



Synergistic antibiotic interactions against *Bacillus oleronius*, a potential causative agent of rosacea



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Abstract

Rosacea, a condition which enlarges facial blood vessels causing redness of the skin, affects more than 3 million people in the United States each year. While there is no cure for rosacea, many treatments have been found effective in reducing its symptoms. The causes of this disorder remain poorly understood. It is believed that an overabundance of the microscopic human hair follicle mite, *Demodex*, is associated with a hypersensitivity immune response in rosacea patients. However, a growing body of evidence suggests that this hypersensitivity reaction is specific to a bacterial commensal of the *Demodex* mite called *Bacillus oleronius*, suggesting the bacteria as a causative agent in rosacea pathogenesis. Therefore, some rosacea treatment strategies include oral or topical antibiotics. Our current study explores the synergistic interaction of four common topical antibiotics, Clindamycin, Bacitracin, Polymixin B, Neomycin used in the treatment of facial acne, and methylglyoxal, an antibacterial component found in Manuka honey. Our results showed that *B. oleronius* was 128 times more sensitive to Clindamycin in the presence of MGO. In isolation the minimum inhibitory concentration (MIC) of Clindamycin was 1 µg/mL, but was reduced to 7.5 ng/mL in the presence of a sublethal concentration of MGO. The MIC in isolation of Bacitracin was 0.5 µg/mL, but in the presence of a sublethal concentration of MGO was reduced to 97.8 ng/mL.

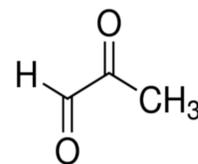
Rosacea

- Rosacea is a common, but poorly understood, disorder that affects mostly the face
- Common symptoms include redness and acne-like bumps on the forehead, cheeks, nose, and chin
- While there is no cure, it can be controlled with the use of oral and topical antibiotics



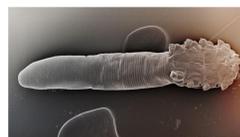
Manuka Honey & Methylglyoxal

- Manuka honey is from the nectar of the Manuka tree found in New Zealand
- Manuka honey has been found to have antibacterial properties
- Methylglyoxal (MGO) is a main component in Manuka Honey, and is found in most types of honey but usually in small quantities
- Hydrogen peroxide is another component which could be used for future research

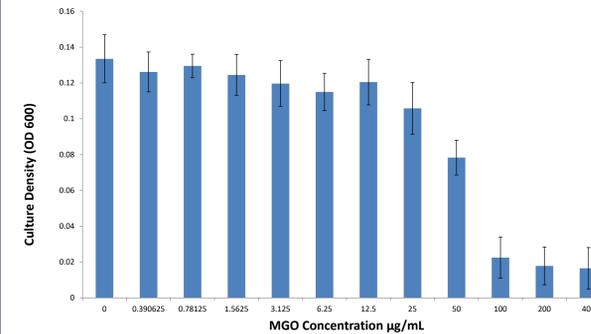


Demodex mite & *Bacillus oleronius*

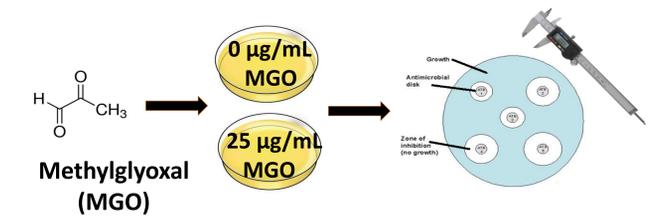
- Demodex, a microscopic mite, that resides in human hair follicles on the face
- Rosacea patients have 10 times more Demodex mites on the skin than the average person
- The bacteria *Bacillus oleronius* is found in the midgut of the Demodex mite
- It is believed that Rosacea is a hypersensitivity reaction due to *B. oleronius*



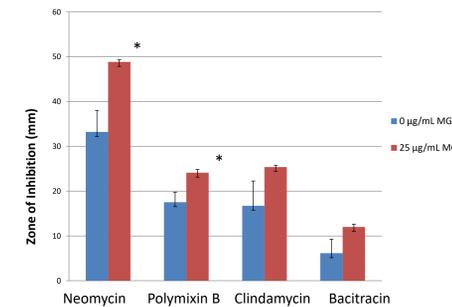
Experimental Design and Results



- The MIC of MGO was 100 µg/mL
- The mean of 3 biological replicates is shown
- Error bars indicate SEM

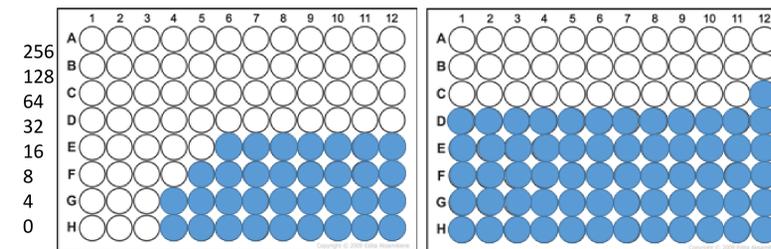


- Using a sublethal concentration of MGO, a disc diffusion assay was performed and the zone of inhibition was measured



- Compared to the control, the zone of inhibition increased significantly in the presence of MGO for 2 of the tested antibiotics
- The mean of 3 biological replicates is shown
- Error bars indicate SEM

1:2 Dilutions of MGO (µg/mL)



1:2 Dilutions of Clindamycin

- In isolation the MIC of Clindamycin was 1 µg/mL
- In the presence of a sublethal concentration of MGO, it was reduced to 7.5 ng/mL

	MIC of Antibiotic	MIC of Antibiotic in the presence of MGO	MIC of MGO	MIC of MGO in the presence of Antibiotic	FICI
Clindamycin	1.0 ± 0 µg/mL	0.025 ± 0.013 µg/mL	109.37 ± 15.62 µg/mL	3.413 ± 0.487 µg/mL	0.061 ± 0.014 µg/mL
Bacitracin	500 ± 0 ng/mL	97.8 ± 97.6 ng/mL	100.0 ± 15.32 µg/mL	31.25 ± 0 µg/mL	0.35 ± 0.061 µg/mL
Neomycin	28.8 ± 3.2 ng/mL	6.8 ± 1.8 ng/mL	76.8 ± 12.8 µg/mL	8.0 ± 0 µg/mL	0.337 ± 0.025 µg/mL
Polymixin B	500 ± 0 µg/mL	4.786 ± 0 ng/mL	64.0 ± 0 µg/mL	4.786 ± 0 ng/mL	0.75 ± 0 µg/mL

- Results represent the mean of 5 experiments
- FICI score <0.5 represents synergy

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