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Inhibition of synthesis of essential metabolites

An antimetabolite is a substance that prevents a cell from carrying out a metabolic reaction. Antimetabolites function in two ways: 1-by competitive inhibition of enzymes, and 2 by erroneous incorporation into nucleic acids.

1-Competitive inhibition

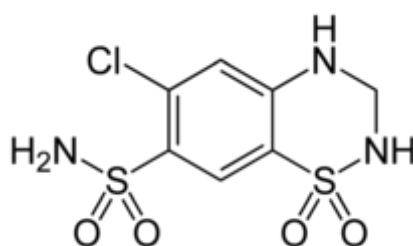
In this type of inhibition, an enzyme is inhibited by a substrate that binds to its active site but cannot react. This slows or completely stops the enzyme's function.

Sulfonamides

This group of molecules is produced entirely by chemical synthesis. In 1935, the parent compound sulfanilamide became the first clinically effective antibacterial agent.

Mechanism of action

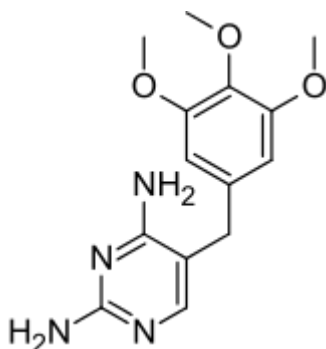
Sulfonamides act in competition with *para*-aminobenzoic acid (PABA), for the active site of dihydropteroate synthetase an enzyme that catalyzes an essential reaction in the synthesis pathway of tetrahydrofolic acid (THFA) which is required for the synthesis of purines and pyrimidines and therefore for nucleic acid synthesis. Fig(1). Sulfonamides are therefore bacteriostatic and inhibit growth and multiplication of bacteria.



Structure of Sulfonamides

Trimethoprim

Trimethoprim is a bacteriostatic antibiotic used mainly in the prophylaxis and treatment of urinary tract infections. It belongs to the class of chemotherapeutic agents known as dihydrofolate reductase inhibitors.



Structure of Trimethoprim

Mechanism of action

Trimethoprim, like sulfonamides, prevent THFA synthesis, but at later stage by binding to dihydrofolate reductase and inhibits the reduction of dihydrofolic acid to tetrahydrofolic acid. THFA is an essential precursor in the thymidine synthesis pathway and interference with this pathway inhibits bacterial DNA synthesis. Fig (1).

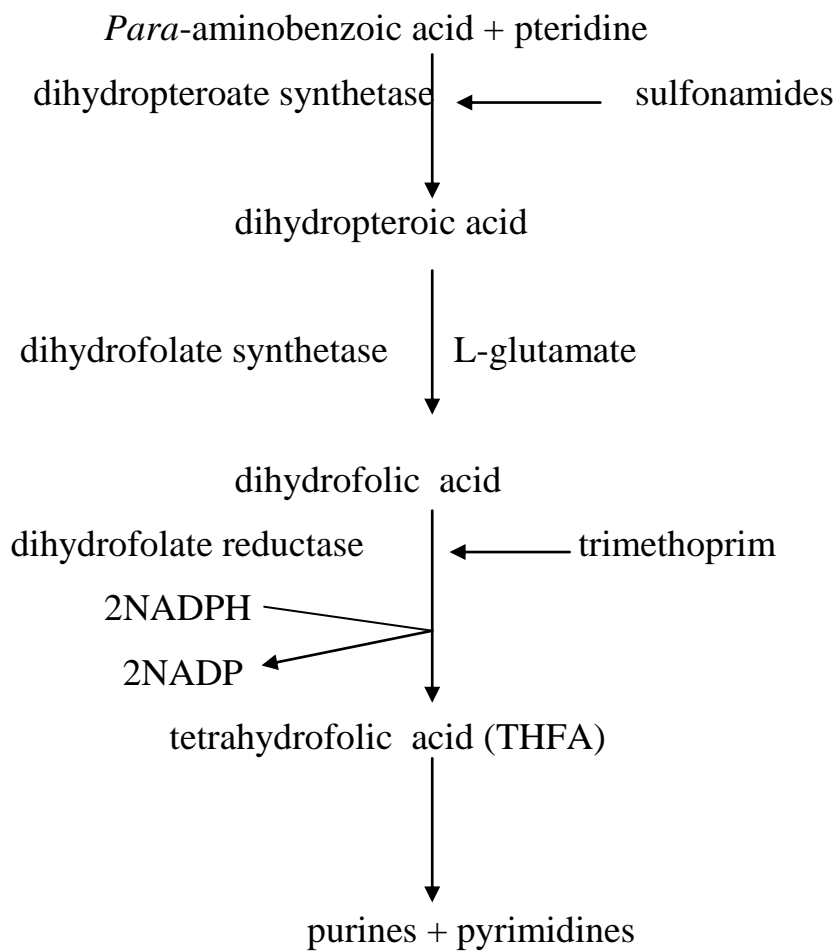


Figure (1):Inhibition the synthesis of tetrahydrofolic acid by sulfonamides and trimethoprim.

2-Erroneous incorporation into nucleic acids

Some antibiotics have similar structure and stereochemistry to purines and pyrimidines found in microorganisms. Thus, these purine and pyrimidine analogs mimic metabolites in nucleic acid synthesis ,and when incorporated they can not form the proper base pairs during replication and transcription.