EFFECTS OF ADRENERGIC DRUGS ON CILIARY EPITHELIUM*

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The action of parasympathomimetic drugs like acetylcholine and physostigmine on ciliary epithelium of frog's oesophagus, rabbit trachea and gill plates of mytilus edulis was extensively studied by Burn *et al.* (1, 2, 6).

Burn (2) also observed a stimulating effect of adrenaline on the ciliary epithelium of rabbit's trachea. Noradrenaline was without any effect.

Cilia lining the oesophagus of the frog can be accelerated or decelerated in their movements by stimulation of the vagus or the sympathetic nerves respectively (7).

In the experimental laboratory of this department, experiment on the action of acetylcholine-like drugs on the ciliary epithelium of frog is a regular undergraduate exercise. In one of such exercises, we used adrenline and it was observed that adrenaline caused both stimulation and depression in various sets of the experiment, and noradrenaline was either depressant or without any effect. This prompted us to study the effects of adrenergic drugs in detail on the ciliary epithelium of frog.

MATERIALS AND METHODS

Pithed frogs were taken and muscle coat of oesophagus was stripped by careful dissection so that a semitransparent or transluscent strip of ciliated mucus membrane was isolated. A piece 20 mm long was mounted, in a frog muscle chamber, having an improvised glass cover with a slit in midline. The strip was hanging free in the muscle chamber and was not stretched or allowed to hang too loosely. Through the slit in the glass lid, poppy seeds of selected size were dropped and the time was measured in sec till these travelled a distance of 32 mm. Fresh seeds were used every time and the mean for 10 seeds was determined. Ten such experiments were made with each drug concentration.

Strips were bathed in oxygenated frog Ringer solution or with the solution containing drugs in various concentrations for 5 min. Following this the solution was drained off from below and record made as described above.

The effects of noradrenaline bitartrate, adrenaline hydrochloride and isoprenaline sulphate in concentrations of 1×10^{-5}, 1×10^{-4}, 2×-10^{4} and 1×10^{-3}, and of tolazoline-hydrochloride and propranolol hydrochloride in concentrations of 5×10^{-5}, 1×10^{-4}, 2×10^{-4}, and 1×10^{-3} were recorded.

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The effects of sympathomimetic amines were also studied after exposure of the strip to alpha and beta-receptor blockers for 5 min.

To exclude the possibility of drugs acting through the remaining submucosal coat or muscle fibres from the undersurface of the strip, a series of experiments were devised in which the drug solutions were applied to the under surface only. The results excluded any such possibility as this procedure did not modify the normal movements of cilia. But when the drug level was further raised, to submerge the upper surface also, the typical drug effects were obtained.

The results were expressed as the mean % change in the rate of movement of cilia as described by Burn (2).

RESULTS

It can be seen from Table I that noradrenaline was depressant to the movements of cilia in all the concentrations used in the experiments. Maximal effect was observed with 2×10^{-4} concentration. Further increase in concentration, was less depressant to the movement.

Adrenaline elicited biphasic effect on the movement. Lower concentration of adrenaline (1×10^{-5}, 1×10^{-4} and 2×10^{-4}) were stimulant to cilia while a higher concentration (1×10^{-3}) was depressant. This depressant effect was found to be variable as it was observed in some experiments that this concentration of adrenaline produced initial stimulation, followed by depression of cilia.

Isoprenaline, like adrenaline elicited biphasic action i.e. stimulation in lower concentrations (1×10^{-5}, 1×10^{-4} and 2×10^{-4}) and depression in higher (1×10^{-3}) concentration.

Tolazoline was seen to be depressant in all the concentrations. Optimal effect was seen with 2×10^{-4} concentration. Though itself a depressant, tolazoline blocked the noradrenaline, adrenaline and isoprenaline induced depression of cilia. In concentration of 2×10^{-4}, tolazoline potentiated the stimulant effect of adrenaline and isoprenaline.

Propranolol was stimulant in lower concentrations (5×10^{-5}, 1×10^{-4} and 2×10^{-4}) and depressant in a higher concentration (1×10^{-3}). Concentration of 2×10^{-4} which was distinctly stimulant to cilia blocked the stimulant effects of adrenaline and isoprenaline. Propranolol failed to antagonize the depressant effects of noradrenaline (2×10^{-4}). However, it exerted a blocking effect on the depression produced by noradrenaline (1×10^{-3}).

DISCUSSION

Effects of catecholamines and those of alpha- and beta-receptor blocking drugs on ciliary epithelial movements suggest the presence of alpha- and beta-receptors in the epithelial cells. Since noradrenaline caused depression and isoprenaline caused stimulation, it appears that in ciliary epithelium alpha-receptors are inhibitory and beta-receptors are excitatory in

TABLE I

Mean % change in rate (sec) of movement of cilia of frog's oesophagus
(Each value is the mean of 10 experiments)

Drug and concentration	*% change in rate ± S.E.*			
		Tolazoline 1 x 10-4	*Tolazoline* 2 x 10-4	*Propranolol* 2 x 10-4
Noradrenaline				
1 x 10-5	- 31.20±0.32	- 8.12±0.12	—	—
1 x 10-4	- 33.25±0.39	- 9.27±0.15	—*	—*
2 x 10-4	- 60.70±0.48	- 42.28±0.36	- 36.57±0.42	- 65.48±0.62
1 x 10-3	- 46.01±0.38	- 39.00±0.29	- 32.21±0.51	- 23.67±0.29
Adrenaline				
1 x 10-5	+109.21±2.14	—	+130.72±0.92	- 23.62±0.23
1 x 10-4	+101.43±2.46	—	+126.83±0.98	- 26.83±0.32
2 x 10-4	+ 30.34±1.23	—	+ 66.50±0.72	- 16.84±0.14
1 x 10-3	- 15.73±0.32	—	+167.35±0.58	- 26.10±0.18
Isoprenaline				
1 x 10-5	+ 40.38±0.42	—	+ 89.22±2.65	- 16.86±0.29
1 x 10-4	+ 49.23±0.56	—	+102.65±2.70	- 13.12±0.34
2 x 10-4	+ 85.81±0.98	—	+142.70±2.34	- 11.73±0.23
1 x 10-3	- 39.42±0.41	—	+112.62±2.52	- 16.73±0.20
Tolazoline				
5 x 10-5	- 7.82±0.24	—	—	—
1 x 10-4	- 16.63±0.18	—	—	—
2 x 10-4	- 26.44±0.22	—	—	—
1 x 10-3	- 6.77±0.12	—	—	—
Propranolol				
5 x 10-5	+ 11.10±0.21	—	—	—
1 x 10-4	+ 52.20±0.42	—	—	—
2 x 10-4	+ 34.72±0.29	—	—	—
1 x 10-3	- 24.27±0.28	—	—	—

Mean control rate of movement of cilia was 40 sec. for 20 mm.
- = % decrease in control rate
+ = % increase in control rate
Probabililty of all the values in the Table excepting those marked* was between $< .05$ and $> .001$

nature. The study of Sinha (8) who showed a slowing of the ciliary movement by ephedrine corraborates the present results. Adrenaline had a mixed action on ciliary epithelium. It is known that adrenaline can excite beta - receptors at concentrations lower than those needed for exciting alpha - receptors. Our observations confirm this since adrenaline caused depression in higher concentrations (overshadowing the effect on beta - receptors) and stimulation in lower concentrations. Tolazoline was depressant by itself, inspite of this, it was able to block the depression caused by noradrenaline. Similarly propranolol which was stimulant by itself blocked stimulation due to isoprenaline.

The stimulant effect of isoprenaline and adrenaline was potentiated by tolazoline. This could be due to block of depressant alpha - receptors leaving unopposed the beta - receptor action of these compounds (4). Propranolol reduced the depressant action of noradrenaline. This could be due to its stimulant action in concentration of 2×10^{-4}.

Isoprenaline induced depression instead of stimulation in higher concentration. This could be due either to beta - receptor blockade by isoprenaline as suggested by Butterworth (3) or due to direct stimulation of alpha - receptor by isoprenaline as tolazoline completely reversed this effect.

The concentrations used were selected after a preliminary screening in which only adrenaline (1×10^{-6}) elicited slight stimulation while all other drugs were without any appreciable effect. It seems that the alpha- and beta- receptors in the ciliary epithelium of frog are poorly sensitive to the catecholamines. This is consistent with the observations of Burn (2) who found adernaline stimulant in 5×10^{-5} and in higher concentrations and noradrenaline (1×10^{-4}) without any effect on rabbit trachea.

SUMMARY

1) Experiments on frog isolated strip of ciliary epithelium devoid of muscular attachments are described.

2) Effects of catecholamines tolazoline and propranolol are suggestive of the alpha– and beta- sympathetic receptors in ciliary epithelium.

3) Alpha—receptors appear to be inhibitory and beta—receptors excitatory in nature.

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