

EFFECTS OF CURCUMIN ON THE GASTRIC EMPTYING OF ALBINO RATS

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Abstract : Curcumin (diferuloylmethane), a polyphenol, is an active principle of the perennial herb *Curcuma longa* commonly known as turmeric. Turmeric (*CURCUMA LONGA* L.) is a medicinal plant extensively used in Ayurveda, Unani, and Siddha medicine as a home remedy for various diseases including biliary diseases, cough, hepatic diseases, wound healing. However studies on the effect of curcumin on the gastric emptying are nearly nonexistent. It is hypothesized that curcumin may have an effect on gastric emptying. For this reason the present study was aimed to study the effect of curcumin on gastric emptying. Rats were divided into 5 groups (Group I – Group V), based on the time interval between administration of curcumin/vehicular fluid to administration of barium sulphate (Group I – 1 hr, Group II – 8 hrs, Group III – 16 hrs, Group IV – 24 hrs, Group V – 48 hrs). Each group was further divided into two sub-groups, Group A (control) and Group B (experimental), containing 6 rats each. Rats in experimental group were administered curcumin intragastrically, in the dose of 1 gm/kg body weight, suspended in normal saline (0.9% NaCl). The controls were given vehicular fluid intragastrically, in volume equal to the experimental animals. It was observed that there was a decrease in the gastric emptying in all the experimental groups.

Key words : gastric emptying curcumin barium sulphate

INTRODUCTION

Medicines derived from plants have played a pivotal role in the health care of

many cultures, both ancient and modern. The Indian system of holistic medicine known as Ayurveda uses mainly plant-based drugs or formulations to treat various ailments

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including cancer. Of the approximately 877 small molecule drugs introduced worldwide between 1981 and 2002, most (61%) can be traced back to their origins in natural products (1-4).

Curcumin (diferuloylmethane), a polyphenol, is an active principle of the perennial herb *Curcuma longa* commonly known as turmeric. TURMERIC (*CURCUMA LONGA L.*) is a medicinal plant extensively used in Ayurveda, Unani, and Siddha medicine as a home remedy for various diseases. For that reason a number of references to the plant are found in classical ayurvedic text such as Charaka Samhita, Sushuruta Samhita, Ashtanga Hridya and Sharangdhar Samhita. These texts described the use of turmeric for a number of disorders pertaining to many systems including abdominal pain, joint pain, swelling and snake bite etc (5-7).

Studies, in the human being and in the experimental animals have shown the beneficial effect of curcumin on the function of gastrointestinal tract. It increases bile secretion in anesthetized dogs and rats. It elevates the activity of pancreatic lipase, amylase, trypsin and chymotropism. Sodium curcuminat inhibit castor oil induced diarrhoea suggesting action of drug on the smooth muscle cells of gastrointestinal tract (8-12). However studies on the effect of curcumin on the gastric emptying are nearly nonexistent. It is hypothesized that curcumin may have an effect on gastric emptying. For this reason the present study was aimed to study the effect of curcumin on gastric emptying.

MATERIALS AND METHODS

Experimental animals

Albino rats of wistar strain, weighing 130-170 gm, of either sex, raised under standard laboratory conditions were obtained from Indian Veterinary research institute, Izat Nagar, Bareilly, Uttar Pradesh. The animals were housed in polycarbonate cages of size 35 cm × 23 cm × 16 cm. Four rats per cage were kept. The animals were fed cooked food ad libitum with free access to water. All experiments in rats were carried out in accordance with the recommendation of guidelines for care and use of laboratory animals approved by Institutional Animal Ethics Committee.

Drugs curcumin

Curcumin was obtained in the form of capsule containing 500 mg of curcumin from INDSAFF, Batala. Curcumin (diferuloylmethane), a polyphenol, is an active principle of the perennial herb *Curcuma longa* commonly known as turmeric. The yellow-pigmented fraction of turmeric contains curcuminoids, which are chemically related to its principal ingredient, curcumin. The major curcuminoids present in turmeric are demethoxycurcumin (curcumin II), bisdemethoxy-curcumin (curcumin III), and the recently identified cyclocurcumin. The major components of Commercial curcumin are curcumin I (77%), curcumin II (17%), and curcumin III (3%) (1).

Dosage

Dose of curcumin was calculated as per

1 gm/kg body weight (13). The capsule containing 500 mg of curcumin was dissolved in normal saline (0.9% NaCl) to make 5 ml suspension of the drug, so that each ml of the suspension consists of 100 mg of curcumin.

Barium sulphate

Barium sulphate (Trade name- microbar-HD manufactured by Eskay Fine chemicals) purchased from medical store.

Weighing scale

Electronic weighing scale ACE-1000 was used to weigh the gastric content. This scale can measure up to 0.1 gm accurately.

Hot air oven

Used to dry up the washed out gastric content at 70°C–75°C for 8 hours.

Acute toxicity study

Six rats were taken for acute toxic effect of curcumin. The animals were fasted overnight and the curcumin was administered intragastric in the dose of 2 gm/kg body weight. Animals were observed continuously for first 3 hrs and were monitored for three days for mortality and general behavior of animals, signs of discomfort and nervous manifestations. No mortality and adverse effects were observed with this dose.

Gastric emptying study

Sixty rats were divided into 5 groups

(Group I – Group V), based on the time interval between administration of curcumin/vehicular fluid to administration of barium sulphate (Group I – 1 hr, Group II – 8 hrs, Group III – 16 hrs, Group IV – 24 hrs, Group V – 48 hrs). Each group was further divided into two sub-groups, Group A (control) and Group B (experimental), containing 6 rats each. Rats in Group B were administered curcumin intragastrically by the naso-gastric tube reaching up to the lower 1/3rd of esophagus, in the dose of 1 gm/kg body weight, suspended in normal saline while rats in Group A were given vehicular fluid (0.9% NaCl) in equal volume as that of curcumin suspension given to experimental group.

After requisite time as per Group I–Group V, in both, Group A and Group B, rats were administered 4 ml of barium sulphate suspension containing 3.2 gm of barium sulphate in isotonic saline, through a naso-gastric tube reaching up to lower third of the esophagus. 30 min after barium sulphate administration the animals were sacrificed by cervical dislocation. Abdomen was opened by midline incision and ligatures were applied at the oesophagogastric junction and gastroduodenal junction. The stomach was striped out carefully.

The stomach was cut open and washed for its luminal contents into a beaker with normal saline (0.9% w/v) till no barium particles can be visualized under mucosal surface. The stomach washing was centrifuged at 3000 rpm for 5 min in a clinical centrifuge. The sediments were dried in hot air oven (70°C–75°C) for 8 hours. The total weight of luminal contents was measured with electronic balance.

Statistical analysis

Mean and standard error of all the observations were calculated and comparisons were done between experimental and control groups by applying Student's t test (unpaired). Comparisons of the effect of curcumin on the gastric emptying among different experimental groups were done applying one way ANOVA.

RESULTS

After the intra-gastric administration of single dose of curcumin, there was decrease in gastric emptying in all the experimental groups as compared to control groups. On applying Student's t test, decrease in gastric emptying in Group I to Group III was statistically significant, while in Group IV and Group V it was statistically insignificant as compared to control groups. On applying one way ANOVA between different experimental groups, there was statistically

significant decrease in gastric emptying in Group I as compared to other Groups. While comparing Group II and Group III with Group IV and Group V, there was statistically significant decrease in gastric emptying as compared to Group V. However the difference among Group IV and Group V was statistically insignificant (Table I).

DISCUSSION

The results of the present study revealed that there was delay in gastric emptying following intragastric administration of curcumin. Limited information exists about the mechanism by which curcumin delays gastric emptying. Gastric emptying is dependent on the organization of motor activity in the proximal stomach, antrum pylorus and duodenum (14-16). The delivery of nutrients from stomach to small intestine is closely regulated, largely as the result of feedback from chemoreceptors and mechanoreceptors (17). It has been demonstrated that vagal stimulation increases the release of nitric oxide (NO) from the gastric myenteric plexus, which mediates nonadrenergic, noncholinergic (NANC) relaxations and accommodation reflex of the stomach (18, 19). NO synthase inhibitors given i.v. at doses that inhibit NO synthase, delay gastric emptying through mechanisms which are unrelated to changes in arterial blood pressure (20).

In animal studies inhibition of NO synthase is associated with suppression of proximal gastric relaxation, stimulation of antral, pyloric and duodenal motility and slowing of gastric emptying (21-26). Chan MM et al. reported that curcumin inhibits nitric oxide synthesis by inhibiting nitric oxide

TABLE I: Comparisons of effect of curcumin on gastric residue (Mean±SE) following intragastric administration of single dose of curcumin (1 gm/kg body wt) in different groups.

Groups	% portion of barium sulphate recorded in stomach		P value
	Control (n=6)	Experiment (n=6)	
Group I	23.60±3.837	59.38±3.608	<0.0001
Group II	24.14±3.754	46.88±2.282 [#]	0.0005
Group III	23.83±3.894	40.63±1.398 ^{###}	0.0019
Group IV	23.44±3.904	31.25±1.745 ^{###}	0.0976
Group V	23.72±4.394	23.44±2.387 ^{###,***,^^^}	0.956

Comparison of control with experimental group was done by t test and inter-groups (I-V) comparison among experimental group was done by one-way ANOVA. # mark represents comparison with group I, * mark represents comparison with group II and ^ mark represents comparison with group III ^,*,#<0.05; ^^,*,#<0.01; ^^^,***,###<0.001.

synthase gene expression (27). Sreejayan N, Rao MNA reported that curcumin has nitric oxide scavenging property (28).

The delayed gastric emptying as observed in our study could be explained by the NOS inhibitory action (27) and scavenging property (28) of curcumin, however other mechanisms may also be involved. Further experimental work needs to be done to establish its mechanisms of its action.

In conclusions present study suggests that curcumin delays gastric emptying. It

may be used as an adjuvant for treatment of diseases in which gastric emptying is increased such as Zollinger-Ellison syndrome.

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