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Research Article

A REVIEW ON POISONOUS BUT BENEFICIAL PLANT – JAYAPALA (*Croton tiglium*)

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ABSTRACT

Plants and their extract have the potential to cure the infirmity of mankind. From ancient times herbal plants are used for treatment. *Croton tiglium* Linn belongs to the family of Euphorbiaceae is widely distributed throughout the plain of India. Jayapala (*Croton tiglium*) is one among the upa vishas and a well-known plant in Indian system of medicine as certain number of formulations includes this drug as an ingredient after proper purification. The word Upavisha means nearer to visha i.e. drugs which possess the same qualities of visha, but not that much potent. Also it is one of the known purgative drugs in Ayurveda with huge therapeutic values. This review article includes overall information about the plant *Croton tiglium*, its botanical description, toxicological aspect, treatment in both Ayurveda and Modern toxicology, its shodhana (purification) processes, FT- IR, GC-MS for component identification.

INTRODUCTION

Plants are the prime source of medicine in Ayurveda. Several compounds have been isolated from medicinal plants and introduced for the service of mankind; however most of these medicines have been withdrawn due to their toxicity or side-effects. Traditionally, plants having various classes of phytochemicals are still in use either in their crude form or after proper processing. Though most of the plant drugs are safe, yet few are toxic for human health. These poisonous/toxic plants are categorized as *viṣa* (poison) and *upaviṣa* (toxic but not lethal for human health) in Ayurvedic texts (table 1) and also listed in the schedule-E of Drugs and Cosmetics Act 1940 (table 2). Jayapala (*Croton tiglium*) is one among the upavishas and a well-known plant in Indian System of Medicine

Table 1 List of plants having Visa properties

Visa	Binomial nomenclature	Family
Vatsanabha	Aconitum ferox wall	Ranunculaceae
Mustaka	Aconitum chasmanthum stapfex Holmes	Ranunculaceae
Srngivisa		
Kalakuta		
Saktuka		

Table 2 List of plants having Upavisa properties.

Upavisa	Binomial nomenclature	Family
Arka	Calotropis procera	Asclepiadaceae
Snuhi	Euphorbia neriifolia Linn.	Euphorbiaceae
Langali	Gloriosa superb Linn.	Liliaceae
Karavira	Nerium indicum mill.	Apocynaceae
Gunja	Abrus precatorius Linn.	Fabaceae
Ahiphena	Papaver somniferum Linn.	Papaveraceae
Dhattura	Datura metal Linn.	Solanaceae

Table 3 Ayurvedic poisonous plant listed in the schedule E of D&C Act 1940

Poisonous Plants	Binomial nomenclature
Aphipena	Papaver somniferum
Arka	Calotropis procera
Bhallataka	Semecarpus anacardium
Bhanga	Cannabia eativa Linn.
Danti	Baliospermum monatanum Mull.Arg
Dhattura	Datura metal Linn.
Gunja	Abrus precatirius Linn.
Jayapala	Croton tiglium
Karavira	Nerium indicum
Langali	Gloriosa superba
Parasika yavani	Hyoscyamus nibar Linn.
Snuhi	Euphorbia neriifolia Linn.
Vatsanabha	Aconitum chasmanthum
Visamusti	Strychnos nux-vomica

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Hence, to promote and introduce their use for medicine, such plant drugs must be detoxified or purified before their use. The detoxification or purification process of any toxic material used for medicinal purposes is termed as "*Śodhana*". The concept of *Śodhana* in Ayurveda not only covers the process of purification/detoxifcation of physical as well as chemical impurities but also covers the minimization of side effects and improving the potency/therapeutic efficacy of the purified [1,2].

Importance of Purification of Poison

The poisonous plants reported in ancient scriptures of Ayurveda are still being used widely in a number of diseases after processing with proper shodhana. Ayurvedic physicians successfully employed these drugs after proper shodhana. The concept of shodhana was mentioned for the first time in Charaka Samhita in the context of Danti Dravanti Kalpadhyaya. To reduce the 'Vikasi' property of *Danti* root, Charaka mentioned it as 'Samaskara'. Acharya Vagbhata also mentioned shodhana of drugs of plant origin in detail, in the context of Bhallataka Rasayana for 'Bhallataka' (*Semicarpus anacardium*). It is reported that aconite (Vatsanabha) purified by cow urine is converted to cardiac stimulant, whereas raw aconite is cardiac depressant. It is clearly mentioned in 'Bhava Prakasha' that the bad/toxic effects attributed to 'Ashodhita Vishas' (unpurified poisonous substances) are minimized when these are used after being subjected to shodhana . Hence 'Vishas' should be essentially subjected for shodhana before being used in therapeutics.

***Croton tiglium*[3]**

Croton tiglium, known as purging croton or jayapala. The upavisha Jayapala which belong to Euphorbiaceae family commonly known as *Croton tiglium* is one of the known purgative drugs in ayurveda with huge therapeutic values. In Ayurveda upavishas are those groups of drugs whose toxicity is less in nature and which are not so lethal but produce certain toxic symptoms on consumption or administration which can be controlled by the therapeutic measures.

Figure 1 Flower stalk of *Croton tiglium*

Taxnonomy

Kingdom - Plantae
Clade - angiosperm
Order - malpighiales
Family - Euphorbiaceae
Genus - Croton
Species - *C. tiglium*

Figure 2 Seeds of ***Croton tiglium***

Table 4 Vernacular names of *Croton tiglium*

Language	Names
English	Croton
Hindi	Jamalgota
Malayalam	Neervalam
Tamil	Neervalam
Kannada	Japala
Telugu	Nepalamu
Sinhala	Jayapala
Nepal	Japalbeej

Figure 3 Inner section of *Croton tiglium seeds*

Distribution

Croton plant grows all over India, especially in the waste lands of North India, grown in many varieties for their brightly coloured foliage.

Morphology

The plant is a small evergreen tree of almost 4.5-6m in height with ash coloured smooth bark and young shoots sprinkled with stellate hairs. Leaves are oblong to ovate- lanceolate, obtuse or rounded at the two glanded base, acuminate membraneous, yellowish green in colour and minutly toothed. Flowers are small, unisexual, males on slender pedicels, females larger on short thick pedicels. Fruits are ovoid or oblong, 3 gonous capsules, seeds are smooth, testa is black, enclosing reddish brown oily endosperm.

Parts Used

The plant parts used for medicinal purpose are seeds and seed oil.

Pharmacognostical Characterstics

Macroscopic

Seeds are albuminous, ovate, oblong, slightly quadrangular, convex on dorsal and flattened on ventral surface, about 12mm in length and resemble castor seed in shape, dull cinnamon brown, often mottled with black due to abrasion in testa, caruncle easily detached and usually absent, hilum on ventral side less distinct than that of castor seed, its raphe runs along ventral surface of seed terminating in a dark chalaza at opposite extremity, kernel is yellowish and oily, consisting of a large endosperm, enclosing papery cotyledons and a small radicle, it has no marked odour. Kernel gives at first oily taste followed by an unpleasant acridity taste.

Microscopic

Seeds show three parts namely, hard testa, epidermis and endosperm. Hard testa consist of an epidermal layer, covered externally with a thick cuticle and composed of oval and tangentially elongated cells, it is filled with a brownish content. Epidermis is a layer of radially elongated cells, slightly bend at middle, its upper half portion filled with reddish brown contents and lower half filled with yellow contents, inner most zone consist of tangentially elongated, thin walled cells. Endosperm consists of polygonal parenchymatous cells filled with oil globules, a few cells having rosette crystals of calcium oxalate central region of endosperm shows a dicotyledonous embryo consisting of thin walled parenchymatous cells.

Phytochemical Properties

Seed and oil extracted from the seed is extremely toxic. Seed oil is commented to have tumour promoting phorbol diesters. Active principles of *Croton tiglium* are crotin (toxalbumin), crotonoside (glycoside) and oil. Oil contains powerful vesicating resin composed of crotonoleic acid, methyl crotonic acid, and several other fatty acids[4].

Pharmacological Properties

The seeds and oil of jayapala with acrid, bitter taste has thermogenic, emollient, drastic purgative, digestive carminative, anthelminthic, antiinflamatory, vermifuge, detergent, diaphoretic, expectorant, vesicant irritant and rubifacient. They are also useful in abdominal disorders, convulsions, ophthalmia, cough, catarrh. It has various activities like molluscidal activity, **t**umor- enhancing activity, larvicidal activity, gastrointestinal activity, anticonvulsant activity, antimicrobial activity, antidermatophytic activity and antioxidant activity[5].

Traditional Uses

It is most powerful laxative, which have stimulative action on bowel movement causing severe cramps during defecation and loose tools.

Modern Scientific Use

Antitumor Activity[6,7]

Phorbol esters present in *Croton tiglium* are well known potent tumor promoting agent. according to Kim *et al*. (1993) isoguanosine has considerable activity against various cell lines both *in vitro* and *in vivo* tests especially against solid tumor and ascetic tumor.

Gastrointestinal activity[8]

Croton tiglium oil increase or decrease gastrointestinal motility by affecting contractile frequency and amplitude of intestinal smooth muscle depending on the dose of oil.

Analgesic activity[9]

From ancient era *Croton tiglium* was used as traditional medicine due to its analgesic effect. A recent study proves that leaves of *Croton tiglium* contain crotonine and pyragine, which is derivative of crotonine which is main integer of analgesic property.

Antinociceptive effect[10]

A study on mice, for antinociceptive effect of *Croton tiglium*, showed good antinociceptive effect of *Croton tiglium*.

Anti-HIV activity[11]

Scientists have tried to develop anti HIV agents from natural sources. It was apparent that the methanol and water extracts of the seeds of *Croton tiglium* significantly inhibited the infectivity and HIV-1-induced cytopathic effect (CPE) on MT-4 cell. *Croton tiglium* seeds contain anti-HIV-1 phorbolesters, 12- Oacetlyphorbol -13- decanoate and 12-O-decadienoylphorbol-13-(2-methyl butyrate) that inhibit the cytopathic effect of HIV-1 on MT-4 cells; TPA (12-Otetradecanoyl phorbol-13-acetate) is even more active than the mentioned phorbol esters against HIV-1.

Source of bio Energy[12]

Utilization of commonly available bio energy crops a potential source of biodiesel.

Table 5 External applications of *Jayapala* in various diseased conditions[13]

Application	Disease condition
Adhimansa	Cancer
Amvata	Rheumatism
Arbuda	Tumor
Bhangadara	Fistula-in-ano
Dhanurvata	Tetanus
Gandamala	Cervical lymphadenitis
Granthi	Cyst
Jwara	Fever
Kandu	Itching
Kushtha	Skin Diseases
Napumsakata	Impotency
Nasaroga	Disease of nose
Pitika	Carbuncle
Rasayana	Rejuvenation
Sannipata Roga	Disease due to vitiation of *Dosha*
Shandhatva	Impotence
Shirashoola	Headache
Shoola	Pain
Switra	Vitiligo
Udararoga	Diseases of abdomen
Udavrta- anaha	Distension of abdomen
Dhvajabhanga	Failure of penile erection
Unmada	Mania
Vataroga	Disease due to *Vatadosha*
Vibandha	Constipation
Virechanartha	For purgation
Visha	Poison
Yoniroga	Disorder of Vagina

Adverse effects

Diarrhoea, severe cramp, burning in abdomen, vomiting, dizziness, ulceration on internal administration. It causes blistering, itching, burning sensation on external application[14].

Antidote for croton poisoning

Borax powder and vacha (calamus) root ash is used as strong antidote for all parts of croton poisoning.

Shodhana

Śodhana is a unique process of detoxification which is employed. In Ayurveda, *Śodhana* is a unique process of detoxification which is employed partly to purify/detoxify and partly to potentiate the effect of various kinds of drugs used in Ayurvedic medicine with a view to reduce their toxic contents/effects as well as to enhance their therapeutic properties. The toxicity of *C. tiglium* seeds is due to the presence of phorbol esters and crotonic acid along with other constituents. These constituents are oil soluble that may have been removed by cow's milk during the process of *Śodhana*. Reduction in the level of these constituents after the purification reduced the toxicity of *C. tiglium* seeds. Reduction in the toxicity of *C. tiglium* seeds helps aid the therapeutic activity of the seeds after the purification process.

Procedure for sodhana process in Croton tiglium

Kumbhinī (*Croton tiglium*) is widely used for constipation, dyspepsia, dysenteria, intestinal inflammation, and other gastrointestinal disorders.Seeds contain an irritating oil, a toxic protein constituent, "crotin" (composed of a "crotonglobulin" and a "crotonalbumin") and also strong purgative principles such as phorbol esters and crotonic acid. *Kumbhinī* seeds are purified by *svedana* with *Godugdha* in a *dolā yantra* for 3 h, after removing its raphae which are later triturated with lemon juice. The phorbol content and toxicity of the croton oil has been reported to significantly reduced, whereas its pharmacological potency increased after the *Śodhana* process. Significant changes were observed in the physicochemical parameters of seeds after *Śodhana*. The quantity of major purgative principles phorbol ester and crotonic acid in unpurified and purified samples were determined by HPLC. The content of the phorbol ester in unpurified and purified sample was found to be 5.2 mg/100 g and 1.8 mg/100 g of dried seeds of *C. tiglium*, respectively. The quantity of crotonic acid in unpurified seeds of *C. tiglium* was found to be 0.102 mg/100 g of dried seeds. Crotonic acid content was found to be absent in the purified seed extract of *C. tiglium*[15]

Component identification of the ethyl acetate-partitioned, heat reflux ethanolic extracts from C. tiglium.

To examine what compounds within the *C. tiglium* extracts have the antidermatophytic activities, the final ethyl acetate preparations from the heat reflux ethanolic extracts of *C. tiglium* stem and seed were separately subjected to GC-MS analysis. In the GC profiles, any peak with a volume higher than 1% of the total peak areas was examined and their components were identified by matching to the built-in data. Table 6 shows ten major components in the stem extract while showing eight components in the seed preparation. Among the ten major components in the stem extract, one (hexadecanoic acid,ethyl ester) was also detected abundantly in the seed extract.The top four abundant compounds in the stem extract were oleic acid, ethyl ester (20.87%), hexadecanoic acid (palmitic acid, 20.77%), hexadecanoic acid, ethyl ester (14.11%), and oleic acid (14.04%)[16].

Table 6 GC-MS identification of ethyl acetate soluble components of the heat reflux ethanolic extracts of *Croton tiglium*.

Groups	Compound	Stem	Seed
Esters	Bis (2-ethylhexyl) phthalate	5.23	—
	Decanoic acid, ethyl ester	—	6.44
	Dodecanoic acid, ethyl ester	—	5.74
	Hexadecanoic acid, ethyl ester	14.11	17.78
	Tetradecanoic acid, ethyl ester	—	4.39
	15-Methyl-11-hexadecenoic acid, methyl ester	1.87	—
	Heptadecanoic acid, ethyl ester	—	0.95
	Linoleic acid, ethyl ester	—	35.90
	Octadecanoic acid,ethyl ester	5.56	24.47
	Oleic acid, ethyl ester	20.87	—
Alcohols	Stigmasterol	—	4.33
Acids	Hexadecanoic acid	20.77	—
	Oleic acid	14.04	—
Alkanes	Dodecamethylcyclohexasiloxane	2.68	—
	Eicosane	7.90	—
	Tetradecamethyl cycloheptasiloxane	1.49	—

Preparation of Extract[17]

The commonly employed technique for separation of active substance from crude drug is called as 'Extraction' which involves the use of different solvents. The plant material used for extraction should be properly authenticated or identified. The choice of the plant material for extraction depends upon its nature and the components required being isolated. The dried powdered plant material is commonly used for extraction. The solvent used for extraction is called menstrum and the residue is known as marc.

Methods for Plant Extraction

There are various methods of extraction. Some of them are described below:

Maceration

The word maceration means softening. It is the simplest method of crude drug extraction and was official in I.P.1966. The process consists of keeping the crude drug in intimate contact with whole menstrum in a closed vessel with occasional shaking for seven days, straining, pressing the marc, mixing the liquids and finally clarifying by subsidence or filtration. The process may take up to 14 days in some cases for complete extraction. The drug: menstrum ratio should be 1: 10.

Infusion

Infusions are usually prepared from vegetable drugs containing water soluble and easily extractable principles. The process consisted of moistening the drug with water, macerating it with boiling water, straining and making up the volume.

Digestion

This is a modified maceration process in which extraction is accomplished at a higher temperature at which the active ingredients are not adversely affected. Use of higher temperature provides for enhanced solvent action of menstrum and constant mechanical agitation of the system accelerates establishment of equilibrium in a short time.

Decoction

Decoction is also employed for extracting vegetable drugs containing water-soluble and heat-soluble constitutes. The process consisted of boiling the drug with water, cooling, expressing, straining liquid and finally make up the volume.

Percolation

Percolation is extraction process in which granulated or powdered drug is deprived of its contents by the descent of a suitable menstrum through it. In Greek, the word 'percolate' means 'to pass through'. The process implies a slow passage of menstrum under the influence of gravity through a column of the drug. During this movement, the menstrum goes on extracting the drug particle layer wise, it being replaced by other layers above as it moves downwards.

Ultrasonic Extraction

The speed of drug extraction is enhanced by application of ultrasonic vibrations. The mixture of the drug and the menstrum is subjected to ultrasonic waves of 20 to 450 kilocycles/second followed by extraction in a soxhlet extractor. The treatment with ultrasonic vibrations provides rapid and superior extraction.

Sucessive Solvent Extraction

Soxhlet Extractor

A Soxhlet extractor is a piece of laboratory apparatus invented in 1879 by Franz Von Soxhlet. It was originally designed for the extraction of a lipid from a solid material. However, a Soxhlet extractor is not limited to the extraction of lipids. Typically, a Soxhlet extraction is only required where the desired compound has a limited solubility in a solvent, and the impurity is insoluble in that solvent. If the desired compound has a high solubility in a solvent then a simple filtration can be used to separate the compound from the insoluble substance.

Principle and Working of Soxhlet Apparatus

Normally a solid material containing some of the desired compound is placed inside a thimble made from thick filter paper, which is loaded into the main chamber of the Soxhlet extractor. The Soxhlet extractor is placed onto a flask containing the extraction solvent. The Soxhlet is then equipped with a condenser. The solvent is heated to reflux. The solvent vapour travels up a distillation arm and floods into the chamber housing the thimble of solid. The condenser ensures that any solvent vapour cools, and drips back down into the chamber housing the solid material. The chamber containing the solid material slowly fills with warm solvent. Some of the desired compound will then dissolve in the warm solvent. When the Soxhlet chamber is almost full, the chamber is automatically emptied by a siphon side arm, with the solvent running back down to the distillation flask. This cycle may be allowed to repeat many times, over hours or days. During each cycle, a portion of the non-volatile compound dissolves in the solvent. After many cycles the desired compound is concentrated in the distillation flask. The advantageof this system is that instead of many portions of warm solvent being passed through the sample, just one batch of solvent is recycled. After extraction the solvent is removed, typically by means of a rotary evaporator, yielding the extracted compound. The nonsoluble portion of the extracted solid remains in the thimble, and is usually discarded[17].

Fourier Transform – Infra Red Spectroscopy[18]

Fourier Transform – Infra Red Spectroscopy Study (FTIR) IR data acquired with FT-IR spectrometer FT/IR-4100 –Jascoasia portal. About 20 mg of the CS before and after purification was taken on a microspatula and grounded well with required quantity of KBr salt. Sample admixed with KBr with trituration aided by mortar and pestle until to get a uniform fine powder of sample- KBr mixture. Further mixture was loaded in pellet die and subjected to 5000-10,000 psi in pelletizer. Resulting pellet was placed in FTIR sample holder and expose to IR radiation to get the spectra.

FT-IR analysis of un-purified croton seeds shows the presence of most significant functional groups such as alcohol, alkane, nitro, acid and aldehyde and while compared to un-purified sample, the FT-IR spectra of purified sample shows the addition to two more functional groups, that is alkene and amine in addition of these functional groups are might be importance of the purification process.

FTI-R analysis of un-purified croton seeds shows the presence of bio-active functional groups such as alcohol, alkane, nitro, acid and aldehydes. Whereas the report of purified CS shows the presence of two functional groups, that is alkene and amine along with the existing ones. Addition of these functional groups justifies the importance of the purification process.

CONCLUSION

In ayurvedic classical references there are many medicinal herbs indicated in different diseases. Upavisha like Jayapala is the one used with medicinal combinations to prepare formulations. Natural products identified from traditional medicinal plants have always paved the way for development of new types of therapeutics. *Croton tiglium* has been used to treat various diseases for more than hundreds of years. As the seed oil is purgative. When taken internally or applied externally to the skin, it produces severe symptoms of toxicity. As the seeds are having poisonous properties it should be used carefully after proper shodhana mentioned in various Ayurvedic text.

As per the concept of Ayurveda, "even a strong poison can be converted to an excellent medicine if processed and administrated properly. On the other hand, even the most useful medicine may become a poison if handled incorrectly." *Śodhana* processes as per Indian system of medicine in the development of herbal formulations with application of modern technology to assess its safety and efficacy. Studies have shown that the toxic constituents are transferred into media rendering the drug nontoxic. Specific media has definitely an important role in making a drug act without causing side-effects/adverse effects.

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