The activity of pyrimethamine and sulfadoxine against two strains of *Plasmodium falciparum* has been studied in vitro by a radioisotopic technique. Low level antagonism of pyrimethamine resulted from the inclusion of \( p \)-aminobenzoic acid, \( p \)-aminobenzoylglutamic acid or folic acid in the test medium. Sulfadoxine activity was antagonised slightly by \( p \)-aminobenzoic but not by \( p \)-aminobenzoylglutamic acid, and antagonised markedly by folic acid at concentrations above \( 4 \times 10^{-8} \) M. At \( 10^{-7} \) M folic acid, a concentration lower than that of normal RPMI medium 1640, sulfadoxine activity was reduced 7000 to 9000-fold in comparison with controls. These results are of importance in terms of the utilisation of folates by *P. falciparum*, the susceptibility of the parasite to antifolate drugs and the in vitro determination of parasite susceptibility.