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Changes in the regional protein metabolism in the central nervous system (CNS) of diabetic rats: Protection by *Cichorium intybus* (Chicory)

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ABSTRACT - Protein content, ammonia and activity levels of Glutamate dehydrogenase (GDH) in the cerebrum, medulla oblongata of noarmal and alloxan – diabetic rats were measured. Protein content decreased in the regions of the brain studied during the diabetic state. Ammonia levels were also increased in the brain of alloxan diabetic rats. The activity level of glutamate dehydrogenase in the broad compartments of the brain was decreased during alloxan induced diabetes. Chicory offered marked protection, it brought down the levels of blood glucose and brain ammonia.

KEYWORDS - Protein metabolism, CNS, Diabetes, Ammonia, GDH, Cichorium intybus, protection.

Abnormalities of protein metabolism in various tissues of mammals during diabetes have been reported (1,2,3,4). Decrease in the rate of nuclear protein biosynthesis has been demonstrated in rat liver during diabetes. Tragl et al (2) reported marked decrease in hepatic ribosomal protein synthesis in rats during experimental diabetes. Total plasma protein levels were not affected significantly in diabetic rats (3). However, no information is available on the regional distribution of protein concentration and changes occurring in their levels during alloxan diabetes in diabetic mammals are meager. Hence, in view of the need for such a study, the present brain investigation was initiated. The paper provides information pertaining to the changes occurring in the levels of proteins and ammonia in the broad compartments of the brain of diabetic rat. Information has also been provided on the distribution of Glitamate dehydrogenase and changes occurring in its activity level in different regions of rat brain during alloxan-diabetes.

Protective effects of feeding Cichorium intybus (chicory) for 10 days have been examined as Chichorium intybus is widely used in Unani (Indian) system of medicine to control blood sugar level during diabetes.

Immature Albino rats (both sexes) of Wistar strain, ranging in weight form 65-85 g were used they were housed in cages at room temperature (25± 2^0C) and fed standard pellet diet (Hindustan Lever Ltd., Bombay). Water was available ad libitum.

Diabetes was induced by intravenous injection of freshly prepared aqueous solution of alloxan monohydrate (40 mg / kg body weight) (5). Control group was injected with the same dosage of mammalian Ringer (6). Blood was extracted for glucose analysis (7) from the tail vein by a sterilized syringe. Rats with fasting blood glucose ranging from 200-220 mg/100ml were considered diabetic and were analyzed 120 hours after alloxanization. Animals with fasting blood glucose less than 200 mg/100 ml were rejected.

A set of 9 rats were fed on *Cichorium intybus* leaves (30% + 70%) standard rat feed for 15 days and then rendered diabetic. Rats were decapitated and the brain was dissected from the ventral side. The adhering blood vessels were removed by keeping the brain immersed in mammalian Ringer $0^{0\ C}$ in a pertridish kept on ice (0^0 C). cerebrum and medulla oblongata were separated with sterilized bent forceps and scalpel, weighed (in the sartorius balance) with Ringer and immediately used for analyses.

Proteins were precipitated from the aqueous extract (10% W/V) by trichloro acetic acid (BDH) and estimated (7). Ammonia levels were measured in the un centrifuged extracts by Van slyke and Cullen's aeration method (7). The activity levels of GDH were estimated by modified triphenyl tetrazolium chloride reduction method (8). Tables 1 and 2, summarize the results obtained. It is seen from the results that the weight of the different regions of the brain showed considerable decrease during diabetes (Table 1). The blood sugar demonstrated 115% elevation as a function of diabetic state (Table 1).

Table 1: Brain weight and blood glucose levels of normal and alloxan –diabetic rats.

Brain weight			Blood glucose		
Normal	Diabetic	Chicory fed Diabetic	Normal	Diabetic	Chicory fed Diabetic
1.68 ± 0.05	1.42 ± 0.13	1.50 ± 0.4	102.3 ± 2.4	220.4 ± 3.15	160.0 ± 3.0

values are mean ± S.D. of 6 observations

In general, the protein content decreased in the cerebrum and medulla oblongata on in vivo administration of alloxan (Table 2). Paralleling the decrease in proteins, the activity levels of Glutamate dehydrogenase also decreased considerably on alloxanization (Table 2). However, the levels of ammonia exhibited significant increase in the brain during the diabetic state (Table2). The protein content of the cortical region of the region of the control group is more compared to the medullary regions of the brain. On the other hand, the level of ammonia is the lowest in this region. A similar trend is exhibited ion the exhibited in the experimental animals also. However, a remarkable feature was that the cerebrum demonstrated the least response for the changes in ammonia and protein levels of GDH in the diabetic state. Maximum response for the changes in ammonia and protein levels was exhibited by the medulla oblongata on inducing alloxan diabetes (Table 2). Such a differential response is related to the differences in the functional status of the concerned compartment of the brain.

Table 2: Changes in the levels of Protein, Ammonia and GDH activity in different regions of the brain of allocan – diabetic and chicory fed diabetic rats

	Cerebrum			Medulla Oblongata		
	Control	Diabetic	Chicory fed Diabetic	Control	Diabetic	Chicory fed Diabetic
Protein mg/g n=4	72.4 ± 4.7	62.2 ± 5.0	69.3± 3.0	66.7 ± 4.0	43.4 ± 4.0	59.2 ± 6.1
Ammonia mg N_2 /g	0.07 ± 0.01	0.09 ± 0.001	0.79 ±0.01	0.62 ± 0.04	0.92 ± 0.02	0.67 ± 0.01
GDH Mg NTC reduced /g/h	178 ± 6.2	120 ± 5.1	159 ± 4.4	150 ±6.0	60 ± 4.5	111 ± 7.2

$P < 0.01$ (between control and diabetic) ; $P<0.05$ (between diabetic and chicory fed diabetic)

The general decrease in levels of protein and activity levels of Glutamate dehydrogenase in the cerebrum and medulla oblongata of diabetic rats appears to be a direct consequence of insulin deficiency/ absence caused by alloxan. A similar effect of insulin deficiency to accelerate the catabolism of proteins and to depress protein synthesis in vertebrates has earlier been shown (9). However, Nayeemunnisa (10) demonstrated an increase in protein and RNA levels in the fore, mid and hind brain of diabetic frogs. The results of Peterson et al., (11) also support protein synthesis during diabetic state in rats.

The general increase in the level of ammonia in the brain of diabetic animals points to the fact that deamination of amino acids is proceeding at a rapid

rate in the diabetic state. The decrease in the activity level of GDH also suggests that regulation of ammonia toxicity in the brain by the processes of deamination and amination is affected markedly during the diabetic state. In support of this, during the course of present study, marked elevation in the free amino acid content in different regions of the brain of alloxan- diabetic rats has been observed. However, amino-transferase (AAT and AIAT) activites have been observed to be accelerated in the brain of diabetic rats (12). In the light of these facts presented above, it is likely that ammonia levels increase and protein content decreases in the diabetic state in rats. Such an increase in the level of ammonia may be connected to the disturbance in the ornithine cycle.

Feeding on chicory prior to alloxan administration brought down the blood glucose levels significantly ($P < 0.01$) and promoted protein synthesis. Chicory categorically decreased ammonia production ($P < 0.0001$) and protected the brain from ammonia toxicity.

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