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# PHYTOCHEMICAL AND PHARMACOLOGICAL ACTIVITIES OF *PERGULARIA TOMENTOSA L.* - A REVIEW

**Nabil Ali Al-Mekhlafi[1*] and Anwar Masoud[1]**

[1]Biochemical Technology Program, Department of Chemistry, Faculty of Applied Science, Thamar University, P.O. Box 87246, Thamar, Yemen

**Abstract:**

*Plants have been one of the important sources of medicines even since the dawn of human civilization. There is a growing demand for plant based medicines, pharmaceuticals, food supplements, health products, cosmetics etc. Pergularia tomentosa L. (Asclepiadaceae) is a perennial twinning herb widely distributed in the Sahara desert, Horn of Africa, Arabian Peninsula to the deserts of southern and eastern Iran, Afghanistan and Pakistan. A wide range of chemical compounds including cardenolides, cardenolide glycoside and taraxasterol-type triterpenes etc. have been isolated from this plant. P. tomentosa has been exploited in traditional medicine as laxative, tumors, warts, depilatory, abortifacient, skin diseases and anthelmintic agents. Moreover, antioxidant, antibacterial, antifungal, insecticidal and cytotoxic activities of this species are documented. The aim of the present review is to summarize and highlight the traditional uses, phytochemical and pharmacological aspects of P. tomentosa.*

**Keywords**: *Pergularia tomentosa, cardenolides, taraxasteroltriterpenes, ghalakinoside, calactin*

*Corresponding author:

**Nabil Ali Al-Mekhlafi,**
*Biochemical Technology Program,*
*Department of Chemistry*
*Faculty of Applied Science, Thamar University*
*P.O. Box 87246, Thamar, Yemen*
*Cell: +967772203999*
*Email: nabilali7@tu.edu.ye*

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## INTRODUCTION:

Medicinal plants, since times ancient, have been used in virtually all cultures as a source of medicine. Medicinal plants are used medicinally in different countries and natural sources of compounds that can be used against many diseases [1]. The World Health Organization (WHO) estimated that 80% of the world's populations rely on traditional medicines for some aspect of their primary health care needs. According to WHO, around 21,000 plant species have the potential for being used as medicinal plants [2].

Nowadays, natural source are responsible for about half of the approved drugs that are currently available [3].

Phytochemicals are chemical compounds produced by different parts of plants like root, leaves, stem, bark, fruits and seeds. Phytochemicals are responsible for the medicinal activity of plants; that have protected humans from various diseases [4].

The milkweed family Asclepiadeceae comprises 200 genera and 2500 species of perennial shrubs and herbs distributed throughout the tropics and temperatures areas of the world mostly in the Sahara region [5]. *P. tomentosa* is a member of the Asclepiadeceae family. It commonly used in the traditional medicine for many purposes. It contained a wide range of chemicals including cardiac glycosides, flavonoids, saponin glycosidesalkaloids, tannins, anthraquinones and other compounds. The bioactivity studies showed that this plant exerted antioxidant, cytotoxic, antibacterial, antifungal and other effects.

Therefore, the aim of the present review is to highlight the traditional and folk medicine uses, chemical constituent and pharmacological effects of *Pergularia tomentosa*

**Synonyms:** Daemia tomentosa (L.) Pomel,

Telosma tomentosa (L.) M.R. Almeida Fl.Maharashtra,

Daemia cordata (Forssk.) R.Br. ex Schult.[6] [7]

**Common names: Arabic**: ghoulga, demya, leben el hamir

**Baluchistan**: Roossuk or Roosunk
**Targui**: tashkat, dellakal, tellakh, sellaha
**French**: pergulaire
**English**: Pergularia
**Nigeria:** fatakko, malaiduwa, bakambi, damargu rafi, sallenke
**Mauritania**: *ARABIC (Hassaniya)* umu éjlud = mother of skins, hide (AN)
**Ivory Coast:** *GAGU* monbula (K&B) *SHIEN (Chiehn)* sokolu (K&B)
**MALI**: *DOGON* pɣ́liõ pɣ́pɣ́liõ (C-G) *TAMACHEK* sellakha (RM) teshilshit (Rodd) [8]

**Scientific classification**

| | |
|---|---|
| **Kingdom**: | plantae |
| **Subkingdom**: | Tracheobionta |
| **Super division**: | Spermatophyta |
| **Division**: | Magnoliophyta |
| **Class**: | Magnoliopsida |
| **Subclass**: | Asteridae |
| **Order**: | Gentianales |
| **Family**: | Asclepiadaceae |
| **Genus**: | Pergularia |
| **Species**: | tomentosa |

**Description:**

This plant can reach 1 m, the perennial shrub about 50-60 cm. along with older woody stems around which the younger ones wind. Erect green hairs cover the stems and the leaves are opposite, entire, 1-2 cm. long, heart-shaped, with long stalks that are also covered with green hairs. Also small flowers with 5 yellow-whitish free petals are present. The fruits are oblong, globulous follicules, covered in fleshy bristles. A white sticky fluid from the leaves and fruits are secreted at the slightest touch of the plant. It flowers in spring in the northern Sahara and any time of year in the central Sahara [7].

**Morphology**

The plant is a twining grey, cane scent under shrub, with the young branches twining around the old ones. Leaves are rather small, 1.5-3.0 cm long, cordate, petiolate and opposite. The inflorescence is axillary umbels on peduncles longer than the leaves. The flowers are whitish-yellow with a pedicel much longer than the flowers. Calyx five-parted brownish hirsute; corolla 8 mm broad, with a tube little longer than the calyx and five-parted limb with ciliate margin. The fruit is a pair of spiny follicles, each 3-6 cm long, inflated below, attenuated into a long, hooked beak. The seed is dark brown in colour, ovate, 0.3-1.0 cm long, truncate at the apex, winged and densely velvety pubescent on both sides. The root system consists of a main woody taproot with smaller rootlets and branches Figure 1. [9,10].

**Geographical Distribution**

The plant is widely distributed across the Sahara desert, and eastward across the Horn of Africa through Sinai (Egypt), southern Israel, Jordan and the Arabian Peninsula to the deserts of southern and eastern Iran, Afghanistan and Pakistan [11]


**Fig. 1: flowers, leaves and fruits of *Pergularia tomentosa***

**Traditional Medicine Uses**

The milk extract from the *Pergularia tomentosa* leaves has been used in the treatment of skin diseases, such as tinea capitis, in Egypt, this plant is used as a laxative, depilatory, anthelmintic, poultice, abortifacient and for skin diseases. In Morocco, the leaves are applied as poultice on snake and scorpion bites and the latex is applied externally to mature furuncles and abscesses and to extract spines from the skin,[12,13]. In addition, it was used as anthelmintic, for tumors, warts and skin diseases in Yemen [14].

A decoction of the leaves, stems and roots is used for the treatment of constipation, piles, asthma, bronchitis and tuberculosis [10,15].

In côte d'Ivoire, the crushed plant with chillies is used against dysentery and as an anthelmintic, leaf-sap used as eye and nosedrops for headache [8]. In Morocco and other countries the latex is used as a cosmetic depilatory [11].

**Part Used Medicinally**

The leaves, latex and roots are used medicinally. These are collected in spring and they are prepared as an infusion, decoction, powder and mixed with other plants, and taken by mouth or used externally [7].

**Physicochemical Properties**

Physicochemical characteristics of the fruit of *P. tomentosa* were: total ash 7.8%, water soluble ash: 4.5%, acid insoluble ash: 0.3%. Pericarp: Petrolum Ether soluble extractive 3,06%, alcohol soluble extractive 6.01%. Seeds: Petrolum Ether soluble extractive 8.88% and alcohol soluble extractive 5.46%.

The fruit of *P. tomentosa* contained many minerals and trace elements in ppm: potassium 384.8, sodium 56.2, lead 0.12, magnesium 77.29, Iron 18.10, Calcium 477.6, Manganese 38.98 [10].

All the plant parts showed high percentages of carbohydrates and crude fiber range from 53.27-61.31% and 16.33-23.17% respectively. Mineral element composition of the plant showed higher amount of phosphorus and potassium in the rootand stemand sodium, magnesium and calcium in the leaf extract [16].

**Phytochemical Constituents**

Generally, phytochemicals are responsible for the medicinal activity of plants. Phytochemical analysis of plant extracts revealed the presence of cardiac glycosides, saponin glycosides, alkaloids, tannins, flavonoids, anthraquinones steroids and volatile oil [17].

Twenty-five compounds were isolated and identified from various parts of the *P. tomentosa.* The structure of these compounds has been presented in figure **2** and **3**. The main class secondary metabolites were isolated from this species include cardenolides, cardenolide glycoside and taraxasterol-type triterpenes. A few of them have been studied for biological activity. Phytochemistry of different parts of the plant is described below.

**Roots**

From the ethanolic extract of the roots of this species a new ghalakinoside and along with the known calactin have been isolated [18] as well as three new cardenolide glycosides, 3′-O-α-D-glucopyranosylcalactin (1), 12-dehydroxyghalakinoside (2), and 6′-dehydroxyghalakinoside (3) were isolated from the roots of *P. tomentosa* and their structures were established on the basis of spectroscopic methods [19].

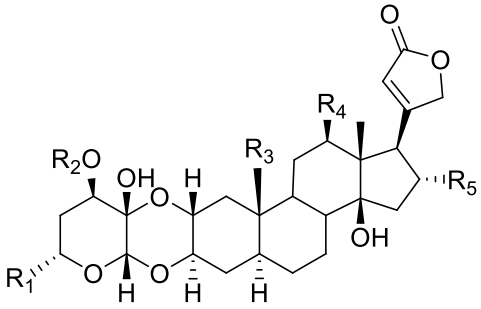
Previous phytochemical investigations of the roots of *P. tomentosa* led to the isolation of two new cardenolide glycosides 6′-hydroxycalactin (6) and 6′-hydroxy-16R-acetoxycalactin (7) along with known cardenolide glycoside, 16R-hydroxycalactin (8) [20].

**Whole Plant**

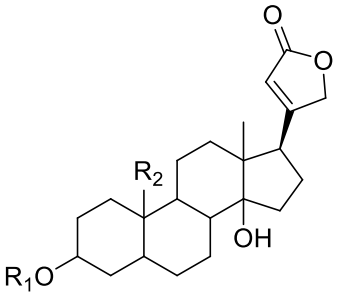
From the ethanolic extract of the whole plant of *P. tomentosa* two new triterpenes, pergularine A (18) and pergularine B (19) were isolated, In addition, eight known compounds were isolated from the plant including 3-acetyltaraxasterol (14), 3-taraxasterol (15), 16a-hydroxytaraxasterol-3-acetate (16), α-amyrin (17), 3-epi-micromeric acid (20), oleic acid (23), (9Z,12Z)-octadecadienoic acid (24) and (9Z,12Z)-octadecadienoic acid glucoside (25)[21].

**Leaves**

Three cardenolides, desglucouzarin (11), coroglaucigenin (12) and uzarigenin (13) in addition to β-sitosterol glucoside (26) were isolated from leaf samples. The cardenolides, ghalakinoside (4), calactine (5), and pergularoside (9) were also identified in the leaves of *Pergularia tomentosa* [5]. Other compound which was isolated from the leaf samples is 22- α-hydroxy-3,4-secostict-4(23),1(2)-en-3-oic acid (21) [22]. A new 16α-acetoxycalotropin (10) was isolated from the methanolic leaf extract of Egyptian plants of this species [23].Chromatographic fractionation of hexane extract of *Pergularia tomentosa* resulted in the isolation of lupeol acetate (22) [24], fifteen phenolics and flavonoids and four cardenolides were also identified in leaves extracts of *P. tomentosa* by used LC-MS techniques [25]




| | R1 | R2 | R3 | R4 | R5 |
|---|---|---|---|---|---|
| 1 | Me | B-D-Glc | CHO | H | H |
| 2 | $CH_2OH$ | H | $CH_2OH$ | H | H |
| 3 | Me | H | $CH_2OH$ | OH | H |
| 4 | $CH_2OH$ | H | $CH_2OH$ | OH | H |
| 5 | Me | H | CHO | H | H |
| 6 | $CH_2OH$ | H | CHO | H | OCOCH3 |
| 7 | $CH_2OH$ | H | CHO | H | OH |
| 8 | Me | H | $CH_2OH$ | H | H |
| 9 | $CH_2OH$ | OH | CHO | OH | OAc |
| 10 | Me | H | CHO | H | |




| | R1 | R2 |
|---|---|---|
| 11 | Glc | CH3 |
| 12 | H | OH |
| 13 | H | CH3 |

Desglucouzarin(11)
Coroglaucigenin (12)
Uzarigenin (13)

3 -O-α-D-glucopyranosylcalactin (1), 12-dehydroxyghalakinoside (2), 6 -dehydroxyghalakinoside (3) ghalakinoside (4) calactin (5), 6'-hydroxycalactin (6), 6'-hydroxy-16R-acetoxycalactin (7), 16R-hydroxycalactin (8), Pergularotoside (9), 16α–acetoxycalotropin (10)

**Fig. 2: cardiac glycosides from *Pergularia tomentosa* plant**

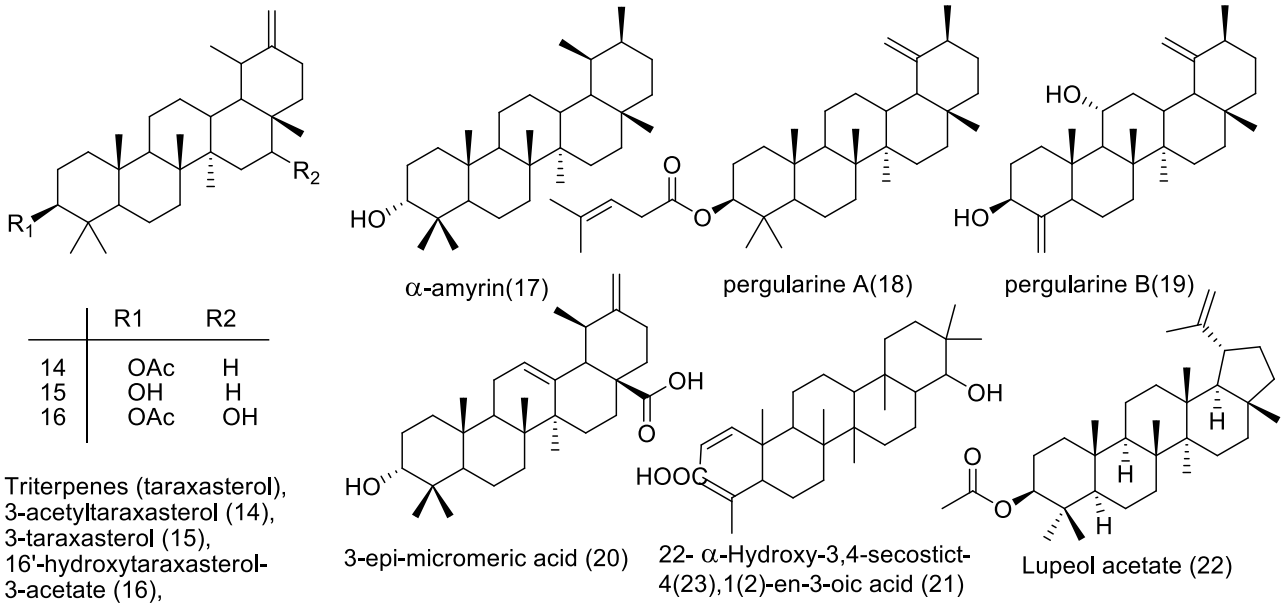



**Fig 3: Triterpenes from *Pergularia tomentosa* plant.**

**Pharmacological Activities**

**Cardiotonic Activity**

The extracts from this plant showed cardiotonic activity. Hifnawy *et.al.* (2014) reported that ghalakinoside showed an increase in the force of myocardial contraction and the heart rate was affected at very high dose levels, they also showed variable changes in the mean arterial blood pressure which were reversible except at the lethal dose of calactin in *in vivo* experiments in rabbits. Meanwhile, only mild reversible bradycardia with high dose levels has been observed. Higher doses of ghalakinoside and calactin showed changes in cardiac rhythm (dysrythmia) ended with a heart block [26].

**Antibacterial and Antifungal Activity:**

The antibacterial effect of the different fractions (hexane, ethylacetate and n-butanol) of the whole methanolic extract of combined mixture of plants (*Vitex doniana, Diospyros mesipiliformis, Acacia polycantha, Pirinari macrophylla, Ficus sycomorus* and *Parkia biglobosa*) and that of *Pergularia tomentosa*.Combined mixture of plants is used in ratio of 1:1were studied against wide ranges of bacteria (*Staphylococcus aureus (MTTC 96), Staphylococcus aureus (MTTC 2940), Escherichia coli (MTTC 739), Micrococcus luteus (MTCC 2470), Bacillus subtilis (MTCC 121), Streptococcus mutants (MTCC 890), Raoultella planticola (MTCC 530), Klebsiella pneumoniae and Salmonella typhimurium*) by disc diffusion method. Among the three fractions, the ethylacetate fraction of combined mixture of plants has marginal antibacterial activity with 8.0, 7.0 and 7.0 mm zone of inhibitions for *M. luteus*, *B. subtilis* and *S. typhimurium*, respectively. Minimum inhibitory concentration (MIC) for the combined mixture of plants was greater than 1000 for M. luteus and S. typhimurium and 87.5 µg/ml for B. subtilis[24]. Antibacterial activity of Ghalakoside isolated from *Pergularia tomentosa* was carried out against two Gram-positive (B. cereus and Staphylococcus aureus) and three Gram-negative (*S. marcescens*, *E. coli* and *P. putida*). It showed strong antibacterial activity against Gram-positive (*B. cereus*) and Gram-negative (*S. marcescens*) and so the lengths of clearing zone diameters were at concentrations 50 and 100 µg/disc (13.2, 10.3 mm, respectively). The minimum inhibitory concentration was 10 µg/disc (5.5 mm). It also exhibited weak antibacterial activity against Gram-negative P. putida and Gram-positive S. aureus. It was inactive against E. coli for all tested concentrations[27].

The antidermatophytic activity of column fractions hexane and chloroform obtained from *Pergularia tomentosa* leaveswere evaluated against *T. rubrum*, *T. mentagrophyte* and *M. gypseum*. Different concentrations of the subfraction (10, 20, 40, 80 and 160 mg/ml) were applied. The results showed that the subfraction chloroform (number 4) was active against *T. rubrum*, *T. mentagrophyte* and *M. gypseum* at all the concentrations used. The minimum inhibitory

concentrations of this fraction revealed low MIC values of 10 mg/ml against all test organisms. Whereas, the hexane subfraction2 and 4 inhibited the growth of *T. rubrum* at all the concentrations used[28].

The antifungal activities of the different parts from of *Pergularia tomentosa* were screened for activity by the fractional method following an increased gradient of polarity against *Fusarium oxysporumf. sp. Lycopersici*. The aqueous extracts of stems and leaves, n-butanol extract of fruits, and ethyl acetate extract of fruits showed positive results. The most potent effective fungicide with a minimum concentration (0.25mg/ml) were obtained from the fruit n-butanol extract. Whereas, ethyl acetate extract of fruits showed an inhibition of 75% at 2mg/ml. Aqueous extract of stems has a total inhibitory value of the fungi growth at a concentration higher than or equal to 20mg/mL. Aqueous extract of leaves shows an inhibition of 25% of the fungal growth at 20mg/mL[29].
More recently, Sulieman et al., (2017) reported antibacterial effect of Pergularia tomentosa along with other plants studied [30].

**Antioxidant Activity**
The methanolic and aqueous extracts which contained many flavonoids exerted an antioxidant activity against DPPH radicals, peroxyl radicals, hydroxyl radicals, and hydrogen peroxide [31].

The DPPH free radical scavenging method were used to detected oxidative activity of *Pergularia tomentosa* roots, stems, leaves, and fruits extracts showed the most powerful antioxidant activity was detected in leaves and fruits extracts [29].

The methanol and hot aqueous extract of this species showed DPPH free-radical scavenging activity (10.5% at 50µg/ml and 4.8% at 50µg/ml, respectively), compared with the standard reference (Ascorbic acid) (99.1% at the same concentration)[14].

Crude extract, basic, acidic, methanolic and hexane fractions were prepared from the whole plant of *P. tomentosa*, antioxidant activityand reducing power were evaluated for this fractions. The crude extract haven highest antioxidant activity, followed by the basic fraction compared to acidic and methanolic fraction. Hexane has the lowest activity[32]

The ethanolic, acetonic and aqueous extracts from *Pergularia tomentosa* were screening in HaCaT cells and skin explants. All extracts showed no significant effect on the HaCaT cell viability and apoptosis rate [33].

Recently, it has been shown that *P. tomentosa (Daemia cordata)* has a strong capacity to neutralize DPPH radical [34]

**Cytotoxic Activity**
The cytotoxic activity of ghalakinoside isolated from roots of *P. tomentosa* was evaluated against 9-KB cells. The results showed that the ghalakinoside possessed strong activity, with ($ED_{50}$, 2.9 x $10^{-2}$µg/ml)[18].

Eight cardenolide glycosides (6′-hydroxycalactin, 6′-hydroxy-16R-acetoxycalactin, 16R-hydroxycalactin, 3′-O-R-D-glucopyranosylcalactin, 12-dehydroxyghalakinoside, 6-dehydroxyghalakinoside, ghalakinoside and calactin) isolated from the roots of *P. tomentosa* were tested for their cytotoxic activity against six different human cancer cell lines (U-373, BxPC-3, PC-3, LoVo, A549, and MCF-7)in vitro and for their ability to inhibit Na+/K+-ATPase activity. All compounds showed very potent antiproliferative agents, calactin compound showed the most potent cytotoxicity against PC3, BxPC3, LoVo , A549, MCF-7 and U373 cells with $IC_{50}$ values of 0.02, 0.08, 0.05, 0.02, 0.04 and 0.2 µM respectively. All eight cardenolides displayed $IC_{50}$ values 10 times lower for A549 cells than in the five other cancer cell lines of different origin study of Na+/K+-ATPase inhibition showed $IC_{50}$ values of these compounds were 0.5, 1.2, 1.7, 0.5, 0.4, 0.7, 0.3 and 0.4µM, respectively, in addition, the cytotoxic properties preventing the morphologic changes seen in cancer cell lines.[20].

A study by Hamed et al. 2006 revealed apoptotic activity of *Pergularia tomentosa* for Kaposi sarcomathe antiproliferative effects of compounds 1-5 were examined against the Kaposis'sarcoma (KS) cell line[19]

Moreover, the cytotoxic effects of roots aqueous extract of *Pergularia tomentosa* were evaluated in human tumor cell, linecervix carcinoma (Hela), liver carcinoma (Hepg 2) and U251 brain cell lines. The highest activity was achieved with Hela cell line where $IC_{50}$ value was 7.5 µg/ml, followed by Hepg2 where $IC_{50}$ was 9.97 µg/ml and lastly the U251 with $IC_{50}$ 10 µg/ml [26]

**Insecticidal Activity**
It has been reported that the crude methanol extract of *Pergularia tomentosa* and its isolated cardenolides had potent antifeedant activity against S. littoralis [35]. However, the alkaloids extract from aerial part of *P. tomentos a*is reported to have insecticidal activity against the fifth instar larvae of *L. migratoria.* The

highest rate of mortality was found at 100% at 240 µg/ larvae [36].

A comparative experimental study of ethanolic leaf extracts from four selected local plants from Saudi Arabia against the larval stages of the dengue fever vector, *Aedes aegypti*. *Pergularia tomentosa* showed larvicidal properties but at a lesser efficacy [37].

**Molluscicidal Activity**

The cardenolide extract from *Pergularia tomentosa* showed molluscicidal activity against the land snail Monachaobstructa.The analyzed extracts possess strong antifeedant effect against land snails. The $LD_{50}$ value after 24 h of treatmentwas60.9 µg/snail [38].

**Toxicity**

The extract of this plant revealed pharmacological and biological activities. When the extract tested for toxicity, the ghalakinoside compound showed the highest toxicity followed by calactin, the median of the lethal doses were 4.6 mg/kg and 5 mg/kg respectively [26]

## CONCLUSION:

The extensive survey literature reviewed that *Pergularia tomentosa* L. is an important medicinal plant with diverse pharmacological spectrum. Few novel chemical constituent isolated from the *Pergularia tomentosa* showed cytotoxic, antibacterial, antifungal, antioxidant and insecticidal properties. *Pergularia tomentosa* L. should be considered as a promising source of many drugs because of its effectiveness.

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