

# ANTI MALARIAL DRUG QUININE AND ACTIVATED CHARCOAL EFFECT ON HAEMTOLOGICAL PARAMETERS IN RATS

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## ABSTRACT

The efficacy of oral administration of activated charcoal in ameliorating the harmful effect of quinine on haematological parameters- packed cell volume (PCV), haemoglobin concentration (Hb) and erythrocyte count (Rbc) in animal model was studied. Quinine alone ( $P < 0.05$ ) or activated charcoal alone ( $P < 0.01$ ) significantly reduced the parameters studied compared with control. Although there was no significant difference in the values of the parameters studied when activated charcoal was administered 10 minutes before or after oral ingestion of quinine hitherto the reduction in the values of PCV, Hb and Rbc were similar to that obtained with activated charcoal alone; which suggests that oral administration of activated charcoal as early as possible may have a beneficial effect in reducing the toxicological effects of quinine on blood parameters

**Key words:** Blood picture; charcoal-therapeutic-use; quinine, animal.

**Running title:** Effect of activated charcoal and quinine on blood profile.

## INTRODUCTION

Malaria is one of the major public health problems in the malaria endemic areas of the world, and chemo prophylaxis is the effective means of control in the define group of people. Thus quinine an isomer of quinidine is one of the alternatives anti malarial drug used in the management and treatment of malaria infection. Along its needed effects, quinine has been reported to cause some side effects such as birth defects, stillbirth in experimental animals and in humans (Micromedex Thomson health care 2000), alter cardiovascular functions (Anigbogu and Badru, 2000) and is rapidly absorbed in the gastrointestinal track (Orisakwe and Akintonwa 1991). These features are likely to lead to haematological disturbances. Despite the wide spread use of antimalarial drugs in the tropics, and in did, in Nigeria quinine is easily assessable over-the-counter and there is the possibility of accidental or deliberate consumption of it, and will present high potential for hazard, relatively little is known about the effect of the drug on blood profile. The distribution in blood cells and the possible mechanism of entry of these drugs into the erythrocytes has been described

(Coker et al 1991). Literature search reveals that activated charcoal is an adsorbent that ameliorates gastrointestinal decontamination after poisoning (Anjaneyulu and Rao, 1993; Manoguerra, 1997; Holsen and Aarebrot 1997; Larsen and Cummings, 1998), have nutritional benefits (Tobioka and Garri11o, 1995), inhibits drugs in the gastrointestinal track (Orisakwe and Akintonwa 1991; Johnson et al, 1995; Idid and Lee, 1996; Tomimaru et al, 1996; Salgia and Kosnik, 1999) and is highly effective in reducing plasma level of drugs over a period of time (Idid and Lee, 1996; Akintonwa and Orisakwe, 1990; Salgia and Kosnik, 1999). Multiple doses of activated charcoal do not enhance the clearance of drug after administration of high-dose intravenous of drug (Johnson et al 1995). Hitherto, there is thus no quantitative study on the effect of activated charcoal and/or quinine on haematological parameters. Hence we have under taken a study to determine whether activated charcoal and/or quinine affect packed cell volume (PCV), haemoglobin concentration (Hb) and erythrocyte count (Rbc) of the blood using animal model and speculate on the benefits of charcoal in

reducing the toxicological effects of anti malarial drugs on blood profile

## METHODS AND MATERIALS

**Experimental animals:** Experiments were carried out using 60 albino rats of the Wistar strain. The animals were maintained in the departmental animal facility and were allowed free access to water and commercially available feed for three weeks. Rats weighing between 155 and 275g were used for the experiments. The animals were divided into four groups. One group was treated with an oral dose of quinine or another group with activated charcoal and the third group was treated with either quinine and followed by activated charcoal or activated charcoal and followed by quinine 10 minutes later. The remaining group (control) was treated with only oral dose of a normal saline.

**Drug administration:** Commercially available quinine was used for the study. Activated charcoal was obtained\* from mango tree (Bonsu, 1997). Quinine dose (11.78mg/5ml) was given to the rats using body weight adjusted dosage. Activated charcoal was administered in 10ml normal saline as 1-2% slurry.

**Collection of blood samples and analysis:** Rats were anaesthetized with diethyl ether after which blood samples were obtained from the tails of the rats into sodium citrate anti-coagulant container 24 hour after administration of the drugs. Samples of the blood were immediately subjected to standard haematological analysis. The packed cell volume (PCV) of each sample was determined by using Hawksley micro haematocrit centrifuge at 3000 rpm for 5 minutes, haemoglobin concentration (Hb) by Sahli's method and erythrocyte count (Rbc) by the use of the haemocytometer method (Deice and Levis 1991). The erythrocyte indices were calculated from the values obtained from the PCV, Rbc and Hb.

**Statistically analysis:** Values obtained were subjected to variance approach commonly known as the ANOVA using the two factors, factorial fixed effect model. Duncan's multiple range tests was used to compare the means. Test of significance was carried out using student's "t" test.

## RESULTS

The results were analyzed using the analysis of variance approach (ANOVA) and showed that the values of the haematological parameters (PCV, Hb and Rbc) at constant activated charcoal to drug ratio was not dependent on the increasing drug concentration. F column factor < F tabulated i.e.  $0.089 < 3.35$  and F interaction < F tabulated i.e.  $0.082 < 2.73$ . Table 1 compares the mean values of the hematological parameters (PCV, Rbc and Hb) studied in the rats. The results showed that oral administration of quinine significantly ( $P < 0.05$ ) reduced PCV, Rbc and Hb in albino rats compared with control. Rats treated with only quinine recorded reduced PCV (22.5%), Hb (9.75%) and Rbc(25%) compared control. The PCV, Hb and Rbc values obtained for the groups of animals treated with activated charcoal only or with activated charcoal 10 minutes after or before oral ingestion of quinine were slightly reduced compared with the control values ( $P < 0.01$ ). Table 2 compares the erythrocyte indices calculated from the values obtained for the PCV, Rbc and Hb. Activated charcoal with or without quinine slightly reduced the indices. The difference was not significant ( $p > 0.05$ )

## DISCUSSION

The study clearly showed the impact of quinine and activated charcoal on blood profile in the studied rats. The results of the study demonstrate the ability of activated charcoal 1-2% to reduce packed cell volume, haemoglobin concentration and red blood cell count in blood and therefore, also prevented quinine from exacting its side effects on blood profile. The observation that activated charcoal reduced packed cell volume in blood is in harmony with the work of Garillo *et al* (1995). The administration of activated charcoal 10 minutes before or after oral ingestion of quinine remarkably prevented quinine from interfering with the packed cell volume, haemoglobin concentration and erythrocyte count in blood compared with when quinine alone was administered and stressed the importance of immediate administration of activated charcoal and its

Table 1. The effect of activated charcoal and quinine on the haematological parameters in rats

Drug	PCV (%)	% diff	Hb(mg/dl)	% diff	RBC( $\times 10^6$ (mm <sup>3</sup> ))	% diff
Control	30.5	-	12.25	-	4.16	-
Activated charcoal	28.2	7.5	11.78	3.5	4.0	3.9
Quinine	22.5	23.7	9.75	19.6	3.1	25
Activated charcoal followed by quinine	28.63	6.0	11.60	5.0	4.0	3.9
Quinine followed by activated charcoal	29.2	7.5	11.73	3.9	4.2	3.4

Table 2 Comparison of the erythrocyte indices.

Drug	MCHC (g/dl)	% Diff.	MCV (um <sup>3</sup> )	%Diff.	MCH (pg)	%Diff.
Control	43.02	-	74.4	-	32.0	-
Activated charcoal	42.0	2.4	70.5	5.3	29.5	78
Quinine	43.4	0.88	72.5	2.6	31.4	1.9
Activated charcoal followed by quinine	40.5	5.9	71.7	3.7	39.0	3.5
Quinine followed by activated charcoal	40.2	6.6	72.5	2.6	29.3	8.4

consequences on counteracting with the inhibitory compounds in quinine, which perhaps is capable of affecting the haematological profiles. Perhaps the molecules of activated charcoal compete with that of quinine for certain position in the membrane in which the quinine molecules may have to be if they are to exert their inhibiting effects on blood. However the observation made in this study is consistent with the view of Idid and Lee (1996) that the administration of activated charcoal as early as possible will help in the reduction of drug absorption from the gastrointestinal track. In fact it has been suggested that activated charcoal does not enhance the elimination of substances which have already been absorbed into the systemic circulation, but constitutes a useful method for the removal of the compounds remaining in

the gastrointestinal track (Tomimaru *et al* 1996). The effect of quinine on the haematological parameters studied perhaps might probably depend on the pH of the drug; which, the presence of activated charcoal evidently neutralized the extent to which the drug-induced reduction in the haematological parameters. It has been suggested that pH changes influenced drug induced erythrocyte shape change and consequently blood profile (Glaser, 1982). In fact it has been demonstrated that in tissue culture or aqueous sucrose solution the extent of sucrose hydrolysis in the media containing activated charcoal was directly proportional to the pH (Wann *et al*, 1997.). However, the results of the present study suggest that 1-2% of activated charcoal have a beneficial effect in reducing the toxicological effects of anti

malarial drug quinine on blood profile when given as early as possible.

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