The development of parasite resistance to first-line antimalarial medicines, especially the ACTs, has made the research and development of novel antimalarial medications vital. *Globimetula oreophila*, a plant used in traditional medicine to treat malaria, is an example of a natural product that may provide new antimalarial drugs with fewer side effects, less drug resistance, and greater efficacy than synthetic drugs. This study aims to evaluate the antiplasmodial properties of *G. oreophila*’s fractions. After collection and authentication, the leaves were air-dried and reduced in size using a pestle and mortar. The pulverized plant was macerated in 70% ethanol and fractionated with solvents in the increasing polarity of n-hexane, chloroform, ethyl acetate, and n-butanol to produce the various fractions. The antiplasmodial activity of the n-hexane, chloroform, ethyl acetate, and n-butanol fractions of *Globimetula oreophila* leaf extract was assessed using an in vivo method in *Plasmodium berghei*-infected mice. In the mice, the fractions’ median fatal dose (LD$_{50}$) was calculated to be more than 5000 mg/kg. At doses of 125, 250, and 500 mg/kg, the fractions significantly ($p < 0.001$) reduced the parasitemia level. The fractions of *G. oreophila* showed significant in vivo antiplasmodial activity, which upholds the earlier in vivo findings for the crude extract as well as its folkloric use.

Funding: This research received no external funding.

Institutional Review Board Statement: This study was conducted by the Declaration of Helsinki and approved by Ahmadu Bello University Zaria, Committee on Animal Use and Care (ABUCAUC) with an approval number: ABUCAUC/2023/061.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to ethical concerns about plagiarism.

Conflicts of Interest: The authors declare no conflicts of interest.

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.