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**REVIEW ARTICLE** **OPEN ACCESS**

# A Review on Medicinal Value and Pharmacological Profile of *Walsuria trifoliata*

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**ABSTRACT**
*The research surrounding Walsura trifoliata, a botanical treasure, has unveiled a multitude of pharmacological potentials that beckon scientific exploration. The roots of this plant have yielded promising results in the inhibition of α-glucosidases, hinting at its anti-diabetic properties. Meanwhile, its leaves, when subjected to extraction, have revealed a trove of activities such as antimicrobial, anti-inflammatory, anti-diarrheal, and anti-cancer effects, suggesting a rich source of therapeutic compounds. The ethanol extract, in particular, emerged as a formidable contender against a spectrum of microorganisms, with significant action against Staphylococcus aureus and Bacillus cereus, and moderate inhibition against Candida albicans. Methanol extracts proved to be effective in reducing oxidative damage, they fell short of surpassing the benchmark set by butylated hydroxytoluene (BHT), standard antioxidant. Furthermore, the research journey unveiled a arresting aspect—Walsura trifoliata's potential in the synthesis of nanoparticles. Using eco-friendly methods, the plant has been instrumental in crafting both gold and silver nanoparticles. These nanoparticles exhibited distinctive characteristics, such as surface plasmon resonance, stability, and size distribution, offering promise in various applications. It's plant's chemistry, novel apo-tirucallane triterpenoids—piscidinone A and B—were discovered in its leaves and twigs. These compounds, with unique tetracyclic rings and substituted pyran rings, have demonstrated moderate cytotoxicity against several cancer cell lines, igniting hope in the realm of cancer research. Last but not least, the phytochemical exploration led to the isolation of Lupenol, a compound brimming with anti-inflammatory, anti-diarrheal, and anti-cancer qualities. Discovery of this active phytocompound opens new avenues for harnessing the plant's therapeutic potential.*
***Keywords:*** *Ayurvedic, cytotoxicity, Inflammation, triterpenoids, sterols.*

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## INTRODUCTION

*Walsuria trifoliate*, a rare evergreen tree belonging to the Meliaceae family, is found abundantly throughout the tropical regions of South Asian countries. *Walsuria trifoliate* thrives in arid, deciduous soils at elevations ranging from 200 to 300 meters. Recognized for its therapeutic potential, this tree has a history of use in traditional medicinal practices. Indigenous communities have harnessed the healing properties of this plant to address various ailments, including skin allergies, astringency, and diarrhea. These clinical challenges are particularly prevalent among tribal populations, who often face difficulties due to limited access to clean water and a lack of awareness regarding hygienic dietary practices and sanitation. The bark of *Walsuria trifoliate* has been documented to possess stimulant, expectorant, and emetic properties. Furthermore, its fruit has been traditionally employed as a means of fishing by acting as a piscicidal agent. Notably, this plant exhibits diverse pharmacological activities, including anti-diabetic, anti-inflammatory, anticancer, antimicrobial, and antioxidant properties. These characteristics underscore the plant's significance not only in traditional medicine but also in contemporary research and potential future therapeutic applications. [1-4].

**Figure 1: Plant, Leaves florets and Figs of *Walsuria trifoliata***

**Taxonomy [5]**

| | |
|---|---|
| **Botanical name** | **:** *Walsura trifoliate* |
| **Author** | **:** Harms, Hermann August Theodor (1830) |
| **Family** | **:** Meliaceae |
| **English names** | **:** Walsura |
| **Indian names** | **:** Kannada : Male sagada, Valursi<br>Tamil : cattuvakku, Valsura<br>Telugu : Vaalarasi, Valsura, Valsuri |
| **Synonyms** | **:** *Heynea trifolia A. Juss.*<br>*Walsura piscida Roxb.*<br>*Walsura trifolia (A. Juss.) Harms.*<br>*Walsura ternate Roxb.* |

**DESCRIPTION AND HABITAT**

This tree is characterized by its small stature, featuring brittle branches with pubescent branchlets. Its leaves are trifoliate, oblong, and ovate-lanceolate in shape, often with obtuse or emarginate apexes. The lower surface of the leaves has a glossy appearance. When it comes to its flowers, they are white in color, and the tree typically bears solitary seeds. The fruit of this tree is ovoid, and the seeds are pale brown, enveloped by a white, fleshy aril. *Walsuria trifoliate* is found in a variety of forest types, including dry deciduous, semi-evergreen, and evergreen forests. Its distribution encompasses regions in India and Sri Lanka, making it a notable presence in these areas.

**PHARMACOLOGICAL ACTIVITIES**

**Inhibition of α-glucosidases**

The roots of *Walsuria trifoliate* were subjected to a series of extraction processes. They were first shade-dried, then powdered, and subsequently extracted for 72 hours using three different solvents: hexane, ethyl acetate, and methanol. The yields from these extractions were as follows: methanol yielded 0.82%, hexane yielded 1.625%, and ethyl acetate yielded 6.57%. To assess the effects of these extracts on digestion, a procedure was followed. Specifically, the area above the cecum and below the duodenum of the small intestine was rinsed with cold saline. The resulting tissue was homogenized with 12 ml of maleate buffer (100mM, pH 6.0). The resulting mixture contained 200-1000 mg/ml of the sample extract and 100 ml of maleate buffer (pH 6.0) with 2% of each sugar substrate solution. This combination underwent a 10-minute incubation at 37°C, followed by a 5-minute period, and then absorbance was measured at 550nm. The results revealed that the concentrations of methanol and acarbose required for a 50% inhibition were 690.10+/-1.44 mg/ml and 290.90+/-1.82 mg/ml, respectively. It's noteworthy that compared to methanol, both hexane and ethyl acetate extracts exhibited lower inhibitory effects in this context [6].

**Antimicrobial activity**

The ethanol extract of *Walsuria trifoliate* was evaluated for its antimicrobial properties using the disc diffusion method. In this experiment, 20ml of media containing specific microbial strains was employed. To prepare the bacteria, a loop with a diameter of 6mm was inserted into 5mm of nutritional broth and then cultured at 35°C for 6 hours. Subsequently, nutritional agar was transferred to Petri plates and inoculated with 1mm of broth at an optical density of 0.6. To serve as positive controls, common antibiotics such as ampicillin, tetracycline, gentamycin, and clotrimazole were used, while water and ethanol were employed as negative controls. The plates were then incubated at a temperature of 37°C for 24 hours, and the resulting incubation zones were observed. The results of this experiment showed that the methanol extract exhibited significant activity against Staphylococcus aureus and Bacillus cereus, moderate inhibition on Bacillus coagulans and Candida albicans, and less activity against Aspergillus fumigatus. On the other hand, the aqueous extract displayed significant and moderate activity against Bacillus cereus, Bacillus coagulans, and Bacillus stearothermophilus. However, the petroleum benzene extract showed lower activity compared to the other two extracts in this context [7].

**Antioxidant activity [8]**

**Reducing ability**

In this experiment, various extract concentrations (ranging from 200 to 1000mg/ml) were emulsified using distilled water. These emulsified extracts were then mixed with 2.5 ml of 0.2M phosphate buffer (pH 6.6) and 2.5 ml of 1% K3Fe[CN]6. The resulting mixture was heated to 50°C for 20 minutes. After this process, the absorbance was measured using 2.5 ml of 10% trichloro acetic acid (TCA) in distilled water and 0.5 ml of 0.1% FeCl3 at 700nm. The results indicate that the reductive capabilities of the methanol extracts from water, hexane, and ethyl acetate were compared to those of BHT (butylated hydroxyl toluene). It appears that the plant extracts exhibited a lesser degree of reduction of Fe+ ions compared to the standard BHT. This suggests that the plant extracts may have lower antioxidant activity when compared to BHT in this specific assay.

**DPPH radical scavenging**

In this experiment, the methanol DPPH solution (0.15%) was mixed with successive dilutions of the plant extracts (ranging from 200 to 1000mg/ml). The absorbance of the mixture was then measured at 515nm after 10 minutes. The anti-radical activity was quantified and expressed in terms of mg/ml ($IC_{50}$), which represents the concentration required to scavenge 50% of the free radicals. The results showed that the methanol extract exhibited the strongest scavenging activity with an $IC_{50}$ concentration of 620.02+/-1.9mg/ml. In comparison, vitamin C, a known antioxidant, had an $IC_{50}$ concentration of 330.10+/-1.14 mg/ml. This indicates that the methanol extract has a higher anti-radical activity compared to the extracts made from hexane and ethyl acetate, suggesting its potential as an effective natural antioxidant.

**Hydroxyl scavenging**

In this study, the interaction of ferric-EDTA with various reactive species such as H2O2, ascorbic acid, and hydroxyl radicals resulted in the production of the substrate deoxyribose and hydroxyl radicals. The purpose of this experiment was to assess whether plant extracts could prevent damage to sugar when incubated with the reaction mixture. The results indicated that the concentration required for 50% inhibition (IC50) of the damage to deoxyribose was determined to be 710.50% for ethyl acetate and 240.45+/-1.42 mg/ml for methanol. These values reflect the effectiveness of the respective extracts in preventing damage to deoxyribose, with the lower IC50 value for methanol suggesting it has a higher protective effect.

***In vitro* Anti-inflammatory activity**

**Nitric oxide assay**

In this experiment, murine macrophages (RAW264.7 cells) were cultured after being pre-incubated with LPS (lipopolysaccharide) at a concentration of 1mg/ml for 24 hours. The cell density was approximately $91.5x10^5$ cells/ml. Nitrate levels in the culture media were used as an indicator of nitric oxide (NO) production. To measure the nitrate levels, Griess reagent was employed. Specifically, 100ml of cell culture media was mixed with 100ml of Griess reagent, and this mixture was incubated continuously for 10 minutes at 100°C. Following the incubation, the absorbance was measured at 540nm. The results indicate that at a concentration of 100mg/ml, both fraction 4 and fraction 7 exhibited substantial activity in terms of NO production, with values of 78.085% and 80.16%, respectively. This suggests that these fractions have a notable impact on nitric oxide production in the cultured macrophages [9].

***In vitro* cytotoxicity in MTT assay**

In this cell culture experiment, RAW 264 cells were grown in 96-well plates for 18 hours before being treated with LPS (lipopolysaccharide) at a concentration of 1mg/ml. Additionally, the cells were exposed to a plant extract at a concentration of 100 mg/ml. After 24 hours of incubation, 4 hours of MTT (3-(4,5-

dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) was added to the medium. The MTT forms crystals within the living cells, which were then dissolved in DMSO (dimethyl sulfoxide). The absorbance of the resulting solution was measured at 540nm after the supernatant was removed. This measurement allowed for the calculation of the percentage of dead cells in comparison to the control group. Regarding cytotoxicity, fractions 4 and 7 were observed to exhibit some level of cytotoxicity. Fraction 4 yielded 80mg with an RF (retention factor) value of 0.48, while fraction 7 yielded 35mg with an RF value of 0.62 after being eluted with a mixture of chloroform and ethyl acetate. These findings suggest that these fractions may have an impact on cell viability, potentially affecting cell health or growth [9].

From the leaves and twigs of *Walsura trifoliata*, researchers have isolated two intriguing novel apo-tirucallane triterpenoids, named piscidinone A and B. These compounds were characterized through in-depth spectroscopic analysis, particularly NMR and mass spectrometry. Piscidinone A and B possess tetracyclic rings and feature a unique substituted pyran ring in their side chains. Their biosynthetic origin is believed to be linked to the apo-tirucallane triterpenoids. Additionally, the cytotoxicity of compounds 1 and 2 was assessed against various cancer cell lines, including HT-29, MCF-7, Hela, A-549, B-16, IEC-6, L-6, and PC-3, demonstrating moderate activity with IC50 values ranging from 14.33 to 50.63 μg/mL across these cell lines [10].

**Synthesis of Gold Nanoparticles**

The researchers used the fresh green harvested stem bark of *Walsuria trifoliate* to extract gold nanoparticles (AuNPs) via an eco-friendly process. The results revealed an absorbance peak at 500nm, indicating the presence of surface plasmon resonance (SPR) property in the AuNPs, along with good stability characterized by a zeta potential value of approximately 24.4 mV and an average particle size of 24.4 nm. Transmission electron microscopy (TEM) showed spherical and monodisperse AuNPs with an average size of approximately 28.74 nm. While antibacterial studies were conducted, specific results regarding the zones of inhibition against bacterial species [11].

**Synthesis of Silver Nanoparticles**

In this study, silver nanoparticles (AgNPs) were synthesized using the aqueous leaf extract of *Walsuria trifoliate* through an eco-friendly bio-reduction method. UV-Visible spectroscopy confirmed the presence of AgNPs with a distinct peak at 434 nm, indicative of their surface plasmon resonance (SPR) property. FT-IR spectral analysis aimed to identify biomolecules involved in capping and stabilizing the nanoparticles, revealing broad peaks. TEM analysis determined the AgNPs' size (approximately 24.48 nm) and offered insights into their dispersion and morphology. The study conducted antibacterial assays, noting that smaller AgNPs exhibited antimicrobial activity, with a more significant impact on gram-negative bacteria (E. coli and Pneumonia), suggesting their potential as effective agents against such microbes [12].

**PHYTOCHEMICAL SCREENING**

Phytochemical screening of the *Walsuria trifoliate* shows the presence of saponins, alkaloids, fatty acids, phenols, steroids and carboxylic acids [5]. In a phytochemical investigation of the methanolic extract from *Walsura trifoliata* bark, researchers identified and isolated two new compounds: a phenylpropanoid-substituted flavan-3-ol (compound 2) and an anthraquinone glycoside (compound 3). Additionally, a known compound, chrysophanol (compound 1), was also identified. The structures of these compounds were determined through the interpretation of NMR (Nuclear Magnetic Resonance) and Mass spectral data [13]. A series of compounds, including piscidenone, piscidinol G, piscidinol F, piscidinol A, piscidinol B, piscidinol C, piscidinol D, piscidinol E, and piscidofuran, have been isolated from the plant. These compounds likely represent a diverse range of chemical constituents found within the plant and may have various biological activities acting as fish poison [14-16]. In a recent study, five novel apotirucallane-type terpenoids, named Piscidinols H-L (1-5), have been successfully isolated from the leaves of Walsura trifoliate. The researchers determined the complete chemical structures of these compounds through extensive spectroscopic analysis, with a particular focus on techniques like NMR (Nuclear Magnetic Resonance) and mass spectrometry [17]. A prominent molecule containing a phenylpropanoid unit and (2R, 3S)-flavanol has been successfully isolated from the leaves of *Walsura trifoliata*. The structural confirmation of this compound was established through extensive spectroscopic evidence, with a primary focus on 2D-NMR (Two-Dimensional Nuclear Magnetic Resonance) techniques. This discovery contributes to our understanding of the chemical constituents present in *Walsura trifoliata* leaves and their potential applications in various fields [18]. The crude methanolic leaf extract of Walsura trifoliolata underwent phytochemical screening, which identified approximately 22 different compounds using GC-MS analysis. Among these compounds, Lupenol, an active phytocompound, was discovered. Lupenol is known for its anti-inflammatory, anti-diarrheal, and anti-cancer properties, which align with previous research findings. The isolation of Lupenol from Walsura trifoliolata is a fascinating discovery that has garnered the interest

of many scientists, highlighting the potential of this plant species as a source of valuable bioactive compounds with diverse medicinal properties [19].

## CONCLUSION

The exploration of *Walsura trifoliata*'s pharmacological potential has unveiled a rich tapestry of bioactivities within this botanical marvel. Its roots exhibit promising anti-diabetic properties, while its leaves offer a diverse array of therapeutic effects, including anti-inflammatory, anti-diarrheal, and anti-cancer activities. The plant's extracts have also displayed robust antimicrobial capabilities, particularly the ethanol extract, which shows promise against various microorganisms. *Walsura trifoliata* further showcases its potential in nanoparticle synthesis, with both gold and silver nanoparticles bearing unique properties. These nanoparticles hold great potential for applications in medicine, diagnostics, and imaging. The discovery of novel apo-tirucallane triterpenoids, piscidinone A and B, in the plant's leaves and twigs adds intrigue to its chemistry. These compounds exhibit moderate cytotoxicity against cancer cell lines, offering promise in the realm of cancer therapeutics. Moreover, the isolation of Lupenol, an active phytocompound with anti-inflammatory, anti-diarrheal, and anti-cancer attributes, underscores the therapeutic treasure trove within *Walsura trifoliata*. As we peer into the future, further research can elucidate the precise mechanisms behind these pharmacological activities and explore clinical applications. Additionally, the nanoparticles synthesized from this plant hold potential for diverse technological advancements. The ongoing phytochemical exploration may reveal more bioactive compounds, while bioinformatics and molecular modeling can aid in drug development inspired by nature.

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