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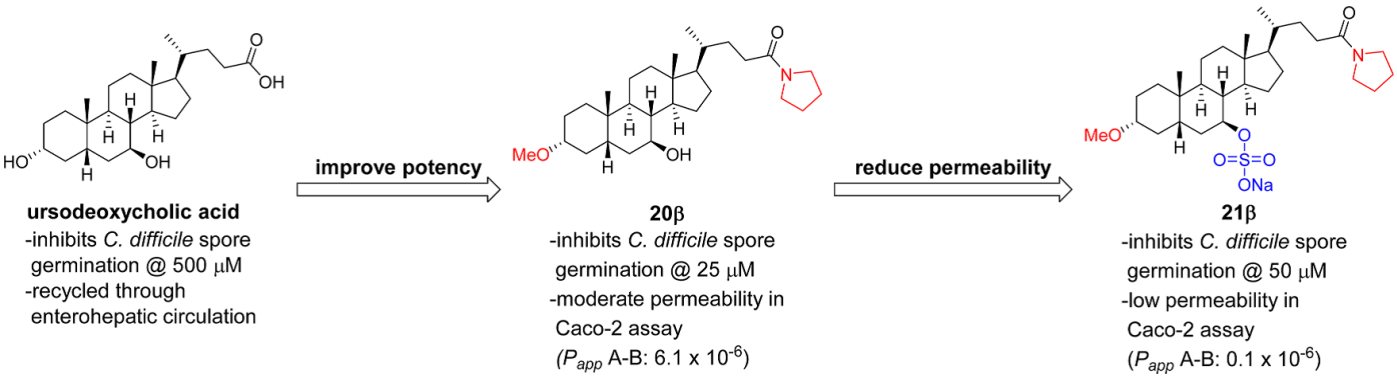
Pharmacological agents to prevent recurrent C. diff infection (20150362)

Cholic and bile acid derivatives that inhibit Clostridium difficile spore germination to prevent or treat C. diff infection.

Technology No. 20150362



ursodeoxycholic acid
-inhibits *C. difficile* spore germination @ 500 μM
-recycled through enterohepatic circulation

20β
-inhibits *C. difficile* spore germination @ 25 μM
-moderate permeability in Caco-2 assay
(P_{app} A-B: 6.1 x 10^{-6})

21β
-inhibits *C. difficile* spore germination @ 50 μM
-low permeability in Caco-2 assay
(P_{app} A-B: 0.1 x 10^{-6})

IP Status: US Patent Pending; **Application #:** 15/998,547

Applications

- C. diff prevention and/or treatment
- Alternative to antibiotics or fecal microbiota transplantation (FMT)
- Hospitals
- Oral therapeutics

Benefits

- Could prevent, treat, and/or reduce risk of developing a Clostridium-associated infection
- Will not kill useful and necessary microorganisms (microbiota)
- Remains stable in acidic stomach environment
- Avoids reuptake into the enterohepatic circulation in the colon

Features

- Cholic and bile acid derivatives

- Therapeutic compounds inhibit taurocholate-induced spore germination
- Offers a non-antibiotic alternative to treating C. diff
- May replace FMT (fecal microbiota transplant) therapy
- Resistant to 7α-dehydroxylation by colonic flora

Inhibits C. diff germination to prevent and treat infection

Newly developed cholic and bile acid derivatives could inhibit Clostridium difficile spore germination, which could prevent, treat, and/or reduce the risk of developing Clostridium-associated infections. The therapeutic compounds inhibit taurocholate-induced spore germination. They are expected to remain stable under highly acidic conditions (such as those in the stomach), to avoid reuptake into the liver and to remain resistant to 7α-dehydroxylation by colonic flora. The antigerminants should prevent germination of Clostridium difficile spores and could be used to prevent and treat C. diff infections.

No antibiotics or fecal microbial transplant (FMT) required

Bile acids produced in the gallbladder are able to inhibit germination of Clostridium difficile spores, but orally dosed bile acids do not reach the large intestine in large enough quantities to be effective. Several reasons are responsible: they break down in the stomach, reuptake receptors pull them from the gut, and/or bacterial enzymes break them down. Standard C. difficile treatments use antibiotics that disrupt indigenous microbiota and often fail to eradicate bacterial spores, increasing recurrence of infection. These newly developed bile acid derivatives could replace secondary bile acids or their analogues inhibitory to C. diff. Because germination in the human colon is critical in C. diff pathogenesis, these novel pharmaceuticals could treat this disease, particularly in patients who have had multiple rounds of antibiotic treatment with no results. With further development, the drug candidates could replace currently available treatments and provide an antibiotic-free option that does not require fecal microbial transplant (FMT).

Phase of Development

- In Vitro assessment.

Desired Partnerships

This technology is now available for:

- License
- Sponsored research
- Co-development

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Researchers

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References

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