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Utilization of *Oxalis corniculata* Linn as a traditional medicine and its bioactivity

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Abstract

Oxalis corniculata Linn. (Oxalidaceae) has been long used as traditional medicine and has been recorded in traditional medicine systems such as Ayurveda, Unani and Siddha. This study explains the relationship between the use of *O. corniculata* as traditional medicine and its bioactivity. The method used in this research is library research online, especially from Google Scholar, using the keywords *O. corniculata*, uses of *O. corniculata* and bioactivity of *O. corniculata*. The results obtained were synthesized so as to provide comprehensive information about the botany, benefits and bioactivity of *O. corniculata*. In traditional medicine *O. corniculata* is used to treat liver disorders, jaundice, skin diseases, and urinary tract. *O. corniculata* bioactivity as an antioxidant, anti-microbial, anti-neurodegenerative, anti-diabetic mellitus, anti-cancer, anti-implantation, anxiolytic, and hepatoprotective. The *O. corniculata* contains a rich source of essential fatty acids such as palmitic, oleic, linolenic and stearic acids with various pharmacological activities. The bioactivity of *O. corniculata* as an antimicrobial can be developed as an alternative food ingredient as well as neurodegenerative as well as a natural preservative.

Keywords: *Oxalis corniculata*; Anti-microbial; Linoleate; Neurodegenerative

1. Introduction

Oxalis corniculata Linn. (Oxalidaceae) is a of the important medicinal plants originating from the tropics and subtropics. The use of *O. corniculata* as a traditional medicine has been recorded in traditional medicine systems such as Ayurveda, Unani and Siddha [1]. This plant is able to adapt to various environmental conditions [2], therefore this plant is easily found in various landscapes such as yards, roadsides, gardens, fields and abandoned land. Although adaptable, *O. corniculata* populations show different morphological responses to changes in environmental conditions [2].

Tibuhwa [3] stated that apart from being used as traditional medicine, *O. corniculata* is traditionally used as a raw vegetable. In traditional medicine, *O. corniculata* is used to treat liver disorders, jaundice, skin diseases, and urinary tract [4]. The *O. corniculata* is proven to have various pharmacological activities such as liver tonic, appetizer, diuretic, anthelmintic, emmenagogue, anti-inflammatory, analgesic, antipyretic, blood purifier [4]. The bioactivity of *O. corniculata* includes anti-inflammatory, anxiolytic, anticonvulsant, antifungal, antiulcer, antinociceptive, anticancer, antidiabetic, hepatoprotective, hypolipidemic, abortive, antimicrobial and wound healing [5]. The methanol extract of *O. corniculata* leaves contains embelin as the main compound reported to have anticancer, antioxidant, antitumor, and anti-inflammatory activities [6].

The use of plants as food ingredients is related to their nutritional content, while as traditional medicinal ingredients they are related to the content of their secondary metabolites. The phytochemical *O. corniculata* content includes

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flavonoids, tannins, phytosterols, phenols, glycosides, fatty acids, galactoglycerolipids and essential oils [6]. Important minerals contained in *O. corniculata* such as sodium, potassium, calcium, and nitrogen [5]. The essential fatty acids found in *O. corniculata* such as palmitic, oleic, linolenic and stearic acids have various pharmacological activities such as antioxidant, anti-cancer, anthelmintic, anti-inflammatory, antimicrobial, astringent, diuretic, febrifuge, cardio-relaxant, and the nature of the stomach [9]. The methanol extract of *O. corniculata* contains Vitamin E and squalene which have bioactivity as antioxidants [10]. Sitosterol compounds, betulin, 4-hydroxybenzoic acid, ethyl gallate, methoxy flavones, apigenin, and 7-O- β -D-glucopyranoside have been isolated from the whole of *O. corniculata* [5].

The use of *O. corniculata* as traditional medicine is often questioned because of its high oxalate content, which can form insoluble salts with physiological calcium. Extraction of *O. corniculata* leaves was carried out using different solvents and methods, and extract analysis studies showed that the oxalate content decreased on drying of the material. The methanolic extract of stems and leaves of *O. corniculata* which had lower oxalate was obtained using sequential extraction [11]. Until now, in-depth studies on the bioactivity of *O. corniculata* are very limited. This study aims to explain the use of *O. corniculata* as a traditional medicine and its bioactivity so that its potential as a nutraceutical can be improved.

2. Methods

The method used in this research is library research online. The main sources are reports, research results, journals, and books obtained from Google Scholar using the keywords *O. corniculata*, uses of *O. corniculata* and bioactivity of *O. corniculata*. The results obtained were synthesized so as to provide comprehensive information about the botany, benefits and bioactivity of *O. corniculata*.

3. Results and discussion

3.1. Botany of *Oxalis corniculata* Linn

The largest genus of the Oxalidaceae family is *Oxalis* L., which is mostly distributed in Southern Africa and South America, and consists of more than 500 species [12]. One type of *Oxalis* that is widely used as traditional medicine and food is *O. corniculata*. The origin of this species is not known with certainty, but it is a cosmopolitan species. In some areas of Malesia, this species does not appear to be widely found until the 1970 [13,14].

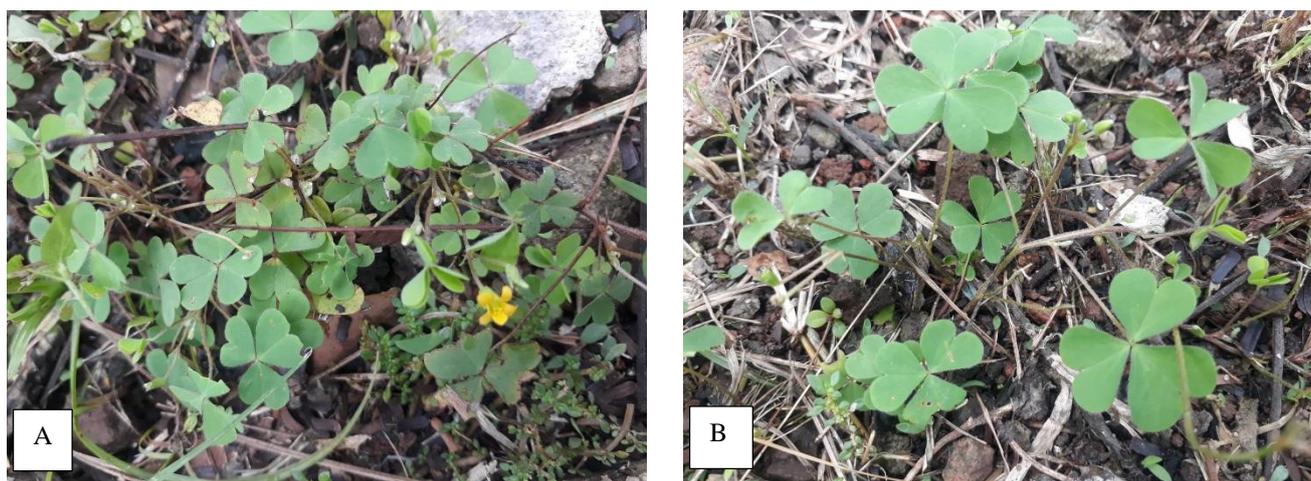


Figure 1 *Oxalis corniculata*. A. Habit and flower; B. The leaves

Description: *O. corniculata* has a habitus of perennial herbaceous plants which more often have creeping stems and roots in the internodes, also reported to be inclined to erect (Figure 1A). Modification of the main root to be thick and woody was also found. Plants usually with several stems emerging from the roots. The cusps are often very small. Leaves with slender stalks, cylindrical, measuring 1–5.5 cm and sometimes up to 10 cm. Leaf blade with three leaflets, each leaf heart-shaped breech (Figure 1B), measuring 4–20 × 5–18 mm with a split tip to approximately half the length of the leaf, each lobe rounded. Flowers are arranged in a reduced umbrella-type arrangement with only 1 or a few flowers. Flowers with free crown lobed lanceolate, green, yellow crown, free with edges near the base that appear attached to each other, measuring 3.5–10 × 1–7 mm with rounded or heart tips. Stamens as many as 10 with different lengths,

generally can be divided into two groups long and short. the pistil is usually free. The fruit is a capsule that breaks when ripe, transversely in the form of a star with a size of 9–20 × 2–4 mm. Ripe fruit will release red or white seeds when touched [13,14].

3.2. Uses and Bioactivities

In traditional medicine, *O. corniculata* is used to treat liver disorders, jaundice, skin diseases, and urinary tract [4]. The *O. corniculata* has anti-inflammatory, anxiolytic, anticonvulsant, antifungal, antiulcer, antinociceptive, anticancer, antidiabetic, hepatoprotective, hypolipidemic, abortive, antimicrobial and wound healing activities [5]. In the following, the bioactivity of *O. corniculata* will be studied further as an antioxidant, anti-microbial, anti-neurodegenerative, anti-diabetic mellitus, anti-cancer, anti-implantation, anxiolytic, and hepatoprotective.

3.2.1. Antioxidants

Free radicals are the main cause of various disease disorders in humans such as cancer, heart problems, and diabetes mellitus. Many human diseases are caused by oxidative stress involving excessive production of free radicals which can be ameliorated by the antioxidant activity of plant extracts [15]. Compounds that are able to inhibit free radicals are known as antioxidants. The search for antioxidant compounds continues to be carried out, especially plants that can be used as food ingredients, including *O. corniculata*. The *O. corniculata* can be an important food source of antioxidants with high scavenging ability and rich in biomolecules which are the precursors of most of the biologically active chemicals of medical importance [16].

Antioxidant bioactivity is related to phenolic content, therefore plants containing phenolic rutin, salicylic acid and benzoic acid [17]. The total phenolic and flavonoid content found in the ethanolic extract of *O. corniculata* was 2.11±0.08 mg/100mg dry weight equivalent to gallic acid (GAE)/100mg dry weight and 4.45±0.15 mg/100mg dry weight equivalent with quercetin (QE) [17]. The total amount of phenol and flavonoid was influenced by the solvent and the order of solvent for phenol content was methanol extract > aqueous extract > chloroform extract > ethyl acetate extract > n-hexane extract while for flavonoids were methanol extract > chloroform extract > aqueous extract > ethyl acetate extract > extract n-hexane [15]. The *O. corniculata* methanol extract contains Vitamin E and squalene which have antioxidant bioactivity [10]. The extract of *O. corniculata* contains bioactive compounds such as steroids, phenolic groups, saponins, tannins, flavonoids, carbohydrates, coumarins, alkaloids and terpenoids which are associated with their antioxidant activity [17].

When explored further, reports on the use of *O. corniculata* as an antioxidant are more prominent than other bioactivities and have been reported by Durgawale et al [10], Ahmad et al [18], Swami & Malpathak [6], Khyadea et al [17], Ahmed et al [19], Tibuhwa [16], and Borah et al [20]. Frequently used reference compounds such as gallic acid, rutin, ascorbic acid for in vitro antioxidant assays [7]. In laboratory experiments the antioxidant bioactivity can be tested with 1,1-Diphenyl-2-picrylhydrazyl (DPPH), Nitric oxide and 2,2-Azinobis 3-ethyl benzothiazoline 6-sulphonic acid (ABTS). The ethanolic extract of *O. corniculata* has antioxidant activity through free radical scavengers tested with DPPH, Nitric oxide and ABTS [17]. DPPH test, the ethyl acetate fraction showed the highest free radical scavenging activity, 24.0% with a concentration of 1 mg/mL [19]. The methanol and ethanol extracts of *O. corniculata* showed significant activity in all antioxidant assays compared to the reference antioxidant ascorbic acid [16].

The bioactivity of *O. corniculata* as an antioxidant is influenced by the polarity of the solvent used and its flavonoid and vitamin C content. The total phenolic content in the ethyl acetate extract was higher than that of the aqueous extract, chloroform and hexane, while the flavonoid content in the methanol extract was higher than that of the ethyl acetate, hexane and water extracts so that it had antioxidant activity [19]. The *O. corniculata* contained vitamin C found to be 0.414 mg/gm fresh weight, and vitamin E was found to be 137.36 mg/gm fresh weight [20].

3.2.2. Anti-microbial

Various researchers reported the bioactivity of *O. corniculata* to inhibit the growth of microbes such as *Escherichia coli* [1,3,21-24], *Salmonella typhi* [1,21,24], *Staphylococcus aureus* [23,24], *Bacillus subtilis* [21, 25], *Shigella dysenteriae* [21], *Staphylococcus faecalis*, *Pseudomonas vesicularis*, *Aeromonas hydrophilia*, *Staphylococcus cohnii*, *Serratia ficaria* [1], *Candida albicans* [3], *Giardia lamblia*, *Eentamoeba histolytica* [26], *Pseudomonas aeruginosa*, *Streptococcus epidermis* [25], *Salmonella typhiimurium*, and *Vibrio cholerae* [24]. The *O. corniculata* is often used to treat various diseases such as dysentery [26], skin diseases [23], toothache, diarrhea [3]. One of the common causes of dysentery is *E. histolytica* [26] while skin infections can be caused by *S. aureus* and *E. coli* [23]. Anti-amoebic *O. corniculata* extract was related to the content of galacto-glycerolipid (GGL) compounds [26]. The bioactivity *O. corniculata* as an antimicrobial is also very potential to be developed as a natural product for natural food preservatives [24].

The bioactivity of *O. corniculata* as an antimicrobial is influenced by various factors including the type of microbe, the compound used for extraction and concentration. The ability of the aqueous extract of *O. corniculata* to inhibit the growth of *S. aureus* and *E. coli* was directly proportional to the concentration [23]. The inhibition zone of *O. corniculata* leaf ethanol extract was higher for *P. vesicularis* compared to *E. coli*, while the methanol extract had a higher inhibition zone for *E. coli* than *Aeromonas hydrophilia* [1]. The order of bacteriostatic and bactericidal rates of various *O. corniculata* extracts was EoAa>AqOc>EtAa = AqAa>EtOc [22]. Secondary metabolites in *O. corniculata* ethanol extract have potential as antibiotics replacing oxacillin, amoxicillin, ampicillin, amoxicillin-clavulanic acid, tetracycline, streptomycin, ciprofloxacin, ceftriaxone, cefazolin, cefuroxime, cefotaxime, ceftazidime and cefixime [22].

The differences in the bioactivity of the extracts were thought to be related to differences in the content of secondary metabolites. The activity of *O. corniculata* extract as an antimicrobial is related to the content of its secondary metabolites including 5-hydroxy-6,7,8,4 tetramethoxyflavone and 5,7,4 trihydroxy-6,8-dimethoxyflavone [21]. The ethanol extract of *O. corniculata* leaves contains catechins and quercetin (flavonoids) while the aqueous extract contains chlorogenic acid polyphenols [22] and the antibacterial activity is related to phenolic compounds [27]. The bioactivity of *O. corniculata* against *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Streptococcus epidermis* is thought to be related to the content of glycosides, saponins, tannins and terpenoids [25].

The *O. corniculata* leaf extract has microbial activity against *S. aureus*, *Salmonella typhi*, *E. coli*, *S. typhiimurium*, *V. cholera*. *E. coli* showed the highest sensitivity and *V. cholera* showed the lowest activities; therefore, it is very potential to be used as a food preservative. The main components of *O. corniculata* leaves are flavonoids with rutin > p-hydroxybenzoic acid > perulic acid [24]. The *O. corniculata* contains flavonoids, alkaloids, tannins, steroids, polyphenols, glycosidic compounds, lipids and essential oils. The leaves of the plant contain medicinal substances such as isovitexine, flavonoids, and vitexine-2-O-beta-D-glucopyrunoside [9].

3.2.3. Anti-neurodegenerative

Neurodegeneration refers to the condition of neuronal death that occurs as a result of long-term progressive disease [28,29,30]. Parkinson's disease (PD) is a type of neurodegenerative disorder characterized by the development of rigidity, resting tremor and postural instability [31]. Phytochemicals from plant medicines may provide a better and safer alternative to synthetic molecules [29]. Neurodegenerative disorders, including Alzheimer's disease (AD), Parkinson's disease (PD) and Huntington's disease (HD), present a large health and financial burden on every healthcare organization in the world. Oxidative stress has long been associated with neurodegeneration, either as a cause or as part of a downstream outcome caused by other factors [30] Thus, the use of antioxidants to counteract cellular oxidative stress in the nervous system has been suggested as a potential treatment option for neurological disorders. Over the past decade, significant research has focused on the potential use of natural antioxidants to target oxidative stress [30].

Various types of commercial drugs are used to treat PD, but herbal medicines are believed to be safer so that exploration continues to be carried out including *O. corniculata*. Treatment with *O. corniculata* reversed changes in locomotor and muscle coordination in MPTP-induced (1-methyl,4-phenyl-1,2,3,6-tetra hydroxyridine) Parkinson's mice and was directly proportional to the dose used. Its anti-neurodegenerative bioactivity is related to its antioxidant activity. Memory retention and increased uptake by *O. corniculata* extract could be due to the presence of antioxidants such as flavonoids, coumarins, tocopherols and phenolic acids and their power in scavenging reactive oxygen species [31]. The extract of *O. corniculata* at doses of 250 and 500 mg/kg concurrently with MPTP significantly restored peroxide and antioxidant levels to near normal in the brains of test animals [28].

3.2.4. Anti-diabetes Mellitus

Diabetes mellitus (DM) is a metabolic disorder that causes blood glucose levels to be above normal, so it is also known as hyperglycemia. In a laboratory experiment, diabetes was induced by a single intraperitoneal injection of the drug streptozotocin (STZ). Edible administration of (*Pteropyrum scoparium* and *O. corniculata*) or a mixture thereof has shown a protective effect against STZ-induced hyperglycemia [33].

3.2.5. Anti-cancer

Cancer is one of the main causes of human caused by uncontrolled cell growth. Anticancer bioactivity is often associated with its antioxidant properties. The ethanolic extract of *O. corniculata* has anticancer activity on Ehrlich ascites carcinoma (EAC) induced in swiss albino rats. The *O. corniculata* ethanolic extract showed significant antitumor in EAC bearing mice and dose dependent reduction in body weight, tumor volume, packed cell volume, tumor cell count and increased mean survival time (MST) and percentage increase in life span in EEOC treatment animals [33].

3.2.6. Hepatoprotective

Hepatoprotective is a compound that is able to restore or protect the liver and its functions. Methanol extract of leaves and stems of *O. corniculata* has promising hepatoprotective activity [11]. The *O. corniculata* exerts anti-hepatic effects by regulating signaling pathways (such as cancer pathway, hepatitis B signaling pathway and PI3K-Akt) [34]. The crude methanol extract *O. corniculata* ameliorated carbon tetrachloride (CCl₄)-induced lung injury in rats [15,18]. The bioactivity of *O. corniculata* as hepatoprotective is thought to be related to the content of flavonoids, alkaloids, terpenoids, saponins, cardiac glycosides, phlobatannins and steroids [15].

3.2.7. Anti-implantation

Anti-implantation compounds are compounds that inhibit the attachment of the embryo to the uterus, therefore these compounds can be used to prevent pregnancy or for abortion, therefore their use must be strictly controlled. Petroleum ether and whole plant ethanol extracts of *O. corniculata* were administered orally at doses of 100 and 200 mg/kg body weight from day 1 to 7 of gestation to evaluate the maximal anti-implantation activity on day 10 (76.42%) with high-dose petroleum ether extract. Pregnant rats treated from day 8 to 14 of gestation showed maximum abortifacient activity (78.55%) with high dose petroleum ether extract [35].

4. Conclusion

In traditional medicine *O. corniculata* is used to treat liver disorders, jaundice, skin diseases, and urinary tract. Bioactivities of *O. corniculata* as an antioxidant, anti-microbial, anti-neurodegenerative, anti-diabetic mellitus, anti-cancer, anti-implantation, anxiolytic, and hepatoprotective. The *O. corniculata* contains a rich source of essential fatty acids such as palmitic, oleic, linolenic and stearic acids with various pharmacological activities.

Compliance with ethical standards

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