INHIBITION OF IN VITRO GROWTH OF PLASMODIUM FALCIPARUM BY ANTIBIOTICS

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SUMMARY

This study reported the *in vitro* sensitivity of *Plasmodium falciparum* to 4 antibiotics : tetracyclines, chloramphenicol, the chloramphenicol derivative (thiamphenicol), and cycloheximide. Results obtained from the 48 hours *in vitro* drug test revealed the slow effect of tetracycline and chloramphenicol groups which are prokaryotic protein inhibitors, on the parasite growth as compared with cycloheximide, as eukaryotic protein inhibitor, since the inhibitory effects from these first 3 antibiotics (at IC_{50}) were not observed in the first 24 hours of drug exposure whereas the retardation was already seen in the culture exposed to cycloheximide. Using K isolate, tetracycline seems to be the most potent antibiotic. The IC_{50} of this K-isolate to tetracycline, chloramphenicol, thiamphenicol and cycloheximide were 3.0×10^{-8} M, 4.0×10^{-4}M, 9.0×10^{-5} M and 3.0×10^{-7} M, respectively. Although the IC_{50} for the chloramphenicol group is high, no effect of these 2 antibiotics on red blood cell causing the hemolysis was detected. A variation in drug responsiveness to chloramphenicol among various Thai isolates variation in degree of Fansidar sensitivity was also found, but there was no statistically significant correlation between the degree of chloramphenicol sensitivity and Fansidar sensitivity.

The effect of thiamphenicol on malarial parasites was more pronounced when the cultures were exposed to this drug for a long period of time (96 hours).

Comparing the antimalarial sensitivity of chloramphenicol with that of thiamphenicol, parasites seem to be more sensitive to the later by a factor of 5. Saponin-lysis was used to partially remove the parasitized erythrocyte membrane, however removal of this putative membrane barrier did not result in an enhanced inhibitory action of chloramphenicol or thiamphenicol, as judged by parasite uptake of ^{3}H-isoleucine.

Using ^{3}H-isoleucine incorporation to measure the effect of each of the 4 antibiotics on protein biosynthesis of P. falciparum K isolate in isoleucine-free medium during 6 hours, no inhibition could be observed, even in the presence of varying concentrations of each of 3 prokaryotic protein inhibitors, whereas there was a direct correlation between the concentration of cycloheximide and the extent of protein inhibition. These results are consistent with the eukaryotic nature of P. falciparum and also confirm the difference between malarial and prokaryotic ribosomes.

No inhibition in ^{3}H-hypoxanthine incorporation could be detected during 8 hours in the presence of any of the 4 prokaryotic protein inhibitors, however there was a decrease in the uptake of ^{3}H-hypoxanthine in the presence of cycloheximide in the first 3 hours of incubation.