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Review

Review on research of the phytochemistry and pharmacological activities of *Celosia argentea*

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ABSTRACT

Celosia argentea L., Amaranthaceae, is widely used as traditional medicine with a long history in China. It is a unique source of *Semen Celosiae* whose contributions include purging the hepatic pathogenic fire, improving eyesight, and treating other eye diseases. Over 79 compounds from this plant were isolated and identified, mainly including saponins, peptides, phenols, fatty acids, and amino acids, of which saponins have been considered as the characteristic and active constituents of *Celosia argentea*. Experimental evidences manifested that *Celosia argentea*, with its active compounds, possesses wide-reaching biological activities such as hepatoprotection, tumor treatment, anti-diarrhea, anti-diabetes, anti-oxidant, anti-hypertension, and for treatment of a number of eye diseases. The objective of the study was to provide an overview of the ethno-pharmacology, chemical constituents, pharmacology, and related clinical applications of *Celosia argentea*, and to reveal their therapeutic potentials, and secure an evidence base for further research works on *Celosia argentea*.

Introduction

People have been using medicinal plants since the dawn of human history. For many of these plants, when and how exactly the isolation and extraction of their medicinal properties have started are unknown. A large number of wild and cultivated plants are being used for treating various disorders and diseases around the world, particularly in some developing countries. Even the uses of some medicinal plants have been supported by long-term practices and systemic theories. With the increasing knowledge of phytochemistry and pharmacology, people have come to clear understanding of the chemical compositions and mechanisms of medicinal plants.

Celosia argentea L., commonly called *Qingxiang* (青葙), is an annual herb that belongs to the Amaranthaceae family. Theoblate, black or reddish black seeds, commonly called *Qingxiangzi* (青葙栀) in Chinese, are usually collected in autumn when the infructescence matures, then the plant is picked or cut, then dried, and the seeds are collected and then refined. The dried ripe seed is for clinical use. *Semen Celosiae* was initially recorded in Shen Nong Ben Cao (Shen, 1997) which is deemed as the earliest classical herb in China, and is frequently used in traditional Chinese medicine for treating eye diseases, ulcer, to serve as anthelminthic, to treat trauma to blood, hygro-paralysis etc. According to records of traditional Chinese medicine theory, *Semen Celosiae* is reputed for purging hepatic pathogenic fire to improve eyesight (Committee for the Pharmacopeia of PR China, 2010). Recently, with the increasing extensiveness of studies on chemical constituents of Chinese Medicinal Materials, the compounds of *C. argentea* are also being isolated and characterized, including saponins, peptides, phenols, fatty acids, amino acids, minerals, and so on. Modern pharmacological studies manifested that *Semen Celosiae* possesses miscellaneous bioactivities such as hepatoprotection (Hase et al., 1996, 1997; Sun et al., 2010; Wang et al., 2010; Xue et al., 2011; Wu et al., 2013), anti-tumor (Hayakawa et al., 1998), anti-diarrhea (Sharma et al., 2010), anti-diabetes (Vetrichelvan et al., 2002), anti-oxidant (Molehin et al., 2014) and so on. In addition, with respect to its high-nutritive value, it is also highly consumed as a leafy vegetable in some areas (Nadkarni, 1982; Kiritikar and Basu, 1987).

In this paper, *C. argentea* is reviewed on biological and pharmacognostic characterization, traditional and folk uses, chemical constituents, pharmacological activities, and toxicology, which will be significant for the exploitation of new drugs and full utilization of this plant. The possible tendency and perspective for future investigation of this plant are also discussed.

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Method

In the present review, information on *C. argentea* L., Amaranthaceae, were gathered through searching scientific databases including Web of Science, ScienceDirect, PubMed, Scopus, Springer Link, VIP, and CNKI. In addition, related Chinese classic herbal literature were also examined and searched.

Biological and pharmacognostic characterizations

Celosia argentea L. (Figs. 1 and 2), an annual herb, belongs to the Amaranthaceae family. This genus consists of sixty species worldwide, but only two species in China, *C. argentea* and *Celosia cristata*, while in other countries and regions, *C. cristata* is still grouped in the *C. argentea* as a variant (*C. argentea* var. *cristata*) (Fig. 3). As for the consanguinity to *C. argentea*, *C. cristata* is usually used as an adulterant consciously or unconsciously.

C. argentea is a herbaceous plant whose upright stem varies between 30 cm and 100 cm in height. Flowers are bisexual, pink or white in terminal elongated spikes of 2.5–15 by 2–2.5 cm, crowded ovate bracteoles, oblanceolate, and curved. The inflorescence is cylindraceous or trochiformis on the top of stems and branches. *Semen Celosiae* is splendent oblate seed, with a diameter of 1–1.5 mm, black or reddish-black surface, middle-eminence, hilum in latero-scoop, and with its seed coat thin and crumbly. Albuminous cell is filled with starch grains and aleuron grains, and contains fatty oil drops and calcium oxalate prisms (Ma, 2012). However, note that the *Semen Celosiae* is the most important part for medicine in *C. argentea*, but due to the equivocal profile, coloration, and texture, it is hard to distinguish the *Semen Celosiae* from *Semen Cristata*. Therefore, both sequence-related amplified polymorphism system (SRAP) and HPLC fingerprints techniques were used in the detection and evaluation of *C. argentea* objectively (Guo et al., 2008; Wang et al., 2008a,b; Feng et al., 2009).

Fig. 1. The plant of *Celosia argentea*. (A) The aerial parts and (B) the inflorescence.

Fig. 2. The seeds of *Celosia argentea* (*Semen Celosiae*).

Fig. 3. The plant of *Celosia cristata*.

Because *C. argentea* grows in warm and wet climate, and is lax to the edaphic condition, it is widely distributed in China, and in other subtropical and tropical regions of the world, such as Sri Lanka, South Asia, Africa, and America (Kiritikar and Basu, 1987; Board, 2003). The wide distribution of *C. argentea* supports its extensive applications.

Traditional and folk uses

Semen Celosiae was initially recorded in *Shen Nong Ben Cao* (Shen, 1997) and included in the 2010 edition of Chinese Pharmacopeia (State Committee of Pharmacopeia, 2010). Described in Shen Nong Ben Cao, *Semen Celosiae* is of bitter taste and slightly cold, and it could purge the liver of pathogenic fire, improve eyesight, and eliminate nephelium (Shen, 1997). The leaf and stem of *C. argentea*, also of bitter taste and slightly cold, could purge the skin pathogenic fire, treat ulcer, and stop surgical trauma-induced bleeding. 'Qingxiangzi' has also been reported in series of Chinese herbal and medical classics, such as *Ben Cao Gang Mu* (Li, 2003), *Ben Cao Qiu Zhen* (Huang, 1987), *Zheng Zhi Zhun Sheng* (Wang, 1993), *Yi Zong Jin Jian* (Wu, 1987).

Semen Celosiae is frequently accompanied with other traditional Chinese medicine as a complex prescription for treating various eye and eye-related diseases. It has impressive clinical effects, mainly from classic prescriptions made and as seen and read in ancient Chinese medical record. *Semen Celosiae*, with *Semen Cassiae*, *Fructus Leonuri*, and *Cornu Saigae tataricae* could cure liver hyperpyrexia induced by conjunctival congestion, eye swell, nephelium, blurred vision, and other eye diseases (Wang, 1993). Along with *Rhizome Rehmanniadride*, *Radix Scrophulariae*, and *Semen Plantaginis*, it is good for treating blurred vision induced by hepatic asthenia and

Box 1: The traditional and clinical usages of *Celosia argentea* in China

Preparation name	Main compositions	Indications	Preparation name
Qing xiang wan (青箱益)	*Semen Celosiae, Radix Rehmanniae, Semen Cuscutae, Fructus Leonuri Japonici, Raidix Aaposhnikoviae, Fructus Schisandrae Chinensis, Radix Pedicularis Davidii, Radix Bupleuri, Rhizoma Alismatis, Semen Plantaginis*, poria	Indicated for hepatic asthenia to pyreticosis, ocular hyperemia, ophthalmodynia, phengophobia, dryness of eye, eye nebula, blurred vision (治肝阳积热, 眼目红肿疼痛, 羞明, 涩巨难开, 眼主翳膜, 视物昏暗)	Yi Zong Jin Jian[a] (医宗金鉴)
Qing xiang zi wan (青箱苓益)	*Semen Celosiae, Radix Gentianae, Radix Scutellariae Baicalensis, Fructus Gradeniae, Radix Sophorae Flavescentis, Cortex Phellodendri Amurensis, Trichosanthes kirilowii* Maxim, *Rhizoma Coptidis*	Indicated for typhoid fever, inner stagnation of pathogenic heat, polydipsia (伤寒后, 结热在洋, 烦渴)	Ji Yan Fang[a] (集试方)
Long Nao Qing Xiang Wan (龙脑青箱益)	*Semen Celosiae*, Borneol, *Radix Ginseng, Semen Plantaginis, Poria alba, Rhizomza seu, Radix notopterygii, Herbal asari, Rhizoma Gastrodiae, Radix Saposhnikoviae, Concha Haliotidis* (bruising and lecigating), *Calculus bovis, Flos inulae, Moschus, azurite ore*	Indicated for external pathogen induced liver asthenia, epiphora induced by wind, blurred vision (肝脏风阳, 时多冷泪, 眼目昏暗)	Tai Ping Sheng Hui Fang[a] (太平圣惠方)
Qing Xiang Zi San 1 (青箱栀散)	*Semen Celosiae, Radix Sophorae Flavescentis, Rhizoma Coptidis, Omphalia, Realgar, Semen Persicae, Herba Polygoni Avicularis, Radix Indigoferae Szechuanensis*	Indicated for pedo-ascarid, cardiodynia, emesia (小儿蛔虫发作, 心痛, 多吐)	Tai Ping Sheng Hui Fang[a] (太平圣惠方)
Preparation name	**Main compositions**	**Indications**	**References**
Qing Xiang Zi San 2 (青箱栀散)	*Semen Celosiae, Rhizoma et Radix Notopterygii, Raidix Saposhnikoviae, Concha Haliotidis, Radix Glycyttizae, Radix Saposhnikoviae, Concha Haliotidis, Radix Glycyttizae, Periostracum Cicadae, Periostracum Serpentis, Spice Schizonepetae, Radix Atracylodis*	Indicated for blurred vision owing to senility (年深日近, 目视昏暗)	Sheng ji zong lu[a] (圣济总录)
Qing Bai Gao (青归膏)	*Semen Celosiae*, Galbanum	Promote tissue regeneration, indicated skin ulceration (主肌, 治痈疡烂潭)	Jie Wei Yuan Sou[a] (解围元薮)
Huan Su Tang (还索汤)	*Semen Celosiae, Flos Dendranthematis, Periostracum Cicada, Folium Mori, Flos Eriocauli Sexangulars, Herba Menthae Haplocalycis, Spica Prunellae Vulgaris*	Indicated for conjunctival congestion, lacrimation induced by irritation of the wind, phengophobia, failure to open eyes, even with ophthalmodynia, superficial and rapid pulse (目赤, 恶风流泪羞明, 不能开视, 甚且作痛, 脉浮数)	Nei Ke Gai Yao[a] (洋科概要)
Proved by The National Standard Compilation of Chinese Medicine (NSCCM)			
Yu Lan Jiang Tang Jiao Nang (玉兰降糖胶囊)	*Semen Celosiae, Radix Scutellariae, Folium Mori, Fructus Arctii, Radix Wahlenbergiae Marginatae, Herba Scutellariae Barbatae, Rhizoma et Radix Dispori Cantoniensis*	Clear heat and nourish Yin, promote the production of body fluid to quench thirst, indicated for internal heat due to yin deficiency caused by diabetes, type 2 diabetes and complications	NSCCM[b]
Yang Gan Huan Jing Wan (养肝还睛益)	*Semen Celosiae, Radix Codonopsis,* almond, *Fructus Lycii, Radix Cyathulae, Radix Saposhnikoviae, Flos Dendranthematis, Pulvis Cornus Bubali Concentratus, Radix Rehmanniae preparata, Semen Cuscutae* (parching processing), poria, *Rhizoma Dioscoreae oppositae, Cornu Saigae tataricae, Semen Cassiae, Radix Asparagi cochinchinensis*	Pacify liver and the external pathogen, nourish the liver and improve eyesight, indicated for blurred vision, photophobia, mydriasis (平肝息风, 养肝明目,用于阴阳肝旺所致视物模糊, 畏光流泪, 瞳仁散大)	NSCCM[b]
Ming Mu Er Shi Wu Wei Wa n (明目二十五味益)	*Semen Celosaie, Radix Genseng,Semen Cassiae obtusifoliae, Rhizoma smilacis Glabrae, Fructus Lycii,Concha Haliotidis,Fructus Leonuri Japonici, Fructus Tribuli,Radix Ophiopogonis Japonici, Flos Buddlejae, Fructus Toosendan, Radix Rubiae cordifoliae, Radix Achyranthis bidentatae, Flos Dendranthematia Indici*	Nourish Yin, purify the hepatic pathogenic fire, indicated for conjunctival congestion, dim eyesight, dryness of eye, nephelium, hypopsia (平肝息风, 养肝明目 用于阴阳肝旺所致视物模糊, 畏光流泪, 瞳仁散大)	NSCCM[b]

Box 1: (*Continued*)

Preparation name	Main compositions	Indications	References
Chu Yi Ming Mu Pian (除翳明目片)	*Semen Celosaie, Spice Prunellae, Flos Buddlejae, Fructus Gradeniae, Flos Dendranthemtis, Radix Paeoniae Rubra,Cortex Moutan Radicis, Herba Menthae Haplocalycia, Semen Plantaginis, Herba Equiseti Radix Saposhnikovia, Rhizoma Chuanxiong, Fructus Frsythiae Suspensae, Fructus Arctii*	Clear heat, purge fire, dispel wind-evil and remove nebula, indicated for pathogenic wind-fire disturbance, conjunctival congestion, sore pain, pupil nebula, photophobia, and tearing (清热泻火, 祛风退翳。用于风火上扰, 目赤肿痛, 眼生星翳, 畏光流泪)	NSCCM[b]
Shi Hu Ye Guang Wan (石斛夜光益)	*Semen Celosiae, Herba Dendrobii Nobilis, Radix Ginseng, Radix Dioscoreae Oppositae, Poria, Radix Glycyrrhizae, Herba Cistanches Deserticolae, Fructus Lycii, Semen Cuscutae, Radix Rehmanniae, Radix Rehmanniae preparata, Fructus Schisandrae Chinensis, Radix Asparagi Cochinchinensis, Radix Ophiopgonis Japonici, Semen Armeniacae Amarum*	Nourish yin, tonify kidney, clear liver and improve eyesight, indicated for both liver and kidney deficiency, asthenic yin causing excessive pyrexia, internal oculopathy, dim vision and blurred vision (滋阴池肾, 清肝明目,用于肝肾两亏, 阴阳火旺, 洋障 目瞎, 视物昏花)	Pharmacopeia of the People's Republic of China (2010)[b]
Approved by the China Food and Drug Administration (CFDA)			
Zhang Yi San (障翳散)	*Semen Celosiae, Radix Salviae Miltiorrhizae, Flos Carthami, Fructus Leonuri Japonici, Semen Cassiae Obtusifoliae, Periostracum Cicadae, Myrrha, Radix Astragali Mongolici, Thallus Laminariae Japonicae, Thallus Sargassi Pallidi, Caulis ristolochiae, Man-shuriensis, Calamina, Margarita, Amber*	Remove blood stasis, remove nebula, indicated for senile cataract and corneal nebula (行滞祛阙,退障消翳。用于老年性归洋障及角膜翳。)	CFDA[b]
Zhang Yan Ming Pian (障眼明片)	*Semen Celosiae, Rhizoma Acori Tatarinowii, Semen Cassiae Obtusifoliae, Herba Cistanches Deserticolae, Radix Puerariae Lobatae, Radix Codonopsis, Fructus Viticis Simplicifoliae, Fructus Lycii, Semen Plantaginis, Radix Paeoniae Alba, Fructus Macrocarpii, Radix Glycyrrhizae, Semen Cuscutae, Rhizoma Cimicifugae foetidae, Nux Prinsepiae*	Tonify liver and kidney, remove nebula and improve eyesight, indicated for the early and middle senile cataract (池补肝肾, 退翳明目 用于初期及中期老年性归洋障)	CFDA[b]
Fu Fang Shi Hu Pian (复方石斛片)	*Semen Celosiae, Radix Ginseng, Cornu Saigae Tataricae, Fructus Schisandrae Chinensis, Fructus Lycii, Radix Chuanxiong, Rhizoma Dioscoreae Oppositae, Radix Rehmanniae, Radix Angelicae Sinensis, Pulvis Cornus Bubali Concentratus, Radix Scutellariae Baicalensis, Fructus Gradeniae, Radix Saposhnikoviae, Herba Dendrobii Nobilis, Fructus Aurantii Submaturus* (parch processing)	Nourish the liver and kidney, benefit Qi and improve eyesight, indicated for internal oculopathy, hypopsia, mydriasis, hyalosis induced blurred vision and epiphora induced by wind (滋养肝肾, 补气明目 用于昏眇洋障, 视力减退, 瞳神散大及云雾移睛引起的视物昏朦, 迎风流泪等症)	CFDA[b]

[a] Cited from the website: http://www.viki8.com.
[b] Cited from the website: http://db.yaozh.com.

heat in blood (Wu, 1987). More important information about prescriptions of *Semen Celosiae* is given in Box 1, in which it acts as principal, ministerial or adjunctive drug. Moreover, it can also be used as a messenger drug, but this will not be explained in this review.

Apart from the records in published works, *C. argentea* also has extensive officinal value in folk use. Around the area of Limu Mountains of the Hainan Island, China, its radix extract is used to treat stomachache (Zheng et al., 2013). In some rural areas India, *C. argentea* is used to for postpartum hemorrhaging (Tamara and Sarah, 2005) and aperients (Bhatia et al., 2014), skin allergies (Sujogya, 2014), anti-dysentery, and anti-diarrhea (Raju and Reddy, 2005). Although folk application mainly depended on experience or passed on from earlier generations, with the lack of systematical theory and scientific evidence as a guide, it is very important to provide the trails for related study and exploitation.

Phytochemistry

Chemical composition is the pharmacodynamics basis of herbs. The chemical constituents of *C. argentea* have long been the pursuit of many researchers, and the multiple classes of chemical constituents have been isolated and identified in different investigations, including saponins, peptides, phenols, fatty acids, amino acids, minerals, among others (Box 2).

Saponins

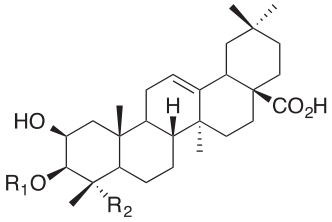
Saponins are attached to a large family, and in *C. argentea*, they mostly exist as oleanane-type triterpenoid saponins which are thought to be the major hepatoprotective compounds of *Semen Celosiae*. Two oleanolic acid saponins named celosin A (**1**) and celosin B (**2**) were isolated from

Box 2: Chemical constituents of *Celosia argentea*

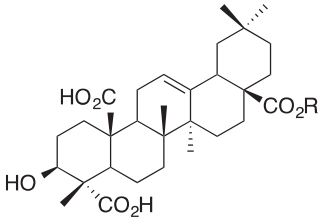
Class	Chemical constituents	Part of plant	Reference
Saponins	Celosin A (**1**)	Seed	Xue et al. (2011)
	Celosin B (**2**)	Seed	Xue et al. (2011)
	Celosin C	Seed	Sun et al. (2010)
	Celosin D	Seed	Sun et al. (2010)
	Celosin E	Seed	Wu et al. (2011)
	Celosin F	Seed	Wu et al. (2011)
	Celosin G	Seed	Wu et al. (2011)
	Celosin I (**4**)	Seed	Wu et al. (2013)
	Celosin II (**5**)	Seed	Wu et al. (2013)
	Celosin H	Seed	Pang et al. (2014)
	Celosin I	Seed	Pang et al. (2014)
	Celosin J	Seed	Pang et al. (2014)
	Cristain (**3**)	Seed	Wang et al. (2010)
Cycpeptide	Moroidin (**6**)	Seed	Morita et al. (2000)
	Celogentins A	Seed	Kobayashi et al. (2001)
	Celogentins B	Seed	Kobayashi et al. (2001)
	Celogentins C	Seed	Kobayashi et al. (2001)
	Celogentins D	Seed	Hayato et al. (2003)
	Celogentins E	Seed	Hayato et al. (2003)
	Celogentins F	Seed	Hayato et al. (2003)
	Celogentins G	Seed	Hayato et al. (2003)
	Celogentins H	Seed	Hayato et al. (2003)
	Celogentins J	Seed	Hayato et al. (2003)
	Celogentins K	Seed	Hayato et al. (2004)
	Celogenamide A	Seed	Morita et al. (2004)
Phenols	Lutin	Leaf	Molehin et al. (2014)
	Epigallocatechin (**7**)	Leaf	Molehin et al. (2014)
	Gallic acid	Leaf	Molehin et al. (2014)
	Caffeic acid	Leaf	Molehin et al. (2014)
	Rosmarinic acid	Leaf	Molehin et al. (2014)
	Quercetin	Leaf	Molehin et al. (2014)
	4-*O*-β-d-apifuranosyl-(1→2)-β-d-glucopyranosyl-2-hydroxy-6-methoxyacetophenone	Leaf	Shen et al. (2010)
Fatty acids	Arachic acid	Seed	Lin et al. (2002)
	Arachidonic acid	Seed	Zhu and Xu (2002)
	Linolenic acid	Seed	Lin et al. (2002)
	Hexadecanoic acid	Seed	Zheng et al. (1995), Lin et al. (2002)
	Palmitoleic acid	Seed	Lin et al. (2002)
	Octadecanoic acid	Seed	Zheng et al. (1995), Lin et al. (2002)
	Octadecanoic monoenoic acid		
	Oleinic acid	Seed	Lin et al. (2002)
	Linoleic acid	Seed	Lin et al. (2002)
Amino acids	Ala, Gly, Arg, Lys, Glu, Val, Met, Ile, Aba, Phe, Ser, Tyr, Pro, Leu, His, Asp, Cys, Cystine, Thr, Ornithine	Seed and leaf	Zheng et al. (1995), Lin et al. (2002)
Minerals	K, Ca, Mg, Na, Fe, Mn, Cu, Zn, S, Si, Ti, Cd, As, Hg, Cr, V, Pb, Mo.	Seed and leaf	Zheng et al. (1995), Lin et al. (2002)
Others	β-Sitosterol	Seed	Fu et al. (1992)
	Cholesteryl palmitate	Seed	Fu et al. (1992)
	3,4-Dihydroxyl benzaldedyde	Seed	Fu et al. (1992)
	p-Hydroxybenzoic acid	Seed	Fu et al. (1992)
	3,4-Dihydroxy benzoic acid	Seed	Fu et al. (1992)
	n-Butyl-β-d-fructose glycoside	Seed	Fu et al. (1992)
	Sucrose	Seed	Fu et al. (1992)
	Stigmasterol	Seed	Xue et al. (2006)
	Oleanolic acid	Seed	Xue et al. (2006)
	β-Carotene	Seed	Xue et al. (2006)
	Daucosterol	Seed	Xue et al. (2006)
	Ascorbic acid	Leaf	Faboya (1990)
	citrusi C	Leaf	Sawabe et al. (1999)
	3-*O*-β-glucopyranosyl-1*H*-indole	Leaf	Sawabe et al. (1999)
	(3*Z*)-hexenyl-(1-*O*-α-rhamnopyranosyl-β-glucopyranoside)	Leaf	Sawabe et al. (1999)
	(3*Z*)-hexenyl-1-*O*-β-glucopyranoside	Leaf	Sawabe et al. (1999)
	(7*E*)-6,9-dihydromegastigma-7-ene-3-one-9-*O*-[β-glucopyranoside	Leaf	Sawabe et al. (1999)

the ethanol extract of *Semen Celosiae*, and determined by using spectral analysis including 1D- and 2D-NMR. Their structures are assigned as 2-hydroxy-23-aldehyde-3-*O*-[-L-arabinopyranosyl-(1→2)-D-glucuronopyranosyl]-oleanolic acid and 2-hydroxy-23-carboxy-3-*O*-[-D-galactopyranosyl-(1→2)-D-glucuronopyranosyl] oleanolic acid, respectively (Xue et al., 2011). In another study, their contents were determined, and the result showed that contents of celosin A and celosin B in eight *Semen Celosiae* samples on medical markets were obviously different from each other, ranging from (0.0512 ± 0.0016)% to (0.114 3 ± 0.0008)% and (0.0109 ± 0.0019)% to (00815 ± 0.0009)% (Wang et al., 2007). The other triterpenoid saponins cristatain (**3**), celosin C∼G (Sun et al., 2010; Wu et al., 2011), celosin I (**4**) and celosin II (**5**) (Wu et al., 2013) were isolated from *Semen Celosiae*, successively. The contents of celosin I for ten samples were determined by HPLC-ELSD, ranging from 0.1667% to 0.3132%, which were far

higher than those of celosin A and celosin B (Wang et al., 2013). Another study indicated that there was an obvious difference in the content of celosin I and celosin II among *Semen Celosiae* species of various origins across China, and suggested that the sun light may be a key factor influencing the content of the two saponins (Chen et al., 2015).



1 R_1=Glc-Ara; R_2=CHO
2 R_1=Glc-Gal; R_2=CO_2H
3 R_1=Glc; R_2=CO_2H



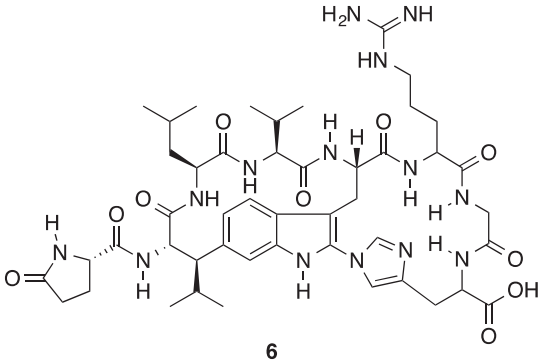
4 R=Fuc-Rha-Glc-Xyl
5 R=Fuc-Rha-Glc-Xyl-Ara

In addition, the cristatain and celosins A–D were also isolated in *C. cristata* (Wang et al., 2010). In general, these celosins have analogous or unique properties such as anti-inflammatory, anti-tumor, hepatoprotective, among others.

Celosins H, I, and J, isolated and characterized from *Semen Celosiae* by NMR, MS, and chemical evidences, were characterized as 3-*O*-β-D-xylopyranosyl-(1→3)-β-D-glucuronopyranosyl-polygalagenin 28-*O*-β-D-glucopyranosyl ester, 3-*O*-β-D-glucuronopyranosyl-medicagenic acid 28-*O*-β-D-xylcopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)-β-D-fucopyranosyl ester, and 3-*O*-β-D-glucuronopyranosyl-medicagenic acid 28-*O*-α-L-arabino-pyranosyl-(1→3)-[β-D-xylcopyranosyl-(1→4)]-α-L-rhamnopyranosyl-(1→2)-β-D-fucopyranosyl ester, respectively (Pang et al., 2014).

Peptides

During the search for bioactive compounds from medicinal plants, Japanese researchers found a series of anti-mitotic bicyclic peptides from *Semen Celosiae*. The group of Kobayashi isolated the moroidin (**6**) from *Semen Celosiae* and re-described its assignment of the stereo-structure (Morita et al., 2000). It was the first time to find moroidin in *C. argentea*. Then other celogentins (celogentins A–H, J) were isolated and described from *Semen Celosiae* gradually by using extensive NMR, MS/MS, and CD spectra (Kobayashi et al., 2001; Hayato et al., 2003). All these cyclic peptides contained a bicyclic ring system, an unusual —*C*—*N* bond formed by Trp and His residues, and an unusual amino acid, β-substituted Leu (β-Leu). Besides, celogentin K (Hayato et al., 2003) and celogenamide A (Morita et al., 2004) were isolated from *Semen Celosiae*, in which the structure of celogentins K, has a 3-hydroxyoxindole ring, was a little different from that of other cyclic peptides in *C. argentea*.



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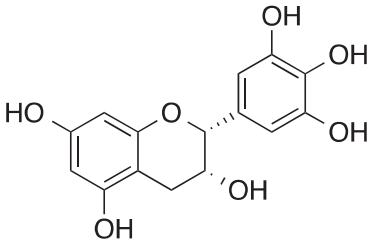
Phenols and their glycosides

Phenols have been reported to produce diverse biological effects, and in *C. argentea*, they were supposed to be anti-inflammatory (Bhujbal et al., 2008) and anti-oxidant (Molehin et al., 2014). The phenolic content of the aqueous extract of three varieties of *Celosia* species was assessed, the result showing that *Celosia laxa* had significantly ($p < 0.05$) higher total phenol and flavonoid contents than the red variant of *C. argentea* and the green variant of *C. argentea* (Molehin et al., 2014). Besides, rosmarinic acid and phenol glycoside were the two major compounds identified by high-performance liquid chromatography-diode-array detector in *C. laxa*, rutin and epigallocatechin (**7**) were the prominent phenolics present in the green variant of *C. argentea* while the red variant of *C. argentea* had epigallocatechin as the most abundant phenolic compound.



7

Moreover, a new phenolic glycoside was isolated from the MeOH extract of the plant *C. argentea*, and was characterized as 4-*O*-β-D-apifuranosyl-(1→2)-β-D-glucopyranosyl-2-hydroxy-6-methoxyacetophenone (Shen et al., 2010).

Fatty acids and amino acids

Fatty acids are one of the main energy sources of the body, in particular, the unsaturated fatty acids that are important to growth, intelligence development, memory, and other physiological functions. Several studies have focused on the fatty acids of *Semen Celosiae*, especially the unsaturated fatty acids. Zheng et al. (1995) isolated and compared five fatty acid contents in *C. argentea* and *C. cristata*, finding that the difference in contents is not significant. Lin et al. (2002) used the Soxhlet extraction method to extract the fatty acids and determined the radio by Shimadzu GC-17A and chemical detection with FID. The result revealed that the unsaturated fatty acids reached 79.276%. The main compositions of fatty acids were oleinic acid (27.995%) and linoleic acid (44.522%). Besides, *Semen Celosiae* also contained linolenic acid and arachic acid.

Amino acids are an important nitrogen source of the body, especially the essential amino acids. Some amino acids are cell signal molecules and regulate gene expression and the protein phosphorylation cascade. *C. argentea* contains various kinds of amino acids, and their contents were determined by using a Hitachi 835-50 automatic amino acid analyzer. The result showed that the total amino acid content was 131.87 mg/g, and the essential amino acid contents reached 42.85% of the total amino acids (Lin et al., 2002). In non-essential amino acids, aspartic acid and glutamic acid contents were higher than others, reaching 10.95 mg/g and 15.75 mg/g, respectively. In another study, the contents of free aspartic acid and glutamic acid were 24.57 mg/100 g and 38.57 mg/100 g, respectively, and after hydrolysis, their contents reached 1077 mg/100 g and 2025 mg/100 g, respectively (Zheng et al., 1996).

Minerals

Minerals are important in plant growth and development, and in maintaining human health. Some necessary trace elements for

bio-system such as Fe, Mn, Cu, and Zn, participate in metabolism, and are closely related to immune function. *C. argentea* consists of over eighteen minerals (Zheng et al., 1996; Markandeya et al., 2013), in which the contents of Al, Fe, Ni, Mn, Cu, K, Ti, and Se were far higher than those in *C. cristata*. A study on minerals of *C. argentea* showed that the content of Fe, Mn, Cu, and Zn were 197, 56, 30, and 160 μg/g, respectively (Lin et al., 2002), while another study estimated seven metal elements in Gannan *Semen Celosiae* and showed that the values of Zn, Co, Ni, Fe, Cr, Mg, and Cu were 33.26, 1.39, 0.72, 219.33, 0.35, 283.88, and 5.64 μg/g, respectively (Huang and Jiao, 2013).

Others

Apart from the above mentioned compositions, other compounds have also been reported. Lutein and β-carotene (Belanger et al., 2010) were isolated from *C. argentea*, while *n*-butyl-β-D-fructoside, β-sitosterol, cholesterylpalmitatie, 3,4-dihydroxyl benzaldedyde, *p*-hydroxybenzoic acid, 3,4-dihydroxy benzoic acid and fructofuranoside were isolated from *Semen Celosiae* (Fu et al., 1992). Daucosterol, stigmasterol, and oleanolic acid were isolated from the petrol-ether fraction and the EtOAc fraction of EtOH extraction of *Semen Celosiae*, respectively (Xue et al., 2006).

Pharmacological activities

With our increasing knowledge of chemistry and improvements in related experimental conditions, we have begun to use scientific methods to unmask the truth about pharmacological mechanisms of various subjects such as *C. argentea*. Increasing attention on *C. argentea*'s pharmacological activities and its mechanism on hepatoprotection, anti-infection, anti-tumor, anti-diarrhea, anti-diabetes, anti-oxidant, and its therapeutic effect on eye diseases indicated that *C. argentea* has enormous potential for further study and exploitation.

Hepatoprotective effect

As is known, liver is the most important channel of *C. argentea* for treatment functions. In the long-term administration practice, hepatoprotection is a main effect of *C. argentea*. The hepatoprotective effect of *Semen Celosiae* is supported by many modern scientific pharmacological studies. Hase et al. (1996) found that the celosian, an acidic polysaccharide from the *Semen Celosiae*, is a potent anti-hepatotoxic agent for chemical and immunological liver injury models in animals. Celosian is also an immunostimulating agent in addition to its anti-hepatotoxic effects (Hase et al., 1997). It induces tumor necrosis factor-α (TNF-α) production, the production of interleukin-1 beta (IL-1 beta), and nitric oxide (NO) in macrophage cell line J774.1 in a concentration-dependent manner (1–1000 μg/ml). Moreover, celosian induces IL-1 beta secretion in human mononuclear cells. In addition, celosian also enhanced the gamma interferon (IFN-gamma) production activity of concanavalin A (Con A) in mice spleen cells although celosian alone did not significantly influence IFN-gamma production.

Intragastric administration of celosin A and B with doses 1, 2, and 4 mg/kg per day to Kunming mice for three days significantly prevented the increase of AST, ALT, and ALP caused by CCl_4 effectively (Xue et al., 2011). Celosin C and D also significantly prevented the increase of AST, ALT, and ALP caused by CCl_4 effectively within a concentration of 1–4 mg/kg compared with the control group. At the same time, both celosins decreased the value of MDA significantly while those of GSH-PX, CAT, and SOD increased significantly (Sun et al., 2010). The hepatoprotection of celosin I and celosin II is similar to celosin A–D, and the oral administration of celosin I and celosin II prevented the increase of AST and ALT effectively but the decrease of ALP was not significant within the concentration of 2–8 mg/kg (Wu et al., 2013). The values of MDA, GSH-PX, CAT, and SOD were related to oxidization, and celosins could prevent such biochemical changes caused by CCl_4, suggesting that such hepatoprotective effects of celosins may involve their anti-oxidant activity. However, not all existing findings are clear, and further investigation is necessary.

Therapeutic effect on eye diseases

For a long time, *Semen Celosiae* has been used as an effective herb for treating eye diseases, especially in China and Japan. Compatible with other herbs (*Radix rehmanniae*, *Radix Scrophulariae*, *Semen Plantaginis* etc.), *Semen Celosiae* is being used to treat ceratitis, epipephysitis, iridocyclitis, opticatrophy, among others.

Huang et al. (2004b) researched the effects of four Chinese herbs, which pass through the liver channel, on improving eyesight and on protecting oxidative injury of lens and apoptosis of lens epithelial cells, finding that by improving the anti-oxidant ability of lens, the water extract of *Semen Celosiae* could decrease the oxidative damage of lens, inhibit lens epithelial cells apoptosis, and reduce lens opacity, better than Catalin eye drops. Lens opacities in *Semen Celosiae* group were much lighter than that in Fenton group. The content of SOD, GSH and GSH-Px in the lenses of *Semen Celosiae* group were higher than Fenton group ($p < 0.01$). The rats of LEC apoptosis in the lenses of *Semen Celosiae* (30.0 ± 2.3) was significantly lower than that in H_2O_2 (92.0 ± 2.55) and pirenoxine sodium (56.0 ± 9.9) group ($p < 0.05$). Another study on these four Chinese herbs focused on their regulation of gene expression related apoptosis of LEC (Huang et al., 2004a), in which, both Bcl-2 and Bax in LEC were expressed, and the Bcl-2 was a higher one than Bax. Compared with the normal group, the expressions of both Blc-2 and Bax in the H_2O_2 group were changed, in which the Blc-2 expression decreased while the Bax expression increased (Ridit Test, $p < 0.01$), while compared with H_2O_2 group, the Blc-2 expression increased and the Bax expression decreased, which were more approximate to the normal ones and more potent than Pirenoxine sodium. Due to the absence of blood normal vessel, lens obtained the nutrient substance from circumstance. Under normal conditions, the concentration of amino acid in lens is higher than surroundings, especially the acidic amino acid such as glutamic acid. When the lens in the situation of cataract, the content of free amino acid has reduced, the content of trace elements such as zinc, selenium, and cuprum has also reduced. With respect to *C. argentea* in these constituents, it might improve eyesight by adjusting the metabolism in lens.

Liu et al. (2007) observed the treatment of 20% water extract of *C. argentea* on senile cataract, compared with an effective drug, Catalin eye drops, the therapeutic effect of *Semen Celosiae* on senile cataract was not significant. Intimately, with iontophoresis group, the number of improvement by *Semen Celosiae* was eighteen eyes (Catalin eye drops: twenty eyes; the total eye diseases was twenty, respectively), while in the eyedropper application group, the number of improvements by *Semen Celosiae* was seventeen eyes (Catalin eye drops: nineteen eyes; the total eyes diseases was twenty, respectively). In both administration routes, there were no iriditis, cornea injury, or choroiditis side effects.

Anti-tumor and immunomodulatory activities

A number of studies revealed that *C. argentea* is a potent agent for tumor treatment. Hayakawa et al. (1998) researched the anti-metastatic effect of *Semen Celosiae* extracts, finding that intraperitoneal administration of *Semen Celosiae* extract for seven days before tumor inoculation significantly inhibited liver metastatis caused by intra-portal injection of colon 26-L5 carcinoma cells

in dose-dependent manner. *In vitro* experiments showed that water extract of *C. argentea* also mediated macrophages to produce white blood cells to lodge (Hayakawa et al., 1998). The anti-tumor foundation of *C. argentea* is due to the characteristic of immune regulation, including induced IL-12, IL-2and IFN-γ, resulting to the immune state of B dominance and activation of the cells to achieve the antitumor state. Co-culture of celosian and Con A increased IFN-γ secretion two-fold compared with Con A alone, indicating that celosian not only activates macrophages but also affects T-cells function. Another study showed significant immunomodulating activity of aerial parts of *C. argentea* (Devhare et al., 2011). The 70% ethanol extract and water extract were screened for delayed type hypersensitivity, neutrophil adhesion test, and cyclophosphamide-induced myelosuppression to assess the effect on immunity in Swiss albino mice at the dose of 50 and 100 mg/kg, *i.p.*

In the existing reports on antitumor activity of *C. argentea*, triterpenoid saponins are the most frequently reported class of compounds. Celosin A (**1**) was reported to be effective in the apoptosis of human cervical cancer HeLa cell l (Huang et al., 2013) and HepG2 Cell (Cheng et al., 2013). Wu et al. (2011) tested four triterpenoid saponins (celosin E–G and cristatain (**3**)) from *Semen Celosiae* for their antitumor activities toward five human cancer cell lines, finding that all four triterpenoid saponins had a certain degree of inhibition of cancer cells. The antitumor activity of cristatain was more potent than others, especially the cristatain I C_{50} values on SHG44, HCT116, CEM, MDA-MB-435, and HepG2 that were 23.71 ± 2.96, 26.76 ± 4.11, 31.62 ± 2.66, 27.63 ± 2.93, and 28.35 ± 2.32, respectively, while the IC 50 values of celosin E, F, and G were all more than 100 μg/ml.

Anti-diarrhoeal activity

C. argentea could effectively inhibit castor oil induced diarrhea and charcoal meal induced diarrhea. Sharma et al. (2010) evaluated the anti-diarrhoeal effect of *C. argentea* leaves extract by using castor oil induced diarrhea, charcoal meal test, and PGE induced diarrhea models. Results suggested that the extract of *C. argentea* leaves inhibited diarrhea within a dose of 100 to 200 mg/kg and that it may act centrally and may inhibit PGE to give anti-diarrhoeal effects. The extract of *C. argentea* leaves showed protection against PGE2 induced enteropooling which might be due to the inhibition of the synthesis of prostaglandins, and decreased the propulsive movement in the charcoal meal study, particularly at the dose of 200 mg/kg, it becomes more efficacious than the standard drugatropine (2 mg/kg).

Anti-diabetic activity

In folklore practice, the decoction of *Semen Celosiae* has been reported to be useful in diabetes mellitus, and its systematic and scientific investigation has been conducted gradually. Vetrichelvan et al. (2002) studied the anti-diabetic activity of alcoholic extract of *C. argentea* seeds (ACAS), finding that ACAS showed positive reduction in blood glucose levels, and this effect was dose-dependent and reached a maximum level within 4–6 h. The fall in blood glucose in rats 6 h after the administration of ACAS showed 27.7% at 250 mg/kg and 38.8% at 500 mg/kg. The continuous treatment with ACAS for a period of fifteen days produced a significant decrease in the blood glucose levels of diabetic rats. Another study also supported this folklore practice, in which both ethanol extract and water extract of *C. argentea* possessed significant hypoglycemic activities, especially the butanol fraction and polysaccharides (Shan et al., 2005). The part of crude polysaccharides significantly increased plasma insulin levels in diabetic mice, more potent than glibenclamide (2 mg/kg). The crude polysaccharides also significantly increased the spleen weight of diabetic mice, while the butanol fraction and the alcohol part of the water extract showed a tendency to increase weight of the pancreas of the diabetic mice, presuming that the extract of *C. argentea* might be able to treat pancreas injury of the alloxan-diabetic mice and at the same time, might contribute to the other organs in relation to glycometabolism.

Anti-infectious activity

In early 1969, *C. argentea* was reported to exhibit antibacterial activity against *Bacillus subtilis*, *S. aureus*, *Salmonella typhi*, *Escherichia coli*, *Agrobacterium tumefaciens*, and *Mycobacterium tuberculosis* (Bhakuni et al., 1969). Further, Gnanamani et al. (2003) researched the antibacterial activity of *C. argentea* leaf extracts on eight burn pathogens, finding that the alcohol extract of *C. argentae* showed sensitivity in the order *Shigella* sp., *Pseudomonas* sp., *Staphylococcus* sp., *Streptococcus* sp., *Vibrio* sp., *Klebsiella* sp., *E. coli* and *Salmonella* sp. Regretfully, the promising antibacterial compounds is not clear, and the goal of elucidating their active antibacterial compounds will be part of the focus of this study.

Anti-oxidant activity

The aqueous extract of *C. argentea* leaves attenuated cadmium-induced oxidative stress in the animals, with the best result at the dose of 400 mg/kg b.w. (Malomo et al., 2011). The inhibitation of H_2O_2, DPPH, and ABTS radicals by various parts extract of *C. argentea* was valued and the details of aerial part, seed, root for H_2O_2, DPPH, and ABTS were 67.13 (0.8 mg/ml), 70.81 (100 μg/ml), 62.25 (100 μg/ml), 79.12 (0.8 mg/ml), 88.18 (100 μg/ml), 86.05 (100 μg/ml), 51.14 (0.8 mg/ml), 36.16 (100 μg/ml), and 30.80 (100 μg/ml), respectively (Rub et al., 2013). The anti-oxidant activity of the extract may be attributed to the phenolic and flavonoid components of the extract. The induction of anti-oxidant enzymes and scavenging of free radicals may account for the mechanism of action of the extract as an anti-oxidant.

Anti-mitotic activity

Anti-mitosis in the moroidin (**6**)/celogentin families in *Semen Celosiae* has been reported. It was reported that moroidin strongly inhibited the polymerization of tubulin, and the inhibitory activity (IC_{50} 3 μM) of the tubulin polymerization by moroidin was more potent than that (IC_{50} 10 μM) of colchicine (Morita et al., 2000). Next, related studies indicated that all of celogentins A–H, J, and moroidin possess a certain degree of anti-mitotic activity; some of them were rivals to vinblastine and are even more potent. Among them, celogentin C is the more potent in inhibiting tubulin polymerization than vinblastine (Kobayashi et al., 2001; Hayato et al., 2003). This difference of bioactivity among celogentins and moroidin might be related to the ring size and conformation suitable for interaction with tubulin.

Other bioactivities

What is more, *C. argentea* has been known to have other pharmacological activities. The alcohol extracts of *C. argentea* promote cell motility and proliferation of primary dermal fibroblasts at 0.1–1 μg/ml but did not alter these responses in primary keratinocytes. In an initial examination of molecular mechanisms, the *C. argentea* extract did not alter fibroblast and keratinocyte responses to the wound repair-associated epidermal growth factor receptor ligands. This may be due to mitogenic and motogenic promotion of dermal fibroblasts.

Acute toxicity evaluations

According to Chinese Pharmacopeia, *Semen Celosiae* can diffuse the papillae, and is not for application in patients with glaucoma. No more side effects were recorded in related literature and the investigation of its related toxicity was lacking. Vetrichelvan et al. (2002) studied the possible toxic effects and changes in behavioral pattern of *Semen Celosiae*, in which rats were treated with different doses of alcoholic extract of *Semen Celosiae* (0.5–5 g/kg, *p.o.*) and kept under close observations for 12 h daily for a week, recording all symptoms including changes in awareness, mood, motor activity, posture, motor co-ordination, muscle tone, and reflexes for seven days. The results indicated that none of the treated animals showed any visible symptoms of toxicity and there were no signs of symptoms like restlessness, respiratory distress, diarrhea, convulsions, coma etc. at a dose as high as 5 g/kg. In our celosin-related studies, the result of total celosins' preliminary acute toxic test on mice indicated that LD_{50} was 713.4 mg/kg, while in the long-term toxicity test, total celosins just showed a certain degree of irritation on the epidermic cell, and heal or lessen in the termination of convalescent (unpublished).

In general, *C. argentea* is a safe medicinal product even in larger dosages. Note however that the different conditions (methods, objects, active fractions, active component contents, and so on) could lead to different results, and may be conflicting. Therefore, it is crucial that additional studies are undertaken to confirm and further support positive findings on the efficacy of *C. argentea*.

Approximate species: *C. cristata*

C. cristata L., Amaranthaceae, an annual herb, is widely distributed in Southern China and other subtropical and tropical regions of the world, such as Africa, India and South America. The Inflorescence is included as a common medicine by pharmacopeia (Committee for the Pharmacopeia of PR China, 2010), and the seed commonly known as *Jiguanhuahi* in Chinese is the adulterants of *Semen C. argentae*. *C. cristata* contains saponins (Wang et al., 2010; Sun et al., 2011), phenols (Wang et al., 2008a,b), betalains (Cai et al., 2005), fatty acids (Weng et al., 1997, 1998), amino acids, mineraland others (Prakash et al., 1995; Chi et al., 2010; Zhang et al., 2014). It serves as a hepatoprotective (Wang et al., 2010; Sun et al., 2011), immunomodulatory (Jiang et al., 2003), anti-osteoporosis (Li et al., 2003, 2006; Chen et al., 2005) and anti-oxidant (Kim et al., 2015) agent, among others. Although there is great similarity on chemical constituents and pharmacological activities between *C. argentea* and *C. cristata*, it is best to distinguish use until more constituents are divided and more precise data on pharmacological activities show that both can Substitute each other.

Conclusion

C. argentea has been widely used in traditional Chinese medicine with a long history China. It is reputed for purging hepatic pathogenic fire, improving eyesight, treating conjunctival congestion, eye swell, nephelium, and blurred vision. It induces hyperpyrexia of the liver, hepatic asthenia, and heat in blood. It also serves as an anti-tumor, immunomodulatory, anti-diarrhea, anti-diabetes, anti-infection, and anti-oxidant agent, among others. Most of these properties have been validated by pharmacological studies both *in vitro* and *in vivo* animal models, and clinical studies. Yet a further study is still urgently needed to gain a better understanding of *C. argentae* and provide better service for clinical use. *C. argentea* contains saponins, cyclic-peptides, phenols, fatty acids, amino acids, minerals, of which saponins are the main pharmacological active agents and might be the promising target for further studies due to their bioactivities. Although researches on the pharmacological effects and the mechanisms of saponins have been performed, complete understanding remains elusive. Moreover, the pathways of their distribution, absorption, metabolism, and excretion are almost nonexistent and need to be urgently examined and clarified by pharmacokinetic studies. Thus far, many studies are significant but limited to the level of active fractions or crude extracts. Accordingly, more promising bioactive chemical class of compounds or individual compounds should be identified using bioactivity-guided isolation strategies. The possible mechanism of action as well as potential synergistic or antagonistic effects of multi-component mixtures derived from *C. argentea* also need to be evaluated integrating pharmacological, pharmacokinetic, bioavailability-centered, and physiological approaches. In addition, no serious side effects or marked toxicity of *C. argentea* have been reported, but further relative systematic toxicity and safety evaluation studies are still needed to assure safety for clinical application.

Conflicts of interest

The authors declare no conflicts of interest.

References

Belanger, J., Balakrishna, M., Latha, P., Katumalla, S., Johns, T., 2010. Contribution of selected wild and cultivated leafy vegetables from South India to lutein and beta-carotene intake. Asia Pac. J. Clin. Nutr. 19, 417–424.

Bhakuni, D.S., Dhar, M.L., Dhar, M.M., Dhawan, B.N., Mehrotra, B.N., 1969. Screening of Indian plants for biological activity. Part II. Indian J. Exp. Biol. 7, 250–262.

Bhatia, H., Sharma, Y.P., Manhas, R.K., Kumar, K., 2014. Ethnomedicinal plants used by the villagers of district Udhampur, J&K, India. J. Ethnopharmacol. 151, 1005–1018.

Bhujbal, S.S., Chitlange, S.S., Suralkar, A.A., Shinde, D.B., Patil, M.J., 2008. Anti-inflammatory activity of an isolated flavonoid fraction from *Celosia argentea* Linn. J. Med. Plants Res. 2, 52–54.

Board, F.o.C.e., 2003. Flora of China. http://foc.eflora.cn/.

Cai, Y.Z., Sun, M., Corke, H., 2005. HPLC characterization of betalains from plants in the Amaranthaceae. J. Chromatogr. Sci. 43, 454–460.

Chen, R.B., Zhang, Y.Y., He, J.M., Wu, W.D., Guo, M.L., 2015. Simultaneous Determination of Two Major Triterpenoid Saponins Celosin I and Celosin II in Celosiae Semen by HPLC-ELSD. Chinese J. CHM 7, 185–190.

Chen, Z.Y., Li, W.L., Zhao, H., Song, X.F., Guo, X.L., Wei, H.J., 2005. Effect of *Celosia cristata* L. flavonoid on expression of bone morphogenetic protein and function of tubular reabsorption of rats with diabete mellitus. Chinese J. Clin. Rehabil 39, 188–190.

Cheng, Q.L., Li, H.L., Huang, Z.Q., 2013. Study on apoptosis of HepG2 cell induced by celosin A from *Celosia Semen* and its mechanism. Chinese J. Exp. Tradit. Med. Form. 19, 200–204.

Chi, X., Guo, M.L., Song, H., Chen, Y.D., 2010. Study on chemical constituents of *Celosia cristata* seed. J. Jilin Agric. Univ. 32, 657–660.

Devhare, S.V., Nirmal, S.A., Rub, R.A., Dhasade, V.V., Zaware, B.B., Mandal, S.C., 2011. Immunomodulating activity of *Celosia argentea* Linn aerial parts. Lat. Am. J. Pharm. 30, 168–171.

Faboya, O.O.P., 1990. The effect of pre-process handling conditions on the ascorbic acid content of green leafy vegetables. Food Chem. 38, 297–303.

Feng, N., Xue, Q., Guo, Q.H., Zhao, R., Guo, M.L., 2009. Genetic diversity and population structure of *Celosia argentea* and related species revealed by SRAP. Biochem. Genet. 47, 521–532.

Fu, H.Z., Meng, X.Y., Li, S.S., Wu, L.J., 1992. Study on the chemical constituents of *Semen Celosiae*. Chinese Tradit. Herbal Drugs 23, 344–345.

Gnanamani, A., Priya, K.S., Radhakrishnan, N., Babu, M., 2003. Antibacterial activity of two plant extracts on eight burn pathogens. J. Ethnopharmacol. 86, 59–61.

Guo, Q.H., Guo, M.L., Xue, Q., Feng, N., Zhang, H.M., 2008. Establishment and optimization of sequence-related amplified polymorphism system for *Celosia argentea*. Chinese Trad. Herbal Drug 39, 264–266.

Hase, K., Basnet, P., Kadota, S., Namba, T., 1997. Immunostimulating activity of celosian, an antihepatotoxic polysaccharide isolated from *Celosia argentea*. Planta Med. 63, 216–219.

Hase, K., Kadota, S., Basnet, P., Takahashi, T., Namba, T., 1996. Protective effect of celosian, an acidic polysaccharide, on chemically and immunologically induced liver injuries. Biol. Pharm. Bull. 19, 567–572.

Hayakawa, Y., Fujii, H., Hase, K., Ohnishi, Y., Sakukawa, R., Kadota, S., Namba, T., Saiki, I., 1998. Anti-metastatic and immunomodulating properties of the water extract from *Celosia argentea* seeds. Biol. Pharm. Bull. 21, 1154–1159.

Hayato, S., Hiroshi, M., Shigeo, I., Jun'chi, K., 2003. New antimitotic bicyclic peptides, celogentins D–H, and J, from the seeds of *Celosia argentea*. Tetrahedron 59, 5307–5315.

Hayato, S., Hiroshi, M., Motoo, S., Jun'ichi, K., 2004. Celogentin K, a new cyclic peptide from the seeds of Celosia argentea and X-ray structure of moroidin. Tetrahedron. 60, 2489–2495.
Huang, G.X., 1987. Ben cao qiu zhen. People's Medical Publish House Beijing, pp. 167.
Huang, X.R., Qi, M.X., Wang, Z.Y., Wang, Y., 2004a. Effects of four Chinese herbs which pass through liver-channel on expression of Bcl-2 and Bax in rat lens epithelial cells. Chinese J. Clin. Pharmacol. Ther. 9, 322–325.
Huang, X.R., Qi, M.X., Wang, Z.Y., Wang, Y., 2004b. Effects of four Chinese herbs which pass through liver-channel on improving eyesight and protecting oxidative injury of lens and apoptosis of lens epithelial cells. Chinese J. Clin. Pharmacol. Ther. 9, 441–446.
Huang, Z.Q., Cheng, Q.L., Li, H.L., Huang, C., 2013. The study for apoptosis of human cervical cancer HeLa cell induced by celosin A from *Celosiae Semen* and its mechanisms. Acta Pharmacol. Sin. 34, 7.
Huang, Z.Q., Jiao, L.Y., 2013. Determination of seven metal elements in Gannan *Semen Celosiae* by atomic absorption spectrometry. Guangdong Wei Liang Yuan Su Ke Xue 20, 6–9.
Jiang, X.M., Guo, H., Sun, W.Q., Tong, D.Q., Chen, Y., 2003. Research of *Celosia cristata* on increasing immunity and suppressor tumor of S180 ascites cancer mice. J. Beihua Univ. (Natural Science) 4, 123–124.
Kim, Y.S., Hwang, J.W., Sung, S.H., Jeon, Y.J., Jeong, J.H., Jeon, B.T., Moon, S.H., Park, P.J., 2015. Antioxidant activity and protective effect of extract of *Celosia cristata* L. flower on *tert*-butyl hydroperoxide-induced oxidative hepatotoxicity. Food Chem. 168, 572–579.
Kiritikar, K.R., Basu, B.D., 1987. Indian Medicinal Plants, vol. I., 2nd ed. International Book Distributors, pp. 2052–2055.
Kobayashi, J., Suzuki, H., Shimbo, K., Takeya, K., Morita, H., 2001. Celogentins A–C, new antimitotic bicyclic peptides from the seeds of *Celosia argentea*. J. Org. Chem. 66, 6626–6633.
Li, S.Z., 2003. Ben cao gang mu. China Pictorial Publishing House, Beijing, pp. 77.
Li, W.L., Tian, Y.H., Shen, G.X., 2003. Effect of flavonoid of *Celosia cristata* on mineralization and ICF-1 expression. China J. Publ. Health 19, 1392–1393.
Li, W.L., Zhao, H., Chen, Z.Y., Wei, H.J., Guo, X.L., 2006. Preventive effect of *Celosia cristata* L. flavonoid on osteoporosis in ovariectomized rats. China J. Publ. Health 22, 165–166.
Lin, W.Q., Chen, Z., Liu, J.Q., 2002. The chemical constituents of *Perilla frutescens* (L.) Britt. var. *acute* (Thunb.) and *Celosia argentea* L. seeds grown in Fujian province. Chinese Acad. Med. Magazing Organisms, 57–59.
Liu, A., Cao, M.F., Xu, C.Y., Jin, W.E., Pan, X.D., Yu, H.Q., Guan, L.H., 2007. The clinical observation of treatment of 20% water extracts of *Semen Celosiae* on senile cataract. J. Fujian College TCM 17, 10–11.
Ma, X.G., 2012. Comparative study on *Semen Celosiae*, Semen critata and *Semen amarathus*. Strait Pharm. J. 24, 27–30.
Malomo, S.O., Ore, A., Yakubu, M.T., 2011. In vitro and *in vivo* antioxidant activities of the aqueous extract of *Celosia argentea* leaves. Indian J. Pharmacol. 43, 278–285.
Markandeya, A.G., Firke, N.P., Pingale, S.S., Salunke-Gawali, S., 2013. Quantitative elemental analysis of *Celocia argentea* leaves by ICP-OES technique using various digestion methods. Int. J. Chem. Anal. Sci. 4, 175–181.
Molehin, O.R., Adefegha, S.A., Oboh, G., Saliu, J.A., Athayde, M.L., Boligon, A.A., 2014. Comparative study on the phenolic content, antioxidant properties and HPLC fingerprinting of three varieties of *Celosia* species. J. Food Biochem. 38, 575–583.
Morita, H., Shimbo, K., Shigemori, H., Kobayashi, J., 2000. Antimitotic activity of moroidin, a bicyclic peptide from the seeds of *Celosia argentea*. Bioorg. Med. Chem. Lett. 10, 469–471.
Morita, H., Suzuki, H., Kobayashi, J., 2004. Celogenamide A, a new cyclic peptide from the seeds of *Celosia argentea*. J. Nat. Prod. 67, 1628–1630.
Nadkarni, A.K., 1982. Indian Materia Medica. Bombay: Popular Prakashan 1, 90–91.
Pang, X., Yan, H.X., Wang, Z.F., Fan, M.X., Zhao, Y., Fu, X.T., Xiong, C.Q., Zhang, J., Ma, B.P., Guo, H.Z., 2014. New oleanane-type triterpenoid saponins isolated from the seeds of *Celosia argentea*. J. Asian Nat. Prod. Res. 16, 240–247.
Prakash, D., Nath, P., Pal, M., 1995. Composition and variation in vitamin C, carotenoids, protein, nitrate and oxalate contents in *Celosia* leaves. Plant Foods Hum. Nutr. 47, 221–226.
Raju, V.S., Reddy, K.N., 2005. Ethnomedicine for dysentery and diarrhoea from Khammam district of Andhra Pradesh. Indian J. Trad. Know. 4, 443–447.
Rub, R.A., Patil, M.J., Ghorpade, P., Siddiqui, A., 2013. Evaluation of antioxidant potential of *Celosia argentea* extracts. Pharmacogn. J. 5, 140–141.
Sawabe, A., Obata, T., Nochika, Y., Morita, M., Yamashita, N., Matsubara, Y., Okamoto, T., 1999. Investigation of functional molecules in African *Celosia argentea* L. Stud. Plant Sci. 6, 290–296.
Shan, J.J., Ren, J.W., Yang, J., Zhao, Y.M., 2005. Hypoglycemic effect of *Celosia argentea* fractions in alloxan-induced diabetic mice. China Pharm. J., 40.
Sharma, P., Vidyasagar, G., Singh, S., Ghule, S., Kumar, B., 2010. Antidiarrhoeal activity of leaf extract of *Celosia argentea* in experimentally induced diarrhoea in rats. J. Adv. Pharm. Technol. Res. 1, 41–48.
Shen, N., 1997. Shen nong ben cao. Liaoning Science & Technology Press, Shenyang, pp. 40.
Shen, S., Ding, X., Ouyang, M.A., Wu, Z.J., Xie, L.H., 2010. A new phenolic glycoside and cytotoxic constituents from *Celosia argentea*. J. Asian Nat. Prod. Res. 12, 821–827.
State Committee of Pharmacopeia, 2010. Pharmacopoeia of the People's Republic of China, vol. I. China Medicine Science and Technology and Publisher, Beijing, pp. 184.
Sujogya, K.P., 2014. Ethno-medicinal uses and screening of plants for antibacterial activity from Similipal Biosphere Reserve, Odisha, India. J. Ethnopharmacol. 151, 158–175.
Sun, Z.L., Gao, G.L., Xia, Y.F., Feng, J., Qiao, Z.Y., 2011. A new hepoprotective saponin from *Semen Celosia cristata*. Fitoterapia 82, 591–594.
Sun, Z.L., Wang, Y., Guo, M.L., Li, Y.X., 2010. Two new hepaprotective saponins from *Semen Celosiae* Fitoterapia 81, 375–380.
Tamara, T., Sarah, P.D., 2005. Medicinal plant use in the practice of midwifery in rural Honduras. J. Ethnopharmacol. 96, 233–248.
Vetrichelvan, T., Jegadeesan, M., Devi, B.A., 2002. Anti-diabetic activity of alcoholic extract of *Celosia argentea* Linn. seeds in rats. Biol. Pharm. Bull. 25, 526–528.
Wang, J.J., Zhang, X.M., Huang, Z.W., 2008a. Simultaneous determination of quercetin, luteolin and kaempferol in *Celosia cristata* L, by RP-HPLC. Northwest Pharm. J. 23, 354–356.
Wang, K.T., 1993. Zheng Zhi Zhun Sheng Publishing House of ancient Chinese Medical Books. Beijing, 128.
Wang, Y., Guo, M.L., Wang, X.K.J.Y., 2007. HPLC ELSD in determination of celosin A and celosin B contents in *Semen Celosiae*. Acad. J. Second Military Med. Univ. 28, 1245–1247.
Wang, Y., Guo, M.L., Wang, X.K., Yin, J., 2008b. HPLC fingerprintsin seed of *Celosia argentea*. China J. Chinese Mater. Med. 33, 51–53.
Wang, Y., Lou, Z.Y., Wu, Q.B., Guo, M.L., 2010. Fitoterapia 81, 1246–1252.
Wang, Y.M., Yu, Y., Li, H.J., 2013. Assay of celosin I in *Celosiae Semen* by HPLC-ELSD. Chinese Tradit. Patent Med. 35, 1957–1961.
Weng, D.B., Wang, H.F., Cao, X.Z., Zhu, S.L., Huang, X.F., 1997. Analysis on fatty acids in some different species of *Celosia cristata* L. seed oil by gas chromatography. Acta Nutr. Sin. 19, 246–249.
Weng, D.B., Zhu, S.L., Huang, X.F., Wang, H.F., 1998. Study on *Celosia cristata* L. seed-analysis of fatty acid and report on the acute oral toxicity test. J. Nanjing Normal Univ. (Engineering and Technology Edition) 21, 64–69.
Wu, Q., 1987. Yi zong jin jian. Publishing House of Ancient Chinese Medical Books, Beijing, pp. 103.
Wu, Q., Wang, Y., Guo, M., 2011. Triterpenoid saponins from the seeds of *Celosia argentea* and their anti-inflammatory and antitumor activities. Chem. Pharm. Bull. 59, 666–671.
Wu, Q.B., Wang, Y., Liang, L., Jiang, Q., Guo, M.L., Zhang, J.J., 2013. Novel triterpenoid saponins from the seeds of *Celosia argentea* L. Nat. Prod. Res. 27, 1353–1360.
Xue, Q., Sun, Z.L., Guo, M.L., Wang, Y., Zhang, G., 2011. Two new compounds from *Semen Celosiae* and their protective effects against CCl_4-induced hepatotoxity. Nat. Prod. Res. 25, 772–780.
Xue, Q., Guo, M., Zhang, G., 2006. Study of chemical constituents of *Semen Celosia*. Pharm. Care Res. 6, 345–347.
Zhang, H.C., Zhang, T.T., Du, B., Cheng, D.Y., Li, Z.G., 2014. Chemical constituents of *Celosia cristata* L. Chinese Trad. Patent Med. 36, 122–125.
Zheng, Q.H., Cui, X., Zhou, P., Li, S.L., 1995. A comparative study of fatty acids and inorganic elements in *Semen Celosiae* and cockscomb. J. Chinese Med. Mat. 18, 466–467.
Zheng, Q.H., Cui, X., Zhou, P., Li, S.L., 1996. A comparative study of amino acids and inorganic elements in *Semen Celosiae* and cockscomb. J. Chinese Med. Mat. 19, 86–87.
Zheng, X.L., Wei, J.H., Sun, W., Li, R.T., Liu, S.B., Dai, H.F., 2013. Ethnobotanical study on medicinal plants around Limu Mountains of Hainan Island, China. J. Ethnopharmacol. 148, 964–974.
Zhu, D., Xu, Q., 2002. Analysis on fatty acid in *Celosia Argentea* L. seed oil by gas chromatography. Chinese J. J. jiangxi Normal University (natural sciences edition) 26, 110–112.