ORIGINAL ARTICLE

Effects of Thymoquinone Obtained from Seeds of Nigella Sativa on Volume & Acidity of Stimulated Gastric Secretion

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ABSTRACT

Aim: To study the effects of thymoquinone obtained from seeds of nigella sativa on volume & acidity of stimulated gastric secretion.
Design: Quasi experimental.
Place & duration: Pharmacology Department College of Medicine, University of Dammam, Saudi Arabia. in 2012.
Methods: Thirty rabbits of local breed, weighing 1-1.5kg were used. The animals were kept on fasting for 48 hours, after that the pylorus of each animal was ligated. Normal saline(2 ml), Thymoquinone 5 mg/kg and Carbachol 600μg/kg &body weight were administered intraperitoneally.
Results : Thymoquinone reduced the volume, free and total acidity of gastric secretion, which were statistically highly significant when compared with Carbachol (P<0.01).
Conclusion: Thymoquinone can be used effectively in the treatment of peptic ulcer and all other conditions like dyspepsia, gastritis & reflux esophagitis which are due to hyper gastric acidity.
Keywords: Thymoquinone, gastric 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 achlorhydric 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. Nigella sativa belongs to the botanical family of Ranunculacae. It commonly grows in Europe, Middle East and Westren Asia. In different countries it is called by different names for example, habbat al-baraka, Kali jeera. In the light of Hadeth "Use this Black seed, it has a cure for every disease except death" (Sahih Bukhari), The Nigella sativa (N. sativa) seeds, are frequently used in Saudi Arabia, Middle East and many other countries since ancient times as a natural remedy for many ailments. Nigella sativa seeds contains many active ingredients including thymoquinone (Nigellone)[2]. Keeping in view, multiple uses of N.sativa many investigators conducted various in vitro & in vivo studies on laboratory animals &human beings in order to know their pharmacological actions. These include anti-inflammatory[3], anti-inflammatory, analgesic and anti-pyretic activity[4] .

METHODOLOGY

Thirty rabbits of local breed were selected for the present study. Healthy animals of both sexes were used in the study. All the agents were injected intraperitoneally (I.P) on the basis of per Kg body weight. 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 8 animals. Group 1 was treated with normal saline, group 2 with Carbachol 600 µg /kg body weight , Group 3 with Thymoquinone 5mg/kg + Carbachol after 15 minutes. Gastric juice was obtained from each rabbit by pylorus ligation method described by Vischer et al[15].

Animals were anaesthetized with ether in a big gloss desicator, weight was found out. Abdomen was opened by a mid line incision and pylorus was isolated & ligated with silk suture. Then abdominal wall was closed with suture clamps. This enabled us to know about the inhibitory effect of the drug after stimulation by Carbachol. After termination of anesthesia, animals regained consciousness. After 4 hours, each animal was slaughtered, abdomen was reopened, cardiac end of the stomach was ligated & was cut from both ends outside the knot. Incision was given to stomach at greater curvature. The gastric juice thus obtained was titrated against o.1 N NaOH solution by the method described by Varley [16].

For calculation of free, combined & total acidity. This method is being used successfully by various researchers since 1954. According to this method, one ml of centrifuged gastric juice was titrated against 0.1 N NaOH using Topfer,s reagent as an indicator for determination of free acidity and 1% phenolphthalein as an indicator for combined acidity. Acidity of the gastric juice was calculated by using the formula NIVI=N2V2. The sum of the two titrations was considered as total acidity. The data were entered into SPSS-IBM Version 19. *p* value of <0.05 was considered to be statistically significant

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RESULTS

The detail of results is given in tables 1.

\Table 1: Effects of Thymoquinone on the volume and acidity of gastric secretion induced by Carbachol in fasting rabbits

Drug	Volume of gastric secretion (ml)	Acidity (meq/dl of gastric secretion)	
		Free	Total
Normal saline	13.500 ±1.414	1.825 ±.353	3.025 ±.148
Pvalue(compared with Carbachol)	0.000	<0.01	<0.01
Carbachol	28.125±2.031(8)	6.225±1.188 (8)	7.650±1.243(8)
Thymoquinone+ Carbachol	13.625±1.355 (8)	2.412±.626 (8)	3.750±.833 (8)
P Value (compared with carbachol)	0.000	<0.01	<0.01

*Carbachol was injected 600 µg/kg body weight &Thymoquinone 5 mg/kg body weight. All the drugs were injected intraperitoneally (I P).

DISCUSSION

N.sativa seed and its components are frequently used as a natural remedy for many ailments. A lot of work has been done to evaluate the pharmacological basis of their uses. Most studies confirm its value in folk medicine as analgesic, anti-inflammatory,anti-oxidant, anti-cancer, anti-microbial, anti-parasitic, antihypertensive and as an immune stimulant. The basic neurotransmitters or hormones that directly stimulate secretion by the gastric glands are acetylcholine, gastrin and histamine[17]. The release of acetylcholine, histamine and gastrin is dependent upon Ca ions influx [18.] Induction of hypercalcaemia through intravenous administration of calcium, is usually associated with increased gastric volume and acidity[5].

In an *in vitro* study,it was demonstrated that *N. sativa*, effectively inhibited the release of histamine from mast cells, possibly through decrease in intracellular calcium and inhibition of protein kinase C. *According to a research, N. sativa* extract produced a significant hypotensive effect in spontaneously hypertensive rats comparable to that of 0.5 mg/kg/day of oral calcium channel blocker nifedipine[6]. *N. sativa* antagonized methacholine induced contractions of isolated guinea-pig tracheal chain[7.] This shows that Nigella sativa has also anticholinergic activity which could be the cause of anti-gastric secretory function.

Our study is in consistent with other workers who concluded that calcium channel blocker Verapamil significantly reduces gastric acid secretion[8].

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 are 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[9]

In our study we observed that thymoquinone, obtained from Nigella sativa significantly reduced gastric secretion & acidity. Our study is in agreement with that of El-Dakhakhani et al[10]. They observed effect of *N. sativa* oil on gastric secretion and ethanol-induced ulcer in rats. In our study, we found out that thymoquinone significantly reduced Carbachol stimulated gastric acidity. From above discussion it is clear that thymoquinone obtained from the seeds of Nigella sativa can significantly decrease gastric acidity either by decreasing histamine release or blocking histamine H_2 receptors. *It is also* having calcium channel blocking activity which reduce the release of acetylcholine & histamine.

CONCLUSION

This extract may be effectively used in patients having peptic ulcer & other diseases related to hyper gastric acidity conditions.

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