

PHARMACOLOGY-III
UNIT-II
TOPIC: Chloramphenicol



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*Shaping Lives...
Empowering Communities...*

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CHLORAMPHENICOL

Chloramphenicol is active against a wide range of gram-positive and gram-negative organisms. However, because of its toxicity, its use is restricted to life-threatening infections for which no alternatives exist.

A. Mechanism of action

The drug binds to the bacterial 50S ribosomal subunit and inhibits protein synthesis at the peptidyl transferase reaction. Because of the similarity of mammalian mitochondrial ribosomes to those of bacteria, protein synthesis in these organelles may be inhibited at high circulating levels, producing bone marrow toxicity.

B. Antimicrobial spectrum

Chloramphenicol, a broad-spectrum antibiotic, is active not only against bacteria but also against other microorganisms, such as rickettsiae. *Pseudomonas aeruginosa* is not affected, nor are the chlamydiae. Chloramphenicol has excellent activity against anaerobes. The drug is either bactericidal or (more commonly) bacteriostatic, depending on the organism.

C. Resistance

Resistance is conferred by the presence of an R factor that codes for an acetyl coenzyme A transferase. This enzyme inactivates chloramphenicol. Another mechanism for resistance is associated with an inability of the antibiotic to penetrate the organism. This change in permeability may be the basis of multidrug resistance.

D. Pharmacokinetics

Chloramphenicol may be administered either intravenously or orally. It is completely absorbed via the oral route because of its lipophilic nature, and is widely distributed throughout the body. It readily enters the normal CSF. The drug inhibits the hepatic mixed-function oxidases. Excretion of the drug depends on its conversion in the liver to a glucuronide, which is then secreted by the renal tubule. Only about 10 percent of the parent compound is excreted by glomerular filtration. Chloramphenicol is also secreted into breast milk.

E. Adverse effects

The clinical use of chloramphenicol is limited to life-threatening infections because of the serious adverse effects associated with its administration. In addition to gastrointestinal upsets, overgrowth of *Candida albicans* may appear on mucous membranes.

Anemias: Hemolytic anemia occurs in patients with low levels of glucose 6-phosphate dehydrogenase. Other types of anemia occurring as a side effect of chloramphenicol include reversible anemia, which is apparently dose-related and occurs concomitantly with therapy, and aplastic anemia, which although rare is idiosyncratic and usually fatal.

Gray baby syndrome:

This adverse effect occurs in neonates if the dosage regimen of chloramphenicol is not properly adjusted.

Neonates have a low capacity to glucuronylate the antibiotic, and they have underdeveloped renal function.

Therefore, neonates have a decreased ability to excrete the drug, which accumulates to levels that interfere with the function of mitochondrial ribosomes.

This leads to poor feeding, depressed breathing, cardiovascular collapse, cyanosis and death. Adults who have received very high doses of the drug can also exhibit this toxicity.