Onosma L.: A review of phytochemistry and ethnopharmacology

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ABSTRACT

The genus *Onosma* L. *(Boraginaceae)* includes about 150 species distributed world-wide in which only about 75 plants has been described for its morphology and less than 10 plants for their chemical constituents and clinical potential. The phytochemical reports of this genus revels that it comprise mainly aliphatic ketones, lipids, naphthazarins, alkaloids, phenolic compounds, naphthoquinones, flavones while most important are shikonins and onosmins. The plants are traditionally used as laxative, anthelmintic and for alexipharmic effects. The plants are also equally use in eye, blood diseases, bronchitis, abdominal pain, stangury, thirst, itch, lecoderma, fever, wounds, burns, piles and urinary calculi. The flowers of various plants are prescribed as stimulants, cardiotonic, in body swelling while leaves are used as purgative and in cutaneous eruptions. The roots are used for coloring food stuffs, oils and dying wool and in medicinal preparations. This review emphasizes the distribution, morphology, phytochemical constituents, ethnopharmacology, which may help in future research.

Key words: Alkannin, hispidone, naphthoquinones, Ratanjot, shikonin

INTRODUCTION

The genus *Onosma* L. (*Boraginaceae*) represents about 150 known species in Asia[1] including 29 species in China,[2] 95 species in Turkey[3] and 8 in Pakistan,[4] but recent studies and revisions have increased the number of species in this genus to over 230 species.[5] The name *onosma* for this genus was introduced into modern botanical nomenclature by Linnaeus, which is derived from a Latin word "osma" originated from a Greek word, "osma" means smell.[6] All species grow in dry or moist and sunny habitats usually in rock crevices and popularly known as rock garden plants.[3]

Onosma L. is a species-rich genus with complicated patterns of morphological, karyological variation and taxonomic treatments within the groups of this genus are highly controversial. Many similar species were described based on minor morphological differences and consequently they have often been confused. In addition, in the European area, their distribution is rather fragmented and classifications have often been done on the basis of geographically limited studies,[7] which appears to be partly artificial and there is a need for re-investigation that new data may provide useful reference in a future classification.[3] According to "The Plant List" of Royal Botanic Garden, Kew and Missouri Botanical Garden, includes 387 scientific plants names of species rank for this genus in which only 37 are accepted species names and further 19 scientific plant names are of infra-specific rank. This list also shows that only 9.6% names are accepted and 6.2% names are synonyms while 84.2% names are still un-assessed.

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DISTRIBUTION

Onosma L. includes numerous species distributed in Asia, Eurasia, Mediterranean regions and Europe mainly in Iran, Syria, Turkey, China, Pakistan, India and Sri Lanka, etc., This genus has been divided into three sections named as *Onosma*, Protonosma and Podonosma while section *Onosma* was further divided into two subsections as asterotricha (Boiss.) Gurke and Haplotricha (Boiss.) Gurke.[3,8] In flora Iranica region, 39 species growing in Iran[9] while Anatolia is an important center of origin for *Onosma* comprising about 95

species, 48 of which and one verity are endemic for Turkey.[10]

In Switzerland, genus *Onosma* is represented by two rare species inhabiting calcareous steppe meadows one is *Onosma helvetica* (A. DC.) Boissier located in Ollon (VD) ans in Haut-Valais and second is *Onosma pseudoarenaria* Schur distributed in central Valais.[11]

In Romania, *Onosma visianii* Clementi spread mostly in Dobrogea's barren places, steppe, on calcareous soils while *Onosma setosum* Ledeb., *Onosma arenaria* Waldst. et Kit., *O. pseudoarenaria* Schur and *Onosma viride* (Borb.) Jav. are endemic, spread in barren regions such as Cluj, Hunedoara and Ploiesti, *Onosma taurica* Pall. ex Willd. spread in stony, grassy, calcareous areas from Timisoara and Constanta. Teppner enumerates only *Onosma heterophylla* (sin. *viride*), *Onosma helveticum* Boiss. spread in Transylvania, *Onosma lypskyi*, *O. visianii* Clementi, *O. taurica* Pall. ex Willd., *Onosma rigida* Ledeb. spread in Dobrogea and *O. arenaria* Waldst. et Kit. spotted in the Danube Delta, without mentioning *O. pseudoarenaria* Schur. while in Transylvania that is the only existing species.[12]

Moreover, Johnston (1954) studied light microscopy of the pollens of 45 species of *Onosma*[13] and Qureshi and Qaiser (1987) studied pollen characteristics of 9 plants[14] while Maggi *et al.* (2009) studied pollen morphology of five *Onosma* species.[15] Binzet and Akcin (2011) also reported pollen characteristics of some *Onosma* species in Turkey[16] and recently Mehrabian *et al.* (2012) was done numerical analysis of pollen characteristics in 24 *Onosma* species growing in Iran and tries to evaluate the usefulness of the palynological data in the taxonomy of the genus and also use such data to illustrate the species affinity.[17]

The anatomical and ecological properties of some *Onosma* species were studied[18] by Akcin (2004), Akcin and Engin (2005).[19] Binzet and Orcan (2009) investigated the anatomical structure and palynological characteristics of *Onosma roussaei* DC. and *Onosma giganteum* Lam.[20] while chromosome numbers of different species of *Onosma* were reported by Teppner in 1981 and 1988.[21,22] The nutlet micro morphologies of some *Onosma* species were also studied by Akcin in 2007.[23] The distribution of some species is summarized in Table 1.

MORPHOLOGY

Table 1: Distribution of plants of genus *Onosma* L.

Plant name	Altitude (m)	Habitat/origin	Type*	Life#	Plant height (cm)	Flowering/fruiting time
O. adenopus	2800-3500	China	H	P	20-30	August-September
O. album	3000	Yunnan	H	P	40-60	July
O. bourgaei	2000	Turkey, Armenia	H	P	30-50	Summer
O. bracteatum	3500-4500	India, Iran	S	P	38	August-October
O. caucasica	400-1000	Turkey	H	P	20-40	Summer
O. cingulatum	2000-2800	Yunnan	H	A	50-70	July
O. confertum	2300-3300	Sichuan, Yunnan	H	P	30-70	July-October
O. decastichum	1300	C Yunnan	H	P	45	October
O. dichroantha	900-2400	Iran, Pakistan	H	B	70	March-May
O. echioides	1600	Italy	H	P	17-30	Summer
O. elegantissimum	900-1800	Slope in Greece	S	P	-	May-June
O. exsertum	1800-2100	Guizhou, Sichuan	H	P	100	June
O. forrestii	3300	Sichuan, Yunnan	H	P	-	July-October
O. fistulosum	1600-3000	SW Sichuan	H	B	100	July-September
O. glomeratum	3700	Xizang, Leiwuqi	H	-	20-30	August
O. gmelinii	1200	Kazakhstan, Russia	H	P	25-40	May-June
O. hispidum	3000-4000	Kashmir, Kumaun	H	P	70-80	-
O. lijiangense	2700	NW Yunnan	H	P	30-40	August
O. liui	2300-3400	Sichuan	H	-	60	July
O. luquanense	1900	N Yunnan	H	B	40-70	October
O. maaikangense	2300-3800	Sichuan, E Xizang	H	P	30-40	June-August
O. mertensioides	3900-4000	Meadows, Sichuan	H	P	15-30	July
O. multiramosum	1600-3100	Sichuan, Yunnan	H	P	30	August
O. paniculatum	2000-2300	Bhutan, NE India	H	B	40-80	June-September
O. polioxanthum	350-2150	Iran	S	P	20-25	May-July
O. potaninii	1700-3200	S Gansu, Sichuan	H	P	15-30	May-August
O. pyramidale	2770	India	H	P	35	July-August
O. sinicum	1700-3200	N Sichuan	H	P	15-30	May-August
O. tornensis	200-500	Europe	H	P	15-25	-
O. waddellii	3000-4000	Xizang	H	P	15-25	Aug-September
O. waltonii	3700	Xizang	H	P	15	August
O. wardii	2200-2800	NW and W Yunnan	H	P	60	November
O. zayueense	3300	SE Tibet	H	P	35	August

*H=Herb, *S=Shrub, #A=Annual, #B=Biennial, #P=Perennial

The genus *Onosma* L. contains biennial or perennial herbs, scabrous and leaves are petiolate or sessile with entire margin. Cymes are scorpioid and solitary at stem apex while branches forming a panicle, which are usually elongated in fruit, bracteate. Flowers are actinomorphic, pedicellate or sessile while calyx parted to or nearly to base with 5 lobes, linear or linear-lanceolate, equal and usually enlarged after anthesis. Corolla is blue, yellow, white or red in color, tubular with campanulate or retrorse with conical and usually gradually expanded from base upward, throat unappendaged while nectary are ring like or lobed with dentate margin. Anthers are coherent laterally into a tube or sagittate, which is pellucid and emarginated with sterile apex. Style is included or slightly exerted with capitate stigma. Gynobase is flat with 4 nutlets, erect, ovate-triangular, length and width subequal, adaxially ribbed and abaxially slightly convex, attached to basal scar.[2]

In addition to the setae with an enlarged base known for many genera of the *Boraginaceae* family, many species of *Onosma* have setae with usually 4-20 rays arising from the base, these are referred to as stellate setae. The central seta is occasionally absent from these hairs, but usually it is distinctly longer and stouter than the rays. The presence or absence of stellate setae is widely used as a major character in the genus, but in a number of species there may be a wide range of variation in the presence, frequency and length of the stellate setae. Petal morphology has major taxonomic importance and corolla color, shape and size are used as taxonomic characters in this genus.[24] However, detailed observations of the micromorphology and anatomy of petals of most of the *Onosma* species are lacking[25] as described in Table 2. The genus presents considerable taxonomic difficulties, particularly in central and south east Europe, which cannot be resolved without experimental investigation.

PHYTOCHEMISTRY

The literature survey revealed that very little phytochemical work has been carried out on the genus *Onosma* L. and only some naphthaquinones, alkaloids and phenolic compounds have so far been reported.[83] Alkannins and Shikonins are chiral-pairs of naturally occurring isohexenylnaphthazarins, found in the external layer of the roots of many species that belongs mainly to the genera Alkanna, Lithospermum, Echium, *Onosma* and Arnebia of the *Boraginaceae* family [Table 3].[84]

From the alkaloid extract of *O. arenaria* Waldst. and Kit. The uplandicine, a 1, 2-unsaturated pyrrolizidine alkaloid esterified with acetyl and echimidinyl moieties and its structure was confirmed by mass spectroscopy (Electron impact and positive Fast atom bombardment), 1H-and 13C-nuclear magnetic resonance (NMR) analysis. Furthermore, nine minor alkaloids were identified on the basis of mass spectral data and/or Kovats retention indices.[1]

When roots of *Onosma argentatum* Hub.-Mor. were extracted with n-hexane-dichloromethane mixture (1:1), subjected to silica gel column chromatography and elution was performed with a n-hexane-ethyl acetate mixture with gradient elution, deoxyshikonin, acetyl shikonin, 3-hydroxy-isovaleryl shikonin, 5,8-O-dimethyl acetyl shikonin were obtained.[35,88]

The *Onosma bracteosum* Hausskn. and Bornm. and *Onosma thracicum* Velen. Exhibits oleic and α-linolenic acids quantified at higher levels in endemic *O. bracteosum* while other fatty acids and α-tocopherol were observed at higher concentrations in *O. thracicum*.[10]

The study of Onosma echioides C. B. Clarke non Linn. showed an alkannin or shikonin content with naphthoquinone derivatives i.e. deoxyalkannin or deoxyshikonin and 5, 8-dihydroxy-2-(4-methyl-6-oxo-5,6-dihydro-2H-pyran-2-yl) -[1,4] naphthoquinone and arnebin-6 were found and characterized in the extracts using high-performance liquid chromatography-mass spectrometry (HPLC-MS) apparatus equipped with an Electro spray ionosat ionization source.[89] Volatile components obtained by hydrodistillation from the aerial parts (leaves and flowers) of O. echioides L. var. columnae Lacaita were investigated by gas chromatography and gas chromatography–MS where 64 volatile components were identified, hexadecanoic acid and phytol were predominant in the flower oils while phytol and hexahydrofarnesyl acetone were the major components in the leaf oils. Alkanes, fatty acids and aldehydes constituted the major fraction in the flower oils while oxygenated diterpenes and ketones were predominant in the leaf oils.[15]

Onosmins A and B have been isolated from *Onosma hispidum* Wall. ex G. Don and their structures were established as 2-[(4-methylbenzyl) amino] benzoic acid and methyl 2-[(4-methylbenzyl) amino] benzoate through spectroscopic studies, including 2D-NMR. The known compounds are apigenin, 6, 4'-dimethoxy-3, 5, 7-trihydroxy-flavone, 6, 7-dimethoxy-3, 5,4' trihydroxy-flavone and apigenin 7-O-beta-D-glucoside are also reported from this species.[85] In 2006, from its ethanolic extract of root bark, isolation of 4-hydroxy-3-methoxy cinnamic acid (ferulic acid) and 4-hydroxy-3-methoxy benzoic acid (vanillic acid) was performed.[90] Hispidone, a new flavanone has been isolated and assigned the structure (2S)-5, 2'-dihydroxy-7, 4', 5' trimethoxy-flavanone by spectroscopic methods and in addition to this benzoic acid and 4-hydroxy benzoic acid are also reported from this species.[84]

Onosma paniculata Bureau and Franchet-HPLC analysis of the active petroleum ether-soluble extract pointed to several shikonin derivatives using preparative HPLC, seven fractions were collected from which β-hydroxyisovalerylshikonin,

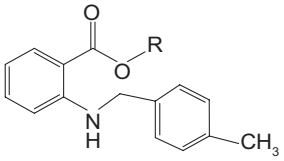
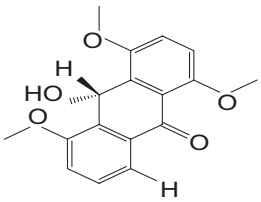
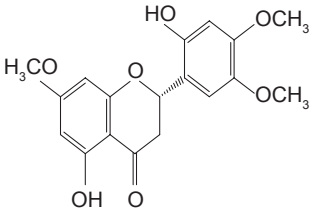
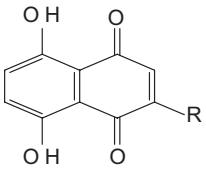
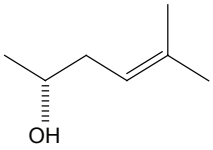
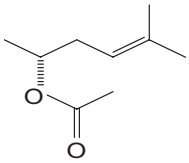
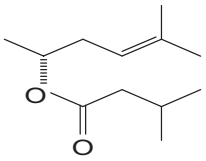
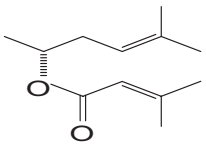
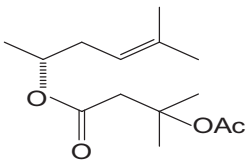
Table 2: Unresolved plants of genus *Onosma* L.

Plant name	Proposed resolution	References
O. aleppica	Found in Judean Desert	[26]
O. ambigens	Found in Turkey, Nutlet and pollen morphology are reported	[16,17,27-30]
O. ampliata	Reported in Danube Delta, Syn *Onosma visianii* Clementi	[31]
O. angustifolia	Syn *Onosma echioides*	[32-34]
O. anisocalyx	Syn *Onosma echioides*	[34]
O. argentata	Endemic species of Turkey	[35]
O. aucheriana	Syn *O. rigidum Ledeb Onosma montana* Sm.	[36-39]
O. auriculata	Found Mediterranean, Turkey	[5]
O. bisotunensis	New species from western Iran, nearest relative, *O. hebebulbum*	[34,40]
O. canescens	Subspecies of *Onosma echioides*	[34]
O. cassium	Reported from Turkey and nutlet study reported	[32,41,42]
O. chitralicum	Reported from Pakistan	[43]
O. cinerascens	Subspecies of *Onosma helvetica*	[44]
O. dasytrichum	Palynological study was reported	[45]
O. epirotica	Syn of *Onosma heterophylla* Gri.	[17]
O. gigantea	Pollination study is reported	[46]
O. graecum	Reported from Datca Peninsula	[47]
O. graniticola	Reported in Danube Delta	[31]
O. graeca	Plant from Greece and karyology, genome size reported	[48,49]
O. halophilum	Found in Erciyes Dauy (Kayseri, Turkey)	[10,16,50]
O. hebebulbum	New species from western Iran	[40]
O. helvetica	Karyotypes and genome size, chorology reported	[11,51,52]
O. isauricum	Micromorphological and anatomical study reported	[25,32]
O. javorkae	Sub species of *Onosma echioides* L	[53]
O. khorassanica	Species from northeast of Iran	[54]
O. kaheirei	Plant reported from Ikaria	[22,55]
O. kotschyi	Found in Iran, Palynological study reported	[45,56]
O. leptanthum	Karyogram study was done	[21]
O. limitaneum	Resemble with *O. glomeratum* reported from Afghanistan, NW India, Iran and Pakistan	[14,57]
O. liparioides	Reported from Uzumlu-Sakaltutan, Iran	[9,35,58]
O. longilobum	Havachoobe (root) drug	[59-61]
O. lucana	Subspecies of *Onosma helvetica*	[51]
O. maroccana	Subspecies of *O. maroccana*	[62]
O. mattirolii	Found in Tomorr, Albania	[63]
O. mersinana	Anatomical, palynological and pollen studied	[5,16,20,64]
O. microcarpum	*O. anisocalyx* PON., subspecies of *0. microcarpum* DC.	[65-68]
O. mirabilis	New species from turkey	[20]
O. molle	Found in Soulful, Irano-Turan	[69]
O. nydeggeri	Reported from turkey	[20,66]
O. nanum	Syn of *O. decipiens*	[70]
O. olivieri	Palynological study reported	[45]
O. paradoxa	Found in Greece	[39]
O. propontica	Anatomical study reported	[66,71]
O. pyramidale	Found in Himalaya, India, Nepal	[72]
O. riedliana	Found in southern Turkey	[27,28,66]
O. rostellata	Nutlets study reported	[51]
O. sericea	Karyotype study reported	[5,49]
O. sieheana	Palynological study reported	[5]
O. sintenisii	Anatomy, palynology reported	[16,28]
O. sorgeri	Karyotype study reported	[49]
O. spruneri	Found in Tomorr, Albania	[63]
O. stellulatum	Remarks to the plant with genotoxic effect	[63,73,74]
O. stenoloba	Palynological study reported	[5,45]
O. stenosiphon	Reported in Iran, burn healing, palynological study reported	[75,76]
O. stridii	Plant reported from Greece	[52,77]
O. thomsonii	Found in Pakistan	[14]
O. thracica	Reported from Bulgaria	[78-80]
O. trachycarpa	Species found in Turkey	[37]
O.tricerosperma	A species of Portuguese flora	[81]
O. velenovskyi	Syn of *O. tauricum*	[82]

PON=Ponert

acetylshikonin, dimethylacrylshikonin and a mixture of α-methylbutyrylshikonin and isovalerylshikonin was isolated[91] and a HPLC method using diode-array detection used for simultaneous quantification of eight naphthoquinone

Table 3: Structures of some phytoconstituents found in genus *Onosma* L.

R	Name	Occurrence	Ref
			
R=H	Onosmin A	*O. hispidum*	[57]
R=CH3	Onosmin B	*O. hispidum*	[57]
	Onosmone	*O. limitaneum*	[85]
	Hispidone	*O. hispidum*	[84]
			
			
	Alkannin or arnibin 4	*O. echioides, O. paniculata*	[86]
	Acetylalkannin or arnibin 3	*O. paniculata*	[86]
	Isovalerylalkannin	*O. heterophylla*	[86,87]
	β, β-dimethylacrylalkannin or arnebin-1	*O. paniculata*	[86]
	β -acetoxyisovalerylalkannin	*O. paniculata*	[86,87]

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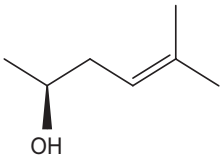
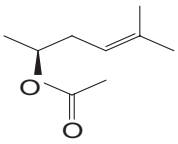
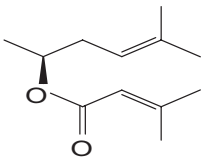
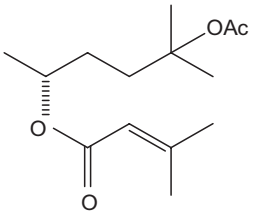
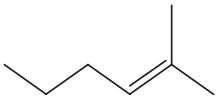
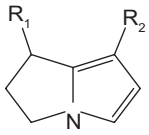
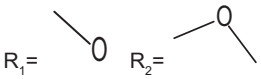
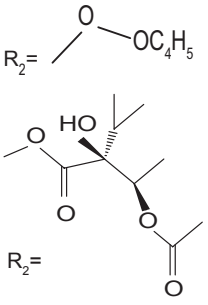
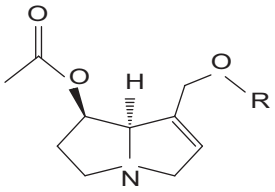
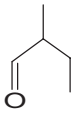
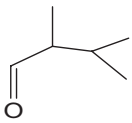
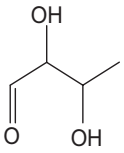
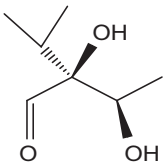
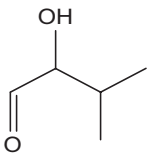
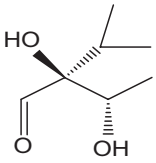
R	Name	Occurrence	Ref
	Shikonin	*O. conferitum, O. hookeri, O. tauricum, O. livanovii, O. visianii, O. sericium, O. setosum, O. polyphyllum, O. zerizaminium*	[86,87]
	Acetylshikonin	*O. confertum, O. hookeri, O. paniculatum, O. echioides*	[86,87]
	β, β -dimethylacrylshikonin	*O. confertum, O. paniculatum, O. hookeri, O. zerizaminum*	[86,87]
	acetylarnebin-2	*O. heterophylla*	[86]
	deoxyalkannin, deoxyshikonin, or arnebin-7	*O. confertum, O. heterophylla*	[86]
	5,6-dihydro-7,9-dimethoxy-7H-pyrrolizine	*O. arenaria*	[1]
	9-(Butyryl1-2-ene) supinidine	*O. arenaria*	[1]
	3'-acetylsupinine	*O. arenaria*	[1]
	7-acetyl-9-(2-methylbutyryl) retronecine	*O. arenaria*	[1]
	7-acetylretronecine	*O. arenaria*	[1]

Contd...

Table 3: Structures of some phytoconstituents found in genus *Onosma* L.

R	Name	Occurrence	Ref
	7-Acetyl-9-(2,3dimethylbutyryl) retronecine	*O. arenaria*	[1]
	7-Acetyl-9-(2,3-dihydroxybutyryl) retronecine	*O. arenaria*	[1]
	Uplandicine	*O. arenaria*	[1]
	7-Acetyl-9-(2-hydroxy-3-methyl butyryl) -retronecine	*O. arenaria*	[1]
	7-Acetyl-lycopsamine	*O. arenaria*	[1]

derivatives isolated from Onosma exsertum Hemsl., Onosma confertum W.W. Smith, Onosma hookerii Clarke var. longiflorum Duthie, O. hookerii Clarke and Onosma waltonii Duthic and these six species of Onosma are also used by peoples of Tibet and Yunnan, which contains various types and considerable amounts of naphthaquinones.[92]

ETHNOPHARMACOLOGY

The plants of genus *Onosma* L. contains alkannin and shikonin, flavonoids, ferulic and vanillic acids, which may responsible for anti-inflammatory, wound healing, analgesic and its antibacterial actions. A study was showed that these phytochemicals have significant anti-inflammatory and anti-pain action without the gastric damage as caused by indomethacin.[87] The anticancer activity was reported in *Onosma limitaneum*[85] and antioxidant with antimicrobial activities in *O. argentatum*.[57]

The roots extract of *O. argentatum* Hub.-Mor. was investigated for their ability to stimulate the growth of human amnion fibroblasts, wound healing activities might be partly due to an additive effect of the shikonin derivatives.[88] The root extract also has spasmolytic and antipyretic activity.[93]

The roots extract of *O. arenaria* possess naphthazarin derivatives showed cytotoxicity on human cervix adenocarcinoma cells and leukemia K562 cells and in another study also showed that β-hydroxyisovalerylalkannin, acetylalkannin and the pigment fraction exhibited high cytotoxicity on non-malignant peripheral blood mononuclear cells (PBMC) as well on healthy PBMC activated by phytohaemagglutinin.[94] In an experimental study the *Onosma armeniacum* K. has shown to possess antiulcer and antioxidative properties.[95]

Aqueous, methanolic and dichloromethane extracts of Auchers golden-drop (*Onosma aucheriana*) exhibited interesting antileishmanial activities on the intracellular amastigote form of the parasite also shown to induce nitrous oxide production by human macrophages.[36]

The effect of *Onosma bracteatum* Wall extract on degranulation of rat peritoneal mast cells and cell inhibitory effect in immunologically induced degranulation of mast cells was found significant.[96] The hydro-alcoholic extract of this plant used in asthma as it stabilizes the mast cell activity, rheumatoid arthritis and showed a significant role in the marked reduction of bronchial hyper-responsiveness on decreasing the infiltration of the eosinophils and the neutrophils in rodents.[97,98] This plant is also used in the Unani system of medicine for stress, disturbances of the

body homeostasis or with the disturbances of the normal body physiology such as psychological (behavioral changes), immunological and hormonal imbalances which causes the pathogenesis of certain chronic diseases such as Alzheimer's disease, Parkinson's disease, hypertension, weakness of the immune system of the human body, asthma, diabetes, heart ailments, cancer,[99] antioxidant[100] with wound healing activity.[101,102]

The antioxidant activity was investigated in *Onosma chlorotricum* Boiss and Noe[103] while *Onosma griffithii* vatke possess spasmogenic activity.[104] *O. chlorotricum* Boiss and Noe[103] and *Onosma dichroanthum* Boiss. have spasmolytic activity,[105] and acetones extract of roots of *O. dichroanthum* Boiss. leads to produce potent free radical scavenging effect.[106]

O. griffithii was also screened parasiticidal activity against *Leishmania* major based on the IC 50 (Inhibitotry concentration) values, found effective, similarly moderate antifungal activity was displayed by the crude methanolic extract against *Aspergillus flavus* and *Fusarium solani* while against the *Staphylococcus aureus*, the aqueous fraction demonstrated moderate antibacterial activity.[107]

Sharma *et al*. (2004), unveiled the effect of *O. echioides* extract on two-stage skin carcinogenesis and on tumor promoter induced markers and oxidative stress in Swiss mice. Pre-treatment of *O. echioides* extract in both studies on single topical application of benzoyl peroxide followed by exposure to ultraviolet B radiation induced significant oxidative stress and elevated the marker parameters of tumor promotion.[108]

The chemical investigation of the ethanolic extract of the root bark of *O. hispidum* Wall following antibacterial and crude ethanolic extract and methanol fraction exhibited substantial bioactivity against species of corynebacteria, enterococci, staphylococci and streptococci, in which ferulic acid was found more bioactive compared with the vanillic acid[90,109] and hispidone, a flavanone isolated from this plant have cholinesterase inhibition property[84] while root extract possess wound healing,[110] antitussive[90] and antidiabetic activity.[111]

The effect of brassinolide on cell growth, shikonin and its derivative formation in *Onosma paniculatum* cell culture was also studied.[112] It is concluded that the pigment yields of callus and suspension cultured cells were increased and maximum yield of pigments was obtained when 10(-6) M of ascorbic acid was added to the medium[113] while its petroleum ether extract induces cell death in a caspase dependent manner.[114] A crude elicitor preparation of culture of *Aspergillus* spices could also accelerate shikonin derivatives formation but irreversibly arrest cell growth in *O. paniculatum* cell cultures.[115]

A study also shows genotoxic effects of over ground and underground parts of species *Onosma stellulata in-vitro* conditions was conducted by using Allium-test, along with observation of chromosomes abnormalities, causing genotoxic effects in mitosis at meristematic cells of Onion.[1,116]

TRADITIONAL USES

Traditionally, genus *Onosma* L. plants are used as a stimulant in rheumatism, bladder pain, kidney irritation, palpitation of heart[57] and roots for their diuretic, cooling, astringent and demulcent action. While in India, it is used in the treatment of hypertension, fever and nervous conditions. In Turkey, these plants are used to treat inflammatory disorders such as tonsillitis, hemorrhoids and bronchitis and pain.[82]

O. hispidum Wall. used in the treatment of fevers, pain relief, wounds, bites, infectious diseases, stings and flowers are used as a cardiac tonic and stimulant while bruised roots are applied externally to cutaneous eruptions.[111]

The roots of *O. argentatum* Hub.-Mor. are used traditionally in Turkey for wound healing, burn and in traditional medicine of Lorestan province, oily extract of root of a plant known as Tashnehdary (*O. chlorotricum*) are used topically for wound healing.[103]

An extract, used orally, is prepared from the roots of *O, armeniacum* K. by villagers who heat the roots with butter and filter then used as a folk medicine in Turkey to treat wounds, burns, dyspnea, hoarseness, hemorrhoids, abdominal aches, stomach ulcers and gynecological problems.[95]

O. bracteatum Wall., known as Gaozaban in the Unani system of medicine and as Sedge in the Middle East and traditionally used as a tonic that helps in building the body's immune resistance with regulation of urine output[99] also reported to be used in the treatment of asthma, bronchitis, tonic, alterative, demulcent, diuretic and spasmolytic. A decoction is used in the treatment of syphilis, rheumatism, leprosy, restlessness in febrile excitement, relieving excessive thirst, useful in irritation of the bladder, palpitation of the heart, stomach and strangury, also folk medicine for the treatment of the wound and skin diseases.[102]

The leaves of *O. echioides* DC. are alterative and powder has given to children as a purgative. Flowers are used as a cordial, stimulant in the treatment of rheumatism and palpitations of the heart while root is bruised, used to treat skin eruptions.[117]

The dried roots of *O. paniculata* Bureau and Franchet are used in traditional Chinese medicine for the treatment of various diseases including cancer.[91]

INDUSTRIAL USES

O. hispidum Wall. has been reported to be the source of Ratanjot, a red dye yielding root, commonly used for coloring food stuffs, oils and medicinal preparations. Owing to its color, it has also been used as an adulterant in spices like chilli powder and food preparations. Its use as a visible coloring agent for Vanaspati has been suggested but feeding trials on rats have shown this coloring matter to be non-toxic in low doses and toxic in high concentrations while causing destruction of liver cells after continued feeding. The color imparted to Vanaspati is completely removed by simple chemical treatment with alkali solution and to a substantial extent by exposure to direct sunlight or heating. Infect, the dye does not appear to be suitable for coloring Vanaspati.[110,118]

The combination of mordants like alum: Chrome, alum copper sulfate, alum: Ferrous sulfate, chrome: Copper sulfate, chrome: Ferrous sulfate, copper sulfate: Ferrous sulfate with roots, in the ratio of 1:3, 1:1 and 3:1 were studied for colorfastness properties and light, washing, rubbing and perspiration fastness of the dyed samples gives fair to excellent fastness grades.[119]

DISCUSSION

Genus *Onosma* L. has controversial and complicated patterns of morphological, karyological and taxonomical data. The numerous similar plants were described on the basis of minor difference in morphological characteristics. Either these plants have only one or two references or the sub-species of other accepted plants. Most of these plants belong to the same species, but due to lack of taxonomical data, some researchers use a different name, which may be due to some morphological changes by different climate conditions. Table 2 enumerates such type of plants, which are available in literature but not have so sufficient data to identify or to prove that these species are exist or not and also provides available references for these individual names. The plant list of Royal botanical garden, Kew and Missouri botanical garden shows that only about 37 plants have correct taxonomical data. The plants of this genus are abundantly distributed in Turkey, China, Iran, Pakistan, Syria, India and Sri Lanka besides these, Switzerland, Romania and Anatolia. This genus distinctly differ in external nutlet characters, size, shape, color and ornamentation and sculpturing of the nutlet surface patterns with petal morphology like corolla color, shape and size. As for as phytochemicals are concerned the alkanins and shikonin are abundantly found in this genus, which are chiral pairs of naturally occurring isohexenylnaphthazarins with some specific phytochemicals such as hispidone, onosmins, onosmone and uplandicine. Besides these, flavonoids, ferulic and vanillic acids are also found, which may be responsible for anti-inflammatory, wound healing, analgesic and antibacterial activities.

The plants of this genus possess anticancer, antioxidant, antimicrobial, antipyretic, anti-diabetic, antitussive and spasmolytic activities and traditionally used in rheumatism, bladder pain, kidney irritation, palpitation of heart while roots are used in astringent, demulcent, diuretic, hypertension, fever, pain and inflammatory disorders and extensively used for so many medicinal purposes by the local peoples. The main aim of this review is to establish permanent genus literature in plant resource information to facilitate future studies and human interventions in the world.

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