SHORT COMMUNICATION

EFFECTS OF CURCUMIN ON THE INTESTINAL MOTILITY OF ALBINO RATS

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Abstract: Curcumin has been used in traditional medicine as a household remedy for various diseases including biliary diseases, cough, hepatic diseases, wound healing. For past few decades, extensive work has been done on biological activities of curcumin. This study was carried out to provide scientific basis for the use of curcumin in gastrointestinal disorders. Animals 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 A were given vehicular fluid (0.9% NaCl) while the rats in Group B were administered curcumin intra-gastrically 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. After the intra-gastric administration of single dose of curcumin, there was decrease in length of small intestine traversed by BaSO₄ in all the experimental groups as compared to control groups. These data suggests that curcumin decreases intestinal motility in albino rats, and this may partly explain the traditional use of curcumin in different disorders like diarrhea, abdominal cramps and irritable bowel syndrome.

Key words: curcumin intestinal motility

INTRODUCTION

India has a rich history of using plants for medicinal purposes. Worldwide interest in natural products as preventive and therapeutic agents has led to a greater appreciation of the rich heritage of traditional system of medicine. Turmeric (Curcuma longa L) is a medicinal plant extensively used in Ayurveda, Unani and Siddha medicine as home remedy for various diseases. Curcuma longa L, botanically
related to ginger family, is perennial plant having a short stem with pyriform rhizomes. Curcumin, the main yellow bioactive component of turmeric has been shown to have a wide spectrum of biological actions. Apart from its daily use in the kitchen as condiment and spice, curcumin has been used in cough, fever, liver diseases, wound healing and inflammatory conditions of joints (1-8). Recent studies, in the human beings and the experimental animals have shown the beneficial effect of curcumin on the function of the gastrointestinal tract. It increases bile secretion in the anesthetized dogs and rats (9). It elevates the activity of pancreatic lipase, amylase, trypsin and chymotrypsin (10). Sodium curcuminate inhibit castor oil induced diarrhoea suggesting action of drug on the smooth muscle cells of gastrointestinal tract (11). However, studies on the effect of curcumin on the gastrointestinal tract motility are nearly nonexistent. For this reason the present study was aimed to study the effect of curcumin on the motility function of gastrointestinal tract in albino rat.

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, Barellie, 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%) (12).

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 5ml suspension of the drug, so that each ml of the suspension consist of 100 mg of curcumin.

Barium sulphate

Barium sulphate (Trade name–Microbar–HD manufactured by Eskay Fine Chemicals) was purchase from local medical store.

Measurement of intestinal length

A metal meter scale fitted on hard board was used to measure the length of intestine and distance traveled by the barium.
Acute toxicity study

Six rats were taken to study the acute toxic effect of curcumin. The rats were fasted overnight and the curcumin was administered intragastric in the dose of 2 gm/kg body weight. Rats were observed continuously for first 3 hr 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.

Motility 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 intra-gastrically 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 gastroduodenal junction and ileocecal junction. The small intestine was stripped of the mesentery and taken out of the abdomen and laid over a board fitted with a meter scale. The upper surface of board was kept continuously wet with normal saline. The length of the intestine was measured by placing it closely along the meter scale. The position of the barium head was located and measured from the point of gastroduodenal junction. To ascertain accurately the position of barium head, the intestine was cut open along its length. The position of barium head was visualized.

Statistical analysis

Mean and SE 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 intestinal motility among different experimental groups were done using one-way ANOVA.

RESULTS

After the intra-gastric administration of single dose of curcumin, there was decrease in length of small intestine traversed by BaSO₄ in all the experimental groups as compared to control groups. The decrease in intestinal motility was maximum one hour after curcumin administration. On applying Student t test, decrease in length of small intestine traversed by BaSO₄ 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 intestinal motility in Group I to Group III as compared to Group IV and Group V (Table I).
TABLE I: Comparisons of effect of curcumin on intestinal motility (Mean±SE) following intragastric administration of single dose of curcumin (1gm/Kg body wt) in different groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>% length of small intestine traversed by BaSO4 (n=6)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>81.14±1.237</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Group I</td>
<td>82.48±2.739</td>
<td>0.048</td>
</tr>
<tr>
<td>Group II</td>
<td>82.37±3.249</td>
<td>0.017</td>
</tr>
<tr>
<td>Group III</td>
<td>81.68±1.453</td>
<td>0.152</td>
</tr>
<tr>
<td>Group IV</td>
<td>84.50±1.784</td>
<td>0.448</td>
</tr>
</tbody>
</table>

Comparison with control was done by t test and inter-group comparison was done by one-way ANOVA. * mark represents comparison with group I, II and III; † mark represents comparison with group IV. ** <0.01; *** <0.001; †<0.05.

DISCUSSION

In the present study, curcumin was found to have an inhibitory effect on intestinal motility. Srinivasan (14) showed the spasmolytic activity of curcumin. Huang et al (15) found that sodium curcuminate antagonized the contractions of guinea pig ileum induced by various agonists. It was more active against nicotine-induced contraction on isolated guinea pig ileum (15). Makhlouf (16) found that contraction of all smooth muscles, including those of gastrointestinal tract, absolutely depends on the presence of Ca++. Agonists – induced contraction may be related to the release of intracellular Ca++ from the sarcoplasmic stores in addition to its influx mainly through L-type Ca++ channels from extracellular fluid. Consequently, smooth muscle contraction can be abolished by antispasmodic drugs through the inhibition of Ca++ and its entry or release into the cell (16).

Turmeric is well known universally for its culinary and medicinal properties. In line with its potential as a gastrointestinal relaxant, Gilani et al (17) tested its crude extract in isolated rabbit’s jejunum and found it to decrease the spontaneous rhythmicity of jejunum. Later Gilani et al (17) found that the crude extract of turmeric even relaxed the potassium induced contractions in isolated rabbit jejunum; relaxation was mediated through the blockade of Ca++ influx (18). Bolton (19) concluded that the contraction caused by high dose of K+ (>30 mM) are dependent on the entry of Ca++ into the cells through the voltage dependent channels (VDC). Godfraind et al (20) concluded that a substance which can inhibit K+ induced contraction is considered to be a calcium channel blocker. Thus, inhibition of high K+ induced contraction of rabbit jejunum by turmeric extract may reflect the restricted Ca++ entry via VDCs (20). Hamilton et al (21) and Dyer et al (22) described curcumin as a Ca++ antagonist. Gnanasekar N, Perianayagam J.B. (11), demonstrated that sodium salt of curcumin significantly inhibit castor oil induced diarrhea. Bennett et al (23) in their study, concluded that prostaglandins might be involved in contractions mediated by cholinergic nerves by increasing the response to released acetylcholine. Prostaglandins might modulate responsiveness to other stimuli since they also reverse the inhibition of histamine-induced ileal contractions by NSAID. Eckenfels Vane (24) observed that following pretreatment of the guinea-pig colon with Indomethacin, the initial contractor effect of histamine was unaffected but the contraction was not maintained unless Prostaglandin E2 was added.

Curcumin since is known to decrease prostaglandin synthesis. The present finding of decrease in intestinal motility following curcumin administration can be related to the above mentioned mechanisms i.e. its
calcium antagonist action and inhibition of prostaglandins synthesis.

Conclusions
Curcumin decreases intestinal motility probably through multiple modes of actions. It may be used as an adjuvant for the treatment of abdominal cramps, diarrhea, and irritable bowel syndrome.

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REFERENCES