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COMPARATIVE EFFECTS OF PLANT EXTRACT ON GASTRIC SECRETION

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ABSTRACT

OBJECTIVE: To compare the effects of extracts from medicinal plants Ammi Visnaga & Olea eurpea on Volume and acidity of stimulated gastric secretion in rabbits.

METHODS: The present study was carried out in department of Pharmacology & therapeutics, Saidu Medical College Swat Pakistan between July 2008 to June 2009. Thirty rabbits weighing 1-1.5kg were included. They were divided in to groups A, B &C each having 10 animals. After fasting for 48 hours, pylorus of each animal was ligated. To group A Carbachol, group B extracts of Ammi visnaga and group C Olea europea followed by Carbachol after 15 minutes to groups B & C were administered intraperitoneally. After 4 hours, stomach was removed, volume was measured, contents centrifuged & estimation for acidity was done by method of titration. Data was subjected to statistical analysis.

RESULTS: In groups B & C, reduction in volume, free and total acidity of gastric juice was observed. All these reductions were found statistically highly significant when their means were compared with that of group A ($P<0.001$).

CONCLUSION: Extracts can be used effectively in the treatment of hyper acidity conditions and peptic ulcer after evaluation of their effects in human being.

KEY WORDS: Ammi Visnaga, Olea Europea, gastric acid secretion.

INTRODUCTION

Peptic ulcer is one of the most common ailments, with which a physician comes across in the clinical practice. Increased acid production from gastric mucosa is responsible for peptic ulceration in majority of the patients. Ulcers are not found in ahlorhydric patients and almost always occur in patients with Zollinger- Ellison (Z.E) syndrome which is characterized by very high acid secretion[1]. Inhibition of over production of gastric acid is a desirable therapeutic goal in the treatment of peptic ulcer. It has been documented that 38 medicinal plants including fruits of Ammi visnaga and leaves of Olea europea contain natural calcium channel blocker[2] In a study with the help of spectrophotometer and high performance liquid chromatography (HPLC), it was observed that Khelin and visnagin are present in the fruit of Ammi visnaga[3]. Khellin and visnagin were identified from Ammi visnaga fruit and were proved that all of them have calcium channel blocking mode of action[4]. Methanol extract from the fruit of Ammi visnaga showed significant calcium channel blocking activity[5]. Ammi has nematocidal activity against nematodes[6]. It has also insecticidal and repellant activity[7]. In an experiment it was observed that Ammi has bactericidal activity against fifty five micro-organism except pseudomonas aerugenosa[8]. Visnagin which is found in fruit of Ammi visnaga causes vasodilatation and reduces blood pressure by inhibiting calcium ion influx into the cell. It has also anti-inflammatory effect in microglial cells[9,10]. Thirty percent ethanol extract from the leaves of Olea europea has significant calcium channel blocking activity[1].

Induction of hypercalcaemia through intravenous administration of calcium is usually associated with increased gastric volume and acidity[12,13]. The acid stimulating ability of calcium; is well known and there is extreme sensitivity to calcium in patients with Z.E. syndrome[14,15]. Histamine release from peritoneal mast cells is critically dependent

upon extracellular Ca^{++} concentration, so non-availability of Ca^{++} may cause reduced effects of histamine on acid production in the stomach. Calcium channel blockers have been mainly used in cardiovascular system as inhibitors of muscle contraction. In the stomach, motility and acid secretion have been shown to be dependent upon calcium ions. The aim of this study was to evaluate & compare the effects of extract from the fruits of Ammi visnaga and leaves of Olea europea on volume and acidity of Carbachol induced gastric secretion.

MATERIALS AND METHODS.

It was Quasi experimental.

It was conducted in Pharmacology department Saidu Medical College Swat Pakistan between September 2008 and June 2009 and was approved by ethical committee. Thirty rabbits of local breed were selected for the present study. Healthy animals of both sexes weighing 1-1.5kg were used in the study. All the animals were kept fasting for 48 hours with free availability of water before they were subjected to experimental procedure. The animals were divided into 3 groups each containing 10 animals. Group A was Carbachol treated, Group B was Ammi vinaga + Carbachol treated and Group C. was Olea europea+Carbachol treated.

The operative procedure was the one adopted by Vischer et al[16]. Animals were anaesthetized with ether, abdomen was opened and pylorus was ligated with silk suture. Then abdominal wall was closed with suture clamps and intraperitoneal (I.P) injection of Carbachol 600µg/Kg body weight were administered to group A, 500mg/Kg body weight of Ammi visnaga to group B and 500 mg/Kg body weight of Olea europea to group C, followed by Carbachol 600µg/Kg body weight after 15 minutes to group B and C. The rabbits were deprived of water for four hours after administration of drugs. Then the rabbits were sacrificed, the thorax and abdomen were opened, oesophagus was ligated and the stomach was removed quickly. The contents of the stomach were collected. The volume of gastric juice was measured. Then the contents were centrifuged, filtered and subjected to titration for estimation of free and total acidity by the method described by Varley (1962)[17]. One ml of centrifuged and filtered gastric secretion was titrated against 0.1 N Na OH using Topfer,s reagent as an indicator for determination of free acidity and 1% phenolphthalein as an indicator for combined acidity. The sum of the two titrations was total acidity. The data was analyzed statistically using student "t" test.

RESULTS

The mean values of volume, free acidity, total acidity of gastric secretion in group A (Carbachol treated group) and group B (Ammi visnaga + Carbachol treated) were compared. There was reduction in the mean values of all the parameters mentioned above. These reductions were found to be statistically highly significant. ($P<0.001$). A similar reduction was observed when we compared means values of volume, free acidity and total acidity of gastric secretion in group A (Carbachol treated group) and group C (Olea europea+Carbachol treated) group. These reductions were also found to be statistically highly significant ($P<0.001$). All these values and changes are shown in Table 1.

When we compared the mean values of volume, free and total acidity for Ammi visnaga + Carbachol and Olea europea+Carbachol treated groups, it was observed that these differences in all the three parameters between groups B and C were non significant ($P> 0.5$). All these values and changes are shown in Table 2.

TABLE I

Comparison between the effects of extract from Ammi visnaga and Olea europea on volume and acidity of Carbachol stimulated gastric secretion in fasting rabbits.

Drug	Volume of gastric secretion(ml)	Acidity (m.Eq./dl of gastric secretion)	
		Free	Total
Carbachol	28.7±0.650 (10)	6.39±0.408 (10)	7.64±0.408 (10)
Ammi visnaga + Carbachol	13.8 ±0.578 (10)	2.41±0.216 (10)	3.57±0.276 (10)
P. Values *	<0.001	<0.001	<0.001
Olea europea +Carbachol	16. 5±0.763 (10)	3.15±0.375 (10)	4.02±0.353 (10)
P.Values **	<0.001	<0.001	<0.001

Each value represents mean of total observations

Figures in parenthesis indicate the number of animals in each group

± Indicates standard error of mean

P. values when compared with Carbachol

* P value between Carbachol & Ammi visnaga +Carbachol

** P value between Carbachol & Olea europea +Carbachol

TABLE 2

Differences between the effects of extracts from Ammi visnaga and Olea europea on volume and acidity of Carbachol induced gastric secretion in rabbits.

Drug	Volume of gastric secretion(ml)	Acidity (m Eq./dl of gastric secretion) Free	Total
Ammi visnaga + Carbachol	13.8 ±0.578 (10)	2.41±0.216 (10)	3.57±0.276 (10)
Olea europea +Carbachol	16. 5±0.763 (10)	3.15±0.375 (10)	4.02±0.353 (10)
P value	>0.05	>0.05	>0.05

Each value represents mean of total observations
Figures in parenthesis indicate the number of animals in each group
± Indicates standard error of mean
P. values when compared with Carbachol.

DISCUSSION

Acid secretion in the stomach is controlled at a different levels by neural, hormonal and paracrine mechanisms. When these regulatory mechanisms malfunction, acid and pepsin autodiagest the mucosa resulting in the ulceration of oesophagus, stomach and duodenum[18]. Histamine, acetylcholine or Carbachol are potent secretogogues for the parietal cells of gastric mucosa leading to the production of Hcl[19].

Acetylcholine and gastrin act through calcium ions. Carbachol being a cholinomimetic drug increases free intracellular calcium ions which, in turn activate protein kinase by phosphorylation and lead to increased production of gastric acid. In this study we observed that Ammi visnaga reduced the volume free acidity and total acidity. All these reductions were statistically highly significant when compared with the mean values in Carbachol treated group. Similar reductions were also observed by Olea europea in all the parameters.

Our study is in consistent with other workers who concluded that calcium channel blocker Verapamil significantly reduces gastric acid secretion[20,21]. Similarly our study is also in agreement with the animal study of Jan et al by observing that Verapamil significantly reduced gastric acid secretion[22]. Both the extracts containing natural calcium channel blockers inhibit the calcium ions influx, which may be responsible for the observed reductions in volume and acidity of gastric secretion. Besides, calcium channel blockers inhibit lipoxygenase pathway during metabolism of arachidonic acid. So leukotriene, the injurous substance is not formed and all the arachidonic acid is metabolized through cyclooxygenase pathway. This will lead to the production of prostaglandin which couples with Gi protein and inhibits adenyl cyclase and thus decrease HCl production[23].

Release of histamine from mast cells is critically dependent on extracellular calcium ions, so by blocking calcium ions, can block histamine release which is a potent agent for HCl secretion[24].

When we compared the differences in the mean values of volume, free acidity and total acidity by Ammi visnaga and Olea europea, the changes were found non significant. This indicates that both the extracts can effectively reduce gastric secretion. Calcium channel blockers are also used in controlling contraction of cardiovascular smooth muscles[25], allergic reaction[26] and prevention of premature labor[27]. All these actions are due to the calcium channels blocking activity.

It is concluded that this extract may be beneficially used in hyper acid secretary conditions and peptic ulcer. Further studies in this regard for evaluation of these effects are suggested in human subjects.

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