Gastro-intestinal transit (fecal pellet output)

A MODEL TO STUDY ANTI-DIARRHEIC OR LAXATIVE ACTIVITY OF CANDIDATE SUBSTANCES (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 transit, the fecal pellet output in mice or rats is a simple, reliable and widely used method.

Species

- Mouse (BALB/c)
- 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 gastro-intestinal transit on normal animal.
- Evaluation is non-invasive, allowing monitoring of compound response over time.
- Each model is validated by clinically relevant compounds: antidiarrheal (Loperamide) or laxative ($MgSO_4$) agents

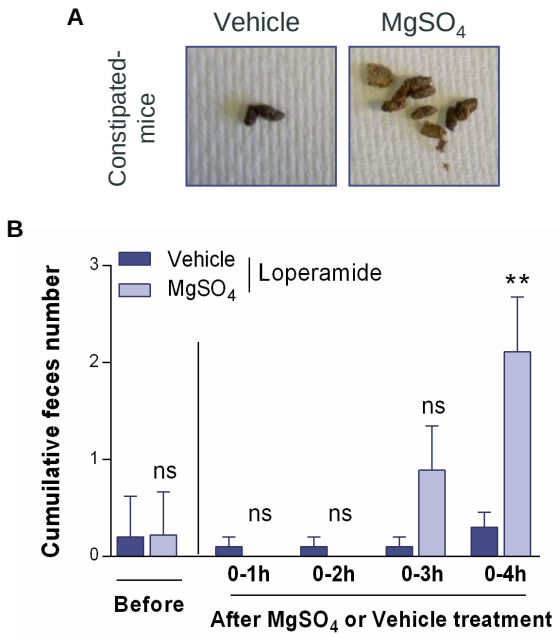
Model Description

- Constipation is induced by oral administration of loperamide.
- Diarrhea is induced by oral administration of castor-oil.
- Tested compounds can be administered *via* various routes (i.v., i.p., s.c., p.o., intracolonic).
- Feces of each animal are collected every hour (up to 6h monitoring).

Parameters evaluated

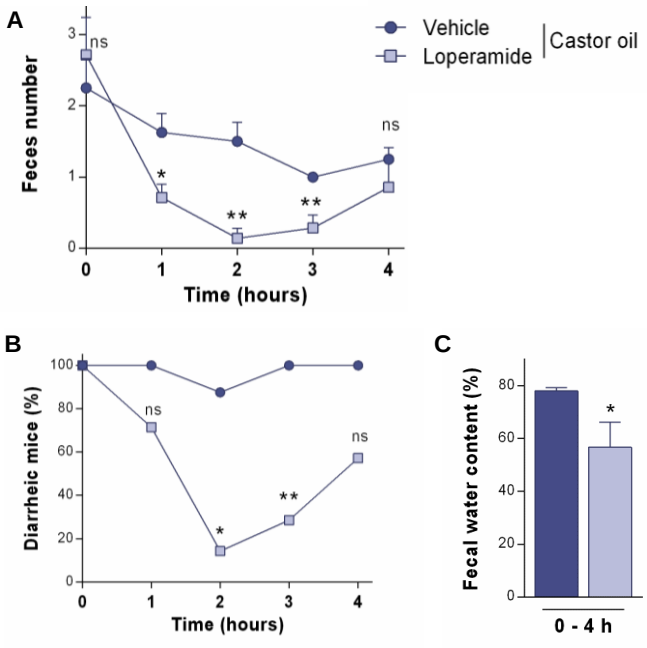
- Number and weight of feces
- Stool consistency scores from 0 to 3 (normal, loose, mushy or liquid)
- Fecal water content (%)
- % of diarrheic or constipated animal
- Diarrheal latency
- % diarrhea: number of feces with score ≥ 2 relative to total number of feces

Curative oral treatment with MgSO4 displays laxative effect on constipated mice



Constipation was induced by oral administration of loperamide at T= -1h. $MgSO_4$ or saline was administered on constipated-mice at T= 0h.
ns P>0.05, ** P<0.01. (n=9-10/group).

Curative oral treatment Loperamide displays anti-diarrheal activity on diarrheic mice



Diarrhea was induced by oral administration of Castor oil at T= -2h. Loperamide or water was administered on diarrheic-mice at T= 0h.
ns P>0,05, * P<0.05, ** P<0.01. (n=7-8/group).