

MINI REVIEW



RECORDS OF PHARMACEUTICAL  
AND BIOMEDICAL SCIENCES



Minireview on terpenoids, flavonoids, and phenolic constituents with  
Biological Activity of *Chrysanthemum coronarium*

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Abstract

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Annual chrysanthemum, botanically known as *Chrysanthemum coronarium* L. (*Glebionis coronaria* L.), is an annual herbaceous plant with aromatic flavour which is popularly known as garland chrysanthemum or edible chrysanthemum belonging to the daisy family Asteraceae. *C. coronarium* is known in many parts of the world since it is widely distributed in the Mediterranean regions, Japan, China, and occasionally introduced and naturalized elsewhere. The plant has been used as a food ingredient, additive, beverage, and medicine in several countries since ancient times. *C. coronarium* is rich in beta-carotene, iron, potassium, calcium, dietary fibres, and various physiologically active secondary metabolites, including flavonoids, phenolic acids derivatives, terpenoids (sesquiterpenes lactone, diterpenes, monoterpenes), glycerides, phytosterols, polyacetylenes, anthraquinones and essential oils. Furthermore, biological studies revealed that *C. coronarium* possessed antioxidant, anti-inflammatory, anticancer, insecticidal, astringent, antimicrobial, antifungal, food production, immune-modulatory, nematocidal, anti-cholesterol, and anti-angiogenesis activities. In order to maximize the medicinal and nutritional benefits of *C. coronarium*, more research on the active ingredients in this plant is necessary. This is because the plant extract is unquestionably a good source of components that strengthen health and may be utilized for both nutritional and therapeutic purposes.

**Keywords:** *Chrysanthemum coronarium*, secondary metabolites, flavonoids, terpenoids, biological studies, antioxidant, anticancer.

**Introduction:**

Plants have been used in folk medicine since ancient times as pharmaceuticals and thought to provide nutritional powers for people (Zayyat *et al.*, 2018). Asteraceae, or generally known as an aster or crown daisy, is one of the most cultivated plant families that is commonly used for medicinal purposes. This family has more than 23,600 recognized species which further

spread into 13 subfamilies (Kuate, Victor, 2017). The genus *Chrysanthemum*, also called mums, is a well-known member of the Asteraceae family, representing one of the most ancient ornamentals and medicinal flowers cultivated in the world, and includes many important medicinal species such as *Chrysanthemum coronarium* (Hadizadeh *et al.*, 2022).

*Chrysanthemum coronarium* L. (Asteraceae family), is an annual herbaceous plant widely distributed in the Mediterranean regions, where it is cultivated for ornament, and it is elsewhere. *C. coronarium* (Table 1) is a glabrous or slightly hairy, with leaves oblong to obovate and florets yellow or ligules yellow at base and white distally (Basta *et al.*, 2007). Egyptian traditional medicine used *C. coronarium* in treatment of headaches, digestive disorders, and skin issues. Furthermore, in East Asia, the plant is consumed as a healthy vegetable and dietary food because the edible portion contains abundant nutrients and fresh flavour (Ibrahim *et al.*, 2007), (Elachouri *et al.*, 2023).

Previous studies investigated biological activities of essential oils and so non-volatile secondary metabolites of *C. coronarium*, the results showed antifungal, antiviral, antimycotic, nematocidal, anti-inflammatory, immunomodulatory, antibacterial, hypoglycemic, anti-hyperlipidemic, anticarcinogenic, insecticidal, mitogenic, astringent, dietary food, and antiangiogenic activities (Polatoğlu *et al.*, 2017). These activities could be linked to the plant's phytochemicals. These compounds reported were mainly terpenoids, flavonoids, and phenolic acids (Wan *et al.*, 2017), (Attard & Cuschieri, 2009)

**Table 1:** The systematic classification of *Chrysanthemum coronarium*

Phylum	Spermatophyta
Subphylum	Dicotyledonae
Subdivision	Angiospermae
Class	Dicotyledonae
Order	Asterales
Family	Asteraceae
Genus	<i>Chrysanthemum</i>
Species	<i>Chrysanthemum coronarium</i>

That could help to explain why this genus is used in medicine as well as food and we will focus on *C. coronarium*.

## 2- Chemical constituents reported in *C. coronarium*:

The chemical composition of *C. coronarium* was previously investigated and numerous secondary metabolites belonging to various chemical classes were reported, mainly terpenoids (sesquiterpene lactones, diterpenes, monoterpenes), flavonoids, and phenolic acids derivatives.

### 2. 1. Terpenoids

*Chrysanthemum coronarium* has been found to contain a new

sesquiterpene lactone, dihydrocucumbrin A, in addition to the known cucumbrin A (El-Masry *et al.*, 1984). Ha, Tae-Jung, *et al.* isolated thirteen sesquiterpene lactones from the flower of *C. coronarium* including 1-epi-dihydrochrysanolide, pyrethrosin, reynosin, and tigloyl-cucumbrin (Ha, Tae-Jung, 2003). Diterpene ent-kaurane-3 $\beta$ ,16 $\beta$ -diol was also separated from chloroform extract of the air-dried leaves of *C. coronarium* (Ragasa *et al.*, 1998). In addition, monoterpenes phytol and 8-hydroxy-linalol 8-*O*- $\beta$ -D-glucopyranoside, were isolated from MeOH extract of the aerial parts of *C. coronarium* (Song M. C. *et al.*, 2003), Table 2.

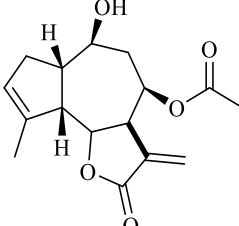
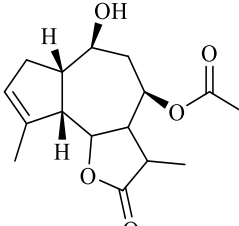
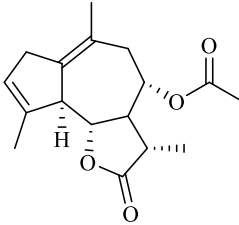
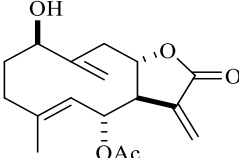
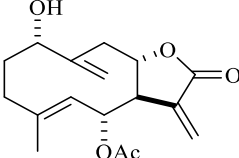
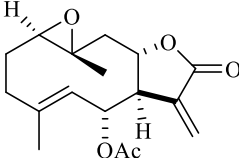
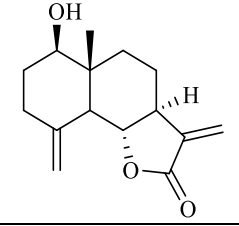
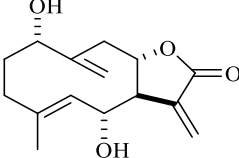
### 2. 2. Flavonoids

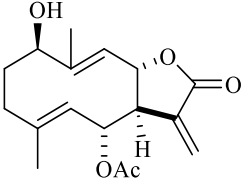
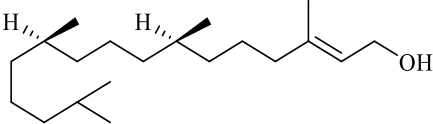
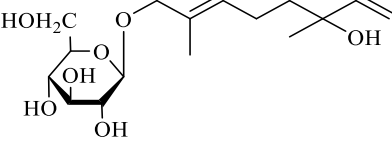
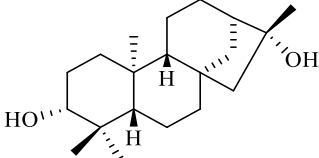
Nine flavonoid derivatives were isolated from the aqueous methanolic extract of the aerial parts of *C. coronarium*. Including apigenin, apigenin 7-*O*-glucoside, luteolin, luteolin 7-*O*-glucoside, kaempferol, kaempferol 3-*O*-glucoside, quercetin, quercetin 3-*O*-glucoside and naringenin 5-*O*-glucoside (Ibrahim *et al.*, 2007). Abd-alla *et al.* separated and identified five flavones, including 5,7-dihydroxy-3,6,4'-trimethoxy-flavone, scutellarin-6,7-dimethyl ether, 6-methoxy quercetin-7-*O*- $\beta$ -D-glucopyranoside, apigenin-7-*O*-[2''(6''-*O*- $\beta$ -D-acetylglucopyranosyl)]-6''-*O*-acetyl-glucopyranoside, and apigenin-7-*O*-(2''-*O*- $\beta$ -D-glucopyranosyl)- $\beta$ -D-glucopyranoside (Abd-alla *et al.*, 2014), Table 3.

### 2. 3. Phenolic Acids derivatives

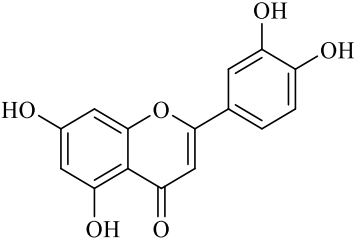
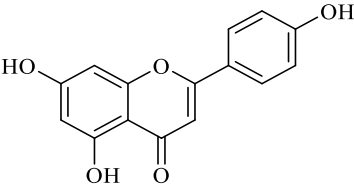
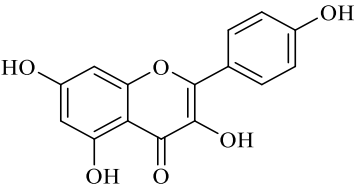
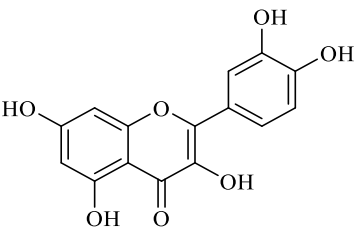
*C. coronarium* has been found to contain Quinic acid derivatives: 3,5-dicaffeoyl-4-succinylquinic acid, and 3,5-dicaffeoyl-quinic acid, were isolated from dried-leaves of *C. coronarium* (Chuda *et al.*, 1996). And seven caffeoylquinic acids were isolated from the aerial parts by Wan, Chunpeng, *et al.*, like 5-*O*-caffeoylquinic acid, 4-*O*-caffeoylquinic acid, 4,5-di-*O*-caffeoylquinic acid, and 3,4-di-*O*-caffeoylquinic acid (Wan *et al.*, 2017). The aerial parts of *C. coronarium* L. were extracted with MeOH, and gave methyl *trans*-ferulate, in addition to some well-known compounds (Song, M. C. *et al.*, 2003), Table 4.

Table 2: Terpenoids

Name	Structure	Reference
Cumambrin A		(El-Masry <i>et al.</i> , 1984)
Dihydrocumambrin A		(El-Masry <i>et al.</i> , 1984)
8 $\alpha$ acetoxy-11 $\beta$ ,13dihydrokauniolide		(Abdelgaleil <i>et al.</i> , 2020)
1-Epi- dihydrochrysanolide		(Lee <i>et al.</i> , 2003) (Ha, Tae-Jung, 2003)
Dihydrochrysanolide		(Lee <i>et al.</i> , 2003) (Ha, Tae-Jung, 2003)
Pyrethrosin		(Lee <i>et al.</i> , 2003)
Reynosin		(Lee <i>et al.</i> , 2003)
1 $\alpha$ -Hydroxy-1-desoxotamirin		(Lee <i>et al.</i> , 2003)

<b>Tulirinol</b>		<b>(Lee et al., 2003)</b>
<b>phytol</b>		<b>(Song M. C. et al., 2003)</b>
<b>8-hydroxylinalol 8-O-β-D-glucopyranoside</b>		<b>(Song M. C. et al., 2003)</b>
<b>ent-kaurane-3β,16β-diol</b>		<b>(Ragasa et al., 1998)</b>

**Table 3: Flavonoids**

<b>Name</b>	<b>Structure</b>	<b>Reference</b>
<b>Luteolin</b>		<b>(Ibrahim et al., 2007)</b>
<b>Apigenin</b>		<b>(Ibrahim et al., 2007)</b>
<b>Kaempferol</b>		<b>(Ibrahim et al., 2007)</b>
<b>Quercetin</b>		<b>(Ibrahim et al., 2007)</b>

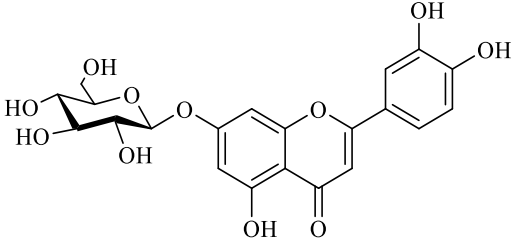
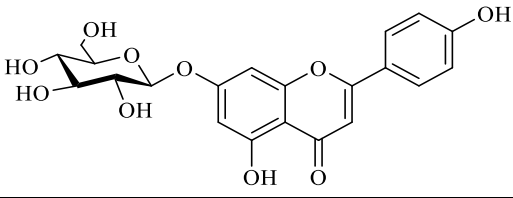
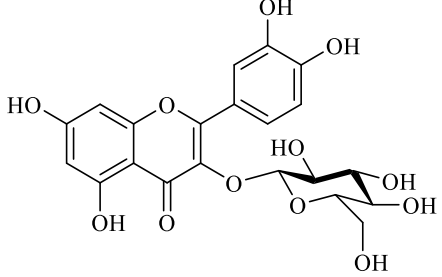
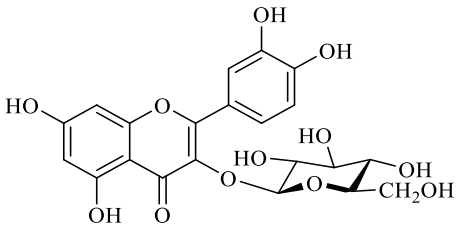
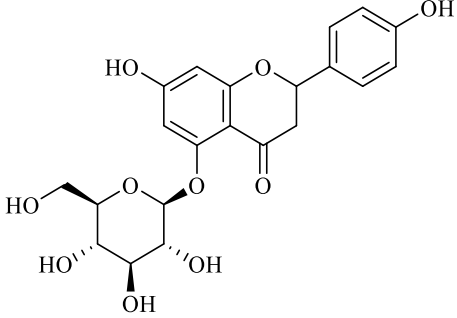
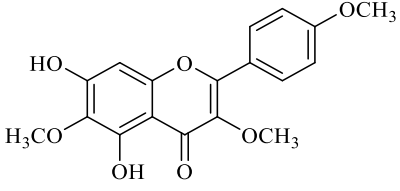
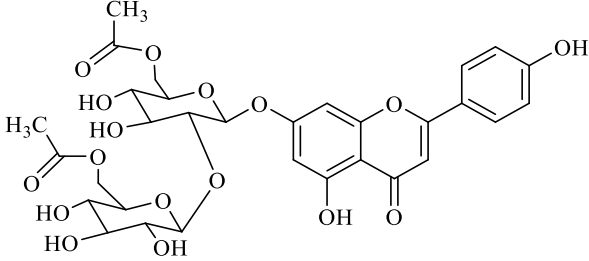
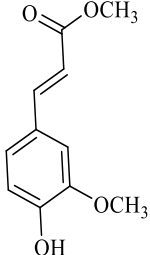
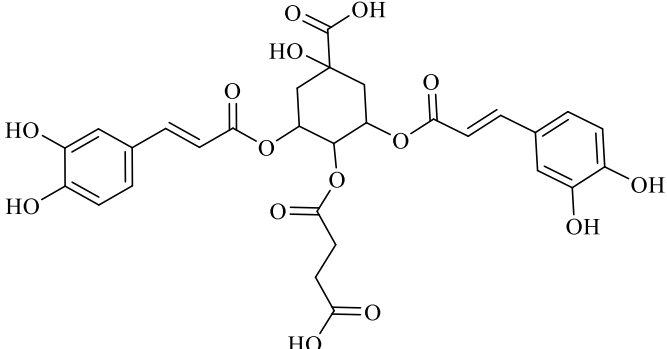
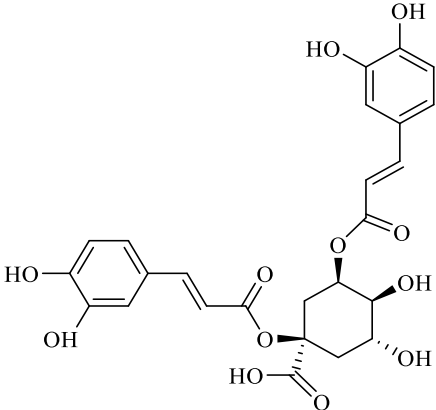
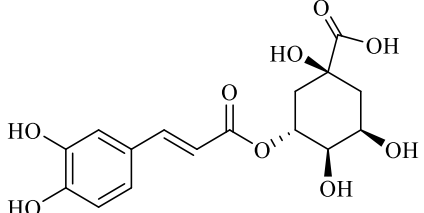
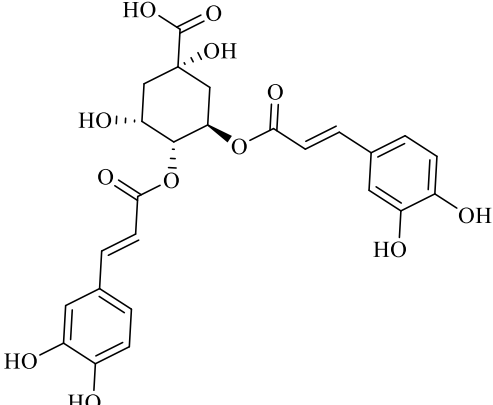
<p><b>Luteolin 7-O-glucoside</b></p>		<p>(Ibrahim <i>et al.</i>, 2007)</p>
<p><b>Apigenin 7-O-glucoside</b></p>		<p>(Ibrahim <i>et al.</i>, 2007)</p>
<p><b>Kaempferol 3-O-glucoside</b></p>		<p>(Ibrahim <i>et al.</i>, 2007)</p>
<p><b>Quercetin 3-O-glucoside</b></p>		<p>(Ibrahim <i>et al.</i>, 2007)</p>
<p><b>Naringenin 5-O-glucoside</b></p>		<p>(Ibrahim <i>et al.</i>, 2007)</p>
<p><b>5,7-dihydroxy-3,6,4'-trimethoxyflavone</b></p>		<p>(Abd-alla <i>et al.</i>, 2014)</p>
<p><b>Apigenin-7-O- [2'' (6'''-O-acetylglucopyranosyl)]-6''-O-acetylglucopyranoside</b></p>		<p>(Abd-alla <i>et al.</i>, 2014)</p>

Table 4: Phenolic acids derivatives

Name	Structure	Reference
<b>Methyl trans-ferulate</b>		<b>(Song <i>et al.</i>, 2008)</b>
<b>3,5-dicaffeoyl-4-succinylquinic acid</b>		<b>(Chuda <i>et al.</i>, 1996)</b>
<b>1,5-di-O-caffeoylquinic acid</b>		<b>(Wan <i>et al.</i>, 2017)</b>
<b>3-O-caffeoylquinic acid</b>		<b>(Wan <i>et al.</i>, 2017)</b>
<b>3,4-di-O-caffeoylquinic acid</b>		<b>(Wan <i>et al.</i>, 2017)</b>

### 3. Biological activities reported from *C. coronarium*:

Various studies proved the diverse bioactivities of *Chrysanthemum coronarium* as follows:

#### 3. 1. Antioxidant activities

Study using DPPH assay revealed the ethyl acetate extract possess the highest activity rather than the chloroform and total extracts of *C. coronarium* (Donia, 2014). Mahdi and coworkers tested the antioxidant activity of *C. coronarium* and found that aqueous or methanolic solvents were more effective at extracting bioactive compounds with potent antioxidant properties from leaves or other parts of *Glebionis coronaria* (*C. coronarium*) plants than petroleum ether. (Mahdi *et al.*, 2023). During comparison between different solvent extracts using DPPH, ABTS and Fe<sup>+3</sup>-reducing power test, the results showed that the methanolic and ethanolic extract had higher antioxidant activity value than the other extracts (Belhachat *et al.*, 2023)

#### 3. 2. Antibacterial

Based on an investigation by Ivaschenko (2017), the ethanolic extract of *C. coronarium* exerted an antibacterial effect against *Staphylococcus aureus* bacteria. This effect was suggested to be strongly correlated with the essential oil and phenol content in the plant (Ivashchenko, 2017). Mahdi *et al.* used agar well diffusion method to screen the antibacterial activity of *C. coronarium* extracts. It was observed that water and methanolic extracts inhibited the growth of *Listeria monocytogenes*, *Bacillus cereus* and *Staphylococcus epidermidis*. However, petroleum ether extracts did not show any antibacterial effect against the investigated bacterial species (Mahdi *et al.*, 2023). The essential oil of *C. coronarium* exhibited a good antimicrobial activity against the gram-positive bacteria *Bacillus cereus* and *Staphylococcus aureus* and its potency was qualitatively assessed by the presence or absence of inhibition zones and zone diameter (Hosni *et al.*, 2013).

#### 3. 3. Anticancer

Three isolated sesquiterpene lactones: 1 $\alpha$ -Hydroxy-1-desoxotamirin, Dihydrochrysa-nolide and 1-Epi-dihydrochrysanolide were examined for their in vitro cytotoxic against A549, PC-3, and HCT-15 cell lines. The obtained IC<sub>50</sub> showed that the plant exhibited promising cytotoxic activity against A549, PC-3, and HCT-15 cell lines (Lee *et al.*, 2002). A study by Bardaweel *et al.* reported that the essential oil of *C. coronarium* exhibited anticancer properties on human breast cancer (MCF-7), human ductal breast epithelial tumor (T47D), human colon adenocarcinoma (Caco-2), as well as human epithelial carcinoma (HeLa) (Bardaweel *et al.*, 2015). The methanol extract of the aerial parts of *C. coronarium*, at concentration range of 25 to 400  $\mu$ g/mL, significantly inhibited (10– 50 %) the proliferation of

six human tumor cell lines, A375.S2 (IC<sub>50</sub> = 127.6  $\mu$ g/mL), WM1361A (IC<sub>50</sub> = 75.7  $\mu$ g/mL), CACO-2 (IC<sub>50</sub> = 106.4  $\mu$ g/mL), HRT18 (IC<sub>50</sub> = 123.2  $\mu$ g/mL), MCF-7 (IC<sub>50</sub> = 138.5  $\mu$ g/mL), and T47 (IC<sub>50</sub> = 79.8  $\mu$ g/mL) (Abu-Rish *et al.*, 2016)

#### 3. 4. Hepatoprotective, Reno-protective, and Gastroprotective activities

An *in vivo* experiment conducted by Donia (2017), evidenced the hepatoprotective of *C. coronarium* against tetrachloromethane (CCl<sub>4</sub>) intoxication in rats. The plant reduced the elevated serum levels of liver marker enzymes ALT, AST, total bilirubin, total protein, and albumin (Donia, 2014). Kim and his team examined the renoprotective effect of *C. coronarium* in experimental animals. The results showed that the plant extract attenuated adenine - induced renal injury and might offer a new option as a renoprotective agent or functional food supplement to manage chronic kidney disease (CKD) (Kim *et al.*, 2023). A recent study concluded that *C. coronarium* leaves could be a promising food for the protection of the gastric mucosa against ethanol-induced lesions. This study revealed that the methanolic extract of the plant decreased total and free gastric acidity (53.80 $\pm$ 7.038 and 17.8 $\pm$ 2.375 respectively) for the 500 mg/kg dose of *C. coronarium* and (60.40 $\pm$ 4.490 and 24.8 $\pm$ 1.855 respectively) for the 250 mg/kg dose of the plant extract (Belmamoun *et al.*, 2024)

#### 3. 5. Insecticidal

The methanolic extract of *C. coronarium* leaves and flowers were investigated separately as insecticidal on the confused flour beetle *Tribolium confusum* through toxicity by ingestion. The obtained findings demonstrated that the flower extract had a significant insecticidal effect greater than those of leaves extract. These results were based on a considerable mortality rate (91%), after giving methanol extract for 14 days. This effect is most likely caused by the proliferation of toxic sesquiterpenes in flower heads of *Chrysanthemum* species (Haouas *et al.*, 2008). Another study by Haouas *et al.* investigated the potency of the essential oil isolated from *C. coronarium* on *Tribolium confusum* pupae. Obtained results showed that the tested essential oils have an effective insecticidal activity (Haouas *et al.*, 2013). A recent study suggested that the high insecticidal activity of the *Chrysanthemum* species could be elaborated by the collective synergistic effect of the phyto-chemical compounds present in

the oil, such as santolinatriene, camphor, yomogi alcohol, bornyl acetate, cis-chrysanthenyl acetate, and hexadecan-oic acid (Polatoğlu *et al.*, 2017).

### 3. 6. Anti-cholesterol

Methyl *trans*-ferulate isolated from *C. coronarium* was evidenced to be effective as anti-hypercholesterolemia and atherosclerosis due to the inhibition activity of hACAT-1, hACAT-2, and LDL-oxidation (Song *et al.*, 2008). Abd-Alla research team reported the therapeutic value of petroleum ether, ethyl acetate, and methanol extracts of *C. coronarium* in the management of hypercholesterolemia in rats. Their results showed that the ethyl acetate and methanol extracts have remarkable results more than the petroleum ether of the plant (Abd-alla *et al.*, 2014).

### 3. 7. Dietary Food

*C. coronarium* has also been used as dietary food products, as it has been reported to contain a low amount of fat, but a high amount of protein, carbohydrates, and vitamin C (Ivashchenko *et al.*, 2019). Also, the same study mentioned that *C. coronarium* contained calcium which play a role in the skeleton formation, coagulation of blood and muscles concentration.

## 4. Conclusion:

*C. coronarium* are growing all over the world. It is used in folk medicine for treatment of different disease. Here we just report a brief review for the chemical constituent and biological activity of the plant.

## 5. conflict of interest

The authors report no declaration of conflict of interest.

## 6. References

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