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Analgesic and Anti- Inflammatory Effect of Zingiber Officinale in Albino Mice

Samia Elzwi[1*] and Hamid Albarsi[1]

[1] *Department of Pharmacology, faculty of medicine, Benghazi University*

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الملخص

نبات الزنجبيل هو جزء رئيسي من الغذاء في انحاء كثيره من العالم وتشير البحوث الجديدة ان الزنجبيل له العديد من التأثيرات الدوائية نتيجة لوجود المواد الفعالة مثل القنقرول والشقول ويعتبر الزنجبيل هو احد اعضاء العائلة الزنجبيلية وينشأ في جنوب شرق أسيا ولكنه الان موجود في اجزاء مختلفة من الارض حيث ينمو في المناخ الملائم الزنجبيل يحتوي علي مكونات مضادة للالتهابات الزنجبيل الطازج والمجفف يحتوي علي سته قنقرول نشط و قنقرديون بالإضافة الي مكونات صمغيه تما استخلاصها بواسطة الهكسان والميثانول وتبين انها مسئوله عن منع الالتهاب الناتج بواسطه الليبوكسوجييدز والسيكلوكسجنيز وعلي الرغم من استعمال الزنجبيل بكثره في الطب الشعبي فأن الملومات العلمية عن فوائده قلياه جدا لهذا فأن هده الورقة تدرس تأثير المستخلص الكحولي المائي للزنجبيل كمضاد لالتهابات الناتجة عن حقن القوارض بماده الكراجنين في قدم الحيوان وكدلك تدرس تأثير النبات كمسكن للإلام الناتجة عن استخدام حمض الخليك وتبين ان الزنجبيل يمكن ان يخفف الالم ويزداد تأثيره كلما زادت الجرعة المستخدمة .

الكلمات المفتاحية:

حامض الاستيك - مسكن للالم - مضاد للالتهاب – الكارجنين - الزنجبيل .

Abstract

Zingiber officinale (ginger) is common part of the diet in many parts of the world, Recent research has found ginger to have various pharmacological properties due to a variety of active constituents, including shogoals and gingerols. It is a member of zingiberaceae family originated in Southeast Asia and has been introduced to many parts of the globe where it proliferates in suitable environment. Ginger contain constituents with anti-inflammatory properties. The fresh and dried ginger both contains active 6 – gingerol and gingerdion along with other resinous pungent principle, extracted with n-hexane and methanol that are responsible for inhibition of inflammatory metabolite's production by lipooxygenase and cyclooxyganse. The present paper aimed to determine anti- inflammatory effects of Zingiber officinale extract in experimental animals .The anti-inflammatory activity was assessed by using carrageenan it showed that the plant extract has anti-inflammatory effect in rats by using acetic acid model. The present paper indicated that plant extract has analgesic activity in dose dependent pattern.

Keywords:

Acetic acid, Analgesic effect, Anti-inflammatory effect, Carrageenan, Zingiber officinale.

1. INTRODUCTION

Ginger (Zingiber officinale) is a medicinal plant that has been widely used in Chinese, and Tibb Unani herbal medicines all over the world, since antiquity, for a wide array of unrelated ailments that include muscular aches, sore throat, constipation, arthritis, indigestion, vomiting and infectious diseases. Currently, there is a renewed interest in ginger, and several scientific investigations aimed at isolation and identification of active constituents of ginger, scientific verification of its pharmacological actions and of its constituents, and verification of the basis of the use of ginger in several diseases and conditions[1]. Ginger grows best in tropical and subtropical areas, which have good rainfall with hot and humid conditions during the summer season. It is a member of zingiberaceae family originated in Southeast Asia and has been introduced to many parts of the globe where it proliferates in suitable environment. Belief in the medicinal properties of ginger existed in ancient Indian and oriental cultures where ginger has been used alone or as a component in herbal remedies. This practice continues today in many areas of the world including Africa ,Brazil ,China and ,Mexico. Ginger has introduced to Europe and other areas by Dutch, Portuguese Arab and Spanish explorers or traders from around the 13th to 16th centuries.

Constituents. 1.Carbohydrates: starch is major constituents up to 50%. 2. Oleo-resin: gingerol homologues (major, about 33%) include derivatives with methyl side chain, shogaol homologues (dehydration products of gingerols), zingerone (degradation product of gingerols) , 1- dehydrogingerdione and 6- gingersulfonic acid[2]. 3. Lipids 6-8%: They include free fatty acids e.g palmitic acid, oleic acid, linoleic acid, caprylic acid, capric acid, lauric acid, myristic acid, pentadecanoic acid, heptadecanoic acid, stearic acid, linolenic acid, arachidonic acid ,triglycerides, phosphatidic acid, lecithins and gingerglycolipids A, B and C[3]. 4. Volatile oil: They constitute 1-3% they are complex predominately Hydrocarbons, zingiberene (major components) and B-bisabolene. Other sesquiterpenes include zingiberol, zingiberenol. 5. Other constitutes: Include amino acids as arginine, aspartic acid, cystine, glycine, isoleucine, leucine, serine, threonine and valine. Proteins constitute about

*Correspondence:

Dr. Samia Elzwi
Department of Pharmacology, faculty of medicine, Benghazi University
doclal560@yahoo.com

9%.Diterpenes (galanolactone), vitamins especially nicotinic acid (niacin) and vitaminA as well as minerals are also present[4,5].

The aim of present paper to study analgesic and anti-inflammatory effects of Zingiber officinale (ginger extract) in rodents.

2. METHODOLOGY

A. Experimental animals :

Albino mice of either sex weighing 20-30 g, and male Wistar strain rats , weighing 200-250 g were maintained in the animal house of Faculty of Medicine – Al Arab Medical University,

The mice and rat were rats were bred in the faculty animal house. All animals were housed in standard polypropylene cages (48×35×22 cm)Benghazi, Libya and kept under controlled room temperature (20±5 ◦C; relative humidity 60-70%) in a 12 h light-dark cycle. The animals were given a standard laboratory diet and free water . Food was withdrawn 12 h before and during the experimental hours.

B. Preparation of Zingiber officinale extract:

Maceration method: In this method fresh ginger rhizome was cut into small pieces , dried, and then pulverized into coarse powder and weighing about400 g of powder. It was macerated in 1000 ml hydroalcoholic solution (70% Ethanol, 30% distilled water) for seventy two hours The extract was then shaken, filtered by using filter paper and the solution was evaporated in a rotatory evaporator under reduced pressure until dryness. Evaporation and removal of the solvent give hydroalcoholic extract of ginger out of 400 g of crude plant, 8 g of hydroalcoholic extract of ginger were obtained and kept for use in pharmacological experiments[6].

C. Study of analgesic activity of Zingiber officinale (ginger) extract in mice

Hydroalcoholic extract of ginger was evaluated for its analgesic activity in albino mice, weighing 20-25g. The animals had access to water and food, but they were deprived of food 12 hour before experimentation. Mice were divided into six groups each consisting of five mice All animals were individually weighed and the doses of extract and control material were calculated accordingly. The investigation of analgesic activity by chemical method was performed by recording the number of writhes induced by i.p. injection of 0.1 ml/10 g of 1% acetic acid in mice

Group1: given normal saline with 0.5 % Tween-80 (1ml i.p) –ve control.

Group2: given acetic acid in a dose of 0.1ml/10g.

Group 3: given hydroalcoholic extract of ginger in a dose of 150 mg /kg (i.p)

Group4: given hydroalcoholic extract of ginger in a dose of 300mg /kg (i.p)

Group 5 : given hydroalcoholic extract of ginger in a dose of 450mg /kg (i.p)

Group 6: given acetylsalicylic acid in a dose of 150mg/kg (i.p)

All groups (except –ve control) were injected by acetic acid 40 min after receiving different treatment. Acetic acid (i.p) caused pain sensation with constriction of abdomen, turning of trunk and extension of hind legs[7]. This contraction of the body is termed as writhing. Any substance that has analgesic activity is supposed to reduce the number of writhes in mice within a given time and with respect to the control group. Five minutes after the administering acetic acid, the number of writhes was counted for fifteen minutes for each mouse The writhes = (The mean for every different group/control mean) ×100. Also, the percentage dose- effect of the extract on writhes was calculated as follow: Dose-effect (%)= (Total writhes per dose (T)/ Total writhes for control group (C) ×100. And the % of inhibition of writhes was calculated. % inhibition =100- (T/C×100) The values were all compared statistically with normal saline control group.

D. The hydroalcoholic extract of ginger was evaluated for anti- inflammatory effect. of extract by as:

Rats were divided into three groups each consisting of 5 rats.

1. Control group: given normal saline containing 0.5 % Tween - 80 in a dose of (1 ml (i.p)
2. Extract group: given hydroalcoholic extract of ginger in a dose of 400mg/kg (i.p)
3. Indomethacin group: given indomethacin in a dose of 5mg/kg (i.p)

Zero time, the volume of right and left paws were measured in all group by using a plethysmometer .Then after 1 hour inflammation was induced by carrageenan sodium gel 1%in a dose of 0.1 ml (s.c) in sub plantar region of the right hind paws at zero time. The volume of the injected paws and contra-lateral paws were measured at 0-30min-1hr-2hr-3hr-4hr-5hr post administration of carrageenan using plethysmometer. Swelling was determined by subtracting the volume of left paw from the right hind paw.

3. DATA AND RESULTS

The analgesic effect of Zingiber officinale are presented in the table (1). The percentage inhibition of writhes are 51.36%, 71.36% , 77.84% and 82.5% in the animals treated with 150 mg/kg, 300 mg/kg, 450 mg/kg of zingiber officinale extract and acetylsalicylic acid respectively.

The data shows that a 50% inhibition obtained at 150 mg/kg and % inhibition increase by increase the dose. By using one way ANOVA and Post Hoc indicated that150mg/kg treated group shows highly significant decrease in the number of writhes ($p<0.001$) compared to acetic acid treated group, and there is highly significant increase ($p<0.001$) in the number of writhes compared to control. In addition ginger extract at 150 mg/kg shows highly significant ($p<0.001$) compared to extract at 450 mg/kg and acetylsalicylic acid groups.

The data in the table (1) reveals that 300 mg/kg treated group shows a highly significant reduction in the number of writhes ($p<0.001$) compared to acetic acid treated group, and there is a high significant increase ($p<0.001$) in the number of writhes compared to control group. And the effect of extract at 300 mg/kg is non-significant ($p>0.05$) compared to acetylsalicylic acid group .At dose of 450 mg/kg there was a high significant reduction ($p<0.001$) in the number of writhes compared with acetic acid treated group and increase in the number of writhes compared to control. In addition extract at a dose of 450mg/kg shows significant ($p<0.05$) compared to extract at 150 mg/kg and non-significant ($p>0.05$) compared to acetylsalicylic acid group.

Acetylsalicylic acid cause highly significant decrease in the number of writhes ($p<0.001$) compared to acetic acid group.

Table (1): Analgesic Effect Of Different Dose of Zingiber officinale Extract and Acetylsalicylic Acid on Acetic Acid –Induced Writhing

Groups	Number of Writhes	% of Writhes	Dose-effect %	% Of inhibition
Control	0	0	0	100
Acetic acid	37	100	100	0
Ginger extract 150mg/kg	*18**	48.64	48.64	51.36
Ginger extract 300 mg/kg	10.6**	28.64	28.64	71.36
Ginger extract 450mg/kg	8.2**	22.16	22.16	77.84
Acetylsalicylic acid 150 mg/kg	6.5**	17.56	17.56	82.5

**-Significant different from acetic acid treated group
*-- Significant different from ginger extract at 450mg/kg and acetylsalicylic acid 150mg/kg

Anti-inflammatory effect of Zingiber officinale on carrageenan – induced inflammation in rats

Results in figure (3) shows no significant change in paw edema produced in paw of rats in (Zingiber officinale +carrageenan treated (groups at all tested times compared to the zero time. The data reveals no significant change in the edema on the paw of rats in (indomethacin+ carrageenan) treated groups at all tested times compared to the zero time. The data also shows a significant increase in the edema in the paw of rats in carrageenan treated group at all tested times compared to the zero time this change is significant ($p<0.05$) at 3 hours. The data reveals a significant reduction ($p<0.05$) in the edema produced in the paw of rats in (Zingiber officinale +carrageenan treated) groups at 3 hour and 5 hour, and there is a significant reduction ($p<0.05$) in the edema produced in the paw of rats in (indomethacin + carrageenan treated group) at 2, 3, 4 hours compared to (carrageenan treated) group at same time.

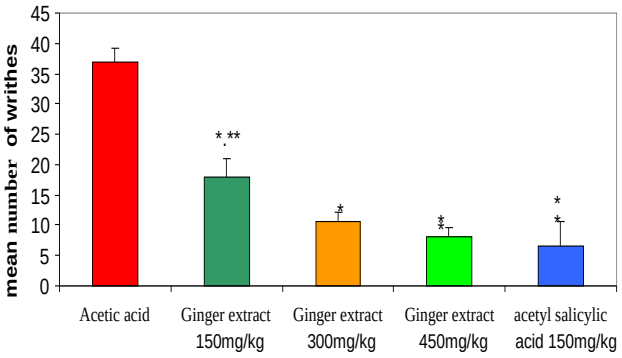

Figure 1: Effect of ginger extract on acetic acid – induced writhes in mice

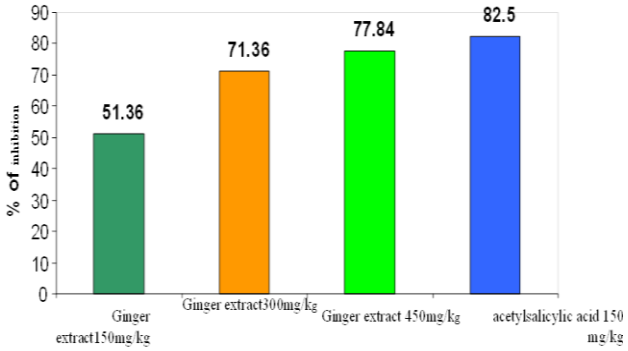

Figure2: Effect of ginger extract on acetic acid induced writhes in mice

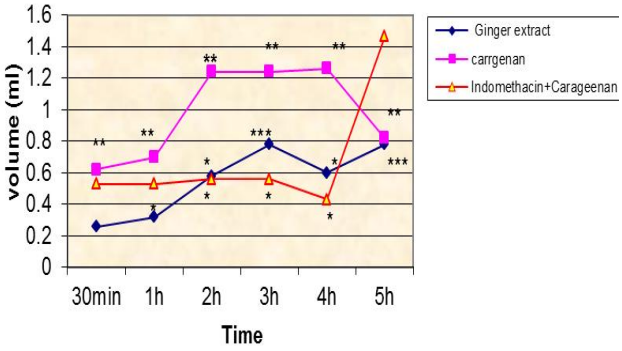

Figure 3: Anti-inflammatory effect of ginger extract on oedema on paw of rat induced by carrageenan

4. DISCUSSION

On the basis of the common uses of this plant in traditional folk medicine the analgesic effect of the rhizome extract of Zingiber officinal was evaluated using acetic acid- induced writhing in mice. The abdominal constriction response induced by acetic acid is a sensitive procedure to establish peripherally acting analgesia. This response is thought to involve local peritoneal receptors, the nociceptive activity of acetic acid- induced writhing is due to the release of tumor necrosis factor alpha (TNF- alpha), interleukin I beta and interleukin 8 by resident peritoneal macrophage and mast cells[8]. This is in accordance with previous studies[9] who demonstrated analgesic effect of Zingiber officinale extract by using acetic acid. Ginger extract in (150mg/kg, 300mg/kg, and 450mg/kg i.p) reduced the number of writhes induced by acetic acid and that the analgesic activity of the extract was increased in dose dependent pattern. methods in mice. Zingiber officinale extract (50- 800 mg/kg i.p) produced dose – dependent analgesic effect against chemically induced nociceptive pain in mice . Young in 2005 studied the analgesic activity of 6- gingerol[10], which is the pungent constituent of ginger. Intraperitoneal administration of 6 – gingerol (25mg/kg- 50mg/kg) produced an inhibition of acetic acid induced writhing response and formalin – induced licking in the late phase. Furthermore, Mahmmood et al, 2004 illustrated that methanol extract of rhizome of Curcuma xantorrhiza[11] (member of zingiberaceae family) showed significant analgesic activity at an oral dose of (300 mg/kg b.w) with 50.50% inhibition of acetic acid – induced writhing in mice. Whereas at a dose of (150mg/kg b.w), the extract showed moderate activity with 33.22% inhibition of acetic acid – induced writhing. The mechanism of analgesic effect of ginger is thought to be related to one of its constituents known as

shagoal. This substance has inhibitory effect on the release of substance p, a neurotransmitter that is used by sensory neurons involved in perception of intense pain[12]. Essential oils constituents such ass(-) – linalool antagonize different pain response elicited by exposure to a chemical stimulus such as acetic acid –induced writhing[13]. The present paper showed that hydroalcoholic extract of Zingiber officinale rhizomeat adose of 450mglkg (i.p) inhibited carrageenan – induced edema in rats. This is in agreement with previous studies[14] (Kottarapat et al, 2013). Who investigated the anti-inflammatory effect of Zingiber officinale essential oils in rats. In this study oral extract at 200mg/kg and 500mglkg reduced significantly the exudate volume. Many substance have been proposed as inflammatory mediator released locally at site of inflammation and having properties that cause or enhance the signs and symptoms of inflammation[15]. Carrageenan- induced edema is a biphasic response. The first phase is mediated through the release of histamine, serotonin and kinin whereas the second phase is related to the release of prostaglandin and slow reacting substance which peak at 3 hours. All mediator appear to be dependent upon an intact complement system for their activation and release[16]. It has been shown by Perper et al, 1974 That in the early phase of edema the predominant cells are polymorph nuclear whereas in advanced stages mononuclear cells predominant[17]. In further support of the present results a study was done in Mahhad University of medical science Iran by Hasssanbad et al, 2005[18]. For anti-inflammatory effect of aqueous extract of ginger root in diabetic mice . In this study addition of Zingiber officinale to drinking water reduced inflammation , she found that that anti-inflammatory effect of ginger was not dose related and oral consumption of ginger (200mg/100ml) is as effective as nitric acid synthase inhibitor.NG- nitro-arginine methyl ester hydrochloride. The mechanism of anti-inflammatory effect of ginger may be due to presence of gingerols, shogaols, and diarylheptanoide which may inhibit inflammatory prostaglandins. These substance are dual inhibitor of eicosanoid synthesis .Furthemore ginger extract and ibuprofen were significantly more effective than placebo in the symptomatic treatment of osteoarthritis. They concluded that ginger could be used as alternative to nonsteroidal anti-inflammatory drugs and as supplement drug in patients with osteoarthritis[19]. The anti-inflammatory effects of ginger essential oil were evaluated in streptococcal cell wall-induced rheumatoid arthritis model in female Lewis arthritis. Daily Intraperitoneal injection of 28 mg/kg ginger essential oil inhibited the chronic joint inflammation without any effects in initial acute phase of joint inflammation or granuloma formation at the site of streptococcal cell wall deposition in liver. Ginger essential oil acts as phytoestrogen without any in vivo effect on estrogen target organ[20].

5. CONCLUSION

Ginger is a perennial plant that grows in India, China, Mexico and several other countries. The rhizome is used as both spice and in herbal medicine and is common added to Food preparation. Carrageenan –induced rat paw edema is a valuable test used in predicting the value of anti-inflammatory agents acting by inhibiting the mediator s of acute inflammation and acetic acid is used as chemical substance for pain induction in mice .The present paper revealed that ginger extract has analgesic activity against acetic acid induced writhing in mice and anti-inflammatory action against carrageenan induced inflammation in rat.

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