



MAYTENUS EMARGINATA (WILLD.): A PROMISING DRUG FOR CANCER THERAPY

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ABSTRACT

There are hundreds of medicinal plants that have a long history of curative properties against various diseases and ailments. *Maytenus emarginata* (Willd.) (Family: Celastraceae) is an evergreen tree that holds a place of exceptional arrogance among the various plants because of its immense medicinal uses of great significance. Plant extracts of the celastraceae have been used for centuries throughout South America and China as insect repellents and insecticides in traditional agriculture, and also for the treatment of a plethora of medical ailments from stomach complaints and fever to rheumatoid arthritis and cancer. Phytochemical investigation of *Maytenus emarginata* (Willd.) has been compiled for the study of clinical use of this plant. The active compounds include emarginatine [A], [B], [E], [F], [G] and emarginatinine are discussed briefly with the recent advances and mechanism of their action. This article briefly reviews the botany, distribution, ecology, uses of the plant and as a drug for cancer therapy. This is an attempt to compile and document information on different aspect of *Maytenus emarginata* and its potential use as a drug source for different tumor cells.

Key words: *Maytenus emarginata* (Willd.), Emarginatine, Emarginatinine, Cancer therapy, Tumor cells.

INTRODUCTION

Chemotherapy is a kind of treatment that uses drugs to attack cancer cells. It is called a "systemic treatment" since the drug, entering through the blood stream, travels throughout the body and kills cancer cells at their sites. The drugs may rarely be intended to have a local effect, but in most cases, the intention is to destroy cancer cells wherever they may exist in the body. Chemotherapeutic drugs are chemically designed to target cells that are dividing and growing rapidly.

Once they reach the cancer cells, they act to retard their growth, eventually resulting in their destruction. Chemotherapy works by stopping or slowing the growth of cancer cells, which grow and divide quickly. The era of cancer chemotherapy began in the 1940s with the first use of nitrogen mustards and folic acid antagonist drugs. Cancer drug development has exploded since then into a multi-billion dollar industry. The celastraceae family, commonly known as bittersweet family, is indigenous to tropical and sub-tropical regions of the world, including North Africa, South America, and many parts of East Asia, Particularly China [1,2].

Plants of this family generally grow as small trees, bushes or lianas and have resinous stems and leaves. They have been valued since antiquity because their extracts have useful medicinal properties [3]. The crude plant extracts of the celastraceae in traditional medicine and agriculture is astonishing, and includes stimulant, restorative, male contraceptive, anti-tumor, anti-leukemic, anti-bacterial, insecticidal and insect repellent activities [4].

Maytenus emarginata (Willd.) belongs to family celastraceae, is an evergreen tree that tolerates various types of stresses of the desert, locally known as "Kankero" in Hindi, "Thorny staff tree" in English. Traditionally species of *Maytenus* has been used for fever, asthma, rheumatism and gastrointestinal disorders worldwide.

Recently some biomolecules from *Maytenus* species has been reported to be active against HIV-Protease [5] Carcinoma and leukemia [6]. Ulcers [7] and MDR (Multi Drug Resistance) [8]. Various parts of this plant contain immense medicinal properties which are mentioned under:

- **Root-** Used in gastrointestinal troubles, especially dysentery [9].
- **Stem-** Tender shoots of the plant help for mouth ulcer. The bark is ground to a paste and applied with mustard oil to kill lice in the hair.
- **Leaf-** Pulverized leaves of *Maytenus emarginata* are given in milk to children as a vermifuge [10]. A decoction of the leafy twigs is used as a mouthwash to relieve toothache. Ash of leaves used

to heal up sores and wound gives cooling effect. The leaves are burnt and mixed with ghee to form an ointment used to heal sores [11]. The tender leaves are chewed raw in the treatment of jaundice.

- **Fruit-** The fruits are used in medicines to purify blood [12].

BOTANICAL CLASSIFICATION:

Kingdom	:	Plantae
Phylum	:	Magnoliophyta
Class	:	Magnoliopsida
Order	:	Celastrales
Family	:	Celastraceae
Genus	:	Maytenus

BOTANICAL NAME: *Maytenus emarginata* (Willd.)Ding Hou

SYNONYMS:

- *Celastrus emarginatus* Willd.
- *Gymnosporia emarginata* (Willd.) Thw.
- *Gymnosporia Montana* (Roth) Benth.

COMMON NAMES:

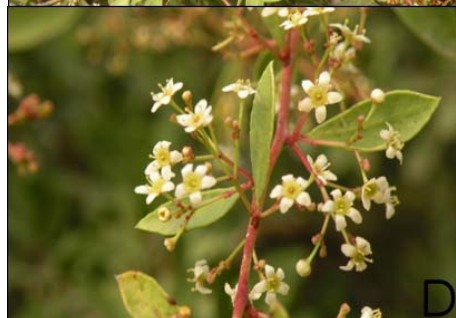
Hindi	:	Vinger, Kankero, Baikal, Malkangni
English	:	Thorny staff tree
Sanskrit	:	Vikankata, Sudhavridsha
Bengali	:	Bakundri, Vaichigacha
Kannada	:	Tandrasi, Tandraja, Haalu manike, Malega, Malkaamguni
Malayalam	:	Katou-patsjotti, Kanguni
Marathi	:	Baefal, Baekar, Bhaarooolee, Bharatti, Bharuli, Harmocha, Vekal, Vekar, Yekkadadi
Tamil	:	Kattangi, Nandunarani, Valulu-Vai
Telugu	:	Chinni, Danthi, Sinni, Danti, Chinni tuppaa, Chinni chettu Goddali-cippa
Gujarati	:	Vickado

BOTANICAL DISCRIPTION

The members of Celastraceae family generally are trees and shrubs comprising about 55 genera and 850 species that are sometimes climbing or vining [13]. *Maytenus emarginata* is a small, compact tree, 3-5 meter high; young branches purple, often spiny, with leaves and flowers on the spines. All the botanical descriptive characters of this plant are listed in Table 1.

Table 1: Botanical Description of *Maytenus emarginata* (Willd)

Plant type	Evergreen, Dioecious tree, Very hardy plant.(Figure.A) Habit:- Scandent shrub or small tree Name code:- 202785
Growing requirements	Light requirement: - Full sun with midday shade Soil tolerances: - Sandy soil, limestone Best season:- Monsoon Drought tolerance:- Various types of stresses of the desert
(a) Bark	Pale brown, smooth, cracked (Figure. B)
(b) Leaf	Thick, coriaceous and usually longer than 40mm, apex rounded, alternate on young branchlets, fasciculate on older ones (Figure. C)
(c) Flower	Bisexual or sometimes functionally unisexual, actinomorphic, white or cream colored 5-7mm in diameter (Figure. D) Male flower:- Stamens slightly shorter than petals, stigmas absent, disc green, 5-lobed Female flower: - Stamines shorter than stamens of male flower, ovary 3-locular, green, style as long as ovary.
(d) Fruit	Capsule, berry, 6-12mm long, green becoming red (Figure. E)
(e) Root	Tap root, Cream yellow in color (Figure. F)
Pest and diseases	Trouble free

**Figure A. *Maytenus emarginata* (Willd.) Plant****Figure B. Bark****Figure C. Leaf****Figure D. Flower****Figure E. Fruit****Figure F. Root****DISTRIBUTION:**

The species is globally distributed in Paleotropics. Within India, it is common in dry scrub forests throughout, particularly on poor soils in Central and Western peninsular India. The genus *Maytenus* distributed in drier parts of Central, South-Western and North-Western India.

It is found throughout in India (Madhya Pradesh, Uttar Pradesh, Punjab, Maharashtra, Gujarat, Delhi, Bihar, Tamilnadu, and Rajasthan).

In Rajasthan its found in Ajmer: Ajmer-Udaipur road, kota: Shahabad, Pali: Gurupratap singh village, Sirohi: Vadakhoda, Tonk: Rajmahal, Doogor Beed (Nagaur), Fahelpur Beed (Sikar), Siker Beed (Siker), Nokha (Bikaner), Karni Mata Oran, Deshnoke (Bikaner), Shri Balaji (Nagaur), Chohta (Barmer), Shri Mukam-Nokha (Bikaner), Khejarali (Jodhpur), Nursery of Rajasthan University, Jhalana Dungi (Jaipur).

ECOLOGY:

Growing at elevations from near sea level and locally abundant on the coast on sand at the edge of mangrove forest or secondary forest, at forest margins, in thickets on branches and hillsides and on sea cliffs, often on limestone. Long, hot summers are needed for production of flowers and fruits.

PROPAGATION:

Maytenus emarginata is an out breeding tree therefore it shows great variability. Sow seed under glass in season of autumn. Remove suckers, which may appear at some distance from the parent plant in spring season. Root semi-ripe cuttings with bottom heat in summer.

GROWTH PATTERNS:

Maytenus emarginata (Willd.) grow in moderately fertile, moist but well-drained soil in full sun with midday shade. Fruit appears in January to February and fruit ripens start from March to April. Flowers appears in October to January. Develops new leaves from June to August as shown in Table-2. The best season for collecting of this plant for medicinal uses is monsoon.

Table 2: General growth pattern of *Maytenus emarginata* (Willd)

Month	J a n	F e b	M a r	A p r	M a y	J u n	J u l	A u g	S e p	O c t	N o v	D e c
Plant Parts												
New leaf												
Flower												
Fruit												
Fruit ripen												

MAYTENUS EMARGINATA:- PROMISING DRUG FOR ANTICANCER:

The majority of chemotherapeutic drugs can be divided into alkylating agents, antimetabolites, anthracyclines, plant alkaloids, topoisomerase inhibitors and other antitumor agents [14].

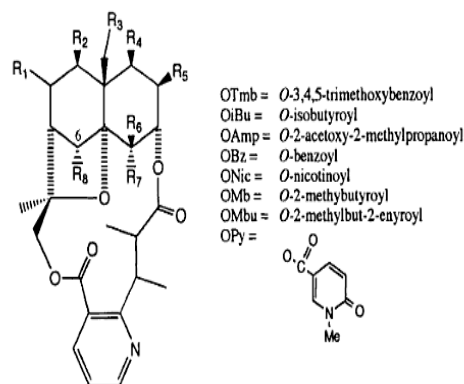
Over the last 30 years or so, a large number of secondary metabolites exhibiting a wide range of bioactivity have been extracted from the Celastraceae. The bioactive metabolites of the genus Maytenus in plants belongs to family Celastraceae, which are widely used as folk medicines in South America [15].

Many characteristic bioactive compounds, such as maytansinoids [16] with antitumor activity, quinoid triterpenes [17, 18] and triterpene dimmers [19, 20] with cytotoxic activity, sesquiterpene pyridine alkaloids [21, 22] with insect antifeedant [23] and immunosuppressive activities [24] and sesquiterpene polyesters [25] with anti-tumor promoting activity [26] are reported from genus Maytenus or the family Celastraceae.

In the search for potential antitumor agents from the plant family Celastraceae, several cytotoxic sesquiterpene pyridine alkaloids are present [27, 28] which are as mentioned under:-

- Emarginatine A (Fig.1a) [Molecular formula: C₄₃H₅₀N₂O₁₉ . Molecular weight: 898.859g/mol] which were isolated from the stems and branches of *Maytenus emarginata*, is based on the euonyminol skeleton and contains a C-3 - C-13 evonic acid dilactone bridge, was slightly less active than emarginatinine, which differs only by containing a C-3 - C-13 hydroxywilfordic acid dilactone bridge (ED₅₀ = 4.0 vs. 2.1 µg mL⁻¹, respectively) [27]. Its structure was determined with MS, UV, IR and one and two- dimensional ¹H and ¹³C NMR, and confirmed by X-ray analysis [29].
- Emarginatine B (Fig.1b) [Molecular formula: C₄₈H₅₂N₂O₁₉, Molecular weight: 960.929g/mol] has been isolated from *Maytenus emarginata* and its structure determined EIMS, UV, IR and ¹H and ¹³C NMR comparison with (Fig. 1a). Emarginatine B was found to be significantly more cytotoxic than Figure 1a against human KB cells, with an ED 50 = 0.4µg/ml [30].
- Emarginatine E (Fig.1c) exhibited cytotoxicity against KB (ED₅₀ = 1.7µg/ml) and COLO-205 (ED₅₀ = 4.1µg/ml) cancer cells [31].
- Emarginatine F (Fig.1d) [Molecular formula: C₄₆H₅₀N₂O₁₈, Molecular weight: 918.891g/mol] were showed best cytotoxicities against the human melanoma cell line RPMI-7951 (ED₅₀ < 0.1µgml⁻¹), and against the meduloblastoma cell line TE-671 (ED₅₀ = 0.21 µgml⁻¹).
- It also showed interesting results against the murine leukemia cell line P-388 (ED₅₀ = 0.69 µgml⁻¹) and against the human colon adenocarcinoma cell line HCT-8 (ED₅₀ = 1.29 µgml⁻¹). However, an ambiguous result was obtained for cytotoxicity against the human lung carcinoma cell line A-549 (ED₅₀ = 5.5 µgml⁻¹).
- Emarginatine G (Fig.1e) [Molecular formula: C₄₅H₅₂N₂O₁₉ , Molecular weight: 924.896g/mol] has been isolated from *Maytenus emarginata*. Structure of this compound were determined with MS, IR, UV, one and two-dimensional NMR [27]. It is also evaluated against tumor cells [32].

Chemical structures of above these compounds (Fig. a - e) are as under:



S.No	Compound	R1	R2	R3	R4	R5	R6	R7	R8
Fig.1a	Emarginatine A	β -OAc	OAc	OAc	OAc	OPy	CH3	OH	OAc
Fig.1b	Emarginatine B	α -OAc	OBz	OAc	OAc	OPy	CH3	OH	OAc
Fig.1c	Emarginatine E	α -OAc	OH	OAc	OH	OPy	CH3	OH	OAc
Fig.1d	Emarginatine F	α -OH	OAc	OAc	OBz	OPy	CH3	OH	OAc
Fig.1e	Emarginatine G	β -OAc	OAc	OAc	OMbu	OPy	CH3	OH	OAc

- Emarginatinine (Fig. 2) were isolated from the stems and branches of *Maytenus emarginata* and its structure established using one and two-dimensional ¹H NMR. Emarginatinine was cytotoxic against KB cells with ED₅₀ = 2.1 μ g/ml (Kuo et al, 1994).

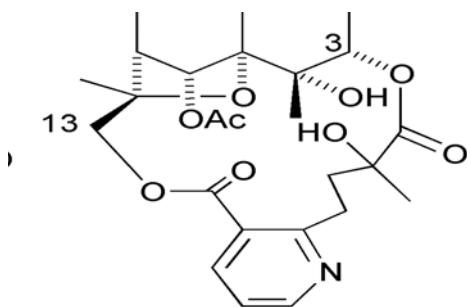


Figure 2: Chemical structure of Emarginatinine

CONCLUSION:

The present study revealed that *Maytenus emarginata* shows significant antitumor properties that support its use in the treatment of cancer. These new leads could be further modified through analog studies to yield useful compounds or to be subjected to biochemical and pharmacological investigation to increase the understanding of cancer cell biology. The sesquiterpene pyridine alkaloids reviewed above are only one division of antitumor agents from *Maytenus emarginata* plant. The number of the alkaloids and their analogs discussed above has already been in preclinical or clinical trials and some of them are now used in clinics. This property could be exploited for the advantage of cancer patients. Continuing investigation on this plant-derived alkaloids will undoubtedly result in the development of more selective and effective novel anticancer drugs.

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