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Mini-Review

Pharmacognosy, Phytochemical, and Pharmacology of Wijaya Kusuma (*Epiphyllum oxypetalum* (DC.) Haw.) – An Update Review

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Abstract

In Indonesia, *Epiphyllum oxypetalum* (DC.) Haw. is known as Wijaya Kusuma. The plant is grown for home decorating and used widely as medicine in some areas. This narrative review discusses the pharmacognosy, phytochemical, and pharmacology aspects of *E. oxypetalum*. The review is limited to original articles and abstracts available in Science Direct, PubMed, and Google Scholar. The keyword used to search the articles was "*Epiphyllum oxypetalum*". The plant contains proteins, amino acids, alkaloids, saponins, terpenoids, steroids, flavonoids, tannins, glycosides, and resins. The plant has pharmacological activities such as anti-inflammatory, antimicrobials, antidiabetic, and antioxidant properties. Researchers interested in developing *E. oxypetalum* as a medicinal plant might use this review as a reference.

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INTRODUCTION

Indonesia has a lot of biodiversity and plants that can be used as a source of traditional medicine. Plants used as a source of medicine have existed since ancient times, both hereditary and scientifically proven. Plants have been an integral part of pharmacotherapy throughout history. Medicinal plants have an essential role in the discovery of bioactive molecules¹. One of the plants that have the potential to be developed as a medicinal plant is *Epiphyllum oxypetalum* (DC.) Haw. or Wijaya Kusuma (family: Cactaceae).

Epiphyllum oxypetalum is an ornamental with much history and is widely used to decorate homes. The plant has the potential to be employed as a medicine. *Epiphyllum oxypetalum* is a plant native to Southern Mexico, but it can also be found in North America and Southeast Asia. The plant is also known as night-blooming cereus because of its likeness to a lotus flower. In Indonesia, *E. oxypetalum* has a story that is particularly popular in Central Java. It is said, if someone sees the flowers blooming, then his wishes will come true and achieve success. Another popular myth in the culture is that the *E. oxypetalum* flower does not always bloom, depending on the planter. Many people plant this flower, hoping that it will bring them luck².

Epiphyllum oxypetalum may reach a height of 2-6 m, are ancient with a green hue, and have dark green leaves. The trunks and shoots of these plants can reach a diameter of 2 cm or more, are woody, and have many branches. The leaves on these plants are low sideways and lancet-shaped. Glossy green leaves on the upper surface and underside of sharp-pointed leaves, thinning, wavy, and serrated leaves, the top of narrow leaves in a linear fashion with the interest of 1.6 to 1.8 mm, nocturnal (bloom at night) funnel-shaped, and scented³. The growth of flowers is heavily influenced by light and wind⁴. *Epiphyllum oxypetalum* is growing in an area with no light, and only a tiny breeze does not blossom until it is fully mature. The temperature has a significant impact on the growth of plant germination⁵.

Many *E. oxypetalum* research articles have been published, but there is no review of this plant's pharmacognosy, phytochemical, and pharmacological aspects. In an era with more scientific publications than ever, article reviews are an essential type of scientific writing. Article reviews were intended to highlight key aspects of contemporary research and compare them to prior studies on related subjects⁶. Based on this, we highlight the potential of this plant from pharmacognosy, phytochemical, and pharmacological aspects through a narrative review. This review is aimed to provide researchers with a summary of information on *E. oxypetalum*'s potential as a medicinal plant.

PLANT CLASSIFICATION

Table I shows the classification of *E. oxypetalum*. Species information is essential for the identification stage of medicinal plants. This is useful to prevent errors in collecting and using plant samples⁷.

 Table I.
 Classification of E. oxypetalum²

| Classification | Identity |
|----------------|--|
| Kingdom | Plantae |
| Subkingdom | Tracheobionta |
| Phylum | Magnoliophyta |
| Class | Magnoliopsida |
| Sub Class | Hamamelidae |
| Order | Caryophyllales |
| Family | Cactaceae |
| Genus | Epiphyllum |
| Species | Epiphyllum oxypetalum |
| Synonims | Cereus oxypetalum, Epiphyllum purpusii, Phyllocactus oxypetalus, Phyllocactus purpursii, Cactus oxypetalus, Epiphyllum acuminatum, Phyllocactus acuminatus, Phyllocactus guyanensis, Phyllocactus grandis, Cereus latifrons Pfeiffer, Epiphyllum latifrons |
| Local Name | Wijaya Kusuma (Indonesia); tan hua (China); bakawali (Melayu); queen of the night; orchid cactus; beauty under the moon (International); brahma kamala, nishagandhi (India); kadupul (Sinhala). |

PHARMACOGNOSY

The identification of a plant is critical for the advancement of traditional medicine. Observations at the microscopic and macroscopic levels help to achieve this objective⁸. Devi *et al.*³ reported that the transverse section of *E. oxypetalum* leaf from Bangalore district, Karnataka, India showed the presence of upper epidermis, paracytic stoma, cystolith crystal, mesophyll with midrib vascular tissue, mesophyll with the upper epidermis, needle-shaped crystals, starch grains, xylem vessels, phloem, sclerenchyma of bundle sheath, and pith tissue, xylem vessels, phloem layer, sclerenchyma patches of *E. oxypetalum* microscopically show the presence of star-shaped calcium oxalate crystals, tetracytic stoma, anisocytic stoma, starch grains, and xylem vessel with spiral wall thickening.

The epidermis is the cell layer that protects the surface of leaves, flowers, fruits, seeds, stems, and roots. The epidermis protects tissues from external effects and is a regulator of gas exchange in the leaves. Stomata and trichomes are formed from the epidermis⁹. Anisocytic stomata are observed in *E. oxypetalum* leaves. Anisocytic stomata have three adjacent cells of different sizes around each guard cell¹⁰. Stomata are involved in gas exchange by controlling water loss during transpiration and absorbing CO₂ during photosynthesis. Because of the importance of stomata in the photosynthesis process, it will impact the generation of metabolites in plants¹¹. Mesophyll tissue contains chloroplasts in cells¹².

Non-specific characteristics like a loss of drying and ash content impact the quality of plant material. Loss in drying and total ash value of *E. oxypetalum* dried leaves was $2 \pm 0.10\%$ and $4.6 \pm 0.4\%^3$. Ingale and Mansoori¹³ reported that the loss on drying in the stem extract was 22.6158 g/100 g, and the leaves extract was 10.4658 g/100 g. Meanwhile, the ash content of the stem extract was 2.0625 g/100 g, and the leaves extract was 2.6024 g/100 g.

The loss on drying aims to provide a maximum range linked to the number of compounds lost during the drying process, whereas the ash content intends to offer an overview of the internal and external mineral content from the starting process to the generation of the extract¹⁴. The location where the plant samples were gathered, and the extraction solvent might

impact the concentration of chemicals in the plant. Environmental elements such as nutrition supplies, pH, growth location, humidity, and light are the key factors that influence the concentration of chemicals in a plant¹⁵. *Epiphyllum oxypetalum* was sampled from several sites across India for this study. As a result, environmental factors significantly impact the concentration of chemicals in plants, resulting in a wide range of results in each research. Microbial contamination is caused by excess moisture, whereas microbial decomposition is suppressed by low water content³.

PHYTOCHEMICAL

Epiphyllum oxypetalum leaf powder has a carbohydrate content of $0.0237 \pm 0.001 \text{ mg}/0.5 \text{ mL}^3$, protein content was 14 mg/g, lipids content was 4.6 mg/g, and niacin content was 0.18 mg/g^{16} . While, the levels of phenolics, flavonoids, tannins are 19.09 $\pm 0.08 \text{ g}/0.6 \text{ mL}$, $8.728 \pm 0.02 \text{ g/mL}$, and $31.32 \pm 0.08\%$, respectively³. The leaves and flowers of *E. oxypetalum* have been extensively studied in the research, as well as the development of pharmaceuticals. Several studies on the chemical composition of this plant have been published. **Table II** summarizes the chemical composition of *E. oxypetalum*.

Plant chemicals are selectively soluble in suitable solvents. The extraction method used and the sample at various sites in each study can impact compound results. Maceration and soxhlet are two typical procedures researchers use to extract chemical components of *E. oxypetalum*. Maceration does not go through a heating process, so it is unlikely that the compounds contained are damaged¹⁷. The long maceration process allows the compound to be extracted completely. Soxhlet extraction is a highly effective hot extraction process. However, it should be noted that hot extraction can damage the samples' compounds for thermolabile compounds¹⁸.

The choice of solvents considerably impacts the extraction efficiency of any traditional technique. The polarity of the substance to be studied is the most significant consideration when selecting a solvent. In choosing a solvent for bioactive component extraction, consider molecular affinity between the solvent and the solute, mass transfer, the use of a co-solvent, environmental safety, human toxicity, and financial feasibility¹⁹.

Based on **Table II**, flowers and leaves of *E. oxypetalum* are reported to have metabolites that play a role in pharmacological activity. Alkaloids play a role in activities such as anticancer, antimalarial, and antihyperglycemic. Saponins play a role in antibacterial and antioxidant activities. Tannins play a role in antibacterial activity. Flavonoids have antioxidant properties²⁰. Most of these compounds can be dissolved in either methanol, ethanol, or water¹⁹.

| Part of plant | Sample location | Extraction method and type of extract | Chemical component | |
|---------------|---|--|--|--|
| Flowers | Hosur, Krishnagiri | Maceration, hexane extract | Alkaloids, saponins, terpenoids ²⁰ | |
| | district, Tamil Nadu, | Maceration, chloroform Extract | Proteins and amino acids, terpenoids ²⁰ | |
| | India | Maceration, ethanol extract | Alkaloids, terpenoids ²⁰ | |
| | Maceration, water extract | | Steroids, flavonoids, tannins ²⁰ | |
| | Denpasar and Badung, Bali, Indonesia | Fractionation, petroleum ether fraction | Alkaloids, triterpenoids and saponins ²¹ | |
| Leaves | Bangalore district, | Soxhlet extraction, methanol Extract | Carbohydrates, proteins, tannins, phenols | |
| | Karnataka, India | Soxhlet extraction, water extract | alkaloids, flavonoids, sterols, saponins ³ Carbohydrates, proteins, tannins, alkaloids | |
| | | Somer extraction, water extract | sterols, saponins ³ | |
| | | Soxhlet extraction, petroleum ether extract | Carbohydrates, tannins, sterols, alkaloids ³ | |
| | | Soxhlet extraction, ethanol extract | Carbohydrates, proteins, tannins, phenols alkaloids, sterols, saponins ³ | |
| | Bangalore district, Karnataka, India | Soxhlet extraction, sequentially ethanol extract | Carbohydrates, proteins, tannins, phenols alkaloids, saponins, glycosides, steroids terpenoids, resins ¹⁶ | |
| | | Soxhlet extraction, sequentially acetone extract | Saponins, glycosides, proteins, steroids terpenoids, phenols, resins, tannins ¹⁶ | |
| | | Soxhlet extraction, sequentially petroleum ether extract | Glycosides, proteins, steroids, terpenoids resins ¹⁶ | |

Table II. Chemical composition of E. oxypetalum

Several chemical constituents of *E. oxypetalum* were identified using the gas chromatography-mass spectroscopy (GC-MS) method^{20,22,23}. The summary can be seen in **Table III**. Hexadecanoic acid was detected in leaves and flowers. This compound

is reported to have potential as an antioxidant, flavor, pesticide, hemolytic, and other. Ethanol extract of E. oxypetalum leaves also contains flavonoids ([7- hydroxy-3(1,1-dimethyl prop-2enyl) coumarin) and fatty acids (oleic acid, nonadecanoic acid, and hexadecanoic acid)²⁰.

| Table III. Che | emical constituents identified in E. oxypetal | lum | |
|----------------|---|--|--|
| Part of plant | Extraction method and type of extract | Chemical component | |
| Flowers | Maceration; | Hexadecanoic acid, ethyl ester | |
| | chloroform, ethanol, | Nonadecanoic acid | |
| | hexane and aqueous extracts | Oleic acid | |
| | | 11-tridecen-1-ol | |
| | | 1-octadecyne Hexadecanal, | |
| | | | |
| | | Spiro[androdt-5-ene-17,1-cyclobutan]-2-1-3-hydroxy | |
| | | 1,6;3,4-dianhydro-2-deoxy betaDLyxo- hexopyranose | |
| | | di-n-decylsulfone, | |
| | | 7-hydroxy-3(1,1-dimethyl prop-2enyl) coumarin | |
| | | Pterin-6-carboxylic acid ²⁰ | |
| Leaves | Soxhlet extraction; | 4-hydroxy-2-methylacetophenone | |
| | ethanol extract | Megastigmatrienone | |
| | | 4-((1E)-3-hydroxy-1-propenyl)-2 methoxyphenol | |
| | | n-hexadecanoic acid | |
| | | Octadecanoic acid | |
| | | Phytol | |
| | | Cholesta-22,24-dien-5-ol, 4,4-dimethyl | |
| | | Stigmasterol | |
| | | 22-stigmasten-3-one | |
| | | Heptacosane | |
| | | Nonadecane, 2- methyl- | |
| | | Spinasterone | |
| | | 4,22-stigmastadiene-3-one | |
| | | Tetracosane | |
| | | Hentriacontane | |
| | | Stigmast-4-en-3-one | |
| | | Testosterone cypionate ²⁴ | |
| | Cold percolation, methanol extract | 10-octadeconoic acid, methyl ester; 1,2-benzenedicarboxylic acid, butyl | |
| | * | octyl ester; 1,2-benzenedicarboxylic acid, mono (2-ethylhexyl) ester; | |
| | | Cyclopropanebutanoic acid, 2-[(2-[(2 | |
| | | [(2pentylcyclopropyl)methyl]cyclopropyl)methyl]cyclopropyl)methyl]-, | |
| | | methyl ester; 17-(1,5-dimethylhexyl)-10,13-dimethyl-3 | |
| | | styrylhexadecahydrocyclopenta(a)phenanthren-2-one; Ergosteryl acetate; | |
| | | Ethanol, 2-(9-octadecenyloxy)-,(Z)-; | |
| | | Glycine,N-[(3a,5a,7a,12a)-24-oxo-3,7,12 tris [(trimethylsilyl) oxy]cholan-24- | |
| | | yl] -, methyl ester; (5a) pregnane -3,20 a-diol, 14a, 18a-[4-methyl-3-oxo- (1- | |
| | | oxa-4-azabutane-1,4-diyl)]-, diacetate; and Rhodopin ²³ | |

Several structures of essential compounds in E. oxypetalum are presented in Figure 1. A molecular docking study reported that megastigmatrienone and testosterone cypionate found in *E. oxypetalum* leaves have the potential to be developed as an antiviral²².

PHARMACOLOGY

The summary of pharmacological activity from E. oxypetalum is shown in Table IV. Because animal tests are expensive, time-demanding, and susceptible to ethical controversy, in vitro procedures are frequently preferred over in vivo assays25. According to Table IV, most *E. oxypetalum* research has been done *in vitro*. The leaves are more studied than the flowers. Flowers may be more challenging to obtain because not all plants planted can produce flowers.

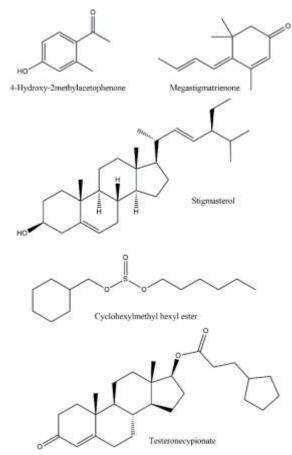


Figure 1. Several chemical structures identified in E. oxypetalum^{20,22,23}

Alcohols, both ethanol and methanol, as polar solvents, are more often used in the test. This solvent can extract metabolites with a wider polarity, such as polyphenols, flavonoids, tannins, alkaloids, glycosides, terpenoids, and steroids²⁶. The extraction methods that are widely used are maceration and soxhlet extraction. Both of these methods are commonly used in the extraction of medicinal plants²⁷. However, currently, the use of non-conventional extraction techniques (such as ultrasonic-assisted extraction or microwave-assisted extraction) is auspicious to be applied in the development of this plant to produce effective, efficient extracts and environmentally friendly^{28,29}. The plant metabolites play a role in the pharmacological effects of plants. Each pharmacological activity of the plant will be discussed at separate points.

Antioxidant

Antioxidants are chemical substances that, when consumed sufficiently, can prevent damage produced by the oxidation process³⁰. In other words, the body needs a substance such as an antioxidant that helps protect against free radical attack³¹. The method that has been used to test antioxidant activity is the DPPH method and hydrogen peroxide scavengers which were tested on samples of methanol extract, ethanol extract, water extract, and petroleum ether fraction. DPPH•, on the other hand, is not a natural radical, but its reaction mechanism with antioxidants is close to that of peroxyl radicals ROO•³². When the DPPH solution is mixed with a substrate that can donate a hydrogen atom, it gives rise to a reduced form with a loss of purple color³³. In this test, ascorbic acid, Trolox, gallic acid, butylated hydroxytoluene (BHT), and butylated hydroxyanisole (BHA) are often used as references³⁴.

The secondary metabolites, such as flavonoids and saponins, contribute to this activity. Saponins can reduce superoxide by forming hydroperoxide intermediates to prevent damage by free radicals. The antioxidant mechanism of steroids is by scavenging reactive species, such as superoxide and chelating metals (Fe^{2+} and Cu^{2+})³⁵. While flavonoids are polyphenols that can donate hydrogen atoms to free radicals, the antioxidant activity of polyphenolic compounds can be generated from a neutralization reaction or at the termination of a chain reaction³⁶.

| Methanol extract and petroleum ether fraction Methanol extract Ethanol extract and aqueous extract | Antioxidant, in vitro, diphenylpicrylhydrazine, DPPH method Antihyperuricemia; in vivo Antioxidant, in vitro, DPPH and hydrogen peroxide | The methanol extract and petroleum ether fraction (at 8000 ppm, 60 minute) was able to able to reduce DPPH free radicals by 70.00% and 155.1%, respectively ³⁷ . The extract (400 mg/Kg BW) can reduce 63.50% of uric acid on mice induced by <i>melinjo</i> and chicken liver juice raw ³⁷ . |
|--|--|--|
| Ethanol extract and aqueous extract | in vivo Antioxidant, in vitro, | of uric acid on mice induced by <i>melinjo</i> and chicken liver juice raw ³⁷ . |
| extract | | |
| Alashal subset 1 | scavenger methods | Both of extracts at 2000 and 500 μg/mL was able to inhibit DPPH radical and hydrogen peroxide scavenging ³⁸ . |
| Alcohol extract and water extract | Anti-inflammatory, <i>in vitro</i> , human red blood cell membrane stabilisation and inhibition of protein denaturation method | Using <i>in vitro</i> techniques, the percentage inhibition of alcohol and aqueous extract was highest at 300 µg/mL, but in animal studies, the percentage inhibition of alcohol and aqueous extract was highest at 600 and 200 mg/Kg BW, respectively ³⁹ . |
| Silver nano particles (AgNPs) synthesized from aqueous extract | Anti-bacteria, <i>in vitro</i> , tested using by Kirby- Bauer disc diffusion method | AgNP synthesized from aqueous extract of <i>E.</i> oxypetalum indicated the presence of anti- bacterial activity against <i>Propionibacterium acne</i> , <i>Pseudomonas aeruginosa</i> , and <i>Klebsiella</i> pneumoniae ⁴⁰ . |
| Extract | Wound healing and kidney hispathological, <i>in vivo</i> | The combination of <i>Catharanthus roseus</i> and <i>E.</i> oxypetalum leaf extract at a concentration of 15% (topically) provided the best wound healing in guinea pigs compared to the administration of each extract alone. Histopathological parameter showed that both extracts were safe for the kidneys ⁴¹ . |
| Ethanol extract 96% | Anti-inflammatory, in vivo | In diabetic mice, topical treatment (ointment) of the extract of <i>E. oxypetalum</i> leaves accelerated wound healing time, with 20% <i>E. oxypetalum</i> extract displayed the highest effect ⁴² . |
| Petroleum ether, acetone, and ethanol extracts | Antimicrobe, <i>in vitro</i> , disc diffusion method | The maximum inhibition zone was indicated by acetone and petroleum ether extracts against <i>Escherichia coli</i> (14 mm); acetone extract against <i>Staphylococcus aureus</i> (14 mm); acetone and ethanol extracts against <i>Klebsiella pneumonia</i> (10 mm and 10 mm, respectively); and petroleum ether extract against <i>Bacillus subtilis</i> (12 mm). All extracts were tested at a concentration of 100 μ g/mL. All extracts showed no activity against fungal pathogen ¹⁶ . |
| Methanol extract | Anti-inflammatory, <i>in vitro</i> , inhibition of albumin denaturation | The extract showed anti-inflammatory activity with a percent inhibition was 32% ³⁷ . |
| Methanol extract | Anti diabetic, <i>in vitro</i> , α-amylase inhibitory assay Antivirus, <i>in silico</i> study using molecular docking | The extract showed the percent inhibition of α -amylase was 26% ³⁷ . |
| Several active compounds (4- hydroxy-2- methylacetophenone, Stigmasterol, 6-octen-1-ol, 3,7-dimethyl, Megastigmatrienone, Cyclohexylmethyl hexyl | | Megastigmatrienone (5.02 kcal/mol) from <i>E.</i> oxypetalum leaves had higher binding interactions against <i>Treponema pallidum</i> , followed by megastigmatrienone (4.58 kcal/mol) with liver cirrhosis, and testosterone cypionate (7.084 kcal/mol) with Zika virus ²² . |
| | Silver nano particles (AgNPs) synthesized from aqueous extract Extract Ethanol extract 96% Petroleum ether, acetone, and ethanol extracts Methanol extract Methanol extract Several active compounds (4- hydroxy-2- methylacetophenone, Stigmasterol, 6-octen-1-ol, 3,7-dimethyl, | membranestabilisationand inhibition of protein denaturation methodSilvernanoparticles (AgNPs) synthesized from aqueous extractAnti-bacteria, in vitro, tested using by Kirby- Bauer disc diffusion methodExtractWound healing hispathological, in vivoand kidney hispathological, in vivoEthanol extract 96%Anti-inflammatory, in vivoPetroleumether, acetone, and ethanol extractsAnti-inflammatory, in vitro, disc diffusion methodMethanol extractAnti-inflammatory, in vitro, disc diffusion methodMethanol extractAnti-inflammatory, in vitro, assay Several active compounds (4- hydroxy-2- methylacetophenone, Stigmasterol, 6-octen-1-ol, 3,7-dimethyl, Megastigmatrienone, CyclohexylmethylAnti-inflammatory, in vitro, assay Several active compounds (4- hydroxy-1 methyl, Megastigmatrienone, Cyclohexylmethyl |

Table IV. Pharmacological activities of *E. oxypetalum*

Antihyperuricemia

Determination of uric acid levels was determined by the enzymatic method using uric acid reagent FS-TBHBA (2,4,6-tribromo-3-hydroxybenzoic acid). The mechanism in this method is that the enzyme uricase oxidizes uric acid with the help of H₂O and O₂ into allantoin, CO₂, and H₂O₂. The H₂O₂ formed will react with 4-amino antipyrine and FS-TBHBA to form pink quinonimine; the peroxidase enzyme catalyzes the reaction⁴³. Compounds that play a role in lowering uric acid levels are flavonoids. The flavonoid group of compounds inhibits the activity of xanthine oxidase and superoxidase, thereby reducing the formation of uric acid⁴⁴.

Anti-inflammatory

Epiphyllum oxypetalum has pharmacological activity as an anti-inflammatory. In a study by Dwita *et al.*⁴², *E. oxypetalum* leaf extract contains secondary metabolites such as alkaloids, flavonoids, tannins, saponins, and steroids. Several studies have demonstrated the mechanism of flavonoids in wound healing by modulating the expression of cytokines and nitric oxide in the inflammatory phase.

Antidiabetic

The antidiabetic activity of methanol extract of *E. oxypetalum* leaf showed inhibition of α-amylase. α-amylase is helpful as a hypoglycemic agent to control hyperglycemia, especially in patients with type 2 diabetes mellitus. This enzyme delays carbohydrates and prolongs carbohydrate digestion time, causing a reduction in the rate of glucose absorption and consequently reducing the postprandial rise in plasma glucose⁴⁵. Secondary metabolite compounds such as phenolics, flavonoids, alkaloids, and steroids have antidiabetic activity⁴⁶.

Antibacterial

The chemical content of the *E. oxypetalum* leaf extract has the potential as an antibacterial, both against gram-negative and gram-positive bacteria, compared to antifungals¹⁶. When paired with antibiotics, nanoparticle technology using silver (silver nanoparticles, AgNPs) synthesized from an aqueous extract of *E. oxypetalum* is more effective. This formulation is both environmentally friendly and cost-effective and may be precious in biomedical applications⁴⁰.

AgNPs can be used effectively against many drug-resistant bacteria because their large surface area and small size make them easy to interact with substances and enhance their antibacterial efficacy. AgNPs can be a new generation of antimicrobial with broad-spectrum activity. Biological methods for the synthesis of nanoparticles have several advantages over chemical and physical methods because these methods do not involve chemical toxins, and sometimes reactions take place at very high temperatures. Using plants to synthesize nanoparticles can be an advantage over microorganisms because it eliminates the culture maintenance process⁴⁰.

The phenolic compounds contained in *E. oxypetalum* are one of the compounds suspected of having antibacterial activity¹⁶. Alkaloids are thought to have the ability as an antibacterial that can interfere with the peptidoglycan components of bacterial cells so that the cell wall layer is not formed completely. Terpenoids are other plant metabolites with antimicrobial, antifungal, antibacterial, and antiviral properties. The flavonoids act as an antibacterial agent by building complex molecules with proteins that damage the bacterial cell membrane's integrity. These substances can degrade cell walls and interfere with cell permeability. In addition to flavonoids, a type of polyphenolic compounds that have antibacterial action, particularly tannins⁴⁷.

Toxicity study

Safety is a major consideration in the development of medicinal plants. Eleven compounds found in methanol extract of *E. oxypetalum* leaves, through GC-MS analysis, were evaluated for their toxicity using QSAR – Toxicity Estimation Software Tool (TEST). Some of them were predicted to possess high to extreme toxicity against Daphnia *magna, Tetrahymena pyriformis,* and *Pimephales promelas,* such as oleic acid, eicosyl ester; hexadecanoic acid, 1-(hydroxymethyl)-1,2- ethanediyl ester; 17-pentatriacontene; cyclopropanebutanoic acid,2-[(2-[(2-pentylcyclopropyl)methyl]cyclopropyl)methyl]-,methyl ester; 17-(1,5-dimethylhexyl)-10,13-dimethyl-3-styrylhexadeca hydrocyclopenta(a)phenanthren-2-one; and ergosteryl acetate²³.

Among the chemicals found in *E. oxypetalum*, 0-octadecenoic acid, methyl ester and ethanol, 2-(9-octadecenyloxy)-, (Z) were harmless to development. Meanwhile, 1,2-benzenedicarboxylic acid, butyl octyl ester; 1,2-benzenedicarboxylic acid, mono(2-ethylhexyl) ester; cyclopropanebutanoic acid,2-[(2-[(2-[(2-[(2-[(2-pentylcyclopropyl)methyl]cyclopropyl)methyl]-,methyl ester; 17-(1,5-dimethylhexyl)-10,13-dimethyl-3-styrylhexadecahydrocyclopenta(a)phenanthren2-one; ergosteryl acetate; glycine,N-[(3a,5a,7a,12a)-24-oxo-3,7,12-tris[(trimethylsilyl)oxy]cholan-24-yl]-,methyl ester; and (5a)pregnane-3,20a-diol,14a,18a-[4-methyl-3-oxo-(1-oxa-4-

azabutane-1,4-diyl)]-,diacetate were poisonous. In oral rats, however, all compounds were predicted to have a low toxicity to nontoxic. Through *in silico* research, the usage of animals for toxicity estimates can be reduced²³. This study was suspected that *E. oxypetalum* leaves are safe for humans and could be used to produce new medications in the future. Of course, before that, scientific evidence of *in vivo* toxicity from extracts and individual compounds of *E. oxypetalum* leaves in animal models is required.

FUTURE PROSPECTS

Based on the information provided, the *E. oxypetalum* plant in the future has the potential to be developed into a source of medicinal ingredients. So, it can be used as a raw material for natural medicine to treat various diseases. The flower and leaves of this plant contain chemical compounds in the form of primary and secondary metabolites. Steroid chemicals dominate the chemical substances detected in this plant, such as testosterone cypionate, stigmasterol, and others. No active chemical compounds against specific pharmacological actions have been isolated on this plant. These isolates will determine quality standards from the extracts or fractions production. In the future, it will also be essential to investigate the plant's roots to complete the information about the plant. The pharmacological activity of *E. oxypetalum* has the potential as an anti-inflammatory, a source of antioxidants, and antimicrobials. The chemical compounds discovered in these plants, particularly steroids, need to be researched further to see whether they may be used for additional therapeutic purposes, such as hormone treatment for fertility, contraception, or even aphrodisiacs.

CONCLUSION

Epiphyllum oxypetalum contains chemical compounds such as carbohydrates, proteins, amino acids, alkaloids, saponins, terpenoids, steroids, flavonoids, tannins, glycosides, and resins. This plant has pharmacological activity such as antiinflammatory, antimicrobial, antidiabetic, and a source of antioxidants. *Epiphyllum oxypetalum* is a plant that is safe because it is not toxic. *Epiphyllum oxypetalum* has the potential to be investigated and developed further so that the plant's benefits can be shared with the rest of the community..

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AUTHORS' CONTRIBUTION

Chandra Adam Lesmana: conceptualization, investigation, data curation, resources, visualization, writing - original draft, and writing - review & editing. **Ni Putu Ermi Hikmawanti**: conceptualization, methodology, project administration, supervision, validation, visualization, writing - original draft, and writing - review & editing. **Agustin Yumita**: conceptualization, supervision, validation, writing - original draft.

DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors have declared no conflict of interest.

REFERENCES

- Sholikhah EN. Indonesian medicinal plants as sources of secondary metabolites for pharmaceutical industry. Berkala Ilmu Kedokteran J Med Sci. 2016;48(4):226-39. doi:10.19106/JMedSci004804201606
- Rohmad Y. Bunga Wijaya Kusuma (Mitos & Legenda, Klasifikasi Ilmiah, Budidaya, Khasiat Herbal, Komunitas). 1st Ed. Malang: Kebun Wijayakusuma; 2015.
- 3. Devi KRS, Narayana SL, Menghani P, Georgekutty J. Microscopic, pharmacognostic and phytochemical screening of Epiphyllum oxypetalum (dc) haw leaves. J Pharmacogn Phytochem. 2018;7(6):972–80.
- Harmiatun Y, Sianipar H, Silahi M. Fenologi Pembungaan Pada Tanaman Wijaya Kusuma. J Pro-Life. 2016;3(3):183–94. doi:10.33541/jpvol6Iss2pp102
- Ortiz TA, Moritz A, de Oliveira MA, Lone AB, Nakatani SH, Takahashi LSA. Optimal conditions for germination of seeds of Epiphyllum oxypetalum. African J Agric Res. 2014;9(34):2630–7. doi:10.5897/AJAR2014.8934
- 6. Agarwal S. Writing a Review Article: For the Beginners in Research. Int J Sci Res. 2014;3(10):813-5.
- Hostettmann K, Wolfender JL, Terreaux C. Modern Screening Techniques for Plant Extracts. Pharm Biol. 2001;39(suppl 1):18–32. doi:10.1076/phbi.39.s1.18.0008
- Ichim MC, Häser A, Nick P. Microscopic Authentication of Commercial Herbal Products in the Globalized Market: Potential and Limitations. Front Pharmacol. 2020;11:876. doi:10.3389/fphar.2020.00876
- Anu O, Rampe HL, Pelealu JJ. Struktur Sel Epidermis dan Stomata Daun Beberapa Tumbuhan Suku Euphorbiaceae. J MIPA. 2017;6(1):69–73. doi:10.35799/jm.6.1.2017.16160
- Haryanti S. Jumlah dan Distribusi Stomata pada Daun Beberapa Spesies Tanaman Dikotil dan Monokotil. Buletin Anatomi Fisiologi. 2010;18(2):21–8. doi:10.14710/baf.v18i2.2600
- 11. Setiawati T, Syamsi IF. Karakteristik Stomata Berdasarkan Estimasi Waktu dan Perbedaan Intensitas Cahaya pada Daun Hibiscus tiliaceus Linn. di Pangandaran, Jawa Barat. J Pro-Life. 2019;6(2):148–59. doi:10.33541/jpvol6Iss2pp102
- Rasyid M, Irawati MH, Saptasari M. Anatomi Daun Ficus Racemosa L. (Biraeng) dan Potensinya di Taman Nasional Batimurung Bulusarung. J Pendidikan Teori Penelitian Pengembangan. 2017;2(6):861–6. doi:10.17977/jptpp.v2i6.9548
- 13. Ingale S, Mansoori MS. Proximate Composition of Epiphyllum Oxypetalum Stem Leaves. World J Pharm Res. 2015;23(1):29–34.
- Ahn JY, Kil DY, Kong C, Kim BG. Comparison of Oven-drying Methods for Determination of Moisture Content in Feed Ingredients. Asian-Australas J Anim Sci. 2014;27(11):1615-22. doi:10.5713/ajas.2014.14305
- 15. Hikmawanti NPE, Hanani E, Maharani S, Putri AIW. Kadar Piperin Ekstrak Buah Cabe Jawa dan Lada Hitam dari Daerah dengan Ketinggian Berbeda. J Jamu Indones. 2021;6(1):16–22. doi:10.29244/jji.v6i1.176
- Upendra RS, Khandelwal P. Assessment of nutritive values, phytochemical constituents and biotherapeutic potentials of Epiphyllum oxypetalum. Int J Pharm Pharm Sci. 2002;4(Suppl 5):421–5.
- 17. Handoyo DLY. The Influence of Maseration Time (Immeration) on the Vocity of Birthleaf Extract (Piper Betle). J Farmasi Tinctura. 2020;2(1):34–41. doi:10.35316/tinctura.v2i1.1546
- Susanty, Bachmid F. Perbandingan Metode Ekstraksi Maserasi dan Refluks terhadap Kadar Fenolik dari Ekstrak Tongkol Jagung (Zea mays L.). J Konversi. 2016;5(2):87–93. doi:10.24853/konversi.5.2.87-92

- 19. Azmir J, Zaidul ISM, Rahman MM, Sharif KM, Mohamed A, Sahena F, et al. Techniques for extraction of bioactive compounds from plant materials: A review. J Food Eng. 2013;117(4):426–36. doi:10.1016/j.jfoodeng.2013.01.014
- 20. Jayashree P, Shalini M, Meenambiga SS, Suganya V. Phytochemical Screening and GC-MS Analysis of Epiphyllum oxypetalum flower extracts. Res J Pharm Technol. 2020;13(12):5893–7. doi:10.5958/0974-360X.2020.01028.8
- 21. Artini NPR, Aryasa IWT. Aktivitas Antioksidan Ekstrak Bunga Wijaya kusuma (Epiphyllum oxypetalum). J Ilmiah Medicamento. 2018;4(2):107–12. doi:10.36733/medicamento.v4i2.864
- Biswal RA, Jayashree P, Mirunaalini K, Pazhamalai V. Molecular docking studies of bioactive compounds from the leaves of Epiphyllum oxypetalum against Treponema pallidum, Zika virus and liver cirrhosis. J Appl Pharm Sci. 2019;9(11):69–77. doi:10.7324/JAPS.2019.91109
- 23. Sripriya N, Kumar RM, Karthick NA, Bhuvaneswari S, Prakash NKU. In silico evaluation of multispecies toxicity of natural compounds. Drug Chem Toxicol. 2021;44(5):480-6. doi:10.1080/01480545.2019.1614023
- 24. Dandekar R, Fegade B, Bhaskar VH. GC-MS analysis of phytoconstituents in alcohol extract of Epiphyllum oxypetalum leaves. J Pharmacogn Phytochem. 2015;4(1):149–54.
- 25. Alternimi A, Lakhssassi N, Baharlouei A, Watson DG, Lightfoot DA. Phytochemicals: Extraction, Isolation, and Identification of Bioactive Compounds from Plant Extracts. Plants. 2017;6(4):42. doi:10.3390/plants6040042
- 26. Tiwari P, Kumar B, Kaur M, Kaur G, Kaur H. Phytochemical screening and Extraction: A Review. Int Pharm Sci. 2011;1(1):98–106.
- 27. Abubakar AR, Haque M. Preparation of Medicinal Plants: Basic Extraction and Fractionation Procedures for Experimental Purposes. J Pharm Bioallied Sci. 2020;12(1):1–10. doi:10.4103/jpbs.jpbs_175_19
- Mosić M, Dramićanin A, Ristivojević P, Milojković-Opsenica D. Extraction as a critical step in phytochemical analysis. J AOAC Int. 2020;103(2):365–72. doi:10.5740/jaoacint.19-0251
- 29. Khadhraoui B, Ummat V, Tiwari BK, Fabiano-Tixier AS, Chemat F. Review of ultrasound combinations with hybrid and innovative techniques for extraction and processing of food and natural products. Ultrason Sonochem. 2021;76:105625. doi:10.1016/j.ultsonch.2021.105625
- 30. Gulcin İ. Antioxidants and antioxidant methods: an updated overview. Arch Toxicol. 2020;94(3):651-715. doi:10.1007/s00204-020-02689-3
- 31. Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn Rev. 2010;4(8):118-26. doi:10.4103/0973-7847.70902
- 32. Munteanu IG, Apetrei C. Analytical methods used in determining antioxidant activity: A review. Int J Mol Sci. 2021;22(7):3380. doi:10.3390/ijms22073380
- 33. Alam MN, Bristi NJ, Rafiquzzaman M. Review on in vivo and in vitro methods evaluation of antioxidant activity. Saudi Pharm J. 2013;21(2):143–52. doi:10.1016/j.jsps.2012.05.002
- 34. Sadeer NB, Montesano D, Albrizio S, Zengin G, Mahomoodally MF. The versatility of antioxidant assays in food science and safety chemistry, applications, strengths, and limitations. Antioxidants. 2020;9(8):709. doi:10.3390/antiox9080709
- 35. Topçu G, Ertaş A, Kolak U, Öztürk M, Ulubelen A. Antioxidant activity tests on novel triterpenoids from Salvia macrochlamys. Arkivoc. 2007;7(7):195–208.
- 36. Syarif RA, Muhajiri, Ahmad AR, Malik A. Identifikasi Golongan Senyawa Antioksidan dengan Menggunakan Metode Perendaman Radikal DPPH Ekstrak Etanol Daun Cordia myxa L. J Fitofarmaka Indones. 2015;2(1):83–9.

- 37. Artini NPR, Aryasa IWT. Efektivitas Bunga Wijaya Kusuma (Epiphyllum oxypetalum) Terhadap Penurunan Kadar Asam Urat Tikus Wistar. J Muhammadiyah Med Lab Technol. 2019;2(2):37–46. doi:10.30651/jmlt.v2i2.2584
- 38. Dandekar R, Fegade B, Bhaskar VH. In Vitro Evaluation of Free Radical Scavenging Activities of Epiphyllum oxypetalum. World J Pharm Res. 2015;4(7):1301–9.
- 39. Dandekar R, Fegade B, Naik A. Evaluating of Anti Inflammatory Activity of Alcohol and Aqueous Extract of Epiphyllum oxypetalum Leaves. World J Pharm Pharm Sci. 2015;4(7):851–8.
- 40. Paralikar P. Biogenic Synthesis of Silver Nanoparticles Using Leaves Extract of Epiphyllum Oxypetalum and its Antibacterial Activity. Austin J Biotechnol Bioeng, 2014;1(7):1–5.
- Humaira S, Berata IK, Wardhita AAGJ. Gambaran Histopatologi Ginjal Marmut yang Diberi Ekstrak Daun Tapak Dara (Cantharanthus roseus) dan Wijayakusuma (Epiphyllum oxypetalum). Indones Med Veterinus. 2020;9(1):12–20. doi:10.19087/imv.2020.9.1.12
- Dwita LP, Hasanah F, Srirustami R, Repi, Purnomo R, Harsodjo S. Wound healing properties of Epiphyllum oxypetalum (DC.) Haw. leaf extract in streptozotocin-induced diabetic mice by topical application. Wound Med. 2019;26(1):100160. doi:10.1016/j.wndm.2019.100160
- 43. Artini NPR, Wahjuni S, Sulihingtyas WD. Ekstrak Daun Sirsak (Annona muricata L.) sebagai Antioksidan pada Penurunan Kadar Asam Urat Tikus Wistar. J Kimia J Chem. 2012;6(2):127–37.
- 44. Sonia R, Yusnelti, Fitrianingsih. Efektivitas Ekstrak Etanol Daun Durian (Durio zibethinus (Linn.)) sebagai Antihiperurisemia. J Kefarmasian Indones. 2020;10(2):130–9. doi:10.22435/jki.v10i2.2148
- Momina SS, Rani VS. In vitro Studies on α-Amylase and α-Glucosidase Inhibitory Activity of Some Bioactive Extracts. J Young Pharm. 2020;12(2):72–5. doi:10.5530/jyp.2020.12s.50
- 46. Ebrahimi E, Shirali S, Afrisham R. Effect and mechanism of herbal ingredients in improving diabetes mellitus complications. Jundishapur J Nat Pharm Prod. 2017;12(1):e31657. doi:10.5812/jjnpp.31657
- 47. Ibrahim A, Kuncoro H. Identifikasi Metabolit Sekunder dan Aktivitas Antibakteri Ekstrak Daun Sungkai (Peronema canescens JACK.) Terhadap Beberapa Bakteri Patogen. J Trop Pharm Chem. 2012;2(1):8–18. doi:10.25026/jtpc.v2i1.43