Antimalarial drug-primaquine and reduced glutathione (GSH)

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The effects of antimalarial drug, primaquine, on the status of erythrocyte reduced glutathione (GSH) and glutathione reductase (GR) activity in albino rats (Charles foster) are investigated. GSH levels and GR activity in primaquine treated rats are significantly ($p<0.001$) reduced. Apparently oxidation of GSH and the reactions which maintain the GSH level are altered with primaquine treatment.

The adequate level of reduced glutathione (GSH) is important for oxidant defense, since it protects erythrocyte against haemolysis caused by intracellular and membrane oxidation. Primaquine (8-aminoquinoline) is an antimalarial drug. Studies suggest that it is an oxidant drug and haemolytic disorders may result from the administration of primaquine. The present work has been therefore undertaken to examine the oxidative effect of primaquine on erythrocyte reduced glutathione in albino rats.

Experimental Procedure

Young albino rats (Charles foster, 250-300 g) maintained on commercial rat diet (Lipton India Ltd.) were divided into two groups. Group I (control) rats were provided feed and water ad libitum. Group II rats were administered one dose of primaquine phosphate orally, equivalent to 0.25 mg of base/kg body wt/day. After 14 days of drug administration, blood samples from control and primaquine treated rats were obtained from the caudal vein. For in vitro studies whole blood from control rats was incubated with 1mM primaquine phosphate for 1 h. Reduced glutathione (GSH), glutathione reductase (GR) activity (in vivo) and haemoglobin content were estimated by the methods described earlier.

Results and Discussion

The data presented in Table 1 show that the administration of primaquine to albino rats brought about a significant ($p<0.001$) decrease in the erythrocyte GSH content and GR activity. While in vitro study show no significant ($p<0.1$) change in GSH content as compared to control. As no relation has been found between the GSH concentration and glutathione synthetase activity. This means GSH oxidation to GSSG (oxidized form) may be the reason for the decreased GSH content. Determination of GSSG might prove this point; however, GSSG is known to combine with cellular proteins by disulphide-interchange reactions or GSSG may be transported across the erythrocyte membrane and thus a large proportion may be lost from the erythrocyte in spite of its enhanced formation.

Individual susceptibility to oxidant effect of drugs arises not only through differences in the pathway of reducing power generation but also with inefficiencies in the metabolism of drugs. The drug metabolites are more active than the parent compound in increasing mechanical fragility.

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<th>Condition</th>
<th>In vivo study</th>
<th>In vitro study</th>
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<tr>
<td></td>
<td>GSH content</td>
<td>GR activity</td>
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<td></td>
<td>mg/100 mL RBC</td>
<td>mg/g Hb</td>
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<tr>
<td>Control (Gp I)</td>
<td>24.66±0.76</td>
<td>1.73±0.02</td>
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<td>Primaquine treated (Gp II)</td>
<td>10.03±0.45*</td>
<td>1.07±0.03*</td>
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* Values are means of at least three experiments (in duplicate) ± S.D.
* $p<0.001$ highly significant as compared to control.
** $p<0.1$ not significant as compared to control.
which is a significant aspect of red cell function and decreasing glutathione content of erythrocytes. In vitro experiments with primaquine on GSH partly confirms the same. The decrease in GSH content of erythrocytes after primaquine treatment may be due to an increased oxidation of GSH induced by the drug/metabolites and decreased activity of GR, an enzyme responsible for the reduction of GSSG to GSH.

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References