JTCM 中医杂志 Journal of Traditional Chinese Medicine

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J Tradit Chin Med 2013 August 15; 33(4): 535-537
ISSN 0255-2922

LITERATURE STUDY

Evaluation of adverse events reported in Traditional Iranian Medicine following administration of aqueous extract of *Herba Portulacae Oleraceae* seed

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Accepted: June 6, 2013

Abstract

OBJECTIVE: To find scientific reasons for adverse events reported in Traditional Iranian Medicine (TIM) following administration of aqueous extract of *Herba Portulacae Oleraceae* seed including itching and tingling of whole body, tachycardia, anxiety, dyspnea and severe nausea.

METHODS: Electronic databases including PubMed, Scopus, and Web of Science were searched up to April 2013 to find papers focused on phytochemistry and biological activities of this plant.

RESULTS: Among chemical constituents present in *Herba Portulacae oleraceae*, catecholamines, adenosine and niacin can cause adverse events similar to those reported in TIM.

CONCLUSION: Because of the short duration of action of adenosine, catecholamines and niacin seems to be the major role in appearance of adverse events reported in TIM for *Herba Portulacae Oleraceae* seed. Mechanisms with consideration of receptor types and pharmacokinetics of catecholamine and niacin are warranted to confirm this hypothesis.

Key words: Portulaca oleracea; Drug toxicity; Catecholamines; Niacin; Medicine, Iranian traditional

INTRODUCTION

Herba Portulacae Oleraceae (PO) from the family Portulacaceae is an annual plant which grows in many areas of the world. It is a herbaceous plant, with branched, decumbent or fairy ascending stems of up to 50 cm, and which are reddish, fleshy and glabrous. The leaves are flat, fleshy, and spatulate. The flowers are yellow and solitary or in axillary groups of two or three. The seed are reniform, black, and maintain their germinative capacity for eight to ten years.[1,2]

Its popular common names in English are Purslane, Moss rose, Portulache, Verdolaga, Little Hogweed, Pursley, and Pigweed. It is thought that PO was cultivated more than 4000 years ago.[1] It is also a well-known medicinal plant in Traditional Iranian Medicine (TIM) and is used alone or in compounds for many medicinal purposes. The names mentioned in traditional Iranian manuscripts for PO are Khorfe, Baghla-al-Homgha, Farfakh, Rejla, Hasib, Baghla-al-Layyena, Baghla mobarake, Baghla fateme, Baghle-al-Zahra, and Tourak.[3]

PO is widely used not only as an edible plant, but also used for its medicinal properties. In TIM, aerial parts and seeds of PO have been used for treatment of fever,

uterus pain, diabetes, aphtous ulcers and diarrhea.[3] Arzani, leaved in 17th century, is a great Iranian scientist and physician who have authored many books. In one of his famous book, Mofarrah-al-Gholoub, he reported some serious adverse events following administration of aqueous extract from PO seed in a patient. In this patient, adverse events including itching and tingling of whole body, tachycardia, anxiety, dyspnea and severe nausea became rapidly apparent after ingestion of mentioned extract.[4] Arzani also quoted that because the temperament of PO from the perspective of TIM is cold and moist, these observed adverse events that are all related to hot dystemperament are unpredictable and thus, he could not find any reason for them.[4,5] Therefore, we decided to find scientific reasons for these reported adverse events from PO.

METHODS

Electronic databases including PubMed, Scopus, and Web of Science from 1966 to 2013 (up to April) to find papers focused on phytochemistry and biological activities of this plant.

The search terms were: "Portulaca oleracea" or "Purslane". Reference lists of the retrieved articles were also reviewed for additional applicable studies.

RESULTS

Review of papers revealed that nutritional value of PO is related to carbohydrates, proteins, fatty acids like omega-3, vitamins (A, C, E and B complex), beta-carotene and minerals (potassium, magnesium, sodium).[6-9] Different phytochemical studies indicated that flavonoids, tannins, coumarins, monoterpene glycoside, alkaloids, N-trans-feruloyltyramine, dopamine, noradrenaline, adenosine and melatonin are among bioactive constituents of PO.[10-14]

Pharmacological activities attributed to PO are antibacterial, analgesic, anti-inflammatory, skeletal muscle relaxant, wound-healing, antioxidant, bronchodilator, reducing locomotor activity and anti-convulsant effect.[14-20]

No adverse event like those reported by Arzani for PO was found in investigated documents.

But some phytochemicals identified in PO including catecholamines, adenosine and niacin (vitamin B3) may lead to adverse events similar to those reported by Arzani. Shi *et al* [11] reported catecholamines including noradrenaline and dopamine from different parts of PO (Table 1). Frequent adverse reactions from catecholamines include tachycardia, palpitation, vasoconstriction, dyspnea, nausea and vomiting, headache, and anxiety.[21,22]

Adenosine, a natural nucleoside in human, also exists in PO extract.[12] Adenosine should be administered intravenously because of rapid metabolism in blood and tissue. The most reported adverse reactions from adenosine injection are facial flushing, headache, dyspnea, chest pressure, nervousness, and nausea.[21,22]

Table 1 Reported contents of phytochemicals may responsible for adverse events of Portulaca oleracea

Dried parts	Phytochemicals (%)			
	Dopamine	Noradrenaline	Adenosine	Niaci
Leaves	0.074	0.69	ND	0.006
Seeds	0.054	0.59	ND	-

Note: ND: not determined.

Niacin or vitamin B3, a water soluble vitamin, is available in many foods. Some studies reported niacin in PO leaves although no data was found for seeds. The reported value of niacin was (0.44±0.01) mg in 100 g of wet leaves and 6 mg in 100 g dry leaves.[8,23] Adverse reactions reported from niacin are flushing, palpitation, tachycardia, dizziness, headache, pruritus, urticarial, abdominal pain, nausea, vomiting, hypersensitivity reactions (rare) and dyspnea.[21,22,24]

CONCLUSIONS

Among phytochemicals of PO with similar adverse events reported by Arzani, adenosine doesn't seem to be responsible, because adenosine has rapid tissue metabolism and thus, has a very short duration of action especially following oral administration.[21,22]

PO contains abundant catecholamines, noradrenaline and dopamine, and they were demonstrated to be the major bioactive constituents.[11] Catecholamines such as noradrenaline and dopamine are very potent. Dopamine dosage for injection in adults is 1-5 mcg/kg^{-1}·min^{-1} up to 20 mcg/ kg^{-1}·min^{-1} and onset of action is 5 min with duration of 10 min. Metabolism occurs by monoamine oxidase in renal, hepatic, plasma to 75% inactive metabolites and 25% noradrenaline. Noradrenaline usual range in adults is 8-30 mcg/min by injection and metabolism via catechol-o-methyltransferase and monoamine oxidase.[22] According to maximum dose about 16 gram for PO seed in TIM books[3] and determination of dopamine and noradrenaline in PO seed by Chen *et al*,[11] with consideration of receptor distribution and pharmacokinetics of them, catecholamines may be responsible for adverse events reported in 17th century from aqueous extract of PO seed.

We couldn't find any data about amount of niacin in PO seed although Bangash *et al* [8] determined (0.44 ± 0.01) mg niacin in 100 g of PO wet leaves. If we hypothesize niacin content of PO seeds is more than its leaves, niacin may be another agent responsible for reported adverse events.

Exact evaluation of PO mechanisms with consideration of receptor types and pharmacokinetics of catecholamine and niacin are warranted to confirm these theories.

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