

Crassocephalum crepidioides (Bioactivity and Utilization)

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Abstract. *Crassocephalum crepidioides* (Asteraceae) is a wild plant that has long been used as food and traditional medicine. The use of plants as food ingredients is related to their nutritional content, while as traditional medicine they are related to their bioactive compounds. This study aims to explain the nutritional content and bioactivity of *C. crepidioides*. The method used in this study is a literature review on various scientific articles published online using the keywords *C. crepidioides*, bioactivities of *C. crepidioides* and uses of *C. crepidioides*. The results obtained were synthesized so as to explain the benefits and bioactivity of *C. crepidioides*. Ethnobotanically *C. crepidioides* is used to treat stomach ulcers, indigestion, wounds, ulcers, burns, treatment of wounds, gastric ulcers, and conditions related to the skin. In some countries *C. crepidioides* has been cultivated and traded. The bioactivity of *C. crepidioides* includes antioxidant, antibacterial, anti-hyperlipidemia, antidiabetic mellitus, antimalarial and anti-cancer. Utilization of *C. crepidioides* as a traditional medicine and food ingredient so that it has potential as a nutraceutical.

Keywords: *Crassocephalum crepidioides*; antibacterial, nutraceutical

1 Introduction

Crassocephalum crepidioides is a species belonging Asteraceae, which has been long been used as a food ingredient [1] and traditional medicine [2]. The local ethnic in Indonesia such as Sundanese used the young leaves of *C. crepidioides* as lalaban (a vegetable that is eaten fresh) [3]. Dairo & Adanlawo [1] stated that *C. crepidioides* is a good source of protein for human and animal nutrition. This plant is easy to find in the surrounding environment, especially disturbed field such as yards, roadsides, gardens and in rice fields. Its short life cycle and the production of many seeds facilitate its dispersal. *Crassocephalum crepidioides* is a weed plant that is spread in tropical Asia, including Indonesia [4].

Based on ethnomedicine research, the *C. crepidioides* is used to treat stomach ulcers, indigestion, wounds, ulcers, burns [2], treatment of wounds, gastric ulcers, and conditions related to the skin [5]. Local people of Lam Dong, Vietnam use *C. crepidioides* to treat wounds [6]. Adjatin et al. [7] stated that *C. crepidioides* has cultivated by local communities in Benin (Africa) as a vegetable, which their consumed or to commercial purposes because of its good nutritional content. The ethnic Bajau in Belud (Sabah) have been consumed as edible wild vegetables and have been traded in traditional markets [8]. Utilization of *C. crepidioides* as a traditional medicine and food ingredient so that it has potential as a nutraceutical.

The bioactivity of *C. crepidioides* as a traditional medicine is related to its secondary metabolite content, while its use as a food ingredient is related to its nutritional content. *C. crepidioides* methanol extract contains phenolic compounds, has antioxidant activity and affects anticholinesterase activity [9]. *C. crepidioides* contains phenolic acids (gallic, chlorogenic, caffeic, and ellagic acids) and flavonoids (catechins, rutin and quercetin) [9]. On the other hand, *C. crepidioides* also has nutritional values such as crude protein, crude fiber, ash content, amino acid values of threonine, and tyrosine. Total amino acids (19.01 ± 0.08 mg/g) while total non-essential amino acids (11.23 ± 0.06 mg/g) [1].

Although there have been many studies on *C. crepidioides*, there is a comprehensive study on its benefits and bioactivity. This study aims to explain the relationship between the use of *C. crepidioides* as a food ingredient and traditional medicine and its bioactivity so that its potential as standardized traditional and herbal medicine can be increased.

2 Research Methods

The method used in writing this article is a literature review of research results published online at Google Scholar using the keywords *C. crepidioides*, bioactivities of *C. crepidioides* and uses of *C. crepidioides*. The results obtained were then synthesized so that they could explain the botany, benefits and bioactivity of *C. crepidioides*.

3 Result and Discussion

3.1 Botany of *Crassocephalum crepidioides*

Asteraceae is a family that is considered the most diverse and one of the largest in most flowering plants having about 1620 genera and 23,000 species [10]. Many species in the Asteraceae family have higher economic value because they are widely used as traditional medicines and food ingredients, one of which is *C. crepidioides*.

C. crepidioides is an erect, low-branched perennial, 6.0 to 12.0 cm tall with soft roots. The stems are green sometimes with purple pigmentation when the plant is young or when flowering. Leaf lyrate or elliptic pinnatifid, lobed with 1-2 lobes, margin serrated or coarsely toothed, apex acute, alternating, pubescent 14.6-18.9 cm long and 7.7 to 9.5 cm wide, provision length from 1.8 - 3.9 cm long and 1.4 - 1.9 cm wide, petiole length from 3.7 - 4.2 cm, with bearded double head peduncle between 3.6 to 16.1 cm (Figure 1) [11].



Fig1. *Crassocephalum crepidioides*. Left. Habits; Center. Leaf; Right. Flowering.

Crassocephalum crepidioides germination at temperatures ranging from 10 to 30 or 10 to 40 °C and pH levels are within 4 to 10 [12]. *C. crepidioides* is widespread in tropical or subtropical regions but is mostly available in tropical Africa. *C. crepidioides* usually occurs in large populations in open dumps, wastelands or along roadsides in almost all vegetation zones in southwest Nigeria [11].

3.2 Uses And Bioactivities

Secondary metabolites is metabolites produced through secondary metabolic processes that plants uses as adaptations. Some secondary metabolites have been long used by humans as traditional medicine and as phytopharmaceuticals such as essential oils. The use of *C. crepidioides* as a traditional medicine is related to its secondary metabolites. The hexane fraction of *C. crepidioides* has compounds such as hexadecenoic methyl ester and linolenic acid has activity as hypocholesterolemia. The benzo furanone and benzofuran of *C. crepidioides* has anticancer and antiviral activity whereas the phenolic and flavonoid compounds has antioxidant, anti-inflammatory activity [2].

C. crepidioides has long been used as a food ingredient and traditional medicine. *C. crepidioides* is used to treat stomach ulcers, indigestion, wounds, ulcers, burns [13], treatment of wounds, gastric ulcers, and skin-related conditions [5]. The use of *C. crepidioides* as a traditional medicine is related to its bioactivity and will be discussed further.

Antioxidant

Free radicals are often associated with various diseases such as heart disease, diabetes mellitus and cancer, therefore the search for compounds that inhibit free radicals or also known as antioxidants continues to be carried out. Foodstuffs that also have bioactive compounds as antioxidants have advantages compared to other medicinal ingredients because their toxicity has been tested, including *C. crepidioides*. In laboratory experiments, the antioxidant activity in vitro can be tested using the compound 1,1-diphenyl-2-picrylhydrazyl (DPPH), 2,2-azinobis (3-ethylbenzo-thiazoline-6-sulfonate (ABTS) [9]. Aqueous extract of *C. crepidioides* has strong activity to scavenge superoxide anion free radicals, hydroxyl radicals and 1,1-diphenyl-2-picrylhydrazyl [14]. Carbon tetrachloride (CCl₄) causes liver damage through increased activity of aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Isochlorogenic acid, quercetin and kaempferol glycosides were identified as active components of *C. crepidioides* with strong free radical scavenging action [14].

The activity of *C. crepidioides* as an antioxidant is related to the content of its secondary metabolites. *C. crepidioides* methanol extract contains phenolic compounds that have antioxidant activity and affect anticholinesterase activity [9]. *C. crepidioides* contains phenolic acids (gallic, chlorogenic, caffeic, and ellagic acids) and flavonoids (catechins, rutin and quercetin) [9]. The unbleached *C. crepidioides* methanol extract had higher inhibition of antioxidants, acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) than the boiled *C. crepidioides* extract. This is related to *C. crepidioides* extracts that are not pale have a higher phenolic concentration compared to boiled *C. crepidioides* [9].

The content of secondary metabolites in plants is influenced by the substances used for extraction. *C. crepidioides* ethanol extract containing TPC and TFC was compared with hot water extract and aqueous extract. This results in different antioxidant activities. IC₅₀ DPPH test shows that distilled water > hot water > ethanol, while IC₅₀ ABTS shows hot water > distilled water > ethanol. There is a high negative correlation between TPC in *C. crepidioides* leaf extract with IC₅₀ DPPH and ABTS test. Following the same trend, there was also a high

negative correlation between TFC in *C. crepidioides* leaf extract with IC50 DPPH and ABTS tests [8].

Anti-Cancer

Cancer is a disease caused by uncontrolled cell growth, therefore plants used or potentially as cancer drugs are plants that produce compounds that can inhibit cell growth. *C. crepidioides* extract slowed the growth of S-180 tumor cells in mice. The RAW 264.7 macrophage supernatant stimulated by cultured *C. crepidioides* was cytotoxic to S-180 cells. *C. crepidioides* cytotoxicity is associated with nitric oxide (NO) production via the NF- κ B signaling pathway critical for transcriptional activation of the iNOS gene. Isochlorogenic acid is a *C. crepidioides* content that induces NF-B activation and iNOS expression [15].

Anti-Malaria

Malaria is one of the diseases in tropical countries including Indonesia that cannot be fully controlled, so the search for anti-malarial bioactive compounds continues to be carried out, including *C. crepidioides*. Three derivatives of dihydroisocoumarin *C. crepidioides* have antimalarial activity, namely 7-butyl-6,8-dihydroxy-3(R)-pent-11-enylisochroman-1-one (1), 7-but-15-enyl-6,8-dihydroxy-3(R)-pent-11-enylisochroman-1-one (2), and 7-butyl-6,8-dihydroxy-3(R)-pentyloisochroman-1-one (3) [16].

Anti-Bacterial

Various types of pathogenic bacteria cause various infectious diseases in humans. The bioactivity of *C. crepidioides* as an antimicrobial is related to the content of its secondary metabolites such as flavonoids, polyphenols, saponins and tannins [4]. *C. crepidioides* essential oil has antibacterial activity [17], inhibits the growth of Gram-positive bacteria such as: *Salmonella typhi* [4,17], *Staphylococcus aureus*, *Bacillus subtilis*) and Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) [17]. the inhibition depends on the concentration of *C. crepidioides* leaf extract with a concentration of 10% (\pm 9.82), at a concentration of 30% (\pm 10.82) while the control is positive (\pm 8.87) [4].

The main content of *C. crepidioides* leaf essential oil is -caryophyllene and cubebene, while the stem essential oil is mostly thymol and 4-cyclohexibutyramide. The results of the lethality test of brine shrimp showed that the stem essential oil (LC50 = 9.10 g/mL) was as toxic as the leaf essential oil (LC50 = 9.2 g/mL). The essential oil is active against all bacterial strains but low when compared to the standard antibiotic, Gentamicin [17].

Anti Hiperlipidemia

Hyperlipidemia is a condition where blood lipid levels are above normal, which can directly or indirectly affect heart function. To induce hyperlipidemic rats can be done with a diet high in fat and triton WR-100 (iso-octyl polyoxymethylene phenol). Some indicators of hyperlipidemia can be measured by total serum cholesterol (TC), high density lipoprotein cholesterol (HDL-c), triglycerides (TG), very low-density lipoprotein cholesterol (VLDL-c), low density lipoprotein cholesterol (LDL-c) and index atherogenic (AI).

The hyperlipidemic mice treated with *C. crepidioides* extract significantly reduced serum TC, TG, LDL-c and VLDL-c levels, but serum HDL-c levels significantly increased. Triton-induced hyperlipidemic mice resulted in significantly reduced serum TC, TG, LDLc, VLDL-c levels but significantly increased serum HDL-c levels [18,19].

Anti-Diabetes Mellitus

Diabetes mellitus is a metabolic disorder caused by blood glucose levels above normal, thus affecting the homeostasis of the circulatory system [2]. Experiments in the laboratory to induce diabetic mice were given STZ. Methanol extract and *C. crepidioides* fraction at concentrations of 50, 100, and 200 mg/kg significantly prolong bleeding (58-200%), clotting (65-133%), prothrombin (176-441%), and thromboplastin (209-518%) times in diabetic rats compared to control rats (LD50 5000 mg/kg). Research shows that *C. crepidioides* has anticoagulant and antianemic activity. Canned *C. crepidioides* leaves are a potential source of novel anticoagulants and nutraceuticals for the management of thrombotic disorders in diabetes [2].

Anti-Injury

Open injury is of the entrances for various microbes that cause various infections in humans. The main goal in wound healing is to reduce the size or close the exposed tissue through the formation of new tissue. The hydroethanolic extract of *C. crepidioides* (CCLE) at a dose of 50 mg/kg/day reduced wound closure time by about 3.5 days. The granulation tissue on day 7 after surgery of the treated group showed a 2.8-fold decrease in inflammatory cell density, a 1.9-fold increase in fibroblast density, and a higher vascular count. The wound healing activity of CC leaves is related to its activity as an antioxidant, anti-inflammatory, fibroblast proliferation, wound contraction, and the effect of angiogenesis [6].

Anti-Coagulant

Various diseases in humans often have implications for the occurrence of blood clotting disorders. Compounds or drugs that are used to inhibit the blood clotting process are referred to as anti-coagulant compounds. *C. crepidioides* leaf extract and methanol fraction significantly lengthened clotting time, prothrombin and thromboplastin time in blood. The highest elongation effect was recorded with the hexane fraction with a concentration of 10 mg/mL. Bioactivity as an anti-coagulant is thought to be related to the *C. crepidioides* phytochemical content such as unsaturated fatty acids and esters, phenolic compounds, flavonoids, and coumarins [5].

4 Conclusion

- a. Ethnobotanically *C. crepidioides* is used to treat stomach ulcers, indigestion, wounds, ulcers, burns, treatment of wounds, gastric ulcers, and conditions related to the skin. In some countries *C. crepidioides* has been cultivated and traded.
- b. The bioactivity of *C. crepidioides* includes antioxidant, anti-bacterial, anti-hyperlipidemia, antidiabetic mellitus, antimalarial and anti-cancer. Utilization of *C. crepidioides* as a traditional medicine and food ingredient so that it has potential as a nutraceutical.

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