ORIGINAL ARTICLE

Significant Hepatic Degeneration Would Lead to Periportal Inflammation and Congestion in the Liver of Albino Rats After Consumption of Garlic (Allium Sativum)

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ABSTRACT

Background: The wide use of the garlic as self medication in the patients with diabetes mellitus and hypertension necessitates the use of its safer dose range and duration as it is completely metabolized in the liver.
Aim: To evaluate the adverse effects of garlic (allium sativum) extracts on liver of adult albino rats.
Methods: In this experimental study a total of 45 wistar albino rats of both sexes weighing between 250-350 grams were selected randomly. Two different doses of 500 and 1000 mg/kg of fresh garlic extract by orogastric tube for thirty days were given to the animals. After this period histopathological analysis was then performed on the livers of the sacrificed rats.
Results: In the presentstudy, hepatic necrosis and significant inflammation and congestion in the portal triad is noted in both experimental group B and C as compared to control group A (P-value < 0.001).
Conclusion: It is concluded that there is a need to evaluate safer dose and duration of usage of garlic in general public due to its harmful effects on liver
Keywords: Garlic (allium sativum), liver, portal triad, albino rats.

INTRODUCTION

Garlic (Allium sativum) of Alliacae or onion family, is the native to central Asia. It is naturalized throughout the world as a conventional medicine and traditional food to improvethe physical and mental health.[1]Garlic cloves were buried in King Tutankhamun's tomb in Egypt due to its religious significance (1341 BC–1323 BC).It is even cited in the Egyptian Codex Ebers**,** a 3,500 years old document, as a useful supplement in the treatment of heart diseases, malignancies, worms infestations, ant to treat thesnake bites.The use of the garlic was documented by the Greek physician, Hippocrates, known as the father of medicine and during the middle ages by Hildegard von Bingen[2]. According to Bible Jewish prisoners were fed on garlic and other allium vegetables as it increased the physical stamina.It was also used by workers in building the pyramids.A leading physician of the 16th century, Pietro Mattiali of Siena, prescribed garlic to help mothers during complicated childbirth.There is evidence that during the earliest Olympics in Greece, garlic was consumed by the athletes to improve the physical strength and productivity[3].

Allicin (allyl 2-propenethiosulfinate or diallylthiosulfinate) is the principal bioactive compound present in the garlic extract or in the raw garlic homogenate. When garlic is in the garlic a compound known as alliin is converted into the allicin by action of allinase enzyme. This enzyme was activated during the cutting or crushing the garlic[4].

Different studies for garlic extract in mice and rats have reported LD50 values greater than 32g/kg[5]. The garlic extract in dose of 2 g/kg damages the gastric and intestinal epithelial mucosal membrane, results in bleeding ulcers and slough off the villus structure of jejunum. In a study, hepatotoxic effects revealed atrophy of hepatocytes with pyknosis of their nuclei and vacuolar degeneration along with inflammatory cell infiltration in the hepatocytes[6].

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MATERIALS AND METHODS

This experimental study was conducted in Department of Anatomy, Shaikh Zayed Postgraduate Medical Institute, Lahore in collaboration with Department of Zoology Quaid-e-Azam Campus, University of the Punjab Lahore**.** 45 wistar albino rats of both sexes weighing between 250-350 grams were selected for this study. After 14 days of acclimatization the animals were randomly divided into three groups. Each group comprised of 15 animals. Group A was control, the animals of this group were not given garlic extracts but instead received distilled 4ml/kg body weight of water by orogastric tube for 30 days. The other two groups B & C were experimental. Garlic extract 500 mg/kg and 1000 mg/kg was given respectively to the rats of experimental groups B & C through the orogastric tube for 30 days.

Garlic bulbs were purchased from the local market and then its extract was obtained from PCSIR, Laboratories Complex Lahore, which was prepared by soaking garlic paste in purified water. From 25 g of raw garlic, 1 ml of garlic extract was obtained which contained approximately 90 mg of allicin. Two concentrations of extract were prepared 0.2 and 0.3 g/ml corresponding to doses of 500 and 1000 mg/kg body weight of animals respectively.[7]At the end of study the rats of all groups were weighed properly before dissection and recorded in proforma. On the day 7 all the rats were euthanized by giving morphine 0.3–0.5 mg/kg intraperitoneally,as an analgesic agent. The anaesthetic agent sodium pentabarbitol was administered intraperitoneally with dose of 45 mg/kg.After dissection the histologic parameters recorded were inflammation and congestion in the periportal areas.

Statistical analysis:The qualitative data for inflammation and congestion in portal triad was reported by using frequency and percentage of each group. Comparison among groups was made by using Chi-square test. P-value <0.05 was considered significant.

RESULTS

Presence of necrosis of hepatocytes along with inflammation and congestion in portal triad was seen in all (100.0%) animals of experimental groups B and C and the portal triad was normal in all animals of control group A (Fig 1). The difference among the groups was statistically significant (P-value < 0.001, Table 1). The inflammation and congestion in the portal triad area was statistically significant for group B and C in comparison with group A (P-value <0.001) and statistically insignificant difference was observed between group B and C (P-value 1.000, Table 2).

Fig. 1: Photomicrographs of the liver of the albino rats A) Control group showing area of portal triad (PT), B &C Experimental groups showing Portal triad surrounded by inflammatory cells (Blue Arrow), Bile ductule (Yellow Arrow) and Hepatic artery (Red Arrow)and Necrosis (N). D) showing Periportal congestion.

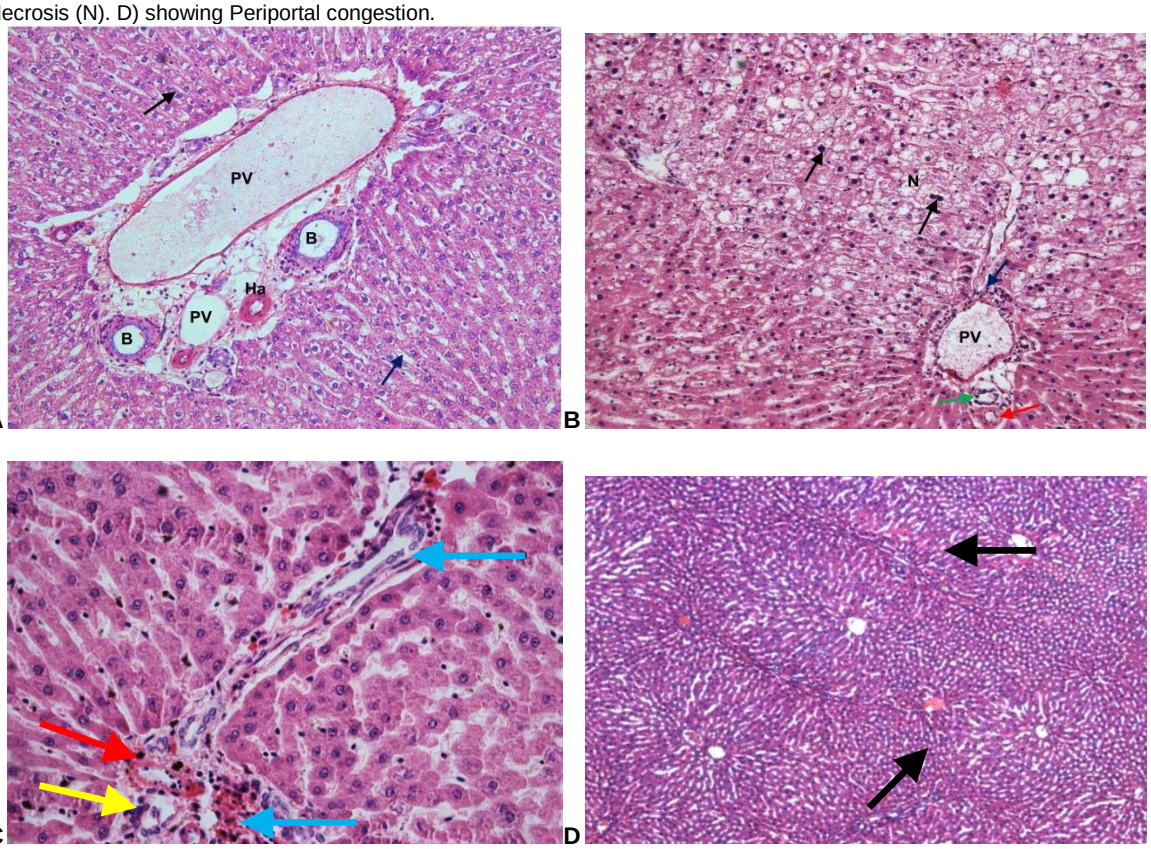

Table 1: Inflammation and congestion in portal triad of rats in control and experimental groups after administration of garlic extract

Groups	Present	Absent	Total
A	0	15(100%)	15(100%)
B	15(100%)	0	15(100%)
C	15(100%)	0	15(100%)

Chi-square = 45.0 p-value <0.001, A-Control Group, B-Experimental Group, C-Experimental Group, N-Number of Animals

Table 2: Comparison of inflammation and congestion in portal triad of rats in control and experimental groups after administration of garlic extract

Group I	Group 2	CHI-Square	DF	P-value
Group A	Group B	26.0	1	< 0.001**
	Group C	26.0	1	< 0.001**
Group B	Group C	0.0	1	1.000++

A-Control Group, B-Experimental Group, C-Experimental Group
DF-Degree of freedom, **Highly significant difference (P<0.01)
++Non-significant difference (P>0.05)

DISCUSSION

The present research work was performed to evaluate the toxic effects of the garlic on the liver of the albino rats. As its main sulphated component is allicin that is completely metabolized in the liver so it is proved to exert the harmful effects on the hepatocytes and portal triad of the liver. Portal triad is the important and distinctive arrangement of the structures located at the periphery of each classical hepatic lobule. It includes the branches of the portal vein, bile duct and hepatic artery, bound together in the perivascular fibrous capsule and they ramify within the substance of liver. Any significant changes in this area would most likely lead to the hepatic dysfunction[8].

In this present study, effects of garlic were observed in doses of 500 and 1000 mg/kg which was given for 30 days and the histological effects on liver were observed. Congestion and inflammation in portal triad was seen in all

(100%) animals of group B and C and the triad was normal in all animals of control group A. (Figs. C & D) The difference among the groups was statistically significant (P-value < 0.001, Table 1 & 2). The mechanism to develop the periportal inflammation may be due to the induction of the hepatotoxicity that is mainly produced by lipid peroxidation and release of toxic oxidative metabolites[9]. The other probable mechanism can be the mitochondrial dysfunction that result in decreased ATP production and development of cell necrosis[10]. The hypotensive effect of the garlic and vasodilatation leads to ischemic changes at tissue level. These all possible factors lead to initiation of inflammatory response by the leukocytic infilteration in the periportal area and associated kupffer cell activation. The proinflammatory mediators also lead to perfusion failure of the hepatocytes and microvascular dysfunction as noted by the Brigitte Vollmer in his study regarding liver injury[11]. These same findings of hepatic necrosis and inflammatory cell accumulation in the portal triad were observed by Banerjee and Maulik in their research work after administration of garlic to albino rats[7]. Salahy documented the hepatic degeneration and necrosis in carnivorous fish after giving them 2 g/kg garlic juice[12]. The necrotic tissue is the main cause of the inflammation in the portal areas which ultimately leads to increase in the blood flow and vasodilatation.These findings coincide with the findings observed by Maulik after administration of 500 mg/kg garlic extract.[13]Same type of cell injuries in the portahapatis zones were documented by Egen Schwind by usage of 200mg/ml of garlic powder in isolated perfused rat liver[14]. This study also coincides with the findings of Ebomoyi, who studied the effect of aqueous fresh garlic (Allium sativum) cloves extracts on liver and pancreas of Wistar ratsin dose of 500 mg/kg body weight. The results of his research showed that the vascular changes in the liver and the pancreas were associated with increased blood flow and caused dilatation[15].

CONCLUSION

The use of garlic extract in high doses for longer time caused significant cellular damage and vasodilatation in liver of albino rats. It is worth noting that garlic is completely metabolized in liver and that is the main cause of its toxicity. The possible mechanism behind its damaging effect is oxidative stress at cellular level. Most lethal effect as indicated in this research work is significant periportal hepatic necrosis with inflammation and congestion. It must be kept in mind while prescribing garlic to hypertensive and diabetic patients because it is not safe as used in excess. There is a need to evaluate safer dose and duration of usage of garlic in general public.

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