

# Preclinical evaluation of a novel membrane-intercalating agent shows antibacterial activity with no generation of bacterial resistance

Membrane fluidity is key to the function of prokaryotic and eukaryotic cells. We have developed chitosan-coated esters of dodecanoic acid as membrane intercalating agents with anti-inflammatory and antibacterial properties. These can be targeted to Gram-positive or negative bacteria by alteration of charge and decoration on the chitosan coat, and bacteria show no innate or evolved resistance to these agents on exposure.

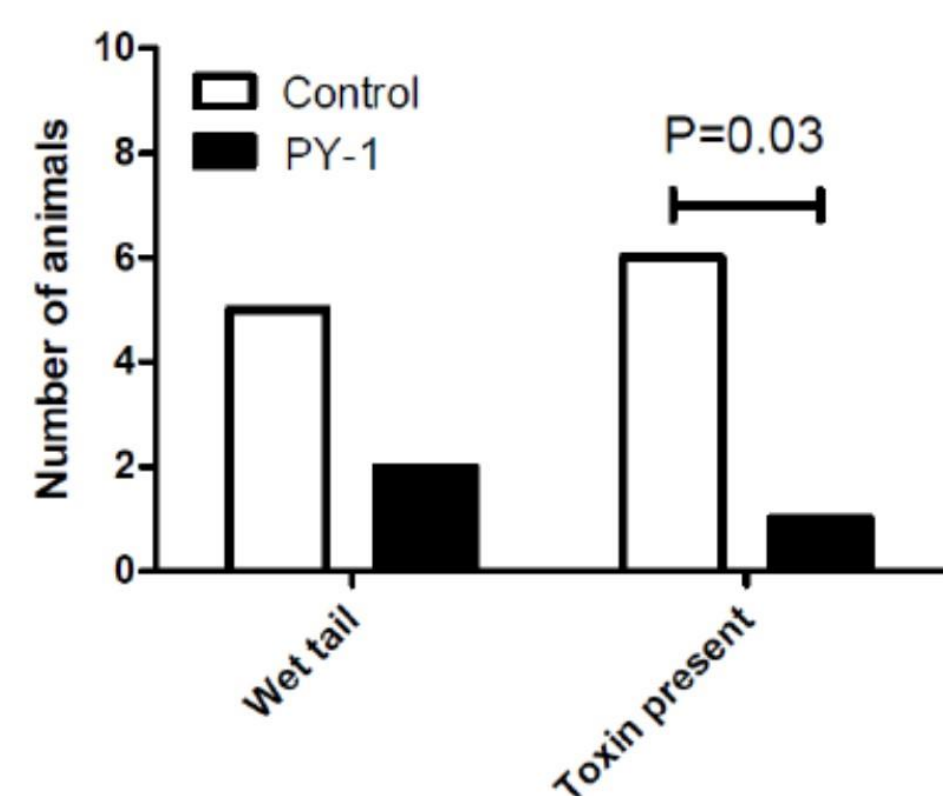
## Background

We have observed previously that modification of bacterial membranes by the insertion of lipids with cyclic or branched moieties causes an increase in membrane stability and in bacterial heat tolerance. Where bacteria are unable to alter these lipids their ability to adapt becomes compromised as an increase in stability causes decreased fluidity and ability of the membrane to function.

Natureza have developed these lipids into orally dosable chitosan-coated particles (PY-1 for Gram positives and fungi and PY-3 for Gram negatives) that show activity against many of the WHO priority pathogens and have also shown that these are active in *in vivo* models.

Organism	MIC (µg/mL)
<i>E coli</i>	>5000
<i>C difficile</i>	18
<i>Streptococcus spp</i>	18
<i>Lactobacillus spp</i>	>5000
<i>Bifidobacterium spp</i>	>5000
<i>Staphylococcus spp</i>	18

*In vivo* activity against *C. difficile* in a hamster model



## PY-1

### Activity against *Candida auris*

Can be formulated as capsules or a topical preparation

No resistance:

- Exposure to agents on agar plates with increasing gradient concentrations of agents (MEGA plates)
- Exposure to long term subinhibitory concentrations of agents

No resistance developed, no change in MIC over 6 months

Organism	MIC (µg/mL)
<i>Salmonella</i>	6
<i>E. coli</i>	6
<i>Enterobacter</i>	6
<i>Klebsiella</i>	6
<i>Acinteobacter</i>	6
<i>Pseudomonas</i>	6
<i>Shigella</i>	6
<i>Staphylococcus</i>	60

## PY-3

Broad spectrum of activity

Active against ESBL+ bacteria, ESKAPE pathogens

Active against carbapenem resistant bacteria

No resistance seen in any of the target bacteria tested

No resistance developed on extended testing

Activity against *Pseudomonas*

Aerosolisable with particle size that can reach the alveoli

Anti inflammatory

Indications: COPD; CF lung infections



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