Project Notes:

Project Title:

Name: Ishana Saroha

Note Well: There are NO SHORT-cuts to reading journal articles and taking notes from them. Comprehension is paramount. You will most likely need to read it several times, so set aside enough time in your schedule.

Contents:

Knowledge Gaps:

This list provides a brief overview of the major knowledge gaps for this project, how they were resolved and where to find the information.

Knowledge Gap	Resolved By	Information is located	Date resolved
Can bacteriocins and bacteriophages be combined? Is there evidence that this is good combination?			
What is difference between bacteriocins and bacteriophages?			

Literature Search Parameters:

These searches were performed between (Start Date of reading) and XX/XX/2019.
List of keywords and databases used during this project.

Database/search engine	Keywords	Summary of search
Google	Bacteriocins	Lots of general research papers, as well as papers on bacteriocins from a variety of substances. Some papers just have general information on different research that has been done on bacteriocins.
Google	Bacteriocins in soil bacteria	Results are research papers on specific bacteriocins from soil bacteria, as well as methodology followed to extract the bacteriocins and isolate them, and then measure their antimicrobial properties
Google	Bacteriocins in lactic acid bacteria	Results are research papers on specific bacteriocins from lactic acid bacteria, as well as methodology followed to extract the bacteriocins and isolate them, and then measure their antimicrobial properties

Tags:

Tag Name	
bacteriocins	Lactic acid bacteria
Soil bacteria	Antibiotic adjuvant

Article #1 Notes: Title

Article notes should be on separate sheets

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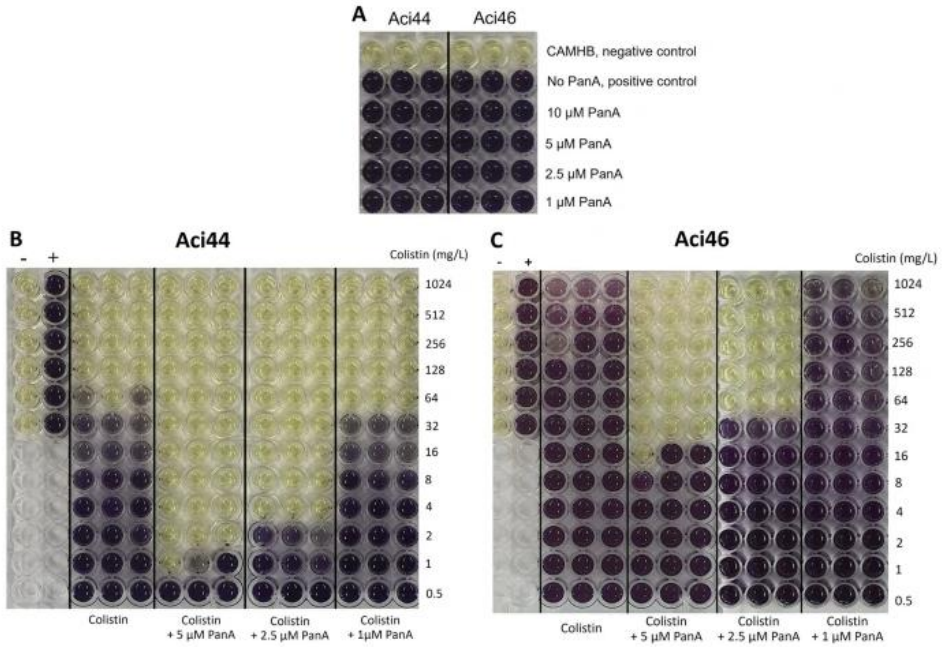
Source Title	
Source citation (APA Format)	
Original URL	
Source type	
Keywords	
#Tags	
Summary of key points + notes (include methodology)	
Research Question/Problem/ Need	
Important Figures	
VOCAB: (w/definition)	
Cited references to follow up on	
Follow up Questions	

Article #1 Notes: Enhancing effect of natural adjuvant, panduratin A, on antibacterial activity of colistin against multidrug-resistant Acinetobacter baumannii

Article notes should be on separate sheets

Source Title	Enhancing effect of natural adjuvant, panduratin A, on antibacterial activity of colistin against multidrug-resistant Acinetobacter baumannii
Source citation (APA Format)	Nalumon Thadtapong, Chaturongakul, S., Chanita Napaswad, Dubbs, P., & Sunhapas Soodvilai. (2024). Enhancing effect of natural adjuvant, panduratin A, on antibacterial activity of colistin against multidrug-resistant Acinetobacter baumannii. *Scientific Reports*, *14*(1). https://doi.org/10.1038/s41598-024-60627-0
Original URL	https://www.nature.com/articles/s41598-024-60627-0
Source type	Journal Article
Keywords	adjuvant
#Tags	
Summary of key points + notes (include methodology)	This research paper talks about panduratin A., a natural adjuvant, and its ability to enhance the antibacterial effectiveness and efficiency of colistin against multidrug-resistant Acinetobacter baumannii (MDR-AB). Antibiotic adjuvants are nonantibiotic compounds that enhance antibiotic activity, either by blocking resistance or by boosting the host response to infection. MDR-AB is known for its ability to develop resistance to multiple antibiotics, including those of last resort like colistin, and they pose a serious threat in clinical settings. Researchers hypothesized that combining panduratin A with colistin could increase the antibacterial activity, thus potentially reducing the required dosage of colistin and mitigating its adverse effects. This research is crucial as it explores alternative treatment strategies against multidrug-resistant bacteria, potentially offering new options to work against infections that are increasingly difficult to treat using just conventional antibiotics. Colistin is a polymyxin antibiotic medication used as last-minute treatment against multidrug-resistant Gram-negative infections such as pneumonia, due to its ability to disrupt bacterial cell membranes. The emergence of colistin-resistant bacterial strains has caused immediate need for new approaches to enhancing its effectiveness or reduce dosage required, in order to minimize potential toxicity to patients. This study aimed to explore whether panduratin A, a natural compound found in certain plants – such as finger roots – can work to enhance the antibacterial

	activity of colistin against MDR-AB. This could potentially widen the possibilities of using colistin for other treatments, and improve treatment outcomes. To carry out this research, various strains of MDR-AB were cultured under controlled conditions. Researchers performed antimicrobial susceptibility testing to determine the minimum inhibitory concentration (MIC) of both colistin alone and with combinations of different concentrations of panduratin A. Improvements were measured using methods such as MBC/MIC ratio, fractional inhibitory concentration (FIC), and fractional bactericidal concentration (FBC), to quantify interactions between panduratin A and colistin, and identify any improvements in activity. Results from this study showed that panduratin A enhances the antibacterial activity of colistin against MDR-AB strains, evident by lower MIC values and biofilm amounts in agar diffusion assays when compared to colistin alone. The research concludes that panduratin A shows promise as a natural adjuvant to enhance the antibacterial activity of colistin against multidrug-resistant Acinetobacter baumannii. These findings highlight the potential for combination therapies utilizing natural compounds to combat antibiotic resistance effectively. This pertains to my prospective ideas for my science fair project because I am thinking about doing some sort of biology project, and would like to read more about different topics within the field, such as antibiotic adjuvants. I wanted to read a research paper that tested a natural antibiotic adjuvant and how it improved performance of an antibiotic. This specific paper showed that finger roots can significantly improve performance of a specific antibiotic, colistin, so I can use this information in further research, perhaps by testing other natural products that have similar properties to finger roots and seeing if they have stronger antibiotic adjuvants and can better enhance existing antibiotics. Further research into the safety, efficacy, and pharmacological properties of panduratin A in clinical settings could create new possibilities for future clinical trials and application in patient care.
Research Question/Problem/ Need	This research paper talks about panduratin A., a natural adjuvant, and its ability to enhance the antibacterial effectiveness and efficiency of colistin against multidrug-resistant Acinetobacter baumannii (MDR-AB).

Important Figures	**Figure 1**  Evaluation of antibiotic activity of panduratin A (PanA) on *A. baumannii* Aci44 and Aci46. (**A**) cell viabilities of Aci44 and Aci46 in four different panduratin A concentrations (0 [or no PanA], 1, 2.5, 5, and 10 µM) were observed by MTT-staining. Uninoculated CAMHB cultures were used as negative controls. MIC determination of colistin alone and combined compounds against Aci44 (**B**) and Aci46 (**C**) using microdilution assay and MTT staining. Viable cells stained purple while dead cells were not stained and shown in yellow. The experiments were tested in three biological replicates.
VOCAB: (w/definition)	Panduratin A: natural antibiotic adjuvant A. baumannii: bacterial pathogen associated with hospital-acquired infections MDR: multi-drug resistance MBC/MIC ratio: shows bactericidal nature of an antibiotic Colistin: antibiotic used to treat infections caused by gram negative bacteria
Cited references to follow up on	
Follow up Questions	Could panduratin A be effective against other multidrug resistant pathogens, or is it only limited to Acinetobacter baumannii? Do bacteriocins work against multiple bacteria strains or only specific ones that are related? Is there a risk of resistance developing to the combination of panduratin A and colistin?

Article #2 Notes: Vaccine for superbugs? New shot shows promise in early tests

Article notes should be on separate sheets

Source Title	Vaccine for superbugs? New shot shows promise in early tests
Source citation (APA Format)	Pappas, S. (2023, December 7). *Vaccine for superbugs? New shot shows promise in early tests*. Livescience.com; Live Science. https://www.livescience.com/health/medicine-drugs/vaccine-for-superbugs-new-shot-shows-promise-in-early-tests
Original URL	https://www.livescience.com/health/medicine-drugs/vaccine-for-superbugs-new-shot-shows-promise-in-early-tests
Source type	Article
Keywords	Superbugs
#Tags	
Summary of key points + notes (include methodology)	This article talks about a new promising approach to prevent hospital-acquired infections, which kill tens of thousands of people annually and are often due to antibiotic-resistant superbugs. There are too many pathogens, so patients cannot receive vaccines for each pathogen separately, and they need immediate protection. Traditional vaccines target specific pathogens and require time to create immunity, but this new vaccine provides broad, short-term protection by boosting innate immune responses. At first, researchers aimed to develop a vaccine against Staphylococcus aureus, a common hospital pathogen, using a combination of bacterial proteins and adjuvants. They found that adjuvants alone were just as effective as the combined vaccine, meaning that the vaccine's efficiency was from its ability to enhance innate immunity. Specifically, the vaccine had three adjuvants: aluminum hydroxide, monophosphoryl lipid A, and fungal mannan. It protected against various fungi and antibiotic-resistant bacteria like E. Coli. The vaccine was tested in mice, and researchers found that its protection lasted 28 days. The reason why this vaccine worked was activating macrophages and modulating cytokine levels, potentially improving survival after infection. If successful in human trials, this

	vaccine could significantly reduce hospital infections, limit antibiotic use, and help stop the rise of antibiotic-resistant superbugs. Researchers are preparing for clinical trials and navigating regulatory approval processes, aiming to begin human testing within the next 12 to 18 months. This innovative vaccine represents a promising new strategy in ongoing efforts to fight against hospital-acquired infections and antibiotic resistance. This article pertains to my prospective ideas for my science fair project because it focuses on exploring innovative approaches to combat antibiotic resistance by providing one example of a combination of antibiotic adjuvants and their effectiveness. This vaccine's success in improving responses to antibiotics highlights the potential for future drugs to do the same. The evidence that adjuvants alone are just as effective as being combined with proteins shows the importance and capability for more adjuvants to be used in medicine, and provide opportunity for further research, such as studying properties of the different adjuvants to determine what makes them so effective, especially when combined. This activity can later be replicated in other combinations in labs, to see if there are stronger or more efficient combinations that can be created and used.
Research Question/Problem/ Need	Researchers aimed to develop a vaccine against Staphylococcus aureus, a common hospital pathogen, using a combination of bacterial proteins and adjuvants.
Important Figures	
VOCAB: (w/definition)	Superbug: a microbe that is resistant to multiple antibiotics/medicines Staphylococcus aureus: a common hospital pathogen
Cited references to follow up on	
Follow up Questions	The protection lasted for 28 days in mice; how can immunity be prolonged in humans? How do the adjuvants specifically enhance innate immune responses? Besides this new vaccine approach, what methods are being used to help combat superbugs in hospital settings?

Article #3 Notes: Dangerous 'superbugs' are a growing threat, and antibiotics can't stop their rise. What can?

Article notes should be on separate sheets

Source Title	Dangerous 'superbugs' are a growing threat, and antibiotics can't stop their rise. What can?
Source citation (APA Format)	Lanese, N. (2023, October 1). *Dangerous "superbugs" are a growing threat, and antibiotics can't stop their rise. What can?* Livescience.com. https://www.livescience.com/health/medicine-drugs/dangerous-superbugs-are-a-growing-threat-and-antibiotics-cant-stop-their-rise-what-can
Original URL	https://www.livescience.com/health/medicine-drugs/dangerous-superbugs-are-a-growing-threat-and-antibiotics-cant-stop-their-rise-what-can
Source type	Article
Keywords	Superbugs, antibiotics, antibiotic resistant bacteria
#Tags	
Summary of key points + notes (include methodology)	This article talks about an infection with drug-resistant Klebsiella pneumoniae in a survivor of the 2016 Brussels Airport bombing. The superbug was finally released from her body when antibiotics were combined with a new treatment, showing a high need for new treatments and increased protection against antibiotic-resistant bacteria. Every year, different bacterial strains are becoming increasingly resistant to common antibiotics that are considered essential for public health. Bacteria are building resistance against antibiotics due to random DNA mutations or horizontal gene transfer, allowing them to quickly spread mutations to more bacteria. Drug companies have been working to develop new antibiotics that can attack these microbes, looking past traditional antibiotics for unique remedies and treatments that will help combat the rise of superbugs. Some possible treatments include phage therapy, CRISPR technology, and designer molecules like peptide nucleic acids (PNAs) and lysins. Phage therapy uses bacteria-infecting viruses - bacteriophages - to kill germs by invading

	their cells and splitting them open from the inside; bacteria are unlikely to develop resistance to phage therapy, and it is very precise with its targets, making this a good option for further research. CRISPR can be used to target specific DNA sequences and kill them, rather than damage multiple sequences. Lastly, lab-made molecules are very promising, because they can be designed to block bacterial cells from building essential proteins that are crucial to their survival. They target proteins that cells cannot change without damaging themselves, so these designer molecules are unlikely to cause drug resistance. All three of these options are very promising, and provide possible remedies that pertain to my prospective science fair project. I can use these three ideas to develop a project and conduct research, and they are more likely to be successful than other possible remedies, due to their promise of lower chances of drug resistance.
Research Question/Problem/ Need	Treatement of an infection with drug-resistant Klebsiella pneumoniae in a survivor of the 2016 Brussels Airport bombing
Important Figures	
VOCAB: (w/definition)	Klebsiella pneumoniae: common bacteria found in intestines
Cited references to follow up on	
Follow up Questions	Are there patterns in resistant bacteria, and can they be used to predict new treatment options? How does the combination of antibiotics with the new treatment specifically help with the release of the superbug? Are bacteriocins effective against superbugs?

Article #4 Notes: Broadening and Enhancing Bacteriocins Activities by Association with Bioactive Substances

Article notes should be on separate sheets

Source Title	Broadening and Enhancing Bacteriocins Activities by Association with Bioactive Substances
Source citation (APA Format)	Zgheib, H., Drider, D., & Belguesmia, Y. (2020). Broadening and Enhancing Bacteriocins Activities by Association with Bioactive Substances. *International Journal of Environmental Research and Public Health*, *17*(21), 7835. https://doi.org/10.3390/ijerph17217835
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC7663325/
Source type	Journal Article
Keywords	Bacteriocins, Bioactive Substances, Antibiotics, Cytotoxicity, Antibiotic Resistance
#Tags	
Summary of key points + notes (include methodology)	This research paper discussed the potential of combining bacteriocins, which are antimicrobial peptides produced by bacteria that demonstrate antiviral, anticancer, antibiotic, and antibiofilm activities, with different bioactive molecules, such as antibiotics, phages, nanoparticles, and essential oils, to enhance their therapeutic properties, effectiveness, and stability, while addressing issues like antibiotic resistance. Research found that combining bacteriocins with antibiotics could possibly reduce the development of resistance, as the combination of these substances lead to reduced potential cytotoxicity and total amount of antibiotics administered. Overall, this promises the future of bacteriocin-based combinations in different applications to address antibiotic resistance.
Research Question/Problem/ Need	Overall, this article talked about combining bacteriocins with different bioactive substances to measure effectiveness with regards to antibiotic resistance, bioavailability, stability, and other research areas.
Important Figures	

VOCAB: (w/definition)	Bacteriocins: antimicrobial peptides produced by bacteria that demonstrate antiviral, anticancer, antibiotic, and antibiofilm activities. They kill bacteria.
Cited references to follow up on	
Follow up Questions	1. Do bacteriocins offer potential to be a more efficient method for preventing antibiotic resistance instead of using antibiotic adjuvants? 2. If one has better performance for antibiotic resistance than the other one (bacteriocins vs antibiotic adjuvants), what makes it better? 3. If one performs much better than another, are there other substances with similar properties that can be tested for use to help with antibiotic resistance, including substances that haven't been researched much in this regard? 4. Bacteriocins demonstrate antiviral, anticancer, antibiotic, and antibiofilm properties. If bacteria are exposed to this, do their properties change? Do they respond to antibiotics differently?

Article #5 Notes: Bacteriocins from plant pathogenic bacteria

Source Title	Bacteriocins from plant pathogenic bacteria
Source citation (APA Format)	Holtsmark, I., Eijsink, V. G. H., & Brurberg, M. B. (2008). Bacteriocins from plant pathogenic bacteria. *FEMS Microbiology Letters*, *280*(1), 1–7. https://doi.org/10.1111/j.1574-6968.2007.01010.x
Original URL	https://academic.oup.com/femsle/article/280/1/1/515599
Source type	Journal Article
Keywords	Bacteriocins, plants, bacteria, antimicrobial
#Tags	

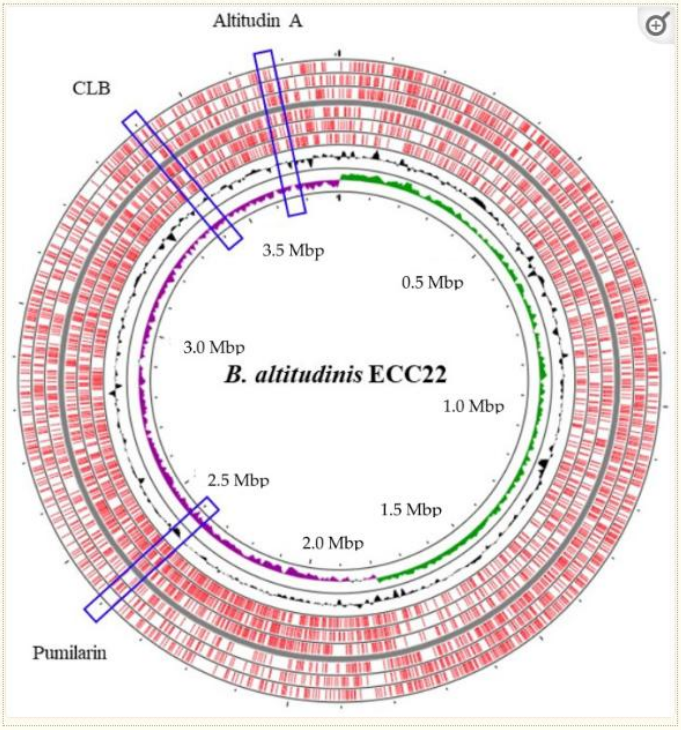
Summary of key points + notes (include methodology)	- Different classes of bacteriocins
	  o Class 1: lantibiotics: have modified amino acids. Their activities result in membrane destabilization, pore formation and/or inhibition of cell-wall synthesis by binding to specific lipids
	  o Class 2: nonmodified peptides. Receptors are proteins not lipids
	  o Class 3: heat-labile proteins
	- Current best-known bacteriocins from gram-negative bacteria come from E. Coli
	- This study examined the role of different bacteriocins in plant pathogenic bacteria. Typically, these substances are known to enhance the competitiveness of the producing organism, but there are some signs that show they also have regulatory functions. Researchers aimed to study these functions to see other applications of bacteriocins, and found that they target species of bacteria that are closely related, meaning they are from the same bacteria family. This makes them a good substance for replacing antibiotics, as their performance can be directed towards specific bacteria with low side effects when compared to existing antibiotics.

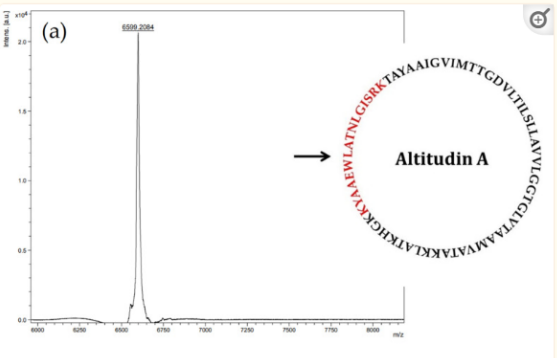
Research Question/Problem/ Need	What are the roles and functions of bacteriocins produced by plant pathogenic bacteria?
Important Figures	
VOCAB: (w/definition)	Lantibiotic: class of bacteriocins, characterized by unique post-translational

	modifications (differences in their structure) Gram-positive vs gram-negative bacteria: they differ based on their cell wall structure Peptide: short chains of amino acids that have various functions Sporulation: process when bacteria form spores, resistant form to survive harsh conditions from environment Auto-inducing peptide pheromone: signaling molecule that can stimulate the production of other molecules in bacterial populations Colicins: type of bacteriocin formed by E. Coli Microcin: small peptides with antimicrobial activity, produced by some gram-negative bacteria
Cited references to follow up on	
Follow up Questions	1. What are the genetic and biochemical variations among various bacteriocins produced by these plant pathogenic bacteria? 2. How do bacteriocins disrupt bacteria cell functions? 3. Do target bacteria ever develop resistance to bacteriocins? If so, how does this happen? Is the process similar to that with traditional antibiotics?

Article #6 Notes: Production of Pumilarin and a Novel Circular Bacteriocin, Altitudin A, by Bacillus altitudinis ECC22, a Soil-Derived Bacteriocin Producer

Source Title	Production of Pumilarin and a Novel Circular Bacteriocin, Altitudin A, by Bacillus altitudinis ECC22, a Soil-Derived Bacteriocin Producer
Source citation (APA Format)	Lafuente, I., Sevillano, E., Nuria Peña, Cuartero, A., Hernández, P. E., Cintas, L. M., Estefanía Muñoz-Atienza, & Borrero, J. (2024). Production of Pumilarin and a Novel Circular Bacteriocin, Altitudin A, by Bacillus altitudinis ECC22, a Soil-Derived Bacteriocin Producer. *International Journal of Molecular Sciences*, *25*(4), 2020–2020. https://doi.org/10.3390/ijms25042020
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10888436/
Source type	Journal Article
Keywords	Circular bacteriocins
#Tags	
Summary of key points + notes (include methodology)	This study addresses the problem of antibiotic resistance by comparing different bacteriocins from soil bacteria. They chose to focus on Bacillus altitudinis ECC22 and studied it through further genome sequencing. Bioinformatic analysis showed specific gene clusters responsible for synthesizing two circular bacteriocins, pumilarin and altitudin A, and a bacteriocin similar to closticin 574. The antibiotic activities of pumilarin and altitudin A were confirmed through in vitro synthesis and recombinant E. Coli cells, but the colisticin-like bacteriocin did not show any antimicrobial activity. Purification and isolation of the bacteriocins showed that they are mainly effective against other Bacillus strains.

Research Question/Problem/ Need	They wanted to identify and characterize some novel bacteriocins from soil bacteria, specifically Gram-positive bacteria like Bacillus, and evaluated their antimicrobial properties.
Important Figures	 Figure 1 *Bacillus altitudinis* ECC22 genome map generated using the CGView server. The red squares represent the coding sequences (CDS). The black plot shows the GC content, the green plot shows the CG skew +, and the purple plot shows the CG skew –. The position of the gene clusters for pumilarin, altitudin A, and the closticin 574-like bacteriocin (CLB) are highlighted with a blue rectangle.

	 Figure 5 MALDI-TOF MS analysis of fractions 12 (**a**) and 15 (**b**) after the second RP-HPLC round of purification of the CFS of *B. altitudinis* ECC22. The peptides with a molecular mass (*m*/*z*) of 6598.93 and 7089.15 are for altitudin A and pumilarin, respectively. The full amino acidic sequences of altitudin A and pumilarin are in the right side of the figures. In red, the sequences containing the circularization site, identified by LC-MS/MS after digestion of fractions 12 and 15. The black arrow shows the head-to-tail circularization of the native bacteriocins.
VOCAB: (w/definition)	*Bacillus altitudinis*: bacteria strain Whole genome sequencing determines the complete DNA sequence of an organism's genome Circular bacteriocins: have a circular peptide structure IV-CFPS: used to produce proteins outside of living cells LC-MS/MS: liquid chromatography-mass spectrometry (identify compounds in a mixture)
Cited references to follow up on	
Follow up Questions	1. Does the structure of a bacteriocin impact its performance? 2. How can genome sequencing be used to evaluate the performance of a bacteriocin? What is the method used to do this? 3. When isolating bacteriocins, do you need to focus on one bacteria strain at a time, or can they be extracted from multiple types of strains of bacteria at once?

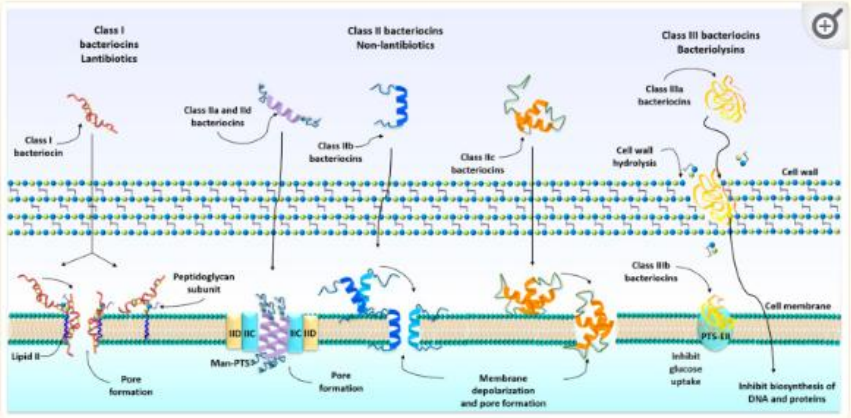
Article #7 Notes: Bacteriocins: Properties and potential use as antimicrobials

Source Title	Bacteriocins: Properties and potential use as antimicrobials
Source citation (APA Format)	Darbandi, A., Asadi, A., Mahdizade Ari, M., Ohadi, E., Talebi, M., Halaj Zadeh, M., Darb Emamie, A., Ghanavati, R., & Kakanj, M. (2021). Bacteriocins: Properties and potential use as antimicrobials. *Journal of Clinical Laboratory Analysis*, *36*(1). https://doi.org/10.1002/jcla.24093
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8761470/
Source type	Journal Article
Keywords	Bacteriocin, food-born pathogen, lactic acid bacteria
#Tags	
Summary of key points + notes (include methodology)	This article looks at bacteriocins produced by lactic acid bacteria, and their potential to be antimicrobial agents against food-borne pathogens, including Staphylococcus aureus, Pseudomonas fluorescens, and Listeria monocytogenes. It also talks about the structure, classification, mechanisms of action, safety, and antimicrobial properties/effectiveness of these bacteriocins, and their ability to preserve foods and potential medication-related applications of these bacteriocins.
Research Question/Problem/ Need	What is the performance of some bacteriocins produced by lactic acid bacteria?
Important Figures	
VOCAB: (w/definition)	Lactic acid bacteria: group of bacteria involved in the fermentation of lactose to lactic acid, and known for their role in food preservation and probiotic health benefits Food-borne pathogens: bacteria that cause illness through contamination of food Probiotic: live microorganisms that provide health benefits when

	consumed in large amounts, associated with gut health
Cited references to follow up on	
Follow up Questions	1. What is the exact process used to extract these bacteriocins? 2. What other substances can bacteriocins be extracted from? 3. What are the safety profiles of these bacteriocins when used in food products, and how do they impact human health? 4. Is there potential for foodborne pathogens to develop resistance to these bacteriocins?

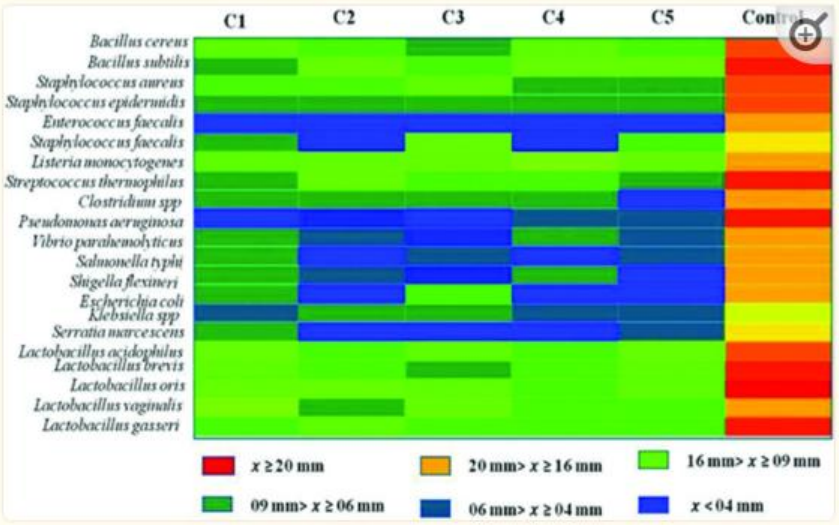
Article #8 Notes: Bacteriocins from Lactic Acid Bacteria. A Powerful Alternative as Antimicrobials, Probiotics, and Immunomodulators in Veterinary Medicine

Source Title	Bacteriocins from Lactic Acid Bacteria. A Powerful Alternative as Antimicrobials, Probiotics, and Immunomodulators in Veterinary Medicine
Source citation (APA Format)	Hernández-González, J. C., Martínez-Tapia, A., Lazcano-Hernández, G., García-Pérez, B. E., & Castrejón-Jiménez, N. S. (2021). Bacteriocins from Lactic Acid Bacteria. A Powerful Alternative as Antimicrobials, Probiotics, and Immunomodulators in Veterinary Medicine. *Animals*, *11*(4), 979. https://doi.org/10.3390/ani11040979
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8067144/
Source type	Journal Article
Keywords	bacteriocins, antimicrobials, lactic acid bacteria, probiotics
#Tags	
Summary of key points + notes (include methodology)	This article talks about the potential for bacteriocins to combat antimicrobial resistance in public and animal health. Lactic Acid Bacteria were used, and bacteriocins were extracted from them and then compared

	to see if they could find any novel bacteriocins. These bacteriocins also have immunomodulatory effects, which are very useful for veterinary medicine.
Research Question/Problem/ Need	What are some bacteriocins extracted from lactic acid bacteria, and how is their antimicrobial performance?
Important Figures	 Figure 1 Mode action of bacteriocins. Bacteriocins act directly on the membrane or through a specific receptor on the target cell and form pores in the bacterial cell membrane, which leads to cell death.
VOCAB: (w/definition)	Immunomodulatory: ability to modify or regulate one or more immune functions Probiotic: live microorganism that provides health benefits when consumed
Cited references to follow up on	
Follow up Questions	1. Do these bacteriocins have the same impact on animals vs people? 2. How effective are bacteriocins compared to traditional antibiotics in treating bacterial infections in veterinary medication? 3. Can bacteriocins be combined with probiotics to enhance performance?

Article #9 Notes: Characterization and profiling of bacteriocin-like substances produced by lactic acid bacteria from cheese samples

Source Title	Characterization and profiling of bacteriocin-like substances produced by lactic acid bacteria from cheese samples
Source citation (APA Format)	Afrin, S., Hoque, M. A., Sarker, A. K., Satter, M. A., & Bhuiyan, M. N. I. (2021). Characterization and profiling of bacteriocin-like substances produced by lactic acid bacteria from cheese samples. *Access Microbiology, 3*(6). https://doi.org/10.1099/acmi.0.000234
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8374546/
Source type	Journal Article
Keywords	antimicrobial activity, bacteriocin, cheese, lactic acid bacteria
#Tags	
Summary of key points + notes (include methodology)	This research paper focuses on bacteriocins from lactic acid bacteria from cheese samples. Researchers took 25 LAB isolates (Lactobacillus spp.) with five strains demonstrating the ability to produce bacteriocins. Then, they used an agar-well-diffusion assay to study the antimicrobial activity of these bacteriocins. This showed inhibition of pathogens such as Bacillus subtilis, Staphylococcus aureus, and Listeria monocytogenes, while other pathogens such as E. faecalis and Salmonella typhi showed resistance. For the best bacteriocin production, the LAB cultures were harvested during exponential growth phase. Overall, this information suggests that bacteriocins from Lactobacillus spp. Have antimicrobial properties.

Important Figures	 Fig. 2. Inhibition zone map of extracted bacteriocins against indicators strains. Here, C1: *L. plantarum*, C2 : *L. paracasei* ss *paracasei*, C3: *L. rhamnosus*, C4: *L. farciminis*, C5: *L. bifermentans*, *x*: antimicrobial activity and ciprofloxacin used as a positive control.
VOCAB: (w/definition)	Agar spot assay: lab technique used to assess antimicrobial performance by observing their effects on a solid growth medium
Cited references to follow up on	
Follow up Questions	1. What LAB strains produce the best performing bacteriocins? 2. How can these bacteriocins be incorporated into foods for food preservation (perhaps even the food that has the bacteria it was extracted from?) 3. What are the mechanisms so that bacteriocins inhibit the growth of the pathogens being tested? 4. How does the agar spot assay show antimicrobial performance through growth?

Article #10 Notes: Isolation and Identification of Bacteriocin Producing Microbial Strains from Rhizosphere Soil

Source Title	Isolation and Identification of Bacteriocin Producing Microbial Strains from Rhizosphere Soil
Source citation (APA Format)	Vahid, A., Mallik, S., & Tyagi, M. (2024). Isolation and Identification of Bacteriocin Producing Microbial Strains from Rhizosphere Soil. *International Journal of Pharmaceutical Sciences and Research*, *86*(2). https://doi.org/10.36468/pharmaceutical-sciences.1309
Original URL	https://www.ijpsonline.com/articles/isolation-and-identification-of-bacteriocin-producing-microbial-strains-from-rhizosphere-soil-5409.html
Source type	Journal Article
Keywords	Antibiotics, rhizosphere, bacteriocin, agar diffusion assay, Streptococcus
#Tags	
Summary of key points + notes (include methodology)	In this paper, bacteriocin-producing pathogens were isolated from local rhizospheric soil samples and tested for antimicrobial activity against common pathogens such as *Pseudomonas, Aeromonas, Bacillus,* and *Escherichia coli* using the agar well diffusion method. Out of 11 tested isolates, five showed significant antimicrobial activity against the pathogenic bacteria. These strains were closely related to *Streptococcus*, *Enterococcus*, and *Gemella berger*, suggesting that these bacteria have strong potential for antimicrobial production.
Research Question/Problem/ Need	What are some bacteriocins in rhizospheric soil samples, and do they have high antimicrobial performance?

Important Figures	None in the paper.
VOCAB: (w/definition)	Rhizospheric soil: soil that surrounds plant roots
Cited references to follow up on	
Follow up Questions	1. Does the "layer" where the soil comes from impact the soil bacteria, and therefore the bacteriocins? 2. Can the specific strains that the five best isolates were closely related to be further tested to see if they produce good bacteriocins? 3. Can other soil bacteria be tested and compared for better antimicrobial performance? What are some differences between these strains, and how may that contribute to the performance of the bacteriocin?

Article #11 Notes: Mechanisms of bactericidal action of Eugenol against *Escherichia coli*

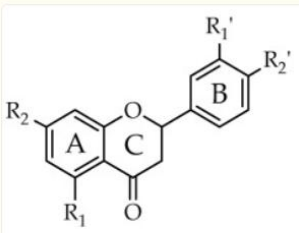
Source Title	Mechanisms of bactericidal action of Eugenol against *Escherichia coli*
Source citation (APA Format)	ımar, G. E., & Lawrence, R. (2021). Mechanisms of bactericidal action of Eugenol against Escherichia coli. *Journal of Herbal Medicine*, *26*, 100406. https://doi.org/10.1016/j.hermed.2020.100406
Original URL	https://www.sciencedirect.com/science/article/abs/pii/S2210803320300774
Source type	Journal Article
Keywords	Antibiotics, adjuvants, Eugenol, MIC
#Tags	#eugenol #adjuvant #antibiotic #MIC
Summary of key points + notes (include methodology)	- Eugenol has antibacterial properties - Is effective against a variety of pathogens - Has MIC ranging from 0.0312 to 8 microgram per microliter - MBC is 2-4 times higher - Has quick bactericidal action against E. Coli - Reduced bacteria levels in 4 hours - Disrupts cytoplasmic membrane (shown by ATP leakage) - Increases membrane depolarization - Alters membrane permeability - Leads to intracellular content leakage and potential cell damage
Research Question/Problem/ Need	What is the bactericidal action of Eugenol against E. Coli?
Important Figures	None in the paper.
VOCAB: (w/definition)	Membrane depolarization: cell membrane changes from negative to more positive, due to rapid opening of sodium channels in the membrane

Cited references to follow up on	
Follow up Questions	1. How well does Eugenol perform as an antibiotic adjuvant compared to existing used adjuvants? 2. If Eugenol is able to enhance the performance of antibiotics, what type of adjuvant is it classified as (what is its mode of action)? 3. Is Eugenol more likely to perform well as an adjuvant when compared to other potential adjuvants?

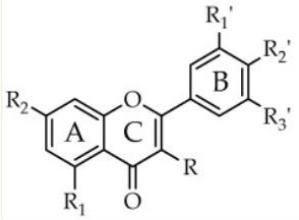
Article #12 Notes: Structure-Activity and Lipophilicity Relationships of Selected Antibacterial Natural Flavones and Flavanones of Chilean Flora

Source Title	Structure-Activity and Lipophilicity Relationships of Selected Antibacterial Natural Flavones and Flavanones of Chilean Flora
Source citation (APA Format)	Echeverría, J., Opazo, J., Mendoza, L., Urzúa, A., & Wilkens, M. (2017). Structure-Activity and Lipophilicity Relationships of Selected Antibacterial Natural Flavones and Flavanones of Chilean Flora. *Molecules : A Journal of Synthetic Chemistry and Natural Product Chemistry*, *22*(4), 608. https://doi.org/10.3390/molecules22040608
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC6154607/
Source type	Journal Article
Keywords	Naringenin, Flavonoid, MIC, adjuvant
#Tags	#naringenin #adjuvant #antibiotic #MIC
Summary of key points + notes (include methodology)	- Naringenin is a naturally-occurring flavonoid - Flavonoid is known for their antimicrobial properties, and due to their structural diversity, these plant derived compounds are a good model for studying potential novel antibacterial mechanisms - Flavonoids are widely distributed in plants - MIC in e coli: 4.00 µg/µL - This looked at eight naturally occurring flavonoids against range of gram positive and gram negative bacteria - Findings show that gram negative bacteria had more targeted range than gram negative bacteria. - Study the relationship between lipophilicity of flavonoids and their antibacterial activity, by determining partition coefficients and diffusion rate - Found that active flavonoids have diffusion coefficients between 9.4 × 10−10 and 12.3 × 10−10 m²/s, with lipophilicity values ranging from 2.0 to 3.3 - the amphipathic nature of flavonoids—containing both hydrophilic and hydrophobic regions—is crucial for their antibacterial activity, and lipophilicity analysis could predict their effectiveness

Research Question/Problem/ Need	What is the antimicrobial action of several different flavonoids against a range of gram positive and gram negative bacteria?
Important Figures	Figure 1.



Flavanones	R_1	R_2	R_1'	R_2'
Naringenin	OH	OH	H	OH
Pinocembrin	OH	OH	H	H
7-*O*-Methyleriodictyol	OH	OCH_3	OH	OH



Flavones	R	R_1	R_2	R_1'	R_2'	R_3'
Quercetin	OH	OH	OH	H	OH	OH
Galangin	OH	OH	OH	H	H	H
3-*O*-Methylisorhamnetin	OCH_3	OH	OH	OCH_3	OH	H
3-*O*-Methylgalangin	OCH_3	OH	OH	H	H	H
3,7-*O*-Dimethylgalangin	OCH_3	OH	OCH_3	H	H	H

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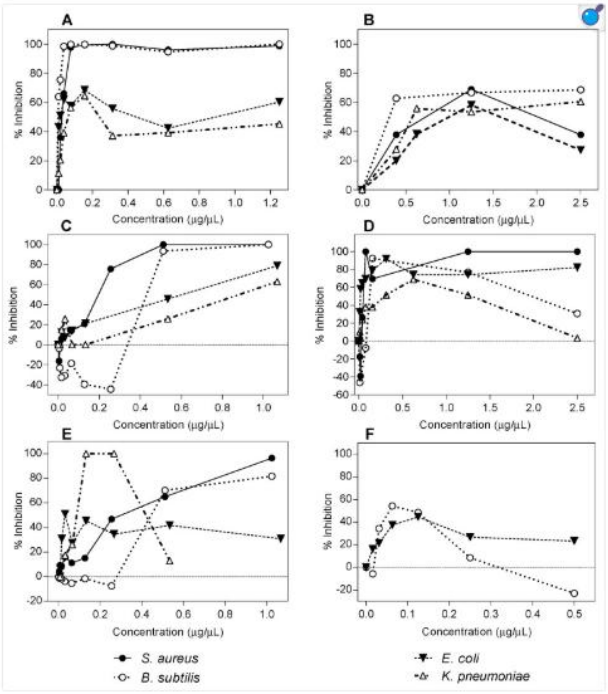
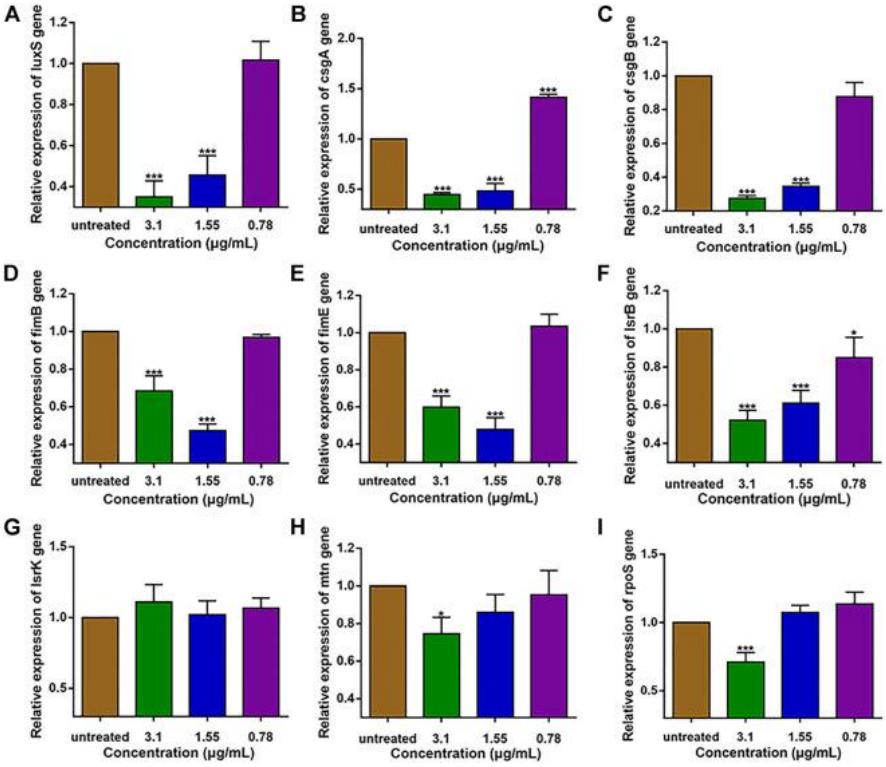
Flavonoids used in this study.

	Figure 2.  Effect of flavonoids on the stationary phase bacterial growth. Bacteria (2×10^8 ufc/mL, 10 µL in a final volume of 150 µL) were incubated stationary at 37 °C for 18 h in the presence of different concentrations of flavonoids in lysogeny broth (LB) in 96-well micro dilution plates. The final optical density (O.D.) in each well was measured in an Enzyme-Linked ImmunoSorbent Assay (ELISA) detector at 540 nm. (**A**) pinocembrin; (**B**) 7-*O*-methyleriodictyol; (**C**) galangin; (**D**) quercetin; (**E**) 3-*O*-methylgalangin; and(**F**) 3,7-*O*-dimethylgalangin. The graphs are representative of the results of three replicates.
VOCAB: (w/definition)	Flavonoid: a group of naturally occurring plant compounds known for their antioxidant, anti-inflammatory, and antimicrobial properties Lipophilicity: ability of a compound to dissolve in fats, oils, lipids and how they can pass through cell membranes and other hydrophobic environments Diffusion coefficient: measures how easily molecules can diffuse through a medium, such as cell membrane
Cited references to follow up on	
Follow up Questions	1. What is the activity of this flavonoid, naringenin, against other bacteria? What if it is combined with other compounds, such as antibiotics? 2. Are there other flavonoids that could perform better than naringenin that are also from citrus fruit? 3. Are there other factors that contribute to the antibacterial effectiveness of flavonoids beyond their lipophilicity?

Article #13 Notes: 1,8-Cineole inhibits biofilm formation and bacterial pathogenicity by suppressing *luxS* gene expression in *Escherichia coli*

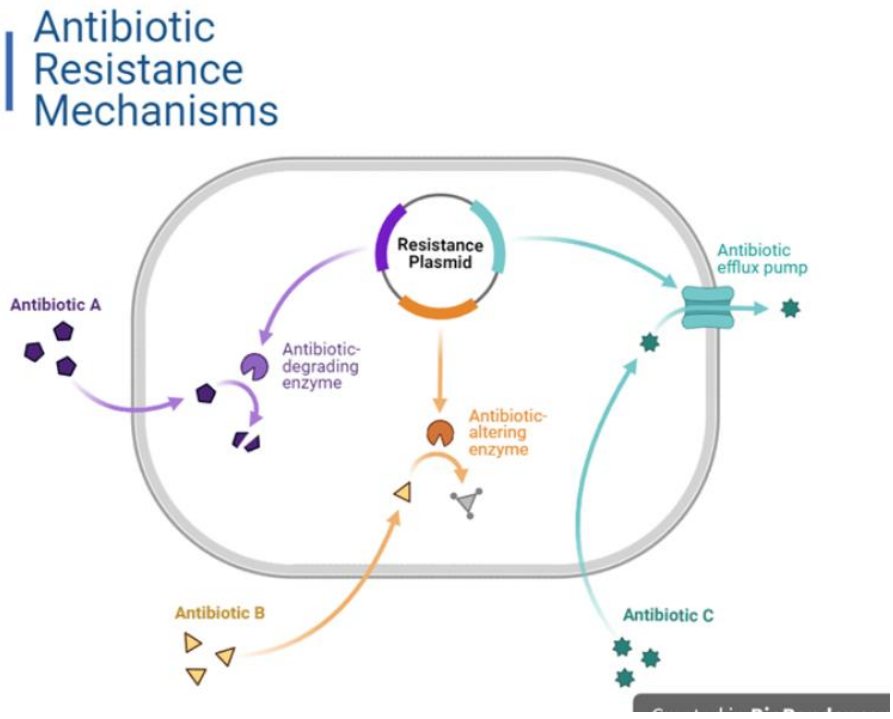
Source Title	1,8-Cineole inhibits biofilm formation and bacterial pathogenicity by suppressing *luxS* gene expression in *Escherichia coli*
Source citation (APA Format)	Wang, Y., Zhang, Y., Song, X., Fang, C., Xing, R., Liu, L., Zhao, X., Zou, Y., Li, L., Jia, R., Ye, G., Shi, F., Zhou, X., Zhang, Y., Wan, H., Wei, Q., & Yin, Z. (2022). 1,8-Cineole inhibits biofilm formation and bacterial pathogenicity by suppressing luxS gene expression in Escherichia coli. *Frontiers in Pharmacology*, *13*. https://doi.org/10.3389/fphar.2022.988245
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC9624193/
Source type	Journal Article
Keywords	1, 8-cineole; quorum sensing; biofilm; *Escherichia coli*; LuxS gene; pathogenicity
#Tags	#eucalyptol #adjuvant #antibiotic
Summary of key points + notes (include methodology)	- Looks at potential for eucalptol to be used to combat bacterial infections and antibiotic resistance - Used against E. Coli O101, which is known for its virulence and biofilm formation - Found that eucalyptol inhibits expression of GQ genes, including luxS gene, with 65% inhibition rate - Hypothesized that eucalpytol can reduce formation of biofilm and pathogenicity of e coli - Deleting the luxS gene improved the bacteria's ability to form

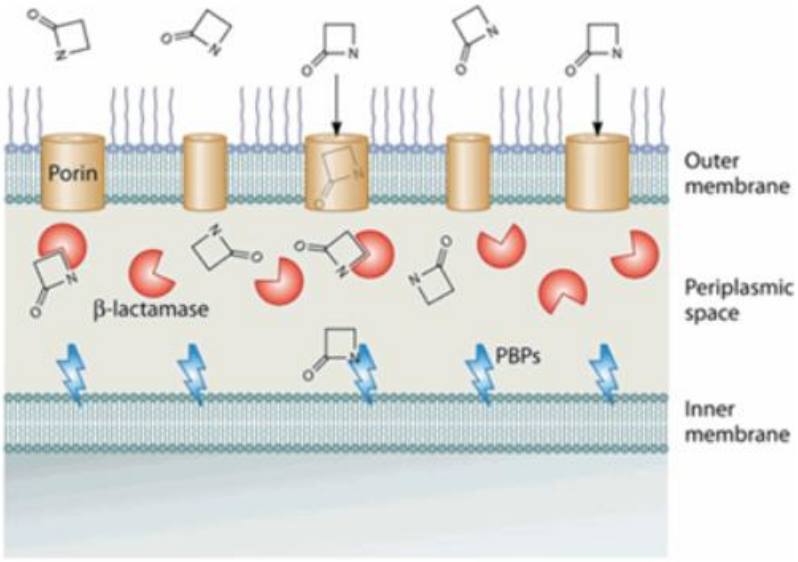
	biofilms, move, and cause disease. With this gene, the eucalyptol did not have much effect on the bacteria's gene expression or phenotype - MIC: 6.2 µg/ml
Research Question/Problem/ Need	Can 1,8-cineole inhibit the pathogenicity of *E. coli* O101 by suppressing the luxS gene expression?
Important Figures	 Expression of QS-related and virulence genes in *E. coli* O101 after 18 h inhibition by non-inhibitory 1,8-cineole concentrations. **(A–I)**: *luxS, csgA, csgB, fimB, fimE, lsrB, lsrK, mtn, rpoS.* The results represent means ± standard deviations for three independent experiments. *$p < 0.05$, **$p < 0.01$ and ***$p < 0.001$ *versus* the control group.
VOCAB: (w/definition)	Quorum sensing (QS): used for bacterial communication and virulence
Cited references to follow up on	
Follow up Questions	1. Does the deletion of the luxS gene in *E. coli* O101 affect its ability to form biofilms and its motility? 2. How will eucalyptol perform when combined with an antibiotic? 3. What is significant about the luxS gene expression? 4. How did researchers know to target this specific gene? Can

	similar thought process be followed for other genes/compounds?

Article #14 Notes: **Antibiotic Adjuvants for Combatting Antimicrobial Resistance**

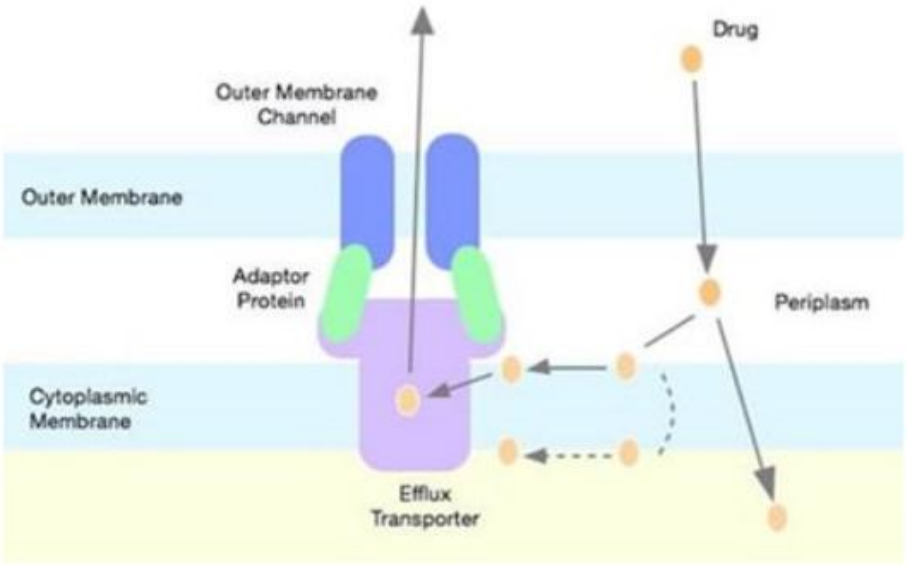
Source Title	**Antibiotic Adjuvants for Combatting Antimicrobial Resistance**
Source citation (APA Format)	*Antibiotic Adjuvants for Combatting Antimicrobial Resistance*. (n.d.). ASM.org. https://asm.org/Articles/2023/January/Antibiotic-Adjuvants-for-Combatting-Antimicrobial
Original URL	https://asm.org/articles/2023/january/antibiotic-adjuvants-for-combatting-antimicrobial
Source type	Webpage Article
Keywords	Types of adjuvants
#Tags	#adjuvants #betalactamaseinhibitor #effluxpumpinhibitor #outermembranepermeabilizer
Summary of key points + notes (include methodology)	- AMR is huge global threat as bacteria become resistant to existing antibiotics - Due to overuse and misuse of antibiotics - One potential solution is the use of antibiotic adjuvants: compounds that enhance the performance, or efficacy, of existing antibiotics instead of having to completely replace them - They don't directly kill bacteria, they inhibit resistant mechanisms - Beta lactamase inhibitors: o Most effective in clinical use

	○ Protect beta lactam antibiotics, like penicillin ○ Prevent beta lactamase from breaking down antibiotics - Efflux pump inhibitors: ○ Block bacterial pumps that expel antibiotics from the bacterial cell, allowing higher concentrations of the drug to stay inside the cell ○ They arent used currently in clinical settings due to toxicity concerns.. - Outer membrane permeabilizers: ○ Help the entry of antibiotics into bacterial cells, especially in gram negative bacteria like e coli
Research Question/Problem/ Need	What are the three different types of antibiotic adjuvants, and what are their mechanisms of action?
Important Figures	



Interactions between β -lactam antibiotics and β -lactam interactive proteins in gram-negative bacteria. β -lactamases intercept the antibiotic molecules so they can't bind to PBPs.

Source: Bush K. and Bradford P.A./Clinical Microbiology Reviews, 2020.

	 Bacteria can pump antibiotics out of the cell through efflux pumps. Source: Schlenk/Wikimedia Commons
VOCAB: (w/definition)	AMR: antimicrobial resistance Efficacy: performance
Cited references to follow up on	
Follow up Questions	1. Are there natural compounds that have similar mechanisms of action like beta lactamase inhibitors? 2. Are there natural compounds that have similar mechanisms of action like efflux pump inhibitors? 3. Are there natural compounds that have similar mechanisms of action like outer membrane permeabilizer?

Article #15 Notes: Outer membrane permeability and antibiotic resistance

Source Title	Outer membrane permeability and antibiotic resistance
Source citation (APA Format)	Delcour, A. H. (2009). Outer Membrane Permeability and Antibiotic Resistance. *Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics*, *1794*(5), 808–816. https://doi.org/10.1016/j.bbapap.2008.11.005
Original URL	https://www.sciencedirect.com/science/article/abs/pii/S1570963908003592?via%3Dihub
Source type	Journal Article
Keywords	Outer membrane permeabilizer
#Tags	#adjuvant #outermembranepermeabilizer
Summary of key points + notes (include methodology)	- Most antibiotics target intracellular process in order to kill bacteria, but this requires penetration of the cell envelope in order to be effective - In gram negative bacteria, the outer membrane is a significant barrier for compounds trying to enter the cell. - There are two main pathways for the antibiotic to cross: lipid-mediated pathway for hydrophobic compounds, and general diffusion porins for hydrophilic antibiotics. Due to structure and composition of the outer membrane, especially its lipid and proteins, they play a crucial role in determining bacterial sensitivity of the antibiotics - Outer membrane permeabilizers work by creating holes in this membrane, so the antibiotic can seep through and fill the cell. - outer membrane permeabilizers are compounds that enhance the ability of antibiotics to penetrate the outer membrane of Gram-negative bacteria (eg. *Escherichia coli*, or E. Coli), since this membrane is typically more

	protective and restricts the entrance of many antibiotics, making Gram-negative bacteria more difficult to treat than Gram-positive bacteria (Delcour, 2010). The permeabilizers work by disrupting or destabilizing the outer membrane, interacting with the lipid components (lipopolysaccharide layer) and causing pores or channels in the membrane which allow antibiotics to enter the cell (Delcour, 2010).
Research Question/Problem/ Need	What is the mechanism of action of outer membrane permeabilizers (how do they work as adjuvants)?
Important Figures	None in the paper.
VOCAB: (w/definition)	Hydrophilic: tend to dissolve in water Cytotoxicity: being toxic to cells, leading to cell damage or death or harmful effects of drugs on human cells
Cited references to follow up on	
Follow up Questions	1. How can this be tested in natural compounds, to see if they perform similar to outer membrane permeabilizers? What to study, what data to collect, how to analyze? 2. Are there any natural compounds that have been researched that have strong potential to perform similar to outer membrane permeabilizers? 3. Are there any natural compounds with mechanisms of action that are directly related to that of outer membrane permeabilizers?

Article #16 Notes: **Beta-Lactamase Inhibitors**

Source Title	**Beta-Lactamase Inhibitors**
Source citation (APA Format)	Khanna, N. R., & Gerriets, V. (2020). *Beta Lactamase Inhibitors*. PubMed; StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK557592/
Original URL	https://www.ncbi.nlm.nih.gov/books/NBK557592/
Source type	Article
Keywords	Beta Lactamase Inhibitors, Adjuvants
#Tags	#antibiotics #adjuvants #betalactamaseinhibitors
Summary of key points + notes (include methodology)	- These inhibitors are co-administered with beta-lactam antibiotics to combat AMR - Their main function is to inhibit beta-lactamase enzymes, which deactivate the beta lactam ring in all beta lactam antibiotics - This inhibition helps prevent antibiotic resistance, especially in bacteria that produce these enzymes (most commonly, gram negative bacteria such as E Coli) - They also target beta-lactamase producing staph bacteria, but there are other resistance mechanisms (such as penicillin-binding proteins) that make beta-lactamase inhibitors less effective for staph infections - These inhibitors are crucial for managing infections that involve resistant pathogens - β-lactamase inhibitors are designed to inhibit the action of enzymes called beta-lactamases that break down the beta-lactam ring in antibiotics, protecting them from degradation (Khanna & Gerriets, 2022). The inhibitors do this by binding to the enzymes and blocking their ability to hydrolyze the beta-lactam ring, thus preserving the antibiotic's activity against pathogens (Khanna & Gerriets, 2022).
Research Question/Problem/ Need	What is the mechanism of action of beta lactamase inhibitors?
Important Figures	None in the paper.

VOCAB: (w/definition)	Beta lactam ring: a four-membered ring that is a key structural component of beta-lactam antibiotics
Cited references to follow up on	
Follow up Questions	1. How can this be tested in natural compounds, to see if they perform similar to beta lactamase inhibitors? What to study, what data to collect, how to analyze? 2. Are there any natural compounds that have been researched that have strong potential to perform similar to beta lactamase inhibitors? 3. Are there any natural compounds with mechanisms of action that are directly related to that of beta lactamase inhibitors?

Article #17 Notes: Efflux pump inhibitors for bacterial pathogens: From bench to bedside.

Source Title	Efflux pump inhibitors for bacterial pathogens: From bench to bedside.

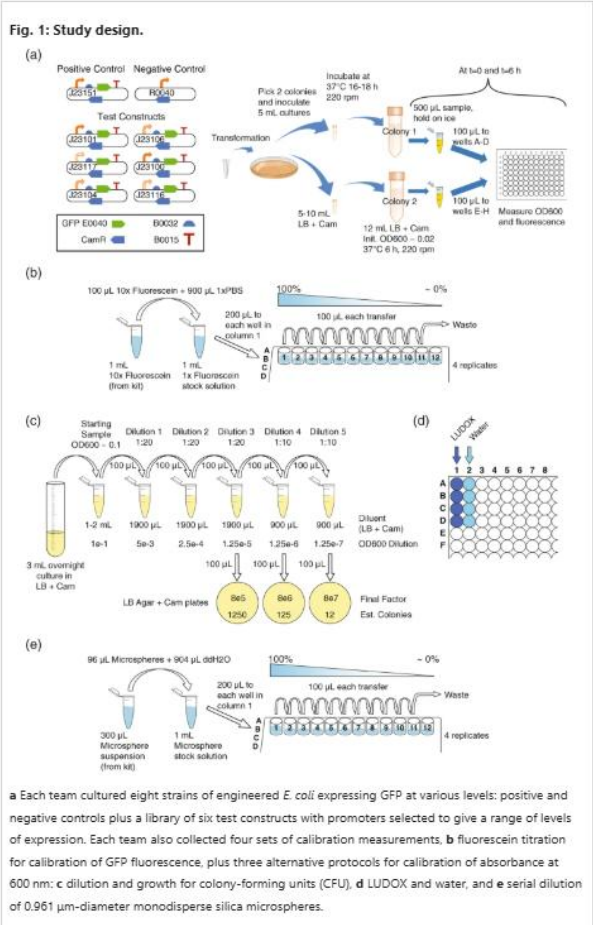
Source citation (APA Format)	Pathania, R., Sharma, A., & Gupta, V. (2019). Efflux pump inhibitors for bacterial pathogens: From bench to bedside. Indian Journal of Medical Research, 149(2), 129. https://doi.org/10.4103/ijmr.ijmr_2079_17
Original URL	https://doi.org/10.4103/ijmr.ijmr_2079_17
Source type	Journal Article
Keywords	Adjuvant, antibiotics, efflux pump inhibitor
#Tags	#adjuvants #antibiotics #effluxpumpinhibitors
Summary of key points + notes (include methodology)	- Efflux pump inhibitors are compounds that work against efflux pumps, which are membrane-bound proteins that actively transport a wide range of antimicrobial agents such as antibiotics out of bacterial cells, thus reducing the drug's effectiveness (Sharma et al, 2019). The inhibitors do this by binding to the pump or interfering with its ability to use energy (such as ATP), preventing it from effectively removing antibiotics from the bacterial cell and restoring the cell's susceptibility to the antibiotic (Sharma et al, 2019). - these pumps are membrane bound transport proteins found in many bacterial cells that expel toxic substances, such as antibiotics, out of the cell - this leads to AMR by reducing intracellular drug concentrations, causing bacteria to be less susceptible to the antibiotic - the pumps use proton gradients or ATP hydrolysis as an energy source to pump out substances, so the inhibitors bind to the pump and prevent or reduce its ability to remove antibiotics - types of efflux pumps: Major Facilitator Superfamily (MFS): These pumps use proton gradients to move drugs across the membrane. ..... ATP-Binding Cassette (ABC) Transporters: These are energy-dependent pumps that utilize ATP hydrolysis to expel drugs. ..... Resistance-Nodulation-Division (RND) Family: Found mostly in Gram-negative bacteria, these pumps use proton gradients to expel drugs. ..... Small Multidrug Resistance (SMR) Family:

	Found mainly in Gram-positive bacteria, these pumps also utilize electrochemical gradients to pump out drugs. ..... Multidrug and Toxic Compound Extrusion (MATE) Family: Use sodium or proton gradients to transport drugs out of cells. - types of inhibitors: competitive inhibition, non-competitive inhibition, substrate depletion, disruption of pump expression - examples: verapamil, CCCP (Carbonyl Cyanide m-Chlorophenyl Hydrazone), Reserpine
Research Question/Problem/ Need	What is the mechanism of action of efflux pump inhibitors?
Important Figures	None in the paper.
VOCAB: (w/definition)	Susceptibility: the state or fact of being likely or liable to be influenced or harmed by a particular thing
Cited references to follow up on	
Follow up Questions	1. How can this be tested in natural compounds, to see if they perform similar to efflux pump inhibitors? What to study, what data to collect, how to analyze? 2. Are there any natural compounds that have been researched that have strong potential to perform similar to efflux pump inhibitors? 3. Are there any natural compounds with mechanisms of action that are directly related to that of efflux pump inhibitors?

Article #18 Notes: **Robust estimation of bacterial cell count from optical density**

Source Title	**Robust estimation of bacterial cell count from optical density**
Source citation (APA Format)	Beal, J., Farny, N. G., Haddock-Angelli, T., Selvarajah, V., Baldwin, G. S., Buckley-Taylor, R., Gershater, M., Kiga, D., Marken, J., Sanchania, V., Sison, A., & Workman, C. T . (2020). Robust estimation of bacterial cell count from optical density. *Communications Biology*, *3*(1), 1–29. https://doi.org/10.1038/s42003-020-01127-5
Original URL	https://www.nature.com/articles/s42003-020-01127-5

Source type	Journal Article
Keywords	Optical density, bacteria count estimate
#Tags	#opticaldensity #bacteriacountestimate
Summary of key points + notes (include methodology)	- Optical density, or OD, is commonly used to estimate density of a cell culture. - OD cannot be used to compare between instruments without standardized calibration protocol - It is difficult to relate OD to actual cell count - The most common method used to estimate the number of cells in a liquid culture is to prepare a liquid suspension of it and use optical density measurements at a wavelength of 600 nm (OD600). This is particularly used in plate readers since the measurements are fast, inexpensive, simple, automated, and high throughput. - Use a spectrophotometer to calculate the OD, then use this value to figure out how many of that bacterial culture is needed to be added to each well in the plates for BMD assay and checkerboard assay o When preparing cuvettes for the spectrophotometer, do not directly put the washed O/N bacteria culture into it. Instead, do a 1 to 10 dilution with growth media (M9) and multiply the resulting OD by 10 *Look at the graphs they use to display data
Research Question/Problem/ Need	How to estimate bacterial cell count from optical density value?

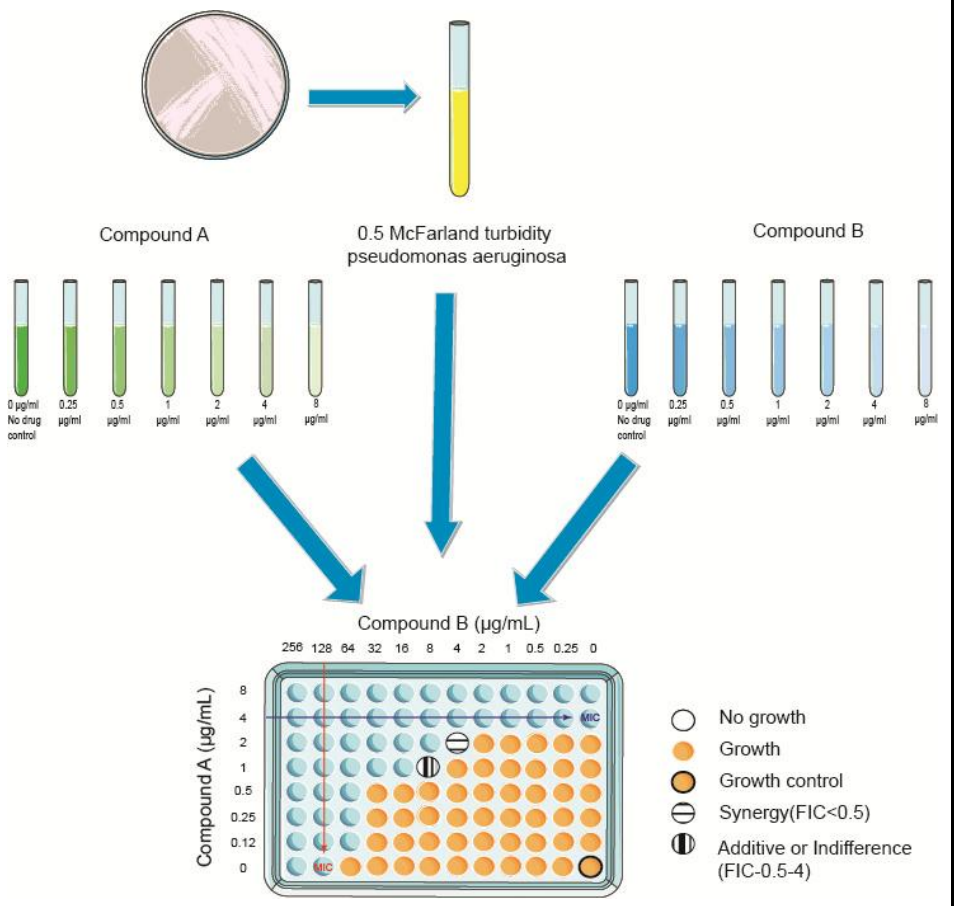
Important Figures	 **Fig. 1: Study design.** **a** Each team cultured eight strains of engineered *E. coli* expressing GFP at various levels: positive and negative controls plus a library of six test constructs with promoters selected to give a range of levels of expression. Each team also collected four sets of calibration measurements, **b** fluorescein titration for calibration of GFP fluorescence, plus three alternative protocols for calibration of absorbance at 600 nm: **c** dilution and growth for colony-forming units (CFU), **d** LUDOX and water, and **e** serial dilution of 0.961 µm-diameter monodisperse silica microspheres.
VOCAB: (w/definition)	CFU: Colony forming units
Cited references to follow up on	
Follow up Questions	1. Does the number of bacterial cells per mL of a bacteria depend on the bacteria strain? 2. How much of an impact does the size of bacterial cells have on the number of bacteria in the culture? 3. How does optical density compare to absorbance?

Article #19 Notes: Antimicrobial Synergy Testing/Checkerboard Assay

Source Title	Antimicrobial Synergy Testing/Checkerboard Assay
Source citation (APA Format)	*Antimicrobial Synergy Testing/Checkerboard Assay - Creative Diagnostics*. (n.d.). Antiviral.creative-Diagnostics.com.

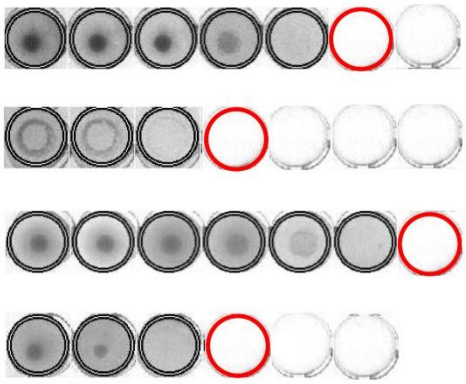
	https://antiviral.creative-diagnostics.com/antimicrobial-synergy-testing-checkerboard-assay.html
Original URL	https://antiviral.creative-diagnostics.com/antimicrobial-synergy-testing-checkerboard-assay.html
Source type	Website article
Keywords	Synergy, checkerboard assay
#Tags	#synergy #checkerboard assay

Summary of key points + notes (include methodology)	- Antibacterial synergy test, also known as checkerboard assay, is used to determine how two antibacterial agents interact.
	- Determine the MIC and MBC of each substance individually and combined
	- Calculate FIC (fractional inhibitory concentration) to determine combined effect of the antibiotics
	  ○ Lower FIC = stronger synergistic effect
	- Methodology
	  ○ Prepare stock solutions of each substance, along with at least two sequential dilutions to ensure concentrations exceed double the MIC.
	  ○ Plate setup:
	  ▪ Add 50 µl of Mueller-Hinton broth to each well of a microdilution plate.
	  ▪ Dilute the first antibiotic (A) sequentially along the vertical axis (ordinate) and the second antibiotic (B) along the horizontal axis (abscissa).
	  ○ Inoculum preparation
	  ▪ Prepare the bacteria culture to 5×10^5 CFU/ml and inoculate 100 µl into each well.
	  ○ Incubate
	  ▪ Incubate the microtiter plate at 35°C for 48 hours under aerobic conditions.
	  ○ Calculate FIC index
	  ▪ FIC Index = (A/ MIC A) + (B / MIC B)
	  • A and B are the MICs of each antibiotic in combination in a specific well.
	  • MIC A and MIC B are the MICs of each antibiotic tested individually.
	  ○ Interperate the FIC index
	  ▪ **FIC < 0.5**: Synergistic effect (the antibiotics work better together).

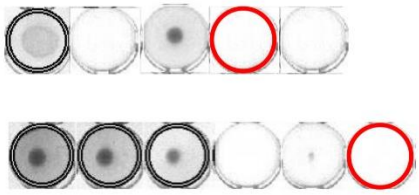
	▪ **FIC > 4**: Antagonistic effect (the antibiotics interfere with each other). ▪ **FIC 0.5–4**: Additive or indifferent effect (no significant interaction).
Research Question/Problem/ Need	How to perform a checkerboard assay and determine synergy?
Important Figures	
VOCAB: (w/definition)	Synergy: combined effect is greater than sum of individual effects
Cited references to follow up on	
Follow up Questions	1. How can this be done with the natural compounds and antibiotics? 2. How to determine what ranges to use of the compounds/drugs? 3. Should MIC tests be done on the individual compounds and drugs prior to this assay to determine ranges? What should be observed in those previous assays, and how can they be used to determine what ranges to use?

Article #20 Notes: MIC determination of non-fastidious and fastidious organisms

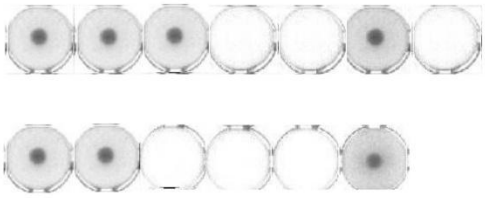
Source Title	MIC determination of non-fastidious and fastidious organisms
Source citation (APA Format)	*eucast: MIC determination*. (n.d.). Www.eucast.org. https://www.eucast.org/ast_of_bacteria/mic_determination
Original URL	https://www.eucast.org/ast_of_bacteria/mic_determination
Source type	Webpage article
Keywords	MIC
#Tags	#MIC
Summary of key points + notes (include methodology)	- in order for the MIC value to be determined, these criteria must be met: - Sufficient growth, i.e. obvious button or definite turbidity, In the positive growth control. - Pure culture: Check for purity by subculturing from the growth-control well immediately after inoculation onto a non-selective agar plate for simultaneous incubation. - Read results manually, never use mirror - Read the MIC as the lowest concentration of the antimicrobial agent that completely inhibits the growth of the organism, based

	on what can be seen with just the eye - Most agents will give a definite endpoint, but some have trailing endpoints with a gradual fading over a couple of wells. Unless there is an exception, they should be read at the definititive stop. - Occasionally a skip may be seen, meaning a well with no growth bordered by wells that have growth. This could be due to incorrect inoculation, contaminations, heterogenous resistance, or other possible explanations. When a single skipped well occurs, retest the isolate or read the highest MIC value so that false susceptible isolates are not reported. Do not report any MIC values for anti microbial agents that have multiple skipped wells. More explanation with images under “figures”
Research Question/Problem/ Need	How to determine MIC based on plate images?
Important Figures	Turbidity without pellet • Haze or turbidity without a pellet is often seen for *Pseudomonas* spp. and *Acinetobacter* spp. This should be regarded as growth and the endpoint read at the first well with complete inhibition (clear broth). 

Examples skipped wells



Retest or read the highest MIC value!



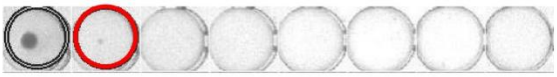
Results invalid!

Gram-negative organisms with bacteriostatic antimicrobial agents

- Disregard pinpoint growth (tiny buttons) when trailing growth occurs.

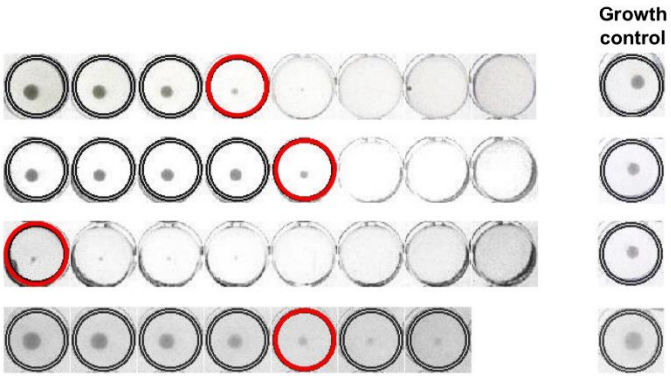
Tigecycline

Tigecycline



Eravacycline

Eravacycline

	0 Trimethoprim and trimethoprim-sulfamethoxazole Read the MIC at the lowest concentration that inhibits ≥80 % of growth as compared to the growth control. 
VOCAB: (w/definition)	Turbidity: how cloudy or hazy a liquid is
Cited references to follow up on	
Follow up Questions	1. Is it necessary to figure out MIC values specific to each antibiotic, or can I use overall trends in the bacteria growth? 2. Do different bacteria pallet sizes form based on the type of bacteria being used? 3. For trailing MICs, how to determine which is the best point to call MIC?

Patent #1 Notes: VACCINE ADJUVANTS, TRANSFECTION REAGENTS, AND METHODS OF USING THE SAME

Source Title	VACCINE ADJUVANTS, TRANSFECTION REAGENTS, AND METHODS OF USING THE SAME

Source citation (APA Format)	Talaat, A., & Touray, B. (2024). VACCINE ADJUVANTS, TRANSFECTION REAGENTS, AND METHODS OF USING THE SAME (U.S. Patent No. 20240335527). U.S. Patent and Trademark Office.
Original URL	https://ppubs.uspto.gov/dirsearch-public/patents/html/20240335527?source=US-PGPUB&requestToken=eyJzdWIiOiI5ODBmNzYyYS04MTc4LTRhMTYtYTBhNi1iMTE1N2U5YzNhM2UiLCJ2ZXIiOiJjYmJmNzA5OC03MmFlLTQxMTQtOWYzYS1mMmVkNjU0NDM3YTYiLCJleHAiOjB9
Source type	Patent
Keywords	adjuvant
#Tags	
Summary of key points + notes (include methodology)	In this invention, an adjuvant was added to enhance the performance of an mRNA vaccine, as this is an advancement in nucleic acid vaccinations. The background of the invention talks about using mRNA vaccines to combat infection diseases and different cancers, and the promise that nucleic acid vaccines have to do this. These vaccines address safety concerns related to live attenuated vaccines and are very scalable and cost-effective. Specifically, this invention patents the role of adjuvants to enhance these vaccines' immunogenicity. Unlike live attenuated vaccines need adjuvants in order to elicit a strong immune response.
Research Question/Problem/ Need	How can adjuvants be used to enhance the performance of a vaccine?
Important Figures	
VOCAB: (w/definition)	Adjuvant: substance that can be added to an antibiotic to enhance its performance
Cited references to follow up on	

Follow up Questions	1. Can adjuvants be added to other vaccines to enhance their performance? 2. Can bacteriocins be added to other vaccines to enhance their performance? 3. How exactly does adding the adjuvant help with the performance of the vaccine?

Patent #2 Notes: Bacteriocin for new application

Source Title	Bacteriocin for new application

Source citation (APA Format)	Gabant, P., & Jaumaux, F. (2024). Bacteriocin for new application (U.S. Patent No. 20240285726). U.S. Patent and Trademark Office.
Original URL	https://ppubs.uspto.gov/dirsearch-public/patents/html/20240285726?source=US-PGPUB&requestToken=eyJzdWIiOiI5ODBmNzYyYS04MTc4LTRhMTYtYTBhNi1iMTE1N2U5YzNhM2UiLCJ2ZXIiOiJjYmJmNzA5OC03MmFlLTQxMTQtOWYzYS1mMmVkNjU0NDM3YTYiLCJleHAiOjB9
Source type	Patent
Keywords	Bacteriocin
#Tags	
Summary of key points + notes (include methodology)	This is a patent on the use of bacteriocins from the pathogen Staphylococcus aureus. It focuses on bacteriocin peptides and peptidomimetics. These compounds are explored for their potential in medical treatments, surface disinfection, and cosmetic applications. The background of the patent highlights the role of microbial populations in maintaining health, and challenges caused by antibiotic-resistant bacteria. This invention introduces bacteriocins produced by the pathogen Staphylococcus aureus, and specific bacteriocin peptides or peptidomimetics that are effective against skin infections caused by these bacteria (especially MRSA) and preserve beneficial skin bacteria like Staphylococcus epidermidis. The invention includes peptides, which are designed for treating, preventing, or delaying infections, and specifically target skin infections caused by Staphylococcus aureus. The compositions cover pharmaceutical and cosmetic compositions containing these peptides, and the methods section covers methods for topical application, enhance skin hygiene, and disinfect surfaces that have been contaminated with harmful pathogens.
Research Question/Problem/ Need	How can bacteriocins from Staphylococcus aureus be used?
Important Figures	
VOCAB: (w/definition)	Staphylococcus aureus: skin bacteria Peptidomimetic: a synthetic compound that mimics the structure and function of peptides Microbiota: the community of microorganisms that live in a specific environment MRSA: Methicillin-resistant Staphylococcus aureus Ex-vivo method: a procedure performed outside a living organism

	Selective inhibition: the ability to inhibit certain bacteria while allowing others to survive
Cited references to follow up on	
Follow up Questions	1. Are bacteriocins from different staph bacteria similar? 2. If they are not similar, what is it about their structures that make them different? What is similar between them? 3. How can these bacteriocins be used in real life scenarios in place of an antibiotic? For example, this is a skin bacterium, so how can the bacteriocin help prevent diseases from the skin bacteria?