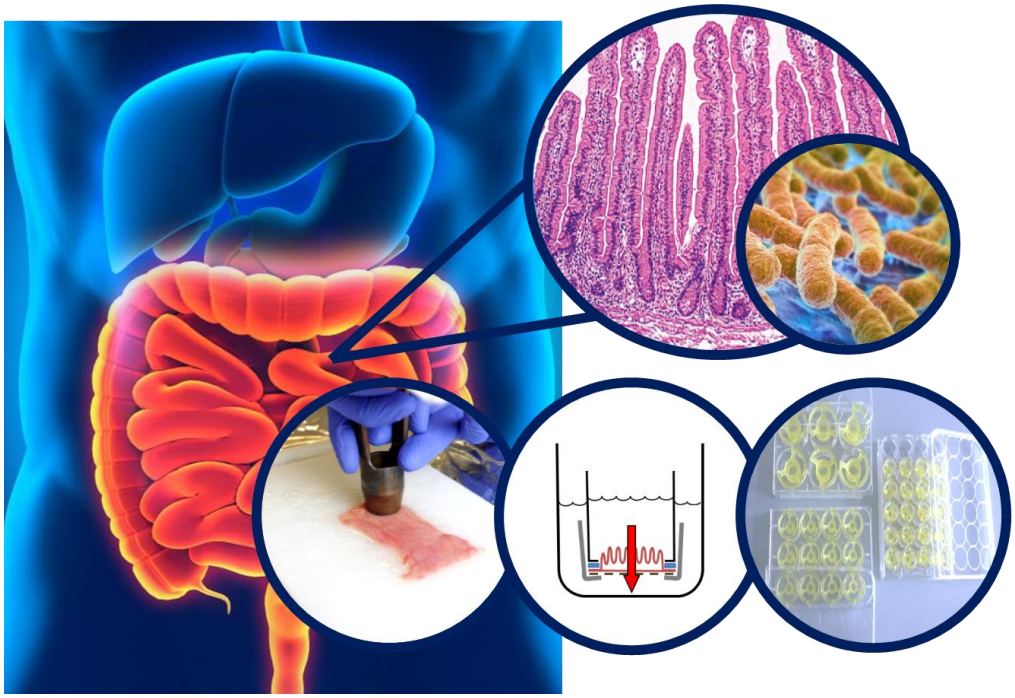
InTESTine™

INTESTINAL ABSORPTION, METABOLISM & INFLAMMATORY RESPONSES



TNO innovation for life

The TNO InTESTine™ system is developed to study the absorption and translocation of pharmaceutical, biological and nutritional compounds across the intestinal wall in a physiologically relevant model. In this medium-throughput system, fresh ex vivo intestinal tissue from human or animal origin is mounted into a two compartment model with an apical and basolateral side.
In order to study regional differences in absorption, tissue from different intestinal regions (duodenum, jejunum, ileum & colon) can be tested in parallel under controlled conditions.

The morphology and function of the intestinal tract changes from duodenum to colon with respect to thickness of the mucus layer, height of the villi, pore size of the tight junctions, expression levels of transporters, receptors and/or metabolizing enzymes. Additionally, intestinal processes can be studied following exposure to digested samples, and in the absence or presence of microbiota. This clearly demonstrates the additional value of InTESTine™ compared to monolayer cultures (e.g. Caco-2 cells) in order to study absorption, metabolism and/or food-drug and excipient-drug interactions of orally administered compounds.

YOUR ADVANTAGE

- Unique opportunity to study processes that determine oral absorption across multiple and various intestinal regions
- Resembling the in vivo situation with respect to the mucus layer, villi, tight junctions, transporters, receptors and enzymes
- Tailored made study design with various relevant opportunities, as TNO has broad expertise in intestinal physiology, active drug transporters, immune response and microbiome analysis
- InTESTine™ is well applicable for screening for toxicity (safety), early immune responses, and the release of gut hormones (e.g. GLP-1, PYY, CCK, GLP-2)

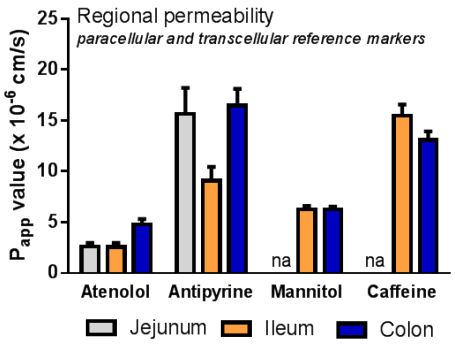


Figure 1. Regional intestinal apparent permeability (Papp) of several compounds across human jejunum, ileum and colon tissue mounted in the InTESTine™ model.

FEATURES OF INTESTINE™

Within the InTESTine™ system, freshly isolated intestinal tissue is used, most commonly derived from human donors or pigs, but also intestinal tissue of rats, dogs or chicken can be applied. The gastrointestinal tract of pigs, like humans omnivorous, shows great similarities with the human GI tract. The main advantage of using pig tissue is the high availability along the whole GI tract, enabling to study window of absorption (Figure 1). The easy set-up and horizontal mounting of tissue in InTESTine™ enables the system to be incubated in a humidified oxygenated incubator at 37°C on a rocker platform thereby reducing the unstirred water layer, evaporation and possible foaming. The horizontal mounting of tissue also enables the direct contact of test compounds with the epithelial tissue. Multiple devices can easily be arrayed allowing medium throughput analyses of your compound of interest in the InTESTine™ platform in a cost-effective way.

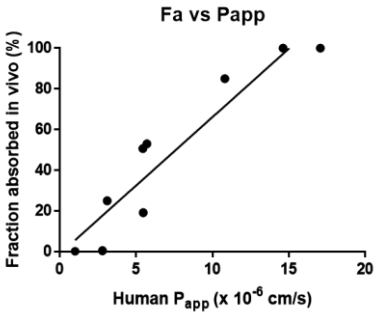


Figure 2. Human Papp, data obtained by the TNO InTESTine™ model, shows a good correlation with the in vivo fraction absorbed of drugs. Data derived from the InTESTine™ model can therefore be well applied to predict oral drug absorption.

COMBINED SERVICES

TNO InTESTine system can be easily combined with other platforms and techniques:

- Microbiome screening and analysis
- *In silico* PBPK modeling of absorption, first pass metabolism and/or bioavailability
- *In vitro* digestion, e.g. by the TNO dynamic gastrointestinal model (TIM, stationed at our spin off Triskelion), which highly simulates gastrointestinal luminal processes (collected samples can be dosed to InTESTine™)
- Our developing technology microfluidic gut-on-a-chip model which allows extended exposure to test compounds, combination with TNO I-screen for studying host microbe interactions and inflammatory responses

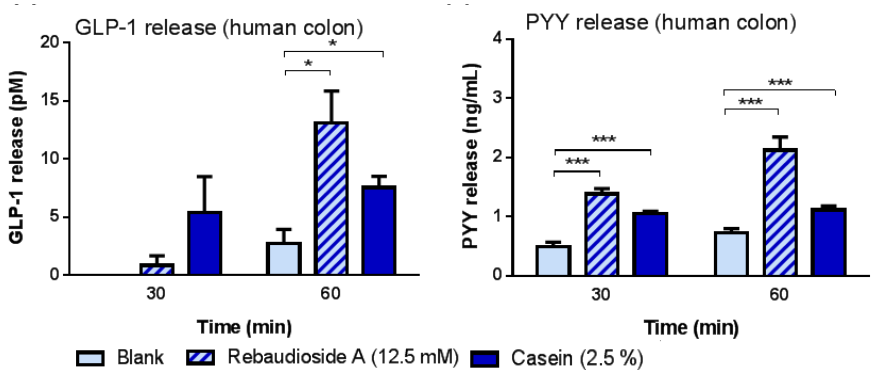


Figure 3. Secretion of gastrointestinal hormones GLP-1 and PYY to the apical and basolateral side upon stimulation of human colon tissue mounted in the InTESTine™ model.

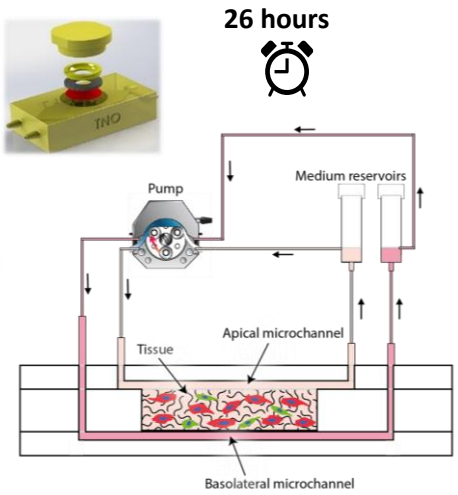


Figure 4. Schematic representation of our microfluidic gut-on-a-chip model which allows extended exposure to test compounds and the study of host-microbe interactions

REFERENCES

- Stevens et al., European Journal of Pharmaceutical Sciences 137 (2019) 104989
- Westerhout et al., European Journal of Pharmaceutical Sciences 63 (2014) 167-177

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TNO HEALTHY LIVING

TNO initiates technological and societal innovation for healthy living and a dynamic society.

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