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A Comparison of the Responses of Lower Vertebrate Intestines to Prostaglandin E_1 and E_2

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SUMMARY

1. The isolated strips of guinea-pig, fowl and reptiles (snake and tortoise) showed consistenly excitatory responses to PGE_1 and E_2, which were dose-dependent.
2. Frog intestine revealed inhibitory responses to both PGE_1 and PGE_2 except a small of PGE_2 (1-10 ng/ml) caused slight contraction.
3. The intestines of pieces showed inconsistent responses to PGE_1 and E_2. In fresh-water fish(carp), PGE_1 produced relaxation under the dose of 50 ng/ml, and contraction by the large doses, but PGE_2 consistently caused contraction in dose-dependent manner. However, the strips of sea-water fish revealed the different responses to PGE compound: PGE_1 caused relaxation and PGE_2 conversly contraction even though in small degree.
4. These results that there are genera differences in the responses of the longitudinal strips of intestine to PGE_1 and PGE_2 was assumed to be possibly correlated with evolutionally primitive function of gut.

INTRODUCTION

Some of the naturally occurring prostaglandins (PGs) were reported to be biosynthesized in many tissues (Flower, 1974), and these substances are also known to be found in all other gastrointestinal tissues including the stomach of man, rat and the small intestine of man, guinea-pig and rabbit, and the large intestine of swine (Bennett and Fleshler, 1970), and further, PGE and PGF types were found to be present in the rat stomach and released spontaneouly in vitro and acetylcholine or transmural electrical stimulation accelerated the PGs formation from precursors bound to membrane phospholipid, However, the responses of lower vertebrate intestine under the genus mammal to PGs were rarely reported, so that this paper is aimed to see the genera differences in the intestinal responses to PGE_1 and PGE_2.

METHODS

The experimental animals acquired near Busan city, Korea were as follows: 1. Mammal; guineapig, 2. Fowl; Gallus gallus domesticus, 3. Reptile; snake (Elaphe rupodorsata (Cantor)) and tortoise (Amyda japonica), 4. Amphibia; frog(Rana nigromaculata) 5. Pisces; fresh-water fish, carp (Carassius carassius) and sea-water fish, eel (Anguilla japonica) and Ditrema temminck: Bleeker.

This experiment was carried out from May to 30th September 1974.

The upper and middle portion of intestine were used and the lower portion discarded ;

lower vertebrates. The segments of guinea-pig and fowl were mounted in organ baths containing 15ml Tyrode solution (37°C) and those of reptiles, amphibia and pisces were suspended in Frog-Ringer solution(at room temperature). All these were gassed with oxygen and muscle activity recorded with an isotonic lever (magnification 10 : 1). The preparations were pretreated with 10^{-6}g/ml of atropine and guanethidine, respectively and bathed for 30~60 min until the tension being stabilized, and then washed out with working solutions.

RESULTS

1. Excitatory responses of intestines

Isolated terminal ileum of guinea-pig and intestinal strips of fowl under gizzard contracted to small amounts of PGE_1 and PGE_2 in dose-dependent manner from 0.1 up to 100 ng/ml and the contraction height of fowl intestine even in large dose was less than those of guinea-pig.

The gut segments of snake and tortoise also showed contraction but the strips of the latter exhibited high senstive and dose-dependent response to both PGE_1 and PGE_2 at picogram level and snake intestine showed much slower response than do those of other lower vertebrates. (Table 1).

2. Inhibitory and inconsistent responses of intestine

The isolated upper intestine of frog consistenty revealed dose-dependent relaxation but PGE_2 showed the dual responses, that is, when

Table 1. Excitatory responses of isolated intestine to PGE_1 and PGE_2

PGE Concentration g/ml	Mammal	Fowl	Reptiles	
	Guinea-pig	*Gallus gallus domesticus*	Snake *Elaphe rupodorsata*	Tortoise *Amyda japonica*
	Contraction (mm), Mean±SD			
	PGE_1 PGE_2	PGE_1 PGE_2	PGE_1 PGE_2	PGE_1 PGE_2
10^{-10}	5.1±2.5(7) 2.4±1.3(7)	10.0±4.1(5) 6.3±2.2(6)	— —	24.4±11.5(9) 8.8±3.5(12)
10^{-9}	9.5±4.2(6) 15.2±6.1(6)	16.2±4.8(6) 21.5±6.7(6)	8.4±4.1(7) 11.6±3.0(8)	50.2±16.3(11) 26.5±6.0(12)
10^{-8}	57.0±24.1(6) 54.2±13.5(6)	48.7±11.0(6) 29.4±10.3(7)	13.5±4.4(12) 25.4±4.8(8)	58.7±14.4(9) 53.8±9.1(9)
10^{-7}	90.6±18.3(6) 80.0±15.5(5)	55.4±12.3(6) 41.6±14.1(6)	19.0±6.2(7) 40.3±10.2(7)	62.8±13.9(8) 57.3±13.5(8)
10^{-6}	— —	— —	28.5±11.5(7) 37.2±12.6(6)	— —

Numbers in brackets indicate numbers of observations

1 ng/ml PGE_2 applied, six out of 9 preparations caused no response and the remained three produce mild contraction and by 10 ng/ml PGE_2 ten out of 14 induced contraction, one had no response and 3 strips showed inhibitory response.

By 30 ng/ml PGE_2 six out of 12 preparations relaxed and others contracted in small height in amplitude and 50 ng/ml PGE_2 showed relaxation in 9 out of 12 and the remained 3 preparations contracted. PGE_2 100 ng/ml consistently produced the inhibitory responses as shown in Fig. 1. The intestinal strips of frog responded inhibitory more sensitively to PGE

Table 2. Inhibitory and inconsistent responses of isolated intestine to PGE_1, PGE_2 and $PGF_{2\alpha}$

PGs	Amphibia			Fish							
Concentration	Frog, Rana nigromaculata			Fresh-water fish, Carassius carassius			Sea-water fish: Eel, Anguilla japonica		Sea-water fish: Ditrema temmincki Bleeker		
g/ml	Responses, Contraction(+) and Relaxation(−), Mean±SD(mm)										
	PGE_1	PGE_2	$PGF_{2\alpha}$	PGE_1	PGE_2	$PGF_{2\alpha}$	PGE_1	PGE_2	PGE_1	PGE_2
10^{-9}	−10.5±2.7 (6)	+4.0±2.2 (9)#	—	0(4)	0(5)	—	0(6)	0(9)	0(5)	0(5)
10^{-8}	−18.7±5.4 (16)	+13.6±5.1 (14)#	+4.6±2.1 (4)	##(7)	+10.2±4.5 (7)	+9.3±3.8 (4)	−13.5±2.1 (6)	+7.1±3.3 (6)	−4.6±1.1 (8)	+6.4±2.0 (5)
10^{-7}	−37.3±13.5 (6)	−42.0±18.6 (8)	+18.7±5.3 (7)	+10.5±5.7 (10)	+21.2±6.3 (10)	+33.6±10.4 (4)	−19.0±7.2 (5)	+12.4±4.6 (6)	−12.5±3.4 (5)	+9.1±4.1 (5)
10^{-6}	—	—	+21.8±4.4 (4)	+18.1±7.6 (9)	+41.0±7.9 (7)	+37.2±11.0 (4)	−22.7+11.0 (5)	+18.7±5.7 (5)	−9.0±2.7 (6)	+11.2±5.3 (4)

Numbers in brackets indicate numbers of observations.
#, See the text.　　##, Three preparations out of 7 showed slight inhibitory response.

Fig. 1. Dose-response curves to PGE_1, PGE_2 and $PGF_{2\alpha}$ as the mean response of intestinal strips from frog, which was compared with the action of epinephrine(*Epi*).

Fig. 2. Effects of PGE_1 and PGE_2 on the intestinal strips of carp, Carassius carassius.

compounds than epinephrine.

The middle portion of intestinal strip (fresh-water fish) was initially applied with 10^{-8}g/ml acetylcholine to see the responsiveness to the stimulant and thereafter, by applying 50 ng/ml PGE_1 they slowly and slightly relaxed, but

PGE_1 from 100 to 1,000 ng/ml consistently contracted the segment. In contrast to PGE_1, PGE_2 strongly caused contraction even by the dose of 5 ng/ml in dose-dependent up to 100 ng/ml. $PGF_{2\alpha}$ also induced contraction but less potent than PGE_2 (Fig. 2).

As a sea-water fish the intestine of eel, which is oviparous fish, was relaxed by PGE_1 but conversly contracted by PGE_2. And the intestinal strips of Ditrema temmincki Bleeker, which is characteristically viviparous fish, revealed the similar responses as shown in those of eel (Table 2).

DISCUSSION

Recent works have shown that relatively large amounts of PGs may be released after nerve stimulation (Horton and Main, 1967; Ramwell et al., 1965; Davies et al., 1967; Gilmore et al., 1968; Shaw, 1966), so that in this experiment atropine and guanethidine were previously treated in the bath to exclude the actions of adrenergic and cholinergic fibers.

In each instance the longitudinal muscle strips were used and the effects of PGE_1 and E_2, sometimes with $PGF_{2\alpha}$ have been compared on the five genera, of which were mamml, fowl, reptile, amphibia and pisces. Not only the intestines of domestic fowl but those of reptiles (snake and tortoise) were consistently responded with contraction by the small amounts of PGE compound like as shown in guinea-pig ileum and other mammals (Bennet and Fleshler, 1970). However, the isolated intestine of frog revealed inhibitory responses to both PGE_1 and E_2 except the small dose of PGE_2 (10 ng/ml) showed inconsistency. There can be seen much more inconsistent responses of the intestines of pisces to PGE, that is, the intestine of carp was contracted by PGE_1 and E_2, in this case the small amount of PGE_1 caused trivial contraction, irregularly. The intestinal strips of sea-water fish showed inhibitory responses to PGE_1, and excitatory to PGE_2, but both of responses were insensitive.

A clear role for PGs in gut motility has not yet been established, but recently interest has been focused on the role of PGs in the action of neurotransmitters of autonomic nervous system and on the maintenance of smooth muscle tone in the rabbit jejunum and guinea-pig ileum (Hedqvist and Wennmalm, 1971; Samuelsson and Wennmalm, 1971; Wennmalm, 1971; Ferreira et al., 1972; Kadlec et al., 1974, and Botting and Salzmann, 1974).

It is interesting to observe that the longitudinal strips of intestine obtained from lower vertebrates under amphibia phylogenetically in contrast to the animals above reptile have shown a variety of responses to PGE_1 and E_2 as inhibitory or excitatory, and these are seemed to be possibly correlated with evolutionally primitive function of gut.

It is harder to rationalize the effects of PGs but these genera differences in the action of PGE compounds may presumably be the same case as the fact indicated by Campbell and Burnstock (1968), concerning the vagal supply to the gut of lower vertebrates as interpreting that the vagal outflow is primitively inhibitory, but that these fibers are accompanied by excitatory fibers.

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