

**Useful drugs and cancer causing chemicals in  
Kenya medical and toxic plants**

**Professor Gerald M. Mugeru**

**Inaugural Lecture**

**University of Nairobi  
Education Lecture Theatre II  
22<sup>nd</sup> November 1977**

**USEFUL DRUGS AND CANCER  
CAUSING CHEMICALS IN  
KENYA MEDICINAL AND TOXIC  
PLANTS**

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Professor Gerald Munene Mugeru was appointed to the Chair of Veterinary Pathology and Microbiology in 1971 at the age of 36 years. He first joined the Department in 1965 as a Lecturer. He was promoted to Senior Lecturer and Head of the Department in 1968. He has been Dean of the Faculty of Veterinary Medicine from 1971 to 1975.

Well known in Veterinary and Medical circles particularly for his research into liver and kidney cancer.

He was born in Kirinyaga District of Central Province. He got his Primary education in Kirinyaga and Nyeri and Secondary School at Alliance High School. On leaving Alliance High School, Kikuyu, in 1954 Professor Mugeru went to Makerere where he gained Diploma in Veterinary Medicine. He taught large animal medicine and surgery at Makerere Veterinary School in 1960-1961.

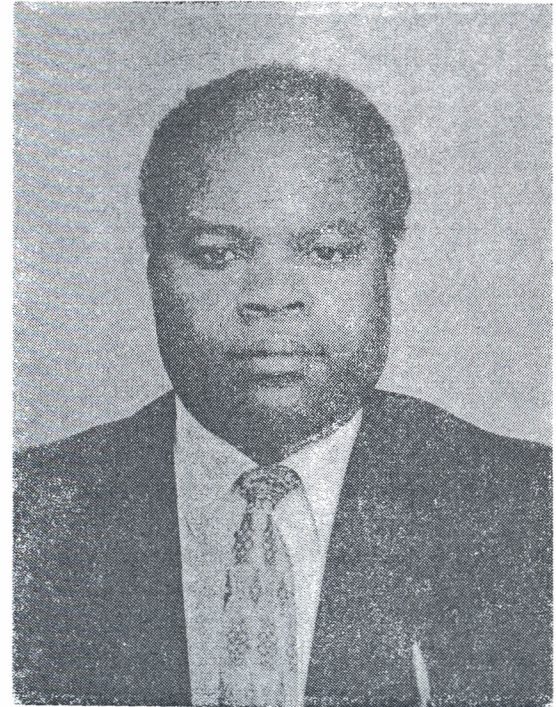
In 1962, on a scholarship to Michigan State University, he took his M.Sc. in Veterinary Pathology and Microbiology and three years later was awarded his Ph.D. with a thesis entitled "Cycad Toxicosis and Carcinogenesis in Animals".

This thesis was of vital interest not only to veterinary scientists but also to the medical profession because it dealt with the cancer-inducing properties of a palm-like plant eaten by cattle and humans in East Africa. There thus arose the possibility that it could be an agent in causing cancer of the liver and kidney, a common human disease in East Africa.

The Department of Veterinary Pathology and Microbiology is responsible of teaching veterinary students diseases of domestic and wild animals and causes of the diseases. The Department also teaches the students the methods of diagnosing diseases of animals. The Department is very active in research in animal diseases and basic medical science.

Professor Mugeru has published more than forty scientific articles. The subject of the lecture today is one of major research project in the Department.

Professor Mugeru is married to a Nurse Tutor with two sons and two daughters. When not teaching, carrying out research or writing he is often travelling abroad to attend veterinary and scientific conferences.



*Professor Gerald M. Mugeru*

# USEFUL DRUGS AND CANCER CAUSING CHEMICALS IN KENYA MEDICINAL AND TOXIC PLANTS

By

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*Professor of Veterinary Pathology*

Kenya has a great variety of plants containing powerful active principles having medicinal or toxic properties. Some of the toxic principles have beneficial effects in treatment of disease conditions if given in small quantities which does not effect the animal or man but affects only the causative agent or improves the function of certain body organs.

A large number of our plants of medicinal value are common weeds generally found in the country which have not been carefully and systematically studied. A number of medicinal plants and toxic plants have been studied chemically and physiologically and their action on the animal body has been studied, and has confirmed their use by traditional medicinal people as a drug or as poison used in the art of poisoning. Physiologically active components have been separated at the Department of Veterinary Pathology and Microbiology of the University of Nairobi. The active components have been tested on laboratory animals for treatment of various disease conditions and proved effective against several types of cancer, bacterial infection, parasitic infections, Hypertension, cardiac diseases, and other conditions. Other plants valued by traditional medicine men have been found inert by physiological tests and contain no active constituents. The therapeutic or medicinal activity of plants usually depends on the presence of what are known as active principles. All plants contain a structural Framework based on cellulose and ligning the vital cells contain protoplasm, such nutrients as sugars, starches, insulin, and chlorophyll which help to form them. Most plants exhibit in addition substances having individual properties. When such substances exert an influence on the structure or function of animal body. They are known as "active principle." It is the presence of such principles that therapeutic value of the plant depends. The active principles have been extracted from leaves, stems and roots of medicinal and toxic plants. The plants are collected in large quantities, dried chopped up and ground into a fine powder. About one Kilogram of ground material

is used for extraction isolation and fractionation. The plant extracts are tests against animal tumours. Bacterial infections using both Gram positive and gram negative organisms, parasites and the physiological effect and toxic effect on the animal body. The National Institute of Health at Washington U.S.A. in their National Cancer Institute has also been collecting material from plants in Kenya and have been testing the plant extract for their antitumour activities in animal tumour system.

## 1. Anticancer Drugs

### (a) Indicine-N-oxide

This is a pyrrolizidine alkaloid isolated from plants of *Heliotropium* species. These plants are perennial herbs with large leaves and long spikes of white flowers. They are common in Kenya Highlands especially on the Forest edge. Two species of *Heliotropium* are used in traditional medicine in East Africa. The juice of the leaves of the *Heliotropium Scothae* pendles (Mugwata Ngundu) which grow in great abundance in Nyambeni Hills in Meru District and Kangaita Forest in Kirinyaga District is used by the tribes around Mt. Kenya for treatment of wounds, local inflammation and insect bites. The leaves are also boiled in water and the mixture taken for treatment of gonorrhoea. In Tanzania *Heliotropium supium/martelli* or *Heliotropium Indicum* boiled leaves is used as a Febrifuge, especially in Febrile attacks to which women are subject after childbirth. It is also used as a colic remedy for children and as expectrant, the fresh juices of the two species in Tanzania is applied to sore eyes, gums, boils, sores caused by biting insects and for cure of snake bites. The *Heliotropium* species mixed with other plants ground and suspended in water has been used for treatment of East Coast Fever in cattle as drench after the animal swollen lymph nodes have been branded with a hot iron bar by the Kikuyu tribe around Mt. Kenya. Indicine-N-oxide possess significant antitumour activities against following experimental tumour lines. Mouse leukemia 1210, P388 lymphocytic leukemia. Melanosarcoma B-16 and walk 256 carcinosarcoma.

The mechanism of action is by inhibition of mitotic division. The drug acts on tissues which are rapidly dividing as cancer cells, bone marrow, thymus, lymphocytes in the lymph nodes and spleen,

tests, ovaries and skin germinal layer. The drug is currently on human clinical trial at the National Cancer Institute with leukemia, solid carcinoma and sarcomas.

### (b) Thalicipine

Thalicipine is a dimeric isoquinoline alkaloid of *Thalictrum* spp. of the family Ranunculaceae. It has been isolated from *Thalictrum dyscarpum*, *Thalictrum Minus* and *Thalictrum rhynchocarpum*. *Thalictrum rhynchocarpum* (Mumori Kikuyu) is a glabrous perennial herb bearing much divided leaves with orbicular segments. It is common at the forest edges in Mount Kenya especially Kangaita area of Kirinyaga District and Kamuruana Hill. Ground leaves and roots have been used as a purgative and as homicidal poison. Thalicipine is active against the following experimental tumours, the walker 256 carcinosarcoma and mouse leukemia L-1210. Thalicipine inhibit the incorporation of thymidine into DNA and uridine into RNA. It also inhibits the early steps nucleotide triphosphate biosynthesis. This inhibition of nucleic acids thereby prevent cell growth. Thalicipine is at third stage of clinical test at National Cancer Institute in Washington.

### *Vinca Alkaloids*

These are alkaloids isolated from *Vinca rosea* or *catharanthus roseus*. This is a much branched herb up to 1m. tall with white or rose coloured flowers. The plant is a native of Madagascar and is commonly cultivated as an ornamental plant throughout the tropics. It is commonly seen growing in bushes in dry areas like Machakos District. Two alkaloids from this plants vinblastine and vincristine are established in cancer chemotherapy as of clinical value. The two alkaloids are active in several animal tumour system such as Murine P1534 and P388 leukemia. In human these alkaloids are used for treatment of lymphomas, especially Hodgkin's disease, children acute leukemia choriocarcinomas and embryonal or mesenchymal carcinoma such as Wilm's tumour, neuroblastoma, rhabdomyosarcoma and carcinoma of the testis. Responses have also been obtained with some frequency in oat cell carcinoma of the lungs breast carcinoma and some central nervous system neoplasms.

### *Maytansine:*

Maytansine is a novel ansa marcolide isolated from plants of celastraceae family. *Maytansine sergalensis* (Mwenyike Embu) *Maytansine buchananii* (Mdiziadzia Digo) *Maytansine Mossambicensis* (Muthuthi Kikuyu) Extracts from these plants have been used in traditional medicine in humane for treatment of venereal diseases, rheumatic pains and swellings of various kinds. Maytansine is active against experiment animal tumours including sarcoma 180, Lewis Lung carcinoma, B16 melanoma and Walker 256 carcino-carcinoma. It inhibit the incorporation of thymidine into DNA in the cells and induces mitotic arrest at metaphase stage. Maytansine is currently undergoing Clinical trials in human at National Cancer institute in Washington.

### *Bruceatin*

Bruceatin is Quassinoid isolated from *Brucea antidysenterica* (Mukuriahungu, or Murianugu — Kikuyu). This is a tall tree and its powdered roots and leaves have been used by the Kikuyu for relieve of abdominal pain. In Ethiopia the juice from the leaves has been used for treatment of warts. Bruceatin is active against animal experimental tumours including P388 leukemia, L1210 leukemia, Lewis lung carcinoma B16 melanoma and Walker 256 carcinosarcoma. The mechanism of antitumour action of Bruceatin is through an effect on protein synthesis.

### *Vernolepin and Vernomenin*

These are elemenolide dilactones isolated from *vernonia hymenolepis* (Mucatha Kikuyu). The two chemicals have tumour-inhibitory activity against Walker 256 carcinosarcoma in rat.

### *Gnidin, Gnitrin, Gnidicin*

These are diterpenoid isolated from *Gnidia lamphratha* and *Gnidia kraussiana* which are perenial herbs up to 50 cm. high with a herbaceous stem found commonly in Machakos district and known to be very poisonous to livestock. These diterpenoid have a high activity against P388 leukemia in mice.

### *Lapachol*

3 (methyl-2 butenyl)-2-hydroxy-14 naphthoquinone and its derivative dichloroallyl lawsone are quinones isolated from plants of the family bignoniaceae. Lapachol occurs in *Lawsonia inermis* which is grown in Coast Province of Kenya as medicinal plant and used for various treatment in the Coast. Lapachol has a significant antitumour activities against Walker 256 carcinosarcoma. The Dichloroallyl lawsone is a considerably more potent antitumour agent to walker tumour than lapachol.

### *Conclusion*

Recent developments in the field of anticancer drugs isolated from plants are yielding chemical compounds active against many different experimental tumour system. These compounds provided a basis from which attempts can be made to develop practical drugs. Since there is merit in the concept of chemotherapy of cancer, principles from plants should play an increasingly important role in this field as more become available.

### (2) *Antimicrobial Drugs*

Over the last thirty years an intensive effort has been made to uncover new clinically useful, antibiotics. This search has resulted in the preparation in more or less homogeneous form of more than one thousand antibiotics. However, of this large number only about a dozen or so have found significant clinical use. For a number of reasons, the search for new antibiotics has been mostly intensive among the lower plants especially streptomycetes and a few fungi. Certain disease entities however, remain serious problem and some of the major antibiotics have considerable drawbacks in terms of limited antimicrobial spectrum or serious side effect.

These factors call for a continuous search for a new antimicrobial agents and especially those that can be safe and effective against clinical infections caused by fungi, viruses, mycobacteria and gram-negative organisms.

It is rational therefore to suppose that clinically and commercially significant new antimicrobial agents with activities supplemental to

and structures widely different from those in current use might be found in sources which have hitherto not as thoroughly explored as traditional microorganisms. A new area that might spring to prominence in future as a source of these agents is higher plants. Alkaloids and organic acids from plants which have been reputed to have medicinal values have been extracted and have been screened against gram-positive and gram-negative bacteria and fungus in vitro using agar dilution-streak. The criteria of useful activity are inhibition of one or more of the test organisms and reproducibility of the activities in following organisms *Pseudomonas aureginosa*, *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pyogenes* and *Candida albicans*. Pure extracts from *Heliotropium Scottae* have shown activities against *Pseudomonas aureginosa*, *Bacillus subtilis*, *Staphylococcus aureus*, *Streptococcus pyogenes* and *Candida albicans*. The active principles are Indicine-N-oxide or an organic acids. *Dracaena usambarensis* (Mronje Digo). This is a well branched tree to 30 ft high with black and rugged bark. It is very common in Coast Province. Roots have been used for treatment of gonorrhoea. The extract from this plant have shown activities against *Staphylococcus aureus*, *Pseudomonas aureginosa*, *Bacillus subtilis*, *Escherichia coli*. The active principles in *Dracaena* are organic acids. *Aerva Persica*. This is a wooly erect perenial herb which grow in dry parts of Southern Meru District, and Narok. The flowers are ground into a paste with water and is given to cattle as a remedy for East Coast Fever. An alkaloid extracted from the flower of the plant has shown activities against *Staphylococcus aureus*, *Streptococcus pyogenes* and *Candida albicans*.

*Thalictrum rhynchocarpum*. Thalicarpine isolated from *Thalictrum rhynchocarpum* which is described in anticancer drugs has shown activities against *Pseudomonas aureginosa*, *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus* and *Candida albicans*.

*Warbugia ugandensis* (Muthaiga-Kikuyu). This is a forest tree about 90 - 140 ft tall. It is very common in Muguga Forest in Kiambu District. It is used for treatment of various conditions. An organic acid isolated from the plant bark has shown activities against *Pseudomonas aureginosa*, *Bacillus subtilis* and *Staphylococcus aureus*.

*Maytenus mossambicensis* (Muthuthi-Kikuyu). This is a shrub which grow in Mt. Kenya area especially Kamuruana hill in Kirinyaga

District. Roots and leaves from the plant has been used for treatment of various diseases. An organic acid isolated from the plant has shown activities against *Pseudomonas aureginosa*, *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pyogenes* and *Candida albicans*.

*Withania somnifera* (Mwanzo-Kamba). A small shrub growing in dry areas of Eastern Province and Masai land. The plant is used for treatment of diarrhoea. An alkaloid isolated the plant leaves has shown activities against *Staphylococcus aureus* and *Streptococcus pyogenes*.

### Conclusion

While no compound from higher plant has come into significant clinical use as antibiotic, this study has indicated availability of large range of extractable antimicrobial agents with high potentiality and encourages the belief that clinically active agents may be found and earn a significant place in human and Veterinary therapy.

### 3. Anti-Theileria activities.

East Coast Fever (E.C.F.) is the most important tick-bone disease of cattle in Eastern and Central Africa. There is no drug for treatment of the disease and no vaccine. Alkaloids isolated from *Maytenus* spp., *Heliotropium scottle*, *Thalictrum rhynchocarpum*, *Aerva persica* and *Spirostachys venenifera* have demonstrated anti-Theileria activities. These alkaloids induces rapid necrosis of lymphocytes in Thymus, lymph nodes, Spleen and lymphocyte precursor in the bone marrow also causing destruction of *Theileria parva* in lymphocytes.

### (4) Other Drugs

#### Cardiac glucosides

These are drugs used to strengthen a weakened heart and thus allows the heart to function efficiently. Their primary action is to increase the force of ventricular contraction by direct action on the myocardium, thus increasing cardiac output and secondarily reducing the venous pressure.

Cardiac glucosides occur in *Strophanthus Kombe* and other *Strophanthus* Spp. *Thevetia Peruviana*, *Calotropis Procera*, *Carissa*



edulis, Acokantheria Longiflora, Eleodendron buchananii, Omithogalum Longibracteatum, Urginea altissima, and Bowiea volubilis.

### *Hypotensive Drugs*

Ruavolfia caffra (Mutu) growing in the lower area of Kirinyaga District and Ruavolfia mombasiana growing in the Coast regions of Kenya contain an alkaloid termed reserpine. Reserpine is used for treatment of hypertension. Ruavolfia mombasiana has higher content of reserpine than the commercially current used Rauwolfia serpentina a shrub found in India, Pakistan, Burma, Slam and Java.

### *Antinflammatory Drugs used for treatment of gout Colchicine*

Colchicine relieves the pain and inflammatory response of acute gouty arthritis. Colchicine occur in Gloriosa simplex which is a climbing herb and widely distributed in Kenya.

### *Antispasmodic Drugs*

These drugs depresses the function of the parasympathetic division of the autonomic nervous system and because they relieve spasms of smooth muscle tubes, such as the gastrointestinal tract bronchi, ureters and bile ducts, they are commonly known as antispasmodic drugs. The group of these drugs have been isolated from a number of plants of solanaceae family. In Kenya the plant known as Datura Stramonium which is a bushy annual herb attaining a height of about 1.5 m. which grows on the road side and non-cultivated land. The plant contain antispasmodic alkaloids either as hyoscyamine or hyoscine is the predominant alkaloid.

### *Drugs for treatment of Asma*

Ephedrine. This is used for the treatment of asma and hay fever to constrict the capillaries in the nose in the treatment of colds and sustain the blood pressure in spinal anaesthesia and other forms of hypotension such as circulatory collapse, shock and haemorrhages. The seeds of Sida Cordifolia which is an erect woody shrubs very common as weed in Machakos District contain alkaloid ephedrine.

### *Conclusion*

A large number of toxic plants in Kenya contain powerful toxic principles and these toxic principles when introduced in small quantities have beneficial effects in treatment of disease conditions and their properties and actions are similar to the imported and often expensive remedies and form an excellent substitute as in atropine group of drugs, for asthma and hypertension.

The utilization of Kenya shrubs for production of drugs should be encouraged. It is therefore hoped that this lecture will give an impetus to organised and well co-ordinated research on indigenous drugs using different disciplines and professional herbalists in the country. The identification of indigenous plants used for drugs and establishment of medicinal plants by pharmaceutical industry will be of great economic advantage to the country and will save Kenya a lot of needed foreign currency.

### *(5) Carcinogenic Chemicals*

Plants, including those used as food and medicine by man and animals, are potential sources of carcinogenic chemicals.

### *Cycads:*

These are palm-like plants which are distributed in nine genera. The two genera found in coastal region of East Africa (Kenya, Tanzania and Malagasy) are cycas and Encephalartos. In Kilifi and Lamu districts of Kenya the stem and seeds of cycas thouorsii or cycas circinalis (swahili mtapo or mtapuu) and Encephalartos hildebrandtii (swahili mtapo mwitu or mtapu mwitu) provide a source edible starch. The starch prepared from these plants is used as an emergency starch supply for families during famine or wherever there is shortage of food. There are several stages of preparation of these starches to remove the toxic factor. The starch before it is detoxicated is toxic to man and livestock (Mugera+Nderito 1967) Mugera and Nderito (1968) induced tumours in the liver, kidneys and lungs of rats after chronic ingestion of starchy kernel prepared from Encephalartos hildebrandtii.

The toxic and carcinogenic factors in these plant is cycasin, methylazoxy B-D glucoside which is hydrolysed in the animal intestine

to an aglycone methylazoxymethanal  $\text{CH}_3\text{NO: NCH}_2\text{OH}$ . Methylazoxymethanal is the proscimate carcinogenic chemical liberated from the cycasin by the action of the intestinal bacterial B-glucosidase in the intestinal tract. Methylazoxymethanal is carcinogenic by both the oral and the intraperitoneal routes, while cycasin is active only by the oral route.

#### PLANTS CONTAINING PYRROLIZIDINE ALKALOIDS

Pyrrrolizidine alkaloids occur in several genera of plants like *Senecio*, *Crotalaria* and *Heliotropium*. Many of these alkaloids are of considerable Veterinary and Medical interest and economic importance, because of their toxic action on grazing animals, probably on human population as they find their way to the food by contamination of cereals and their use as herbal medicine. The toxic action of Pyrrrolizidine alkaloids takes the form of chronic liver damage.

In East Africa *Senecio moorei* (Kikuyu Muguruka) contain a toxic and carcinogenic alkaloid Ruwenine. The plant causes deaths to livestock in many part of East Africa. Kamau and Mugeru 1975 induced tumours of the liver in rats after prolonged feeding with dried young shoots of *Senecio moorei*. In Kenya *Cynoglossum geometricum* (Kikuyu Muramata) and *Heliotropium scottii* (Kikuyu Mugwatangondu) and *Heliotropium indicum* are used in herbal medicine and several species of *Crotalaria* are used in Tanzania and Ethiopia for herbal medicine. *Gynoglossum* and *Heliotropium* species contain indicine-N-oxide. Mugeru and Ward (1976) have induced tumour of the liver to rats after several injection with indicine-N-oxide. *Crotalaria* Spp. contain a pyrrrolizidine alkaloid termed monocrotine. Schoental and Head (1955) induced hepatoma in rats after treatment with monocrotine. The work of Schoental (1968); Schoental + Coady 1969; Schoental, Fowler and Coady 1970, Kayanel Heath 1969 and Schoental and Caranagh 1972 has demonstrated that the pyrrrolizidine alkaloids can induce acute and chronic disease of the liver and tumours of the liver, lungs and certain other organs even with a single dose.

#### BRACKEN FERN

Bracken Fern is widely distributed in East African highlands. Ingestion of the plant produces accumulative type of poisoning and

symptoms occur after the plant has been consumed for two or more months. The major toxic manifestation following ingestion by cattle is chronic enzootic haematuria. Bracken Fern poisoning has been associated with the tumour of urinary bladder in Kenya cattle in Limuru area and other areas next to the Forest. (Mugeru + Nderito (1968). Feeding studies has demonstrated that Bracken Fern induce tumours in urinary bladder of cows. (Evans + Mason 1965; Price and Pamukeu). Feeding experiments in rats has shown that all parts of the bracken Fern are carcinogenic (Hirono, Fushimi, and Mori 1973) carcinogenic component of Bracken Fern is shikimic acid (Evan and Osman 1974).

#### Conclusion:

It is important in Kenya, as in every other country, to screen plants that are used as traditional remedies in every area of the country. Priority should be given to plant species which belong to the genera known to contain pyrrrolizidine alkaloids. Such hepatotoxic plants are a hazard to health not only of the people who ingest them directly but if ingested by lactating Females their milk will be toxic. The milk of lactating cattle which has ingested the plant is also toxic. This is of great practical importance as the very young for whom milk is the principal constituent of diet, are many times more susceptible than the adults to the toxic pyrrrolizidine alkaloids.

The public should be educated about the danger of these plants in their farms as they cause great losses of livestock and are dangerous to humane life. It is likely that more than realized, some unexplained incidences of cancers of different organs in man and animals may be due to the ingestion, at some previous occasions, of insiduously acting toxic or medicinal plants.

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