MICROBIAL BIOTECHNOLOGY

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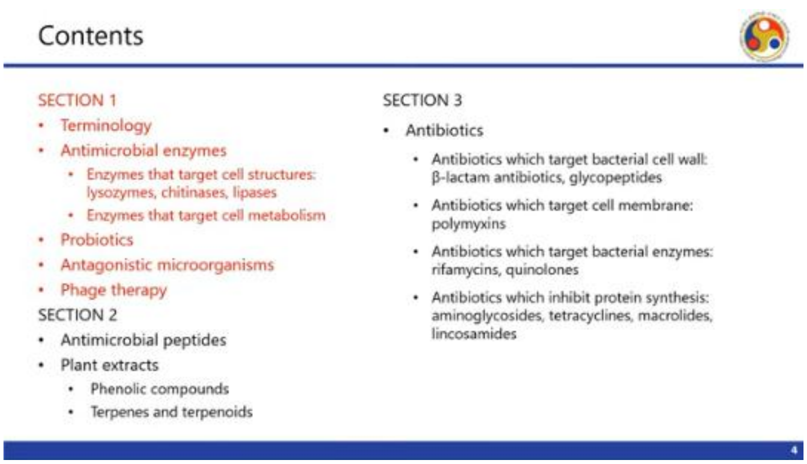
Lecture-18
Lec 18: Control methods: Biological methods

Hello everyone. Welcome back to my course on microbial biotechnology. We are in module number 5, discussing the control of microorganisms. Today, we will discuss the biological methods of microbial control. Under this, we will discuss the application of enzymes, antibiotics, plant extracts, bacteriophages, antimicrobial peptides, and living organisms themselves—how they are used to control microbes.

Biological agents provide a reliable alternative for the control of microorganisms. Apart from the physical and chemical methods we have already discussed, living organisms or the products of their metabolic activities are used to regulate the population of harmful microorganisms or pests. In contrast to chemical methods, biological agents may help manage the target organism in a more sustainable and environmentally friendly manner. In this lecture, we will discuss the various biological agents I have already shown you in that diagram, and we will begin with a few terminologies useful for today's discussion. So, antagonism is the inhibition of growth or survival of one organism by another, which can be of two types: direct, which causes inhibition through direct interaction or release of inhibitory substances, or indirect, where inhibition occurs through environmental modification or resource consumption.

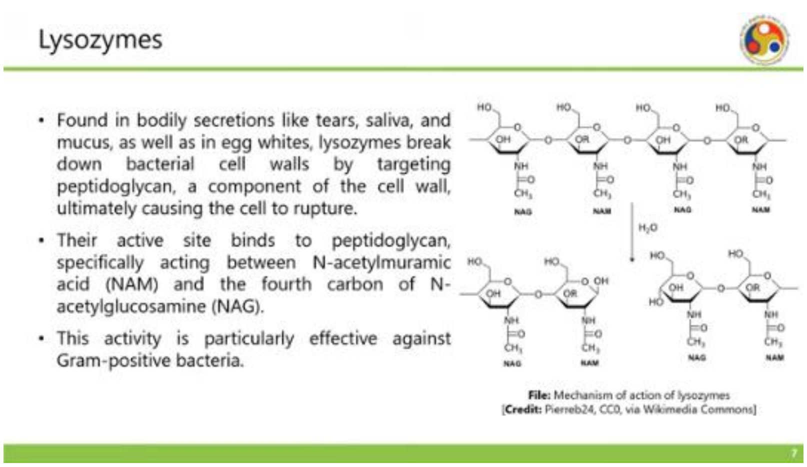


There is another concept called predation, which refers to the act of one microorganism consuming another for nutrients or energy. Then there is competition, which refers to the rivalry between microorganisms for shared resources in their environment. We begin with antimicrobial enzymes. These are proteins that inhibit the growth or kill microorganisms. The enzymes act by disrupting essential structures or processes within microbial cells.

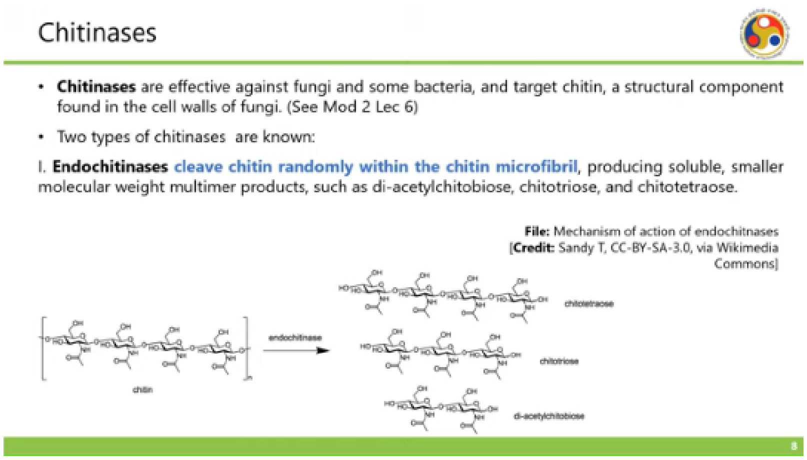
These enzymes can be naturally occurring within the body or can be applied externally in various products for their antimicrobial effects. Their mode of action varies, but they generally disrupt critical components of microbial cells, making them valuable in various industries like healthcare, food preservation, and hygiene products. So, one of the very common known enzymes is lysozyme. It is found in bodily secretions like tears, saliva, and mucus, as well as in egg whites.

Lysozyme breaks down bacterial cell walls by targeting peptidoglycan, a component of the cell wall, ultimately causing the cell to rupture. So, we can see the mechanism of action of lysozyme over here, where it is attacking between the NAG and NAM residues and breaking them into smaller parts. Thereby, disrupting the whole structure. The active site binds to peptidoglycan, specifically acting between N-acetylmuramic acid and the fourth carbon of N-acetylglucosamine.

These activities are particularly effective against gram-positive bacteria. We have another class of enzymes called chitinases. As the name suggests, chitinases are effective against chitin. It will degrade it. So, it is basically used against fungi and some bacteria.



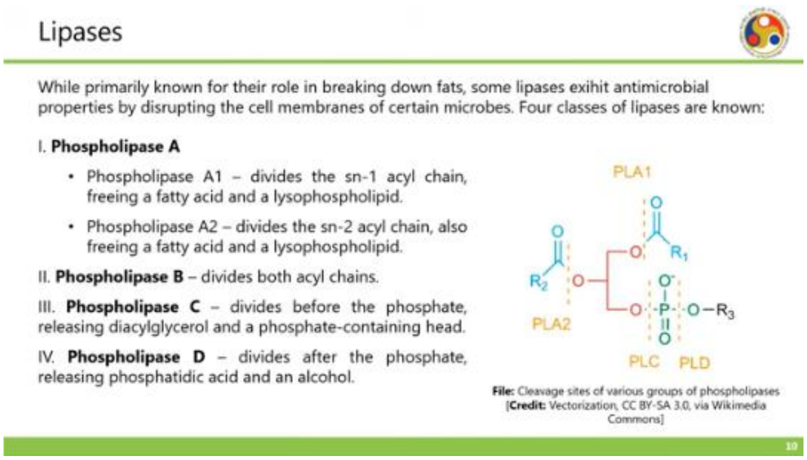
And they target chitin, a structural component found in the cell walls of these fungi. There are two types of chitinases. Endochitinases, which cleave chitin randomly within the chitin microfibril, producing soluble smaller molecular weight multimer products such as diacetylchitobiose, chitotriose, and chitotetraose. So, this is the mechanism of action of endochitinases as shown in the figure.



So, these endochitinases break down the long chitin microfibril into smaller components which may be composed of two units, three units, and four units, and accordingly named as diacetylchitobiose, chitotriose, and chitotetraose. Then we have exochitinases, which are further categorized into two subtypes. One is the chitobiosidases, which act upon the non-reducing end of the chitin microfibrils, sequentially releasing diacetylchitobiose, Then we have beta-1,4-N-acetylglucosaminidases, which break down multiple products like diacetylchitobiose, chitotriose, and chitotetraose into the monomers of N-acetylglucosamine.

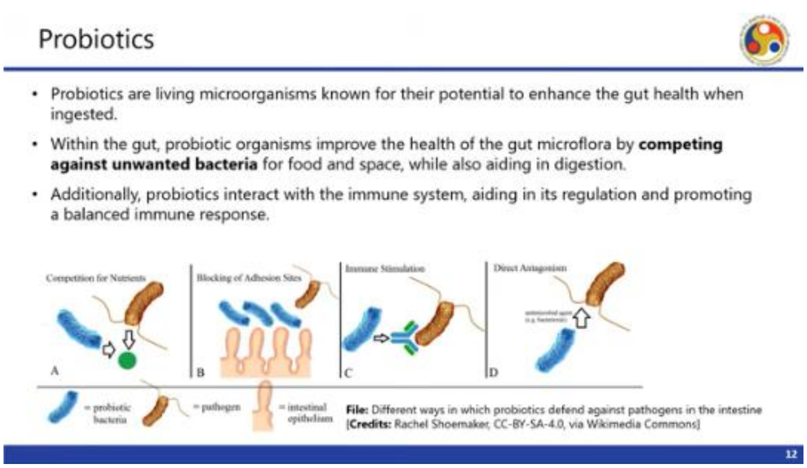
Another class of important enzymes are the lipases. While primarily known for their role in breaking down fats, some lipases exhibit antimicrobial properties by disrupting the cell membrane of certain microbes. Four classes of lipases are known. Number one is the phospholipase A. The phospholipase A1 cleaves the SN1 acyl chain, freeing a fatty acid and a lysophospholipid. Then there is phospholipase A2, which cleaves the SN2 acyl chain, also freeing a fatty acid and a lysophospholipid.

Then we have phospholipase B. This divides both acyl chains. Then we have phospholipase C, which divides before the phosphate, releasing diacylglycerol and a phosphate-containing head. Then we have phospholipase D, which divides after the phosphate, releasing phosphatidic acid and alcohol. Now let us discuss certain enzymes that target cell metabolism, such as lactoperoxidase. This is present in milk and saliva.



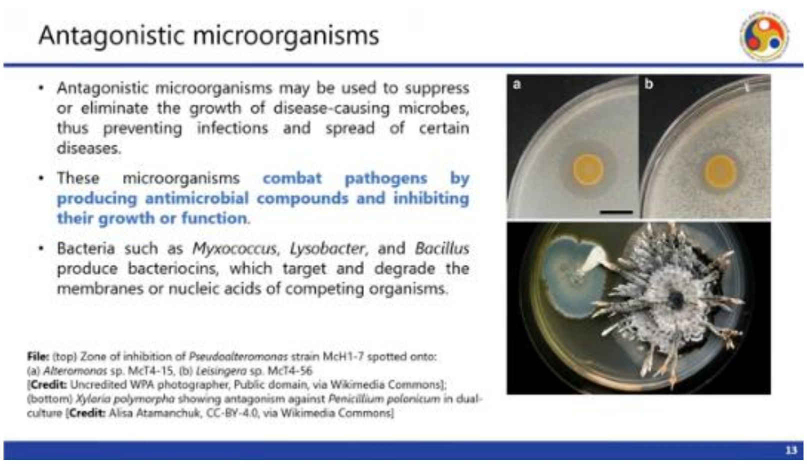
Lactoperoxidase generates antimicrobial compounds by catalyzing reactions with hydrogen peroxide. These compounds inhibit bacterial growth by interfering with their metabolism. Then we have proteases, which break down proteins. Some proteases have been shown to interfere with the cell membrane or cell wall integrity of bacteria, thereby affecting their viability. Let us now discuss probiotics,

which are living microorganisms known for their potential to enhance gut health when ingested. Within the gut, probiotic organisms improve the health of gut microflora by competing against unwanted bacteria for food and space while also aiding in digestion. So in this picture, we can see the different mechanisms that we will discuss. These probiotics interact with the immune system, also aiding in its regulation and promoting a balanced immune response.



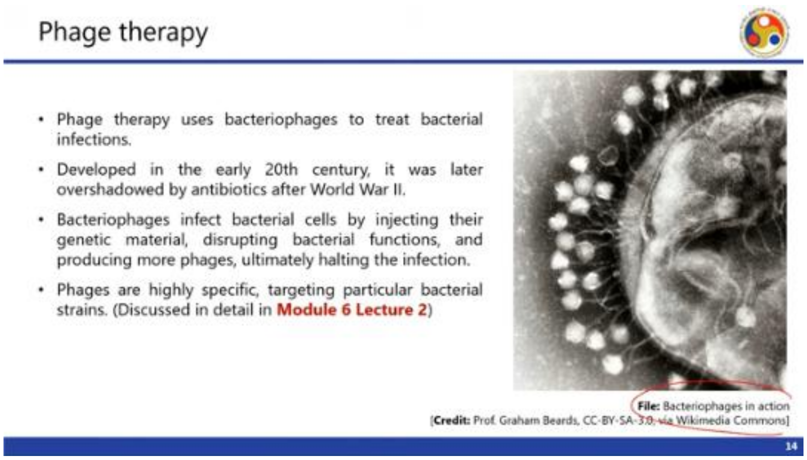
So, here we can see the probiotic competing for nutrients with the harmful bacteria or sometimes the probiotic microorganisms will block the adhesion sites and do not allow the harmful bacteria to adhere. Then they also stimulate the immune systems as already discussed and sometimes they directly antagonize the harmful bacteria. Let us discuss about some antagonistic microorganisms may be used to suppress or eliminate the growth of disease-causing microbes, thus preventing infection and spread of certain diseases. These microorganisms combat pathogens by producing antimicrobial compounds and inhibiting their growth or function.

We have bacteria like myxococcus, lysobacter and bacillus which produce bacteriocins and target and degrade the membrane or nucleic acid of the competing organisms. Here, we can see the zone of inhibition of pseudo-alteromonas strain spotted in this figure, A, alteromonas species and B, Lissingera species. Then in the bottom we can see Gylaria polymorpha showing antagonism against Penicillium polonicum in a dual culture. One of the very interesting therapies is the use of viruses to control microbial growth. So we call it also sometimes as fast therapy.

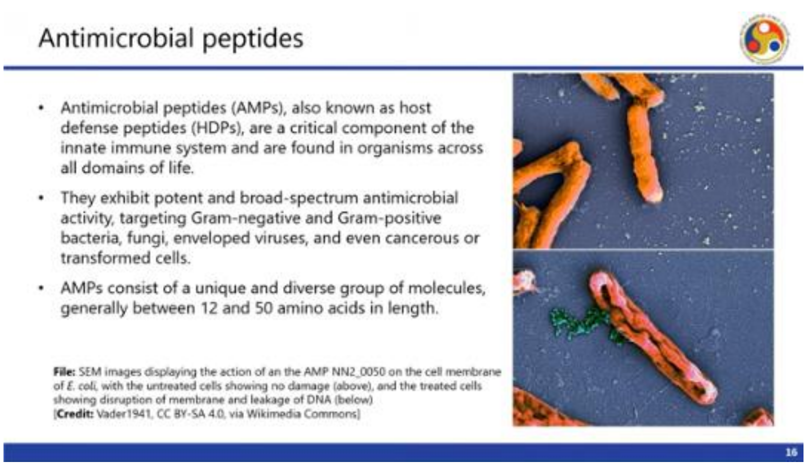


Basically, it uses bacteriophages to treat bacterial infections. It was developed in the early 20th century and was later overshadowed by antibiotics after World War II. Bacteriophages infect bacterial cells by injecting their genetic material, disrupting bacterial functions and producing more fuzzes ultimately halting the infection. Fuzzes are highly specific targeting a particular bacterial strain.

So here, we can see a bacteriophage in action. This is a magnified microscopic photograph—an electron microscopic photograph. So now, Let us move to Section 2, where we will discuss antimicrobial peptides, plant extracts, phenolic compounds, terpenes, and terpenoids. Antimicrobial peptides, also known as host defense peptides, are a critical component of the innate immune system and are found in organisms across all domains of life.



They exhibit potent and broad-spectrum antimicrobial activity, targeting Gram-negative and Gram-positive bacteria, fungi, enveloped viruses, and even cancerous or transformed cells. Antimicrobial peptides consist of a unique and diverse group of molecules, generally between 12 and 50 amino acid residues in length. Here, we can see the same image displaying the action of antimicrobial peptide NN2-0050 on the cell membrane of E. coli, with untreated cells showing no damage here and treated cells showing membrane disruption and leakage. This picture clearly shows that AMPs can be very effective in inhibiting or controlling bacterial growth.



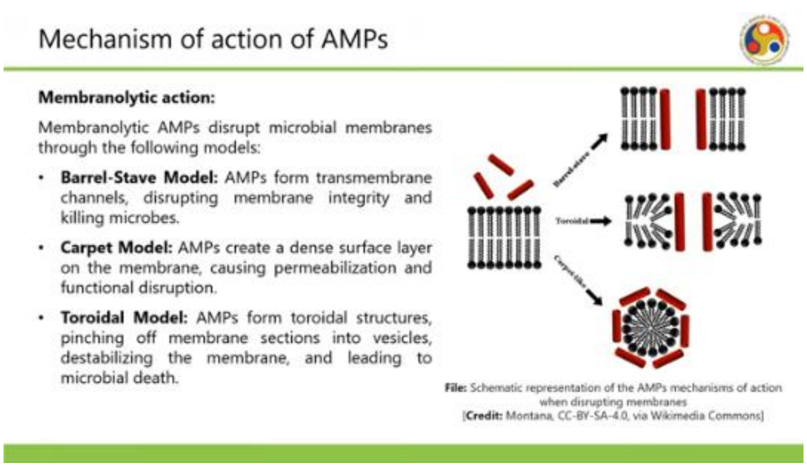
Some examples of AMPs are produced across the whole tree of life, such as in bacteria, fungi, cnidaria, insects, arthropods, amphibians, frogs, birds, mammals, etc. The mechanism of action can be seen from that picture of what was happening to the bacterial cell. These AMPs typically carry a net positive charge, enabling them to interact with negatively charged molecules on the surface of bacteria and cancer cells, such as phosphatidylserine, O-glycosylated mucins, C-allylated gangliosides, and heparan sulfates.

The mechanisms of action are broadly categorized into membranolytic and non-membranolytic activities, although the exact mechanism is not fully understood.

In non-membranolytic action, AMPs penetrate the cell and interact with intracellular molecules essential for the survival of the organism. Intracellular mechanisms include disrupting cell wall synthesis, altering the cytoplasmic membrane, activating autolysins, and inhibiting the synthesis of DNA, RNA, or proteins, as well as specific enzymatic functions. Let us have a brief discussion on the mechanism of action of antimicrobial peptides. They primarily act through membranolytic action. Membranolytic AMPs disrupt microbial membranes through the following modes.

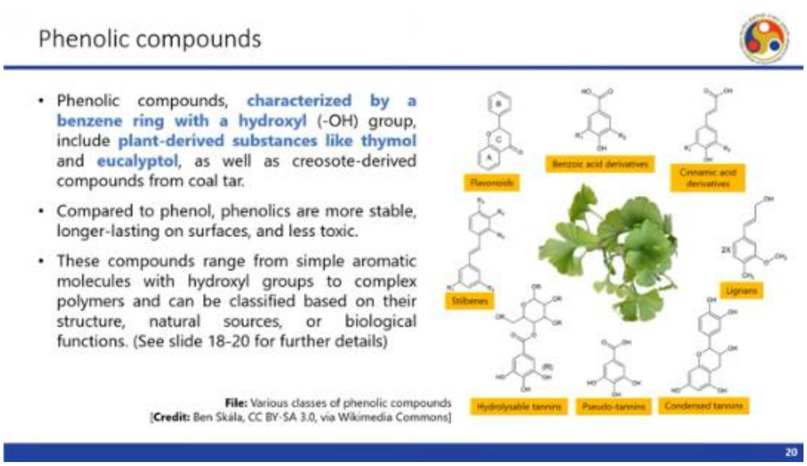
Barrel-stave model, so here you can see this. AMPs form transmembrane channels, disrupting membrane integrity and killing the microbes. A channel is formed, so material can either enter or exit the cell. Then there is the carpet model. Here you can see AMPs create a dense surface layer on the membrane, causing permeabilization and functional disruption.

Then we have the toroidal model. Here, AMPs form toroidal structures, pinching off membrane sections into vesicles, destabilizing the membrane, and leading to microbial death. Let us now discuss plant extracts and their applications in controlling microbial growth. Plant extracts are widely recognized for their antimicrobial properties, exhibiting the ability to inhibit the growth and survival of microorganisms. These extracts contain various compounds like alkaloids, phenols, flavonoids, and essential oils, among others, which possess antimicrobial effects.



The antimicrobial action includes disrupting the cell walls or membranes of bacteria, fungi, and viruses, thereby impeding their growth and causing their death. Additionally, these extracts might interfere with vital microbial metabolic processes, hindering their proliferation and viability. Some of the phenolic compounds used are shown here, such as flavonoids, benzoic acids, derivatives, cinnamic acid, lignans, condensed tannins, pseudotannins, hydrolyzable tannins, and stilbenes. All these phenolic compounds are characterized by a benzene ring with a hydroxyl group. They include plant-derived substances like thymol and eucalyptol, as well as creosote-derived compounds from coal tar.

Compared to phenol, phenolics are more stable, longer-lasting on surfaces, and less toxic. These compounds range from simple aromatic molecules with hydroxyl groups to complex polymers. They can be classified based on structure, natural sources, or biological functions. Phenolic compounds may target multiple sites within bacterial cells, and their mechanism of action varies based on their functional groups and aromatic rings. Phenolics may disrupt and depolarize the cell membrane, causing leakage of cellular content.



Here, you can see how the membrane is disrupted and leakage is taking place. Phenolics may intercalate DNA bases and base pairs, altering the structure of DNA. Phenolics may hinder enzymatic activity within bacterial cells. They also hinder vital processes, such as the synthesis of nucleic acids and proteins. Phenolic compounds can be classified into various groups, each with different mechanisms of action, and here you can see the typical structure of each.

Phenolic compounds: mechanism of action

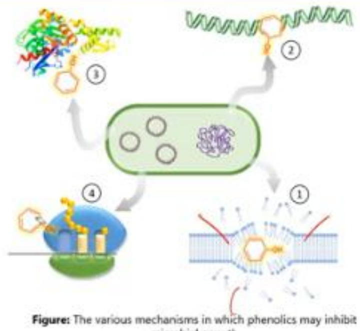
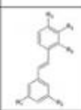
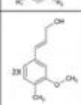
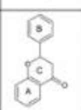


Figure: The various mechanisms in which phenolics may inhibit microbial growth
(Generated by R. Lama, TA for MOOCs Course)

- Phenolic compounds may target multiple sites within bacterial cells, and their mechanisms of action vary based on their functional groups and aromatic rings (Lobiuc *et al.*, 2023):
  1. Phenolics may disrupt and depolarize the cell membrane, causing leakage of cellular content
  2. Phenolics may intercalate DNA base pairs and alter of DNA structure
  3. Phenolics may hinder in enzymatic activity within bacterial cells
  4. Phenolics may hinder vital processes such as the synthesis of nucleic acids and proteins

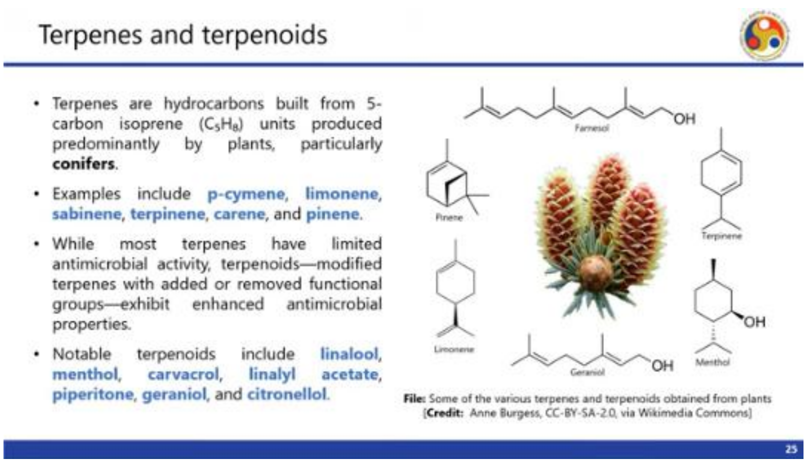
Here you have the phenolic acids like benzoic acid derivatives, cinnamonic acid derivatives. Their mechanism action is antibacterial effect increases significantly with the pH values. Then we have still beans which in combination with antibiotics can be used in treating infections caused by multidrug resistance bacteria. Then lignans, which due to structural properties, antimicrobial activity of lignans is influenced by the stereochemistry of the molecules. Then we have flavonoids, which act against bacteria such as S. aureus and Pseudomonas aeruginosa with a very low minimum inhibitory concentration.

Phenolic compounds: classification (*contd...*)

Group	Structure	Examples	Mechanism of action
Stilbenes		• R_1,R_2,R_3=OH, R_4,R_5=H: Resveratrol. • R_1,R_2=OCH_3, R_3=OH, R_4, R_5=H: Pterostilbene.	In combination with antibiotics, some stilbenes can be useful in treating infections caused by multidrug-resistance bacteria.
Lignans		Dibenzylbutanes, dibenzylbutyrolactones, Terahydrofurans, Furofurans	Due to structural properties, antibacterial activity of lignans is influenced by the stereochemistry of molecules.
Flavonoids		Flavones, Flavonols, Isoflavones, Flavanones, Anthocyanidins (flavylium salt), Flavanols	Flavonoids act against bacteria such as *S. aureus* and *P. aeruginosa* with a very low minimum inhibitory concentration (MIC) value (0.062 µg/mL).

Then tannins can be hydrolyzable or non-hydrolyzable and there are also certain pseudotannins and we have corresponding examples like galotannins and also we have complex tannins and low molecular mass phenolics like gallic acid. Overall the tannins compounds act against bacteria causing disintegration of bacterial colonies by interfering with the bacterial cell wall and inhibiting fatty acid biosynthesis pathways. Let us have a discussion on the terpenes and terpenoids. Terpenes are hydrocarbons built from 5-carbon isoprene units produced predominantly by plants, particularly the conifers. So some of the terpenes and terpenoids obtained from plants can be seen in this figure like limonene, pinene, then farnesol, terpenene, and menthol.

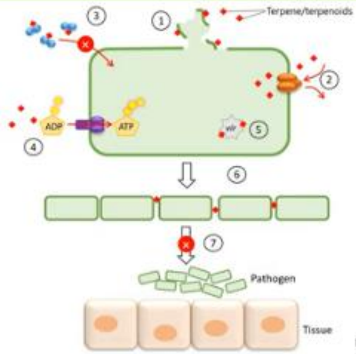
Most terpenes have limited antimicrobial activity. Terpenoids, modified terpenes with added or removed functional groups exhibit enhanced antimicrobial properties. Notable terpenoids include linalool, menthol, carvacrol, linalyl acetate. Then we have piperitone, then geraniol and citronellol. The mechanism of action of the terpenes and terpenates remain mostly unknown.



They may inhibit microbial growth in any of the following manners, such as disruption of the cell membrane, as can be seen here in this picture. They may also modulate the efflux pump. Then we have inhibition of oxygen uptake. Oxygen is not entering due to this inhibition.

Then we have alteration in oxidative phosphorylation, as seen in point number 4. So, they also act by inhibition of the virulence factor, reduction of cell adherence ability or capability, and suppression of biofilm development. So, overall, they may have multiple mechanisms of action. So here is a table which provides examples of the test organisms against which the particular class of tapinoids is effective. For example, monotapin and monotapinoids have been tested against Enterobacter, E. coli, Salmonella, and Klebsiella pneumoniae.

Mechanism of action



- The precise antibacterial mechanism of terpenes and terpenoids remains mostly unknown; they may inhibit microbial growth in any of the following manner (Mahizan *et al.*, 2019):
  1. Disruption of cell membrane
  2. Modulation of efflux pump
  3. Inhibition of oxygen uptake
  4. Alteration in oxidative phosphorylation
  5. Inhibition of virulence factor
  6. Reduction of cell adherence ability
  7. Suppression of biofilm development

Figure: The various mechanisms in which terpenes/terpenoids may inhibit microbial growth [Generated by R. Lama, TA for MOOCs Course]

and also against tobacco mosaic virus and cucumber mosaic virus. They act by various means, such as efflux pump inhibition, growth inhibition, biofilm inhibition, cell membrane disruption, and again, growth inhibition. Then we have sesquiterpenes and sesquiterpenoids, like zentorazole and farnesole, which are effective against Staphylococcus, Bacillus, and also act by reduction of cell adherence ability, biofilm formation, and potentiation effect or combination therapy. Diatapins and diatypenoids have been tested against Pseudomonas aeruginosa, E. coli, S. aureus, and C. albicans.

Table: Classification of terpenes/terpenoids (*cont…*)

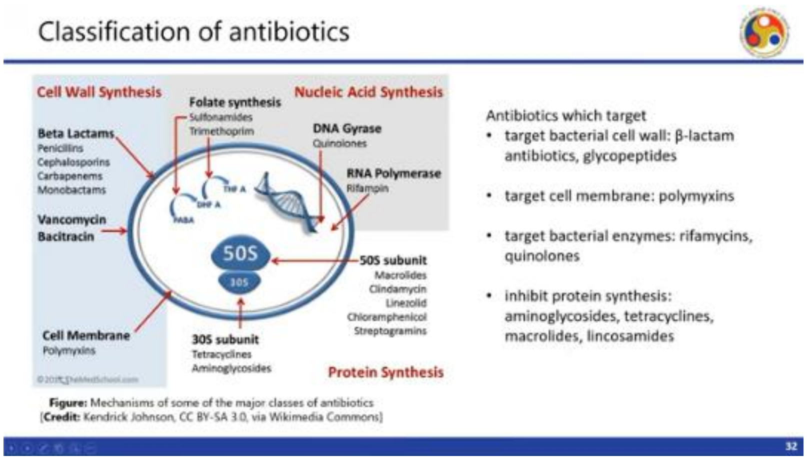
Terpenoid Class	Chemical Compound	Test Organism	Antimicrobial Effect
Diterpenes and diterpenoids	(-)-Carvone, Dihydrocarveol, (-)-Carveol	*P. aeruginosa, E. coli, S. aureus, C. albicans*	Growth inhibition
	Salvipisone	*S. aureus, S. epidermidis*	Bacterial cell adherence prevention Biofilm development inhibition
	Salvipisone, Aethiopinone	*S. aureus, Enterococcus faecalis, S. epidermidis*	Biofilm production inhibition
		MRSA, MRSE	Synergistic activity alongside antibiotic
Triterpenes and triterpenoids	25-Dien-3-one, Oleanic acid, Bonianic acid A, Bonianic acid B, Ergosterol peroxide, Ursolic acid	*Mycobacterium tuberculosis*	Synergistic activity alongside antibiotic
	Oleanic acid, Ursolic acid	*B. cereus, Vibrio cholera, K. pneumoniae, S. pneumoniae*	Growth inhibition

And then you have these similar effects, like antibacterial growth inhibition, bacterial cell addition prevention, and biofilm development inhibition. They also show some synergistic activity alongside antibiotics, particularly against MRSA and other MRSA organisms. And then we have tritrapins and tritrapinoids tested against Mycobacterium tuberculosis. These show synergistic activity alongside the antibiotics used.

Then you have P. cereus, Vibrio cholera, Pneumonia, and they act by inhibiting growth. Let us now discuss antibiotics, which are very effective biocontrol agents. These are the most important bacterial agents used to combat bacterial infections. They are used to treat and prevent infections by killing bacteria or inhibiting their growth. Although initially used exclusively to describe substances produced by microorganisms with antagonistic effects on bacteria, antibiotics now encompass all drugs with antibacterial properties.

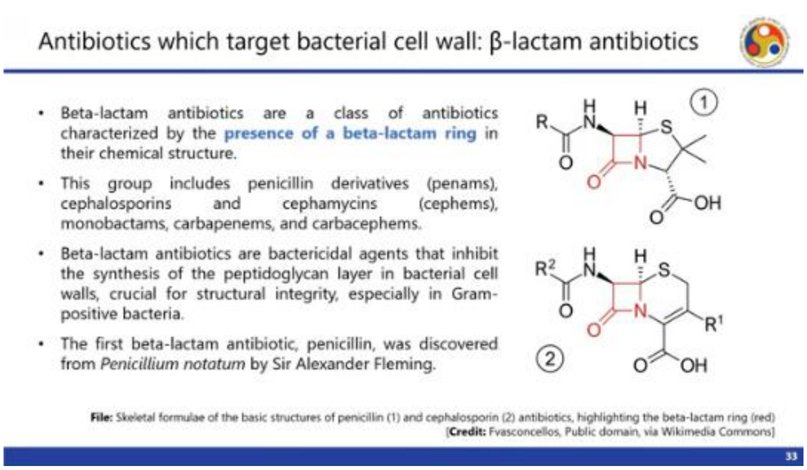
The use of moldy bread in topical treatments for wounds in ancient China, Egypt, and Greece might have been the first instance of antibiotic use, but they lacked scientific understanding. The modern era of antibiotics began with Alexander Fleming's accidental discovery of penicillin, a substance produced by the mold Penicillium notatum that could kill bacteria. Following penicillin, other antibiotics, including streptomycin, tetracycline, and chloramphenicol, were discovered between the 1940s and the 1960s, a period often referred to as the golden age of antibiotics. New antibiotics continue to be developed, but the emergence of antibiotic-resistant bacteria has become a significant challenge due to the overuse and misuse of antibiotics. We can classify antibiotics based on their target.

Some target bacterial cell walls, like beta-lactam antibiotics, as you can see here. Then some target the membrane, like the polymyxins. Certain antibiotics target bacterial enzymes, like rifamycins and quinolones. Here, we can see RNA polymerase being targeted. Then some target or inhibit protein synthesis, like aminoglycosides.

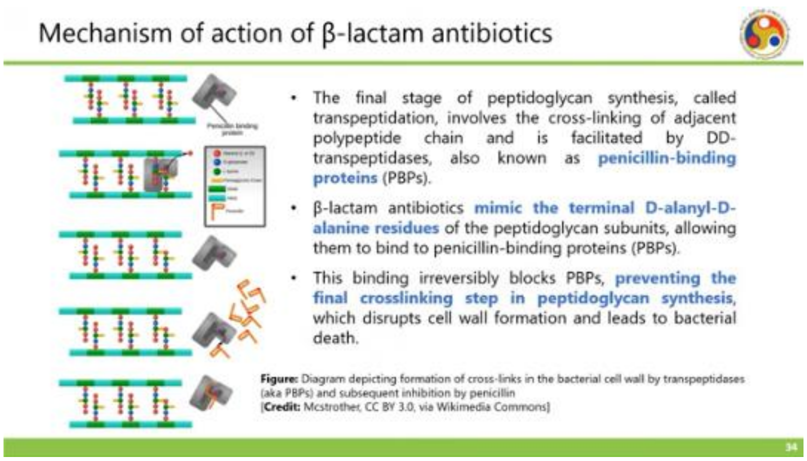


Then you have the tetracyclines, macrolides, or lincosamides. We have a large number of antibiotics, and their mode of action is different, as seen in this picture. So, let us discuss a few of them. Particularly, let us start with beta-lactam antibiotics, which target the bacterial cell wall. These are a class of antibiotics characterized by a beta-lactam ring, highlighted in red here in their chemical structure.

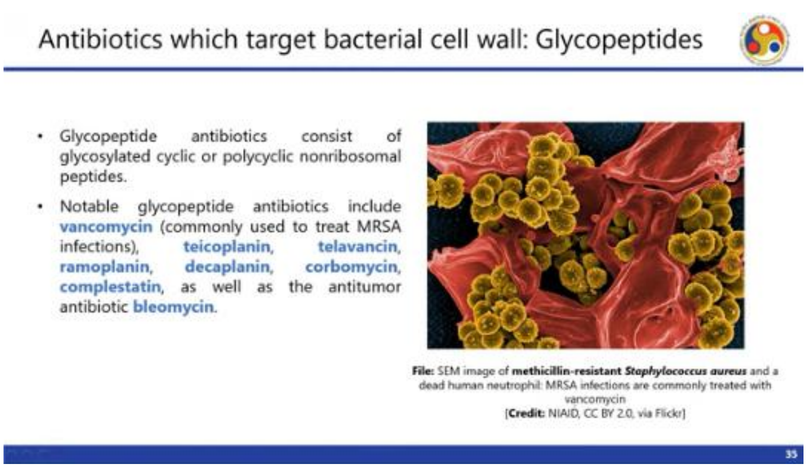
The group includes penicillin derivatives, penams, cephalosporins, cephamycins, monobactams, carbapenems, and carbacephems. Beta-lactam antibiotics are bactericidal agents that inhibit the synthesis of the peptidoglycan layer in bacterial cell walls, which is crucial for structural integrity, especially in gram-positive bacteria. The first beta-lactam antibiotic, penicillin, was discovered from Penicillium notatum by Sir Alexander Fleming—an accidental discovery, as mentioned. The final stage of peptidoglycan synthesis, called transpeptidation, involves cross-linking adjacent polypeptide chains and is facilitated by DD-transpeptidases, also known as penicillin-binding proteins, as seen here.



Beta-lactam antibiotics mimic the terminal D-analoyl D-alanine residue of the peptidoglycan subunit, allowing them to bind to penicillin binding proteins. These binding irreversibly blocks the peptide binding. Penicillin binding proteins preventing the final cross-linking step in peptidoglycan synthesis which disrupts the cell wall formation and leads to bacterial death. Let us now discuss about the glycopeptides, which are antibiotics that target the bacterial cell wall. Glycopeptide antibiotics consist of glycosylated cyclic or polycyclic non-ribosomal peptides.



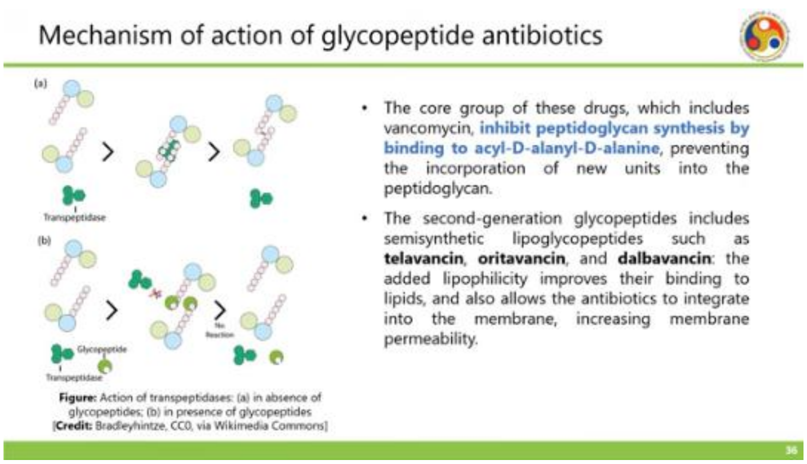
Notable glycopeptide antibiotics include vancomycin, ticoplanin, telavensin, Ramoplanin, Decaplanin, Carbomycin, Complextatin as well as the anti-tumor antibiotic Gliomycin. So, this is a same image of Methylysin resistance Staphylococcus aureus and a dead human neutrophil. These MRSA infections are commonly treated with Vancomycin. Let us discuss about the mechanism of action of glycopeptide antibiotics.



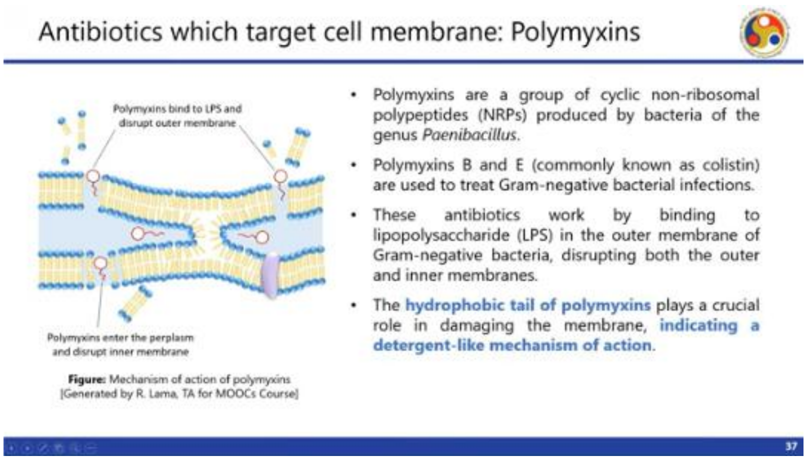
So, here we can see these enzyme transpeptides and then we have this glycopeptide. So, in figure 1 you can see there is no any glycopeptide. And in figure B, there is glycopeptide.

So due to the presence of the glycopeptide, these cross-linking do not happen over here, but it is happening in the absence of the glycopeptide. So, the core group of these drugs which include vancomycin inhibit peptidoglycan synthesis by binding to acyl-D-analyl-D-alanine preventing the incorporation of new units into the peptidoglycan.

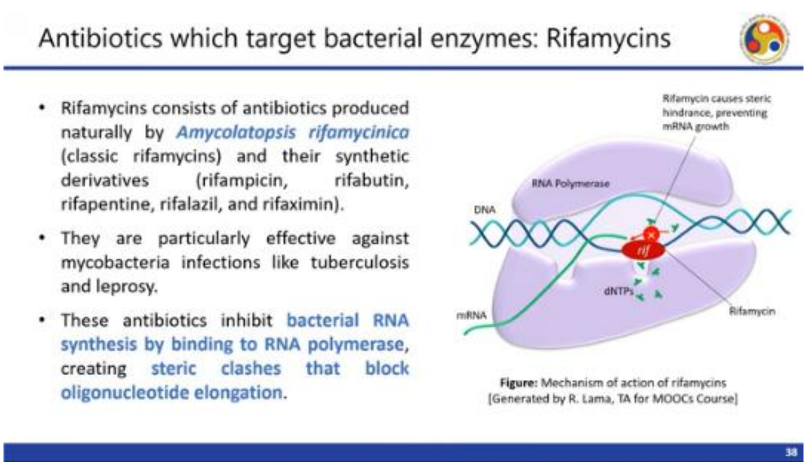
The second-generation glycopeptides include semi-synthetic lipoglycopeptides such as telavancin, oritavancin, and dalbavancin. The added lipophilicity improves their binding to lipids and also allows the antibiotics to integrate into the membrane, increasing membrane permeability. Let us discuss the polymyxins, which target the cell membrane. Polymyxins are a group of cyclic non-ribosomal polypeptides produced by bacteria of the genus Paenibacillus. Here, you can see in this picture that polymyxins bind to the LPS and disrupt the outer membrane, and the polymyxin also enters the periplasm and disrupts the inner membrane.



Polymyxins B and E, commonly known as colistin, are used to treat Gram-negative bacterial infections. These antibiotics work by binding to lipopolysaccharide in the outer membrane of Gram-negative bacteria, disrupting both the outer and inner membranes. The hydrophobic tail of polymyxins plays a crucial role in damaging the membrane, indicating a detergent-like mechanism of action. Let us now discuss antibiotics that target bacterial enzymes. For example, the rifamycins, which consist of antibiotics produced naturally by Amycolatopsis, rifamycin, etc., and their synthetic derivatives.

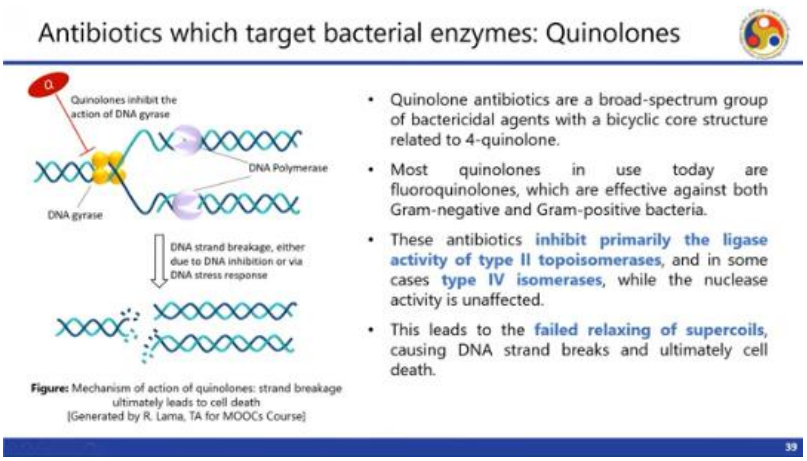


Here, we can see the mechanism of action of rifamycin. Rifamycin causes steric hindrance, preventing mRNA growth in this picture, as you can see here. They are particularly effective against mycobacterial infections like tuberculosis and leprosy. In fact, it is administered as a drug regularly. These antibiotics inhibit bacterial RNA synthesis by binding to RNA polymerase, creating steric clashes that block the elongation of the oligonucleotide.



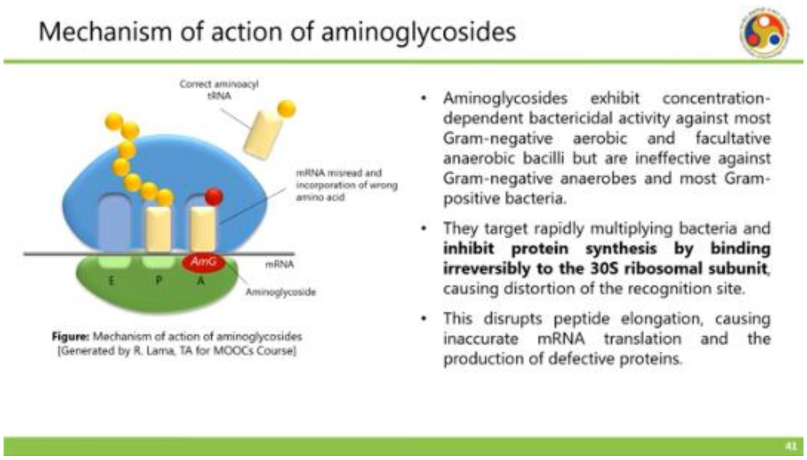
Another class of antibiotics which target bacterial enzymes are the quinolones. They are a broad-spectrum group of bactericidal agents with a bicyclic core structure related to quinolones. Most quinolones in use today are fluoroquinolones, which are effective against both gram-negative and gram-positive bacteria. These antibiotics primarily inhibit the ligase activity of type 2 topoisomerases and, in some cases, type 4 isomerases, while the nuclease activity is unaffected. This leads to the failed relaxation of supercoils, causing DNA strand breaks and ultimately cell death.

So, here you can see the mechanism of action of quinolones: strand breakage will ultimately lead to cell death. So, quinolones inhibit the action of DNA gyrase, as you can see here, and this leads to DNA strand breakage either due to DNA inhibition or via the DNA stress response. So, at this point, the DNA will break, and this will lead to cell death. There are other classes of antibiotics, like aminoglycosides, which inhibit protein synthesis. They contain amino-modified glycosides.



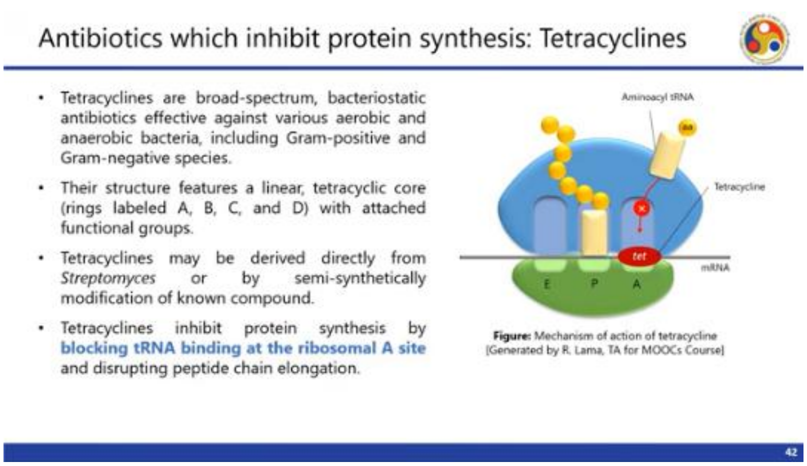
They are primarily effective against gram-negative aerobes and certain anaerobic bacilli, with limited activity against gram-positive and anaerobic gram-negative bacteria. One example is streptomycin, derived from Streptomyces. This was the first aminoglycoside used in the modern treatment of tuberculosis. Unlike most aminoglycosides, streptomycin lacks the common 2-deoxystreptamine moiety. Other aminoglycosides, such as kanamycin, tobramycin, gentamicin, and neomycin, contain these structural features as well.

In this picture, you can see the mechanism of action of aminoglycosides. The aminoglycosides exhibit concentration-dependent bacterial activity against most gram-negative aerobic and facultative anaerobic bacilli. But they are ineffective against gram-negative anaerobes and most gram-positive bacteria. They target rapidly multiplying bacteria and inhibit protein synthesis by binding irreversibly to the 30S ribosomal subunit, causing distortion of the recognition site. This disrupts peptide elongation,



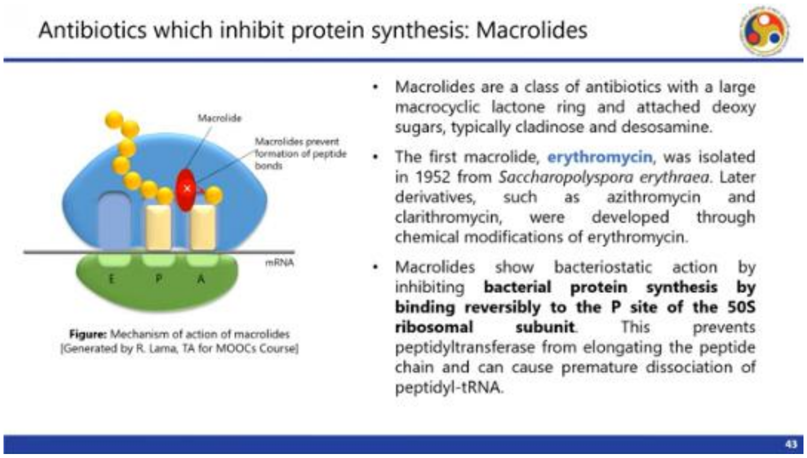
causing inaccurate mRNA translation and the production of defective proteins. Tetracyclines also act by inhibiting protein synthesis. They are broad-spectrum bacteriostatic antibiotics, effective against various aerobic and anaerobic bacteria, including gram-positive and gram-negative species. Their structural features are a linear tetracyclic core, rings labeled as A, B, C, and D with attached functional groups.

Tetracyclines may be derived directly from Streptomyces or by semi-synthetic modification of known compounds. They inhibit protein synthesis by blocking the tRNA binding at the ribosomal A site and disrupting peptide chain elongation. Macrolides are another class of antibiotics that inhibit protein synthesis. They have a large macrocyclic lactone ring and attached deoxysugars, typically cladinose and desosamine. The first macrolide, erythromycin, was isolated in 1952 from



Saccharopolyspora erythraea. Later derivatives such as azithromycin and clarithromycin were developed through chemical modification of erythromycin. Macrolides show bacteriostatic action by inhibiting bacterial protein synthesis by binding reversibly to the

P-site of the 50S ribosomal subunit. This prevents peptidyl transferase from elongating the peptide chain and can cause premature dissociation of peptidyl tRNA. Let us also look into the action of lincosamides, which consist of a pyrrolidine ring linked to a pyranose moiety via an amide bond, functioning in a way similar to macrolides.



Lincomycin is naturally produced by bacterial species, namely Streptomyces lincolnensis, rociolus, and celestis. Clindamycin is derived via 7S chloro-substitution of the 7R hydroxyl group of lincomycin and is widely used in the treatment of a number of bacterial infections, including osteomyelitis, strep throat, pneumonia, acne, and some cases of methicillin-resistant Staphylococcus aureus. So, with this, we come to the end of today's lecture. Thank you for your kind attention.