IN-SILICO IDENTIFICATION OF NATURAL INHIBITORS OF HUMAN TOPOISOMERASE AND KINASES TOWARDS TREATMENT OF VISCERAL LEISHMANIASIS.

MUHINDO JENIPHER

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DECLARATION

I declare that this research project is my original work and has not been submitted elsewhere for examination, a ward of a degree or publication. Where other people's work or my own work has been used; this has properly been acknowledged and referenced in accordance with the Busitema University requirements.

Signature..... Date.....

MUHINDO JENIPHER

APPROVAL

This undergraduate research project report has been submitted for examination with my/our approval as research supervisor(s).

Signature..... Date.....

Dr. Andima Moses

Senior Lecturer

Department of chemistry

P.O Box 236, Tororo

mandima@sci.busitema.ac.ug

DEDICATION

I dedicate this research project to my father Mr.Bwambale Sostin and Forum for African Women Educationalists-Uganda Chapter (FAWE-U).

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ACRONYMS

VL: Visceral leishmaniasis

PKDL: Post kala azar dermal leishmaniasis

CL: Cutaneous leishmaniasis

MCL: Mucocutaneous leishmaniasis WHO: World Health Organization

CADD: computer aided drug design

GSK-3: Glycogen synthase kinase 3

6BIO: 6-bromoindirubin-30-oxime

LCDK1: leishmanial cyclin-dependent kinase-1

LGSK-3:leishmanial Glycogen synthase kinase 3

DNA: De-oxyribo nucleic acid.

WHO: World health organisation.

ADMET: Adsorption,distribution,metabolism,excretion and toxicity

MOE: molecular operating environment

PDB: protein data bank

ABSTRACT

Leishmaniasis is endemic in 98 countries and is closely associated with poverty more than a million new cases are reported per year and 350 million people are at the risk of contracting the infection. For the most severe form of leishmaniasis VL, approximately 300,000 new cases are estimated to occur annually resulting in approximately 40,000 deaths. Current treatment options against leishmaniasis are expensive and laden with serious side effects a longside wide spread

resistance by the parasite: In this study therefore, natural inhibitors of leishmanial topoisomerase and kinases were identified form a data base of natural products isolated from Ugandan medicinal plants using in silico docking experiments.

According to this research I found out that the best docked ligands are Grandibracteoside B and Grandibracteoside A with binding energies of -33.6003 Kcal/mol and -33.7991Kcal/mol respectively.so these compounds can be modified chemically and tested in-vitro for further research.

CHAPTER ONE: INTRODUCTION

1.1 Background

Leishmaniasis is a parasitic disease that presents four main clinical syndromes/forms: Cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis (MCL), visceral Leishmaniasis/kalaazar (VL), and post kalaazar dermal leishmaniasis (PKDL). Visceral Leishmaniasis (VL) represents the most severe form of tropical disease and without proper diagnosis and treatment, is associated with high fatality [1]. Visceral leishmaniasis (VL), a chronic disease caused by parasites of the *Leishmania donovani* complex, is characterized by irregular fever, enlargement of the spleen, liver and weight loss.