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Review Article

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Rauvolfia tetraphylla L. (Apocynaceae): A Pharmacognostical, Phytochemical and Pharmacological Review

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ABSTRACT

Rauvolfia consists of approximately one thousand species, evergreen trees and shrubs belonging to the family: Apocynaceae. 'Reserpine' is common phytochemical from Rauvolfia species which was broadly indicated as an antihypertensive drug. Rauvolfia tetraphylla L. a small tree shrub and a frequently available species of Rauvolfia which is prevalently used in Ayurvedic and unani system of medicines and also a part of folk remedies of most Asian countries. This review discusses pharmacognosy, phytochemistry, and pharmacological activities of R. tetraphylla. The leaf, stem and root of R. tetraphylla were pharmacognostically studied. Preliminary phytochemical study of different extracts revealed the presence of various phytoconstituents like reducing sugars, sugars, carbohydrates, alkaloids, amino acids, steroids, tannins, flavonoids, phenols, saponins, fixed oils, fats, gums, and mucilages. The stems and branches (air-dried) of R. tetraphylla provided a new labdane diterpene characterized as 3β-hydroxy-labda-8(17),13(14)-dien-12(15)-olide. Three antipsychotic indole alkaloids (IA) are namely, α-yohimbine, isoreserpiline, and 10-methoxy tetrahydroalstonine in R. tetraphylla leaf. Five new indole alkaloids rauvotetraphylline, together with eight known analogues, were isolated from the aerial parts of R. tetraphylla. Different activities including antibacterial, antifungal, anti-inflammatory, antioxidant, cytotoxic, cardio tonic and cardio protective was found from pharmacological view. In conclusion, from view point of pharmacognosy, phytochemistry and pharmacology R. tetraphylla is important medicinal herb.

Keywords*:* Rauvolfia; Apocynaceae; *R. tetraphylla;* Pharmacognosy; Phytochemistry; Pharmacology

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INTRODUCTION

Synthetic drugs are effective in controlling different diseases but these synthetic drugs are out of reach of millions of people (Kumar et al., 2010). Plants with their enormous arrays of secondary metabolites from a reservoir of low molecular weight organic compounds that is mostly untapped as a basis of pharmaceuticals (Srivastava et al., 1996). Medicinally, plants are an important therapeutic aid for a range of ailments (Fakruddin et al., 2012) and plants are used as a source of many potent and powerful drugs in different countries (Srivastava et al., 1996). In contemporary medicines, plants have an extremely important position as the raw material for some important drugs. According to the estimation, an around 70,000 plant species have been used for medicinal purposes. Medicinal herbs provide the starting material for the synthesis of conventional drugs. The curative action of medicinal plant is due to the presence of multifaceted chemical constituents. Regarding the Indian estimation, more than 2500 plant species having medicinal value, Sri Lanka around 1400 and Nepal around 700 (Kumar et al., 2010). The World Health Organization (WHO) approximations that 80% of the inhabitants of some Asian and African countries at present uses herbal medicines for some aspect of primary health care because of superior cultural acceptability, affordability, better compatibility with the human body along with fewer side effects (Jakaria et al., 2015; Dash et al., 2014; Parekh et al., 2005). The genus of Rauvolfia is evergreen trees and shrubs in the *Apocynaceae* family. It is consists of approximately one thousand species in the genus and mostly be found in tropical regions (Joyti et al., 2012; Harisaranraj et al., 2009; Anitha and Kumari, 2006). The species of Rauvolfia is mostly known for its phytochemical 'Reserpine' which was broadly indicated

as an antihypertensive drug (Kumar et al., 2011). *Rauvolfia tetraphylla* L., a small tree shrub that will attain 6 feet (~ 2 meters) in heights (Rao et al., 2012). It is a frequently available species of Rauvolfia which is prevalently used in Ayurvedic and unani system of medicines and also a part of folk remedies of most Asian countries (Behera et al., 2016). From medicinal point of view, *R. tetraphylla* is significant in the treatment of cardiovascular diseases, hypertension and a variety of psychiatric diseases (Faisal and Anis, 2002). Economically, it is also important because of the presence of alkaloids, which are localized in the roots (Patil and Jeyanthi, 1997). It is reported that, the roots are useful in the treatment of hypertension, cardiovascular diseases and as a tranquilizing agent. For intestinal problems, the extract of the root of *R. tetraphylla* is valuable. It is believed that roots are used to stimulate uterine contraction in case of difficult delivery (Harisaranraj et al., 2009). The black dye yielding from fruits and the extract of the herb is mixed with castor oil applied to skin ailments (Anitha and Kumari, 2006). The present review discusses pharmacognosy, phytochemistry, and pharmacological activities of *Rauvolfia tetraphylla*.

PHARMACOGNOSTICAL STUDY

Pharmacognostical study of leaf, stem and root was done by Joyti et al., (2012) and only study of root was also done by Amjad et al. (2014).

Study of leaf

Macroscopic characters

Leaf in whorls of 4, unequal, 5–9× 3–4cm, elliptic-ovate in shape; Apex was acute and base is round, entire margin, and reticulate venation. Both surfaces were pubescent, color was dark green. Odor characteristic, texture was smooth.

Microscopic characters

On surface preparation, the leaf showed that upper epidermis was devoid of stomata and it had numerous uniserate, muticellular trichomes. But in lower epidermis innumerable paracytic stomata were observed and trichomes similar to that of upper epidermis were examined. Transverse section of the midrib of leaves illustrated a single layer of upper and lower epidermis with a thin cuticle. In epidermis, abundant uniserated and muticellular trichomes were seen. Just below the upper epidermis 5–7 layer of collenchymatous cells (which changed pink after addition of a staining agent, saffranin), which were polygonal in shape and lesser than parenchymatous cells. Similar collenchymatous cells were observed above the lower epidermis too. The vascular bundles composed of xylem at the center with phloem on both the sides which makes them bicollateral vascular bundle. Additional areas of the midrib contained parenchymatous cells. The mesophyll tissue composed of higher in position palisade and lower spongy parenchyma cells. Chlorophyll was availble in the entire of the section (Figure 1 and 2).

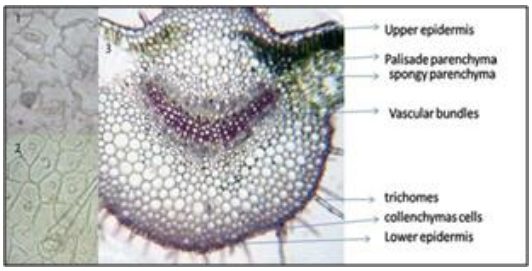

Figure 1: Transverse section of Leaf

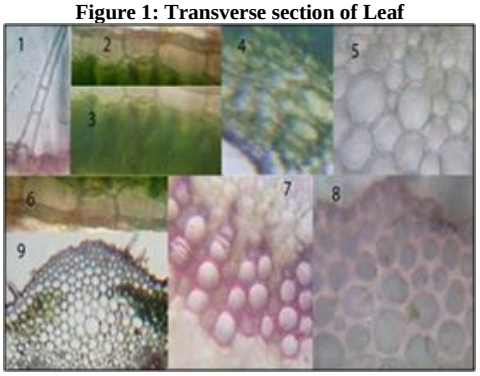

Figure 2: Leaf characters

(1: trichomes 2: upper epidermis 3: upper palisade 4: lower spongy parenchyma 5: parenchyma of mid rib 6: lower epidermis 7: vascular bundles 8: Collenchymatous cells)

Study of stem

Macroscopic characters

Stem was round, its length and breadth was 12-19× 0.2-05, Surface was rough, hairy, outwardly green and internally creamish yellow. Odor characteristic, texture was rough and fibers.

Microscopic characters

Transfer section of stem views the single layer of epidermis with uniserate, muticellular trichomes. Just below the epidermis cortex is filled with 10-12 layer of parenchymatous cells which are oval to oblong in shape of different size. At the end of cortex, the patches of non-lignified fibers which has yellowish ting. After the cortex is vascular bundle here xylem in the center and phloem in both the side so it is bicollateral vascular bundle. In center the big pith which is filled with parenchymatous cells, but at places we can see the stone cells in cortex and pith region (Figure 3 and 4).

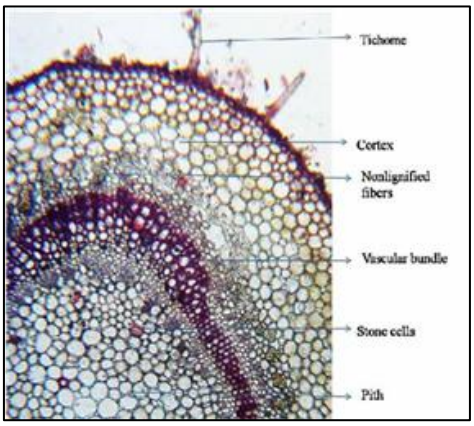

Figure 3: Transverse section of Stem

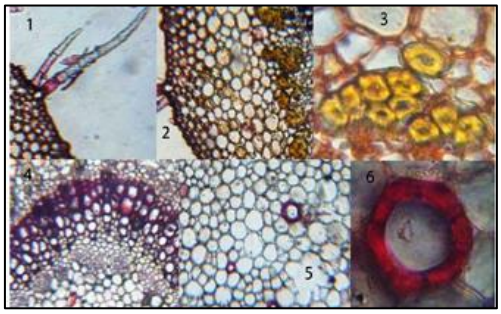

Figure 4: Stem characters

(1: trichomes 2: cotex 3: nonlignifed fiber 4: vascular bundle 5: pith 6: stone cell)

Study of root

Macroscopic character

Pieces of roots was about 8 to 15cm long and 0.5 to 2cm in thickness. The root was sub cylindrical in shape, curved, outer surface was grayish-brown to reddish-brown and its inner surface creamish yellow, longitudinal fissures are seen in outer surface, fracture was splintery short. Slight odor and bitter in taste**.**

Microscopic character

Root comprises of simple rectangular cork about 15 layers, big cortex which are made up of parenchyma cells and it is filled with simple starch grain and at places it observe presence of oil resin in cortex. Presence of stone cells in cortex is the character which helps to different from R. serpentina. Thick walled Medullary rays which are uniseriate or biseriated, which are arises from end of cortex region that's above the cambium, which are almost rectangular in shape. Xylem is lignified xylem fibers and xylem parenchyma cells are seen in the stellar. There is small pith at the center. Starch grains and twin prismatic crystals are seen the section (Figure 5 and 6).

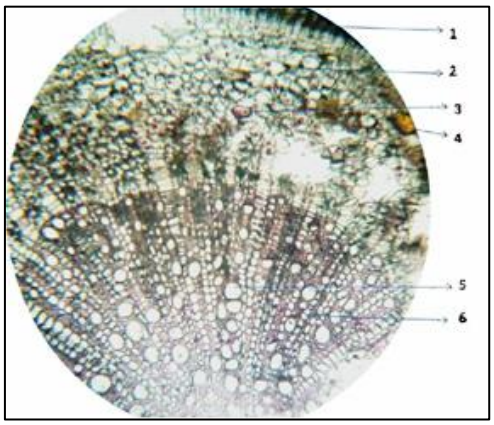

Figure 5: Transverse section of Root
(1: Cork 2: cortex3: stone cells 4: oil resin 5: xylem 6: Medullary rays)

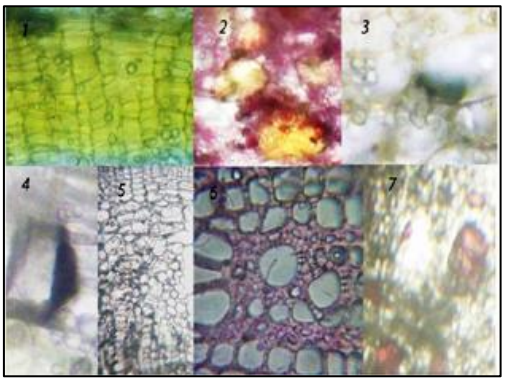

Figure 6: Root characters
(1: cork 2: oil resin 3: starch grains4: prismatic crystals 5: cortex 6: xylem and Medullary rays 7: stone cells)

PHYTOCHEMISTRY

Cold extracts of the plants samples showed the presence of compounds including carbohydrates, alkaloids, tannins, phenols and flavonoids along with absence of fixed oil and saponins. In this assay total alkaloids (TA), total terpenoides (TT), total glycoside (TG) of alcohol, water and 50% alcohol extracts of the powdered drugs of four samples were also carried out (Thinakaran et al., 2009). Another test results of preliminary phytochemical study of aqueous and methanol extracts revealed the presence of various phytoconstituents like carbohydrates, alkaloids, steroids, tannins, phenols, saponins, fixed oils, fats, gums, mucilages and flavonoids and absence of proteins, and volatile oil (Kavitha et al., 2012).

In an additional study of phytochemical screening of cultured plant extracts also revealed the presence of steroids, reducing sugars, sugars, alkaloids, phenols, flavonoid, saponins, tannins and amino acids (Nandhini and Bai, 2014). Moreover, in another study, alkaloids were present in leaf as well as fruit samples, this was predictable as a number of alkaloids have been reported from the related species of this family which are namely serpentine, reserpine, ajmalacine and many of these have proven medicinal records. Beside the acetone extracts of both leaf and fruits showed the presence of flavanoids, tannin and saponin as well (Behera et al., 2016).

The air-dried stems and branches of R. tetraphylla provided a new labdane diterpene characterized as 3β-hydroxy-labda-8(17),13(14)-dien-12(15)-olide on the basis of several spectroscopic studies comprising UV, IR, MS and NMR (H, C and HMQC). This is the first report of a new terpenoid constituent from *R. tetraphylla*, an important medicinal plant broadly known for the source of a diversity of alkaloids (Brahmachari et al., 2011). Three antipsychotic indole alkaloid (IA) such as, α-yohimbine, isoreserpiline, and 10-methoxy tetrahydroalstonine in *R. tetraphylla* leaf simultaneously quantified by developed simple isocratic HPLC method (Verma et al., 2012).

From another research, five new indole alkaloids rauvotetraphyllines A–E (1–5)(Figure 7), together with eight known analogues, were isolated from the aerial parts of *R. tetraphylla*. The structures were recognized by means of spectroscopic methods (Gao et al., 2012).

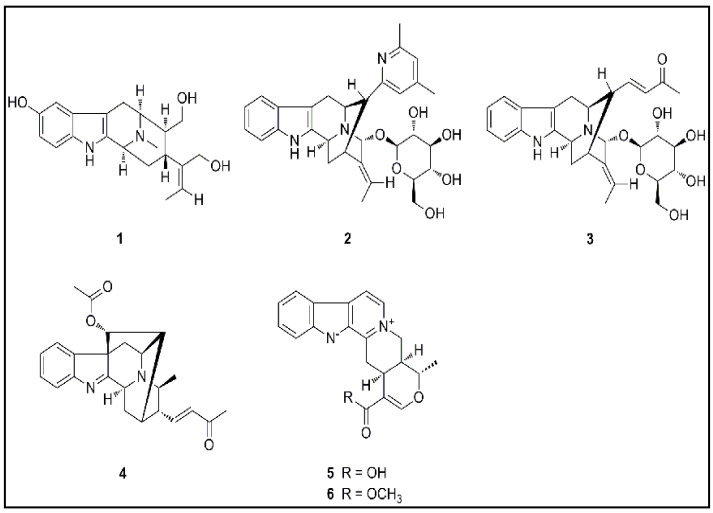

Figure 7: Five new indole alkaloids rauvotetraphyllines A–E (1–5)

It is reported that this plant root contains nearly 30 alkaloids including reserpine, ajmalicine, reserpitine, sarpagine, deserpidine, rescinnamine, serpentine, ajmalidine, alloyohimbine, chandrine, corynathine, iscajmaline, neo ajmaline, papaverine, raunatine, raunoline, rauwolscine, reserpiline, reserpinine, reserpoxidine, serpinine, thambine and yohimbine. Reserpine is working as tranquilizer and also lowers the blood pressure. Serpentine, a weak hypotensive agent and sarpagine has only fleeting effect on blood pressure. The alkaloid yohimbine is hypotensive, a depressant of cardiovascular system and also a hypnotic. Ajmaline stimulates respiration, bowel movement and also useful in the management of arrhythmic heart disorders (Anitha and Kumari, 2006). From another report, the root of this plant includes various monoterpene indole alkaloids and reserpine is reported to present in more than 50% of total alkaloids (Anitha and Kumari, 2013).

According to the assay by using HPTLC coupled with mass spectrum, identified major compounds were 3-isoreserpine, ajmalicine, ajmaline, reserpine and yohimbine from R. tetraphylla (Nandhini and Bai, 2014).

PHARMACOLOGICAL ACTIVITIES

Antibacterial activity

Antibacterial activity of ethanol extract from *R. tetraphylla* was tested against bacterial species of *Escherichia coli*, *Streptococcus lactis*, *Enterobacter aerogenes*, *Alcaligenes faecalis*, *Pseudomonas aeruginosa*, and *Proteus vulgaris*. Extracts showed maximum activity against *E. coli*, *E. aerogenes*, *A. faecalis* (Suresh et al., 2008).

In addition, another in vitro study of antibacterial activity was done for extracts against four gram positive (*Streptococcus pneumoniae*, *Staphylococcus aureus*, *Bacillus cereus*, *Bacillus pumilis*) bacteria and four gram negative bacteria included Escherichia coli, *Enterobacter aerogenes*, *Pseudomonas aeruginosa*, Streptomyces marienensis by using cylinder plate assay. Ethyl acetate, methanol and hydroalcoholic extracts (70% v/v ethanol) of *R. tetraphylla* showed good zone of inhibition against tested bacterial strains at dose of 150µg/cup compared to hexane extract (Rao et al., 2012).

Moreover, in vitro antibacterial activity of aqueous, alcoholic, and chloroform extracts of leaf of *R. tetraphylla* against various gram-positive and gram-negative bacteria including *Bacillus cereus*, *Bacillus subtilis*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Streptococcus agalactiae*, *Lactobacillus acidophilus* and *Escherichia coli* was studied by using disc diffusion method with standard antibacterial drugs as a positive control. Methanol extract of both plants have produced good and comparable antimicrobial activity against most gram positive and gram negative bacteria except against *S. typhimurim* and *E. coli.* Chloroform extract of *R. tetraphylla* was also effective against majority of bacteria (12.00± 0.58 to 14.67±0.88 mm) but water extracts of the plants did not show any antibacterial activity (Patel et al., 2013).

Antifungal activity

Ethanol leaf extract of *R. tetraphylla* also done for antifungal activity against fungal species of *Fusarium oxysporum*, *Alternaria helianthii*, *Curvularia lunata*, *Aspergillus niger* and *Penicillium* spp. by using disc diffusion technique. Among different fungi, investigated *A. niger* and *Penicillium* spp were found to be more responsive to crude extract when compared to others (Suresh et al., 2008).

Another study of aqueous and methanol leaf extracts of *R. tetraphylla* was investigated for antifungal activity against four fungi (*Aspergillus niger*, *Aspergillus flavus*, *Rhizopus indicus* and *Mucor indicus*) using the paper disc diffusion technique. Methanol extract produced antifungal activity against three fungi excluding *M. indicus* (Kavitha et al., 2012).

Anti-inflammatory activity

Hydro-alcoholic extract (70% v/v ethanol) at 200, 400 and 800 mg/kg doses and methanol, ethyl acetate and hexane extracts at doses 100, 200 and 400 mg/kg of R. tetraphylla root bark were examined for anti-inflammatory activity in Carrageenan induced rat paw oedema model. In this activity, the thickness of paw was measured every one (01) hour up to six (06) hours. The extracts of hydro-alcohol and methanol (fraction) of R. tetraphylla root bark at three different doses produced significant ($p<0.001$) reduction when compared to vehicle treated control group (Rao et al., 2012).

Antioxidant activity

Methanol extract of fruit and n-hexane, dichloromethane, and methanol leaf extracts of R. tetraphylla were investigated for in vitro antioxidant activity at different concentrations (5, 50 and 100µg). Antioxidant ability is expressed as equivalents of ascorbic acid. Leaf n-hexane and methanol extracts was found to be significantly active at 5µg when compared with Butylated hydroxy anisole (BHA), and at 50µg concentration the methanol leaf extract found be very high. The fruit methanol extract was found to be active and the activity proportionally increased with dose, but not as that of Butylated hydroxy anisole (BHA). The experimental results show that the activity exhibited by the solvent extracts is dose dependent (Vinay et al., 2016).

In another study, leaf and fruit extracts (Hexane, Chloroform, Acetone, and Methanol) of R. tetraphylla were investigated for their antioxidant activity. All the extracts showed good antioxidant activity in DPPH radical scavenging assay compared with ascorbic acid at the doses 15.62, 31.25, 62.5, 125, 250, 500, and 1000µg/ml. In addition, in the nitric oxide antioxidant assay, all extracts produced good antioxidant activity compared with standard quercetin at the doses 25, 50,100, 200, and 400µg/ml except hexane extract which showed only mild antioxidant potential (Behera et al., 2016).

Cytotoxic activity

Leaf and fruit extracts (Hexane, Chloroform, Acetone, and Methanol) of R. tetraphylla were examined for their cytotoxic activity by using brine shrimp lethality assay. Chloroform leaf extract as well as acetone extract of fruit showed significant cytotoxic activity (Behera et al., 2016).

In another cytotoxicity study, R. tetraphylla fruit extract was done using by using Allium cepa root model. Root tips of Allium cepa were treated with fruit extracts at various concentrations. The mitotic indices of control and treatments were calculated and the chromosomal aberrations were also studied. The study revealed that the fruit extracts of R. tetraphylla at different concentration has significant effect on mitotic index and can induce chromosomal aberrations. Thus, R. tetraphylla fruit extract caused cytotoxicity (Kavitha et al., 2016).

Cardio tonic activity

An effect of *R. tetraphylla* aqueous leaf extract was done on frog heart in situ preparation. The aqueous leaf extract of R. *tetraphylla* produced significant positive ionotropic effects. It was unaffected by beta-blocking drug propranalol and more affected by Ca2+ channel blocker nifedipine, whereas slightly less negative chronotropic effects unaffected by atropine. Thus, suggesting extract produced cardio tonic activity parallel to cardiac glycosides. The extract has also blood pressure lowering effect (Thinakaran et al., 2009).

Cardio protective activity

Study was done to evaluate the cardiac protective activity in *R. tetraphylla* by using rat model. Myocardial infarction was induced in experimental rats by intraperitoneal injection of isoproterenol hydrochloride. Each group of rats were treated with combination of isoproterenol and *R. tetraphylla* leaves and also treated separately. Latterly of the experimental period, the blood was collected rat from groups and examined biochemical estimation. The leaf extract of *R. tetraphylla* has cardio protective potential. The leaf extract of R. tetraphylla pretreatment improved cardiac functions, the effect which can be attributed to its capability of maintaining redox status, via restoration of endogenous antioxidants, controlling lipid peroxide formation and preserving cardiac marker enzyme activities of CK, LDH, AST and ALT. Histo architecture of myocyte and its preservation by R. tetraphylla pretreatment reconfirms these effects. The probable mechanisms action of *R. tetraphylla* due to the attendance of phytochemicals as phenolic groups that might directly or indirectly involved in its cardioprotective effects (Nandhini and Bai, 2015).

CONCLUSION

It is concluded that R. tetraphylla contains a numbers of phytochemical consituents. The extract possesses antibacterial and antifungal properties and it can be used effectively as an herbal drug in treatments of several microbial diseases. The plant is also reported to possess anti-inflammatory, antioxidant, cytotoxic and cardio tonic, cardio protective activities. The present review also showed that it is useful in a number of diseases. Therefore, it is essential that more clinical and pharmacological studies should be conducted to investigate unexploited potential of this plant. The researchers have isolated numerous phytoconstituents from this plant. However, further investigations are necessary to isolate and purify novel pharmacologically active and industrially important compounds.

REFERENCES

[1] S Anitha; BDR Kumari. *Pakistan J Bio Sci* **2006**,9(3), 422-424.
[2] S Anitha; BDR Kumari. *Asian J Pla Sci*. **2013**,12, 28-33.
[3] DR Behera; RR Dash; S Bhatnagar. *Int J Pharmacog Phyto Res*. **2016**, 8(7), 1164-1167.
[4] G Brahmachari; LC Mandal; D Gorai; M Avijit; S Sarkar; S Majhi. *J Che Res*, **2011**, 35(12), 678-680.
[5] PP Dash; AK Chaturvedi; A Mishra; D Chaturvedi. *Int J Nat Prod Res*, **2014**, 4, 95-99.
[6] M Fakruddin; KSB Mannan; RM Mazumdar; H Afroz. *BMC Complement Altern Med*. **2012**, 12, 232.
[7] M Faisal; M Anis. *J Physiol Mol Biol Pla*. **2002**, 8(2), 295-99.
[8] Y Gao; DS Zhou; LM Kong; P Hai; Y Li; F Wang; JK Liu. *Nat Prod Bioprospect*. **2012**, 2, 65.
[9] R Harisaranraj; K Suresh; S Saravanababu. *Aca J Pla Sci*. **2009**, 2(3), 195-198.
[10] AAM Iqbal; I Ansari; M Khan. *Int J Pharm Phytopharmacol Res*. **2014**, 3(4), 289-295.
[11] M Jakaria; M Parvez; R Zaman; Arifujjaman; MI Hasan; MA Sayeed; AM Ali. *Res J Bot*. **2015**, 10, 98-103.
[12] T Joyti; K Brijesh; KRH Venkatesh. *J Pharm Sci Inn*. **2012**,1(6),57-60.
[13] S Kumar; R Malhotra; D Kumar. *Pharmacogn Rev*. **2010**, 4(7), 58-61.
[14] A Kumar; MK Bhardwaj; AK Upadhyay; A Tiwari; BD Ohdar. *J Chem Pharm Res*. **2011**, 3(2), 907-910.
[15] R Kavitha; T Deepa; P Kamalakannan; R Elamathi; S Sridhar. *Int J Pharm Sci Rev Res*. **2012**, 12(1), 142-144.
[16] KR Kavitha; MV Shijil Kumar; CR Lalitha. *Int J Adv Res*. **2016**, 4(1), 1258-1264.
[17] VS Nandhini; GV Bai. *Int J Adv Pharma Ana*. **2014**, 4(2), 81-87.
[18] VS Nandhini; GVS Bai. *South Indian J Bio Sci*., **2015**, 1(2), 97-102.
[19] J Parekh; D Jadeja; S Chanda. *Turk J Biol*. **2005**, 29, 203-10.
[20] VM Patil; M Jeyanthi. *Curr Sci*. **1997**, 72(12),961-65.
[21] UD Patel; HB Patel; BB Javia. *Wayamba J Ani Sci*. **2013**, 1377753231, 723-28.
[22] GB Rao; PU Rao; ES Rao; TM Rao; DVS Praneeth. *Asian Pac J Trop Biomed*. **2012**, 2(10), 818-821.
[23] J Srivastava; J Lambert; N Vietmeyer. *World Bank Technical* **1996**, 320.
[24] K Suresh; SS Babu; R Harisaranraj. *Ethnobot Leaf*. **2008**, 12, 586-590.
[25] T Thinakaran; A Rajendran; V Sivakumari. *Asian J Env Sci*. **2009**, 4(1), 81-85.
[26] KN Vinay; VV Lakshmi; ND Satyanarayan; GR Anantacharya. *Int J Pharm Sci Res*. **2016**, 7(4),1705-1709.
[27] RK Verma; S Gupta; MM Gupta; SK Srivastava. *J Liq Chro Rel Tech*. **2012**,35(7), 937-950.