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Phytochemistry and Ethnopharmacology of Some Medicinal Plants Used in the Kurdistan Region of Iraq

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The majority of Kurds inhabit a region that includes adjacent parts of Iran, Iraq, Syria and Turkey. This review shows that the traditional medicine is still used by Kurdish peoples and underlines the medicinal value of a great number of plants used locally. The medicinal uses include the treatment of a variety of diseases, ranging from simple stomach-ache to highly complicate male and female disorders; even sexual weakness and kidney stones are treated by plants. The majority of the plants that are used are for curing gastro-intestinal disorders and inflammation, followed by urinary tract disorders, skin burns, irritations and liver problems. In the last part of this paper, we also report the first results of our ongoing research project on the constituents of some uninvestigated Kurdish medicinal plants. The *C*-glycosylflavone embinin, the α-methylene acyl derivative 6-tuliposide A, and the iridoids aucubin and ajugol were isolated for the first time from *Iris persica*, *Tulipa systole* and *Verbascum calvum*, respectively. These plants are traditionally used against inflammation, pain, and skin burns.

Keywords: Kurdistan-Iraq, Phytochemistry, Ethnopharmacology, Traditional uses, Secondary metabolites.

Kurdistan, which means the homeland of the Kurds, is not a state, but an ill-defined geo-cultural region where about 20-million Kurdish people form the major population. They have been constituted ethnically as a homogeneous community since the dawn of history, developing their unique culture and language. The word Kurdistan was first used by the Seljuks in the 12th century as a name for a province including the lands between Azerbaijan and Luristan (for example, Senna, Dainawar, Hamadan, and Kirmanshah), as well as certain adjoining areas to the west of Zagros (Shahrazur, Khuftiyan) [1]. Nowadays, the largest part of Kurdistan is a highland, roughly encompassing the northwestern Zagros and the eastern Taurus mountain ranges [2]; however, in the southeast, it spreads across a belt of foothills to the Mesopotamian plain. Greater Kurdistan is thus a geographically contiguous territory, of about 409,650 square kilometers and 1,000 kilometers in length from north to south, which includes parts of southeastern Turkey (Northern Kurdistan), northern Syria (Western Kurdistan), northern Iraq (Southern Kurdistan), and western Iran (Eastern Kurdistan) (Figure 1). Though the well-known Kurdish sentiment that they have "no friends but the mountains" reveals the cultural and even political significance of the landscape, the reality of the human settlement in Kurdistan belies this rather romantic vision. In fact, the majority of the Kurdish population lives now in towns, and a large diaspora is present in distant countries such as Germany, Sweden, and Canada. Likewise, habit differences between remote villages on mountains and large cities, and varied experiences with modernization, as well as Arab, Persian, and Turkish nationalisms, are marked by contrasting patterns of rural and urban life-styles; however, residents still recognize a common Kurdish culture [3].

About 8.35 million (2013 estimate) Kurds live in Iraqi Kurdistan or Southern Kurdistan, who constitute approximately 19% of Iraq's overall population. The country is officially known as the Kurdistan Region; being governed by a Regional Government and a Parliament, it is the only autonomous region of Iraq and even of the entire Greater Kurdistan. The land itself is unique in its natural diversity, due to the mountainous nature of the north and the east, while rolling hills and sometimes plains make up the western and southern parts.

The country is generously watered by a number of clear springs, water courses and rivers, among which are the biblical Tigris, and lakes. The climate is harsh in winter and snow covers the high summits for many months of the year. In the plains, rainfall varies between 200 and 400 mm a year, although it may reach between 700 and 2000 and even 3000 mm on the plateau between the different chains of mountains. However, in the valleys, the climate is continental and even arid on the plains. In the mountains, high mountain-pastures stretch over many kilometers and provide pasturage for herds of goats and sheep. In places, edible wild plants grow, sought after by shepherds and simple folk for their medicinal properties and carefully collected, mostly by women [4].

In Kurdistan, the use of plants as medicines has, indeed, been described throughout history in the form of traditional medicines, potions and oils, and has constituted the only medicinal remedies for the people living in remote villages in the mountains. In Kurdistan, the knowledge of the effects and uses of herbs is not only the property of specialists or herbalists, such as in other traditional medicinal systems; instead, it is part of the cultural heritage of any family and it is orally transmitted through generations. Any market, locally known with the names of souk and bazaar, in towns as well as in villages, contains a section where medicinal wild plants are sold.

Figure 1: Map of mainly Kurdish settled regions (Kurdistan).

In Kurdish traditional medicine the physical characteristics of the herbs and plant parts, including size, shape, color, texture and taste, have traditionally served as important criteria in their selection for therapeutic purposes, while several procedures are used to obtain the beneficial phytochemical components from selected species. The majority of plant-based remedies are consumed orally in the form of a fresh plant, e.g *Tulipa systole* bulbs for pain killing, *Iris persica* for treating tumors and inflammation, *Anethum graveolens* for flatulence and *Hypericum perforatum* for topical treatment and pain relief. Other common preparations are teas or different drinks containing diluted or concentrated chemical ingredients, e.g. with *Urtica dioica* for treating gastrointestinal tract problems. The tea is generally prepared using different parts of a plant, as an infusion or as a decoction, e.g. with *Prangos peucedanifolia* against kidney disorders. Another common way of administration is through a poultice, which is made by grinding or crushing selected plant parts, which are then mixed with hot water or other liquids to create a medicinal paste or plaster. The resulting mixture is used to treat joint inflammation and pain, e.g. with *Eremurus persicus*, or it is placed directly on wounds, bruises, burns, e.g with *Verbascum calvum*, insect, e.g. with *Plantago loeflingii,* and animal bites, rashes, swellings, wrinkles or dermatological irritations.

Indeed, plants in Kurdistan are used for many purposes, ranging from medicinal to cosmetic and ritual applications. As an example, 133 different uses have been recorded for the 82 species of plants and 16 mixtures of plant products sold at the great Qaysari Market in the city of Erbil, the capital of the Kurdistan Region of Iraq. About a dozen major biological system disorders treated with plants and other uses have been identified (Figure 2). Herbs for treating digestive system disorders clearly dominate the reported plant uses with 117 out of 449 reports (26.1%). This could be due to the abundance of these problems among the Kurdish society, and/or due to the broad applicability of this term as it includes different uses, e.g. reduction of cholesterol level, abdominal pain, flatulence, and colic. Other disease categories that are frequently reported (< 8 %) are genito-urinary disorders, including aphrodisiacs, endocrine system disorders, including diabetes, and integumentary system disorders, including all skin affections [5].

Interestingly, 64% of the herbal products sold in the Qaysari Market have their origin outside the Kurdistan Region and Iraq, traded from such distant countries as China, India, and Libya. Therefore, we decided that it would be interesting to gain information about medicinal plants collected in the wild only in Kurdistan and used locally. In our view, this ethnobotanical information could make the basis from which to start an ambitious research project on the phytochemistry of Kurdish medicinal plants. They, to our knowledge, are mostly little or completely uninvestigated. The survey was carried out on isolated mountains called Halgurd, Shireen, Korek, Safeen, Sakran, Bamo, Khalafy, Hawraman, Qarachux and Penchwen, which belong to the Districts of Rawandus, Choman, Mergasoor and Kanymasy, near the northern border with Turkey, Kalar, Penchwen, Halabja, and Sharazoor, stretching mostly in the east, near the Iran border, and Shaqlawa, and Zraraty not far from the city of Erbil.

The ethnobotanical compilation presented here is primarily based on information collected from local herbalists (herbal healers) and elderly via about 80 recorded interviews and direct documentation. The information about plant parts, varieties, modes of use and preparation of traditional herbal remedies were in some cases compared with previous studies for further confirmation. The surveys were spread across seasons, from June 2011 to August 2014, to obtain the maximum information and also to cross-check the data provided by local informants. The plants have been identified by Prof. Abdul Hussain Al Khayyat from the Department of Biology-College of Education in the Salahaddin-Erbil University; voucher specimens have been deposited in the Education Salahaddin University Herbarium (ESUH).

The plants have been divided into two tables. In Table 1 we listed plants which are not endemic to Kurdistan, but which also grow in nearby countries and for which some phytochemical data already

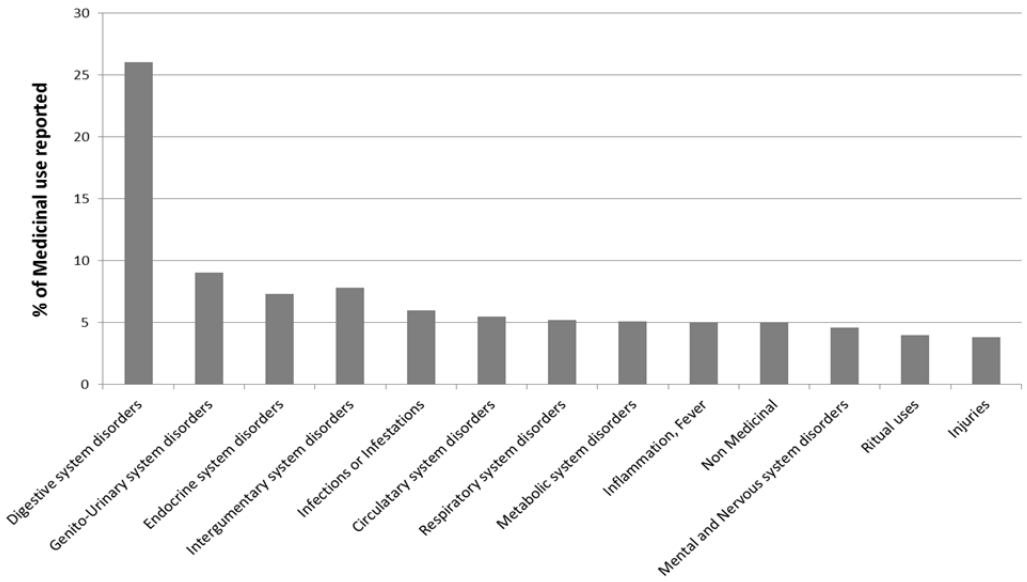


Figure 2: Diversity and percentage of the medicinal plant use reported in the Qaysari Market, Kurdistan-Iraq (adapted from reference [5]).

Table 1: List of medicinal plants, disease treated, part used and modes of drug preparation in the investigated areas.

Family	Botanical name	Voucher no.	Part/Preparation	Traditional use
Adiantaceae	*Adiantum capillus* Sw.	7232	Leaf/Decoction	Kidney stone
Apiaceae	*Cuminum cyminum* L.	7406	Seed/Dried direct use	Lactation regulation
	Prangos peucedanifolia Fenzl	6828	Aerial parts/Decoction	Kidney disorders, hemorrhoids
	Prangos pabularia Lindl.	7322	Aerial parts/Decoction	Stimulant
	Prangos ferulacea Lindl.	7330	Aerial parts/Decoction	Kidney and bladder inflammation
	Anethum graveolens L.	7423	Herb/Fresh and dried	Flatulence
	Coriandrum sativum L.	7336	Fruit/ Decoction	Intestinal disorders
	Scorzonera papposa L.	7323	Aerial/Fresh	Increase of breast milk
	Calendula arvensis Boiss	7233	Flower/Pounded	Burn and skin injuries
	Anthemis nobilis L.	7297	Flower/Tea	Stomach disorders, common cold, tonic, wounds
	Calendula officinalis L.	7234	Leaf/Decoction	Ulcer, abdominal pain
	Achillea falcata L.	7235	Aerial parts/Infusion	Diuretic
	Achillea filipendulina Lam.	7236	Aerial parts/Decoction	Carminative and stomach disorders
	Arctium lappa Kalm.	7281	Root/Decoction	Diuretic
	Lactuca sativa L.	7337	Leaf/Fresh	Emollient for skin
	Onosma rostellatum Lehm.	7359	Root/Maceration	Bladder pain, kidney disorders
Brassicaceae	*Eruca sativa* Mill.	7299	Seed/Oil	Sexual weakness, hair loss
	Lepidium persicum Boiss	7393	Leaf/Pounded	Burns
	Lepidium latifolium L.	7361	Leaf/Maceration	Burn inflammation
	Brassica nigra W.D.J. Koch	7360	Seeds/Direct use	Stomach disorders, emetic, stimulant
Caryophyllaceae	*Dianthus caryophyllus* L.	7298	Flower/Tea	Cardiotonic, fever, anti-stress
	Vaccaria pyramidata Medik.	7335	Seed/Maceration Arial parts/Pounded	Diuretic, vulnerary Externally skin itching
Clusiaceae	*Hypericum perforatum* L.	7280	Leaf/Decoction	Kidney stone, liver diseases, stomach disorders, inflammation
Cyperaceae	*Cyperus rotundus* L.	7364	Root/Decoction	Diuretic, hemorrhoids
Equisetaceae	*Equisetum arvense* L.	7329	Arial parts/Decoction	Kidney disorders
Euphorbiaceae	*Euphorbia macrocarpa* Boiss. & Buhse	7346	Latex/External application	Inflammation
	Euphorbia aucheri Boiss	7405	Latex/Direct use	Fungal infections
Fabaceae	*Vicia villosa* Roth	7279	Seed/Fresh internal use	Headache
	Trifolium purpureum Loisel.	7237	Herb/Fresh	Intestinal disorders
	Cassia acutifolia Delile	7421	Leaf/Infusion	Hemorrhoids
	Astragalus micraucistrus L.	7422	Root/Decoction	Diabetes
	Trigonella foenum-graecum L.	7296	Seed/Decoction	Kidney stones, bowel irritation, hypoglycemic, inflammation
Iridaceae	*Crocus biflorus* Mill.	7295	Flower/Infusion	Dyspepsia, arthritis, for delaying menstrual cycle
	Iris postii Mouterde	7230	Arial parts/Decoction	Inflammation
	Iris persica L.	7229	Root, Leaves /Fresh, Decoction	Wound inflammation, antitumor
	Crocus sativus Ten.	7238	Stigma/Direct use	Fever
Lamiaceae	*Salvia limbata* C.A.Mey.	7278	Arial parts/Decoction	Cold, stomach disorders
	Salvia euphratica Montbret & Aucher	7263	Flower/Decoction	Hypoglycemic, antibacterial, fever
	Salvia indica L.	7264	Leaf/Infusion	Stomach, intestinal disorders
	Salvia smyrnaea Boiss	7265	Leaf/Infusion	Intestinal disorders
	Salvia adenocaulon P.H.Davis	7358	Leaf/Infusion	Gastro intestinal disorders
	Nepeta congesta Fisch. & C.A.Mey.	7249	Leaf/Maceration	Antiasthma, antispasmodic
	Salvia officinalis L.	7379	Flower/Decoction	Reduce cholesterol level, antibacterial
	Thymus vulgaris M.Bieb.	7328	Arial/Dried direct use	Fungal infections, immunostimulant, abdominal pain, nephritis
Liliaceae	*Tulipa systole* Stapf.	7201	Root/Fresh, Leaf/Decoction	Inflammations, pain
	Allium schoenoprasum L.	7403	Leaf/Infusion	Carminative and diuretic
Malvaceae	*Hibiscus esculentus* L.	7363	Fruit/Decoction	Diuretic, emollient

Myrtaceae	*Eucalyptus camaldulensis* Dehnh.	7424	Leaf/Maceration, Gum/Direct application	Throat sore, diarrhea
	Eucalyptus incrassata Labill.	7404	Leaf/Maceration	Throat sore
Oleaceae	*Fraxinus ornus* Scop.	7334	Leaf/Infusion	Tonic
Plantaginaceae	*Plantago loeflingii* L.	7248	Leaf/Fresh directly	Wounds, vulnerary
Poaceae	*Agropyron repens* P.Beauv.	7344	Root/Decoction	Bladder disorders
Primulaceae	*Anagallis arvensis* L.	7407	Flower/Maceration	Dermatological wound healing
Ranunculaceae	*Nigella sativa* L.	7294	Seed/Dried direct use	Tonic, immunostimulant, stomach disorders, asthma, antibacterial
Resedaceae	*Reseda alba* L.	7410	Root/Decoction	Stomach disorders
Rhamnaceae	*Paliurus spina-christi* Mill.	7324	Fruit/Infusion internal	Diuretic
Rosaceae	*Geum urbanum* L.	7380	Flower/Decoction	Stomach and digestive problems
Rutaceae	*Citrus aurantifolia* Christm.	7327	Fruit/Tea	Liver, heart diseases, diuretic, spleen, common cold
Scrophulariaceae	*Verbascum calvum* Boiss.& Kotschy	6823	Leaf/Decoction	Burn inflammations
	Verbascum ponticum Stef.	7357	Leaf/Direct External	Mycodermatitis
	Verbascum alceoides Boiss. & Hausskn	7247	Leaf/Pounded	Mycodermatitis
	Verbascum assurense Bornm. & Hand.-Mazz.	7425	Leaf/Infusion	Anti-parasitic
	Verbascum froedinii Murb.	7381	Leaf/Decoction	Mycodermatitis, burns
Solanaceae	*Hyoscyamus albus* L.	7293	Leaf/Decoction	Narcotic
	Hyoscyamus niger L.	7239	Leaf/Decoction	Sedative and narcotic
Thymelaeaceae	*Daphne mucronata* Royle	7356	Steam/Internal	Hemorrhoids
	Daphne acuminata Stocks	7428	Steam/Internal	Hemorrhoids, inflammations
Urticaceae	*Urtica dioica* L.	7333	Leaf/Decoction	Diabetes, throat disease, inflammations
Zingiberaceae	*Zingiber officinale* Roscoe	7241	Rhizome/Paste	Hyperglycemia, hemorrhoids

Table 2: List of medicinal plants endemic to the areas under study, with part used, mode of drug preparation, and disease cured.

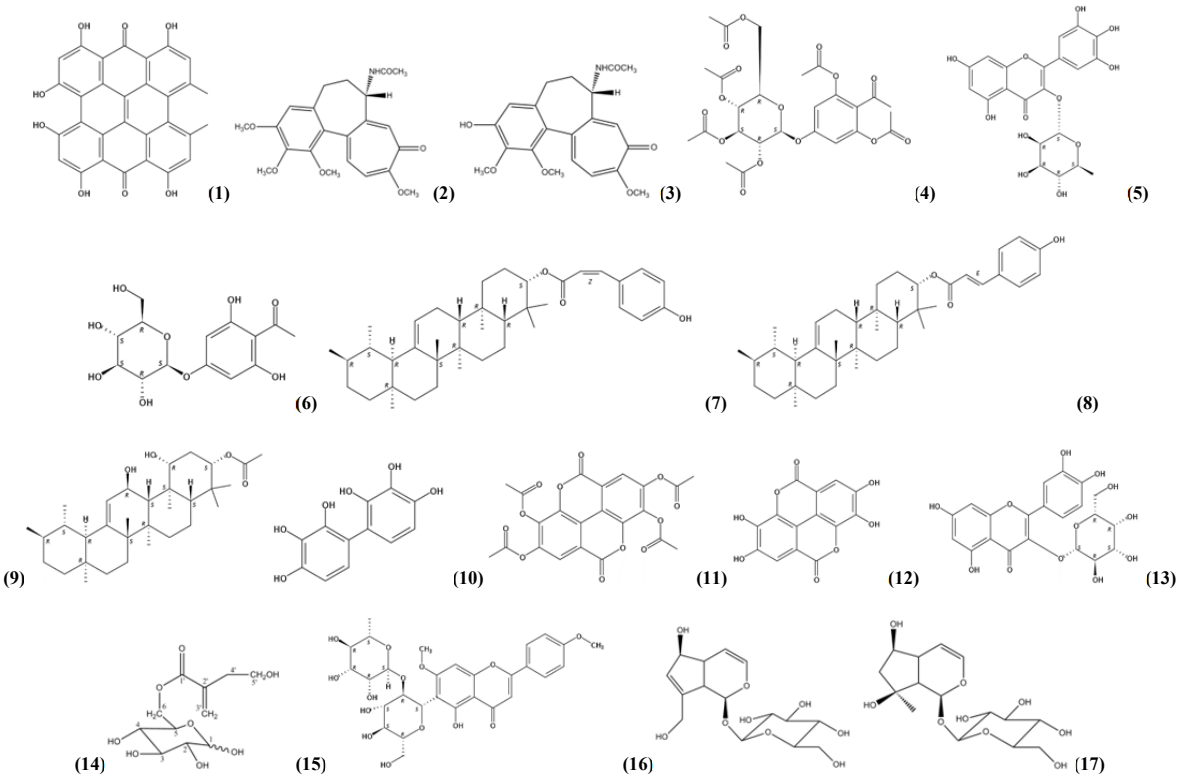
Family	Botanical name	Voucher no.	Part/preparation	Traditional use	Reported phytochemical components
Alliaceae	*Allium anacoleum* Hand.-Mazz.	7426	Bulb/Dried	Reduce blood sugar	none
	Allium arlgirdense Blakelock	7246	Leaf/Fresh	Anemia, Diuretic	none
	Allium qaradaghense Feinbrun	7389	*		none
	Allium trachycoleum Wendelbo	7266	Bulb/Fresh internal use	Analgesic	none
	Allium fedtschenkoi Nábělek	7409	*		none
Clusiaceae	*Hypericum asperulum* Jaub. & Spach	7311	Herb/Decoction	Stomach disorders, Jaundice	essential oil [6]
	Hypericum lysimachioides Wall.	7240	Herb/Decoction	Stomach disorders, ulcer, kidney stones	fatty acids [7], essential oil [8]
Colchicaceae	*Colchicum kotschyi* Boiss.	7326	*		Alkaloids [9], phenolic compounds [9]
Euphorbiaceae	*Euphorbia aucheri* Boiss.	7405	Latex/Direct use	Fungal infections	Flavanoids, phenolic gallate [10], acetophenone glycoside [10]
	Euphorbia iberica Boiss.	7284	Latex/Direct use	Fungal infections, skin pimples	triterpenoids, diterpenes [11], polyphenols [12] [13], essential oil [14]
Iridaceae	*Iris gatessi* Foster	7310	Root/Fresh	Liver diseases, Inflammation	none
Fabaceae	*Medicago noeana* Boiss.	7394	*		none
	Astragalus caryolobus Bunge	7300	*		none
	Astragalus fieldianus Hub.-Mor.	7427	*		none
	Astragalus ensifer Nábělek	7283	Gum/Direct use, Root/Decoction	Stomach disorders, diabetes	none
	Astragalus carduchorum Boiss. & Hausskn	7362	*		none
	Astragalus helgurdensis C.C.Towns.	7245	*		none
	Astragalus venulosus Boiss.	7355	Gum/Pounded	Throat pain	none
	Astragalus kirrindicus Boiss.	7331	*		none
Liliaceae	*Bellevalia olivieri* (Baker) Wendelbo	7291	*		none
Linaceae	*Linum velutinum* Steud. ex Planch.	7292	*		none
Malvaceae	*Alcea arbelensis* Boiss. & Hausskn.	7429	*		none
Rosaceae	*Alchemilla kurdica* Rothm.	7325	Leaves/Infusion	Diuretic	none
	Agrimonia repens L.	7282	*		none
Rubiaceae	*Asperula stricta* Boiss.	7408	*		none
	Asperula xylorrhiza Nábělek	7430	*		none
	Asperula insingnis (Vatke) Ehrend.	7387	*		none
	Galium nabelekii Ehrend. & Schönb.-Tem.	7290	*		none
	Galium kurdicum Boiss. & Hohen.	7267	Herb/Infusion	Labor pain	none
Violaceae	*Viola modesta* Fenzl.	7244	*		none

* The plant has been indicated as a medicinal plant; however, there is no general consensus by informants about its therapeutic use.

exist in the literature. Instead, in Table 2 we listed plants that are endemic to the regions under study. The majority of them are still phytochemically uninvestigated and even a general consensus about their therapeutic applications does not exist.

A variety of diseases are treated with different preparations of the plants listed in the two tables, ranging from simple stomach-ache to highly complicated male and female disorders. Even herbal remedies for curing sexual weakness and kidney stones have been reported. The maximum number of plants is used for curing gastro-intestinal disorders and inflammation, followed by urinary-tract disorders, skin burns, irritations and liver problems. A few medicinal plants are used for curing more than just one disease, in the same and/or different places, depending on the therapeutic property attributed to the plant in that region.

A few significant examples nicely confirm the therapeutic importance of active substances isolated from reported plants, though, as often occurs for traditional remedies, the bioactivity of isolated compounds is not strictly related to the uses of plants.



Among the *Clusiaceae*, a decoction of the leaves of *Hypericum lysimachioides* is a very common remedy for healing wounds and inflammation by the people living in villages of the Hawraman mountains; the phenolic derivative hypericin (**1**) has been isolated [2], which is very well known for its antiviral [15-17] and anticancer [18] activities. In the traditional medicine, a decoction of the flowers of *Colchicum kotschyi* (Colchicaceae) is topically used to relieve pain. The indole alkaloids colchicine (**2**) and 3-demethyl-colchicine (**3**) have been isolated [19, 9]. Colchicine is a potent anti-inflammatory [20] and anticancer compound [21]; moreover, it suppresses the local cardiac production of inflammatory cytokines in patients with an acute coronary syndrome [22], thus exerting beneficial effects in a variety of cardiovascular disorders, including acute and recurrent pericarditis [23].

The latex of *Euphorbia aucheri* and *E. iberica* (Euphorbiaceae) is directly used for skin fungal infections by the people living on the Bamo Mountain near to the Iran-Iraq border. Three polyphenols, phloracetophenone acetylglucoside (**4**)**,** myricetin 3-*O*-rhamnopyranoside (**5**)**,** and phloroacetophenone 4-*O*-β-D-glucopyranoside (**6**) were isolated for the first time from *E. aucheri* [13]. On the other hand, three triterpenoids [11], 3-(*Z*)-coumaroyl α-amyrin (**7**), 3-(*E*)-coumaroyl α-amyrin (**8**), the mono-acetate (**9**), and four polyphenolic compounds [12, 13], 4,4'-bipyrogallol (**10**), ellagic acid tetra-acetate (**11**), ellagic acid (**12**) and 3-*O*-β-D-galactosyl quercetin (**13**) were isolated from *E. iberica.*

Starting from the ethnobotanical information reported in this paper, we decided to investigate *Tulipa systole*, *Iris persica*, and *Verbascum calvum*, for which no phytochemical reference is reported in the literature.

The genus *Tulipa* (Liliaceae) is of great economic, horticultural, esthetic, ecological, conservational, and taxonomic interest. A pair of fresh bulbs of *T. systole*, which grows under and between rocks, is traditionally eaten as a herbal anti-inflammatory remedy and for pain-relief. The antioxidant properties of *T. systole* have been evaluated [24] and 6-tuliposide A (**14**) has recently been isolated by our research group from an ethanolic extract of the roots.

The genus *Iris* (Iridaceae**)** comprises over 300 species [25]; most of them have medicinal importance and are used for the treatment of cancer, inflammation, bacterial and viral infections, among other diseases [26]. Moreover, a plethora of bioactive metabolites have been isolated [27]. *I. persica* is commonly employed in the Kurdish traditional medicine for the treatment of wound inflammation. In initial studies of this plant we have isolated the C-glycosylflavone embinin (**15**) from a methanolic extract of the leaves.

Verbascum calvum (Scrophulariaceae) is employed in the Kurdish traditional medicine for the treatment of burns and other skin diseases. We have isolated the iridoids aucubin (**16**) and ajugol (**17**), which are very well-known for their potent anti-inflammatory activity [28]; in contrast, they had no activity against the growth of several tumor cell lines.

In conclusion, this short review has demonstrated that traditional medicine is still widely practiced by Kurdish peoples and has established the value of a great number of plants used as herbal medicines. However, in Kurdistan, as well as in other Middle East countries, the use of herbal remedies as medicines would require an ad-hoc legal regulation and licensing, in order to ensure supply of controlled and safe vegetable products of verified therapeutic efficacy and containing standardized bioactive compounds. Moreover, these medicinal plants represent potential sources of new phytotherapeutic agents for different diseases. The great number of endemic plants, their growth in remote highlands of Kurdistan and the lack of phytochemical studies offer appealing opportunities for novel investigations to scholars in chemistry and biology. In this context, on the basis of the ethnobotanical information collected in

different parts of Kurdistan, a couple of years ago we embarked on a long-term project aimed at the study of uninvestigated Kurdish medicinal plants. Our preliminary results on the components of extracts of *I. persica*, *T. systole* and *V. calvum*, reported in this paper, are the first steps in this direction.

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