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Evaluation of the Anti-inflammatory Activity of the Seeds Extracts of Prickly Pear (*Opuntia ficus-indica* L.)

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ABSTRACT

The prickly pear cactus Opuntia ficus-indica (OFI) or nopal is a plant that is well adapted to arid and semi-arid climates like that of Algeria, it has been used in traditional folk medicine because of its role in treating a number of diseases including diabetes, hypertension, gastric mucosa pain, cardiovascular and anti-inflammatory diseases in many countries over the world. The objective of this work is to evaluate the hydro-ethanolic and aqueous extracts of (OFI) seeds (500 mg/kg, p.o.) for in vivo anti-inflammatory activity. The anti-inflammatory activity of OFI was tested in rats weighting 200-300 g by following method physiological saline (0.09%) for control group, the both extracts (500 mg/kg) and brexin (12 mg/kg) was administered (p.o.) for 30 min before an edema was induced in the rat paw by subcutaneous injection of carrageenan. The rat-paw volume was measured 1 h 30 min and 3 h and 6 h after injection. The OFI showed significant reduction of edema in carrageenan induced rat paw edema model for 44%, 50% at 1 h 30 min and 3 h for hydro-ethanolic respectively, compared to the aqueous extract which reduces the increase in paw volume with the same percentage of 25%, for the reference brexin (12 mg/kg) exhibited % reduction in paw volume 72.71%, 71.32% and 28.72% after 1 h 30 min, 3 h, 6 h respectively compared to control group. Furthermore the phytochemical tests detect the presence of flavonoids, tannins, sterols, and alkaloids in the seeds of prickly pear cactus (OFI). The obtained results of the present investigation revealed that the extract of OFI seeds (aqueous, hydro-ethanolic) has significant anti-inflammatory activity.

Keywords: Brexin, Anti-inflammatory activity, *Opuntia ficus-indica*, Nopal seeds

INTRODUCTION

Inflammation or phlogosis is a pathophysiological response of living tissues to injuries that leads to the local accumulation of plasmatic fluid and blood cells, which involves a complex sequence of bio-chemical events closely associated to the pathogenesis of various diseases such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute gout, migraine [1-3].

Nowadays, although the synthetic anti-inflammatory drugs are dominating the market, the element of toxicity from these drugs cannot be ruled out. Many drugs both Non-steroidal Anti-inflammatory Drugs (NSAIDs) and corticosteroids, have been developed but their safety profile studies have shown that none of them is clearly safe. Due to adverse reactions of synthetic and chemical medicines causing gastrointestinal irritation and reappearance of symptoms after discontinuation, herbal medicines have made a comeback to improve our basic health needs. Many plants and herbs such as ginger, turmeric and olive oil, have been shown to exhibit potent anti-inflammatory effects [4].

Currently available drugs such as opiates and NSAIDs are not useful in all cases due to their adverse effects. In this respect, new compounds with improved pain management capacity and fewer side effects are searched every nook and corner of the world. During this process, the investigations of the efficacy of plant-based drugs used in the traditional medicine have been paid great attention because they are cheap and have little side-effects [5,6].

In this context the world appears to be increasingly interested in the health benefits of foods, it is generally accepted that the beneficial effects of herbal remedies can be obtained from active constituents present in the whole plant, parts of the plant (flowers, fruits, roots), or combinations thereof, whether in crude or processed state [7].

Synthetic and natural antioxidants are of particularly importance in maintaining the oxidative stress level under the critical point in human organism. These roles have been attributed, in part, to their biological active constituents, such as liposoluble and water soluble vitamins (E and C, respectively) and polyphenolic substances [8].

As plants produce a significant amount of antioxidants to prevent oxidative stress, they represent a potential source of new compounds with antioxidant activity. Some of these plants the nopal or cactus (*Opuntia ficus-indica*) commonly known as prickly pear belongs to the family Cactaceae contain about 130 genera and nearly 1500 all well adapted to arid lands and to a diversity of climates and are naturalized in several areas all over the world, including the Mediterranean basin, it is a member of the succulent plant and an important nutrient and food source [9].

Cactus pear grows throughout Algeria and the fruits are consumed exclusively as fresh fruit. The extracted pigments from prickly pear fruits are used as additives in food, cosmetic, and pharmaceutical preparations [10]. This shrub used in traditional medicine. It is known for its virtues healing, an antioxidant effect, antiulcer, diuretic and anti-inflammatory [11-14].

MATERIALS AND METHODS

Vegetable material

The fruits have were collected in the North-West of Algeria at the Relizane city the month of August 2013 a number of 920 fruits which correspond to 90 kg of the peeled fruits.

Preparation of fruit

The fruits were sorted, washed with running water to remove the glochides and the impurities, peeled by the hand. The seeds were separated from juicy pulp, abundantly washed 8 times, with water distilled then dried with the room temperature for 1-3 days, the dried plant materials were grounded into fine powder using the electric blender. The plant was identified in Laboratory of Ecology and Management of Natural Ecosystems of the University of Tlemcen (Algeria). A voucher specimen of the plant was deposited in the Laboratory.

Preparation of the extracts

The two extracts are obtained by cold maceration under agitation of the crushed powder of seeds of the fruits of *Opuntia*, the maceration lasted 2 h at room temperature during 2 h a weight of 2 g in 25 ml of water distilled for the aqueous extract which corresponds the first extract (Ext Aq), and of 2 g in 25 ml of a mixture of distilled water and ethanol for hydro-ethanolic extract (Ext Etoh 50%), then filtered and solvent was evaporated one using a rotavapor R-200 (Germany) of Buchi. The extraction yields for the aqueous extract and the ethanol extract are respectively: 8.5%, 14.5%. The 2 concentrates are solubilized in a solution of 1% Carboxymethyl Cellulose (CMC) and administered orally to rats.

Phytochemical prospecting

The phytochemical tests to detect the presence of flavonoids, tannins, sterols, and alkaloids were used by simple qualitative methods. The tests were based on the visual observation of color change or formation of precipitate after the addition of specific reagents.

Experimental animals

The study was carried out according to the directives of the journal official of the European Community (JOCE), on rats Sprague Dawley of a Swiss race coming from the breeding of the laboratory of biology of the Faculty of Science in Rabat. The rats are of the two sexes, of equal number 2-3 mon old, weighing 200-300 g and gathered by batches of 10, the animals are healthy and vaccinated, were housed in polypropylene cages at a temperature of 24 ± 2°C and relative humidity of 60%-70%. All experiments were conducted after overnight fasting but there was free access to water.

Anti-inflammatory drug activity

The anti-inflammatory drug activity was evaluated by measuring the edema induced by the carrageenan according the following method [15]. Chemical inflammation was caused by injection of 0.1 ml of the carrageenan with 1% in an isotonic saline solution under plantar aponeurosis of the left hind paw of the rat. The 2 extracts (Aqueous, hydro-ethanolic) of *Opuntia* was dissolved and dispersed in physiological saline (0.09%) and administrated by orally for pre-treated groups of rats at 500 mg/kg dosage. Physiological saline (0.09%) was given to the control group at the same volume as vehicle 30 min prior to carrageenan injection. Increasing of carrageenan induced inflammatory paw volume was measured before 1 h and a half, 3 and 6 h after the injection with a plethysmometer [16]. The anti-inflammatory activity of *Opuntia* extracts was compared with that of 12 mg/kg brexin. The percentage inhibition of the inflammation was calculated from the following formula:

$$\text{Inhibition}\% = 1 - (VT - V0)\,Le / (VT - V0)\,Lt \times 100$$

Where VT is the increased volume of the paw at 1 h 30 min, 3 h, 6 h and V0 is the initial volume of the paw, Le is the treated bath (extract or reference brexin), Lt is the control group of rats. A significant reduction of the volume of the paw compared to the pilot batch was regarded as anti-inflammatory drug effect.

Statistical analysis

The results are expressed in (M+/-DS) the average+Derivation standard. The negative value indicates that the absolute volume of the edema of the pilot batch was smaller than the volume of the treated batch.

RESULTS AND DISCUSSION

The injection of 0.1 ml of carrageenan induced to the creation of a paw edema which increased gradually with a maximum of (1.730 ± 0.764 ml) at 3 h. The both extracts of *Opuntia* showed a significant inhibition of the edema of paw in the rats, of which the hydro-ethanolic extract causes an important inhibiting effect with a significant difference ($P<0.01$), and a percentage of 44% at 1 h 30 min and 50% at 3 h, compared to the aqueous extract which reduces the increase in paw volume with the same percentage of 25% for 3 h after pretreatment. For the batch of reference (brexin) reduces the volume of the edema with a percentage of inhibition of 72%, this reduction was maintained for 3 h after pretreatment. The results are expressed in Table 1.

Table 1: Effect of *Opuntia ficus-indica* seeds extracts and brexin on the edema induced by the carrageenan and the percentage of inhibition

Treatment	Doses (mg/kg)	30 min	% inhibition	1 h, 30 min	% inhibition	3 h	% inhibition	6 h	% inhibition
Controls	0	0.975 ± 0.091	-	1.025 ± 0.247	-	1.730 ± 0.764	-	0.935 ± 0.177	-
Brexin	12	0.835 ± 0.63	10.47	0.675 ± 0.008	72.71	0.375 ± 0.0354	71.32	0.590 ± 0.084	28.72
Ext Aq	500	1.007 ± 0.092	- 6.20	1.530 ± 1.211	25	1.477 ± 0.912	25.18	0.820 ± 0.322	14.19
Ext Etoh (50%)	500	0.885 ± 0.008	-1.16	1.075 ± 0.785	44.09	0.720 ± 0.070	50.31	0.635 ± 0.0495	24.46

The negative value indicates that the absolute volume of the edema of the pilot batch was smaller than the volume of the treated batch

The paramount test most largely used to evaluate the activity of a new agent anti-inflammatory drug and its capacity to reduce the edema induced by the injection of an agent irritating in the paw of the rat represented by the carrageenan, the latter is a mucopolysaccharide sulphated coming from Rhodophyceae, it caused inflammation typically associated with activation of cyclooxygenase. This inflammation is biphasic indeed; it is known that, in the live animal, carrageenan in a first phase causes around 1 h to the synthesis of chemical mediators such as histamine and serotonin which maintain inflammation [17]. In 1 s phase represented by a swelling, this molecule of reference mainly induces the synthesis of prostaglandins, proteases and lysosomes [18]. This last step is sensitive to prostaglandin synthesis antagonists and to natural anti-inflammatory or synthetic drugs such as the glucocorticoids [19-21].

The present experimental investigation revealed that the effects of extracts of *O. ficus-indica* (aqueous and hydro-ethanolic) at a dose of 500 mg/kg appearing as those of the reference brexin, after the 1st h, they produce a significant inhibition of induced carrageenan edema of the paw at 3rd h of experimentation at the time of the prostaglandin release in the inflammatory site, it is found that the extracts contain anti-serotonin compounds and antihistamines. The efficacy of the hydro-ethanolic extract of *Opuntia* seeds may be related to the chemical profile of this extract, particularly to the presence of polyphenolic compounds, among which flavonoids are able to inhibit the oxidants released by leukocytes and other phagocytes in the inflammatory site [22-26]. Also the flavonoids are known to target prostaglandins, which are involved in the late phase of acute inflammation and pain perception [27].

These compounds are known to be biologically active. Furthermore, numerous studies have evocated the analgesic and anti-inflammatory actions of the genus *Opuntia* by using either fruit extract, the lyophilized cladodes, or the phytosterols from fruit and stem extracts [28]. The β-sitosterol identified as the active anti-inflammatory principle from the stem [29].

CONCLUSION

The results of this study, which supplement the data literature confirms that *O. ficus-indica* is an interesting plant that could be used in the treatment of inflammation, in addition to the cactus stem, the extract seeds has an interesting potential like new molecule anti-inflammatory drug.

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