

Review Article

Overview of Phytochemical and Pharmacological of Gandarussa Extract (*Justicia Gendarussa* Burm)

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Abstract: *Gandarussa* plant (*Justicia gendarussa* Burm.F.) was a herbal plant that contains chemical compounds such as alkaloids, saponins, flavonoids, polyphenols, essential oils, tannins and steroids. The presence of these chemical compounds can be used as medicinal ingredients, namely headaches, rheumatism and sprains. *Justicia gendarussa* Burm.F. has long been used as an anti-inflammatory and pharmacologically, this plant has been reported that have antibacterial, analgesic, anthelmintic, anti-cancer, anti-inflammatory, antioxidant, anti-HIV, toxicity, sedative hypnotic and male contraception drugs.

Keywords: *Justicia gendarussa* Burm.F., Phytochemical, Pharmacological.

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INTRODUCTION

Justicia Gendarussa Burm .F. included in the family Acanthaceae, which are scattered in Asia, such as China, Philippines, India, Indonesia, Malaysia, Sri Lanka, Pakistan, Thailand and the Andaman Islands. *J.gendarussa* grew wild in the forest or river embankments and can also be planted as a medicinal plant or hedge plant [1].

Gandarussa plant (*Justicia gendarussa* Burm.F.) was known by various regional names such as, Sumatera: *Besi-besi* (Aceh), *Gandarussa* (Melayu); Java: *Handerasa* (Sunda), *Gonorusa* (Sunda), *Gondorusa* (Central Java), *Ghandarusa* (Madura); Nusa Tenggara: *Gandarisa* (Bima,), *Puli* (Maluku) [2].

Justicia gendarussa classification [3]

Kingdom	: Plantae
Division	: Tracheophyta
Class	: Magnoliopsida
Order	: Lamiales
Family	: Acanthaceae
Genus	: <i>Justicia</i>
Species	: <i>gendarussa</i>

The morphology of *Justicia gendarussa* is a shrub, erect, up to 2 m in height. The stem is rectangular, woody, the young leaves are dark purple and when the leaves are old they turn shiny brown (Figure 1). *J.gendarussa* has single lanceolate leaves, 3-12 cm length, 1.5-3.5 cm width, pinnate, opposite, flat leaf edges tapered, and dark green leaf has short stalk (Figure 2). *J.gendarussa* has small white flowers that arranged in the form of malay or closed grain, spread, and out of the tip of the stalk [2].



Fig-1: Gandarussa plant [4]



Fig-2: Gandarussa leaves [2]



Fig-3: Gandarussa Flowers [2].

J.gendarussa is one of herbal plants used in the Ayuverda medical system. Ayuverda is one of the traditional healing methods that have been used for a long time. Ayuverda treatment helps to restore balance between body, heart, mind and environment. Treatment with the Ayuverda system can be started by consuming herbal ingredients, yoga, massage therapy, and meditation [3].

J.gendarussa has pharmacological effects such as fever, cough, jaundice, mouth sores, arthritis, cephalgia, hyplegia, facial paralysis, otalgia, hemicranias, bronchitis, chronic rheumatism, liver disorders, respiratory disorders, indigestion, anti-inflammatory, and anti-cancer [5].

DATA COLLECTION

This review article used study literature technique by looking for theoretical references that were relevant to the cases or problems found. Collecting National and International articles with a span of 10 years (2010-2020) and using official books. The searching data in this review article used online media with trusted sites such as Google Scholar, Scienedirect, Pupmed, Pupchem and NCBI with the search keyword "*Justicia gendarussa Burm F*".

PHYTOCHEMICAL

Screening of ethanol extract (C_2H_5OH) Gandarussa root (*Justicia gendarussa Burm.F.*) showed that were several chemical compounds such as carbohydrates, flavonoids, alkaloids and saponins. While hexane (C_6H_{14}) and chloroform extract ($CHCl_3$) Gandarussa root (*Justicia gendarussa Burm.F.*) contained steroid [6]. Ethanol (C_2H_5OH) and aqueous extract (H_2O) that obtained of Gandarussa stem (*Justicia gendarussa Burm.F.*) showed that there were tannins, flavonoids, glycosides, terpenoids and phenolic compounds [5].

Phytochemical screening of aqueous (H_2O), ethanol (C_2H_5OH), hexane (C_6H_{14}), and chloroform extract ($CHCl_3$) in Gandarussa leaves (*Justicia gendarussa Burm.F.*) showed that were glycosides, tannins, phenolic, flavonoids, terpenoids, carbohydrates, tannins, alkaloids and saponins [6, 5]. Chloroform ($CHCl_3$), methanol (CH_3OH), and petrelum ether (pe) extract in Gandarussa leaves (*Justicia gendarussa Burm.F.*) showed that were flavonoids, essential oils, resins, and carbohydrates. *J.gendarussa* identified chemical elements from various leaf extracts using *Gas Chromotography - Mass Spectrometer GC-MS*, the result showed there were 23 bioactive phytochemical compounds [3]. *J.gendarussa* is a Phytol and β -sitosterol producer which included in the phenolic, terpenoid, and alkaloid parts. Phytol is acyclic terpen alcohols that were found as essential oils in aromatic plants [7, 8].

In Skudai and Muar areas, Gandarussa leaves (*Justicia gendarussa Burm.F.*) were collected to determine the distribution of 2 flavonoid compounds, namely naringenin and kaempferol using *Gas Chromotography - ionization (GC-IFD)* detector analysis. The distribution of naringenin and kaempferol of Gandarussa (*Justicia gendarussa Burm.F.*) was higher in old leaves than in young leaves, due to physiological, environmental and soil geographic factors [9]

PHARMACOLOGICAL

Anti-bacteria

One of the pharmacological activities contained in Gandarussa (*Justicia gendarussa Burm.F.*) is antibacterial. Antibacterial is a compound that can control bacterial growth. This study was used to evaluate the antimicrobial activity by using disc diffusion and broth dilution methods. Sample of aqueous extract (H_2O) of Gandarussa stem showed that the antibacterial activity can inhibit maximum the bacteria *Shigella flexneri* (26.20 mm), *Proteus mirabilis* (24.50 mm), *Escherichia coli* (21.40 mm) *B. Subtilis* (20.25 mm), *S. paratyphi A* (19.50 mm) by both methods. Different from ethanol extract (C_2H_5OH) of Gandarussa stem has less inhibitory activity. An

aqueous extract of Gandarussa leaves showed significant antimicrobial activity to *Staphylococcus aureus* (26.33 mm). In the ethanol extract (C₂H₅OH), Gandarussa leaves showed little inhibitory activity to some organisms [5]. Extracts of methanol, chloroform and petroleum ether of Gandarussa leaves showed that the antibacterial activity was strong to *P. pneumonia* and *P. vulgaris* [3].

This study stated (*Justicia gendarussa* Burm .F.) extracts and solvent fraction of methanol, petroleum ether (pe), carbon tetrachloride, chloroform, and water have antibacterial activity to *B. cereus*, *B. subtilis*, *S. aureus*, *Staphylococcus aureus*, *Sarcina lutea*, *E. coli*, *Pseudomonas aeruginosa*, *Salmonella paratyphi*, *Shigella boydi*, *S. dysenteriae*, *Vibrio mimicus*, and *Vibrio parahemolyticus* [10].

Testing of the root, stem and leaves of Gandarussa (*Justicia gendarussa* Burm .F.) using ethanol extract (C₂H₅OH) disc diffusion method and broth microdilution test was tested on four positive gram bacteria, namely *S. epidermidis*, *S. pyogenes*, *S. aureus*, dan *E. faecalis*. Six gram-negative bacteria, namely *S. boydii*, *S. dysenteriae*, *S. typhi*, *P. vulgaris*, and *E. coli* showed moderate antibacterial activity against the tested bacteria. The hexane and chloroform extract showed relatively high antibacterial activity against the tested bacteria. Alkaloid compounds, flavonoids, and saponins in the Gandarussa plant (*Justicia gendarussa* Burm .F.) supported antimicrobial activity, such as alkaloids are known to have antimicrobial activity that is anti-parasitic. Antibacterial activity of flavonoid was able to form extracellular complex proteins, dissolves and complexes with bacterial cell walls. Saponins also participate in antimicrobial activity in pathogenic bacteria and fungi [6].

Gandarussa stem (*Justicia gendarussa* Burm .F.) which extracted using aqueous and hexane, was tested with antimicrobial such as *Escherichia coli*, *Staphylococcus aureus* and *Candida albicans* by the disc diffusion method. Aqueous extract of Gandarussa (*Justicia gendarussa* Burm .F.) showed the largest inhibition zone of 5 mm to *Escherichia coli* and 3 mm to *Staphylococcus aureus* at concentration of 50 µg/ml and was more effective against *Candida albicans* fungi than hexane extract [11].

Anthelmintic

Anthelmintic is a compound to eradicate worms and excreted it through the digestive tract. Gandarussa (*Justicia gendarussa* Burm .F.) is a plant that has anthelmintic activity with chemical compounds containing stigmasterol, lupeol, and 16-hydroxy lupeol. Methanol extract of leaves and stems of Gandarussa (*Justicia gendarussa* Burm .F.) has anthelmintic activity. Testing of paralysis and death of *Pheretima posthuma* worm was carried out with test concentrations of 10, 20, 30, 40 and 50 mg/ml. The

methanol extract of leaves with a concentration of 50 mg/ml caused paralysis in worm at 35.3 minutes and death at 70.7 minutes. While the stem methanol extract caused paralysis in worm at 41.3 minutes and death at 89.3 minutes. Albendazole which was used as a positive control caused paralysis and death in worm at 17 and 48 minutes [12].

Analgetic

Gandarussa (*Justicia gendarussa* Burm .F.) is a plant that has activity as an analgesic with chemical compounds such as steroids, terpenoids, flavonoids, and alkaloids. An analgesic is a compound or drug that is used to reduce pain or pain caused by various stimuli to the body, both mechanical, chemical, and physical. Pain can cause damage to tissues that trigger the release of pain mediators such as bradykinin and prostaglandins which eventually activate pain receptors in peripheral nerves and is passed on to the brain. Research on the n-hexane fraction of Gandarussa leaves (*Justicia gendarussa* Burm .F.) has activity as an analgesic. The identification of the n-hexane fraction of Gandarussa leaves (*Justicia gendarussa* Burm .F.) containing steroids and terpenoids that can stimulate lipomodulin protein biosynthesis which can inhibit the enzymatic phospholipase activity, was responsible enzyme for the release of arachidonic acid which blocks cyclooxygenase and lipoxygenase, inhibiting prostaglandins, leukotrienes, prostacyclin, and thromboxane [13].

Anti inflammation

Gandarussa (*Justicia gendarussa* Burm .F.) is a plant that has been used as a medicine to treat inflammation (anti-inflammatory). Since ancient times, inflammation is a complex biological response of blood tissues to harmful stimuli such as pathogens, cells that were damaged, or irritated. The ethanol extract of Gandarussa leaves (*Justicia gendarussa* Burm .F.) which was cold macerated has anti-inflammatory effect with concentration of 50-200 µg/ml which could weaken NO (Nitric Oxide) production and reduce MMP-9 gene expression in macrophages that induced with lipopolysaccharide (LPS) 1 µg. NO and MMP-9 have an important role in tissue damage and inflammation through degradation of matrix protein with proteolytic activity of cytokines. NO is produced by macrophages without lipopolysaccharide induction (LPS) showed no significant results compared to treatment. In this study, dexamethasone as a standard drug which inhibited 85% of NO production in macrophage cells [14].

Methanol extract of Gandarussa root (*Justicia gendarussa* Burm .F.) showed anti-inflammatory activity, the dose used was 100 mg/kg significantly inhibited edema formation 5 hours after carrageenan induction. It showed that the root extract of Gandarussa (*Justicia gendarussa* Burm .F.) has high edematogenic activity that caused total cyclooxygenase activity, providing

anti-inflammatory effects by reducing prostaglandin production through inhibition of COX and key enzymes in prostaglandin synthesis [15].

Extract of Gandarussa leaves (*Justicia gendarussa Burm .F.*) contained Phytol compound which have anti-inflammatory activity by releasing histamine (26.92 %), serotonin and bradykinin (49.90%), and prostaglandins (68.03%) compared to the diclofenac standard 5 mg/kg. Chloroform extract of Gandarussa (*Justicia gendarussa Burm .F.*) produced β -sitosterol. β -sitosterol is one of the phytosterols which could help to reduce cholesterol by limiting the amount of cholesterol that entered the body, thereby increasing the prostate to help to reduce swelling (inflammation) using a mouse model of acute inflammation, β -sitosterol effect of leukocyte accumulate, cytokine doses, cytokine doses, and oxidative stress, showed potential anti-inflammatory activity by releasing histamine (30.07%), serotonin and bradykinin (52.25%) and prostaglandins (69.43%)[7, 8].

Extract of Gandarussa leaves (*Justicia gendarussa Burm .F.*) could reduce the level of urine F2-isoprostan which was carried out in experimental animals, was Wistar rat (*Rattus norvegicus*). F2-isoprostan is a non-classical *eicosanoid* and has potent biological activity as a mediator of inflammation leading to pain perception. This study showed that the result of urine F2-isoprostan in rat decreased after 4 weeks in excessive physical treatment and *Justicia gendarussa Burm F* leaf extract, was 5.46 ± 0.655 ng/ml to 3.61 ± 0.389 ng/ml [16].

The flavonoid compound of Gandarussa root (*Justicia gendarussa Burm .F.*) which has anti-inflammatory activity is apigen. Methanol extract of root of *Justicia gendarussa Burm .F.* fractionated then isolated to obtain apigen compound. This study stated 89% inhibition of edema at dose of 10 mg/kg in carrageenan induced rat [17].

Anti-cancer

Anticancer potential of Gandarussa (*Justicia gendarussa Burm .F.*) with in vitro culture, ethanol, chloroform and ethyl acetate extracts were used to analyze cytotoxicity against liver carcinoma cell line (HepG2) and cervical cancer cell line (HeLa) by testing using *multi tie tamper* (MTT). The result showed that the ethanol extract of Gandarussa (*Justicia gendarussa Burm .F.*) has cytotoxicity activity against liver carcinoma cancer cell lines (HepG2) and (HeLa) with IC_{50} values 19.8 μ g/ml and 43.8 μ g/ml. Chloroform and ethyl acetate extracts had IC_{50} values above 50 so they were unable to inhibit liver carcinoma (HepG2) and cervical cancer (HeLa) cells [18].

This study stated that Gandarussa leaves (*Justicia gendarussa Burm .F.*) using 96% ethanol extract and aqueous extract showed the result of LC_{50}

which were carried out using the *Brine Shrimp Lethality Test* (BSLT) method. 96% ethanol extract of Gandarussa leaves (*Justicia gendarussa Burm .F.*) showed anticancer potential with LC_{50} valued 713.34 μ g/ml. Aqueous extract of Gandarussa leaves (*Justicia gendarussa Burm .F.*) showed the greatest potential as an anticancer with the smallest LC_{50} valued 24.64 μ g/ml. It showed that extract of Gandarussa leaves (*Justicia gendarussa Burm .F.*) has the potential to be developed as an anti-cancer [19].

Antioxidant

Gandarussa (*Justicia gendarussa Burm .F.*) has antioxidant activity with the amount of phenolic compounds in the methanol extract of Gandarussa leaves (*Justicia gendarussa Burm .F.*) 280.41 ± 0.58 mg/g equivalent to gallic acid, while the flavonoid content was 165.52 ± 0.65 mg/g equivalent to quersetin. In the DPPH test, the IC_{50} value of Gandarussa (*Justicia gendarussa Burm .F.*) was $71, 31 \pm 0.42$ μ g/ml while the IC_{50} value of ascorbic acid was 14.11 ± 0.24 μ g/ml [20].

Sedativ and hypnotics

The ethanol extract of Gandarussa (*Justicia gendarussa Burm .F.*) with doses of 250 and 500 mg/kg in rat could make sedative and hypnotic effect that was almost same as 3 mg/kg diazepam. The sedative and hypnotic activity of the ethanol extract of Gandarussa (*Justicia gendarussa Burm .F.*) was caused by chemical compounds such as flavonoids and terpenoids [21].

Anti hiv

Extraction of Gandarussa stem and bark (*Justicia gendarussa Burm .F.*) was fractionated and isolated to obtain 2 compounds, justiprocumins A and B which believed that have anti-HIV activity. Both of these compounds were identified as glycosides arynalphthalide lignans (ANL) where arynalphthalide lignan was constituent of chemical that contributed to the activities of anti-HIV, giving a value of IC_{50} 21 nm better than the value of the IC_{50} drugs in clinical use of zidovudine (AZT) [22].

This study stated that 70 % fractionated of Gandarussa ethanol extract (*Justicia gendarussa Burm .F.*) could be developed into anti-HIV drug because the ethanol fraction cannot induce IFN- γ production. Based on the WHO standard which stated that the phytopharmaceutical dosage requirements for anti-HIV drug should not have IFN- interferon inducing activity [1].

Toxicity

In a study was conducted by Berna Elya examined the value of LD_{50} and liver function based on the activity of the aminotransferase enzym which was carried out on the test animals, male and female mice which were divided into 5 groups, group 1 as the control group, 2-5 were given the ethanol extract of

Gandarussa leaves (*Justicia gendarussa* Burm .F.) with doses of 4,8,16, and 32 g/kg (highest dose). The LD₅₀ test was determined by the number of deaths in the test group for 24 hours of treatment with one time giving of the test material. The result showed that the test material up to the highest dose was non-toxic with LD₅₀ value 31.99 g/kg bb (male group) and 27.85 g/kg bb (female group). Measurement of aminotransferase enzyme activity using the colorimetric method showed that the liver function was not different between the control group and the test group by giving the test material solution with dose of 4 g/kg - 16 g/kg bb [23].

Male contraception drugs

Research was conducted to determine the reversibility of the effects of Gandarussa leaves ethanol extract on the weight index of the reproductive organs of mice were testes, epididymis and vas deferens; the quality of the spermatozoa of mice were immotility, viability and abnormalities of spermatozoa and concentration of spermatozoa. This study used three doses of the extract were 0.065 mg/kg bb; 0.130 mg/kg bb and 0.195 mg/kg bb that were given for 22 days. To determine the reversibility of the effect, observations were made on one group of mice that were left alive for one month after giving the extract dose of 0.195 mg/kg bb. The result showed that the ethanol extract of Gandarussa leaves affected the index weight of the testes, epididymis and vas deferens with the largest reduction achieved by extract 0.195 mg/kg bb, significantly compared to control (P = 0.000; a = 0.05) for all spermatozoa quality parameters. Gandarussa leaves ethanol extract could affect the spermatozoa concentration of mice, significantly compared to control (P = 0.000; a = 0.05). Gandarussa leaves extract has a reversible effect on the index of reproductive organ weight and spermatozoa quality of mice. After one month of giving the extract, it could be seen from the absence of significant differences with control (P index of testicular organ weight 0.479; P index of epididymal organ weight and vas deferens 0.614; P motility 0.484; P viability 0.992; P abnormality = 1; a 0.05), whereas the spermatozoa concentration showed an irreversible effect (P> 0.05) [24].

CONCLUSION

Gandarussa (*Justicia gendarussa* Burm.F.) was a plant that has chemical compounds spread in every part of the plant, has benefits for treating various diseases such as antibacterial, analgesic, anthelmintic, anti-cancer anti-inflammatory, antioxidant, anti-HIV, toxicity, sedative hypnotic, and male contraceptive drugs.

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