IJPSR (2012), Vol. 3, Issue 11 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 27 July, 2012; received in revised form 17 September, 2012; accepted 21 October, 2012

TO ESTABLISH THE ULCEROGENIC POTENTIAL IF ANY, OF GINGER-JUICE *ZINGIBER OFFICINALE* ROSCOE (ZINGIBERACEAE) ON IMPORTANT PARAMETERS OF GASTRIC ULCERATION

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Keywords:
Ginger-juice, Total Acidity, Gastric volume, pH, Ulcerogenic, Ulcer index

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ABSTRACT

The aim of this study was to investigate the possibility of gastric-ulceration by ginger-juice (*Zingiber officinale* Roscoe) in rat. (A) Albino rats (n=6-12) were administered G.J at two doses (2ml & 4 ml/rat, p.o) as single administration and chronic treatment over period of 30 days. Following this assessment was done for possible gastric lesion. Effect of treatment with G.J acutely and chronically (30 days) administered, was assessed. Parameters used during assessment were total acidity, gastric volume & pH and ulcer index 'UI' (acute and chronic). Acute & chronic administration of G.J (2ml & 4ml/rat, p.o) caused an increase in pH and vol. of gastric content, a decrease in total acidity and no significant change in ulcer index.

INTRODUCTION: A Ginger is one of the most important and oldest spices, consisting of the prepared and sun-dried rhizomes of *Zingiber officinale* (Zingiberaceae). It is cultivated in many tropical countries. It is produced all over India from ancient times. It has a good commercial value and is claimed to have many medicinal uses. Because of differences in cultivation pattern, harvesting technique and climatic conditions it's commercial value differs and so also the medicinal actions and uses. It is referred by different names in the languages of different regions and countries.

It is widely consumed almost all over the world however in tropical countries or warm regions like Asia, it is more popular [1]. Because of its typical taste and a pleasant odor it's widely used as flavoring agent in numerous food recipes, beverages, pickles, many popular soft drinks etc [2].

From the ancient times it is included in many traditional medicinal systems for treatment of number of diseases. It is widely claimed as a Stomachic, aromatic, carminative, aphrodisiacs, diaphoretic, antiemetic, allergic rhinitis and gastric stimulant and for treating migrane headache. It is also used an antispastic against intestinal colic. Ginger oil is used in mouthwashes and liquors [3].

Many varieties of ginger are found such as processed, coated or unscraped, unbleached (natural) and bleached ginger having different types of active principles present in the ginger. Many scientists have investigated the ginger oil and found about 50 constituents, mainly aroma, Starch, Volatile oil, Zingiberene, Gingerol, Oleoresin (Gingerin), Zingiberol, Zingerone, Shagaol etc. The acetone extract of ginger contains Zingerberone and ether extract contain Zingerone (Pungent principles).

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IJPSR:
ICV (2011)- 5.07

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www.ijpsr.com

In view of the available literature, we have tried to screen some actions of ginger-juice; as crude form of ginger. We presume that crude form contains majority of active principles, may be in very low concentrations. Keeping in minded some of its potential therapeutic applications we have carried out animal experiments to investigate the effects of ginger-juice on gastric-ulceration.

Digestant: Langer et al., (1998) [4] have studied that ginger stimulates digestion. In ancient times ginger was used in gastro-intestinal problems (stimulation of digestion). Today it is used mainly to prevent the symptoms of travel sickness.

Phalphale et al., (1997) [5] have investigated the clinical efficacy of Ruchamax in treatment of anorexia in goats. Ruchamax is an herbal preparation that contains one of the main components of *Z. officinale*. It was given in a dose of 5 gm twice daily for 3 to 5 days. Appetite was restored in all goats between 3 and 7 days after treatment. The rumen motility increased from 1- 5 per 3 minute before treatment to 4-6 per minute. Total bacterial and protozoal counts increased after treatment. It is concluded that Ruchamax is an effective digestive stimulant.

Kalpana *et al.,* (1996) [6] have studied the possible influence of ginger on digestive enzymes of intestinal mucosa in female Wister rats. They proved that ginger prominently enhanced intestinal lipase, disaccharides, sucrase and maltase activity.

Masson *et al.,* (1994) [7] have studied the effect of salivary stimulant on rumen water kinetics, in vitro, fermentation rate and net growth of rumen microorganisms in buffaloes. A positive co-relation between increased rumen dilution rate and increased microbial growth has been demonstrated in ruminents. Osmotically active agents had been employed as means to increase rumen fluid dilution rate. Since, rumen liquid dilution rate is dependent on salivation. The effect of feeding *Z. officinale* (0.4 gm/kg) on rumen water kinetics and efficiency of microbial growth was studied in buffaloes. Ginger supplementation resulted in a significant increase in rumen fluid dilution rate and total rumen fluid outflow rate, with increased net growth of rumen microorganisms.

MATERIAL AND METHODS: The fresh ginger rhizomes were bought from local market of Surat, Gujarat.

Preparation of ginger-juice: The commercially available ginger was obtained from the local market. It was confirmed from the botanist that it was *Zingiber officinale*. The rhizome of ginger after cleaning and scrapping the superficial skin was cut into small pieces. With the help of mixer-grinder the pieces were made in to paste. The paste was taken on a white clean cloth and the liquid was squeezed out. The juice so obtained was used in the experiments. The stock of juice was kept in a refrigerator for maximum period of 15 days and the required quantity was used for the experiments after removing particulate matter from it.

500 gm ginger rhizomes yielded about 250ml juice.

The liquid portion which was obtained in the course of filtration looked like yellowish hazy opalescent liquid. It was administered orally in acute or chronic experiments. The doses were either 2 ml to 4 ml per rat.

To study the Ulcerogenic potential of ginger-Juice: The rats were divided into following groups, each group consisting of 6-12 animals.

Control groups: Two control groups were taken. One received the vehicle (2% suspension of gum acacia 2ml p.o) for 30 days and the second group received the vehicle (2% suspension of gum acacia 4ml p.o) for 30 days. They were sacrificed 6 hours after the last dose of vehicle.

Test groups: Two test groups were taken. One received 2ml ginger-juice orally for 30 days and the second group received the 4ml ginger-juice orally for 30 days. The animals kept fasting overnight on the last day of experiment were sacrificed after 6 hours of last dose of ginger-juice, by anaesthetizing with intra-peritonial injection of sodium pentobarbitone (50 mg/kg i.p).

The abdomen was opened with a vertical incision. The stomach was tied at both ends to allow the contents to remain inside. Then the stomach was removed. Subsequently the following parameters were assessed for each rat.

Measurement of the volume of gastric content: The stomach was opened along the greater curvature and the contents were scraped gently with the help of a blunt wooden spatula in to a measuring cylinder to measure the volume of the gastric contents. The measuring cylinder was a minimum graduation of 0.1ml.

Estimation of gastric pH: The stomach content was allowed to settle and the supernatant was decanted off in a clean container. The pH was measured by microprocessor based pocket size pH meter (pH scan-2, Eutech Cybernetics Pvt.Ltd., Singapore). The pH meter could measure the pH up to one decimal digit with ± 0.1 pH variation.

Estimation of Total Acidity: The estimation of total acidity was done by titration method. The gastric content was titrated against 0.01 N NaOH to pH 8.0, using the phenolphthalein as an indicator.

The gastric contents were centrifuged and the supernatant was taken in a clean test tube. To this, 0.02 ml of phenolphthalein was added with micropipette (Finpipette). Sodium hydroxide solution of the strength of 0.01 N was added drop by drop using glass pipette with minimum graduation 0.1 ml. The titration was considered completed as soon as the faint pink colour appeared.

[The amount of HCl was expressed in terms of milli equivalent per liter (m Eq/L)]

Measurement of Ulcer Index: The stomach was opened along with greater curvature and was averted. The specimen was kept in 2% formalin solution for ten minutes. It was then rinsed gently with distilled water and examined under a dissecting microscope (magnification 20X). The numbers of ulcers were counted and the size of each one was measured and a score was given according to the method described by Robert et al., (1979) [8] and was termed as the Ulcer Index (UI).

The ulcer index scoring was done as described below:

Score-0: No ulcer.	Score-3: Ulcer > 2mm < 4mm.
Score-1: Punctiform ulcer.	Score-4: Ulcer > 4mm
Score-2: Ulcer < 2mm.	

Each ulcer was scored separately and the ulcer index of the individual sample was determined by summing up the individual scores.

RESULT:

Gastric Ulceration:

Effect of ginger-juice on gastric ulceration:

1. To study the possible effect of ginger-juice on gastric ulceration, the following parameters were studied in each rat: (a) gastric pH (b) total gastric acidity (c) volume of gastric contents and (d) ulcer index. The values are expressed as mean ± standard error of mean (SEM). Ginger-juice administration was as per description in 'material and methods'. The comparison was done with the vehicle control group.

a. **Vehicle treated control group:** This group comprised of 10 rats, which received 2% suspension of gum acacia in distilled water. One milliliter of suspension was administered to each rat orally through gastric tube.

The mean pH in this group was 2.84±0.2 and mean total acidity was 85.5±3.84mEq/L. The volume of gastric content was 2.52 ml±0.18 and the mean ulcer index (UI) in the control group was 0.8±0.32 (**see table 1**). Such a low mean ulcer index indicates lack of ulcer.

TABLE 1: VALUE OF DIFFERENT GASTRIC PARAMETERS IN VEHICLE CONTROL GROUP

Parameter	Mean	SEM
PH	2.84	0.2
Total Acidity (mEq/L)	85.5	3.84
Volume (ml)	2.52	0.18
Ulcer Index	0.8	0.32

It shows the value of different parameters in the control group comprising of 10 rats, which received vehicle (1ml 2% gum acacia) by oral administration.

b. **Groups treated with ginger-juice (as chronic treatment):** Ginger-juice was administered orally in doses of 2ml/rat, p.o. (30days) and 4ml/rat, p.o. (30days), in groups comprising of 6 and 12 rats respectively. The effects of ginger-juice were seen on various parameters mentioned above. The results are showed in **table 2**.

TABLE 2: EFFECT OF CHRONIC TREATMENT WITH GINGER-JUICE ON PH, GASTRIC VOLUME, TOTAL ACIDITY AND ULCER INDEX IN RATS

Group	PH	TA (mEq/L)	Volume (ml)	UI
Control (vehicle) (n=10)	2.84±0.20	85.5±3.84	2.52±0.18	0.80±0.32
Ginger-juice (2ml/rat) (n=6)	5.21±0.14	51.60±2.11	5.55±0.20	0.00±0.00
Ginger-juice(4ml/rat) n=12)	5.31±0.16	51.69 ±2.13	5.51±0.22	0.00±0.00

It shows the effect of ginger-juice (2ml/rat, 30days, and (4ml/rat, 30days') on different parameters like pH, Total acidity, Volume of gastric content and Ulcer index in the rats. The statistical significance vis a vis the vehicle treated control is presented as *P<0.05 **P<0.01 ***P<0.001

Results indicate that administration of ginger-juice over period of 2ml/rat over period of 30 days as well as 4ml/rat for 30 days caused an increase in pH and volume of gastric content; decrease in total acidity and no significant change in ulcer index. This rule out the ulcerogenic potential of ginger-juice even in higher doses given in 'chronic form'.

DISCUSSION: Acute & chronic administration of G.J (2ml & 4ml/rat, p.o) caused an increase in pH and vol. of gastric content, a decrease in total acidity and no significant change in ulcer index. Ginger Juice in crude form rules out the ulcerogenic potential even for higher doses in 'Chronic form'. Oral administration of ginger-juice 2ml and 4ml for 30 days did not exhibit ulcerogenic potential. Ginger Juice in crude form rules out the ulcerogenic potential even for higher doses in Ginger-juice itself did not produce ulcer but rugosity of mucosa was increased as compared to control group.

With chronic treatment of ginger-juice for 30 days there was significant rise in pH,vol. of gastric content, significant fall in total acidity, and UI.

It remains to study about the exact mechanism of inhibition of acid secretion. As chronic study also exhibits the rise in pH, it appears that the neutralization of acid is ruled out. Reduction of gastric volume is suggestive of the inhibitory mechanism of secretary process. Possibility of anti-acetylcholine, antihistaminic and anti-proton pump cannot be ruled out presently.

Various authors have reported ulcer protection by acetone, ethanolic extract and active principles isolated, from ginger.

Yamahara et al., (1998); Sertie et al., (1992) [9] [10] have shown ulcer protection by acetone and ethanolic extract, active principles Zingiberene (terpenoid) and 6-Gingerol (the pungent principle), 6-Gingesulfonic acid and 6-Shagoal are other active principles shown to have ulcer protective effect [11] [12], however have shown ulcer protection by crude drug. It is noted that the mucosal damaged induced by 70% ethanol and the mucin content of the deep mucosa was reduced. Zingiber officinale rhizome protected the ulcer by action at this level. Goso et al., (1996) [12] also reported that pretreatment of *Zingiber officinale* rhizome increased the gastric mucin.

Our result and that of Goso suggest that ginger does contain certain active principles, which are orally bio-available from crude preparation. This is ulcer protective. This may not produce gastric lesion.

CONCLUSION: Acute & chronic administration of G.J (2ml & 4ml/rat, p.o) caused an increase in pH and vol. of gastric content, a decrease in total acidity and no significant change in ulcer index. Ginger Juice in crude form rules out the ulcerogenic potential even for higher doses in 'chronic form'.

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How to cite this article:
Prasad SS, Sinha A, Patel K, Dumatar C, Vajpeyee SK and Bhavsar VH: To establish the Ulcerogenic Potential if any, of Ginger-Juice *Zingiber officinale* Roscoe (Zingiberaceae) on important parameters of Gastric Ulceration. *Int J Pharm Sci Res*. 3(11); 4472-4476.