Pharmacological Insights into Portulaca oleracea: Anti-Inflammatory and Muscle Relaxant Perspectives

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Abstract

Introduction: Portulaca oleraceacommon Purslane is an annual succulent in the family Portulacaceae.
Objectives: The aim of this study was to overview therapeutic effects of Portulaca oleracea especially its Anti-inflammatory and muscle relaxant properties.
Methods: This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases .The initial search strategy identified about 73 references. In this study,58studies was accepted for further screening and met all our inclusion criteria [in English, full text, therapeutic effects of Portulaca oleracea and dated mainly from the year 1993 to 2016.The search terms were “Portulaca oleracea”, “therapeutic properties”, “pharmacological effects”.
Result: while Portulaca oleraceais possesses lots of therapeutic effect, itsanti-inflammatory and muscle relaxant, antioxidant as well as antitumor activities was reviewed. An aqueous extract of Portulaca oleracea leaves and stems showed relaxant activity in a dose-dependent manner.The study of Phytochemistry of Portulaca oleracea was shown that this plant contain alkaloids other than its other chemical compoundsincluding oleracimine , oleracimine A , and oleraconeA,oleracone B , and β-carboline. These alkaloids are responsible for its anti-inflammatory effect.Postsynaptic alpha-adrenoceptors, inhibition of trans-membrane Ca influx, potassium ions, Ca2+ mobilization, and K+ ion contribute to the relaxant activity of the herb.
Conclusion: Portulaca oleraceaiswas shown that its anti-inflammatory effect is mostly due to the presence of oleraconeA, oleracone B. Among its alkaloids compound i.e. oleracimine , oleracimine A , and oleracone A , oleracone B , β-carboline , the two first was diagnosed to be responsible for its anti-inflammatory effect. The relaxant activity of Portulaca oleraceais is due to Postsynaptic alpha-adrenoceptors, inhibition of trans-membrane Ca influx, potassium ions, Ca2+ mobilization, K+ ion.Portulaca also possesses some of the claimed traditional uses of the wild species in the relief of pain and inflammation. In this study Anti-inflammatory and muscle relaxantproperties of this plant are presented using published articles in scientific sites.

Keywords:
Artemisia annua, therapeutic properties, pharmacological effects,Anti-inflammatory, muscle relaxant.

Introduction

1.1. Background

The use of medicinal herbs and herbal medicines is an age-old tradition (1-4) and the recent progress in modern therapeutics has stimulated the use of natural product worldwide for diverse ailments and diseases (5-17).

Portulaca oleraceaor popularly called Purslane is an annual succulent in the family Portulacaceaeextending from North Africa and Southern Europe through the Middle East and the Indian Subcontinent to Malaysia and Australasia(18).It is a warm-climate, herbaceous succulent annual plant. It is eaten extensively as a potherb and added in soups and salads around the Mediterranean and tropical Asian countries and has been used as a folk medicine in many countries(19). Diverse compounds have been isolated from Portulaca oleracea, such as flavonoids, alkaloids, polysaccharides (20), fatty acids, terpenoids, sterols, proteins vitamins and minerals (18). Portulaca oleracea possesses a wide spectrum of pharmacological properties such as neuroprotective(21), hepatoprotective(22), antidiabetic(23), antioxidant(24),antifatigue(25), anti-inflammatory(26), and anticancer activities(24, 27). Its leaves are used for diarrhea, postpartum bleeding(28), and intestinal bleeding(29).

Mechanism of action of AP is to prevent the vascular inflammatory process through the inhibition of intracellular ROS production and NF-κB activation as well as the reduction of adhesion molecule expression in TNF-α-induced HUVEC. Besides, AP prevents the development of diabetic endothelial dysfunction for the development of diabetes and its vascular complications.in addition, the ethanol extract of plant increase the colon length, decreasing body

weight loss and the disease activity index score, reducing the mRNA expressions of pro-inflammatory cytokines (TNF-α, IL-1β and IL-6) and the protein expressions of TNF-α and NF-kB p65. purslane had prophylactic and curative value on cholestasis-induced liver fibrosis through inhibition of oxidative stress, decreasing the expression of profibrogenic cytokines, collagenolytic activity and activation of hepatic stellate cells. AP prevents the vascular inflammatory process through the inhibition of intracellular ROS production and NF-κB activation as well as the reduction of adhesion molecule expression in TNF-α-induced HUVEC.

1.2. Statement of problem

In fact, medicinal herbscontaining natural composition are able to treat and cure many diseases. The diversity of natural compounds in herbs and their different role in preventing and treating different diseases from one hand and naturalness and compatibility with body as well as having no adverse effects trigger people have more interest to their application and researchers have much more inclination towards studies on them and recognize their curativeeffects, but there is stillelusion about their efficacy, pharmacological dosage, toxicity. To achieve this purpose, lots of studies have been carried out to concentrate on the ability of herb to generate favorable chemical and pharmacological profile.

1.3. Objective of research

This review article is aimed to overview chemical compounds and popular usages of Portulaca oleracea well as its anti-inflammatory and muscle relaxantproperties in details.

Materials and methods

This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases .The initial search strategy identified about 73 references. In this study, 58studies was accepted for further screening and met all our inclusion criteria [in English, full text, therapeutic effects of *Portulaca oleraceaL* and dated mainly from the year 1993 to 2016.The search terms were “Portulaca oleraceaL”, “anti-inflammatory” , “muscle relaxant”, “pharmacological effects”.

2.1. Inclusion and exclusion criteria

Inclusion criteria were the following key words were used to search for the relevant articles published from March 1993 to March 2016, their Full text should be available, to be in English. Articles included were consisted of clinical trials, in vitro, in vivo, review, or meta-analysis studies. Exclusion criteria were relating to other properties of this herb than its traditional usage and its anti-inflammatory and muscle relaxant activities, just abstract was available, not in the time line of study. Those article that did not match our inclusion criteria (be in other languages than English, between the time line of study) were excluded from the study.

Results

3.1. Anti-inflammatory effect

In an animal study, the anti-inflammatory of Portulaca oleracea L. was examined.The result showed that Oleracone as a novel alkaloid showedsignificantanti-inflammatory effect, with quick distribution and high bioavailability (30). Vascular inflammatory process of an aqueous extract of Portulaca oleracea wasinvestigated. AP prevents the vascular inflammatory process through the inhibition of intracellular ROS production and NF-κB activation as well as the reduction of adhesion molecule expression in TNF-α-induced HUVEC. These results suggested that AP might have a potential therapeutic effect by inhibiting the vascular inflammation process in vascular diseases such as atherosclerosis (31).

The protective effect of the aqueous extract of Portulaca oleracea L. (AP) on diabetic vascular complications was investigated. It was found that the insulin immunoreactivity of the pancreatic islets remarkably increased in AP treated db/db mice compared with untreated db/db mice. Taken together, AP suppresses hyperglycemia and diabetic vascular inflammation, and prevents the development of diabetic endothelial dysfunction for the development of diabetes and its vascular complications(32).

Oleracimine fromPortulaca oleracea L. was used to investigate the anti-inflammatory effects on lipopolysaccharide-stimulated macrophages. The results showed that oleracimine (1) remarkably inhibited nitric oxide production and could dose-dependently decrease the secretions of interleukin 6, tumor necrosis factor α, nitric oxide, and

prostaglandin E2 in cell culture supernatants as well as the mRNA of cyclooxygenase-2 and inducible nitric oxide synthase(33).

In an animal study, the protective inflammatory effects of the ethanol extract from Portulaca oleracea L. on dextran sulphate sodium-induced UC .The results demonstrated that the ethanol extract from POL could exhibit the effective protection for the DSS induced UC by increasing the colon length, decreasing body weight loss and the disease activity index score, reducing the mRNA expressions of pro-inflammatory cytokines (TNF-α, IL-1β and IL-6) and the protein expressions of TNF-α and NF-kB p65. These results may prove that this plant can be used in UC through the oxidative stress and inflammatory activities (34).

The anti-inflammatory ability with lipopolysaccharide (LPS) stimulated macrophages of Portulaca oleracea L. was examined.Oleracone was a novel alkaloid first isolated from Portulaca oleracea L. and possessed unique structure in natural products, whose anti-inflammatory activity effecting on nitrite oxide production and several pivotal pro-inflammatory cytokines was found at the concentration of 50 μm. Oleracone as novel alkaloid presented remarkably anti-inflammatory effect, which was rapid distributed in rat with high bioavailability of 74.91 ± 10.7%(35).

Therenoprotective effect of the aqueous extract of Portulaca oleracea (AP) on diabetic nephropathy accelerated by renal fibrosis and inflammation in type 2 diabetic db/db mice was investigated. This study also showed that treatment with AP significantly decreased water intake and urine volume in diabetic db/db mice ($p < 0.05$). Furthermore, NF-κB p65 activation in renal tissues markedly increased in untreated db/db mice, which was significantly suppressed by AP treatment. These findings suggest that AP attenuates diabetic nephropathy through inhibition of renal fibrosis and inflammation in db/dbmice (36).

The protective effect of the aqueous extract of Portulaca oleracea L. (AP), an edible plant used as a folk medicine, on diabetic vascular complications was investigated. It was also found that the insulin immunoreactivity of the pancreatic islets remarkably increased in AP treated db/db mice compared with untreated db/db mice. Taken together, AP suppresses hyperglycemia and diabetic vascular inflammation, and prevents the development of diabetic endothelial dysfunction for the development of diabetes and its vascular complications(37).

Anti-inflammatory properties of Portulaca oleracea L. subsp. sativa (Haw.) Celak. (a cultivar) was investigated. The 10% ethanolic extract of the aerial parts (dried leaves and stem) showed significant anti-inflammatory and analgesic after intraperitoneal and topical but not oral administration when compared with the synthetic drug, diclofenac sodium as the active control. Results indicate this cultivar species of Portulaca also possesses some of the claimed traditional uses of the wild species in the relief of pain and inflammation(38).

It was investigated whether an aqueous extract of Portulaca oleracea (AP) prevents the TNF-α-induced vascular inflammatory process in the human umbilical vein endothelial cell (HUVEC). AP prevents the vascular inflammatory process through the inhibition of intracellular ROS production and NF-κB activation as well as the reduction of adhesion molecule expression in TNF-α-induced HUVEC. These results suggested that AP might have a potential therapeutic effect by inhibiting the vascular inflammation process in vascular diseases such as atherosclerosis (31).

Anti-inflammatory effect of Purslane in hepatic fibrosis progression was assessed..Thestudy suggested that purslane had prophylactic and curative value on cholestasis-induced liver fibrosis through inhibition of oxidative stress, decreasing the expression of profibrogenic cytokines, collagenolytic activity and activation of hepatic stellate cells (39).

3.2. The muscle relaxant properties

The juice and aqueous extracts from the plant Portulaca oleracea was tested for muscle relaxant properties on isolated nerve-muscle preparations. Ethanolic extracts caused an initial augmentation of twitch height in chick biventercervicis preparations and then blockade which appeared to be mediated by an action directly on muscle fibres rather than on neuromuscular transmission. Solvent fractionation of the crude ethanolic extract followed by bioassay on the chick biventercervicis preparation showed that muscle paralysis increased with increasing polarity: i.e. water fraction >butanol> ethyl acetate approximately equal to crude extracts. It was concluded that the neuromuscular activity of extracts of Portulaca oleracea is caused by high concentrations of potassium ions(40).

An aqueous extract of Portulaca oleracea leaves and stems produced a dose-dependent relaxation of guinea pig fundus, taenia coli and rabbit jejunum and a dose-dependent contraction of the rabbit aorta. Phentolamine reduced the relaxant effect of the extract on gut smooth muscle and abolished the contractile response on the aorta as well as the pressor response on blood pressure. Guanethidine and tetrodotoxin had no effect on extract-induced relaxant or contractile responses. The extract may, therefore, act in part on postsynaptic alpha-adrenoceptors and by interference with transmembrane calcium influx(41).

An aqueous extract of the stems and leaves of Portulaca oleracea abolishes the twitch contraction of the directly stimulated rat hemidiaphragm preparation. There was a positive correlation between the concentration of K+ ions in the extract and the effects of potassium chloride of similar molarity. It is concluded that the K+ ion content of Portulaca oleracea is at least partly responsible for the relaxant effect observed on the isolated rat diaphragm(42).
The effects of aqueous (AEE), dialysable (DIF) and methanol (MEE) extracts of Portulaca oleracea stems and leaves were compared with those of dantrolene sodium and methoxyverapamil (D-600) with respect to inhibition of twitch tension on the rat phrenic nerve-hemidiaphragm and with respect to contracture induced by nicotinic agonists on the frog rectus abdominis preparations. it appears that the Portulaca oleracea extracts mimic, in part, the effect of D-600 and dantrolene on the rat hemidiaphragm and frog rectus abdominis muscles; therefore, the muscle relaxant properties of the extracts may be due, in part, to inhibition of trans-membrane Ca influx, interference with the Ca-induced Ca release process and/or inhibition of the release of intracellular Ca from stores in the sarcoplasmic reticulum(43). The aqueous extract of Portulaca oleracea used topically showedmuscle relaxant property(44).
The aqueous extract of Portulaca oleracea produced skeletal muscle relaxation in rats following i.p. or oral administration, as assessed by the prolongation of pull-up time. The i.p. route of administration was more effective. When compared with chlordiazepoxide, diazepam and dantrolenesodium, the extract proved a more effective skeletal muscle relaxant. The LD50 in an acute toxicity test in mice was 1040 mg/kg i.p(45).

The skeletal muscle relaxant properties of an aqueous extract of Portulaca oleracea were examined on the twitch and tetanus tension evoked by electrical stimulation using the rat phrenic nerve-hemidiaphragm and frog sciatic nerve-sartorius muscle preparations and on contractures induced by nicotinic agonists using the rat rectus abdominis muscle preparation. The observations indicate that the aqueous extract possesses unique skeletal muscle relaxant properties which do not appear to involve interference with cholinoceptor mechanism(s). It appears that the mechanism of action of the extract may involve interference with Ca2+ mobilization in skeletal muscle(46).
The effects of the extract on the locomotor activity, threshold to noxious stimulus, anti-convulsant activity and relaxant effects on the skeletal muscle were studied. The anti-nociceptive activity of the extract in rats was attenuated by naloxone pre-treatment indicating the involvement of opioid receptors in its anti-nociceptive effects. It is indicated from the results of the present study that P. oleracea v. sativa possesses varied effects on both the central and peripheral nervous system and the plant should be exhaustively studied for other neuropharmacologicaleffects (47).

3.3. Antioxidant effect
Antioxidant activities of three phenolic alkaloids, i.e., oleracein A (OA), oleracein B (OB) and oleracein E (OE), isolated from Portulaca oleracea were determined. The DPPH radical scavenging activities of these phenolic alkaloids were lower than caffeic acid but higher than ascorbic acid and alpha-tocopherol, being in the following order: OB > OA > OE. OE was most potent in preventing formation of malondialdehyde (MDA) with an EC(50) value of 73.13 microM, close to that of caffeic acid (72.09 microM). It was demonstrated that phenolic alkaloids served as a new class of antioxidant agents in this plant(48).

The protective effect of betacyanins from Portulaca oleracea L. against the D-galactose (D-gal)-induced neurotoxicity in mice was assessed. Betacyanins from Portulaca oleracea markedly reversed the D-gal-induced learning and memory impairments.These results suggest that the neuroprotective effect of betacyanins against D-gal-induced neurotoxicity might be caused, at least in part, by an increase in the activities of antioxidant enzymes with a reduction in lipid peroxidation. In comparison with vitamin C (VC), the betacyanins had a more pronounced effect on ameliorating cognition deficits in mice(49).

The protective effects of ethanolic and aqueous extracts of Portulaca oleracea L. (P. oleracea) on human lymphocyte DNA lesions were evaluated with the comet assay. It was found that the aqueous extract of P. oleracea significantly inhibited DNA damage, while there was no effect of the ethanolic extract. These data suggest that the aqueous

extract of P. oleracea can prevent oxidative DNA damage to human lymphocytes, which is likely due to antioxidant constituents in the extract(50).

The antioxidant properties of Portulaca oleracea L., known as Purslane was investigated. Phenolic extracts from all three-plant parts from both locations showed protective effects on DNA against hydroxyl radicals. This work suggests the possibility of benefit to human health from its consumption, related to the high antioxidant activity of purslane, even the stems, usually discarded in daily consumption(51).

Different antidiabetic activity between fresh and dried POL, including hypoglycemic and antioxidant activities both in vivo and in vitro was compared. Results indicated that both fresh and dried POL possessed antidiabetic activities, besides stronger activity was observed in the fresh herb. These findings provided evidence for the application and development of fresh POL in the treatment of diabetes mellitus(52).

The present investigation suggests that the processing enhance the functionality and improves the availability of bioactive substances of these vegetables. In addition, they also exhibited more potent antioxidant activity. Therefore these natural weeds from the crop land ecosystem could be suggested as cost effective indigenous green vegetables for human diet and potential feed resources for animals. Further extensive studies on role and importance of those weeds in sustaining the agro biodiversity are also needed(53).

The impact of oral administration of purslane (Portulaca oleracea) extract or fish oil and their co-treatments in the modulation of radiation-induced damage was evaluated.It could be concluded that purslane extract and fish oil may have therapeutic potential to improve hepatic and renal functions as well as oxidative stress in irradiated rats. Moreover, their co-administration showed a better improved liver function(54).

Purslane ethanolic extract effects were evaluated on antioxidant indices and sex hormone in D-gal aging female mice.These findings indicate that Purslane can attenuate aging alternations induced by D-gal and aging in female reproductive system(55).

This study examined the ability of tropical vegetables to reduce oxidative stress induced by vitamin A deficiency.This study evidences that the ingestion of purslane or malanga leaves may have a protective effect against oxidative stress caused by vitamin A deficiency(56).

3.4. Antitumor effect

theanti-tumor effects in vivo of unique polysaccharide component (POP) from Portulaca oleracea was analyzed and it was found that POP could significantly inhibit the growth of transplantable sarcoma 180 and potentiate the animal's immune responses including an increase in the number of white blood cell (WBC) and CD4(+) T-lymphocytes, as well as the ratio of CD4(+)/CD8(+).it is suggested that the anti-tumor effect elicited by POP could be associated with its immunostimulating properties(57).

cis and trans-isomers of feruloyl amides were evaluated for their antitumor activity. Long-term stability tests did not show any significant changes. Among all compounds and conversion mixtures collected, compound 6 exhibited the strongest inhibition of IL-6-induced STAT3 activation in Hep3B cells, with an IC50 value of 0.2 μM. This study is the first verification of the conversion rates and an equilibrium ratio of feruloyl amides. These results indicate that this natural material might provide useful information for the treatment of various diseases involving IL-6 and STAT3 (26).

Discussion

The Phytochemistry of Portulaca oleracea was shown that this plant contain flavonoids, alkaloids, polysaccharides (20), fatty acids, terpenoids, sterols, proteins vitamins and minerals (18). Each of the aforementioned chemical compound is divided into some subdivisions.

Three novel carbon skeleton alkaloids, named oleracimine (**1**), oleracimine A (**2**), and oleracone A (**3**), with one novel azulene carbon skeleton compound, oleracone B (**4**), and one known compound, β-carboline (**5**), were first isolated from Portulaca oleracea(58).

Oleracone as a novel alkaloid showed significant anti-inflammatory effect(30).oleracimine possessed unique structure in natural products, whose anti-inflammatory activity effecting on nitrite oxide production and several pivotal pro-inflammatory cytokines was found at the concentration of 50 μm. oleracimine remarkably inhibited nitric oxide production and could dose-dependently decrease the secretions of interleukin 6, tumor necrosis factor α, nitric oxide, and prostaglandin E2 in cell culture supernatants as well as the mRNA of cyclooxygenase-2 and inducible nitric oxide synthase(58) .Intraperitoneal and topical use of the aerial parts of plant showed significant anti-inflammatory and analgesic effect but its oral administration do not have such an effects(59).

the muscle relaxant properties of the extracts may be due, in part, to inhibition of trans-membrane Ca influx, interference with the Ca-induced Ca release process and/or inhibition of the release of intracellular Ca from stores in the sarcoplasmic reticulum (43), Ca2+ mobilization in skeletal muscle(60),the K+ ion(42)). It was concluded that the neuromuscular activity of extracts of Portulaca oleracea is caused by high concentrations of potassium ions (40). Postsynaptic alpha-adrenoceptors is responsible for its relaxant activity as well as interference with transmembrane calcium influx ((41)).An aqueous extract of Portulaca oleracea leaves and stems showed that its relaxant activity is done in a dose-dependent manner (41).

Conclusion

Portulaca oleraceais was shown that its anti-inflammatory effect is mostly due to the presence of oleraconeA, oleracone B. Among its alkaloids compound i.e. oleracimine , oleracimine A , and oleracone A , oleracone B , β-carboline , the two first was diagnosed to be responsible for its anti-inflammatory effect .The relaxant activity of Portulaca oleraceais is due to Postsynaptic alpha-adrenoceptors**,** inhibition of trans-membrane Ca influx, potassium ions, Ca2+ mobilization, and K+ ion.Portulaca *also possesses some of the claimed traditional uses of the wild species in the relief of pain and inflammation. In this study Anti*-inflammatory and muscle relaxantproperties of this plant are presented using published articles in scientific sites.

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