

ribose 5-phosphate is catalyzed by PRPP synthetase (ribose phosphate pyrophosphokinase, Figure 22.6). This X-linked enzyme is (end-product inhibition). [Note: The sugar moiety of PRPP is ribose, and, therefore, ribonucleotides are the end products of *de novo* purine synthesis. When deoxyribonucleotides are required for DNA synthesis, the ribose sugar moiety is reduced (see p. 297).]

B. Synthesis of 5'-phosphoribosylamine

Synthesis of 5'-phosphoribosylamine from PRPP and glutamine is shown in Figure 22.7. The amide group of glutamine replaces the pyrophosphate group attached to carbon 1 of PRPP. The enzyme, called by the purine 5'-nucleotides AMP and GMP—the end products of the pathway. This is the committed step in purine nucleotide biosynthesis. The rate of the reaction is also controlled by the intracellular concentration of PRPP. [Note: The intracellular concentration of PRPP is normally far below the K_m for the amidotransferase. Therefore, any small change in the PRPP concentration causes a proportional change in the rate of the reaction (see p. 59).]

C. Synthesis of inosine monophosphate, the "parent" purine nucleotide

The next nine steps in purine nucleotide biosynthesis leading to the synthesis of inosine monophosphate (IMP, whose base is hypoxanthine) are illustrated in Figure 22.7. This pathway requires ATP as an energy source. Two steps in the pathway require N^{10} -formyltetrahydrofolate (see p. 267).

D. Synthetic inhibitors of purine synthesis

Some synthetic inhibitors of purine synthesis (for example, the sulfonamides¹), are designed to inhibit the growth of rapidly dividing microorganisms without interfering with human cell functions (see Figure 22.7). Other purine synthesis inhibitors, such as structural analogs of folic acid (for example, methotrexate²), are used pharmacologically to control the spread of cancer by interfering with the synthesis of nucleotides and, therefore, of DNA and RNA (see Figure 22.7).

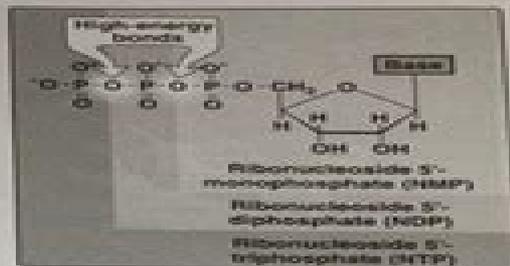


Figure 22.4
Ribonucleoside monophosphate, diphosphate, and triphosphate.

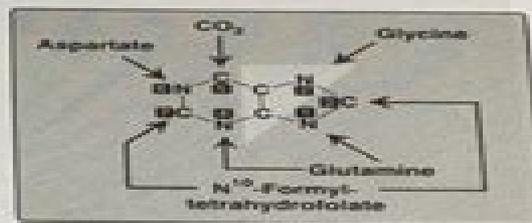


Figure 22.5
Sources of the individual atoms in the purine ring. The order in which the atoms are added is shown by the numbers in the black boxes (see Figure 22.7).

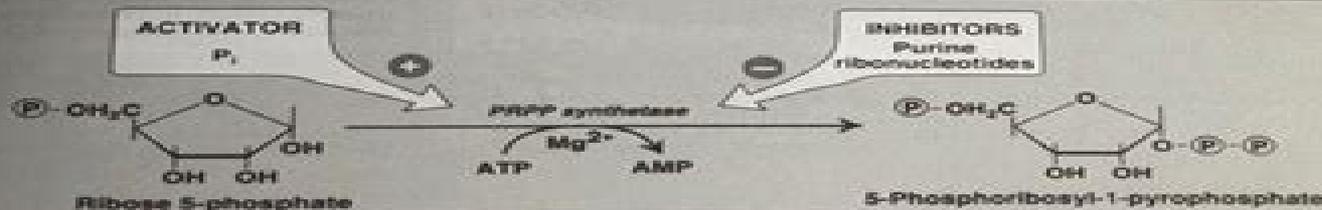


Figure 22.6
Synthesis of 5-phosphoribosyl-1-pyrophosphate (PRPP), showing the activator and inhibitors of the reaction.

^{1,2} See Chapter 30 in *Lippincott's Illustrated Reviews: Pharmacology* for a discussion of sulfonamides and methotrexate.

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