Emergence of new and re-emergence of old infections continue to elude prospects of reducing morbidity and mortality caused by microbial infections. Trends of resistance to currently in use antimicrobials and antimalarials threaten to increase mortality caused by these infections. This study explores the potential of marine invertebrates as a source for new antimicrobials and antimalarials. The lactate dehydrogenase method was used to assay marine sponges for activity against Plasmodium falciparum, while the disc diffusion method was used to assay the extracts for antibacterial and antifungal activity. Extracts of some marine sponges from the Zanzibar Island exhibited both antiplasmodial and antimicrobial activities. Among the 55 marine sponge extracts that were tested 23 (41.8%) inhibited Plasmodium falciparum W2 strain by more than 50% at both 250 and 50 µg/ml concentrations. Moderate polar extracts were more active against Plasmodium falciparum W2 strain than polar and non-polar extracts. None of the 12 extracts that were tested on Plasmodium falciparum strain D6 exhibited inhibitory activity reaching 50%. Among 18 marine sponge extracts that were tested for antimicrobial activity 12 (66.7%) showed activity against one or more of the bacteria and fungi used ranging from weak to strong on an arbitrary criterion. The ethyl acetate extracts of Agelas mauritania and Oceanopia sp. exhibited high activity against the fungi Candida albicans and Cryptococcus neoformans. The best antibacterial profile was exhibited by ethyl acetate extracts of Aplysinopsis sp., Halichondrida sp. 1 and Oceanopia sp. In conclusion, these results support the need for intensified efforts to search for active antimalarial and antimicrobial compounds from the Zanzibar marine sponges.