ORIGINAL ARTICLE

Comparison between the Effects of Thymoquinone Obtained from Seeds of Nigella Sativa & Ranitidine on Volume & Acidity of Stimulated Gastric Secretion

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ABSTRACT

Aim: To compare the effects of thymoquinone& Cimetidineon volume and acidity of Carbachol induced gastric section.
Design: Quasi experimental.
Place & duration of study: Pharmacology Department, College of Medicine University of Dammam, Saudi Arabiain 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. Thymoquinone 5 mg/kg, Carbachol 600µg/kg & Ranitidine 2.5 mg/kg body weight were administered intraperitoneally. Pylorus ligation method was used for getting gastric contents & titration method was used for finding out acidity.
Results: Thymoquinone reduced the volume, free and total acidity of gastric secretion, which were statistically highly significant when compared with Carbachol ($P<0.01$) but when we compared the results of Thymoquinones with that of Ranitidine, it was non siginificant.
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.
Key words: Thymoquinone, Ranitidine , Gastric secretion

INTRODUCTION

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 Bukhare), 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)[1]. Due to 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[2] Anti-inflammatory analgesic and anti-pyretic activity[3] antimicrobial[4]. Antifungal[5]. hypoglycemic effects[6], antituberculous[7]. TQ administration can prevent and improve murine DSS-induced colitis. TQ could serve as a potential therapeutic agent for the treatment of patients with inflammatory bowel disease. It prevents colitis & diarrhea[8].

METHODOLOGY

Twenty four 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 bases 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 Carbachol 600µg/kg body weight, Group 2 with Thymoquinone 5mg/kg& group 3 with Ranitidine 2.5 mg/kg body weight.. After15 minutes Carbachol 600 µg /kg body weight was injected to Group 2 & 3. Gastric juice was obtained from each rabbit by pylorus ligation method described by Vischeret 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.

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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 thus obtained was subjected to statistical analysis for any significance. The data were entered into SPSS-IBM Version 19. P value of <0.05 was considered to be statistically significant.

RESULTS

The detail of results is given in tables 1, 2.

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

Drugs	Gastric secretions (ml)	Acidity (m.Eq/dl of gastric secretion)	
		Free	Total
Carbachol	28.125±2.03 (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 Values (compared with carbachol)	0.000	0.000	0.000
Ranitidine+ Carbachol	13.212±1.174 (8)	2.012±.432 (8)	3.075±.989 n(8)
P Values (Compared with Carbachol)	0.000	0.000	0.000

*Carbachol was injected 600 µg/kg body weight Thymoquinone 5 mg/kg&Ranitidine 2.5 mg /kg body weight. All the drugs were injected intraperitoneally(I P).

Table 2: Comparison between the effect of Thymoquinone & Ranatidine on the volume and acidity of gastric secretion induced by Carbachol in fasting rabbits

Drugs	Volume of gastric secretion (ml)	Acidity (meq/dl of gastric secretion)	
		Free	Total
Thymoquinone +Carbachol	13.625±1.355 (8)	2.412±.626 (8)	3.750±.833 (8)
Ranitidine+ Carbachol	13.212±1.174 (8)	2.012±.432 (8)	3.075±.989 (8)
P values(Compared with Thymoquinone + Carbachol)	0.268	0.216	0.265

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[9]. The release of acetylcholine, histamine and gastrin is dependent upon Ca ions influx[10] Induction of hypercalcaemia through intravenous administration of calcium, is usually associated with increased gastric volume and acidity[11].

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. In a study, 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[12].

N. sativa antagonized methacholine induced contractions of isolated guinea-pig tracheal chain[13.] 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[14].

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 and inhibits adenylcyclase and thus decrease HCl production[15]

Release of histamine from mast cells is critically dependent on external calcium ions, so by blocking calcium ions can inhibit, histamine release which is a potent agent for HCl secretion[16.] 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 [17]. They observed effect of N. sativa oil on gastric secretion and ethanol-induced ulcer in rats. There is significant increase in mucin content, glutathione level as well as a significant decrease in mucosal histamine content and ulcer formation.

Conclusion: Extract may be effectively used in patients having peptic ulcer & other diseases related to hyper gastric acidity conditions.

Approval by ethical committee: It was approved from the ethical & research committee of the institute.

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