

## REVIEW OF SOME EUPHORBIACEAE PLANTS IN *USADA TARU* *PRAMANA* AND ITS PHARMACOLOGICAL ACTIVITIES

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### ABSTRACT

**Background:** World Health Organization (WHO) states that up to 65% of the world's population uses traditional medicines. Indonesia is one of the countries where most people still use traditional medicine, especially in Bali. The traditional Balinese plant-based medical system that has existed for a long time and is still inherited today is *Usada Taru Pramana*. One of the many plants found in *Usada Taru Pramana* is the Euphorbiaceae. **Objective:** This work aims to review some of the Euphorbiaceae plants written in *Usada Taru Pramana*, which have a variety of potential pharmacological activities. **Method:** This article review using a primary and secondary data sources. **Results:** Some parts of the Euphorbiaceae plants in *Usada Taru Pramana* contain important phytochemical constituents such as phenols, alkaloids, flavonoids, saponins, tannins and essential oils. Some of the potential pharmacological activities that have been tested are anti-inflammatory, analgesic, and antibacterial. **Conclusion:** The Euphorbiaceae plants in *Usada Taru Pramana* have a variety of phytochemical constituents and correlates with its pharmacological activities. Further research needs to be conducted to explore other Euphorbiaceae plants species in *Usada Taru Pramana* to find compounds and other pharmacological activities to deal with various diseases in the community.

**Keywords:** *Usada Taru Pramana*, Euphorbiaceae, Phytochemical Constituents, Pharmacological Activities.

### INTRODUCTION

World Health Organization (WHO) states that up to 65% of the world's population uses traditional medicines and medicines from natural ingredients (Kemenkes RI 2007)<sup>[1]</sup>. Indonesia is one of the countries where most people still use traditional medicine and have a variety of traditional medical systems based on natural ingredients, especially in Bali. The use of plant-based medicines is a popular approach to health care in Indonesia, especially Bali. The traditional Balinese plant-based medical system that has existed for a long time and is still inherited today is *Usada Bali*. *Usada* is a term for the Balinese system of treatment written on papyrus with Balinese language and script

and compiled into a text of medical knowledge, how to concoct medicine, how to treat or treat traditionally or traditional Balinese medicine<sup>[2]</sup>. The word *Usada* comes from the word *ausadhi* (Sanskrit), which means plants that contain medicinal properties. There are various types of *Lontar Usada*, one of which is *Lontar Usada Taru Pramana*. *Taru pramana* is derived from the word “taru”, meaning plant and “premana” means strength or efficacy. *Usada Taru Pramana* is a papyrus that tells the plants to come to Mpu Kuturan to express their respective properties that can be used as medicines<sup>[3]</sup>. *Usada Taru Pramana* contains a description of the method of treatment

(*usada*) in the form of dialogue in the disclosure of how to treat it<sup>[4]</sup>. Parts of plants that can be used in medicine are from the leaves, flowers, fruits, seeds, bark, sap, roots, rhizomes and all parts of the plant.

*Usada Taru Pramana* consists of approximately 182 plants with diverse properties and uses. These plants come from various family, including Liliaceae, Fabaceae, Moraceae, Lauraceae, Asteraceae, Piperaceae, Zingiberaceae, Euphorbiaceae, and others. One of the many plants found in *Usada Taru Pramana* is the Euphorbiaceae. Euphorbiaceae is a large family of flowering plants with about 300 genera and 8.000 species. This allows the Euphorbiaceae plants to be the largest plant with many species. The implication is that there is a higher chance that some species of plants will have medicinal properties. Most Euphorbiaceae plants are herbaceous, but several other species are found as shrubs or trees in the tropics<sup>[5,6]</sup>. The distribution of Euphorbiaceae plants spread in the territory of Indonesia, Malaysia, and America. Some Euphorbiaceae plants are written in *Usada Taru Pramana* such as cat tail (*Acalypha hispida*), buni (*Antidesma bunius*), jarak (*Ricinus communis*), candlenut (*Aleurites moluccana*), and others<sup>[7,8]</sup>. Traditionally, the Euphorbiaceae plants are used to treat eye pain, dizziness, plaque, thrush, sore throat, and pain throughout the body.

The Euphorbiaceae plants have been widely used as traditional medicine by various methods of treatment. However, scientific evidence is needed to ensure that the Euphorbiaceae plants are scientifically proven to have healing activity. In this review, we have summarized some of the Euphorbiaceae plants in *Usada Taru Pramana* along with some phytochemical compounds and pharmacological activities. The existence of scientific evidence from several studies is expected to further

convince the public that the plants contained in *Usada Taru Pramana* do have pharmacological activities and are beneficial to health.

## METHODS

This primary data source was obtained from the derivation of *Usada Taru Pramana* papyrus by Putra (1999)<sup>[8]</sup>. This process of finding secondary data sources is obtained by searching on google, google scholar, and NCBI with the keywords “phytochemical constituents of *Acalypha hispida*, *Antidesma bunius*, *Ricinus communis*, *Jatropha curcas*, *Pedilanthus tithymaloides*, *Aleurites moluccana*, and *Sauropus androgynus*“ and “pharmacological activities of *Acalypha hispida*, *Antidesma bunius*, *Ricinus communis*, *Jatropha curcas*, *Pedilanthus tithymaloides*, *Aleurites moluccana*, and *Sauropus androgynus*“. Secondary data sources used are journals that have been published for the past ten years. The use of data over the last ten years is applied of no last ten years of data is supported.

## RESULTS

The result obtained from the primary data source in the form of derivation *Usada Taru Pramana* is several Euphorbiaceae plants and the plant's parts used. The phytochemical constituents and pharmacological activities were obtained from the various data source in this review. The result obtained from the primary data source is listed in Table 1.

## DISCUSSION

### 1. *Acalypha hispida*

In *Usada Taru Pramana*, the *Acalypha hispida* plant or *ekor kucing* is known as a crop of white langurs and has efficacy as an eye remedy. *Ekor kucing* plus onions and fennel are then ground, filtered, and precipitated as an eye medicine.

**Table 1. Some Euphorbiaceae Plants in *Usada Taru Pramana* and Its Phytochemical Constituents and Pharmacological Activities**

No	Species	Parts	Phytochemical Constituents	Pharmacological Activities
1	<i>Acalypha hispida</i>	Leaves <sup>[7,8]</sup>	Phenol compounds, flavonoids, glycosides, steroids, saponins, hydroxyantraquinones, gallic acid, corilagin, and triterpenoids <sup>[11]</sup>	Antibacterial, Antioxidant <sup>[12,13,14,15]</sup>
2	<i>Antidesma bunius</i>	Leaves, Fruits, Roots, Barks <sup>[7,8]</sup>	Polyphenols, terpenoids, glucoside, saponins, tannins, biflavonoids, anthocyanins, luteolin, rutin, resveratrol, and quercetin <sup>[16,17]</sup>	Antiinflammation, Antibacterial <sup>[18,19]</sup>
3	<i>Ricinus communis</i>	Leaves, Roots <sup>[7,8]</sup>	Steroids, saponins, alkaloids, flavonoids, and glycosides <sup>[20]</sup>	Antiinflammation, Antinociceptive, Analgesic <sup>[21,22,23]</sup>
4	<i>Jatropha curcas</i>	Roots, Latex <sup>[7,8]</sup>	Phenols, tannins, free amino acids and phytic acid <sup>[24]</sup>	Antiinflammation, Wound Healing, Antibacterial <sup>[25,26]</sup>
5	<i>Pedilanthus tithymaloides</i>	Leaves <sup>[7,8]</sup>	Alkaloids, flavonoids, terpenoids, phenols, tannins, saponins, glycosides, sterols, and amino acids <sup>[27]</sup>	Antiinflammation, Antinociceptive <sup>[28,29]</sup>
6	<i>Aleurites moluccana</i>	Seeds, Bark <sup>[7,8]</sup>	Alkaloids, polyphenols, flavonoids, coumarin, tannins, steroids, and triterpenoids <sup>[30]</sup>	Antibacterial, Antinociceptive <sup>[31,32,33]</sup>
7	<i>Sauropus androgynus</i>	Leaves <sup>[7,8]</sup>	Sterols, resins, tannins, saponins, alkaloids, flavonoids, terpenoids, glycosides, phenols, cardiac glycosides, and acidic compounds <sup>[34]</sup>	Antiinflammation, Antibacterial, Anti-obesity <sup>[35,36,37,38]</sup>

The eye disease in question is conjunctivitis caused by a bacterial infection. In general, the bacteria that cause conjunctivitis are Gram-positive and Gram-negative bacteria. Examples of Gram-positive bacteria are *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, and *Streptococcus viridians* and examples of Gram-negative bacteria are *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Serratia marcescens*, *Proteus* sp., and *Enterobacter* sp.<sup>[9,10]</sup>.

Phytochemical screening of water and methanol extracts of plant leaves showed the presence of phenol compounds, flavonoids, glycosides, steroids, saponins, phlaccacin, and hydroxyantraquinones. Isolated compounds from plants include

gallic acid, corilagin, triterpenoids, flavonoids such as quercetin and kaempferol derivatives<sup>[11]</sup>. The leaves of *Acalypha hispida* are reported to contain several phytochemical compounds and have antibacterial activity. *Acalypha hispida* leaf extract contains carbohydrates, cardiac glycosides, anthraquinone glycosides, tannins, alkaloids, steroids, saponins, and flavonoids.

The methanol extract of *Acalypha hispida* leaves inhibits more bacteria than other extracts of *Acalypha hispida* solvents such as ethanol, chloroform, and water. In testing the antibacterial activity by the Kirby-Bauer agar diffusion method, the ethanol extract of the leaves of *Acalypha hispida* with a concentration of 80% has the highest antibacterial activity than the

other extracts, producing a diameter of inhibition zone of 18,50 mm in *Escherichia coli* bacteria and 19,33 mm in *Staphylococcus aureus*<sup>[12,13]</sup>. Other studies report that the methanol extract of *Acalypha hispida* leaves produces a minimum bactericidal concentration (MBC) against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Salmonella typhi* with each MBC of 250 mg/mL. All extracts were able to kill *Escherichia coli* bacteria, but methanol extract produced the lowest MBC of 125 mg/mL while other solvent extracts produced MBC 250 mg/mL. This shows that the methanol extract of *Acalypha hispida* leaves has stronger antibacterial effectiveness compared to other extract solvents and is more effective against *Escherichia coli* bacteria compared to other bacteria<sup>[14,15]</sup>.

Other studies report the presence of antioxidant activity in the extract of *Acalypha hispida* leaves. The results of antioxidant activity testing using the Water Soluble Tetrazolium Salt-1 (WST-1) reduction method showed that the ethanol extract of *Acalypha hispida* leaves had antioxidant activity (SOD like activity) with the percentage of inhibition at a concentration of 10 µg/mL, 100 µg/mL, and 1000 µg/mL, which is 11,27%, 15,20% and 22,06%. Ethanol extract fraction of *Acalypha hispida* leaves which has the best antioxidant activity (SOD-like activity) is ethyl acetate fraction with inhibition percentage at concentrations of 10 µg/mL, 100 µg/mL, and 1000 µg/mL, which is equal to 63,14%, 91,95% and 100%<sup>[12]</sup>. The antioxidant activity can be related to secondary metabolites found in *Acalypha hispida*, namely flavonoids and phenols.

## 2. *Antidesma bunius*

Leaf, fruit, root, and bark *Antidesma bunius* contains polyphenols, terpenoids, glucoside, saponins, tannins, biflavonoids, anthocyanins, luteolin, rutin, resveratrol, quercetin, procyanidin, catechins,

amentoflavone, corinagines (1-O-galloyl) 3,6-O-hexahydroxydiphenoyl-β-glucopyranoside), gallic acid (3,4,5-trihydroxybenzoic), elagic acid, vicinin II, ferulic acid, citric acid, benzoic acid, malic acid, lactic acid, oxalic acid, acetic acid, ascorbic acid, and caffeic acid<sup>[16]</sup>.

The methanol extract of *Antidesma bunius* leaves contains saponins, tannins, flavonoids, steroids, phlobatin, coumarin, alkaloids, emodin, and anthraquinones<sup>[17]</sup>. *Antidesma bunius* leaf extract also has anti-inflammatory and antibacterial activity. Anti-inflammatory measurement was carried out by looking at the ability of *Antidesma bunius* leaf extract to reduce swelling in the legs of experimental animals which were injected with 1% carrageenan solution. After being injected with carrageenan, the rat showed swelling and redness in the legs, and the mouse could not walk nimbly as before injection. The principle in this method is to measure the volume of the swollen sole of a test animal that has been induced by an inflammatory agent. Ethanol extract and ethyl acetate fraction of *Buni* leaves (*Antidesma bunius*) have effective anti-inflammatory activity at a dose of 200 mg/kg body weight. Antiinflammatory effect of leaf extract *Antidesma bunius* showed the most effective activity to reduce oedema in rat feet, ethanol extract 200 mg/kg body weight and ethyl acetate fraction 200 mg/kg body weight showed the same value to positive control namely sodium diclofenac. The anti-inflammatory effect is thought to be caused by the activity of secondary metabolites found on the leaves of *Antidesma bunius*, namely flavonoids, triterpenoid steroids, glycosides, and saponins<sup>[18]</sup>.

*Antidesma bunius* fruit has the potential for antibacterial activity especially against Gram-positive bacteria such as *Bacillus cereus* and Gram-negative bacteria such as *Salmonella thypimurium*. It is known that the inhibitory power is strong (at extract concentrations of 80%),

moderate (at concentrations of 40%), and low (at concentrations of 10-1,25%) against the *Bacillus cereus*. Whereas against test bacteria *Salmonella Typhimurium* is strong inhibitory (at concentrations of 80 and 40%) and low (at concentrations of 20-1,25%). The average diameter of inhibition zone formed in the fruit extract of *Antidesma bunius* against *Bacillus cereus* bacteria at a concentration of 80; 40; 20; 10; 5; 2,5; and 1,25% each was 18,4; 12; 9,4; 8,4; 7,4; 7; and 6,4 mm, while against *Salmonella Typhimurium* at a concentration of 80; 40; 20; 10; 5; 2,5; and 1,25% respectively of 26,7; 21; 11; 10; 8; 7; and 4,3 mm<sup>[19]</sup>.

### 3. *Ricinus communis*

Phytochemical studies of *Ricinus communis* show the presence of steroids, saponins, alkaloids, flavonoids, and glycosides. The dried leaf of *Ricinus communis* shows alkaloid content, ricinin (0,55%), kaempferol-3-OD-glucopyranoside, xylopyranoside quercetin, quercetin-3-O-D-glucopyranoside, camphor,  $\alpha$ -sesquiterpenoid ( $\beta$ -caryophyllene), quercetin gallic acid, gentisic acid, routine, and epicatechin. Indole-3-acetic acid has been extracted from the root. The seeds contain 45% glycosides from ricinoleic acid, isoricuric acid, stearic acid and dihydroxysteine, lipase and ricinin. GLC studies of castor oil showed palmitic acid (1,2%), stearic acid (0,7%), oleic acid (3,2%), linoleic acid (3,4 ricinoleate (89,4%) and dihydroxy stearic. GC-MS analysis of *Ricinus communis* showed several compositions of essential oils such as cineol (30,98%),  $\alpha$ -pinene (16,88%), camphor and lupeol<sup>[20]</sup>.

Leaf extract of *Ricinus communis* has an inflammatory activity based on the potential anti-inflammatory test using paw carrageenan oedema for acute inflammation testing in Wistar rats. In the carrageenan-induced paw oedema model, subplantar carrageenan administration

resulted in significant paw oedema formation compared to normal paw at consecutive hours of up to 24 hours. The methanol extract of the leaves of *Ricinus communis* (250 and 500 mg/kg body weight) each showed a cellular protective effect during the formation of oedema and in all stages of acute inflammation. This effect is supported by the protective effect of flavonoids against carrageenan-induced foot oedema in rats<sup>[21]</sup>.

In addition to anti-inflammatory activity, other studies report that the methanol extract of *Ricinus communis* leaves has antinociceptive and analgesic activity. The methanol extract of *R. communis* leaves reduced the writhing of acetic acid-induced rats significantly at doses of 100, 125 and 150 mg/kg body weight. The ethanol extract of the leaves of *Ricinus communis* showed analgesic effects in phase I and phased II pain that was formalin-induced. Each phase is associated with neurogenic and inflammatory pain. The methanol extract of *Ricinus communis* leaves inhibits a significant dose-dependent neurogenic and inflammatory phase. The methanol extract of *Ricinus communis* leaves at a dose of 150 mg/kg body weight showed significant inhibition of neurogenic and inflammatory phases ( $p < 0,001$ ) which was comparable to standard drugs (diclofenac). The mechanism of the analgesic effect of the methanol extract of *Ricinus communis* leaves is caused by the inhibitory effect or release of endogenous substances which induce nerve endings of pain similar to NSAIDs<sup>[22,23]</sup>.

### 4. *Jatropha curcas*

Phytochemical analysis of various parts of *Jatropha* plant revealed variations in the total content of phenols, tannins, free amino acids and phytic acid. The leaves contain phenols, tannins, and free amino acids<sup>[24]</sup>. 15% latex of *Jatropha curcas* has anti-inflammatory activity potential because it can accelerate the healing

process of the inflammatory phase of the wound. The results showed that the cream of 10% and 15% latex of *Jatropha curcas* stimulated a moderate immune reaction against CD68 in wound healing. These extracts show good antioxidant, coagulant and anticoagulant, analgesic, and anti-inflammatory properties. Similar results were observed for the effect of n-hexane leaf extract of *Jatropha curcas*, which showed a hemostatic effect and a significant reduction in bleeding time. Latex from tree branches has been used in healing wounds, refractory lesions, and septic gums and as a barrier to bruising. There are several secondary metabolic compounds extracted from the leaves of *Jatropha curcas*, which are involved in the wound healing process. *Jatropha curcas* leaves and sap extracts contain a considerable amount of phenolic compounds and saponins which are responsible for antimicrobial and antioxidant activity. Quercetin and routine flavonoids can enhance the wound healing process in the early phase, that is, regulation of expression of vascular endothelial growth factor (VEGF) for the growth of new blood vessels and the formation of type III collagen. However, flavonoid compounds play a role in the initial phase of wound healing (the inflammatory phase) to increase the activity of the immune system such as interleukin-2, lymphocyte proliferation, and macrophages. In addition, sesquiterpenoids are responsible for antimicrobial and analgesic effects. Meanwhile, proteins such as curcaine are responsible for wound healing. *Jatropha curcas* leaves and sap contain phenolic compounds and saponins which have antioxidant and anti-inflammatory activity. Flavonoids as antioxidants can reduce free radicals and will bind to free radicals that damage cell membranes. Flavonoids that accumulate in latex *Jatropha curcas* play an important role in the inflammatory phase by increasing interleukin-2,

lymphocyte proliferation, and macrophages. Saponins can increase monocyte proliferation which will ultimately increase the number of macrophages that secrete growth factors that are important for the wound healing process<sup>[25]</sup>.

*Jatropha curcas* leaf extract has the potential for antibacterial activity. The result of methanol extract of *J. curcas* leaves which use maceration method has inhibitory against *Staphylococcus epidermidis* at a concentration of 50 ppm (6,67 mm) and is increasing at a concentration of 100 ppm (19,33 mm). Inhibition zone diameters in reflux *Jatropha curcas* leaves extracts showed inhibition in all concentration series. The smallest inhibition zone is shown at a concentration of 3,125 ppm (9,33 mm) and has positive correlation with increasing concentration. The biggest inhibition zone at a concentration of 100 ppm was 22,67 mm. Reflux extracts provide greater resistance than methanol maceration extracts against *Staphylococcus epidermidis* and *Staphylococcus aureus*. The methanol extract of *Jatropha curcas* leaves resulting from maceration and reflux has strong antibacterial activity against both *Staphylococcus epidermidis* and *Staphylococcus aureus* but still below the standard antibiotic drug, such as clindamycin<sup>[26]</sup>.

### 5. *Pedilanthus tithymaloides*

Phytochemical screening reveals the presence of alkaloids, flavonoids, terpenoids, phenols, tannins, saponins, glycosides, sterols, amino acids, kaempferol 3-O-β-D-glucopyranoside, quercitrin, isoquercitrin, and scopoletin. The relevant phytochemical groups are identified as steroids in hexane and ethyl acetate, triterpenes in hexane, tannins in ethyl acetate, coumarin in ethyl acetate and saponins in hexane and ethyl acetate extract<sup>[27]</sup>.

Methanol and chloroform extracts of *Pedilanthus tithymaloides* leaves have anti-inflammatory activity based on the results of inflammatory induction test of swollen feet with carrageenan. Methanol extract significantly reduced carrageenan-induced foot oedema after three hours of injection at all doses tested compared to the positive control group indomethacin ( $p < 0,001$ ). Significant reduction in feet oedema was also given by chloroform extract at doses of 200 and 400 mg/kg body weight compared to the positive control group indomethacin ( $p < 0,05$ ). Methanol extract dose of 400 mg/kg body weight showed inhibition of oedema paw that was almost the same (62,28%) as observed with the indomethacin group (65,80%) whereas in chloroform extract with the same dose showed inhibition of 49,29% after five hours carrageenan injection. It is known that carrageenan-induced inflammatory reactions occur in two phases: the initial phase (0-2,5 hours after injection) resulting from the release of serotonin, bradykinin, and histamine, then the advanced phase is associated with the release of prostaglandins. Methanol and chloroform extracts of *Pedilanthus tithymaloides* leaves produced inhibition after the third hour of carrageenan-induced inflammation, showing a selective inhibitory effect on prostaglandin synthesis. The mechanism of anti-inflammatory activity of leaves of *Pedilanthus tithymaloides* is thought to originate from the blocking of synthesis and release of prostaglandins, which correlate naturally with therapeutic doses of most clinically effective anti-inflammatory agents<sup>[28]</sup>.

Methanol and chloroform extracts also showed peripheral antinociceptive activity in the inflammatory pain model induced by acetic acid. Oral administration of methanol and chloroform extracts (100, 200, and 400 mg/kg body weight) resulted in a reduction in the amount of writhing ( $p < 0,001$ ) of 22%, 39,3%, and 48,48%, respectively and 36,36%, 66,67%, and

79,17% compared to the inhibition (90,9%) produced by diclofenac sodium (10 mg/kg body weight). This nociceptive activity is associated with an increase in PGE2 and PGF2a levels in peritoneal fluid and inhibits synthesis of prostaglandin and cyclooxygenase<sup>[29]</sup>.

#### 6. *Aleurites moluccana*

*Aleurites moluccana* bark extract contains various phytochemical compounds such as alkaloids, polyphenols, flavonoids, coumarin, tannins, steroids, and triterpenoids. Various phytoconstituents such as flavonoids and triterpenes, hydrocarbons, sterols, amino acids and carbohydrates are present in the leaves of *Aleurites moluccana*. The methanol extract of *Aleurites moluccana* leaf showed the presence of two C-glycoside flavonoids namely Swertisin and 2-O-rhamnosylswertisin. *A. moluccana* seeds contain glycerides, fatty acids such as linoleic acid, palmitic acid, stearic acid, myristic acid, oils, proteins and vitamin B<sup>[30]</sup>.

The disk diffusion test results showed significant *Aleurites moluccana* extract activity against Gram-positive (*Staphylococcus aureus* and *Streptococcus pyogenes*) and Gram-negative bacteria (*Pseudomonas aeruginosa* and *Klebsiella pneumoniae*). Results for MIC and MBC against *Staphylococcus aureus* showed the lowest MIC in acetonitrile bark extract (195 µg/mL) whereas *Streptococcus pyogenes* had the lowest MIC in methanol extract from the same bark (781 µg/mL). *Pseudomonas aeruginosa* showed very low MIC shown in methanol extracts of bark (98 µg/mL). Finally, for *Klebsiella pneumoniae* all extracts showed high MIC, but the lowest in the group was shown in cutaneous acetonitrile extract<sup>[31,32]</sup>.

The results of the isolation and identification of the methanol extract of *Aleurites moluccana* leaf showed two main flavones of C-glycosida, namely swertisin and 2-O-rhamnosylswertisin, which have

potential antinociceptive activity. The antinociceptive pharmacological effect of *A. moluccana* extract was evaluated in a mechanical hypernociception model induced by flogistic agents such as carrageenan, PGE2, and CFA. Oral administration of *Aleurites moluccana* extract (500 mg/kg body weight) can reduce mechanical hypernociceptive caused by carrageenan injection, with inhibition of  $36 \pm 4\%$  and ID50% of 443 (400-490) mg/kg body weight. Significant results were obtained with animals injected with CFA, which *Aleurites moluccana* extract dose 500 mg/kg body weight orally reduced the hypernociceptive threshold up to six hours after CFA injection, with  $48 \pm 4\%$  inhibition at 500 mg/kg doses. *Aleurites moluccana* extract, dose 125 to 500 mg/kg body weight, has been proven effective in preventing mechanical hypnosis from being induced by PGE2 for up to one hour after irritant injection. The reduction percentages are  $26 \pm 10\%$  and  $33 \pm 3\%$ , for 250 and 500 mg/kg body weight. Swerticin isolate compound and 2-O-rhamnosylswertisin dose of 30 mg/kg body weight was effective in inhibiting the hypernociceptive response, when compared to the control group, with inhibitions of  $70 \pm 2\%$  and  $50 \pm 5\%$ , respectively. Furthermore, 2-O-rhamnosylswertisin is able to significantly inhibit mechanical sensitization induced by CFA or PGE2, with each inhibiting  $25 \pm 3\%$  and  $94 \pm 6\%$ <sup>[33]</sup>.

### 7. *Sauropus androgynus*

Phytochemical detection of *Sauropus androgynus* leaves reveals the presence of sterols, resins, tannins, saponins, alkaloids, flavonoids, terpenoids, glycosides, phenols, catechols, cardiac glycosides, and acidic compounds such as phenolic acids, chlorogenic acid, caffeic acid, and ferric acid. Analysis of ethanol extract of *Sauropus androgynus* leaves using gas chromatography-mass spectrometry (GC-MS) revealed the presence of phytols and

squalene. Seven bioactive compounds from methanol extract from the aerial portion of *Sauropus androgynus*, including three lignans glycosides, a lignans glycosides, glycosides<sup>[34]</sup>.

The methanol, ethanol, and water extracts of *Sauropus androgynus* leaves contain bioactive compounds which have pharmacological properties and are responsible for anti-inflammatory activities such as tannins, flavonoids, alkaloids, phenols, and steroids. Leaves extract in doses of 200 mg/kg body weight and 400 mg/kg body weight has resulted in a significant increase in heat plate reaction time in doses depending from 0 to 90 minutes compared to 100 mg/kg body weight. Leaf extract in both doses of 100 mg/kg body weight also produced significant inhibition with average plate reaction time. Extracts of 100, 200 and 400 mg/kg body weight and 100 mg/kg Papaverine and 100 mg/kg Phenylbutazone (positive control) significantly reduce the volume of paw oedema that is not dose-dependent. There is also substantial inhibition of oedema of feet volume induced in extracts and in animals treated with medication. The results of this study indicate that *Sauropus androgynus* leaf extracts show activity in varying degrees of inflammation, pain and fever by activating cyclooxygenase, prostaglandin levels, especially PGE2, significantly increasing and their production triggers inflammation, pain and fever. The significant reduction, as well as the inhibitory effect of extracts on carrageenan-induced oedema foot volume, is an indication of the plant's anti-inflammatory potential<sup>[35]</sup>.

*Sauropus androgynus* leaves extract at a concentration of 5 mg/mL is the lowest concentration that can inhibit the growth of bacterial strains after incubation when compared to controls. Chloramphenicol and gentamicin are used as standard antibiotics for Gram-positive and Gram-negative bacteria. The Kirby-Bauer disk



diffusion method is used to determine the inhibition of bacterial growth by plant extracts. Six bacterial strains were used to test the antimicrobial activity of *Sauropus androgynus*. Among the six organisms investigated, three were Gram-positive, namely *Bacillus cereus*, *Bacillus subtilis*, *Staphylococcus aureus* and the other three were Gram-negative organisms, namely *Escherichia coli*, *Klebsiella pneumoniae*, and *Salmonella typhimurium*. *Sauropus androgynus* methanol leaf extract showed more inhibitory effect on Gram-positive bacteria when compared with ethanol extract. Methanol leaf extract also shows the best inhibitory effect on Gram-negative bacteria when compared with ethanol and water extracts<sup>[36,37]</sup>.

*Sauropus androgynus* leaf extract has anti-obesity activity. The extract can reduce body weight and eating index, increase stool weight and consistency comparable to orlistat, decrease retroperitoneal fat index, affect organ index by increasing the weight of the liver and testes. The best dose of *Sauropus androgynus* leaf extract in reducing body weight is 400 mg/kg body weight. *Sauropus androgynus* leaf extract with a dose of 400 mg/kg body weight has a bodyweight reduction activity of mice closer to the comparison (orlistat) than extract dose of 100 mg/kg body weight and 200 mg/kg body weight. *S. androgynus* leaf extract group 100, 200, and 400 mg/kg body weight had significant differences compared to the negative control group ( $p < 0,05$ ). The content of flavonoids in the leaves of *Sauropus androgynus* can reduce body weight through the mechanism of action to reduce food intake and reduce lipid accumulation in the liver<sup>[38]</sup>.

## CONCLUSION

The Euphorbiaceae plants in *Usada Taru Pramana* have a variety of phytochemical constituents and correlate with its pharmacological activities. The secondary metabolite compounds found in

the Euphorbiaceae plants are phenols, alkaloids, flavonoids, saponins, tannins and essential oils. Most of the Euphorbiaceae plants in *Usada Taru Pramana* have the potential for anti-inflammatory, analgesic, and antibacterial. Further research needs to be carried out to explore other Euphorbiaceae plants species in *Usada Taru Pramana* to find compounds and other pharmacological activities to deal with various diseases in the community.

## CONFLICT OF INTEREST

No conflict of interest in this paper. This paper was written independently without being affiliated by another party.

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