An innovative inflammation-targeting platform for ulcerative colitis treatment

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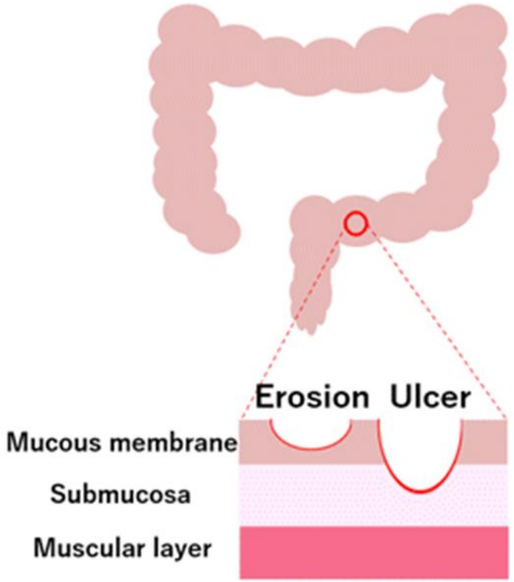
JULY 13-18, 2025

NEXT-GENERATION DELIVERY INNOVATIONS

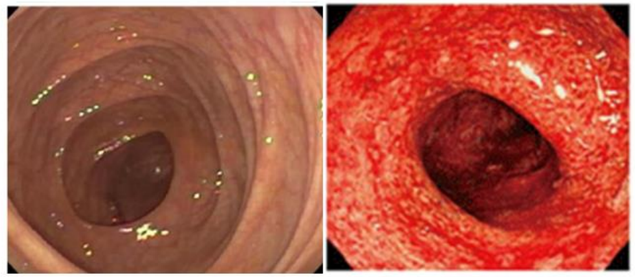
Ulcerative colitis (UC)

UC is a long-term condition where the colon and rectum become inflamed. As of 2025, an estimated 10 million people worldwide have ulcerative colitis.



Erosions and ulcers occur continuously from the rectum in the large intestine mucosa

Endoscopic findings

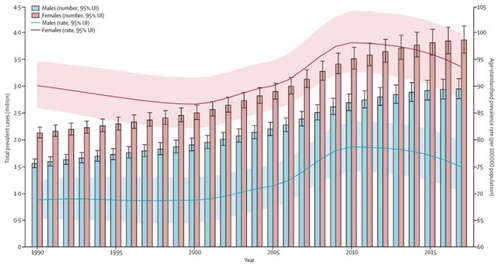


Normal | Ulcerative colitis

- **Symptoms** such as diarrhea, bloody stools and abdominal pain
- Onset mainly in young people to elderly people
- Repeat active period and remission period

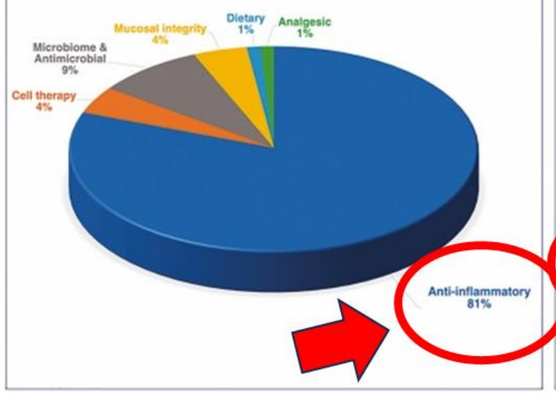
Needs long-term treatment

Incident of IBD

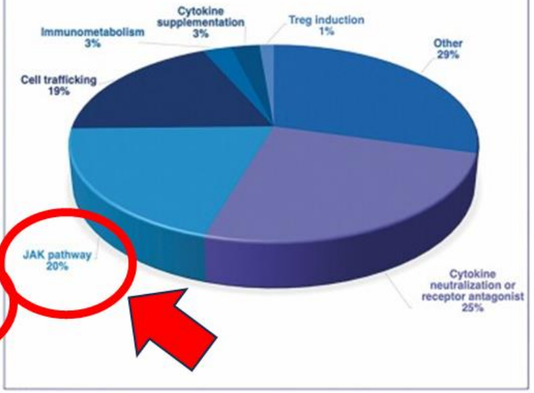


The Lancet Gastroenterology and Hepatology,
Volume 5, Issue 1 P17-30January 2020

Therapeutic Modalities in Clinical Development (P2 & P3)

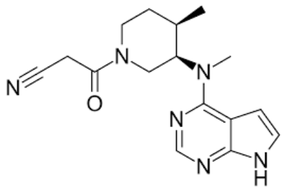


Anti-inflammatory MoAs

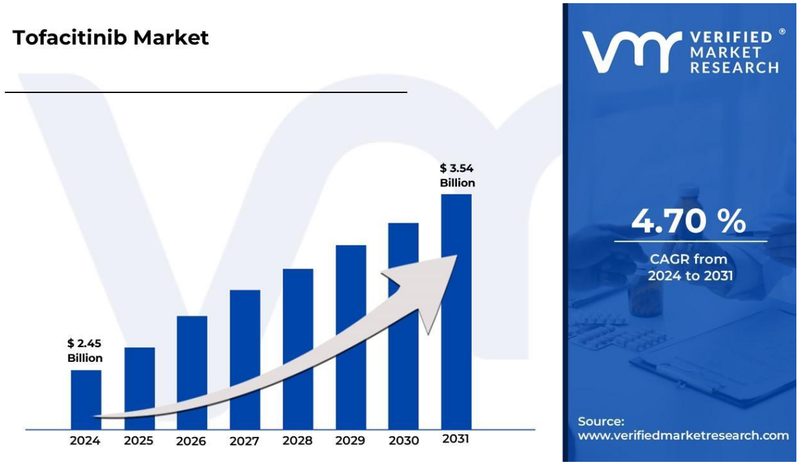


Tofacitinib (Xeljanz®): a small molecule JAK inhibitor

FDA approved for UC, represented a paradigm shift in a field dominated by biologics.



Chemical structure of tofacitinib



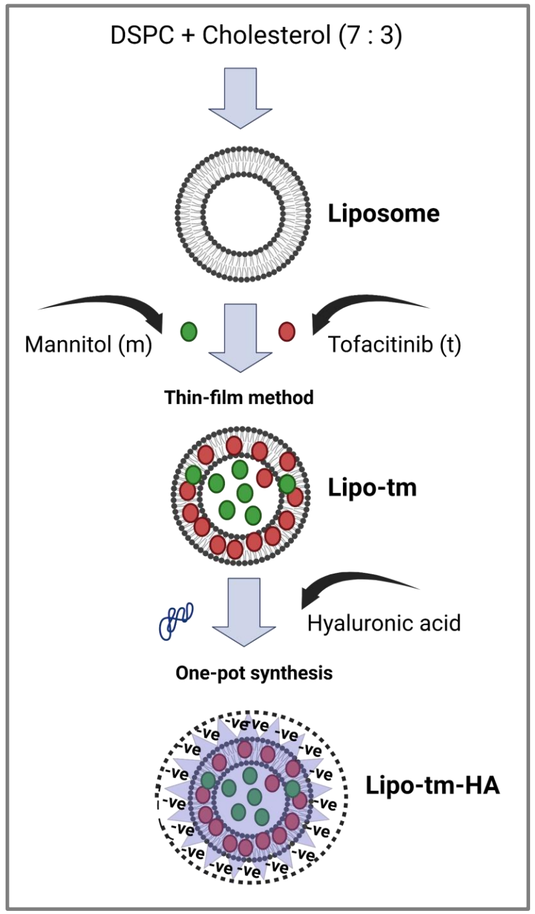
Tofacitinib—Concerns !

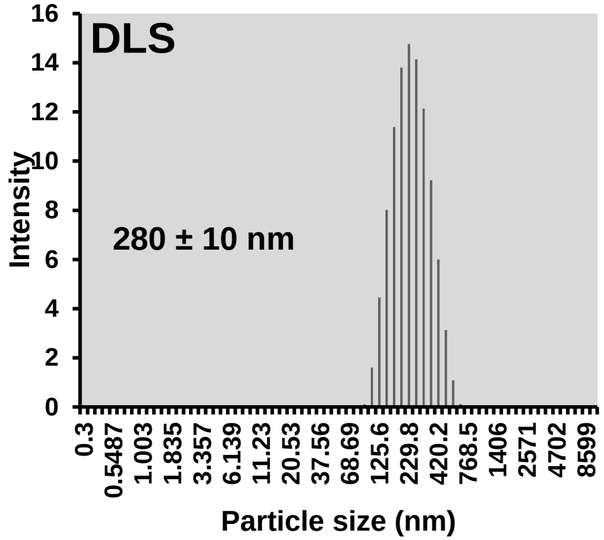
- ❑ Distribute entire body indiscriminately
  - ❑ Potential teratogenicity and fetolethality which leads to avoidance of tofacitinib in women of child bearing age.
  - ❑ It carries an FDA black box warning due to serious infections, mortality, malignancy major adverse cardiovascular events and thrombosis.

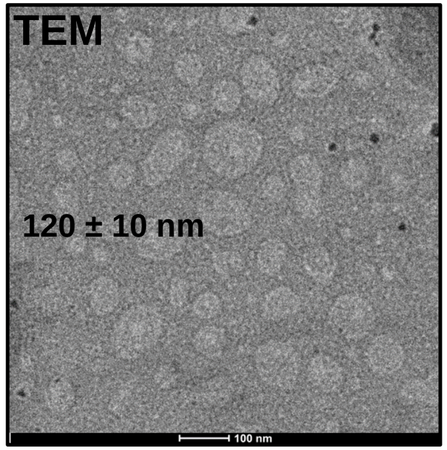
Source:
FDA Drug Safety Communication, 2021
Lewis et al. Gastroenterology, 2023
Sandborn et al N. Engl. J. Med. 2017

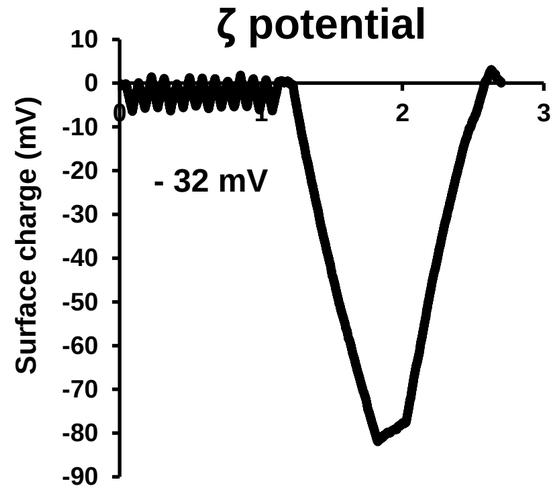
A great clinical need to enhance tofacitinib safety to expand IBD access

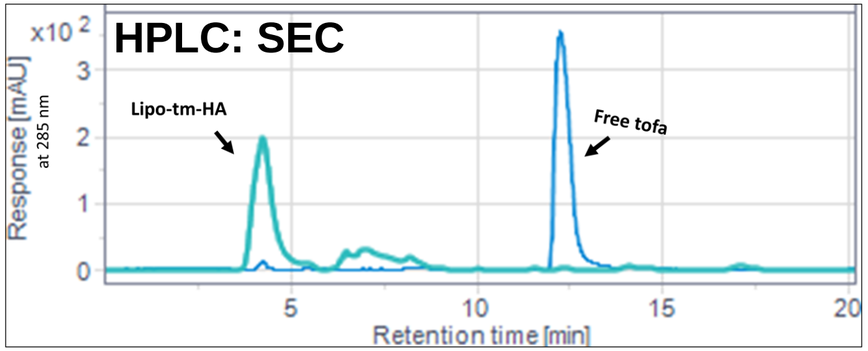
Innovative drug delivery platform: Lipo-tm-HA

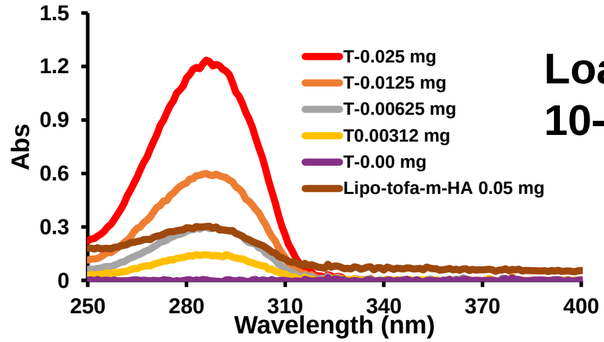








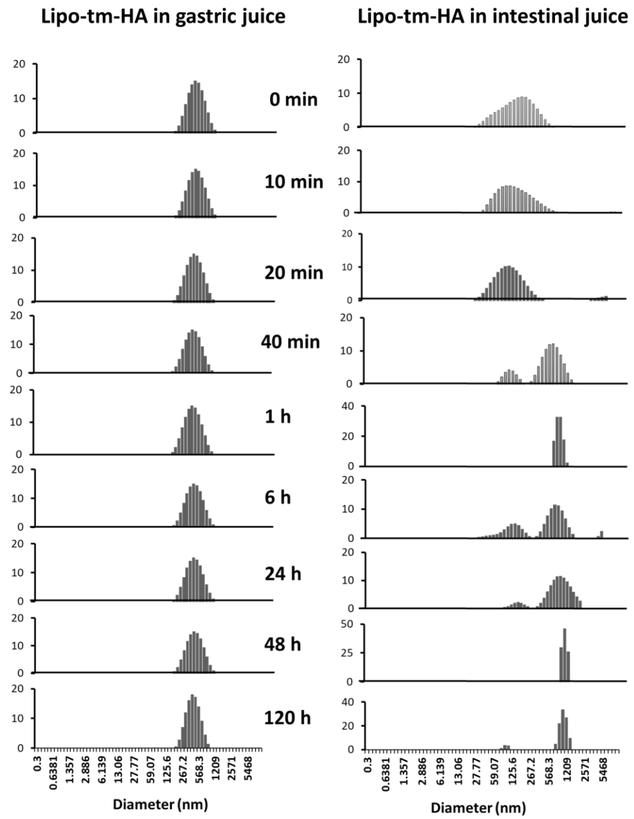




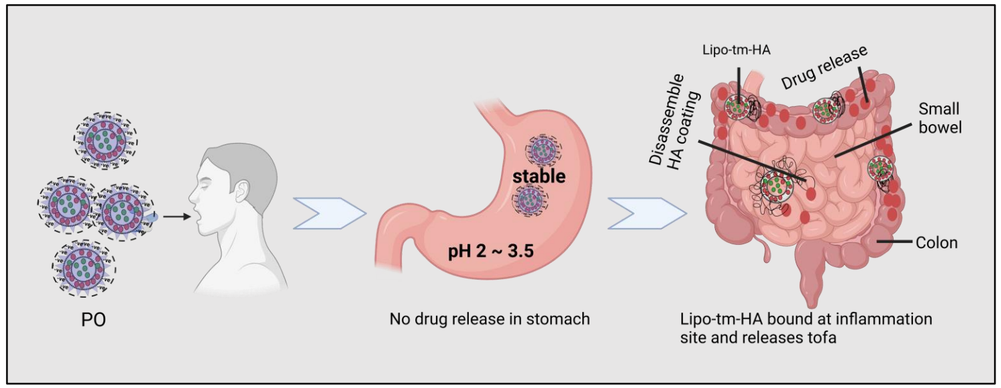
Loading: 10-12%

Lipo-tm-HA avoids gastric environment

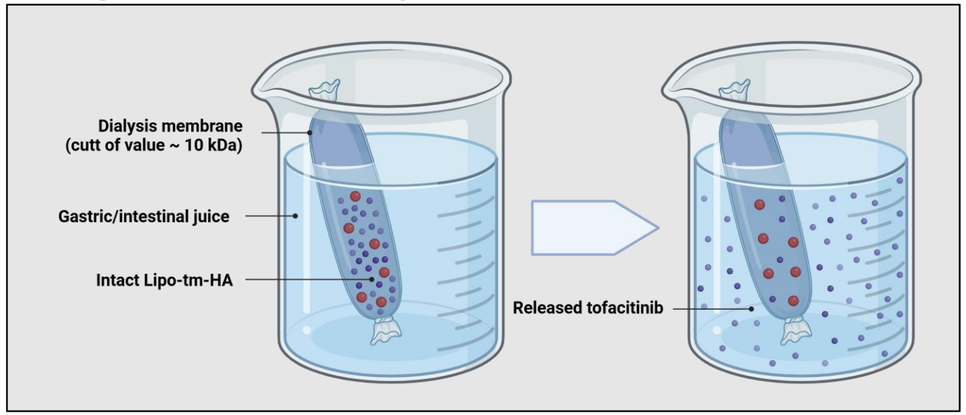
Stability study by DLS



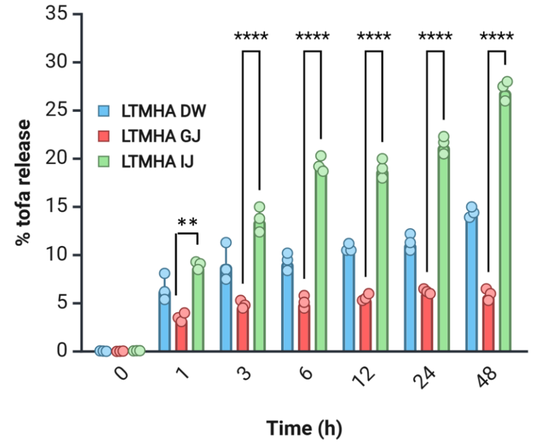
Proposed hypothesis:



Drug release study



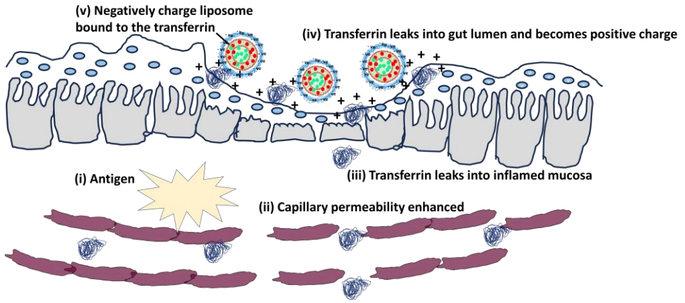
Hyaluronic acid coating protects the liposomal formulation in gastric milieu



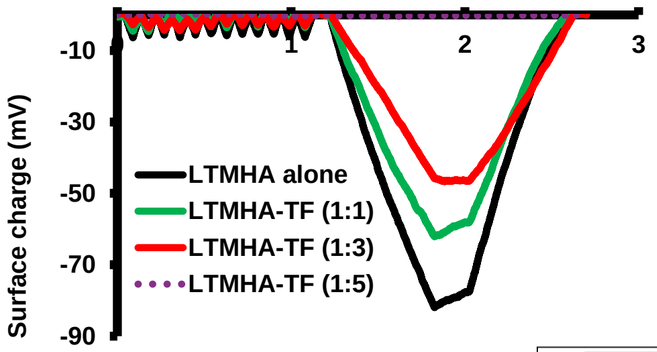
Higher drug release in intestinal juice

Dual targeting of inflamed colon

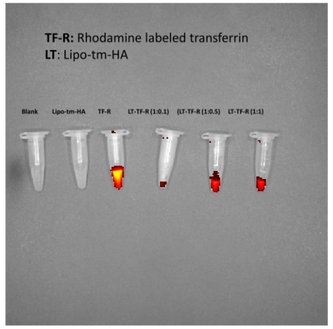
Target-1: Transferrin binding in inflamed colonic mucosa

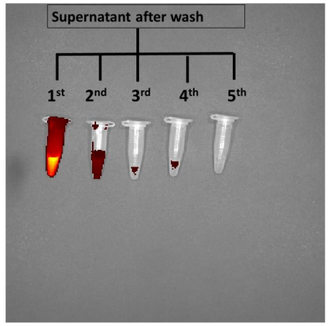


Charge neutralization



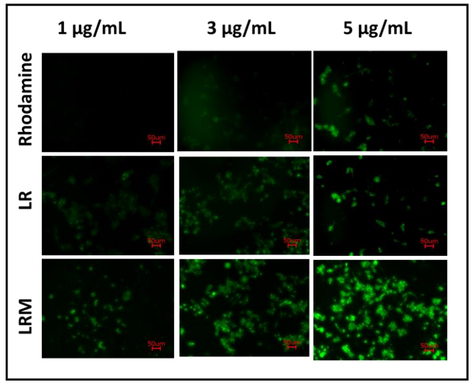
Binding confirmed by fluorescent label transferrin



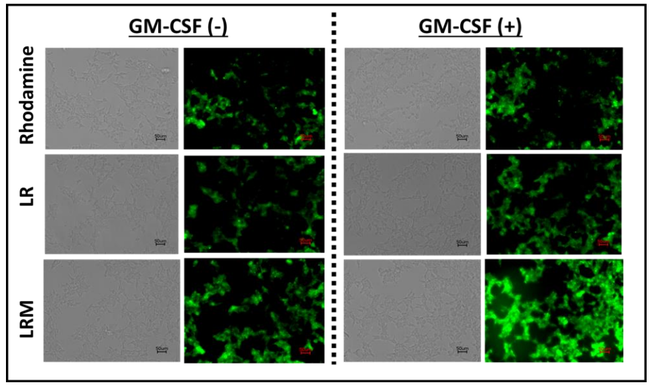


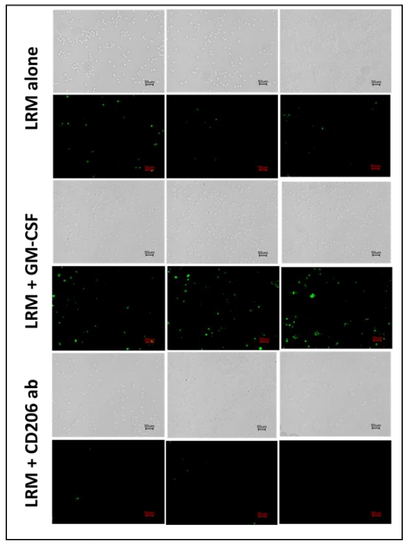
Target-2: Macrophage through mannose receptor (CD206)

Dose dependency in RAW 264.7 macrophage

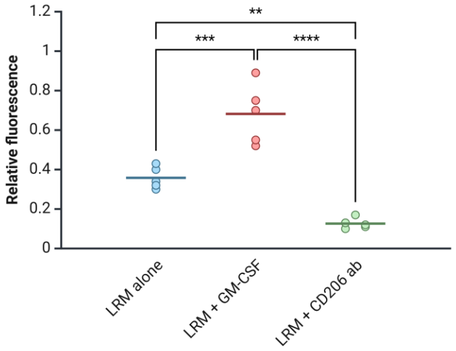


Granulocyte-Macrophage Colony-Stimulating Factor



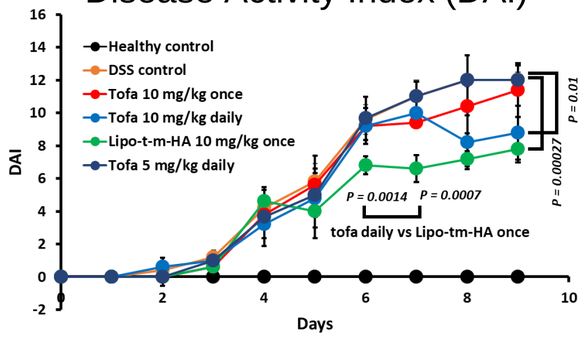


Mannose receptor mediated uptake

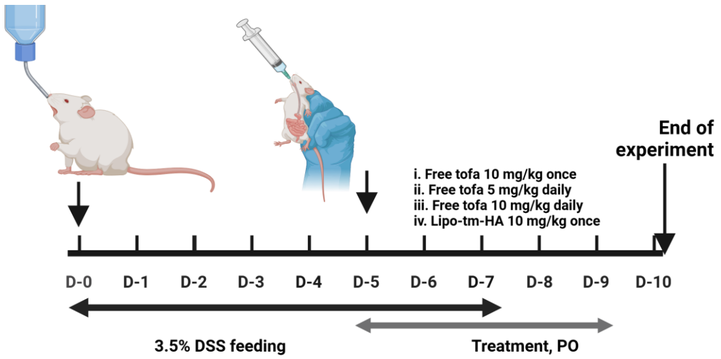


Enhanced therapeutic effect by targeting inflamed colon

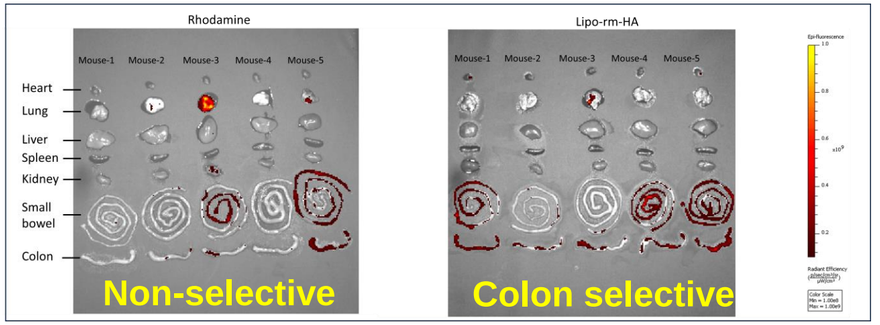
Disease Activity Index (DAI)



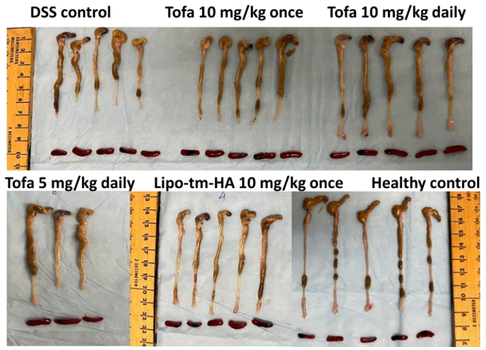
Experimental design: therapeutic efficacy

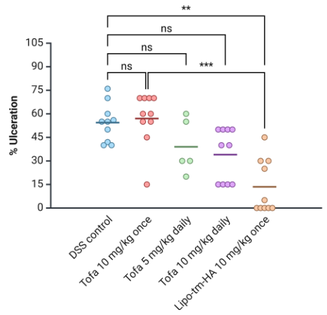


Biodistribution in colitis mice

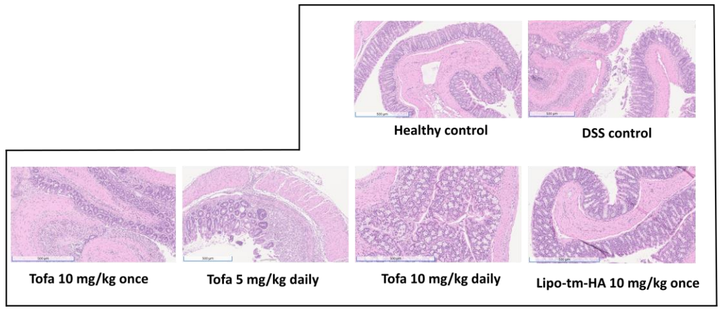


Colon image at day 10.

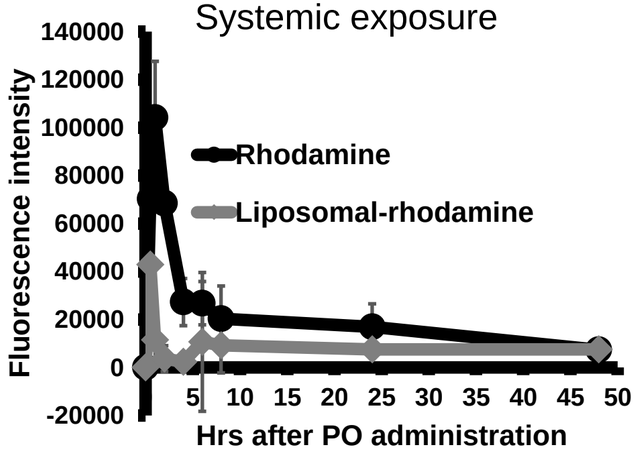




H&E staining of colon tissue



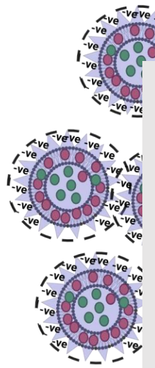
Systemic exposure



Single-dose Lipo-tm-HA (10 mg/kg) outperformed daily free tofacitinib

Concluding remark

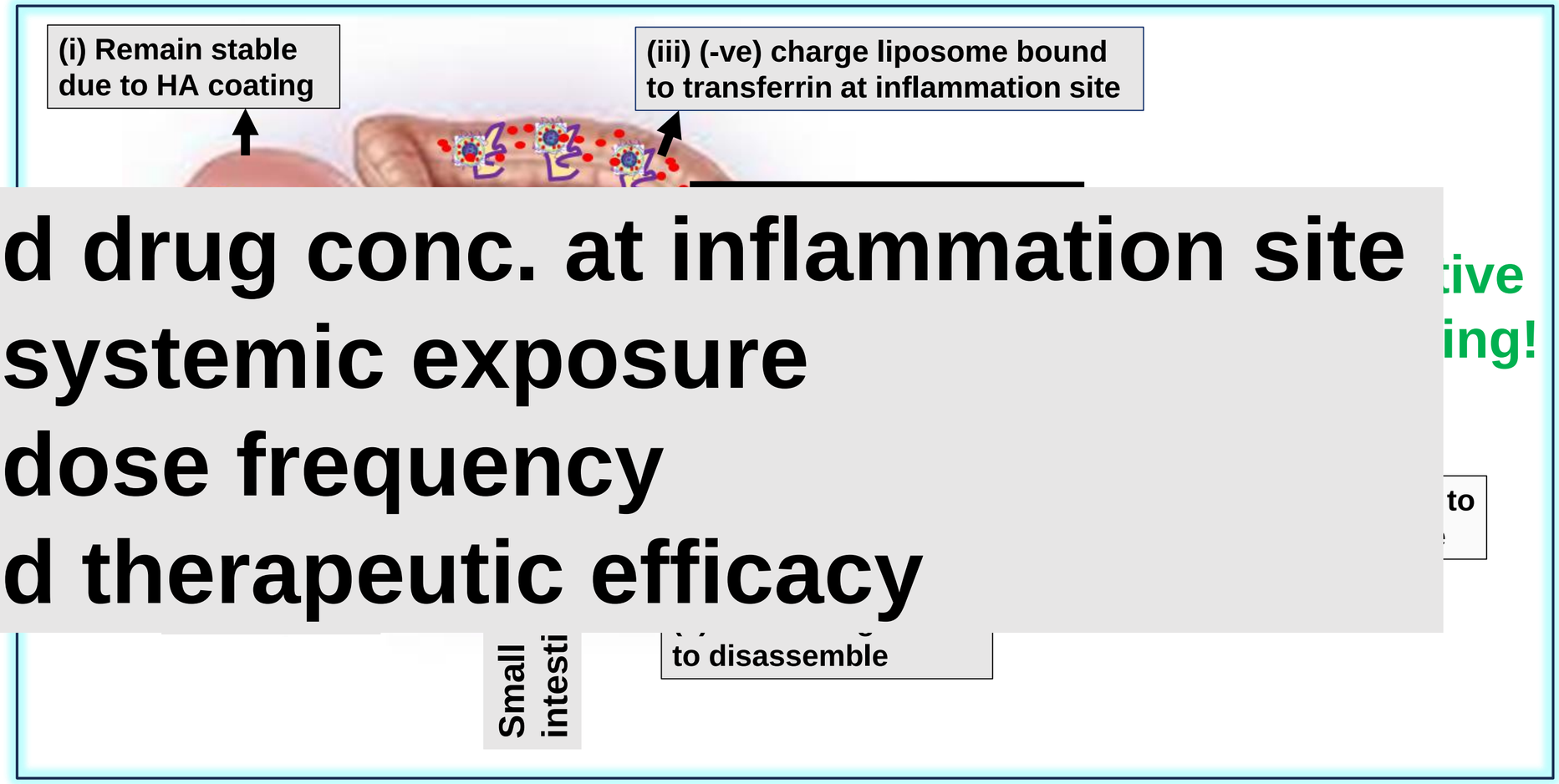
Administered orally



PO

Lip

- **Size ~ [illegible] nm**
- **Loading of 10-12% tofa**



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ing!

- ❖ **Improved drug conc. at inflammation site**
- ❖ **Reduce systemic exposure**
- ❖ **Reduce dose frequency**
- ❖ **Improved therapeutic efficacy**

Acknowledgement

Professor Florin M. Selaru, MD, MBA
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