REVIEW ARTICLE

RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

# Chemistry and biological activities of *Cichorium endivia:* A mini review

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## Abstract

*Cichorium endivia* L. is a wild edible plant and widely distributed in the Mediterranean region. Traditionally, it had been used to relief of mild digestive disorders symptoms such as flatulence, feeling of abdominal fullness, and slow digestion, and loss of appetite. It is a bitter-leafed vegetable with simple, alternate and sessile leaves forming an inflorescence. Recently, *C. endivia* gained attention because of its therapeutic and biological activities such as antimicrobial, hepatoprotective, antioxidant and antiproliferative. In this review, we summarize the most important chemical constituents and biological activities *C. endivia*.

**Keywords:** *Cichorium endivia; chemical constituents; biological activities.*

## 1. Introduction:

*Cichorium endivia* L. subsp. *Pumilum* Jacq., (Arabic name: Shikorya or Sereis), commonly known as chicory, is a wild edible plant and belongs to family Asteraceae. It is a bitter-leafed vegetable with simple, alternate and sessile leaves forming an inflorescence. Additionally, the leaves are slightly pubescent, pale to dark green, sometimes reddish along midrib and the flowers are blue **(Figure 1) (Aisa *et al*., 2020)**.

It is widely distributed in the Mediterranean region and cultivated in many countries in Asia, Europe and North America **(Khalil & Kamel, 2015; Amer, 2018).** *C. endivia* L. is valuable nutritionally with a high content of vitamin C, minerals and dietary fibres **(Kopeck, 1998; Koudela & Petříková, 2007).** So that, it sometimes used as a vegetable in salad and in the traditional folklore was used to relief of mild digestive disorders symptoms such as flatulence, feeling of abdominal fullness, and slow digestion, and loss of appetite **(Masoud *et al.*, 2018)**. In addition, it is famous among the Egyptian farmers and is preferred to be eaten with cheese as a common Egyptian meal **(Abou-Zeid, 2015; Masoud *et al.*, 2018).** Furthermore, leaves decoction was used for poisoning, bacterial infection, rheumatism **(Azaizeh *et al.*, 2006)** and diabetes **(Al Khateeb *et al.*, 2012)**.

*C. endivia* L. showed many biological activities such as antimicrobial **(Amer, 2018)**, hepatoprotective, **(Chen *et al*., 2011),** antioxidant **(Papetti *et al*., 2002)** and antiproliferative **(Wang *et al*., 2012; Alshehri & Elsayed, 2012)**.

Phytochemical investigation of *C. endivia* L. revealed presence of many bioactive compounds, such as flavonoids **(Saleh *et al*., 1975; Mascherpa *et al*., 2012; Hegazy *et al.*, 2015**) coumarins **(Khalil and Kamel, 2015)**, Sesquiterpenes and their glycosides **(Seto *et al.*, 1988; Kisiel and Michalska, 2003)**, phenolic acids **(Kisiel and Michalska, 2006; Papetti *et al*., 2008)** and nitrogenous compounds **(Chen *et al*., 2011; Wang *et al*., 2012; Aisa *et al*., 2020)**.

## 2. Phytochemical constituents reported in *Cichorium endivia L.*:

A review on the phytochemical compounds and the pharmacological activities of *Cichorium endivia* L. was done and it revealed that the chemical compounds isolated and identified from the *C. endivia* belong to various chemical classes including sterols, triterpenes, sesquiterpenes, flavonoids, phenolic and organic acids, phenolic glycosides, coumarins, nitrogen containing compounds along with many other miscellaneous compounds as summarized in the tables **(1-7)**.

### Table 1: Sterols and triterpenoids:

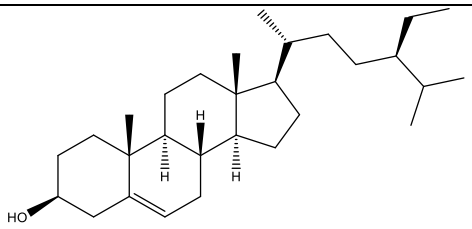
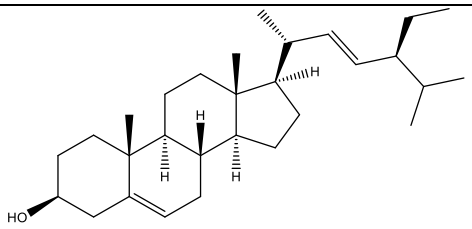
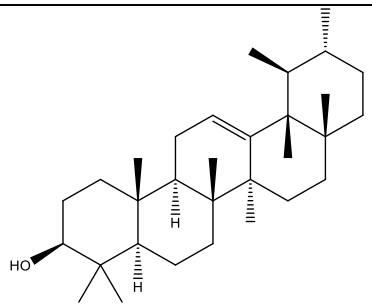
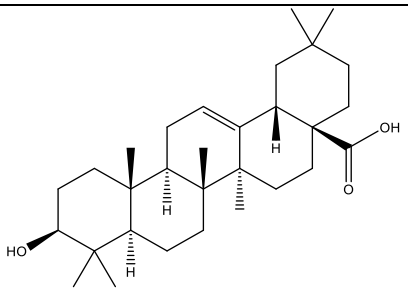
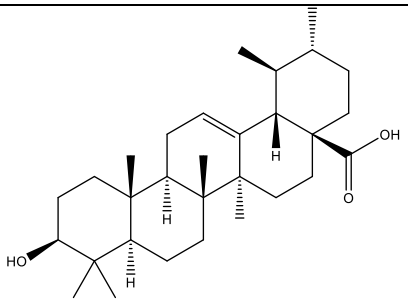
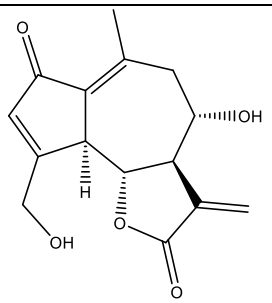
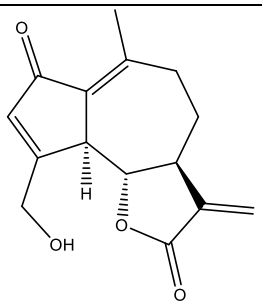
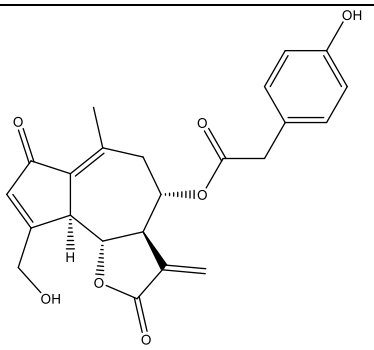
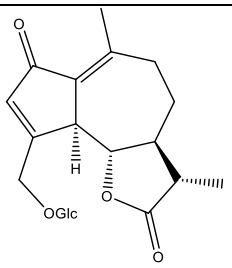
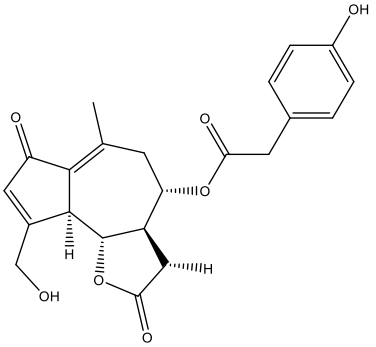
| Compound Name | Compound Structure | Reference |
|---|---|---|
| β-Setosterol |  | **(Hegazy *et al*., 2015)** |
| Stigmasterol |  | **(Hegazy *et al*., 2015)** |
| α-Amyrin |  | **(Hegazy *et al*., 2015)** |
| Oleanolic acid |  | **(Hegazy *et al*., 2015)** |
| Ursolic acid |  | **(Hegazy *et al*., 2015)** |

**Table 2: Sesquiterpenes:**

| Compound Name | Compound Structure | Reference |
|---|---|---|
| Lactucin |  | **(Seto *et al*., 1988)** |
| 8-deoxylactucin |  | **(Seto *et al*., 1988)** |
| Lactucopicrin |  | **(Seto *et al*., 1988)** |
| 11β, 13- dihydrolactucin |  | **(Seto *et al*., 1988)** |
| 11β, 13- dihydrolactucopicrin |  | **(Kisiel and Michalska, 2006)** |

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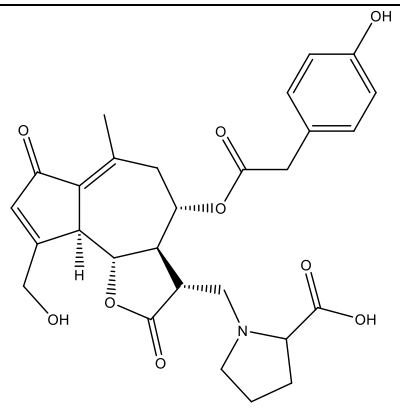
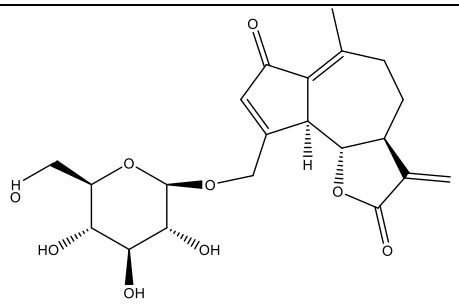
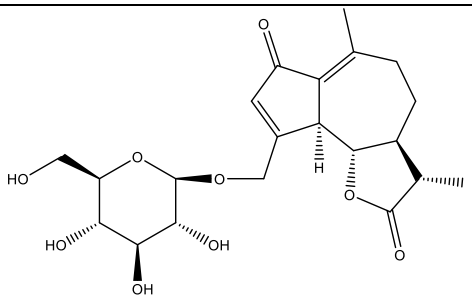
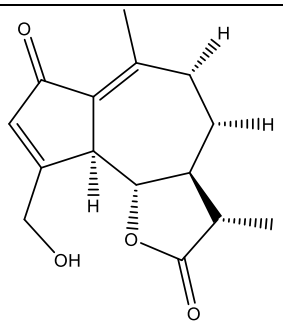
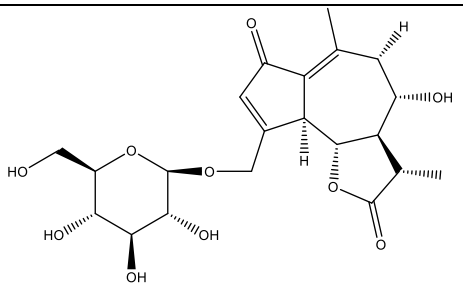
|---|---|---|
| 11 β,13-Dihydro-13-prolyl-lactucopicrin |  | **(Warashina and Miyase, 2008)** |
| Crepidiaside A |  | **(Seto *et al*., 1988)** |
| Crepidiaside B |  | **(Seto *et al*., 1988)** |
| Jacquinelin |  | **(Warashina and Miyase, 2008)** |
| Cichorioside B |  | **(Warashina and Miyase, 2008)** |

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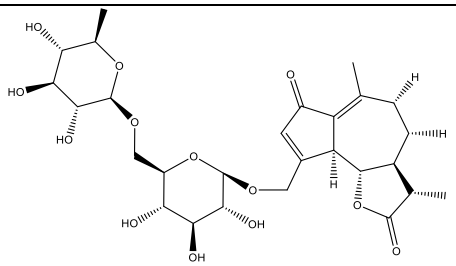
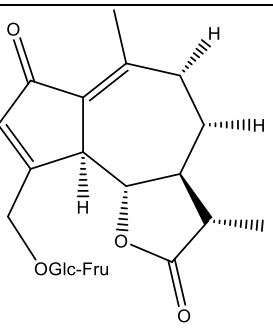
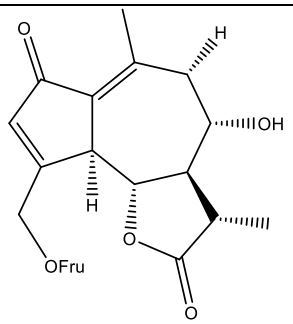
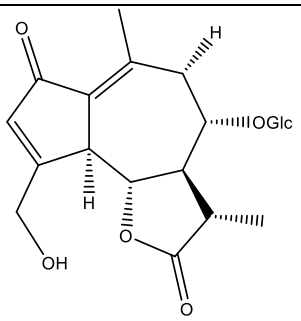
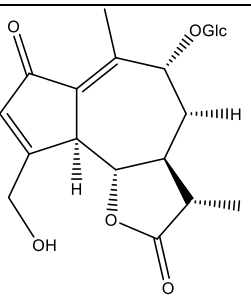
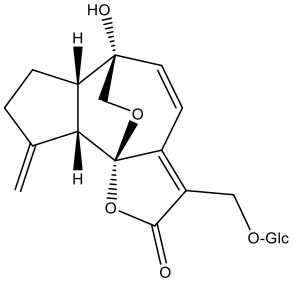
|---|---|---|
| Cichorioside D |  | **(Warashina and Miyase, 2008)** |
| Cichorioside E |  | **(Warashina and Miyase, 2008)** |
| Cichorioside F |  | **(Warashina and Miyase, 2008)** |
| Cichorioside G |  | **(Warashina and Miyase, 2008)** |
| Cichorioside H |  | **(Warashina and Miyase, 2008)** |
| Cichorioside J |  | **(Warashina and Miyase, 2008)** |

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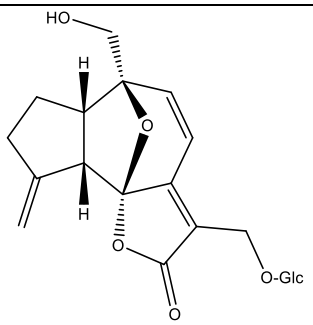
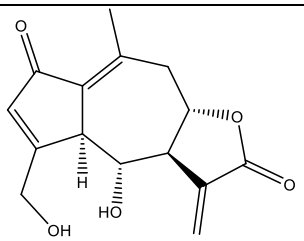
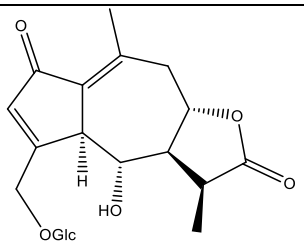
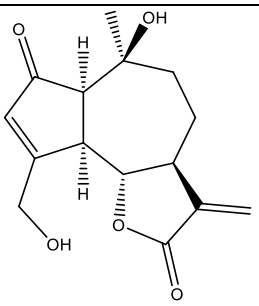
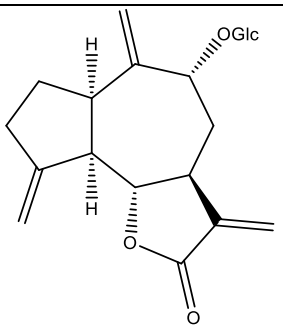
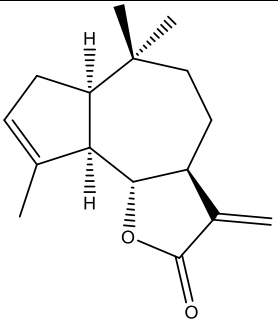
|---|---|---|
| Cichorioside K |  | **(Warashina and Miyase, 2008)** |
| Intybulide |  | **(Kisiel and Michalska, 2006)** |
| Cichorioside I |  | **(Warashina and Miyase, 2008)** |
| Hieracin II |  | **(Kisiel and Michalska, 2006)** |
| Ixerisoside D |  | **(Kisiel and Michalska, 2006)** |
| Macrocliniside G |  | **(Kisiel and Michalska, 2006)** |

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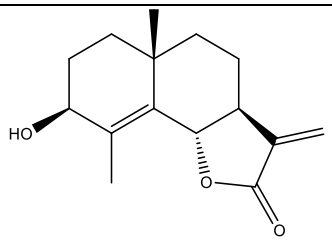
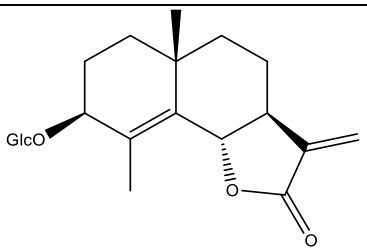
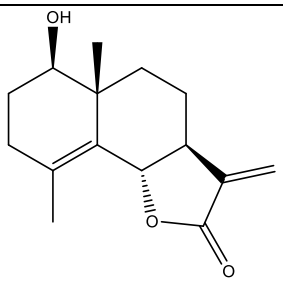
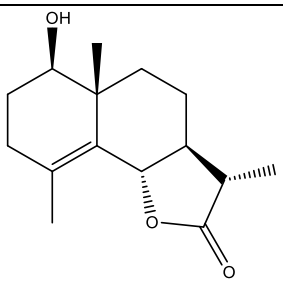
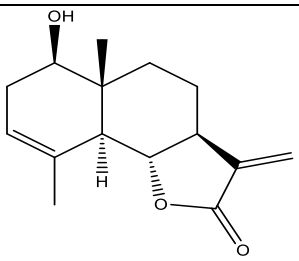
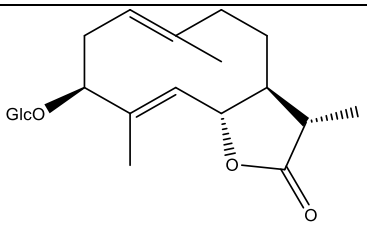
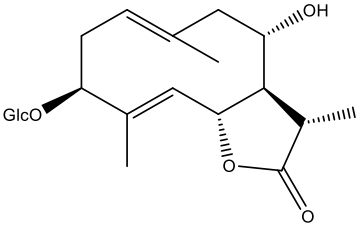
|---|---|---|
| Cichoriolide A |  | **(Seto *et al*., 1988)** |
| Cichorioside A |  | **(Seto *et al*., 1988)** |
| Magnolialide |  | **(Kisiel and Michalska, 2006)** |
| Artesin |  | **(Kisiel and Michalska, 2003)** |
| Santamarine |  | **(Kisiel and Michalska, 2003)** |
| Sonchuside A |  | **(Seto *et al*., 1988)** |
| Cichorioside C |  | **(Warashina and Miyase, 2008)** |

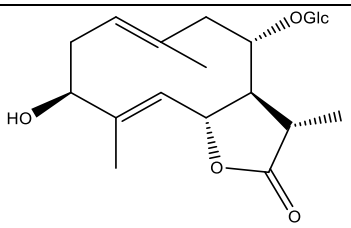
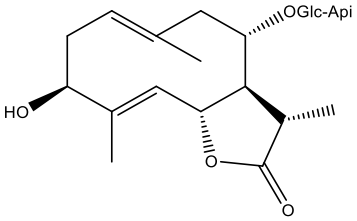
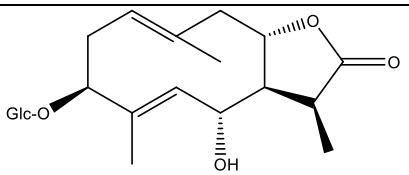
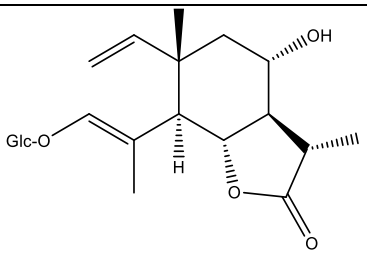
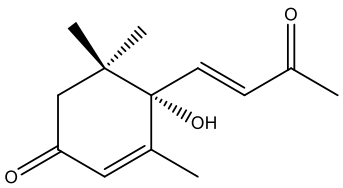
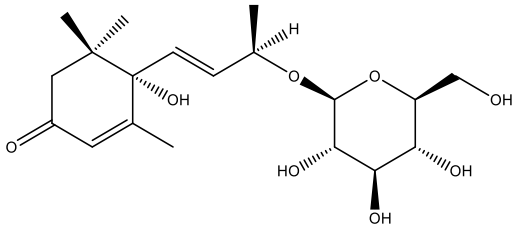
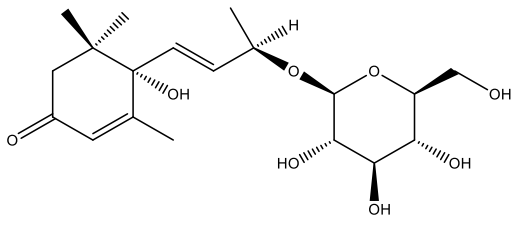
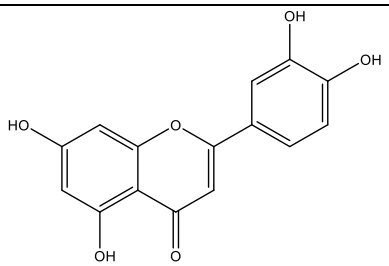
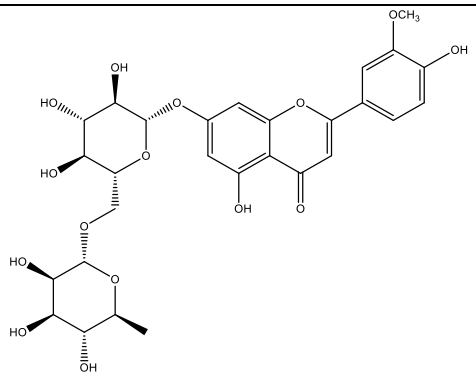
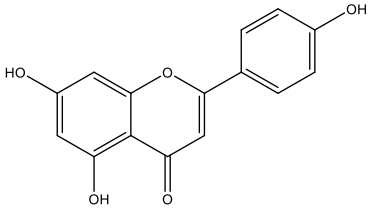
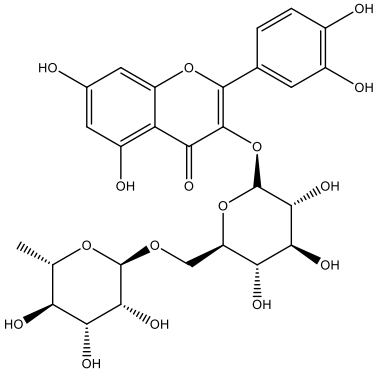
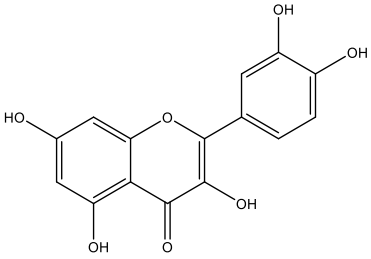
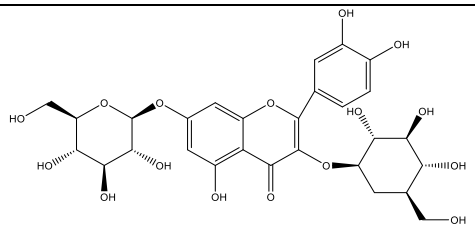
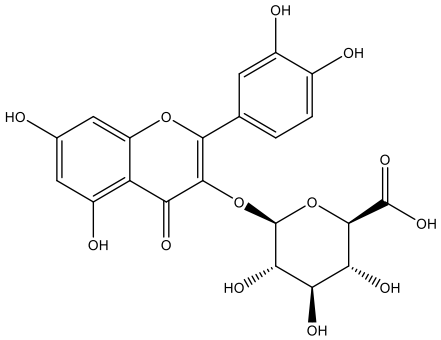
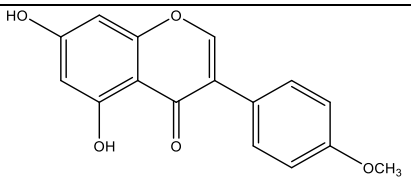
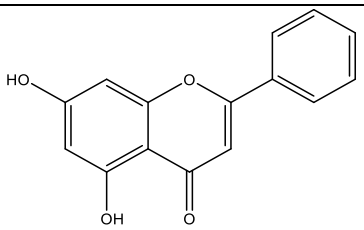
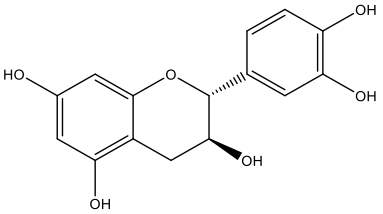
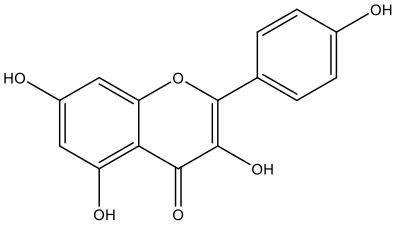
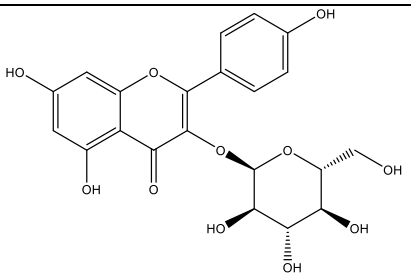
| | | |
|---|---|---|
| Hypochoeroside A |  | **(Warashina and Miyase, 2008)** |
| Cichorioside L |  | **(Warashina and Miyase, 2008)** |
| Cichorioside M |  | **(Warashina and Miyase, 2008)** |
| Cichorioside N |  | **(Warashina and Miyase, 2008)** |
| (6S, 7E)-6-hydroxy-4,7-megastigmadien-3,9-dione (S (+)-dehydrovomifoliol |  | **(Kisiel *et al.*, 2004)** |
| (6S, 7E, 9R)-6,9-dihydroxy-4,7-megastigmadien-3-one 9-O-b-glucopyranoside (roseoside) |  | **(Kisiel *et al.*, 2004)** |
| (6S, 7E, 9S)- 6,9-dihydroxy-4,7-megastigmadien-3-one 9-O-b-glucopyranoside (diastereomer) |  | **(Kisiel *et al.*, 2004)** |

**Table 3: Flavonoids*:***

| Compound Name | Compound Structure | Reference |
|---|---|---|
| Luteolin |  | **(El-Shafey and AbdElgawad, 2012)** |
| Luteolin-3'-methoxy-7-rutinoside |  | **(Hegazy *et al*., 2015)** |
| Apigenin |  | **(Hegazy *et al*., 2015)** |
| Rutin |  | **(Hegazy *et al*., 2015)** |
| Quercetin |  | **(Hegazy *et al*., 2015)** |

| | | |
|---|---|---|
| Quercetin-3,7-di-O-glucoside |  | **(Mascherpa *et al*., 2012)** |
| Quercetin-monoglucuronide |  | **(Mascherpa *et al*., 2012)** |
| 5,7-dihydroxy 4'-methoxy isoflavone |  | **(Hegazy *et al*., 2015)** |
| Chrysin |  | **(Hegazy *et al*., 2015)** |
| Catechin |  | **(Hegazy *et al*., 2015)** |
| Kaempferol |  | **(Chen *et al*., 2011)** |
| Kaempferol-3-O-β-D-glucoside (Astragalin) |  | **(Chen *et al*., 2011)** |

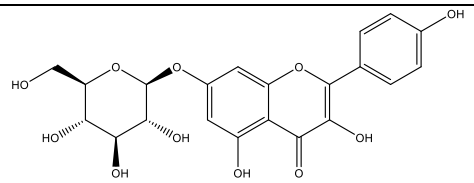
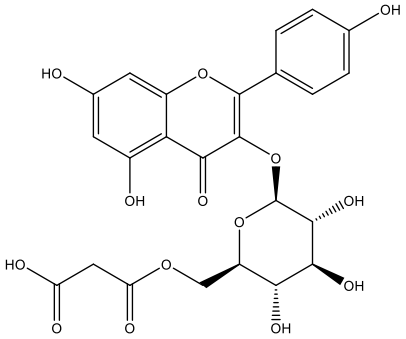
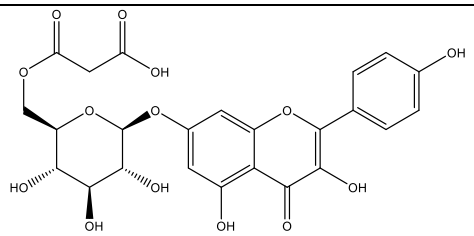
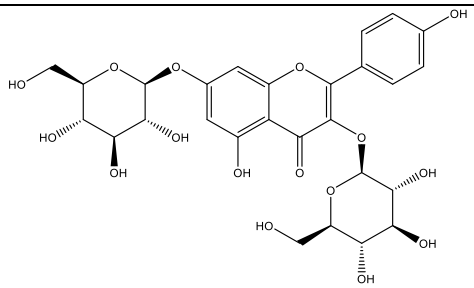
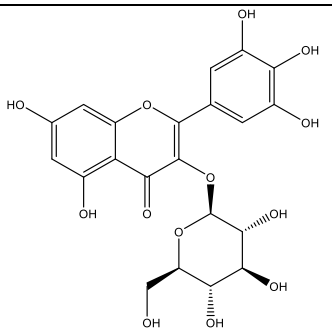
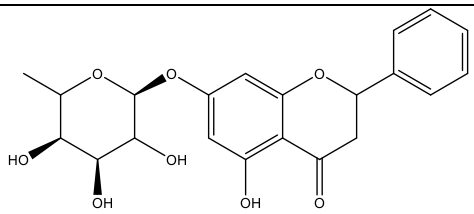
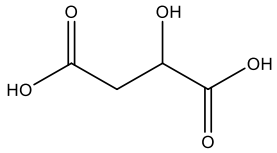
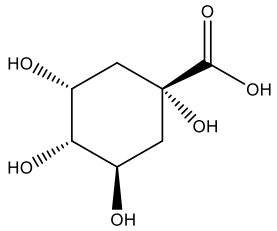
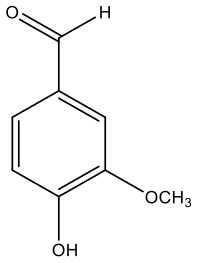
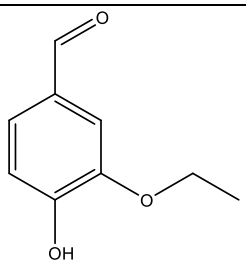
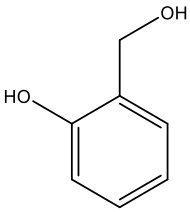
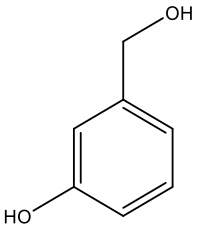
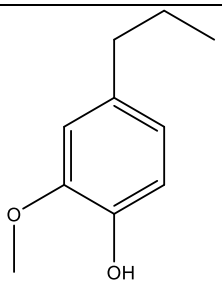
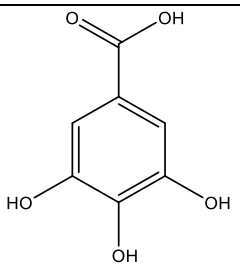
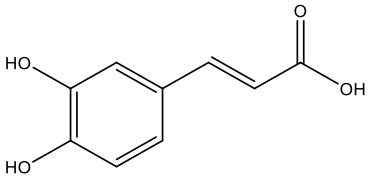
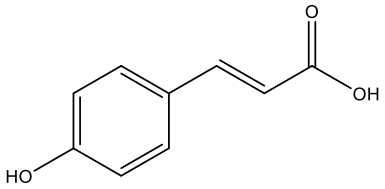
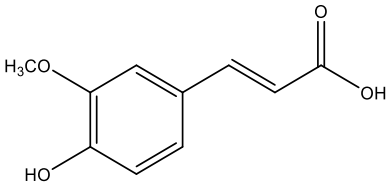
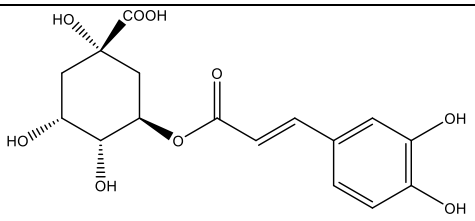
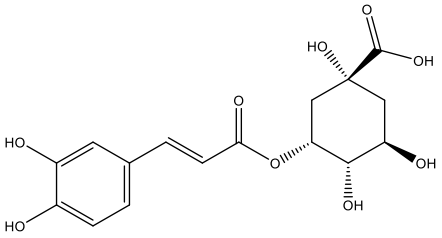
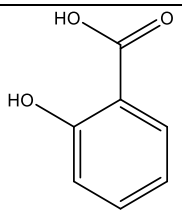
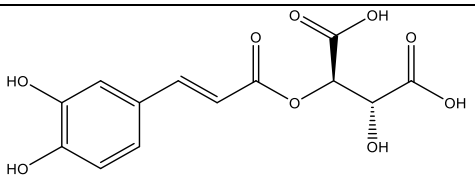
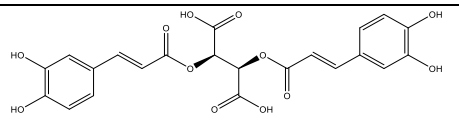
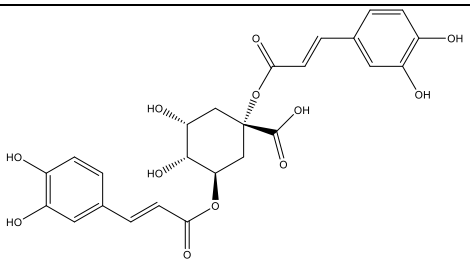
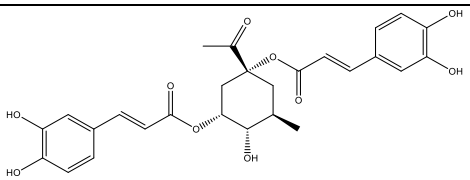
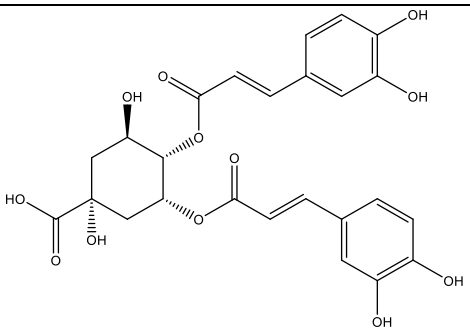
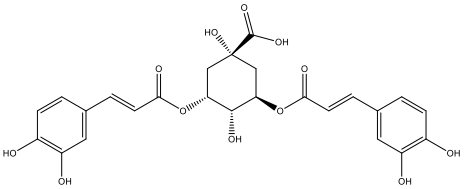
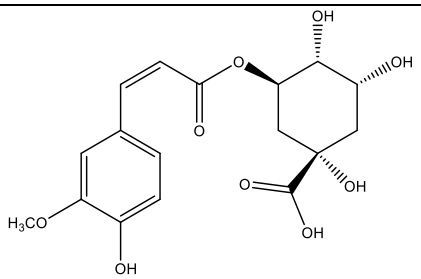
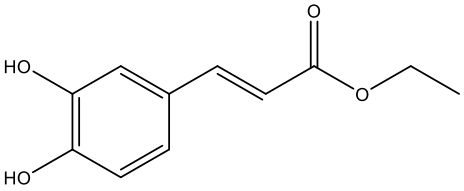
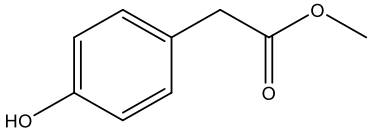
| | | |
|---|---|---|
| Kaempferol-7-O-glucoside |  | **(Mascherpa *et al.*, 2012)** |
| Kaempferol-3-O-(6″-malonyl)-glucoside |  | **(Mascherpa *et al.*, 2012)** |
| Kaempferol-7-O-(6″-malonyl)-glucoside |  | **(Mascherpa *et al.*, 2012)** |
| Kaempferol-O-diglucoside |  | **(Mascherpa *et al.*, 2012)** |
| Myricetin-3-O-glucoside |  | **(Mascherpa *et al.*, 2012)** |
| Pinocembrin-O-rhamnoside |  | **(Mascherpa *et al.*, 2012)** |

**Table 4: Organic and phenolic acids and their derivatives:**

| 1. **Compound Name** | **Compound Structure** | **Reference** |
|---|---|---|
| Malic acid |  | **(Mascherpa *et al*., 2012)** |
| Quinic acid |  | **(Mascherpa *et al*., 2012)** |
| Vanillin |  | **(Hegazy *et al*., 2015)** |
| Ethyl vanillin |  | **(Enk *et al*., 2004)** |
| Salicyl alcohol |  | **(Enk *et al*., 2004)** |
| ٣-hydroxy benzenemethanol |  | **(Enk *et al*., 2004)** |
| Dihydroeugenol |  | **(Enk *et al*., 2004)** |

| | | |
|---|---|---|
| Gallic acid |  | **(Hegazy *et al*., 2015)** |
| Caffeic acid |  | **(Mascherpa *et al*., 2012)** |
| *p*-Coumaric acid |  | **(Hegazy *et al*., 2015)** |
| Ferulic acid |  | **(Hegazy *et al*., 2015)** |
| Chlorogenic acid (3-caffeoylquinic) |  | **(Hegazy *et al*., 2015)** |
| 5-caffeoylquinic (5-CQA) (Neochlorogenic acid) |  | **(Mikropoulou *et al*., 2018)** |
| Salicylic acid |  | **(Hegazy *et al*., 2015)** |
| trans-caftaric acid |  | **(Mascherpa *et al*., 2012)** |

| | | |
|---|---|---|
| Chicoric acid |  | **(Mascherpa *et al*., 2012)** |
| 1,3-dicaffeoylquinic acid |  | **(Mascherpa *et al*., 2012** |
| 1,5-di-O-caffeoylquinic acid |  | **(Singab *et al*., 2010)** |
| 3,4-dicaffeoylquinic acid |  | **(Papetti *et al*., 2008)** |
| 3,5-Di-O-caffeoylquinic acid |  | **(Papetti *et al*., 2008)** |
| 5-feruloylquinic acid |  | **(Mascherpa *et al*., 2012)** |
| Ethyl trans-caffeate |  | **(Kisiel and Michalska, 2006)** |
| Methyl p-hydroxyphenylacetate |  | **(Kisiel and Michalska, 2006)** |

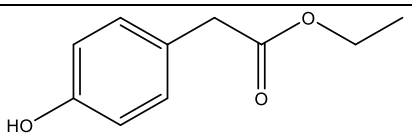
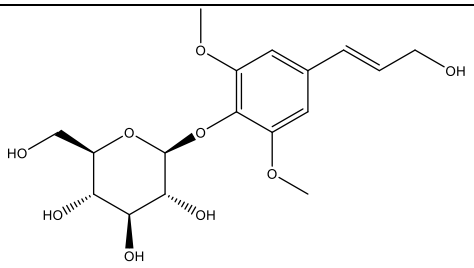
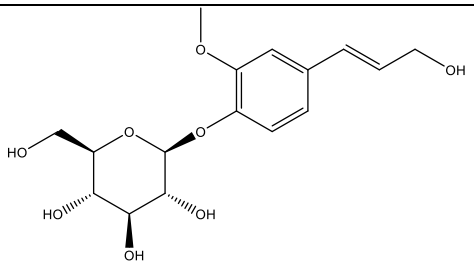
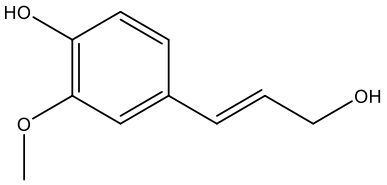
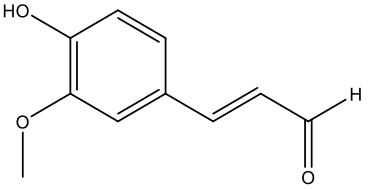
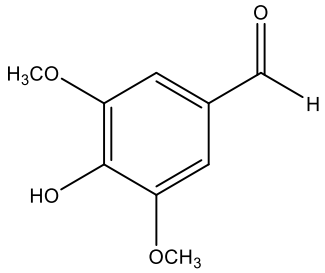
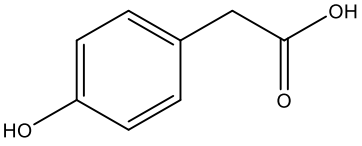
| | | |
|---|---|---|
| Ethyl p-hydroxyphenylacetate |  | **(Kisiel and Michalska, 2006)** |
| Syringin |  | **(Kisiel and Michalska, 2003)** |
| Coniferin |  | **(Kisiel and Michalska, 2003)** |
| Coniferyl alcohol |  | **(Kisiel and Michalska, 2003)** |
| Coniferyl aldehyde |  | **(Kisiel and Michalska, 2003)** |
| Syringaldehyde |  | **(Kisiel and Michalska, 2003)** |
| 4-Hydroxy phenyl acetic acid |  | **(Khalil and Kamel, 2015)** |

**Table 5: Coumarins:**

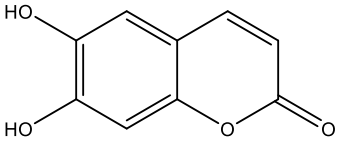
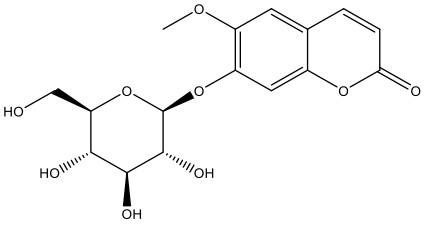
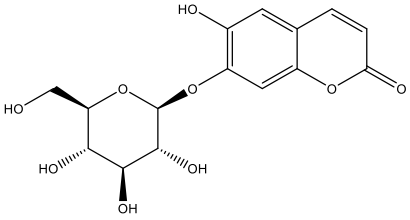
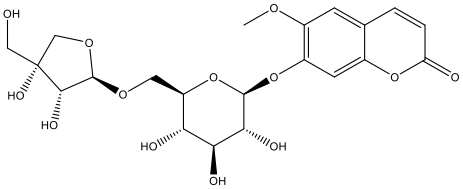
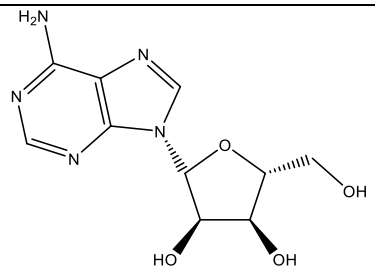
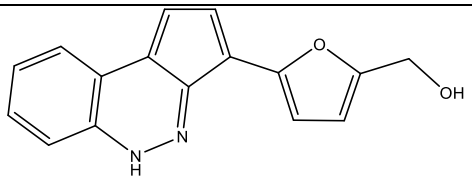
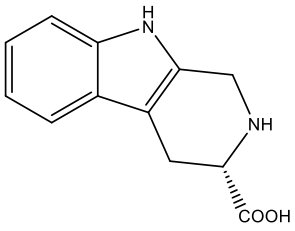
| Compound Name | Compound Structure | Reference |
|---|---|---|
| Aesculetin |  | **(Singab *et al*., 2010)** |
| Scopolin |  | **(Khalil and Kamel, 2015)** |
| Cichoriin |  | **(Khalil and Kamel, 2015)** |
| Hymexelsin |  | **(Khalil and Kamel, 2015)** |

**Table 6: Nitrogen containing compounds:**

| Compound Name | Compound Structure | Reference |
|---|---|---|
| Adenosine |  | **(Chen *et al*., 2011)** |
| 2-furanmethanol-(5'→11)-1,3-cyclopentadiene-[5,4-c]-1H-cinnoline |  | **(Chen *et al*., 2011)** |
| (3S)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid |  | **(Wang *et al*., 2012)** |

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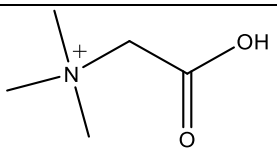
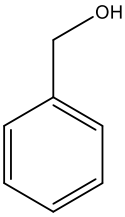
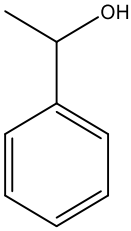
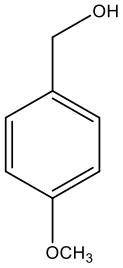
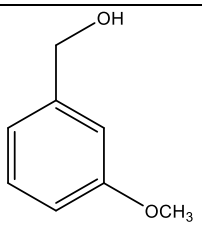
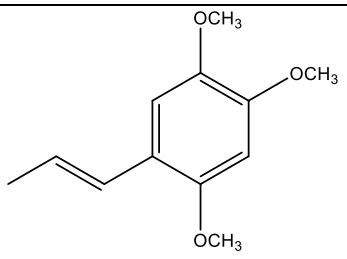
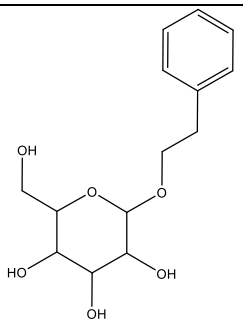
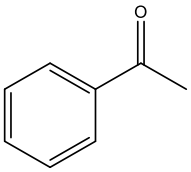
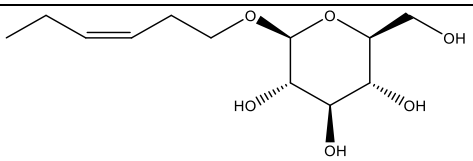
|---|---|---|
| Betaine |  | **(Aisa *et al*., 2020)** |

**Table 7: Other miscellaneous compounds*:***

| Compound Name | Compound Structure | Reference |
|---|---|---|
| Benzyl alcohol |  | **(Enk *et al*., 2004)** |
| Phenylethyl alcohol |  | **(Enk *et al*., 2004)** |
| *p*-anisyl alcohol |  | **(Enk *et al*., 2004)** |
| *m*-anisyl alcohol |  | **(Enk *et al*., 2004)** |
| *cis*-asaron |  | **(Enk *et al*., 2004)** |

| | | |
|---|---|---|
| 2-phenylethyl-β-D-glucopyranoside |  | **(Chen *et al*., 2011)** |
| Acetophenone |  | **(Schmidt and Schreier, 1986)** |
| z-3-Hexenyl-β-D-glucoside |  | **(Khalil and Kamel, 2015)** |

## 3. Biological activities reported in *Cichorium endivia L.*:

Studies on Cichorium endivia L. revealed that it possesses a wide range of biological activities including anti-oxidant, antimicrobial, insecticidal, anthelmintic anti-Blastocystis, anti-diabetic antihyperglycemic, antihyperlipidemic, anti-inflammatory, antiangiogenic and cytotoxic activities as summarized in Table 8.

**Table 8: Biological activities reported in *Cichorium endivia* L.:**

| **I- Anticancer activity** | | |
|---|---|---|
| **Active Compounds / extracts** | **Details** | **Reference** |
| 3S-1,2,3,4-tetrahydro β-carboline-3-carboxylic acid | Remarkable *in-vitro* cytotoxicity against HCT-8 and HepG2 cell-lines. | **(Wang et al., 2012)** |
| Hydro-ethanolic extract | Significant *in-vivo* protective effect of sun light-activated extract against the dimethylbenz[a]anthracene (DMBA) induced benign breast tumors to female rats by reducing the lobular hyperplasia and fibroadenoma induced in the mammary glands. | **(Al-Akhras *et al*., 2012)** |
| 3S-1,2,3,4-tetrahydro β-carboline-3-carboxylic acid | Significant *in-vivo* anti-proliferative effect on human Colorectal Cancer cell line HCT-8, and induction of apoptosis of HCT-8 cells via the suppression of NF-κB signaling pathway in a dose-dependent manner. | **(Wang et al., 2012)** |
| Methanolic root extract | Polyphenolic extract from roots using methanol showed significant *in-vitro* cytotoxic activity against breast cancer | **Alshehri and Elsayed, 2012)** |

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| | cell line (MCF7) with remarkable changes in the gene expression for the DNA cancer markers. | |
| aqueous decoction | Remarkable *in-vitro* cytotoxic activity in C5N cells which represent an immortalized highly differentiated non-tumorigenic cell line | **(Mikropoulou *et al*., 2018)** |
| **II- Antimicrobial activity** | | |
| Methanolic extract<br><br>Ethanolic extract | Methanolic extract at 24ºC showed antibacterial activity against both gram negative bacteria: *Klebsiella pneumoniae* (ATCC 10031) and *Pseudomonas aeruginosa* (ATCC 27853) as well as gram positive bacteria: *Bacillus cereus* (ATCC11778).<br>Hot methanolic extract at 60ºC was potent against *Pseudomonas aeruginosa* (ATCC 27853*), Enterobacter aerogenes* (ATCC 13048), *Klebsiella pneumoniae* (ATCC 10031) and *Bacillus subtilis* (ATCC 6633).<br>Ethanolic extract showed antibacterial activity against *Staphylococcus aureus* (ATCC 29213), *Bacillus cereus* (ATCC11778) and *Klebsiella pneumoniae* (ATCC 10031) Of both *ex-vitro* and *in-vitro* growing plantlets and callus cultures. | **(Al Khateeb *et al*., 2012)** |
| Methanolic seeds extract<br><br>Methanolic leaves extract<br>Methanolic roots extract | Methanolic seeds extract showed high antimicrobial activity against Gram-positive bacteria: *Staphylococcus aureus* (ATCC 25923) and *Bacillus cereus* (ATCC 33018), Gram-negative bacteria: *Salmonella typhimurium* (NCTC 12023/ATCC 14028) and *Escherichia coli* ATCC 25922) and the fungi: *Candida albicans* (CAIM-22).<br>Methanolic leaves and roots extract showed a high antibacterial activity against Gram-positive bacteria: *Staphylococcus aureus* (ATCC 25923) and *Bacillus cereus* (ATCC 33018). | **(Amer, 2018)** |
| Water, ethanolic, methanolic and acetone extracts | Marked antifungal activity against *Aspergillus aflatoxiformans* and *Aspergillus ochraceous* while the methanolic extract is the more potent. | **(Mostafa and El-Sayed, 2021)** |
| **III- Antioxidant activity** | | |
| Ethanolic extract | Significant antioxidant activity by inhibition of intracellular reactive oxygen species (ROS) production thus protection against hepatic damage induced by tert-butyl hydroperoxide (*t*-BHP)- in HepG2 cell line *in-vitro*. | **(Chen *et al*., 2011)** |
| Ethanolic extract | Potent antioxidant and anti-lipid peroxidative effects | **(Chen *et al*., 2011)** |

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| | shown by remarkable reduction in malondialdehyde (MDA) level in the mice's liver tissue treated with *t*-BHP *in-vivo*. | |
| Kaempferol<br>Kaempferol-3-O-β-D-glucoside<br>Adenosine and 2-furanmethanol-(5'→11)-1,3-cyclopentadiene-[5,4-c]-1H-cinnoline | Potent antioxidant activity of kaempferol followed by kaempferol-3-O-β-D-glucoside<br>Moderate antioxidant activity of adenosine and 2-furanmethanol-(5'→11)-1,3-cyclopentadiene-[5,4-c]-1H-cinnoline in Oxygen Radical Absorbance Capacity (ORAC) Assay. | **(Chen *et al*., 2011)** |
| Aqueous suspension of leaves powder | Significant decrease in liver superoxide dismutase (SOD) activity, and significant increase in antioxidant enzymes; glutathione-S-transferase (GST) activity and glutathione (GSH) levels *in-vivo* in Streptozotocin (STZ)-induced diabetic rats. | **(Kamel and Marzouk, 2011)** |
| Methanolic extract | The methanolic extract growing ex-vitro plantlets and callus cultures show significant antioxidant potential due to high total phenol content. | **(Al Khateeb *et al*., 2012)** |
| Aesculetin<br>Quercetin<br>Astragalin<br>Caffeic acid | Marked *in-vitro* DPPH radical scavenging activities. | **(Khalil and Kamel, 2015)** |
| **IV-Anti-inflammatory activity** | | |
| Ethyl acetate root extract | Significant reduction serum level of IL-6 both in acutely inflamed mice *in-vivo* caused by lipopolysaccharide LPS and in rats with liver fibrosis. | **(Han *et al*., 2021)** |
| Ethyl acetate root extract | Significant improve in the damage of colon tissue, reduction of the inflammation of colon, improvement of the lesions in the colonic tissue and reducing necrosis *in-vivo* in rats with colitis caused by 2,4,6-trinitrobenzensulphonic acid (TNBS) -ethanol enemas. | **(Han *et al*., 2021)** |
| Lactucin | Significant reduction in levels of inflammatory mediators' production (IL-6, nitric oxide NO).<br>Significant inhibition of mRNA expression of genes responsible for production of inflammatory mediators (iNOS, COX-2, IL-6, IL-1β).<br>Significant inhibition of Protein Expression iNOS, COX-2 induced by lipopolysaccharide LPS- in RAW264.7 Cells in-vitro. | **(Han *et al*., 2021)** |

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| | Significant inhibition of the phosphorylation and activation of the MAPK-AKT signaling pathway in RAW264.7 cells induced by lipopolysaccharide LPS in-vitro.<br>Suppress the phosphorylation of ERK1/2 and p38 signaling pathways, leading to the inhibition of NO production in RAW 264.7 cells. | |
| **V-Hepatoprotective activity** | | |
| Root extract | Normalize some morpho-functional liver features *in-vivo* in rats with hepatitis induced by CCl4 as it can decrease cell of necrosis, glycogen content and increase the number of cells with remarkable protein synthesis activity. | **(Krylova *et al*., 2006; Masoud *et al*., 2018)** |
| Ethanolic extract | Marked reduction in (*t*-BHP)-induced cell death thus protection against hepatic damage in HepG2 cell line *in-vitro*. | **(Chen *et al*., 2011)** |
| Ethanolic extract | Significant reduction in serum levels of ALT and AST in *t*-BHP-induced acute liver injury *in-vivo* in mice model thus protection against hepatic tissue damage. | **(Chen *et al*., 2011)** |
| Ethyl acetate root extract | Significant improve of liver congestion and normalization of the color of liver.<br>Significant improve in the histopathological changes including reduction of the collagen fibrillar content in liver fibrosis in rats.<br>Significant reduction of serum levels of AST and γ-GT in liver injury-hepatic fibrosis *in-vivo* model in rats caused by 2,4,6-trinitrobenzensulphonic acid (TNBS) -ethanol enemas.<br>Can improve *in-vitro* the impaired intestinal microbes in the gut of rats with liver fibrosis making the intestinal flora close to the normal level.<br>Significant improve of liver fibrosis through the "gut-liver axis" via decreasing intestinal inflammation and promoting probiotic growth (*Bifidobacterium Adolescentis*). | **(Han *et al*., 2021)** |
| **VI-Antidiabetic activity** | | |
| Aqueous suspension of leaves powder | Significant decrease in serum levels of the enzymes: aminotransferases (AST, ALT), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH) activities *in-vivo* in Streptozotocin (STZ)-induced diabetic rats similar to the diabetic drug (glibenclamide) effects. | **(Kamel and Marzouk, 2011)** |

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| **VII-Analgesic and sedative activities** | | |
| Lactucin<br>lactucopicrin<br>11,13-dihydrolactucin | Marked analgesic and sedative activities in thermal models *in-vivo* in mice. | **(Wesołowska *et al*., 2006)** |
| **VIII-Skin protective activity** | | |
| Ethanolic root extract | Can absorb radiation in the UVB spectrum and prevent in-vivo UVB-induced erythema of human skin.<br>Can in-vitro prevent pyrimidine dimer formation, cell death, and IL-6 mRNA expression in a human keratinocyte cell line after UVB irradiation, so that it can be useful as sunscreen. | **(Enk *et al*., 2004)** |
| **IX-Effect on germination and seedling growth of maize** | | |
| Luteolin | Enhances germination and seedling growth of maize in normal conditions.<br>Eliminate the harmful effect of salinity on seedling growth and germination of maize.<br>Stimulates α-amylase activity thus improves mobilization of starch and enhances the accumulation of soluble sugars.<br>Partially enhances the antioxidative defense. | **(El-Shafey and AbdElgawad, 2012)** |
| **X-Antihypertensive activity** | | |
| Methanolic extract | *Ex-vitro* growing plants and growing callus showed high Angiotensin Converting Enzyme (ACE) inhibitor activity which can be a useful therapy for hypertensive patients by controlling blood pressure. | **(Al Khateeb *et al*., 2012)** |

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