INTRODUCTION
Clinical evidence indicates that oral administration of chloroquine (CHQ) evokes adverse effects on glucose homeostasis and kidney function in African children (Jarzyna et al., 2001). These complications are partly ascribed to transiently high plasma CHQ concentration and/or malaria parasites (Gustafsson et al., 1983). We have, however, reported that topical application of pectin CHQ matrix patches formulation sustained controlled release of CHQ into the bloodstream (Musabayane et al., 2003).

OBJECTIVES
The purpose of the study was to determine whether CHQ delivered via the transdermal route can reduce malaria parasites and ameliorate the side effects associated with oral CHQ.

MATERIALS AND METHODS
Patch preparation
The pectin CHQ matrix patch was prepared using a protocol similar to that previously described with slight modifications (Musabayane et al., 2003). Briefly, pectin was dissolved in de-ionised water followed by agitation at 700 rpm. Chloroquine dihydrochloride was then added to the mixture and dried at 37°C for 30 minutes. Following this, the dimethyl sulfoxide, sodium lauryl sulphate, vitamin E and eucalyptus oil were added to the mixture. Following this, an aliquot of the mixture (1 mL) was transferred to separate petri dishes and frozen at -5°C for 18 hours following which a 2% CaCl₂ solution was added to the mixture to allow for cross linking. The patches were then stored in the refrigerator at 4°C until use.

Induction of malaria
Malaria was induced in male Sprague-Dawley rats with a single intraperitoneal injection of Plasmodium berghei (10⁵ parasitised RBC).

Oral glucose tolerance (OGT) responses
Oral glucose tolerance responses (OGT) to CHQ delivered orally (60 mg/kg) or transdermally (53 mg/kg) were monitored in groups of non-infected and Plasmodium berghei-infected male Sprague-Dawley rats giving a chloroquine load of 18.5 fold. Infected rats treated with deionized water (3 mL/kg p.o.) or drug free pectin acted as controls. Blood glucose was monitored at 15 min intervals for the first hour and hourly thereafter for 3 h.

Sub-chronic effects of CHQ
Blood glucose and renal function were monitored over a 21-day period divided into pre-treatment (days 0-7), treatment (days 8-12) and post-treatment (days 13-21) in separate groups of non-infected and infected control animals. Malaria-infected animals were administered twice daily (60 mg/kg p.o.) by means of a bulb-ended steel needle whilst the CHQ patch (53 mg/kg) was applied once at the beginning of the treatment period.

Statistical analysis
All data presented as means ±SEM. Graph Pad Instat software (version 5) using one way analysis of variance (ANOVA) followed by Tukey-Kramer multiple comparison test was used. p values <0.05 were considered significant.

RESULTS
However, the blood glucose concentration remained stable throughout the experiment following twice a day topical application of the CHQ patch by comparison to both non-infected and infected baseline values (Figure 2).

CHQ effects on renal electrolyte handling
An elevation of mean urinary K+ output in non-infected and infected animals following oral administration of CHQ was observed (Figure 3). The current study has also shown hyperkalaemia and elevated urinary K+ outputs in malaria infected control animals. Reduced urinary K+ outputs were also shown in P. berghei infected animals treated with oral and CHQ. However, transdermal application of CHQ had no significant effect on renal electrolyte handling (Figure 4).

CONCLUSION
Transdermally delivered CHQ equally reduced P. berghei parasitaemia by comparison with twice daily oral CHQ. Also, CHQ patch has the potential to circumvent the adverse effects of oral CHQ administration.

REFERENCES