Gastro-intestinal transit (charcoal meal test)

A MODEL TO STUDY ANTI-DIARRHEIC OR LAXATIVE ACTIVITY OF CANDIDATE COMPOUNDS (EFFICACY AND SIDE EFFECTS)

Model

Transit and motility disorders (constipation or diarrhea) account for 67 % of the side effects described for drugs (analgesics, anti-inflammatory, antidepressants drugs...) and account for 23% of adverse events encountered in Phase I studies. In addition, constipation and diarrhea are common health problems affecting the quality of life.
To study the effect of a candidate compound on gastrointestinal motility, the progression of a charcoal meal through the gastrointestinal tract in mice or rats is a simple, reliable and widely used method.

Species

- Mouse (BALB/c or C57BL/6)
- Rat (Sprague-Dawley)

Interest

- Evaluation of anti-diarrheal efficacy of drug candidates on diarrheic animal.
- Evaluation of laxative efficacy of drug candidates on constipated animal.
- Rapid and relevant evaluation of compound potential side effects on small intestine motility on normal animal.
- Each model is validated by clinically relevant compounds: antidiarrheal (Atropine, Loperamide) or laxative ($MgSO_4$) agents

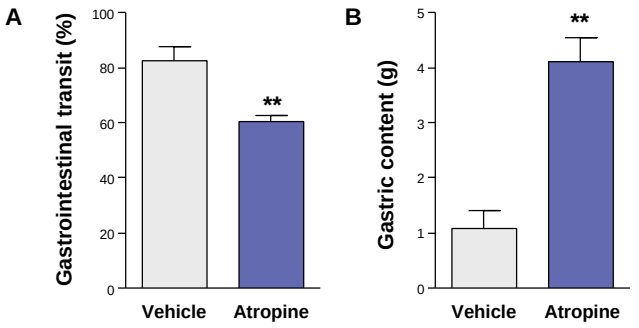
Model Description

- Constipation is induced by oral administration of loperamide.
- Diarrhea is induced by oral administration of castor-oil.
- Animals receive an administration *per os* of charcoal suspension 20 to 30 minutes before sacrifice.
- Total length of the small intestine and distance travelled by the charcoal are measured.
- Tested compounds can be administered *via* various routes (i.v., i.p., s.c., p.o., intracolonic).

Parameters evaluated

- Distance travelled by the charcoal (recorded as % of small intestine length)
- Quantification of gastric content

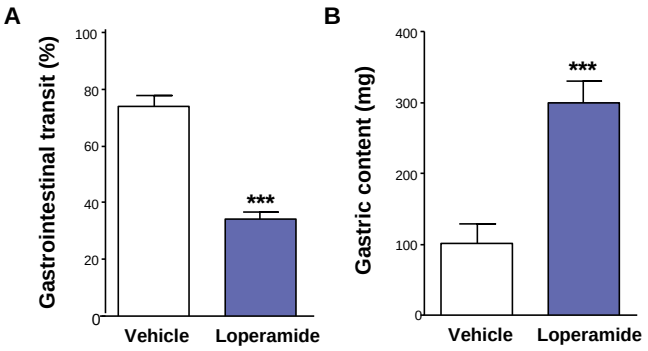
Effect of Atropine on small intestinal motility in normal Sprague-Dawley rats



Atropine (3 mg/kg) administered intraperitoneally 30 min before the charcoal gavage significantly decreased gastrointestinal transit (A) and increase gastric content (B). Evaluation was performed 30 min after charcoal administration.
** P< 0.01, n=5-10/group

Similar results were obtained in C57BL/6 and BALB/c mice.

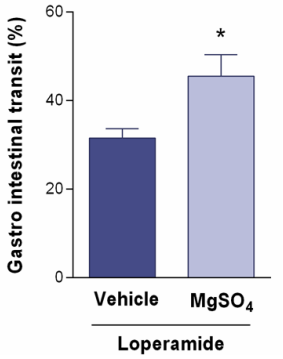
Effect of Loperamide on small intestinal motility in normal BALB/c mice



Loperamide (5 mg/kg) administered orally 30 min before the charcoal gavage significantly reduced gastrointestinal transit. Loperamide effect on intestinal motility (A) was paralleled by a significant increase in gastric content (B). Evaluation was performed 20 min after charcoal administration.
*** P< 0.001, n=7/group

Similar results were obtained in C57BL/6 mice and Sprague-Dawley rats.

Pre-treatment with $MgSO_4$ improves small intestinal motility in constipated mice



$MgSO_4$ or saline vehicle was administered 30 min before loperamide and 30 min latter charcoal meal oral administration was performed. Evaluation was done at 20 min post-charcoal.
* P< 0.05, n=7/group