

**PHYTOCHEMICAL INVESTIGATIONS OF *LONCHOCARPUS*
ERIOCALYX (HARMS), *ALYSICARPUS OVALIFOLIUS* (SCHUMACH)
AND *ERYTHRINA ABYSSINICA* (DC) FOR ANTIPLASMODIAL,
LARVICIDAL, MOSQUITOCIDAL AND ANTIMICROBIAL ACTIVITIES**

**BY
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**A THESIS SUBMITTED IN FULFILLMENT OF THE REQUIREMENTS
OF THE DEGREE OF DOCTOR OF PHILOSOPHY (Ph.D) IN
CHEMISTRY**

DEPARTMENT OF CHEMISTRY

MASENO UNIVERSITY

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DECLARATION

This thesis has never been previously presented for examination for a Doctor of Philosophy degree of Maseno University or in any other University. This is my original research and all sources of information have been duly supported by the relevant references.

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DEDICATION

This Thesis is dedicated to the late Prof. Job Isaac Jondiko Ogoche for being an icon in Natural Products Chemistry and steering it to the level it is today and my late parents Mzee Gabriel Ochung' Waga and Mama Penina Ajwang' Ochung' for imparting in me the zeal to be a-go-getter.

ABSTRACT

Management of parasitic disease continues to be a burden and a major public health problem the world over today. Malaria is most lethal of the parasitic vector-borne diseases due to drug and vector resistance to the available chemotherapeutics and vector management strategies, respectively. Bacterial and fungal infections are opportunistic to persons with compromised immunity yet the available drugs are associated with occasional treatment failures while antibiotic resistance is growing relentlessly. Drug research and development (R&D) is out-paced by the rate of resistance by these disease causing organisms. This has necessitated a fall back to natural botanical sources such as *Lonchocarpus eriocalyx* (Harms), *Alysicarpus ovalifolius* (Schumach) and *Erythrina abyssinica* (DC). Root decoction from *L. eriocalyx* is used to manage fever, malaria and as a mosquito repellent, *A. ovalifolius* is used for bleeding piles and cough relief while concoctions from *E. abyssinica* are used to manage fever, malaria and fungal infections. However, the phytochemicals responsible for these activities have not been fully identified. This study evaluated crude extracts and pure isolates for antiplasmodial, larvicidal, mosquitocidal and antimicrobial activities, isolated and characterized compounds from active extracts. Air-dried and pulverized plant parts were sequentially soaked in solvents of varying polarities and subsequently subjected to chromatographic fractionation. Structures of isolated compounds were elucidated using physical and spectroscopic methods and compared with literature data. Concentrations inhibiting 50% of parasite and micro-organisms (IC_{50}) of active extracts and isolates were also determined. The stem bark of *L. eriocalyx* yielded lupeol (**27**), quercetin (**65**), apigenin (**68**), friedelin (**133**), β -sitosterol (**134**), lupenone (**135**), β -sitosterol-3-*O*-glucoside (**136**), chrysin (**137**), morinhydrate (**138**), quercetin-3-*O*-glucoside (**139**), 4',5-dihydroxystilbene-3-*O*-glucoside (**140**) and rutin (**141**). Quercetin, apigenin, β -sitosterol, β -sitosterol-3-*O*-glucoside, quercetin-3-*O*-glucoside, plumbagin (**142**), orientin (**143**), mohanimbine (**144**), koenimbine (**145**) and koenidine (**146**) were obtained from root bark of *A. ovalifolius* while the leaves of *E. abyssinica* yielded 7-hydroxy-4'-methoxy-3-prenylisoflavone (**147**) and erythrininate A (**148**). Koenidine was the most active against W2 and D6 strains of *P. falciparum* with IC_{50} values of **63.07 \pm 0.01** and **54.19 \pm 0.04 μ g/mL**, respectively. However the activity of mefloquine used as a positive control was superior. Mohanimbine was highly active against *A. gambiae* larvae with **82.3 \pm 0.01%** mortality although this activity was lower than temephos used as a positive control. The DCM extracts of *E. abyssinica* showed intermediate activity against *S. aureus* with zones of inhibition of **15.3 \pm 0.1 mm** compared to amoxyllin (**19.5 \pm 0.1 mm**). This extract also inhibited the growth of *C. albicans* with **13.2 \pm 0.1 mm** zone of inhibition compared to fluconazole (**17.3 \pm 0.2 mm**). Terpenoids, flavonoids and carbazole alkaloids were the major constituents of the three plants. This research has confirmed the presence of bioactive secondary metabolites in these plants and scientifically validates their use in folk medicine. The isolates can be used as templates and developed into drugs to support the existing strategies in the management of parasitic diseases.

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LIST OF ABBREVIATIONS

^{13}C NMR	Carbon-13 Nuclear Magnetic Resonance
CC	Column chromatography
COSY	Correlation Spectroscopy
CDCl_3	Deuterated chloroform
CD_3OD	Deuterated methanol
CFU	Colony Forming Units
D6	Chloroquine-sensitive strain of <i>Plasmodium falciparum</i>
DEPT	Distortionless Enhancement by Polarization Transfer
DMSO-d_6	Deuterated dimethyl sulphoxide
EDTA	Ethylenediaminetetraacetic acid
ESIMS	Electro Spray Ionisation Mass Spectroscopy
HMBC	Heteronuclear Multiple Bond Coherence
HMQC	Heteronuclear Multiple Quantum Coherence
^1H NMR	Proton Nuclear Magnetic Resonance
HSQC	Heteronuclear Single Quantum Coherence
Hz	Hertz
IC_{50}	Inhibitory concentration that kills 50% population
IR	Infra red
Me	Methyl
MS	Mass Spectroscopy
RDA	Retro-Diels-Alder
SD	Standard Deviation

UV-Vis	Ultraviolet-Visible Spectroscopy
W2	Chloroquine-resistant strain of <i>Plasmodium falciparum</i>
br s	Broad singlet signal in NMR
br t	Broad triplet signal in NMR
d	Doublet signal in NMR
dd	Doublet of doublets signal in NMR
<i>J</i>	Coupling constant
m/z	Mass to Charge ratio
m	Multiplet signal in NMR
t	Triplet signal in NMR
s	Singlet signal in NMR
TLC	Thin Layer Chromatography

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