

EFFECTS OF PROPYLENE GLYCOL ON THE INTESTINAL SMOOTH MUSCLES OF EXPERIMENTAL ANIMALS

By

D.S. SHAH

Department of Pharmacology, Municipal Medical College, Ahmedabad.

INTRODUCTION

Propylene Glycol ($\text{CH}_3\text{CHOHCH}_2\text{OH}$, Sp.gr. 1.036) is a dihydroxy alcohol, which is being extensively used as a drug solvent. It has been reported earlier that Propylene Glycol has an anticholinergic effect on intestinal muscles (1). On the other hand, it has been reported to enhance the effect of Acetylcholine on the superior cervical ganglion, nictitating membrane and neuromuscular junction (2). In the present work, the action of Propylene Glycol is studied on Guineapig ileum using agonists like Histamine and 5-hydroxytryptamine, in addition to Acetylcholine for inducing contractions. In order to find out the probable mechanism of its action, the effects of Propylene Glycol in presence of Alpha and Beta receptor blocking agents, were studied on the rabbit Jejunum.

MATERIALS AND METHODS

Guineapig ileum-Adult female Guineapigs (wt. 500 to 800 gms) were killed by a blow on the head and cutting the throat. Pieces of ileum (about 2 to 3 cms) were mounted in an isolated thermostatic organ bath containing Tyrode solution at 37°C being bubbled with oxygen (3).

Submaximal contractions were obtained with 1×10^{-8} G/ml of Acetylcholine, 2×10^{-7} G/ml of Histamine and 3×10^{-7} G/ml of 5-hydroxytryptamine respectively. Propylene Glycol was added in the organ bath, in concentration of 20.72×10^{-3} G/ml (0.02 ml/ml) and was allowed to act for 1 or 14 minutes at the end of which, the agonists were added in the same doses to find out any modification of their effects. The recovery time was found by adding the agonists in the same doses at regular intervals till the initial effects were obtained. Experiments were also carried out similarly to study the effects of double concentration of Propylene Glycol (41.44×10^{-3} G/ml or 0.04 ml/ml).

Rabbit jejunum

Pieces of jejunum (2 to 3 cms) were obtained from freshly killed adult rabbits (wt. 1.1 Kg. to 1.3 Kg) of either sex, and were mounted in an isolated thermostatic organ bath containing Tyrode solution at 37°C being bubbled with Oxygen and 5 percent Carbon dioxide (3).

Graded doses of Propylene Glycol, ranging from 1.29×10^{-3} G to 20.72×10^{-3} G/ml

(0.00125/ml to 0.02 ml/ml) were added in the organ bath and their effects were observed for 30 seconds.

The effect of Propylene Glycol was also studied in presence of Tolazoline (6×10^{-6} G/ml) and Propranolol (1×10^{-5} G/ml) which were allowed to act for 3 minutes prior to addition of Propylene Glycol, and was compared with that of Epinephrine (1×10^{-7} G/ml) in presence of similar doses of Tolazoline and Propranolol. The number of experiments carried out on Rabbit Jejunum was ten (Fig. 3).

RESULTS

Guinea pig ileum : The results show that Propylene Glycol antagonises the effects of all the three agonists. (Fig. 1, Table 1). The antagonistic effect is more marked in higher con-

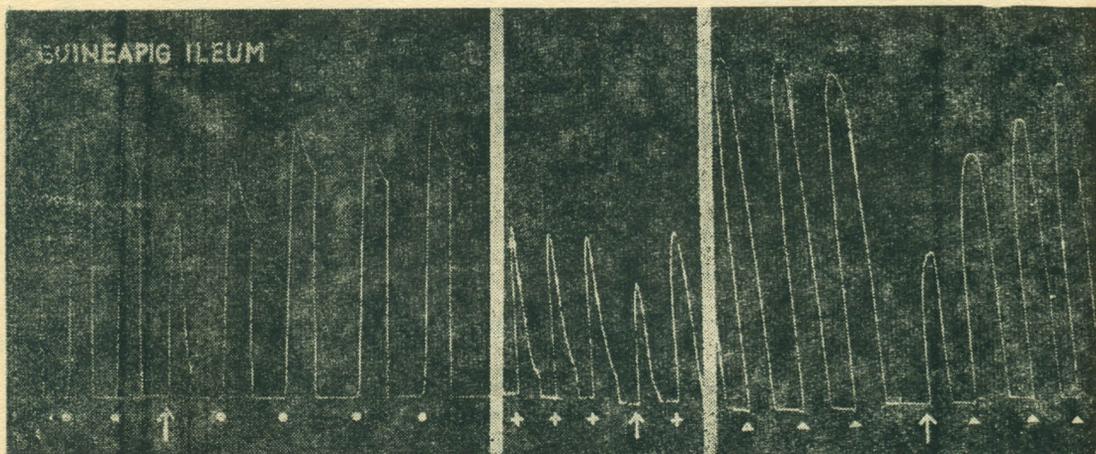


Fig. 1

Showing the effect of 20.72×10^{-3} G/ml of Propylene Glycol on contractions of Guinea pig ileum induced by Histamine, 5-hydroxytryptamine and Acetylcholine. Time interval 1 minute.

- ⊙- 2×10^{-6} G/ml of Histamine was added
- + - 3×10^{-6} G/ml of 5-hydroxytryptamine was added
- △- 1×10^{-8} G/ml of Acetylcholine was added
- ↑ - 20.72×10^{-3} G/ml of P.G. was added followed by the respective agonists after fourteen minutes.

centration and on increasing the time interval for which it is allowed to act (Table 1, Fig. 2). The recovery is comparatively quicker with 5-hydroxytryptamine (10 minutes) while slower with Acetylcholine (20 minutes).

Rabbit jejunum—In concentrations, ranging from 1.29×10^{-3} G/ml to 10.36×10^{-3} G/ml, Propylene Glycol decreases the height of pendular movement without any change in the tone of the intestinal muscles. In higher concentrations (20.72×10^{-3} G/ml), the pendular movement is inhibited completely and the tone is also decreased (Fig. 3). The recovery is immediate after removing the drug solution.

TABLE I

Showing the effect of Propylene Glycol on intestinal contractions of Guinea pig, induced by Histamine, Acetylcholine, and 5-hydroxytryptamine.

Conc. of Agonist/ml	Conc. of Propylene glycol/ml	Time in min. for which Propylene glycol was kept in bath	Mean Percentage inhibition	Recovery in minutes
Histamine 0.2 μ g	20.72 mg	14	43.97 \pm 1.76 (6)	15
Acetylcholine 0.01 μ g	20.72 mg	14	35.31 \pm 8.78 (6)	20
5 hydroxytryptamine 0.3 μ g	20.72 mg	14	34.40 \pm 12.26 (5)	10
Histamine 0.2 μ g	20.72 mg	1	36.82 (3)	15
Histamine 0.2 μ g	41.44 mg	1	83.95 (3)	15
Histamine 0.2 μ g	41.44 mg	14	96.55 (1)	20
Acetyl choline 0.01 μ g	41.44 mg	1	77.94 (2)	15
Acetyl choline 0.01 μ g	41.44 mg	14	96.15 (1)	20
5-hydroxytryptamine 0.01 μ g	41.44 mg	1	90.00 (1)	10
5-hydroxytryptamine 0.03 μ g	41.44 mg	14	94.29 (2)	10

\pm S.E.

() No. of Experiments.

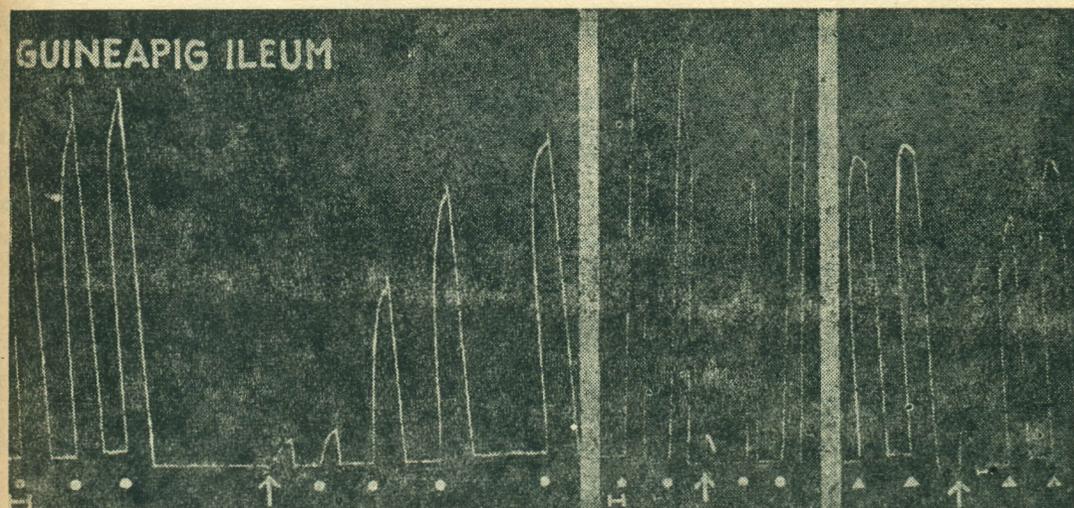


Fig. 2

Showing the effect of 41.44×10^{-3} G/ml of Propylene Glycol on contractions of Guinea pig ileum induced by Histamine and Acetylcholine. Time interval 1 minute.

○ - 2×10^{-6} G/ml of Histamine was added

△ - 1×10^{-8} G/ml of Acetylcholine was added

↑ - 41.44×10^{-3} G/ml of Propylene Glycol was added for 1 minute, 14 minutes and 14 minutes respectively before adding the respective doses of Agonists.

The inhibitory effect of Propylene Glycol on Rabbit jejunum is observed even in presence of Tolazoline as well as Propranolol, which completely block the relaxant effect of Epinephrine (Fig. 3).

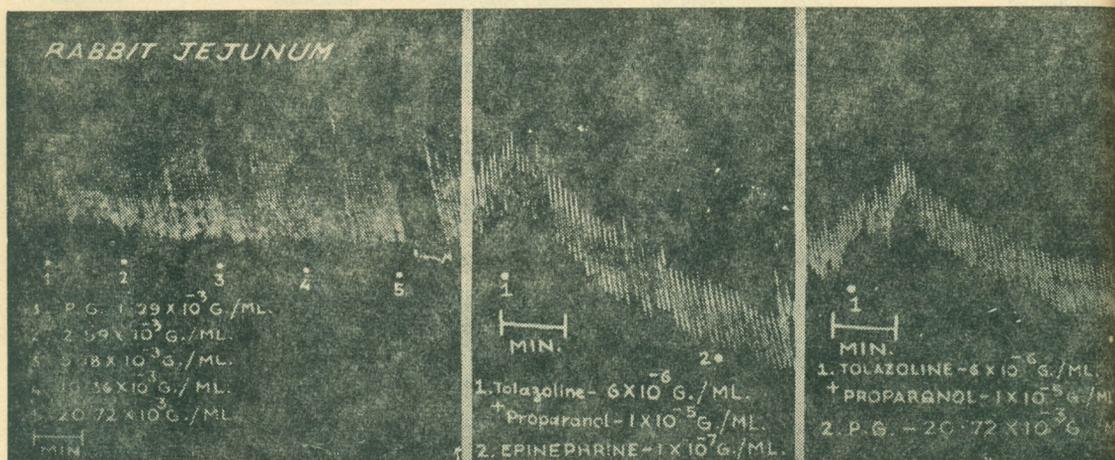


Fig. 3
Showing the effect of P.G. on Rabbit Jejunum

DISCUSSION

It is evident from the present investigation that Propylene Glycol possesses an inhibitory effect on the smooth muscles of intestine in both the species. The antagonistic effect of Propylene Glycol against the various agonists, Acetylcholine, Histamine and 5-hydroxytryptamine to a more or less similar degree may be interpreted as a direct depressant effect like Papavarine or a sympathomimetic effect because the inhibitory effect of epinephrine on intestine is manifested in a lower sensitivity to smooth muscle stimulants of all types (4). However, the observations that Propylene Glycol retains its inhibitory effect in presence of Tolazoline and Propranolol on rabbit jejunum rules out any sympathomimetic action (Fig. 3).

The concentrations of Propylene Glycol which have shown the relaxant effect are very large as compared to other known smooth muscle relaxants and it would not be practicable to use it therapeutically for this purpose. However its relaxant effect must be kept in mind and simultaneous control readings must be carried out, using similar volumes of Propylene Glycol when it has been employed as a drug solvent in various pharmacological investigations.

SUMMARY

1. Propylene Glycol, in relatively large concentrations exert a smooth muscle relaxant effect on rabbit jejunum and Guineapig ileum.

2. The mechanism of this action of Propylene Glycol is probably due to a direct spasmolytic or Papavarine like effect.
3. The spasmolytic effect of Propylene Glycol must be kept in mind in screening of drugs which have been dissolved in Propylene Glycol.

ACKNOWLEDGEMENT

I thank Dr. M.D. Desai, Dean, Municipal Medical College, Ahmedabad, for permitting me to carry out this work, and also Mr. R.S. Macwan for technical assistance.

REFERENCES

1. Frommel, E. et F, Vallet-De l effect anticholinergique due propylenglycol., *Arch. Sci. Geneva.*, 4:127, 1951.
2. Sollmann, T.A. Manual of Pharmacology and its applications to Therapeutics and Toxicology., *Philadelphia. W.B. Saunders Company.* 129, 1957.
3. Staff, Department of Pharmacology University of Edinburgh. Pharmacological Experiments on Isolated Preparations, Edinburgh *E. & S. Livingstone Ltd.* 58, 1968.
4. Turner, R.A. Screening methods in Pharmacology, New York. *Academic Press.* 45, 1965.