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Pharmacological potential of Orchis mascula- A review

Ali Esmail Al-Snafi
Department of Pharmacology, College of Medicine, Thi qar University, Iraq.
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Abstract: Orchis mascula was used traditionally as astringent, demulcent, expectorant, nutritive, restorative, invigorator and sexual tonic. In addition to its aphrodisiac effect, it was also used in the treatment of male sexual disorders like erectile dysfunction and impotence, and also as a nervine tonic that to treat stress and mental disorders. Orchis mascula contained alkaloids, saponins, tannins, phenolics, terpenes, sterols and flavonoids. The pharmacological studies showed that Orchis mascula possessed cardiovascular, hypolipidemic, antioxidant, antiepileptic, DNA protective, antimicrobial, cytotoxic, aphrodisiac, smooth muscle relaxant, and many other effects. The current review was designed to shed some light on the chemical constituents and pharmacological effects of Orchis mascula.
Keywords: constituents, pharmacological effects, Orchis mascula

I. INTRODUCTION:

Plants produced many secondary metabolites which represented an important source of many pharmaceutical drugs. Recent reviews showed that medicinal plants possessed wide range of pharmacological effects[1-14]. *Orchis mascula* was used traditionally as astringent, demulcent, expectorant, nutritive, restorative, invigorator and sexual tonic. In addition to its aphrodisiac effect, it was also used in the treatment of male sexual disorders like erectile dysfunction and impotence, and also as a nervine tonic that to treat stress and mental disorders. *Orchis mascula* contained alkaloids, saponins, tannins, phenolics, terpenes, sterols and flavonoids. The pharmacological studies showed that *Orchis mascula* possessed cardiovascular, hypolipidemic, antioxidant, antiepileptic, DNA protective, antimicrobial, cytotoxic, aphrodisiac, smooth muscle relaxant, and many other effects. The current review was designed to shed some light on the chemical constituents and pharmacological effects of *Orchis mascula*.

Plant profile:
Synonyms:

Androrchis mascula, Androrchis mascula subsp. lapalmensis, Androrchis mascula subsp. longicalcarata, Androrchis mascula subsp. maghrebiana, Androrchis pinetorum, Androrchis tenera, Orchidactyla kromayeri, Orchis compressiflora, Orchis kromayeri, Orchis lapalmensis, Orchis mascula var. acutiflora, Orchis mascula subsp. acutiflora, Orchis mascula f. acutiflora, Orchis mascula var. albiflora, Orchis mascula var. albiflora, Orchis mascula var. bicolor, Orchis mascula f. borbasiana, Orchis mascula f. brevibracteata, Orchis mascula f. brevicalcarata, Orchis mascula f. cochleata, Orchis mascula f. comosa, Orchis mascula f. fimbriata, Orchis mascula f. kotuliana, Orchis mascula subsp. lapalmensis, Orchis mascula f. laxa, Orchis mascula subsp. longibracteatoides, Orchis mascula subsp. longicalcarata, Orchis mascula f. longicalcarata, Orchis mascula subsp. maghrebiana, Orchis mascula f. maghrebiana, Orchis mascula var. maritzii, Orchis mascula subsp. mascula, Orchis mascula var. minima, Orchis mascula f. minor, Orchis mascula var. monsignatica, Orchis mascula var. obtusata, Orchis mascula var. obtusiflora, Orchis mascula subsp. occidentalis, Orchis mascula subsp. pinetorum, Orchis mascula var. pinetorum, Orchis mascula f. platyloba, Orchis mascula f. podolica, Orchis mascula f. reichenbachiana, Orchis mascula f. tatrensis, Orchis mascula var. tenera, Orchis mascula subsp. tenera, Orchis mascula subsp. wanjkovii, Orchis masculolatifolia, Orchis monsignatica, Orchis morio var. mascula, Orchis morio f. mascula, Orchis obtuse, Orchis obtusiflora, Orchis parreissii, Orchis pinetorum, Orchis pinetorum, Orchis speciosa var. alba, Orchis speciosa var. rosea, Orchis stabiana, Orchis tenera, Orchis tenera f. herculiana, Orchis verna, Orchis vernalis, Orchis wanjkovii, Orchis wilmsii[15].

Taxonomic classification:
Kingdom: Plantae, **Phylum**: Tracheophyta, **Division**: Spermatophyta**, Subdivision**: Angiospermae, **Class**: Liliopsida, **Order**:Asparagales, **Family**: Orchidaceae, **Genus**: Orchis, **Species**: *Orchis mascula*[16].

Common names:

This name orchis comes from the Greek Orchis, meaning (testicle), due to the appearance of the paired subterranean tuberoids. Its common names were: **Arabic**: Sahlab, Sahlab thakari, Khasa Althalab; **English**: Salep, Salep orchid, Early purple orchid; French: Orchis mâle; Hindi: Salap, Salab; **Persian**: Thalab Nar, **Portuguese**: Satirião-macho; **Spanish**: Campanos[17].

Distribution:

It is distributed in Albania, Algeria, Austria, Baleares, Baltic States, Belarus, Belgium, Bulgaria, Canary Islands., Central European Rus, Corse, Czechoslovakia, Denmark, East Aegean Is., East European Russia, Finland, France, Froyar, Germany, Great Britain, Greece, Hungary, Iran, Iraq, Ireland, Italy, Krym, Lebanon-Syria, Madeira, Morocco, Netherlands, North Caucasus, Norway, Poland, Portugal, Romania, Sardegna, Sicilia, South European Russi, Spain, Sweden, Switzerland, Transcaucasus, Turkey, Ukraine and Yugoslavia[16].

Traditional uses:

Various kinds of Orchis under the name of Sahlep were used for making a wholesome and nutritious drink of the same name. It was rich in mucilage, which formed a soothing and demulcent jelly that was used in the treatment of irritations of the gastro-intestinal canal. One part of Salep to fifty parts of water was sufficient to make a jelly[17].

It was used traditionally as astringent, demulcent, expectorant, nutritive, restorative, invigorator and sexual tonic. In addition to its aphrodisiac effect, it was also used in the treatment of male sexual disorders like erectile dysfunction and impotence, and also as a nervine tonic to treat stress and mental disorders[18-19].

Furthermore, the plant was also used for the treatment of hypertension and dyslipidemia and given in all forms of wasting diseases[20].

Part used:

Dried tubers of the plant, whole herb and seeds[17, 21].

Description:

Orchis mascula is a polycarpic perennial herb with two ellipsoid to sub-globose tubers, 15–35 × 10–20 mm, positioned 3–10 cm underground; roots few, rather slender. Stem 20–60 cm, erect, stout, cylindrical, pale green, often purplish, and angled above, sometimes hollow at the base, with 3–5 leaves in lower half and with sheaths above. Leaves 5–20 cm long, 0.5–3 cm wide, bright or greyish-green, broadly to narrowly oblong–lanceolate to oblong, acute or obtuse at apex, keeled, usually with rounded black–purple spots, the lower leaves spreading, the upper more erect and clasping. Inflorescence a spike, 4–15 × 3–5 cm, ovoid or cylindrical, rather lax, especially below, with 10–45 flowers. Bracts 12–20 mm long, 1.0–1.5 cm wide, usually as long as ovary, purple-tinged, narrowly linear-lanceolate, long-acute at apex, membranous, one-veined or the lower three-veined. Flowers reddish-violet, magenta, lilac, rose, pale pink or white, scentless or with an unpleasant smell of cats. No nectar is produced. Outer perianth segments 6–8 mm long, ovate or oblong-lanceolate, the two lateral deflexed, the median more or less erect; inner obliquely ovate-lanceolate. Labellum 8–15 × 7–18 mm, deep reddish-violet to pale rose or magenta, paler at the base and dotted with darker purple, three-lobed; lateral lobes 1.2–3.7 × 1.7–5.9 mm, ovate or orbicular, obtuse, crenulate towards the apex, middle lobe 1.7–5.1 × 2.5–7.9 mm, almost square, slightly larger, truncate to two-lobed, crenulate with a ± distinct central notch and sometimes with a lateral notch on either side. Spur 10–15 × 1–3.5 mm, at least as long as ovary, stout, cylindrical, straight or curved upwards, horizontal or ascending, blunt or truncate. Column short, with a small point at the apex. Anthers ovate 1.2–2.5 mm, purplish or greenish-grey; pollinia 2, dark green, or yellow when the flowers are white; caudicles 1.4 × 0.15 mm, yellow and transparent, enclosed in a rose-violet bursicle, strongly elastic. Two stigmas, confluent on the roof and sides of the chamber, edged with a purplish line. Rostellum three-lobed. Ovary sessile, purple-tinged. Capsule 17–20.3 × 4.4–5.2 mm, erect. Seeds very numerous and tiny (length: 0.39 (± 0.13) mm, width: 0.18 (± 0.03) mm), mean volume 6.43 (± 3.98) × 10^{-3} mm^3; testa transparent[22].

Chemical constituents:

The preliminary phytochemical screening showed that the crude extract of *Orchis mascula* contained alkaloids, saponins, tannins, phenolics, terpenes, sterols and flavonoids[9]. The tuber of *Orchis mascula* contained glucoside, bitter substance, saponins 4%, starch 2.7- 21.92%, mucilage 48%, moisture 10.62%, sugar 1%, nitrogenous compounds 5 %, albumen, a trace of volatile oil and ash 2% containing chiefly phosphates and chlorides of potassium and lime. Glucomannan contents reached 43.67 ± 0.95% [17-19, 23].

The polysaccharides isolated from *Orchis mascula* were fractionated through ion-exchange and purified using gel filtration column chromatography. The chemical composition of the polysaccharide showed carbohydrates (91.5%), ash (13.01%), moisture (4.03%), carbon (39.21%) and hydrogen (5.87%). Molecular weight of the polysaccharides was 48kDa[24].

Phenolic compounds such as gallic acid, catechin, chlorogenic acid and syringic acid were identified in the plant[25].

Pharmacological effects:

Cardiovascular and hypolipidemic effects:

The effects and possible modes of action of *Orchis mascula* in hypertension and dyslipidemia was studied. In spontaneously hypertensive rats, the crude extract of *Orchis mascula* significantly ($p<0.05$) reduced systolic blood pressure to 174.2±9.63 vs. 203.4±7.13 mmHg, and improved endothelial dysfunction by increasing acetylcholine-induced relaxation. In normotensive anesthetized rats, the crude extract of *Orchis mascula* at 10 and 30 mg/kg caused a dose-dependent decrease in the mean arterial pressure. *Orchis mascula* also decreased serum triglycerides to 29.28±6.99 vs. 93.84±5.7mg/100 ml ($p<0.001$), low-density lipoprotein-cholesterol to 5.99±1.27 vs. 21.9±3.5mg/100 ml ($p<0.05$) and atherogenic index to 0.096±0.017 vs. 0.36±0.08mg/ 100 ml ($p<0.05$). *Orchis mascula* significantly reduced lipid levels in tyloxapol and high fat diet-induced hyperlipidemia. It also reduced gain in body weight with a reduction in daily diet consumption. In isolated rabbit aorta, crude extract of *Orchis mascula* caused concentration-dependent relaxation of both phenylephrine and high K^+ (80mM)- induced contractions and caused a rightward shift of the calcium concentration–response curves similar to the effect of verapamil[23].

A polyherbal formulation (POL-10) contained *Orchis mascula* as one of its ingredient was evaluated in hypertension and dyslipidemia in rats. In spontaneously hypertensive rats, POL-10 significantly ($p<0.05$) reduced blood pressure to 183.2±2.97 vs 198.1±5.2 mmHg, improved endothelial dysfunction ($p<0.01$) by increasing acetylcholine-induced relaxation up to 46.0± 6.7% vs 24.6±3.8% and decreased serum triglycerides to 54.5±3.3 vs. 93.84±5.7 mg/dl ($p<0.001$). In high fat diet-induced hypercholesterolemia, POL-10 caused reduction in total cholesterol, low density lipoproteins levels and the atherogic index. It decreased triglycerides levels in tyloxapol-induced hyperlipidemia and increased high-density lipoprotein cholesterol and reduced atherogenic index in normotensive rats[26].

The antidyslipidemic, antihypertensive and endothelial modulatory properties of two herbal formulations, (ZPTO and ZTO, contained *Zingiber officinalis, Piper nigrum, Terminalia belerica* and *Orchis mascula*), were studied in different animal models included, tyloxapol and high fat diet-induced dyslipidemia and spontaneously hypertensive rats. In tyloxapol-induced hyperlipidemic rats, both ZPTO and ZTO caused significant reduction in serum triglyceride and total cholesterol. In high fat diet-fed rats, ZPTO decreased triglyceride, low-density lipoproteins cholesterol and atherogenic index. ZTO also showed similar effects with more capability to reduce atherogenic index, body weight and raising high-density lipoproteins. In spontaneously hypertensive rats, both formulations markedly reduced systolic blood pressure, atherogenic index and triglyceride levels, ZTO being more potent in reversing endothelial dysfunction, but it was devoid of cardiac stimulatory effect. ZTO also reduced low-density lipoproteins cholesterol and improved glucose levels in spontaneously hypertensive rats[27].

Ambrex, a polyherbal formulation consisted of *Withania somnifera, Orchis mascula, Cycas circirnalis, Shorea robusta* with amber was investigated for antioxidant effect in high fat diet fed rats and to investigate the possible mechanisms focusing on the gene expression involved in adipogenesis and inflammation in 3T3-L1 cell line. The serum total cholesterol and triglycerides were significantly decreased in ambrex treated hyperlipidemic rats compared to untreated rats. The activities of catalase, superoxide dismutase and reduced glutathione were significantly augmented in the serum, liver, and heart of hyperlipidemic rats treated with ambrex compared to control. Ambrex treated rats also showed significant reductions in malondiadehyde levels in the serum, liver and heart compared to untreated rats. Furthermore, ambrex treatment inhibited pre-adipocyte differentiation of 3T3-L1 cells *in vitro* by suppression of peroxisome proliferator activated receptor gamma, sterol regulatory binding proteins, tumor necrosis factor-α, inducible nitricoxide synthase, leptin, and upregulation of thioredoxin 1 (TRX1) and TRX2 mRNA expression[28].

Antioxidant effect:

Antioxidant capacity of *Orchis mascula* extracts was determined using DPPH method, total antioxidant status, total oxidant status and oxidative stress index. The plant extracts exhibited low antioxidant activity. Total antioxidant status value was 3.719 mmol/l, total oxidant status value was 18.664 μmol/l and oxidative stress index value was 0.505[25].

Polysaccharide isolated from *Orchis mascula* showed total antioxidant activity (21.81-72.1% at 50-250 μg/ml), DPPH radical scavenging activity (23.5-77.98% at 10-160 μg/ ml), hydroxyl radical scavenging activity (13.01-71.43% at 25-125 μg/ml), superoxide radical scavenging activity (927.01-68.27 at 50-250 μg/ml) and reducing power activity (0.405-1.789% at 10-160 μg/ml)[24].

The antioxidant activities of two herbal formulations, (ZPTO and ZTO) containing (*Zingiber officinalis, Piper nigrum, Terminalia belerica and Orchis mascula*) were carried out using DPPH radical-

scavenging assay. Both formulations showed antioxidant effects, but ZTO showed more potent antioxidant effect than ZPTO[27].

A polyherbal formulation (POL-10), contained *Orchis mascula* as one of its ingredient, was evaluated for antioxidant effect. It exhibited strong antioxidant activity in different *in vitro* assays[26].

Central nervous effects:

The antiepileptic effect of hydroalcholic extract of *Orchis mascula* tuber (orally 30 min before induction of seizures) was evaluated against seizures, seizure-induced oxidative stress and cognitive deficit in pentylenetetrazole and maximal electroshock-induced seizures in rats. The extract produced 33.3%, 50% and 66.7% protection in pentylenetetrazole model and 16.7%, 16.7% and 33.3% at 250, 500 and 1000 mg/kg, respectively, in maximal electroshock-induced seizures. Pre-treatment with the extract significantly decreased the retention transfer latency in elevated plus maze test, and an increase in the retention latency in passive avoidance test. Oxidative stress induced by seizures was also attenuated as indicated by significant increase in GSH and decrease in MDA levels in extract treated groups. Furthermore, pentylenetetrazole and maximal electroshock-induced seizures, caused a significant decrease in AChE and BChE activities, which was prevented by the extract[29].

DNA protective effect:

DNA protective activity of *Orchis mascula* extracts was studied using pBR322 supercoil DNA. The plant extracts showed weak DNA protective effect[25].

Antimicrobial effect:

The antimicrobial activity of *Orchis mascula* extracts was investigated using modified agar dilution method. The plant extracts showed no antimicrobial activity[25].

Cytotoxic effect:

Polysaccharide isolated from *Orchis mascula* possessed anticancer activity against A549 lung and AGS human gastric carcinoma, it inhibited cell proliferation (7.23-55.78% and 8.11-59.03%) at concentration of 50-250 µg/ml respectively[24].

The cytotoxic activity of *Orchis mascula* extracts was studied against A549 cancer cell line. The plant extracts (methanol and dichloromethane) did not show cytotoxic effects on A549 cells[24].

Aphrodisiac effect:

The aphrodisiac nature of a the plant was studied by observing mounting behavior, hormones levels and semen parameters in male mice. Crude extract showed significant increase in mounting behavior, remarkable increase in the organ weights, sperm counts, the protein, haemoglobin and testosterone content as compared to control group[30].

Smooth muscle effect:

POL-10, A polyherbal formulation contained *Orchis mascula* as one of its ingredient, exhibited calcium channel blocking (CCB) activity by inhibition of high K^+- induced contractions and rightward shift of Ca^{++} concentration-response curves similar to that of verapamil in isolated smooth muscle preparation[26].

Other effects:

The effect of salep concentration (0.5-1.5%) on the rheological characteristics of ice cream mixes, prepared from nonfat cow's milk, was investigated using a controlled stress rheometer. The time-dependent flow behavior of ice cream mix has been studied, the samples showed slightly thixotropic behavior, which was positively correlated with salep content[31].

Salep of high-glucomannan (*O. mascula* ssp. *pinetorum* contained glucomannan > 40 g/100 g) showed a significant and positive effect on the viscosity values and overrun levels and contributed to the sensory qualities of the ice cream, and thus is suitable for ice cream making[32].

II. CONCLUSION:

The current review highlighted the chemical constituents and pharmacological effects of *Orchis mascula* as a plant with wide range of pharmacological activities to be utilized in medical practice as a result of its effectiveness and safety.

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