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Review Article

Plants of the Genus Heracleum as a Source of Coumarin and Furanocoumarin

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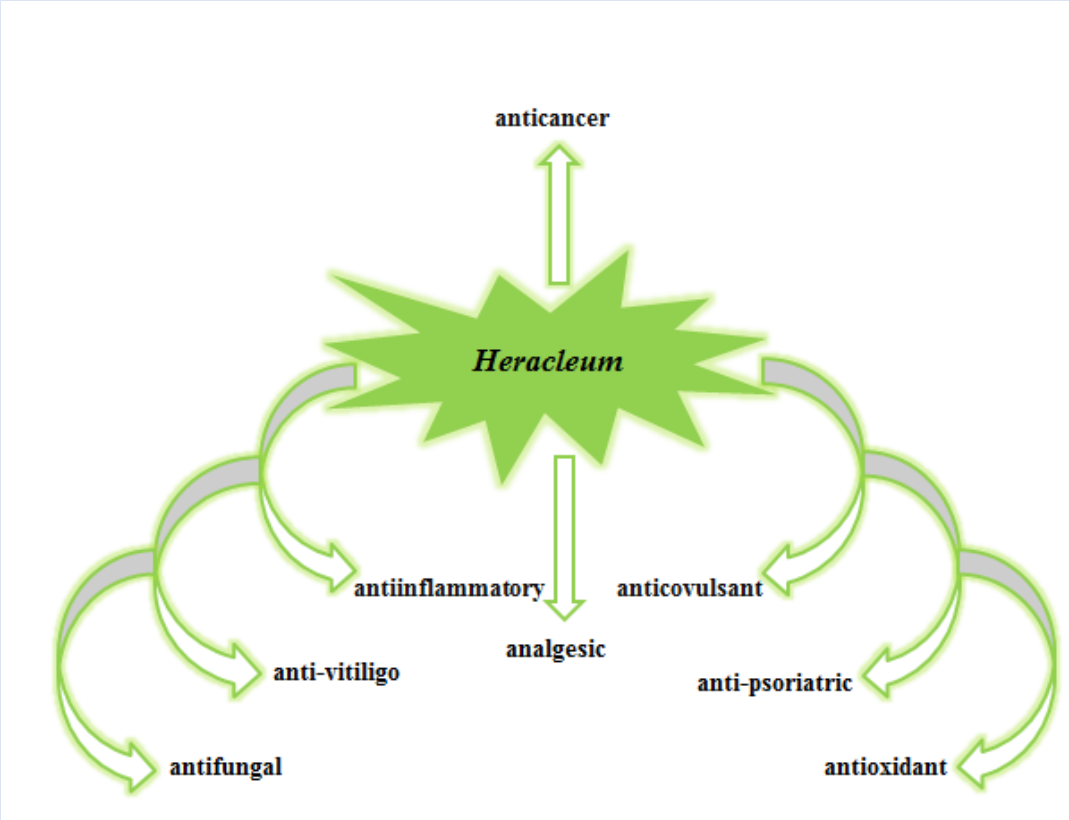
Abstract: Heracleum is one of the greatest genera of the Umbelliferae family that has more than 120 species. This genus is represented by 109 species in Asia. Common names for the genus or its species include hogweed and cow parsnip. This paper discusses the phytochemistry, ethnopharmacological use and pharmaceutics of Heracleum species. Many kinds of metabolites have been isolated and identified, that furanocoumarins are among the significant ones. Modern pharmacological studies demonstrated that Heracleum and its active compounds have extensive biological activity, particularly in anticonvulsant, anti-inflammatory, antifungal, anticancer, anti-psoriatric, anti-vitiligo and antioxidant activities. In clinical test, Heracleum has successfully been utilized to treat psoriasis, vitiligo, carminative, stomachs, pain killer and anticonvulsant.

Keywords: Heracleum, furanocoumarins, coumarins, anticovulsant, anti-inflammatory.

Graphical Abstract:



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Biography

- **Zahra Hosseinzadeh** was born in Meshkin shahr, Ardebil (Iran) in 1988. She completed her BSc (2011) degree from Science College, Urmia, Urmia University and MSc (2005) Degree from Tarbiat Moallem University, Tabriz (Iran) in Phytochemistry. At present she is pursuing her PhD degree at Organic Chemistry, Zanjan University (Iran) under the guidance of Pro. Ali Ramazani. Her area of research interest is synthesis of biological active compounds and development new synthetic methodologies.

- **Ali Ramazani** has completed his Ph.D under the supervision of Professor Issa Yavari in the Department of Chemistry at the Tarbiat Modares University (TMU) in the Tehran-Iran. He currently works as a full professor in Chemistry at the University of Zanjan in the Zanjan-Iran. His studies focused on organic synthesis and nanochemistry and he has published more than 350 papers. He is an Editorial Board Member of the international Journal Nanochemistry Research. He has received several national and international awards, including the 2013 khwarizmi international award, several top-cited author awards and best-paper awards from leading ISI Journals, Best Researcher Awards, and the Best Lecturer Awards at the University of Zanjan.

- **Nima Razzaghi-Asl** obtained his PhD degree in medicinal chemistry in 2013 under the supervisor of Dr Ramin Miri. Later on, he is currently working as associate professor in the School of Pharmacy of Ardabil University of Medical. He has been actively involved design and modeling of potentially bioactive molecules, synthesis of potentially bioactive heterocyclic compounds and structure activity relationship study of heterocyclic compounds.

1. Introduction

Heracleum (Apiaceae) also known as hogweed and is one of the greatest genera of the Umbelliferae family that has more than 120 species Drude (1897-1898) categorized the genus Heracleum in Umbelliferae tribe Peucedaneae subtribe Tordyliinae. Pimenov and Leonov (1993) ordered Heracleum in tribe Tordylieae W.D.J. Koch, that its arrangement in this tribe has been confirmed by the results of phylogenetic analyses of molecular data [1-4]. This genus is represented by 109 species in Asia, including 10 species in Iran. Four of the Iranian spices are indigenous, [5] and four of them are endemic [6]. In traditional medicine, some Heracleum species are used as antipyretic, analgesic, diaphoretic, [7] antiseptic, carminative, digestive and also as a flavouring agent and spice for foods for rheumatic disease, lumbago, gastralgia, and injuries from falls, fractures, contusions and strains [8]. Several compounds including coumarins, furanocoumarins, anthraquinones, stilbenes, furanocoumarin dimers, and flavonoids have been isolated and identified from various species of this genus [9-12].

Studies on the essential oils and extracts of different species of Heracleum have shown different biological properties such as cytotoxic activity for Heracleum sibiricum, [13] antioxidant and antimicrobial activity for Heracleum nepalense [14], immunostimulant in Heracleum maximum [15] and anticonvulsant effect for H. persicum [16]. H. persicum has been known as “Golpar” in Iran and is used as flavouring agent and spice for food in many parts of Iran. In some areas of the country, Golpar is used as a flavouring agent for making pickles. The leaves and fruits of this genus are

used as a flavoring agent, antiseptic, carminative, digestive and analgesic in the Iranian folk medicine [17-19].

The genus Heracleum is also a famous origin of furanocoumarins (e.g. bergapten, byakangelicol, phellopterin, xanthotoxin, isopimpinellin, and imperatorin) that show biological effects of broad spectrum [20]. They are significant drugs in vitiligo and psoriaris treatment [20, 21].

Thus, this review discusses to classify updated information on chemical constituents, biological activity and clinical studies performed on the extracts, and the main active constituents isolated from different species of plants of the genus Heracleum in the therapy of the rheumatic and in painful disorders.

2. Botanical Description and Distribution

Heracleum genus has biennial or perennial plants, tall and robust. Height is usually 100-500 cm. This genus grows from a yellow branched root system 40-60 cm deep, that reaches 15 cm in diameter at the crown when ripe. Leaves are ternately compound and on the upper surface the leaves are hairless and below slightly hairy. Lower leaves are divided into three or more segments. On the upper surface, the leaves are hairless and below slightly hairy. The hollow stem of giant hogweed is coarse and ridged with protruding white hairs that are noticeable at the node and base of the petiole. The green stem with purple blotches is often contrast easily with the white hairs. The blossoming on cow parsnip is ordered as a composite umbel with thousands of very small, white flowers or pinkish and petals 9-12 mm. fruits are egg-shaped or oval; 18 mm long by 4-10 mm, barely winged, hairless to hairy, dividing into two mericarps; each with 3–5 lengthened oil canals [22-26].

Convenient features to identify plants with purple-stemmed genus, would be the glabrous and lobed leaves shape of them. Surface glabrous and the canals oil can also be used to identify species [25].

Heracleum grows mainly in the mountain areas alongside streams, cultural landscapes, grasslands, and wetlands. They are found quite in the moderate northern hemisphere and high mountains as far south as Ethiopia. Two principal centers of Heracleum are disclosed; the Caucasus and the Sino-Himalayan regions. In agreement to the data, aggregated in the ASIUM database of Botanical Garden of Moscow State University, there are 30 species of genus Heracleum in the Causasus and Transcaucasian area; 24 species are reported from Turkey and 11 from Iran. 32 species of this genus have been recorded in the Sino-Himalayan area (25 in SW China, nine in Indian Himalaya, and eight in Nepal). The category and distribution of West Asian Heracleum plants is presented in Table1. The overwhelming majority of Heracleum species are endemic to china (out of 29 species, 21 are endemic) although some are found in western, eastern and central Caucasus and western, central, eastern and southwestern Transcaucasia. In China, 29 species are known from China, which are chiefly reported from the Hengduan Mountains of southwestern China. These species have mainly famed in the pharmaceutic uses and some are significant principle in traditional Chinese medicine. Species of this genus can lead to an intense photodermatitis as they include abundant diversity of chemical compounds and be weedy or highly invasive [27-34].

3. Ethno-Pharmacological Use

Certain species of Heracleum have been used in traditional Asian medicine and have proven to have remarkably therapeutic activities [35]. Several Heracleum species have been used traditionally for many purposes in different countries. In traditional medicine, some Heracleum species are used as antipyretic, analgesic, diaphoretic, antiseptic, carminative, and digestive, and also as a flavoring agent and spice for foods for rheumatic disease, lumbago, gastralgia, and injuries from falls, fractures, contusions and strains. The fruits and leaves of this genus are also used as antiseptic, carminative, digestive and analgesic in the Iranian folk medicine [17, 36-41].

H. sphondylium which is known as “cow parsnip” in Europe is used against diarrhea. It is known as tavsanclotu and used against dysentery in Turkey. The roots of Heracleum candicans Wall and Heracleum yunngningense HAND.–MASS are applied in Chinese traditional medicine as an antipyretic and diaphoretic agent in local region of PR China [44-46]. In the Indian system of medicines, Heracleum candicans DC finds use as an aphrodisiac, nerve generally furanocoumarins, furanocoumarin dimer, tonic and also in the therapy of dermal illnesses.

Eastern Canadian First Nations communities use Heracleum maximum as a conventional Asian medicine and have demonstrated to have ailments that include tuberculosis [47-50]. In Thai folk medicine, the fruits of H. siamicum were used as a carminative herbal drug [51]. In Ayurveda, H. rigens has been traditionally used for urinary disorders, cough, hyperacidity, wounds, abdominal disorders, and cardiac diseases and vomiting, in addition, in Siddha, it is used for treating constipation, stomachache, diarrhoea, headache, phlegm, gastric disorders and indigestion [52]. Heracleum rapula, with the Chinese name ‘‘Baiyunhuagen’’, is commonly used in Chinese traditional medicine to dispel wind, remove dampness, expel cold, relieve pain, dredge all channels and

vessels, promote blood circulation, and relax muscles and tendons [53].

4. Chemical Constituents

A great variety of species of plants belonging to the genus Heracleum have been phytochemically and pharmacologically investigated and many molecules have been isolated and identified. In this context, different classes of organic compounds of medicinal interest have been reported, including coumarins and generally furanocoumarins, furanocoumarin dimer, coumarin glycosides, anthraquinones and stilbene derivatives, and flavonoids (Table 2, Figures 1-9).

However, it should be considered that coumarins and furanocoumarins are the most plenty compounds so far verified in this genus. The genus Heracleum is a rich of furanocoumarins (such as bergapten, byakangelicol, phellopterin, xanthotoxin, isopimpinellin, and imperatorin), showing the pharmacological effects. They are used as drug for the vitiligo and psoriaris treatment [54-56].

Among the all studied species, H. candicans Wall, H. rapula, H. yunngningense and H. grandiflorum have been used more than the other species. Although a majority of these compounds are chemically identified, their complete biological activity remain totally unknown.

Table 1. The category and distribution of West Asian Heracleum species

Distribution	Category
Russia	H.apiifolium Boiss, H. chorodanum (Hoffm.) DC, H. grandifloru Steven ex M.Bieb, H. leskovii Grossh, H. ponticum (Lipsky) Schischk.ex Grossh, H. roseum Steven, H.scabrum Albov, H.sibiricum L, H.sibiricum L^2, H.sibiricum L^3. H.transcaucasicum
Turkey	H.argaeum Boiss, H.crenatifolium Boiss, H.humile Sm, H.lasiopetalum Boiss, H.marashicum Yildiz, H.pastinaca Fenzl, H.peshmenianum Ekim, H.platytaenium Boiss, H.sphondylium L. subsp. Velen, H. sphondylium ssp. ternatum, H. platytaenium, H.sphondylium.subs .artvinense, Heracleum platytaenium
Armenia	H.pastinacifolium K. Koch, H.schelkovnikovii Woronow, H,trachyloma Fisch, H.transcaucasicum Manden
Iran	H.anisactis Boiss, H.lasiopetalum Boiss, H.rechingeri Manden, H.persicum Desf, H. pastinacifolium C. Koch, H.transcaucasicum Manden, H.gorganicum, H. rawianum
Georgia	H.antasiaticum Manden, H.asperum (Hoffm.) M.Bieb, H.yclocarpum K.Koch, H. freynianum Sommier, H.ossethicum Manden, H.sosnowskyi Manden, H.sibiricum L, H.calcareum var. colchicum, H.chorodanum, H.dissectum, H.dulce, H.lehmannianum, H.mandenovae, H.moellendorffii, H.pastinacifolium, H.ponticum, H.pubescens, H.roseum, H.sommieri, H.sosnowskyi, H.stevenii, H.trachyloma, H.wilhelmsii,H.voroschilowii
Afghanistan	H.afghanicum Kitam
Chin	H.souliei, H.bivittatum Boiss, H.millefolium Diels, H.canescens Lindl, H.sibiricum, H.pyrenaicum, H.hemsleyanum, H.grandiflorum, H.cyclocarpum, H.platytaenium, H.ossethicum, H.lehmannianum, H.mantegazzianum, H.trachyloma,H.sosnowskyi,H. wolongense, H.tiliifolium, H.mollendorffii var mollendorffii, H. fargesii , H. dissectifolium, H.yungningense , H.forrestii, H.subtometellum, H.oreocharis, H.stenopterum, H.scabridum, H.rapula, ,H.franchetii, H.stenopteroides
Iraq	H. rawianum C.C.Towns
Azarbaijan	H. pastinacifolium C. Koch, H. grandiflorum Bie
Ukraine	H. carpaticum Porc, H. ligusticifolium M.Bieb, H. sibiricum L

Table 2. Chemical components isolated from plants of the genus Heracleum

Species	Class	Compound	Ref.
H. persicum	furanocoumarin	xanthatoxin	[57]
		pimpinellin	[58]
		isopimpinellin	
		bergapten	
		isobergapten	
		sphondin	
	flavonoid	quercetin	[59]

H. maximum	furanocoumarin	bergapten	[60]
		isobergapten	
		angelicin	
		sphondin	
		pimpinellin	
		isopimpinellin	
		isopentenyloxyisobergapten	
		6-isopentenyloxyisobergapten	
	polyacetylene	falcarindiol	
H. lacianitum	furanocoumarin	sphondin	[61]
H. candicans Wall		xanthotoxin	[62]
	alkyl coumarins	isophellodenol C	[63]
	spirobifuranocoumarins	candibirin B-E	[64]
	trifuranocoumarins	canditririns A	
		canditririns B	
	spirotrifuranocoumarin	canditririns C-E	
	spirotetrafuranocoumarin	canditetrarin A	
	tetrafuranocoumarin	canditetrarin B	
	furanocoumarin glucosides	candinosides A	[65]
		candinosides B	
		candinosides C	
		candinosides D	
	ester coumarin	candinols A	[66]
		candinol B	
		candinol C	
	furanocoumarin dimers	candibirins F-H	
	furanocoumarin	heraclenol	[66-68]
		bergapten	
		angelicin	
		imperatorin	
		heraclenin	
		xanthotoxol	
		psoralen	
		isopsoralen	
		8-geranoxypsoralen	
		sphondin	
		isoheraclenin	
		candicanin	
		(+)-Marmesin	[68]
H. mantegazzianum	furanocoumarin	pimpinellin	[69]
		imperatorin	
		phellopterin	
		xanthotoxin	
		isobergapten	
		angelicin	
		isopimpinellin	

		bergapten	
H. rapula	intermolecular rearranged biiridoid glucosides	rapulasides A	[30]
		rapulasides B	
	coumarin	osthol	[70]
	furanocoumarin	xanthotoxin	[71]
		isoimperatorin	
		isophelopterin	
		phellopterin	
	tricoumarin	rapultririn A	[72]
		demethylsuberosin	
		8-hydroxybergapten	
		xanthotoxol	
		8-hydroxybergaptol	
	coumarin glucosides	glucosylpsoralen	
		marmesin	
		30 –hydroxymarmesin	
		heraclenol	
	biocoumarin	moellendorffiline	
		rivulobirin A	
		rivulobirin B	
	furanocoumarin	8-geranyloxypsoralen	
		heraclenin	
		imperatorin	
		R-heraclenol	
		O-isopropylideneheraclenol	
		bergapten	
		isopimpinellin	
		sphondin	
		isobergapten	
		pimpinellin	
		angelical	
		pregnenolone	
		(+)-Marmesin	
H. rawanium	furanocoumarin	angelicin	[73]
		allobergappten	
		sphondin	
	sterol	stigmasterol	
		β-sitosterol	
H. sibiricum	furanocoumarin	bergapten	[74]
		pimpinellin	
		isopimpinellin	
		sphondin	
		phellopterin	[75]
		xanthotoxin	
		heraclenin	
		byakangelikol	

		imperatorin	
		byakangelicin	
H. rigens		5-(3-methyl but-2-enyloxy)7 methoxy coumarin	[76]
		isopimpinellin	
		8-hydroxy furanocoumarin	
		5-methoxy furanocoumarin	
H. sosnowsky		angelicin	[77]
		bergapten	
		methoxalen	
		imperatorin	
	protein	arabinogalactan	[78]
	carbohydra	pectic polysaccharides	
H. leskowii	coumarin	umbelliferone	[79]
	furanocoumarin	xanthotoxin	
		angelicin	
		isopimpinellin	
		bergapten	
		imperatorin	
		isoimperator	
H. nepalense		sphondin	[80]
		bergapten	
		pimpinellin	
		isopimpinellin	
		quercetin-3-O-β-D-glucopyranoside	
H. platytaenium		psoralen	[81]
		bergapten	
		xanthotoxin	
		pimpinellin	
		isopimpinellin	
		sphondin	
		byakangelicin	
		heraclenol	
	glycosylated dihydrofurocoum	apterin	
	sterol	stigmasterol	
H. pastinacifolium	coumarin	umbelliferone	[82]
	furanocoumarin	bergapten	
		isobergapten	
		sphondin	
		pimpinellin	[83]
		isopimpinellin	
		xanthotoxin	
		allobergapten	
		osthole	
H. grandiflorum		umbelliferone	[84]
		scopoletin	
		isopimpinellin	

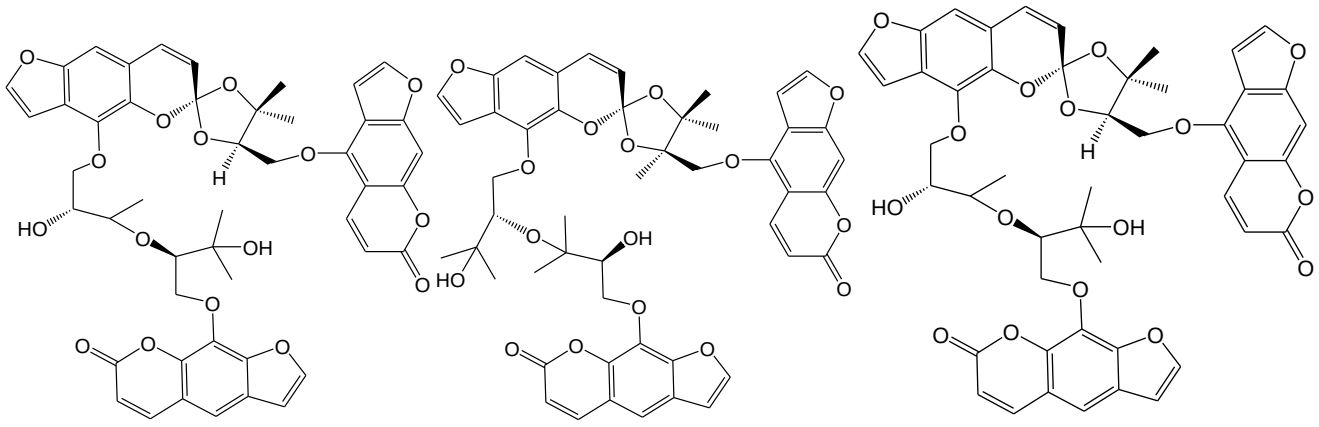
		marmesin	
		columbianetin	
		sphondin	[85]
		isobergapten	
		pimpinellin	
		psoralen	
		bergapten	
		xanthotoxin	[84]
		heraclesol	
		byacangelicin	
H. candolleanum	monoterpenoids	2-exo,3-endo-Camphanediol	[86]
		2-Pinene-4,10-diol	
H. yunngningense	coumarin	yunngnin A	[34]
		yunngnin B	
		yunngnoside A	
		yunngnoside B	
	polyacetylen	falcarindiol	
	phenylpropanoids	ferulic acid	
	phenylpropanoids	phydroxyphenethyl ferulate	
	coumarin	imperatorin	
		umbelliferone	
	furanocoumarin	phellopterin	
		moellendorffiline	
		xanthotoxin	
		umbelliprenine	
		vaginidiol	
		(+)-heraclenol	
		8-geranyloxypsoralen	
		apterin	
		heratomol-6-O-b -D-glucopyranoside	
		isofraxidin	
		scopoletin	
		hermandiol	
		angelicin	
		pimpinellin	
		isobergapten	
		isopimpinellin	
		sphondin	
		6-isopentenyloxyisobergapten	
		bergapten	
		mellendorffiline	
H. transcaucasicum	furomethoxyheraclin	furomethoxyheraclin	[87]
H. moellendorffii Hance	polyacethelene	panaxynol	[88]
		falcarindiol	
	furanocoumarin	bergapten	

		osthol	[88, 89]
		isopimpinellin	
		sphondin	
		4'-hydroxy-columbianetin	
		moellendorffiline	
		isobergapten	[90, 91]
		psoralen	
		pimpinellin	
H. montanum	flavonoid	quercetin	
H. souliei	pluramycin-type	heraclemycins A–D	[92]
		β-indomycinone	
		saptomycin A	
H. sphondylium L	flavonoid	quercetin	
	furanocoumarin	bergapten	[92]
		n-pentacosane	
		n-heptacosane	
		n-octacosane	
		n-nonacosane	
		n-triacontane	
H. sphondylium L		n-hentriacontane	
		ceryl alcohol	
	sterol	β-sitosterol	
	furanocoumarin	xanthotoxin	[93]
H. aconitofolium		sphondin	[94]
		imperatorin	
		bergapten	
		xanthotoxin	
		byacangelicin	
H. lehmannianum	neutral lipid	hydrocarbons	[95]
		triacylglycerols (TAGs)	
		free fatty acids(FFs)	
		triterpenols	
		sterols	
	phospholipids	phosphatiadylcholines (PCs)	
		phosphatidylinositols (PIs)	
		phosphatidylethanolamines (PEs)	
		N-AcyI-PEs	
		N-Acvl-lyso-PEs	
		phosphatidylglycosides (PGs)	
H. lehmannianum		Lyso-PC	
		Lyso-Pls	
	glycolipids	sterol glycoside esters	
		methylgalactosyldiglycerides (MGDGs)	
		digalactosyldiglycerides (DGDGs)	
H.canescens	furanocoumarin	osthol	[96]
		methyl 3,4,5trimethoxybenzoate	

		heraclenin	
		8-geranyloxypsoralen	
	sterol	sitosterol	[97]
	furanocoumarin	imperatorin	
H.canescens		psoralen	
		alloimperatorin	
		xanthotoxin	
		imperatorin	
		isoheraclenin	
		heraclenol	
		isogosferol	
		alloisoimperatorin	
H. leskovii		bergapten	
		xanthotoxin	
		isopimpinellin	
		osthole	
		psoralen	
		phellopterin	
		heracol	
		byacangelicin	
		angelicin	
		sphondin	
		isobergapten	
		6-isopentenyloxy-5-methoxyangelicin	
		heraclesol	
H. lanatum		xanthotoxin	[98]
		bergapten	[99]
		psoralen	
H. crenatifolium		bergapten	
		pimpinellin	
		isopimpinellin	
		sphondin	
		isobergapten	
		byak-angelicol	
H. antasiaticum		heracol	
H. thomsoni		heratomin	[100]
		heratomol	
		Ianatin	
		isobergapten	
		isoimperatorin	
		impemtorin	

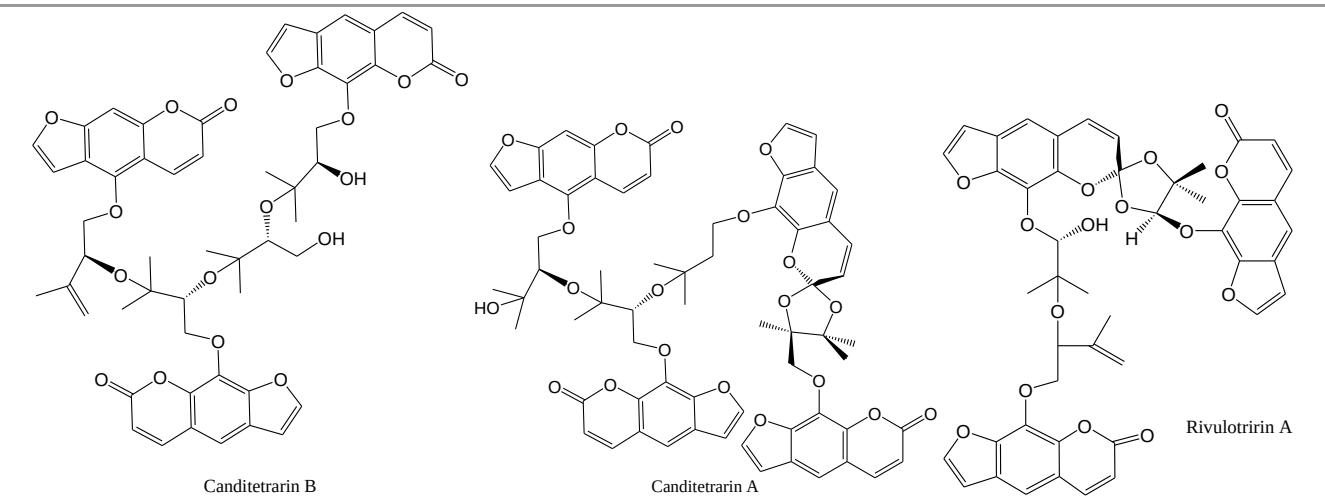
2-exo,3-endo-Camphanediol 2-Pinene-4,10-diol

Figure 1. Monoterpenoids isolated from the seeds of Heracleum candolleanum.



Canditririn D Canditririn E Canditririn C

Figure 2. Spirotrifuranocoumarin isolated from H. candicans.



Canditetrarin B Canditetrarin A Rivulotririn A

Figure 3. Furanocoumarins isolated from H. candicans.

Clearly, the complication of the admixture and the existence of the multiple compounds in low concentrations cause to be the isolation and identification of these substances very arduous. Some studies have specified the existence of multiple furanocoumarins in H. yunngningense (Table 1), the authors of this review cannot recognize any of these compounds from the same species but gathered in China. So, different environmental conditions affect the chemical compounds [101].

Concerning the part of the plant most investigated, we have observed that in general the whole plant material is used, since these species are commonly small herbs and are employed in this manner in folk medicine. Our research team has carried out phytochemical studies of this genus via bioassay-guided isolation, allowing the identification of different compounds with pharmaceutical effects existing in the active fractions or extracts. In this way, we have isolated the principal furanocoumarin existing in H. platytaenium, reffering to sphondin that exhibits antioxidant and anticholinesterase activity [82]. It is worth noting that this furanocoumarin has been utilized as a pattern to prepare novel active molecules, especially 4'-Aminomethyl-4,5',8-trimethylpsoralen and 4,5,8 trimethylpsoralen (trioxalen) derivatives [102]. Besides angelicin, we also have isolated 8 furanocoumarin, steroid compound and a dihydrofurocoumarin glycoside that will be conversed in more detail in the biological section (Table 3).

However, it is also important to demonstrate that the genus Heracleum is a main origin of furanocoumarins (e.g. bergapten, byakangelicol, phellopterin, xanthotoxin, isopimpinellin, and imperatorin), that demonstrate pharmaceutical properties of broad spectrum [53-55]. They are typical phototoxic compounds leading to photodermatitis upon exposure to UV light [103]. In humans and experimental animals, chronic furanocoumarin treatment, in combination with UV light, is used in the therapy of psoriasis and vitiligo [21,57].

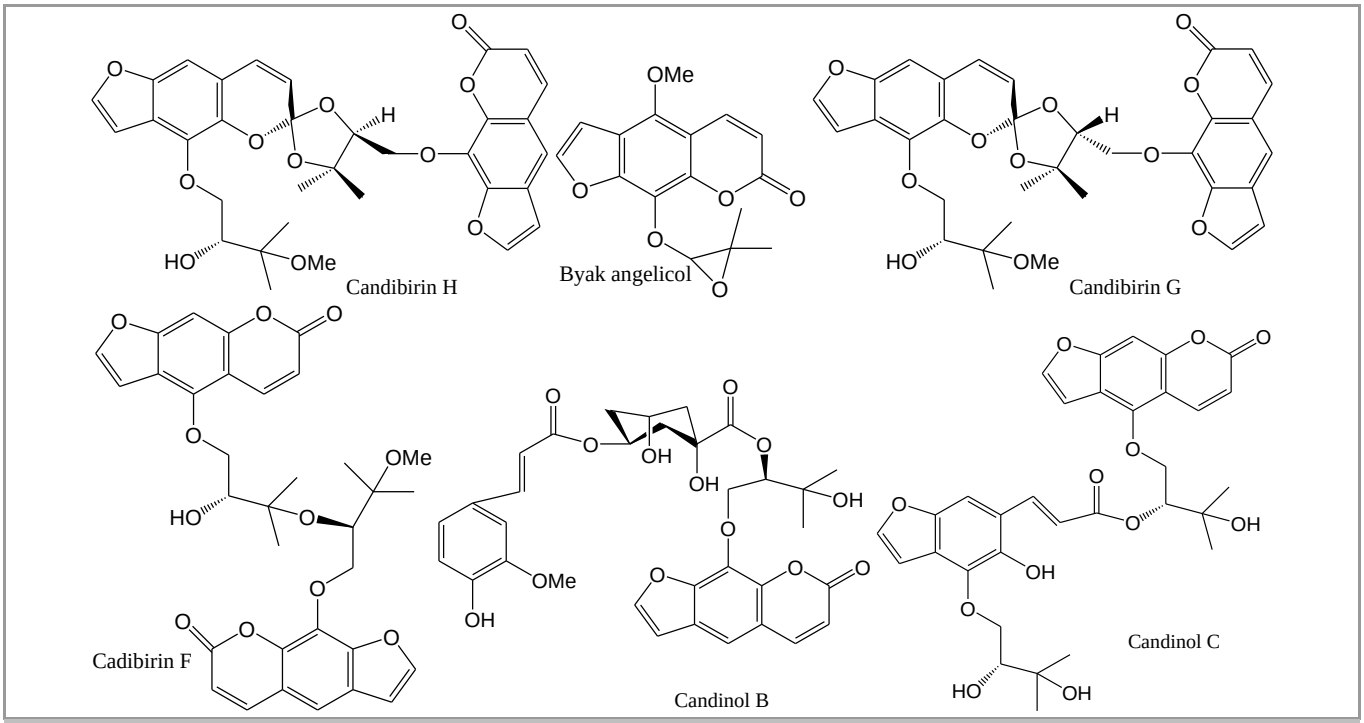


Figure 4. Furanocoumarins isolated from H. candicans.

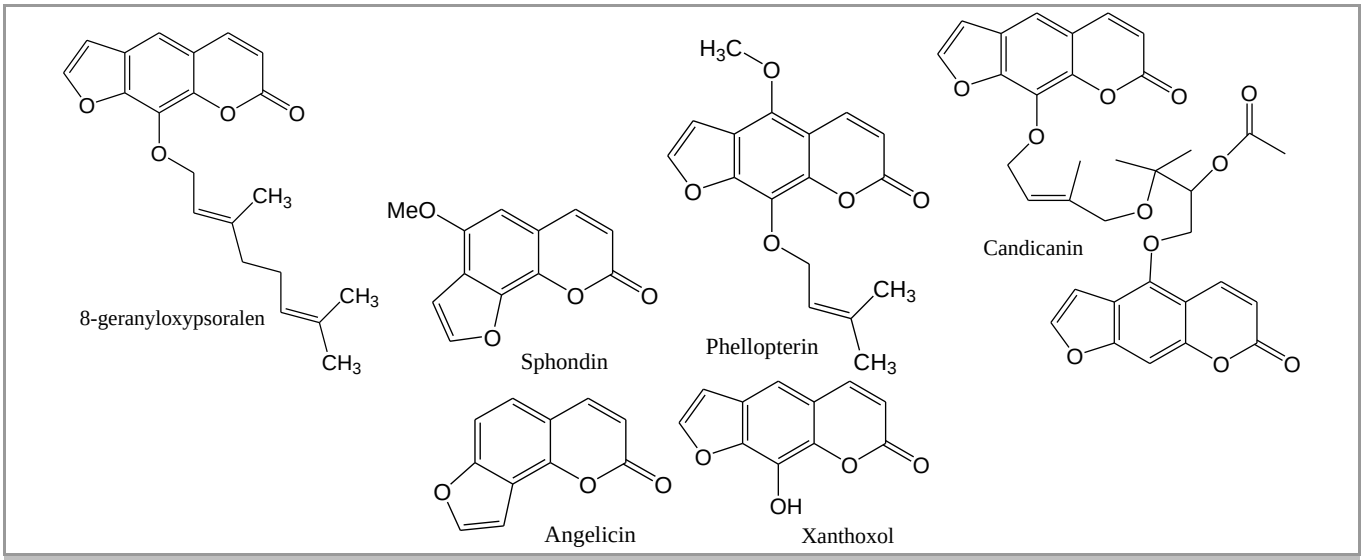


Figure 5. Furanocoumarins isolated from H. candicans.

5. Chemical Constituents

Up to now, it still abides a worldwide health preference to extend new remedial methods for therapeutic a countless of diseases, and to establish those discoveries in an surrounding of stability [104]. Owing to the variety, wide metabolic span, and provided. Accessibility, plants demonstrate a potentially worth origin of biologically important constituents that should be probed for their

capability pharmaceutical utilize. About 6.5 billion patients are applying medicinal plants in some formation on a relatively orderly foundation, and the use of plant-based traditional pharmaceuticals in the world is ongoing to increase as the population extends

[105]. Heracleum pharmacological effects have enticed wide consideration. Orally, Heracleum has traditionally been utilized to therapy impotency, treatment of skin diseases, epilepsy, urinary disorders, gastric disorders, stomachache, phlegm, cough, hyperacidity, wounds, abdominal disorders, and cardiac diseases, vomiting, antipyretic, diaphoretic, analgesic, dysentery, diarrhea laryngitis, and bronchitis [36-40]. A general overview on the present situation of modern biological assay is reported in supplemental (Table 3)

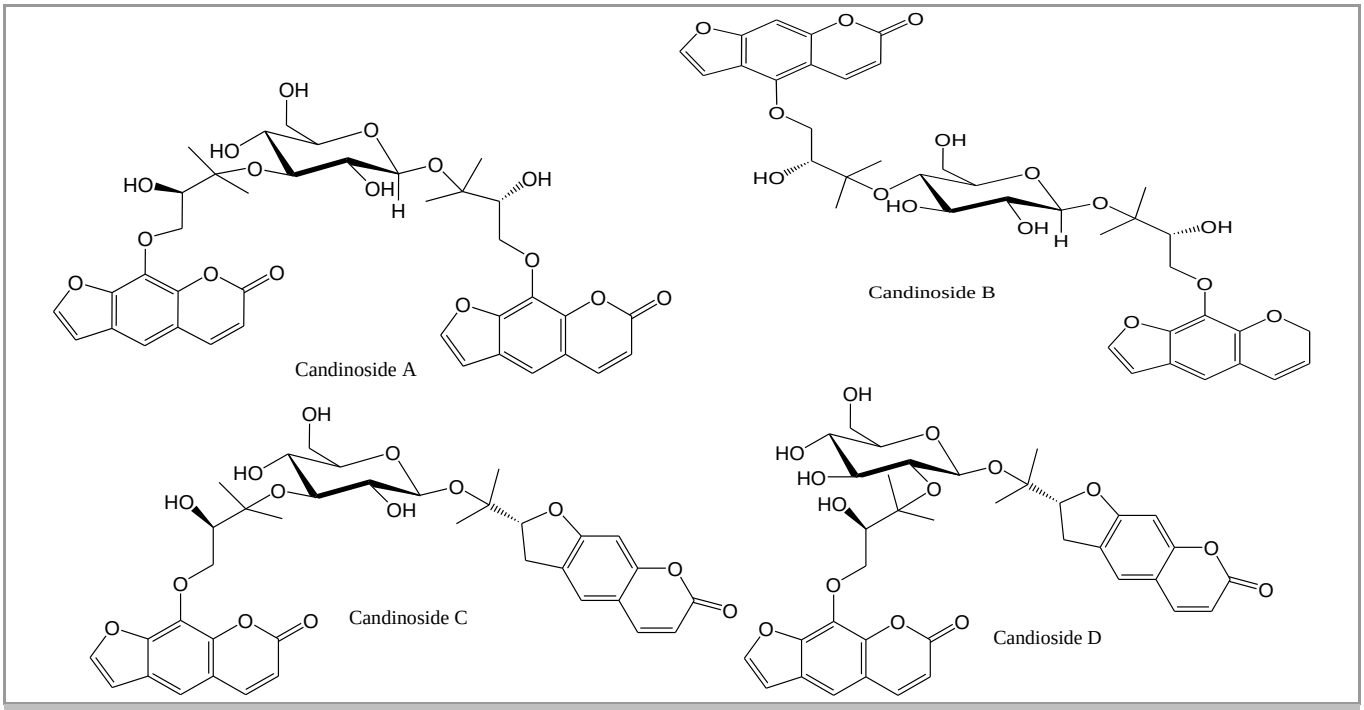


Figure 6. Furanocoumarin glucosides isolated from H. candicans.

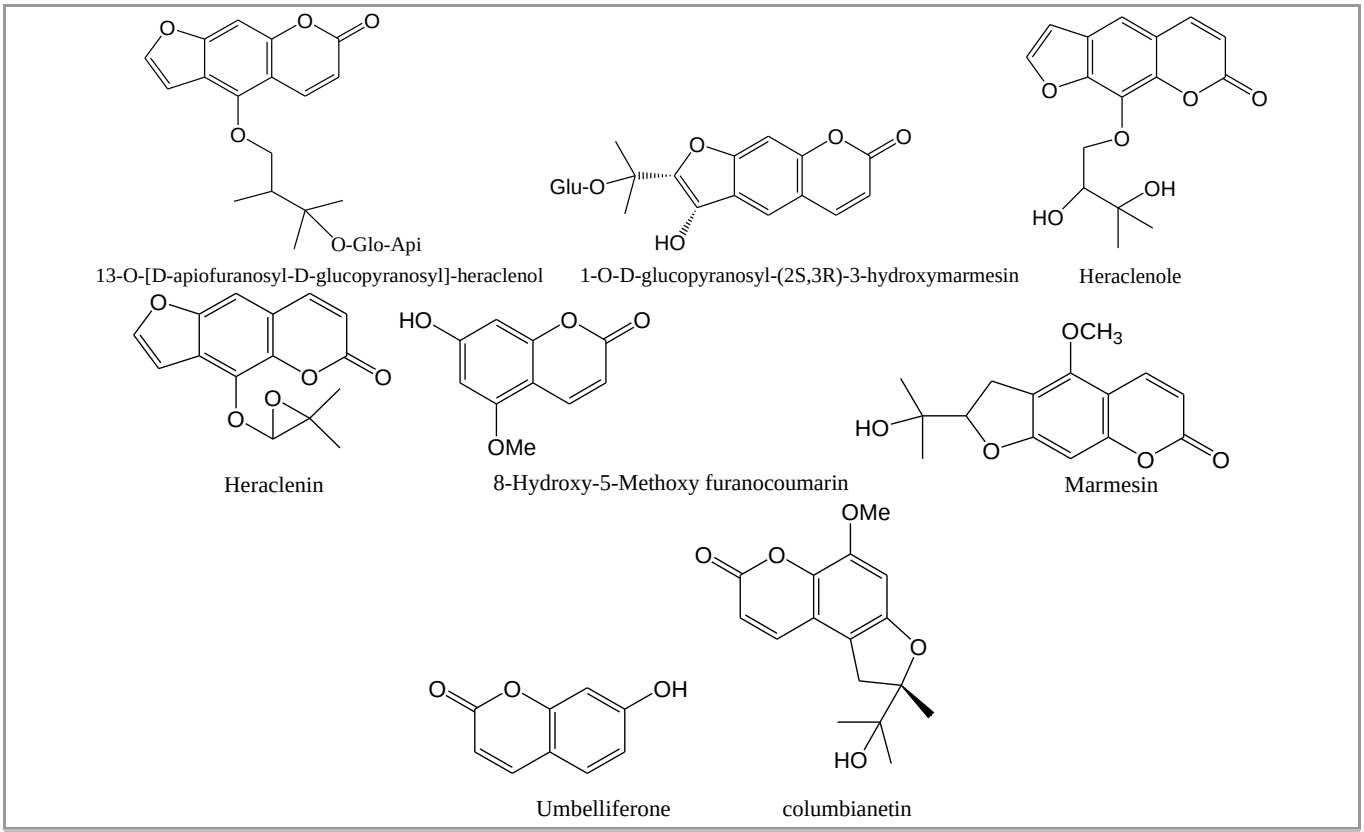


Figure 7. Furanocoumarin isolated from Heracleum species.

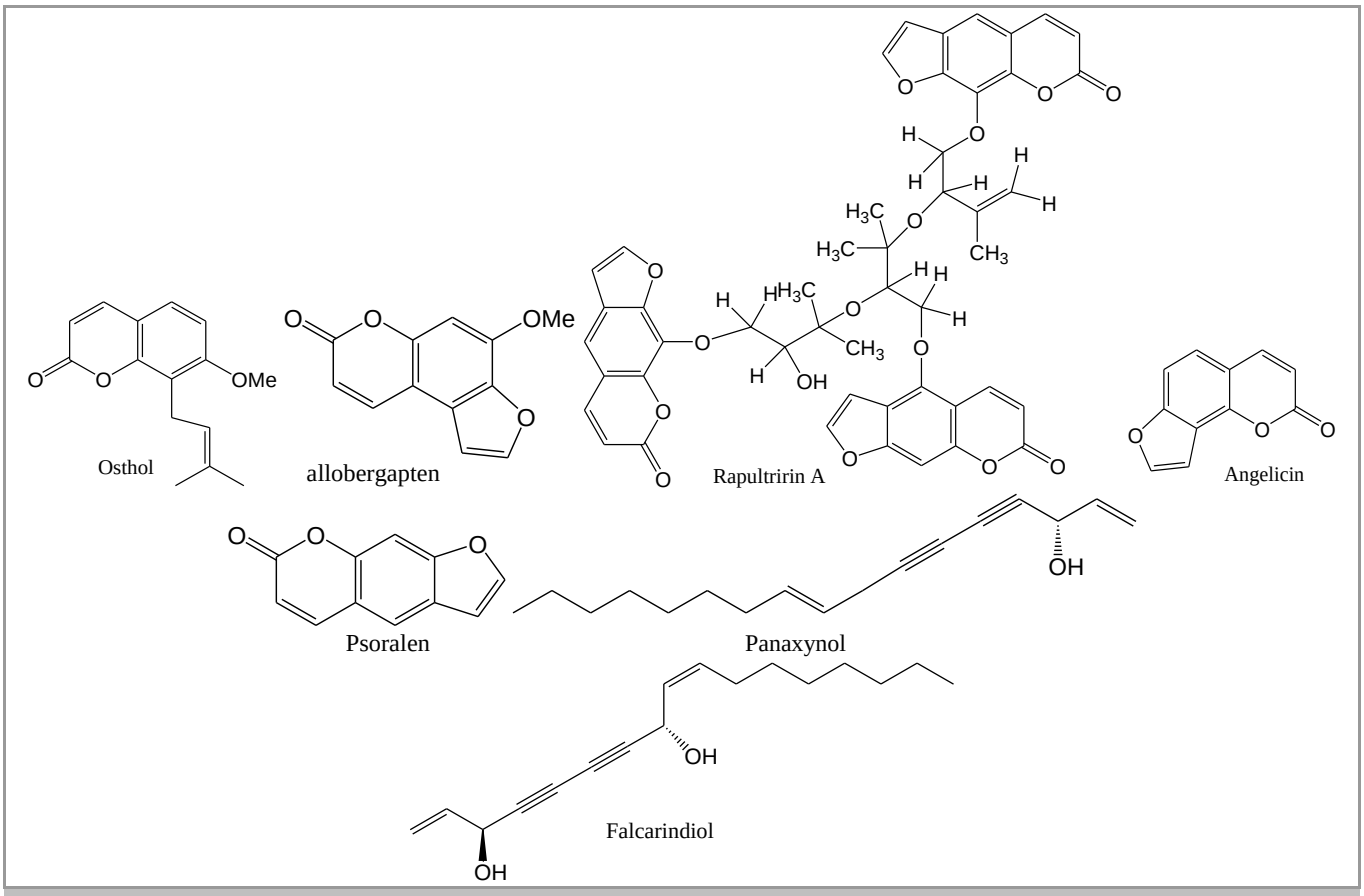


Figure 8. Furanocoumarin isolated from Heracleum species.

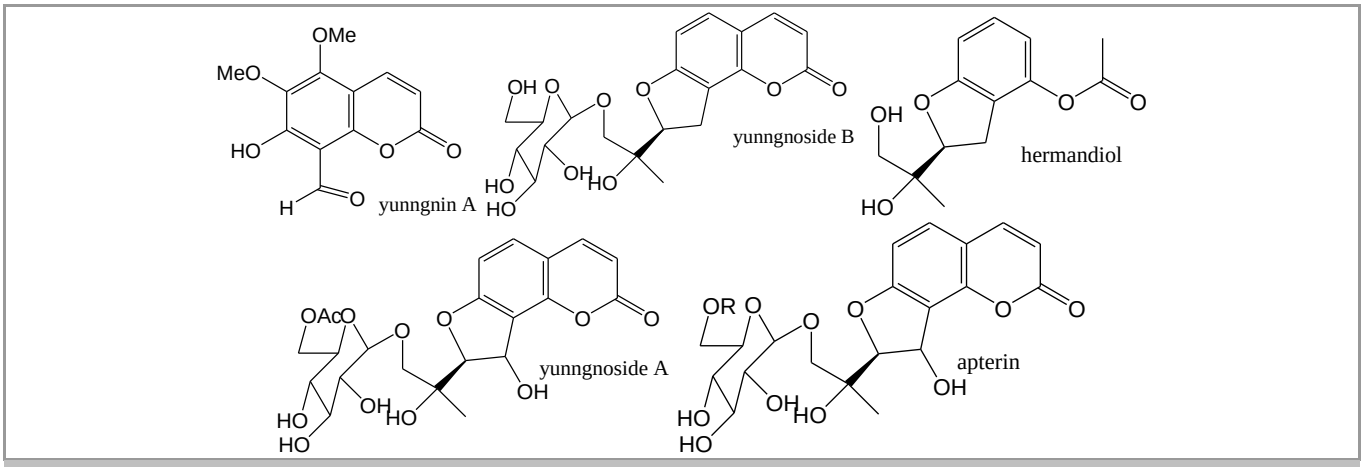


Figure 9. Furanocoumarins isolated from Heracleum yunngningense.

Table 3. Biological Activity of the Isolated Constituents of Some Species of Heracleum.

Species	Compound	Pharmacological Activity	Ref.
H. candicans	heraclenin	anti-inflammatory	[21]
		anti-coagulant	[106]
		skin photosensitizing	[107]
	bergapten	melanogenesis stimulation activity	[108]
H. lanatum	psoralen	anti-psoriatric	
H.canescens		anti-vitiligo	
H.moellendorffii Hance		antifungal	[106, 109]
H. platytaenium		anticancer	[110]

H. candicans Wall	xanthotoxin	treat leucoderma	[62]
		suntan lotions	
H. crenatifolium	bergapten	anticonvulsant	[101]
H. persicum	aconitine	anticonvulsant	[110]
	sphondin	anti-inflammatory, analgesic	[58, 111]
		folliculogenesis	[111]
	ergosterol	antifungal	[112]
		anti-AF	
H. nepalense	bergapten	anti-inflammatory	[113]
H. souliei	heraclemycin C	antitubercular	[92]
H. mantegazzianum	xanthotoxin	antimicrobial	[114]
	pimpinellin		
	phellopterin		
H. moellendorffii	psoralen	antiarrhythmic	[115]
H. platytaenium	xanthotoxin	Anti AChE	[82]
	isopimpinellin	Anti BChE	
	pimpinellin		
	psoralen	antioxidant	
	pimpinellin		
H.laciniatum	sphondin	anti-inflammatory	[111]
H rapula	Rapulasides A,B	Inhibitor platelet aggregatio	[69]
H. maximum	falcarindiol	antimycobacterial	[15]
	6-isopentenyloxyisobergapten		
H. moellendorffii	panaxynol		[90]
	falcarindiol		

6. Conclusions

In a clinical test, Heracleum has successfully been utilized to treat the psoriasis, vitiligo, carminative, stomachs, pain killer, and anticonvulsant. Modern in vitro and in vivo pharmacological studies have increasingly confirmed the traditional use of the Heracleum plants. The raw extracts and constituents from the aerial parts or roots have plenty sorts of pharmacological effects, particularly in the betterment of carminative, digestive, stomachs, antiproliferative, antimycobacterial, inhibitor platelet aggregation, anti-inflammatory, antioxidant, anticholinesterase, antimicrobial, antitubercular, analgesic, anticancer, anti-vitiligo, anti-psoriatric, anti-coagulant, anti-inflammatory, and antifungal effects. Most of the pharmacological activity of Heracleum plants can be illustrated by a more content of furanocoumarins present in the genus, particularly psoralen and xanthotoxin. Recently

phytochemical and pharmaceutical investigation of the constituents isolated from the genus Heracleum have attracted much attention, but the pharmaceutical researches so far have mainly been performed in vitro and in vivo with animals. Thus, pharmaceutical investigation in humans are crucially necessary to verify this conventional phytotherapy. The compounds of the genus Heracleum, their pharmaceutical and cytotoxicity properties should be more studied with both in vitro and in vivo studies. Also, due to profile, their remedial performance and economical attentions, the total furanocoumarins and/or active constituents may be developed into novel drugs for the therapy of different diseases, particularly psoriasis and vitiligo.

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