REVIEW ARTICLE

RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

Metabolites and Biological Activities of some *Pulicaria* species (Asteraceae): mini-review

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Abstract

Medicinal plants are a prominent source of secondary metabolites and bioactive innovative molecules with interesting and remarkable biological activities. The Sinai Peninsula is considered an exceptional reservoir of many indigenous medicinal plants that have been used for treatment of many ailments; *Pulicaria* is a promising medicinal genus and one of the widest spread desert plants growing wild in Egypt. Some plants within the genus are used as traditional herbal medicines. *Pulicaria* is a well-known natural source of several bioactive compounds and used in traditional medicine in the many countries. Most importantly, previous studies of *Pulicaria* species allowed the isolation of various compounds such as flavonoids and terpenes. Our review tends to support the therapeutic value of this genus. Many recent studies suggested that most of the reported biological activities of *Pulicaria* are due to its high content of polyphenols, particularly flavonoids. This review highlights the phytochemical constituents of this important and valuable genus as well as its different reported biological activities.

Keywords: *Pulicaria*; phenolics; terpenes; flavonoids; biological activity

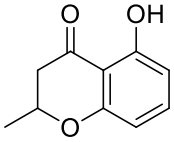
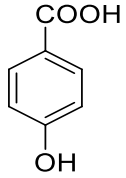
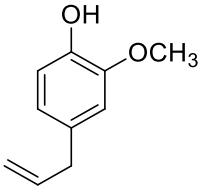
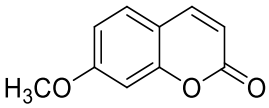
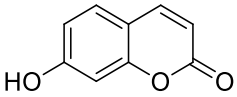
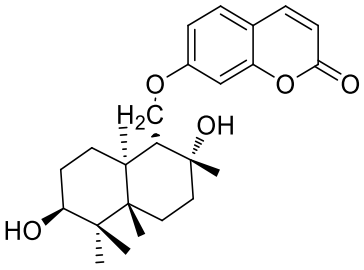
1. Introduction:

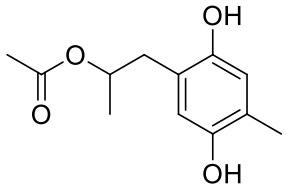
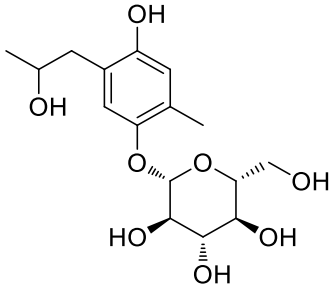
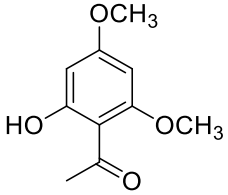
Natural products display an important role in the synthesis and discovery of new drugs also as a source of bioactive agents; **(Gordaliza, 2007)**. Disease ailments are changing the patterns, and the new diseases are emerging due to changing environments. The drug manufacturers are always on the lookout for new resources to develop effective and safe drugs for the increasing demands of the world population **(Khazir *et al.*, 2014);** Medicinal plants are rich sources of secondary diverse molecules with various therapeutic properties. Among these plants families, Asteraceae family continues to play a remarkable role in the development of drugs used in modern medicine **(Hussien *et al.*, 2016)**. Several members of this family are characterized by phytochemical compounds such as acetophenones, caffeoylquinic acids, phloroglucinol, polyphenols, pyrrolizidine alkaloids, polyacetylenes, chalcone, flavonoids, and diterpenoids. Several species of the family Asteraceae are characterized by analgesic, anti-allergic, antibacterial, antidiabetic, antifungal, antiviral, antiinflammatory, antimigraine, antioxidant, antiproliferative, antipyretic, antitumor, antiulcer, cardiotonic **(Maroyi, 2019).** The genus *Pulicaria*, belonging to the tribe Inuleae of the family Asteraceae, consists of 100 species with a distribution from Europe to North Africa and Asia, particularly around the Mediterranean **(Williams *et al.*, 2003)**. It is known as "Dethdath", and the flower branches are used for preparing a powerful sneezing powder as an insect repellent and as an herbal tea. Various types of chemical constituents within the genus *Pulicaria* have been reported, including phenolic derivatives, monoterpene derivatives, sesquiterpenes, diterpenes, flavonoids, triterpenes,

steroids, essential oils **(Liu *et al.*, 2010)**. *Pulicaria* is a well-known natural source of several bioactive compounds and used in traditional medicine in the many countries. Most importantly, a number of compounds from *Pulicaria* species have been found to possess potent bioactivities, they could be promising candidates for the development of potential drugs and value-added products **(Hussein *et al.*, 2017)**.

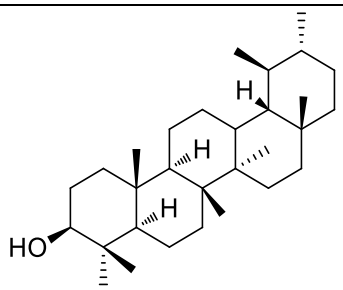
2. Chemical constituents reported from *Pulicaria species*:

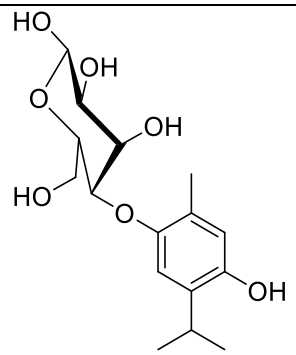
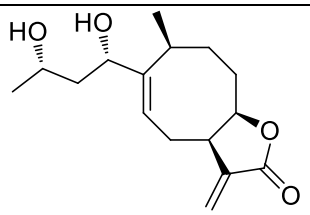
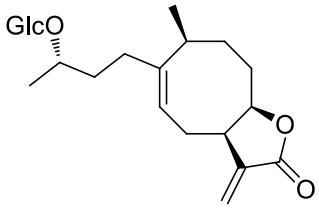
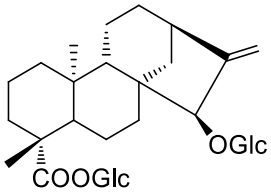
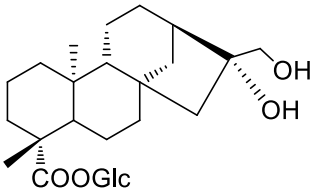
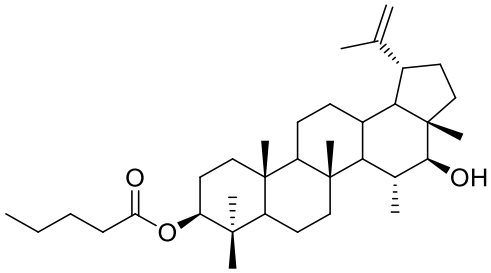
Examples of phenolic derivatives isolated from *Pulicaria* species:

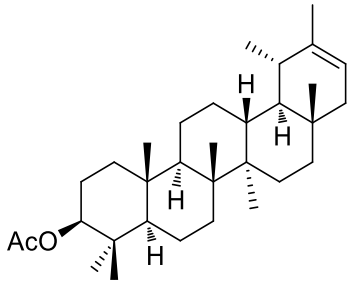
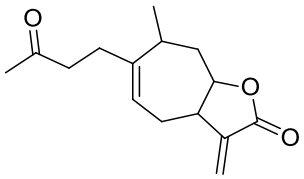
NO	Names & Structures	Species	References
1	 **5-Hydroxy-2-methyl-2,3-dihydro-4H-chromen-4-one**	*P. wightiana*	**(Das *et al.*, 2006)**
2	 ***p*-Hydroxybenzoic acid**	*P. paludosa* *P. gnaphalodes*	**(Liu *et al.*, 2010)** **(Eshbakova *et al.*, 2016)**
3	 **Eugenol**	*P. paludosa*	**(Liu *et al.*, 2010)**
4	 **Herniarin**	*P. gnaphalodes*	**(Eshbakova *et al.*, 2016)**
5	 **Umbelliferone**	*P. gnaphalodes*	**(Eshbakova *et al.*, 2016)**
6	 **Feshurin**	*P. gnaphalodes*	**(Eshbakova *et al.*, 2016)**

7	 **2-(2-acetoxy propyl), 5-methyl hydroquinone**	*P. jaubertii*	**(Elshamy *et al.*, 2018)**
8	 **2-(2-hydroxy propyl), 5-methyl hydroquinone-4-*O*-*β*-D glucopyranoside**	*P. jaubertii*	**(Elshamy *et al.*, 2018)**
9	 **1-Acetyl-2-hydroxy-4,6-dimethoxybenzene**	*P. undulata*	**(Mustafa *et al.*, 2020)**

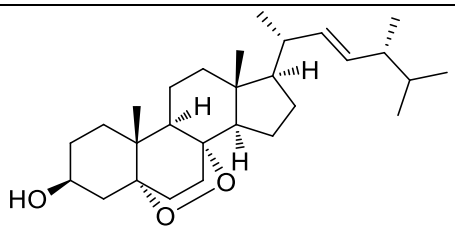
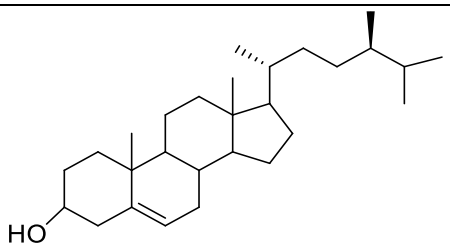
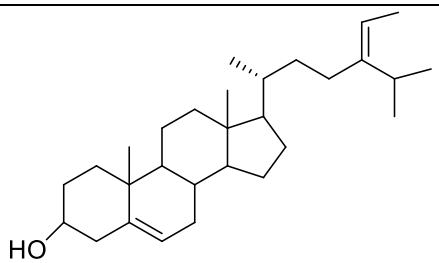
Examples of some terpenoidal compounds isolated from *Pulicaria species:*

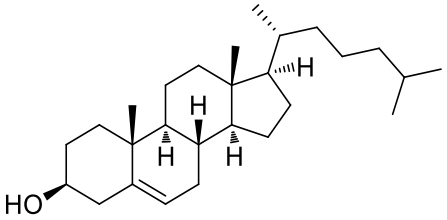
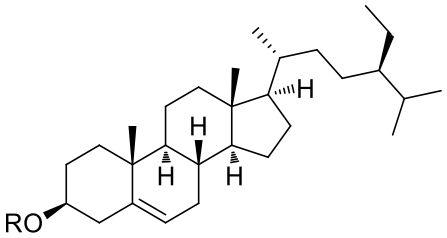
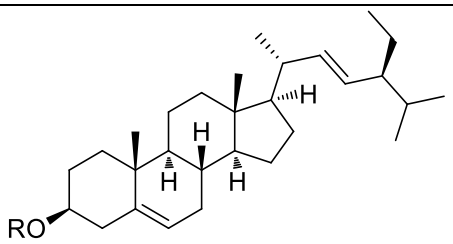
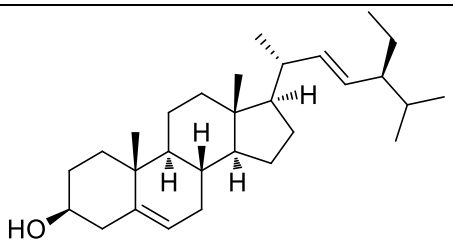
NO	Names & Structures	Species	References
1	 ***α*-Amyrin**	*P. incise*	**(Wang *et al.*, 2015)**

2	 **Thymoquinol 2-*O*-*β*-D-glucopyranoside (zataroside-B)**	*P. jaubertii*	**(El-Ghaly *et al.*, 2016)**
3	 **8-epi-Ivalbin**	*P. undulata*	**(Hussien *et al.*, 2016)**
3	 **Ivalin**	*P. undulata*	**(Hussien *et al.*, 2016)**
4	 **Crispioside A**	*P. undulata*	**(Hussien *et al.*, 2016)**
5	 **Crispioside B**	*P. undulata*	**(Hussien *et al.*, 2016)**
6		*P. undulata*	**(Abdallah, 2019)**

	undulaterpene A		
7	 **Pseudotaraxasteryl acetate**	*P. undulata*	**(Abdallah, 2019)**
8	 **Tomentosin**	*P. undulata*	**(Abdallah, 2019)**

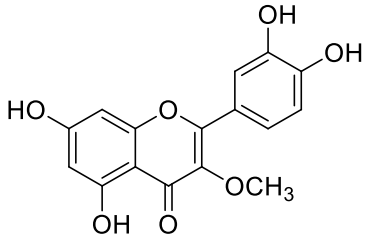
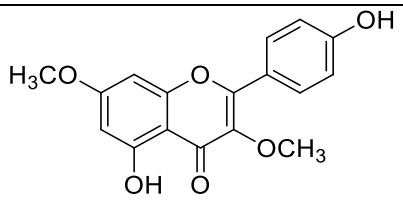
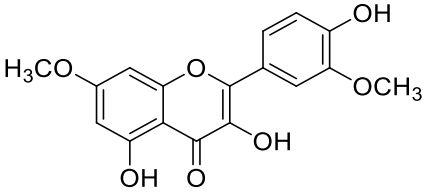
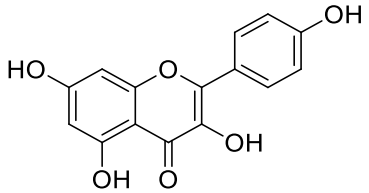
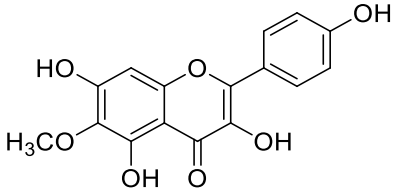
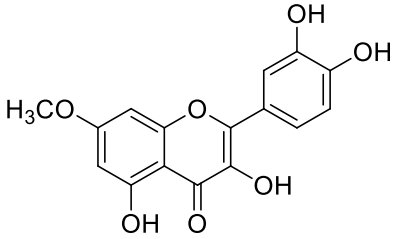
Examples of some steroidal compounds isolated from *Pulicaria* species*:*

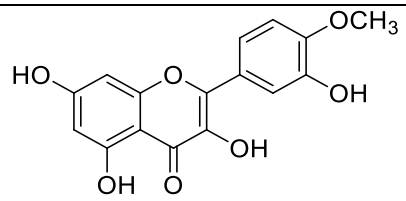
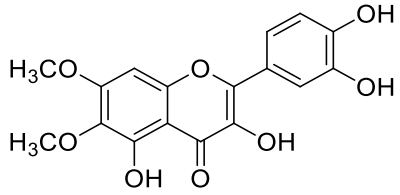
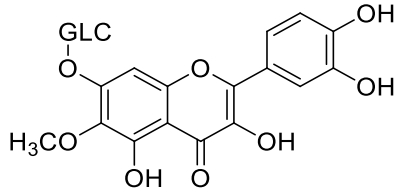
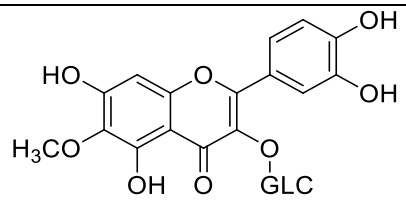
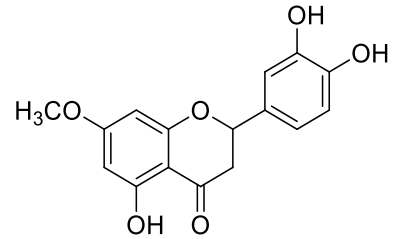
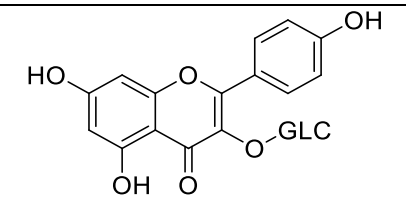
NO	Names & Structures	Species	References
1	 **Ergosterol peroxide**	*P. canariensis*	**(Triana *et al.*, 2005)**
2	 **Campesterol**	*P. incisa*	**(Hassanien *et al.*, 2009)**
3	 **Δ^5-Avenasterol**	*P. incisa*	**(Hassanien *et al.*, 2009)**

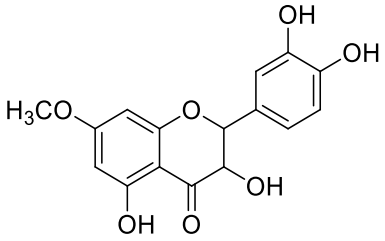
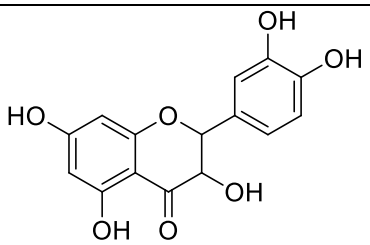
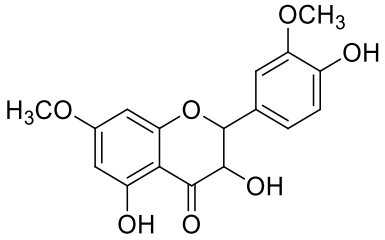
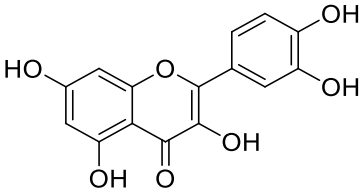
4	 **Cholesterol**	*P. salviifolia*	**(Liu *et al.*, 2010)**
5	 ***β*-Sitosterol-3-*O*-glucoside** **R= glucose**	*P. incisa*	**(Ewais *et al.*, 2014)**
6	 **Stigmasterol -D-glucopyranoside** **R=glucoside**	*P.gnaphalodes* *P. jaubertii*	**(Eshbakova *et al.*, 2016)** **(El-Ghaly *et al.*, 2016)**
7	 **Stigmasterol**	*P. angustifolia* *P. undulata*	**(Athayde *et al.*, 2019)** **(Abdallah, 2019)**

Examples of some flavonoids compounds isolated from *Pulicaria species:*

Number of flavonoids has been identified since the first study on the genus *Pulicaria*, and they represent a large group of the known *Pulicaria* compounds.

No	Names & Structures	Species	References
1	 **Quercetin 3-*O*-methyl ether**	*P. orientalis*	**(Liu *et al.*, 2010)**
3	 **Kaempferol 3,7-dimethyl ether**	*P. orientalis*	**(Liu *et al.*, 2010)**
4	 **quercetin 7, 3`-di-Omethylether (rhamnazin)**	*P. jaubertii*	**(El-Ghaly *et al.*, 2016)**
5	 **Kaempferol**	*P. gnaphalodes*	**(Eshbakova *et al.*, 2016)**
6	 **6-Methoxykaempferol**	*P. undulata*	**(Hussien *et al.*, 2016)**
7	 **Quercetin 7-*O*-methylether (rhamnetin)**	*P. jaubertii*	**(El-Ghaly *et al.*, 2016)**

No	Names & Structures	Species	References
8	 **Quercetin 3`-*O*-methylether (isorhamnetin)**	*P. jaubertii*	**(El-Ghaly *et al.*, 2016)** **(Elshamy *et al.*, 2018)**
9	 **Quercetagetin 6, 7-dimethyl ether (Eupatolitin)**	*P. undulata*	**(Hussien *et al.*, 2016)**
10	 **Patulitrin**	*P. undulata*	**(Hussien *et al.*, 2016)**
11	 **Patuletin 3-*O*-*β*-D-glucopyranoside**	*P. undulata*	**(Hussien *et al.*, 2016)**
12	 **7-*O*-Methyleriodictyol**	*P. undulata*	**(Hussein *et al.*, 2017)**
13	 **Kaempferol 3-glucoside (Trifoliin)**	*P. incisa* *P. dysenterica*	**(Hussein *et al.*, 2017)** **(Williams *et al.*, 2000)**

No	Names & Structures	Species	References
14	 **Taxifolin 7-methyl ether (padmatin)**	*P. undulata*	**(Elshamy *et al.*, 2018)**
15	 **Dihydroquercetin (taxifolin)**	*P. jaubertii*	**(Elshamy *et al.*, 2018)**
16	 **Dihydroquercetin 3‘,7-dimethyl ether**	*P. jaubertii*	**(Elshamy *et al.*, 2018)**
17	 **Quercetin**	*P.jaubertii*	**(Elshamy *et al.*, 2018)**

3. Reported biological activities of *Pulicaria undulata:*

Antimicrobial Activities:

P. dysenterica MeOH extract was found to be effective as an antibacterial agent against *Vibrio cholera*, *Staphylococcus aureus*, and *Bacillus cereus* using the disc-diffusion assay technique. **(Basta *et al.*, 2007).**

The essential oil of *P.odora* L. exhibited a significant antibacterial activity at low quantities when tested against seven bacteria *Bacillus cereus, Streptococcus C, Proteus vulgaris, Enterococcus faecalis, Escherichia coli, Pseudomonas aeroginosa,* and *Enterococcus* at different concentrations **(Ezoubeiri *et al.*, 2005)**.

The chemical composition of the essential oil obtained from the leaves of *Pulicaria undulata* was analyzed by GC-MS. Major compounds of *P. undulata* oil were the oxygenated monoterpenenes, carvotanacetone and 2,5-dimethoxy-*p*-cymene. The oil showed the strongest bactericidal activity against *Staphylococcus aureus* and methicillin-resistant *S. aureus,* as well as *Candida albicans* **(Ali *et al.*, 2011)**.

The essential oil of *P. gnaphalodes* progressively inhibited Leishmania major growth **(Asghari *et al.*, 2014)**.

Cytotoxic Activities:

Emam *et al.* assess the anticancer activity of *Pulicaria undulata* extract *in vitro* in the treatment of hepatocellular carcinoma (HepG2) cell line and stated that *P. undulata* could be promising therapeutic agent for treatment of hepatocellular carcinoma **(Emam *et al.*, 2019).**
Crude extract of *P. undulata* and the isolated compounds inhibited the proliferation of MCF-7 cells and HepG2 cells at various levels, and the cytotoxic activity increased in a dose-dependent manner by measuring their ability to scavenge the radical DPPH **(Hussien *et al.*, 2016).** Moreover, the essential oil of *Pulicaria undulata* showed moderate cytotoxic activity against MCF-7 breast tumor cells, with an IC_{50} of 64.6 ± 13.7 µg/mL **(Ali *et al.*, 2011).** *P. crispa* and *P. incisa* showed potential cytotoxic effect against HepG-2 and MCF-7 cell line **(Wang *et al.*, 2015)**; Cytotoxic activities of the compounds isolated from *P. canariensis* were tested against the human myeloid leukemia cell line by the MTT assay **(Triana *et al.*, 2005).**
In 2008, during biological activity studies on the species *P. crispa*, 2, 3-Dihydro-5,10-epiaromatin was evaluated *in vitro* for anticancer activity in an established human bladder carcinoma cell line, EJ-138. It demonstrated promising activity in this cell line **(Stavri *et al.*, 2008).**

Antihypertensive activity:

The standardized extract of *P. jaubertii* significantly reduced SBP in L-NAME–induced hypertensive rats. The possible antihypertensive activity of the alcoholic extract may be due to its flavonoids and phenolic contents **(El-Ghaly *et al.*, 2016).**

Other Activities:

Antispasmodic activities of *P.glutinosa* have been demonstrated **(Abdallah, 2019)**, and *P. dysenterica* showed an antihistaminic effect **(Mahfouz *et al.*, 1973)**. Karim *et al.* reported that *P. incisa* was used as a tonic and a tea substitute, antispasmodic, hypoglycemic and as an ingredient of a local perfume in the Sudan **(Karim *et al.*, 1992)**. The plant is also used as a traditional medicine for treating heart diseases by Bedouins **(Mansour *et al.*, 1990; Saleh, 2003);** also *P. undulata* succeeded to have anti-ulcerative protective effect **(Fahmi *et al.*, 2019).**

4. Conclusion

In this review, we discussed some of the isolated phytochemicals and the biological activities of *Pulicaria* species. There is now a tendency to the use of complementary remedies for treating and decreasing symptoms of many diseases; our review showed that this genus is a valuable source of several metabolites especially flavonoids, ,sesquiterpenes, monoterpenes and titerpenes and it possesses several medicinal uses that were previously reported; more studies should be focused on this genus.

5. Conflict of interest

The authors report no declaration of conflict of interest.

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