International Journal of Research and Review
www.ijrrjournal.com E-ISSN: 2349-9788; P-ISSN: 2454-2237

Review Article

Alkaloids and Non Alkaloids of *Tabernaemontana divaricata*

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ABSTRACT

Tabernaemontana divaricata is a garden plant which commonly known as *Chandani*, has been used as a traditional medicine with many pharmacological properties. Plants produce a lot of antioxidants to control the oxidative stress caused by sunbeams and oxygen, they can represent a source of new compounds with antioxidant activity. The beneficial properties of T. divaricata are antioxidant, anti-infection, anti-tumour action, analgesia and the enhancement of cholinergic activity in both peripheral and central nervous systems. In traditional medicine Tabernaemontana divaricata is used to treat various diseases like epilepsy, abdominal tumours, eye infections, fractures, fever, headache, inflammation, mania, oedema, leprosy, diarrhea. Many primary and secondary metabolites are present in the different parts of Tabernaemontana divaricata .The review reveals that alkaloids and non alkaloids present in the extract of parts of Tabernaemontana divaricata which can be applicable in various research applications. Total 66 alkaloids isolated and identified from T. divaricata. 34, Non-alkaloids including the enzymes, pyrolytic oil, hydrocarbons, terpenoid and phenolic acids are also listed in this review.

Keywords: *Tabernaemontana divaricata, Alkaloids, Non alkaloids*

INTRODUCTION

Tabernaemontana divaricata is commonly known as *Chandani* from the family *Apocynaceae*. The plant is an evergreen shrub growing to a maximum height of six feet and found in all parts of the India. Normally a Plant produces various metabolic products for their growth and development. The components which are essential for the growth and survival for the producer plant are known as primary metabolites. Secondary metabolites are plant substances which are derived biosynthetically from primary metabolites. Flavanoids, alkaloids, terpenoids, phenols, tannins, saponins, steroids etc belong to this class. The presence of phenolic group imparts anti oxidant activity to flavonoids, phenols and tannins. Anti oxidant substances can block the action of free radicals which are responsible for the pathogenesis of various diseases. [1] This species has been extensively investigated and a number of chemical constituents such as alkaloids, triterpenoids, steroids, flavonoids, phenyl propanoids and phenolic acids were isolated from leaves, roots and stems of the plant. [2-10]

Plants produce a lot of antioxidants to control the oxidative stress caused by sunbeams and oxygen, they can represent a source of new compounds with antioxidant activity. Free radicals are atoms or groups of atoms with an odd number of electrons and can be formed when oxygen interacts with certain molecules. Once highly reactive free radicals are formed, they can start chain reactions. Their major threat comes from the damage they can do when they react with important cellular components such as DNA or cell membranes.

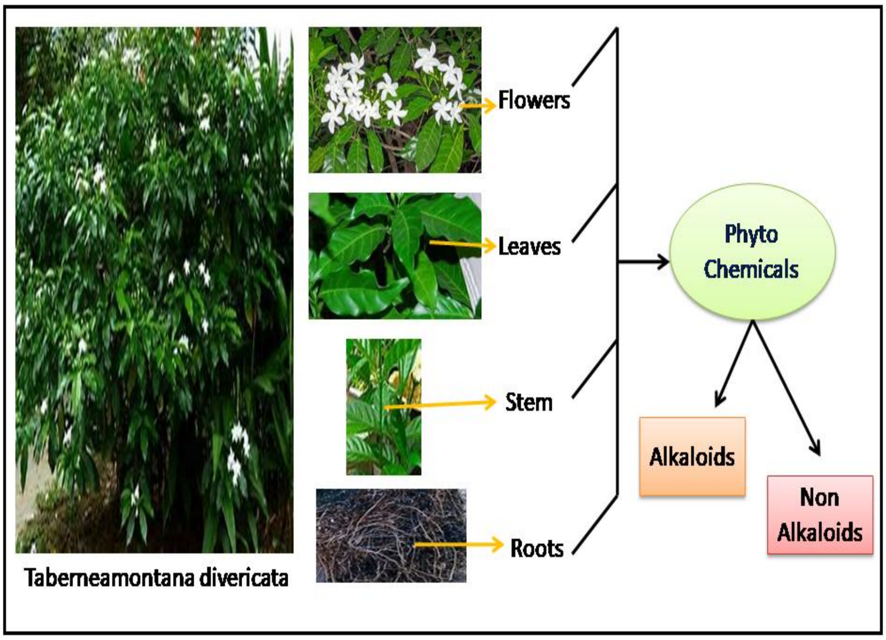

Figure 1: Alkaloid and Non alkaloids study of Tabernaemontana divaricata

Cells may function poorly or die if this occurs. To prevent free radical damage, the body has a defence system of antioxidants. [11] Antioxidants can give free radicals, which become companions to their unpaired electrons, thus eliminating the threat of gene alteration which can lead to cancer. [12-13] Medicinal plants have attracted the attention of not only professionals from various systems of medicine, but also the scientific community belonging to different disciplines. Herbal drugs, being generally harmless in prescribed doses, are becoming popular all over the world and the WHO currently encourages, recommends and promotes inclusion of these drugs in national health care programmes. [14-15]

T. divaricata was first described by Linnaeus in 1753. T. divaricata has four typical characteristics including: (i) evergreen shrub forms shaped like symmetrical mounds 6-feet high, (ii) horizontal branches having the appearance of an attractive, almost horizontal shrub (the species name, divaricata, means an obtuse angle), (iii) large, shiny, deep green leaves, 6 or more inches in length and 2 inches wide, and (iv) waxy blossoms with white, five-petal pinwheels, gathered in small clusters on the stem tips. T. divaricata has been used in traditional medicine and for other purposes. The phytochemistry and a number of chemical constituents from the leaves, stems, and roots have been reported previously. [16] Constituents studied include alkaloids, and non-alkaloid constituents such as terpenoids, steroids, flavonoids, phenyl propanoids, phenolic acids and enzymes. [17-52] Since 1974, 66 different alkaloids of T. divaricata have been identified. The phytochemical data for each alkaloid provide information about its biosynthesis. Such information can assist in the search for new application and, medically interesting compounds that may be useful against diseases. In traditional medicine Tabernaemontana divaricata is used to treat various diseases like epilepsy, abdominal tumours, eye infections, fractures, fever, headache, inflammation, mania, oedema, leprosy, diarrhea. [53]

2. Phytochemical constituents of T. divaricata

2.1. Alkaloids of T. divaricata:

Alkaloids of T. divaricata are arranged in 11 main classes: Vincosan, Corynanthean, Vallesiachotaman, Strychnan, Aspidospermatan, Plumeran, Eburan, Ibogan, Tacaman, Bis-indole and Miscellaneous. At least 66 alkaloids were extracted from T. divaricata by several methods such as thin layer chromatography (TLC), high performance liquid chromatography (HPLC) and gas chromatography-mass spectrophotometry (GC-MS). The currently known 66 alkaloids isolated from T. divaricata is shown in Table 1.

Table 1 : Alkaloids isolated from different parts of T. divaricata

S.N.	Alkaloids	Plant Part
1	11-Methoxy-N-methyldihydropericyclivine	Leaves, Flowers, Roots
2	12-Hydroxyakuammicine	Cell Suspension Culture
3	19,20 Dihydrotabernamine	Roots
4	19,20-Dihydroervahanine A	Stems
5	19-Epivoacangine	Leaves, Flowers, Root
6	19-Epivoacristine	Leaves
7	19-Heyneanine hydroxyindolenine	Whole Plant
8	19-Hydroxycoronaridine	Root Bark
9	3-Oxocoronaridine	Root Bark
10	3-Oxovoacangine	Whole Plant
11	3S-Cyanocoronaridine	Stems, Barks
12	3S-Cyanoisovoacangine	Stems, Bark
13	5-Hydroxy-6-oxocoronaridine	Root Bark
14	5-Hydroxyvoaphylline	Leaves
15	5-oxo-11-hydroxy voaphylline	Leaves
16	5-Oxocoronaridine	Root Bark
17	6-Oxocoronaridine	Root Bark
18	Apparicine	Cell Suspension Culture
19	Catharanthine	Cell Suspension Culture
20	Conodurine	Roots
21	Conodusarine	Stems, Barks
22	Conofoline	Leaves
23	Conolidine	Stems, Barks
24	Conolobine A	Stems, Barks
25	Conolobine B	Stems, Bark
26	Conophyllidine	Leaves
27	Conophylline	Leaves
28	Conophyllinine	Leaves
29	Coronaridine	Leaves
30	Coronaridine hydroxyindolenine	Root Barks
31	Dregamine	Leaves, Stems, Barks, Roots
32	Ervaticine	Leaves
33	Ervatinine	Leaves
34	Heyneanine	Root Bark
35	Hyderabadine	Leaves
36	Ibogamine	Whole Plant
37	Isovoacangine	Leaves, Flowers, Roots
38	Isovoacristine	Leaves, Flowers, Roots
39	Lahoricine	Leaves
40	Lochnericine	Leaves
41	Mehranine	Leaves
42	N1-Methylvoaphylline	Leaves
43	N-methylvoafinine	Leaves
44	O-Acetylvallesamine	Cell Suspension Culture
45	Pachysiphine	Leaves
46	Pericyclivine	Cell Suspension Culture
47	Perivine	Cell Suspension Culture
48	Pseudovobparicine	Root, Bark
49	Stemmadenine	Cell Suspension Culture
50	Taberhanine	Leaves
51	Tabernaelegantine A	Roots
52	Tabernaemontanine	Leaves
53	Tubotaiwine	Cell Suspension Culture
54	Vallesamine	Cell Suspension Culture
55	Voacamine	Leaves, Stems, Barks, Roots
56	Voacangine	Leaves
57	Voacangine hydroxyindolenine	Whole Plant
58	Voacristine	Whole Plant
59	Voacristine hydroxyindolenine	Whole Plant
60	Voafinidine	Leaves

Table 1: to be continued…		
61	Voafinine	Leaves
62	Voaharine	Leaves
63	Voalenine	Leaves
64	Voaphylline	Leaves
65	Voaphylline hydroxyindolenine	Cell Suspension Culture
66	Vobasine	Leaves, Stems, Barks, Roots

2.2. Non-alkaloids of T. divaricata:

Non alkaloidal constituents such as terpenoids, steroids, enzymes, and hydrocarbons have also been isolated from T. divaricata. Terpenoid-indole alkaloids are formally derived from a unit of tryptamine, obtained by decarboxylation of tryptophan catalyzed by the enzyme tryptophan decarboxylase (TDC), and a C10 unit of terpenoid origin (secologanin). Several studies demonstrated about the role of those enzymes that regulate biosynthesis and metabolism of terpenoids in T. divaricata. [54] The five known enzymes that were detected for the first time in T. divaricata cell suspension culture: isopentenyl diphosphate isomerase, prenyl transferase, squalene synthetase, qualene 2,3 oxide cycloartenol cyclase and squalene 2,3-oxide cyclase. These enzymes act as key regulatory agents in controlling the flux of carbon into the cytosolicmicrosomal pathway of terpenoid synthesis. [55] Other five enzymes from T. divaricata cell lines including tryptophan decarboxylase, strictosidine synthase, strictosidine glucosidase, isopentenyl pyrophosphate isomerase and geraniol 10 hydroxylase. [56] In addition, the enzyme strictosidine a-D-glucosidase was partially purified from cell suspension cultures of T. divaricata. [57] Another non-alkaloidal enzyme, squalene synthase, was also partially purified from a membrane-rich fraction obtained from cell suspension cultures of T. divaricata. [58] Farnesyl diphosphate synthase enzyme from T. divaricata cultured cells by chromatography and Western blotting assay also were studied. [59]

Many plant species produce a wide range of chemical products that are not involved in primary metabolism and called secondary metabolites. [60] Secondary metabolites are metabolic intermediates or products found as differential products in restricted taxonomic groups and are not essential to the growth and life of the producing organism. They are biosynthesized from one or more primary metabolites by a wider variety of pathways than those available in primary metabolism. [61] Alkaloid and terpenoids are main secondary metabolites that have many physiological and pharmacological properties to living cells. [62] However, their biosynthesis is normally restricted to certain developmental stages of the organism. Some of that biosynthesis is the phase-dependent formation for some enzymes. [63] Therefore, the expression of secondary metabolites is based on the process of plants' differentiation. Thus, it is not surprising that the synthesis of secondary metabolites does not occur in the meristematic cells of intact plants. [64] Moreover, some studies suggested that cell cultures of plants could produce secondary metabolites when they stopped being meristematic and rather acquired a certain degree of biochemical modification and maturation. [65]

Other non alkaloidal constituents, saw discovery of free radical scavenging enzymes such as superoxide dismutase, catalase, ascorbate peroxidase, glutathione reductase and phenolic peroxidase in T. divaricata from roadside plants in India. [66] Their discoveries indicated that T. divaricata was a very good scavenging system to combat the effects of air pollution. Other non alkaloidal compounds in T. divaricata such as pyrolytic oil, solid char, amino acid and hydrocarbon were also found to have some beneficial effects. The stems and leaves of Indian T. divaricata have pyrolytic oil and solid char that can be converted into petroleum and ethanol, which can be exploited to produce gasohol fuel. [67] The hexane extract from old leaves, roots, flowers and stems of T. divaricata was rich in hydrocarbons. [68] Some isolated eight non alkaloid compounds from the root bark of T. divaricata such as a -amyrin acetate, lupeol acetate, a-amyrin lupeol, cycloartenol, b-sitosterol, campesterol, benzoic acid and aurantiamide acetate. Non-alkaloids isolated from different parts of T. divaricata is shown in Table 2.

Table 2: Non-alkaloids isolated from different parts of T. divaricata

S.N.	Non Alkaloids	Plant Part
Enzyme:		
1	Anthranilate synthase	Cell Culture
2	Isopentenyl diphosphate	Cell Culture
3	isomerase	-
4	Prenyl transferase	-
5	Squalene synthetase	-
6	Qualene 2,3–oxide	-
7	cycloartenol cyclase	-
8	Squalene 2,3-oxide: cyclase	-
9	Tryptophan decarboxylase	Cell Culture
10	Strictosidine synthase	-
11	Strictosidine glucosidase	-
12	Isopentenyl	-
13	pyrophosphate isomerase	-
14	Geratinol 10-hydroxylase	-
15	Strictosidine b–D-glucosidase	Cell Culture
16	Squalene synthase	Cell Culture
17	sopentenyl diphosphate	Cell Culture
18	isomerase	-
19	Farnesyl diphosphate synthase	-
20	Superoxide dismutase	-
21	Catalase,	-
22	Ascorbate peroxidase	-
23	Glutathione reductase	-
24	Phenolic peroxidase	-
25	Pyrolytic oil and solid char	Stems, Leaves
26	Hydrocarbon	Leaves, Roots, Flowers, Stems
Other (Terpenoid & Phenolic Acid)		
27	a–amyrin acetate	Root Bark
28	Lupeol acetate	-
29	a-amyrin lupeol	-
30	Cycloartenol	-
31	b-sitosterol	-
32	Campesterol	-
33	Benzoic acid	-
34	Aurantiamide acetate	-

The terpenoids, phenolic acid, and plant metabolites exhibit pharmacological properties such as anti-inflammatory and anti-oxidant activity invitro. [69] Recent investigations have shown that the antioxidant properties of plants could be correlated with oxidative stress defense and different human diseases including cancer, atherosclerosis and the aging process. The antioxidants can interfere with the oxidation process by reacting with free radicals, chelating free catalytic metals and also by acting as oxygen scavengers. [70-72]

3. CONCLUSION

Many primary and secondary metabolites are present in the different parts of Tabernaemontana divaricata .The review of chemical analysis reveals that alkaloids and non alkaloids present in the extract of parts of Tabernaemontana divaricata which can be applicable in various research applications. There are still many T. divaricata alkaloids and their derivatives, whose activities have not yet been investigated. Hence much contribution in the production of more research is expected from this plant other active biochemical components with the help of advanced study in future.

4. ACKNOWLEDGEMENT

The authors acknowledge the help received from everyone for encouragement of this review work and kind blessings to publish this paper.

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How to cite this article: Kulshreshtha A, Saxena J. Alkaloids and non alkaloids of *Tabernaemontana divaricata*. International Journal of Research and Review. 2019; 6(8):517-524.

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