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Anti-Inflammatory Effects of Ginger and Parsley Extracts on Rats Paw

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Abstract

Inflammation is the natural reaction of the body to an antigen, this reaction might be continues even after the elimination of the antigen, entering a chronic stage and targets normal cells of the body and causes extensive damage. The present study was conducted to investigate the effects of Ginger (Zingiber) and Parsley (Baqdounes) extracts as anti-inflammatory on rats paw. A total of thirty male albino rats were divided into six groups (5 rats each) and fed on the basal diet. Groups 1 and 2 were received orally 1 ml/100g of saline solution and kept as positive and standard groups, respectively. Groups 3 and 4 were given orally ginger extract for two weeks at a dose of 100 and 200 mg/kg of b. wt., respectively. Groups 5 and 6 were given orally parsley extract for two weeks at a dose of 100 and 200 mg/kg b. wt, respectively. At the end of experimental period (14 days), the second group was given intraperioteneally Feldene (Piroxicam) as anti-inflammatory agent in a dose of 4 mg/kg of body weight. After one hour of the treatment, each rat in all groups was injected with 0.1 ml of formalin 4% in the plantar side of the left hind paw. The paw thickness (inflammation) caused by formalin was measured using skin caliber every two hours until 8 hours after injection. The present results showed that ginger and parsley extract had a significantly positive effect as anti-inflammatory which was more detectable with increasing doses of plant extracts. Results concluded that regular intake of ginger and parsley had anti-inflammatory effect.

Keywords: Acute and chronic inflammation – Ginger – Parsley – Rats.

Introduction

Inflammation is a complex immune process defined by the sequential release of mediators such as pro-inflammatory cytokines including interleukin-1 (IL-1) and tumor necrosis factor (TNF) and anti-inflammatory cytokines (IL-10) in

addition to reactive oxygen and nitrogen species. These mediators initiate inflammatory response, recruit and activate other cells to the site of injury and subsequently resolve inflammatory process. The inhibition of such mediators, especially pro-inflammatory cytokines may prevent or suppress a variety of inflammatory diseases **(Kim *et al.*, 2003).**

Risk factors for inflammation are known and may attack body cells at various parts of the body causing inflammatory diseases which may be acute or chronic. Acute inflammation usually takes place first in response to the attack of the risk factor (s). As soon as the risk factor (s) is removed, the acute inflammatory response will stop. Visualize, acute inflammation does not lead to oxidative and nitrosative stress or any serious adverse effect. However, when the risk factor (s) continues to exist, the acute inflammation will progress to chronic inflammation. Chronic inflammation plays the major role in the pathogenesis of all inflammatory diseases. If the risk factor (s) continues to exist, the acute inflammation will progress to chronic inflammation. Chronic inflammation plays a major role in the pathogenesis of all inflammatory diseases **(James and Lily, 2007)**.

In recent years, focus on traditional plants research has increased all over the world and large evidence has been found to show immense potential of medicinal plants used in various traditional systems.

Ginger (Zingiber officinale) has been cultivated for thousands of years as a cooking spice and flavoring agent. It has been used in traditional medicine for ailments muscholar aches, fever, sore throats, pain, indigestion and vomiting (**Ali et al., 2008)** and treat inflammation such as osteoarthritis **(Leach and Kumar, 2008)**. Ginger is rich source of antioxidant, analgesic and antipyretic properties **(Jana et al., 1999)**. Ginger is introduced into various tropical countries where diverse chemo types have been developed **(Wichtl, 2004)**. The major pungent constituents of ginger are 6-gingerol and 6-shogaol that have been shown to have many interesting pharmacological effects, such as anti-oxidant, antitumor promoting and anti-inflammatory effects **(Young et al., 2005)**.

Parsley, (Petroselinum Crispum) family Umbelliferae, locally known as Baqdounes, has been used medicinally for many centuries' in Mediterranean, European and Asian countries. It is widely used as a salad ingredient, a healthy garnish, and capable of disguise foul odors (**Ghazanfar, 1994**). Parsley is used in medicine for gastrointestinal disorders and to cure jaundice **(Kreydiyyeh *et al.*, 2001)** and for flushing the efferent urinary tract, as a diuretic **(Kreydiyyeh and Usta, 2002)**. The phytochemical screening of parsley leaves revealed the presence of tannins, flavonoids, sterol and triterpenes **(Al-Howiriny *et al.*, 2003)**. Folk medicines are used parsley for menstrual disorder ailments, as an emmenagogue, galactagogue and stomachic. Results of many investigations were pointed out to the antioxidant properties of parsley. it contains flavonoid apigenin as one of the components of parsley plant that express strong antioxidant effects by increasing the activities of antioxidant enzymes and decreasing the oxidative damage to tissues. It has potentially anticancer properties **(Mimica-Dukić and Popović, 2007)**. With these facts, the present study was planned to find out the possibility of anti-inflammatory activity of ginger and parsley extracts in male albino rats.

Materials and Methods

Materials:

Plants: Dried powder ginger and fresh parsley was purchased from the Herbs and Medicinal Plants market, in the local market from Cairo, Egypt.

Animals and diet: Thirty male rats of Sprague-Dawley strain weighing 175 ± 5 g were obtained from the Laboratory Animal Colony, Helwan, egypt. Basal diet constituents were purchased from El-Gomhorya Company for Pharmaceutical and Chemical, Cairo, Egypt.

Drugs: Feldene (Piroxicam) is an anti-inflammatory agent was obtained in the form of ampoules form the local pharmacy in Cairo, Egypt.

Methods:

Preparation of plant: Fresh parsley was washed with tap water and soaked in a water bath to remove possible potential pathogenic micro-organisms.

Afterwards, the parsley was dried by cotton cloth to remove the excess liquid prior to drying. Air drying was achieved at room temperature for 72 hr. Then a grinder mill and sieves were used to obtain a powder particle size. The dried ginger and parsley were finely grinded into fine powders and kept for further use.

Preparation of herbs extract: Dried fine powder of both ginger and parsley were soaked separately in 90% ethyl alcohol for 5 days. Then extracts were concentrated at low temperature (50Cº) using a Rotary evaporator apparatus (manufactured in Basil, Switzerland) until all the ethyl alcohol had been removed to give an extract sample. Dried extract was dissolved in a mixture of carboxymethylcellulose and few drops of Tween 80 as a suspending agent to obtain 10% and 20% concentration liquid extract.

Preparation of basal diet: The basal diet (AIN-93M) was prepared according to **Reeves *et al.*, (1993).** It consists of casein 20%, soybean oil 5%, Choline chloride 0.20%, vitamin mixture 1.0%, mineral mixture 4.0%, fibers 5%, L-Cystine 0.18%, sucrose 10% and the reminder was corn starch.

Experimental design: Animals were maintained under standard conditions of humidity, temperature, alternating 12-hour light-dark cycle, fed on the basal diet and water *ad libitum* for one week for acclimatization before starting the experimental. After acclimatization period, all animals (n= 30) were randomly assigned to six groups (5 rats each) as follows: Groups 1and 2 were feed on the basal diet only, received orally of saline solution at a dose of 1 ml/100g body weight (b. wt.) and kept as a positive control and standard groups, respectively. Groups 3 and 4 feed on the basal diet and given orally ginger extract by tube feeding for two weeks at a dose of 100 and 200 mg/kg of b. wt, respectively. Groups 5 and 6 fed on the basal diet and given orally parsley extract by tube feeding for two weeks at a dose of 100 and 200 mg/kg of body weight, respectively.

Induction of inflammation: Anti-inflammatory study was achieved as described by **Northover and Subramanian, (1962)**. It depends upon induction of pedal inflammation in rats paw by 0.1ml of formalin 4%. At the end of

experimental period (14 days), the second group was given (I/P) intraperioteneally Feldene (Piroxicam) as anti-inflammatory agent in a dose of 4 mg/kg of b.wt. After one hour of the treatment with extracts and anti-inflammatory agent, each rat in all groups was injected with 0.1 ml of formalin 4% in the plantar side of the left hind paw. The paw thickness caused by formalin was measured using skin caliber every two hours till 8 hours after injection. The difference between subsequent readings gave the actual edema volume. Anti-inflammatory effect was assessed by the reduction in the thickness of rat's paw.

Statistical analysis: The results were expressed as mean ± SD and statistical significance was assessed using one-way analysis of variance (ANOVA) test. Statistical analyses were performed using the SPSS software (Statistical Package for the Social Sciences, version 16.00, Chicago, USA).

3- Results

The effect of ginger extract at the two different doses (100 and 200 mg/kg of body weight) on paw's thickness (edema) of rats showed that rats given anti-inflammatory agent (standard group) had significant reduction in paw's thickness compared with positive rats at the 2, 4, 6 and 8 hrs post administration (Table 1).

Rats treated orally with ginger extract at 100 mg/kg of b. wt. had significantly reduction at $p<0.05$ in paw's thickness (mm) at the 2, 4 and 6 hrs post administration, while at the eight hour post administration, there was no significant difference, compared with that treated with anti-inflammatory agent as recorded in Table 1. Tabulated results revealed that rats given orally extract at a dose of 200mg/kg b. wt. had significant decreased ($p<0.05$) in paw's thickness compared with that treated with anti-inflammatory agent and those treated with extract at a dose of 100mg/kg b. wt. at the 2, 4, 6 and 8 hrs post administration.

The effect of parsley extract at the two different doses (100 and 200 mg/kg of b. wt) on paw's thickness in rats is tabulated in Table 2. It revealed that treated rats with anti-inflammatory agent had significant reduction at $p<0.05$ in paw's

thickness compared to the positive rats, at the 2, 4, 6 and 8 hrs post administration. Administration of parsley extract at a dose of 100 mg/kg b. wt. caused significantly reduction ($p<0.05$) in paw's edema at the 2, 6 and 8 hrs, post administration, while, at the four hours post administration, there was no significant differences compared that treated with anti-inflammatory agent. On the other hand, administration of parsley extract at a dose of 200mg/kg b. wt. caused significant ($p<0.05$) decreased in paw's thickness (mm) at the 2, 4, 6 and 8 hrs post administration compared with that treated with anti-inflammatory agent. The parsley extract at dose 200 mg/kg had significantly anti-inflammatory effect in reducing paws thickens in treated rats at the 2, 4 and 8 hours post administration more than that treated with extract at dose of 100 mg/kg b. wt.

Table 1: Effect of ginger extract on the paws thickness (mm) after induction of pedal rat's inflammation

Time after inflammation induction	Paw's thickness (mm) as Mean ± SD			
	Positive group	Standard group	Treated group with 100 mg/kg b.wt.	Treated group with 200 mg/kg b.wt.
At the 2 hrs	**a** 6.82 ± 0.08	**b** 5.74 ± 0.09	**c** 5.24 ± 0.09	**d** 5.04 ± 0.05
At the 4 hrs	**a** 7.48 ± 0.10	**b** 5.28 ± 0.20	**c** 4.92 ± 0.10	**d** 4.70 ± 0.10
At the 6 hrs	**a** 7.78 ± 0.13	**b** 4.86 ±0.13	**c** 4.34± 0.05	**d** 4.08 ± 0.08
At the 8 hrs	**a** 7.46 ± 0.09	**b** 4.38 ± 0.08	**b** 4.04 ± 0.05	**c** 3.92 ± 0.08

Different superscript letters in the same row denotes significant differences at P<0.05

Table 2: Effect of parsley extract on the paws thickness (mm) after induction of pedal rat's inflammation

Time after inflammation induction	Paw's thickness (mm) as Mean ± SD			
	Positive group	Standard group	Treated group with 100 mg/kg b. wt.	Treated group with 200 mg/kg b.wt.
At the 2 hrs	**a** 6.82 ± 0.08	**b** 5.74 ± 0.09	**c** 5.58 ± 0.08	**d** 5.36 ± 0.05
At the 4 hrs	**a** 7.48 ± 0.10	**b** 5.28 ± 0.20	**b** 5.26 ± 0.10	**c** 4.92 ± 0.10
At the 6 hrs	**a** 7.78 ± 0.13	**b** 4.86 ±0.13	**c** 4.44± 0.20	**c** 4.52 ± 0.10
At the 8 hrs	**a** 7.46 ± 0.09	**b** 4.38 ± 0.09	**c** 4.20 ± 0.07	**d** 4.06 ± 0.09

Different superscript letters in the same row denotes significant differences at P<0.05

Recorded data in Table 3 demonstrated the comparison of anti-inflammatory effect between ginger and parsley extracts. It showed that administration of ginger extract at the two different doses (100 and 200mg/kg b. wt) caused significant reduction ($p<0.05$) in rat paw's thickness, compared with parsley extract at the same doses at the 2, 4, 6 and 8 hrs post administration. The anti-inflammatory effect of ginger was more detectable with increasing extract doses as shown in Fig 1and 2.

Table 3: Comparison the effect of ginger and parsley extract on the paws thickness (mm) after induction of pedal rats inflammation

Groups	Parameters as Mean ± SD of paws thickness (mm) after induced for:			
	Two hours	Four hours	Six hours	Eight hours
Positive control group	**a** 6.82 ± 0.08	**a** 7.48 ± 0.08	**a** 7.78 ± 0.13	**a** 7.46 ± 0.09
Standard group	**b** 5.74 ± 0.09	**b** 5.28 ± 0.16	**b** 4.86 ± 0.13	**b** 4.38 ± 0.08
Treated groups with ginger at dose of: 100 mg/kg b.wt	**e** 5.24 ± 0.09	**c** 4.92 ± 0.11	**d** 4.34 ± 0.05	**d** 4.04 ± 0.05
200 mg/kg b.wt	**f** 5.04 ±0.05	**d** 4.70 ± 0.10	**e** 4.08 ± 0.08	**e** 3.92 ± 0.08
Treated groups with parsley dose of: 100 mg/kg b.wt	**c** 5.58 ± 0.08	**b** 5.26 ± 0.05	**cd** 4.44 ± 0.15	**c** 4.20 ± 0.07
200 mg/kg b.wt	**d** 5.36 ± 0.05	**c** 4.92 ± 0.08	**c** 4.52 ± 0.08	**d** 4.06 ± 0.09

Different superscript letters in the same column denotes significant differences at P<0.05

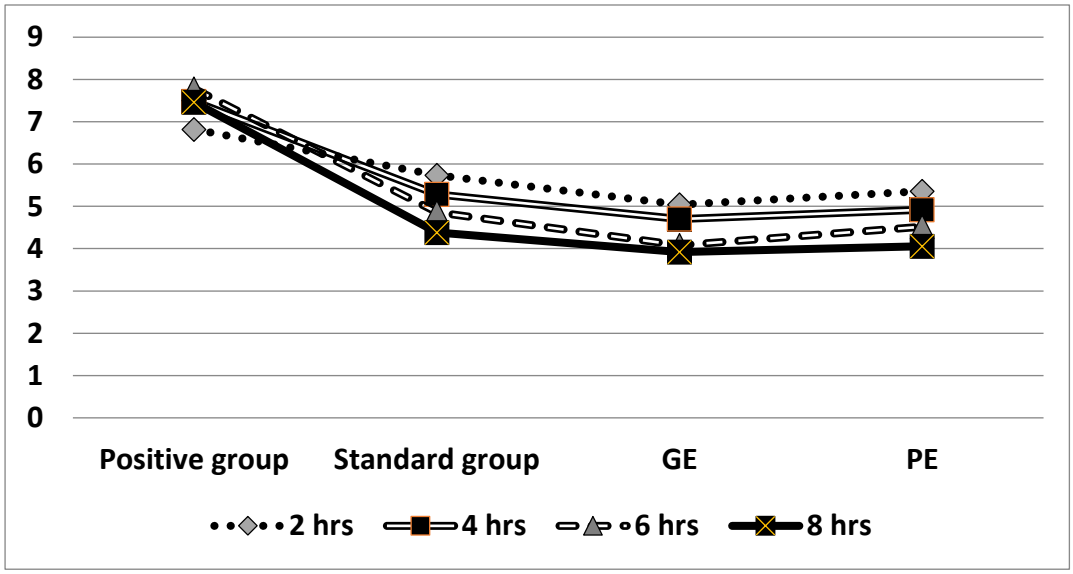

Figure 1: Comparison effect of ginger (GE) and parsley (PE) extract at a dose of 100 mg/ kg of b wt on the rats paws thickness (mm).

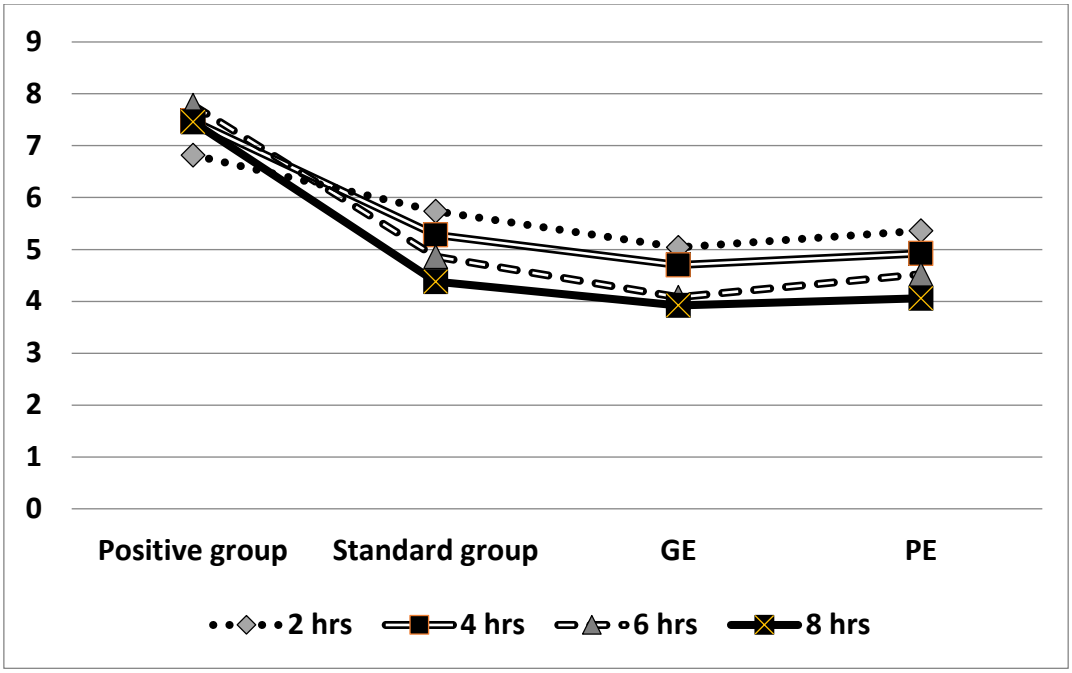

Fig 2: Comparison effect of ginger (GE) and parsley (PE) extract at a dose of 200 mg/ kg of b wt on the rats paws thickness (mm).

4-Discussion

In an effort to identify the anti-inflammatory effect of ginger and parsley extracts we performed an experimental study on 30 male albino rats. Inflammation was induced by formalin comprises an early neurogenic response mediated by substance P which is secreted by nerves and inflammatory cells such as macrophages, eosinophils, lymphocytes, and dendritic cells and bradykinin followed by a tissue mediated response, where histamine, 5-hydroxytryptamine, prostaglandins and bradykinin are involved **(Wheeler-Aceto and Cowan, 1991)**. Moreover, reactive oxygen species (ROS) are formed in both physiological and pathological conditions in mammalian tissues. The uncontrolled production of free radicals is considered to be an important factor in tissue damage which can induce pathophysiological changes. Free radicals also play an important role in inflammation that can mediate tissue destruction **(Kottarapat *et al.*, 2013).** The inflammatory process is itself a pathological process, whereas the natural anti-inflammatory response that ensues after acute inflammation tends to reverse tissue homeostasis

towards normality and should therefore be regarded as a true defensive reaction of the affected tissue **(Srdan, 2012)**.

The present study was conducted to investigate the effects of Ginger (Zingiber) and Parsley (Baqdounes) extracts as anti-inflammatory on paw rats.

The present study revealed that treated rats with ginger and parsley extracts at 100 and 200 mg/kg of b. wt had significant anti-inflammatory effect as showed by decreasing signs and paw's thickness (edema), compared with that treated with anti-inflammatory agent at the 2, 4 and 6 and 8 hrs post administration.

Previous studies founded that ginger (*Zingiberofficinale*) had anti-inflammatory effect which was not dose-related **(Srivastava and Mustafa, 1992)** and decrease inflammation swelling, and pain (**Young *et al*., 2005).** In addition, **Minghetti et al., (2007)** reported that gingerola (the active constituent of fresh ginger), dried ginger extract and a dried gingerol-enriched extract potent anti-inflammatory effects. **Lantz *et al.*,(2007)** demonstrated that ginger has long been used in the world as a popular spice food as well as a medicinal herb because of its high content of anti-inflammatory properties.

The anti-inflammatory effect of ginger may be related to its constituents. The main principles constituent in ginger are the series of pungent oleoresin constituents known as gingerols, with gingerol being the major component. Gingerols are the most pharmacologically active components **(Park and Pezzuto, 2002).** There are more than 50 types of antioxidants are extracted from ginger rhizome. The major pharmacological activities of ginger are 2 and 6-Gingerol **(Shukla and Singh, 2007).** Shogoals, gingerol, and are the ingredients that prevent the biosynthesis of Leukotrienes and Prostaglandins by inhibiting 5-lipoxygenase and prostaglandin synthesize (**Chang et al., 1993**). Ginger can inhibit NF-κB (Nuclear factor κB) activation, TNFα expression and CRP production **(Lantz et al., 2007)**. **Manju and Nalini, (2005) and Kota et al., (2008**) reported that the anti-inflammatory effects of ginger may be related to its inhibitory affect COX-2, lipoxigenase, NFκB and TNFα activity, which are caused by reduction of inflammatory factors such as IL6, IL1β, and IL2. The 6-gingerol have inhibitor influence on the arachidonic acid metabolites

include lowering formation of Thromboxan B2, Prostaglandin 2D and platelet aggregation. In addition to, anti-oxidative effects of ginger is related to glutathione enhancement, SOD activity induction and ROS reduction. Recently, **Kottarapat *et al.*, (2013)** founded that the essential oil of ginger scavenges superoxide, hydroxyl radicals and inhibit tissue lipid peroxidation. Therefore, it had antioxidant, anti-inflammatory and anti-nociceptive properties. Ginger oil displayed strong anti-inflammatory activity in chronic inflammation model and the mode of action may be due to the inhibition of prostaglandin release.

On the other hand the present study showed that parsley extract has anti-inflammatory properties as it appeared in reducing paw's edema in rats with inflammation. The anti-inflammatory effective of parsley may be related to its antioxidant properties **(Hempel et al., 1999)** and decrease oxidative stress **(Nielsen et al., 1999)** and scavenge hydroxyl radical in addition to protecting against ascorbic acid-induced membrane oxidation (**Fejes et al., 2000**). **Al-Howiriny et al., (2003)** mentioned that preliminary qualitative phytochemical screening of parsley leaves revealed the presence of flavonoids, tannins, sterols and/or triterpenes. In addition, the ethanolic extract of parsley was found to suppress carrageenan-induced rat paw edema significantly at higher doses (2g/kg) and significantly inhibited the edema formation after 3 h of administration. Recently, **Al-khazraji (2015)** showed that parsley effectively suppressed the edema produced by the histamine, which indicates that the parsley extract exhibit have anti-inflammatory properties by either the inhibition of the synthesis, release or action of inflammatory mediators via histamine, serotonin and prostaglandin that might be involved in the inflammation.

5- Conclusion

Rats given orally ginger and parsley extracts at 100 and 200mg/kg of b. wt. had significant anti-inflammatory effect as showed by the reduction in paw's thickness in treated rats Therefore, the intake of ginger and parsley had anti-

inflammatory effects by reduceing pain and swelling and can be used in the treatment, prevention and decreasing the signs of acute inflammations.

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