

SERUM UREA AND ENZYMES IN RAT ON INTRAGASTRIC ADMINISTRATION OF GARLIC OIL AND GARLIC EXTRACTS

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HYPOGLYCEMIC, hypolipidemic, fibrinolytic and antibacterial activities of garlic principles are well known¹⁻⁸. Garlic is generally considered as a safe flavouring adjuvant of foods. The recommended levels are 800–1300 ppm of garlic or 10–15 ppm of garlic oil⁹. However, very high doses of garlic principles are toxic. The LD₅₀ value for allicin in mice is 60 mg per kg body wt⁹. Nakagawa *et al.*¹⁰ observed that when young rats were fed a high dose of fresh garlic juice, some died within 21 days and the body wt of the still living ones was considerably reduced. Hypertrophy of the spleen, liver and adrenal glands, followed by decreased erythrocyte counts, were regular features in high-dose raw garlic-administered rats¹⁰. The active principles of aqueous extracts of garlic are sulphoxides; in garlic oil the active principle is diallyl disulphide¹. Sulphoxides and disulphides can undergo exchange reactions with various sulphhydryl compounds in the body spontaneously at physiological pH and temperature^{11,12}. Titrable SH groups are found on the cell membranes of RBC, and cells of liver and kidneys¹¹. The diallyl disulphide of garlic oil is absorbed and metabolized chiefly in the liver¹³. We therefore studied liver and kidney function in rats administered high doses of garlic principles.

White male albino rats, 6–8 months old and weighing 200–300 g, were obtained from the Central Food Technological Research Institute, Mysore. They were divided into five groups of six animals each and fed standard laboratory diet *ad libitum*.

One gram of garlic was crushed with 3 ml water and filtered. The filtrate was used as aqueous extract of garlic. Crushed garlic was steam-distilled. The distillate was extracted with ether. The ether layer was separated, clarified with anhydrous sodium sulphate and evaporated at 55°C. The oil left behind was used as garlic oil.

Control rats (group 1) were fed intragastrically 2 ml normal saline per 100 g body wt 3 h before sacrifice. Group 2 rats were fed 2 ml aqueous extracts of garlic per 100 g body wt 3 h before

sacrifice. Group 3 rats were fed 6.7 mg garlic oil suspended in 2 ml normal saline per 100 g body wt. Group 4 rats were fasted for 24 h and fed 2 ml normal saline per 100 g body wt and sacrificed 3 h later. Group 5 rats were also fasted for 24 h and fed 6.7 mg garlic oil suspended in 2 ml normal saline per 100 g body wt 3 h before sacrifice. All the rats were sacrificed by decapitation. Blood was collected in a clean beaker and allowed to clot. Urea¹⁴, creatinine¹⁵, LDH (EC 1.1.1.27)¹⁶, alkaline phosphatase (EC 3.1.3.1)¹⁷, AST (EC 2.6.1.10)¹⁸ and ALT (EC 2.6.1.2)¹⁸ were estimated in the clear serum. All the estimations were carried out using diagnostic reagent kits from SPAN Diagnostic Pvt. Ltd, Surat, India. *In vitro* addition of garlic extracts or garlic oil did not have any effect on the estimation of urea by the method used.

Statistical analysis was by Student's *t* test.

The results are shown in table 1. Group 2 rats showed significantly higher ($P < 0.01$) levels of urea and AST in serum, while ALT, alkaline phosphatase and LDH levels were unaffected. Feeding garlic oil to fed rats (group 3) did not change any of the above parameters within 3 h ($P > 0.1$). Rats fasted for 24 h (group 4) also showed only normal levels of urea, AST, ALT, alkaline phosphatase and LDH in serum. However, when 24-h-fasted rats were fed garlic oil (group 5) serum urea increased and alkaline phosphatase decreased significantly ($P < 0.01$). Administration of garlic extracts or garlic oil had no effect on serum creatinine.

Diallyl disulphide present in garlic oil and the sulphoxides present in aqueous extracts of garlic are known to undergo exchange reactions with SH groups of enzymes and other proteins that have titrable SH groups^{11,12}. Thus garlic principles have been demonstrated to inhibit the activities of a variety of enzymes, including alkaline phosphatase¹. The low levels of alkaline phosphatase in group 5 rats (fed garlic oil in the fasted state) may be due to such inhibition by garlic oil absorbed from the intestines and still present in the blood. Rats fed a similar quantity of garlic oil in the fed state (group 3) show no change in alkaline phosphatase probably because absorption of garlic oil might have been delayed.

Earlier workers have used a dose of 10 mg garlic oil or 1 ml garlic extracts per 100 g body weight of fed rats for hypolipidemic studies^{5,6}. Yet administration of two-thirds of this dose of garlic oil to fasted rats raises urea and inhibits alkaline phosphatase in serum. Similarly administration of twice the optimal dose of garlic aqueous extracts to fed rats raises urea

Table 1 Effects of feeding garlic principles on serum urea and enzymes in fed and starved albino rats

Group	Treatment	Urea (mmol/l)	Creatinine (μ mol/l)	LDH	Alkaline phosphatase	AST	ALT
1	Control	4.1 \pm 0.38	127 \pm 39	164 \pm 23	376 \pm 45	120 \pm 20	32 \pm 5.7
2	Garlic aqueous extracts	6.27* \pm 1.05	169 \pm 22	169 \pm 15	387 \pm 108	170* \pm 21	38 \pm 5.4
3	Garlic oil	4.05 \pm 0.22	99 \pm 54	148 \pm 22	380 \pm 29	142 \pm 16	23 \pm 5
4	24-h-fasted	4.0 \pm 0.33	167 \pm 22	175 \pm 14.2	250 \pm 24	130 \pm 13	25 \pm 2.6
5	24-h-fasted garlic oil	9.4* \pm 1.3	132 \pm 18	298 \pm 259	15.5* \pm 4.4	172 \pm 51	43 \pm 20

Results are mean \pm SD for six observations.

*P < 0.01.

and AST levels within 3 h. Thus administration of an overdose of aqueous extracts of garlic to fed rats or a normal dose of garlic oil to fasted rats may cause changes in urea and enzymes in the serum.

The authors are grateful to Dr A. Subba Rao, Department of Biochemistry, J. S. S. Medical College, Mysore, for help.

26 December 1988; Revised 14 February 1989

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