RESULTS

In the present study, it was observed that addition of different doses (0.01, 0.02 and 0.04 ml/ml) of the phosphate buffer, the solvent used for dissolving domperidone,was without any effect on the intestinal motility when added to the bath (Fig. I). On the other hand, addition of domperidone in a dose of 2 µg/ml dissolved in 0.02 ml phosphate buffer produced a stimulant effect on the intestinal rhythmic contraction of isolated rabbit's intestine. The stimulant action affected both tone and amplitude of contraction (Fig. I).

It was also observed that addition of domperidone in different doses of 2, 4 and 8 µg/ml produced a dose dependent stimulation of rhythmic contractions of rabbit's intestine. However, the dose of 1 µg/ml was devoid of any stimulant effect on intestinal motility (Fig. II).

The site and mode of action of domperidone was investigated on isolated rabbit's intestine. It was found that domperidone, added in a dose of 2 µg/ml, produced stimulant effect of the rhythmic intestinal motility, which was abolished after the addition of nicotine large dose (Fig. III).

Fig. I:

A record showing effect of different doses of phosphate buffer compared to domperidone on isolated rabbit's intestine.

- Addition of phosphate buffer at different dose levels of 0.01, 0.02 and 0.04 ml/ml produced no effect on rhythmic contraction of isolated rabbit's intestine.
- Addition of domperidone, in a dose of 2 µg/ml dissolved in a volume of 0.02 ml/ml phosphate buffer, produced stimulation of rhythmic contraction of isolated rabbit's intestine.

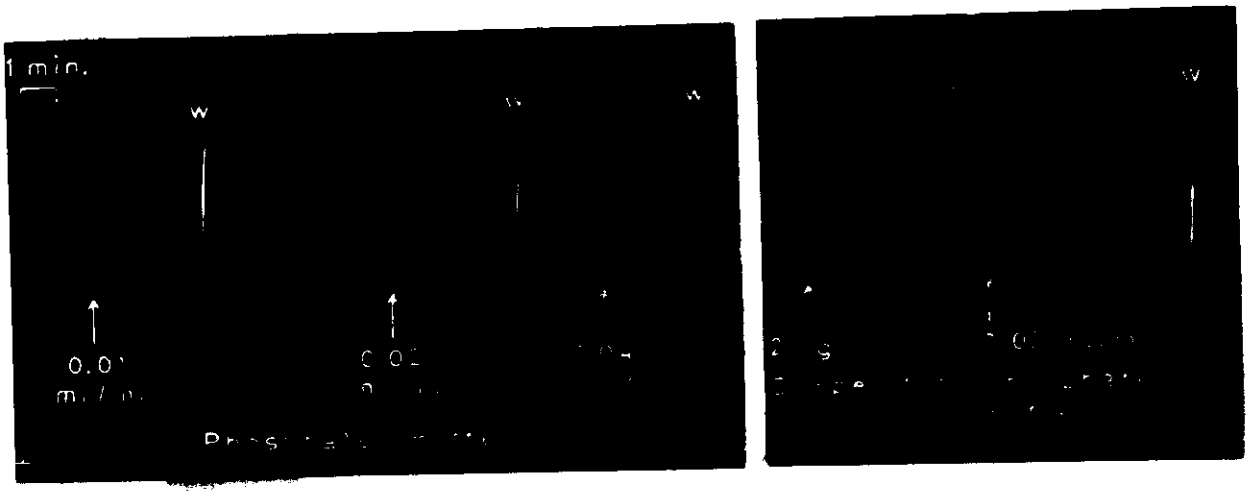

1 min.

Fig. II:

A record showing dose response curve of domperidone on rhythmic contractions of isolated rabbit's intestine.

- Addition of domperidone, in a dose of 1 µg/ml, produced no effect on rhythmic contractions of isolated rabbit's intestine.
- Addition of different doses of 2, 4 and 8 µg/ml produced dose dependent stimulation of rhythmic contractions of isolated rabbit's intestine.

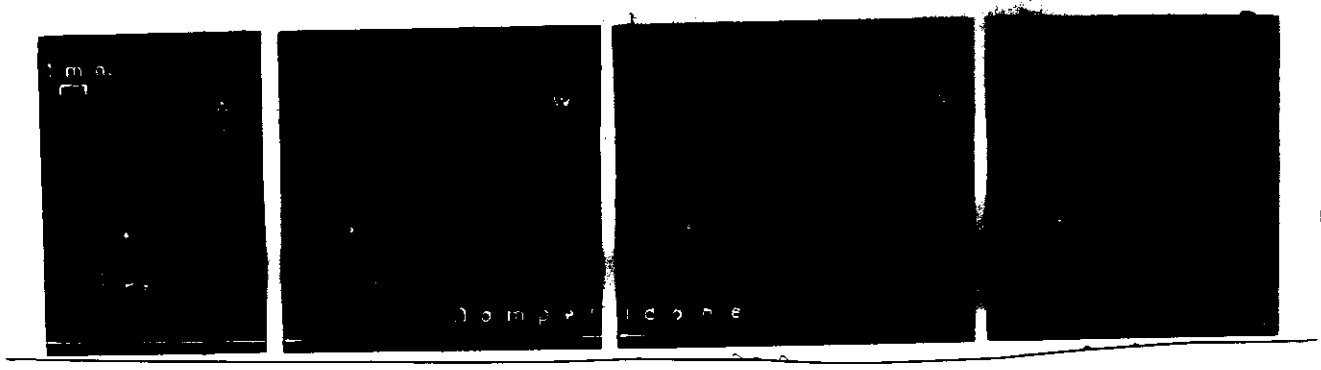


Fig. III:

A record showing site and mode of action of domperidone on isolated rabbit's intestine.

- Addition of domperidone, in a dose of 2 µg/ml, produced a stimulant effect on contractions of isolated rabbit's intestine.
- Addition of nicotine, in a dose of 0.5 µg/ml, produced an increase in the tone of intestinal contractions.
- Addition of nicotine, in a dose of 5 µg/ml, produced stimulant action in amplitude of contraction of isolated rabbit's intestine.
- Re-addition of nicotine on a previous dose of 0.5 µg/ml did not change intestinal contractions.
- Re-addition of domperidone, in a dose of 2 µg/ml, after nicotine 5 µg/ml, domperidone did not produee any effect on intestinal contractions.

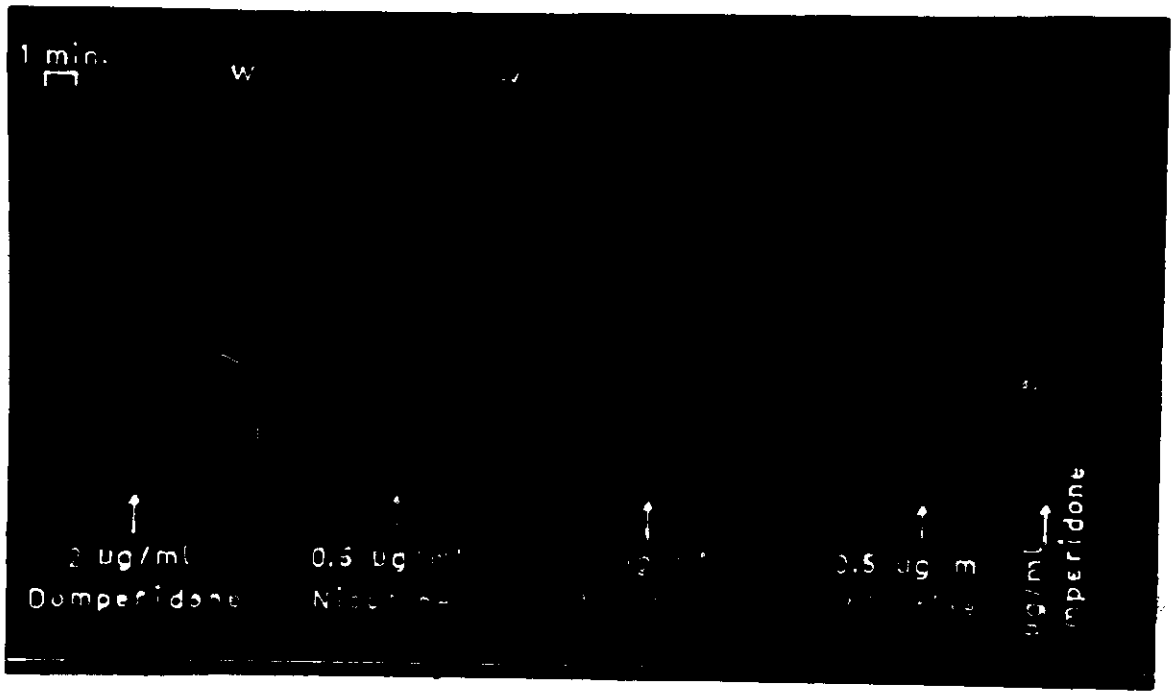
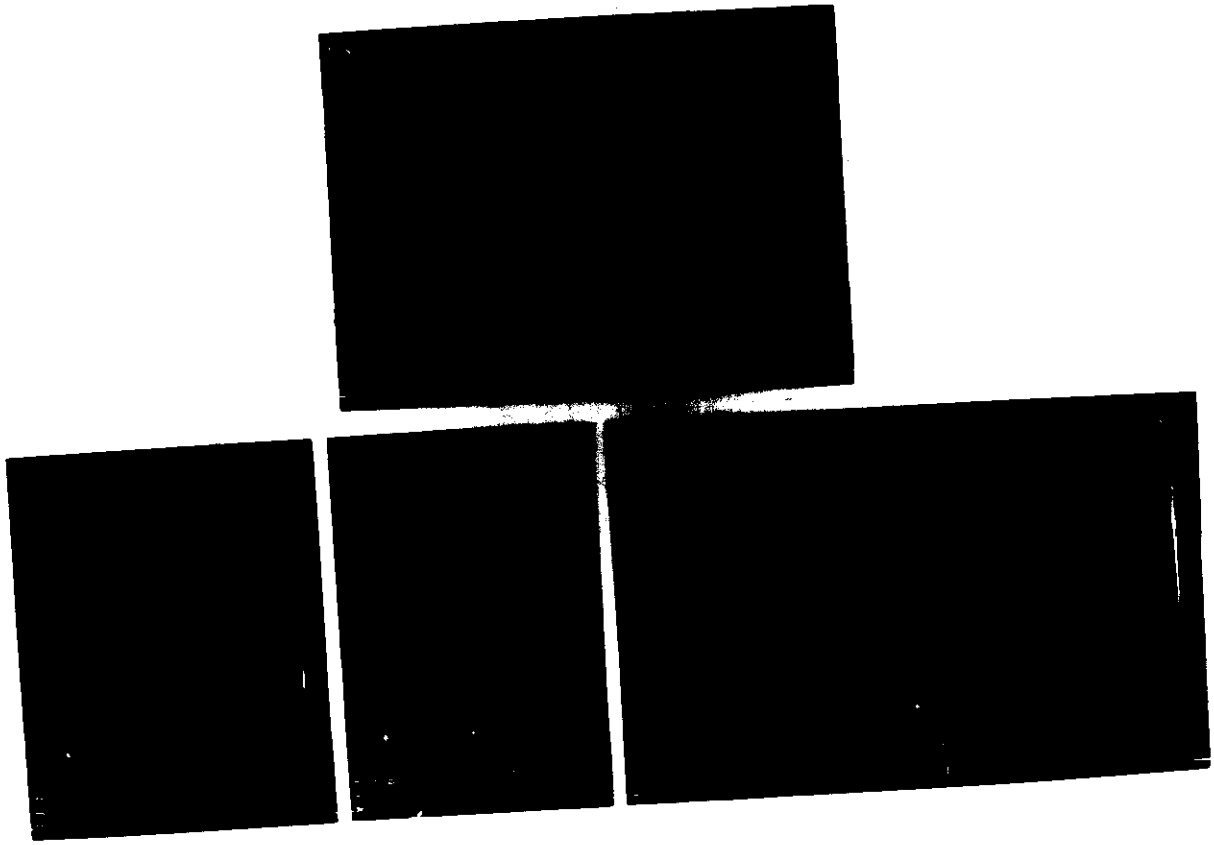

1 min.
2 ug/ml
Domperidone
0.5 ug/ml
Domperidone

Fig. IV:

A record showing interaction of domperidone with barium chloride and acetylcholine on isolated rabbit's intestine.

- Addition of barium chloride, in a dose of 5 µg/ml, produced a marked increase in tone of intestinal contractions.
- Addition of acetylcholine, in a dose of 0.1 µg/ml, produced marked increase in tone of intestinal contractions.
- Addition of domperidone, in a dose of 2 µg/ml, induced temporary stimulation of intestinal motility.
- Re-addition of acetylcholine, in the above mentioned dose, produced a reduced stimulant effect in intestinal motility.
- Re-addition of barium chloride, in the aforementioned dose, produced a marked reduced stimulant effect in intestinal contractions.

1 Min.
W
W
W
W
BaCl2



Concerning the effect of domperidone on rat fundus strip, it was found that addition of domperidone in a dose of 2 µg/ml does not produce any change in the tone or induce any stimulant effect on rat fundus strip (Fig. VI). On the other hand, domperidone added in the previous dose was found to reduce the stimulant effect of 5-hydroxytryptamine (5-HT) to less than 50%. Rat fundus strip regained its normal sensitivity to 5-HT after repeated washings (Fig. VI).

Experiments were also carried out to screen the pharmacological effects of domperidone on different segments of guinea pig ileum.

In experiments using the proximal segment, it was found that domperidone at a dose of 2 µg/ml reduced almost completely the contractile effect induced by histamine (0.4 µg/ml) (Fig. VII).

The normal response of guinea pig ileum to histamine was restored after repeated washings (Fig. VII).