PHYTOCHEMICAL INVESTIGATION OF *BRIDELIA MICRANTHA* AND *TABERNAEMONTANA VENTIRCOSA* FOR CYTOTOXIC PRINCIPLES AGAINST DRUG SENSITIVE LEUKEMIA CELL LINES

RENEE ROSEBELLA MUNAYI

THIS THESIS IS SUBMITTED IN PARTIAL FULFILMENT FOR THE MASTER OF SCIENCE IN INDUSTRIAL CHEMISTRY IN THE CHEMISTRY DEPARTMENT, UNIVERSITY OF NAIROBI

2016

DECLARATION

DECLARATION

This thesis is my original work and has not been presented for a degree in any other University.

25/04/2016

Renee Rosebella Munayi

Reg. No. I56/67098/2013

This thesis has been submitted for examination with our approval as University supervisors.

Dr. Leonidah Kerubo Omosa,

Omosa 25/04/2016

Prof. Jacob Ogweno Midiwo,

24/04/2016

Department of Chemistry,
University of Nairobi,
P. O. Box 30197, 00100,
Nairobi-Kenya

ii

DEDICATION

This research thesis is dedicated to my parents Mr. Calvin Munayi and Mrs. Judy Munayi for their support, encouragement and inspiration.

ACKNOWLEDGEMENT

I would like to sincerely thank my supervisors Dr. Leonidah Kerubo and Prof. Jacob Midiwo for their parental and professional guidance throughout the course of this work. May God continue to bless you.

My sincere thanks to Dr. Matthias Heydenreich, University of Potsdam and Professor Muhammad Ilias and his colleagues from the University of Mississippi for the 1-D and 2-D (^{13}C and ^{1}H) NMR spectra and Professor Thomas Efferth from the University of Mainz, Germany for availing the facilities for carrying out the cytotoxicity assays. Mr. Patrick Mutiso of the herbarium, School of Biological Sciences for identifying and collecting the samples.

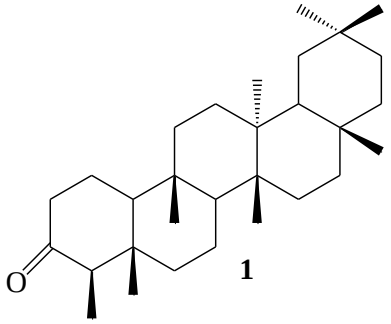
I would like to express my thanks to my colleagues at the Natural Products Laboratory, Ms. Veronica Masila, Mr. Boniface Muemi, Mr. George Kwesiga, Mr. Robert Wafula and Ms. Phylis Kitur for the supportive role they played during my research. I would also like to thank the teaching and technical staff of the Department of Chemistry, University of Nairobi for creating a conducive environment suitable for my research.

I would like to express my gratitude to my family, for their patience, moral and financial support. My parents are highly appreciated for their love, sacrifices and in molding me to be a responsible person.

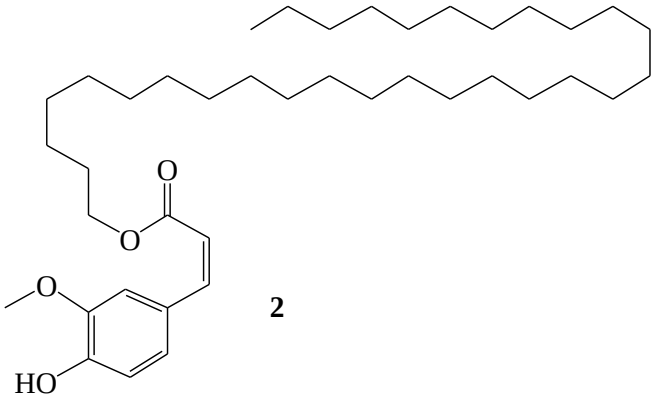
Most importantly, I am thankful to the Almighty God for His grace throughout this research period.

ABSTRACT

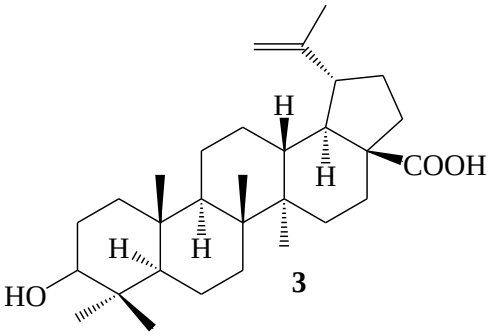
There are various treatment options that are available for the treatment of cancer. However, development of multidrug resistant cancer has become a global health challenge in the fight against cancer. *Bridelia micrantha* (Euphorbiaceae) has been used traditionally by people within the vicinity of Kakamega Forest for the treatment of tumors and related ailments. Despite its widespread use, its cytotoxicity has not been fully established. *Tabernaemontana ventricosa* (Apocynaceae) is known to contain indole and *bis*-indole alkaloids that have shown to elaborate anticancer principles. However, these cytotoxic principles have not been fully documented. This study therefore sought to investigate the phytochemical and anticancer principles of both *B. micrantha* and *T. ventricosa* to produce lead compounds to combat drug sensitive and multidrug resistant (MDR) cancer as well as validate the traditional uses of *B. micrantha* so as to improve the existing traditional knowledge. The stem bark of *Bridelia micrantha* and root bark of *Tabernaemontana ventricosa* were subjected to extraction by cold percolation and the crude extracts underwent chromatographic separation leading to the isolation of six compounds. The compounds were characterized using spectroscopic methods and identified as friedelin (**1**), *trans*-triacontyl-4-hydroxy-3-methoxycinnamate (**2**), betulinic acid (**3**), catechin (**4**), stigmasterol (**5a**) and *β*-sitosterol (**5b**). The crude extract and isolated compounds from *B. micrantha* were tested for their cytotoxicity and anticancer activity towards drug sensitive leukemia cell lines. The crude extract of *B. micrantha* showed a cell viability of 31.5% at the tested concentration (10µg/ml) with an IC_{50} value of 9.43µg/ml and thus showed good activity towards the drug sensitive leukemia cell lines. The compound, *trans*-triacontyl-4-hydroxy-3-methoxycinnamate (**2**) showed an interesting cell viability of 31.13% at 1 µg/mL. However, friedelin (**1**), betulinic acid (**3**) and catechin (**4**) showed cell viability of <30% (cell inhibition of <70%) at the tested concentration of 1µg/ml and were thus considered inactive. From this study, the stem bark of *B.* mainly used for the management of cancer by people within Kakamega Forest, showed good anticancer activity and should therefore be subjected to efficacy trials for possible anticancer use



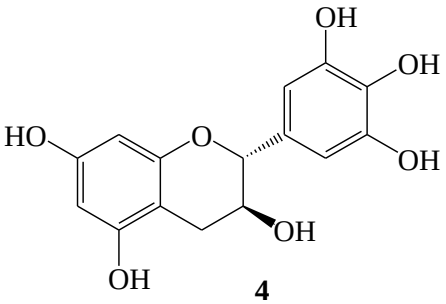
1



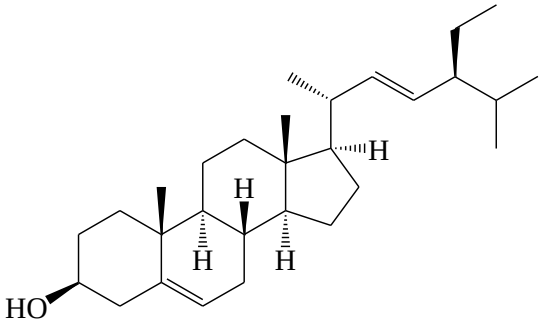
2



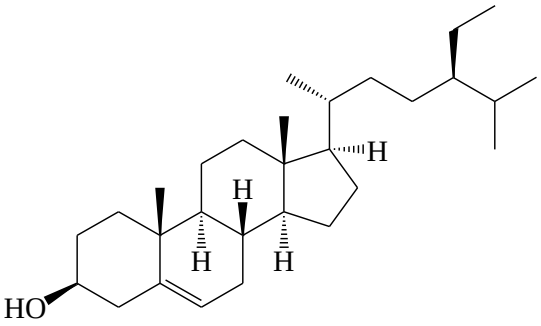
3



4



5a



5b