- 2. Anderson, O. R., Radiolaria, Springer-Verlag, New York, 1983.
- 3. Johnson, D. A., Schneider, D. A., Nigrini, C. A., Caulet, J. P. and Kent, D. V., Marine Micropaleontol., 1989, 14, 33-66.
- Caulet, J. P., Nigrini, C. and Schneider, D. A., Marine Micropaleontol., 1993, 22, 111-129.
- Riedel, W. R. and Sanfilippo, A., in *Initial Reports*, *DSDP* (eds Bader, R. G. et al.), U.S. Govt. Printing Office, USA, 1970, vol. 4, pp. 503-575.
- Riedel, W. R. and Sanfilippo, A., in *Initial Reports*, *DSDP* (eds Winterer et al.), U.S. Govt. Printing Office, USA, 1971, vol. 7 (2), pp. 1529-1672.
- 7. Riedel, W. R. and Sanfilippo, A., Micropaleontology, 1978, 24, 61-96.
- 8. Johnson, D. A., in *Initial Reports*, DSDP (eds Borch Von der et al.), U.S. Govt. Printing Office, USA, 1974, vol. 22, pp. 521-575.
- Nigrini, C., in *Initial Reports*, DSDP (eds Mayer, L. et al.), U.S. Govt. Printing Office, USA, 1985, vol. 85, pp. 511-551.
- Theyer, F., Mato, C. Y. and Hammond, S. R., Marine Micropaleontol., 1978, 3, 377-395.
- Johnson, D. A. and Nigrini, C., Marine Micropaleontol., 1985, 9, 489-523.
- Shackleton, N. J., Baldauf, J. G., Flores, J. A., Iwai, M., Moore, T. C. Jr., Raffi, I. and Vincent. E., in *Proc. Ocean Drilling Program., Sci. Results* (eds Pisias, N. G. et al.), College Station TX (Ocean Drilling Program), USA, 1995, vol. 138, pp. 517-536.
- Moore, T. C., Jr., in Proc. Ocean Drilling Program, Sci. Results (eds Pisias, N. G. et al.), College Station TX (Ocean Drilling Program), USA, 1995, vol. 138, pp. 191-232.
- Kling, S. A., in *Introduction to Marine Micropaleontology* (eds Haq, B. U. and Boersma, A.), Elsevier, New York, 1978, pp. 203-244.
- Pessagno, E. A. and Newport, R. L., Micropaleontology, 1972, 18, 231–234.
- 16. Berger, W. H., Science, 1968, 159, 1237-1239.
- Casey, R. E., in *Micropaleontology of Oceans* (eds Funnell, B. M. and Riedel, R. M.), Cambridge University Press, Cambridge, 1971, pp. 331-341.
- Petrushevskaya, M. G., in *Micropaleontology of Oceans* (eds Funnell, B. M. and Riedel, W. R.), Cambridge University Press, Cambridge, 1971, pp. 309-317.

- 19. Keany, J., Nature, 1973, 246, 139-141.
- 20. Molina-Cruz, A., Marine Micropaleontol., 1977, 2, 315-352.
- Johnson, D. A. and Nigrini, C., Marine Micropaleontol., 1980, 5, 111-152.
- Johnson, D. A. and Nigrini, C., Marine Micropaleontol., 1982, 7, 237-281.
- 23. Molina-Cruz, A., Marine Micropaleontol., 1984, 9, 53-75.
- Kruglikova, S. B., Paleogeogr. Paleoclimatol. Paleoecol., 1989, 69, 303-320.
- 25. Morley, J. J., Marine Micropaleontol., 1989, 13, 293-307.
- Moore, T. C. and Lombari, G., Marine Micropaleontol., 1981, 6, 581-597.
- 27 Kennett, J. P., Deep-Sea Res., 1970, 17, 125.
- 28. Keany, J. and Kennett, J. P., Deep-Sea Res., 1972, 19, 529.
- Casey, R. E., Palaeogeogr. Palaeoclimatol. Palaeoecol., 1972, 12, 115–130.
- 30. Keigwin, L. D., Jr., Micropaleontology, 1976, 22, 419-442.
- Mullineaux, L. S. and Westberg-Smith, M. J., Micropaleontol., 1986, 32, 48-71.
- 32. Savin, S., Annu. Rev. Earth Plant. Sci., 1977, 5, 319-355.
- 33. Woodruff, F., Savin, S. M. and Douglas, R. G., Science, 1981, 212, 665-668.
- 34. Ingle, J. C. Jr., Soc. Econ. Paleontol. Mineral., 1981, 159-180.
- 35. Barron, J. A. and Keller, G., Micropaleontology, 1983, 29, 150-181.
- Nigrini, C., in Proceedings of Ocean Drilling Program, Sci. Resustrs (eds Prell, W. J. et al.), College Station, TX (Ocean Drilling Program), USA, 1991, vol. 117, pp. 89-126.
- Romine, K. and Lombari, G., Geol. Soc. Am. Mem., 1985, 163, 273-290.
- Kennett, J. P., Keller, G. and Srinivasan, M. S., Geol. Soc. Am. Mem., 1985, 163, 197-236.

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Side effects of some medicinal plants

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Herbal drugs are playing an important role in health care programmes worldwide, especially in developing countries. This is primarily due to the general belief that herbal drugs are without any side effects besides being cheap and locally available. The article gives an account of 21 medicinal plant species which are being used, on large scale, for treatment of particular diseases, reported to be having serious side effects. Medicinal plants, before being allowed to be used as drugs, should also be tested for side effects, if any.

LATELY, there is a resurgence of interest in herbal medicines for treatment of various ailments chiefly because of prohibitive cost of allopathic drugs, unavail-

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ability in remote areas and also due to popular belief that herbal medicines are without any adverse side effects. Moreover, as is well known, the herbal medicine system has originated as a result of continuous trial and use of various plants/plant parts by people inhabiting areas rich in floral wealth and the information so generated has been passed from one generation to another through the word of mouth only.

This resurgence and popularity of herbal products have led to quantum jump in the number of herbal products swarming the market without any regard for their quality, efficacy and often new combination of plants are released in the market as a proclaimed remedy for a particular disease. Unfortunately, no accurate information about the rational use of these products is available. This puts the gullible at the risk of contracting more complications than remedy for a minor ailment. In the absence of any concerted effort to study atleast the toxicity of herbal products/plants, the traditional medicine fails to convince the potential user of its efficacy and adverse effects, if any vis-à-vis allopathic medicines which are backed by sound scientific research.

Knowledge regarding the adverse effects of herbs/ herbal drugs, if any, both short and long term is as important as their proclaimed medicinal uses. The claim that herbal medicines have no adverse side effects does not hold true, atleast in all cases, in view of the latest studies, which have shown that extracts of many medicinal plants used in various forms in different herbal preparations have adverse side effects in low as well as high doses.

In Table 1, 21 plants popularly used in the treatment of various diseases are listed and the toxic aspects of the vital component employed in curing the diseases are highlighted alongside.

The fact that herbal medicines contain ingredients to maintain health and to cure ailments is well known. However, the fact that they may contain toxic substances which are harmful or even dangerous to health is least

Table 1. Toxicity of certain medicinal and aromatic plants

Name	Constituents/part used ^{9,10,11}	Use ^{9,10,11}	Toxicity	Ref.
Tylophora asthamatica	Tylophorine, tylophorinine and pergularinine from leaves	Treatment of asthma, dysentery and useful in catarrh	A dose of 12-100 mg pure alkaloid suspended in peanut oil, given to male rats caused inactivity, respiratory distress, salivation, nasal discharge and diarrhoea LD ₅₀ -35.32 mg/kg	1
Prunus virginiana and Sambucus canadensis	i) Berries ii) Shoot, leaves, bark or roots	Used for the treatment of inflammation of both kidney and liver. Drug is very efficacious in dropsy	Ingestion of the official parts of these plants causes symptoms like corrosion of upper alimentary tracts, especially the stornach, inactivation of oxidative enzyme, formation of cyanohemoglobin, reflex stimulation of respiration etc. and death; absorbed orally	2
Allium sativum (Garlic)	Essential oil (diallyl disulphide)	Syrup of garlic is a valuable medicine for asthma, cough, difficulty in breathing, being of particular virtue in chronic bronchitis	Garlic oil feeding (10 mg/100 g body weight, intragastrically) to rats after 24 h fasting was found lethal. However, similar dose was well tolerated in fed state. A dose of 2 ml/100 g body weight, intragastrically causes rise in urea and D-asparatate aminotransferase and inhibition of alkaline phosphate in serum. Liver showed histological changes	3
Vinca rosea (Linn)	Vincristine, vinblastine	Used as chemotherapeutics in cancer and for treating diabetes	A continuous treatment of sexually mature male rats and rats in pubertal transition with vincristine at dose levels of 10 and 20 and 5 and 10 µg respectively per day caused gross morphological and gravimetric changes in the reproductive system. Treatment resulted in drastic regression of the entire male reproductive system, suggesting that vincristine would cause male reproductive toxicity.	4
Colchicum autumnale and Gloriosa superbu	Colchicine from seeds and tubers	Treatment of gout, rheumatism and in plant breeding work for polyploidization	Ingestion of bulbs and seeds caused severe abdominal pain, nausea, vomiting, profuse watery bloody diarrhea, hematuria, rapid and weak pulse, ascending paralysis of the central nervous system and death by respiratory paralysis.	2,5
Matricaria recutita L.	Coumarins (umbelliferone and its methyl ether) volatile oil (0.24-1.9%)	Used for flatulent nervous dyspepsia, travel sickness, nasal catarrh, nervous diarrhea, restlessness and specifically for gastro-intestinal disturbance with associated nervous irritability in children.	Allergic reactions to chamomile are common. Two reports of anaphylactic reaction have been documented. In both cases the symptoms were abdominal cramps, thickness of the tongue and a tight sensation in the throat, angioedema of the lips and eyes and upper air way obstruction. Oral and dermal LD_{50} (rabbits): > 5 g/kg; Oral LD_{50} (mouse): 2.5 ml/kg	6

Table 1. (Contd)

Name	Constituents/part used ^{9,10,11}	Use ^{9,10,11}	Toxicity	Ref.
Acorus calamus	Volatile oil, alkaloid- choline	Traditionally indicated for acute and chronic dyspepsia, gastritis and gastric ulcers, intestinal colic and anorexia	Feeding studies in rat using the Indian calamus oil (high-beta-asarene) have shown death, growth depression, hepatic and heart abnormalities and serious effusion in abdominal and/or peritoneal cavities. LD ₅₀ value of volatile oil: Rat (oral): 777 mg/kg, Rat (intraperitoneal): 221 mg/kg Guinea pig (dermal): > 5 g/kg	6
Cassia senna and C. angustifolia	Anthraquinones: dianthrone glycosides, primarily sennosides A and B with sennosides C and D	Used in constipation	Senna causes mild abdominal discomfort such as colic or cramps. Prolonged use results in diarrhea with excessive loss of K, atonic nonfunctioning colon may also develop. Excessive use and abuse causes finger clubbing and the development of cachexia and reduced serum globulin concentration. LD ₅₀ in mice (intravenous injections): Sennosides A and B: 4.1 g/kg Rhein-8-glycoside: 400 mg/kg	6
Rosmarinus officinalis	Flavonoids (diosmetin, diosmin); phenols (caffeic, chlorogenic); terpenoids (carnosol, oleanolic acid and ursolic acid)	Indicated for flatulent dys- pepsia, headache, sciatica, myalgia and inter-coastal neuralgia and its essential oil is used in perfumery.	Rosemary oil is moderately irritating when applied undiluted to rabbit skin. Bath preparations, cosmetics and toiletries containing rosemary oil may cause erythema and dermatitis in hypersensitive individuals LD ₅₀ value of Rosmarinic acid in mice: 561 mg/kg of body weight	6
Eucalyptus globulus	Volatile oil (0.5-3.5%) eucalyptol (70-80%)	Leaves and oil have been used as an antiseptic, febrifuge and expectorant	Undiluted eucalyptus oil is toxic and should not be taken undiluted internally. A dose of 3.5 ml has proved fatal. Symptoms of poisoning include epigastric burning, nausea, vomiting, dizziness, muscular weakness, a feeling of suffocation, cyanosis, delirium and convulsions.	6
Humulus lupulus	Flavonoids: astragalin, kaempferol, quercetin; volatile oil (0.3-1.0%)	Used for neuralgia, insomnia, excitability, priapism, mucous colitis, topically for crural ulcers and specifically for restlessness associated with nervous tension headache and/or indigestion and for flavoring beer	Respiratory allergy caused by handling of hop cones. A subsequent patch test using dried, crushed flowerheads proved negative. Positive patch test reaction have been documented for fresh hop oil, humulon and lupulon. Contact dermatitis to hops which is attributed to pollen has long been recognized.	6
Glycyrrhiza glabra	Coumarins: glycyrin, heniarin; flavonoid: flavonols; terpenoids: glycyrrhizin, glycoside; volatile oil (0.047%)	Effect the adrenal glands. Used for bronchial catarrh, bronchitis, chronic gastritis, peptic ulcers, colic and primarily adreno- cortical insufficiency	Excessive or prolonged ingestion has resulted in symptoms like hypertension, hypokalaemia and weight gain, but also in low levels of plasma renin activity, aldosterone and antidiuretic hormone. Consumption of liquorice 10-45 g/day causes raised blood pressure, together with a block of aldosterone/renin axis and electro-cardiogram changes.	6
Capsicum frutescens (Chilli)	Capsaicin	Commonly used Indian spice in cooking food, powerful local stimulant without narcotic effect, largely used as a condiment and most useful in atory of the intestine and stomach	Cheek pouch application of chilli extract in golden hamsters showed high mortality. Toxicity was observed in liver, cheek pouch, stomach and kidney of animals. Liver cirrhosis was observed in 49% of hamsters. Kidney showed degeneration of glomeruli and diarrhea was also observed in many hamsters. Pyperplasia was observed in all. No tumor was observed in anyone. But gross tumors were found in cheek pouch of hamster which were treated with DMN-OAC (N-acetoxy methyl-methyl nitrosamine) and chilli.	7

Table 1. (Contd)

Name	Constituents/part used ^{9,10,11}	Use ^{9,10,11}	Toxicity	Ref.
Digitalis purpurea and Nerium oleander	Cardiac glycosides	Digitalis is used in cases of heart, diseases. It increases the activity of all forms of muscle tissues, but more especially that of heart and arterioles. Causes high rise in blood pressure. It improves the nutrition of heart by increasing the amount of blood.	Ingestion of flowers, leaves or seeds causes symptoms such as vomiting, bradycardia, heart block, inverted T-wave with a prolonged PR interval and depressed ST segment of the ECG, coupled rhythm, abdominal pain, yellow or green vision with an inability to see the blue, depression, confusion memory defects and death by ventricular fibrillation.	2
Madhuca butyracea (Indian butter tree)	Saponins	Fat used as ointment in rheumatism, emollient for chapped hands, etc.	Acute doses of saponins caused mortalities in albino rats and LD_{50} and LD_{90} values were 330 and 430 mg/kg body weight respectively. Severe diarrhea, restlessness and histopathological changes were observed in liver and kidney.	8
Plantago major (Plantain)	Benzoic acid, caffeic acid and cinnamic acid	Used for cystitis with haematuria, and specifically for hemorrhoids with bleeding and irritation	Allergic contact dermatitis to <i>Plantago</i> has been reported. Green part of plant releases an irritant principle (isothiocyanate) upon enzymatic hydrolysis. Seed may cause sensitization and dermatitis. LD ₅₀ value in rat: Intraperitoneal injection: I g/kg By mouth: > 4 g/kg	6
Aconitum nepellus	Aconitine	Aconite used in ointment and sometimes given as hypodermic injection. Also used in cardiac failure. Applied locally to skin to diminish the pain of neuralgia, lumbago and rheumatism.	Symptoms of poisoning are tingling and numbness of tongue and mouth and a sensation of ants crawling over the body, nausea and vomiting with epigastric pain, laboured breathing, irregular and weak pulse, cold and clammy skin, bloodless and giddiness features.	5

known. The object of this review is not to minimize the role of plants in providing health care but to highlight the dangers inherent in some plant species. It is advisable to avoid them since the main objective of taking herbal medicines is to improve one's health and not to be harmed. Herbal medicines should also be subjected to extensive scientific and pharmacological screening before being recommended as drug.

- Stanley, Abraham, Averal, Horne Iona and Akbarsha, M. A., Indian J. Exp. Biol., 1993, 31, 380-382.
- Grieve, M., in A Modern Herbal (ed. Leyel, C. F.), Tiger Books International, London, 1992, p. 912.
- Newall, Carol A., Anderson Linda A and Phillipsen, David, J., in Herbal Medicines: A Guide for Health Care Professionals, The Pharmaceutical Press, London, 1996, p. 296.
- Agarwal, R. C. and Bhide, S. V., Indian J. Exp. Biol., 1988, 26, 377-382.
- Lalitha, T., Vishwanatha, S. and Venkataraman, L. V., *Indian J. Exp. Biol.*, 1990, 28, 642-647.
- Chopra, R. N., Nayar, S. L. and Chopra, I. C., in Glossary of Indian Medicinal Plants, CSIR, New Delhi, 1956, p. 330.
- Anonymous, in The Useful Plants of India, CSIR, New Delhi, 1986, p. 918.
- Anonymous, in The Wealth of India, CSIR, New Delhi, 1956, vol. I-XI.

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Dikshit, T. S. S., Raizada, R. B. and Mulchandani, N. B., Indian J. Exp. Biol., 1990, 28, 208-212.

Haley, Thomas J., in Handbook of Toxicology (eds Haley, Thomas J. and Berndt, William O.) Hemisphere Publishing Corporation, Washington, 1987, pp. 592-645.

Joseph, P. K., Rao, K. Ramesha and Sundaresh, C. S., Indian J. Exp. Biol., 1989, 27, 977-979.