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A comprehensive review of Cuphea (Lythraceae)

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ABSTRACT

A wide range of phytochemical constituents have been reported from genus Cuphea are tannins , flavonoids, triterpenes, sterols, aromatic acids, carbohydrates, unsaturated fatty acids and alkanes. This genus is biologically studied for cytotoxic activities, antiviral activities, antimicrobial activities, anti-Helicobacter pylori activities, antiprotozoal activities, cardiovascular activities, antioxidant activities and anti-diuretic activities. It has been evaluated for the cytological parameters, reduction of plasma cholesterol and losing weight.

Keywords: antioxidant, Cuphea, cytotoxic, flavonoids, lythraceae, triterpenes.

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INTRODUCTION

Cuphea is a New World genus and the largest of the 32 genera of Lythraceae with about 260 species of herbaceous perennials and small shrubs.[1,2] The genus Cuphea distributed from East USA to the South of Argentina.[3] It has been used in traditional medicine in this region. Medicinal herbs and plant extracts are now generally considered as effective medicines to be respected, appreciated and they play a major role in modern pharmacy. World Health Organization estimated that about 80% of the world's population relies on herbs for their primary healthcare needs. The knowledge of how plants actually affect human physiology remains largely unexplored.[4,5] It has been widely used in ancient traditional medicine in South and Central Americas.[6] In this review a comprehensive account of the morphology, phytochemical constituents, biological activities and traditional uses are included in view of the many recent findings of importance on this plant.

Species of Cuphea have deserved much attention as a potential source of seed lipids rich in short and median chain fatty acids. [7-11] In addition to their economic importance, such fatty acids have been assigned a taxonomic significance. [12, 13]

TAXONOMY OF CUPHEA:

Kingdom: Plantae
Subkingdom: Tracheobionta
Super-division: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Order: Myrtales
Family: Lythracea
Genus: Cuphea [14, 15]

Taxonomically, Cuphea is divided into two subgenera and thirteen sections, defined by one to a few "key" characters in a now largely outdated monograph.[16-18] The genus has grown since 1903 by nearly 40% and new species continue to be discovered.[19] As the genus has become better known through sectional revisions[20-26] new information, particularly from previously uninvestigated pollen and seed characters, indicates the presence of a number of species groups that are at variance with the present taxonomy.

Synonyms:

Waxweed

I. Morphology:

Morphological synapomorphies of *Cuphea* include: Sticky or glandular hairs covering stems, leaves, and flowers.[3,20,27] Flowers: characterized by interpetiolar emergence of flowers;[28] the ribbed floral tube which terminates in 6 deltate calyx lobes;[2] the unique seed dispersal mechanism; 11 stamens; a unilateral free-standing nectariferous organ, the “disc”, at the base of the ovary; septal walls reduced to two thin threads; oblate pollen.[29,30] Seeds: are characterized by dispersion via erection of the placenta and attachment through coordinated slits in the capsule and floral tube. [18], [20] In addition, the seeds contain inverted, spiral, mucilaginous trichomes in the exotestal cells, [21, 31] feature shared with four other genera of the Lythraceae but otherwise unknown in other angiosperms. [32]

II. Phytochemical constituents isolated from cuphea:

Aqueous extract from dried and ground aerial parts of *C. carthagenensis* was sequentially partitioned with immiscible solvents. Chromatographic and spectral analyses identified the presence of quercetin-3-sulfate.[33] Bioassay-guided fractionation of the crude extract of the aerial part of *C. pinetorum* gave four flavonoid glycosides, quercetin-3-O-rhamnopyranoside, luteolin-7-O-glucopyranoside, apigenin-7-O-rhamnopyranoside and apigenin-7-O-glucopyranoside, as well as squalen and β -sitosterol.[34]

The extract of *C. wrightii* afforded friedelan-3- β -ol, ferneol, germanicol, ursolic acid, 3-O- β -glucopyranosyl- β -sitosterol, glucoluteolin, hyperin and mannitol. [35] Two new ellagitannin dimers, cuphiins D1 and D2, and six known compounds including 1,2,3,6-tetra-O-galloyl- β -D-glucose, 1,2,3,4,6-penta-O-galloyl- β -D-glucose, tellimagrandin II, oenothien B and woodfordin C and myricitrin have been isolated from the aerial part of *C. hyssopifolia*.[6] *C. pinetorum* roots extract led to the isolation of kaempferol and quercetin.[36]

From 16 species of *Cuphea* 35 flavonoids were obtained. Apigenin-C-glycoside and isorhamnetin-3-O-galactoside were isolated from *C. acino*. Quercetin-3-O-arabinoside, quercetin-3-O-glucoside, rutin and quercetin-3-O-arabinoside were isolated from *C. adenophylla*. Isorhamnetin-3-O-galactoside and myricetin-3-O-galactoside were isolated from *C. cipoensis*. Quercetin, quercetin-3-O-galactoside, quercetin-3-O-(glucose-glucuronic acid), rhamnetin-3-O-galactoside, myricetin-3-O-galactoside and myricetin-3-O-glucoside were isolated from *C. diosmifolia*. Apigenin-C-glycoside, quercetin-3-O-arabinoside, quercetin-3-O-galactoside and quercetin-3-O-glucosyl-glucosyl-glucoside were isolated from *C. disperma*. Myricetin-3-O-glucoside, myricetin-3-O-rhamnoside and myricetin-3-O-(glucose-rhamnose) were isolated from *C. linarioides*. Kaempferol-3-O-(glucose-galactose), kaempferol-3-O-(glucose-rhamnose), quercetin, quercetin-3-O-galactoside, quercetin-3-O-(galactose-rhamnose) and myricetin were

isolated from *C. pseudovaccinium*. Luteolin-7-O-galactoside, luteolin-7-O-(Glucose-glucuronic acid), quercetin-3-O-galactoside, quercetin and myricetin-3-O-glucoside were isolated from *C. sclerophylla*. Quercetin, quercetin-3-O-arabinoside, quercetin-3-O-(glucose-rhamnose), rhamnetin-3-O-glucoside and isorhamnetin-3-O-arabinoside were isolated from *C. crulsiana*. Myricetin-3-O-galactoside was isolated from *C. sperguloides*. Quercetin-3-O-arabinoside, quercetin-3-O-galactosyl-galctoside, rutin, rhamnetin-3-O-glucoside, isorhamnetin-3-O-xyloside and myricetin were isolated from *C. pulchra*. Quercetin-3-O-galactoside, quercetin-3-O-(galactose-glucose) and rhamnetin-3-O-galactoside were isolated from *C. rubrovirens*. Quercetin-3-O-arabinoside, quercetin-3-O-glucoside, quercetin-3-O-(glucose-rhamnose) and isorhamnetin-3-O-galactoside were isolated from *C. teleandra*. Quercetin-3-O-galactoside, quercetin-3-O-glucoside, quercetin-3-O-(arabinose-glucose), isorhamnetin-3-O-(glucose-rhamnoae), myricetin-3-O-arabinoside, myricetin-3-O-galactoside and myricetin-3-O-(arabinose-galactose) were isolated from *C. lutescens*. Kaempferol-3-O-galactoside, Quercetin-3-O-galactoside, myricetin-3-O-arabinosyl-arabinoside and myricetin-3-O-galactosyl-galactosyl-galactoside were isolated from *C. ericoides*. Quercetin-3-O-arabinoside, quercetin-3-O-galactoside, quercetin-3-O-(galactose-glucose), quercetin-3-O-(galactose-glucuronic acid), quercetin-3-O-glucosyl-glucoside, quercetin-3-O-(glucose-glucuronic acid), rutin and myricetin-3-O-galactoside were isolated from *C. sessilifolia*. [1]

Kaempferol, quercetin, gallic acid and its methyl ester and 3,4-dihydrobenzoic acid were isolated from the aqueous extract of *C. aperta*, while mixtures of n-alkanes, α -amyrin, β -amyrin, lupeol, stigmasterol, sitosterol, campestenone, sitostinone, stigmastenone were isolated from its hexane extract.[37] The aerial parts of *C. carthagenensis* afforded the saturated fatty acids lauric and myristic, the latter also being found in *C. epilobifolia* together with the unsaturated fatty acid linolenic, while two other unsaturated fatty acids, oleic and linoleic, were isolated from *C. infundibulum* as well as D-galactose. All three species of *Cuphea* contained mannitol, β -sitosterol, β -amyrin, betulinic acid, and epifriedelinol. Ursolic acid and ergosterol were obtained from *C. carthagenensis* as well as a new natural triterpenoid, 3- β -hydroxyfriedel-7-ene (Carthagenol). [38] Production of seed oil is dominated by an array of medium-chain fatty acids. [21]

III. Biological activities of cuphea:

Cytotoxic activities

Four macrocyclic hydrolyzable tannin dimers, cuphiin D1, cuphiin D2, oenothien B and woodfordin C isolated from *C. hyssopifolia* were evaluated the antitumor activities [39]. The mechanism of Cuphiin D1, isolated from *C. hyssopifolia*, induced antitumor effect on human promyelocytic leukemia (HL-60) cells was explored.[40] Cuphiin D1, isolated from *C. hyssopifolia*, significantly inhibited the growth of human cervical carcinoma.[41] The investigation of Cuphiin D1, isolated from *C. hyssopifolia*, has an effect on the proliferation and cytokine secretion of human peripheral blood mononuclear cells.[42] The cytotoxic effect of

different fractions from acetone-water extract of *C. aequipetala* using several cell lines was revealed.[43]

Antiviral activities:

The antiviral effect of the aerial parts of *C. carthagenensis* against two viruses: Herpes simplex virus type 1 and poliovirus type 2 was studied. The hydroethanolic extract of *C. carthagenensis* showed the best activity against Herpes simplex virus type 1 (HSV-1) and no antipoliovirus activity. [44]

Antimicrobial activities:

Water extracts (infusion and decoction) of *C. carthagenensis* exhibited activity against *Staphylococcus aureus*, *Micrococcus luteus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*. [45] Aqueous extract of *C. carthagenensis* demonstrated activity against *Staphylococcus aureus* and *Salmonella choleraesuis* causing bovine mastitis. [46] Aqueous and ethanolic extracts of *Cuphea* species showed antimicrobial activity against *Escherichia coli* and *Staphylococcus aureus*. [47] The extract of *C. aequipetala* showed high activity against *Helicobacter pylori*. [48]

Antiprotozoal activities:

The methanolic extract of the roots of *C. pinetorum* showed activity against *Entamoeba histolytica* and *Giardia lamblia*. [36] The crude extract of the aerial parts of *C. pinetorum* showed activity against *Entamoeba histolytica* and *Giardia lamblia*. [34] Kaempferol obtained from *C. pinetorum* showed antiprotozoal activity against *Giardia lamblia* in suckling female mice. [49] The extracts of *C. carthagenensis*, *C. glutinosa* and *C. ingrata* were assayed on epimasigote form of *Trypanosoma cruzi*. [50]

Cardiovascular activities:

The butanolic fraction from the aerial parts of *C. carthagenensis* showed vasorelaxant effect in rings of the rat thoracic aorta [51]. The extract of *C. carthagenensis* showed angiotensin converting enzyme inhibition. [52]

Antioxidant activities:

The extract of *C. carthagenensis* leaves showed antioxidant activity against the superoxide anion and hydroxyl radical. [53]

Anti-diuretic activities:

The extract of *C. mesostemon* showed anti-diuretic effect on the toad urinary bladder as an epithelium analogue to the distal nephron of mammals. [54]

General activities:

The aqueous extract of *C. calophylla* showed effect on mitosis as indicative of presumable antimitotic and genotoxic actions. [55] The aqueous extract of *C. carthagenensis* showed reduction of plasma cholesterol of rats fed on a high calorie diet. [56] The extract of *C. carthagenensis* pre-clinical data indicated a potential role in the control of hyperlipidemia which is associated with obesity. [57]

IV. Traditional uses of genus cuphea:

Aerial parts of *C. aequipetala* are used in treatment of stomach ache and diarrhea.[48] The decoction of the entire plant is taken orally for treating cancer.[58] *C. aperta* is used in treatment of arterial hypertension.[37] Aerial parts of *C. calophylla* are used in treatment of hypertension [55]. Its hot water extract is used to induce diuresis. [59]

Aerial parts of *C. carthagenensis* are used in treatment of high levels of cholesterol and triglycerides [56] that indicate a potential role in losing weight. [57] The infusion and decoction of aerial parts is used orally for the prevention and control of bovine mastitis. [46] The whole plant of *C. carthagenensis* is used in treatment of fever, arterial hypertension, cardiovascular diseases and constipation. It is used also as diaphoretic and diuretic. [44] Leaves decoction of *C. carthagenensis* is taken orally and used for treatment of vaginal infections, weakness and anemia.[60] The astringent plant decoction of *C. carthagenensis* is taken as a general remedy and some drink it as a treatment for gonorrhoea.[38] It is used as a remedy for malaria and often taken to alleviate symptoms of syphilis.[61,62]

The aqueous infusion of the fresh aerial parts of *C. epilobifolia* is taken orally for the treatment of rheumatism. [63]

Leaves and stems of *C. glutinosa* are used as antimalarial, diuretic, depurative of blood, and antihypertensive. *C. glutinosa* is used against palpitations and for nervous diseases.[64-67] The decoction of *C. glutinosa* is used as emmenagogue.[68] Aerial parts of *C. ingrata* are used as antipaludic, cardiotoxic, antisiphilitic and diaphoretic.[61] Leaves and flowers of *C. hyssopifolia* are used as insecticide and tonic and in treatment of fever and cough.[69] The aqueous infusion of the fresh mature leaves of *C. racemosa* is taken orally for the treatment of urinary tract infection.[5] The plant decoction of *C. speciosa* is used as a general cure-all.[70] Also it is considered as infallible cure for haemorrhoids.[71]

C. strigulosa is used in the treatment of burns, herpes, skin infection, pimples (disease caused by the Rainbow spirits). Either used as steam bath with leaves followed by a tepid bath or cooked leaves can be put as a dressing on the skin for a faster relief of burns [72]. The decoction of the entire plant is used as an antidiarrhetic and as a stomachic.[73] *C. utriculosa* leaves are used as skin cleanser and in treatment of lice.[74] The whole plant of *C. wrightii* is used for respiratory illness.[75]

CONCLUSION

Genus *Cuphea* (Lythraceae) is widely distributed and has phytochemical constituents; tannins, flavonoids, triterpenes, sterols, aromatic acids, carbohydrates, unsaturated fatty acids and alkanes. The genus appears to have a broad spectrum on several ailments. Mostly, the aerial parts of genus have been explored for cytotoxic activities, antiviral activities, antimicrobial activities, anti-*Helicobacter pylori* activities, antiprotozoal activities, cardiovascular activities, antioxidant activities and anti-diuretic activities. The biological studies reported in the present review confirm the therapeutic value of the genus and its wide traditional uses. However, less information is available regarding the clinical and toxicity studies of this genus. The genus is pre-clinically evaluated to some extent; if these claims are scientifically and clinically evaluated then it can provide good remedies and help mankind in various ailments.

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