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The medical importance of *Iris pallida* – A review

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Abstract

Iris pallid (Family: Iridaceae) was used traditionally asantispasmodic, aperient, aromatic, attenuant, carminative, detoxicant, diuretic, emetic, emmenagogue, expectorant, fixative, laxative, pectoral, purgative and sedative. It contained oils and aromatic constituents, fat, resin, a large quantity of starch, mucilage, phenolics, flavonoids and glucosides. *Iris pallida* possessed many pharmacological effects included anti-inflammatory, antioxidant, anti-aging, anticancer, antiparasitic and antimicrobial activities. The current review will highlight the chemical constituents and pharmacological effects of *Iris pallida*.

Keywords: Constituents; Pharmacology; Inflammatory; Antioxidant; Anti-aging; *Iris pallida*

1. Introduction

Plants generally produce many secondary metabolites which are bio-synthetically derived from primary metabolites and constitute an important source of chemicals which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives. Recent reviews showed that the medicinal plants possessed wide range of biological effects included central nervous, cardiovascular, antioxidant, endocrine and reproductive, gastro-intestinal, respiratory, antidiabetic, antimicrobial, antiparasitic, dermatological, anticancer, anti-inflammatory, antipyretic, analgesic, immunological and many other pharmacological effects[1-15]. *Iris pallid* (Family: Iridaceae) was used traditionally as antispasmodic, aperient, aromatic, attenuant, carminative, detoxicant, diuretic, emetic, emmenagogue, expectorant, fixative, laxative, pectoral, purgative andsedative. It contained oils and aromatic constituents, fat, resin, a large quantity of starch, mucilage, phenolics, flavonoids and glucosides. *Iris pallida* possessed many pharmacological effects included anti-inflammatory, antioxidant, anti-aging, anticancer, antiparasitic and antimicrobial activities. The current review discussed the chemical constituents and pharmacological effects of*Iris pallida.*

2. Plant profile

2.1. Synonyms

Iris australis var. *mandraliscae*, *Iris australis* var. *tinaei*, *Iris fulgida* , *Iris germanica* subsp. *pallida*, *Iris glauca*, *Iris gloriosa* , *Iris hortensis*, *Iris mandraliscae*, *Iris marchesettii*, *Iris moggridgei*, *Iris odoratissima*, *Iris pallida* subsp. *mandraliscae*, *Iris pallida*var. *odoratissima*, *Iris pallida* subsp. *pallida*, *Iris pallida* var. *rosea*, *Iris pallida* subsp. *sicula*, *Iris pallida* subsp. *tinaei*, *Iris pallida ecaerulaea*, *Iris plicata*, *Iris propendens*, *Iris sicula*, *Iris swertii*, *Iris tinaei*, *Iris pallida* subsp. *cengialti*, *Iris pallida* subsp. *illyrica* [16].

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2.2. Taxonomic classification

Kingdom: Plantae;
Subkingdom: Viridiplantae;
Infrakingdom: Streptophyta;
Superdivision: Embryophyta;
Division: Tracheophyta;
Subdivision: Spermatophytina;
Class: Magnoliopsida;
Superorder: Lilianae;
Order: Asparagales;
Family: Iridaceae;
Genus: Iris;
Species: *Iris pallida*[17].

2.3. Common names:

The common word (iris) that gave the name of the genus, originated from Greek designating "rainbow" presumably due to the wide variety of colors that these flowers can have. However, the common names of*Iris pallida* were:

Arabic: Sausan, Sausan flurancy;
English: Dalmatian iris, fragrant-root iris, orris, sweet iris;
French: iris pâle;
German: bleiche Schwertlilie;
Portuguese: íris;
Spanish: lirio pálido;
Swedish: silveriris [18-20].

3. Distribution

It is native to Dalmatian coast, However, it was distributed in Europe (Former Yugoslavia, Italy, Albania, Bulgaria, Romania, France); Asia-temperate (Lebanon, Iraq, Palestine), Africa (Canary Islands) and Northern America (USA)[19, 21].

3.1. Description

Stems 1–3-branched, 6–10 dm. Rhizomes branching, forming extensive clumps, 1.5–2 cm diam. The leaves are bluish-green in color, and sword-shaped, 40–50 cm (16–20 in) in length, and 2.5–3 cm (0.98–1.18 in) in width. Inflorescences with terminal unit 3-flowered, branch units 2–3-flowered; distal branches subtended by scarious bracts, lower one to 15 cm, herbaceous, green; spathes completely silvery white, 2–3.5 cm, scarious. Flowers often very fragrant; perianth light blue-violet to mauve-purple, one form with blue pigment limited as stipples or stitches along margin and/or along veins, with ground color white on both petals and sepals; floral tube 1–1.3 cm; sepals slightly reflexed, obovate, 7.8–8.3 × 5–5.3 cm, with wedge-shaped claw marked with brown veins, beard yellow with white tips; petals blue-violet, in some forms lighter than sepals, with some brown veining at base and on claw, obovate, 8 × 5 cm; ovary trigonal, 6-grooved, 1–1.5 cm; style violet, fading paler along margins, keeled along midrib, 2–2.4 × 1 cm, crests rounded, 1.4 cm, apex acute; stigmas rounded, margins entire; pedicel very short, 2–3 mm. Capsules borne on ends of stems and branches, oblong, trigonal, 6-grooved, 4–5 × 1.5–2 cm. Seeds in 2 rows per locule, dark brown, compressed, cubical, wrinkled [21-23].

3.2. Traditional uses

The root wasused as antispasmodic, aperient, aromatic, attenuant, carminative, detoxicant, diuretic, emetic, emmenagogue, expectorant, fixative, laxative, pectoral, purgative andsedative [24].

The peeled and dried rhizomes of *Iris germanica* as well as its variety *florentina* and *Iris pallida*were known as orris root or as rhizoma iridis and were used for centuries in medicinal treatments, while today they are most important particularly for production of orris butter[25]. Rhizomes of *Iris pallida* (orris root) were used in perfume and medicine. The juice of the fresh root is a strong purge of great efficiency in the treatment of dropsy. Orris olderived from the dried root, was used as a flavouring in soft drinks, sweets, chewing gum etc. It was much used as a fixative in perfumery, as an ingredient of toothpastes, for the treatment of coughandas breath fresheners [21, 24-26].

Parts used: Rhizomes with the roots and oil [24, 27].

3.3. Chemical constituents

The chief constituent of the root was the Oil of Orris, also known as Orris Butter, which constitutes about 0.1 to 0.2 percent of the dried root; it is a yellowish white, semisolid mass. Other constituents of Orris root were fat, resin, a large quantity of starch, mucilage, a bitter principle and a glucoside named Iridin. The aromatic constituent of Orris root was irone, which gives the dried, aged root its characteristic violet like odor [28-30].

The essential oils obtained from the leaves and rhizomes of *Iris pallida* from Ukraine were 0.03% and 0.20%, respectively. 26 components were identifiedin the leaves and 18 in the rhizomes. The major terpenes in the essential oil of the leaves were squalene (6%), hexahydrofarnesylacetone (8%) and neophytadiene (up to 6%). Among them, myristic acid (56%), capric acid (14.50%), lauric acid (15.42%), α-irone (2.85%) were found as the major constituents of the essential oil of the rhizomes of *I. pallida*. α-irone and γ-irone contents are accepted as the most significant criteria of the commercial quality of Iris essential oil [26].

Quantitative analysis of the phenolic compounds of *I. pallida* revealed that it contained gallic acid2.362 ± 0.076,mangiferin 0.849 ± 0.029,caffeic acid 0.227 ± 0.033,tectoridin 1.642 ± 0.023,germanaism B 0.534 ± 0.015,irisolidone-D- glucoside0.325 ± 0.030,iristectorigenin B 0.354 ± 0.004, nigricin 0.317 ± 0.003,irigenin 3.199 ± 0.034, 5,6-dihydroxy-7,8,3′,5′- tetramethoxy isoflavone 0.457 ± 0.003 and irisolidone 0.264 ± 0.004 mg/g [31].

The highest number of (iso)flavonoids was detected in I. *pallida* leaves and roots, which consisted of 35 and 38 (iso)flavonoids, respectively, while less than half of them were detected in the rhizomes of this species [32].

Iris pallida rhizomes wasrich in flavonoids (resinoids of I. *pallida* rhizomes contained 120 ± 3.3 mg/g isoflavones). One isoflavanone (2,3-dihydroirigenin) and one benzophenone (2,6,4'-trihydroxy-4-methoxybenzophenone) only were identified in I. *pallida* resinoid[33]. However, Isoflavones isolated from different parts of *Iris pallida* were included: iristectorigenin A, irisflorentin, irilone, irigenin, 8-hydroxyirigenin, nigricin, nigricanin, iris kumaonin methyl ether, irisflogenin and 2,3-dihydroirigenin [34]. 0.1–0.7 % of iridals and their esters were extracted from the leaves of *I. pallida* [35].

However, the ironecontents of*Iris pallida* was 1386 mg/kg dry mass, and 866 g/plant in fress mass. Four irone isomers (Trans-α, cis-α, cis-γ and β- irone) were identified in *Iris pallida* [36].

The average composition of the irone oil produced by the enzymatic method employed on four batches of fresh *Iris pallida* rhizomes: 4% of (+)-trans-α-irone, 0.6% of (-)-trans-γ-irone, 31.6% of predominantly dextrorotatory cis-α-irone, 49.8% of (+)-cis-γ-irone, traces of β-irone, and 13.8% of other unidentified components [37].

The isomeric ironesin *Iris pallida*were developedon oxidative cleavage of the methylated triterpenoids iripallidal or its isomer iriflorental. Their possible precursor was the squalene is the C 30-compound isoiridogermanal which was found in rhizomes of *Iris pallida* [38].

Methionine was readily incorporated into cycloiridals of *Iris pallida dalmatica*, thus indicating that the methylation of iridals via S-adenosyl- L - methionine led to the formation of the irone moiety of the bicyclic compounds. The cycloiridals, C31-triterpenoids, also served as precursors of the irones [39].

To increase the production of a mixture enriched in cis-γ-irone,the iris rhizomes, parts of these rhizomes, iris extracts, or iris wastes were incubated with two bacterial strains, in the presence of a plant cell culture medium (*Serratia liquefaciens* and *Pseudomonas maltophilia*).Incubation of *Iris pallida* rhizomes with these strains increased theproduction of irones. After eight days, irone content reached 1 g per kg of dry rhizome, whereas only 400 mg per kg were obtained by the traditional procedure using rhizomes stored for three years [37, 40].

4. Pharmacological effects

4.1. Anti-aging and dermatological effects

Sweet iris acts on consequences of natural aging at the conjunctive level of the dermis and the upper layer of the epidermis, at the level of the dermis, the sweet iris stimulates the synthesis of constituents of the extra-cell matrix - collagens, glycosaminoglycans, elastin and proteoglycans - while limiting the action of the enzyme that destroys them. In the same time, it helps to regenerate the epidermis in a well-balanced way by increasing the production and the differentiation of the cells of the epidermis that slows down with ageing. Skin layers can get back their density and their

global balance, which limit the creation of wrinkles. Anti-wrinkle effect of sweet iris was evaluated in women after 28 days of treatment (face): it decrease of the total surface by 24%, decrease of the number of wrinkles by 19% and decrease of the length of wrinkles by 26%. 80% of women declared that their wrinkles seem to have decreased [41].

4.2. Anti-inflammatory and antioxidant effects

The respiratory burst and degranulation of neutrophils are important processes in the maintenance of human health, but they need careful regulation to prevent the development of chronic and auto-immune diseases. Superoxide is a major radical produced by neutrophils and its excessive amount contributes to several acute and chronic diseases, including lung injury, sepsis, or arthritis. The effects of Iris extracts on superoxide anion generation and elastase release triggered by fMLF in CB-primed human neutrophils were studied. The results revealed that the water extracts Iris rhizomes showed anti-inflammatory potential and inhibited superoxide anion generation at 10 µg/ml by 41.0- 45.7%. Both the ethanolic and water extracts of the rhizomes showed enhancing effects on elastase release by human neutrophils and thus may have immune-promoting effects related to degranulation [31].

4.3. Cytotoxic effects

A bicyclic triterpenoid isolated possessed anti-proliferative activity in the NCI 60 Human Cancer Cell Lines with GI_{50} concentrations ranging from micromolar to nanomolar range. Binds to PKCα with high affinity (Ki = 75.6 nM). Also binds to RasGRP3 (Ki = 15.5 nM), a phorbol ester receptor that links DAG/phorbol ester signaling with Ras activation. Binding is competitive with respect to phorbol ester. Itinduced translocation of RasGRP3 from the cytoplasm to fibrillar structures and the nuclear membrane. Also induced phosphorylation of ERK1/2 in a RasGRP3-dependent manner [42-43].

Six different triterpenoids (iridals) were bioassayed on two cultured human tumor cell lines: A2780 and K562 (and for each one a drug-sensitive and a drug-resistant cell line). All of the tested iridals had an IC_{50} in the 0.1 to 5.3 microg/ml range. Some of them were shown to be more effective than doxorubicine [44]. Iridal, a triterpenoidic compound showed anticancer activity against two cultured human tumor cell lines (A2780 and K562) [45].

Eleven iridal type triterpenoids were examined for protein kinase C (PKC) activation and binding activity to PKC. Nine iridals showed dose-dependent activities, and a mutual relation between the two activities was also observed. The structural requirements of the iridals for these activities included (i)a hydrophobic side-chain, (ii)an E-methylidene aldehyde group at the C-1 position, and (iii)a hydroxyl group at the C-26 position [46].

However, the extracts were evaluated for their in vitro cytotoxicity in human fibroblasts usingresazurin assay after 72 h of exposure. No toxicity was observed for fibroblasts (MRC cell line) at the highest tested concentration (670 mg/l) [32].

4.4. Antiparasitic effects

Iridal, a triterpenoidic compound was tested in vitro on *Plasmodium falciparum* chloroquine-resistant and -sensitive strains and in vivo on *P. vinckei*. The IC_{50} obtained in vitro on human malaria strain was ranged from 1.8 to 26.0 microg/ml and the ED_{50} in vivo was 85 mg/kg/day by intraperitoneal route [45].

Iridalsalso showed antitrypanosomal activity with the using of *in vitro* screening assays [47].

4.5. Antimicrobial effects

The antibiofilm activity of 15 methanolic extracts of Iris species was investigated against both mono-(*Pseudomonas aeruginosa, Staphylococcus aureus*) and multi-species oral biofilms (*Streptococcus gordonii, Veillonella parvula, Fusobacterium nucleatum* subsp*. nucleatum,* and *Actinomyces naeslundii*). Among Iris species*, I. pallida*, inhibited both the quorum sensing and adhesion during biofilm formation in a concentration-dependent manner. However, the extracts were less active against maturated biofilms. The inhibition of bacterial adhesion significantly correlated with myristic acid content, and quorum sensing inhibition correlated with the 7-_-hydroxystigmast-4-en-3-one content [32].

Iridal, a triterpenoidic compound was tested against *Candida albicans* and *C. parapsilosis* strains. The minimal antifungal inhibitory concentrations were higher than to 50 microg/ml, whatever the strain of yeast tested [45].

5. Conclusion

This review discusses the traditional uses, chemical constituent, pharmacological and therapeutic effects of *Iris pallid* as promising herbal drug because of its safety and effectiveness.

Compliance with ethical standards

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