

LETTER TO THE EDITOR

EFFECTS OF N-METHYL-N'-NITRO-N-NITROSOGUANIDINE ON CYCLIC
NUCLEOTIDE LEVELS IN RAT COLON

Sir,

(Received on March 15, 1983)

Cyclic nucleotides have been reported to be involved in cell proliferation and malignant transformation (1). Alterations in cyclic nucleotide levels in rat colon have been observed during the early stage of colon carcinogenesis induced by 1, 2-dimethylhydrazine (3). N-Methyl-N'-nitro-N-nitrosoguanidine (MNNG) has been shown to induce colon carcinomas in rats (2); and in this report, the effects of MNNG on cyclic nucleotide levels in rat colon are discussed.

Female Sprague-Dawley rats, weighing 170-200 g, were obtained from Charles River Lab., Wilmington, MA, USA, and used in these studies. MNNG was obtained from Sigma Chemical Co., St. Louis, MO, USA. Radioimmunoassay kits for adenosine 3', 5'-cyclic monophosphate (cAMP) and guanosine 3', 5'-cyclic monophosphate (cGMP) were obtained from Pasteur Institute, Paris, France. All other chemicals were of analytical reagent grade.

MNNG was administered intraperitoneally to the experimental group at a dose of 150 mg/kg of body weight, while isotonic saline solution was administered intraperitoneally to the control group. At appropriate post-treatment intervals, three rats from each group were sacrificed by cervical dislocation. The colons were excised immediately, and stored at -70°C until assayed. The cyclic nucleotides were extracted from the colon specimens according to the method of Stevens and Loven (3), and assayed with the radioimmunoassay kits obtained from Pasteur Institute according to the manufacturer's directions.

As shown in Table I, significant increases in cGMP and decreases in cAMP in the colon tissues of MNNG-treated rats were observed during the first four days post treatment. The maximal changes were recorded on the second day, and a return to normal values was observed by the seventh day post treatment. The cyclic nucleotide

levels in the colon tissues of the control animals remained essentially unchanged during the survey period.

TABLE 1: Effects of MNNG on cyclic nucleotide levels in rat colon.

Post treatment (day)	Cyclic nucleotide levels (pmol/g wet weight)			
	cAMP		cGMP	
	Control	Treated	Control	Treated
0	1502±60	1510±65	50±3	53±2
1	1481±55	756±29*	49±3	123±7*
2	1496±68	390±18*	48±2	210±8*
4	1492±50	800±26*	52±3	129±7*
7	1505±60	1493±62	53±2	51±3

The results are presented as mean ± S.D. (n=3); and * indicates statistical significance at P<0.01.

The results of this study are consistent with the alterations in cyclic nucleotide levels in rat colon following exposures to 1,2-dimethylhydrazine reported by Stevens and Loven (3). These observations demonstrate that cyclic nucleotides play an important role in the initiation of colon carcinogenesis.

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