Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2011, 3(1): 45-54
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

A Review on Phytochemical, Pharmacological and toxicological studies on *Neolamarckia cadamba*

Atul Dubey*, Satish Nayak and D. C. Goupale

Bansal college of pharmacy Kokta, Anand nagar, Bhopal-462021

ABSTRACT

Neolamarckia cadamba is one of such ayurvedic remedy that has been mentioned in many Indian medicinal literatures. This article discusses about the medicinal values of Neolamarckia cadamba. In this communication, we reviewed the morphology, microscopy, phytochemistry of Neolamarckia cadamba and its application in the treatment of various ailments like diabetes mellitus, diarrhoea, fever, inflammation, haemoptysis, cough, vomiting, wounds, ulcers, debility and antimicrobial activity. The major constituents of the plant are triterpenes, triterpenoid glycosides, flavanoids, saponins, indole alkaloids; cadambine, cadamine, isocadambine, isodihydrocadambine. This work discusses the investigations made by various workers related to chemical constituents, pharmacological action and toxicological studies of this plant since years till date.

KEYWORDS: *Neolamarckia cadamba,* Indole alkaloids, Pharmacological action, Antimicrobial action and Toxicological studies.

INTRODUCTION

Neolamarckia cadamba Syn. *A. indicus, A. rich, A.chiensis* (Lam.) Rich. Ex. Walp, *Anthocephalus cadamba* (Family-Rubiaceae) commonly called kadamba enjoys a hallowed position in Ayurveda- an Indian indigenous system of medicine. It is also named as Kadam. Other vernacular names of *Neolamarckia cadamba* have been listed in the Table 1.

Table 1: Vernacular names of *Neolamarckia cadamba*

S. no.	Vernacular names
1	Sanskrit: Kadambah, Vrtta puspa and Priyaka
2	English: Wild cinchona
3	Hindi: Kadamb, Kadam
4	Assam: Roghu, Kadam
5	Tamil: Vellaikkatampu, Arattam and Kadappai
6	Malayalam: Katampu, Attutekka
7	Kannada: Kadamba mara, Kadavala and Neirumavinamara
8	Telugu: Kadambamu, Kadimi chettu
9	Indonesia: Jabon
10	Malaysia: Kalempayan
11	Cambodia: Thkoow

The tree is a medium to large sized deciduous tree attaining a height of 20-40 m and a girth of about 2-2.5 m with clean cylindrical branches and rounded crown. It is frequently found all over the India on the slopes of evergreen forests up to 500 m. It is found in the sub-himalayan tract from Nepal eastwards on the lower hills of Darjeeling terai in West Bengal where it is common; in Chota Nagpur (Bihar), Orissa and Andhra Pradesh, in the Andamans, it is very common in damp places along large streams, and in Karnataka and Kerala on the west coast, and western ghats at low level in wet places. It is also distributed in Thailand and Indo-china and east-ward in Malaysian archipelago to Papua New Guinea [1, 2]. The bark of the plant is reported to possess tonic, bitter, pungent, sweet, acrid, astringent, febrifugal, anti-inflammatory, digestive, carminative, diuretic, expectorant, constipating and antiemetic properties and is given to treat the fever and inflammation of eyes. The flowers are used as vegetable. The leaves are slightly aromatic with unpleasant taste but the decoction of leaves good for ulcers, wounds, and metorrhea. Additionally, it is useful in the treatment of snake-bite. It is often used in the form of powder (nygrodhadi kvatha churna) which is a herbal formulation. A general description about morphology of *Neolamarckia cadamba* has been summarized in Table 2 [3-5]. The analytical parameters and classification of plant mentioned in Table 3[6, 7] and Table 4 [8] respectively.

Table 2: Morphology of *Neolamarckia cadamba*

S. no.	Description
1	Habitat: India, Thailand, Indo-China and East-ward in Malasiyan archipelago to Papua New Guinea
2	Parts used: Barks, Fruits, Leaves, seeds, Flowers and root.
3	Bark: bark is dark brown, roughish with longitudinal fissures peeling off in thin scales.
4	Leaves: leaves coriaceous, entire margin, elliptical-oblong or ovate, pulvinus base, with acute or shortly acuminate.
5	Flowers: flowers are small, yellow or Orange colored with globose heads.
6	Fruits: fruits are fleshy, orange, globose Pseudocarpand yellow when ripe.
7	Seeds: seeds are small and muriculate.

Table 3: Analytical parameters of *Neolamarckia cadamba*

S. no.	Parameters	Result
1	Foreign matters	nmt 2%
2	Total-ash	8-9%
3	Acid-insoluble ash	0.6-1.5%
4	Water-soluble ash	2-2.5%
5	Sulfated ash	4-4.5%
6	Alcohol-soluble extractive value	4-6%
7	Water-soluble extractive value	4.5-5%

Table 4: Classification details of *Neolamarckia cadamba*

1	Kingdom	Plantae - plants
2	Subkingdom	Tracheobionta - vascular plants
3	Superdivision	Spermatophyta – seed plants
4	Division	Magnoliophyta – flowering plants
5	Subclass	Asteridae
6	Order	Rubiales
7	Family	Rubiaceae – madder family
8	Genus	Neolamarckia F. Bosser
9	Species	Neolamarckia cadamba (Roxb.) F. Bosser

Microscopy

The microscopic study of *Neolamarckia cadamba* leaf showed the presence of simple elongated, unicellular trichomes, rubiaceous types of stomata on the lower side of the leaf, starch grains, crystals of calcium oxalate, wedge-shaped vascular bundles, phloem in the form of ring and oil globules. The leaves of *Neolamarckia cadamba* having methyl salicylate aroma when crushed by hands [6, 7]. The bark consists of thin-walled, rectangular cells, phloem fibres some cell consists of chlorophyll and prismatic crystals of calcium oxalate [4].

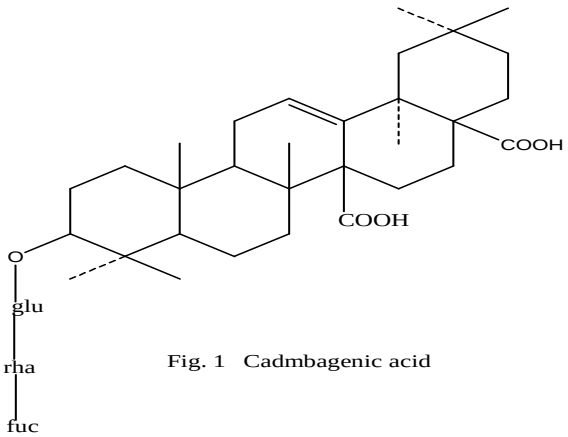

Fig. 1 Cadmbagenic acid

Phytochemistry

Neolamarckia cadamba primarily consist of indole alkaloids, terpenoids, sapogenins, saponins, terpenes, steroids, fats and reducing sugars [1, 4]. The bark also consists of tannins [2] and an astringent principle; which is due to the presence of an acid similar to cincho-tannic acid [5]. A new pentacyclic triterpenic acid isolated from the stem bark *Neolamarckia cadamba* named

cadambagenic acid (18α-olean-12ene-3β-hydroxy 27, 28-dioic acid) (Fig. 1), along with this acid quinovic acid (Fig. 2) and β- sitosterol (Fig. 3) have also been isolated [9].

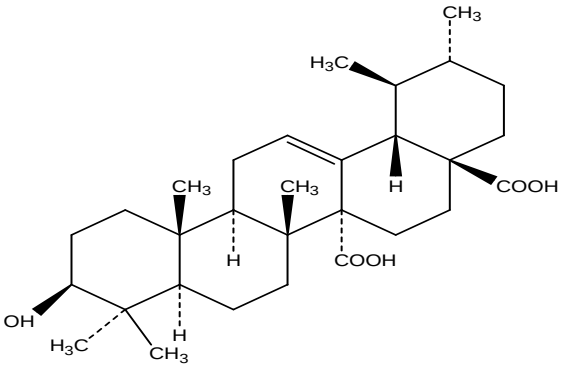

Fig. 2 Quinovic acid

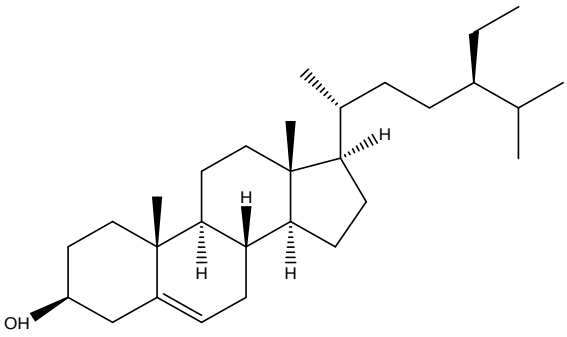

Fig. 3 β - sitosterol

Dried stem bark of *Anthocephalus indicus* has been investigated for its steroidal and alkaloidal constituents having good therapeutic values [10, 11]. Glycosidic indole alkaloids; cadambine ($C_{27}H_{32}N_2O_{10}$) (Fig. 4), 3α-dihydrocadambine ($C_{27}H_{34}N_2O_{10}$) (Fig. 5), isodihydrocadambine ($C_{37}H_{44}N_2O_{15}$) (Fig. 6) [12, 13] and two related non-glycosidic alkaloids; cadamine ($C_{23}H_{23}N_3O_4$) (Fig. 7) and isocadamine isolated from the leaves of *Neolamarckia cadamba* [14].

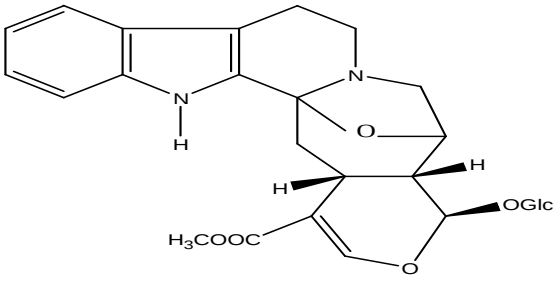

Fig. 4 Cadambine

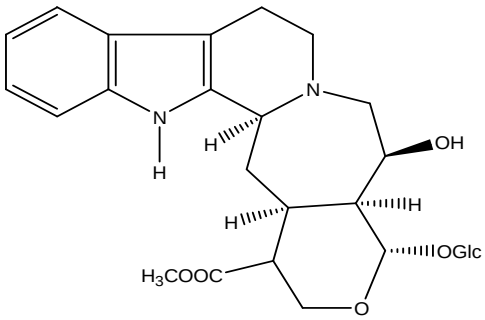

Fig. 5 3α dihydrocadambine

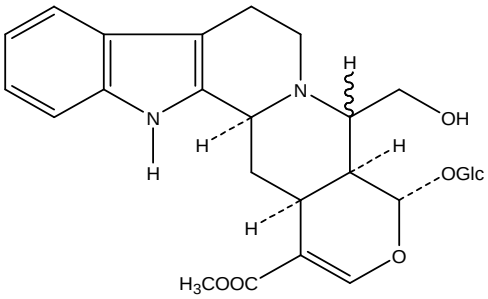

Fig. 6 Isodihydrocadambine

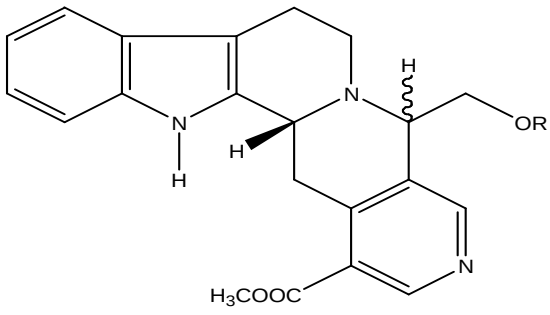

Fig. 7 Cadamine

The isolation and structure of 3β-dihydrocadambine and 3β-isodihydrocadambine (Fig. 8) alkaloids reported from the leaves of *Neolamarckia cadamba* with molecular formula ($C_{37}H_{44}N_{15}O_2$) [15]. A new saponin named saponin B ($C_{48}H_{76}O_{17}$) reported from *Neolamarckia cadamba* (Miq.) [16]. *Neolamarckia cadamba* also contain an acid called chlorogenic acid (CGA) (Fig. 9) [17]. Recently some worker isolated two novel triterpenoid saponins, phelasin A and phelasin B from the bark of *Neolamarckia cadamba* (Roxb.) Miq [18]. Two novel monoterpenoid indole alkaloids, aminocadambine A ($C_{24}H_{27}N_3O_5$) (Fig. 10) and aminocadambine B ($C_{25}H_{29}N_3O_5$) (Fig. 11) obtained from the leaves of *Neolamarckia cadamba*, previously named *Anthocephalus chinensis* [19] whereas some worker biosynthetically synthesized glucosidic indole alkaloid cadambine from its biological precursor secologanin [20] which is the main precursor of various indole alkaloids.

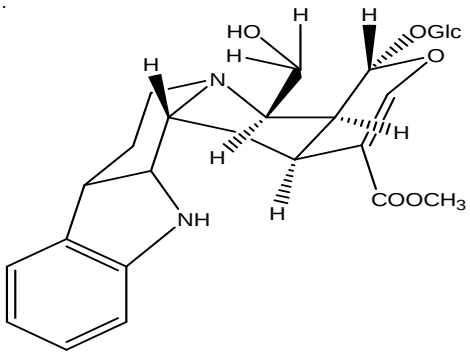

Fig. 8 3β Isodihydrocadambine

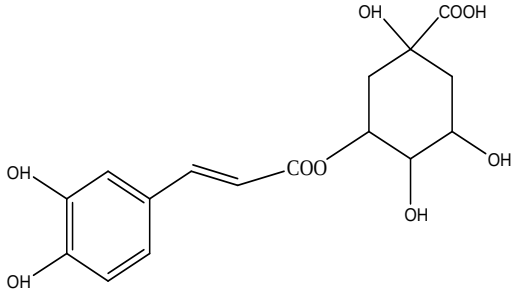

Fig. 9 Chlorogenic acid

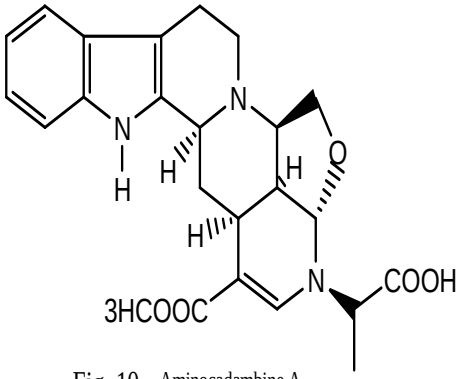

Fig. 10 Aminocadambine A

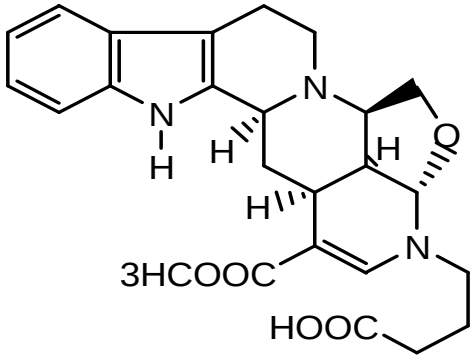

Fig. 11 Aminocadambine B

Three monoterpenoid gluco-indole alkaloids, 3β-isodihydrocadambine, cadambine and 3α-dihydrocadambine isolated from *Nauclea cadamba* (Roxb.) [21]. The flowers of *Neolamarckia cadamba* yield an essential oil and the main constituents of oils are linalool, geraniol, geranyl acetate, linalyl acetate, α-selinene, 2-nonanol, β-phellandrene, α-bergamottin, *p*-cymol, curcumene, terpinolene, camphene and myrcene [2]. Two triterpenoid glycosides, glycosides A and B were isolated from the bark of *Neolamarckia cadamba* and defined as 3-*o*-(α-L-rhamnopyranosyl)-quinovic acid-28-*o*-(β-D-glucopyranosyl) ester and 3-*o*-(β-D-glucopyranosyl)-quinovic acid-28-*o*-(β-D- glucopyranosyl) ester respectively [22] and eight different alkaloids also obtained from *Neolamarckia cadamba* named cadambine, CFJ 83, isomalindan, cadamine, 2 derivs. HFP34, GZM28, malindan, dihydrocadambine (Fig. 12), 2

derivs. GPX71, GPX73, isomalindan, isodihydrocadambine, 2 derivs. GPX51, GPX53, malindan [23]. The seeds of *Anthocephalus indicus* composed of water-soluble polysaccharides D-xylose, D-mannose and D-glucose in the molar ratio 1:3:5 [24].

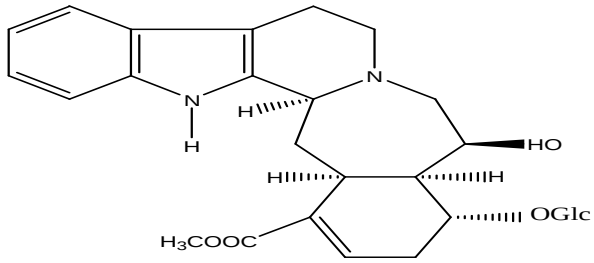

Fig. 12 Dihydrocadambine

Pharmacological Studies

From literature survey it was found that the almost all parts of the plant *Neolamarckia cadamba* is used in the treatment of various diseases. Decoction of leaves is used as gargle in aphthae or stomatitis and in the treatment of ulcers, wounds, and metorrhea. Bark of the plant is used in fever, inflammation, cough, vomiting, diarrhoea, diabetes, burning sensation, diuresis, wounds, ulcers and in the treatment of snake-bite [1, 2, 3, 5].

Antidiabetic activity

The alcoholic extract of the stem bark of *Neolamarckia cadamba*, syn. *Neolamarckia cadamba* has been reported to exhibit antidiabetic (hypoglycemic) potential in alloxan (120-150 mg/kg) induced diabetic rats and rectifying the problems like fatigue and irritation associated with this disease. The experimental studies showed that the 400-500 mg/kg extract of drug are effective in the treatment of diabetes and it is thought to be due to the presence of flavonoids, which stimulate the insulin secretion or possess an insulin-like effect [25, 26]. The alcoholic and aqueous extract of the roots of *Neolamarckia cadamba* also possess the anti-diabetic activity in dose 400 mg/kg body weight and was tested against the normoglycaemic and alloxan induced hyperglycaemic rats [27].

Analgesic, Antipyretic and Anti-inflammatory activities

Extracts of the bark and leaf of *Neolamarckia cadamba* possess the analgesic, antipyretic and anti-inflammatory activities. The defatted aqueous extract of the leaves of *Neolamarckia cadamba* showed significant analgesic and anti-inflammatory activity at varying doses (50, 100, 300 and 500 mg/kg) [28, 29]. The methanolic extract of the bark of *Neolamarckia cadamba* was successfully evaluated for analgesic, antipyretic and anti-inflammatory activities by some workers [30, 31].

Antidiarrhoeal activity

The dry hydroethanolic extract (200-500mg/kg) of the flowering tops of *Neolamarckia cadamba* exhibited a dose-dependent decrease in the frequency of faecal dropping in castor oil induced

diarrheoea in mice. The extract also produced a dose-dependent reduction in intestinal fluids accumulation [32].

Diuretic and Laxative activity
The various extracts of the barks of *Neolamarckia cadamba* were studied for its diuretic and laxative activity and it was found that the methanol extract (300 mg/kg) of the bark of *Neolamarckia cadamba* significantly showed in increases the urinary output (ie., diuresis) as compared with aqueous, chloroform and petroleum ether extract, whereas the chloroform extract (300 mg/kg) produced significant laxative property [33].

Antihepatotoxic effects
Neolamarckia cadamba have been reported to be used for its hepatoprotective activity. The hepatoprotective activity is due to the presence of chlorogenic acid (CGA) isolated from *Neolamarckia cadamba*. It was also found that the intraperitoneal administration of CGA to mice at a dose of 100 mg/kg for 8 days exhibited a better liver protective action than silymarin (SM), in CCl_4 administered mice. The antioxidative activity of CGA is responsible for its hepatoprotective nature. CCl_4 is used as a model of liver injury [17].

Hypolipidemic activity
From the experimental studies carried out by the workers showed the marked decrease in the lipid level in alloxan (150 mg/kg body wt.) induced diabetic rats. Oral administration of root extract (500 mg/kg body wt.) of *Anthocephalus indicus* for 30 days in dyslipidemic animals resulted in significant decrease in total cholesterol, phospholipids, triglycerides and lipid peroxides [34].
Antioxidant activity
The extract of *Neolamarckia cadamba* Syn. *A. indicus* Syn. *A. chinensis* possesses potent antioxidant activity by inhibiting lipid peroxidation and increase in the superoxide dismustase (SOD) and catalase activity [34-36].

Antimicrobial and wound healing activity
Neolamarckia cadamba has been reported for antimicrobial activitites. The plant have been reported to posses potent antibacterial and antifungal activity against *Escherichia coli, Micrococcus luteus, Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhi, Klebsiella pneumonia, Proteus mirabilis, Candida albicans, Trichophyton rubrum, Asperagillus niger, Asperagillus flavus* and *Asperagillus nidulans* [35, 36]. The experimental evidence also shows that *A. cadamba* extract has potent wound healing capacity [35]. The aqueous extract of *A.cadamba* also found effective against *Rathyibacter tritici* a causal organism of tundu disease of wheat [37], and effective against foot and mouth disease of animals [38].

Anthelmintic activity
Aqueous and ethanolic extracts of mature bark of *Neolamarckia cadamba* has been reported for its anthelmentic activity against earthworms, tapeworms, and roundworms [39].

Toxicological studies
The methanolic extract of *Neolamarckia cadamba* barks were studied for its toxicity in mouse models. The results suggested that acute toxicity was found in animal models at doses range higher than 3000 mg/kg and there was no mortality found at 3000 mg/kg dose in animal models. The sub-acute toxicity was carried out at dose 600 mg/kg. From the result it is suggested that *N. cadamba* is non-toxic at doses of 600 mg/kg [30, 40].

Ayurvedic properties and action [4]
Rasa (taste): kasaya, madhur (sweet), lavana
Guna (qualities): ruksa
Virya (nature): sita (cooling)
Vipaka (taste developed through digestion): katu

Formulation and analytical studies
Neolamarckia cadamba have been widely used in the in various ayurvedic formulation in the form of churna (nygrodhadi kvatha churn) and oil (grahanimihira taila) [4]. It is widely used in the form of paste by tribe in Western Ghats for treating skin diseases [35]. Earlier various methods have been developed to analyze *Anthocephalus* extract, these method include HPTLC, TLC, and various spectroscopic techniques like IR, Mass and NMR spectroscopy [41].

CONCLUSION

Research in medicinal plants has gained a renewed focus recently. The main reason is that the other system of medicine associated with number of side effects that often cause to serious problems. Though traditionally *Neolamarckia cadamba* has various medicinal activities but it is time to explore its medicinal values at molecular level with the help of various biotechnological techniques. Few toxicological studies have been reported. The work could also be done in this direction to ensure free utility of the plant.

Acknowledgement
The authors thanks to Head, Department of Pharmacy, Bansal College of pharmacy for providing help in carrying out this work. Thanks are also due to the library of Bansal College of pharmacy for providing necessary journals and reference books to complete this work.

REFERENCES

[1] Prajapati, Purohit, Sharma and kumar, A handbook of medicinal plants: A complete source book. Agrobios (India) publisher, Jodhpur, **2007,** 52-53.
[2] The wealth of India, A dictionary of Indian raw materials and industrial products. NISCAIR press publishers, New Delhi, **2006**, 305-308.
[3] K.R. Kirtikar and B.D. Basu, Indian medicinal plants. Lalit mohan basu publishers, Allahabad, **1999**, 2, 1250-1252.
[4] Ayurvedic Pharmacopoeia of India. Controller of publication, New delhi, **1999**, 1, 64-65.
[5] K.M. Nandkarni's, Indian materia medica. Bombay popular prakashan, Mumbai**, 2002**, 118-119.
[6] D. Patel and V. Kumar, *International journal of green pharmacy*, **2008,** 2, 1, 26-27.

[7] T.R. Shantha, K.G. Vasanthakumar and K. Gopakumar, *Journal of economic and taxonomic botany***, 2008**, 32, 1, 128-148.
[8] USDA, Plant database **1994,** united state department of agriculture. Available online at: http://www.plants.usda.gov/java/reference?symbol=NECA7.
[9] N.P. Sahu, S.B. Mahto and R.N. Chakravarti, *Ind j pharm***. 1974**, 12, 284-286.
[10] S. Prasad and I.C. Bhattacharya, *Ind j pharm*. **1960**, 22, 7, 172-174.
[11] S. Prasad, S.B. Jaiswal and I.C. Bhattacharya, *Ind j pharm*. **1961**, 23, 1, 5-7.
[12] R.T. Brown and S.B. Fraser, *Tetrahedron lett*. 1974, 23, **1957**-1959.
[13] R.T. Brown, S.B. Fraser and J. Banerji, *Tetrahedron lett*., **1974**, 29, 3335-3338.
[14] T. Richard, Brown and L.C. Chapple, *Tetrahedron lett*., **1976**, 19, 1629-1630.
[15] R.T. Brown, S.B. Fraser and L.C. Chapple, *Tetrahedron lett*., **1976**, 17, 2723-2724.
[16] N. Banerji, *Ind j chem*. B, **1977**, 15, 654-655.
[17] A. Kapil, I.B. Koul and O.P. Suri, *Phytotherapy research*. 1995, 9, 3, 189-193.
[18] N.P. Sahu, K. Koike, Z. Jia, B. Achari, S. Banerjee and T. Nikido, *Magnetic resonance in chemistry*. **1999**, 37, 11, 837-842.
[19] Ling-Li Liu, Ying-Tong Di, Qiang Zhang, Xin Fang, Feng Zhu, Dong-Lin Chen, Xiao-Jiang Hao and Hong-Ping He, *Tetrahedron lett*., **2010**, 51,43, 5670-5673.
[20] R.T. Brown, D.M. Duckworth and C.A.M. Santos, *Tetrahedron lett*., **1991**, 32, 1987-1990.
[21] H. Takayama, S. Tsutsumi, M. Kitajima, D. Santiarworn, B. Liawruangrath and N. Aimi, *Chem. Pharm. Bull.*, **2003**, 51, 232-233.
[22] N.P. Sahu, K. Koike, Z. Jia, S. Banerjee, N.B. Mandal and T. Nikaido, *J. Chem. Research*, **2000**, 22-23.
[23] L.F. Sazbo, *Molecules*, **2008**, 13, 1875-1896.
[24] O. Chandra and D. Gupta, *Carbohydrate research*, **1980**, 83, 85-92.
[25] S.K. Bussa and J. Pinnapareddy, *Int. j. pharmacy and technology*, **2010**, 2,2, 314-324.
[26] H. Gurjar, S.K. Jain, R. Irchhaiya, R. Nandanwar, V.K. Sahu and H. Saraf, *Int. j. pharmaceutical Sci. and res.*, **2010**, 1,7, 79-83.
[27] S. Acharyya, D.K. Dash, S. Mondal and S.K. Dash, *Int. j. pharma and bio sciences*, **2010**, 1, 2, 1-9.
[28] R.S. Bachhav, V.V. Buchake, S.S. Aher, R.R. Rode and R.B. Saudagar, *Adv. In pharmacol. And toxicology*, **2009**, 10, 2, 123-130.
[29] H.R. Ambujakshi, S.T. Antony, Y. Kanchana, R. Patel, H. Thakkar and Shyamnanda. *J. pharmacy res.*, **2009**, 2, 8, 1279-1280.
[30] S. Mondal, G.K. Dash and S. Acharyya, *J. pharmacy res*., **2009**, 2, 6, 1133-1136.
[31] K.S. Chandrashekar, A. Borthakur and K.S. Prasanna, *Int. j. plant biology*, **2010**, 1, 1, 30-32.
[32] M.A. Alam, R. Akter, N. Subhan, M.M. Rahman, M.M. Majumder, L. Nahar and S.D. Sarker, *Brazilian J. of pharmacognosy*, **2008**, 18,2, 155-159.
[33] S. Mondal, G.K. Dash, A. Acharyya and H.P. Sharma, *Drug invention today*, **2009**, 1, 1, 78-80.
[34] V. Kumar, F. Mahdi, R. Chander, R. Singh, A.A. Mahdi, K.A. Khanna, S. Bhatt, R.S. Kuswaha, K. Jawad, J.K. Saxena and R.K. Singh, *Indian journal of biochemistry and biophysics*, **2010**, 47, 104-109.
[35] S.P. Umachigi, G.S. Kumar, K.N. Jayaveera, K.D.V. Kumar, A.C.K. Kumar and R. Dhanpal, *African journal of traditional, complementary and alternative medicines*, **2007**, 4, 4, 481-487.

[36] L. Nahar, F.A. Ripa, Rokonuzzaman, A.A. Al-bari, *Journal of applied sciences research*, **2009**, 5, 12, 2285-2288.
[37] K.S. Chandrashekar and K.S. Prasanna, *Journal of chemical and pharmaceutical research*, **2009**, 1, 1, 268-270.
[38] S.K. Bhardwaj and J.S. Laura, *Biosciences, biotechnology research asia*, **2008**, 5, 1, 283-288.
[39] S.C. Dogra, *Indian journal of history of science*, 1987, 22, 2, 164-169.
[40] R.G. Mali and A.A. Mehta, *Natural product radiance*, 2008, 7, 466-475.
[41] S.N. Bhunia, S. Mondal, G.K. Dash and A. Samnata, *Journal of pharmacy research*, **2009**, 2, 11, 1746-1750.
[42] H. Gurjar, S.K. Jain, R. Nandanwar and V.K. Sahu, *International journal of pharmaceutical sciences and research*, **2010**, 1, 7, 108-115.