

# Nano-mupirocin in Mice Necrotizing Fasciitis Model

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## Background

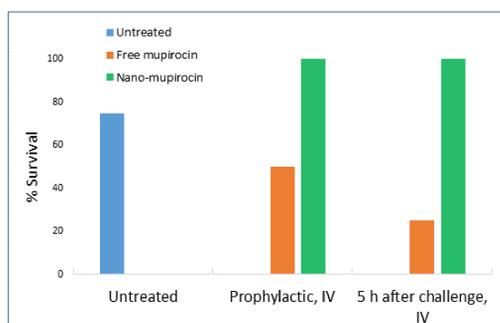
Mupirocin, an antibiotic with a unique mechanism of action (inhibition of isoleucyl-tRNA synthetase) is limited to topical use due to its rapid systemic elimination and high protein binding. Loading mupirocin into PEGylated nano-liposomes to form Nano-mupirocin protects the drug and potentially allows it to be used parenterally against a wider range of bacteria and infections. The activity of Nano-mupirocin in a necrotizing fasciitis model in mice was studied and described herein.

## Method

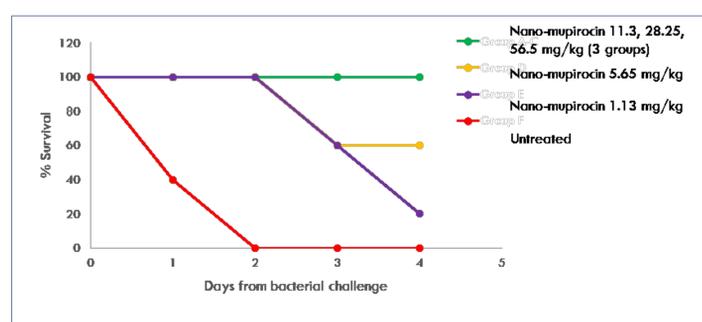
Female BALB/c mice aged 3–4 weeks were injected SC with  $\sim 1 \times 10^8$  CFU, M14 Group A *streptococcus* (GAS) which resulted in skin lesions. Two studies are described: 1) Single dose of 50 mg/kg (free mupirocin or Nano-mupirocin) was administered IV either prophylactically or 5 h after infection. This study included histopathology of the skin lesions taken 48 h after infection. 2) A dose response study of a single IV dose of 1.1–56.5 mg/kg Nano-mupirocin administered 1 h after infection. In addition, skin lesions were extracted and tested for mupirocin content using HPLC method.

## Efficacy: animal survival

Single dose, 50 mg/kg Free mupirocin vs Nano-mupirocin



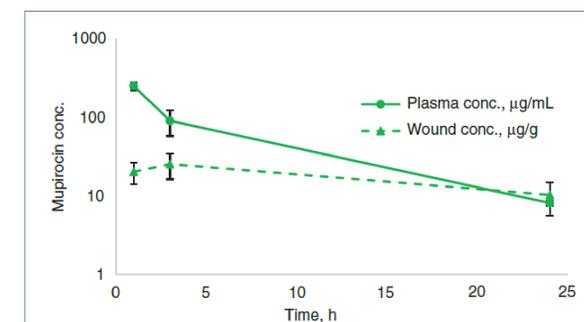
A dose response study, single IV dose



## Biodistribution to infected tissue

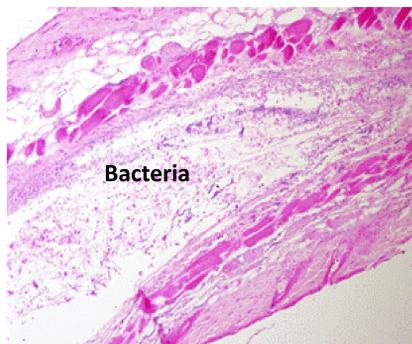
Mupirocin conc. In plasma and skin lesions following Nano-mupirocin, 50 mg/kg IV administration.

No mupirocin was detected in free mupirocin administration group



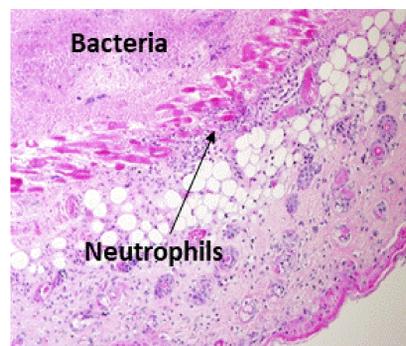
## Efficacy: Histopathology of skin lesions taken 48 h after the bacterial challenge

Control mouse



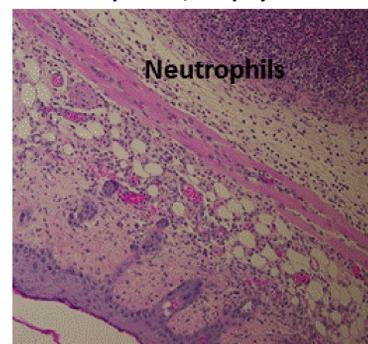
The tissue is necrotic. Bacteria is seen deep in the tissue. No inflammation response. (200x magnification)

Free mupirocin, Prophylactic



The tissue is necrotic. Bacteria is deep in the tissue. Slight inflammation response. (200x magnification)

Nano-mupirocin, Prophylactic



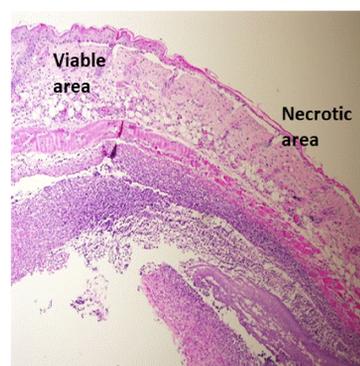
The tissue is viable. Deep in the tissue there are many neutrophils. Very few bacteria deep in the tissue (not seen in the picture). (200x magnification)

Free mupirocin, administered 5 h after the bacterial challenge

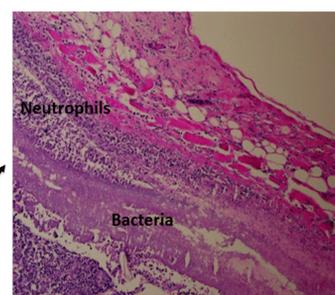


The tissue is necrotic. Bacteria is deep in the tissue. Slight inflammation response. (200x magnification)

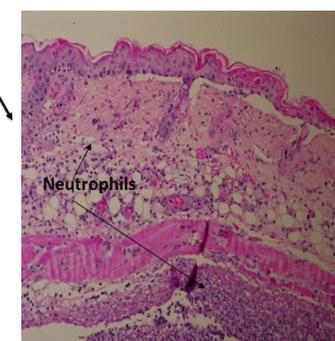
Nano-mupirocin administered 5 h after the bacterial challenge



In the center of the wound there is a necrotic area. In the sides of the wound the dermis is viable showing healing process of these areas. (100x magnification)



Bacteria and inflammation response is seen. (200x magnification)



A strong inflammation response is seen. (200x magnification)

## Conclusions

- Nano-mupirocin efficacy was demonstrated when administered prophylactically or 5 h after the bacterial challenge.
- Dose response study: On the day of 100% control mortality- No death occurred in the lowest dose tested (1.13 mg/kg). Doses above 11.3 mg/kg resulted in 100% survival.
- Nano-mupirocin showed distribution into the skin lesion tissue while no mupirocin was detected for the free mupirocin group.
- The activity of Nano-mupirocin in situ was well supported by the histopathology findings.

**Nano-mupirocin administered parenterally suggest a potential treatment for GAS systemic infections.**

## Reference

Cern A, Michael-Gayego A, Bavli Y, Koren E, Goldblum A, Moses AE, Xiong YQ, Barenholz Y. 2016. Nano-mupirocin: Enabling the parenteral activity of mupirocin. Eur J Nanomedicine 8:139–149.