PSYCHOPHARMACOLOGICAL PROPERTIES AND MECHANISMS OF ACTION OF METHANOLIC LEAF EXTRACT OF THE MALE *CARICA PAPAYA* LINN (CARICACEAE) IN MICE.

EHIZOGIE QUEEN ADEYEYE

2011

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF SCIENCE (PHARMACOLOGY).

BY

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF SCIENCE (PHARMACOLOGY).

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CERTIFICATION

We hereby certify that the work described and reported in this thesis was carried out by ADEYEYE, Ehizogie Queen (PHP 07/08/H/2828) in the Department of Pharmacology, Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife Nigeria, under our supervision.

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DEDICATION

To the almighty God who has made this programme possible.

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LIST OF ABBREVIATIONS

CEWG	Community Epidemiology Work Group
CNS	Central Nervous System
CPR	Chlopheniramine
CPX	Crude Papaya Latex
DAWN	Drug Abuse Warning Network
DDT	Dichloro Diphenyl Trichloroethane
ED	Emergency Department
EPG	Eggs Per Gram
EPM	Elevated Plus Maze
HAL	Haloperidol
ICAA	International Council on Alcohol and Addiction
JNC	Joint National Committee on the Control of Hypertension and Related Diseases
nACHRs	Nicotinic Acetylcholine Receptors
NIDA	National Institute of Drug Abuse

SCP	Scopolamine
WHO	World Health Organization

ABSTRACT

This study investigated the central nervous system effect of the methanolic leaf extract of the male *Carica papaya*, a plant reported to posses psychoactive effects. This activity was with a view to evaluate the psychopharmacological properties and mechanisms of action of the plant extract.

Ninety-six adult male and female mice were divided into sixteen groups of five to six animals per group. The neuropharmacological effects of the methanolic leaf extract of the plant were evaluated by examining the effects on Novelty-induced behaviours (locomotion, rearing and grooming) of the animals. The anxiolytic effect was investigated on Elevated Plus Maze and Holeboard apparatus while its effects on learning and memory were investigated on Y-Maze. Oral doses of 125, 250 and 500 mg/kg of the extract were administered to the test group and the results were compared with the vehicle-treated control groups. Prior administration of scopolamine (3 mg/kg), a muscarinic receptor blocker, chlorpheniramine (10 mg/kg), a histamine receptor blocker and haloperidol (0.1 mg/kg) a dopamine receptor blocker were used to investigate the involvement of Cholinergic, histaminergic and Dopaminergic system in the action of the extract.

The results showed that methanolic extract of dry *Carica papaya* leaves exhibited dose-dependent decrease in locomotor, rearing and grooming behaviours at all doses administered indicating the central inhibitory effect. Holeboard and Elevated Plus Maze tests, models showed that the extract has no anxiolytic effect, while the Y-maze model suggests that the extract has no significant effect on learning and memory. Investigation of the possible mechanism of action using scopolamine, chlorpheniramine and haloperidol showed that the

dopaminergic system is highly involved in the central effect of the extract. There was indication that cholinergic components may also be involved in the action of the extract.

The study concluded that the methanolic leaf extract of male *Carica papaya* has central inhibitory effects but no anxiolytic properties and the mechanism of action is mainly through the inhibition of the dopaminergic system.

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CHAPTER ONE

1.0 INTRODUCTION

Natural products will continue to be important in three areas of drug discovery: as targets for production by biotechnology, as sources of new lead compounds of novel chemical structure, and as the active ingredients of useful treatments derived from traditional systems of medicine (Harvey, 1993). Furthermore, the widespread interest in, and global resurgence of, the use of plant-based products in prophylaxis, treatment and management of several medical conditions call for more broad-based screening and functional bioassays of these materials for proper appraisal of their safety and efficacy.

In Africa, traditional birth attendants use the extract of *Carica papaya* L. (family: Caricaceae) root in the management of difficult labor (Sofowora, 1993). Indigenous populations in some parts of Asia also apply the crude latex of *Carica papaya* L. (the milky sap stored in the articulated laticifer of the plant) intravaginally to the uterine cervix opening to induce abortion (Quisumbing, 1951). Apart from its anecdotal use in the indigenous practice of obstetrics and gynecology, crude papaya latex (CPX) has long been treasured as a purgative and remedy for different gastrointestinal disorders.

In India, CPX is taken orally for indigestion, abdominal colic and intestinal worm infestations (Singh et al., 1980). Fresh papaya latex is also taken orally in Mexico to treat constipation (Zamora-Martinez and Pola, 1992). *Carica papaya*, belongs to the family of Caricaceae, and several species of Caricaceae have been used as remedy against a variety of diseases (Mello et al., 2008; Munoz et al., 2000). Originally derived from the southern part of Mexico, *Carica papaya* is a perennial plant, and it is presently distributed over the whole

tropical area. In particular, *Carica papaya* fruit circulates widely, and it is accepted as food or as a quasi drug. Many scientific investigations have been conducted to evaluate the biological activities of various parts of *Carica papaya*, including fruits, shoots, leaves, rinds, seeds, roots or latex. The leaves of *Carica papaya* have been shown to contain many active components (such as papain, chymopapain, cystatin, tocopherol, ascorbic acid, flavonoids, cyanogenic glucosides and glucosinolates) that can increase the total antioxidant power in blood and reduce lipid peroxidation level, (Seigler et al., 2002).

Moreover, *Carica papaya* leaf juice is consumed for its purported anti-cancer activity by people living on the Gold Coast of Australia, with some anecdotes of successful cases being reported in various publications. *Carica papaya* leaf extracts have also been used for a long time as an aboriginal remedy for various disorders, including cancer and infectious diseases.

Preliminary report reveals that the extract of the dry leaves of *Carica papaya* plant has possible psychoactive effect and recent report (not documented) suggest that the dry leaves of *Carica papaya* plant are being smoked by youths in the south-Western part of the Nigeria and may constitute another potential drug of abuse among youths.

CHAPTER TWO

LITERATURE REVIEW

2.1 ORIGIN AND DESCRIPTION OF *CARICA PAPAYA*

Pawpaw (*Carica papaya*) probably originated in Central America but is now cultivated in all tropical regions of America, Asia and Africa. Today major pawpaw producers are Brazil, Indonesia and India who export the fruit to many countries, including the U.K.

2.1.1 Fruit of *Carica papaya*

The fruit is melon-like, or oval in shape l5-50cm in length and 10-20cm thick.The skin is waxy and thin but fairly though.When the fruit is green and hard it is rich in white latex. As it ripens, it becomes light or deep-yellow externally and the thick wall as succulent flesh becomes aromatic,yellow or red.(Julia, 1987).

2.1.2 *Carica papaya* Tree

Although the pawpaw is often called a tree, it is in fact a giant herbaceous plant, up to 5 m tall. Its hollow stem is grey or green in colour and bears large leaf scars along its entire length. Surmounting the stem is a tuft of large dark green leaves, each up to 75 cm across and deeply divided into approximately 7 leaflets which are in turn further subdivided. The plant is very fast growing, bearing flowers and then fruit within a year of planting. Pawpaws are usually dioecious, with flowers of different sexes being produced on different plants. The trumpet-shaped male flowers are borne in long hanging inflorescences (flower heads) whilst the larger female flowers, which have five free