of aspirin so that it can irritate the epithelium in the gastric mucosal layer. High stomach acid caused by NSAIDs causes wounds to the gastric mucosa to get worse and can cause inhibition of wound healing (Valkhoff, 2012).

Gastric ulcers are wounds that occur in the gastric mucosal layer due to erosion of the gastric mucosal layer. Stomach ulcers can cause pain and tenderness in the stomach. Gastric ulcers are caused by an increase in stomach acid which is caused by a decrease in the work of prostaglandins, thereby reducing the production of mucus which serves as protection of the stomach from aggressive (damaging) factors.

In this study, post-administration of aspirin 200 mg/kgBW was followed by administration of kenikir leaf extract in graded doses in groups P1(700 mg/kgBW), P2(800 mg/kgBW) and P3(900 mg/kgBW). The group of rats given kenikir leaf extract showed an improvement in the mucosal epithelial cells. In groups P1, P2 and P3 gastric ulceration was no longer visible and erosion began to decrease. If the groups P1, P2 and P3 are compared with each other, it can be seen that the P3 group shows a better improvement. Improvements in the P3 group proved that healing gastric ulcers using kenikir leaf extract at a dose of 900 mg/kgBW showed better results with other doses. The content of secondary metabolites in kenikir leaves, especially flavonoid compounds, has a role as an antioxidant and anti-inflammatory that can repair damage to the gastric mucosal layer.

The mechanism of cell regeneration starts from the hemostatic process. This process involves platelets and fibrin which are useful for stopping bleeding (inflammation). Furthermore, an inflammatory process occurs which causes the activation of macrophages and neutrophils to the tissue to phagocytose cell debris, bacterial cells and necrotic cells (damaged). Then neutrophils will undergo apoptosis and make macrophages stimulate growth factor mediators (vascular endothelial growth factor) and fibronectin. The mediators released by these macrophages make stem cells active and then proliferate. In the proliferative process, stem cells will differentiate to form new blood vessels called angiogenesis and epithelialize, in addition, proliferation will trigger the formation of granulation tissue and reduce wound contraction. In this process, cells that are not needed undergo apoptosis and what happens next is

remodeling and maturation, which is the process of forming connective tissue.

These effects are obtained from secondary metabolites contained in kenikir leaf extract. Secondary metabolite compounds such as saponins, tannins and flavonoids are active compounds found in plants that have the ability to provide protection and repair against gastric ulcers (Gricilda, 2014). Saponins are also one of the secondary metabolites found in plants and are known to have the ability to activate protectively in the mucosal layer that plays a role in healing gastric ulcers (Wahyudi, 2018).

### Conclusion

The administration of kenikir leaf extract (*Cosmos caudatus* K.) did not have an effect on the morphological picture of the stomach of rats induced by aspirin but the administration of kenikir leaf extract (*Cosmos caudatus* K.) had an effect on the histological picture of the stomach, namely repairing damage to epithelial cells in the layer with the best dose in the group. P3 (dose of 900 mg/kg BW).

### References

- Andarwulan, Nuri, Ratna Batari, Dinny Agustini Sandrasari, Bardley Bolling, Hanny Wijaya. 2010. Flavonoid Content and Antioxidant Activity Of Vegetables From Indonesia. *Food chemistry*. Vol 121.
- Vimala, G., & Gricilda Shoba, F. (2014). A Review on Antiulcer Activity of Few Indian Medicinal Plants. *International Journal of Microbiology*. 2014, 1-14. <http://dx.doi.org/10.1155/2014/519590>.
- Lintong, Loho, Anggaran. (2013). Gambaran Histopatologik Lambung Tikus Wistar Setelah Diinduksi Aspirin. *Jurnal Biomedik*. 5(3), 38-45. <https://doi.org/10.35790/jbm.5.1.2013.2044>.
- Mustaba, Winaya, dan Ketutberata. (2012). Studi Histopatologi Lambung pada Tikus Putih yang Diberi Madu sebagai Pencegah Ulkus Lambung yang Diinduksi Aspirin. *Indonesia Medicus Veterinus*. 1(4), 471-482.
- Putri, Ramadani dan Maulida. (2019). Efek Gastroprotektif Ekstrak Etanol Daun Pepaya (*Carica papaya* L.) pada Tikus yang Diinduksi dengan Aspirin. *EKSAKTA*. 19 (02), 98-104. <https://doi:10.20885/eksakta.vo119.iss2.art1>.
- Szabo, I.L., Cseko, K., Czemmer, J., dan Mozsik, G. (2013). Diagnosis of Gastritis-Review from Early Pathological Evaluation to Present Day Management. *In Current Topics in Gastritis*. 2012. 3-19. <http://dx.doi.org/10.5772/5284>.
- Valkhoff VE., Sturkeboom MC., dan Kuipers EJ. (2012). Risk Factors for Gastrointestinal Bleeding Associated with Low-Dose Aspirin. *Best Practice Resarch Clinical Gastroenterology*. 26(2), 125-140. <http://doi.org/10.1016/j.bpg.2012.01.011>.



- Wahyudi. 2018. *Pengujian Efektivitas Ekstrak Etanol Daun Afrika (Vernonia Amygdalina Del.) Sebagai Obat Tukak Lambung Pada Tikus Jantan*. Tesis. Medan: Fakultas Farmasi USU.
- Wijaya, Dwi S. (2017). Ekstrak Daun Sirsak Terhadap Ulkus Lambung. *Journal of Holistic and Traditional Medecine*. 1(4), 75-80.