WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 3, 2223-2237. Review Article ISSN 2277– 7105

CRITICAL REVIEW ON THERAPEUTIC AND TOXICOLOGICAL ASPECT OF *UPVISHA: JAYAPALA* (*CROTON TIGLIUM*)

[1]*Dr. Arvind Tumram and [2]Dr. Kundan Meshram

[1]Assistant Professor, Dept. of Agatantra, Govt. Ayurved College, Nagpur.

[2]PhD Scholar, YMT Ayurved Medical College, Mumbai.

Article Received on
18 Jan. 2022,

Revised on 08 Feb. 2022,
Accepted on 01 March 2022

DOI: 10.20959/wjpr20223-23454

***Corresponding Author**
Dr. Arvind Tumram
Assistant Professor, Dept. of Agatantra, Govt. Ayurved College, Nagpur.

ABSTRACT

Ayurveda is the one of the ancient science known to human being which still providing the knowledge about various diseases and their cure. Agadtantra is one of the incredible branch among *Astangas* mentioned in Ayurveda which is used for diagnosis of poison and their management. 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isolated from medicinal plants and introduced for the service of mankind; however most of these medicines have been withdrawn due to their toxicity or side effects. These poisonous/toxic plants are categorized as *viṣa* (poison) and *upaviṣa* (toxic but not lethal for human health) in Ayurvedic texts and also listed in the schedule-E of Drugs and Cosmetics Act 1940. Jayapala (*Croton tiglium*) is one among the upavishas and a well-known plant in Indian System of Medicine. This review article includes overall information about the plant *Croton tiglium*, its botanical description, toxicological aspect, treatment in both Ayurveda and Modern toxicology, its purification processes along with formulations currently used to treat various disorders.

KEYWORDS: Ayurveda, upavishas, Jayapala.

INTRODUCTION

Ayurveda is known as the science health and healing which includes the knowledge of eight branches (*Astangas*), Agadtantra is one of the branch among these *Astangas* which is used for diagnosis of various types of poisonings and their management. According to *Agadatantra Visha* is classified into three- *sthavara, jangama* and *kritrima*. *Sthavara visha* is further classified into *maha visha* and *upavisha* based on its toxicity. In Ayurveda *uapavishsha* are those group 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 therapeutic measure. Jayapala/Jepala (*Croton tiglium* Linn.) is one among the elevan *upavisha* which belongs to the family Euphorbiaceae. The croton plant is a native of India and is grown all through the East Indies. The seeds are poisonous and contain crotin, a toxalbumin. Jamalgota also called Purging Croton, is most powerful laxative, which has stimulant action on bowel movement. It has potent effects, which results in cramps during defecation and loose stools if taken internally. Safety monitoring of medicines in common use should be an integral part of clinical practice.

Jayapala (*Croton tiglium*) is one among the upavishas, still there are many Ayurvedic formulations like *Icchabhedi Rasa*, *Jwarari Rasa*, *Jalodari Rasa* etc. that contains *Jayapala* as one of main ingredients. Though the whole plant is considered as poisonous, Seeds is considered as highly toxic part, so it should be used carefully after proper *Shodhana* process. Improper *Shodhana* procedure or improper use of such drugs can also lead to the manifestation of poisonous signs & symptoms. Safety is the most important consideration before administration of such products. The knowledge and administration of proper antidote can be life-saving in circumstances of its toxicity & it may help to decrease the morbidity & health care costs. The widespread availability of an affordable antidote for such drugs would revolutionize the management of toxicity.

In the current scenario, the tendency of going back to natural medicine with a view that it is relatively safer than that of synthetic ones has raised its world demand. Ayurveda claims that the use of poison like *Jayapala* in therapeutics is safe as they are processed with *Shodhana* procedure.

JAYAPALA/JEPALA

Synonyms-[1]

Sr. N.	Synonym	Meaning
1	*Jayapala*	That wins over diseases
2	*Rechaka*	Purgative nature
3	*Beeja rechaka*	seeds causes purgation
4	*Dantibeeja*	seeds resemble that of danti
5	*Maladravi*	that which causes liquid defecation
6	*Nikumba*	globose fruit
7	*Beeja rechaka*	seed causes purgation
8	*Kumbibeeja*	pot shaped seed
9	*Chitramoola*	root resembles that of chitraka
10	*Sheegra*	fast acting drug
11	*Tindideephala*	

Vernacular Names

English – Croton Hindi - Jamalgota Gujarati - Nepalo, Jamala gota

Malayalam - Neervalam Tamil - nervalam Kannada - Nepal, Japala

Telungu – Nepalamu

Botanical Name: *Croton tiglium* Linn.

Scientific Classification

Kingdom: Plantae

Clade: Angiosperms

Clade: Eudicots

Clade: Rosids

Order: Malpighians

Family: Euphorbiaceae

Subfamily: Crotonoideae

Tribe: Crotoneae

Genus: *Croton*

Classical Categorization

Ayurvedic *Sthavara Visha* – Vegetative *(Phala Visha)*

Modern Science Irritant – Organic Vegetative Poison

Classical References

- The words *danti* and *drawanti* are synonymous of Jayapala found in brihatrayee[2]
- Jayapala is mentioned among the drugs where root is used as the medicine.[3]
- Purgative quality of Jayapala is explained in the event of subsidence of vitiated doshas.[4]
- Nighantu adarsha mentions it under Aamlakyadi varga and Dhanwantari nighantu under Eranda kula. Bhavaprakasa nighantu as well states about Dantibeeja[5]
- The References in Bruhatrayi are as follows:

Charaka samhita		***Susruta samhitha***		***Astanga hridayam***	
Sthana	**Chapter**	***Sthana***	**Chapter**	***Sthana***	**Chapter**
Sutrasthana	1, 2	*Sutrasthana*	11, 39, 42, 44, 45	*Sutrasthana*	15
Vimana sthana	7, 8				
Chikitsa sthana	7, 13, 27, 33	*chikitsa sthana*	2, 18, 31	*chikitsa sthana*	19
Kalpa sthana	1,11, 12	*Uttarsthana*	42, 52	*kalpa sthana*	2
Sidhi sthana	11			*uthara sthana*	30

As per different ancient texts, *Jaypala* included in different *varga* given as bellow:[6]

Ayurvedic texts	Varga
Sharngadhara samhita, Rasendra chudamani, Rasa sara sangraha Ayurveda prakasha, Rasa Tarangini	*Upavisha*
Bhavaprakasha nighantu, Dhanwantara nighantu	*Guduchyadi varga*
Kaiyyadeva nighantu	*Oushadi varga*
Raj nighantu	*Pippalyadi varga*

MORPHOLOGY[7,8]

- It is a small evergreen tree having a height of 15 – 20 feet, the young shoots sprinkled with stellate hairs, bark smooth, ash-colored. 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.[7,8]
- Flowering during January-May and fruiting in March-July

PHARMACOGNOSTICAL CHARACTERSTICS

Macroscopic: Seed are albuminous, ovate, oblong, slightly quadrangular, convex on dorsal and somewhat 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.[9,10]

Microscopic- Seed shows a hard testa, consisting of an epidermal layer, covered externally with a thick cuticle and composed of oval and tangentially elongated cells, filled with brownish content; epidermis followed by a layer of radially elongated cells, slightly bent at middle, upper half portion filled with reddish-brown and lower half filled with yellow contents; inner most zone consists 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.[11]

MEDICINAL PARTS: Seeds, Leaves, Roots, External bark of croton roots, Seed oil (Croton oil, also called Crotonis oleum).

RASA PANCHAKAS[12,13,14,15]

	Rasa	Guna	Veerya	Vipaka	Doshaghnata	Rogaghnata
Raj nighantu	Katu	ushna	ushna	Katu	Kapha vata hara	Krimihara, jataramaya
Dhanvantari nighantu	Katu	usna	Usna	Katu	Kapha vata hara	Krimihara, jataramaya nasana
Kaidev nighantu	Madhura	Laghu, snigdha	Seta	Madhura	Pitha kapha hara	Gara, sopha hara, kasahara, daham hanti
Bhavprakash		Guru, snigdha			Pitha kapha hara	
Ashtang nighantu						Anaha, udaram hanti, sanyasa, sirogada, dhanusthambha, jwarahara, amavatahara

PHARMACOLOGICAL PROPERTIES[16]

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.[22]

THERAPEUTIC INDICATION

- As it is most powerful laxative, which have stimulative action on bowel movement causing severe cramps during defecation and loose tools, thus use in persistent and obstinence constipation.
- Hair Loss (rarely)
- External Application of Croton roots Paste use in Haemorrhoids, Skin tags, Abscess

THERAPEUTIC DOSAGE

- 1/8th to 1/4th *gunja.(Rasatarangini)*
- Purified Jamalgota – 5 mg to 25 mg [6-12 mg powder (API Vol. IV.)]
- Croton root powder – 100 mg to 1000 mg
- External bark of croton roots – 500 mg to 1000 mg
- Croton oil – 1 drop mixed with honey or butter

TOXIC PART

Seed and oil extracted from the seed is extremly toxic. Seed oil is commented to have tumour promoting phorbol diesters.[17]

FATAL DOSE

Seed

1 seed -toxic symptoms

4 seed -death

Oil

3 drops- toxic symptoms for children

20-30 drops- for adults.[18]

FATAL PERIOD

Death -4 to 6 hrs or may be delayed for 3 days or even more.[19]

PHYTOCHEMISTRY (CHEMICAL COMPOSITION)[21]

- **Active principles** of *Croton tiglium* are crotin (toxalbumin), crotonoside (glycoside) and oil.
- Croton seed kernels contain approximately 50 to 60% croton oil.
- Croton seed oil contains powerful vesicating resin and 17 fatty acids.
- Seed and oil extracted from the seed is extremely toxic. Seed oil is commented to have tumour promoting phorbol diesters.

MAIN COMPONENTS[21]

- Linoleic acid
- Oleic acid
- Elcosenoic acid

MECHANISM of action[22]

The toxalbumin present in the seeds is a toxic protien that disable ribosomes and thereby inhibit protien synthesis. It is antigenic in nature, it agglutinates red cells and causes hemolysis and cell destruction.

SIGNS AND SYMPTOMS[23,24,25]

On ingestion: There is hot burning pain from mouth to stomach, salivation, Nausea, vomitting, purging, and bloody stools with griping pain followed by tachycardia, vertigo, great prostration, circulatory and respiratory collapse and death.

Applied to skin: croton oil produces burning sensation, redness and vesication; the vesicles may later suppurate and cause scaring.

Dosage of SeedFatal dose of seed is 4 seeds. A single seed is said to have produced severe symptoms of poisons. Fatal period of Jayapala seed is four to six hours or may be delayed for three to six days. Toxic effect of *Jayapala*seed is burning pain from mouth to stomach, salivation, vomiting, purging with severe griping pain and bloody stool followed by tachycardia, vertigo, great prostration, circulatory, respiratory collapse and death.

According to Ayurveda[26]

Vanti, Bhranti, Atisara, Sula, Atopa, Daurbalya, Atisweda, etc.

TREATMENT

According to modern science[27]

- Stomach wash
- Administration of demulscent drinks, like milk, or egg white
- Morphine with atropine to allay pain and reduce intestinal secretions.
- Glucose and saline re given IV to compact collapse and dehydration.
- Borax is an antidote of croton seed poisoning

According to Ayurveda

- According to Anupanamanjari and Rasajalanidhi Dhanyaka (coriander seeds), pestled with curd and sugar removes troubles due to croton seeds.
- In Kodasseri marga, a traditional malayalam textbook it has been explained that ingestion of Jayapala seeds result in acute diarrhoea and vomitting and for that 16g (4 kazhanju)

lavanga and 8g (2 kazhanju) sundi and musta is made to kahayam and when cooled is given with honey, which is considerd as the best medicine for jayapala poisoning.

PM FINDINGS[28]

- Deaths caused by ingestion of castor plant seeds are rare, because of its indigestible capsule.
- Mucosa of the GIT is congested, softened and inflamed with occasional erosions and submucous hemorrhages.
- Fragments of seeds may be found in the stomach and intestines.
- Dilation of heart, hemorrhages in the pleura, edema and congestion of the liver, kidneys, spleen and lungs may be seen.

MEDICO LEGAL IMPORTANCE[29]

- Accidental poisoning results from swallowing croton oil by mistake.
- Suicide and homicide is rare.
- Root and oil are taken internally as an abortifacient.
- Oil is used as arrow poison.

SHODHANA[30,31]

The poisonous plants reported in ancient scriptures of Ayurveda are still being used widely in a number of diseases after processing with proper shodhana. This 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. Shodhana is done to reduce the toxicity of the seeds.

- According to Rasa Tarangini the seed are taken and cut onto two along the ridge. Then the seeds are boiled in cows milk for 1 yama (3 hours) and dried under sunlight by

keeping the seeds in earthern plate.The earthern plate absorbs the oil content from the seeds thus reducing its toxicity.

- According to Astanga sangraha swedana with gomaya swarasa and goksheera and then mild fry reduces toxicity of oil.
- Kriyakoumudi has elaboratly described many sodhana procedures for jayapala.[30]

- Boil Jayapala seeds in Tandulodaka of brown rice with buffalo dung, remove its outer cover and bud, then it becomes purified.
- Boil in dung milk and Kumari swarasa, Wash it with sudha jala and dried, boil in ghrta for sometime, then remove the oil content and do bhavana for 3 days in jambeera swarasa.

PRAYOGAS IN VISHA CHIKITSA[32,33]

- Neervala Tailam; indicated in cobra poisoning
- In prayoga samuchaya dviteeya paricheda Moorkha visha chikitsa (cobra poisoning): Swetha arka patra swarasa and Jayapala beeja is indicated for pana cures sarva visha.
- Jayapala, saanamoola and mandooka vasa is made bhavana in salt water and is made to pills for nasya cures poison
- Vishahara lepa for vruschika (r.t) paste of jayapala beeja on site of scropion sting relieves pain of the sting

Vishishta Yogas of *Jayapala*[34]

Internal Formulations

S.N.	Name	Ingredients	Indication	Dose & *Anupana*
1	*Ichabedi rasa* (R.S.S)	*Parada, Gandhaka, Tankana, Shunti, Maricha, Jayapala*	*Udararoga, Virechaka*	250 mg Cold water
2	*Jalodhari rasa*(R.S.S)	*Tamarabasma, Kajjali, Haridra, Pippali, Marica, Jayapala, Tamra, Snuhi ksheera*	*Virechana, Jalodhara*	125mg *Jala*
3	*Jwarahari rasa*(R.S.S)	*Parada, Gandhaka, Naga, Sila, Haratala, Tamra, Visha, Pippali, Shunti, Maricha, Jayapala, Dhattura, Arka, Ardraka, Rohita matsya pitta*	*Jwara*	125mg *Jala*
4	*Jwarakesari rasa*(R.S.S)	*Jayapala, Visha, Pippali, Marica, Shunti, Triphala, Parada, Gandhaka,*	*Jwara*	125 mg *Madhu*

		Bhrungaraja swarasa		
5	*Jwaramurari rasa (R.R.S)*	*Visha, Pippali, Marica, Shunti, Nagara, Abhaya, Hingula, Tankana, Jayapala*	*Jwara*	250 mg *Adaraka swarasa, Madhu*
6	*Panchanan vati*(B.R)	*Parada, Gandhaka, Tuttha, Abaraka, Jayapala, Pippali, Aragvadha, Snuhi ksheera*	*Pandu*	250mg *Punarnavastaka kwatha*
7	*Virechana gutika*(S. yog)	*Trivrit, Trikatu, Jayapala.*	*Samyak Virechaka*	250 mg *Ardraka swarasa, Guda*
8	*Plihasardula rasa* (B.R)	*Parada, Gandhaka, Pippali, Shunti, Maricha, Tamra, Manasila, Tuttha, Hingu, Loha, Tankana, Tamra, Varata, Jayapala, Jayanti, Rohitaka, Yavaksara, Saidhava, Vida, Citraka,*	*Gulma, Jwara, Sotha, Vidradhi*	250mg *Madhu*
9	*Krimikasthanala rasa (B.R)*	*Kajjali, Vanga, Haratala, Manahsila, Vidanga, Danti, Jayapala*	*Krimi Roga*	*125mg Madhu*
10	*Sarvanga sundara rasa(R.S.S)*	*Visha, Pippali, Shunti, Maricha, Triphala, Jayapala, Parada, Gandhaka, Tankana*	*Jwara*	*125 to 250 mg Madhu*
11	*Draksasava (B.R)*	*Draksa, Kankola, Pippali, Citrakamula, Lavanga, Jayapala, Twak, Ela, Patra, Nagakesara, Candana, Dhataki, Jati*	*Arsas, Raktaja Vikara*	*12-24ml jala*
12	*Dadimavaleha (Y.R)*	*Dadima, Javanti, Marica, Shunti, Jayapala*	*Aruci, Amlapitta, Atisara, Netraroga*	*12gm Ushna jala*
13	*Yakritplihara lauham (B.R)*	*Parada, Gandhaka, Abhraka, Tamra, Silajatu*	*Jwara, Pandu, Sotha, Halimaka,*	*250mg Jala*
14	*Chintamani rasa (R.Chi)*	*Vatsanaba Jayapala*	*Jwara, Vataroga*	*125 mg Trikatu churna*
15	*Yakrtplihari loha(A.F.I)[10]*	*Parada, Gandaka, Lauha, Abraka, Tamara, Manasila, Haridra, Jayapala, Tankana, Silajatu, Danti, Nishotha, Shunti, Pippali, Bhrungaraja*	*Udararoga, Jwara, Pandu*	*250 mg Jala*

16	*Pratapa martanda rasa (R.S.S)*	*Visha, Hingula, Jayapala, Tankana*	*Jwara*	*60-125mg Ardraka swarasa Madhu*
17	*Rechani vati (B.B.R)*	*Haritaki, Jayapala, Snuhidugdha*	*Vibhandha*	*500mg Jala*
18	*Soolakuthara rasa (S. Yo)*	*Parada, Gandaka, Triphala, Jayapala Etc*	*Sarva Shoola*	*125 mg maricha churna*
19	*Raja virechana gutika (S. yo)*	*Triphala, Trikatu, Gandaka, Jayapala*	*Purgative*	*250mg Jala*
20	*Shotari rasa(B.R)*	*Hingula, Jayapala, Marica, Tankana, Pippali*	*Sotha*	*250mg Ghrita*

External Formulations

S.N.	Formulations	Part used	Bhavana dravya	Indications	Dosage forms
1	*Jayapala beeja lepa (R.T)*	*seed*	*jala*	*visha*	*Lepa*
2	*Jayapalapatra vati (B.Bh.R)*	*Leaf*	*jala*	*visha*	*Lepa*
3	*Naracha rasa (B.R)*	*seed*	-	*Virechana*	*Lepa*
4	*Naracha rasa (R.Y.S)*	*seed*	*Snuhi ksheera*	*Udavarta, Anaha*	*Lepa*
5	*Dantyadi lepa (B.Bh.R)*	*seed*	*jala*	*pitika*	*Lepa*
6	*Chintamani rasa –Taila (R.Y.S)*	*seed*	-	*Vibandha*	*Lepa, Nasya*
7	*Anjanabhairava Rasa(R.Y.S)*	*seed*	*Nimbu swarasa*	*Jwara*	*Anjana*
8	*Ardhanarinateshwara rasa (R.Y.S)*	*seed*	-	*Jwara*	*Nasya*
9	*Ardhanarishwara rasa (R.Sambhava)*	*seed*	*Triphala swarasa- 5 times*	*Jwara*	*Nasya*
10	*Bindhu ghrita (Sh.S)*	*fruit*	-	*Udara roga*	*Lepa*
11	*Bhairava anjana (B.Bh.R)*	*seed*	*Nimbu swarasa – 8 day*	*Jwara*	*Anjana*
12	*Ashwakanchuki rasa (R.Y.S)*	*seed*	-	*Sarvaroga*	*Anjana, Lepa*
13	*Rasadi lepa (B.Bh.R)*	*seed*	*kanji*	*shoola*	*lepa*
14	*Sanjeevakarana rasa (R.Y.S)*	*seed*	*Vatsanabha kwatha- 3 days*	*Sannipata*	*Udharshana*
15	*Soochimukha rasa (R.Y.S)*	*seed*	*Sarpa pita*	*sannipata*	*Lepa*
16	*Taila (R.R.M)*	*Root*	-	*Kushta*	*Abhyanga*
17	*Trayushanadi vati (R.Y.S)*	*seed*	-	*Rasayana*	*Anjana*
18	*Vishamrita rasa (R.Y.S)*	*seed*	*Narikelodaka*	*Jwara*	*Anjana*
19	*Vishari varti (B.Bh.R)*	*Endosperm*	*Nimbu swarasa – 21 times*	*Visha*	*Lepa*
20	*Yonivarti yoga (B.R)*	*seed*	-	*yoniroga*	*varti*

RECENT ADVANCES

Antitumor Activity[35, 36]

Phorbol esters present in *Croton tiglium* are well known potent tumor promoting agent. Isoguanosine has considerable activity against various cell lines both *in vitro* and *in vivo* tests especially against solid tumor and ascetic tumor.

Gastrointestinal activity[37]

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[38]

Leaves of *Croton tiglium* contain crotonine and pyragine, which is derivative of crotonine which is main integer of analgesic property.

Antinociceptive effect[39]

A study on mice, for antinociceptive effect of *Croton tiglium*, showed good antinociceptive effect of *Croton tiglium*. *Scientific Res. Publications*, 2004; 4(1); 1-5.

Anti-HIV activity[40]

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-Odecadienoylphorbol-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.

DISCUSSION AND CONCLUSION

In ancient ayurvedic literature, there are various herbs which are indicated in different diseases, which are still use in current era and their demands are conyinuously increasing in global market also. So to sustain in global market, these herbal formulations must have to follow some standard guidelines for efficacy and safety.

The oral use of unpurified seeds of *Jayapala* and oil is likely unsafe. It produces nausea and violent vomiting. Impure *Jayapala beeja* produces vesicles with yellow exudation and urticaria of the ab-dominal skin. It can cause severe inflammation in intestines and lead to intense abdominal pain and cramps. Purified kernels may be useful for people with severe or

chronic constipation, but the regular or frequent use of *Shudhdha Jayapala* is also unsafe. Its regular use may cause intestinal sluggishness and reduce natural peristalsis. However, *Jayapala* is not indicated in most cases of constipation because of its dangerous effects. The safer laxatives are available in the market. Here, the physician may require potent stimulant laxative in some cases with severe constipation, you should confirm for other causes especially Bowel obstruction (Intestinal obstruction). In this case, you should never use any formulation containing *Jayapala* as an ingredient.

Upavisha like Jayapala is the one used with a medicinal combinations to prepare formulations. It is better to treat various diseases with a herbal drug like Jayapala as an ingredient by following proper procedures like Shodhana Some formulations in visha chikitsa are not widely used in Clinical practice and hence there is a scope of Research in this area.

REFRENCE

1. Indian Medicinal plants, Editd by P.K Warrier, V.P.K Nambiar, C.Ramankutty, Vaidyaratnam P.S.Varier's, AryaVaidya Sala, Kottakal, published by Orient Longman Private Ltd., 3: 223.
2. Acharya Vidyadhar Shukla and Prof. Ravidatta Tripathi, Editor, Charakasamhita of Agnivesha Edited with Vaidyamanorama Hindi Commentary, Volume 2, Kalpasthana, Chapter 12, Chaukhmba Sanskrit Pratishtahan, Delhi, Reprint, 2010.
3. Acharya Vidyadhar Shukla and Prof. Ravidatta Tripathi, Editor, Charakasamhita of Agnivesha Edited with Vaidyamanorama Hindi Commentary, Volume 1, Sutrasthana; Dirghajivitiya-adhyaya, Chapter 1, Chaukhmba Sanskrit Pratishtahan, Delhi, Reprint, 2010.
4. Acharya Vidyadhar Shukla and Prof. Ravidatta Tripathi, Editor, Charakasamhita of Agnivesha Edited with Vaidyamanorama Hindi Commentary, Volume 1, Sutrasthana; Ayushkamiya-adhyaya, Chapter 1, Chaukhmba Sanskrit Pratishtahan, Delhi, Reprint, 2010.
5. https://easyayurveda.com/2017/05/09/jamalgota-purging-croton-croton-tiglium/
6. 2. https://easyayurveda.com/2017/05/09/jamalgota-purging-croton-croton-tiglium/
7. Indian Medicinal plants, Editd by P.K Warrier, V.P.K Nambiar, C.Ramankutty, Vaidyaratnam P.S.Varier's, AryaVaidya Sala, Kottakal, published by Orient Longman Private Ltd., 3: 223.
8. https://vdocuments.mx/documents/big-medicinal-plants.html

9. The Ayurvedic Pharmacopia of India ,Government of India, Ministry of health and family welfare, Department of India systems of medicine and Homeopathy,New Delhi, 1(2): 58-59.
10. https://comsys.com.sg/pdf/Siddha_Herbs.pdf
11. Saranya S *et al*., A Review on Poisonous but Beneficial Plant – Jayapala (Croton Tiglium), *Int J Recent Sci Res.*, 2019; 10(06): 32915-32920, DOI: http://dx.doi.org/10.24327/ijrsr.2019.1006.3566
12. Indian Medicinal plants, Editd by P.K Warrier, V.P.K Nambiar, C.Ramankutty, Vaidyaratnam P.S.Varier's, AryaVaidya Sala, Kottakal, published by Orient Longman Private Ltd., 3: 223.
13. https://comsys.com.sg/pdf/Siddha_Herbs.pdf
14. Acharya PV Sharma, Dhanwantari Nigantu, Chaukhambha Orientalia, 57.
15. Bhavamisha, bhavprakasha, edited by Sri.Brahmasankara Mishra and Sri.Rupalalaji visya, The Khashi Sanskrit series 130, published by Chaukambha Sanskrit Sansthan, 1: 260.
16. Ayurvedic Pharmacopoeia of India, Part I, Volume- 2. Pg.62, Published by Govt. of India, Ministry of Health and Family Welfare.
17. Nagesh Kumar Rao, Text book of Forensic Medicine and Toxicology; Jaypee brothers medical publishers Pvt .Ltd, 2nd edition pgno.476.
18. Dr. K.S. Narayana Reddy; Forensic medicine and Toxicology; 33rd, edition, K. Suguna devi malakpet, Hyderabad, 2014; 689.
19. Dr.K.S. Narayana Reddy; Forensic medicine and Toxicology; 33rd, edition, K. Suguna devi malakpet, Hyderabad, 2014; 555.
20. Prof. P.V. Sharma Dravya Guna Vigyana Chaukhambha Bharati Academy, Varanasi, 2: 428-430.
21. Ayurvedic Pharmacopoeia of India, Part I, Volume- 2. Pg.62, Published by Govt. of India, Ministry of Health and Family Welfare
22. Biswas G. Review of Forensic Medicine and Toxicology. Jaypee brothers medical publishers Pvt. Ltd, 2nd edition pgno.459.
23. Modi's textbook of Medical Jurisprudence And Toxicology, edited by Justice K Kannan, saurabh printers Pvt. Ltd, 24th edition., 137-138.
24. http://www.doctorpedi.net/fordoctor/Poisning_Center/poisoning_Details.aspx?id=65
25. Dr K.S Narayana Reddy, The Essentials Of Forensic Medicine And Toxicology;K Suguna Devi,Om Sai Graphics; 31st edition pg no.515-516.

26. Bhavamishra; Bhavaprakash; edited by Brahmshankara Mishra; Choukamba Sanskrita Samsathana; Varanasi; Vol;1; edition 8th, 402.
27. Modi's textbook of Medical Jurisprudence And Toxicology, edited by Justice K Kannan,saurabh printers Pvt .Ltd,24th edition.pgno.137-138.
28. Review of Forensic Medicine and Toxicology, second edition, Dr. Goutam Biswas, Jaypee Brothers Medical Publishers (P) Ltd., 2012, pg. no. 459.
29. Review of Forensic Medicine and Toxicology, second edition, Dr. Goutam Biswas, Jaypee Brothers Medical Publishers (P) Ltd., 2012, pg. no. 459.
30. https://easyayurveda.com/2017/05/09/jamalgota-purging-croton-croton-tiglium/
31. kriyakoumudiKuttikrishnan menon V.M Kriyakaumudi,1st Ed,Sahitya Pravaraka Co-operative Society Ltd,Kottayam,Kerala,1986,Chapter-kitavishaprakarnam,Sloka
32. Kuttikrishnan menon V.M Kriyakaumudi, 1st Ed, Sahitya Pravaraka Co-operative Society Ltd, Kottayam, Kerala, 1986, Chapter-Sloka-pg-
33. Dr K.P Sreekumari amma, Kodasseri Margam; Kerala Goverment publication series 19, page no. 92.
34. Priyanka *Et Al*., Critical Review on *Jayapala* (Croton Tiglium), World Journal Of Pharmacy And Pharmaceutical Sciences**,** Volume 8, Issue 3, 1665-1673.
35. Kim CW, Moon JC, Kim JB. Cytotoxic effects of extract (cp-2) from the mixture of Coptis and Croton tiglium L. of the various tumor cell lines. *Korean Central J. Med*., 1993; 58: 177-184.
36. Kim JH, Lee SJ, Han YB *et al*. Isolation of isoguanosine from Croton tiglium and its antitumor activity. *Arch. Pharm. Res.*, 1994; 17: 115-118.
37. Pillai NR. Gastrointestinal effects of Croton tiglium in experimental animals. *Ancient Sci. Life*, 1999; 18: 205-209.
38. Wu XA, Zhao YM, Yu NJ. A novel analysis of pyrazine derivatives from the leaves of Croton tiglium *L. J. Asian. Nat. Prod. Res*., 2007; 9: 437-441.
39. Yumnamcha T, Nongthomba U, Devi MD., Phytochemical screening and evaluation of genotoxicity and acute toxicity of aqueous extract of Croton tiglium *L. Int. J.*
40. Sahar EM. Anti-Hiv-1 phorbol esters from the seeds of croton tiglium, *Phytochemistry*, 2000; 53(4): 457-464.