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Rauvolfia serpentina (Sarpagandha): An overview

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ABSTRACT

Rauvolfia serpentina or the Serpentina plant is a climbing or twining herb or shrub, belonging to the natural order Apocynaceae, very well known for its immense therapeutic use in the pharmaceutical world. *R. serpentina* is found to be the most consistently successful and effective drug in curing violent maniacal disorders associated with psychosis, schizophrenia, insanity, insomnia and epilepsy. The pharmacologic actions of *R. serpentina* is due to the presence of alkaloids, carbohydrates, flavonoids, glycosides, phlobatannins, phenols, resins, saponins, sterols, tannins and terpenes. The root extracts are mostly used for its various medicinal properties. It also helps in the treatment of intestinal disorders, particularly diarrhea and dysentery and also as anthelmintic. The present review focuses mainly on chemical composition and importance of *Rauvolfia* alkaloids.

Keywords: Therapeutic uses, *R. serpentina*, alkaloids, ethnobotany, chemical composition

INTRODUCTION

India is one of the richest sources of traditional herbs and medicinal plants. From time immemorial our people are using these herbs to cure all kinds of diseases and illness. Now a days, millions of people are suffering from various types of diseases worldwide, therefore, there is a need to get new formulations of medicine which can cure these diseases. Though there are availability of different pharmaceutical formulations, these seem to be more costly and less affordable. Therefore, there is need to shift from these pharmaceutical formulations to traditional medicines. But over exploitation of these medicinal herbs has resulted in loss of genetic biodiversity. Therefore, we have to be concerned about bringing these medicinal plants into proper cultivation system so that our natural resources stay safe. Ahmed and Barua (2013) have discussed about the good agronomic practices (GAPs) for different medicinal and aromatic plants so that these plants can be brought under cultivation and production system. The therapeutic uses of medicinal plants are safe, economical and effective and are easily available to medium and small farmers. India has been considered as one of the major store house of various indigenous plants that are used to cure diseases of various kind. The local availability of all herbs in our surrounding helps us to use these herbs as home remedies.

Rauvolfia serpentina (L.) Benth. ExKurz. (family: Apocynaceae) is commonly known by different names; Sarpagandha or Chandrika; Sarpagandha in Sanskrit means snakes smell or repellent, refers to the use of the said plant as an antidote for snake-bite. This is also known as Arachortita in Assamese, Barachandrika in Hindi, Harki in Marathi, Chevanamalpodi in Tamil, etc. It is an evergreen, woody, glabrous and perennial shrub with maximum height up to 60 cm. The plant possess tuberous root with pale brown cork and elliptic to lanceolate or obovate leaves in whorls of three (Deshmukh et al., 2012).

DISTRIBUTION

Sarpagandha is an important medicinal plant distributed in the foot-hills of Himalayan range, up to the elevation of 1300-1400 m. and almost all over the country. It is used in preparation of traditional medicine in India, China, Africa and many other countries. It is found in India, Pakistan, Sri Lanka, Burma and Thailand. In India, it is widely distributed in the sub-Himalayan tract from Punjab to Nepal, Sikkim and Bhutan. It is also found in the lower hills of Gangetic plains, eastern and Western Ghats and Andaman and Nicobar island. It is mostly found in moist deciduous forests at altitudes ranging from sea level to an altitude of 1200 m high. In the Deccan, it is associated with bamboo forests (Vakil, 1955).

ETHNOBOTANY

During collection of commercial non-timber and other forest products in Odisha, the tribal people mostly collect the traditional herbs from forests (Rout et al. 2010). In Virudhunagar district of Tamil Nadu, Rajendran and Agarwal (2007) have reported medicinal use of fruits and seeds of this species by the ethnic tribals of India. Chakma community residing in the north-western periphery of Namdapha National Park in Arunachal Pradesh has mentioned the name of *R. serpentina* in a report on traditional medicobotany of India (Sarmah et al. 2008). Mao et al. (2009) have reported this plant as a part of the ethnobotanical wealth of Northeast India. Ethnomedicinal importance of this plant was reported by Dey and De (2010). This plant was described from the wetlands of Terai region of Nepal by Siwakoti (2006). In 2009, Bhattarai has referred to the traditional use of this plant in dysentery, fever, cut wounds, boils, stomach-ache, menstrual problems etc. Rijal (2008) has also mentioned this plant's utility while quantitatively assessing the indigenous plant uses among two Chepang communities in the central mid-hills of Nepal. The tribes of Chhatarpur district, Madhya Pradesh, India use this plant against snake bite (Arjariya and Chaurasia, 2009). This plant has been used by local people of Himalayan mountains for snake bite (Ghorbani et al., 2006). Fresh root of *Aristolochia indica* is grounded along with the roots of *R. serpentina* (vernacular name: Amalpori) and mixed in water and taken twice daily for three days against snake bite by the Kurichayas of Kannur district, Western Ghats, Kerala, India. A decoction of powdered rhizome and leaves is also given in snake bite (Rajith and Ramachandran, 2010). About 10 ml of root paste is taken orally for treatment of snake bite by the forest dwellers of the Daitari range of hills of Odisha, India (Mohapatra et al., 2008).

THERAPEUTIC USES

The roots of this shrub have been used for centuries in ayurvedic medicines. According to Ayurveda, it is the best among all anti-hypertensive drugs. The root is bitter, acrid, pungent and anthelmintic. The drug preparation consists of air-dried roots that are used as antihypertensive and sedative. It is also used for the treatment of various central nervous system disorders associated with psychosis, schizophrenia, insanity, insomnia and epilepsy. This shrub is highly effective in the treatment of high blood pressure. It is also very useful in mental disorders like insanity, mental illness and traumas. But due to indiscriminate collection and over exploitation of natural resources for commercial purposes to meet the requirements of pharmaceutical industry, coupled with limited cultivation and increasing population, it is now an endangered species in India (Mallick et al., 2012). The plant is reported to contain a large number of therapeutically useful indole alkaloids and these alkaloids are largely located in the roots (Kumaria et al., 2013). Mixed with other plant extracts, they have been used in the treatment of cholera, colic and fever. The root was believed to stimulate uterine contraction and recommended for the use in childbirth. A study by Azmi and Qureshi in 2012 showed therapeutic effects of *Rauvolfia* with incomplete hypoglycemic action in diabetic hypertensive patients. The juice of the leaves has been used as a remedy for the opacity of the cornea (Sukumaran, 2008). *Rauvolfia's* juice and extract obtained from the root can be used for treating gastro-intestinal, hepatic and circulatory diseases. The Juice of tender leaves and root extract is used to treat liver pain, stomach pain and dysentery to expel intestinal worms (Anisuzzaman, 2007).

PHYTOCHEMICAL CONSTITUENTS

R. serpentina carries aesthetic value due to its phytochemical properties. The contributions towards the study of its phytochemical composition vary upon the geographical location and species. In 2013, Kumarin et al*.,* reported that the roots of the sarpagandha contains 0.7-3.0 % of total alkaloids and about 0.1 % of the active principle resperine which is an indole alkaloid, present in the root. Hence, root biomass production of this plant could be of economic importance. The thin layer chromatography resulted in extraction of crude alkaloids (Verma and Verma, 2010) was found to be 0.416 mg g^{-1} and 0.217 mg g^{-1} on dry weight basis in roots and leaves of *R. serpentina*. Similarly, Hussain et al*.,* (2015) quantified the phytochemical constituents using GC-MS. This indicated the presence of fats (2%), alkaloid (12.4%) and saponins(7.35%). A total of 147 molecules, reported to be extracted from various plant parts (Fig. 1) and broadly classified into different chemical classes (Fig. 2). The percentage of alkaloid depends on geographical place from where the plant is collected and also the season of collection. Generally samples from Assam have a higher percentage of alkaloid (2.57%) and December is the best month for the collection for getting more percentage of alkaloid (Herbal Monograph). The major phytochemical components are described below in Table 1 followed with a brief discussion about the constituents.

Table 1. Phytochemical composition of R. serpentina in plant sample and expressed as mg 100 g^{-1} dry weight (Harisaranraj et al., 2009)

Phytochemicals	*R. serpentina*
Alkaloids	1.48±0.02
Flavonoids	1.72±0.11
Phenols	1.86±0.11
Tannins	0.51±0.20

Results are mean of triplicate determinations on a dry weight basis ± Standard Deviation

Alkaloids

Alkaloids are large group of organic molecules occurring naturally and contain basic low molecular weight nitrogen atoms. Alkaloids are produced by bacteria, fungi, plants and animals. Basically these alkaloids are produced by more than 20% of the plant species and they use it as defense mechanism against plant pathogens and herbivorous animals. Since ages, alkaloids from different plant extract of *R. serpentina* have been found to be used as potions as well as poisons.

Three types of alkaloids are present in *R. serpentina (*Tyler et al., 1988)

i. Weakly basic indole alkaloids: the principal alkaloids are reserpine, rescinnamine, despiridine and these are tertiary indole alkaloids.

ii. Indoline alkaloids of intermediate bases: reserpiline, ajmaline, iso-ajmaline, rauwolfinine are tertiary indoline alkaloids.

iii. Strong anhydronium bases: serpentine, serpentinine and alsotonine are strongly basic anhydronium alkaloids

While ajmalinine, ajmalicine, chandrine, renoxidine, reserpinine, sarpagine, tetraphyllicine, yohimbine, 3-epi-ayohimbine are the other alkaloids present in *R. serpentina* (Herbal Monograph).

Flavonoids

Flavonoids have the general structure of a 15-carbon skeleton, which consists of two phenyl rings (A and B) and heterocyclic ring of carbon. Flavonoids are widely distributed in plants. An important role of flavonoids is to serve as visual signals by acting as pigments in fruits and flowers, firstly to attract animals as pollinators in flowers and later to attract animals to eat the fruits and thereby help in seed dispersal. These are potent water-soluble antioxidants and free radical scavengers, which prevent oxidative cell damage and have strong anticancerous activity. Flavonoids in intestinal tract also lower the risk of heart disease. As antioxidants, flavonoids provide anti-inflammatory activity used for the treatment of diseases in herbal medicine. (Mittal et al*.,* 2012).

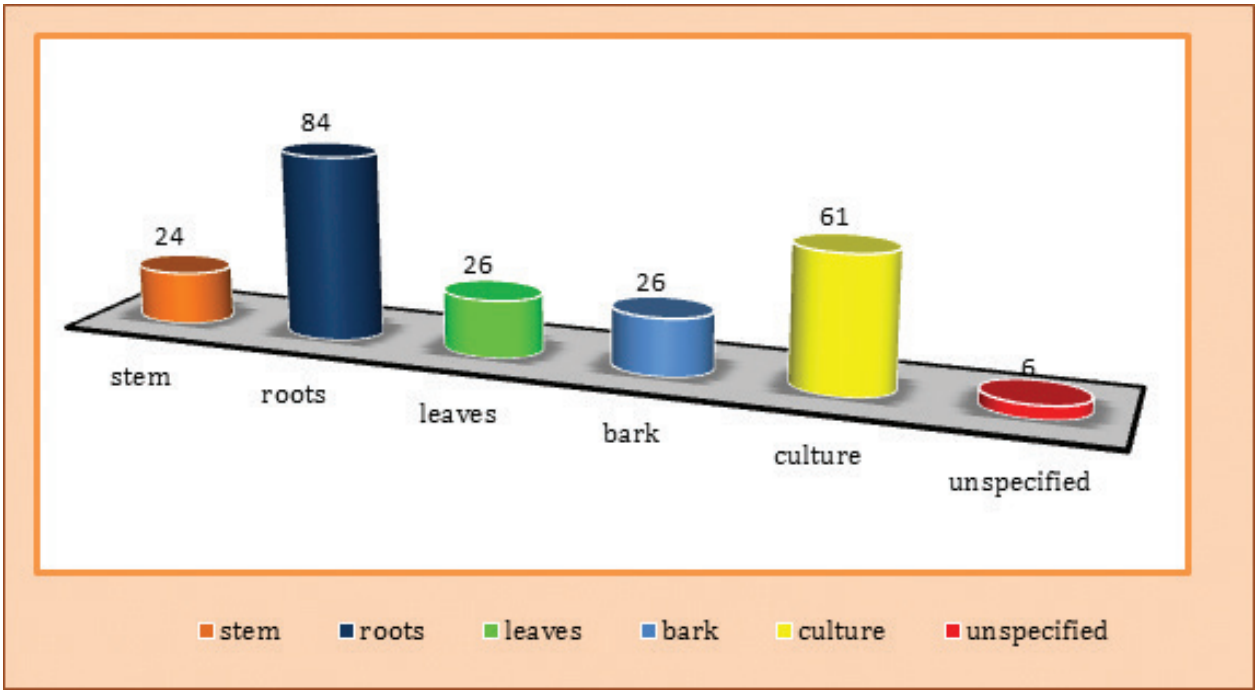

Fig. 1. Distribution of *R. serpentina* plant-derived molecules across various plant parts (Pathania et al., 2015)

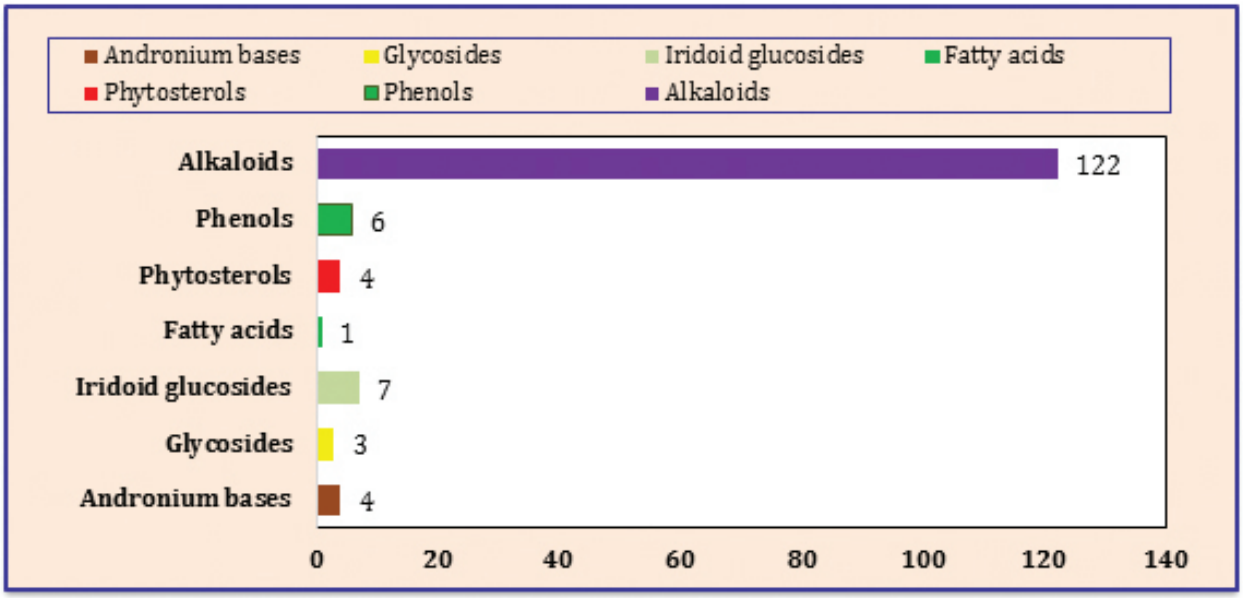

Fig. 2. Number of plant derived molecules of *R. serpentina* (Pathania et al., 2015)

Phenols

A phenol is any of a family of organic compounds characterized by a hydroxyl (-OH) group attached to a carbon atom that is part of an aromatic ring. These phenolic compounds are biosynthesised through shikimate pathway. Phenolsare considered as secondary plant metabolites mostly found in herbs, shrubs, vegetables and trees (Naira et al., 2013). Phenolic compounds also produce allelopathic effect. Presence of high quantity of total polyphenolic compounds in *R. serpentina* shows significant antidiabetic and hypolipidemic properties (Qureshi et al., 2009). It is used as an expectorant and emulsifying agent and antimicrobial compound.

Tannins

The tannins are the secondary compounds that are widely distributed in many plant species, where they play a role in protection from predation sometimes as pesticides and in plant growth regulation. The oxidation inhibiting activity of tannin is due to the presence of gallic acid and diagallic acid. Healing of wounds and inflamed mucous membranes are hastened up due to presence of tannins. Thus, *R. serpentina* helps in treating many disorders by traditional medicine healers in south eastern India (Agoha, 1974).

OTHER IMPORTANT BIOCHEMICAL CONSTITUENTS PRESENT IN ROOTS

Reserpine

Reserpine was isolated in 1952 from the dried root of *R. serpentina*. It is a relatively weak tertiary base occurring in the oleoresin fraction of the roots and is useful in the treatment of hypertension, cardiovascular and neurological diseases (Weiss et al., 2000). The antihypertensive properties of *Rauvolfia* roots are attributed to reserpine (3, 4, 5-trimethyl benzoic acid ester of reserpic acid, an indole derivative of 18 hydroxyyohimbine type). It is the most prominent of all alkaloids and used mainly as a natural tranquillizer. (Banerjee and Modi, 2010). Reserpine is now being utilized as a tool in physiological studies of body functions and in pharmacological studies. Resperine can bind the catecholamine storage vesicles of the nerve cell because of its antihypertensive actions on central nervous system (CNS) and peripheral nervous system. This interferes with the function of autonomic nervous system by depleting the transmitter substance from the adrenergic neurons and possibly by activating the central parasympathetic system (Nammi et al., 2005). Resperine can control heart rate, cardiac contraction, peripheral resistance, sedation and lowering of blood pressure, especially in cases of hypertension exacerbated by stress and sympathetic nervous system activity.

Ajmaline

In 1931, Salimuzzaman Siddiqui first isolated this compound from the roots of *R. serpentina*. He named it ajmaline, after Hakim Ajmal Khan, one of the most illustrious practitioners of Unani medicines in South Asia (Siddiqui, 2013). Ajmaline has been used as a treatment for Wolff-Parkinson-White syndrome which is characterized by arrhythmias with the ventricles contracting prematurely resulting in tachycardia and a shortened refractory period. This compound is considered as a class I anti-arrhythmic agent, which is highly useful in diagnosing hereditary cardiac disorder (Brugada Syndrome) and differentiating between subtypes of patients with this disease (Rolf et al., 2003). The action of ajmaline on systemic and pulmonary blood pressure is similar as of serpentine (Gawade and Fegade, 2012).

Ajmalicine

Ajmalicine or raubasine (alkaloid) is an antihypertensive drug used in the treatment of high blood pressure and also having large number of applications in the treatment of circulatory diseases, especially in providing relief to normal cerebral blood flow. It helps in prevention of strokes and helps in lowering blood pressure (Srivastava et al*.,* 2006). About 3500 kg of ajmalicine is isolated from either *Rauvolfia* or *Catharanthus spp*. annually by pharmaceutical industries for the treatment of circulatory diseases. The ajmalicine is derived from tryptophan which is converted to tryptamine via secologanin, strictosidine and cathenamine. Reduction of cathenamine to ajmalicine is facilitated by enzyme NADPH and tryptophan decarboxylase (TDC). Decarboxylase might be the key enzyme involved in the synthesis of ajmalicine in *Rauvolfia* (Liu et al*.,* 2012).

Serpentine

Serpentine, a type II topoisomerase inhibitor, exhibits antipsychotic properties (Costa-Campos et al., 2004). The enzyme peroxidase (PER) is responsible for oxidation of ajmalicine to serpentine by catalyzing bisindole alkaloid localized in the vacuole (O'Connor and Maresh, 2006).

Saponins

Saponins are a class of chemical compounds found in particular abundance in various plant species and derive their name from the soapwort plant (genus *Saponaria*, family Caryophyllaceae), the root of which was used historically as a soap. Saponins are being promoted commercially to be used as dietary supplement and nutraceuticals. Some of the characteristics of saponins include formation of foams in aqueous solutions, hemolytic activity, cholesterol binding properties and bitterness. (Sodipo et al., 2000). Saponin has the property of coagulating red blood cells. The high saponin content of *R. serpentina* substantiates the use of this extracts to stop bleeding and in treating wounds (Harisaranraj et al., 2009).

Deserpidine

Deserpidine is an ester alkaloid isolated from *Rauvolfia* with antipsychotic and antihypertensive properties that has been used for the control of high blood pressure and for the relief of psychotic behavior (Varchi et al., 2005). It differs from reserpine only by means of absence of a methoxy group at C-11, which is synthesized from reserpine. It is capable of reducing high blood pressure by controlling nerve impulses along various nerve pathways. As a result, they act on the heart and blood vessels to lower blood pressure and also for the relief of psychotic behaviour. Deserpidine also binds and inhibits the angiotensin converting enzyme and competes with angiotensin I for binding at the angiotensin-converting enzyme. It also blocks the conversion of angiotensin I to angiotensin II (Varchi et al., 2005).

Rescinnamine

Rescinnamine, a purified ester alkaloid of alseroxylon fraction in species of *Rauvolfia*; related chemically and pharmacologically to reserpine with similar uses. It is clinically a less potent alkaloid than reserpine and not so effective in lowering blood pressure (Klohs et al., 1954). Rescinnamine inhibits angiotensin converting enzyme, peptidyldipeptidase that catalyzes the conversion of angiotensin I to the vasoconstrictor substance, angiotensin II which stimulates aldosterone secretion by the adrenal cortex. Firstly, it inhibits the Angiotensin Converting Enzyme (ACE) and then blocks the conversion of angiotensin I to angiotensin II. Inhibition of ACE results in decreased plasma angiotensin II. Angiotensin II is a vasoconstrictor and a negative-feedback mediator for renin activity, its lower concentration results in a decreasing in blood pressure and stimulation of baroreceptor reflex mechanisms, which ultimately results in decreased vasopressor activity and aldosterone secretion.

Yohimbine

A pharmacologically well characterized alkaloid Yohimbine, is used as a selective alpha-adrenergic antagonist or alpha-blocker in the blood vessels for the treatment of erectile dysfunction. It dilates blood vessels and increases blood flow in the penis, which helps in improving erectile function (Andersson, 2001).Yohimbine was also explored as a remedy for diabetes in animal and human models carrying polymorphisms of the α2A-adrenergic receptor gene. Antagonism at these receptors relaxes smooth muscle and lowers blood pressure. It works by increasing certain chemicals in the body, which dilates the pupils of the eye (Rosenren et al., 2009).Yohimbine indicated to reverse the effects of xylazine in animals. The combination of yohimbine and 4-aminopyridine may be used for rapid reversal of xylazine-induced sedation in goats (Ndeereha, et al., 2001).

MINERALS AND VITAMINS COMPOSITION

Rauvolfia contains a large number of macro and micro-nutrients and the most abundant macro nutrient is calcium. The presence of calcium helps in treating wounds and coagulation of blood at a faster rate. The sodium content is low (Table 2) that can be an added advantage due to the direct relationship of sodium intake with hypertension in human. The presence of zinc shows that plant can play valuable roles in the management of diabetes, which result

from insulin malfunction. The plant *R. serpentina* is also an excellent source of ascorbic acids, riboflavin, thiamin and niacin (Okwu, 2003). Ascorbic acid is vital for body performance as it plays an important role in normal wound healing (Okwu, 2004) and lack of it impairs the normal formation of intercellular substances throughout the body (including collagen, bone matrix and tooth dentine). The *R. serpentina* is used in herbal medicine as a potential source of useful drugs for the treatment of many diseases as it is a rich source of phytochemicals, minerals and vitamins (Mittal, et al*.,* 2012; Harisaranraj, et al*.,* 2009).

Table 2. Mineral composition of *R. serpentina* and expressed as mg 100 g^{-1} dry weight (Harisaranraj, et al., 2009)

Minerals	*R. serpentina*
Macroelements	
Magnesium	0.10±200
Calcium	0.32±0.10
Potassium	0.04±0.11
Phosphorus	0.18±0.22
Sodium	0.02±0.10
Microelements	
Iron	1.85±0.20
Zinc	5.38±0.11

Results are mean of triplicate determinations on a dry weight basis± Standard Deviation.

R. serpentina are rich source of vitamins (Table 2). Ascorbic acid (vitamin C) was found to be 44.03 mg 100 $g^{-1}$and along with that, Riboflavin, thiamine and niacin were also detected. The presence of phenolic compounds in the plant indicates that this plant may be anti-microbial agent (Harisaranraj et al., 2009).

CONCLUSION

Sarpagandha has promising potential in India especially north east India. The chemical constituents are highly useful and can be utilized for various medicinal purposes. Apart from being used popularly in the treatment of hypertension, mental disorder and schizophrenia, its use in traditional system of medicine in the treatment of gastrointestinal problems, snake bites, skin diseases, malaria, AIDS, asthma etc. must be critically evaluated. So far little work has been done to abridge the vast gap between ethnomedicinal utilization of this plant species and its active principles related to the treatment of various ailments. It is to be noted that the tribal use of the plant species must be verified by further scientific experimentation and this rich folklore can be utilized in herbal therapy and drug discovery. But for the efficient utilization and sustainability of this plant, few strategies have to be followed like; conserving the plant species in small area like herbal gardens or seed banks or gene banks and cultivation of the plant species which are rare and have high medicinal importance.

From the above discussion, it is evident that *R. serpentina* is a major plant species of ethnic use. Over exploitation, loss of habitat, poor seed germination rate etc. are the major factors of decline of this important plant species of south-east Asian countries. Although the roots are the major source of active principles, leaves, stem, fruits, seeds and flowers are also being utilized by the aboriginals to treat different diseases. Several attempts have been made to conserve this threatened and endangered plant either by *in situ*, *ex-situ* or *in-vitro* conservation strategies.

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