**MONOBACTAMS**

**Monobactam: it a monocyclic β-lactum antibiotic, with a side sulfo-group is joined to the nitrogen atom of β-lactum ring.**

**Products**

**Aztreonam Disodium**

* **It binds with high affinity to PBP in Gram-negative bacteria only.**
* **It is inactive against Gram-positive bacteria and anaerobes.**
* **4-methyl β group, increases stability to β –lactamases.**
* **β -Lactamase resistance due to isobutyric acid oximino acyl group**
* **The strong withdrawing group (sulfamic acid) probably makes the β-lactam bond more vulnerable to hydrolysis.**
* **It is used to treat urinary and lower respiratory tract infections, intra-abdominal infections, and gynecological infections.**
* **Less than 1% of an orally administered dose is absorbed.**
* **The disodium salt is very soluble in water, it administered parenterally.**



**LINCOMYCINS**

* **The lincomycins are sulfur-containing antibiotics isolated from Streptomyces lincolnensis.**
* **Lincomycins resemble macrolides in antibacterial spectrum (with additional activity against anaerobic bacteria) and biochemical mechanisms of action. They bind to the 50S ribosomal subunit to inhibit protein synthesis. Its action may be bacteriostatic or bactericidal depending on various factors, including the concentration of the antibiotic.**

**Products**

**Lincomycin Hydrochloride**



* **-The structure contains a basic function, the pyrrolidine nitrogen, by which water-soluble salts may be formed.**
* **It is absorbed moderately well orally and distributed widely in the tissues. Effective concentrations are achieved in bone for the treatment of staphylococcal osteomyelitis but not in the cerebrospinal fluid for the treatment of meningitis.**
* **Adverse effects: diarrhea and pseudomembranous colitis in patients treated with lincomycin (or clindamycin).**

**Clindamycin Hydrochloride**



* **The replacement of the 7-hydroxy group of lincomycin by chlorine resulted in a compound with enhanced antibacterial activity.**
* **Improved absorption and higher tissue levels of clindamycin and its greater penetration into bacteria have been attributed to a higher partition coefficient than that of lincomycin.**
* **It used for the treatment of osteomyelitis, skin, and anaerobic infections.**
* **Adverse effects: clindamycin- associated GI toxicity, which range in severity from diarrhea to an occasionally serious pseudomembranous colitis.**
* **Clindamycin is absorbed rapidly from the GI tract, even in the presence of food.**

**It is available as:**

1. **Water-soluble hydrochloride hydrate.**
2. **The 2-palmitate ester hydrochloride salts in oral dosage forms.**

**The ester serves as a tasteless prodrug, which hydrolyzes to clindamycin in the plasma. The salt form confers water solubility to the ester, which is available as granules for reconstitution into an oral solution for pediatric use.**

1. **The 2-phosphate ester in solutions for intramuscular or intravenous injection. It is very soluble in water (exists as a zwitterionic structure). It is intended for parenteral (intravenous or intramuscular) administration.**

* **All forms are chemically very stable in solution and in the dry state.**

**POLYPEPTIDES**

**Among the most powerful bactericidal antibiotics are those that possess a polypeptide structure. Their clinical use has been limited by:**

1. **Their undesirable side reactions, particularly renal toxicity.**
2. **Lack of systemic activity of most peptides following oral administration.**

**Polypeptide antibiotics variously possess several interesting and often unique characteristics:**

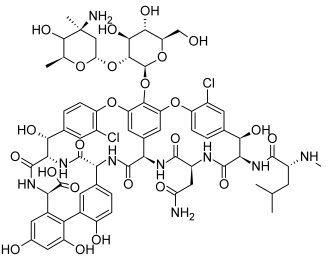
**a- Most of them are cyclic, with a few exceptions (e.g., the gramicidins).**

**b-They frequently contain D-amino acids and/or “unnatural” amino acids.**

**c- Many of them contain non–amino acid moieties, such as heterocycles, fatty acids, sugars, etc.**

**Examples: Vancomycin, Teicoplanin, Bacitracin, gramicidins, polymyxin.**

**Vancomycin Hydrochloride**



**Mechanism of action and spectrum of activity**

**Vancomycin interferes with bacterial cell wall synthesis through binding to peptidoglycan terminus and subsequently inhibit their cross linking. It is effective against Gram-positive bacteria particularly *streptococci*, *staphylococci*, and *pneumococci*. It is not active against Gram-negative bacteria, with the exception of *Neisseria* spp.**

**Uses**

* **Vancomycin is recommended for use when infections fail to respond to treatment with the more common antibiotics or when the infection is known to be caused by a resistant organism.**
* **It is particularly effective for the treatment of endocarditis caused by Gram-positive bacteria.**
* **MRSA**
* **pseudomembranous colitis**

**Resistance**

**Resistance to vancomycin among Gram-positive cocci is rare. This resistance is through the change in the peptidoglycan structure. The resulting peptidoglycan can still undergo cross-linking but no longer binds vancomycin.**

**Administration**

* **IV for the treatment of systemic infections.**
* **Orally for the treatment of local intestinal infection( e.g. pseudomembranous colitis), because it is not absorbed.**

**Adverse effects:**

**Nephrotoxicity, allergy (red man syndrome), Phlebitis.**

**Teicoplanin**

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**The teicoplanin complex is similar to vancomycin structurally and microbiologically but has unique physical properties that contribute some potentially useful advantages.**

1. **While retaining excellent water solubility, teicoplanin has significantly greater lipid solubility than vancomycin. Thus, teicoplanin is distributed rapidly into tissues.**
2. **The complex has a long elimination halflife, resulting from a combination of slow tissue release and a high fraction of protein binding(may be administered on a once-a-day dosing schedule)**
3. **Unlike vancomycin, teicoplanin is not irritating to tissues and may be administered by intramuscular or intravenous injection.**
4. **Orally administered teicoplanin is not absorbed significantly.**
5. **Teicoplanin exhibits excellent antibacterial activity like vancomycin**
6. **Teicoplanin impairs bacterial cell wall synthesis in a manner entirely analogous to the action of vancomycin.**
7. **In general, teicoplanin appears to be less toxic than vancomycin.**
8. **Unlike vancomycin, it does not cause histamine release following intravenous infusion.**
9. **Teicoplanin apparently also has less potential for causing nephrotoxicity than vancomycin.**