Methylglyoxal Potentiates the Effect of Linezolid Against *Staphylococcus aureus*

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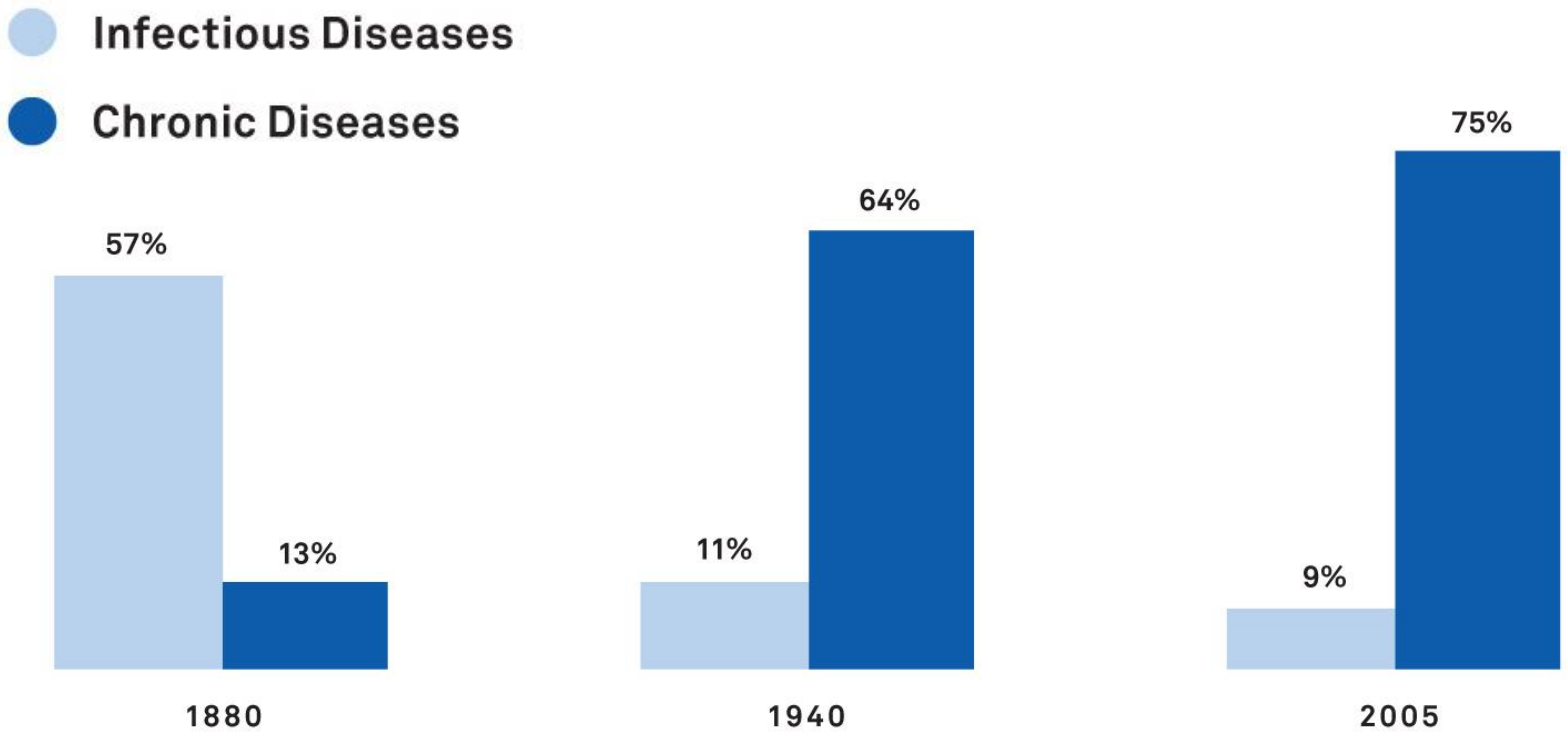
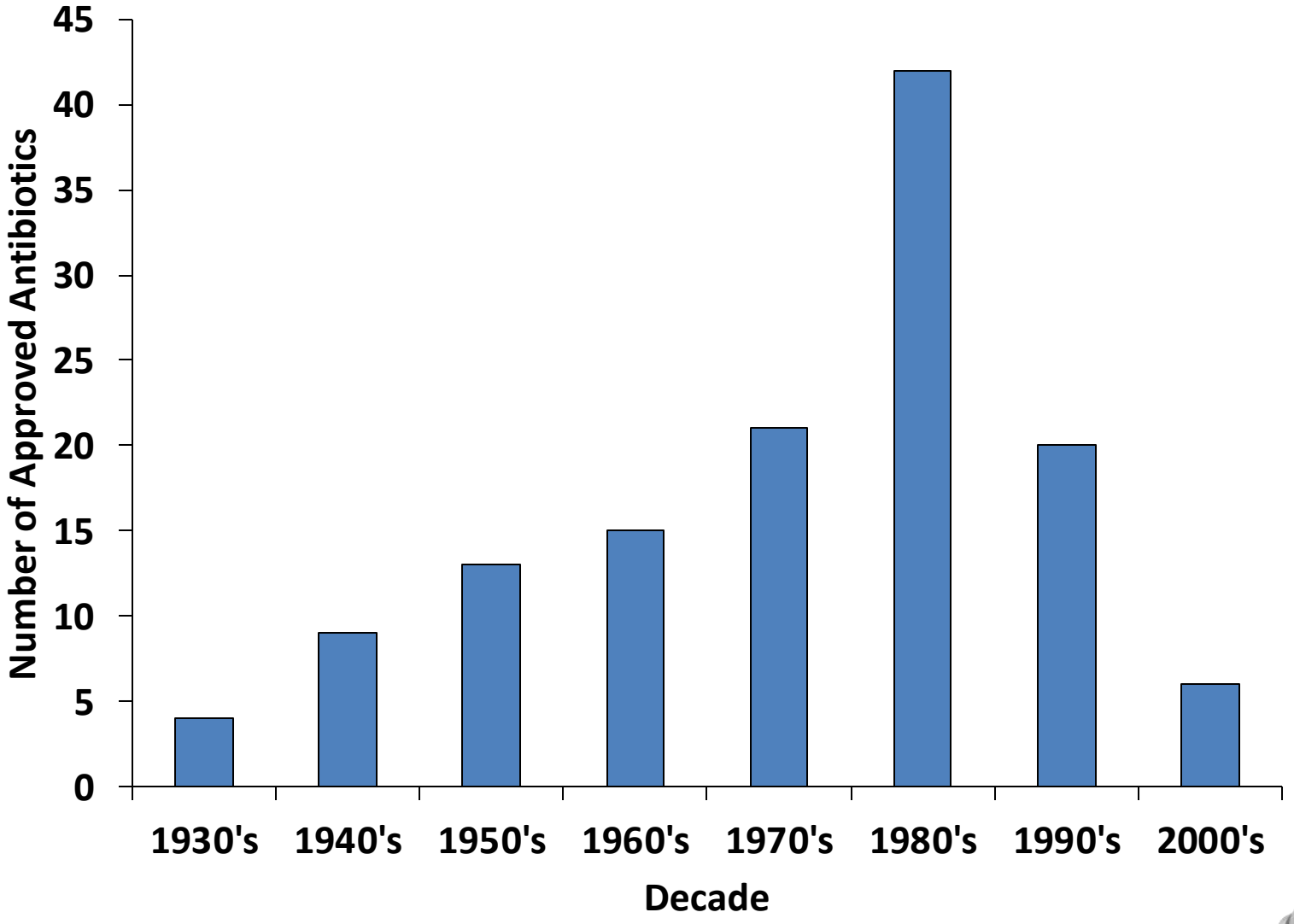
Antibiotics Changed Deaths



Source: The City of New York Summary of Vital Statistics 2005

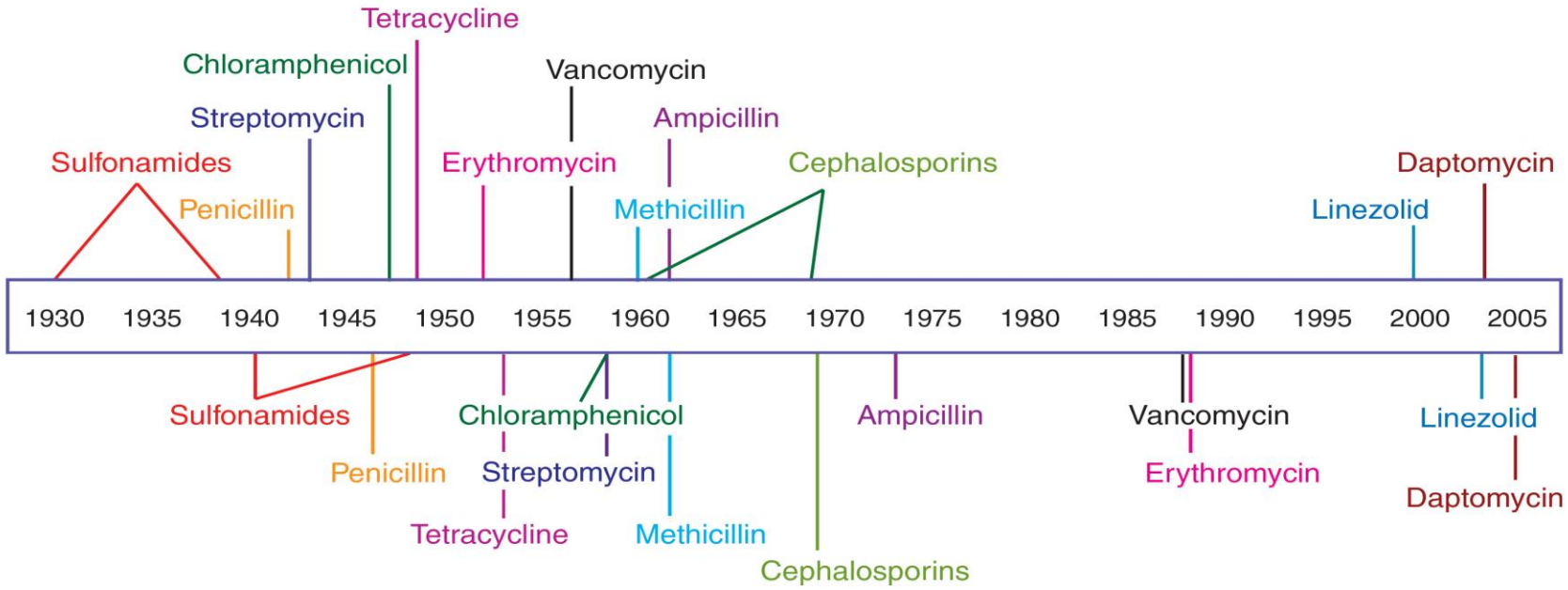
Antibiotic Pipeline Drying Up



The Economist. 2011.

Antibiotic Resistance

Antibiotic Deployment



Antibiotic Resistance Observed

Clatworthy et. al. (2007) *Nat. Chem. Biol.* **3**: 541-548

What can be done?

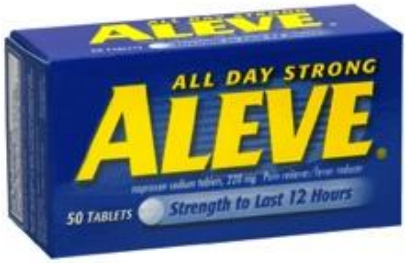
- New antibiotics?
  - Becoming more complex to discover new antibiotic compounds
  - Antibiotics provide a low return on investment compared to other drugs
    - $5 billion in research and testing for each new drug
- Or…

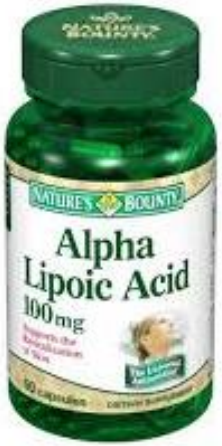
Invigorate Sensitivity

But how?

Here's how:

- Take existing compounds and pair them with current antibiotics to restore sensitivity
  - Over the counter medications
  - Natural compounds/ products



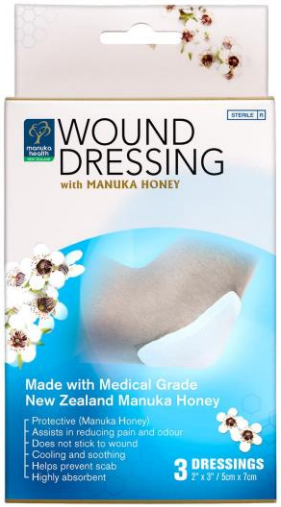


Here's why:

- FDA approved
- Safe
- Cheap and readily available
- Renewed public interest in natural compounds; some already possess antimicrobial properties

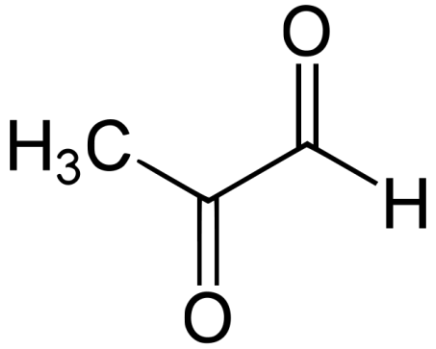
Manuka Honey

- Honey produced in New Zealand from the nectar of the Manuka tree
- Marketed as an antibacterial wound treatment



Can it be used along with antibiotics to increase sensitivity?

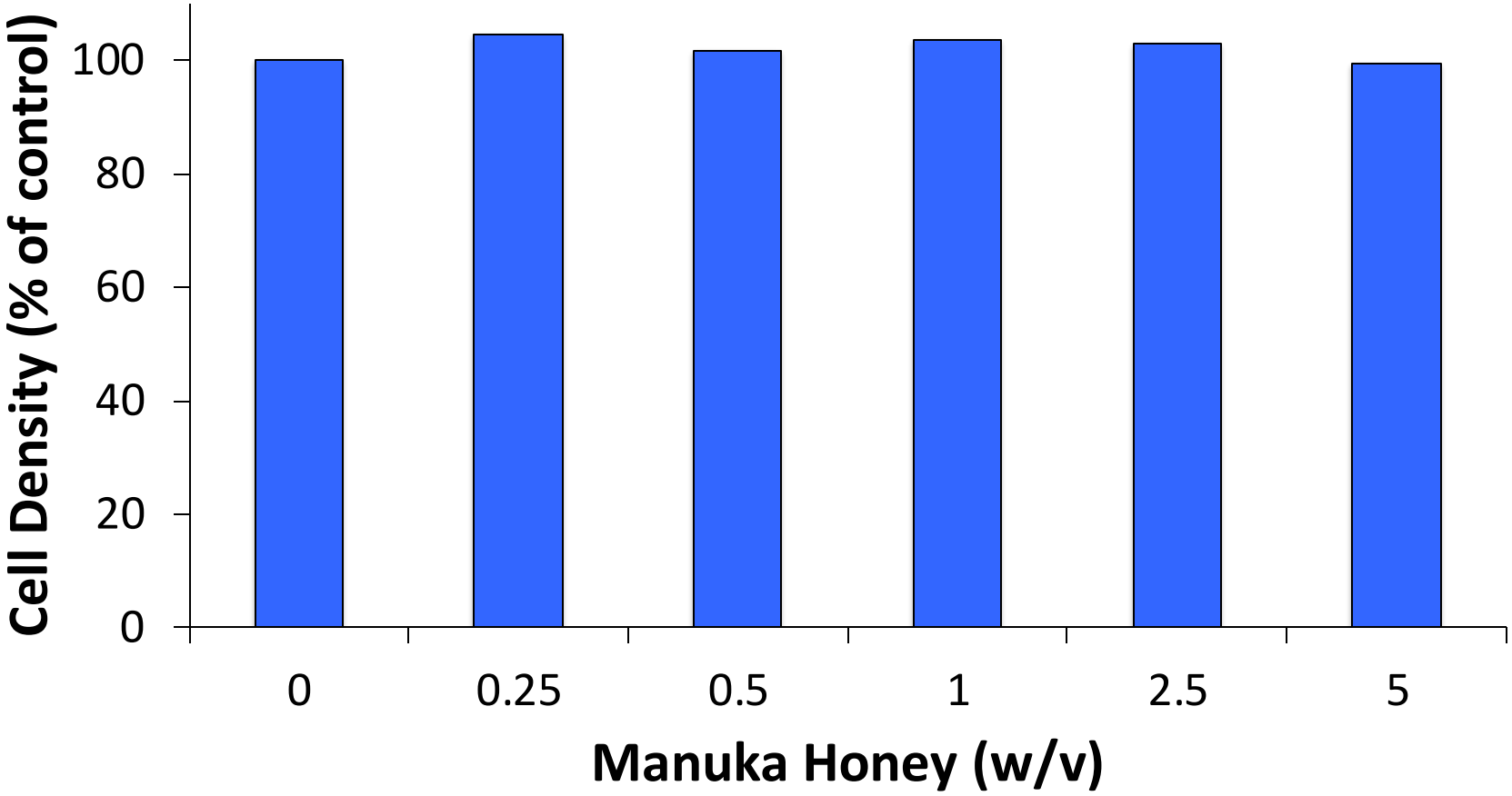
Methylglyoxal (MGO)



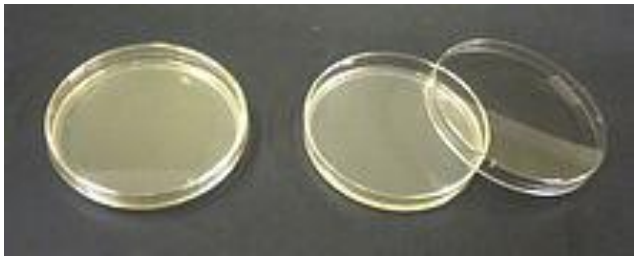
Dietary Methylglyoxal Content		Strength
MGO 100+ MANUKA HONEY	100mg/kg	Minimum
MGO 250+ MANUKA HONEY	250mg/kg	Medium
MGO 400+ MANUKA HONEY	400mg/kg	Strong
MGO 550+ MANUKA HONEY	550mg/kg	Super Strong

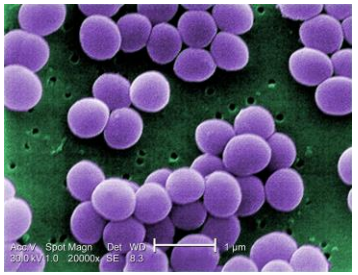
http://www.lifegenki.com/manuka-health-honey-mgo250/manuka-health-honey-mgo250#.VaPH70s2cds

Manuka Honey's Effect on *S. aureus* Growth



Initial Screen For Interactions

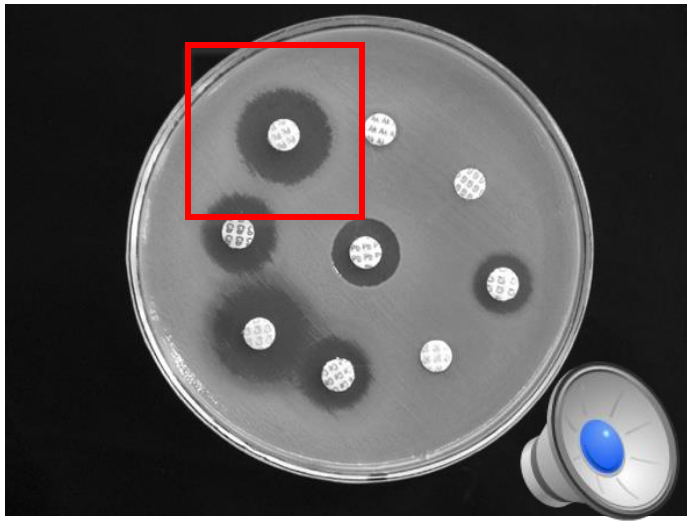


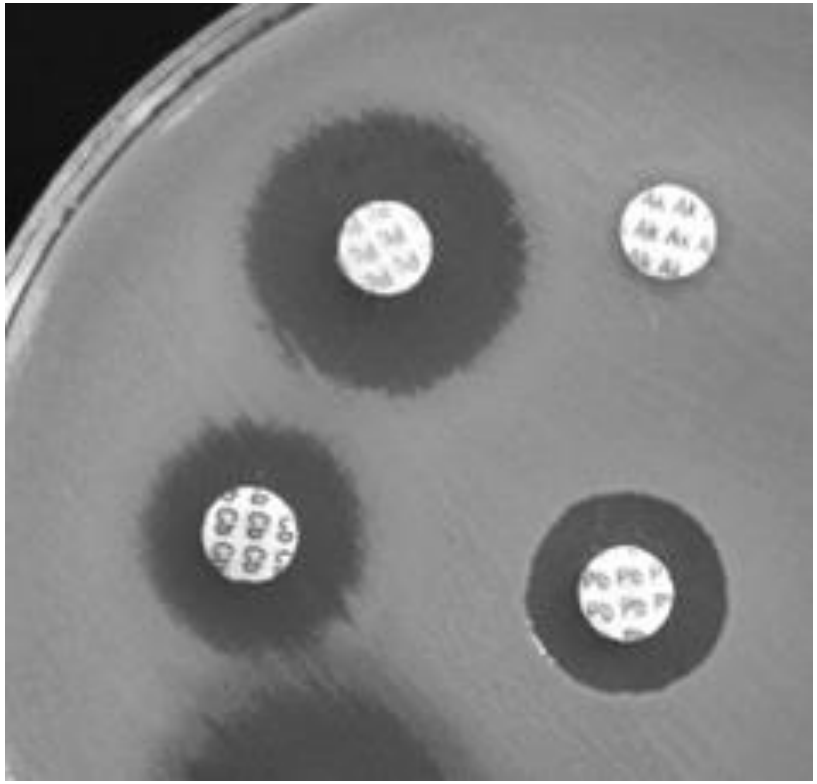


Staphylococcus aureus

Water

5 % Manuka Honey

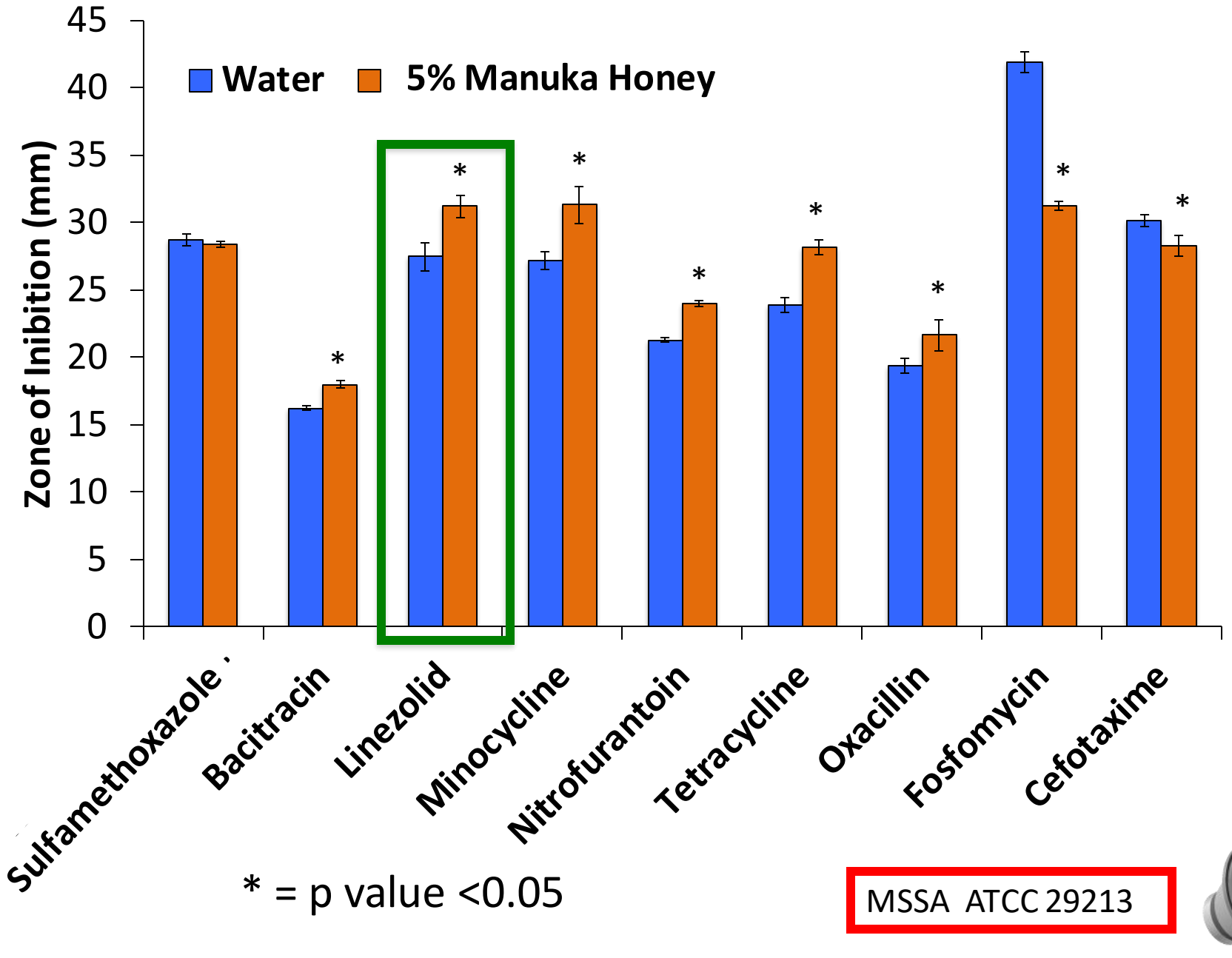




Synergy: **1+1=3**

Additivity: **1+1=2**

Antagonism: **1+1= < 2**

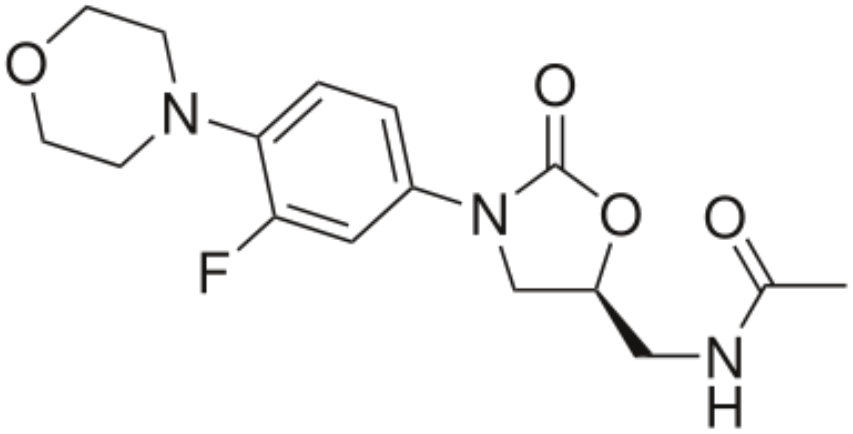


* = p value <0.05

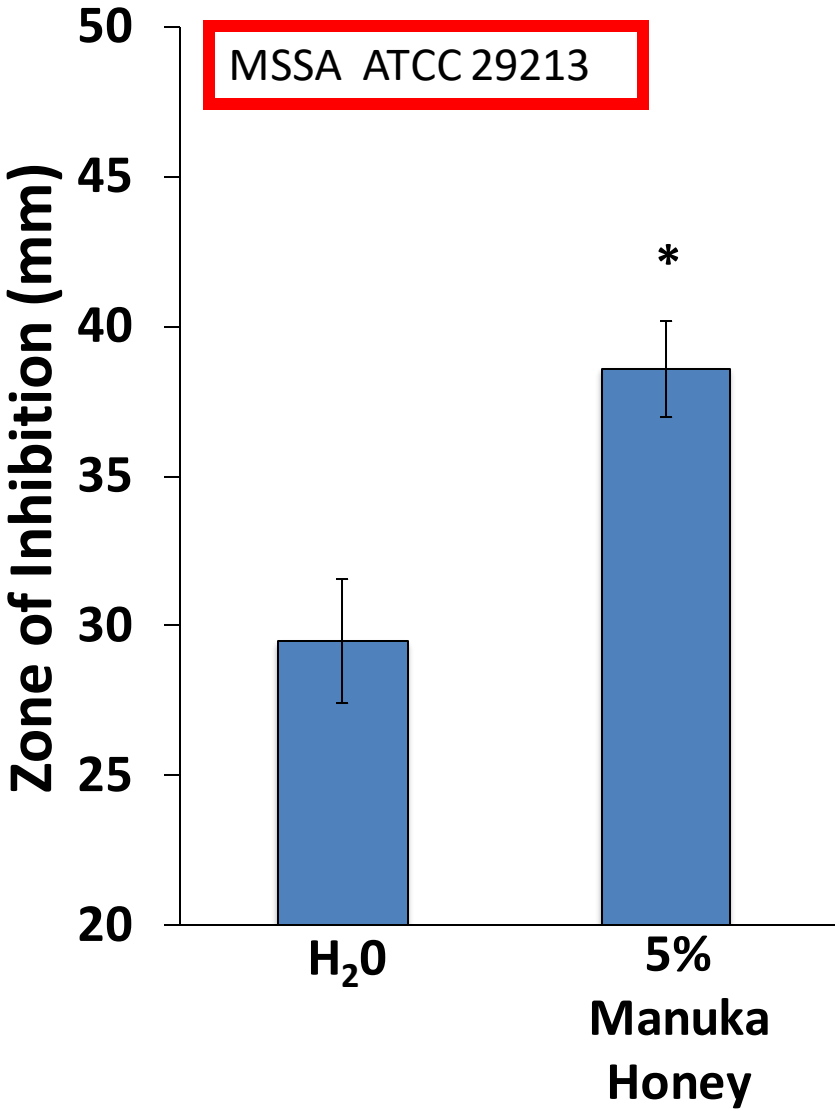
MSSA ATCC 29213

Linezolid: What is it?

- Market name: Zyvox
- Last line defense antibiotic against Gram-positive bacterial pathogens, including MRSA
- Mode of action: inhibiting protein synthesis by preventing the formation of the initiation complex



Is This Manuka Honey Specific?



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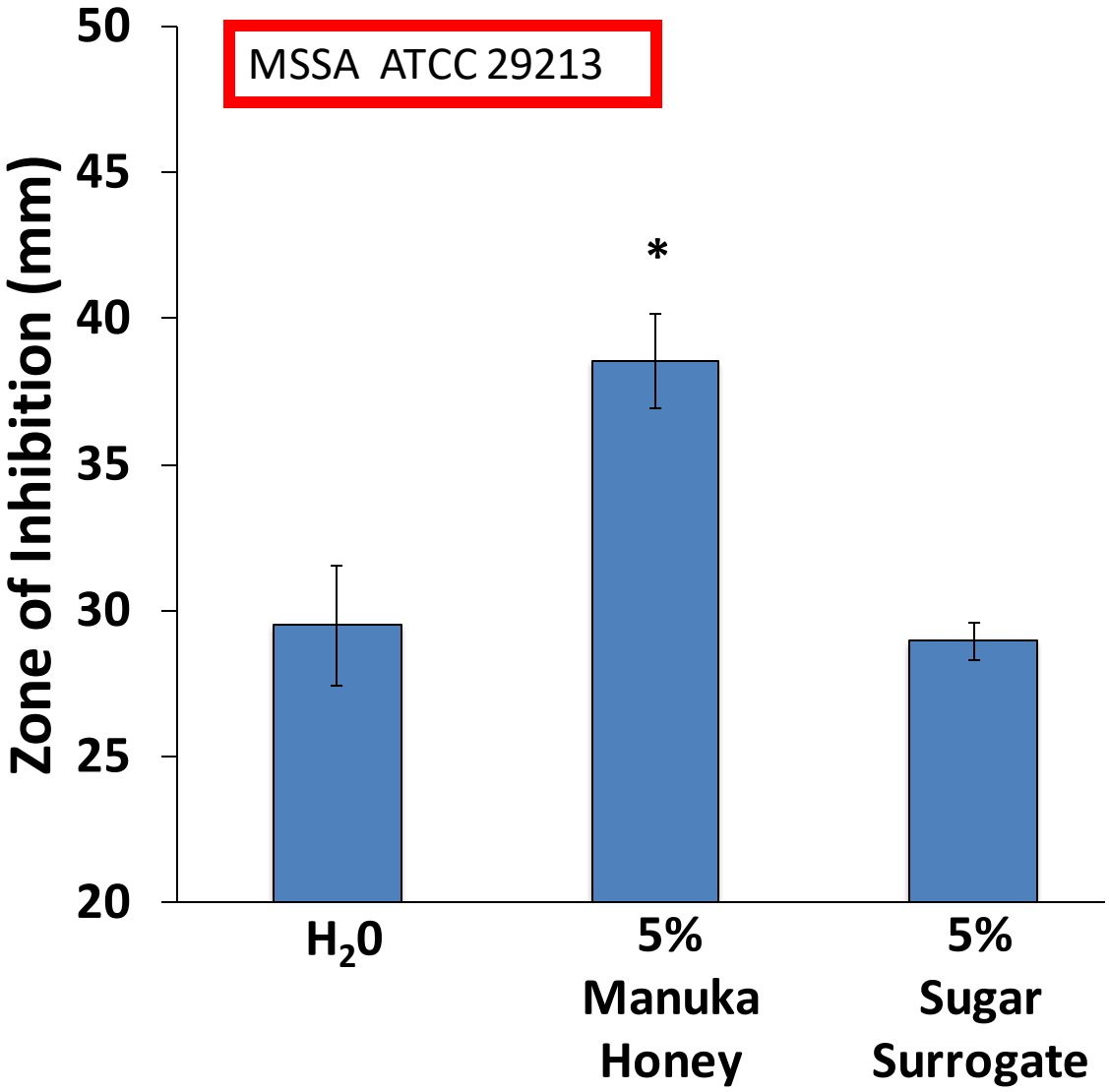

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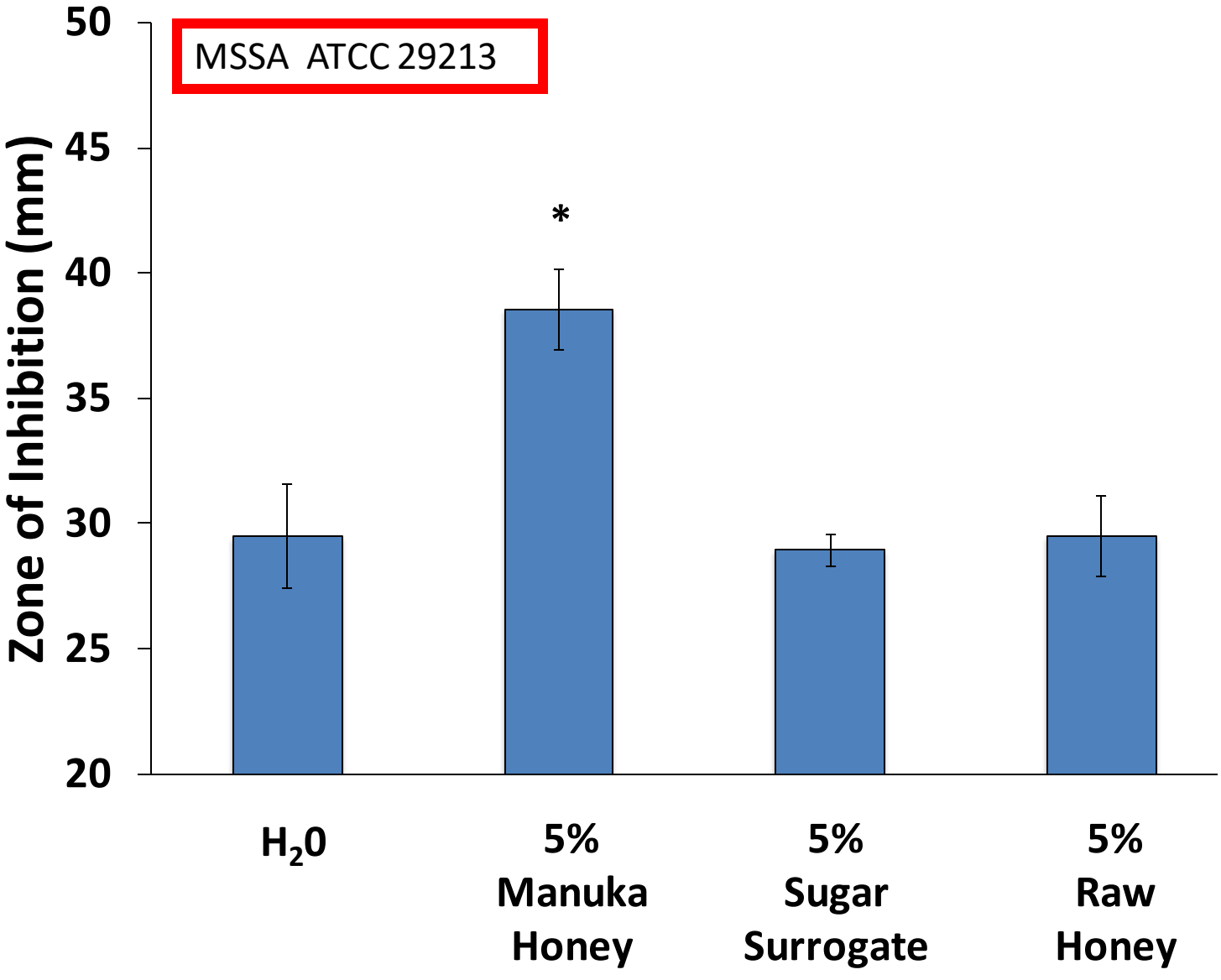
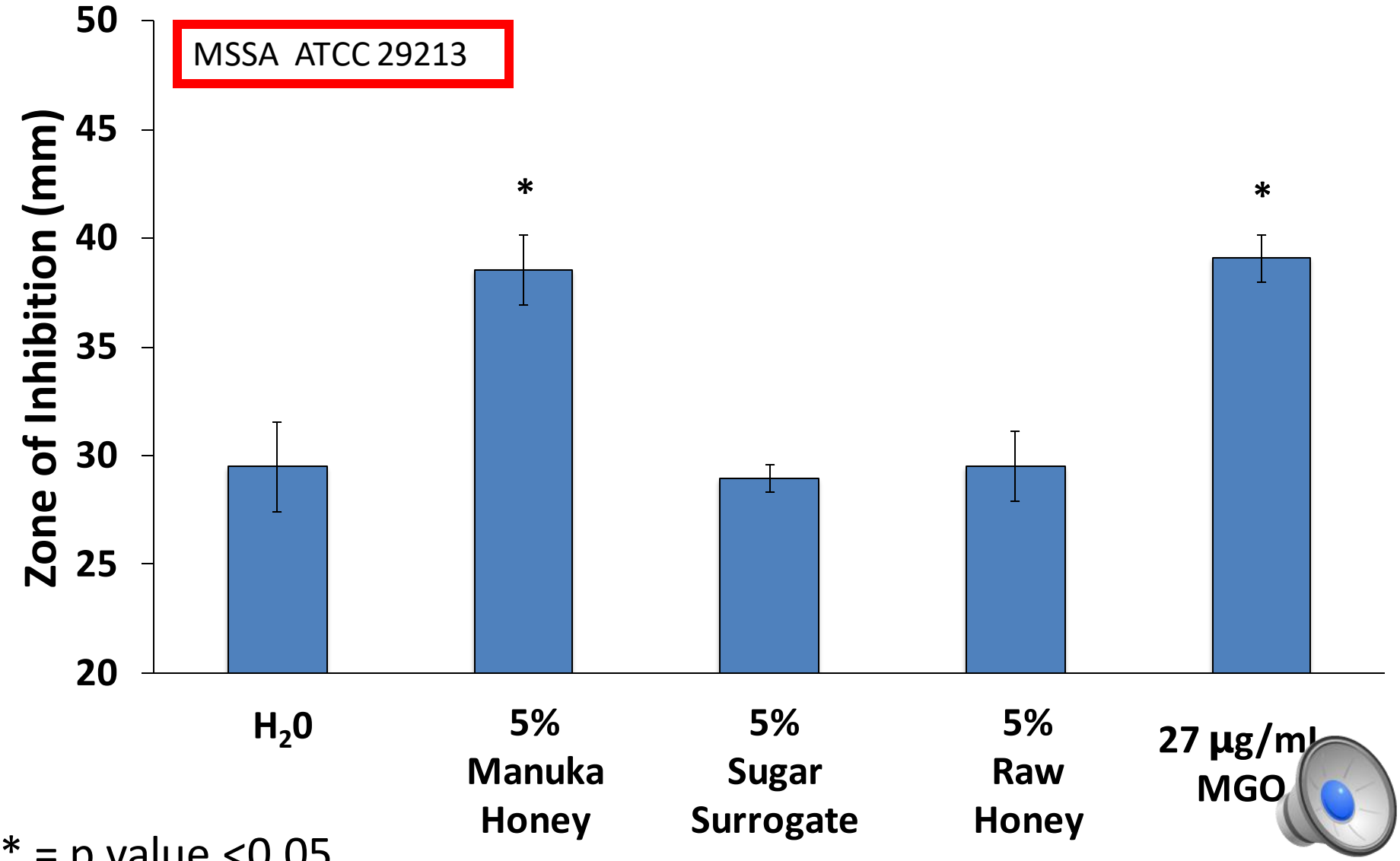


MGO

Is This Manuka Honey Specific?



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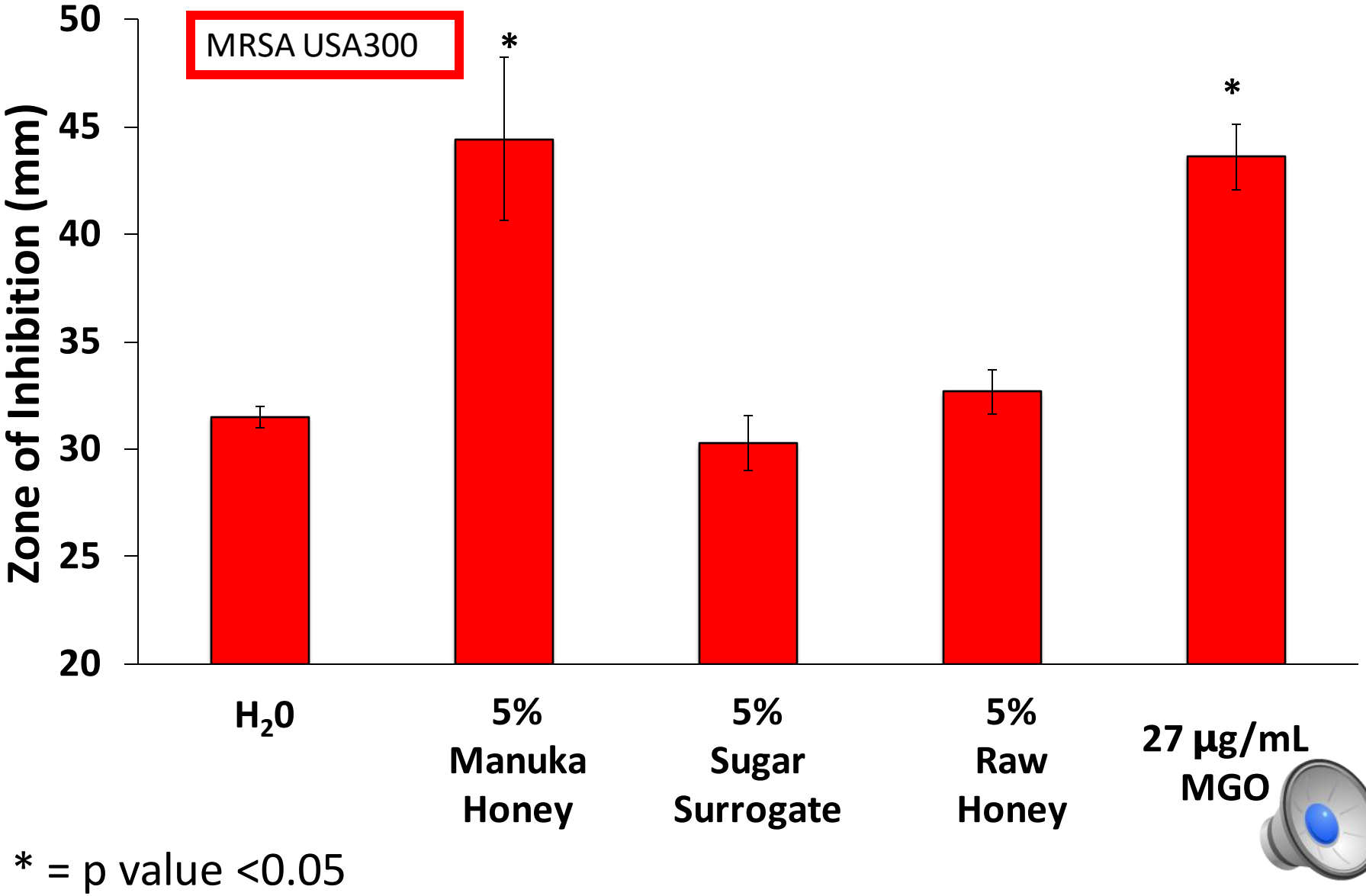

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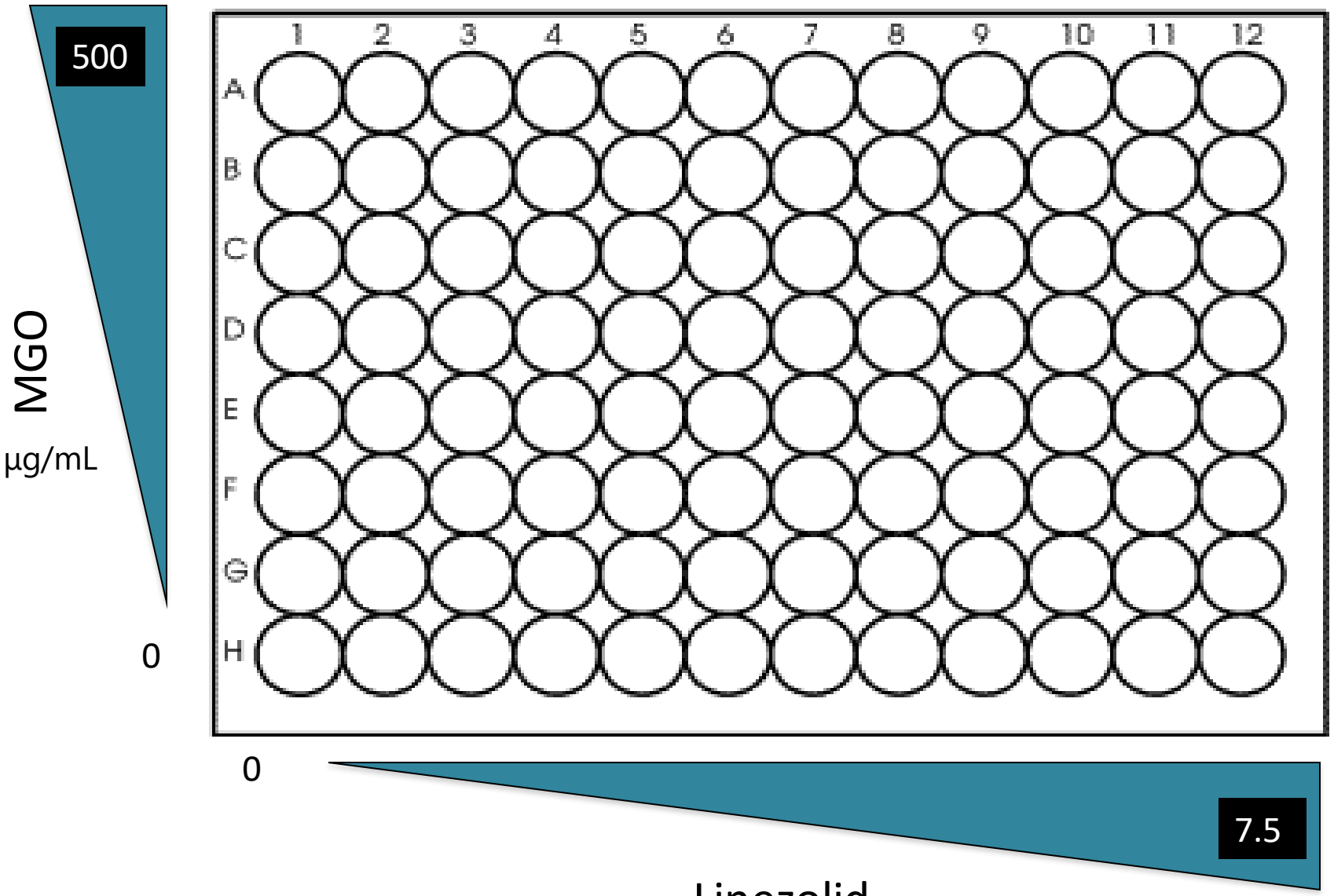
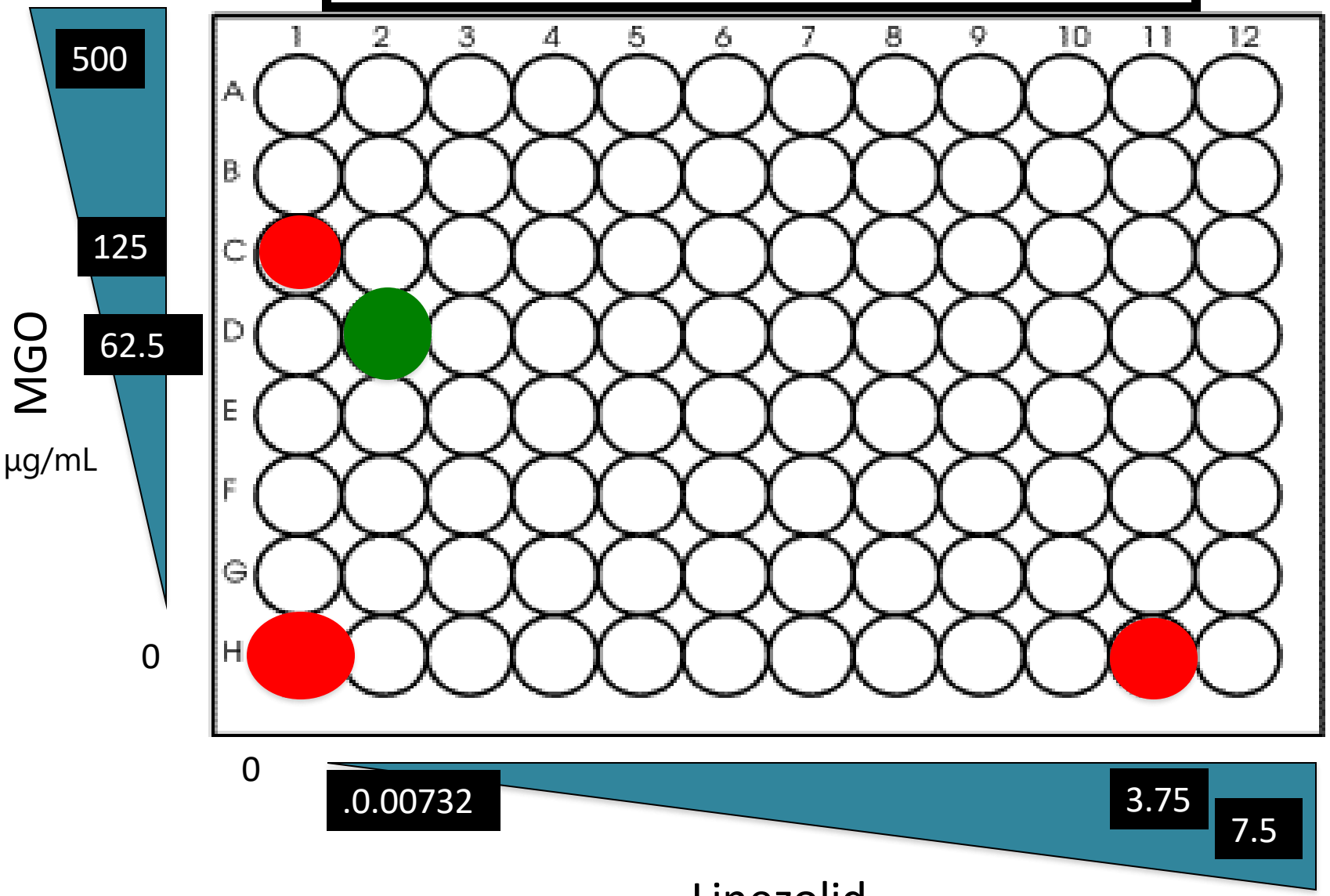


MSSA ATCC 29213

512 times more sensitive



MSSA ATCC 29213

Fractional Inhibitory Concentration Index

FICI Score < 0.5 Indicates Synergy

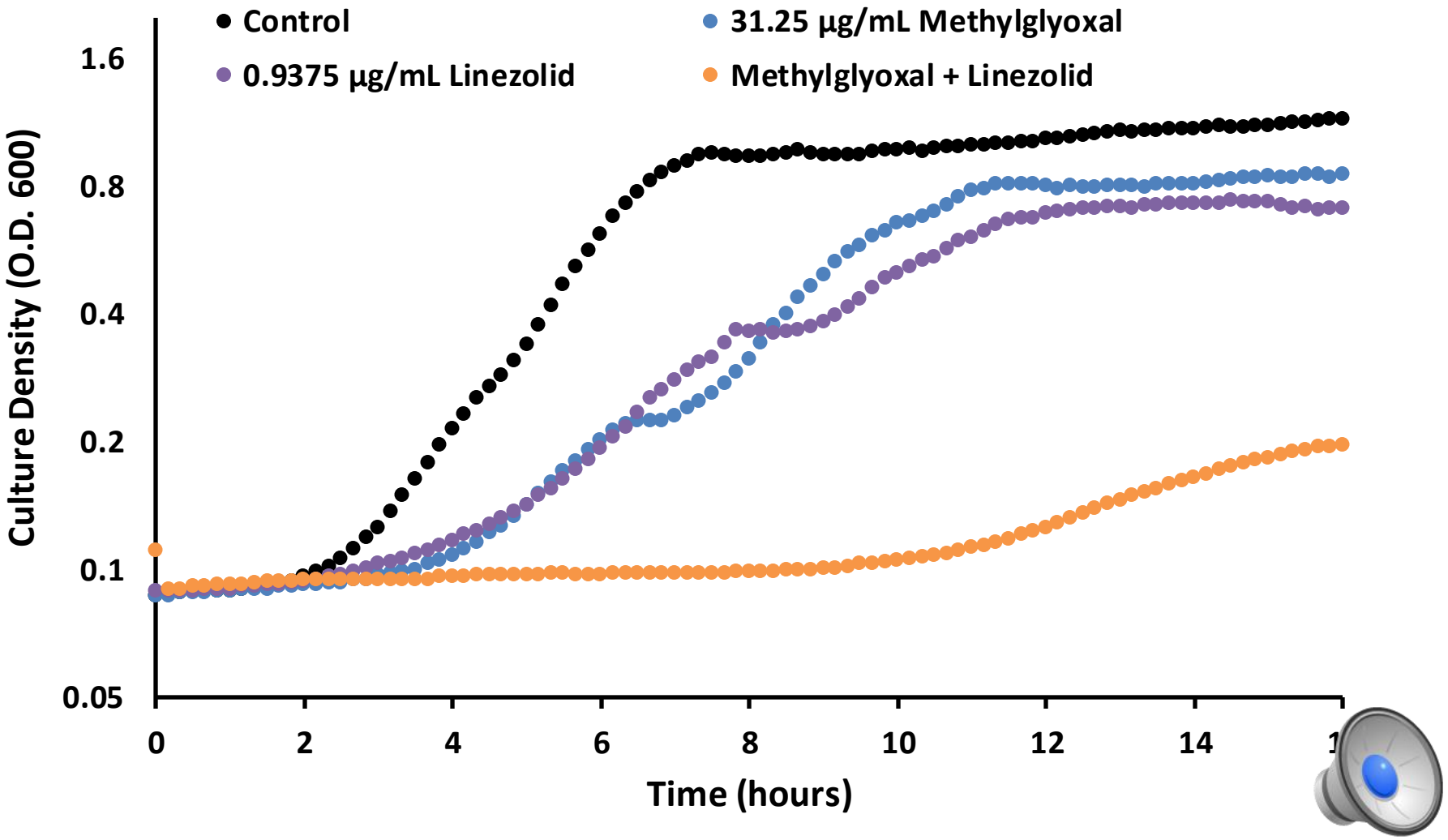
MSSA ATCC 29213

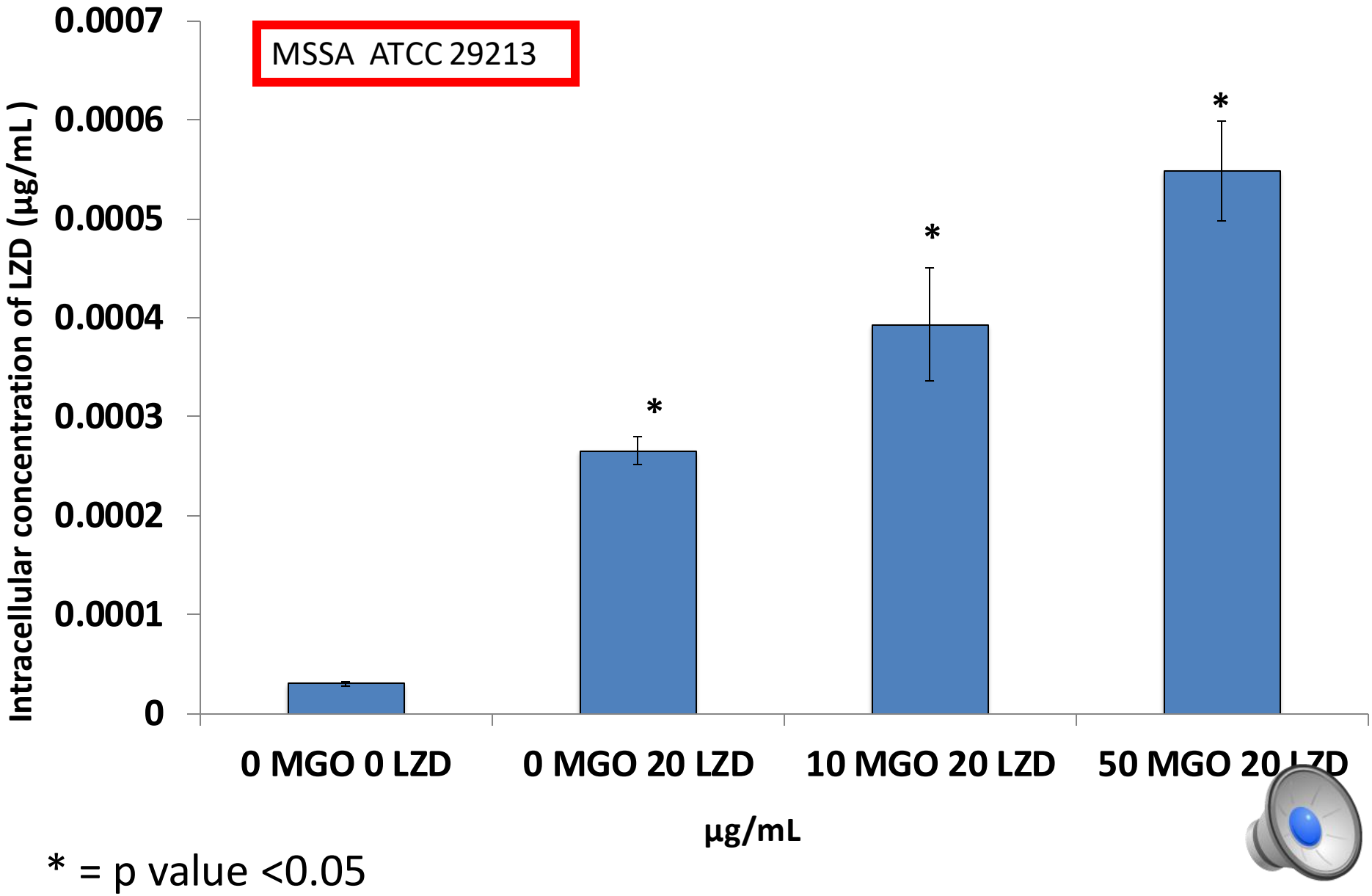
FICI Score: 0.0644

MRSA USA300

FICI Score: 0.25781

MSSA ATTC 29213




MSSA ATCC 29213
Intracellular concentration of LZD (µg/mL)
0.0007
0.0006
0.0005
0.0004
0.0003
0.0002
0.0001
0
*
*
*
0 MGO 0 LZD
0 MGO 20 LZD
10 MGO 20 LZD
50 MGO 20 LZD
µg/mL

* = p value <0.05

Conclusions

- The Synergy is MGO and Manuka specific
- MGO displays synergy with linezolid against MRSA and methicillin sensitive strains of *S. aureus*
- Interaction is partially due to increased drug internalization

Acknowledgements

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HIGH POINT UNIVERSITY

THE SUMMER RESEARCH INSTITUTE SuRI

THE SUMMER RESEARCH PROGRAM IN THE SCIENCES SuRPS

URCW

Manuka Honey: A New Tool in the Battle Against Antibiotic Resistance?

Project Backers

30 Backers | **101%** Funded | **$1,361** Total Donations | **$45.37** Average Donation

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Questions for me n’ my honeys?