

# Graptophyllum pictum (L.) Griff. (Syn: Justicia picta Linn.) and its Effectiveness: A Well-Known Indonesian Plant

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## ABSTRACT

*Graptophyllum pictum* (L.) Griff., a shrubby stove plant, has been used traditionally to treat various diseases. This review summarizes the up-to-date data about its phytochemistry and pharmacological properties and provides a perspective and direction for future research. The phytochemical analysis of *G. pictum* revealed the presence of flavonoids, steroids, glycoside, tannins, saponin, chlorophyll, nontoxic alkaloid, and anthocyanin. Meanwhile, the pharmacological analysis revealed that this plant possessed various activities such as antimicrobial, immunomodulatory, antioxidant, anti-inflammation, anti-analgetic, wound-healing, anti-hemorrhoid, anti-diabetic, and estrogenic effects. However, most of its pharmacological activities were based on the crude extracts and the bioactive compounds responsible for the bioactivities have not been well identified. A further detailed investigation in phytochemistry to identify the bioactive compounds and to investigate the mechanism action of its bioactivities is required. Moreover, a toxicology study is also needed to develop a standardized formulation of *G. pictum* preparation and to fulfill the requirements of modern phytomedicine.

**Key words:** *G. pictum*, Indonesia, Pharmacological, Activities.

## INTRODUCTION

Over the past century, chemical drug development has transformed the world's health care system. Nevertheless, according to the World Health Organization (WHO), about 80% of the world's population still relied on natural resources for health maintenance, especially in Africa, Asia, and Latin America.<sup>1-26</sup> Plants are the most affordable and easily accessible source of raw materials for drug development. They have been traditionally used to treat pathologic conditions or to improve health conditions since hundreds or even thousands of years ago. This ancient medication knowledge has been passed on through generations to generations to keep it in daily life practice as a promising source to defeat diseases, either in the form of traditional preparations or as plant-based active compounds.

As one of the tropical countries, Indonesia has the second biggest potential medicinal plant resource after Brazil. Among more than 40,000 medicinal plants that are used in the world, at least 30,000 of them can be found in Indonesia which reflects almost 90% of medicinal plants in Asia.<sup>27,28</sup> This local heritage in traditional medicine was collected by the experience of ancient people only using the patient as a subject of experiment throughout. Hence, it contains many materials worthy of further research to collect scientific data to confirm the claims of folklore medicinal plants for its efficacy and safety to fulfill the modern standards of therapeutic agents. Moreover, among thousands of medicinal plants in Indonesia, only 45 have been certified as Standardised Herbal Medicine and 21 plants have been developed as Phytomedicine.

*Graptophyllum pictum* L Griff or popularly known as caricature-plant, is a medicinal shrub belong to the family of Acanthaceae. It is most likely native to New Guinea and then extensively spread to India, Mexico, United States, Ghana, Bolivia, and Asia. Currently, it is easily found in some regions in Indonesia and locally known as Daun Ungu, Daun Wungu. *Graptophyllum pictum* has been used widely to treat many diseases such as wound healing, hemorrhoid, antipyretic, analgetics, and menstrual problems.<sup>22</sup> There was a previous review of the biological activities of *G. pictum*,<sup>29</sup> however, a comprehensive review of the present knowledge is needed to provide the perspectives and directions for future research and potential applications. In this review, we document an updated and complete overview of the botany, phytochemistry, traditional uses, and pharmacological activities of *G. pictum*. Moreover, the present knowledge obtained mainly from experimental studies was critically assessed to provide evidence and justification for local traditional uses of *G. pictum* and to propose future research prospects and potential therapeutic uses for this plant.

## METHODS

We searched PubMed and Google Scholar with the term *Graptophyllum pictum*, Handeleum, daun ungu, daun wungu among publishing studies between 1990 until 2020. All related review articles, original articles, case reports were analyzed. Selection Criteria. We included articles published in English or Indonesia. Two reviewers (S.T and S.E) independently evaluated the relevance of the retrieved articles by title and abstract. The studies

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that were not related were excluded. Two independent researchers (S.T and S.E) categorized eligible articles. Information from the articles was tabulated and classified according to mechanisms, and results.

## RESULTS

By searching the electronic database, 50 potential articles were identified. The full text of 39 articles was obtained. Most were published from Indonesia (46 of 50; 92%) (Takayama et al., 2011; Kimura and Sato, 2012; one was published in Japan, two was published in India, Fourteen articles were published in English (28%) and the rest in Indonesian (72%). Six articles were excluded because the article was incomplete (4), the article was about the food coloring effect of *G. pictum* (2).

## VERNACULAR NAMES

*Graptophyllum pictum* is commonly known as Joseph's coat in English,<sup>29</sup> daun prada, puding in Malaysia,<sup>21</sup> Kaala-aduusa, Ysjudemaram India, and Guacamari, Camagua, Guacamayo in Cuba.<sup>22</sup> Meanwhile, in Indonesia, this plant has different names such as Daun Ungu; Daun Putri, Dangora (Ambon) Kabi-Kabi (Ternate); Demung, Tulak, Wungu (Java); Daun Temen-temen, Handeuleum (Sunda); Karotong (Madura).<sup>2</sup>

## BOTANICAL DESCRIPTION

The characteristics of these plants are the erect standing tree, purple to green leaves. It can grow until 2 meters; the widest leaf is 25x11 cm with a shiny surface. The flower's color is a dark red and the fruit's color is brownish-purple.

## TRADITIONAL USES

Traditionally, the leaves and/or flowers of *G. pictum* is considered an emollient, resolvent, laxative, diuretic, and anti-inflammatory.<sup>9,12</sup> In Cuba, the plant is prescribed in the treatment of earache, sores, swellings, and wounds.<sup>22</sup> The Indonesian used it to treat tonsillitis, abscess, and rheumatism.<sup>2,9</sup> Herbarium Amboinense on the eastern and central Indonesian plants mentioned that it has been used to treat breast engorgement and breast abscess.<sup>1-34</sup>

## PHYTOCHEMISTRY

The important phytochemical contents are flavonoids (rutin, heperoside, and quercetin), steroid, glycoside, tannin, saponin, chlorophyll and nontoxic alkaloid.<sup>3,16</sup> Indonesia's National Agency of Drug and Food Control (BPOM) revealed that *G. pictum* contains alcohol, pectin, and formic acid. Moreover, the essential oil content is not less than 0.4% and flavonoid (0.4%), vomifoliol, a triterpenoid compound, as a chemical marker.<sup>8</sup> Budiaji et al.<sup>6</sup> reported that *G. pictum* also contain compounds such as Hexadecanoic acid, ethyl ester; (2E) - 3,7,11,15-tetramethyl-2-hexadecem-1-ol; Pyridine-3-carboxamide, oxime, N- (2-trifluoromethylphenyl); 9-Tricosene; Squalene; Gamma-Tocopherol, Stigmasterol; Beta-sitosterol; 2,5,9-cyclotetradecatrien-1-ol, 2,6,10- trimethyl-13- (1-methylethenyl).

## PHARMACOLOGICAL ACTIVITIES

### Antibacterial activity

0.5 cc of *G. pictum* extract with different concentrations of 100%, 50%, 25%, 12.5%, 6.25%, 3.12%, 1.56%, 0.78%, 0.39%, 0.19%, 0.019%, 0.04% and 0.02% showed inhibition of *Streptococcus mutant* growth.<sup>19</sup> Minimum Inhibition Concentration (MIC) of *G. pictum* ethanol extract to *Staphylococcus aureus* was 25 mg/ml, whereas MIC to *Pseudomonas aeruginosa* was 50 mg/ml.<sup>7,35</sup> The gel preparation of the formula (carbopol 940 and CMC-Na (0.25:0.75) had the best physical and stability properties for 21 days of storage as well as the 9.67 mm

antibacterial inhibitory zone of *Staphylococcus aureus*.<sup>32</sup> The ethyl acetate fraction of *G. pictum*'s ethanol extract has the most active antibacterial activity against *S. aureus* ATCC 25923 with an MKC value of 12.5% compared to n-hexane, ethyl acetate, and water fractions from the ethanol extract purple leaf.<sup>17,31</sup> When examined against *E. coli*, the ethyl acetate was the most active fraction compared to n-hexane, ethyl acetate, and water fractions from the ethanol extract purple leaf and the diameter of the inhibition zone on the ethyl acetate fraction in the 50% concentration is 23,3 mm; 24 mm and 23 mm. The test for the antibacterial activity with the dilution method shows that the MBC (Minimal Bactericidal Concentration) is 12.5%.<sup>15</sup>

The extract of leaf *G. pictum* in a boiled mouthwash of patients using orthodontic appliances showed 40% reduction of the amount colony of *Staphylococcus sp.*, however, the reduction effect was similar to Chlorhexidine 0.2%.<sup>33</sup> Minimum concentration of 12.5 % of methanol extract of *G. pictum* leaf showed inhibition of growth of root canal bacteria which is polymicrobial and 25 % concentration of *G. pictum* leaf of methanol extract demonstrated the similar effect of sodium hypochlorite as an antibacterial irrigation agent.<sup>11</sup> When examined against *Enterococcus faecalis*, MIC of ethanol *G. pictum* extract was 25% concentration with MBC was at 50% concentration of *G. pictum* extract.<sup>5</sup> There was a study which compared the betadine gargle with 90% concentration of *G. pictum* leaf extract as a mouth wash and this study resulted in that *G. pictum* extract leaf had an effect of decreasing saliva viscosity and lowering saliva pH and thus might prevent the growth of *Streptococcus mutans* that encourage caries dentis.<sup>18</sup>

### Antifungi activity

The 50% ethyl acetate fraction of the *G. pictum* was the most active fraction with a 28 mm in diameter and with dilution test capable of showing MBC to 12.5% on *Candida albicans* ATCC 10231.<sup>4</sup> A clinical trial in 10 patients with oral candidosis demonstrated that there was a decrease in hypha and spore of patients using 25% *G. pictum* leaf mouthwash.<sup>37</sup> 40% of ethanol extract of *G. pictum* leaf showed the smallest number of growth of *Candida albicans* in 40 samples of acrylic resin denture.<sup>36</sup>

### Immunomodulator activity

2.5% ethanol extract of *G. pictum* leaf showed enhancement of phagocytosis activity to *Candida albicans* and the effect was greater than isoprinosine (a synthesis immunomodulator drugs).<sup>13</sup> A report from Kusumawati et al showed the ethanol extract of *G. pictum* to phagocytosis and immunoglobulin M and TNF- $\alpha$  to the mice's macrophage.<sup>14</sup> *G. pictum* leaf ethanol extract 3.125%, 6.25%, 12.5%, and 25% concentration showed a decrease of *Streptococcus mutans* adhesion to neutrophil isolate from healthy individuals in vitro. The higher concentrate of *G. pictum* leaf ethanol extract demonstrated the smallest number of *Streptococcus mutans* adhered to neutrophil.<sup>19,23</sup>

### Antioxidant activity

*G. pictum* leaf extract reduces nephrotoxicity induced by gentamicin via impending lipid peroxidation and ameliorating glutathione content and activity of enzymes in the liver and kidney. Healthy adult Wistar albino rats (150 to 250 g) aged 60 to 90 days received *G. pictum* ethanol extract at 300 mg/kg, 150 mg/kg, and 75 mg/kg along with gentamicin and the glutathione (GSH) and Glutathione S-transferases (GST) blood levels were significantly raised.<sup>30</sup>

### Antiinflammatory activity

*G. pictum* leaf ethanol extract exerted inhibition of edema induced by carrageenan in hind paw's mice and this herb also increased the vascular permeability induced by acetic acid. This concluded that *G*

*pictum* exerted an inflammatory effect or the early exudative phase of inflammation.<sup>20</sup> 20% ethanol-extracted cream of *G. pictum* exerted an anti-inflammatory activity to the white male mice that had been induced inflammation using carrageenan.<sup>27</sup>

### Wound healing activity

Mice back that incised treated with 10% and 15% ethanol extract of *G. pictum* leaf showed the healing of the wound from the dryness of wound, skin crusts, and release of skin crusts.<sup>1</sup> A study on Wistar rat as reported by Prasetyo et al. revealed that ethanol extract of *G. pictum* at the dose of 100 mg/kg significantly attenuated anal ulcer by decreasing the total percentage of ulcer area, edema, leukocyte infiltration as well as malondialdehyde, and at the same time increased the superoxide dismutase as compared to the negative control.<sup>17</sup>

### Analgetic property

Pain is a protective response of the body to the stimulus that is caused by actual or potential tissue damage. This response is associated with a localized or generalized unpleasant feeling that is transmitted to the brain by sensory neurons. As a complex pharmacological condition, there are various options for the treatment of pain. One of the currently prominent therapy for pain is using medicinal plants such as *G. pictum*.

*In vivo* study of the analgesic effect of ethanol extract of *G. pictum* leaves in Swiss Webster female mice by heat-induced method showed that the extract at the doses of 100 and 200 mg/kg significantly increased the reaction time by the values of 4.62 and 5.15 seconds compared to negative control with the value of 3.59 seconds ( $p < 0.05$ ). Moreover, it was comparable to the positive control (acetosal 0.42 mg/kg) with a reaction time of 5.83 seconds ( $p > 0.05$ ).<sup>25</sup>

$\beta$ -sitosterol isolated from n-hexane fraction of *G. pictum* leaves was given orally to male mice to investigate its analgesic activity in the writhing reflex model. The compound at the doses of 1, 2, and 4 mg/20g was found to inhibit acetic acid-induced pain by the value of 51.2%, 64.7%, and 72.3% respectively. However, the analgesic activity of fractions was lower than aspirin as the positive control.<sup>10</sup>

### Anti-haemorrhoid activity

A recent study by Hutagalung on male Wistar rats induced by 6% croton oil on the anus for 3 days to develop the haemorrhoid-like condition. Furthermore, *G. pictum* extract was given orally to the rats at a dose of 100 mg/kg on day 4 for 5 consecutive days. The result showed that the extract exhibited the anti-hemorrhoid effect by decreasing anal edema measured by the rectoanal coefficient as well as the number of extra vessels leukocyte. The rats that were treated with *G. pictum* extract experience a less severe anal edema with a rectoanal coefficient that was significantly lower than control group with values of 2.46 and 3.13 respectively. Moreover, the number of extra vessels leukocytes of the treatment group (900.14) was also significantly lower than the control group (1003.28).<sup>10</sup>

### Anti-diabetic effect

The aqueous extract of *G. pictum* was administered orally to alloxan-induced diabetic Sprague-Dawley rats once a day. The group treated by *G. pictum* extract exhibited anti-diabetic activity by lowering blood glucose level at a dose of 100 mg/kg which is comparable to metformin (10 mg/kg) as the positive control.<sup>15</sup>

Similar to the previous study, Rosmiati and Fernando<sup>22</sup> reported that *G. pictum* ethanol extract at a dose of 250 mg/kg successfully decreased blood glucose level of alloxan-induced diabetic male mice as effective as the positive control group that treated with glibenclamide.

Four extracts of *G. pictum* that were obtained from sequential extraction using ethanol, diethyl ether, ethyl acetate, and butanol to investigate

their anti-diabetic effects in alloxan-induced diabetic Sprague-Dawley rats. The extracts were given orally to the rats at a dose of 50 mg/kg for 28 days of the experiment. The result revealed that all extracts decreased blood glucose level with a percentage of decrease ranging from 30 to 37% compared to glibenclamide (0.25 mg/kg) with a value of 56%.<sup>19</sup>

### Estrogenic effects<sup>24</sup>

Oral treatment with hexane leaf extract of *G. pictum* (0.5 mg/0.05 ml olive oil) possessed an estrogenic effect by significantly increasing the diameter of the uterus, mucous layer thickness, lumen epithelial cell height, and glandular epithelial cell height compared to aquadest-treated group. However, the estrogenic effect of *G. pictum* remains significantly lower than Ethinyl estradiol as the positive control.<sup>27</sup>

### Another research on calcium level

A research to evaluate the effect of *G. pictum* extract on calcium level on mice femoral bone post ovariectomy proved that *G. pictum* leaf extract was able to increase the calcium content of the femur. This extract does not affect bone morphometry. This research also showed the optimal dose of *G. pictum* extract is 30 mg/kgBW.<sup>25</sup>

## CONCLUSION AND FUTURE DIRECTION

Herein, we documented the existing phytochemistry and pharmacological properties of *G. pictum*. This plant is a potential herbal therapy for many ailments. A peruse of available scientific references show that the traditional medical uses of *G. pictum* have been evaluated by modern pharmacological studies such as for anti-hemorrhoid, anti-microbial, anti-inflammation, anti-analgesic, and wound healing, etc., which can be explained by the presence of various compounds such as flavonoids, steroids, terpenoids, anthocyanins, etc. The biological activities and bioactive compounds must be of great attention to the researchers. However, future studies are necessary to address issues regarding the composition of the extract, toxicity, explicability of preclinical experiments, and lack of transformation of the preclinical results to clinical efficacy. Therefore, it is extremely important to conduct detailed investigations on the phytochemical and pharmacological, and toxicity properties and develop standardized formulations based on the ingredients.

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