



A review on medicinal aspects of *Chrozophora tinctoria* (L.) A (Euphorbiaceae)

M S Patil¹, Sumai Fatima¹, M B Patil²

¹ Dr. Rafiq Zakaria College for Women, Aurangabad, Maharashtra, India

² Department of Botany, JES'S Arts, Science and Commerce College, Nandurbar, Maharashtra, India

Abstract

Chrozophora tinctoria (L.) A. Juss is an herb belongs to the family Euphorbiaceae having various medicinal and therapeutic importance. The current review article covers an emphasis on the key aspects of plant *Chrozophora tinctoria* with regards to their common uses as well as regarding its biological activity; antimicrobial activity, phytochemical studies, cytotoxicity, cytotoxonomic significance, wound healing potential and anticancer activity.

Keywords: *Chrozophora tinctoria*, euphorbiaceae, phytochemical, medicinal and antimicrobial activity

Introduction

Euphorbiaceae is a flowering plant family, the family of spurge has 228 genera and near about 6,547 species (The Plant List, 2013) [3]. Specially in the tropics, spurges are shrubs or trees and cactus type but mostly they are herbs (Gibbs RD, 1974) [2]. Euphorbiaceae family is seen mainly in the tropics where climate is warm with most of the species in the Indo-Malayan region and tropical America, they extend towards the temperate regions of Southern hemisphere and Northern hemisphere which is not reported from Arctic portion (Lawrence, 1951) [6]. The fruit of *Chrozophora tinctoria* is usually a schizocarp, were it is drupe in some cases, usually capsules three-celled, each cell containing a single seed. Some species constitutes vesicating, poisonous and irritant seed oils which may be obtained. This family contains large varieties of phytotoxins, mainly diterpene esters, alkaloids, glycosides, and ricin-type toxins (Betancur- Galvis LA *et al.*, 2002) [4]. The members of family Euphorbiaceae are usually planted as decorative purpose and some species shown to be fruitful against genital herpes (HSV-2) (Hecker, 1968) [5].

Chrozophora tinctoria A. Juss

Botanical description: An annual prostrate herb, the entire plant thickly outfitted with stellate tomentum; stems about 1 feet long, branched, not stout. Leaves are thick, both surfaces with soft stellate tomentose, 1.25-2.75 to 1.75-2.5 inches, shape ovate and sinuate-toothed or entire to rounded and obtusely lobed; Leaves with 0.5-2.5 inch long petioles. Flowers are born in short racemes lengthening in fruit, the males flowers are numerous which are crowded and stalkless at the top of the raceme, the female flowers are stalked in the lower part, solitary; bracts are narrowly linear, 1/16-1/12 inch long and hairy. Male flowers: Calyx 1/8-1/6 inch long, thickly stellately tomentose. Petals 5, thin membranous, elliptic-lanceolate, 1/10 inch long. About 15 stamens in two whorls. Female flowers: Pedicels frequently extending in fruit. Calyx splitted nearly to the base, thickly stellately tomentose; sepals 5, triangular acute, 1/10 inch long by 1/30 inch wide at the base. Petals such as sepals but narrower and shorter, thickly stellately tomentose. Stellately tomentose ovary and outfitted with silvery scales; styles 3, each very much bifid, usually spreading. Capsules 1/4-3/8 inch in diameter, outfitted with stellate tomentum and silvery scales. Seeds 1/6 inch long with a silvery sheen which shines and a bit tuberculate (The Flora of the Presidency of Bombay by Theodore Cooke, Vol. 2, pg.no.606).

Scientific classification: Kingdom: Plantae; Clade: Angiosperms; Clade: Eudicots; Clade: Rosids; Order: Malpighiales; Family: Euphorbiaceae; Subfamily: Acalyphoideae; Tribe: Chrozophoreae; Subtribe: Chrozophorinae; Genus: *Chrozophora* Neck. Ex A. Juss. (1824), Pax and K. Hoffm. (1919); Species: *Chrozophora tinctoria*.

Chemotaxonomic significance: The flavonoids among all the species of the genus *Chrozophora* is common due to which it reveals the probability to be useful as chemosystematic markers. Various species belonging to *Chrozophora* reported around 35 flavonoids, and from them 6 novel flavonoids have been reported (Marzouk *et al.*, 2015).

Traditional uses: *Chrozophora tinctoria*, is an annual plant and the only species that is used as a source of dyeing material in Carpet, Kilims and in Western Anatolia and benefits the economy of Turkey. Number of countries in Africa, temperate and tropical Asia and Europe is the motherland of *C. tinctoria* where it is oftenly

known as 'Dyer's Croton' (Suleyman B, 2000). Purple colored dyes from lichen species such as *Varialaria*, *Roccella*, and *Lecanora*. These dyes are produced from the flower *Chrozophora tinctoria* were possibly used since antiquity to dye textiles. Purples obtained from the above *Chrozophora tinctoria* plants rried symbolic meanings and in the Early Middle Ages and from the 14th c. on, orcein purples were used in the illuminations of precious manuscripts (M. J. Melo *et al.*, 2013, F. Rosi *et al.*, 2013). *C. tinctoria*, shows most solubility in water, and produces dark red color, but has not shown reaction with wool fiber (Ugulu *et al.*, 2009) [29].

Importance:

***Chrozophora* genus:** The plant is placed Euphorbiaceae family and the only genus in the subtribe Chrozophorinae. The members of the genus are mostly herbaceous, monoecious under shrubs, made up of about 9 species spread in the Mediterranean regions, countries of tropical Africa, West Africa, West Asia, Pakistan and India (Boulos 2000; The Plant List 2013) [12, 3]. In India, 5 species of *Chrozophora* are known to occur. Naturally these plants occur in countries of tropical Africa, Asia and India (Rev. Fr. Jean Ferdinand Caius, 1938; The Plant List, 2013) [3].

Table 1

Name of the Plant	Medicinal and Other Uses	Reference
<i>Chrozophora plicata</i>	Seeds as cathartic, treats vomiting due to poisoning, acute and corrosive properties.	(Manandhar NP, Manandhar S, 2000) [7]
<i>Chrozophora rottleri</i>	Traditionally used for various diseases. In Saudi Arabia and India, useful for the treatment of icterus and works as blood purifier. Fruit juice for cough and cold in Nepal.	(Khare CP, 2007) [8]
	Leaves as a depurgative plant part and very much useful in the treatment of skin related problems.	(Priyanka P, 2010) [9]
<i>Chrozophora tinctoria</i>	Traditionally to treat warts, used as an emetic, cathartic, and for the treatment of fever.	(Gamble, 1967) [28]
<i>Chrozophora</i> plant	Used traditionally to heal skin related problems, jaundice, diarrhea, mouth ulcer, skin burns, wounds, abdominal pain, joint pain and swelling, fever, migraine, menstrual problems, and also to throw out intestinal worms. Provides scientific evidence for their proper use in food, feeds, personal body care, and foods used in medicine, and for the prevention and treatment of infectious diseases and diseases related to oxidative stress.	(Manal <i>et al.</i> , 2014) [10]

Phytochemical analysis: The *Chrozophora* genus results in the separation of several types of secondary metabolites such as terpenes, essential oils, phenylpropanoid glycosides, sterols, xanthenes, chromone and flavonoids (Hashim, 1990) [16]. Various biological activities of *Chrozophora* genus were reported such as an antioxidant (Delazar *et al.*, 2006; Hawas 2007) [13, 39, 17], antimicrobial (Vassallo *et al.*, 2006; Usman *et al.*, 2007) [26, 25] and traditional medicine for the treatment of various ailments (Dipankar *et al.*, 2011) [14]. Many more phytochemical constituents are reported from few species of the genus *Chrozophora*, flavonoid as well as coumarins (Abdel-Sattar, 1985) [11], diterpenoids (Mohamed *et al.*, 1994, 1995; Tabussum *et al.*, 2013) [22, 23, 24], phenylpropanoid glycosides (Mohamed, 2001) [21], anthraquinones, tannins, phenolic acids, saponins and xanthenes (Agrawal & Singh 1988; Usman *et al.*, 2007) [1]. Commonly reported, flavonoids in all the species of the genus *Chrozophora* (Vassallo *et al.*, 2006; Hawas 2007; Tabussum *et al.*, 2013) [26, 17, 24]

Antimicrobial activity: *Chrozophora tinctoria* methanol extract showed low antibacterial activity against *Staphylococcus aureus* and *Klebsiella pneumoniae* and highest inhibition against *Pseudomonas aeruginosa* (Kensa and Yasmin, 2011) [33] and n-hexane extract of *C. tinctoria* showed low antibacterial activity against *Escherichia coli* and notable in *Pseudomonas aeruginosa* and highest inhibition against *Staphylococcus aureus* and *Klebsiella pneumoniae*. However, methanol extract of *C. tinctoria* showed remarkable antibacterial activity against *Escherichia coli* as well as *P. aeruginosa*, *S. aureus*, and *K. Pneumoniae*. However, the aqueous extract showed the lowest antibacterial activity as acetone extract of *C. tinctoria* is effective on both Gram-positive (*S. aureus* and *B. subtilis*) and Gram-negative (*K. pneumoniae* and *P. aeruginosa*) bacteria and the acetone and methanol extracts of *C. tinctoria* showed the greatest antibacterial activity. (Javad *et al.*, 2015) [32]. Leaf extract of *C. tinctoria* shows higher antiradical activity than the stem extract, and the methanol leaf extract had the maximum antiradical activity (Javad *et al.*, 2015) [32]. *C. tinctoria* may be useful in pharmaceutical and phytotherapeutic applications as it has antioxidant and antimicrobial potential. *C. tinctoria* leaves extract revealed the appearance of number of secondary metabolites groups such as alkaloids, mucilage, anthraquinone, saponins, tannins, flavonoids, steroids, terpenoids, glycosides and reducing sugar (Rangari V., 2002) [31].

Table 2

Solvent	Bacteria	Inhibition Zone (mm)	Inhibition (%)	Average (no. of samples = 5)	Reference
Methanol extract	<i>Salmonella typhi</i>	15	54.5	(46.00) NS	Dastagir <i>et al.</i> , 2012
	<i>Pseudomonas aeruginosa</i>	10	69.6		
	<i>Escherichia coli</i>	19	42.4		
	<i>Staphylococcus aureus</i>	25	24.2		
	<i>Klebsiella pneumoniae</i>	20	39.3		
n-hexane extract	<i>Salmonella typhi</i>	18	45.4	(41.16) NS	Dastagir <i>et al.</i> 2012
	<i>Pseudomonas aeruginosa</i>	24	27.2		
	<i>Escherichia coli</i>	30	9.09		
	<i>Staphylococcus aureus</i>	10	69.6		
	<i>Klebsiella pneumoniae</i>	15	54.5		

C. tinctoria is chemically, morphologically and anatomically dissimilar from the other surveyed species. The leaves are thin woolly rombical and midrib shows the presence of lunate vascular bundles assist for species identification (Boulos 2000; Meelad & Dahhan 2000) ^[12, 20] and a prostrate herb, stamens 15 in two whorls (The Flora of the Presidency of Bombay by Theodore Cooke, Vol. 2).

Wound healing ability: Diabetes mellitus is one of the life threatening conditions, which creates barrier in the faster wound healing process. Experiment on the treated group of rats, *Chrozophora tinctoria* showed an increase in the rate of wound reduction (healing) on which it leads to quick healing as established by decreased period of epithelialisation (14.67 ± 0.28 days) when compared to disease control wounds that is 19.83 ± 0.37 days. It reveals that the treatment on wound in diabetic rats with application of hydroalcoholic leaves extract of *C. tinctoria* may be probably favourable for the control of wound healing because it improves the maximum levels of collagen in the granulation tissues. This action is likely due to the presence of active chemical constituents that is a novel chrozophorin, apigenin, rutin, and acetin. The *C. tinctoria* leaves extract has been noticed to reduce the BSL after oral administration of Streptozotocin. This effect is enhanced due to the presence of alkaloids and tannin since, it has well-known coloring properties. This recent studies executes that the process of wound healing process can be raised by the use of hydroalcoholic leaves extract of *C. tinctoria* given through oral and dermal route of administration. Hydroalcoholic leaves extract plays a notable protective role against physically damaged tissues in diabetic rats and reasonably improves wound healing (Maurya H *et al.*, 2016) ^[36].

Cyto-toxicity activity: The cytotoxicity of the *C. tinctoria* plant leaves, roots and stems extracts using brine shrimp assay, antitumor activity using potato disc assay, and phytotoxicity activity using radish seed bioassay studies showed considerable activity.

Table 3: Brine Shrimp Assay

Concentration (ppm)	Mortality (%)			Reference
	Leaves	Roots	Stems	
1000	80	33.3	36.6	Jamil M <i>et al.</i> , 2012 ^[43] ; Ali Esmail Al-Snafi*, 2015 ^[44]
100	30	26.6	20	
10	20	20	20	

Table 4: Antitumor Potato Disc Assay:

Concentration (ppm)	Tumor inhibition (%)			Reference
	Leaves	Roots	Stems	
1000	54.43	58.82	61.96	Jamil M <i>et al.</i> , 2012 ^[43] ; Ali Esmail Al-Snafi*, 2015 ^[44]
100	47.83	49.41	45.65	
10	41.30	17.65	35.87	

Table 5: Radish Seed Phytotoxicity Assay

Concentration (ppm)	Root growth inhibitor (%)			Reference
	Leaves	Roots	Stems	
10000	64.31	56.93	53.49	Jamil M <i>et al.</i> , 2012 ^[43] ; Ali Esmail Al-Snafi*, 2015 ^[44]

1000	13.02	13.13	4.01
100	7.61	2.80	-3.93
10	2.06	1.75	-8.60

The above studies shows considerable mortality (%) in brine shrimp assay at different concentrations, % mortality decreases as the decrease in concentration of plant part extract, antitumor activity in potato disc assay of leaves, root and stem shows % inhibition in which leaves and stem extract at 100 and 10 ppm is considerable and in radish seed phytotoxicity assay of plant extract in which leaf extract shows considerable growth inhibition.

Nevertheless, different concentrations of methanolic extract *Chrozophora tinctoria* shows the effect against *Artemia salina* (a species of brine shrimp) (% mortality) with 100 % mortality at concentration of 100, 300 and 1000 µl and n-hexane extracts of *Chrozophora tinctoria* 100, 48.13 and 100% mortality at concentration of 100, 300 and 1000 µl. The LD₅₀ of *Chrozophora tinctoria* against *Artemia salina* for methanol extract was 47.22 and n-hexane extract was 151.77 µg/ml (Dastagir G and Hussain F, 2014) [37].

Anticancer activity: *In vivo* studies on inhibitory effect of *C. tinctoria* on the skin tumors of mouse during which the tumor induction was done with a single topical application of 7, 12-Dimethylbenze (a) anthracene (DMBA) (40 µg/100 µl acetane/mouse). Tumor promotion was started after seven days by twice-weekly topical application of Benzoyl peroxide (BPO) (20 mg/300 µl acetone/mouse) for a period of 32 weeks. The mice received a single topical dose of *Chrozophora tinctoria* extract (10 mg/gr carbopol gel/mouse) before 4 hours of DMBA application. The result showed higher yield of tumors in the animals (mice) receiving both the drugs DMBA and BPO. Nevertheless, complete inhibition of tumor incidence was noticed among the pretreated *Chrozophora tinctoria* group of animals(mice). The antitumor effect of the plant was step in by its scavenging of free radicals which play an crucial role in the treatment of skin cancer (Hossein R *et al.*, 2006) [39].

Some studies announces the antiproliferative effects of the gallic acid and it has remarkable effects on some cancer cell lines including HeLa by inducing apoptosis and activating caspases (Ji *et al.*, 2009; You *et al.*, 2010, 2011) [40, 42-41].

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