COMPARISON BETWEEN THE EFFECTS OF EXTRACT FROM MEDICINAL PLANT "AMMI VISNAGA AND MYRISTICA FRAGRANS" ON THE VOLUME AND ACIDITY OF CARBACHOL INDUCED GASTRIC SECRETION IN FASTING RABBITS.

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ABSTRACT

BACKGROUND: Peptic ulcer is mostly produced due to the over production of gastric acid. This study was undertaken to find out the effects of extract from the fruits of medicinal plant Ammi visnaga and seeds of Myristica fragrans (both of which contain documented natural Calcium channel blockers) on volume and acidity of Carbachol induced gastric section. Their effects were also compared to find out any difference in their effect.

DESIGN: Quasi experimental.

PLACE & DURATION OF STUDY: Pharmacology Department Saidu Medical College Swat.

METHODS: Thirty rabbits of local breed, weighing 1-1.5kg were used. The animals were kept on fasting for 48 hours, after which the pylorus of each animal was ligated. Carbachol 600µg/kg was injected to group A Extracts of Ammi visnaga and Myristica fragrans 500 mg/kg body weight each and after 15 minutes Carbachol 600µg/kg body weight was administered to group B & C intraperitoneally.

RESULTS: It was found that both the extracts reduced the volume, free and total acidity of gastric secretion, which were statistically highly significant when compared with Carbachol ($P < 0.001$). When the differences of means for both the extracts were compared, all these were found statistically non significant indicating that the extracts have similar effects on all parameters included in study.

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

KEY WORDS: Ammi visnaga & Myristica fragrans, gastric secretion.

INTRODUCTION:

Peptic ulcer is a common disease of the upper gastro-intestinal tract occurring in about 5-10 % of the world's population. The etiology of the disease appears to be multifactorial.

Increased acid production from gastric mucosa is responsible for peptic ulceration in majority of the patients. Ulcers are not found in ahlorhydic 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 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 seeds of Myristica fragrans have

natural calcium channel blocker². Khellin and visnagin were identified from Ammi visnaga fruit and were proved that all of them have calcium channel blocking mode of action³. Methanol extract from the fruit of Ammi visnaga showed significant calcium channel blocking activity⁴. In a study with the help of spectrophotometer and high performance liquid chromatography (HPLC) it was observed that Khellin and visnagin are present in the fruits of Ammi visnaga⁵. In another study it was observed that extract from the seeds of Myristica fragrans showed significant calcium channel blocking activity⁶. The calcium channel blocking agents like Verapamil, nifedipine and diltiazem are commonly used in the treatment of hypertension, angina myocardial infarction and

supraventricular tachycardia⁷. Induction of hypercalcaemia through intravenous administration of calcium, is usually associated with increased gastric volume and acidity.^{8,9} The acid stimulating ability of calcium is well known and there is extreme sensitivity to calcium in patients with Z.E. syndrome.^{10,11} 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. So this study was planned to evaluate the effects of extract from the fruits of *Ammi visnaga* and seeds of *Myristica fragrans* on the volume and acidity of Carbachol induced gastric secretion. Their effects were also compared on these parameters.

MATERIALS AND METHODS

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 visnaga* + Carbachol treated and Group C. was *Myristica fragrans* + Carbachol treated.

The operative procedure was the one adopted by Vischer et al.(1954)¹². 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 600 μg /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 *Myristica fragrans* to group C, followed by Carbachol 600 μg /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)¹³. One ml of centrifuged and filtered gastric secretion was titrated against 0.1 N NaOH using Topfer's reagent for determination of free acidity and 1% phenolphthalein as indicator for combined acidity. The sum of the two titrations was total acidity. The data was analyzed statistically using student "t" test.

RESULTS

The volume, free acidity and total acidity of gastric secretion in group A (Carbachol treated group) was $28.7 \pm 0.650\text{ml}$, $6.39 \pm 0.408\text{ m.Eq./dl}$ and $7.64 \pm 0.408\text{ m.Eq./dl}$ respectively. Similarly the volume, free acidity and total acidity in group B (*Ammi visnaga* Carbachol treated) was $13.8 \pm 0.578\text{ml}$, $2.41 \pm 0.216\text{m.Eq./dl}$ and $3.57 \pm 0.276\text{ m.Eq./dl}$ respectively. The volume, free acidity and total acidity in group C (*Myristica fragrans* and Carbachol treated) was $15.3 \pm 0.597\text{ml}$, $2.9 \pm 0.331\text{m.Eq./dl}$ and $3.86 \pm 0.426\text{m.Eq./dl}$ respectively. These reductions noticed in all the parameters were found to be statistically highly significant when compared with Carbachol group ($P < 0.001$). All these changes are shown in Table 1.

TABLE I

Comparison between the effects of extract from *Ammi visnaga* and *Myristica fragrans* 500mg/kg each on volume and acidity of Carbachol 600 μg /kg bodyweight induced 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)
<i>Ammi visnaga</i> + Carbachol	13.8 ± 0.578 (10)	2.41 ± 0.216 (10)	3.57 ± 0.276 (10)

P. Values	<0.001	<0.001	<0.001
Myristica fragrans +Carbachol	15.3±0.597 (10)	2.9±0.331 (10)	3.86±0.42 6 (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

P. values when compared with Carbachol.

When we compared the mean values of volume, free and total acidity for Ammi visnaga and Myristica fragrans, it was observed that these differences in all the three parameters between groups B and C were found to be non significant. All these changes are shown in Table 2.

TABLE 2

Differences between the effects of extracts from Ammi visnaga and Myristica fragrans 500mg/kg each on volume and acidity of Carbachol 600µg/kg body weight 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±0.21 6 (10)	3.57±0.276 (10)
Myristica fragrans +Carbachol	15.3±0.597 (10)	2.9±0.331 (10)	3.86±0.426 (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

P. values when compared with Carbachol.

DISCUSSION.

Acid secretion in the stomach is controlled at a variety of 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 duodenum¹⁴.

Histamine, acetylcholine or Carbachol are potent secretagogues for the parietal cells of gastric mucosa leading to the production of HCl¹⁵.

Acetylcholine and gastrin act through calcium ions. Carbachol being a cholinomimetic drug increases free intracellular calcium ions which, intern activate protein kinase by phosphorylation and lead to increased production of HCl. In this study we observed that Ammi visnaga reduced the volume free 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 Myristica fragrans in all the parameters. This is due to the calcium channel blocking activity of natural calcium channel blockers present in these extracts.

Our study is in consistent with other workers who concluded that calcium channel blocker Verapamil significantly reduces gastric acid secretion^{16, 17}. The extracts containing natural calcium channel blockers inhibit the calcium 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 leukotrienes, the injurious 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, inhibits adenyl cyclase and thus decrease HCL production.¹⁸

Release of histamine from mast cells is critically dependent on external calcium ions, so by blocking calcium ions, can block histamine release which is a potent agent for HCL secretion¹⁹.

When we compared the differences in the mean values of volume, free and total acidity by Ammi visnaga and Myristica fragrans, the change was found non-significant. This indicates that the extracts have similar effect on decreasing volume, free and total acidity of gastric

secretion. Calcium channel blockers are also used in controlling contraction of cardiovascular smooth muscles²⁰, allergic reaction²¹ and prevention of premature labor.²² All these actions are due to the calcium channels blocking activity. As the extracts also contain calcium channel blocker, so they can also be used for the treatment of the above mentioned diseases and peptic ulcer.

CONCLUSION

It is concluded that these extracts may be beneficially used as a single drug therapy in patients having peptic ulcer & diseases related to hyper gastric acidity. Further studies in this regard for evaluation of these effects are suggested in human subjects.

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