INTERNASIONAL CONFERENCE ON
MULTIDISCIPLINARY APPROACHES IN HEALTH SCIENCE
VOLUME 2, ISSN 3032-4408 (Online)
https://ejournal.poltekkes-denpasar.ac.id/index.php/icmahs

Phytochemical Profile and Potential Health Benefits of Beluntas Leaves (Plucheaindica): A Literature Review

Putu Wira Kusuma Putra[1)]., AA Ngurah Subawa[2)]., I Nyoman Mantik Astawa[3)]., Agung Wiwiek Indrayani[4)]

[1),3),4)] Program studi Doktor Ilmu kedokteran, Fakultas Kedokteran, Universitas Udayana

[2)]Program Studi Pendidikan Dokter, Universitas Udayana

Corresponding author : subawapdki@gmail.com

Article history

Posted : 2024-12-12
Reviewed : 2024-10-29
Received : 2023-10-03

ABSTRACT

Traditional medicine in Indonesia is a cultural heritage consisting of tangible or intangible elements that shape the identity of a community or society. The development of traditional medicine is ongoing in Indonesia, utilizing herbal materials. One of the native Indonesian plants that is widely distributed in several regions and has potential for development is the beluntas plant (Plucheaindica L.). The purpose of this literature review is to provide an overview of the effectiveness of Plucheaindica's components and its potential health benefits as an herbal medicine in Indonesia. Articles were gathered using electronic databases such as PubMed, ScienceDirect, ProQuest, and Google Scholar. The collected articles did not have a time limit. Keywords used in the article collection included (PlucheaIndica L.), beluntas leaves, antioxidants, phytochemistry, anti-inflammation/anti-inflammatory. The current study focuses on the use of the traditional plant Plucheaindica, its nutritional composition, phytochemistry, health benefits, and its role in clinical studies. Based on the literature review, the beluntas plant contains phytochemicals such as alkaloids, flavonoids, tannins, essential oils, and chlorogenic acid, which are strongly associated with mechanisms to reduce the risk of chronic diseases like diabetes, cancer, obesity, and cardiovascular diseases. Additionally, Plucheaindica is beneficial as an antioxidant, antibacterial, anti-inflammatory, cholesterol-lowering, and cell protection agent. Beluntas leaves (Plucheaindica L.) can be processed into various forms such as infusions, capsules, and tea, depending on the intended use, but should adhere to specific dosages.

Keywords : Beluntas Leaves (PlucheaIndica), anti-inflammatory, antioxidants, traditional medicine

Introduction

Traditional medicine has developed over centuries in various countries with diverse techniques, such as Traditional Chinese Medicine in China, Kampo Meridian therapy in Japan, traditional Korean medicine including Sasang in Korea, and Traditional Medicine in Indonesia. There are several clinical practices, each with its own set of concepts, diagnostic evaluation procedures, structures, and reasons for reaching a diagnosis, and accompanying treatment approaches (Birch et al., 2020). Traditional medicine in Indonesia is a cultural heritage consisting of tangible or intangible elements that shape the identity of a community or society. This heritage has been passed down from past generations through creativity, work, and knowledge, and has been preserved for the future. Indonesian cultural heritage includes traditional foods and beverages that can be used as medicine, processed using local products and procedures, and is rich in regional characteristics (Setyowati et al., 2023).

Bali Province is one of the regions in Indonesia with a rich culinary culture and a cultural tourism sector that attracts many tourists. Traditional medicine known as “Usadha” has emerged as an important component of Balinese Traditional Medicine. Various traditional Balinese drinks, known as “Loloh,” processed using spices or herbs, have been empirically proven as remedies by the Balinese people (Widhiantara&Jawi, 2021). Loloh has functional qualities and can be used to experimentally treat various disorders. These traditional beverages contain active compounds that can promote beauty, health, and body care. The general public is increasingly aware of the benefits related to nature.

One of the native Indonesian plants widely distributed in several regions and with potential for development is the beluntas plant (Plucheaindica L.), which belongs to the Asteraceae family and contains alkaloids, flavonoids, tannins, essential oils, chlorogenic acid, sodium, potassium, magnesium, and phosphorus, while its roots contain flavonoids and tannins (Rolnik&Olas, 2021; Yuliani et al., 2015). Beluntas is often used as a traditional medicine to eliminate body and mouth odor, stimulate appetite, address digestive disorders in children, relieve pain from rheumatism, bone pain, and lower back pain, reduce fever, and treat leucorrhea and irregular menstruation, due to its phytochemical content (Suriyaphan, 2014). It is mentioned that beluntas leaves contain various compounds such as lignans, terpenes, phenylpropanoids, benzoids, alkanes, sterols, catechins, hydroquinone phenols, saponins, tannins, and alkaloids (Ruan et al., 2018). The compounds in beluntas leaves exhibit several biological activities, including anti-inflammatory, antipyretic, hypoglycemic, diuretic, and various pharmacological activities (Chiangnoon et al., 2022; Defitiana et al., 2019; Sirichaiwetchakoon et al., 2020).

Empirically, beluntas plants are frequently used in traditional medicine to eliminate body and mouth odor, stimulate appetite, address digestive disorders, relieve pain from rheumatism, bone pain, and lower back pain, reduce fever, and treat leucorrhea and irregular menstruation (Lestari et al., 2020a; Manu, 2013). Due to its potential to boost immune function, some literature reports its benefits as an immunostimulant against COVID-19 (Jha et al., 2021) and for anti-hyperglycemia, dyslipidemia, and obesity (Sirichaiwetchakoon et al., 2020). Beluntas contains phytochemicals such as alkaloids, flavonoids, tannins, essential oils, and chlorogenic acid, which are strongly associated with mechanisms to reduce the risk of chronic diseases such as diabetes, cancer, obesity, and cardiovascular diseases (Dwi et al.,

2018; Sirichaiwetchakoon et al., 2020; Sudirman et al., 2017).

To date, there is relatively little scientific literature that comprehensively introduces the phytochemical composition and bioactivities of Plucheaindica against various diseases. Therefore, a literature review to examine the phytochemical content found in Plucheaindica extracts is necessary. This review also highlights the various health benefits of Plucheaindica, such as lowering cholesterol, blood sugar, anti-cancer, antibacterial, antioxidant properties, and anti-inflammatory effects. The findings of this review could serve as material or information sources for researchers interested in studying Plucheaindica extracts more deeply, such as the prospects for developing standardized herbal medicines, phytopharmaceuticals, and its economic prospects as a local resource in Indonesia.

Method

This study aims to collect data on the effectiveness of beluntas leaf extract (Plucheaindica L) in enhancing health, specifically focusing on its anti-inflammatory and anti-cholesterol effects. Articles were collected using electronic databases such as PubMed, ScienceDirect, ProQuest, and Google Scholar. No time limits were applied to the articles collected. The keywords used for article collection included (Plucheaindica L), beluntas leaves, antioxidants, phytochemistry, dyslipidemia, and anti-inflammation/anti-inflammatory. **Inclusion and Exclusion Criteria:** The inclusion criteria are preclinical and clinical studies involving animal models and/or human subjects with experimental methods. Studies must provide interventions using beluntas leaf extract or components of beluntas leaves in other forms, such as tea and other methods.

Result and Discussion

1. Plant Description

The beluntas plant is an upright shrub that often branches profusely and grows to a height of 0.5-2 meters. The leaves of the beluntas plant are hairy and light green. The leaf blades are oval, elliptical, or inverted egg-shaped with a pointed base and serrated edges. The leaves are alternately arranged on short stalks, measuring 2.5-9 cm in length and 1 cm in width.The flowers of the beluntas plant are compound, small, and clustered in flat terminal panicles. Beluntas flowers have purple staminal tubes and pistil stalks with two long purple branches. The fruit of the beluntas plant is a hard, brown capsule. The fruit is very small, measuring about 1 mm in length, and contains small, brownish-white seeds (Fitriansyah et al., 2018).

Here is the taxonomy of the beluntas plant based on the classification from Badan Riset dan Inovasi Nasional (BRIN):

Kingdom: Plantae (Plants)
Subkingdom: Tracheobionta (Vascular Plants)
Superdivision: Spermatophyta (Seed Plants)
Division: Magnoliophyta (Angiosperms/Flowering Plants)
Class: Magnoliopsida (Dicotyledons)
Order: Asterales Link
Family: AsteraceaeGiseke
Genus: Pluchea Cass.
Species: Plucheaindica Less.

2. Nutritional Composition of Plucheaindica

Plucheaindica, commonly known as beluntas, has leaves that are rich in calcium, vitamin C, dietary fiber, and β-carotene (Singdam et al., 2022). The calcium content in Plucheaindica leaves is seven times higher (251 mg/100 g) compared to that in basil leaves, which contain 32 mg/100 g. Additionally, the β-carotene content is twice as high (1225 µg/100 g) compared to basil leaves, which have 812 µg/100 g (Sudjaroen, 2012). The leaves of Plucheaindica, when crushed, have a very

distinctive aroma. These leaves are reported to have a sweet, tangy, and aromatic taste. In several Asian countries, Plucheaindica leaves, whether boiled or fresh, are used as a side dish in chili paste to add a spicy flavor to dishes (Wei et al., 2022).

3. Potential Phytochemical Content of PlucheaIndica

Plucheaindica is also highly interesting for development as a standardized herbal product or phytopharmaceutical due to the various phytochemicals contained in this plant. However, it should be noted that the amounts of different phytochemicals are often influenced by environmental factors, genotype, and their combinations. Plucheaindica contains a range of phytochemicals that can be categorized into several important classes. These classes include flavonoids, alkaloids, tannins, steroids, phenolic acids, and phytosterols (Yuliani et al., 2015). The leaves of Plucheaindica contain flavonoids, which are organic antioxidants. Traditional plants generally contain flavonoids in varying concentrations, with the leaves being the most dominant part. Flavonoids, which are strong antioxidants, have qualities including anti-cancer, anti-allergy, anti-inflammatory, anti-carcinogenic properties, immune system support, and protection of digestive system performance (Buapool et al., 2013; Chiangnoon et al., 2022; Dwi et al., 2018; Nopparat et al., 2019).

a. Phenolic Compounds

It is known that the presence of phenolic compounds with antioxidant characteristics can prevent or reduce the development of diseases associated with oxidative stress (Tan et al., 2018). Total phenolic content can be interpreted as the variety of phenolic compounds contained in an extract, and it is crucial to measure this level due to its relation to significant antioxidant activity (Blainski et al., 2013). Phenolic components with strong antioxidant activity can suppress Reactive Oxygen Species (ROS), a source of oxidative stress commonly linked to cardiovascular diseases, cancer, and neurological disorders (Chacko et al., 2010). Research reports reveal that gamma radiation applied to Plucheaindica leaf extract can enhance antioxidant activity, total phenol content, and reduce microbial contaminants during storage (Ernawati et al., 2021). Herbal tea made from Plucheaindica leaves has also been commercially available in Indonesia and Thailand and has high phenolic compound content as confirmed by phytochemical testing (Widyawati et al., 2014a). Comparative studies have shown that the total phenol content in Plucheaindica essential oil is higher than that of basil leaf oil, with values of 275.21 mg GAE/l of oil and 209.30 mg GAE/l of oil, respectively (Widyawati et al., 2013). Phenolic compounds such as caffeoylquinic acid derivatives have been successfully validated in Plucheaindica leaf extract using HPLC. Quantitatively, ultrasound extraction with 50% ethanol yields the highest concentration of caffeoylquinic acid derivatives in Plucheaindica leaf extracts from various sources in Thailand (Kongkiatpaiboon et al., 2018). In addition to Thailand, the phenolic components of Plucheaindica leaves have also been analyzed from various locations in Malaysia. These phenolic components include 3-O-caffeoylquinic acid, 5-O-caffeoylquinic acid, 3,4-O-dicaffeoylquinic acid, 3,5-O-dicaffeoylquinic acid, and 4,5-O-dicaffeoylquinic acid (Vongsak et al.,

2018). Interestingly, the stage of leaf maturity in Plucheaindica shows varying total phenol content, with young leaf tips showing significantly higher phenolic levels compared to other maturity stages (Vongsak et al., 2018). Research by Sirichaiwetchakoon et al. (2020) found that the total phenolic content in Plucheaindica tea was 107.95 ± 4.87 mg GAE/g. This study indicates that Plucheaindica has an effect on reducing serum lipids, including total cholesterol, triglycerides, and LDL cholesterol.

b. Flavonoids

Flavonoids are a type of active polyphenolic chemical found in plants, derived from the core structure of 2-phenylchromon. Flavonoids are phytochemicals with a C6-C3-C6 structure, characterized by two aromatic rings connected by a three-carbon bond. In plants, they are considered UV-B absorbers that offer protection against UV radiation as a response to "excess light" stress (Agati et al., 2011). Due to their widespread presence in many plants, flavonoids are essential for meeting daily human dietary needs (Ribeiro et al., 2015). Flavonoids are currently classified into flavonols, flavanols, flavones, anthocyanidins, flavanonols, flavanones, and chalcones based on their structure (Lu et al., 2013). Herbal flavonoids have been shown to provide anti-inflammatory, natural antioxidant properties, and therapeutic effects against cardiovascular diseases with minimal side effects and safety concerns (Salaritabar et al., 2017). Flavonoid content has been found in Plucheaindica plants across various regions, including Asia, the Middle East, and the Americas, and has been shown to manage inflammation (Srivastava &Shanker, 2012). Flavonoids (quercetin, kaempferol, myricetin, luteolin, and apigenin), caffeic acid, anthocyanins (Andarwulan et al., 2010), and essential oils have also been identified in Plucheaindica leaf extract (Widyawati et al., 2014a). UV spectrum analysis indicates that flavonoid compounds in Plucheaindica leaf extract absorb at 240–285 nm (band I) and 300–560 nm (band II) (Ernawati et al., 2021). Interestingly, Plucheaindica contains higher levels of flavonoids compared to Plucheasagittalis, which is associated with its antinociceptive effects (Figueredo et al., 2011). Some vegetables in Indonesia, including Plucheaindica, contain 6.39 mg/100 g fw of flavonoids, lower than Cosmos caudatus (52.19 mg/100 g fw) and Polysciaspinnata (52.19 mg/100 g fw) (Andarwulan et al., 2010). Reports indicate that there is no significant difference in flavonoid concentration relative to the geographic altitude of Plucheaindica plant growth. However, the study noted that the choice of solvent in ethyl acetate fractions has higher flavonoid content compared to methanol, water, and n-butanol (Yuliani et al., 2015). Total flavonoid analysis shows that Plucheaindica tea contains 95.33 ± 0.48 mg CE/g of dry weight total flavonoid content. This study found that Plucheaindica tea has a significant effect in reducing total serum cholesterol, triglyceride levels, and LDL cholesterol. The flavonoid content in Plucheaindica has potential use in preventing hyperglycemia, obesity, and dyslipidemia (Sirichaiwetchakoon et al., 2020).

c. Alkaloids

Alkaloids are natural compounds typically containing one or more ring structures with at least one basic nitrogen atom. These low molecular weight structures are mostly found in plants and are generally synthesized from amino acids. Over 20,000 different alkaloids have been reported, with about 20% of all plant species producing alkaloids as secondary metabolites, which exhibit a wide range of structural diversity compared to other secondary metabolites (van Rootselaar et al., 2023). Despite their potential hazards, alkaloid-containing plants have long been used in the production of stimulants, sedatives, narcotics, insecticides, aphrodisiacs, and medications (Ziegler &Facchini, 2008). Alkaloid-containing plants have become a part of daily food consumption. Alkaloid content in the Pluchea genus, which belongs to the Asteraceae family, varies and has only been reported qualitatively in some studies (Ahmed &Kamel, 2013; Hussain et al., 2013; Widyawati et al., 2014b). Despite this, the mechanism of action of alkaloid compounds in plants shows similarities with certain diseases. For example, alkaloid mechanisms exhibit cytotoxic properties during mitosis, especially in the G2 and M phases, or act as topoisomerase inhibitors. Traditional plants with alkaloid content can be purified and compared for effectiveness with commonly used drugs like vincristine and vinblastine in human treatment (Zehnder et al., 2016). Research on Plucheaindica has identified active compounds such as alkaloids (0.316%), tannins (2.351%), and flavonoids (4.18%) (Febrianta et al., 2015).

d. Tannins

Tannins, also known as tannic acid, are water-soluble polyphenols found in various plant foods. Research indicates that tannins not only enhance digestive tract effectiveness but also reduce efficiency in converting digested nutrients into new body components. The treatment of degenerative diseases such as cancer has been associated with the consumption of tannin-rich foods like betel nuts and herbal teas, suggesting that tannins may have anticarcinogenic properties. Natural treatments in Asia use plant extracts containing tannins to alleviate symptoms of diarrhea and inflammation (Baba et al., 2021; Li et al., 2022; Ren et al., 2021). Tannin content has also been identified in Plucheaindica extracts in various studies. The bioactivity of tannins from Plucheaindica has been shown to affect glutamate levels in sperm from white rats, analyzed via HPLC. The reduction in glutamate levels in Plucheaindica extract-treated rats was 1,341.40 mg (100 g/gr), leading to improved sperm quality (Susetyarini, 2015). Quantitative analysis indicates that tannin content in Pluchea spp. ranges from 8.7 to 20 mg TAE/gr, reflecting the therapeutic potential of this plant (Qasim et al., 2017).

e. Saponins

Saponins are amphipathic glycosides with triterpene or steroid structures attached to one or more hydrophilic sugar groups such as glucuronic acid, glucose, galactose, rhamnose, and xylose. Most saponins are either monodesmoside or bidesmoside, meaning they have one or two sugar chains at different locations (Renda et al., 2022; Sharma et al., 2021). Steroidal saponins are among the most

significant active components, drawing attention for their pharmacological activities. Researchers are interested in certain steroidal saponins due to their potential as viable treatments (Xie et al., 2023). The presence of saponin compounds in Plucheaindica leaf extracts has been qualitatively investigated in several studies. Extraction methods such as maceration, percolation, and Soxhlet extraction have all shown the presence of saponins in each respective method (Lestari et al., 2020b). Extracts of Beluntas leaves used as a natural insecticide against Spodopteralitura also demonstrated saponin content in the leaves extracted through maceration for 72 hours (Muta'ali&Purwani, 2015).

4. Health Benefits of Beluntas Plant (Plucheaindica)

a. Antioxidant

Research on the antioxidant activity of chloroform extracts from Beluntas leaves shows strong antioxidant properties with an IC50 value of 107 ppm (Nafisah&Tukiran, 2017). Antioxidant activity was measured using the DPPH scavenging method. DPPH is a stable radical that appears violet in its radical form. Antioxidants react with DPPH through an electron donation mechanism, stabilizing DPPH as evidenced by a decrease in the violet color of DPPH, which gradually turns yellow. This decrease can be measured spectrophotometrically at λ 515 nm. The highest antioxidant activity was observed with PI3, having an IC50 of 16.66 µg/ml for DPPH scavenging activity (Indradi et al., 2017). Additionally, a study by Defitiana et al. (2019) assessed antioxidant activity using the DPPH method (2,2-diphenyl-1-picrylhydrazyl). Maceration of Beluntas leaf powder was performed using ethanol as the solvent. The ethanol extract was tested for antioxidant activity to determine the IC50 value using UV-Vis spectrophotometry at 517 nm. The results showed that the ethanol extract of Beluntas leaves had an IC50 value of 37.25 ppm, indicating strong antioxidant activity.

b. Antibacterial

Studies on the antibacterial activity of ethanol extracts from Beluntas leaves show that it inhibits the growth of Propionibacterium acnes at certain concentrations, as evidenced by the formation of clear zones around the wells. These clear zones indicate inhibition of bacterial growth. The antibacterial compounds found in Beluntas leaves include flavonoids, essential oils, phenolics, tannins, and alkaloids (Hafsari et al., 2015). Another study on the antibacterial activity of Beluntas leaves used the agar diffusion method with cylinder cups. Test solutions of 12%, 24%, 36%, 48%, and 60% were used for each bacterial test. The results showed that ethanol extract of Beluntas (Plucheaindica L.) provided inhibition diameters ranging from 1.203-1.593 cm against Staphylococcus aureus; 1.051-1.430 cm against Bacillus subtilis; and 1.143-1.525 cm against Pseudomonas aeruginosa (Manu, 2013). Plucheaindica L. contains flavonoids, alkaloids, saponins, and tannins. The highest inhibition diameters for Escherichia coli and Bacillus subtilis were obtained from Plucheaindica L. leaf extracts using the Soxhlet method (Lestari et al., 2020a). The antibacterial mechanism of flavonoids involves

forming complex compounds with extracellular and soluble proteins, damaging bacterial cell membranes, and leading to the release of intracellular compounds (Hafsari et al., 2015).

c. Cholesterol-Lowering

Another benefit of Beluntas leaves is their ability to lower cholesterol. This has been demonstrated in studies involving rats fed a high-fat diet and administered Plucheaindica (400 and 600 mg/kg daily), which resulted in significantly lower total triglycerides, total cholesterol, and LDL-C levels compared to the group only fed a high-fat diet. Additionally, the extract reduced perigonadal fat pad weight and adipocyte size while increasing the number of adipocytes per field of view in rats. These results align with our previous findings that PlucheaIndica Tea inhibits lipid and carbohydrate accumulation in adipocytes and interferes with pancreatic lipase activity, leading to a reduction in serum lipid profiles and obesity. Moreover, previous research found that caffeoylquinic acid derivatives, present in PlucheaIndica Tea, can suppress body fat accumulation caused by a high-fat diet by decreasing SREBP-1c regulation and related molecules in C57BL/6J mice. Additionally, caffeoylquinic acid has been reported to have antihyperlipidemic mechanisms by increasing PPARalpha and PPARdelta expression, reducing adiponectin, and enhancing the regulation of LPL and AMPK activity. Beta-caryophyllene, a major component in PlucheaIndica Tea, has also been reported to mitigate palmitate-induced lipid accumulation through AMPK signaling and prevent atherosclerosis in hypercholesterolemic mice (Sirichaiwetchakoon et al., 2020).

d. Diuretic

Treatment with Beluntas plant at doses of 100, 200, and 300 mg/kg, p.o., showed significant increases in Na+, K+, and Cl- excretion in rats. The extract also increased urine volume at all dose levels. The effect observed with a dose of 300 mg/kg was comparable to that of furosemide (20 mg/kg, p.o.), suggesting that Beluntas is an effective diuretic agent (Pramanik et al., 2007).

e. Anti-inflammatory

Beluntas leaves contain alkaloids, flavonoids, tannins, essential oils, chlorogenic acid, sodium, potassium, aluminum, calcium, magnesium, and phosphorus. Flavonoids, essential oils, and tannins are reported to have anti-inflammatory activity. Flavonoids inhibit the action of COX-2, leading to reduced production of prostaglandins. Tannins contribute hydrogen atoms to bind and neutralize free radicals, thereby controlling and reducing lipid autoxidation reactions by protecting cell membranes and reducing inflammation. The essential oil in Beluntas leaves, particularly eugenol, is suspected to have anti-inflammatory effects. Eugenol is reported to inhibit platelet aggregation by blocking thromboxane formation, contributing to its anti-inflammatory effects. Eugenol can also inhibit PGH synthase activity by competing with arachidonic acid at the active site of PGH synthase, thereby blocking the formation of PG (Sudirman et al., 2017). Therefore, the anti-inflammatory effects of Beluntas are likely mediated through one or a combination of these mechanisms.

Conclusion

Based on the literature review regarding the effectiveness of Beluntas leaves

(PlucheaIndica) as an Indonesian herbal remedy, it is evident that Beluntas leaves have significant potential as a herbal material that can enhance health. Specifically, Beluntas leaves offer numerous health benefits, including antioxidant, anti-inflammatory, antibacterial, diuretic, and cholesterol-lowering properties, as well as contributing to cellular health. As an Indonesian herbal plant, Beluntas can be processed into various forms without diminishing its health benefits and effectiveness.

Conflict Of Interest

The author declares that there is no conflict of interest regarding the writing of this article. This article is purely intended to contribute to the knowledge of the use of herbal materials for health.

Acknowledgement

References

Agati, G., Biricolti, S., Guidi, L., Ferrini, F., Fini, A., & Tattini, M. (2011). The biosynthesis of flavonoids is enhanced similarly by UV radiation and root zone salinity in L. vulgare leaves. *Journal of Plant Physiology*, *168*(3), 204–212. https://doi.org/10.1016/j.jplph.2010.07.016

Ahmed, S. A., & Kamel, E. M. (2013). Phenolic constituents and biological activity of the genus Pluchea. *Der Pharma Chemica*, *5*(5), 109–114.

Andarwulan, N., Batari, R., Sandrasari, D. A., Bolling, B., & Wijaya, H. (2010). Flavonoid content and antioxidant activity of vegetables from Indonesia. *Food Chemistry*, *121*(4), 1231–1235. https://doi.org/10.1016/j.foodchem.2010.01.033

Baba, A., Hoshino, T., Ogawa, S., & Takara, T. (2021). Improvement of glucose metabolism and safety of acacia bark-derived proanthocyanidins in healthy Japanese adults: A Randomized, Double-blind, Placebo-controlled, Parallel-group Trial. *Functional Foods in Health and Disease*, *11*(9), 431. https://doi.org/10.31989/ffhd.v11i9.822

Birch, S., Alraek, T., Bovey, M., Lee, M. S., Lee, J. A., Zaslawski, C., Robinson, N., Kim, T.-H., & Bian, Z. (2020). Overview on pattern identification – History, nature and strategies for treating patients: A narrative review. *European Journal of Integrative Medicine*, *35*, 101101. https://doi.org/10.1016/j.eujim.2020.101101

Blainski, A., Lopes, G., & de Mello, J. (2013). Application and Analysis of the Folin Ciocalteu Method for the Determination of the Total Phenolic Content from Limonium Brasiliense L. *Molecules*, *18*(6), 6852–6865. https://doi.org/10.3390/molecules18066852

Buapool, D., Mongkol, N., Chantimal, J., Roytrakul, S., Srisook, E., & Srisook, K. (2013). Molecular mechanism of anti-inflammatory activity of Pluchea indica leaves in macrophages RAW 264.7 and its action in animal models ofinflammation. *Journal of Ethnopharmacology*, *146*(2), 495–504. https://doi.org/10.1016/j.jep.2013.01.014

Chacko, S. M., Thambi, P. T., Kuttan, R., & Nishigaki, I. (2010). Beneficial effects of green tea: A literature review. *Chinese Medicine*, *5*(1), 13. https://doi.org/10.1186/1749-8546-5-13

Chiangnoon, R., Samee, W., Uttayarat, P., Jittachai, W., Ruksiriwanich, W., Sommano, S. R., Athikomkulchai, S., & Chittasupho, C. (2022). Phytochemical Analysis, Antioxidant, and Wound Healing Activity of Pluchea indica L. (Less) Branch Extract Nanoparticles. *Molecules*, *27*(3). https://doi.org/10.3390/molecules270306

35

Defitiana wanita, Rusmini, Ashfia, F., & Yustisia, F. (2019). Uji aktivitas antioksidan ekstrak etanol daun beluntas (Pluchea indica L.) dengan metode DPPH (2, 2-DIFENIL-1-PIKRILHIDRAZIL). *Indonesian Chemistry and Application Journal*, *2*(2), 25. https://doi.org/10.26740/icaj.v2n2.p25-28

Dwi, Y., Werdani, W., & Widyawati, P. S. (2018). *Antidiabetic Effect of Pluchea Indica Less Tea as a Functional Beverage in Diabetic Patients*. *98*(Icpsuas 2017), 164–167.

Ernawati, Suryadi, H., & Mun'im, A. (2021). Effect of gamma irradiation on the caffeoylquinic acid derivatives content, antioxidant activity, and microbial contamination of Pluchea indica leaves. *Heliyon*, *7*(8), e07825. https://doi.org/10.1016/j.heliyon.2021.e07825

Febrianta, H., Yunianto, V. D., & Sukamto, B. (2015). Effects of Pluchea indica Less Leaf Extract and Chlorine to Hematological Profiles of Broiler Chickens. *International Journal of Poultry Science*, *14*, 584–588. https://doi.org/10.3923/ijps.2015.584.588

Figueredo, S. M., Do Nascimento, F. P., Freitas, C. S., Baggio, C. H., Soldi, C., Pizzolatti, M. G., De Ibarrola, M. D. C. C., De Arrua, R. L. D., & Santos, A. R. S. (2011). Antinociceptive and gastroprotective actions of ethanolic extract from Pluchea sagittalis (Lam.) Cabrera. *Journal of Ethnopharmacology*, *135*(3), 603–609. https://doi.org/10.1016/j.jep.2011.03.006

Fitriansyah, M. I., Indradi, R. B., Farmasi, F., & Padjadjaran, U. (2018). Review : Profil Fitokimia dan Aktivitas Farmakologi Baluntas (Pluchea indica L.). *Farmaka Suplemen*, *16*, 337–346.

Hafsari, A. R., Tri, C., Toni, S., & Rahayu, I. L. (2015). Uji Aktivitas Antibakteri Daun Beluntas. (Pluchea Indica (L.) LESS.) terhadap Propionibacterium Acnes penyebab jerawat, *Biomelolekuler 9(1), 142–161.*

Hussain, H., Al-Harrasi, A., Abbas, G., Rehman, N. U., Mabood, F., Ahmed, I., Saleem, M., van Ree, T., Green, I. R., Anwar, S., Badshah, A., Shah, A., & Ali, I. (2013). The Genus Pluchea: Phytochemistry, Traditional Uses, and Biological Activities. *Chemistry & Biodiversity*, *10*(11), 1944–1971. https://doi.org/10.1002/cbdv.201200140

Indradi, R. B., Fidrianny, I., & Wirasutisna, K. R. (2017). *DPPH Scavenging Activities and Phytochemical Content of Four Asteraceae Plants*. *9*(6), 755–759. https://doi.org/10.25258/phyto.v9i6.8173

Jha, N. K., Sharma, C., Hashiesh, H. M., Arunachalam, S., Meeran, M. N., Javed, H., Patil, C. R., Goyal, S. N., & Ojha, S. (2021). β-Caryophyllene, A Natural Dietary CB2 Receptor Selective Cannabinoid can be a Candidate to Target the Trinity of Infection, Immunity, and Inflammation in COVID-19. *Frontiers in Pharmacology*, *12*. https://doi.org/10.3389/fphar.2021.590201

Kongkiatpaiboon, S., Chewchinda, S., & Vongsak, B. (2018). Optimization of extraction method and HPLC analysis of six caffeoylquinic acids in Pluchea indica leaves from different provenances in Thailand. *Revista Brasileira de Farmacognosia*, *28*(2), 145–150. https://doi.org/10.1016/j.bjp.2018.03.002

Lestari, K. A. P., Pranoto, P. P., Sofiyah, S., Musyirah, M., & Pratiwi, F. I. (2020a). Antibacterial Activity of Beluntas (Pluchea indica L.) Leaves Extract using Different Extraction Methods. *Jurnal Riset Biologi Dan Aplikasinya*, *2*(2), 49. https://doi.org/10.26740/jrba.v2n2.p49-54

Lestari, K. A. P., Pranoto, P. P., Sofiyah, S., Musyirah, M., & Pratiwi, F. I. (2020b). Antibacterial Activity of Beluntas (Pluchea indica L.) Leaves Extract using Different Extraction Methods. *Jurnal Riset Biologi*

Dan Aplikasinya, *2*(2), 49. https://doi.org/10.26740/jrba.v2n2.p49-54

Li, Y., Zhu, L., Guo, C., Xue, M., Xia, F., Wang, Y., Jia, D., Li, L., Gao, Y., Shi, Y., He, Y., & Yuan, C. (2022). Dietary Intake of Hydrolyzable Tannins and Condensed Tannins to Regulate Lipid Metabolism. *Mini-Reviews in Medicinal Chemistry*, *22*(13), 1789–1802. https://doi.org/10.2174/1389557522666211229112223

Lu, M.-F., Xiao, Z.-T., & Zhang, H.-Y. (2013). Where do health benefits of flavonoids come from? Insights from flavonoid targets and their evolutionary history. *Biochemical and Biophysical Research Communications*, *434*(4), 701–704. https://doi.org/10.1016/j.bbrc.2013.04.035

Manu, R. R. S. (2013). Aktivitas antibakteri ekstrak etanol daun beluntas (. *Calyptra: Jurnal Ilmiah Mahasiswa Universitas Surabaya*, *2*(1), 1–10.

Muta'ali, R., & Purwani, K. I. (2015). Effect of Beluntas (Pluchea indica) Leaf Extract on Mortality and Development of Spodoptera litura F Larvae. *Jurnal Sains Dan Seni ITS*, *4*(2).

Nafisah, M., & Tukiran, D. (2017). Uji Antioksidan Dan Identifikasi Senyawa Aktif Dari Ekstrak Kloroform Daun Tanaman Beluntas (Pluchea indica L.). Antioxidant Test And Identification Of Active Compounds Form Chloroform Extract Of Beluntas (Pluchea indica L.) Leaf. *UNESA Journal of Chemistry*, *6*(2).

Nopparat, J., Nualla-Ong, A., & Phongdara, A. (2019). Ethanolic extracts of Pluchea indica (L.) leaf pretreatment attenuates cytokine-induced β-cell apoptosis in multiple low-dose streptozotocin-induced diabetic mice. *PLoS ONE*, *14*(2), 1–20. https://doi.org/10.1371/JOURNAL.PONE.0212133

Pramanik, K. C., Biswas, R., Mitra, A., Bandyopadhyay, D., Mishra, M., & Chatterjee, T. K. (2007). Tissue culture of the plant Pluchea indica (L.) Less. and evaluation of diuretic potential of its leaves. *Oriental Pharmacy and Experimental Medicine*, *7*(2), 197–204. https://doi.org/10.3742/opem.2007.7.2.197

Qasim, M., Abideen, Z., Adnan, M. Y., Gulzar, S., Gul, B., Rasheed, M., & Khan, M. A. (2017). Antioxidant properties, phenolic composition, bioactive compounds and nutritive value of medicinal halophytes commonly used as herbal teas. *South African Journal of Botany*, *110*, 240–250. https://doi.org/10.1016/j.sajb.2016.10.005

Ren, Y., Zhang, X., Li, T., Zeng, Y., Wang, J., & Huang, Q. (2021). Galla Chinensis, a Traditional Chinese Medicine: Comprehensive review of botany, traditional uses, chemical composition, pharmacology and toxicology. *Journal of Ethnopharmacology*, *278*, 114247. https://doi.org/10.1016/j.jep.2021.114247

Renda, G., Gökkaya, İ., & Şöhretoğlu, D. (2022). Immunomodulatory properties of triterpenes. *Phytochemistry Reviews*, *21*(2), 537–563. https://doi.org/10.1007/s11101-021-09785-x

Ribeiro, D., Freitas, M., Lima, J. L. F. C., & Fernandes, E. (2015). Proinflammatory Pathways: The Modulation by Flavonoids. *Medicinal Research Reviews*, *35*(5), 877–936. https://doi.org/10.1002/med.21347

Rolnik, A., & Olas, B. (2021). *The Plants of the Asteraceae Family as Agents in the Protection of Human Health*.

Ruan, J., Li, Z., Yan, J., Huang, P., Yu, H., Han, L., Zhang, Y., & Wang, T. (2018). Bioactive constituents from the aerial parts of pluchea indica less. *Molecules*, *23*(9), 1–11. https://doi.org/10.3390/molecules23092104

Salaritabar, A., Darvishi, B., Hadjiakhoondi, F.,

Manayi, A., Sureda, A., Nabavi, S. F., Fitzpatrick, L. R., Nabavi, S. M., & Bishayee, A. (2017). Therapeutic potential of flavonoids in inflammatory bowel disease: A comprehensive review. *World Journal of Gastroenterology*, *23*(28), 5097. https://doi.org/10.3748/wjg.v23.i28.5097

Setyowati, N., Masyhuri, Mulyo, J. H., Irham, & Yudhistira, B. (2023). The hidden treasure of wedang uwuh, an ethnic traditional drink from Java, Indonesia: Its benefits and innovations. *International Journal of Gastronomy and Food Science*, *31*, 100688. https://doi.org/10.1016/j.ijgfs.2023.100688

Sharma, P., Tyagi, A., Bhansali, P., Pareek, S., Singh, V., Ilyas, A., Mishra, R., & Poddar, N. K. (2021). Saponins: Extraction, bio-medicinal properties and way forward to anti-viral representatives. *Food and Chemical Toxicology*, *150*, 112075. https://doi.org/10.1016/j.fct.2021.112075

Singdam, P., Naowaboot, J., Senggunprai, L., Boonloh, K., & Pannangpetch, P. (2022). Pluchea indica Leaf Extract Alleviates Dyslipidemia and Hepatic Steatosis by Modifying the Expression of Lipid Metabolism-Related Genes in Rats Fed a High Fat-High Fructose Diet. *Preventive Nutrition and Food Science*, *27*(4), 384–398. https://doi.org/10.3746/pnf.2022.27.4.384

Sirichaiwetchakoon, K., Lowe, G. M., Kupittayanant, S., Churproong, S., & Eumkeb, G. (2020). Pluchea indica (L.) Less. Tea Ameliorates Hyperglycemia, Dyslipidemia, and Obesity in High Fat Diet-Fed Mice. *Evidence-Based Complementary and Alternative Medicine*, *2020*(Cvd). https://doi.org/10.1155/2020/8746137

Srivastava, P., & Shanker, K. (2012). Pluchea lanceolata (Rasana): Chemical and biological potential of Rasayana herb used in traditional system of medicine. *Fitoterapia*, *83*(8), 1371–1385. https://doi.org/10.1016/j.fitote.2012.07.008

Sudirman, R. S., Usmar, U., Rahim, A., & Bahar, M. A. (2017). Aktivitas Anti-inflamasi Ekstrak Etanol Daun Beluntas (Pluchea indica L.) pada Model Inflamasi Terinduksi CFA (Complete Freund's Adjuvant). *Jurnal Farmasi Galenika (Galenika Journal of Pharmacy) (e-Journal)*, *3*(2), 191–198. https://doi.org/10.22487/j24428744.0.v0.i0.8921

Sudjaroen, Y. (2012). Evaluation of ethnobotanical vegetables and herbs in Samut Songkram province. *Procedia Engineering*, *32*, 160–165. https://doi.org/10.1016/j.proeng.2012.01.1251

Suriyaphan, O. (2014). Nutrition, health benefits and applications of Pluchea indica (L.) Less leaves. *Mahidol University Journal of Pharmaceutical Sciences*, *41*(4), 1–0. https://pharmacy.mahidol.ac.th/journal/_files/2014-41-4_01-10.pdf

Susetyarini, R. E. (2015). The Level of Glutamic Acid in the Semen of Male White Rat (Ratus Norwegicus) after Being Treated with Tannin of Pluchea Indica. *Procedia Chemistry*, *14*, 152–156. https://doi.org/10.1016/j.proche.2015.03.022

Tan, B. L., Norhaizan, M. E., Liew, W.-P.-P., & Sulaiman Rahman, H. (2018). Antioxidant and Oxidative Stress: A Mutual Interplay in Age-Related Diseases. *Frontiers in Pharmacology*, *9*. https://doi.org/10.3389/fphar.2018.01162

van Rootselaar, S., Peterse, E., Blanco-Ania, D., & Rutjes, F. P. J. T. (2023). Stereoselective Mannich Reactions in the Synthesis of Enantiopure Piperidine Alkaloids and Derivatives. *European Journal of Organic Chemistry*, *26*(22). https://doi.org/10.1002/ejoc.202300053

Vongsak, B., Kongkiatpaiboon, S., Jaisamut, S., &

Konsap, K. (2018). Comparison of active constituents, antioxidant capacity, and α-glucosidase inhibition in Pluchea indica leaf extracts at different maturity stages. *Food Bioscience*, *25*, 68–73. https://doi.org/10.1016/j.fbio.2018.08.006

Wei, E., Chan, C., Ng, Y. K., Wong, S. K., & Chan, H. T. (2022). *P harmaceutical S ciences A sia Pluchea indica : An updated review of its botany , uses , bioactive compounds and pharmacological properties*. *49*(1), 77–85. https://doi.org/10.29090/psa.2022.01.21.113

Widhiantara, I. G., & Jawi, I. M. (2021). Phytochemical composition and health properties of Sembung plant (Blumea balsamifera): A review. *Veterinary World*, *14*(5), 1185–1196. https://doi.org/10.14202/vetworld.2021.1185-1196

Widyawati, P. S., Budianta, T. D. W., Kusuma, F. A., & Wijaya, E. (2014a). Difference of solvent polarity to phytochemical content and antioxidant activity of Pluchea indicia less leaves extracts. *International Journal of Pharmacognosy and Phytochemical Research*, *6*(4), 850–855.

Widyawati, P. S., Budianta, T. D. W., Kusuma, F. A., & Wijaya, E. L. (2014b). Difference of solvent polarity to phytochemical content and antioxidant activity of Pluchea indicia less leaves extracts. *International Journal of Pharmacognosy and Phytochemical Research*, *6*(4), 850–855.

Widyawati, P. S., Wijaya, C. H., Hardjosworo, P. S., &Sajuthi, D. (2013). Volatile Compounds of Pluchea indica Less and Ocimum basillicum Linn Essential Oiland Potency as Antioxidant. *HAYATI Journal of Biosciences*, *20*(3), 117–126. https://doi.org/10.4308/hjb.20.3.117

Xie, H., Shi, X., Zhao, D., Wang, B., Jin, Y., & Li, X. (2023). A review: The structures and bioactivities of steroidal saponins from Allium macrostemon Bulbus. *Phytochemistry Letters*, *57*, 210–226. https://doi.org/10.1016/j.phytol.2023.08.018

Yuliani, Y., Yanuwiadi, B., & Leksono, A. (2015). Total phenolic and flavonoid contents of pluchea indica less leaves extracts from some altitude habitats. *International Journal of ChemTech Research*, *8*(4), 1618–1625.

Zehnder •, A., Graham •, J., Reavill •, D. R., & McLaughlin, A. (2016). Neoplastic diseases in avian species. In *Current Therapy in Avian Medicine and Surgery* (pp. 107–141). Elsevier. https://doi.org/10.1016/B978-1-4557-4671-2.00012-4

Ziegler, J., & Facchini, P. J. (2008). Alkaloid Biosynthesis: Metabolism and Trafficking. *Annual Review of Plant Biology*, *59*(1), 735–769. https://doi.org/10.1146/annurev.arplant.59.032607.092730