

ALTERATIONS IN RAT TISSUE GLUTATHIONE S-TRANSFERASE AND ITS ISOZYME (Class Mu) DURING ONION FEEDING

Dietary factors influence xenobiotic metabolism by inducing specific enzymes responsible for detoxification. Among them the glutathione S-transferase (GSTs) are a family of detoxification enzymes involved in cellular protection. They catalyse the conjugation of electrophilic compound with reduced glutathione. Some of the inhibitors of carcinogenesis have been reported to stimulate glutathione S-transferases activity in the liver. Expression of GST Mu has been proposed to be determinant of susceptibility to some types of cancers among cigarette smokers¹. A preliminary study was planned to investigate if onion feeding results in alterations in the levels of GST and GST Mu enzymes in rat tissues.

Male Wistar NIN breed rats weighing 125-150 g were divided into 3 groups and were fed *ad lib*, diet containing 0, 1 and 5% of dried onion powder. At the end of 6 months, animals were sacrificed. Liver, stomach, kidney and lungs were dissected out and tissue homogenates (10% w/v) were prepared in 10 mM potassium phosphate buffer, pH 7.0, containing 1.4 mM 2-mercaptoethanol using polytran, centrifuged at 20,000 g for 40-60 min to obtain the supernatant fractions.

GST activity towards 1-chloro 2, 4-dinitrobenzene and GST Mu activity towards trans-stilbene oxide were measured^{3,4}. The data were analysed using analysis of variance (ANOVA) and group means were tested by Duncan's multiple range test. P values <0.05 were considered significant.

GST and GST Mu activities were significantly increased in the stomach and the liver following onion (1 and 5%) feeding (Table 1). Both GST and GST Mu activities from lung and kidney tissues did not show any significant changes (Table 1).

The activities of ingredients present in onion and garlic have been shown to retard the incidence of benzo(a)pyrene induced neoplasia of lung and forestomach in mouse⁴. It has been also shown that diallyl sulfide and diallyl disulfide inhibited the 7, 12-dimethyl benzanthracene and 12, 0-tetradecanoyl phorbol 13-acetate promoted skin tumour in mice⁵. However, the mechanism by which these chemopreventive effects are brought about is not clearly understood. Results of this study suggest that one mechanism by which onion may exert its anti-cancer effect would be through enhancing the GST mediated detoxification of the xenobiotics. It is also possible that it can inhibit the activity of mixed function oxygenases⁶.

The observation that GST Mu activity is stimulated more at lower levels of onion feeding in liver when compared to the high levels indicates that induction is not dose dependant. In a similar manner it has been shown that a single (500 mg/kg) dose of garlic oil to rats resulted in suppression of several Phase I and Phase II enzymes, whereas, low doses (50 mg/kg) for 5 days resulted in significant increase in several of these enzymes⁷. Present studies also indicate that induction of GST and GST Mu activity by onion is organ specific because stomach and liver only showed induction whereas kidney and lung did not show any alteration.

Table 1. Effect of onion feeding on GST and GST Mu activities in rat.

Onion feeding ^a		Tissues			
		Stomach	Liver	Lung	Kidney
GST (nmol/min/ mg protein)	Control	101 ± 3.5	1144 ± 29	220 ± 18	121 ± 12
	1%	143 ± 10.4 ^b	1544 ± 43 ^b	180 ± 25	111 ± 3
	5%	150 ± 5.2 ^b	1485 ± 28 ^b	184 ± 24	136 ± 10
GST Mu (nmol/min/ mg protein)	Control	1.31 ± 0.05	8.7 ± 95	0.83 ± 0.10	0.46 ± 0.11
	1%	1.93 ± 0.13 ^b	13.2 ± 0.46 ^c	0.75 ± 0.06	0.30 ± 0.03
	5%	1.85 ± 0.06 ^b	11.6 ± 0.45 ^b	0.75 ± 0.10	0.32 ± 0.04

Values are mean±SE of 6 animals,

^aAnimals were maintained on 1 and 5% onion powder diet for 180 days and were killed. ^bP <0.05, ^cP <0.01 treated vs control.

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The K.B. Institute of Pharmaceutical Education & Research, Gandhinagar is organizing a National Workshop on Pharmacokinetics: Basic Concepts to Applications in Drug Research Development on September, 22-26, 1999. The course work is being meticulously designed in collaboration with the scientists of Synchron Research Services Pvt. Ltd., Ahmedabad and other academic and industrial organizations. Leading academicians and industrial scientists like Prof. Neelima Kshirsagar, Prof. M.U.R. Naidu, Prof. H.P. Tipnis, Dr. J.K. Paliwal, Shri Bhupinder Singh Bhoop, Dr. T.P. Gandhi, Dr. A.J. Singh, Dr. Shubha Rani, Prof. N. Gururajan, Dr. B.P. Udwadia and Dr. Shiv Prakash are going to function as faculty members and resource persons. The number of seats for participants are restricted to 30. Scientists working in the industry, National Laboratories and Contract Research organizations and actively involved in this field will be given preference.

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