



PRECLINICAL SCREENING OF LAXATIVES

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INTRODUCTION

- ❑ Laxatives are substances that loosen stools and increase bowel movements.
- ❑ They are used to treat and prevent **Constipation**.
- ❑ High dose of laxatives can cause diarrhoea.

CLASSIFICATION OF DRUGS

- ❑ **Bulk Forming:-** Dietary fiber, Metamucil, Psyllium, Methylcellulose.
- ❑ **Emollient [Stool softener and Lubricants]:-**
Stool softener- Docusate salts (colace, surfak).
Lubricants- Mineral oils.
- ❑ **Hyperosmotic:-** Polyethylene glycol, Sorbitol, Glycerin, Lactulose.
- ❑ **Saline laxatives:-** Sodium phosphate, Magnesium citrate, Magnesium hydroxide (*milk of magnesia*), and Magnesium sulfate (*Epsom salt*).
- ❑ **Stimulants:-** Senna, Cascara.

ANIMAL SCREENING MODEL

□ IN VIVO MODELS:-

- Drug- Induced Constipation in rats
- Charcoal meal methods
- Castor oil- Induced enter pooling
- Low-fiber diet-Induced constipation in rats
- Measurement of colon motility

DRUG- INDUCED CONSTIPATION IN RATS

❑ **Purpose :-** The model is used to determine the laxative properties of test drugs by inducing constipation.

❑ **Procedure:-**

Rats of either gender 180-220 gm where assigned randomly to 3 groups of six each.



Animals were fasted for 12 hrs before the experiment but with *ad libitum* water supplied.



The first group administered with normal saline used as control group.



Second group administered with test drug used as test group.



Third group administered with standard drug methyl cellulose used as standard group.



Every group administered with Loperamide which cause constipation.

❑ **EVALUATION:-** The output of feces (total amount of normal and wet feces) was quantified in all groups by evaluating feces weight & compare with control group.

CHARCOAL MEAL METHOD

□ Procedure:-

For an overnight period appropriate no. of animals are deprived of food.



Each mouse (0.3ml) or rat (0.5ml) in a group is given of suspension of charcoal meal (10% w/v wood charcoal in 5% w/v gum acacia solution).



Test drug I.P. administered 10-30 min before administrating charcoal meal.



After 20 mins animals are sacrificed by cervical dislocation.



The abdomen is opened, the marker's leading-edge is found.



The intestine at the leading edge is instantly immersed in 5% formalin solution to stop the peristalsis.

Evaluation:-

- ❑ The distance travelled by the charcoal leading edge and the complete intestine length are evaluated.
- ❑ More distance travelled shows the laxative properties of test drug.

CASTOR OIL – INDUCED ENTEROPOOLING

□ Procedure:-

Overnight fasted rats were divided into 4 groups of 6 animals.



Group 1:- Normal Saline (2ml/kg I.P.) served as control groups.

Group 2:- Received Loperamide (5mg/kg I.P.)

Groups 3,4 :- Methanol extract mg/kg I.P.)



All groups got castor oil after 1 hour, 2 hrs later the rats were sacrificed.



The small intestine were isolated from the pylorus to the caecum in a graduated tube and volume was measured.

□ **EVALUATION:-**

- The intestine was reweighed and the difference between the full and empty was calculated.
- The differences between full and empty intestine was calculated respectively.