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Oxyria digyna: A review on the nutritional value, phytochemistry and ethnopharmacology

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ABSTRACT: *Oxyria digyna* is an important herb, having a wide geographical distribution. Nutritionally, it has found its place in the meals of various populations living in different parts of the world, both in raw and cooked forms. Traditional uses identified its indications in cancer, depression, hepatitis, jaundice, colic, gastritis, appetite, diuretic, constipation, cough, chest congestion, boils, scurvy. Several pharmacological activities have hastened further experimental exploration of this plant, establishing its efficacy for diabetes, free radical scavenging, gout, and cancer. The important bioactive compounds isolated from this plant are vitexin, orientin, hesperidin, quercetin and stigmasterol. These compounds have extensive effects on human physiology and provide proof that *O. digyna* is potentially unexplored for its pharmacological efficacy. A detailed metabolomic approach is required to fully characterize the plant as a potential nutraceutical candidate with multiple therapeutic potentials.

Keywords: *Oxyria digyna*; Nutritional values; Phytochemistry; Pharmacological effects; clinical status; Therapeutic potential.

1. Introduction

POLYGONACEAE is a family of worldwide distribution, contains about 59 genera and 1384 accepted species being classified under the major group of flowering plants (Angiosperm). Plants in this family received attention due to its bioactive phytoconstituents. The pharmacological activities exhibited by this family include antiproliferative, antidiabetic, anti-inflammatory, cathartic, antioxidant, antimicrobial, antidiarrheal, anthelmintic, acetylcholinesterase inhibition etc., (Ayaz et al., 2020; Fan et al., 2010; Lajter et al., 2013; Mostafa et al., 2011; Singh et al., 2010; Torres-Naranjo et al., 2016). The genus Oxyria Hill is comprised of 16 plant species, but only two are accepted as per the plant name index database https://theplantlist.org i.e., *Oxyria digyna* (L.) Hill and *Oxyria sinensis* Hemsl. The taxonomy of *xyria digyna* is shown in **Table 1 and figure 1**.

The genus Oxyria has been little explored for potential natural compounds. Existing studies have documented the well-known flavonoids, tannins, phytosterols, or glycosidic derivatives.

Some of them are vitexin, hesperidin, orientin, quercetin, epigallocatechin, kaempferol, and stigmasterol (Orhan et al., 2009). These bioactive molecules have been reported to possess numerous pharmacological activities.

Table 1: Taxonomy of *Oxyria digyna* (L.) Hill [Alpine Mountain sorrel]

Kingdom	Plantae (Plants)
Subkingdom	Tracheobionta (Vascular plants)
Superdivision	Spermatophyta (Seed plants)
Division	Magnoliophyta (Flowering plants)
Class	Magnoliopsida (Dicotyledons)
Subclass	Caryophyllidae
Order	Polygonales
Family	Polygonaceae (Buckwheat family)
Genus	*Oxyria* Hill
Specie	*digyna* (Alpine Mountain sorrel)

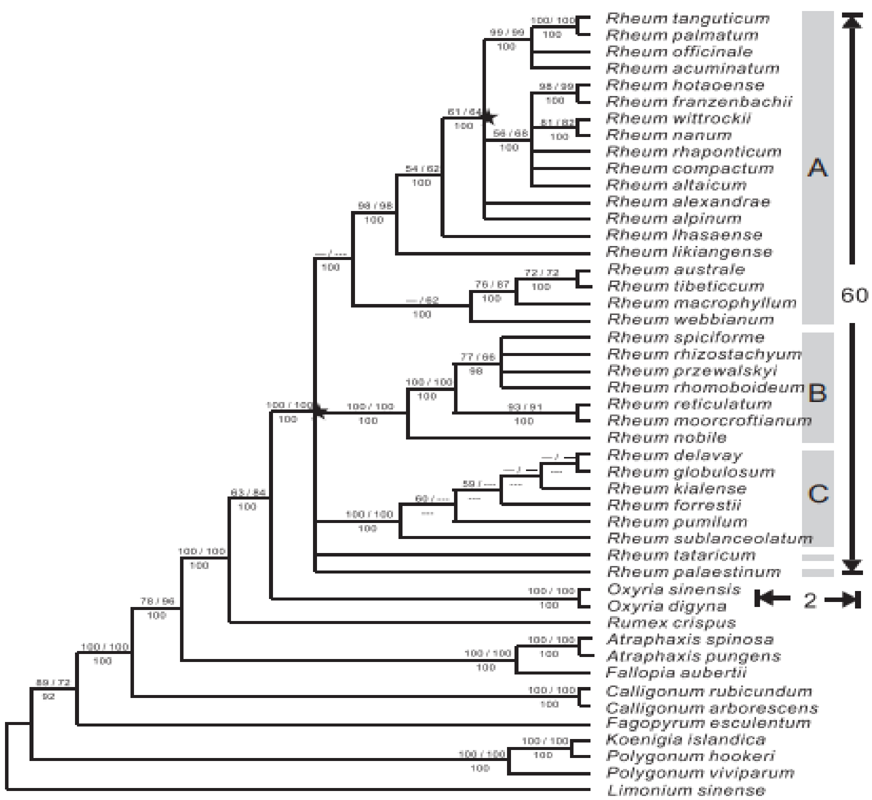

Figure 1: Strict consensus tree exhibiting *Oxyria digyna*

O. digyna has also been used as a component in many traditional cooking recipes consumed from the arctic to the Himalayan regions. It is also a part of traditional healthcare treatments in Chinese, South Asian and Arctic territories (Angmo et al., 2012; Da Cheng Hao and Xiao, 2015; Davis and Banack, 2012). However, a deep metabolomic approach is still required to characterize its pharmacological properties.

1.1 Biological and Traditional Nomenclature

One of the little explored specie of genus Oxyria is *Oxyria digyna*. The word Oxyria originates from Greek**,** meaning 'sour' because of its taste (Gjærevoll and Rønning, 1999). The various synonyms for *O. digyna* are *Acetosa digyna* (L.) Mill., *Donia digyna* (L.) R.Br., *Doniasapida* R.Br., *Lapathum digynum* (L.) Lam., *Oxyria elatior* R.Br. ex Meisn., *Oxyria reniformis* Hook., *Oxyria rotundifolia* Gray, *Rheum digynum* (L.) wahlenb. and *Rumex digynus* L. listed by plants of the world online, http://powo.science.kew.org/.

Bootstrap support values are displayed above branches receiving >50 % values in both MP/ML analyses, while the corresponding posterior probabilities from 'Bayesian analyses' can be seen below branches. Arrows on the right show contrasting numbers of species in Rheum (60) and its sister genus Oxyria (2) (Sun et al., 2012).

O. digyna is commonly known as mountain-sorrel, sour grass, or Alpine mountain-sorrel. Due to its availability in various geographical territories, it has got numerous vernacular naming depicted. Some of them are Tarvaskoonay (Lakki marwat, Pakistan) (Ullah et al., 2014), Khata pat (Azad Jammu and Kashmir) (Mehmood et al., 2018), Da Ghra Shalkhay (Azad Jammu and Kashmir) (Shaheen et al., 2012), Jomo (western Himalayan valley, India) (Rawat et al., 2013), Churki (Shina) (Khan, 2014; Khan et al., 2018), 'Qunguliit' (Inuit families, Canadian northwest territories) (Davis and Banack, 2012), Quunarliarraat (Yup'ik) (Pete and Rasmussen), Quulistat (Cup'ig) (Griffin, 2001), Kugylnik (Siberian Yupik), Qufuliq / Qunulliq (Inupiaq) [Yup'ikeskimos, southwestern Alaska] (Griffin, 2009), Chukru (Himachal Pradesh, India) (Rana et al., 2020), Skyurbutaq (Gilgit-Baltistan, Pakistan) (Hussain et al., 2011), Chumcha / Suchli (Suruand Zanskar valley, Ladakh, India) (Rinchen and Pant, 2014), Chumtswa (western Ladakh, India) (Angmo et al., 2012), Lamanchu (Kashmir, Himalaya) (Singh et al., 2016), Shen Ye Shan Liao and Suan Jiang Cao (Chinese) (Da Cheng Hao and Xiao, 2015).

1.2 Geographical Distribution

The specie *O. digyna* is native to Subarctic and Subalpine regions, and grows in other regions such as Pakistan, Turkey, India, Carpathian basin, Alaskan Arctic regions, China, Kazakhstan, Sweden, Svalbard Archipelago (seabird area), Iceland, Siberia, Somas Lom polo (near Norwegian border), North America, Eurasia and Canadian northwest territories (Asif et al., 2020; Eddudóttir et al., 2020; Hultén and Fries, 1986; Kienast et al., 2001; Song et al., 2009; Wang et al., 2016; Zmudczyńska-Skarbek and Balazy, 2017), and Italy (Gentili et al., 2010; Gentili et al., 2020). Please, refer to **Figure 2**.

Figure 2: Geographical distribution of *Oxyria digyna* in various regions of world.

The vegetation of *O. digyna* was also found in 'poor health' at low alpine territory of central Scandes Mountains of Sweden (12.60° longitude, 62.90° latitude) (Bruun, 2019). Russell reported the plant from the Karakoram-Himalayan region, at latitude of 35° N between Kashmir and Chinese Turkistan. The vegetation at altitude of 12,000-15,000 ft. was similar in many ways to-that of Jan Mayen's at sea level (Russell, 1948). In China, the plant co-occurs with its sister species, *Oxyria* *sinensis*, restricted to the eastern Qinghai-Tibet Plateau. These are the only two species known, of genus *Oxyria* (Sun et al., 2012).

1.3 Plant Description and Development

O. digyna (Polygonaceae) is a wind-pollinated, hermaphroditic, flowering, tufted, perennial, herbaceous plant occurring in diverse habitats from sea level up-to 4500 m (Hultén and Fries, 1986; Wang et al., 2016). The stem is grooved, while the leaves are simple, kidney shaped, long stalked and fleshy as shown in **Figure 3**.

Figure 3: Geographical distribution of *Oxyria digyna* in various regions of world.

O. digyna's flowering time is from May to August, while the harvesting time is June-September. Flowers are greenish with segmented pinkish-white perianth (Mehmood et al., 2018). The fruits are single seeded achene (a small nut; nutlet) with wings. The endosperm is a perisperm, embryo located peripheral and no potential impermeability of seed coat for water was noted. The dormancy class was defined as 'physiological dormancy' of intermediate level (Schwienbacher et al., 2011). The reproductive traits were studied by *Henrik bruun*, who revealed the dispersule and germinule of this plant as nutlets and tepals, while 'ramets' as their reproductive units from the alpine territory of Sweden (Bruun, 2019). A tepal is the outer whorl of flowers that has poor differentiation as sepal or petals.

Many arctic plants have a characteristic close connection between temperature and rapid development in early spring. It allows the maximum growth and maturity in this short growing season. Development of *O. digyna* on Jan Mayen was found while the plants were still covered with several feet of snow. This implies that in early stages, the rapid development is fueled by large reserves of carbohydrate stores in the root and not on newly biosynthesized assimilatory products. This evidence is supported by the declining carbohydrate content of the plant rootstock in early summer (Russell, 1948). Elevated levels of soluble carbohydrates are usually a characteristic of frost-resistant plants in temperate regions (Andersson, 1944).

2. Methods

Traditional, pharmacological, and phytochemical studies on *O. digyna* were searched in online databases including Google scholar, PubMed, Research gate, Science Direct. The literature was searched using plant's scientific name, validated using plant name index database https://theplantlist.org. All the peer review journals were included in the study.

3. Traditional Uses

3.1 A nutritional and functional food

O. digyna is nutritionally an important herb. This is evidenced by its consumption both in raw and cooked form. The plant is used as salad or minced into a specific form of sauce. The plant is consumed in the form of 'chutneys' (a sauce) locally in Bandi Pora district of Kashmir, Himalaya, India. The fresh leaves are available as food, but not medicine, in the trade markets of India (Singh et al., 2016). The leaves are also consumed as salad in the Pakistani territories of Azad Kashmir and deosai plateau of Gilgit Baltistan (Khan, 2014; Shaheen et al., 2012). Consumption of sauce with meals is very common in South Asian region, concentrically in subcontinent region. The people of this territory prepare a sauce by mincing different herbs including coriander, peppermint, spearmint, capsicum fruit as per their taste, commonly known as "chutney" [Urdu and Hindi language]. This spicy sauce is consumed with normal daily meals. Similarly, the plant is cooked as vegetable and eaten in this form. Sometime consumed solitary while also in mixing with other food ingredients.

O. *digyna* is one of the most important traditional food items of the Baffin Island Inuit families (Ulukhaktokmiut), living in the south of Holman, Northwest territories of Canada and Eskimos of North Bering Sea and arctic Alaskan regions (Anderson, 1939; Geraci and Smith, 1979; Kuhnleini and Soueida, 1992). The raw leaves and flowers of the plant are prepared in a concoction (as food) used very commonly by the Kiluhikturmiut Inuinnait, referring to it as 'qunguliit'. It is used with relish due to its pleasant tart flavour. However, the entire shoot is consumed raw, as well as infused beverage prepared by simmering in water (Davis and Banack, 2012). The plant is used as food by the Yup'ik Eskimos of Nunivak island living in southwestern Alaska (Griffin, 2009). The leaves of this plant are used in raw or cooked form in Nevada and by natives of Alaska. It is a good source of ascorbic acid, oxalic acid, and carotene (Turner, 1981). The leaves of *O. digyna* are used as vegetables in Anatolia (Orhan et al., 2009). Traditional nutritional of *O. digyna* are summarized in figure 4.

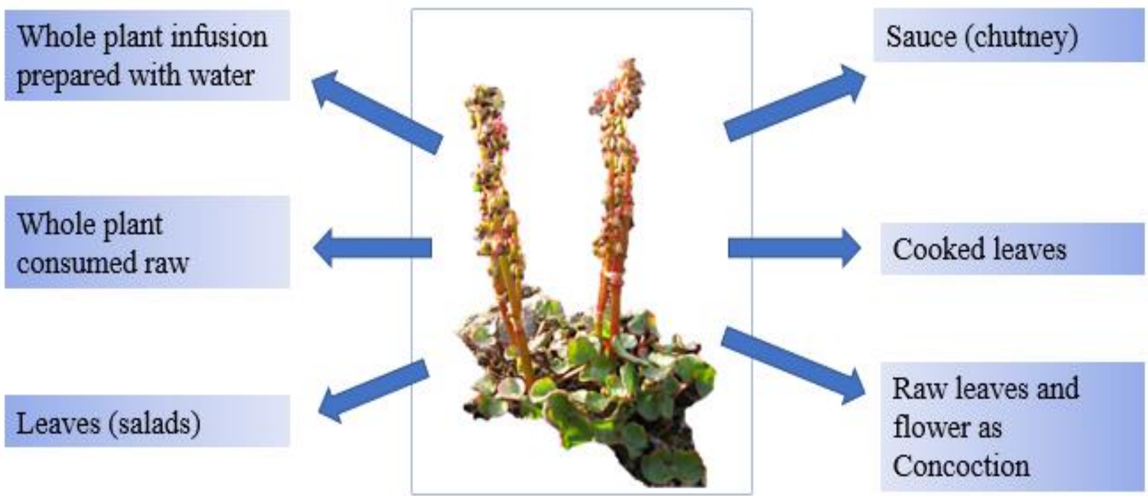

Figure 4: Consumption of *Oxyria digyna* as food in various geographical locations as nutritional herb.

3.2 Ethnopharmacology

Hartwell's series reported the ethnomedicinal use of *O. digyna* against tumors, cancers and warts (Hartwell, 1970). The plant is reported for Appetite disorders in the Indian Kashmir (Singh et al., 2016). O. *digyna* is an important traditional food item for residents of baffin island Inuit families' Northwest territories of Canada. The local healers of the community used the whole plant poultice for chest congestion (Davis and Banack, 2012). The roots are used by indigenous people of Himachal Pradesh, India for treatment of cough, cold and boils. Crushed roots are applied as paste on boils. For cough and cold, a decoction of roots is prepared with boiled water. A small amount of jaggery is added; the mixture is strained and is ready to be used orally twice or thrice a day (Rana et al., 2020).

The whole plant is locally used in Azad Jammu and Kashmir to treat jaundice, constipation (decoction of whole plant), thirst problems, stomach and other liver disorders (Mehmood et al., 2018). In Azad Kashmir, the leaves of O. *digyna* are used to treat scurvy. The stem, root and leaves are cooked and used orally to treat dysentery (Shaheen et al., 2012). The whole plant decoction is used twice or thrice per day to treat indigestion in the Ladakh region (Rinchen and Pant, 2014). The 'Sowa-rigpa' system of traditional healthcare is under practice in Western Ladakh region of India since immemorial timeframe. This traditional practice is now declining due to lack of interest by youngsters of the local community. This system utilizes the leaves and shoot as local remedy for improving digestion; as appetizer, and treatment of gastritis (Angmo et al., 2012). The flowers and leaves are part of the traditional medicines in deosai plateau of Gilgit-Baltistan, Pakistan. The fresh flowers are harvested during spring season, dried and used with green tea (Hussain et al., 2011; Khan et al., 2018). In Chilim Deosi

(Northern Gilgit-Baltistan), the *O. digyna* flowers and leaves are mixed with honey and used one teaspoonful twice a day for children as tonic. The plant is used to treat gastritis and improve appetite (Khan, 2014). The aerial parts of *O. digyna* are used as Stomachic and anti-flatulent. The plant is also reported for its use as fodder in the Lakki Marwat district of Pakistan (Ullah et al., 2014).

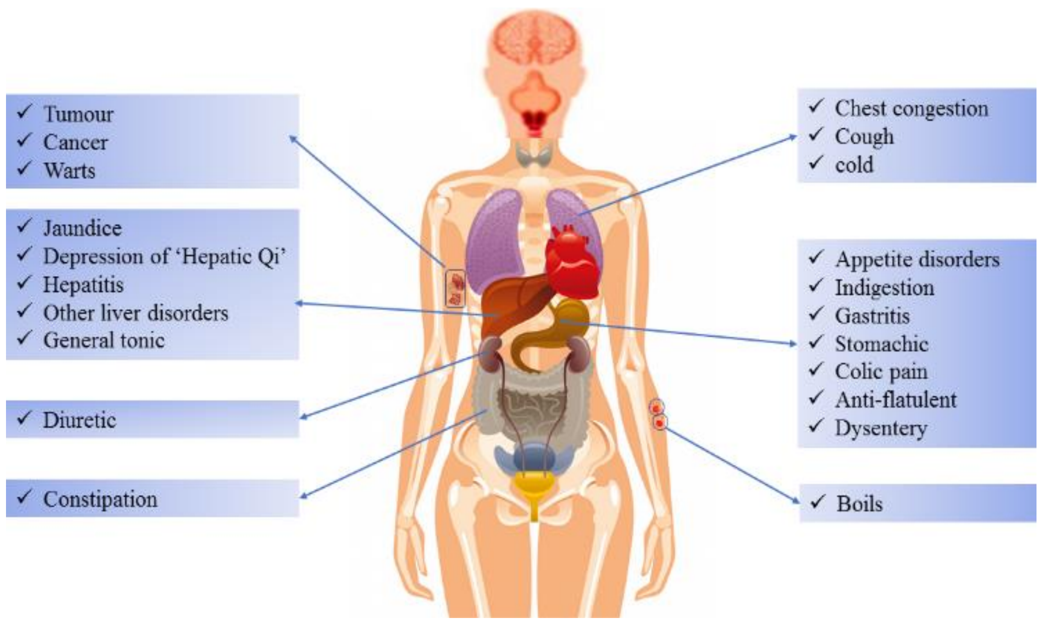

Figure 5: Ethnopharmacology of *Oxyria digyna*.

4. **Nutritious components**

The consumption of *O. digyna* in different geographical locations in raw and cooked form provides proof for its nutritious value. However, this use requires to be evidence based. To date, only a single study explored the functional constituents of this plant. Ascorbic acid and carotene are one of those biomolecules which are responsible for its nutritional candidature (Turner, 1981). Similarly, carbohydrate content has also been revealed, which are the primary source of energy. *Russell* revealed the total carbohydrates such as starch and total sugars found in high levels both in beginning and end of the growing season. Up to 40 % of the alcohol-insoluble material was found. At midsummer, the general carbohydrate level of the plant was considerably lower (Russell, 1948).

5. **Phytochemistry**

5.1 Total phenolic content

The presence of phenolic compounds in this plant was determined with Folin-Ciocalteau reagent (Singleton and Rossi, 1965). Briefly, the Oxyria extract of aerial parts (1.0 g/200ml of 70% ethanol; 150 µl) was mixed with Folin-Ciocalteau reagent (750 µl) and sodium carbonate (600 µl, 7.5%). The reaction mixture was incubated at 40°C for 30 min and the absorption was measured at 760 nm. The total phenolic content of the extract was expressed as gallic acid equivalent (mg/g extract). The total phenolic content of *O. digyna* was 613.0 ± 1.0 mg/g of extract, determined as gallic acid equivalent (Orhan et al., 2009).

5.2. isolated compounds

The three new compounds isolated from the whole plant of *O. digyna* were Oxyria flavonol; 5, 7, 3'-trihydroxy-4-methoxyflavanone-7-O-(2''-O-beta -D-glucopyranosyl)-alpha -L-rhamnopyranoside; and 5, 7, 2', 3', 4'-pentahydroxyflavone-8-C-glucopyranoside based on spectral data. Five known compounds isolated were identified as Vitexin, Orientin, Hesperidin, Quercetin-3-O-beta-D-glucopyranoside and Stigmasterol (Figure 2**:** Geographical distribution of *Oxyria digyna* in various regions of world **6**) (Zhou et al., 2002).

5.2.1 Vitexin

Vitexin is also known as Apigenin-8-C-glucoside and 5, 7, 4-trihydroxyflavone-8-glucoside. It is a C-glycosylated flavone found in various medicinal plants including moss *Tortula muralis, Raphanus sativus,* mung bean, *Pennisetum millet*, *Crataegus* spp., *Cajanuscajan* (Basile et al., 2003; Cao et al., 2011; Edwards et al., 2012; Fu et al., 2007; Fu et al., 2008; Gaitan et al., 1989). Vitexin affect various organ systems in the human body. It possess several pharmacological effects;

briefly, antiviral (Krcatović et al., 2008; Li et al., 2002), antibacterial , antioxidant (An et al., 2012; Borghi et al., 2013; Kim et al., 2005), anti-inflammatory (Dong et al., 2011; Rosa et al., 2016), anti-hypersensitive activity in ovalbumin induced allergic asthma (Venturini et al., 2018), cardio-protection after ischaemic injury (Che et al., 2016; Dong et al., 2008; Dong et al., 2013; Dong et al., 2011), antinociceptive (Gorzalczany et al., 2011; Özkay and Can, 2013; Zhu et al., 2016), antithyroid (Gaitan et al., 1995), anti-cancer (An et al., 2015; Choi et al., 2006; Yang et al., 2013), neuroprotection in hypoxia-ischaemic injury (Min et al., 2015), neuroprotection after scopolamine-induced memory impairment and blocking NMDA receptors (Abbasi et al., 2013; Yang et al., 2014), CYP3A1 enzyme inhibition and CYP2C11 short term induction, then inhibition (Wang et al., 2015), MPTP-induced Parkinson's disease (Hu et al., 2018), Alzheimer's disease (Choi et al., 2014), anticonvulsant (Abbasi et al., 2012), antidepressant (Can et al., 2013), antihypertensive (Je et al., 2014), antispasmodic (Gilani et al., 2006; Ragone et al., 2007) and Liver diseases (Duan et al., 2020; Inamdar et al., 2019).

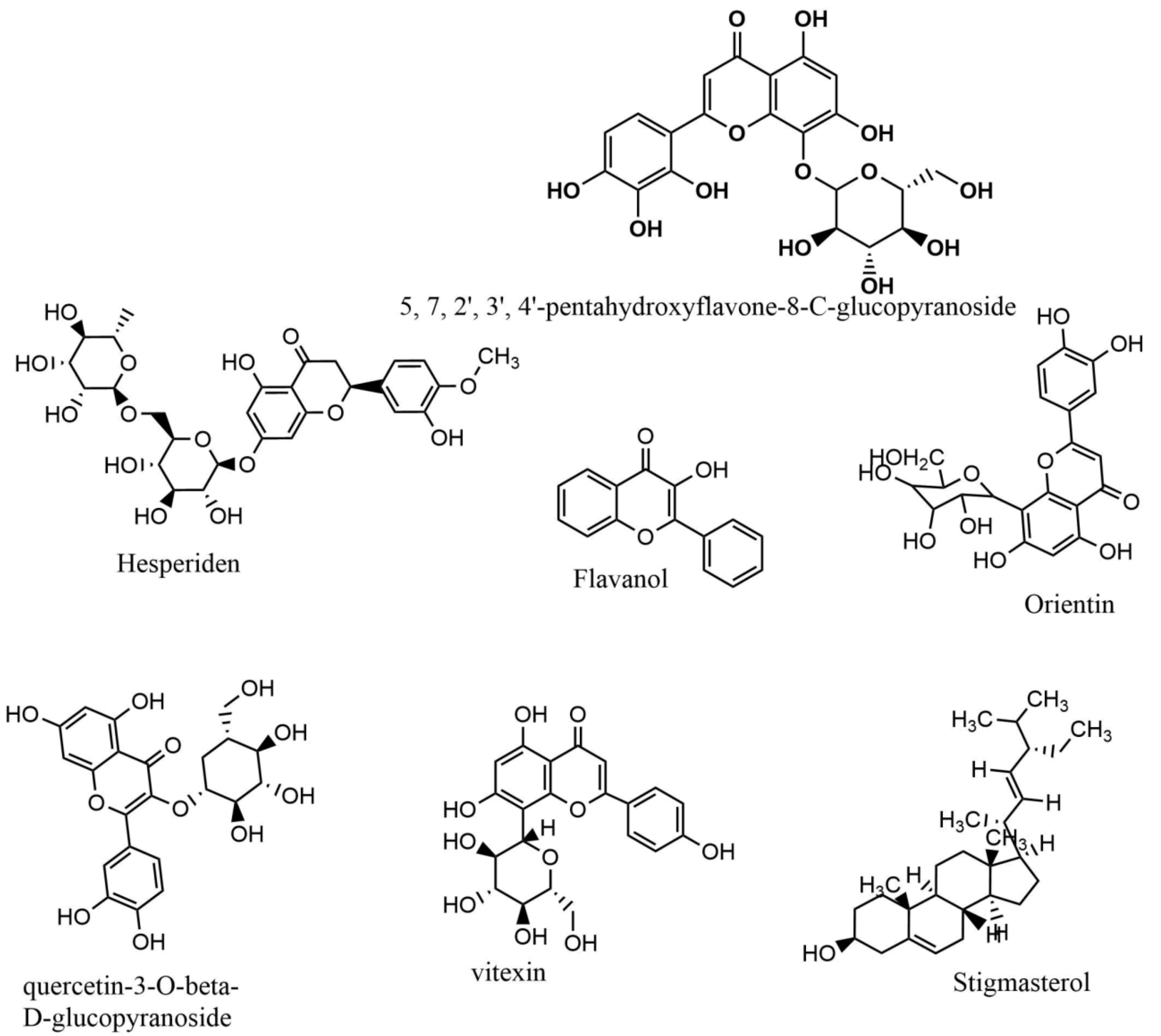

Figure 6: Isolated compounds from Oxyria digyna.

Ilkay orhan et al. isolated it from *O. digyna* for the first time. LC-DAD-MS analysis was performed using high pressure liquid chromatograph (HPLC) coupled to quadrupole mass spectrometer (multimode ionization interface). LC-MS 1 model nitrogen generator was employed for generating Nitrogen drying gas. The parameters for chromatographic separations were Eclipse XDB-C18 column (15 cm x 4.6 mm, 5 µm), mobile phase (gradient elution with acetonitrile and 40 mM formic acid), flow rate (1.0 ml/min), injection volume (10 µl) and detection (254 nm and 330 nm). The calculations of quantitative analysis were performed with external standardization by measurement of peak areas (Orhan et al., 2009). The positive-ion mass spectrum of vitexin was recorded in the total-ion monitoring mode utilizing various fragment or potentials to establish the fragmentation pattern. This spectrum consisted of the protonated molecular ion $[M + H]^+$ at m/z 433 for vitexin. The ethanolic extract of O. *digyna* possess a flavone glycoside, vitexin (Orhan et al., 2009).

5.2.2. Orientin

Orientin is a flavonoid found in various plant species like *Spirodel apolyrhiza* (Kim et al., 2010), *Ocimum sanctum* (Uma Devi et al., 2000) and *Trollius chinensis* Bunge (Li et al., 2002). Some of its pharmacological effects are: Cardio-protection after ischemic injury (Fu et al., 2006), inhibit vascular inflammation (Lee et al., 2014), antithrombotic and antiplatelet (Lee and Bae, 2015), antioxidant(An et al., 2012), antidepressant (Liu et al., 2015), neuroprotective effects (Wang et al., 2017), antinociceptive (Da Silva et al., 2010), anti-Alzheimer's disease (Zhong et al., 2019) and mast cell stabilisation (Dhakal et al., 2020).

5.2.3. Hesperidin

Hesperidin is a well-known flavanone glycoside obtained from citrus fruits including other species from families, Lamiaceae and Betulaceae (Meng et al., 2020). it was isolated in 1828, Some of the plant species having this important phytoconstituent are *Citrus trifoliate* (Abd El Kawy et al., 2020), *Eriocephalus africanus* (Magura et al., 2020), *Citrus sinensis* and *Citrus limon* (Meneguzzo et al., 2020). Hesperidin modify various diseases and have found its potential role in the therapeutics as anticancer (Aggarwal et al., 2020), antidiabetic (Rehman et al., 2020), wound healing (Bagher et al., 2020), metabolic syndrome (Guirro et al., 2020).

5.2.4. Quercetin-3-O-β-D-glucopyranoside

Quercetin is an extensively studied flavonoid with promising pharmacological effects. It is isolated from several species, including *Guierasene galensis* (Parvez et al., 2020), *Lens culinaris* Medik (Rolnik et al., 2020), *Bixa orellana* (de Moura et al., 2020) and *Cleome droserifolia* (Ahmed Youness et al., 2020). The pharmacological effects are exhibited both by the aglycone part as well as by the glycosidic form i.e. neuroprotection (Khan et al., 2020a), anticancer (Ezzati et al., 2020), cardio-protection (Ferenczyova et al., 2020), antiviral (Lopes et al., 2020), allergic conjunctivitis (Ding et al., 2020), anti-Alzheimer (Zhang et al., 2020b), cytoprotective effect (Zhang et al., 2020a), antioxidant (Kumar et al., 2020).

5.2.5. Ascorbic acid

Ascorbic acid is a water-soluble vitamin producing important physiological roles inside human body. O. *digyna* is a rich source of vitamin C in raw form (36 mg/100g) as well as in cooked form (Geraci and Smith, 1979). This implies its use in scurvy, vascular pathologies including thrombotic events, cardio-protection, oxidative stress; wound healing (Chang et al., 2020; Deirawan et al., 2020; He et al., 2020; Kim et al., 2020).

5.2.6. Stigmasterol

Stigmasterol is a monohydroxy alcohol found in various plant species like *Roscoea purpurea*, *Zeamays*, *Lonchocarpus sericeus* Poir., *Adhatoda vasica* Nees (Bag and Barai, 2020; Lifsey et al., 2020; Nandhini and Ilango, 2020; Udo et al., 2020). The pharmacological effect of this phytosterol is highlighted by its role in transintestinal cholesterol excretion, arthritis, cerebral ischemia / reperfusion injury, adjunct in cancer chemotherapy and many more (Khan et al., 2020b; Liang et al., 2020; Liao et al., 2020; Lifsey et al., 2020).

6. Pharmacological Effects

6.1. Free radical scavenging

The free radical scavenging activity was determined with 2, 2-diphenyl-2-picrylhydrazyl (DPPH). Ethanol (75%) was used as solvent and activity was determined at different concentrations of 0.25, 0.5, 1.0, and 2.0 mg/ml as prescribed by M. S. Blois (Blois, 1958). Each solution was mixed with DPPH solution (1.5×10^{-4} M). Remaining amount of DPPH was shown by a decrease in absorption and measured at 520 nm using UV-visible spectrophotometer. Gallic acid and butylated hydroxy anisole (BHA) were employed as reference standard and percent inhibition activity was calculated at each concentration. The ethanolic extract of *O. digyna* exhibited antioxidant effect of 10.8 ± 0.4, 16.2 ± 0.4 and 36.7 ± 2.2 (% inhibition ± standard deviation) at 0.5, 1.0, and 2.0 mg/ml concentration in comparison to the standards, gallic acid (93.2 ± 0.0) and BHA (82.9 ± 0.7). No activity was observed at 0.2 mg/ml concentration. The ethanolic extract of *O. digyna* exhibited very low (< 50%) antioxidant effect (Orhan et al., 2009).

6.2. Ferric reducing antioxidant power assay

The iron-reducing power of *O. digyna* was tested using 1 ml of the extract at various concentrations (0.5, 1.0, and 2.0 mg/ml). Gallic acid and BHA were used as positive control. The assay was commenced by adding 2.5 ml of phosphate buffer (0.1 M; pH 6.6) and 2.5 ml potassium ferricyanide (1%; w/v) with the test solutions. The mixture was then incubated at 50°C for 20 min. 2.5 ml of trichloroacetic (10%) was added and the mixture was agitated vigorously. A solution of 2.5 ml was obtained from this mixture and added with 2.5 ml of distilled water and 0.5 ml of $FeCl_3$ (0.1%; w/v). After a period of 30 min incubation, absorbance was read at 700 nm. The analysis was performed in triplicates according to Oyaizu *et al* (Oyaizu, 1986). The absorbance ± SD at 700 nm were recorded as 0.170 ± 0.1, 0.335 ± 0.1 and 0.698 ± 0.1 at 0.5, 1.0 and 2.0 mg/ml, respectively. The increased absorbance of the reaction mixture signifies the increased reducing power of that respective solution (Orhan et al., 2009). Similarly, in another study, *Paudel* et al (2014) reported an IC_{50} value of >20 μg/mL for DPPH radical scavenging activity (Paudel et al., 2014).

6.3. Antiproliferative activity

The chloroform extract of *O. digyna* whole plant exhibited considerable antiproliferative activity against various cancer cells at 30 μg/ml. The percent growth inhibition reported for HeLa (cervix epithelial adenocarcinoma), MCF7 (breast epithelial adenocarcinoma) and A431 (skin epidermoid carcinoma) cancer cells was 40.65 ± 1.88, 27.21 ± 2.29 and 37.56 ± 1.30, respectively (Lajter et al., 2013).

6.4. Advanced glycation end products inhibition

The inhibitory activity of *O. digyna* stem and leaves ethanolic extract on advanced glycation end products exhibited an IC_{50} value of 7.61μg/mL compared to aminoguanidine (IC_{50} 77.04 μg/ml). Advanced glycation end products are thought to play a role in the progression of diabetic complications (Kim et al., 2013). Progression of protein glycation inside human body promote diabetes complications. This inhibition of protein glycation is a key strategy in preventing diabetic abnormalities (Anis and Sreerama, 2020).

6.5. Xanthine oxidase inhibition

The xanthine oxidase inhibitory potential of *O. digyna* was studied *in vitro* by Vasas *et al* (2015). The whole plant chloroform and methanolic extract (fractionated) exhibited xanthine oxidase inhibition 36.01 ± 8.08 and 56.61 ± 4.06 (% ± SD), respectively, at 400 μg/ml (Orbán-Gyapai et al., 2015). This activity pave the way of this plant as antigout, because xanthine oxidase inhibition leads to reduced production of uric acid (Hyun et al., 2013).

7. Future prospect; Industrial application as Nutraceutical

As discussed above, the very little explored herb, *Oxyria digyna* is a good source of nutritional as well as functional pharmacologic biomolecules. This can serve as nutraceutical product finding a place in the health and financial arena. The flavonoids vitexin, orientin, hesperidin, quercetin-3-O-β-D-glucopyranoside and stigmasterol (phytosterol) have numerous pharmacologic activities, effecting or modifying many organ systems of human body. Combined, these pharmacologic activities may have a synergistic effect, if in a single product. These govern the use of this plant as tonic to improve general health as well as in alleviating pathologies, hence providing a substitute for synthetic sources of vitamins and other products.

8. Conclusions

Only ~5,000 plants have been thus far investigated for medicinal use, queuing 25000 plant species in line. The herbal medicine industry has a growth rate of 7-15% annually. World Health Organization (WHO) recommends plants as major source of alternative medicines in developing countries. The world trade of plant-oriented medicines is growing, creating newer opportunities for developing countries to participate in the herbal drug industry by a sustainable utilization of local medicinal flora creating additional value (Mehmood et al., 2018). In summary, *O. digyna* has important characteristics and properties, such as ethnobotanical, pharmacological, and phytochemical. To date, a scant number of compounds have been isolated from *O. digyna*. This is the first review of the scientific literature on *O. digyna*. The chemical constituents present in this herb include flavonoids, micronutrients, and glycoside derivatives. *O. digyna* affords a potential source of bioactive compounds and nutrients, warranting it's in nutraceuticals, pharmaceuticals and health restoring products.

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References

Abbasi, E., Nassiri-Asl, M., Sheikhi, M., Shafiee, M., 2013. Effects of vitexin on scopolamine-induced memory impairment in rats. Chinese Journal of Physiology 56,184-193.

Abbasi, E., Nassiri-Asl, M., Shafeei, M., Sheikhi, M., 2012. Neuroprotective effects of vitexin, a flavonoid, on pentylenetetrazole-induced seizure in rats. Chemical Biology & Drug Design 80, 274-278.

Abd El Kawy, M.A., Michel, C.G., Kirollos, F.N., El Kerdawy, A.M., Sedeek, M., 2020. In vitro MAO-B Inhibitory Effects of Citrus trifoliata L. Fruits Extract, Self-Nano-Emulsifying Drug Delivery System and Isolated Hesperidin: Enzyme Assay and Molecular Docking Study. Egyptian Journal of Chemistry 63, 897-906.

Aggarwal, V., Tuli, H.S., Thakral, F., Singhal, P., Aggarwal, D., Srivastava, S., Pandey, A., Sak, K., Varol, M., Khan, M.A., 2020. Molecular mechanisms of action of hesperidin in cancer: Recent trends and advancements. Experimental Biology and Medicine 245, 486-497.

Ahmed Youness, R., Amr Assal, R., Mohamed Ezzat, S., Zakaria Gad, M., Abdel Motaal, A., 2020. A methoxylated quercetin glycoside harnesses HCC tumor progression in a TP53/miR-15/miR-16 dependent manner. Natural Product Research 34, 1475-1480.

An, F., Wang, S., Tian, Q., Zhu, D., 2015. Effects of orientin and vitexin from Trollius chinensis on the growth and apoptosis of esophageal cancer EC-109 cells. Oncology letters 10, 2627-2633.

An, F., Yang, G., Tian, J., Wang, S., 2012. Antioxidant effects of the orientin and vitexin in Trollius chinensis Bunge in D-galactose-aged mice. Neural Regeneration Research 7, 2565-2575.

Anderson, J.P., 1939. Plants used by the Eskimo of the northern Bering Sea and arctic regions of Alaska. American Journal of Botany, 714-716.

Andersson, G., 1944. Gas change and frost hardening studies in winter cereals, p 163.

Angmo, K., Adhikari, B.S., Rawat, G.S., 2012. Changing aspects of traditional healthcare system in Western Ladakh, India. Journal of ethnopharmacology 143, 621-630.

Anis, M.A., Sreerama, Y.N., 2020. Inhibition of protein glycoxidation and advanced glycation end-product formation by barnyard millet (Echinochloa frumentacea) phenolics. Food Chemistry 315, 126265.

Asif, M., Iqbal, Z., Alam, J., Majid, A., Ijaz, F., Ali, N., Rahman, I.U., Hussain, S., Khan, A., Qadir, G., 2020. Floristic inventory and biological spectra of Balakot, District Mansehra, Pakistan. Acta Ecologica Sinica 40, 197-203.

Ayaz, M., Ahmad, I., Sadiq, A., Ullah, F., Ovais, M., Khalil, A.T., Devkota, H.P., 2020. Persicaria hydropiper (L.) Delarbre: A review on traditional uses, bioactive chemical constituents and pharmacological and toxicological activities. Journal of Ethnopharmacology 251, 112516.

Bag, B.G., Barai, A.C., 2020. Self-assembly of naturally occurring stigmasterol in liquids yielding a fibrillar network and gel. RSC Advances 10, 4755-4762.

Bagher, Z., Ehterami, A., Safdel, M.H., Khastar, H., Semiari, H., Asefnejad, A., Davachi, S.M., Mirzaii, M., Salehi, M., 2020. Wound healing with alginate/chitosan hydrogel containing hesperidin in rat model. Journal of Drug Delivery Science and Technology 55, 101379.

Basile, A., Sorbo, S., Lopez-Saez, J.A., Cobianchi, R.C., 2003. Effects of seven pure flavonoids from mosses on germination and growth of Tortula muralis HEDW.(Bryophyta) and Raphanus sativus L.(Magnoliophyta). Phytochemistry 62, 1145-1151.

Blois, M.S., 1958. Antioxidant determinations by the use of a stable free radical. Nature 181, 1199-1200.

Borghi, S.M., Carvalho, T.T., Staurengo-Ferrari, L., Hohmann, M.S., Pinge-Filho, P., Casagrande, R., Verri Jr, W.A., 2013. Vitexin inhibits inflammatory pain in mice by targeting TRPV1, oxidative stress, and cytokines. Journal of Natural Products 76, 1141-1149.

Bruun, H.H., 2019. Dataset on reproductive traits of Scandinavian alpine plants. Data in brief 25, 104149.

Can, Ö.D., Özkay, Ü.D., Üçel, U.İ., 2013. Anti-depressant-like effect of vitexin in BALB/c mice and evidence for the involvement of monoaminergic mechanisms. European journal of pharmacology 699, 250-257.

Cao, D., Li, H., Yi, J., Zhang, J., Che, H., Cao, J., Yang, L., Zhu, C., Jiang, W., 2011. Antioxidant properties of the mung bean flavonoids on alleviating heat stress. PloS one 6, e21071.

Chang, C.-Y., Chen, J.-Y., Wu, M.-H., Hu, M.-L., 2020. Therapeutic treatment with vitamin C reduces focal cerebral ischemia-induced brain infarction in rats by attenuating disruptions of blood brain barrier and cerebral neuronal apoptosis. Free Radical Biology and Medicine.

Che, X., Wang, X., Zhang, J., Peng, C., Zhen, Y., Shao, X., Zhang, G., Dong, L., 2016. Vitexin exerts cardioprotective effect on chronic myocardial ischemia/reperfusion injury in rats via inhibiting myocardial apoptosis and lipid peroxidation. American Journal of Translational Research 8, 3319-3328.

Choi, H.J., Eun, J.S., Kim, B.G., Kim, S.Y., Jeon, H., Soh, Y., 2006. Vitexin, an HIF-1α Inhibitor, Has Anti-metastatic Potential in PC12 Cells. Molecules & Cells (Springer Science & Business Media BV) 22.

Choi, J.S., Islam, M.N., Ali, M.Y., Kim, E.J., Kim, Y.M., Jung, H.A., 2014. Effects of C-glycosylation on anti-diabetic, anti-Alzheimer's disease and anti-inflammatory potential of apigenin. Food and Chemical Toxicology 64, 27-33.

Da Cheng Hao, X.-J.G., Xiao, P.G., 2015. Phytochemical and biological research of Polygoneae medicinal resources. Medicinal Plants, 465.

Da Silva, R.Z., Yunes, R.A., de Souza, M.M., Delle Monache, F., Cechinel-Filho, V., 2010. Antinociceptive properties of conocarpan and orientin obtained from Piper solmsianum C. DC. var. solmsianum (Piperaceae). Journal of Natural Medicines 64, 402-408.

Davis, J.D., Banack, S.A., 2012. Ethnobotany of the Kiluhikturmiut Inuinnait of Kugluktuk, Nunavut, Canada. Ethnobiology Letters 3, 78-90.

de Moura, M.C.L., de Araújo, V.L.L., de Sousa, J.A., 2020. Pharmacokinetic, toxicological and pharmacodynamic analysis of flavonoid quercetin isolated seeds of Bixa orellana l. Research, Society and Development 9, 170932242.

Deirawan, H., Fakhoury, J.W., Zarka, M., Bluth, M.H., Moossavi, M., 2020. Revisiting the pathobiology of scurvy: a review of the literature in the context of a challenging case. International Journal of Dermatology.

Dhakal, H., Lee, S., Choi, J.K., Kwon, T.K., Khang, D., Kim, S.-H., 2020. Inhibitory effects of orientin in mast cell-mediated allergic inflammation. Pharmacological Reports, 1-9.

Ding, Y., Li, C., Zhang, Y., Ma, P., Zhao, T., Che, D., Cao, J., Wang, J., Liu, R., Zhang, T., 2020. Quercetin as a Lyn kinase inhibitor inhibits IgE-mediated allergic conjunctivitis. Food and Chemical Toxicology 135, 110924.

Dong, L.-Y., Chen, Z.-W., Guo, Y., Cheng, X.-P., Shao, X., 2008. Mechanisms of vitexin preconditioning effects on cultured neonatal rat cardiomyocytes with anoxia and reoxygenation. The American journal of Chinese medicine 36, 385-397.

Dong, L.-Y., Li, S., Zhen, Y.-L., Wang, Y.-N., Shao, X., Luo, Z.-G., 2013. Cardioprotection of vitexin on myocardial ischemia/reperfusion injury in rat via regulating inflammatory cytokines and MAPK pathway. The American Journal of Chinese Medicine 41, 1251-1266.

Dong, L., Fan, Y., Shao, X., Chen, Z., 2011. Vitexin protects against myocardial ischemia/reperfusion injury in Langendorff-perfused rat hearts by attenuating inflammatory response and apoptosis. Food and chemical toxicology 49, 3211-3216.

Duan, S., Du, X., Chen, S., Liang, J., Huang, S., Hou, S., Gao, J., Ding, P., 2020. Effect of vitexin on alleviating liver inflammation in a dextran sulfate sodium (DSS)-induced colitis model. Biomedicine & Pharmacotherapy 121, 109683.

Eddudóttir, S.D., Erlendsson, E., Gísladóttir, G., 2020. Landscape change in the Icelandic highland: A long-term record of the impacts of land use, climate and volcanism. Quaternary Science Reviews 240, 106363.

Edwards, J.E., Brown, P.N., Talent, N., Dickinson, T.A., Shipley, P.R., 2012. A review of the chemistry of the genus Crataegus. Phytochemistry 79, 5-26.

Ezzati, M., Yousefi, B., Velaei, K., Safa, A., 2020. A review on anti-cancer properties of Quercetin in breast cancer. Life Sciences, 117463.

Fan, P., Terrier, L., Hay, A.-E., Marston, A., Hostettmann, K., 2010. Antioxidant and enzyme inhibition activities and chemical profiles of Polygonum sachalinensis F. Schmidt ex Maxim (Polygonaceae). Fitoterapia 81, 124-131.

Ferenczyova, K., Kalocayova, B., Bartekova, M., 2020. Potential Implications of Quercetin and its Derivatives in Cardioprotection. International journal of molecular sciences 21, 1585.

Fu, X.-C., Wang, M.-W., Li, S.-P., Wang, H.-L., 2006. Anti-apoptotic effect and the mechanism of orientin on ischaemic/reperfused myocardium. Journal of Asian natural products research 8, 265-272.

Fu, Y., Zu, Y., Liu, W., Hou, C., Chen, L., Li, S., Shi, X., Tong, M., 2007. Preparative separation of vitexin and isovitexin from pigeonpea extracts with macroporous resins. Journal of Chromatography A 1139, 206-213.

Fu, Y., Zu, Y., Liu, W., Zhang, L., Tong, M., Efferth, T., Kong, Y., Hou, C., Chen, L., 2008. Determination of vitexin and isovitexin in pigeonpea using ultrasonic extraction followed by LC-MS. Journal of separation science 31, 268-275.

Gaitan, E., Cooksey, R.C., Legan, J., Lindsay, R.H., 1995. Antithyroid effects in vivo and in vitro of vitexin: a C-glucosylflavone in millet. The Journal of Clinical Endocrinology & Metabolism 80, 1144-1147.

Gaitan, E., Lindsay, R.H., Reichert, R.D., INGBAR, S.H., Cooksey, R.C., Legan, J., MEYDRECH, E.F., HILL, J., KUBOTA, K., 1989. Antithyroid and goitrogenic effects of millet: role of C-glycosylflavones. The Journal of Clinical Endocrinology & Metabolism 68, 707-714.

Gentili, R., Armiraglio, S., Rossi, G., Sgorbati, S., Baroni, C., 2010. Floristic patterns, ecological gradients and biodiversity in the composite channels (Central Alps, Italy). Flora-Morphology,

Distribution, Functional Ecology of Plants 205, 388-398.
Gentili, R., Baroni, C., Panigada, C., Rossini, M., Tagliabue, G., Armiraglio, S., Citterio, S., Carton, A., Salvatore, M.C., 2020. Glacier shrinkage and slope processes create habitat at high elevation and microrefugia across treeline for alpine plants during warm stages. Catena 193, 104626.
Geraci, J.R., Smith, T.G., 1979. Vitamin C in the diet of Inuit hunters from Holman, Northwest Territories. Arctic, 135-139.
Gilani, A.H., Khan, A.u., Ghayur, M.N., Ali, S.F., Herzig, J.W., 2006. Antispasmodic effects of Rooibos tea (Aspalathus linearis) is mediated predominantly through K+-channel activation. Basic & clinical pharmacology & toxicology 99, 365-373.
Gjærevoll, O., Rønning, O.I., 1999. Flowers of svalbard. Tapir Academic Press.
Gorzalczany, S., Marrassini, C., Miño, J., Acevedo, C., Ferraro, G., 2011. Antinociceptive activity of ethanolic extract and isolated compounds of Urtica circularis. Journal of ethnopharmacology 134, 733-738.
Griffin, D., 2001. Contributions to the ethnobotany of the Cup'it Eskimo, Nunivak Island, Alaska. Journal of Ethnobiology 21, 91-132.
Griffin, D., 2009. The ethnobiology of the Central Yup'ik Eskimo, Southwestern Alaska. Alaska Journal of Anthropology 7, 81-100.
Guirro, M., Gual-Grau, A., Gibert-Ramos, A., Alcaide-Hidalgo, J.M., Canela, N., Arola, L., Mayneris-Perxachs, J., 2020. Metabolomics Elucidates Dose-Dependent Molecular Beneficial Effects of Hesperidin Supplementation in Rats Fed an Obesogenic Diet. Antioxidants 9, 79.
Hartwell, J.L., 1970. Plants used against cancer. A survey.[Continued.]. Lloydia 33, 97-194.
He, X.Y., Sun, A., Li, T., Qian, Y.J., Qian, H., Ling, Y.F., Zhang, L.H., Liu, Q.Y., Peng, T., Qian, Z., 2020. Mussel-Inspired Antimicrobial Gelatin/Chitosan Tissue Adhesive Rapidly Activated In Situ by H2O2/Ascorbic Acid for Infected Wound Closure. Carbohydrate Polymers, 116692.
Hu, M., Li, F., Wang, W., 2018. Vitexin protects dopaminergic neurons in MPTP-induced Parkinson's disease through PI3K/Akt signaling pathway. Drug design, development and therapy 12, 565.
Hultén, E., Fries, M., 1986. Atlas of North European vascular plants north of the Tropic of Cancer. Koeltz Scientific.
Hussain, I., Bano, A., Ullah, F., 2011. Traditional drug therapies from various medicinal plants of central karakoram national park, Gilgit-Baltistan Pakistan. Pak J Bot 43, 79-84.
Hyun, S.H., Mun, H.Y., Lee, H.B., Kim, H.-K., Lee, J.-S., 2013. Isolation of yeasts from wild flowers in Gyonggi-do province and Jeju island in Korea and the production of anti-gout xanthine oxidase inhibitor. Microbiology and Biotechnology Letters 41, 383-390.
Inamdar, S., Joshi, A., Malik, S., Boppana, R., Ghaskadbi, S., 2019. Vitexin alleviates non-alcoholic fatty liver disease by activating AMPK in high fat diet fed mice. Biochemical and biophysical research communications 519, 106-112.
Je, H.G., Hong, S.M., Je, H.D., Sohn, U.D., Choi, Y.-S., Seo, S.-Y., Min, Y.S., Chung, S.J., Shin, Y.K., Lee, T.J., 2014. The inhibitory effect of vitexin on the agonist-induced regulation of vascular contractility. Die Pharmazie-An International Journal of Pharmaceutical Sciences 69, 224-228.
Khan, H., Ullah, H., Aschner, M., Cheang, W.S., Akkol, E.K., 2020a. Neuroprotective effects of quercetin in Alzheimer's disease. Biomolecules 10, 59.
Khan, K.U., 2014. Ethnobotanical and ethnopharmacognostic exploration of folk medicines of Deosai Plateau. PhD thesis. Hazara University, Hazara, Pakistan.
Khan, K.U., Shah, M., Ahmad, H., Khan, S.M., Rahman, I.U., Iqbal, Z., Khan, R., Abd_Allah, E.F., Alqarawi, A.A., Hashem, A., 2018. Exploration and local utilization of medicinal vegetation naturally grown in the Deusai plateau of Gilgit, Pakistan. Saudi journal of biological sciences 25, 326-331.
Khan, M.A., Sarwar, A.H.M.G., Rahat, R., Ahmed, R.S., Umar, S., 2020b. Stigmasterol protects rats from collagen induced arthritis by inhibiting proinflammatory cytokines. International Immunopharmacology 85, 106642.
Kienast, F., Siegert, C., Dereviagin, A., Mai, D.H., 2001. Climatic implications of Late Quaternary plant macrofossil assemblages from the Taymyr Peninsula, Siberia. Global and Planetary Change 31, 265-281.
Kim, J., Arnaout, L., Remick, D., 2020. Hydrocortisone, ascorbic acid, and thiamine (HAT) therapy decreases oxidative stress, improves cardiovascular function, and improves survival in murine sepsis. Shock 53, 460-467.
Kim, J., Lee, I., Seo, J., Jung, M., Kim, Y., Yim, N., Bae, K., 2010. Vitexin, orientin and other flavonoids from Spirodela polyrhiza inhibit adipogenesis in 3T3-L1 cells. Phytotherapy Research 24, 1543-1548.
Kim, J.H., Lee, B.C., Kim, J.H., Sim, G.S., Lee, D.H., Lee, K.E., Yun, Y.P., Pyo, H.B., 2005. The isolation and antioxidative effects of vitexin fromAcer palmatum. Archives of pharmacal research 28, 195.
Kim, Y.S., Lee, Y.M., Kim, J.H., Kim, J.S., 2013. Screening of Herbal Medicines from China with Inhibitory Activity on Advanced Glycation End

Products (AGEs) Formation (X). Korean Journal of Pharmacognosy 44, 305-311.
Krcatović, E., Rusak, G., Bezić, N., Krajačić, M., 2008. Inhibition of tobacco mosaic virus infection by quercetin and vitexin. Acta Virolog 52, 119-124.
Kuhnleini, H.V., Soueida, R., 1992. Use and nutrient composition of traditional Baffin Inuit foods. Journal of Food Composition and Analysis 5, 112-126.
Kumar, H., Bhardwaj, K., Kuča, K., Kalia, A., Nepovimova, E., Verma, R., Kumar, D., 2020. Flower-Based Green Synthesis of Metallic Nanoparticles: Applications beyond Fragrance. Nanomaterials 10, 766.
Lajter, I., Zupkó, I., Molnár, J., Jakab, G., Balogh, L., Vasas, A., Hohmann, J., 2013. Antiproliferative activity of Polygonaceae species from the Carpathian Basin against human cancer cell lines. Phytotherapy Research 27, 77-85.
Lee, W., Bae, J.-S., 2015. Antithrombotic and antiplatelet activities of orientin in vitro and in vivo. Journal of Functional Foods 17, 388-398.
Lee, W., Ku, S.-K., Bae, J.-S., 2014. Vascular barrier protective effects of orientin and isoorientin in LPS-induced inflammation in vitro and in vivo. Vascular Pharmacology 62, 3-14.
Li, Y.-L., Ma, S.-C., Yang, Y.-T., Ye, S.-M., But, P.P.-H., 2002. Antiviral activities of flavonoids and organic acid from Trollius chinensis Bunge. Journal of Ethnopharmacology 79, 365-368.
Liang, Q., Yang, J., He, J., Chen, X., Zhang, H., Jia, M., Liu, K., Jia, C., Pan, Y., Wei, J., 2020. Stigmasterol alleviates cerebral ischemia/reperfusion injury by attenuating inflammation and improving antioxidant defenses in rats. Bioscience Reports 40.
Liao, H., Bai, M., Zhu, D., Chen, H., Yan, S., Yu, J., Zhu, H., Zheng, W., Fan, G., 2020. Stigmasterol Sensitizes Endometrial Cancer Cells to Chemotherapy By repressing Nrf2 Signal Pathway.
Lifsey, H.C., Kaur, R., Thompson, B.H., Bennett, L., Temel, R.E., Graf, G.A., 2020. Stigmasterol stimulates transintestinal cholesterol excretion independent of liver X receptor activation in the small intestine. The Journal of nutritional biochemistry 76, 108263.
Liu, Y., Lan, N., Ren, J., Wu, Y., Wang, S.t., Huang, X.F., Yu, Y., 2015. Orientin improves depression-like behavior and BDNF in chronic stressed mice. Molecular nutrition & food research 59, 1130-1142.
Lopes, B.R.P., da Costa, M.F., Ribeiro, A.G., da Silva, T.F., Lima, C.S., Caruso, I.P., de Araujo, G.C., Kubo, L.H., Iacovelli, F., Falconi, M., 2020. Quercetin pentaacetate inhibits in vitro human respiratory syncytial virus adhesion. Virus research 276, 197805.
Magura, J., Moodley, R., Maduray, K., Mackraj, I., 2020. Phytochemical constituents and in vitro anticancer screening of isolated compounds from Eriocephalus africanus. Natural Product Research, 1-4.
Mehmood, S.I., Majeed, S., Jannat, Z., Habib, T., 2018. Imaging based ethno botanical studies of district Poonch, Azad Jammu and Kashmir. International journal of herbal medicine 6, 81-91.
Meneguzzo, F., Ciriminna, R., Zabini, F., Pagliaro, M., 2020. Review of Evidence Available on Hesperidin-Rich Products as Potential Tools against COVID-19 and Hydrodynamic Cavitation-Based Extraction as a Method of Increasing Their Production. Processes 8, 549.
Meng, X., Wei, M., Wang, D., Qu, X., Zhang, K., Zhang, N., Li, X., 2020. The protective effect of hesperidin against renal ischemia-reperfusion injury involves the TLR-4/NF-κB/iNOS pathway in rats. Physiology International, 1-10.
Min, J.-W., Hu, J.-J., He, M., Sanchez, R.M., Huang, W.-X., Liu, Y.-Q., Bsoul, N.B., Han, S., Yin, J., Liu, W.-H., 2015. Vitexin reduces hypoxia–ischemia neonatal brain injury by the inhibition of HIF-1alpha in a rat pup model. Neuropharmacology 99, 38-50.
Mostafa, H., Elbakry, A., Eman, A.A., 2011. Evaluation of antibacterial and antioxidant activities of different plant parts of Rumex vesicarius L.(Polygonaceae). Int. J. Pharm. Pharm. Sci 3, 109-118.
Nandhini, S., Ilango, K., 2020. Simultaneous Quantification of Lupeol, Stigmasterol and β-Sitosterol in Extracts of Adhatoda vasica Nees Leaves and its Marketed Formulations by a Validated RP-HPLC Method. Pharmacognosy Journal 12.
Orbán-Gyapai, O., Lajter, I., Hohmann, J., Jakab, G., Vasas, A., 2015. Xanthine oxidase inhibitory activity of extracts prepared from Polygonaceae species. Phytotherapy Research 29, 459-465.
Orhan, I., Kartal, M., Abu-Asaker, M., Şenol, F.S., Yilmaz, G., Şener, B., 2009. Free radical scavenging properties and phenolic characterization of some edible plants. Food Chemistry 114, 276-281.
Oyaizu, M., 1986. Studies on products of browning reaction: antioxidative activity of products of browning reaction. Jpn. J. Nutr 44, 307-315.
Özkay, Ü.D., Can, Ö.D., 2013. Anti-nociceptive effect of vitexin mediated by the opioid system in mice. Pharmacology Biochemistry and Behavior 109, 23-30.
Parvez, M.K., Al-Dosari, M.S., Arbab, A.H., Al-Rehaily, A.J., Abdelwahid, M.A., 2020. Bioassay-guided isolation of anti-hepatitis B virus flavonoid myricetin-3-O-rhamnoside along with quercetin

from Guiera senegalensis leaves. Saudi Pharmaceutical Journal.
Paudel, B., Bhattarai, H.D., Kim, I.C., Lee, H., Sofronov, R., Ivanova, L., Poryadina, L., Yim, J.H., 2014. Estimation of antioxidant, antimicrobial activity and brine shrimp toxicity of plants collected from Oymyakon region of the Republic of Sakha (Yakutia), Russia. Biological research 47, 10.
Pete, M., Rasmussen, M., A Guide to the Ethnobotany of the Yukon-Kuskokwim Region.
Ragone, M.I., Sella, M., Conforti, P., Volonté, M.G., Consolini, A.E., 2007. The spasmolytic effect of Aloysia citriodora, Palau (South American cedrón) is partially due to its vitexin but not isovitexin on rat duodenums. Journal of Ethnopharmacology 113, 258-266.
Rana, D., Bhatt, A., Lal, B., Parkash, O., Kumar, A., Uniyal, S.K., 2020. Use of medicinal plants for treating different ailments by the indigenous people of Churah subdivision of district Chamba, Himachal Pradesh, India. Environment, Development and Sustainability, 1-80.
Rawat, B., Sekar, K.C., Gairola, S., 2013. Ethnomedicinal plants of Sunderdhunga Valley, western Himalaya, India—Traditional use, current status and future scenario. Indian For 139, 61-68.
Rehman, K., Munawar, S.M., Akash, M.S.H., Buabeid, M.A., Chohan, T.A., Tariq, M., Jabeen, K., Arafa, E.-S.A., 2020. Hesperidin improves insulin resistance via down-regulation of inflammatory responses: Biochemical analysis and in silico validation. PloS one 15, e0227637.
Rinchen, T., Pant, S., 2014. Ethnopharmacological uses of plants among inhabitants surrounding Suru and Zanskar valleys of cold desert, Ladakh. Int J Pharm Biol Sci 5, 486-494.
Rolnik, A., Żuchowski, J., Stochmal, A., Olas, B., 2020. Quercetin and kaempferol derivatives isolated from aerial parts of Lens culinaris Medik as modulators of blood platelet functions. Industrial Crops and Products 152, 112536.
Rosa, S.I.G., Rios-Santos, F., Balogun, S.O., de Oliveira Martins, D.T., 2016. Vitexin reduces neutrophil migration to inflammatory focus by down-regulating pro-inflammatory mediators via inhibition of p38, ERK1/2 and JNK pathway. Phytomedicine 23, 9-17.
Russell, R.S., 1948. The effect of arctic and high mountain climates on the carbohydrate content of Oxyria digyna. Journal of Ecology 36, 91-95.
Ryabushkina, N., Gemedjieva, N., Kobaisy, M., Cantrell, C.L., 2008. Brief review of Kazakhstan flora and use of its wild species. Asian and Australasian Journal of Plant Science and Biotechnology 2, 64-71.
Schwienbacher, E., Navarro-Cano, J.A., Neuner, G., Erschbamer, B., 2011. Seed dormancy in alpine species. Flora-Morphology, Distribution, Functional Ecology of Plants 206, 845-856.
Shaheen, H., Shinwari, Z.K., Qureshi, R.A., Ullah, Z., 2012. Indigenous plant resources and their utilization practices in village populations of Kashmir Himalayas. Pak J Bot 44, 739-745.
Singh, B., Sultan, P., Hassan, Q.P., Gairola, S., Bedi, Y.S., 2016. Ethnobotany, traditional knowledge, and diversity of wild edible plants and fungi: a case study in the Bandipora District of Kashmir Himalaya, India. Journal of Herbs, Spices & Medicinal Plants 22, 247-278.
Singh, P., Negi, J.S., Rawat, M.S., nee Pant, G.J., 2010. Quantification of mineral elements of Rheum emodi Wallr.(Polygonaceae). Biological trace element research 138, 293-299.
Singleton, V.L., Rossi, J.A., 1965. Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents. American journal of Enology and Viticulture 16, 144-158.
Song, J., Yao, H., Li, Y., Li, X., Lin, Y., Liu, C., Han, J., Xie, C., Chen, S., 2009. Authentication of the family Polygonaceae in Chinese pharmacopoeia by DNA barcoding technique. Journal of Ethnopharmacology 124, 434-439.
Sun, Y., Wang, A., Wan, D., Wang, Q., Liu, J., 2012. Rapid radiation of Rheum (Polygonaceae) and parallel evolution of morphological traits. Molecular Phylogenetics and Evolution 63, 150-158.
Torres-Naranjo, M., Suárez, A., Gilardoni, G., Cartuche, L., Flores, P., Morocho, V., 2016. Chemical constituents of Muehlenbeckia tamnifolia (Kunth) Meisn (Polygonaceae) and its in vitro α-amilase and α-glucosidase inhibitory activities. Molecules 21, 1461.
Turner, N.J., 1981. A gift for the taking: the untapped potential of some food plants of North American Native Peoples. Canadian Journal of Botany 59, 2331-2357.
Udo, U.E., Echeme, J.O., Igwe, O.U., Sunday, T.P., 2020. β-Stigmasterol is present in the stembark of Lonchocarpus sericeus Poir.(Papilionaceae). Journal of Pharmacognosy and Phytochemistry 9, 1750-1755.
Ullah, S., Khan, M.R., Shah, N.A., Shah, S.A., Majid, M., Farooq, M.A., 2014. Ethnomedicinal plant use value in the Lakki Marwat District of Pakistan. Journal of ethnopharmacology 158, 412-422.
Uma Devi, P., Ganasoundari, A., Vrinda, B., Srinivasan, K., Unnikrishnan, M., 2000. Radiation protection by the ocimum flavonoids orientin and vicenin: mechanisms of action. Radiation research 154, 455-460.

Venturini, C.L., Macho, A., Arunachalam, K., de Almeida, D.A.T., Rosa, S.I.G., Pavan, E., Balogun, S.O., Damazo, A.S., de Oliveira Martins, D.T., 2018. Vitexin inhibits inflammation in murine ovalbumin-induced allergic asthma. Biomedicine & Pharmacotherapy 97, 143-151.

Wang, Q., Liu, J., Allen, G.A., Ma, Y., Yue, W., Marr, K.L., Abbott, R.J., 2016. Arctic plant origins and early formation of circumarctic distributions: a case study of the mountain sorrel, Oxyria digyna. New Phytologist 209, 343-353.

Wang, X., An, F., Wang, S., An, Z., Wang, S., 2017. Orientin attenuates cerebral ischemia/reperfusion injury in rat model through the AQP-4 and TLR4/NF-κB/TNF-α signaling pathway. Journal of Stroke and Cerebrovascular Diseases 26, 2199-2214.

Wang, X.s., Hu, X.c., Chen, G.l., Yuan, X., Yang, R.n., Liang, S., Ren, J., Sun, J.c., Kong, G.q., Gao, S.g., 2015. Effects of vitexin on the pharmacokinetics and mRNA expression of CYP isozymes in rats. Phytotherapy Research 29, 366-372.

Yang, L., Yang, Z.-m., Zhang, N., Tian, Z., Liu, S.-b., Zhao, M.-g., 2014. Neuroprotective effects of vitexin by inhibition of NMDA receptors in primary cultures of mouse cerebral cortical neurons. Molecular and cellular biochemistry 386, 251-258.

Yang, S.H., Liao, P.H., Pan, Y.F., Chen, S.L., Chou, S.S., Chou, M.Y., 2013. The novel p53-dependent metastatic and apoptotic pathway induced by vitexin in human oral cancer OC2 cells. Phytotherapy Research 27, 1154-1161.

Zhang, Q., Hu, J., Liu, M., Shi, Y., De Vos, R.C., Ruan, J., 2020a. Stimulated biosynthesis of delphinidin-related anthocyanins in tea shoots reducing the quality of green tea in summer. Journal of the Science of Food and Agriculture 100, 1505-1514.

Zhang, X.-W., Chen, J.-Y., Ouyang, D., Lu, J.-H., 2020b. Quercetin in Animal Models of Alzheimer's Disease: A Systematic Review of Preclinical Studies. International Journal of Molecular Sciences 21, 493.

Zhong, Y., Zheng, Q.-y., Sun, C.-y., Zhang, Z., Han, K., Jia, N., 2019. Orientin Improves Cognition by Enhancing Autophagosome Clearance in an Alzheimer's Mouse Model. Journal of Molecular Neuroscience 69, 246-253.

Zhou, Y., Zhang, G.L., Li, B.G., Chen, Y.Z., 2002. Three new compounds from Oxyria digyna (L.) Hill. ChemInform 33, no-no.

Zhu, Q., Mao, L.-N., Liu, C.-P., Sun, Y.-H., Jiang, B., Zhang, W., Li, J.-X., 2016. Antinociceptive effects of vitexin in a mouse model of postoperative pain. Scientific reports 6, 19266.

Zmudczyńska-Skarbek, K., Balazy, P., 2017. Following the flow of ornithogenic nutrients through the Arctic marine coastal food webs. Journal of Marine Systems 168, 31-37.