ROLE OF 2-MERCAPTOPROPIONYL-GLYCINE AGAINST ^3H β-RAYS IN THE DEVELOPMENT OF MICE BRAIN

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A CONTINUOUS increase in the tritium concentration in environment from natural and man-made sources and the radiosensitive nature of embryo, have encouraged search for an antiradiation drug to protect embryos from tritiated water (HTO)-induced anomalies. 2-Mercaptopropionylglycine (MPG), a potent radioprotector, when administered either through oral or parenteral route is found strongly effective in very low, non-toxic dose, in both developing and adult mouse against external ^{60}Co-gamma rays[1, 2]. MPG may be equally effective for protection against internal emitters (P-32)[3]. Brain retains relatively more bound ^3H from HTO for longer periods in mice upon a chronic HTO exposure and thus suffers from various losses[4-6]. This has led us to investigate the role of 2-MPG as an antiradiation drug for developing brain against β-rays from HTO.

Groups of pregnant Swiss albino mice at different gestation days (11, 16 & 18) were selected from an inbred colony and maintained on two different series, one on HTO (2.5 μCi or 92.5 kBq/ml of drinking water; 0.005 Gy/day) after a priming injection of HTO of the activity 2.0 μCi/ml body water. HTO was obtained from BARC, Bombay (sp. activity 10 mCi or 370 MBq). Another series (MPG + HTO) was maintained on 2-mercaptopropionylglycine at the level of 2 mg MPG/60 ml drinking water (received from Santen Pharmaceutical Ltd, Japan) mixed with HTO (2.50 μCi/ml drinking water). To this group (MPG + HTO) a priming dose of HTO (approx. 2.00 μCi (74 kBq)/ml of body water) followed by a dose of MPG 20 mg/kg body weight (dissolved in distilled water; 6.4 pH of the solution maintained with 0.1 N NaOH)

Table 1 *Changes in the brain and body weights, and lengths of body and tail lengths (mean ± SEM) after in utero HTO-exposure with or without MPG from different days of gestation upto 7 days post-parturition.*

Initiation day p.c.		No. of animals	Weight of animals (g)	Wt. of brain (mg)	Ratio Brain wt/b.wt.	Length of the body (mm)	Tail length (mm)
0 day	Normal (± SEM)	5	5.04 (100%) ± 0.09	252.00 (100%) ± 4.06	0.0501 (100%) ± 0.0002	75.60 (100%) ± 0.49	28.5 (100%) ± 0.64
11 day	Control (± SEM)	5	4.30 ± 0.12 (85.32%)	247.50 ± 4.17 (98.21%)	0.0590 ± 0.0005	70.40 ± 0.49 (93.12%)	28.20 ± 0.98 (98.95%)
	Drug treated (HTO + MPG) (+ SEM)	6	4.97 ± 0.13 (98.61%) $p < 0.001$	231.60 ± 13.21 (91.90%) $p < 0.01$	0.0468 ± 0.0031	73.80 ± 0.58 (97.62%) N.S.	25.40 ± 0.27 (89.12%) $P < 0.01$
16 day	Control (HTO) (± SEM)	5	2.82 ± 0.04 (55.95%)	250.67 ± 1.22 (99.47%)	0.0875 ± 0.0097	65.60 ± 1.07 (86.77%)	—
	Drug treated (HTO + MPG) (± SEM)	5	3.05 ± 0.10 (60.52%) N.S.	232.40 ± 13.03 (92.22%) $p < 0.001$	0.0768 ± 0.0061	67.00 ± 2.01 (88.62%) N.S.	25.00 ± 0.36 (87.72%)
18 day	Control (HTO)	6	3.18 ± 0.05 (63.10%)	182.25 ± 2.21 (72.32%)	0.0565 ± 0.0007	60.30 ± 0.22 (79.76%)	21.70 ± 0.22 (76.14%)
	Drug-treated	5	2.43 ± 0.10 (48.21%) $p < 0.001$	195.60 ± 6.41 (77.61%) N.S.	0.0812 ± 0.0055	56.00 ± 2.01 (74.07%) $p < 0.01$	20.40 ± 0.49 (71.58%) $p < 0.001$

were injected 30 min before the supply of drinking water on the day the treatment was initiated. The weight of the brain and body, and the lengths of the tail and animal recorded on one week *post partum* are given in table 1. Various parameters of the control and drug-treated litters were also compared to the 1-week-old neonates brought up on ordinary tapwater (normal).

As shown in figure 1 and table 1 (i) the animals of both the sexes in control series (HTO) showed loss of weight in their body and brain. The 16th day group showed the most pronounced decline in body weight whereas the brain weight and the length of the animal and tail were greatly reduced in the 18th day group. A larger deviation from the normal values was noticed in the brain wt to body wt ratio in all the HTO-irradiated groups. (ii) Although animals treated with a combination of MPG + HTO, appeared to show a gain in their body weights by 13.29% ($p < 0.001$) in 11th day and 4.57% (N.S.) in 16th day groups, when compared with those of controls (HTO), they failed to attain the normal (sham-irradiated) values. The 18th day group clearly exhibited a loss of 14.89% ($p < 0.001$) more than the control. The brain weights in HTO + MPG series showed deficits by 6.31% in the 11-day group ($p < 0.01$), and 7.25% in the 16-day group ($p < 0.001$). Moreover, litters born to the 11- and 16-day groups in the HTO + MPG series showed a greater loss in brain weight as compared with controls. An increase of 5.29% in brain weight of HTO + MPG series in the 18-day group is statistically non-significant. A decrease in tail length in all the HTO + MPG series as compared with HTO series of the same group and a decrease in the length of the animals in the HTO + MPG series in the 18-day group have been recorded. The increase in body length in the 11-day and 16-day group is not significant.

It is evident from the above results that the animals of HTO + MPG series showed consistent deficits in many of the studied end-points. The role of MPG possibly exerting a protective effect against body weight losses due to external irradiation as well as HTO-irradiation (in 11- and 16-days groups in present study) cannot be ruled out. However its action on CNS including brain against HTO-induced damage is ambiguous. If MPG protects any other organ of developing animals against HTO-induced damages, their combination, on the other hand, may likely to prove hazardous to the developing brain. Previous studies[2, 7]

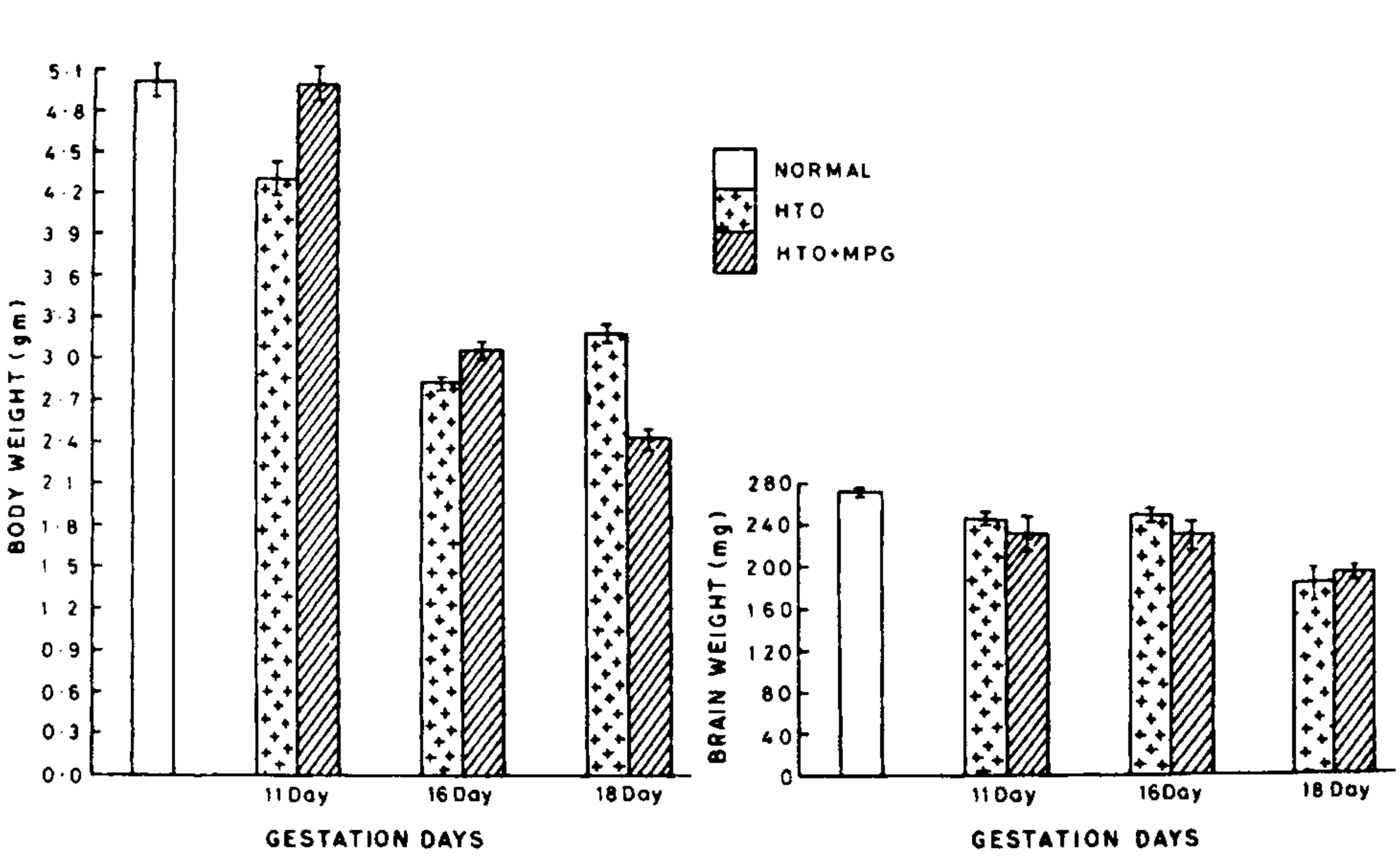

Figure 1. Graph showing changes in body and brain weights after HTO-exposure with or without 2 MPG from 11, 16 and 18th days *post-coitum*.

report that MPG is quite effective for protection against external γ-rays of ^{60}Co and the body weight has been maintained to a greater extent as a result of protection of various organs like gonads[3, 8], intestine [9] etc. While investigating the role of MPG in preventing the HTO-induced deleterious changes in various organs, in combination, its toxicity with regard to developing brain should be understood.

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HISTOENZYMOLOGICAL STUDY ON *OESOPHAGOSTOMUM COLUMBIANUM*

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THE present communication reports the histochemical localization and distribution of dehydrogenases in *Oesophagostomum columbianum*, an important intestinal nematode parasite of sheep, goat and wild antelope.

Adult *O. columbianum* worms were collected in normal saline from the intestine of freshly-slaughtered sheep at the local abattoir. The worms were washed thoroughly with distilled water. Frozen sections of the worms (both sexes) were obtained and processed histochemically as follows: Succinate dehydrogenase (SDH) was localized by nitro-BT method, cobalt-farmazan technique was employed for localization of isocitric, glutamate, malate and α-glycerophosphate dehydrogenase[1].

The results are summarized in table 1 and illustrated in figures 1–5. SDH and isocitric dehydrogenase activities were manifested in the form of granules, being more intense in the musculature, oesophagus and intestine (figures 1, 2). Moderate activity was observed in the cuticle, subcuticle, germinal zone of the ovary and testis, while the growth zone of the ovary exhibited feeble reaction. Glutamate dehydrogenase (GDH) activity was observed in the subcuticle, oesophagus, being more intense in the musculature and intestine (figure 3). Moderate to intense malate dehydrogenase activity was observed in the musculature and intestine,

Table 1 *Distribution and localization of various enzymes in Oesophagostomum columbianum*

Anatomical features of the worm	Enzymes				
	Succinate dehydrogenase	Isocitric dehydrogenase	Glutamate dehydrogenase	Malate dehydrogenase	α-glycerophosphate dehydrogenase
Cuticle	–	+ +	–	–	–
Subcuticle	+ +	+ +	+ +	+	+
Musculature	+ + +	+ + +	+ + +	+ + +	+ +
Oesophagus	+ + +	+ + +	+ +	+ +	+ +
Intestine	+ + +	+ + +	+ + +	+ + +	+ +
Ovary:					
Germinal zone	+ +	+ +	+	–	+
Growth zone	+	+	–	–	+
Testis	+ +	+ +	–	–	+

+ Feeble reaction; + + Moderate reaction; + + + Intense reaction.