

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 4×10^{-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.