

Rowan University

Rowan Digital Works

STEM Student Research Symposium Posters

Apr 23rd, 11:00 AM

Enhancing the Antibiotic Properties of Meropenem with Hydrophobic Ion-Pairing

Krishna Paul
Rowan University

Bidhan Barua
Rowan University

Lark Perez
Rowan University

Follow this and additional works at: https://rdw.rowan.edu/student_symposium

 Part of the [Chemistry Commons](#)

Let us know how access to this document benefits you - share your thoughts on our feedback form.

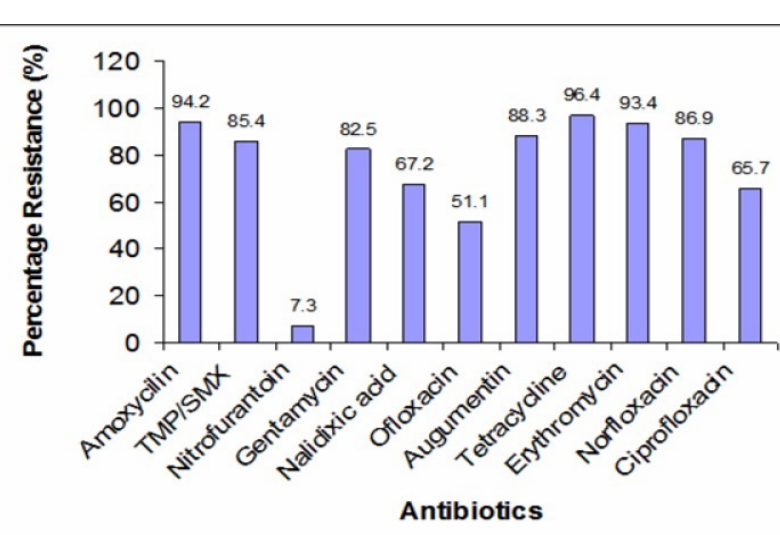
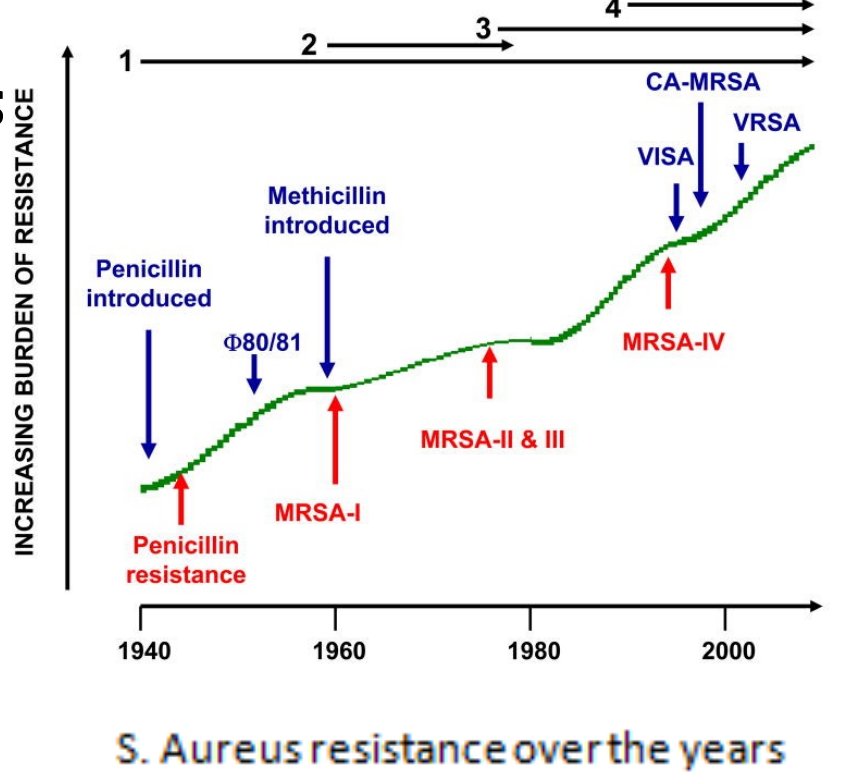
Paul, Krishna; Barua, Bidhan; and Perez, Lark, "Enhancing the Antibiotic Properties of Meropenem with Hydrophobic Ion-Pairing" (2024). *STEM Student Research Symposium Posters*. 10.

https://rdw.rowan.edu/student_symposium/2024/Apr23/10

This Poster is brought to you for free and open access by the Conferences, Events, and Symposia at Rowan Digital Works. It has been accepted for inclusion in STEM Student Research Symposium Posters by an authorized administrator of Rowan Digital Works.

Introduction

Antibiotic Resistance is one of the most urgent global threat to humankind. Most antibiotics are hydrophilic in nature while proteins and peptides are lipophilic. Enhancing lipophilicity of the antibiotic by HIP can increase solubility of the drugs in human and improve antibacterial effect as well.



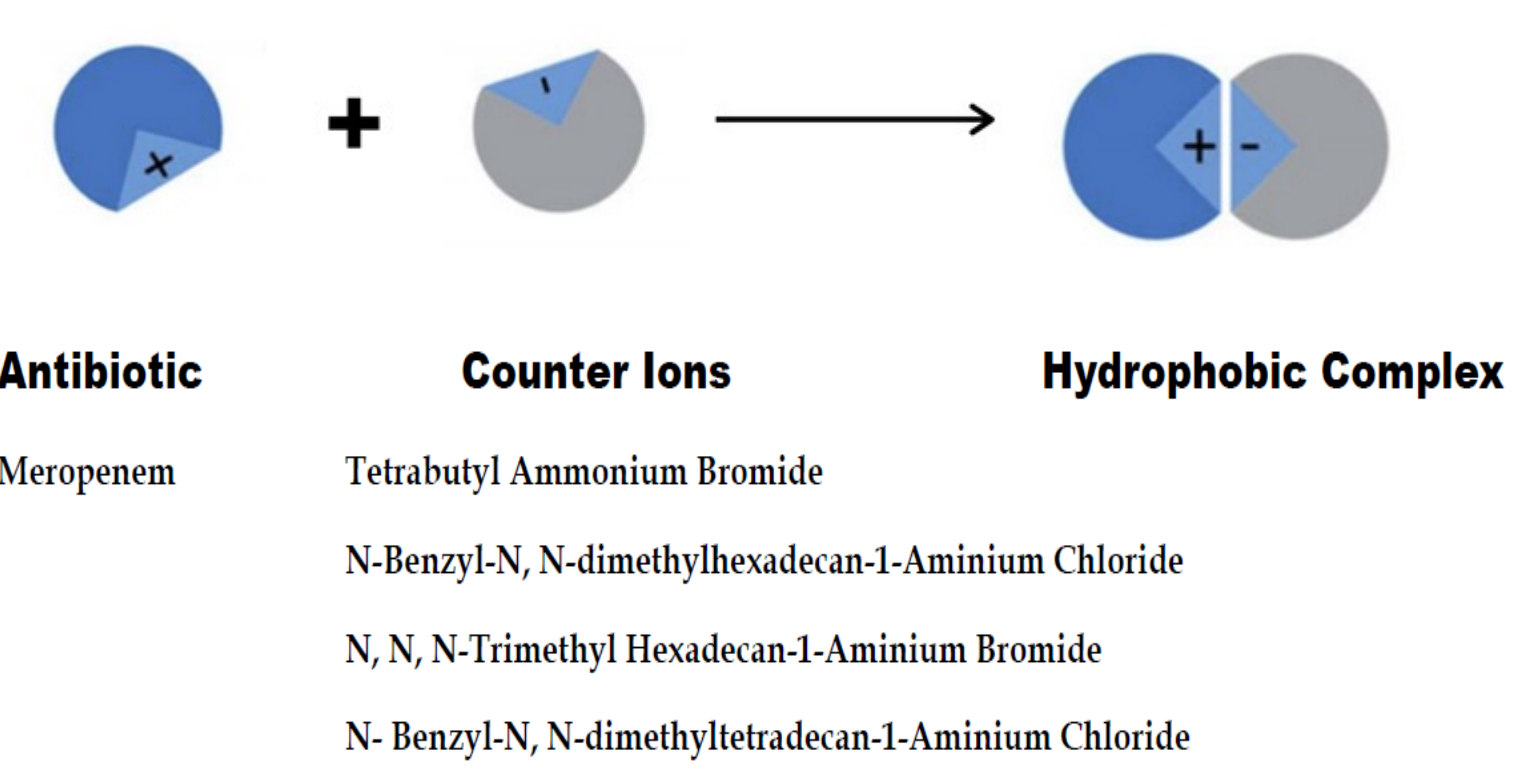
Percentage of E. coli resistance against antibiotics

We hypothesized that formation of a hydrophobic drug complex would change the physical properties of the antibiotic and enhance its antimicrobial activity.

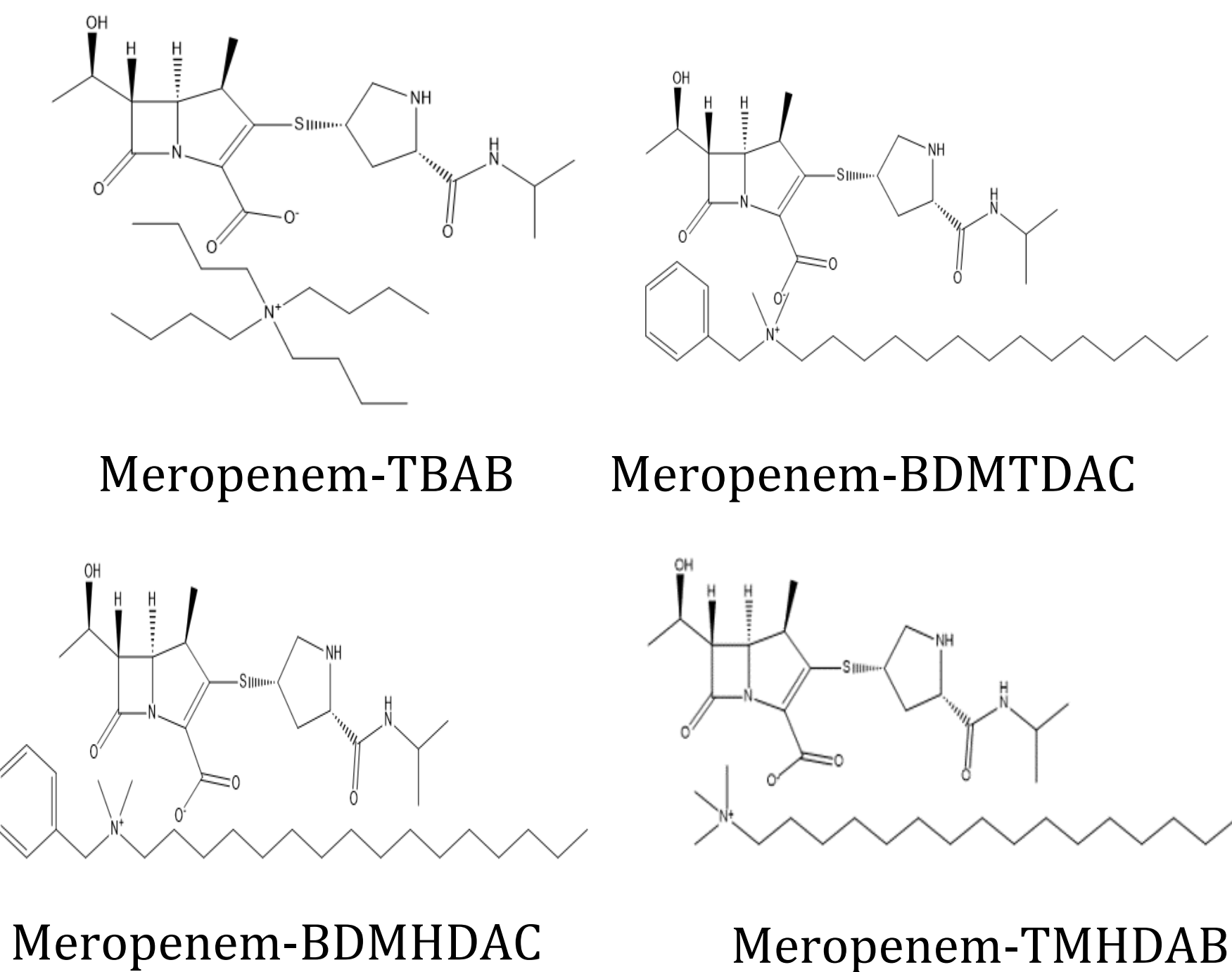
According to CDC, each year Worldwide 1,270,000 Deaths Associated with 5,000,000 deaths

Yearly in the U.S., at least 2,800,000 people get an antibiotic-resistant infection, and more than 35,000 people die.

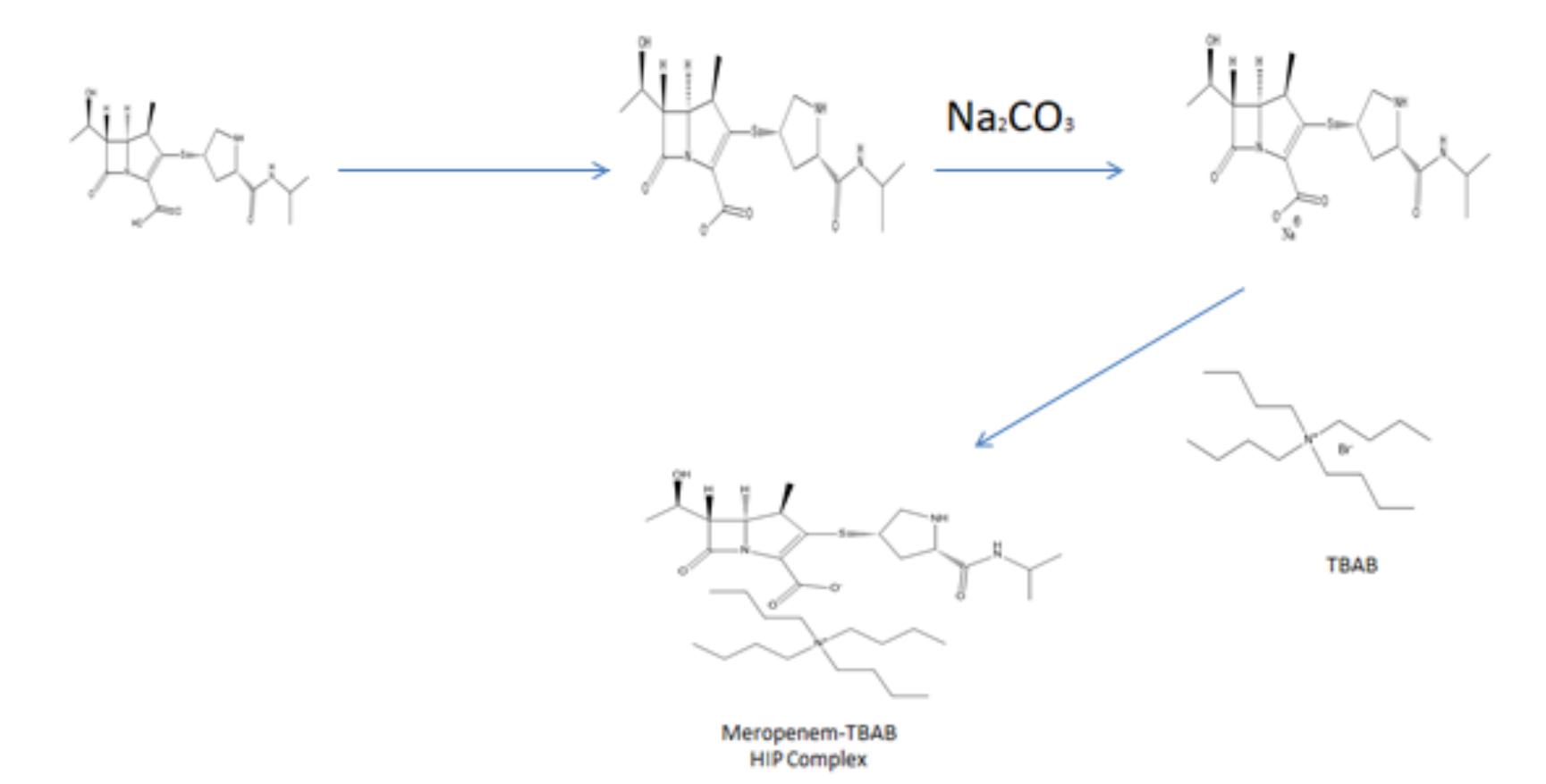
Hydrophobic Ion Pairing



Hydrophobic Complexes



Synthesis and Yield Determination

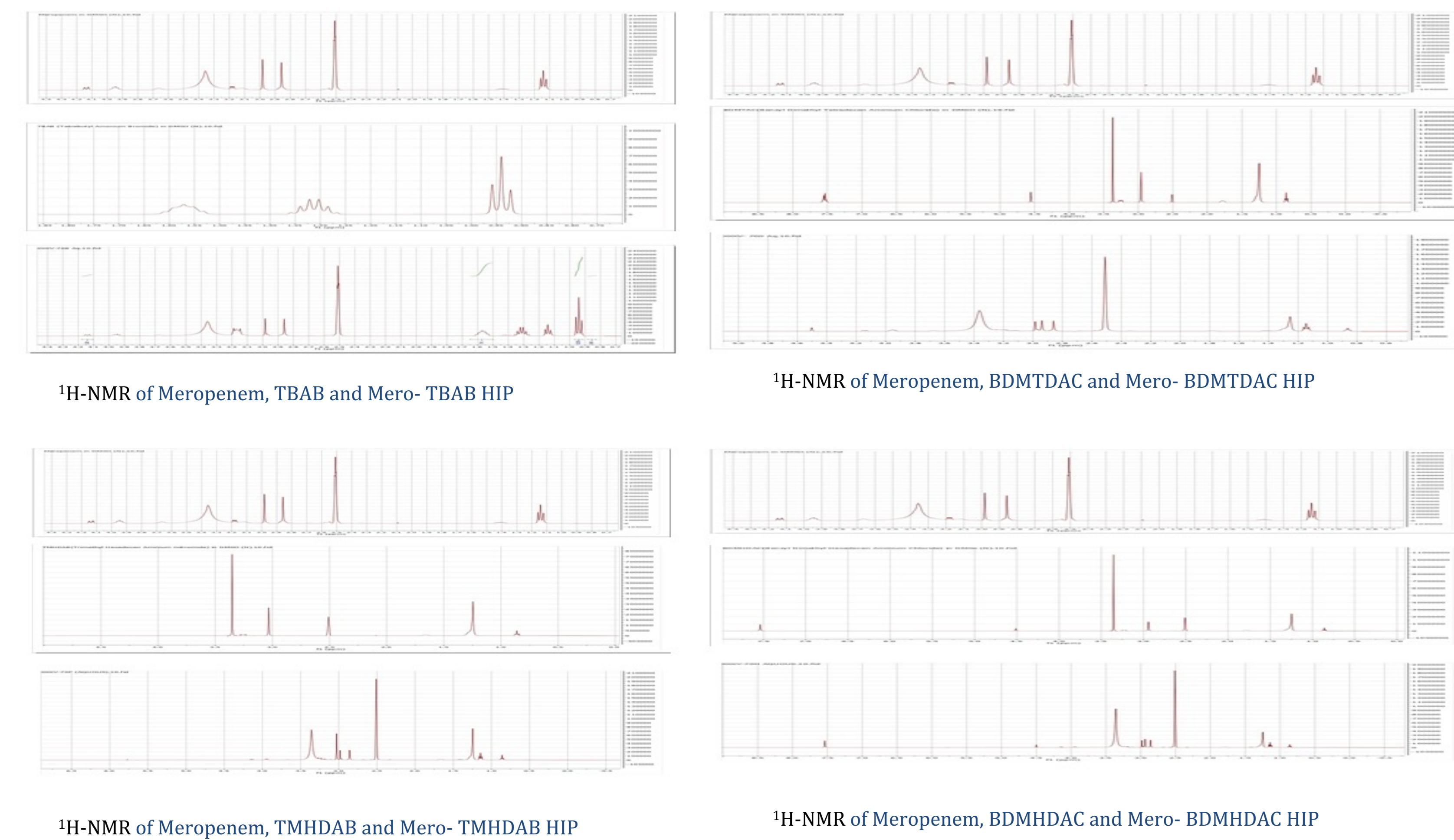


- 1:1 ratio were used for all drugs counterions to synthesize HIP complex.
- Protonated Meropenem in a Sodium Carbonate buffer solution of various pH levels.
- HIP were found in both phases, Aqueous parts were predominant for all counter ions.
- Sodium Carbonate buffer at a pH of 9.2 and 10.6 gave maximum yield.

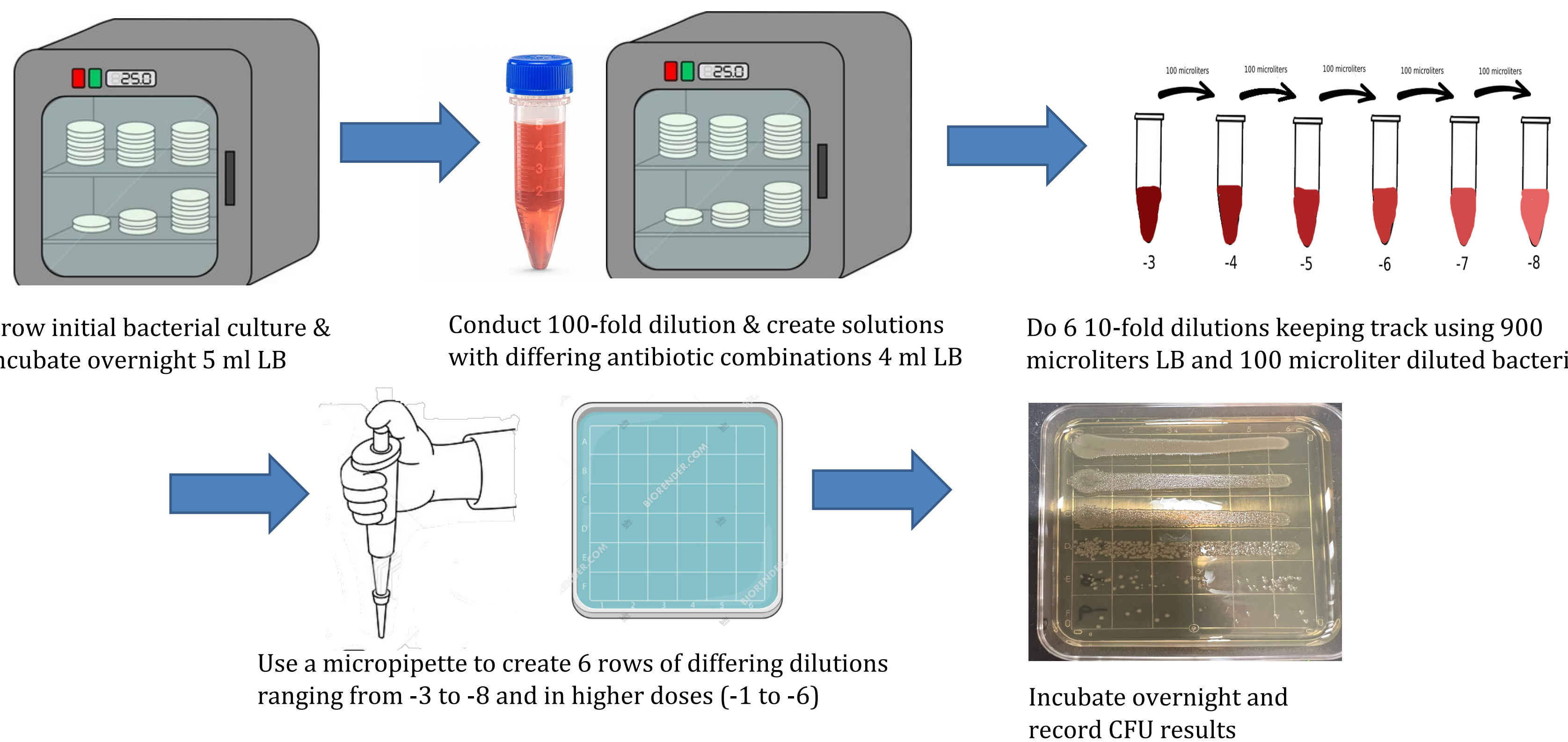
Sample ID	Counter Ions	Meropenem: CI	Weight of HIP	Yields
XXXV-70B (Aq)	TBAB	1.13 : 1	70.1 mg	81.89%
XXXV-70D (Aq)	BDMTDAC	1.17 : 1	72.3 mg	76.83%
XXXV-70F (Aq)	TMHDAB	0.85 : 1	77.9 mg	84.03%
XXXV-70H (Aq)	BDMHDAC	1.08 : 1	74.3 mg	76.21%

Characterization of Hydrophobic Complexes

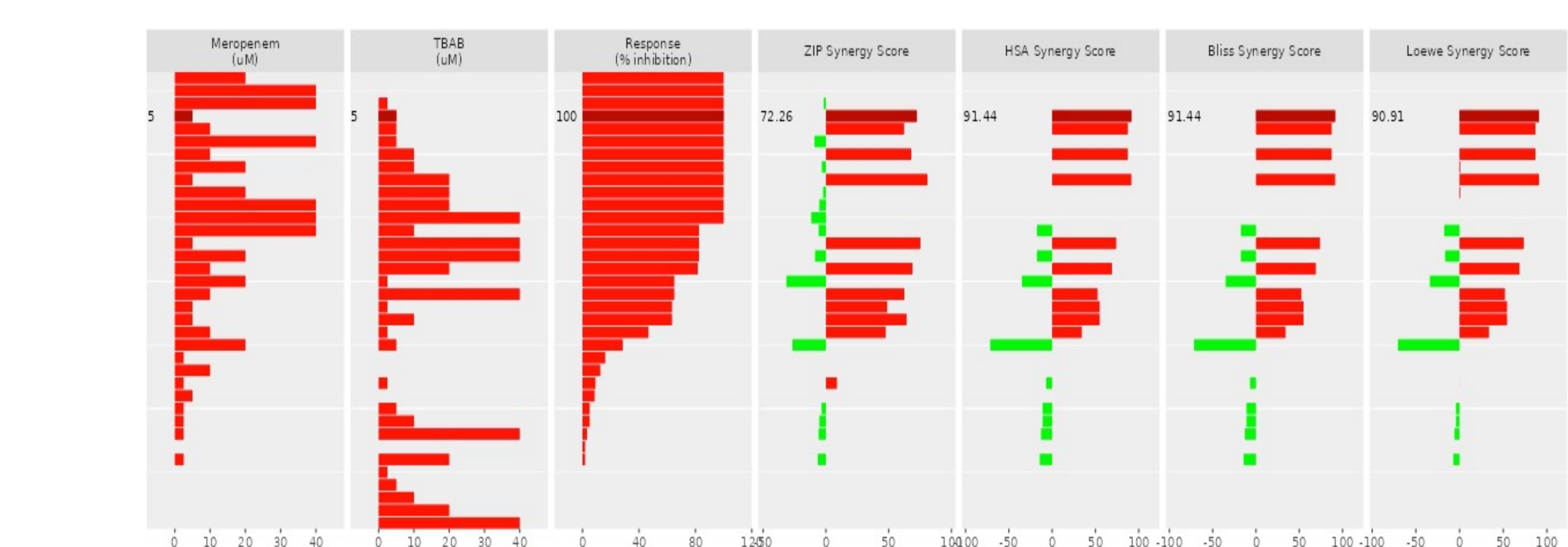
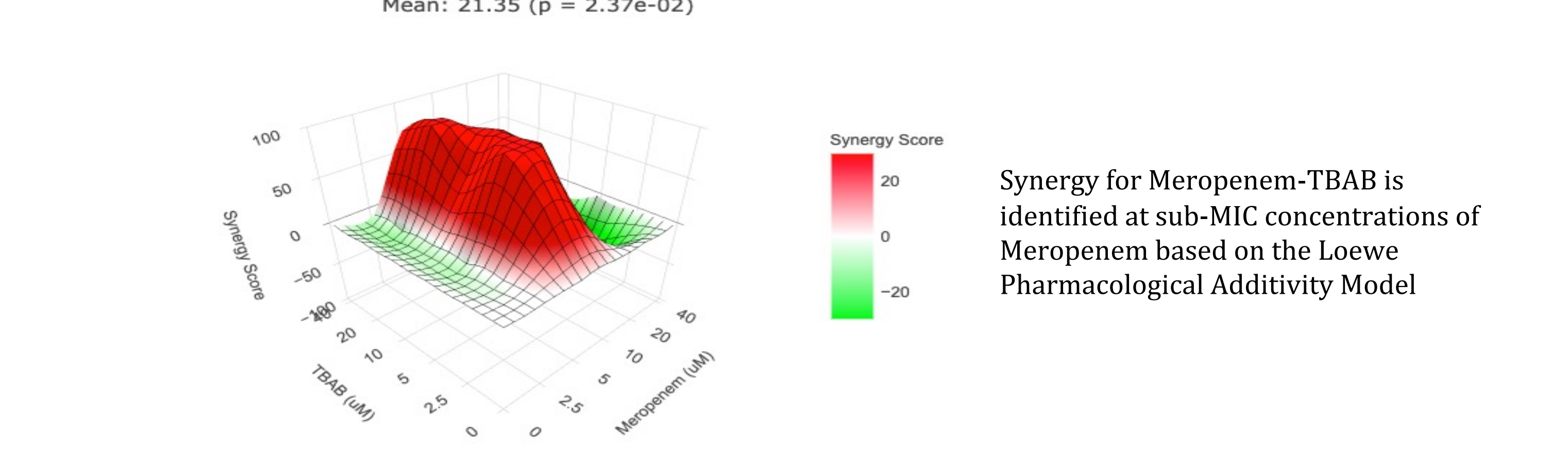
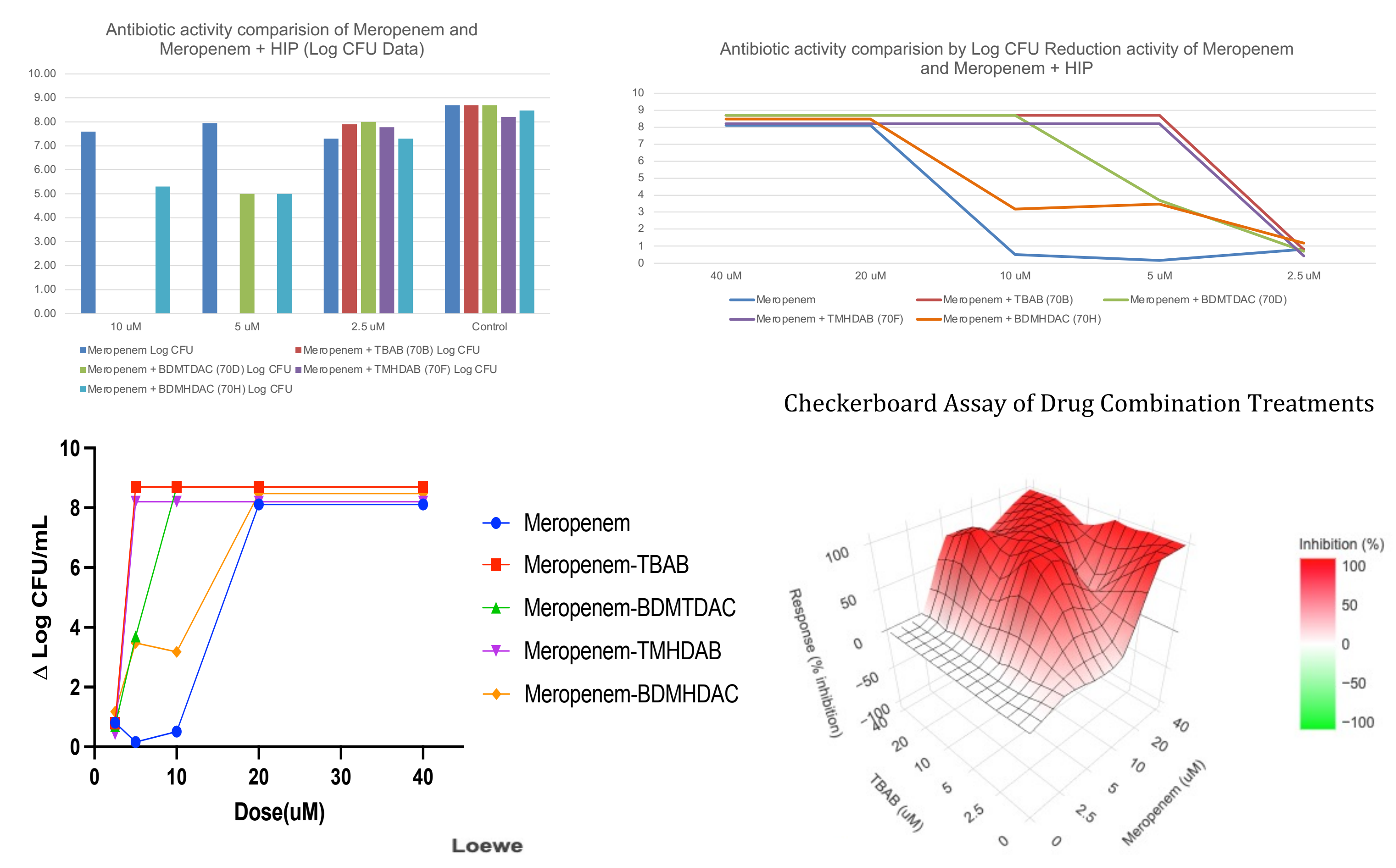
All hydrophobic complexes were characterized using FTIR and ¹H-NMR



Track Dilution MIC Assay of S. Aureus and MEROPENEM + HIP



Assaying Effect on S. Aureus Bacteria



Biological Activity

- Full Drug Synergy Analysis conducted using synergyfinder.com.
- Consensus observed among four major methods for calculating drug synergy.
- Synergy calculation highlighted for the combination of 5uM Meropenem with 5uM TBAB.
- Red bars indicate "synergistic" combinations of the drug with HIP.
- Green bars represent "antagonistic" combinations.
- The Antibiotic activity of Meropenem + HIP was way better than Meropenem itself against S. Aureus.
- At 5uM dose Meropenem + TBAB shows 54 times, Meropenem + TMHDAB shows 51 times, Meropenem + BDMDAC shows 23 times and Meropenem + BDMHDAC shows 22 times better CFU Reduction than Meropenem does.
- Among all the Meropenem + HIP complex Meropenem + TBAB shows the best outcome in all aspect.

Conclusions and Future Work

- Developed an innovative protocol for synthesizing a range of novel Meropenem antibiotic combination with hydrophobic counterions.
- Fully characterized the hydrophobic salts to validate their structural integrity.
- Collected IR and NMR data along with percentage yield to get better idea of complex formation and their future aspect.
- Optimized several Track Dilution with all Meropenem HIP complexes and 96-well plate methodologies against S. Aureus, E. Coli and Pseudomonas.
- Quantified collected data using Loewe Pharmacological Additivity Model.
- Future investigations will further refine parameters for enhancing antibiotic activity through hydrophobic counterion pairing.
- If possible will work on preparing the Meropenem HIP nanoparticles to ensure the best stability and efficacy of the complexes.

References and Acknowledgements

* Correspondance: perezla@rowan.edu

Yayan, J., Ghebremedhin, B., & Rasche, K. (2015). Antibiotic resistance of Pseudomonas aeruginosa in pneumonia at a single university hospital center in Germany over a 10-year period. *PLOS one*, 10(10), e0139836.

Ristroph, K. D., & Prud'homme, R. K. (2019). Hydrophobic ion pairing: encapsulating small molecules, peptides, and proteins into nanocarriers. *Nanoscale Advances*, 1(11), 4207-4237.

Jett, B.D.; Hatter, K.L; Huyche, M.M.; Gilmore, M.S. (1997) Simplified Agar Plate Methos for Quantifying Visible Bacteria. *BioTechniques* 23:648-650.

Counter-Ion Names Full Form

TBAB	Tetrabutyl Ammonium Bromide
BDMHDAC	N-Benzyl-N,N-dimethylhexadecan-1-Aminium Chloride
TMHDAB	N,N,N-Trimethyl Hexadecan-1-Aminium Bromide
BDMDAC	N-Benzyl-N,N-dimethyltetradecan-1-Aminium Chloride