JFSP Vol.9, No.1, January-April 2023, Page: 62-71 pISSN: 2549-9068, eISSN: 2579-4558
Jurnal Farmasi Sains dan Praktis
(JFSP)
http://journal.unimma.ac.id/index.php/pharmacy

LITERATURE REVIEW OF THE PHARMACOLOGICAL ACTIVITIES OF THE EUPHORBIACEAE FAMILY PLANTS

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https://doi.org/10.31603/pharmacy.v9i1.5990

Article info:
Submitted : 06-10-2021
Revised : 10-03-2023
Accepted : 15-03-2023

Publisher:

Universitas Muhammadiyah Magelang

ABSTRACT

Euphorbiaceae family plants are spread in Indonesia and empirically, have been used for a long time as medicine. This article review aims to discuss the pharmacological activities of several plants from the Euphorbiaceae family. This research was conducted by conducting a literature review limited to research in the form of scientific articles. The scientific article in question results from research reviewed and published in Indonesian and English. The steps in the search are divided into several stages, starting from identification, screening, eligibility, and data grouping. The articles used in this article review were obtained by searching the internet from online data search media/search engines such as Google/Google Scholar and journal provider sites such as PubMed, NCBI, and SINTA with the keywords "Euphorbiaceae plants," "Ethnopharmacology, "Ethnobotany and Ethnopharmacy," "Plant Activity and Effectiveness," "Euphorbiaceae family activity," and "Pharmacological activity of Euphorbiaceae. After determining the keywords, the next step is filtering multiple data or duplications and filtering the article's title, abstract, and keywords so that data can be determined to be used or not for the following review.This study is a literature review based on several national or international scientific articles about the pharmacological activity of Euphorbiaceae plants. The literature study found that some plants from the Euphorbiaceae family have pharmacological activities, and the most dominant are antimicrobial, antioxidant, and anti-inflammatory. Moreover, many other activities include analgesic, antipyretic, antithrombotic, anti-hypercholesterolemia, antihyperglycemic, antihistamine, diuretic, and antiseptic.

Keywords: Euphorbiaceae; Medicinal plants; Pharmacological activity

1. INTRODUCTION

Medicinal plants have been widely used since ancient times and are still part of alternative medicine worldwide. No less than 50,000 species of plants have been used for medicinal purposes. The basis for the development of plant-based medicine is carried out by the community based on beliefs, local wisdom, and the observations of previous people (Abe & Ohtani, 2013). Humans are familiar with the functions of plants, especially in handling health problems based on experience and skills or because of interactions from time to time (Mulyani et al., 2020).

The United States produces more than 40 kinds of essential medicines which were later discovered that the raw materials come from plants from tropical countries, including Indonesia (Novianti, 2017). In Indonesia, traditional medicines, also known as herbal medicines, are obtained from plants in their whole form, and only certain parts, animal ingredients, minerals, and essences, are mixed or blended (Adiyasa & Meiyanti, 2021). Plants usage as traditional medicine usually must change the form first, such as being converted into liquid forms, or topical use, such as patches or inhalers (Siregar et al., 2020). Based on the Ministry of Health of the Republic of

Indonesia (2018), the proportion of Family Medicinal Plants (TOGA) utilization in Indonesia reaches 24.6% of the total population. This data shows that the Indonesian people believe in the properties provided by medicinal plants, along with increasing public confidence in the minimum perceived side effects (Sari, 2006).

One family of medicinal plants is Euphorbiaceae (the castor tribe), which has many genera in Indonesia, including Phyllanthus, Euphorbia, Croton, and Ricinus (Siregar et al., 2017). In order to increase the potency of plants belonging to the Euphorbiaceae family, more research needs to be carried out considering the various benefits of plants in this family. Indonesia itself has used plants as traditional medicine empirically, and in-depth research related to the pharmacological activities of plants in this family and their utilization needs to be carried out. This fact is the background for the authors to study the content of active compounds and the pharmacological effects of plants in the Euphorbiaceae family based on scientific literature.

2. METHODS

This research was conducted by conducting a literature review limited to research in the form of scientific articles. The scientific article in question results from research reviewed and published in Indonesian and English. The steps in the search are divided into several stages, starting from identification, screening, eligibility, and data grouping.

The articles used in this article review were obtained by searching the internet from online data search media/search engines such as Google/Google Scholar and journal provider sites such as PubMed, NCBI, and SINTA with the keywords "Euphorbiaceae plants," "Ethnopharmacology, "Ethnobotany and Ethnopharmacy," "Plant Activity and Effectiveness," "Euphorbiaceae family activity," and "Pharmacological activity of Euphorbiaceae. After determining the keywords, the next step is filtering multiple data or duplications and filtering the article's title, abstract, and keywords so that data can be determined to be used or not for the following review.

The next stage is eligibility, carried out by reading thoroughly or partially articles that have yet to be eliminated in the previous stage. It can be determined that these articles can be included in the next stage based on eligibility criteria, where articles published before 2012 are excluded. The results of this stage are articles that meet the requirements and do not meet the requirements.

Furthermore, articles were grouped based on the techniques and approaches, such as qualitative and quantitative research. From previous stages, 30 relevant articles were obtained. The articles, described in tabular form, contain the name of the plant, the part of the plant used, the chemical content of the plant, and the pharmacological activity of the plant in the Euphorbiaceae family according to the context.

3. RESULTS AND DISCUSSION

The articles show that several plants belonging to the Euphorbiaceae family have pharmacological activity. The data consists of only ten plants belonging to the Euphorbiaceae family, known and widely used by Indonesians. The plants in question are in the **Table 1** and **Figure 1**.

3.1. Euphorbia hirta L.

Euphorbia hirta L., commonly called Patikan Kebo, is a species from the *Euphorbiaceae* family. According to research by Karim et al., (2015), this plant has a potent antioxidant activity of 99.21%, even more significant than the antioxidant power of vitamin C. The antioxidant activity of this plant is classified as very strong because it obtained the Inhibitory Concentration 50 (IC_{50}) value, namely 11.50 ppm. This antioxidant effect is produced due to the presence of tannins and flavonoids, especially quercitrin and myricitrin, from the ethanol extract of patikan kebo leaves.

The anti-inflammatory activity of the patikan kebo herb 0.1%, 0.2%, 0.4%, and 0.8% has also been studied by Syarif & Usmar (2014), which reduces oedema volume on the soles of mice-

supported by research on patikan kebo leaf methanol extract, which is rich in anti-inflammatory activity as seen in the inhibition of ear oedema and granuloma formation in rats. Moreover, it showed effectiveness in the thrombotic process, with the most excellent inhibition presentation given by the 200 mg/mL patikan kebo leaf methanol extract, namely 38.00 ± 2.52%, which showed a potent thrombotic effect compared to streptokinase as an antithrombotic standard (45.33 ± 2,67%). As mentioned, the presence of flavonoids, tannins, triterpenoids, and glycosides is believed to have a pharmacological effect, but further research is needed to determine which compounds really have antithrombotic and anti-inflammatory effects (Rahman et al., 2019). The content of alkaloids, flavonoids, and tannins in Euphorbia hirta causes this plant to have good potential in the wound-healing process (Fiandri & Sutarto, 2020).

Table 1. Study results of the pharmacological activity of plants in the Euphorbiaceae family

No	Plant Name	Plant Parts	Chemical Compound	Pharmacological Activity	Reference
1	Euphorbia hirta L.	Leaf	Tannins, flavonoids, triterpenoids, glycosides	Antioxidant, anti-inflammatory dan antithrombotic	(Karim et al., 2015; Rahman et al., 2019)
		Herb	Flavonoids	Diuretic, anti-inflammatory, antibacterial	(Lingga et al., 2014; M. Singh & Sudha, 2018; Syarif & Usmar, 2014)
2	Baccaurea lanceolata (Miq.) Müll. Arg.	Fruit	Phenol, flavonoids, terpenoids	Antibacterial, antioxidant	(Fitriansyah et al., 2018; Hadi et al., 2015)
3	Euphorbia pulcherrima	Leaf	Phenolic	Antibacterial, antioxidant	(Ibrahim et al., 2019; Sopiah et al., 2019a)
4	Aleurites moluccana L.	Bark	Flavonoids, α,β-amyrenone	Antibacterial; Anti-inflammatory	(Mukhriani et al., 2017); (Quintao et al., 2014)
5	Sauropus androgynus (L.) Merr	Leaf	Flavonoids, Phenolic, alkaloids, saponins	Antibacterial, anti-inflammatory, analgesic, increase breast milk production, antithrombotic	(Magdalena et al., 2015; Majid & Muchtaridi, 2018; Ramadheni et al., 2017; Selvi & Bhaskar, 2012)
6	Jatropha curcas L.	Leaf	Flavonoids	Analgesic, antipyretic, antifungal	(Gosal et al., 2020; Ningsi & Fadhilah, 2017; Yensenem et al., 2018)
7	Jatropha multifida L.	Sap	Quercetin, alkaloids, saponins, tannins, phenolic, flavonoids	Antiseptic	(Chairani & Harfiani, 2018)
		Bark	Phenol, flavonoids, terpenoids, alkaloids	Antioxidant	(Fitria et al., 2018)
8	Mallotus paniculatus	Bark	Phenolic, flavonoids, alkaloids, tannins, steroid	Antioxidant	(Junaidi et al., 2016)
9	Phylanthus niruri L.	Herb	Flavonoids, triterpenoids, saponins, tannins	Anti-inflammatory, antidiarrheal, antiulcer	(Mostofa et al., 2017; Sumarny et al., 2013)
		Leaf	Flavonoids	Analgetic	(Alyidrus et al., 2019)
10	Phyllanthus acidus (L.) Skeels	Leaf	Flavonoids, alkaloids, tannins	Antimicrobial, antihyperglycemic, anti-hypercholesterolemia, antihistamine	(Mulqie & Anggadiredja, 2019; Tatto et al., 2017)

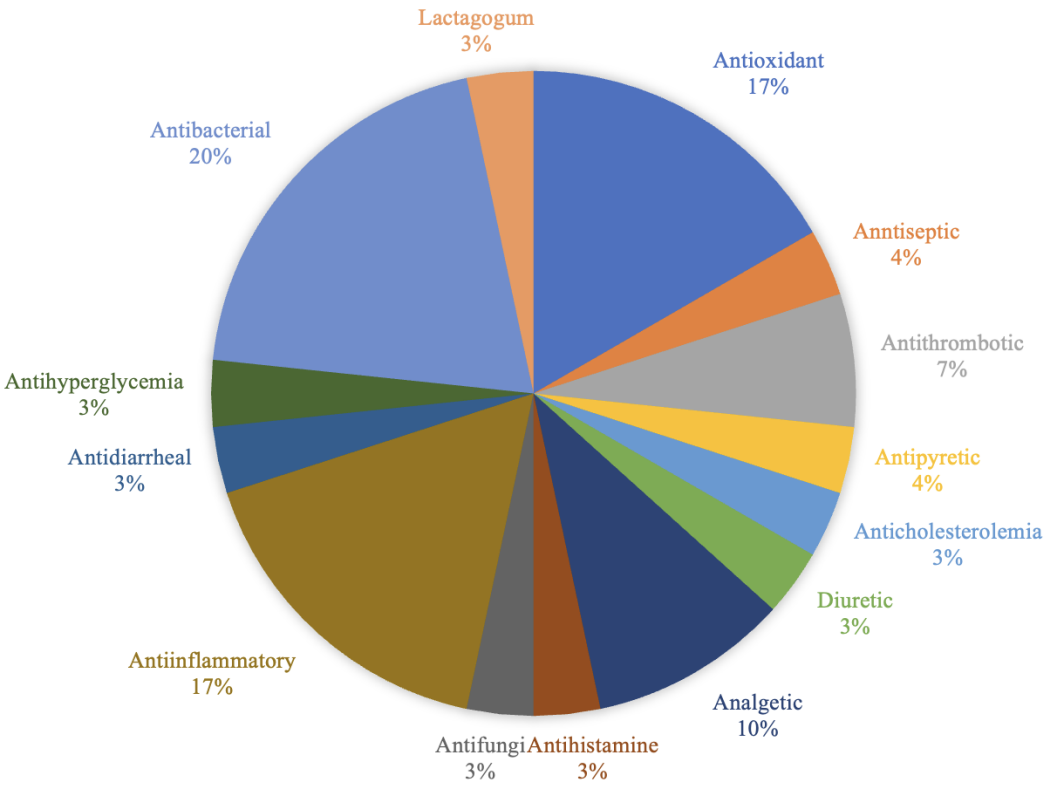

Figure 1. Percentage graph of the most frequently occurring pharmacological activities produced by ten plants of the Euphorbiaceae family

The Patikan kebo plant also has diuretic activity, as evidenced by research conducted by Lingga et al., (2014) which shows a diuretic effect. The diuretic effect is believed to be due to the presence of flavonoid compounds (quercitrin and myricitrin) in patikan kebo extract, which is known to have sufficient OH groups so that they can chelate calcium (Hamdiana et al., 2017). Antibacterial activity was also shown by Patikan kebo, which was able to provide obstacles to the growth of the bacteria Bacillus cereus, Escherichia coli, Salmonella typhi, and Staphylococcus aureus (Singh & Sudha, 2018).

3.2. Baccaurea lanceolata (Miq.) Müll. Arg.

Limpasu, one of the *Baccaurea* species, has antimicrobial activity (Fitriansyah et al., 2018) states that the ethanol extract of spleen fruit has antibacterial activity against Gram-positive bacteria such as *B. subtilis* and *S. aureus*, Gram-negative bacteria such as P. aeruginosa and E.coli as well as *P. acnes* and *S. epidermidis* which are bacteria that cause acne. MIC against these bacteria is 2.5% w/v. It contains phenolic compounds and flavonoids. By the Serampas-Jambi Tribe, the spleen is used to treat athletes' feet (Hariyadi & Ticktin, 2012).

However, from several articles investigated, most of the pharmacological effects shown by the spleen are its activity as an antioxidant, depending on the test method. The antioxidant potential of the pericarpium of *B. lanceolata*. was generated due to the presence of a flavonoid compound in the quercetin group, where the methanol extract showed the most potent antioxidant activity (Zamzani & Triadisti, 2021).

According to another study, spleen fruit has antioxidant activity with an IC_{50} value of 142 ppm which is thought to be produced by the content of terpene group compounds (triterpenes or diterpenes) in the spleen Hadi et al., (2015) steroid content, namely, beta-sitosterol is also thought to be able to provide antioxidant activity (Nastiti & Hadi, 2020)

3.3. Euphorbia pulcherrima

According to Ibrahim et al., (2019) the ethanol extract of poinsettia leaves (*Euphorbia pulcherrima* Wild.) has the potential as an antimicrobial at concentrations of 10 mg/100 µL and

20 mg/100 µL to inhibit *S. aureus* bacteria. This potential is believed to be due to phenolic compounds in poinsettia leaves. In line with this research, related research was conducted by Jannah & Muhimmatin (2021), which stated that poinsettias have an antimicrobial effect on *S. typhi*. Administration of *E. pulcherrima* extracts inhibited the growth of *S. typhi* bacteria, with an average diameter of the inhibition zone of 1.1 mm (MIC 5%).

Another pharmacological effect of the poinsettia is as an antioxidant with the DPPH method. The results showed free radical inhibition activity due to yellow spots on the TLC spots. Compounds that are thought to play a role are flavonoids, tannins, and terpenoids (Sopiah et al., 2019). According to Singh et al., (2012), poinsettia extract can provide an anticonvulsant effect but does not affect the coordination of motor nerve cells and anxiety. The content of the flavonoids spinacetin and patuletin in poinsettia is thought to be able to have an excellent effect as an anti-inflammatory, as evidenced by the decrease in oedema in rats' feet, besides that poinsettia also provides analgesic and sedative effects, and believed to have a muscle relaxant effect (Aljohani et al., 2022).

3.4. Aleurites moluccana L.

Candlenut is a plant of the *Euphorbiaceae* family, known to have antimicrobial effects against several bacteria. Research conducted by Mukhriani et al., (2017) showed that candlenut has antibacterial activity against the growth of several bacteria, namely *E. coli* and several other bacteria, which are believed to be produced by flavonoid compounds that have the most significant inhibition zone at a concentration of 1000 ppm.

Pre-clinical research on a semisolid preparation of dried hazelnut extract showed analgesic, anti-inflammatory, and wound-healing activities. These abilities are presumably due to the presence of flavonoid compounds in the hazelnut extract, namely 2"-O-rhamnosylswertisin (Cesca et al., 2012). A study conducted by Quintao et al., (2014) also stated that the isolate contained in hazelnut, namely α and β-amrinone, can provide acute and chronic anti-inflammatory effects by inhibiting or reducing neutrophil reduction mechanisms.

3.5. Sauropus androgynus (L.) Merr

In a study conducted by Ramadheni et al., (2017), it was explained that the growth of E. coli and S. aureus bacteria could be inhibited by giving katuk leaf ethanol extract, which showed an optimal inhibitory effect at a concentration of 80% with a total administration of 0.1 mL/disc equivalent to 80 mg.

According to Majid & Muchtaridi, (2018) other pharmacological activities provided by katuk leaves are anti-anemia, can help increase milk production in nursing mothers, and are anti-inflammatory. The anti-inflammatory effect of katuk leaves has also been studied by Desnita et al., (2018), where a patch of katuk leaf extract at a dose of 400 mg/kg BB has a percentage of inflammatory inhibition in the range of 66.67-100%, indicating that katuk leaves are pretty effective as an anti-inflammatory. In addition, katuk leaf extract significantly reduces the body temperature in rats, which is influenced by prostaglandin biosynthesis (Selvi & Bhaskar, 2012).

Various compounds will provide different pharmacological effects. Katuk leaves contain antithrombotic effects or can inhibit platelet aggregation, which contain active compounds such as quercetin and kaempferol, phenol, beta-carotene, and anthocyanins. Katuk leaves at a dose of 4.5 mg/g BW had the same bleeding time prolonging effect as aspirin when given to male Wistar rats (Magdalena et al., 2015).

3.6. Jatropha curcas L.

From the results of a study conducted by Yensenem et al., (2018), it was found that *Jatropha curcas* L. extract, or in Indonesia it is called jarak pagar leaf, gave the best analgesic effect at an extract dose of 600 mg/kg BW, where the analgesic effect began to be shown in rats in the 30th minute and decreased pain response until 120th minute. In addition, jatropha leaves showed activity in reducing the temperature in white male rats after induction with the DPT vaccine,

which, at a dose of 7.2 mg/200 g BW occurred a temperature drop. The antipyretic effect is thought to be due to the content of chemical compounds in the leaves, namely flavonoids (Gosal et al., 2020). The existence of antifungal activity was also proven through research conducted by Ningsi & Fadhilah (2017), that the ethanol extract of Jatropha curcas L. with an optimum concentration of 6% w/v inhibited the growth of water fleas, which was equivalent to the positive group of ketoconazole.

3.7. Jatropha multifida L.

Research has been carried out regarding the antiseptic activity of Chinese castor latex (*Jatropha multifida* L.), which can inhibit the growth of Gram-positive and Gram-negative bacteria. Chinese castor sap with various concentrations has strong-antiseptic power. The most vigorous antiseptic activity was shown by the sap of 100% concentration, which resulted in an inhibition zone of *S. aureus* = 14.05 mm and 21.26 mm in *E. coli* (Chairani & Harfiani, 2018).

Research conducted by Fitria et al., (2018) showed that the ethyl acetate extract of Chinese distance stems bark had a high antioxidant activity with an IC_{50} value of 201.61 ppm and an inhibition presentation of peroxide formation of 39.69%, which was thought to be due to the presence of the compound. Chemicals that are antioxidants in the bark of Chinese castor oil are phenols, flavonoids, terpenoids, and alkaloids.

3.8. Mallotus paniculatus

Pila-pila peel methanol extract with the Latin name Mallotus paniculatus shows good antioxidant activity, as evidenced by the significant free radical scavenging activity DPPH/Inhibitory Concentration 50 (IC_{50}), which is 71.94 mm (Junaidi et al., 2016). In line with this research, Bahaman et al., (2020) stated that pila-pila extract has an antioxidant effect. The most exciting thing is that pila-pila extract has a cytotoxic effect on three cancer cells: McF-7, HeLa, and HT-29. In addition, pila-pila also shows antibacterial activity, as evidenced by the formation of inhibition zones on gram-positive bacteria.

3.9. Phyllanthus niruri L.

The anti-inflammatory activity of meniran is evidenced by a decrease in oedema volume in the treatment group by 58% which is greater than the positive control (indomethacin), which only has an oedema reduction effect of 43% (Sumarny et al., 2013). Anti-inflammatory is produced because meniran is rich in phenolic compounds, especially flavonoids, namely quercetin (Porto et al., 2013). Due to the content of phytoconstituents in meniran, such as flavonoids, steroids, triterpenoids, saponins, and tannins, there is another pharmacological effect, namely as an antiulcer as evidenced in the study of Mostofa et al., (2017), where methanol extract of meniran has a potential effect as an antiulcer at a dose of 400 mg /kg by comparison with the standard drug, namely omeprazole.

The antidiarrheal activity was also shown by the Herbal extract of meniran 14.9 mg/200 g BW which was not significantly different ($p < 0.05$) from the positive control group (loperamide dose 0.21 mg/200 g BW) (Sumarny et al., 2013), the antidiarrheal effect is caused by the flavonoid content in meniran by inhibiting intestinal motility and hydro-electrolytic secretion (Wijaya & Soegianto, 2017).

According to Alyidrus et al., (2019), the ethanol extract of meniran leaves showed analgesic activity against male mice induced by acetic acid. Observations were made based on the number of writhings, which was the test animal's pain reaction to pain. The best presentation of the analgesic power of meniran leaves was shown by the 400 mg/kg BW concentration group, namely 96.02%. This analgesic effect is due to flavonoids, which can protect lipid membranes from damage and inhibit COX-I enzymes.

The potential of P. niruri was also stated by (Puspita & Alhebshi, 2019), namely selectively inhibiting the proliferation of leukemia MOLT-4 and K562 cells, cytotoxic to cancer cells but protective to normal cells. Increased p53 resulted in apoptosis in leukemia cells.

3.10. Phyllanthus acidus (L.) Skeels

The presence of flavonoid compounds in the ethyl acetate fraction of ceremai leaves is thought to play a role in antimicrobial activity. Based on research conducted by (Mulqie & Anggadiredja, 2019) ethyl acetate fraction of ceremai leaves provides antibacterial activity against antimicrobial and antifungal-resistant bacteria and antifungal activity carried out using the Autobiographical TLC method.

Ceremai leaf extract dose of 200 mg/kg BW is effective as an antihyperglycemic and anti-hypercholesterolemia in white male rats. The effect is comparable to the positive control, namely metformin, and simvastatin. Compounds that are thought to play a role in this pharmacological activity are alkaloids, flavonoids, and tannins (Tatto et al., 2017).

4. CONCLUSION

This literature review showed that several plants of the Euphorbiaceae family have various pharmacological activities. The most dominant pharmacological activities are antimicrobial, antioxidant, and anti-inflammatory. However, besides that, several other activities include analgesic, antipyretic, antithrombotic, anti-hypercholesterolemia, antihyperglycemic, antihistamine, diuretic, and antiseptic. Based on the findings in this review, more in-depth research can be carried out on plants belonging to the Euphorbiaceae family, given the rich pharmacological activity of these family plants to be used as raw materials for medicine. Apart from that, it is also hoped that there will be collaborative efforts between the government and academics in the pharmaceutical/botanical field to continue to increase research related to Indonesian plants so that the pharmacological activities of a plant become more evident and can have a good impact on the people of Indonesia.

5. CONFLICT OF INTEREST

All authors declared that there was no conflict of interest.

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