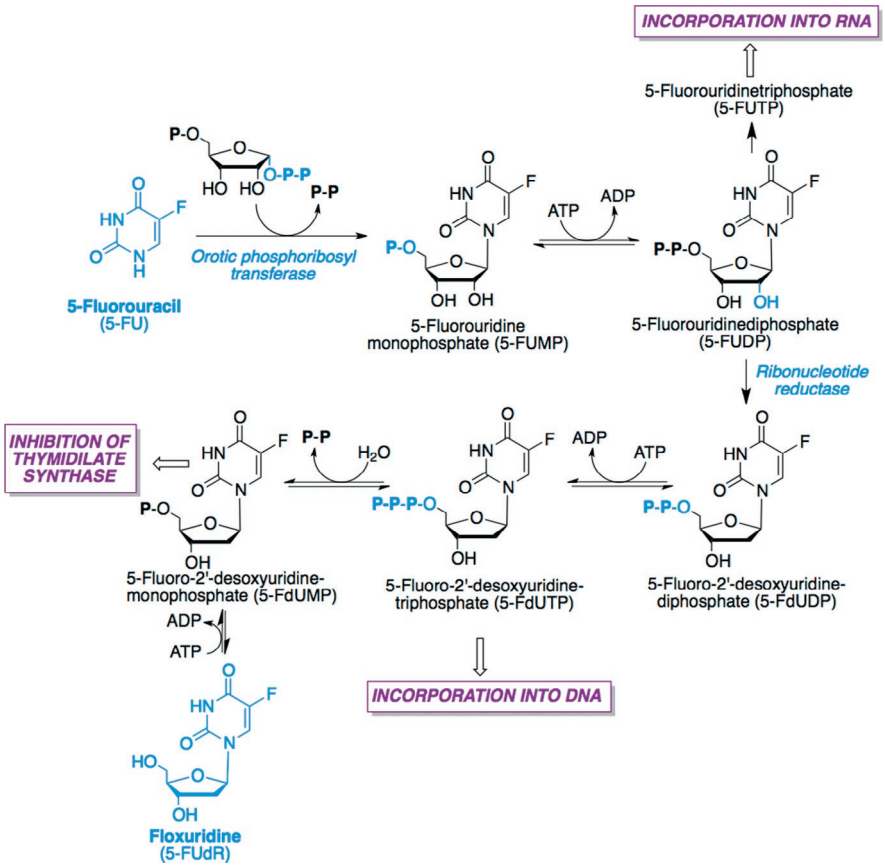

FIGURE 2.16

Antitumor species from the metabolism of 5-fluorouracil and floxuridine.

with the conversion of serine into glycine, with pyridoxal phosphate (PLP) as a cofactor. In the reaction catalyzed by TS, the 5,10-methylenetetrahydrofolate thus formed donates its methylene group to dUMP, being transformed into dihydrofolate (DHF) by a mechanism that is discussed below (see Figure 2.16). DHFR finally closes the cycle by reducing DHF to THF.

4.2 5-FLUOROURACIL AND FLOXURIDINE

The main inhibitors of thymidylate synthase are 5-fluorouracil (5-FU) and its deoxynucleoside floxuridine (5-FUdR), and these fluoropyrimidines represent the most widely prescribed class of anticancer drugs worldwide.[29] In particular, 5-FU is widely used in the treatment of cancers of the aerodigestive tract, breast, head, and neck and especially in colorectal cancers in combination therapies with oxaliplatin and irinotecan.[30,31] Administered as a cream, it is also useful for the treatment of some skin