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Review

Phytochemical and biological studies on *Launaea* Cass. genus (Asteraceae) from Algerian Sahara

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ABSTRACT

Traditional remedies have been employed for the treatment and management of various ailments since the beginning of human civilization. *Launaea* Cass. is a small genus of the family Asteraceae (tribe Lactuceae, subtribe Sonchinae), consisting of 54 species, of which 9 are presented in the flora of Algeria and is mainly distributed in the South Mediterranean, Africa and SW Asia. Plants in the *Launaea* genus have been used ethnobotanically as bitter stomachic, for treating diarrhea, gastrointestinal tracts, as anti-inflammatory, for skin diseases, treatment of infected wounds, hepatic pains, children fever, as soporific, lactagogue, diuretic and as insecticidal. The aim of this review is to present as much information as was established from the available scientific literature. The review covers the ethnopharmacological, biological activity related and phytochemical information on the species from genus *Launaea*, especially those growing in Algerian Sahara and used as medicinal plants.

KEYWORDS: Asteraceae, *Launaea* Cass., ethnopharmacological, biological activities, phytochemical, Sahara

INTRODUCTION

The World Health Organization (WHO) has recognized the potential utility of traditional remedies and strives to preserve the primary health care involving medicinal plants. Thus, there is ample archaeological evidence indicating that medicinal plants were regularly employed by people in prehistoric times. In several ancient cultures botanical products were ingested for biomedically curative and psychotherapeutic purposes [1]. Plants have formed the basis of Traditional Medicine (TM) systems that have been in existence for thousands of years and continue to provide mankind with new remedies, such as, the oldest known medicinal systems of the world: Ayurveda, Arabian medicine, Chinese and Kempo medicine. Although some of the therapeutic properties attributed to plants have proven to be erroneous, medicinal plant therapy is based on the empirical findings of hundreds and thousands of years [2]. One of the most efficient ways of finding new bioactive compounds is collecting data on the use of medicinal plants in traditional pharmacopeia. Nearly 50,000 species of higher plants have been used for medicinal purposes. They are also used in food, cleaning, personal care and perfumery. In systems of traditional healing, major pharmaceutical drugs have been either derived from or patterned after compounds from biological diversity [3]. Natural products have made enormous contributions to human health through compounds such as quinine, morphine, aspirin (a natural product analog), digitoxin and many others. Thus natural products are very important to conduct research on and they can be a source of new compounds [4]. A trend in phytomedicine is the use of new plant origin bioactive compounds with the potential for chemical modification, which will broaden phytomedical

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importance. Molecular biology is also being used in this process and the pharmacological profiles of these compounds are screened using new research equipment and new technology [5-8]. Natural products and their derivatives represent more than 50% of all the drugs in clinical use in the world and in which higher plants contribute to no less than 25% [2].

A dozen potent drugs have been derived from plants including: derived diosgenin; reserpine and pilocarpine. Other natural products are metabolites from fungi, bacteria, algae, and marine organisms. So, the diversity of structures obtained and the different therapeutic activities shown by the natural products make the isolation, identification, synthesis and biosynthesis of new natural compounds a field of enormous interest. Only a small part of the 400,000 vegetable species known have so far been investigated for their phytochemical and pharmacological aspects, and each species could contain up to several thousands of different components [9].

The plant family Asteraceae (Compositae) comprises of a large number of species that have been and are still used as medicinal plants, particularly in folk medicine and used as a food.

Launaea Cass. is a small genus of the family Asteraceae (tribe Lactuceae, subtribe Sonchinae). The genus consists of 54 species, of which 9 are presented in the flora of Algeria and is mainly distributed in the South Mediterranean, Africa and SW Asia. They are perennial to annual herbs, small shrubs or sub shrubs. Many of its plants are used in folk medicine as bitter stomachic, for treating diarrhea, gastrointestinal tracts, as anti-inflammatory, for skin diseases, treatment of infected wounds, hepatic pains, children fever, as soporific, lactagogue, diuretic and as insecticidal. Additionally, crude extracts of some species have been reported to exhibit antibacterial, antiparasitic, antioxidant, cytotoxic, neuropharmacological and insecticidal activities. From a chemical point of view, only ten species of the genus *Launaea* Cass. have been subjected to previous phytochemical investigation, namely, *Launaea acanthoclada, L. arborescens, L. asplenifolia, L. capitata, L. cassiniana, L. mucronata, L. nudicaulis, L. pinnatifida*, *L. resedifolia* and *L. tenuiloba*. Different secondary metabolites including terpenoids, steroids, triterpenoid saponin, sesquiterpene lactones, coumarins, flavonoids, flavone glycosides and phenolic compounds have been reported.

We attempt to present a review on the ethnopharmacological and phytochemical studies and biological activities of plants from the genus *Launaea* Cass., especially those growing in Algerian Sahara and used as medicinal plants.

Botanical taxonomy of the genus *Launaea* Cass.

Asteraceae family (Compositae), known as the aster, daisy or sunflower family, is one of the largest angiosperm families of dicotyledenous flowering plants. It comprises about 1400 genera and more than 25000 species of herbaceous plants, shrubs, and trees, spread throughout the world, and classified over three subfamilies and 17 tribes [10]. Asteraceae plants tend to grow in sunlit places, in temperate and subtropical regions and can share these following characters [11]:

Various members of the aster family are familiar species in natural habitats, while others are cultivated plants in gardens and some are grown as food (*Lactuca sativa*). Many members of Asteraceae are pollinated by insects, which explain their value in attracting beneficial insects and are major honey plants.

The flowers of this family are of two basic types: tubular actinomorphic corollas and those with strap shaped or radiate zygomorphic corollas, often with the same head. Either type may be bisexual or unisexual.

Leaves and stems very often contain secretory canals with resin or latex (particularly common among the Cichorioideae). The leaves can be alternate, opposite, or whorled. They may be simple, but are often deeply lobed or otherwise incised, and conduplicated or revoluted. The margins can be entire or dentate.

The fruit of Asteraceae is a specialized type of achene sometimes called cypsela. One seed per fruit is formed.

Due to their chemo-diversity, the sesquiterpene lactones are the most suitable class of naturals products for chemo-systematic studies within the family [12, 13].

The tribe *Lactuceae* Cass. The tribe Lactuceae (Cichorieae, Asteraceae family) comprises 98 genera and more than 1550 species. The milky latex and the floral structure make the tribe easily distinguishable from all other Asteraceae. The flowering heads are composed of wholly ligulate florets that are usually 5-lobed [10].

According to classification system on flowering plants [14], the classification hierarchy of the genus *Launaea* can be tracked as follows:

Kingdom	:	Plantae
Division	:	Angiosperms
Class	:	Eudicots
Subclass	:	Asterids
Order	:	Asterales
Family	:	Asteraceae
Subfamily	:	Cichorioideae
Tribe	:	Lactuceae (Cichorieae)
Sub-tribe	:	Sonchinae
Genus	:	*Launaea*

The genus *Launaea* Cass. belongs to the tribe Lactuceae of the Asteraceae family and contains about 54 species, most of which are adapted to dry, saline and sandy habits [15]. Plants of this genus have several rows of stems, hairless leaves incised into lobes that are themselves lined with white teeth, membranous scales on the edges, yellow ligules, and elongated chain, prismatic or slightly flattened.

The genus *Launaea* is represented in the flora of Algeria by nine species including five endemics of North Africa: *L. angustifolia*, *L. quercifolia*, and *L. cassiniana* are the endemic plants of the North Africa, with limited distribution [15, 16], whereas *L. acanthoclada* and *L. arborescens* are two endemic plants of the north-west of Africa. The other four species *L. nudicaulis* and *L. residifolia* sprout in Algeria and Tunisia Mediterranean Sea, whereas *L. glomerata* and *L. mucronata* grow in the Saharan Atlas [16].

Three of this species are used in Algerian Sahara ethnopharmacopea as medicinal plants, *L. nudicaulis, L. residifolia and L. arborescens*,

Figure 1. *Launaea arborescens* (Batt.) and flower–south west Algeria.

which is endemic to south west Algeria and south east Morocco [17].

Launaea arborescens (Batt.) Murb, (syn. *Zollikoferia spinosa* DC) is an almost leafless, xerophilous, perennial spiny shrub, 40-120 cm. high, with typical zig-zag shaped stems (Figure 1). The young stems are green, glabrous and erect. The older ones become tough spines. The leaves are narrow and dissected in small lobes, evergreen at the base but shed after flowering from the stems. The flowers are yellow, and abundant flowering occurs from March to June, but flowers and achenes are produced throughout the year. The roots are very deep, the leaves and stems have white latex which is similar in appearance to milk (thus the local name “Oum loubina”) [15-18].

Ethnopharmacolgy and bioactivity of the genus *Launaea* Cass.

It is well known that species from Asteraceae family are used as natural remedies such as: *Anthemis arvensis* L. (anti-inflammatory, emetic, sedative), *Artemisia arborescens* L. (digestive, stimulant, expectorant), *Calendula arvensis* (antispasmodic, burns, diuretic, disinfectant and vulnerary), *Cichorium intybus* L. (blood purification, arteriosclerosis, anti-arthritis, anti-spasmodic, digestive, hypotensive, aperitif and laxative) and *Helychrysum microphyllum* Willd. (expectorant).

Algeria with its large area and diversified climate has a varied flora, which is a source of rich and abundant medical matter and, in particular, Sahara part constitutes an important reservoir of many plants which have not been investigated until today. Among this flora, some *Launaea* plants have been used in the traditional medicine [17-19]. Species of the genus *Launaea* are widely applied in traditional folk medicine throughout their areas of distribution. Many of them are used in folk medicine as bitter stomachic, anti-tumour, insecticides and against skin diseases.

Launaea residifolia (Vernacular name: Lemkar) is a medicinal plant used in folkloric medicine mainly for the treatment of hepatic pains.

Launaea nudicaulis (Vernacular name: Reghama) is used in the traditional medicine to treat gastric burns, pain of stomach, constipation, to relieve fever in children, in the treatment of itches of skin and eczema.

Launaea arborescens (Batt) (Vernacular name: Oum Lbina) commonly used in popular medicine as an antidiarrhoic and antispasmodic, to relieve fever, and as a vermifuge in children. The latex is applied locally to cure sore throats and in the treatment of furuncles. The powdered root mixed with *Artemisia herba-alba* is taken for diabetes. The plant is appreciated by livestock, mainly by camel [17-21].

Many phytochemicals are potent effectors of biologic processes and have the capacity to influence disease risk via several complementary and overlapping mechanisms [22].

More than 4000 sesquiterpenoids structures with around 30 different skeletal types have so far been reported from several tribes of Asteraceae family including the Cichorieae tribe. These natural compounds are responsible for allergic contact dermatitis and exhibit a wide range of bioactivities which include plant growth regulation and antimicrobial activity. Also they are used as schistosomicidal and insect feeding-deterrent agents. In addition, they provoke the toxicity for certain cancer cell lines by inhibition of nuclear DNA synthesis, especially the enzymatic activity in tumour cells of DNA polymerase and thymidylate synthetase [12, 23, 24].

On the other hand, triterpenoids and flavonoids chemio-characteristic of Asteraceae family, including the *Launaea* genus, have been reported to have anti-inflammatory activities, anti-hyperlipidemia, hepatoprotection, antioxidant, cytoprotective, giving protection against cardiovascular disease, and certain forms of cancer [25, 26]. Antibacterial, antifungal and allelopathic potential activities have been proven for many species of *Launaea*. In an antibacterial assay against *Bacillus subtilis* the extracts of *L. nudicaulis* and *L. residifolia* showed 18.5 and 20.5 mm zones of inhibition, respectively, as determined by the disc diffusion method. The antifungal activity against *Aspergillus* spp. was determined by measuring the linear growth in slants on 4^{th} day of incubation. Methanol extracts of *L. nudicaulis* and *L. residifolia* were active at 0.209 mg/ml levels exhibiting 45 ± 6 mm and 37 ± 6 mm linear growth which decreased to 22 ± 5 mm and 28 ± 4 mm, respectively, at 0.838 mg/ml concentration [27].

As a part of our works on medicinal plants of Algerian Sahara, recently we have reported the antibacterial activity of extracts from *Launaea Arborescens* and *L. nudicaulis* which are widely distributed in the south west of Algeria. The methanol extract of the aerial part of *L. nudicaulis* showed high activities against *Candida albicans*, *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The highest inhibition observed in *S. aureus*, a human pathogen, explains the use of this plant against a number of infections for generations. Very interesting antifungal activity against *Candida albicans* and *Saccharomyces cerevisae* and antibacterial activity against *Staphylococcus aureus, Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella entrecocus* have been reported for the methanol extract of *Launaea Arborescens* [18, 28].

Hydroalcoholic extract from aerial parts of *Launaea arborescens* was evaluated for acute and subacute toxicity in *Swiss* mice after ingestions of the extract. The LD50 of the extract is higher than 2.75 g/kg and the subacute treatment did not shows any change in corporal weight and haematological parameters, which suggest that the plant seems to be destituted of toxic effects in mice [29].

Aerial part and roots of *Launeae arborescens* were used to evaluate their extracts for antifungal activity against Fusarium oxysporum f. sp. albedinis Foa. The antifungal test was conducted using disc diffusion technique and relative virulence (RV) test (on potato tuber tissue). For both tests, four extract quantities were used (200, 400, 800 and 1,600 µg). The relative virulence was presented as necrotic tissue weight (mg) of potato tuber tissue. Among all solvents, methanol had the best extraction yield (mean: 6.35%, minimum: 2.27%, maximum: 9.80%) [30].

Coumarins isolated from *L. resedifolia* showed high antibacterial activity against some Gram-positive bacteria such as *Bacillus cereus* and *Staphyllococcus aureus* in minimum inhibitory concentrations of 200 and 400 µg/mL. However, they showed no effect on tested Gram-negative bacteria such as *Serratia* Sp., *Pseudomonas* Sp. and *Escherichia coli* [31]. The ethanol extract of *L. resedifolia* showed neuropharmacological properties in animal models. The extract exhibited an inhibitory effect on the locomotor activity of mice in the open field test, an anti-nociceptive effect by increasing the hot plate reaction time in the hot plate test, and an anti-inflammatory activity in the carrageen-induced paw oedema. This finding has demonstrated that the extract of *L. resedifolia* possesses sedative, analgesic and anti-inflammatory properties, and some effect on body weight. The anti-infl ammatory effect of the plant was found to be as active as the prototype non-steroidal anti-inflammatory drug (NSAID) aspirin [32].

Allelopathic potential effect of aqueous extract of *Launaea procumbens* was observed in the soil application by a significant retarding effect on wheat growth while shoot spray or root dip treatment had no such effect and methanol and chloroform fraction from this specie exhibited efficient antioxidant scavenging activities, attributed to the phenolic and polyphenolic compounds such as myricetin, catechin, vitexin, orientin, hyperoside and rutin, revealed in HPLC [33].

Other research has shown that extracts from *Launaea procumbens* provide effective protection for kidneys against the CCl_4-induced oxidative damage in rats, through antioxidant and free radical scavenging effects of flavonoids and saponins present in this plant, which might be responsible for the elimination of various kidneys insults [34].

Phytochemistry of the genus *Launaea* Cass.

a. Secondary metabolites from the 2ed group of Lactuceae tribe

The biodiversity of metabolite products isolated from Asteraceae makes this family an important phytochemical and commercial source. Several phytochemical studies of some genera of *Lactuceae* tribe (Cichorieae) revealed to be rich in secondary metabolites, specifically sesquiterpene lactones exhibiting the eudesmane, germacrane and guaiane carbon framework. A total of 360 sesquiterpene lactones and related compounds have been isolated from 139 taxa belonging to 31 different genera of the *Lactuceae*. Studies realized for these genera revealed that most sesquiterpenoids within the Cichorieae belong to the guaianolide class, particularly: 92 representatives of costus lactone type, 75 compounds of lactucin type, and 29 representatives of hieracin type [35, 36].

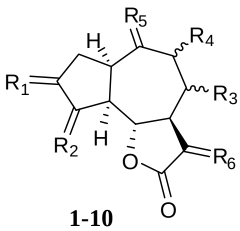
Some phenolic compounds, such as flavonoids and coumarins were also isolated [37-42]. In addition, triterpenes have also been detected [43, 44]. Recently, Sareedenchai and Zidorn indicated that a total of 135 flavonoids have been isolated from 299 species of the Cichorieae (Lactuceae) tribe. The reported compounds encompass flavanones, flavanonols, flavones, flavonols, anthocyanidins, isoflavonoids, chalcones and aurone [45].

Based on the similarity of their sesquiterpenes profiles, Zidorn grouped the 31 genera of the *Lactuceae* into seven main clusters and classified Launaea with the 2ed group characterized by the prevalence of guaianolides, formed by 11 genera, sub-divided into four sub-groups: a) *Scorzoneroides*; b) *Notoseris*, *Lactuca*, and *Cichorium*; c) *Launaea*, *Crepidiastrum*, *Reichardia*, and *Cicerbita* d) *Taraxacum*, *Helminthotheca*, and *Hypochaeris* [35].

Phytochemical investigation of 2ed group of the Cichorieae tribe resulted in the identification and isolation of differents metabolites including:

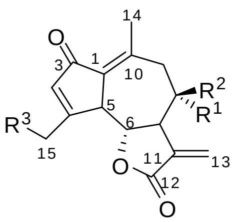
Sesquiterpenoids

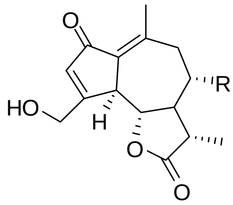
Costus lactone type guaianolides such as dehydrocostruslactone **1**, ixerisoside B **2**, C **3** and D **4**, scorzoside **5**, zaluzanin C **6**, glucozaluzanin C **7,** 11 β,13-dihydrozaluzanin C **8**, 8β-hydroxy-4 β,15-dihydrozaluzanin C **9** and prenantheside C **10** [38, 39]. Lactucin type guaianolides, Lactucin **11**, 8-O-acetate Lactucin **12**, Crepidiaside A **13**, 11β, 13dihydrolactucin **14**, 8-O-acetate, 11β, 13 dihydrolactucin **15** and 8-Deoxylactucin **16**. The eudesmane derivatives santamarin **17**, ixerisoside E **18,** lactuside D **19**, sonchuside C **20** and artesin **21** [39, 46], costinolide type germacranolides such as picriside B **22**, C **23**, sonchuside A **24**, B **25** and cichoerioside C **26**, [41, 47, 48], and melampolides type, lactulide A **27**, lactuside A **28** and B **29** [38, 39, 49, 50] and in some case sesquiterpenoid sulphate, 8-deoxy-15-(3'-hydroxy-2'-methylpropanoyl) lactucin-3'sulfate **30** [51].



1-10

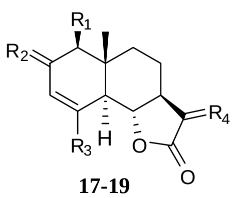
	R_1	R_2	R_3	R_4	R_5	R_6
1	H,H	CH_2	H	H	CH_2	CH_2
2	α H,β OGlc	α CH_3 ,βH	β OH	H	CH_2	CH_2
3	α H,β OGlc	CH_2	H	H	CH_2	α CH_3 ,βH
4	H,H	CH_2	H	α OGlc	CH_2	CH_2
5	H,H	CH_2	H	α OGlc	CH_2	α CH_3 ,β
6	α H,β OH	CH_2	H	H	CH_2	CH_2
7	α H,β OGlc	CH_2	H	H	CH_2	CH_2
8	α H,β OH	CH_2	H	H	CH_2	α CH_3 ,βH
9	α H,β OH	α CH_3 ,βH	β OH	H	CH_2	CH_2
10	α H,β OGlc	CH_2	α OH	H	CH_2	α CH_3 ,Bh





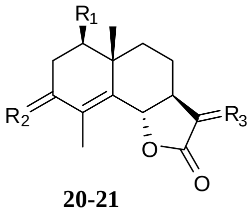
11 : R_1 = R_3=OH , R_2=H
12 : R_1 = OAc , R_2=H , R_3=OH
13 : R_1 =R_2=H , R_3=O-glc

14 : R=OH
15 : R = OAc
16 : R=H



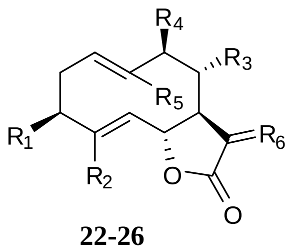
17-19

	R_1	R_2	R_3	R_4
17	OH	H ,H	CH_3	CH_2
18	OH	H ,H	CH_2OGlc	CH_2
19	O-PPA	H ,H	CH_2OGlc	CH_2



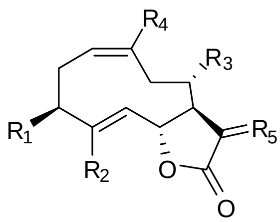
20-21

	R_1	R_2	R_3
20	H	α H, β OGlc	α CH_3, β H
21	OH	H, H	α CH_3, β H



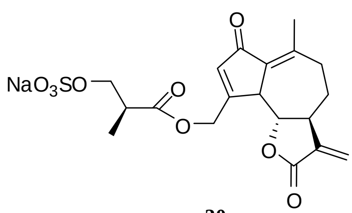
22-26

	R_1	R_2	R_3	R_4	R_5	R_6
22	H	CH_2OGlc	H	H	CH_3	CH_2
23	OGlc	CH_3	H	H	CH_3	CH_2
24	O-Glc	CH_3	H	H	CH_3	α CH_3, β H
25	OGlc	CH_3	H	O-PMP	CH_3	CH_2
26	OGlc	CH_3	OH	H	CH_3	α CH_3, β H



27-29

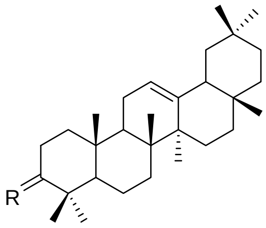
	R_1	R_2	R_3	R_4	R_5
27	OH	CH_3	H	CHO	α CH_3 ,βH
28	OGlc	CH_3	H	CHO	α CH_3 ,βH
29	OGlc	CH_3	H	CH_2OH	α CH_3 ,βH



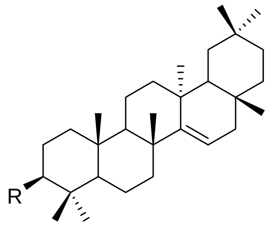
30

Terpenoids

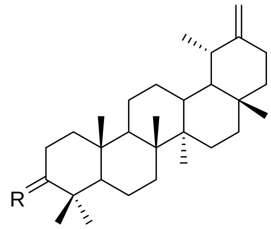
The majority of these triterpenes are pentacyclic and belong to lupane, oleanane, gammacerane and ursane groups, with some tetracyclic compounds such as β-amyrin **31**, β-amyrin acetate **32**, taraxerol **33**, taraxeryl acetate **34**, taraxasterol **35**, taraxasterone **36**, taraxasteryl acetate **37**, ψ-taraxasteryl derivatives **38**, **39**, α-amyrin derivatives **40**, **41**, lupeol **42**, lupenone **43**, and lupenyl acetate **44** [39, 44].



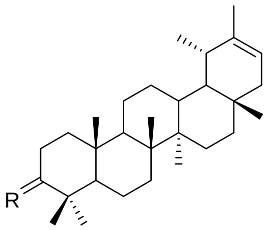
31 R= α H, βOH
32 R= α H, βOAc



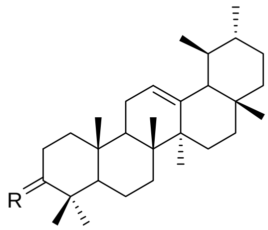
33 R= OH
34 R= OAc



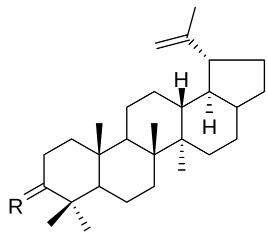
35 R= α H, βOH
36 R= O
37 R= α H, βOAc



38 R= α H, βOH
39 R= α H, βOAc



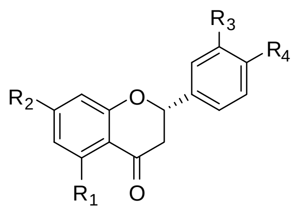
40 R= α H, βOH
41 R= α H, βOAc



42 R=α H, βOH
43 R= O
44 R= α H, βOAc

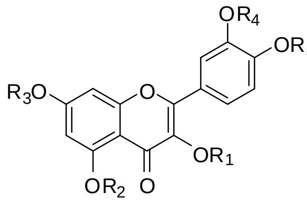
Phenolic compounds

Several phenolic compounds were identified in the aerial parts and roots of some species of the 2ed group of Lactuceae tribe such as small phenolic compounds: *p*-hydroxybenzoic acids, 4- caffeoylquinic, chlorogenic, *trans*-caffeate, methyl and ethyl *p*-hydroxyphenylacetate, and *p*- coumaric**,** affeic acids as well as their glycoside derivatives, dihydroconiferin, syringin and dihydrosyringin [38, 39]. In addition this group of Lactuceae tribe contains various flavonoids and flavonoid glycosides such as flavanone type: 7-hydroxyflavanone **45**, 7-methoxyflavanone **46**, naringenin **47**, naringenin 7-methyl ether **48**, miscanthoside **49**, hesperitin **50,** quercetin derivatives: Isorhamnetin **51**, quercetin 7-*O*-glucoside **52**, quercetin 7-*O*-gentiobioside **53**, hyperin **54**, quercetin 3-*O*-glucuronide **55**, quercetin 3-*O*-rhamnoside **56**, quercetin 3-*O*-rutinoside **57**, isorhamnetin 3-*O*-glucoside **58** and isorhamnetin 3-*O*-glucuronide **59.** Various apigenin, luteolin and isoetin groups were founds in the tribe such as: Apigenin 4'-methyl ether **60**, apigenin 4'-*O*-glucoside **61**, apigenin 7-*O*-glucoside **62**, scutellarin A **63**, apigenin 7-*O*-gentiobioside **64**, linarin **65,** luteolin **66**, luteolin 4'-*O*-glucoside **67**, luteolin 7-*O*-galactoside **68**, luteolin 7-*O*-glucoside **69**, luteolin 7-*O*-rhamnoside **70**, luteolin 7-*O*-gentiobioside **71**, luteolin 7-*O*-rutinoside **72**, luteolin 7,4'-*O*-diglucoside **73**, luteolin 7-*O*-gentiobioside-4'-*O*-glucoside **74**, luteolin 7,3'-*O*-diglucoside **75** and isoetin glycosides, 7-O-glucoside **76**, 7-O-glucoside-2'-O-arabinoside **77**, 7-O-glucoside-2'-O-xyloside **78**, 7-O-glucoside-2'-O-(4-O-acetyl)-xyloside **79.** It is well noted that flavonoids are considered as chemosystematic markers in the tribe Cichorieae of the Asteraceae family. Furthermore, usually coumarin compounds are found in the 2ed group of the Cichorieae tribe such as, umbelliferone **80**, scopoletin **81**, esculetin **82** and cichoriin **83** [41, 45, 52, 53].



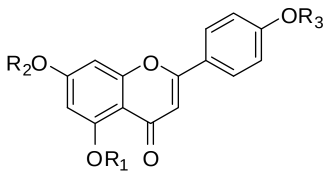
45-50

	R_1	R_2	R_3	R_4
45	H	OH	H	H
46	H	OCH_3	H	H
47	OH	OH	H	OH
48	OH	OCH_3	H	OH
49	OH	O-Glc	OH	OH
50	OH	OH	OH	OCH_3



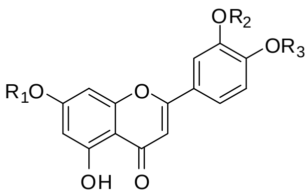
51-59

	R_1	R_2	R_3	R_4	R_5
51	H	H	H	CH_3	H
52	H	H	Glc	H	H
53	H	H	Gen	H	H
54	Gal	H	H	H	H
55	Glu	H	H	H	H
56	Rha	H	H	H	H
57	Rut	H	H	H	H
58	Glc	H	H	CH_3	H
59	Glu	H	H	CH_3	H



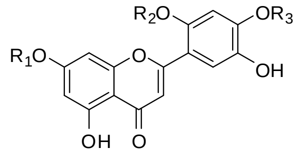
60-65

	R_1	R_2	R_3
60	H	H	CH_3
61	H	H	Glc
62	H	Glc	H
63	H	Glu	H
64	H	Gen	H
65	H	Rut	CH_3



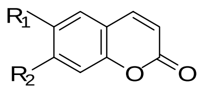
66-75

	R_1	R_2	R_3
66	H	H	H
67	H	H	Glc
68	Gal	H	H
69	Glc	H	H
70	Rha	H	H
71	Gen	H	H
72	Rut	H	H
73	Glc	H	Glc
74	Gen	H	Glc
75	Glc	Glc	H



76-79

	R_1	R_2	R_3
76	Glc	H	H
77	Glc	Ara	H
78	Glc	Xyl	H
79	Glc	4-*O*-acetyl Xyl	H



80-83

	R_1	R_2
80	H	OH
81	OMe	OH
82	OH	OH
83	OH	O-Glc

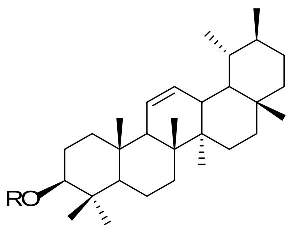
b. Secondary metabolites isolated from the Saharan *Launaea* genus

Different secondary metabolites have been identified from the genus *Launaea*. In addition, few sesquiterpene lactones have been reported from various species of this genus and the occurrence of flavones glycosides is remarkable. The first works in phytochemistry on species of the genus *Launaea* was started in 1969 by Prabhu and Venkateswarlu [54], when they isolated from leaves and roots of launaea pinnatifida two compounds Taraxasterol **35** and Taraxerly acetate **37**. Five year after, in 1974, Bahadur and Sharma [55] reported the presence of palmitic, stearic, oleic and linoleic acids from the roots of *Launaea nudicaulis*. Twenty year ago, in 1989, Gupta *et al.* [56] investigated *Launaea asplenifolia* and isolated nine compounds namely, taraxasterol, taraxasterone, taraxasteryl acetate and the common compounds stigmasterol, ethypalmitate, ethylstearate, hexacosanol, octacosanol and octacosanoic acid.

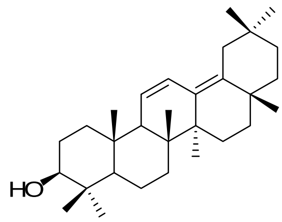
Launaea nudicaulis

The light petroleum extract of *Launaea nudicaulis* leads to the characterization of some Δ^7 and Δ^5 phytosterols: β-sitosterol, brassicasterol, campesterol, stigmasterol, fucosterol, 24β-Δ^7-ergosten-3β-ol and stigmasta-7,24(28)-dien-3-ol [57]. Detailed chemical investigation of *Launaea nudicaulis* yielded some triterpenes such as taraxasterol 35, ψ- taraxasterol 38, β-amyrin 34, 3β- taraxerol 33, α- amyrin 39, and lupeol 41 [58].

Two new ursene type triterpenes, nudicauline A **84**, and nudicauline B **85** have been isolated from the aerial parts of this species, along with olean-11,13(18)-diene **86**, 3β-hydroxy-13(28)-epoxy-urs-11-ene **87** and 3-keto-13(28)-epoxy-urs-11-ene **88** [59]. Additionally, flavone glycosides were reported from the 70% EtOH extract of fresh sample of *Launaea nudicaulis* and identified as apigenin-7-*O*-glucoside **62**, luteolin-7-*O*-glucoside **69**, luteolin-7-*O*-rutinoside **72**, apigenin-7-*O*-gentiobioside **64**, luteolin-7-*O*-gentiobioside **71**, and three glycosides luteolin-7,3'-diglucoside **75**, luteolin-7',4'-diglucoside **73** and luteolin-7-*O*-gentiobioside-4'-*O*-glucoside **74** [60], which are common metabolites within the 2ed group of Lactuceae tribe as indicated above. Moreover, two common coumarins, esculetin **82**, and cichoriin **83**, were also described [61, 62].



84 R= OH
85 R = Ac



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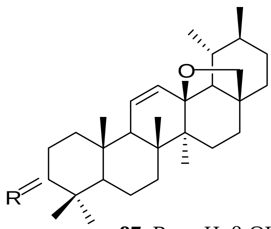
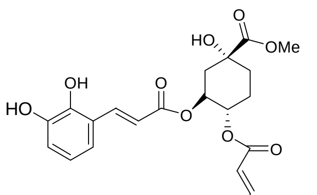


87 R= α H, β OH
88 R = O

Recently, ethyl acetate soluble fraction of methanolic extract of *Launaea nudicaulis* was subjected to chromatographic purification to get four new compounds including a quinic acid derivative Cholistaquinate **89**, a pentahydroxy acetylene analog: trideca-12-ene-4,6-diyne-2, 8, 9, 10, 11-pentaol **90**, a flavone glycoside Cholistaflaside **91** and a sesquiterpene lactone nudicholoid **92**. Cholistaquinate **89** exhibited significant activity in DPPH free radical scavenging assay with an IC50 value of 60.7 mM, whereas, nudicholoid **92** exhibited a moderate inhibitory activity against the enzyme butyrylcholinesterase with an IC50 value of 88.3 mM [63].



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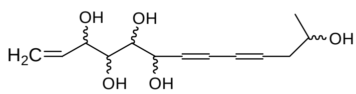

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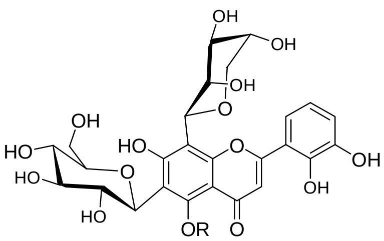

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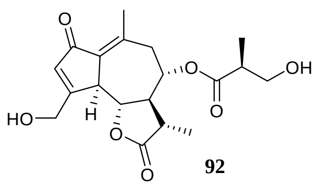


92

***Launaea residifolia* (L.)**

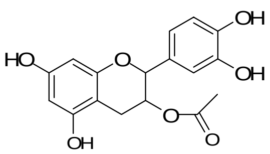
Chemical studie of the plant led to the isolation of triterpenes α-amyrin **40**, lupeol **42**, lupeol acetate **44** and their epimer moretenol together with the Δ^7-stigmasterol. From the aerials parts of *Launaea residifolia* growin in Algeria, four coumarin compounds, cichoriin **83,** esculetin **82**, scopoletin **81** and its isomere isoscopoletin, were isolated [64].

On the other hand, the chemical composition of essential oils from this species (0.9%) has been identified using the ordinary GC-MS technique. Nineteen compounds of essential oil of *L. residifolia* L. were identified representing 86.68% of the total oil. The compounds were identified by spectral comparison to be mainly esters, alcohols, ketones, and terpenes. The principal constituents are dioctyl phthalate (39.84%), Decanoic acid, decyl ester (12.09%), 11-Octadecenal (11.24%), and Eucalyptol (07.31%) [65].

Launaea arborescens

Chemical data on this species are scarce in literature and few published papers describe phenolic components of the plant. In their studies on *Launaea* genus from Spain including *L. arborescens*, Giner *et al.* [66] isolated common phenolic compounds namely, luteolin **66**, luteolin-7-*O*- glucoside **69**, luteolin-7-*O*-rhamnoside **70**, esculetin **82** and its glycoside cichoriin **83**, and simple compounds, ethyl-caffeoate and ferulic acid. The authors remarked that cichoriin **83** was the most abundant compound in all studied species.

We are the first initiators on the phytochemical study of the Algerian sample of *L. arborescens* collected from the Sahara [67]. From the methanol extract of the aerial parts of this species, we have described the isolation of four compounds, two flavonoids, 3- acetyl-5-methoxy-7,3',4'-trihydroxyflavan-3-ol-8-*O*-glycoside **93,** 5,7,4'-trihydroxy-3'- methoxyflavone (chrysoeriol) **94**, one lignan, 4,4'-dihydroxy-3,3'-dimethoxy-7,9':7,9'-diepoxylignan **95**, and a diterpene, methyl-15,16-epoxy-12-oxo-8(17), 13(16), 14-ent-labdatrien-19-oate **96**.



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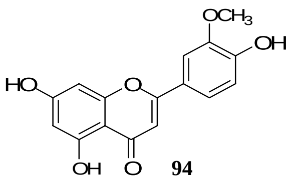

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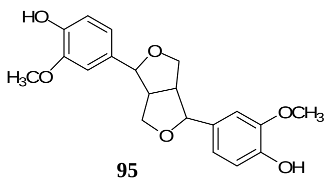

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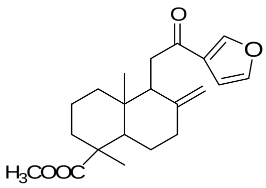

96

A diversity structure of triterpenes oleanane (3β-hydroxy-11α-ethoxy-olean-12-ene) and sesquiterpenes type guaianolides (9α- hydroxy-11β,13-dihydro-3-epi-zaluzanin C, 9α-hydroxy-4α,15-dihydro-zaluzanin C) and costinolide (3β,14-dihydroxycostunolide-3-O-β-Gluc.,3β, 14-dihydroxycostunolide-3-O-β-Gluc.-14-O-p-hydroxyphenylacetate) together with the lactucin-sulfate **30** were chemically characterised from both the aerial parts and roots of *L. arborescens* [68]. The hydrodistillation of the aeriel part of *Launaea arborescens* gave a green yellowish oil in an yield of 0.07% from dried material. Seventeen compounds were identified, representing 84.96% of the total oil. The essential oil of *L. arborescens* was a mixture of different substances, including oxygen-containing monoterpenes, alcohols, aldehydes, and esters. Esters were the dominant group in the oil (58.24%) with dioctyl phthalate (38.6%) and decanoic acid, decyl ester (12.07%) as the main constituents. Alkenes and ketones were the minor constituents of the oil. The terpenoid portion consisted of two oxygenated monoterpenes accounting for 7.24% of the oil. We also found aldehydes in considerable amounts (16.09%) [69].

In a recent study, we were interested in the chiral separation and determination of the diastereomerisation barriers of two flavanone glycosides hesperidin and naringin isolated from the aerial part of *Launeae arborescens*. The chiral separation HPLC screening of diastereomers of hesperidin and naringin by HPLC methods was accomplished in the normal-phase mode using 11 chiral stationary phases and various n-hexane/alcohol mobile phases. The rate constants and activation energy of diastereomerisation (DG#) of flavanones, naringin and hesperidin were determined, respectively, on Chiralpak IC and Chiralpak IA. Separation of (2R/2S)-flavanone glycosides using the Chiralcel OD-H as CSP indicat that Epimer selectivity values (R) ranged from 1.81 for naringin to 1.16 for hesperidin, Chiralpak IA ranged in different conditions from 1.25 to 1.13 for naringin and hesperidin and Chiralpak AD-H presented a good chiral separation of naringin and hesperidin with a selectivity factor towards 1.28. The ChiralpakAD phase presented only the epimer separation of hesperidin with a selectivity factor towards 1.21. Analogously, the resolution factor (Rs) ranged from 2.27 for naringin to 0.97 for hesperidin. The values of R and Rs obtained for naringin were much better than those obtained using another polysaccharide-derived CSP (Chiralpak AD) and a very similar mobile phase (1.51 and 0.7, respectively) [70].

CONCLUSION

The genus *Launaea* has great importance due to its ethnobotanics, phytochemistry and biological activity, and it is a promising source of various secondary metabolites including sequiterpenoids, terpenoids and flavonoids. Some of these isolates compounds have been found to exhibit various biological activities. We have attempted to show the high biodiversity of metabolite products isolated from of the *Launaea* genus as well as their biological significance. This review presents information on the importance of the ethnobotany, phytochemistry and biological activities of the members of this genus, especially the species growing in Algerian Sahara. The given information can be the base for undertaking future research. It is necessary to carry out more studies and to propagate utilization of medicinal plants as a way to diminish the costs of public health programs.

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