

**APOCYNACEAE FAMILY AS A SOURCE OF TRADITIONAL AND
CONVENTIONAL MEDICINE.**

BY

KHALIF AHMED MOHAMUD

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SUPERVISOR: DR. A.GATUMA


**DEPARTMENT OF PHARMACOLOGY AND PHARMACOGNOSY,
SCHOOL OF PHARMACY, COLLEGE OF HEALTH SCIENCES,
UNIVERSITY OF NAIROBI.**

DECLARATION

I declare that this research proposal is my original work and to the best of my knowledge, has not been presented or produced in any other university or any other institution for the award of degree or examination purposes.

Name: KHALIF AHMED MOHAMUD.

Admission: U29/11201/2006.

Signature: 

Date: 20/05/2011

SUPERVISOR. DR AMBROSE GATUMA.

Signature: 

Date: 24/05/11

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ACRONYMS:

W.H.O. - World Health Organisation of the United Nations.

B,P - British Pharmacopoeia.

CNS -Central Nervous System.

1. BACKGROUND TO THE STUDY.

Plants have an important role in the treatment of various diseases by both traditional and conventional or 'modern' medicine. Modern medicine utilises scientific and technological methods to age old practices e.g. a plant that is known to have specific activity against a certain disease is harvested and modern isolation techniques and pharmacological procedures are carried out to find the active substance, that is then purified and presented in various formulations e.g. tablets, capsules, syrups, suspensions etc rather than in the 'crude' form that is normally the case in traditional medicine (Trease and Evans, 2006)Therefore in essence 'modern' medicine borrows heavily from traditional medicine and is an outcome of the evolvement of the knowledge and experience of traditional practitioners. This shows that traditional and modern medicine should have a mutually beneficial relationship in order for both to prosper and for the betterment of the health of patients.

The World Health Organization (WHO) defines traditional medicine as 'therapeutic practices that have been in existence, often for hundreds of years, before the development and spread of modern scientific medicine and are still in use today. This is mostly the case in the African and Asian continents where traditional medicine is widely used .Chinese medicine and herbs are becoming more and more popular in the west.

Conventional medicine has its origins in Mesopotamia and Egypt (Egyptian papyrus ebers c 1600BC),The Unani medicine(Kitab-al-shifa, the magnum opus of Avicenna¹,

¹ Corrupted latin for Abū Alī al-Ḥusayn ibn Abd Allāh ibn Sīnā popularly known as Ibni Sīnā see en.wikipedia.org/wiki/Avicenna

AD 980-1037) which is of Islamic origin and Ayurvedic² medicine (Ayurveda 2500-600 BC). The most ancient form of medicine that used plants were the Unani³ and Ayurvedic medicine both of which have origins in the Mediterranean. The *materia medica* of both unani and ayurvedic medicine is derived from many herbs and the final preparations for administration include pills, syrup, alcoholic extracts, etc, Chinese medicine also has a long history with the earliest known texts being unearthed in Hunnan province and dates from the 4th century BC. It lists over 200 herbs with instructions for 52 pharmaceutical preparations. This shows that plants have been exploited for their medicinal use for ages and are still being used worldwide as a source of conventional medicine, this at times puts a strain on existing plant sources e.g. as a result of demand for new drug galanthine for treatment of Alzheimers disease, *Leucojum aestivum* is now in danger of extinction ((Trease and Evans, 2006), Hence research into cultivation or artificial propagation by cell cultures or use of a related species with the same active ingredient has been tried as a solution.

² **ayurvedic medicine** is a system of traditional medicine native to India^[1] and practiced in other parts of the world as a form of alternative medicine. See <http://en.wikipedia.org/wiki/Ayurveda>

³ Unani is the Arab word for Greek or Ionian and is a development of Arabic medicine which itself was based on the work of Galen (2AD) see trease and evans.

There are many species of plants containing substances of medicinal value which have yet to be discovered, large number of plants are constantly being screened for their possible pharmacological value particularly anti-inflammatory ,hypotensive, amoebicidal, antifertility, cytotoxicity, antibiotic and anti parkinsonism properties.

1.1. INTRODUCTION TO THE APOCYNACEAE FAMILY

The Apocynaceae family (also sometimes called the dogbane family) is made up of about 250 genera and 2000 species of tropical trees, shrubs and vines; it is closely associated with the Asclepiadaceae. A characteristic feature of the family is that almost all species produce milky sap. Leaves are simple, opposite and whorled. Flowers are large and colourful.

Scientifically Apocynaceae can be classified as;

- **Kingdom:** *Plantae*
- **Division:** *Angiosperms*
- **Class:** *Eudicots*
- **Subclass:** *Asterids*
- **Order:** *Gentianales*
- **Family:** *Apocynaceae*

The subfamilies include:

- *Rauvolfioideae*
- *Apocynoideae*
- *Periplocoideae*

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- *Secamonoideae*
- *Asclepiadodeae*

The important genera are arranged under two subfamilies:

TABLE 1: Table of important genera and number of species of apocynaceae family.

A: Plumierioideae		B: Apocynoideae	
Name	No. of Species	Name	No. of Species
<i>Arduina Carissa</i>	35	<i>Echites</i>	6
<i>Allamanda</i>	15	<i>Dipladenia</i>	30
<i>Landolphia</i>	55	<i>Odontadenia</i>	30
<i>Cardopinus</i>	50	<i>Mandevilla</i>	114
<i>Hancornia</i>	15	<i>Baissea</i>	40
<i>Pleiocarpa</i>	3	<i>Funtumia</i>	3
<i>Plumeria</i>	7	<i>Apocyanum</i>	7
<i>Alstonia</i>	50	<i>Nerium</i>	3
<i>Aspidosperma</i>	80	<i>Strophanthus</i>	60
<i>Rhazya</i>	2	<i>Wrightia</i>	23
<i>Amsonia</i>	25	<i>Parsonia</i>	100
<i>Lochnera-catharanthus</i>	5	<i>Lyonsia</i>	24
<i>Vinca</i>	5	<i>Malouetia</i>	25
<i>Tabernaemontana</i>	100		
<i>Voacanga</i>	25		
<i>Alyxia</i>	80		
<i>Rauwolfia</i>	100		
<i>Ochrosia</i>	30		
<i>Cerebra</i>	6		

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In the Apocynaceae family ,the active ingredient/component is found in different parts of the plant eg;

<i>Catharanthus roseus</i> -	Leaves
<i>Strophanthus</i> -	Seeds
<i>Rauwolfia</i> -	Roots
<i>Hollarhena</i> -	Bark
<i>Alstonia</i> -	Bark
<i>Aspidosperma</i> -	Bark

1.2. PHYTOCHEMISTRY

Constituents of the Plumierioideae include a vast range of Indoline alkaloids, over 500 in *Alstonia*, *Aspidospermum*, *Catharanthus*, *Hunteria*, *Pleiocarpa*, *Tabernaemontana*, *Rauwolfia* and *Voacanga*. Steroidal alkaloids occur in *Hollarhena*, and harman- type alkaloids in *amsonia* and *aspidosperma* .

Cardioactive glycosides occur in *Acokanthera*, *Carissa*, *Melodinus*, and in *Apocyanum* ,*Nerium* ,*Strophanthus*. Other constituents of the family are cyanogenetic glycosides, leucoanthocyanins, saponins, tannins, coumarins, phenolic acids, cyclitols and triterpenoids. Widely grown ornamental plants of the family include species of *amsonia*, *Nerium*(oleander), *vinca*, *plumeria*(frangipani), *Thevetia* (yellow oleander) and *Mandevilla* (Chilean jasmine)

RESEARCH QUESTIONS.

1. Which genera in the apocynaceae family have medicinal uses?
2. Which of these genera has been used in traditional medicine?
3. Which of these genera has found use in modern/conventional medicine?
4. Which of these genera have medicinally active ingredients that can be exploited for medical use?

OBJECTIVES

BROAD OBJECTIVES

To carry out a literature review of the apocynaceae family and determine the genera used for traditional and conventional medicine.

SPECIFIC OBJECTIVES.

1. Identify genera of the apocynaceae family that are used in traditional medicine.
2. Identify genera that have found uses in modern/conventional medicine.
3. To establish which genera have been used in both traditional and modern medicine.
4. To determine which genera can be further investigated for their medicinal properties.

JUSTIFICATION OF THE STUDY

The apocynaceae family has shown a significant amount of medicinal diversity within the genera in the family, this makes it a very interesting family to study for their medicinal content.

The main aim of this study is to establish

- What is known about this family with regards to medicinal use.
- What is not known about the family i.e. the knowledge gaps.
- The plants in the genera that are still undergoing study or screening for their medicinal activity.
- The chemical constituents in this family that impart medicinal activity to this plant.

2 LITERATURE REVIEW.

In this section of the proposal, the literature review will be tackled under three subtopics;

- Traditional uses of the apocynaceae family
- Conventional uses of the apocynaceae family
- Studies done on the apocynaceae family

The literature review for the apocynaceae family outlined in this section is by no means exhaustive and a more detailed literature review will be undertaken in the project.

2.1 TRADITIONAL USES OF THE APOCYNACEAE FAMILY.

1. *Acokanthera longifolia*, OL-MORIJOI (Maasai)

A decoction of the roots has been given to people with syphilis, but such treatment must be administered with caution since the plant is known to be toxic.

An infusion of the bark and roots is used as an arrow poison. (Kokwaro, 1993)

Samburu women in Kenya drink the decoction when their menstrual cycle does not stop.

The Boran steep the root for one day in water and drink the extract for stomach problems.

In Ethiopia a pomade is made from leaves and barks with butter for gall bladder problems.

Xhosa , Mpundu ,Zulu, and other peoples in south Africa use leaves and roots as an emetic after a snake bite.

A seven hour macerate of pounded roots is said to be a powerful aphrodisiac (H.D Neuwinger)

2. *Acokanthera schimperi*.

KELYOT (Kipsigis), NAMIKUOKO (Fipa), OLMORIGYE (Maasai)

An infusion of the roots is given to man suffering from syphilis but the dose must be in small quantities (Kokwaro,1993).

Acokanthera schimperi is also the classic hunting poison of east Africa and could almost be called the “national poison plant” of Kenya, such is its widespread and unrivalled use.(H.D Neuwinger)

The ripe fruits of *A.schimperi* and *A.opositifolia* are important as famine food (Medicinal plants of Tropical Africa)

3. *Adenium obesum*.KALUNI(Pokot),MWADIGA(Swahili).

The roots which are poisonous to human are used to kill lice.

Bark infusion used in washing livestock against ticks and lice (Kokwaro, 1993).

4 *Alstonia boonei*, MUJWA (Lunyoro)MUKOGE (Luganda), NSIWA (Lusoga).

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An infusion of stem bark in cold water is drunk and used for bathing for treatment of dizziness. Leaf extracts is used for washing infected breasts .Root and stem infusion is drunk as an antihelminthic or for treating snake bites. An infusion of root stem and leaves is drunk for treating asthma (Kokwaro,1993)

5. *Ancylobothrys petersiana*, (Sandani)

Root decoction drunk for the treatment of influenza, snake bite and as a diaphoretic.

6. *Carissa spinarum/Carissa edulis*, Kamasai(Nyamuha) Kikawam Mukawa(Kamba), Mufumbwe(Hehe)Ochuoga(Luo)Lamuriei(Samburu)Mtanda Mboo(Swahili)Muyonza(uganda)

Used for indigestion and also for lower abdominal pains in pregnancy. An infusion of the roots together with other medicinal plants is used for treating chest pains. Root decoction is also used for malaria ,in treating polio symptoms, chest pain , arthritis , rheumatism , gonorrhoea , constipation, yellow fever, epilepsy , kidney problems or as a cathartic, leaf decoction used for breast cancer (Kokwaro,1993).

Recently a medicine man in Loliondo, Tanzania claimed that he possessed a ‘wonder drug’ that could treat every ailment. This was later discovered to be *Carissa edulis*, a plant well known in Kenya and many studies are still being carried out to verify its medicinal activity. (Daily nation, 23rd March 2011)

7. *Catharanthus roseus*, (Maua, Luo)

Whole plant decoction mixed with the bark of *cassia hirsute*, *harrisonia abyssinica* is drunk for treating abdominal pains (Kokwaro,1993)

Historically Madagascar periwinkle had been used for various treatments, e.g. diabetes mellitus, high blood pressure and infection.(Trease and Evans, 2006)

8. *Diplorhynchus condylocarpus*, Itelembe(Nyika) Mtoga(Rufiji) Msonga (Nyamwezi).

A decoction of the root is part of the medicine drunk for gonorrhoea, testicle inflammation and dysentery. It is also a remedy for sore eyes. Powdered root and bark are used to facilitate birth. It is also a snake bite remedy (Kokwaro,1993)

9. *Hollarhena pubescens*, Mbelembele (Sukuma) Mtimeupe (Swahili) Nalupande (Mweera)

Leaves are pounded and mixed with water which is drunk as cure for stomach pains.

Roots are used in washing children with fever,for stimulating lactation in women and for influenza (Kokwaro,1993)

The roots,barks and seeds were used and found to have anti amoebic activity,effective in dysentery, haematuria, snakebite, bronchitis, antihelminthic (Trease and Evans, 2006).

10. *Rauvolfia caffra*, Mutondwet(Sebei) Mutu(Meru) Mwerere(kikuyu)

A bark decoction is drunk as a medicine for general body swellings ,rheumatism and pneumonia .Leaves used by circumcised boys to sleep on when wounds are still fresh .Root and stem bark used as an ascaricide while the powdered young flowers are for the treatment of sores .Root juice mixed with honey is applied on fractures. The bark is used as an astringent and as a colic remedy. Root decoction or infusion is drunk for

treating roundworms and tapeworms, and it also acts as a purgative. Bark decoction is for coughs, stitch and toothache.(Kokwaro,1993)

11. *Rauvolfia mombasiana* ,Kibombo (Digo)

Roots boiled with other plants and liquid drunk three times daily as a cure for gonorrhoea .this bitter root decoction is also drunk as a remedy for malaria.(Kokwaro,1993)

12. *Saba florida*

Boiled root decoction drunk for treatment of rheumatism.

13. *Schizogygia Coffaeoides*,Mbaika(Bondei),Mpelepele(Swahili)

Extract of root mixed with coconut oil used for “pele” (Swahili), sores on hands .the roots may simply be pounded, mixed with coconut oil and smeared on the sores. Fruits are reported to be toxic (Kokwaro,1993)

14. *Strophanthus eminii*, Msengululu(Nyamwezi),Msungururu(Sukuma)

Roots are soaked in water and children bathed in the liquid to cure fever. Boiled root decoction drunk twice a day as medicine for worms. Young branches are chewed for snake bite treatment. Roots are further used as an emetic, but the seed are reported to be toxic .As a febrifuge, pounded root are soaked in warm water, and apparently the escaping vapor inhaled while bathing the patient. Seeds are used to prepare an arrow poison, and any drug prepared from the plant must be used with care.(Kokwaro,1993)

**15. *Tabernaemontana holstii*, Kibombo(Luhya) Mkombo(Chagga),
Mworongondo(Digo), Nongoli(mwera)**

The latex is used to treat minor cuts or abrasions on the body , merely by permitting the milky sap to drop from cuts ends of the fruits up on the injured surface. Because of the presence of a rubber _like substance in this milky sap a film or a sort of a “new skin” is formed over the injured part. A decoction of the roots is taken as a remedy for stomachache and constipation, and also acts as a purgative. It is also taken to relieve headache and is said to cause people to sleep, i.e. it is a hypotonic. An infusion of the leaves is used as a head wash as a remedy for headache. A decoction of the roots is taken to relieve flatulence. Latex is further applied directly to sore eyes.(Kokwaro,1993)

16. *Tabernaemontana usambarensis*,KITONDO(luhya)

The latex obtained from the stem is allowed to drip from the cut ends of the stem upon an old wound to eliminate secondary infection and the wound soon heals.

17. *Nerium oleander*

The roots are mostly used as a diuretic and in skin disease.(Trease and Vvans)

2.2 CONVENTIONAL USES OF APOCYNACEAE

2.2.1 PLANTS WITH CARDIOACTIVE PROPERTIES

In plants cardiac glycosides appear to be more confined to the angiosperms. Cardenolides are more common and are particularly abundant in the apocynaceae and the asclepiadaceae.

Some of the main genera containing cardiac glycosides in the apocynaceae family include;

- *Adenium*
- *Acokanthera*
- *Strophanthus*
- *Apocyanum*
- *Cerebra*
- *Tanghinia*
- *Thevetia*
- *Nerium*
- *Carissa* and
- *Urechites*

STROPHANTHUS

Seeds of east African *Strophanthus kombe* were formerly official in the British pharmacopoeia (BP) and a tincture prepared from them was used similarly to digitalis.

The principal glycosides are k-strophanthoside, k-strophanthin-B, and cymarins which are all based on the genin strophanthidin.

Strophanthus gratus seeds contain 4-8% of ouabain (G-strophanthin), a rhamnose glycoside more stable than those present in a pure crystalline form and has been used as a standard in biological assays and for preparation of ouabain injections. (Trease and Evans, 2006)

OLEANDER GLYCOSIDES

These groups of glycosides which have an action similar to that of digitalis and have enjoyed some medicinal use characterize *Nerium oleander* and its relatives.

Principal constituents of the leaves are oleandrin and digitalinum verum. Oleandrin is the monoside comprising oleandrigenin (16-acetylgitoxigenin) and L-oleandrose.

The leaves also contain gitoxigenin and digitoxigenin glycosides. A new glycoside, nevidiginoside, has recently been obtained by activity directed isolation using the central nervous system (CNS) depressant effect of a methanolic extract of the leaves on mice.

The seeds of *Thevetia peruviana* (*T. neviifolia*) the yellow oleander, are a rich source of the glycoside thevetin A, which by partial hydrolysis and the loss of two glucose units yields peruvoside, the therapeutic cardioactive properties of which are well known.

Peruvoside consists of L-thevetose linked to the aglycone cannogenin. Thevetin has found use in continental Europe and is considered particularly useful in cases of mild myocardial insufficiency and where digitalis intolerance exists. (Trease and Evans, 2006)

***CATHARANTHUS ROSEUS* (Madagascar periwinkle, *vinca rosea*)**

Is a native of Madagascar and is abundantly naturalized in many regions, particularly in arid coastal locations.

Grown commercially for its medicinal uses in Australia, Africa, India and Southern Europe.

Cultivated as an ornamental plant almost throughout the tropical and subtropical world.

Chemical Constituents

Contains more than 70 alkaloids mostly of the indole type. It has medicinal importance owing to the presence of alkaloids like Ajmalicine, Serpentine and Reserpine, which are well known for their hypotensive and antospasmodic properties.

The most important alkaloids are the antineoplastic Vincristine and vinblastine, .The absolute levels of vinblastine and vincristine are considered far too low to explain the activity of crude extracts of *Catharanthus*. Various studies show the presence of other antineoplastic alkaloids in the plant (El-Sayed, et al. 1983; El-Sayed & Cordell 1981). Crude extracts of *Catharanthus* made using 50% and 100% methanol had significant anticancer activity against numerous cell types in vitro (at <15 mcg/ml) (Ueda, et al. 2002). Greatest activity was seen against multidrug resistant tumor types, suggesting there were compounds in *Catharanthus* that were synergistic or additive with antineoplastic elements by inhibiting resistance to them

Use in cancer.

Vinblastine and vincristine are all administered intravenously in their sulphate form. These solutions are fatal if they're administered any other way and can cause a lot of tissue irritation if they leak out of the vein.

Although these compounds are very similar in structure and have the same basic action, they have distinctly different effects on the body.

Most commonly used in treatment of the following type of cancers:

- Hodgkin's Disease
- Breast cancer
- Acute Lymphocytic Leukemia
- Soft tissue sarcomas
- Multiple Myeloma
- Neuroblastoma

Both vincristine and vinblastine are used in the treatment of various forms of malignant diseases in man. Vincristine is superior to vinblastine for the treatment of lymphosarcoma, but this is in part counter balanced, by its greater toxicity.

Vinca alkaloids are useful in the treatment of both malignant and non malignant diseases.

Though these alkaloids are useful in platelet and platelet associated disorders, it is in treating malignancy that they are truly an indispensable part of the pharmacopoeia.

Vinca alkaloids are exceedingly important in both curative and palliative regimens. The use of vincristine to treat thrombotic thrombocytopenic purpura is reported to be successful. This rare disease cause sporadic thrombosis of small vessels with consequent intravascular hemolysis. Vincristine has also been used successfully in the treatment of drug induced microangiopathic hemolytic anaemia.

The dose requirements of both alkaloids differ markedly, the weekly intravenous dose of vincristine for humans is 0.1-0.2 mg/kg, while that of vinblastine is approximately one tenth of this, Vinblastine is considered to have higher potency in bone marrow depression.

The side effects of these drugs are most probably caused by the metabolites of the alkaloids, since it is assumed that these disindole bases are unable to cross the blood brain barrier.

2.3 STUDIES DONE ON APOCYNACEAE.

Iboga root (*Tabernanthe iboga*), an African narcotic, contains alkaloids of the indole group. The alkaloid ibogaine has received attention as a possible anti addictive drug(P.poplik and P.skolnick)

Rauvolfia serpentina (Indian snakeroot) yields the alkaloids reserpine and rescinnamine which can be used in hypertension.

A study of the leaf extracts of five selected species of Apocynaceae used in traditional medicine (*Alstonia angustiloba*, *Calotropis gigantea*, *Dyera costulata*, *Kopsia fruticosa* and *Vallaris glabra*) were assessed for antiproliferative (APF) and antiplasmodial (APM) activities, and analysed for total alkaloid content (TAC), total phenolic content (TPC) and radical-scavenging activity (RSA).

As *V. glabra* leaf extracts showed wide spectrum APF and APM activities, they were further screened for saponins, tannins, cardenolides and terpenoids.

Leaf extracts of *A. angustiloba*, *C. gigantea* and *V. glabra* displayed positive APF activity. Dichloromethane (DCM) extract of *C. gigantea*, and DCM and DCM:MeOH extracts of *V. glabra* showed strong APF activity against all six human cancer cell lines tested. DCM extract of *A. angustiloba* was effective against three cancer cell lines.

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Against MCF-7 and MDA-MB-231 cell lines, DCM extract of *C. gigantea* was stronger than standard drugs of xanthorrhizol, curcumin and tamoxifen. All five species were effective against K1 strain of *Plasmodium falciparum* and three species (*C. gigantea*, *D. costulata* and *K. fruticosa*) were effective against 3D7 strain. Against K1 strain, all four extracts of *V. glabra* displayed effective APM activity. Extracts of *D. costulata* were effective against 3D7 strain.

Selectivity index values of extracts of *A. angustiloba*, *C. gigantea* and *V. glabra* suggested that they are potentially safe for use to treat malaria. Extracts of *K. fruticosa* had the highest TAC while *D. costulata* had the highest TPC and RSA. Phytochemical screening of extracts of *V. glabra* also showed the presence of terpenoids, tannins and saponins

3.0 METHODOLOGY.

This research is going to be carried out from April to August and involves an extensive literature review of the apocynaceae family regarding its traditional and modern/conventional use.

The main sources of information to be reviewed include:

- 1. Journals.**
- 2. books .**
- 3. articles.**
- 4. internet.**

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