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THE GENUS *ONOSMA* L.: A COMPREHENSIVE REVIEW

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ABSTRACT

In medicinal plant field ethnopharmacological knowledge aggrandizes legibility for prioritizing species selection for future research opportunities. Many plant species representing the genus Onosma have been documented to be important in communities world-wide as evidenced by the numerous records on traditional medicinal and ethno-botanical information. Various species of the genus are used in the traditional medicinal systems in Europe and Asian countries especially in India, China, Turky and Pakistan. The literature on the species distribution and their characterization was compiled from different regional floras, regional revisions and databases. The information related to traditional uses, pharmacological activities and phytochemistry was systematically collected from the scientific databases including reference books, SciFinder, Scopus, PubMed and Google Scholar. Absence of comprehensive literature review on genus Onosma species led to design present study and dig the recorded documents to comparatively gauge magnitude of studies on each of the Onosma species through an exhaustive bibliographic evaluation of scientifically studied species of genus Onosma that are also taxonomically identified and are valued as traditional medicinal remedy for diseases in their countries of origin. The study hinted about lack of scientific literature on most of the species. A comprehensive bibliographic review on the geographical distribution, identification, traditional uses, phytochemistry, pharmacology and toxicology of the genus Onosma is attempted here to give insights into promising future drug discovery strategies.

KEYWORDS: *Onosma, Distribution, Traditional uses, Phyto-Pharmacology*

1. INTRODUCTION

Onosma L. (Family: Boraginaceae) is one of the largest genera of the tribe Lithospermeae Dumort. in Boraginaceae, representing 200 species in Asia and Europe including 29 species in China [1],95 species in Turkey[2], 8 in Pakistan[3], 33 species in Europe[4], and 34 species in Russia and adjacent states[5].

In recent years, numerous studies[6-10] pertaining to genus led to inclusion of the several numbers of species increasing the number to 250 species in the genus Onosma. The botanical nomenclature of Onosma for this genus was introduced by Linnaeus, which is derived from a Latin word "osma" originated from a Greek word, "Osma" means

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smell and accepted to be treated as feminine[11]. Onosma species are traditionally valued as a remedy for rheumatism, bladder pain, kidney irritation and palpitation of heart, laxative, blood diseases, bronchitis, leucoderma, fever, wounds, burns, piles and urinary calculi[12,13]. Phytochemicals including lipids, pyrrolizidine alkaloids, phenolic compounds, naphthoquinones and flavonoids are reported from different Onosma species[14]. Some of the traditional uses of various species have been scientifically validated and are shown to possess antioxidant and anti-inflammatory, spasmolytic, antimicrobial, analgesic, wound healing Potential[15-21].

2. DISTRIBUTION

The genus Onosma L. comprises of numerous species that are distributed mainly in Western and Central Asia, Northwestern Africa and in the Mediterranean region of Europe. It is mainly centered in Iran, Syria, Turkey and Pakistan and also found in Northern India and adjacent Tibet into Burma and China [22]. The distribution pattern of different species in different regions has been discussed by Kumar, et al. in 2013[23]. Distribution of some species of genus Onosma L is presented in Table 1. The flora of China enlists 29 species growing in China. O. hookeri, O. hookeri var. hookeri, O. paniculatum distributed in China as well as North India and Bhutan[1]. Onosma pyramidale Hook.and O. bracteatum is an endemic species from Kali Valley, Eastern Kumaun (Uttarakhand), India[24,25]. Anatolia is an important centre of origin for Onosma as 101 species (107 taxa) are found, of which 50 are endemic including 1 variety from Turkey[26].O. arenaria and O. pseudoarenaria are included in list of endangered species in Slovakia due to climatic factors, O. tornensis, the number of localities of which is constant and O. visianii is the most frequent species in Slovakia[27]. In Romania, O. visianii Clem grows mostly in Dobrogea's barren places, steppe and on calcareous soils while O. setosum Ledeb., O. arenariaWaldst. et kit., O. pseudoarenaria Schur and O. viride (Borb.) Jav. are endemic, spread in barren areas such as Cluj, Hunedoara and Ploiesti; O. taurica Pall. ex Willd. grows in stony, grassy and calcareous areas from Timisoara and Constanta. O. heterophylla (sin. viride) and O. helveticum Boiss. grow in Transylvania; O. lypskyi, O. visianii Clementi, O. taurica Pall. Ex Willd., O. rigida Ledeb. are found in Dobrogea and O. arenaria Waldst. et Kit. is spotted in the Danube Delta[28].

3. MORPHOLOGY AND MICROSCOPY

Genus Onosma encompasses fruticulose herbs bearing a peculiar indumentum that is developed from a big, solitary bristle (seta) growing out of the top of a tubercle, and (found in some groups only) with several rays of smaller setae attached circularly to the base of the tubercle and directed radially called asterosetules or stellate setae[4].The genus Onosma L. contains biennial or perennial, hispid herb or undershrub; leaves are petiolate or sessile, alternate with entire margin. Racemes are simple or cymose, one sided and bracteate, flowers are actinomorphic, sessile or shortly pedicellete, while calyx parted to or nearly to base with 5 lobes, corolla blue, yellow, white or red in color, tubular or ventricose, throat unappendaged while, nectary are ring like or 5 lobed with dentate margin, stamen 5, filaments attached near the middle of the corolla tube linear short or long or dilated at the base, anther lanceolate, acuminate, free conically connivent, ovary deeply 4 lobed, style filiform, stigma capitates 2 lobed. Gynobase is flat with 4 nutlets, ovoid, acute, erect or somewhat incurved, smooth or tuberculate, attached to basal scar[1,4,29].The indumentums of leaf, flowers and stem of Onosma taxa show three separate parts: 1) setae (rarely hairs) that are often slightly raised, or pancake-shaped with multicellular tubercles; 2) setules, which are at times reduced to tiny spinules or produced as hairs, and stellately laid around the base of the seta; and 3) tiny hairs that make a pubescent, puberulous or tomentose surface covering between the setae. The setae are brittle and detachable hispid indumentum that can penetrate the skin and causean irritant rash. Although the stellate setae is a typical feature of this genus, in a number of species a wide range of variation in the presence, frequency and length has been observed. Based on the trichomes features, some taxa are named e.g., O. sericeum Willd. (sericeous setae or silky trichomes), O. asperrima Bornm. (aspersus setae or slightly rough trichomes), O. bulbotricha DC. (bulbous setae), O. chrysochaeta Bornm. (Yellow setae, or golden trichomes), and O. chlorotricha Boiss. & Noë (green setae)[30]. Furthermore, different morphological characters such as corolla color, shape and size are of taxonomic significance in this genus[4,31]. The pollen morphology has been reported to be prolate, sphaeroidea and subprolatae in Asterotricha and Haplotricha subsections respectively[32].

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4. TRADITIONAL USES

Onosma species are traditionally used as a stimulant in rheumatism, bladder pain, kidney irritation and palpitation of heart, laxative and anthelmintic[12]. Different species are used in the treatment of eye and blood diseases, bronchitis, abdominal pain, strangury, itch, leucoderma, fever, wounds, burns, piles and urinary calculi. The flowers are indicated as stimulants, cardiotonic, in body swelling, while the leaf as purgative and in cutaneous eruptions[13].

O. bracteatum leaf, flowers, and seeds are widely used in the indigenous system of medicine as acrid, cooling, antipyretic, diuretic and given in diseases of the chest and lungs, asthma, throat troubles, stomatitis, gingivitis, gonorrohoea and leprosy[25].

O. hispidum root is used to get red dye used for colouring food stuff, oils and medicinal preparation, leaves as cardiac stimulant, in rheumatism and palpitation of heart, cooling, laxative, anthelmintic, diseases of the eye and blood, bronchitis, and abdominal pain [33,34].

O. sericeum Willd., O. microcarpum Steven ex D.C are indicated in the treatment of wounds in rural areas in Turkey, O. argentatum Hub.-Mor. roots are used for wound healing and burns in rural areas of Ilica District (Erzurum, Turkey)[35].

O. armeniacum is used by villagers who heat the roots with butter and filter then use as a folk medicine in Turkey traditionally to heal wounds, burns, dyspnea, hoarseness, hemorrhoids, abdominal aches, stomach ulcers and gynecological problems[36].

5. INDUSTRIAL USES

'Ratanjot', which comprises mainly two plant species (O. hispidum, O. echioides) is regarded as the important herbal drug of indigenous systems of medicine. Besides its medicinal uses 'ratanjot' is also popular in Asia for imparting a pleasing red color to foodstuffs, oils, fats and various galenicals. Shikonin and its derivatives from O. hispidum are used in cosmetic preparations and dusting powder beneficial for skin and for the treatment of haemorrhoids[37].O. hispidum has also been used as an adulterant in spices like chilli powder and food preparations, its use as a visible coloring agent 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[38]. Printed jute fabric with very good wash and rub fastness can be produced from natural dyes extracted from O.echioides by substantive screen printing method, and these can be used as decorative, furnishing and apparel textiles[39].

6. PHYTOCHEMISTRY

Reports on phytochemical work on the genus Onosma L. revealed pyrrolizidine alkaloids (Table 2a) and naphthaquinones (Table 2b), phenolics/flavonoids, fatty acid and wax as key constituents.

Table 2a: Alkaloid constituents of Genus Onosma L.

Sr.No.	Chemical constituents	Speceis	References
1	Intremidine	O.alborosea, O.alborosea Sanguinolenta, O.arenaria subsp. Pennina	[40]
2	Lycopsamine	O.alborosea, O.alborosea Sanguinolenta, O.arenaria subsp. Pennina, O.hispida, O.paniculata, O.dichroantha, O.hypoleuca, O.thomsonii,O.chitralica, O.adenopus	[40,41]
4	O7-acetyllycopsamine	O.alborosea, O.alborosea Sanguinolenta, O.arenaria subsp. Pennina	[40]
5	O7-acetylintermidine	O.alborosea, O.alborosea Sanguinolenta, O.arenaria subsp. Pennina,	[40]
6	Uplandicine	O.arenaria Waldst. and Kit,	[42]
7	5,6-dihydro-7,9-dimethoxy-7H-Pyrrolizine	O.arenaria Waldst. and Kit	[42]
8	Leptanthine	O.leptantha	[43]
9	LeptanthineN-oxide	O.leptantha	[43]
10	Echihumiline	O.leptantha	[43]
11	Echihumiline N-oxide	O.leptantha	[43]
12	N-oxide of 3-O-acetylechihumiline	O.leptantha	[43]

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13	Supinine	O.hispida, O.confertum, O.hookerii Clarke, O.paniculata, O.dichroantha, O.hypoleuca, O.thomsonii, O.chitralica, O.adenopus, O.griffithii, O.weddelli, O.multiramosum, O.apiculata, O.gmelinii, O.ferreri, O.sinica	[41]
14	Europine	O. confertum, O.griffithii, O.weddelli, O.ferreri, O.sinica	[41]
15	Heliotrine	O.hookerii Clarke, O.adenopus, O.griffithii, O.weddelli, O.multiramosum, O.apiculata, O.gmelinii	[41]
16	Echimidine	O.hispida, O.paniculata,O.dichroantha, O.hypoleuca, O.thomsonii, O.chitralica, O.adenopus,	[41]

Table 2b: Alkannin/Shikonin constituents of genus Onosma L.

Sr.No.	Chemical constituents	Species	Reference
1	Deoxyshikonin	O.argentatum, O.exsertum, O.confertum, O.waltonii duthic, O.hookerii Clarke var. longiflorum Duthie, O.hookerii Clarke, O.echioides L, O.visianii	[44,45]
2	Shikonin	O.exsertum, O. confertum, O.waltonii duthic, O.hookerii Clarke var. longiflorum Duthie, O.hookerii Clarke	[45]
3	Acetyl shikonin	O.argentatum, O.exsertum, O.confertum, O.waltonii duthic, O.hookerii Clarke var. longiflorum Duthie, O.hookerii Clarke, O.paniculata,	[44,45, 46]
4	3-hydroxy-isovaleryl shikonin	O.argentatum, O.paniculata	[44,45,46]
5	5,8-O-dimethyl acetyl shikonin	O.argentatum	[44]
6	Acetoxyisovalerylshikonin	O.exsertum, O.confertum, O.waltonii duthic, O.hookerii Clarke var. longiflorum Duthie, O.hookerii Clarke	[45]
7	Isobutyrylshikonin	O.exsertum, O.confertum, O.waltonii duthic, O.hookerii Clarke var. longiflorum Duthie, O.hookerii Clarke,	[45]
8	Alkannin,	O.heterophylla	[47]
9	deoxyalkannin,	O.heterophylla, L, O. graeca	[47,48]
10	β,β-dimethylacrylate alkannin	O.heterophylla, O.graeca	[47,48]
11	Alkannin isovalerate	O.heterophylla	[48]
12	β-hydroxyisovalerylalkannin	O. graeca, O. arenaria Waldst. and Kit	[48,49]
13	acetylalkannin	O. graeca, O. arenaria Waldst. and Kit	[48,49]

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7. PHARMACOLOGY

Recorded literature on genus Onosma L. is suggestive of it being rich source of pyrrolizidine alkaloids, napthaquinone derivatives alkannin and shikonin, phenolics and flavanoids and their glycoside, essential oil and sterols. These bioactives may be responsible for anti-oxidant, anti-inflammatory, anti-tumor, wound healing, analgesic and antibacterial actions exhibited by different species.

7.1 Onosma hispida

Hispidone, a flavanone isolated from O. hispida exerted cholinesterase inhibition property [34]. Onosmins A and B isolated from the plant have been shown to exhibit lipoxygenase inhibition activity[50]. In a study targeting antibacterial activity of the ethanolic extract of the root bark against species of Corynebacteria, Enterococci, Staphylococci and Streptococci, ferulic acid was shown to be more active compared to vanillic acid[51]. Different experimental studies have shown that root extract possessed Antitussive [52], Hypoglycemic [53], wound healing[54], Petroleum ether extract of root of O. hispidum has been shown to exert antidiabetic activity and the aqueous extract has been shown to be having anticancer potential on HepG2 cellline on prolonged exposure due to the presence of appreciable amounts of polyphenols and flavonoids[55].

7.2 Onosma arenaria

Naphthazarin derivatives, β-hydroxyisovaleryl alkannin, acetyl alkannin, and the pigment fraction isolated from the roots of O. arenaria have been reported to possess cytotoxicity against human cervix adenocarcinoma cells (HeLa) and leukaemia K562 cells, as well on non-malignant Peripheral blood mononuclearcells (PBMC)[49].

7.3 Onosma argentatum

Root extract has been reported to possess antioxidant, antibacterial and wound healing activities might be partly due to an additive effect of the shikonin derivatives activities[19,56].

7.4 Onosma paniculatum

Petrol ether extract has been noted to exert growth inhibitory effect, cell cycle influence and caspase-3 dependent induction of apoptosis on leukemia cells, CCRF-CEM and THP-1, and breast cancer cells MDA-MB-231[57]. Napthaquinone from root of O.paniculatum was shown to cause the inhibition of nitric oxide production suggesting the anti-inflammatory potential[58]. Shikonin derivatives from the roots were shown to possess tumor growth inhibitory activity towards melanoma cells by inducing apoptosis, inhibiting caspase-3,7 dependently, increasing the protein levels of cleaved enzyme poly ADPribose polymerase, and double-stranded DNAbreakage [59].

7.5 Onosma leptanhtha

Naphthazarine derivatives (β, β-dimethylacryl shikonin, isovaleryl shikonin and acetyl shikonin) isolated from root extracts have been demonstrated to exert anti-inflammatory effect on carrageenan-induced rat paw edema test and cytotoxic activity against L1210 murine lymphoblastic leukemia cell line and human fibrosarcoma HT-1080 cells[60].

7.6 Onosma echioides

O. echioides plant extract prevented the depletion of the cellular antioxidant, reduced glutathione and its associated enzymes along with the elevation of enzymes involved in the suppression of oxidation processes, along with reduction in the number of tumors in dimethyl-benz(a)anthracene and croton oil induced mouse skin carcinogenesis[61]. A dimer of alkannin/shikonin isolated from the petroleum ether (60–80ºC) extract of the bark was found to exert wound-healing activity against excision and incision wound models in albino rats[62]. Root bark extract has been shown to effectively decrease ROS levels, induce apoptosis and improve the viability of cells in a dose dependent manner in response to mercury-induced oxidative stress in neuroblastoma cells[63]. Hexane extract of the root bark was shown to be effective in management of diabetic neuropathy against streptozotocin-induced diabetes in Sprague Dawley rats[64]. Bark extract has been noted to be devoid of any adverse effect on body weight, food consumption, water intake, serum glucose, and hematology, biochemistry at a fixed dose[65].

7.7 Onosma bracteatum L.

A dealcoholized and detannated extract has been shown to lower the blood pressure and depressed the heart and caused vasoconstriction[16], The methanol extract is shown to have antioxidant activity, decrease lipid peroxides and inhibit caspase-3 on BT549, PC3 and A549 cancer cells[66], The ethanolic extract from the

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aerial parts has been recorded to possess antiallergic, analgesic, anti-inflammatory and wound healing activities[17,18, 20],O. bracteatum extract has been shown to exert protective effect against the stress induced impaired immune functions and the psychological processes like memory[67], The hydroalcoholic extract is shown to have anxiolytic and antidepressant properties[68]. Benzoquinones have been evidenced to display anti-aging potential evaluated through a yeast lifespan assay[69].

7.8 Onosma heterophyllum

The aqueous extract of roots being rich source of phenolics and flavanoids has been shown to possess antioxidant, tyrosinase and α-glucosidase inhibitory activities. The methanol extract is demonstrated to exhibit the highest inhibitory activity on AChE and α-amylase [70].

7.9 Onosma hookeri Clarke

Naphthoquinone-enriched ethanol extract from the roots of O. hookeri Clarke.Var. Longiforumduthi isshown to be a potent antioxidant[71].

8. DISCUSSION

As seen from the data Genus Onosma L. is of substantial importance from the view of its utility as traditional medicine and industrial significance (dye stuff). The plants of this genus are abundantly distributed in Turkey, China, Iran, Pakistan, Syria, India, Sri Lanka, Anatolia, Switzerland and Romania. Looking to the controversial and complex patterns of morphological, karyological and taxonomical data many a times the identity of the similar plants is done on the basis of small difference in morphological characteristics (pollen, nutlet and trichomes). It has been observed that some researchers use a different name for same species of plant due to lack of taxonomical data, which may be due to some morphological changes by different environment conditions. The species of genus Onosma mostly differ in trichomes characters and nutlet characters visually size, shape, color and ornamentation and sculpturing of the nutlet surface patterns with petal features like corolla color, shape and size. Recorded phytochemicals in different species include typical pyrrolizidine alkaloids, abundant isohexenyl naphthazarins (chiral pairs of alkanin and shikonin) and flavonoids onosmins, onosmone and uplandicine that are shown to be responsible for antioxidant, antimicrobial, anti‑inflammatory and anticancer potential.

There is substantial scope for extended as well as new research developmental activities to explore genus Onosma, especially on the Asian species, the comprehensive exemplar literature presented here proffers significant data for future studies. Accordingly, the future research can be targeted for morphological, karyological and taxonomical studies on species for correct identification and further refinements of the geographical distribution; scientific validation of traditional uses of ethnobotanically relevant Onosma species to create new medicinal and functional food products.

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