Schistosomiasis is a parasitic disease caused by blood flukes of the genus *Schistosoma*. It is second to malaria in importance and at present the most effective control method is chemotherapy with use of praziquantel as the drug of choice. With the rising cases of drug resistance and re-infection, the focus is on development of a vaccine that can significantly reduce the incidence of the disease. The ability of genes encoding *S. mansoni* Cu/Zn superoxide dismutase (CT-SOD) and glutathione peroxidase (GPX) to confer significant levels of protective immunity in a murine model of *S. mansoni* have been demonstrated. In addition to anti-oxidant enzymes, a gene encoding Sm-filamin has also been shown to consistently induce a significant level of protection against schistosomiasis in mice. In this study, therefore the aim was to determine whether the protection observed in murine models can be replicated in the olive baboons as no such work has been done in higher mammals. In the study, animals in three groups were inoculated with 500ug each of DNA vaccines containing genes encoding *S. mansoni* CT-SOD, GPX and Sm-filamin respectively. The baboons in the fourth group received 500tg each of a vaccine containing a gene encoding GPX cloned in the reverse orientation (XPG) and the animals in the fifth group were injected with normal saline (0.85% NaCl). The animals were boosted at week 4, 8 and 12, and then rested for 4 weeks. Thereafter, the animals were challenged with 800 *S. mansoni* cercariae per animal percutaneously. The DNA vaccines did not alter the blood parameters, indicating that they are safe for use in animal models. Genes encoding *S. mansoni* anti-oxidant enzymes (CT-SOD and GPX) and Sm-filamin induced production of specific IgG against SEA and the response to SWAP was low, but this immune response was un-protective to baboons against *S. mansoni* infection. The egg output was low in SOD, GPX and XPG vaccinated baboons and highest in Sm-filamin vaccinated and normal saline injected baboons. Worm burdens, gross and histo-hepat-intestinal pathology including the mean hepatic egg-granuloma sizes in vaccinated and nonvaccinated controls were statistically insignificant. Although the baboons inoculated with Sm-pcGPX and Sm-pcXPG had a worm reduction of 7.47% and 2.63% respectively, this was insignificant and below the WHO requirement for vaccine. Those vaccinated with pcCT SOD and Sm-filamin had also insignificant worm reductions as compared to the controls. However, all animals gained weight before inoculation, but lost weight after challenge infection, with those vaccinated with SOD and GPX loosing less weight than other groups and those vaccinated with XPG loosing more weight. Although, these vaccines were able to induce immune responses to some worm antigens, some of them (SOD and GPX) were able to cause less weight loss pi and also low egg output, but worm reduction and pathology in both vaccinated and non-vaccinated were insignificant to indicate any protection. This study recommends several things; these vaccines should be used with a suitable adjuvant in future studies, vaccines should also be combined into one polyvalent vaccine, less weight loss and anti-fecundity effects of SOD and GPX should also be further investigated. Genes encoding other schistosome antigens that have shown protection in murine models should also be tested in non-human primates as a prelude to human clinical trial.