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THE CHEMICAL CONSTITUENTS AND PHARMACOLOGICAL IMPORTANCE OF *CHROZOPHORA TINCTORIA*

Ali Esmail Al-Snafi*

Department of Pharmacology, College of Medicine, Thi qar University, Nasiriyah, Iraq.

ABSTRACT

Chemical analysis of *Chrozophora tinctoria* showed that it contained dye substances, flavonoids, alkaloids, oils, diterpenoids, xanthones, coumarins, chromones, diterpenoids, and phenylpropanoid glycosides. The plant possessed antioxidant, cytotoxic, antibacterial, antifungal, antiparasitic and other biological effects. This review highlight the chemical constituents and pharmacological effects of *Chrozophora tinctoria*.

Key words: *Chrozophora tinctoria*, Chemical constituents, Pharmacology.

INTRODUCTION

Medicinal plants have been identified and used throughout human history. Plants have the ability to synthesize a wide variety of chemical compounds that are used to perform important biological functions. The World Health Organization (WHO) estimates that 80 percent of the population of some Asian and African countries presently use herbal medicine for some aspect of primary health care. In 2001, researchers identified 122 compounds used in modern medicine which were derived from traditional human use. However, the recent pharmacological and therapeutic studies showed that plants possessed wide range of pharmacological activities and can be utilize to maintain disease-free healthy life [1-57]. This review was designed to highlight the chemical constituents and pharmacological effects of *Chrozophora tinctoria*.

Synonyms

Chrozophora hierosolymitana, Chrozophora verbascifolia Baill, Chrozophora oblique, Croton tinctorium L[58-59].

Classification

Kingdom: Plantae, Subkingdom: Tracheobionta, Superdivision: Spermatophyta, Division: Magnoliophyta, Class: Magnoliopsida, Subclass: Rosidae, Order: Euphorbiales, Family: Euphorbiaceae, Genus: *Chrozophora*, Species: *Chrozophora tinctoria*[60].

Common names

Arabic: Ghobbeira, Zeraj, Neel, English: Dyer's-croton, Giradol, Turnsole, French: Maurelle, Tournesol , German: Lackmuskraut, Portuguese: Tornasol, Spanish: Tornasol, Swedish: Tournesolört [61].

Description

The plant has an ash-gray green appearance, because it is densely covered with white, wool-like (tomentose) hairs. The hair is described as stellate (star-shaped) since groups of hair bristles are arranged as radiating out from a common point and so they have the shape of a pointed star. The plant produces few simple branches starting at least one third up of the plant height. The basal stem is thin and yellow-amber in colour. Leaves grow alternately along the stem and are not found in large numbers per plant. The mature leaves have a long petiole (longer than the leaf length) and a rhombic to ovate shape. Leaf margins are sinusoidal (wavy) in a perpendicular plane to the lamina plane. The plant is monoecious hence producing male and female flowers separately, which both are tiny (1-2 mm) and therefore inconspicuous. The male flowers have a 5-sepal calyx, 5 yellow petals and a cluster of 5 central stamens which have dark or black anthers. The female flowers have a 10-sepal calyx around a spherical ovary, no petals and 3 styles which each subdivide into 2 stigma. The male and female flowers outgrow as a raceme at the top of the branch, but they are so densely packed that appear to be a spike. Male flowers are above the basal

***Corresponding Author** **Ali Esmail Al-Snafi** E mail: aboahmad61@yahoo.com

female flowers in the spike-like raceme. Flowers are pollinated by a small-sized species of ants. Without doubt, the most conspicuous part of the plant is its fruit. The fruit is a strange looking capsule with the shape of 3 spherical bodies fused in a rather rounded-triangular structure. Additionally the fruit has perpendicular stubby projections and white scales ontrasting with the dark green wall of the fruit. Each fruit holds 3 seeds. When reaching full maturity, the fruit darkens to a dark green colour and eventually burst open with an incredible strong and sudden twist of its walls, sending the seeds inside to a considerable distance away. The seeds are oval or teeth shaped with a rough texture. They are 4mm in size and grey to light brown colour. The remnants of the fruit wall (found on the soil under the plant) rapidly turn black [62-63].

Distribution

This plant is mainly found in the Mediterranean region and central/south Asia. It is described as native to the following countries: Africa, (Algeria, Egypt, Libya, Morocco, Tunisia and Yemen) temperate and tropical Asia (Kuwait, Saudi Arabia,

Afghanistan, Iran, Iraq, Israel, Jordan, Lebanon, Syria, Turkey, Kazakhstan, Turkmenistan, India and Pakistan), and Europe (Ukraine, Albania, Bulgaria, Greece,Italy, Malta, France, former Yugoslavia, Portugal and Spain) [61,63-64].

Traditional uses

It is an old dye plant widely used in the Middle Ages in the illuminations. Turnsole also called (folium) pigment is more correctly a range of colours from blue through purple to red depending on the PH of the solution. It was considered as another kind of Litmus and sometimes was used for coloring Dutch cheese and certain liquors. Traditionally it is used for the treatment of warts [64-66]. It was also used as an emetic, cathartic, and for the treatment of fever [67]. The leaves are boiled in water and the obtained juice is given orally to relieve chest burning of digestive origin [68].

Chemical constituents

The preliminary analysis of *Chrozophora tinctoria* (whole plant, %) showed that it contained 50.00, organic matter 92.73, crude protein 9.13, neutral detergent fiber 31.06 and acid detergent fiber 54.10 [69].

Analysis of *Chrozophora tinctoria* showed that it contained dye substances, flavonoids, alkaloids, diterpenoids, xanthones, coumarins, chromones, diterpenoids, and phenylpropanoid glycosides [70-74].

However, analysis of *Chrozophora tinctoria* stems, leaves, and seeds collected during winter from two habitats in Sinai (Egypt), showed the presence of tannins, flavonoids, phenolics, alkaloids, glycosides, reducing sugars, chlorides, and sulfates were detected in samples from both habitats. HPLC analysis revealed the presence of arabinose, ribose, fructose, glucose, and raffinose in the free form, and sucrose in the combined form. Ten amino acids were also isolated from the plant [75].

Phytoanalysis of the plant parts showed that the plant contained alkaloids (stems and roots), saponins (leaves, stems and roots), anthraquinones (leaves, stems and roots), terpenoids (leaves), flavonoids, flavones (leaves and roots), tannins (leaves and roots) and cardiac glycosides (stems) [76].

From the aerial parts of the plant, two phenylpropanoid glucosides: 4-O-methyl guaiacylglycerol 9-O- beta- glucopyranoside and 4-O-methyl guaiacylglycerol 8-O-beta-glucopyranoside together with syringin, benzyl alcohol glucoside, isorhamnetin-3-O-beta-glucopyranoside-7-O-alpha-rhamnopyranoside and quercetin-3-O-beta-glucopyranoside-7-O-alpha-rhamn op yranoside have been isolated [74].

The methanol extract of the aerial parts of *Chrozophora tinctoria* yielded five flavonoid glycosides, quercetin 3-*O*-rutinoside (rutin), acacetin 7-*O*-rutinoside , apigenin 7-*O*-β-D-[(6-*p*-coumaroyl)]-glucopyranoside, apigenin 7-*O*- β-D-glucopyranoside and apigenin 7-*O*-β-D-[6-(3,4-dihydroxybenzoyl)]-glucopyranoside (named, chrozophorin) [64]. Three novel dolabellane diterpene glucosides and one new dolabellane diterpenoid have been isolated from the plant [72]. The composition of *Chrozophora tinctoria* oil were: eugenyl methy 3.692%, cyclohexyl ketone 13.742% , 2(4H)- benzofuranone, 5,6,7,7 a- tetrahydro - 4,4,7a – trimeth 50.718%, IH – cycloprop{e} azulen - 7- ol, decahydro - 1,1,7 trimethyl 9.845%, alpha cedrol 3.497%, elemicin 8.558% and capillin 9.948 % [77].

Minerals contents of *Chrozophora tinctoria* were P: 0.15, K: 0.99, Na: 0.11, Ca: 1.38, Mg: 0.32, Fe: 0.010, Cu: 4.40, Mn: 8.30 and Zn: 49.30 %/ dry matter [69].

Pharmacological effects

Antioxidant effects

The free-radical scavenging activity of the methanol extract (RC_{50} = 2.24 x 10^{-1} mg/ml) as well as the isolated five flavonoid compounds (RC_{50} = 4.38 x 10^{-3} , 2.26 x 10^{-2}, 7.69 x 10^{-4}, 8.71 x 10^{-3} and 3.19 x 10^{-4} mg/ml, respectively) were assessed by the DPPH assay [64].

It was suggested that its antitumor effect against chemically induced skin cancer was attributed to its scavenging of free radicals which play an important role in skin cancer [66].

Cytotoxic effects

The cytotoxicity of the plant leaves , roots and stems extracts was studied using brine shrimp assay, antitumor activity using potato disc assay, and phytotoxicity activity using radish seed bioassay. Mortalities (%) of brine shrimps at concentrations of 1000,100 and 10 ppm of the plant leaves , roots and stems extracts were (80,30 and 20), (33.3, 26.6 and 20) and (36.6,20 and 20) respectively. In antitumor potato disc assay, the tumor inhibition (%) at concentrations of 1000,100 and 10 ppm of the plant leaves , roots and stems extracts were (55.43, 47.83 and 41.30), (58.82, 49.41 and 17.65) and (61.96, 45.65 and 35.87) respectively. In radish seed phytotoxicity assay, the percentage root growth inhibition or stimulation (%) at concentrations of

10000, 1000,100 and 10 ppm of the plant leaves , roots and stems extracts were (64.31, 13.02, 7.61 and 2.06), (56.93, 13.13, 2.80 and 1.75) and (53.49, 4.01, -3.93 and -8.60) respectively [76].

Effect of different concentrations of methanolic extracts of *Chrozophora tinctoria* against *Artemia salina* (a species of brine shrimp) (% mortality) showed 100 % mortality at concentration of 100, 300 and 1000 µl. However, n-hexane extracts of *Chrozophora tinctoria* 100, 48.13 and 100% mortality at concentration of 100, 300 and 1000 µl. The LD_{50} of *Chrozophora tinctoria* against *Artemia salina* for methanol extract was 47.22 and n-hexane extract was 151.77 µg/ml [78].

The inhibitory effect of *Chrozophora tinctoria* on mouse skin tumors was studied in vivo, tumor initiation was achieved by a single topical application of 7, 12-Dimethylbenze (a) anthracene (DMBA) (40 µg/100 µl acetane/mouse). After 7 days, tumor promotion was begun by twice-weekly topical application of Benzoyl peroxide (BPO) (20 mg/300 µl acetone/mouse) for a period of 32 weeks. Also before 4 hours of DMBA application , animals received a single topical dose of *Chrozophora tinctoria* extract (10 mg/gr carbopol gel/mouse). Results showed that there were higher yields of tumors in those animals receiving both DMBA and BPO. However, the *Chrozophora tinctoria* pretreated group showed complete inhibition of tumor incidence. The authors concluded that the antitumor effect of the plant was mediated by its scavenging of free radicals which play an important role in skin cancer [66].

Antimicrobial effects

Antibacterial activity of crude plant extract was carried out against six bacterial strains [three gram-positive bacterial strains, Bacillus subtilis (ATCC 6633), Micrococcus leuteus (ATCC 10240), Staphylococcus aureus (ATCC 6538)] and three gram negative ones, Escherichia coli (ATTCC 1522), Salmonella setubal (ATCC 19196) and Bordetella bronchiseptica (ATCC]. The result showed that the plant extract showed antibacterial activity against three bacterial strains (M. leuteus, B. bronchiseptica, S. Setubal) at the concentrations 5-25mg/ml [79].

The antibacterial effect of ethanolic and water extracts of *Chrozophora tinctoria* stems and leaves at different concentrations was evaluated against four endemic bacteria *E coli*, *Staph aereus*, *Ps aeroginesa* and *P mirabilis*. The alcoholic extract of the plant was more potent antibacterial (Diameter of inhibition 10.97mm) than water extract (Diameter of inhibition 5.38mm). The leaves extract was more potent than stems extracts (Diameter of inhibition 8.43 and 7.90 respectively) The concentration of 0mg/l was the more potent (Diameter of inhibition 13.96) followed by the concentration 25mg/l (Diameter of inhibition 11.12mm), then the concentration 10mg/l (Diameter of inhibition 1.03mm) [80].

The crude methanol extract of the plant was tested against seven fungal strains (Fusarium moniliformes, Fusarium solani, Aspergillus niger, Aspergillus fumigatus, Aspergillus flavus, Alternaria sp. and Mucor sp.). The plant extracts showed low antifungal activity against all the seven fungal strains . The percentage inhibition in linear growth was 22.08± 2.2, 2.89± 2.61, 32.73±1, 23.48±2, 18.33± 3.3, 7.14± 3.3 and 28.26± 5.6 respectivily [79].

However, aqueous and methanolic extracts of *Chrozophora tinctoria* showed no antifungal activity against *Rhizoctonia solani*, *Fusarium oxysporum* and *Cochliobolus sativus* [81]. The statistical analysis revealed that 10g and 20g extracts of the plants significantly inhibited the growth of *Lemna minor*[82].

Toxicity

The toxicity of the plant was investigated in Wistar rats. The plant leaves were fed to rats at a concentration of 2% or 10% of the standard diet. When compared with controls, body weight gains and feed efficiency were adversely affected by both doses. Although the rats fed 10% / diet had the lowest growth rate, bouts of soft faeces and entero-hepato-nephropathy, no death occurred among the rats. These changes were accompanied by increases in serum GGT and AST activities, urea and cholesterol concentrations, decreases in total protein and albumin levels, macrocytic hypochromic anaemia and leucopenia [83].

CONCLUSION

Chrozophora tinctoria contained a wide range of secondary metabolites. It possessed antioxidant, cytotoxic, antibacterial, antifungal, antiparasitic and other biological effects. This review discussed the chemical constituents and pharmacological effects of *Chrozophora tinctoria*.

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