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Review of some important plants with antioxidant and other biological activities

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Abstract

The last two decades have witnessed a revival of interest in natural drugs and herbal products primarily due to the widespread belief that 'green' medicines are healthier than synthetic products. This has led to a rapid spurt in demand for health products like herbal teas, ginseng and such other products of traditional medicine. It is increasingly being realized that a majority of the present day diseases are due to the shift in the balance of the pro-oxidant and the antioxidant homeostatic phenomenon in the body. Despite the existence of endogenous defense mechanisms against reactive oxygen species (ROS) like the antioxidant enzymes and dietary antioxidants, it has been observed that whenever either the level of the cellular antioxidant system goes down or when the ROS reach abnormally high levels, oxidative damage to the cells occurs leading to several pathological conditions. Over about 100 disorders like rheumatoid arthritis (RA), hemorrhagic shock, cardiovascular system (CVS) disorders, cystic fibrosis, metabolic disorders, neurodegenerative diseases, gastrointestinal, ulcerogenesis and acquired immunodeficiency syndrome (AIDS) have been reported as ROS mediated. In the present paper, ten 'Rasayana' plants with potent antioxidant activity (*Acorus calamus, Andrographis paniculata, Anogeissus latifolia, Argyreia speciosa, Asparagus racemosus, Boerhaavia diffusa, Convolvulus pluricaulis, Curculigo orchioides, Desmodium gangeticum, Embelia ribes, Picrorhiza kurrooa, Withania somnifera*) are reviewed for their traditional uses, phytochemical and pharmacological aspects.

Key words: Antioxidant, Natrual Products, India, Ayurveda, Rasayana Plants, Ethnobotany

Introduction

The origin of diseases is of multifactorial nature and is now being understood as a vitation in the basic homeostatic balance phenomenon in the body. There is an explosion of global awareness concerning increasing imbalances in the natural ecosystem. Various measures are being taken up to correct the root cause of this imbalance. Human beings constantly struggle against the changing environmental conditions to maintain optimum health and vigour throughout their life. The human body depends on the continuous interaction between internal and external factors. When this interaction is in a state of equilibrium, man enjoys good health and when it fails, either due to internal deficiency or hostile environmental factors, the balance is disturbed and leads to disharmony and disease. The altered homeostatic theory was proposed by Hellstrom (1) which asserts that multiple acquired and genetic factors move the basic homeostatic balance of the body in such a direction that inappropriately activates the defense mechanisms. Therefore, it is essential to diagnose the causes of inappropriate imbalance, which may be the real factor, lack of which is an important step in controlling the disease process. Thus, the ideal cure would be the restoration of factors, which will improve the balance (remove the imbalance) and shift the physiological process in the direction of homeostatic balance. This theory is regarded as a holistic approach to the disorders of multifactorial nature.

It is being increasingly realized that a majority of the present day diseases are due to the shift in the balance of the pro-oxidant and the antioxidant homeostatic phenomenon in the body. Pro-oxidant conditions dominate either due to the increased generation of the free radicals caused by excessive oxidative stress of the current life, or due to the poor scavenging/quenching in the body caused by depletion of the dietary antioxidants (2,3).

Free radicals are fundamental to any biochemical process and represent an essential part of aerobic life and our metabolism. They are continuously produced by body's use of oxygen such as in respiration and some cell-mediated immune functions. They are also generated through environmental pollutants, cigarette smoke, automobile exhaust, radiation, air-pollution, pesticides, etc. (4, 5). Normally, there is a balance between the amount of free radicals generated in the body and the antioxidant defense systems that scavenge/quench these free radicals preventing them from causing deleterious effects in the body (6). The antioxidant defense systems in the body can only protect the body when the amount of the free radicals is within the normal physiological level. But when this balance is shifted towards more of free radicals, increasing their burden in the body, either due to

environmental condition or produced within the body, it leads to oxidative stress, which may result in tissue injury and subsequent diseases (5). Since free radicals play such an important role in the disease scenario, a thorough understanding of the various physiologically significant free radicals is of paramount importance before the search of the radical scavengers or the antioxidant principles to treat the physiological disorders caused by them.

The concept of developing drugs from plants used in indigenous medical systems is much older, while in some cases direct links between local and biomedical use exists, in other cases the relationship is much more complex (7). As 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. There has been a review on some plants of Indian traditional medicine with antioxidant activity (8) and a review of immunomodulators from Ayurveda especially of the Rasayana plants. Ayurvedic pharmacology classifies medicinal plants into different groups according to their actions. One of these is the 'Rasayana' group. The word 'Rasayana' literally means the path that 'Rasa' takes ('Rasa': plasma; Ayana: path). It is believed, in Ayurveda that the qualities of the 'Rasa-dhatu' influence the health of other dhatus (tissues) of the body. Hence any medicine that improves the quality of 'Rasa' ('Rasayana') should strengthen or promote the health of all tissues of the body. In this review, some of the important Indian medicinal plants with antioxidant effects are reviewed for their traditional use, chemistry and pharmacological actions.

Monographs of individual plants

1. Acorus calamus

Acorus calamus Linn. (family, Araceae) is a semi-aquatic, perennial, aromatic herb with creeping rhizomes. Since antiquity, calamus root has been used for medicinal baths, in incense and tea. It is the official drug for flatulent colic and chronic dyspepsia (9). The rhizome is aromatic, stimulant, bitter, tonic, carminative, anti-spasmodic, emetic, expectorant, emmenagogue, aphrodisiac, laxative, and diuretic (10). It has also been ethnobotanically used in asthma and bronchitis (11), body ache (12), cold and cough (13) and inflammation (14). The insecticidal activity of the solvent extracts and steam-distilled volatile principle of rhizome against common houseflies is quite marked (15). α- and β-asarone and 1-allyl-2, 4, 5-trimethoxybenzene from essential oil exhibited spasmolytic activity on isolated guinea-pig trachea and ileum contracted by acetylcholine, histamine, serotonin and barium chloride. Both α- and β-asarone showed cardiac depressant activity, moderate hypotensive action in anaesthetized dogs and anticholinergic activity (16). The major chemical constituents of *A. calamus* are α- and β-asarone (17,18), calacone, telekin, isotelekin, calarene, isocalamendiol, calamendio (19), shyobunone, epishyobunone, isoshyobunone (17,20), acolamone, isoacolamone, acoragermacrone, (+)calamusenone, isocalamusenone, galangin (flavone), acoradin, 2, 4, 5 hydrodxy benzaldehyde, 2, 5 dimethoxy benzoquinone (21), calamensesquiterpeneo (16), triterpenoid saponins viz. 1β, 2α, 3β, 19α - tetrahydroxy-12-en-28-oic tetrahydroxyolean-12-en-3-O-{-β-D-arabinosyl(1→3)}- β-D-arbinopyranoside (22)acid-28-O-{β-D-glucopyranosyl (1→2)}- β-D- galactopyranoside, 3β,22α, 24, 29 and sesquiterpene viz. 2-hydroxyacorenone, 2-acetoxyacorenone, epicorone, 1-hydroxyepiaorane, epiacoronene, acorusnol (23). We have recently reported the antioxidant activity of the *A. calamus* (24).

2. Anogeissus latifolia

Anogeissus latifolia Roxb. Wall. Ex. Bedd. (Family, Combretaceae) is a small or fairly large tree, commonly found in the forests of the Sub-Himalayan region, Siwalik Hills and throughout India up to 1200 m. It is an important timber while the leaves and bark are used for tanning. The bark was first examined by Reddy *et al*. (25) who isolated (+) leucocyanidin from it. Later, ellagic acid and two new glycosides of ellagic and flavellagic acid were reported (26). Ethnobotanically, the bark has been reported to be used in the treatment of various disorders like skin diseases (27), snake and scorpion bite (28), stomach diseases (29), colic (30), cough (31) and diarrhoea (32), though till to date, no biological report has been published. We have reported the antioxidant activity of the plant for the first time (33).

3. Asparagus racemosus

Asparagus racemosus Willd. (family, Liliaceae), commonly known as `shatavari' (Hindi and Sanskrit), is a tall climber under-shrub found all over India. Almost all parts of this plant are used by the Indian traditional system of medicine (Ayurved and Unani) for the treatment of various ailments. In particular, the roots are used in dysentery, diarrhoea, tuberculosis, leprosy, skin diseases, epilepsy, inflammation, and as expectorant (34,35). Antioxidant properties of *A. racemosus* against damage induced by gamma-radiation in rat liver mitochondria have been reported (36). Chemically, the plant has been reported to contain isoflavone mainly 8-methoxy-5, 6, 4-trihydroxyisoflavone 7-O-beta-D-glucopyranoside (37), polycyclic alkaloids, asparagine (38) and phytoecdysteroids (39). *A. racemosus* has been reported as a potential immunoadjuvant that also offers direct therapeutic benefits resulting in less morbidity and mortality (40). Methanol extract of *A. racemosus* roots showed significant antitussive activity (41). Aqueous extract of *A. racemosus* has been reported to possess adaptogenic

activity (42), thus proving the plant as a Rasayana drug and validating the Ayurvedic claim. Antioxidant potential of the plant in diabetic rats has also been reported (43). Presence of isoflavaone in the plant may be one of the reasons for the antioxidant activity.

4. Azadirachta indica

Azadirachta indica A. Juss. (family, Meliaceae; Ayurvedic name Nimba) is commonly known as neem. It is very useful in blood disorders, eye diseases, intermittent fever as well as in persistent low fever. Oil is very useful in leprosy, skin diseases, ulcers, and wounds. The bark contains a resinous bitter principle and is usually prescribed in the form of a tincture or an infusion. It is also regarded as beneficial in malarial fever (10). The antioxidant property of *A. indica* has been reported (44). Neem leaf extracts (100, 200, and 400 mg/ kg) showed its chemoprotective effects on potent gastric carcinogen N-methyl-N'-nitro-N-nitrosoguanidine (MNNG)-induced oxidative stress by decreasing LPO and enhancing the antioxidant enzymes like SOD, CAT, GSH-px and GST in male rats (45). Ethanolic neem leaf extract exerts protective effects against MNNG-induced genotoxicity and oxidative stress by augmenting host antioxidant defense mechanisms (46). *A. indica* extract demonstrated anticancer activity by increasing the distribution of antioxidant elements and GST activity to protect cells in preneoplastic nodules in cancer treated groups (47). Modulatory effects of garlic and neem leaf on hepatic and blood oxidant-antioxidant status may play a key role in preventing cancer development at extrahepatic sites (48).

5. Bacopa monnieri

Bacopa monnieri Linn. Penn. (family, Scrophulariaceae; Ayurvedic name, Brahmi). Leaves and stalks are very useful in the stoppage of urine, which is accompanied by obstinate costiveness. A poultice made of the boiled plant is placed on the chest in acute bronchitis and other coughs in children. Leaves also give satisfactory results in cases of asthenia, nervous breakdown and other low adynamic conditions. It is also given in combination with 'Ghrita' (animal fat), a well-known Ayurvedic medicine (*brahmi ghrita*) in cases of hysteria and epilepsy. It is also useful in insanity, neurasthenia, aphonia and hoarseness (10). *B. monnieri* is clinically used for memory enhancement, epilepsy, insomnia and as mild sedative. It protected the auto-oxidation and $FeSO_4$-induced oxidation of GSH on lower doses (100 µg/ml and below) but on higher concentrations, it enhanced the rate of oxidation. (49). Extract of *B. monnieri* was assessed on rat brain frontal cortical, striatal and hippocampal SOD, CAT and GSH-px activities, following administration for 7, 14 or 21 days which induced a dose-related increase in SOD, CAT and GSH-px activities (50). It showed a dose-dependent free radical scavenging capacity and a protective effect on DNA cleavage and was confirmed by a significant protective effect on H_2O_2-induced cytotoxicity and DNA damage in human non-immortalized fibroblasts (51). Treatment with *B. monnieri* extract significantly increased the antioxidant enzymes such as CAT, SOD, GSH-px and the levels of GSH inhibited lipid peroxidation and reduced the tumor markers (52).

6. Boerhavia diffusa

Boerhavia diffusa L. (family, Nyctagenaceae) is commonly known as punernava. In Ayurvedic literature, two types of punernava, red and white are mentioned, *B. diffusa* and the allied species *B. repanada* and *B. erecta*. In Ayurveda, it is used as an antidote to toxins, rejuvenator and as a Rasayana. It forms a part of formulation used for treatment of bronchial troubles, liver disorders and as diuretic. β-Ecdysone (0.05%), triacontanol and β-sitosterol was isolated from its roots (53). 5,7-dihydroxy-3',4'-dimethoxy-6,8-dimethylflavone was also isolated from roots. Two new rotenoids – boeravinone A and boeravinone B were isolated from roots of plant collected from Nepal and sitosterol, stigmasterol, campesterol and their glucosides and methyl esters of palmitic, heptadecyclic, oleic, stearic, arachidic and behenic acids were also isolated (54). Isolation of a new 12a-hydroxyrotenoid boeravinone C from roots and determination of its structure and absolute configuration (55) have also been determined. Borhavine was isolated from roots and characterized as methyl-3, 10-dihydro-11-1-methoxy-4, 6-dimethyl-10-oxo-1H-furo [3, 4-b] xanthene-3-carboxylate (56). Rawat et al. (57) have reported the hepatoprotective activity of the plant. *B. diffusa* has been found to cause significant decrease in blood glucose and significant increase in plasma insulin levels were observed in normal and diabetic rats (58). Immunosuppressive potential of ethanolic extract of *B. diffusa* has been established (59). Free radical scavenging potential of the plant has also been reported (60) along with an effect on enzymatic system, especially on catalase and adenosine triphosphatase (61), thus validating its use as a potent rejuvenator.

7. Centella asiatica

Centella asiatica L. (Syn. *Hydrocotyle asiatica*; family, Umbelliferrae) is known as mandukparni in the Indian Sub-Continent and gotu kola in the western world. It is considered cool, bitter and a brain tonic. These form part of formulations, which are mainly used as brain tonic, for nerve disorders, for skin diseases and leprosy. Chemically it is reported to contain triterpene acids-brahmic acid, isolbarhmic acid and two saponins brahmoside, and brahminoside, triterpene glucoside thankuniside, and thankunic acid, triterpene-medecassoside and madecassis acid, 11-oxoheneicosanyl-cyclohexane and dotriacnt-8-en-1-oic acid (62). Triterpenoid glycoside 3-0-{α-

Larabinopyranosy1} 2α, 3β, 6β, 23-α-tetrahydroxyurs-12-ene-28-oic acid accompanied by 6 β –hydroxyasiatica acid and asiatic acid have been isolated (63). Ursane and oleanane type triterpene oligoglycosides, centellasaponins B, C, and D, were also isolated from the aerial parts. Asiaticoside produced increase in hydroxyproline, tensile strength and collagen content in streptozotocin diabetic rats where healing is delayed. Topical application of asiaticoside over punch wound increased hydroxyl content, tensile strength and collagen content thereby facilitating healing (64). Antihypertensive activity of *C. asiatica* has also been reported (65). *C. asiatica* partially prevented the decrease in body weight and leucocyte counts caused by cyclophosphamide (CYP) or cisplatin (CP) treatment and also significantly prolonged the life span of these mice; it, however, did not produce protective effects on CYP/CP induced toxicity (66). The antifilarial activity of *C. asiatica* ethanol extracts has been reported (67). *C. asiatica* shows significant antistress activity in all the parameters studied (68) proving its use as a Rasayana. Decreased levels of total ATPase Mg^{2+} ATPase, $Na^{+}K^{+}$ATPase and the increased levels of Ca^{2+} ATPase activity, protects the tissues against peroxidative reactions, thereby protects against cell damage (69). Inhibition of lipid peroxidation by *C. asiatica* was more in the liver followed by brain, kidney, heart, lungs and spleen in the presence or absence of inducers (70). Hexane and EtOAc extracts of *C. asiatica* displayed significant inhibitory activity against *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Pseudomonas cichorii* while n-BuOH extract was found to be inactive (71). The hydroalcoholic extract of *C. asiatica* showed anxiolytic/sedative effect and potentiation of the hypnotic effect of pentobarbitone and anticonvulsant activity against pentyteneletrazol-induced convulsion (72). Asiaticoside exhibits significant wound healing activity in normal as well as delayed healing models and is the main active constituent of *C. asiatica* (73). *C. asiatica* showed encouraging results with significant improvement of performance I.Q., immediate memory score and social quotient in these children after 6 months of treatment (74). Asiaticoside application to excision-type cutaneous wounds in rats led to increased enzymatic and non-enzymatic antioxidants, namely superoxide dismutase, catalase, glutathione peroxidase, vitamin E and ascorbic acid in newly formed tissues. It also resulted in a several fold decrease in lipid peroxide levels as measured in terms of thioparbituric acid reactive substance (75). Aqueous extract of *C. asiatica* is effective in preventing the cognitive deficits, as well as oxidative stress caused by i.c.v. STZ in rats (76). Crude methanol extract of *C. asiatica* for 14 days significantly increased the anti-oxidant enzymes, like superoxide dismutase (SOD), catalase and glutathione peroxidase (GSHPx) and anti-oxidants like glutathione (GSH) and ascorbic acid decreased in lymphoma-bearing mice (77), thus proving the utility of the plant as an antioxidant.

8. ***Convulvulous pluricaulis***

Convulvulous pluricaulis Choice. (family, Convolvulaceae) is a small annual herb with conch shell like flowers and commonly known as shankhpushpi. It is used as a brain tonic, digestive, appetizer, carminative, antidiabetic, antihypertensive and cures skin diseases in the Indian traditional system of medicine. The compounds isolated from *C. pluricaulis* include; 6-methoxy-7-hydroxycoumarin, glucose, maltose and β-sitosterol (78), kaempferol, kaempferol-3-glucoside and 3, 4-dihydroxycinnamic acid along with sugars (79), N-hexacosanol, n-octacosanol, n-triacontanol and n-dotriacontanol, β- and ε-sitosterols (80) and N-tetracontane, n-octacosanol (81, 82). The anticonvulsive (83) and antiulcerogenic (84) effects of *C. pluricaulis* have been reported. It appears that the plant extract is on thyroid function (85). The plant has also been reported as a brain tonic and memory enhancer (86, 87).

9. ***Desmodium gangeticum***

Desmodium gangeticum L. DC. (family, Leguminaceae; Ayurvedic name, Shalparni) is a small shrub of tropical region, which has been used in Indian system of medicine as a bitter tonic, febrifuge, digestive, anticatarrhal, antiemetic, antiinflammatory conditions of chest and various other inflammatory conditions (88). The plant is used in various Indian traditional systems of medicine like Ayurveda and Siddha. The roots of the plant are one of the ingredients of popular Ayurvedic drug – Dashmoola, a potent rejuvenating formulation used in Ayurveda (89). 5-methoxy-N,N-dimethyltryptamine, N,N-dimethyltryptamine, their N-oxides, N-methyl-tetrahydroharman, 6-methoxy-β-carbolinium cation (regenerated from Reinecke salt) from aerial parts of *D. gangeticum* and five phospholipids from the seeds of *D. gangeticum* have been reported (90). A new pterocarpan gangetin from the hexane extract of *D. gangeticum* was isolated and assigned the structure on the basis of chemical and spectroscopic evidence (91). Also reported were gangetinin and desmodin as the two minor pterocarpanoids of *D. gangeticum*. Twelve alkaloids comprising of four broad structural types, viz., carboxylated and decarboxylated tryptamines, β-carbolines and β-phenethylamines from different parts of *D. gangeticum* at different stages of development were also reported (92). Ingham and Dewick (93) isolated antifungal isoflavanoid phytoalexin desmocarpin together with genistein, 2'-hydroxygenistein, dalbergioiden, diphysolone and kievitone from fungus-inoculated leaflets and Behari and Varshney (94) isolated 24-ethylcholesta-5,22-dien-3β-ol, 24-ethylcholest-5-en-3β-ol and 24-methylcholest-5-en-3β-ol from *D. gangeticum*. Yadava and Reddy (95) reported

the isolation and structure determination of 8-C-prenyl-5, 7, 5'-trimethoxy-3', 4'-methylenedioxy flavone (I) from *D. gangeticum*. Yadava and Tripathi (96) isolated a novel flavone glycoside, 4', 5, 7-trihydroxy- 8-prenylflavone 4'-O-a-L-rhamnopyranosyl- (1→6) -β - D-glucopyranoside from the stem of *D. gangeticum*. Anti-inflammatory and analgesic activities of gangetin, a pterocarpenoid from *D. gangeticum* but gangetin did not show any acute toxicity in mice up to an oral dose of 7 g/kg (97). Daily administration of gangetin caused impairment of fertility and also caused a reduction in the vaginal sperm count and an enhancement of pre-implantation losses (98). It also showed inhibitory influence over the reproductive organs due to the antiprolactin nature of gangetin and secondarily to the significant fall in plasma testosterone level (99). Effects of aqueous extracts of *Desmodium gangeticum* on the central nervous system have also been investigated (100). We have reported the antioxidant activity of hydroalcoholic extract of *D. gangeticum* (101).

10. Hemidismus indicus

Hemidesmus indicus R. Br. (family, Asclepiadaceae), commonly known as anantmul and also called as Indian sarsaparilla. In Ayurveda, there is confusion about the differential botanical identification of *H. indicus* and another herb, Sariva (102). As per Ayurveda, it is cooling, sweet, anabolic, aromatic laxative, blood purifier, stimulates the flow of bile and antidote to 'tridosha' and body toxin. It cures skin diseases and ulceration. The compounds identified from *H. indicus* include hexatriacontane, lupeol octacosanoate, β-amyrin acetate, lupeol acetate, α-amyrin, lupeol, β-amyrin and sitsterol (103), pregnane ester diglycoside named desinine (104), hemidesminine a coumarino-lignoid (105), pregnane glycoside, designated indicine I and hemidine (II) (106), two new coumarino-lingnoids, hemidesmin-1 and hemidesmin-2 (107), two novel pregnane glycosides, hemidescine and emidine (108), and three new pregnane diglycosides, medidesmine, hemisine and desmisine (109, 110). *H. indicus* suppressed both the cell-mediated and humoral components of the immune system (111). Oral treatment with the ethanol extract *of H. indicus* roots significantly prevented rifampicin and isoniazid-induced hepatotoxicity in rats (112). *H. indicus* has been reported to possess *in vitro* antioxidant (113, 114), antiulcer (115), and antidiarrhoeal and bacteriocidal (116) actvities. Moreover, inhibition of cutaneous oxidative stress and two-stage skin carcinogenesis (117) and management of renal impairment induced by gentamicin (118) have also been reported.

References

1. Hellstrom, H.R. *Med. Hypothesis*, **53,** 194-199 (1999).
2. Schulz, J.B., Lindnau, J., Seyfriend, J., Dichgans, J. *Euro. J. Biochem.* **267**, 4904-4911 (2000).
3. Dringen, R. *Euro. J. Biochem.* **267**, 4903 (2000).
4. Halliwell, B., Gutteridge, J.M.C., Cross C. E. *J. Lab. Clin. Med.* **119**, 598-620 (1992).
5. Li, Y., Trush M.A. *Cancer Research,* **54,** 1895s-1898 (1994).
6. Nose, K. *Biol. Pharm. Bull.* **23**, 897-903 (2000).
7. Heinrich, M., Gibbons, S. *J. Pharm. Pharmacol.* **53**, 425-432 (2001).
8. Scartezzini, P., Speroni, E. *J. Ethnopharmacol.* **71**, 23- 43 (2000).
9. Parrotta, J.A. *Healing Plants of Peninsular India.* CABI Publishing Oxon, U.K., 2001, pp. 106-107.
10. Kapoor, L.D. *Hand book of Ayurvedic Medicinal plants. CRC Press, Washington D.C.*, pp. 18-19 (2001)
11. Maheshwari, J.K., Singh, K.K., Saha, S. *Bull. Medico-ethnobot Res.* **1,** 318-337(1980).
12. Gupta, R. *Glimpses of Indian Ethnobotany.* 83-90 (1981).
13. Rao, R.R. *J. Econ. Tax. Bot.* **4,** 67-172 (1983).
14. Malhotra, C.L., Balodi, B. *J. Econ. Tax. Bot.* **5,** 841-845 (1984).
15. Agarwal, S.L., Dandiya, P.C., Singh, K.P., Arora, R.B. *J. Am. Pharm. Assoc.***145,** 655-656 (1956).
16. Janssen, A.M., Scheffer, J.J.C. *Planta Med.* **51,** 507-511 (1985).
17. Iguchi, M., Nishiyama, A., Koyamam, H., Yamamura, S., Hirata, Y. *Tetrahedron lett.* **42,** 3729-3732 (1969).
18. Patra, A., Mitra, A.K. *J. Nat. Prod.* **44**, 668-669 (1981).
19. Saxena, D.B. *Phytochem.* **25**, 553-555 (1986).
20. Iguchi, M., Nishiyama, A., Yamamura, S., Hirata, Y. *Tetrahedron lett.* **11**, 855-857 (1970).
21. Patra, A., Mitra, A.K. *Indian J. Chem.* **17B**, 412-414 (1979).
22. Rai R., Siddiqui I.R., Singh, J. *Indian J. Chem.* **37**, 473-476 (1998).
23. Nawamaki, K., Kuroyanagi, M. *Phytochem.* **43(6)**, 1175-1182 (1996).
24. Govindarajan, R., Agnihotri, A.K., Khatoon, S., Rawat, A.K.S., Mehrotra, S. *Nat. Prod. Sci.*, **9(4)**, 264-269 (2004).
25. Reddy, K.K., Rajadurai, S., Nayudamma, Y. *Indian J. Chem.* **3,** 308-310 (1965).
26. Deshpande, V.H., Patil, A.D., Rama Rao, A.V., Venkatraman. *Indian J. Chem.* **14,** 641-643 (1976).
27. Roy, G.P., Chaturvedi, G.P. *Folklore,* **27,** 95-100 (1986).

28. Mishra, R., Billore, K.V. *Nagarjun,* **26,** 229-231 (1983).
29. Jain, S.K., Tarafde,r C.R. *Econ Bot*. **24**, 241-278 (1970).
30. Apparanantham, T., Chelladurai, V. *Anc. Sci. Life,* **5**, 182-185 (1986).
31. Balla, N.P., Sahu, T.R., Mishra, G.P. *J. Econ. Tax. Bot*. **3,** 23-32 (1982).
32. Ramachandran, V.S., Nair, N.C. *J. Econ. Tax. Bot*. **2**, 183-190 (1981)
33. Govindarajan, R., Vijayakumar, M., Rao, Ch.V., Rawat, A.K.S., Shirwaikar, A., Mehrotra, S., Pushpangadan, P. *Biol. Pharm. Bull*. **27(8)**, 1266-1269 (2004).
34. Jain, S.K. Dictionary of Indian Folk Medicine and Ethnobotany. Deep Publications, New Delhi (1991).
35. Nadkarni, A. K., Nadkarni's Indian materia medica, vol. 1. Popular Prakashan. Bombay p. 153 (1976).
36. Kamat, J.P., Boloor, K. K., Devasagayam, T. P., Venkatachalam, S. R. *J. Ethnopharmacol*. **71**, 425-435 (2001).
37. Saxena, V.K., Chourasia, S. *Fitoterpia,* **72**, 307-309 (2001).
38. Sekine, T., Fukaswa, N., Kashiwagi, Y., Murakoshi, I., Ruangrungsi, N. *Chem. Pharm. Bull*. **42**, 1360-1362 (1994).
39. Dinan, L., Savchenko, T., Whiting, P. *Phytochem.* **56(6),** 569-576 (2001).
40. Gautam, M., Diwanay, S., Gairola, S., Shinde, Y., Patki, P., Patwardhan, B. *J Ethnopharmacol*. **91(2-3),** 251-255 (2004).
41. Mandal, S.C., Kumar, C.K.A., Mohanalakshmi, S., Sinha, S., Murugesan, T., Saha, B.P., Pal, M. *Fitoterapia.* **71(6)**, 686-689 (2000).
42. Rege, N.N., Thatte, U.M., Dahanukar, S.A. *Phytother. Res.* **13(4),** 275-91 (1999).
43. Govindarajan, R., Vijayakumar, M., Rao, Ch.V., Vivek Kumar, Rawat, A. K. S., Pushpangadan, P. *Nat. Prod. Sci.***10 (4)**, 177-181 (2004).
44. Rao, A.D., Devi, K.N., Thyagaraju, K. *J. Enzyme Inhibition,* **4**, 85-96 (1998).
45. Subapriya, R., Kumaraguruparan, R., Chandramohan, K.V., Nagini, S. *Pharmazie* **58**, 512-517 (2003).
46. Subapriya, R., Kumaraguruparan, R., Abraham, S.K., Nagini, S., *Drug Chemistry and Toxicology,* **27**, 15-26 (2004).
47. Hanachi P., Fauziah. O., Peng L.T., Wei L.C., Nam L.L., Tian.T.S. *J. Clin. Nutri.* **13,** S170 (2004).
48. Arivazhagan, S., Velmurugan, B., Bhuvaneswari, V., Nagini, S. *J. Medi. Food,* **7**, 334-339 (2004).
49. Tripathi, Y.B., Chaurasia, S., Tripathi, E., Upadhyay, A., Dubey, G.P. *Indian J. Exp. Biol*. **34**, 523-526 (1996)
50. Bhattacharya, S.K., Bhattacharya, A., Kumar, A., Ghosal, S. *Phytother. Res.* **14**, 174-179 (2000).
51. Russo, A., Izzo, A.A., Borrelli, F., Renis, M., Vanella, A., *Indian J. Exp. Biol.* **42,** 776-780 (2003).
52. Rohini, G., Sabitha, K.E., Devi, C.S. *Indian J. Exp. Biol*. **42**, 776-780 (2004).
53. Suri, O.P., Ravikanth, Jamwal, R.S., Suri K. A., Atal, C.K. *Planta Med*. **44,** 180-181 (1982).
54. Kadoda, S., Lami, N., Tezuka, Y., Kikuchi, T. *Chem. Pharm. Bull*. **37(12)**, 3214-3220 (1989).
55. Lami, N., Kadoda, S., Tezuka, Y., Kikuchi, T. *Chem. Pharm. Bull*. **38(6)**, 1558-1562. (1990).
56. Ahmed, B., Yu, C.P. *Phytochem*. **31(12)**, 4382-4384 (1992).
57. Rawat, A.K.S, Mehrotra, S., Tripathi, S.C., Shome, U. *J. Ethnopharmacol*. **56(1)**, 61-66 (1997).
58. Pari, L., Satheesh, M.A. *J. Ethnopharmacol*. **91(1)**, 109-113 (2004).
59. Mehrotra, S., Mishra, K.P., Maurya, R., Srimal, R.C., Singh, V.K. *Intern. Immunopharmacol*. **2(7)**, 987-996 (2002).
60. Mandal, M., Mukherji, S. *J. Environ. Biol*. **22(4)**, 301-305 (2001).
61. Goswami, P., Sarma, T. C. *J. Res. Ayur. Siddha.* **13**, 135-140 (1992).
62. Srivastava, R., Shukla, Y.N. *Indian Drugs*. **33(5)**, 233-234 (1996).
63. Shukla, Y.N., Srivastava, R., Tripathi, A.K., Prajapati, V. *Pharmaceutical Biol*. **38(4)**, 262-267 (2000).
64. Shukla, A., Rasik, A.M., Jain, G.K., Shankar, R., Kulshrestha, D.K., Dhawan, B.N. *J. Ethnopharmacol*. **65(1)**, 1-11 (1999).
65. Hansen, K., Nyman, U., Smitt, U.W., Adsers, A., Gudiksen, L., Rajasekharan, S., Pushpangadan. *Glimpses of Indian Ethnopharmacology* p. 263-273 (1995).
66. Babu, T.D., Padikkala, J. *Amala Research Bulletin*, **14**, 52-56 (1994).
67. Chakraborty, T., Sinha, S.P., Sukul, N.C. *Fitoterapia,* **67(2)**, 110-112. (1996).
68. Sarma, D.N.K., Khosa, R.L., Chansauria, J.P.N., Sahai, M. *Phytother. Res.* **10(2)**, 181-183 (1996).
69. Chandra Prabha, D., Annapurani, S., Murthy, N.K. *Indian J. Nutri. Dietetics.* **33(6)**, 128-132 (1996).
70. Chandra Prabha, D., Annapurani, S., Murthy, N.K. *Indian J Nutri Dietetics*, **33(4)**, 74-79 (1996).
71. Srivastava, R., Shukla, Y.N. Antibacterial activity of *Centella asiatica*. *Fitoterapia.* **68(5)**, 466-467. (1997),

72. Delucia, R., Sertie, J.A., Camargo, E.A., Panizza, S. *Fitoterapia*, **68(5)**, 413-416 (1997).
73. Shukla, A., Rasik, A.M., Dhawan, B.N. Asiaticoside-induced elevation of antioxidant levels in healing wounds. *Phytother. Res.***13 (1)**, 50-54 (1999).
74. Agarwal, S.C., Agarwal, D., Singh, R.H. *South East Asia on Herbs and Herbal Medicines*, 114. (1999).
75. Shukla, A., Rasik, A.M., Jain, G.K., Shankar, R., Kulshrestha, D.K., Dhawan, B.N. *J. Ethnopharmacol*. **65(1)**, 1-11 (1999).
76. Veerendra Kumar, M.H., Gupta, Y.K. *J. Ethnopharmacol* **79**, 253-260 (2002).
77. Jayashree, G., Kurup, M.G., Sudarslal, S., Jacob, V.B. *Fitoterapia*. **74(5)**, 431-434 (2003).
78. Deshpande, S.M., Srivastava, D.N. *J. Indian Chem. Soc*. **46(8),** 758-760 (1969)
79. Bisht, N.P.S., Singh, R. *Planta Med*. **34**, 222-223 (1978)
80. Bisht, N.P.S., Singh, R., Bansal, R.K., Singh, P. *Z. Naturforsch*, **33B,** 249 (1978).
81. Chowdhary, M.R., Kapoor, R.C. *Curr. Sci*. **55,** 917-918 (1986).
82. Mishra, A.S., Verma, J., Kumari, N. *Biojournal*, **61**, 31-36 (1995).
83. Mudgal, V., Udupa, K.N. *J. Res. Indian Med. Yoga Homeopathy*. **12**, 127-129 (1977).
84. Sairam, K, Rao. Ch.V, Goel, R.K, *Indian J. Exp. Biol*. **39(4)**, 350-354 (2001).
85. Panda.S, Kar. A. *Horm. Meta.b Res*. **33(1)**, 16-18 (2001).
86. Singh, R.H., Mehta, A.K., Sarkar, F.H., Udupa, K. *J. Res. Indian Med. Yoga Homeopathy*. **12**, 42-47 (1977).
87. Sinha, S.N., Dixit, V.P., Madnawat, A.V.S., Sharma, O.P. *Indian Med*. **1**, 1-6 (1989).
88. Chopra, R.N., Nayar, S.L., Chopra, I.C. *Glossary of Indian Medicinal Plants. CSIR, New Delhi India Publication*, p. 84 (1956).
89. Ghosal, S., Banerjee, P.K. *Australian J Chem*. **22**, 2029 (1969).
90. Rastogi, S.C., Tiwari, G.D., Srivastva, K.C., Tiwari, R.D. *Planta Med*. **20(2)**, 131-132 (1971).
91. Purushothaman, K.K., Chandrasekharan, S., Balakrishna, K., Connolly, J.D. *Phytochem*. **14(4)**, 1129-1130 (1975).
92. Ghosal, S., Bhattacharya, S.K. *Planta Med*. **22(4)**, 434-40 (1972).
93. Ingham, J.L., Dewick, P.L.Z. *Naturforsch*. **39c,** 531-534 (1984).
94. Behari, M., Varshney, A. *Indian Drugs*, **23**, 434 (1986)
95. Yadava, R.N., Reddy, K.I.S. *J. Inst. Chem*. **70(6)**, 213-214 (1998).
96. Yadava, R. N., Tripathi, P. *Fitoterapia*, **69(5)**, 443-444 (1998)
97. Ghosh, D., Anandkumar, A. *Indian J. Pharmacol*. **15**, 391-402 (1981).
98. Latha, P., Govindasamy, S. *Phytother. Res*. **11(6)**, 466 (1997)
99. Latha, P., Govindasamy, S., Balakrishna, K. *Phytother. Res*. **11(5)**, 372 –375 (1997).
100. Jabbar, S., Khan, M.T.H., Choudhuri, M.S K. *Pharmazie*. **56(6)**, 506-508 (2001).
101. Govindarajan R., Rastogi S., Vijayakumar M., Rawat A.K.S., Shirwaikar A., Mehrotra S., Pushpangadan P. *Biol. Pharm. Bull*. **26**, 1424-1427 (2003).
102. Karnick, C.R. *Herba Hungarica*. 16, 7-12 (1977).
103. Padhy, S.N., Mahato, S.B., Dutta, N.L. *Phytochem*. **12**, 217-218 (1972).
104. Oberai, K., Maneswari, P., Khare, A. *Phytochem*. **24**, 2395-2397 (1985).
105. Mandal, S., Das, P.C., Joshi, P.C., Das A., Chatterjee A. *Indian J Chem*. **30B**, 712-713 (1991).
106. Kamal, P., Sethi, A., Desh, D., Anakshi K., Khare, M.P. *Phytochem*. **30(1)**, 297-300 (1991).
107. Das. P.C, Joshi P.C., Mandal. S, Das. A, Chatterjee. A, *Indian J. Chem*. **31(B)**, 342-345 (1992).
108. Chandra, R., Desh, D., Khare, A. *Phytochem*. **(35)**, 1545-1548 (1993).
109. Desh, R., Srivastava, S., Khare A. *Carbohydr. Chem*. 69-74 (1995).
110. Desh, D., Srivastava, S., Khare, A. *Phytochem*. **(44)**, 145-151(1996).
111. Atal, C.K., Sharma, M.L., Kaul, A., Khajuria, A. *J. Ethnopharmacol*. **18(2)**, 133-41 (1986).
112. Prabakan, M., Anandan, R., Devaki, T. *Fitoterapia,* **71(1)**, 55-9 (2000).
113. Ravishankara, M.N., Shrivastava, N., Padh, H., Rajani, M. *Phytomed*. **9(2)**, 153-60 (2002).
114. Mary, N.K., Achuthan, C.R., Babu, B.H., Padikkala, J. *J. Ethnopharmacol*. **87(2-3),** 187-91(2003).
115. Anoop, J. *J. Ethnopharmacol*. **84(2-3)**, 149-56 (2003).
116. Das, S., Prakash, R., Devaraj, S.N. *Indian J. Exp. Biol*. **41(4)**, 363-6 (2003).
117. Sultana, S., Alam, A., Khan, N., Sharma, S. *Indian J. Exp. Biol*. **41(12)**, 1416-23 (2003).
118. Kotnis, M.S., Patel, P., Menon, S.N. Sane, R.T. *Nephrology*. **9(3)**, 142-52 (2004).