Br. J. Pharmac. (1981), **72**, 8–9

TYPE OF ADRENOCEPTORS INVOLVED IN INDUCTION BY ADRENALINE OF HEPATIC ALKALINE PHOSPHATASE IN MICE *in vivo*

P.L. MARY & J. PRAKASA RAO

Department of Physiology, Christian Medical College, Vellore-632002, Tamil Nadu, India

Study of adrenoceptor agonist drugs in hepatic alkaline phosphatase induction in mice *in vivo* revealed that β-receptors are involved in this process. Use of selective blocking drugs showed that β_2-receptors may be responsible for the induction.

Introduction It has been reported that adrenaline can induce hepatic alkaline phosphatase (Wilfred & Prakasa Rao, 1976). However, the type of adrenoceptor involved in this induction is not known. The present study attempts such a determination.

Methods Experiments were performed on albino mice weighing 21 to 27 g. The drugs were administered subcutaneously by injection and the animals were killed 4 h after the last treatment. The livers were removed quickly, cut into small pieces and washed in ice-cold 0.25 M sucrose solution. They were then homogenized in 50 ml of fresh ice-cold 0.25 M sucrose solution. Suitably diluted aliquots of this homogenate were used for assay of alkaline phosphatase. The assay mixture contained 100 μmol of Tris-HCl, pH 10.2, 2.5 μmol of $MgCl_2$, 2.5 μmol of *p*-nitrophenyl phosphate and the enzyme preparation in a total volume of 0.5 ml. Incubation was carried out at 37°C for 30 min after which 2.5 ml of 0.2 N NaOH was added and the colour due to released *p*-nitrophenol was measured in a spectrophotometer at a wave length of 420 nm (model PMQ II. Carl-Zeiss). One unit of the enzyme was defined as the activity forming 1 nmol of *p*-nitrophenol at 37°C per min. Specific activity was expressed as units per mg of protein. Protein was estimated by the method of Lowry, Rosebrough, Farr & Randall (1951) using crystalline bovine serum albumin as the standard.

Results and Discussion Results shown in Table 1 indicate that adrenaline significantly increased the hepatic alkaline phosphatase activity. This action was blocked by propranolol, the β-adrenoceptor blocking agent but not by the α-blocking drug, phentolamine. The β-agonist isoprenaline was capable of inducing hepatic alkaline phosphatase but the α-receptor agonist, phenylephrine failed to do so. β-Receptors were sub-classified by Lands, Arnold, McAuliff, LuDuena & Brown into β_1 and β_2 types. The effect of isoprenaline was blocked by isopropyl methoxamine

Table 1 Effect of drugs on hepatic alkaline phosphatase activity in mice

Group	Treatment: *−30 min* (*dose per mouse*)	Treatment: *0 min* (*dose per mouse*)	*Specific activity of hepatic alkaline phosphatase* (*unit/mg protein*)
1	Saline	Saline	10.2 ± 0.7
2	Saline	Adrenaline (10 μg)	21.4 ± 0.8*
3	Propranolol (100 μg)	Adrenaline (10 μg)	10.2 ± 1.0
4	Phentolamine (250 μg)	Adrenaline (10 μg)	18.9 ± 0.8*
5	Saline	Phenylephrine (25 μg)	9.8 ± 0.3
6	Saline	Isoprenaline (20 μg)	18.9 ± 1.0*
7	Practolol (2 mg)	Saline	10.0 ± 1.3
8	Practolol (2 mg)	Isoprenaline (20 μg)	17.9 ± 0.9*
9	Isopropyl methoxamine (0.5 mg)	Isoprenaline (20 μg)	8.2 ± 0.5
10	Isopropyl methoxamine (0.5 mg)	Saline	7.9 ± 0.6
11	Saline	Salbutamol (75 μg)	19.5 ± 1.1*

All the drugs were injected subcutaneously dissolved in saline (0.9% w/v NaCl solution). The activity of hepatic alkaline phosphatase, estimated 4 h later, is expressed as specific activity (units/mg protein). The values are means ± s.e. Each group contained six mice. Values marked (*) are significantly different ($P < 0.005$) from the first group.

0007-1188/81/010008-02 $01.00

which is a specific antagonist of β_2-type receptors. Practolol, which blocks β_1-receptors, failed to inhibit the response to isoprenaline. This clearly shows that β_2-receptors are probably involved in this induction, a suggestion which is further supported by the observation that salbutamol, a β_2-receptor agonist was able to induce hepatic alkaline phosphatase.

Financial assistance of the Indian Council of Medical Research is gratefully acknowledged.

References

WILFRED, G. & PRAKASA RAO, J. (1976). Induction of hepatic alkaline phosphatase: phosphodiesterase inhibitors and adrenaline. *Ind. J. Biochem. Biophys.*, **13**, 331, 334.

LOWRY, O.H., ROSEBROUGH, N.J., FARR, A.C. & RANDALL, R.J. (1951). Protein measurement with the folin-phenol reagent. *J. biol. Chem.*, **193**, 265–275.

LANDS, A.M., ARNOLD, A., MCAULIFF, J.P., LUDUENA, F.P. & BROWN, T.G. (1967). Differentiation of receptor systems activated by sympathomimetic amines. *Nature, Lond.*, **214**, 597–598.

(*Received October 1, 1980.*)