JOURNAL OF CRITICAL REVIEWS

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

TOXICOLOGICAL PROPERTIES AND CHEMICAL PROFILING OF NATIVE PLANTS GEOGRAPHICALLY DISTRIBUTED IN AND AROUND THRISSUR DISTRICT, KERALA, INDIA.

Meena K Cheruvathur[1], Shafna Jose[2]

[1]Assistant Professor, Department of Botany, St. Mary's College, Thrissur 680 020, Kerala
[2]Assistant Professor, Department of Chemistry, St. Mary's College, Thrissur 680 020, Kerala.

E mail id: srsantra@gmail.com

Received: 14 March 2020 Revised and Accepted: 8 July 2020

I. INTRODUCTION:

Plants are living factories producing thousands of secondary metabolites. We have a general concept that plants and plant products are harmless. However, more than 700 plants produce physiologically active toxic substances, sufficient to cause harmful effects in human beings and animals. In some plants, one part may be edible while another is poisonous. Lack of toxicological evaluation of natural products leads to the false concept that natural products are safe. Even herbal food ingredients may contain some Phyto-constituents known to produce genotoxic or carcinogenic components after prolonged dose depended exposure. Poisonous plants produce several toxic substances at various concentrations at different organs and cause responses ranging from mild nausea to mortality. Certain animal species may have a specific vulnerability to a potentially poisonous plant. Plant toxins belong to different categories. The reviewed plants are classified into nine based on the significant category of poisons:

1. Plants with Anticholinergic (Antimuscarinic) Poisons:

Neurotransmitter acetylcholine transmits impulses between nerves in the brain and neuromuscular junctions. Tropane alkaloids present in plants resembles acetylcholine and hence competitively inhibit acetylcholine receptors producing the anticholinergic syndrome. Their reaction may affect the heart rate, respiration and functions of the central nervous system. (Diaz, 2015). Tropane alkaloids are observed in about 25 genera and 2000 species of plants. Most are from the family Solanaceae (Brinjal Family) ((Chowański *et al*., 2016; Yamashoji and Matsuda, 2013). Frequently observed plants coming under this group are *Datura stramonium, Datura metal, Datura wrightii* and *Brugmansia.* Potatoes after exposure to sunlight develop green coloure and show the presence of toxin Alpha-solanine belongs to this group (Lee, 2006). Scopolamines present in these plants rapidly penetrate the central nervous system and cause hallucinations at lower doses followed by paralysis and death due to respiratory failures at higher levels (Cornelius *et al.*, 2019; Koleva *et al*., 2012).

2. Calcium Oxalate Crystals:

The standard type of harmful calcium oxalate crystals belongs to Raphides. They are elongated needle-like crystals present within a specialised bag like cell called idioblast. In some plants, it will be filled with irritating mucilage. Upon mechanical stimulation like chewing; crystalline calcium oxalate needles release from idioblasts, move in a projectile fashion, penetrate the mucous membranes and induce the release of histamine and other inflammatory mediators (Konyar *et al*., 2014). Many of the garden plants belong to the Aroideae group possess Calcium oxalate crystals. Examples are Alocasia, *Arisaema, Caladium, Caryota, Colocasia, Dieffenbachia, Epipremnum, Monstera, Anthurium, Philodendron, Spathiphyllum etc.* Among these, most of them contain crystals in all parts of the body. These plants are highly useful as air purifiers and hence widely used as indoor plants. Intake can result in acute irritation and swelling in the mouth, throat and Gastrointestinal tract. Children, as well as pets such as cats and dogs, may nibble on the toxic foliage, are all at risk. General symptoms of poisoning are blistering, difficulty in swallowing and hoarseness. In the case of the eye, it produces extreme pain, keratoconjunctival injection, and in severe cases, ocular damage and vision loss also can be occurred. Extensive dermal contact may produce pain, signs of irritation and swellings (Coté, 2009; Franceschi and Nakata, 2005; Arditti and Rodriguez, 1982).

3. Cardio active Steroids/Cardiac Glycosides:

Cardioactive steroids attached with sugar moieties are termed cardiac glycosides. They inhibit the cellular Na^+/K^+-ATPase pump, which leads to the indirect increase of intracellular $Ca2^{++}$ concentrations in specific cells, like myocardial cells. Poisoning by these agents causes bradycardia and heart block.
Plants coming under this category are: Cerbera odollam: This plant belongs to family Apocynaceae. It is often called Suicide tree because of its elevated cardiotoxic effects which make people opt this plant to attempt suicide (Menezes et al., 2018). The Kernal of the fruit is rich in cerberin, a digitoxin type cardenolide and cardiac glycoside that reversibly block the Calcium channel in myocardial cells resulting from the disruption in cardiac electrical activity that leads to death and is responsible for about 50% of plant poisoning in Kerala, India (Misek *et al.*, 2018; Fok *et al.*, 2018; Tsai *et al.*, 2008; Krishnamoorthy, 2004).

Oleander-The toxic components are the two potent cardiac glycosides, oleanderin and neriine which are isolated from all the organs of the plant body and are very similar to the toxin of the Foxglove plant (Khanet al., 2010).

b). *Cryptostegia Grandiflora, Cryptostegia madagascariensis*

Toxic organs: All parts of these plants are poisonous. Toxin present is Cardioactive steroids resembling digitalis. Substantial ingestion leads to toxicity. Poisoning would be expected to produce clinical findings typical of cardioactive steroid poisoning (Prasad, 2013).

c). *Adenium species*
Toxin: Cardioactive glycosides resembling digitalis (Hossain, 2018). Toxicity depends on the quantity ingested.

d). *Parthenium hysterophorus:***:** It contains a bitter glycoside parthenin, a significant sesquiterpene lactone. Prolonged exposure results in skin inflammation, eczema, asthma, allergic rhinitis, hay fever, black spots, burning and blisters around eyes (Khaket et al., 2015).

e). *Calotropis species.*
The latex of this plant has a direct irritant action on mucous membranes. All parts of this plant contain unidentified vesicant allergen in the latex, calcium oxalate crystals and cardioactive steroids resembling digitalis (Basak t al., 2009).

4. Cyanogenic Compounds:

Cyanogenic glycosides are present in several edible plants and in their seeds. Hydrogen cyanide liberated from the cyanogenic glycosides when fresh plant material is macerated as in chewing. Cyanide is one of the most powerful, rapidly acting, poisons. They inhibit the final step of the mitochondrial electron transport chain and block oxidative processes of cells, causing rapid failure in cellular energy level. This results from the death of the cells. An adult human can withstand 50-60 ppm for an hour without severe consequences. But exposure to concentrations of 200-500 ppm for 30 minutes is usually fatal. E.g., Hydrangea Sp., cassava, bamboo shoots, seeds of apple and pear shows the presence of this toxin (Bolarinwa *et al*., 2016).

a). Cassava (*Manihot esculenta):* Cassava classified into two main types: bitter cassava and sweet cassava. Less than 50 mg/K.G. hydrogen cyanide on fresh weight is present in the storage roots of Sweet cassava. Bitter type may contain up to 400 mg per kilogram. In mild poisoning, abdominal pain, vomiting, lethargy, and sweating will occur. In severe poisonings, coma develops and may be accompanied by convulsions and cardiovascular collapse. Hydrogen cyanide will leach out during thorough washing with water and boiling (Bolarinwa *et al*., 2016; Poulton, 1990; Conn, 1978.

Bamboo shoots are another popular food item containing hydrogen cyanide. The cyanogenic glycoside present in the bamboo shoot will decompose while boiling. Other edible plants containing cyanogenic glycosides include kernels within the pits of some stone fruits (e.g. bitter apricot kernels, seeds of apple), lima beans, etc. (Chaouali *et al*., 2013; Tuncel et al., 2006).
Clinical symptoms of cyanide poisoning are rapid respiration rate and enhanced pulse rate, drop in blood pressure, rapid respiration and pulse, dizziness, vomiting, diarrhoea, headache, mental confusion, twitching and convulsions and blue colouration of the skin due to lack of oxygen (cyanosis) Cyanide can be fatal to human beings, and the acute dose is 1 mg/kg body weight of the organism. Misuse, particularly of preparations from cyanide rich apple seeds results from cases of acute poisoning. In the presence of sulphur-containing amino acids, cyanide is detoxified in the body, by the enzyme rhodanese, to produce thiocyanate. The thiocyanate,

which is the detoxification product of cyanide has the same size as the iodine molecule, and competitively interferes with iodine uptake by the thyroid, effectively increasing the dietary requirement for iodine. Hence goitre and cretinism due to iodine deficiency can be exacerbated by chronic consumption of insufficiently processed cassava. The effect is only seen in iodine-deficient population and can be reversed by iodine supplementation (Tuncel *et al*., 2006)

5. Gastrointestinal Toxins:

These pharmacologically active agents most commonly work by stimulation of cholinergic receptors in the gastrointestinal tract to induce smooth muscle contraction.

a). *Allamanda cathartica,* which is a garden hedge plant, is coming under this category. Bark, leaves, fruit, seeds, and sap of this plant contain a weak gastrointestinal irritant Plumericin (Bonomini *et al*., 2017).

b). *Thevetia peruviana:*

It is extremely poisonous. Usually causes digestive upset and mental confusion. Even the ingestion of one leaf or flower can be fatal to a child. The plant possesses potentially dangerous cardiac glycosides such as thevetins A and B, thevetoxin, nerifolin, peroxide and ruvoside which produce both gastric and cardiotoxic effects, results in death (Kishan *et al*., 2012; Elena *et al*., 2002).

c). *Euphorbia species*

The latex of some species of Euphorbia are poisonous. Toxins differ based on species but include complex diterpene esters (e.g., phorbol esters) and mitogenic lectins. Ingestion may produce gastrointestinal symptoms. Skin exposure may produce an irritant Dermatitis (Goel *et al*., 2007). Ocular exposure may produce irritant keratoconjunctivitis depending on the species of *Euphorbia.*

6. Poisonous alkaloids:

Alkaloids are metabolic by-products derived from amino acids and nitrogenous compounds. They are the largest group of secondary metabolites. More than 20,000 diverse molecules of alkaloids are distributed among 20% of vascular plant families (Yang and Stockigt, 2010). Depending on the position of the nitrogen ring, they show changes in properties. The toxic effects of alkaloids depend upon the specific dosage, the sensitivity of the organism, exposure time, site of action and developmental stages (Kamarul Zaman and Mohamad Azzeme, 2018; Matsuura and Fett-Neto, 2015).

They are:

a). Poisoning by Plants with Mitotic Inhibitor alkaloids:

They inhibit mitosis by interfering with the polymerisation of microtubules. This results in metaphase arrest. Actively dividing cells like bone marrow cells and gastrointestinal cells affected earlier than those slow dividing cells. Direct cellular toxic effects and even death may occur on the dose.

a).*Gloriosa superb*

The whole plant, particularly the tubers containing a potent toxin Colchicine which is capable of inhibiting microtubule formation. Intake may cause initial oropharyngeal pain followed by peripheral neuropathy, bone marrow suppression, cardiovascular collapse and death.(Mendis, 1989).

b). *Catharanthus roseus*: The whole plant is mildly poisonous. It contains Vinca alkaloids (e.g., vincristine), clinically similar to colchicine, a cytotoxic alkaloid capable of inhibiting microtubule formation. It is used in Chemotherapy. Its toxicity is dose-dependent(Ngan *et al*., 2001).

c). Poisoning by Plants with Pyrrolizidine Alkaloids:

Pyrroles produced as a metabolic by-product of pyrrolizidine alkaloids are alkylating agents that injure the endothelium of the liver and lungs. High-dose exposures result from an overproduction of the pyrrole lead to hepatic carcinoma. The pyrrole functions as reactive alkylating intermediates and results in DNA alkylation, DNA cross-linking, liver cell necrosis, genotoxicity, leading to tumours (Cushnie *et al*., 2014; Norton, 2001; Huan *et al.,* 1998; Huan *et al*., 1998; Carballo *et al*., 1992). In humans, it affects principally on the liver by

producing veno-occlusive disease in hepatic veins and causes damages in the liver (WHO, 1988; Huan *et al*., 1998). They are present in plants of the families of Boraginaceae (all genera) (Carballo *et al.*, 1992), Senecionae and Eupatoriae of Asteraceae, and genus *Crotalaria* of Fabaceae and known to hazardous towards livestock (WHO, 1988).

7. Poisoning by Plants with Convulsant Poisons (Seizure):

The toxin of these plants leads to severe convulsions. Mechanisms that result in seizures including antagonism of gamma-aminobutyric acid (GABA) at its receptor on the neuronal chloride channel, imbalance of acetylcholine homeostasis, excitatory amino acid mimicry, sodium channel alteration, or hypoglycemia. Toxicity is fatal.

Duranta repens-a common hedge plant in gardens includes in this group. The fruit is poisonous. It contains a poisonous saponin. Poisoning is reputed to cause increased body temperature, tachycardia, oedema of lips, Gastrointestinal irritation and convulsions.

Strychnine obtained from Strichnos nux-vomica is a tetanic poison, and its analogues antagonise the postsynaptic inhibiting activity of glycine at the spinal cord motor neuron. Strychnine results in hyper excitability of the motor neurons, which manifests as a convulsion (Croteau and Kutchan, 2000).

8. Poisoning by Plants with lysergic acid Alkaloids:

Psychoactive alkaloids, such as ergine and psilocybin, contain the indole structure and a double carbon-nitrogen ring. It is similar to the natural neurotransmitter serotonin. So they ay interfere or compete with the action of serotonin in the brain, causing psychedelic visions, delusions and hallucinations.

Psychoactive alkaloids, such as ergine and psilocybin, contain the indole structure and double carbon-nitrogen ring serotonin, which is a natural neurotransmitter. These alkaloids may interfere or compete with serotonin in the brain, causing psychedelic visions, delusions and hallucinations. Synthetic LSD has two additional ethyl groups (C_2H_5) and is about 100 times more potent. Before it was discovered in morning glories, the First report of ergine was from ergot which is obtained from Claviceps purpurea, a rust fungus that infects grains.

Family Convolvulaceae includes at least 50 genera and more than 1000 species, of high-climbing vines and woody lianas of prostrate and trailing perennials that decorate our fences, trellises and walls with lush green foliage and colourful funnel-shaped blossoms. Some climbers of this family provide us with economically important, nutritious root crops like sweet potatoes and morning glory (Beyer, 2013).

9. Poisoning by Plants with Nicotine-Like Alkaloids

These agents are direct-acting agonists at the nicotinic subtype of the acetylcholine acceptor in the ganglia of both the parasympathetic and sympathetic limbs of the autonomic nervous system (N.N. receptors), the neuromuscular junction (N.M. receptors) and the brain. Examples of plant genera associated with this syndrome *are Laburnum, Lobelia, Nicotiana, Sophora* (Schep et al., 2009).

10.Poisoning by Plants with Toxalbumins:

The toxin is contained within the rigid, water-impermeable coat of the seeds. The toxin will be released if the seed is chewed and digested or the seed coat is broken by mechanical stress. Abrin is a plant lectin (toxalbumin) present within the seeds of *Abrus precatorius* related to ricin, inhibits cellular protein synthesis and may be extremely toxic. The protein toxins derived from these plants work specifically by inhibiting the function of ribosomes, the subcellular organelle responsible for protein synthesis. The toxins typically have two linked polypeptide chains. Absorption of toxin into the circulatory system allows widespread distribution and multisystem organ failure may lead to death.

Examples of plant genera associated with this syndrome: *Abrus, Jatropha and Ricinus.*

Castor oil is procured from seeds of *Ricinus communis* which is a weed along the railway tracks and roadsides of Kerala. It does not contain any toxins. Nevertheless, if the seeds must be chewed or broken open, it activates the toxicity. Unopened seeds can pass with no harm to the animal. If the animal is observed eating the seeds like castor and Abrus, they are harmless when ingested as a whole, since the hard outer shell resists digestion. However, any type of breaking of the seed before swallowing will enable the toxins to be released. Bean causes stomach irritation, pain, diarrhoea, increased heart rate, collapse, convulsions and death. Commercially prepared castor oil does not contain any toxins. The seeds must be chewed or broken open to activate the toxicity.

III. CONCLUSION

Presence of poison is a survival mechanism to discourage herbivory. Different plants contain different types of chemical compounds, and these occur at varying levels depending on a range of variables including the time of the year, the growth stages of the plant, the parts are eaten and the humidity. One by a tenth of poisoning among small children below age six is due to intake of poisonous plants. So we should have a general idea about the toxicity of the plants grown in our premises. Moreover, the presence of a poison means the presence of a potential physiologically active secondary metabolite. We can explore new nano drugs from these plants in a dose-dependent manner.

Acknowledgement

We would like to thank Principal and management of St. Mary's College Thrissur, Kerala for providing the infrastructure for the study. We acknowledge DST-FIST for partially funding the research lab.

IV. REFERENCES

[1] Arditti, J., Rodriguez, E., 1982. Dieffenbachia: Uses, abuses and toxic constituents: A review. J. Ethnopharmacol. 5, 293–302. https://doi.org/10.1016/0378-8741(82)90015-0

[2] Basak, S.K., Bhaumik, A., Mohanta, A., Singhal, P., 2009. Ocular toxicity by latex of Calotropis procera (Sodom apple). Indian J. Ophthalmol. 57, 232–234. https://doi.org/10.4103/0301-4738.49402

[3] Beyer, J., 2013. Herbal Psychoactive Substances, in: Siegel, J.A., Saukko, P.J., Houck, M.M.B.T.-E. of F.S. (Second E. (Eds.), . Academic Press, Waltham, pp. 275–279. https://doi.org/https://doi.org/10.1016/B978-0-12-382165-2.00317-2

[4] Bolarinwa, I.F., Oke, M.O., Olaniyan, S.A., Ajala, A.S., 2016. A Review of Cyanogenic Glycosides in Edible Plants. Toxicol. - New Asp. to This Sci. Conundrum. https://doi.org/10.5772/64886

[5] Bonomini, T.J., Holzmann, I., Thiesen, L.C., Fratoni, E., Muller, A.F.F., Lucinda-Silva, R.M., Yunes, R.A., Malheiros, A., Gonçalves, A.E., Dalmagro, A.P., da Silva, K.A.B.S., de Souza, M.M., Santin, J.R., 2017. Neuropharmacological and acute toxicological evaluation of ethanolic extract of Allamanda cathartica L. flowers and plumieride. Regul. Toxicol. Pharmacol. 91, 9–19. https://doi.org/10.1016/j.yrtph.2017.10.005

[6] Carballo, M., Mudry, M. D., Larripa, I. B., Villamil, E., D'Aquino, M., 1992. Genotoxic action of an aqueous extract of heliotropium curassavicum var argentinum. Mutat. Res. 279, 245 –253.

[7] Carballo, M., Mudry, M.D., Larripa, I.B., Villamil, E., D'Aquino, M., 1992. Genotoxic action of an aqueous extract of Heliotropium curassavicum var. argentinum. Mutat. Res. Toxicol. 279, 245–253. https://doi.org/10.1016/0165-1218(92)90240-Z

[8] Chaouali, N., Gana, I., Dorra, A., Khelifi, F., Nouioui, A., Masri, W., Belwaer, I., Ghorbel, H., Hedhili, A., 2013. Potential Toxic Levels of Cyanide in Almonds (Prunus amygdalus), Apricot Kernels (Prunus armeniaca), and Almond Syrup . ISRN Toxicol. 2013, 1–6. https://doi.org/10.1155/2013/610648

[9] Chowański, S., Adamski, Z., Marciniak, P., Rosiński, G., Büyükgüzel, E., Büyükgüzel, K., Falabella, P., Scrano, L., Ventrella, E., Lelario, F., Bufo, S.A., 2016. A review of bioinsecticidal activity of Solanaceae alkaloids. Toxins (Basel). 8, 1–28. https://doi.org/10.3390/toxins8030060

[10] Conn, E.E., 1978. Cyanogenesis, the Production of Hydrogen Cyanide, By Plants, Effects of Poisonous Plants on Livestock. ACADEMIC PRESS, INC. https://doi.org/10.1016/b978-0-12-403250-7.50035-2

[11] Cornelius, G., Lohiya, G., Sharma, R., 2019. Chemical Constituents and Pharmacological Properties of Datura Stramonium (Thorn Apple) - A Review. Int. J. Eng. Res. Technol. 8, 512–515.

[12] Coté, G.G., 2009. Diversity and distribution of idioblasts producing calcium oxalate crystals in Dieffenbachia seguine (Araceae). Am. J. Bot. 96, 1245–1254. https://doi.org/10.3732/ajb.0800276

[13] Croteau R, Kutchan TM, L.N., 2000. Natural products (secondary metabolites), in: Buchanan B, Gruissem W, J.R. (Ed.), Biochemistry and Molecular Biology of Plants. pp. 1–15.

[14] Cushnie, T.P.T., Cushnie, B., Lamb, A.J., 2014. Alkaloids: An overview of their antibacterial, antibiotic-enhancing and antivirulence activities. Int. J. Antimicrob. Agents 44, 377–386. https://doi.org/10.1016/j.ijantimicag.2014.06.001

[15] Diaz, G.J., 2015. Toxicosis by plant alkaloids in humans and animals in Colombia. Toxins (Basel). 7, 5408–5416. https://doi.org/10.3390/toxins7124892

[16] Elena, M., Enriquez, M., Antonio, L., Ruiz, M., Rosas, M.L., Alfonso, G.I.L., Guerrero, M., Contreras, A.A., Efrain, A., Sepulveda, C., 2002. Acute toxicity of Thevetia peruviana in rodents Acute Toxicity of Thevetia peruviana in Rodents.

[17] Fok H, Victor P, Bradberry S, E.M., 2018. Novel methods of self-poisoning: repeated cardenolide poisoning after accessing Cerbera odollam seeds via the internet. Clin Toxicol (Phila). 36, 304–306. https://doi.org/doi:10.1080/15563650.2017.1369543

[18] Franceschi, V.R., Nakata, P.A., 2005. CALCIUM OXALATE IN PLANTS: Formation and Function. Annu. Rev. Plant Biol. 56, 41–71. https://doi.org/10.1146/annurev.arplant.56.032604.144106
[19] Gaillard Y, Krishnamoorthy A, B.F., 2004. Cerbera odollam: a "suicide tree" and cause of death in the state of Kerala, India. J Ethnopharmacol 95, 123–126. https://doi.org/DOI: 10.1016/j.jep.2004.08.004
[20] Goel, G., Makkar, H.P.S., Francis, G., Becker, K., 2007. Phorbol esters: Structure, biological activity, and toxicity in animals. Int. J. Toxicol. 26, 279–288. https://doi.org/10.1080/10915810701464641
[21] Hossain, M.A., 2018. A review on Adenium obesum: A potential endemic medicinal plant in Oman. Beni-Suef Univ. J. Basic Appl. Sci. 7, 559–563. https://doi.org/10.1016/j.bjbas.2018.06.008
[22] Huan, J.-Y., Miranda, C. L., Buhler, D. R., Cheeke, P.R., 1998. Species differences in the hepatic microsomal enzyme metabolism of the pyrrolizidine alkaloids. Toxicol. Lett. 99, 127–137.
[23] Kamarul Zaman, M.A., Mohamad Azzeme, A., 2018. Plant toxins: alkaloids and their toxicities. GSC Biol. Pharm. Sci. 6, 021–029. https://doi.org/10.30574/gscbps.2019.6.2.0003
[24] Khaket, T.P., Aggarwal, H., Jodha, D., Dhanda, S., Singh, J., 2015. Parthenium hysterophorus in current scenario: A toxic weed with industrial, agricultural and medicinal applications. J. Plant Sci. 10, 42–53. https://doi.org/10.3923/jps.2015.42.53
[25] Khan, I., Kant, C., Sanwaria, A., Meena, L., 2010. Acute cardiac toxicity of Nerium oleander/indicum poisoning (Kaner) poisoning. Hear. Views 11, 115. https://doi.org/10.4103/1995-705x.76803
[26] Kishan, S., Kumar, A.K., Vimlesh, M., Mubeen, U.S., Alok, S., 2012. ISSN 2230 – 8407 A REVIEW ON : THEVETIA PERUVIANA 3, 74–77.
[27] Koleva, I.I., van Beek, T.A., Soffers, A.E.M.F., Dusemund, B., Rietjens, I.M.C.M., 2012. Alkaloids in the human food chain - natural occurrence and possible adverse effects. Mol. Nutr. Food Res. 56, 30–52. https://doi.org/10.1002/mnfr.201100165
[28] Konyar, S.T., Öztürk, N., Dane, F., 2014. Occurrence, types and distribution of calcium oxalate crystals in leaves and stems of some species of poisonous plants. Bot. Stud. 55, 1–9. https://doi.org/10.1186/1999-3110-55-32
[29] Lee, M.., 2006. The Solanaceae: foods and poisons. J R Coll Physicians Edinb. 36, 162-169.
[30] Matsuura, H., Fett-Neto, A., 2015. Plant Alkaloids: Main Features, Toxicity, and Mechanisms of Action. pp. 1–15. https://doi.org/10.1007/978-94-007-6728-7_2-1
[31] Mendis, S., 1989. Colchicine cardiotoxicity following ingestion of Gloriosa superba tubers. Postgrad. Med. J. 65, 752–755. https://doi.org/10.1136/pgmj.65.768.752
[32] Menezes, R.G., Usman, M.S., Hussain, S.A., Madadin, M., Siddiqi, T.J., Fatima, H., Ram, P., Pasha, S.B., Senthilkumaran, S., Fatima, T.Q., Luis, S.A., 2018. Cerbera odollam toxicity: A review. J. Forensic Leg. Med. 58, 113–116. https://doi.org/10.1016/j.jflm.2018.05.007
[33] Misek, R., Allen, G., LeComte, V., Mazur, N., 2018. Fatality Following Intentional Ingestion of Cerbera odollam Seeds. Clin. Pract. Cases Emerg. Med. 2, 223–226. https://doi.org/10.5811/cpcem.2018.5.38345
[34] Ngan, V.K., Bellman, K., Hill, B.T., Wilson, L., Jordan, M.A., 2001. Mechanism of Mitotic Block and Inhibition of Cell Proliferation by the Semisynthetic Vinca Alkaloids Vinorelbine and Its Newer Derivative Vinflunine. Mol. Pharmacol. 60, 225 LP – 232. https://doi.org/10.1124/mol.60.1.225
[35] Poulton, J.E., 1990. Cyanogenesis in plants. Plant Physiol. 94, 401–405. https://doi.org/10.1104/pp.94.2.401
[36] Prasad, H.B., 2013. Poisoning Due to Cryptostegia Grandiflora (Indian 1964, 4–5.
[37] Schep, L., Slaughter, R., Beasley, D.M., 2009. Nicotinic plant poisoning. Clin. Toxicol. (Phila). 47, 771–781. https://doi.org/10.1080/15563650903252186
[38] Tsai, Y.C., Chen, C.Y., Yang, N.I., Yang, C.C., 2008. Cardiac glycoside poisoning following suicidal ingestion of Cerbera manghas. Clin. Toxicol. 46, 340–341. https://doi.org/10.1080/15563650701291766
[39] Tuncel, G; Nout , M; Brimer, L.; Goktan, D., 2006. Cyanogenic glycosides - Information Sheet. Int. J. Food Microbiol.
[40] WHO, I., 1988. ISBN 92 4 154280 2, The United Nations Environment Programme and the World Health OrganizationINTERNATIONAL PROGRAMME ON CHEMICAL SAFETY Pyrrolizidine alkaloids.
[41] Yamashoji, S., Matsuda, T., 2013. Synergistic cytotoxicity induced by α-solanine and α-chaconine. Food Chem. 141, 669–674. https://doi.org/10.1016/j.foodchem.2013.03.104
[42] Yang L, S.J., 2010. Trends for diverse production strategies of plant medicinal alkaloids. Nat Prod Rep 27, 1469–1479. https://doi.org/doi:10.1039/c005378c