Title: Single-dose pharmacokinetics of anti-malarial chlorproguanil and its active metabolite chlorcycloguanil in healthy adult volunteers

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Abstract: Malaria, often referred to as "the King of Diseases", is the single largest cause of disease and death every year in tropical countries. It is possible to prevent malaria infections if those concerned (travelers to, and residents of, endemic areas) are well informed about the dangers of contracting the disease if they do not take preventative measures. The main preventative measure is through prophylaxis (drug taking) which should be used for as long as there is no effective and sure immunising vaccine. While malaria remains a major, worldwide, public health problem and resistance to currently available drugs becomes more prevalent, interest had focused on the understanding of the pharmacokinetic characteristics of available anti-malarial. These are parameters, which govern the time-course of the movement of drugs into, around and out of the body. Previously, many of these drugs had been little studied, and it is now anticipated that increasing information on the disposition of drugs, both current and under development, may improve their rational use and enhance their role as possible tools to combat malaria.In this study, the rate of elimination of both CPG and CCG from the body (circulation) have been shown to be similar to that of proguanil (an analogue of CPG) which is taken daily, and its active metabolite, cycloguanil. This finding has supported the hypothesis that the current recommended weekly dose of CPG hydrochloride (20mg) is inappropriate. Inter-subject variation was found in the extent of metabolism of CPG to CCG, although the magnitude of this variation was found to be less than that reported for proguanil. These results are of general importance in the search for effective chemoprophylactic drugs, and of specific importance in terms of the relationship between efficacy and dosage of CPG hydrochloride as a chemoprophylactic drug.