Inaugural Lecture Series 132

MEDICINAL PLANTS, PARASITES AND SNAILS IN HEALTH

By

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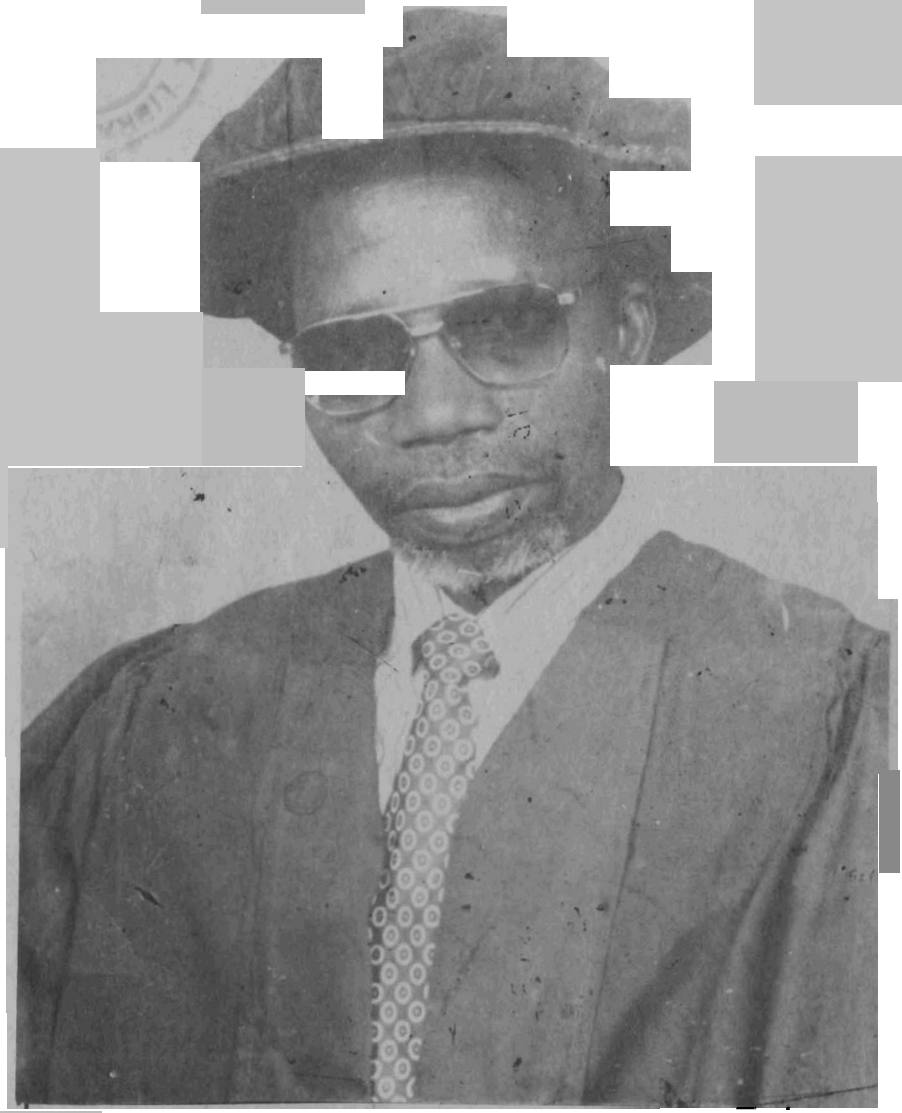
OBAFEMI AWOLOWO UNIVERSITY PRESS LIMITED



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An Inaugural Lecture Delivered at
Oduduwal Hall, Obafemi Awolowo University,
Ile-Ife, Nigeria.

On

Tuesday 16th March, 1999

Obafemi Awolowo University,
Ile-Ife, Nigeria.

Obafemi Awolowo University Press Limited, 1999

ISSN 0189 - 7848

Printed by
Obafemi Awolowo University Press Limited
Ile-Ife, Nigeria.

The creation of heaven and earth is recorded in the Bible (Genesis 1 - 2), stars (Isaiah 40 : 26), and the universe (Job 25 : 7 - 14; Psalm 19 : 1, Isaiah 42 : 5). Recent scientific evidence regarding the theory of evolution of the human race suggests that *Homo erectus* migrated from Africa about one million years ago. However, *Homo sapiens* (which evolved from *Homo erectus*) migrated from Africa about 100,000 - 200,000 years ago. Furthermore, evidence from DNA analysis strongly supports the hypothesis that the original home of the human race is Africa! One may allude to the Yoruba mythology which claimed that Africa, specifically, ILE-IFE, as the centre of the human creation! The evolutionary theory of the "great bang" occurred billions of years ago while we were told in the Bible that the creation took 6 days and that God rested on the seventh day. If we recall a quotation in the Bible- "for a thousand years in thy sight are but as yesterday when it has past and as a watch in the night" (Psalm 90 : 4); days quoted in the Bible could therefore not be interpreted literally. The authors in the Bible thought and wrote like men of their time. "The approach of the authors was the approach of a particular civilization and mentality" (see God speaks to us, *The New American Bible, 1971)* "The views of the author of Genesis on the make up of the universe were as unscientific as those of any amateur at any time; and if he was not writing about the universe's composition at all but religion, then we have no more right to accuse him of error".. The editors concluded that in "scientific matters the Bible speaks as any non-specialist will speak". Many of the discords between scripture and science have arisen out of the attempt to play the scripture in a key note intended by the writer. "God created man in his own image ... and God blessed them, and God said unto them ; Be fruitful and multiply and replenish the earth, and subdue it, andhave dominion .... over everything that moveth upon the earth" (Genesis 1 : 27 - 30). The disobedience of God by Adam and Eve by eating the forbidding fruit marked the beginning of the tribulations of man on earth. "For dust you are and to dust you shall return" (Genesis 3 : 19). God created all forms of life on earth, - plants, animals, parasites and man-kind. There are copius citations in the Bible on : vegetation with healing qualities such as the use of poultice applied, to the ulcer of king Hezekiah (2 Kings 20 :), leaves of fruit trees growing along river on either bank that will be medicinal (Ezekiel 47 : 12). Disease is defined in the *Webster's II New Riverside Dictionary* as an abnormal condition that impairs normal functions. A disease state in our society is regarded as either physical or spiritual in nature. In the Bible, the spiritual aspect is confirmed by many healing miracles of the sick. Some of these diseases are cases of abscess (2 Kings 20 : 7), blindness (Matthew 9 : 27 - 31, Mark 8 : 22 - 26, John 9 : 1 - 7, Luke 8 : 35), dysentery (2 Chronicles 21 : 12 - 19, Acts 28 : 8, fever (Matthew 8 : 14 - 15), itch (Deuteronomy 28 : 27), leprosy (2 Kings 5 : 1) and ulcers (Luke 16 : 20). Although, the aetiological agents of these diseases were not stated, the list provided in this lecture could have been caused by protozoan parasites (*Entamoeba histolytica*), helminths

(Onchocerca volvulus, Trichuris trichiura, Schistosoma mansoni, S. haematobium, Hookworms), bacteria and other agents.

A parasite is defined in the *Oxford Advanced Dictionary* as an animal or plant that lives on or in another and gets its food from it. A professor of Parasitology once claimed that the only parasite he had was his wife! God's creation was good until the work of the evil one. Man became wise and was destined to die. When God sent flood to destroy earth creatures, Noah took both "clean and unclean" animals with him into the ark. Were parasites living a symbiotic relationship between man, animals and plants before the arrival of the evil one or its evolution? It was possible to invent a very potent vaccine against the small pox virus because of the simple nature (not clever, stupid nature !) of this virus. But others such as the AIDS virus, malaria parasites and schistosomes are very clever. For example, the schistosome parasite is immunologically invissible to the host's antigens. Is this the work of the evil one? Are carcinogens, mutagens and toxic components from plants and natural sources the creation of the evil one? Plants, Parasites and snails including man are all destined to die! However, man is endowed with tools to manipulate the good nature in medicinal plants and snails to control the evil one - parasites for better health.

"Ninu gbogbo eranko ti Eledumare da sile aiye, awa omo eniyan losoro" which means the human race is the cleverest and most unpredictable of God's creatures. This dominion of man over living and non-living things is the major attribute possessed by him in conquering his environment and space. Mr. Vice-Chancellor, Sir, this lecture titled "Medicinal Plants, Parasites and Snails in Health" deals with our efforts, and those of others in manipulating plants, parasites and snails for better health. Plants and animals suffer from a range of parasites, including protozoa, nematodes, arthropods and fungi. They show a variety of protective adaptation. Some plants produce chemicals - phytoalexins - specifically in response to attack by micro-organisms and parasites. The anti-nematode effect reported for known phytoalexins suggests that these compounds have nematostatic rather than a nematocidal effect (O'Neill, 1986). The social and economic effects of parasitic diseases (arising from their morbidity and mortality) cannot be estimated. For example, *Entamoeba histolytica* may invade tissues and variable symptoms which include diarrhoea or dysentery with loss of blood, ulceration of the intestine, liver involvement may lead to abscess formation. Three parasites (*Ascaris lumbricoides, Trichuris trichiura* and hookworms - either *Ancylostoma duodenale* or *Necator americanus*) are usually found occurring together in our tropical environment (Fasuyi, 1983; Adewunmi *et al.,* 1993). About one billion persons are infected with these parasites globally. Migrating larvae of *A. lumbricoides*, and hookworms cause pneumonitis or pneumonia while in the lungs. The severity of the disease is dependent on the density of adult

worms and nutritional state of the subject. At high densities, massed worms (*A. lumbricoides*) in the small intestine can cause intestinal obstruction and pain possibly followed by gut perforation or volvulus. High adult *T.trichiura* presence in the colon especially in under-nourished children can result in severe dysentery, anaemia, rectal prolapse and may be fatal. Hookworm disease can cause blood losses of about 0.15 ml per worm per day and anaemia is a prominent symptom in many cases. *Onchocerca volvulus*, the causative agent of river blindness is transmitted by species of the black fly, *Simulium.* Another severe pathological damage due to *O. volvulus* is onchodermatitis which is a range of painful and disfiguring skin changes. A parasitic disease in Nigeria which is very important and often neglected is ***schistosomiasis.*** Schistosomiasis has a long history in Nigeria. It is essentially an infection of rural and agricultural communities. Transmission of the disease is highly focal. The disease affects about 200 million people (WHO, 1990). Four species of the genus *Schistosoma* are important parasites of man, namely, *S. mansoni, S. haematobium* (adult worms in vesical veins of the bladder), *S. japonicum* and *S.intercalatum.* Infection of the trematodes are caused by cercariae liberated from intermediate snail hosts namely *Biomphalaria, Bulinus africanus* and *truncatus* groups, *Oncomelania*, *B. forskalii* and *B. africanus.* Cercarial dermatitis occurs during the cercarial invasive stage. The pathology of the disease is the direct or indirect result of the host's immunological responses to schistosome eggs (Whitefield, 1987). The adult schistosome worm is coated with the host's antigens and therefore immunologically invisible, living relatively harmless in blood vessels, but producing eggs which become trapped in various tissues, including the liver. There they produce enzymes that are antigenic and stimulate local cell-mediated delayed hypersentivity reactions leading to the formation of granulomas. In heavy infections caused by *S. mansoni*, the granulomatous reaction can extend into the gut lumen as pseudopapillomas, with or without egg calcification. This can result in colonic obstruction and blood loss. Eggs trapped in the liver set up a complete series of cellular reactions. This produces liver enlargement and following portal hypertension, spleen enlargement also occurs. Damage to portal circulation causes collateral circulatory shunts to be set up and this allows eggs to by pass the filtering function of the liver. There after eggs are lodged in the lungs in large numbers causing degenerative pulmonary blood vessel changes which later brings about cardiac pathology (Whitefield, 1987). Granulomatous reactions in *S. haematobium* infections lead to fibrosis and calcification induce haematuria, dysuria, hyperplasia of the bladder lining, partial ureteric blockade, and secondary damage to the kidneys (Whitefield, 1987).

FRESHWATER SNAILS

I. Economic snails

There are economic, medical and non-economic snails, all ofwhich are important in the biodiversity of nature. The economic snails are very small forms of livestock (CTA, 1993). There are many species; those with the greatest relevance are the giant or land snails - *Achatina* and *Archachatina* species. Keeping of snails requires good husbandry. Snail meat contains high quality protein (12 - 16.0 %), iron (45.0 - 50.0 mg/kg), and fat (0.5 - 0.8 %) (Cobbinah, 1993). Freshwater Prosobranchs are important sources of animal protein in some parts of Nigeria (Reid, 1989). Some of the local Prosobranchs (also eaten in southeastern states) identified by our group in parts of southwestern Nigeria include *Tympanotonos fuscatus, Potadoma freethi, Pachmelania bryonensis, P. fusca* and *Lanistes ovum* (Adewunmi and Olorunmola, 1998). *T. fuscatus* (Linnaeus, 1758) like *P. bryonensis* (Wood, 1828) are collected in streams and rivers in the southeastern states of Nigeria for food. They form a regular dietary item and are considered inexpensive and tasty (Reid, 1989). *P. freethi* is eaten by villagers near streams and are found in rural markets. Their shells are ground up and included in local poultry feed and scouring powder. *L. ovum* inhabits the same habitat as *P. freethi*, but, it is of less importance than *P. freethi*. Systems for snail farming are available (Runham, 1989). Farmers should form groups in which specialization is possible and continuity of production can be established and sustained.

II. Medical Important snails

Medical important snails serve as intermediate hosts of human and animal parasites (Rollinson and Southgate, 1987; Frandsen and Christensen, 1984). The intermediate host spectra of *Schistosoma mansoni* are *Biomphalaria* species while those of *S. haematobium, S. rodhaini, S. intercalatum, S. mattheei, S. bovis* are *Bulinus africanus* species complex. *S. japonicum* is transmitted bypopulations of the polytypic *Oncomelania hupensis* of which there are six subspecies (Davis, 1980) which are found in China, Taiwan, the Philippines and in Japan. In Nigeria, *B. pfeifferi* transmits *S. mansoni* (Adewunmi *et al.*, 1990b, 1991b, 1993). *B. pfeifferi*, the snail host for *S. mansoni*, was found in the University Dam, Obafemi Awolowo University, Ile-Ife in 1989 with population peaking during February, March and April. *S. mansoni* infections in *B. pfeifferi*, as confirmed by results from mice infections, were found throughout the period of observation. Transmission of *S. mansoni* was demonstrated throughout the year in this man-made dam (Adewunmi *et al.*,1990b). *S. mansoni* infected *B. pfeifferi* were encountered in two of the seven water contact sites. The pattern of occurrence of infection with *S. mansoni* differed markedly between a pond site and a stream site in another study area (Adewunmi *et al.*, 1991b). *B. pfeifferi* shedding cercariae of the mammalian type were found at four contact sites around Erinle dam. *B. pfeifferi* was the predominant schistosomal transmitting snails recovered at all the contact sites around the Erinle dam. Available data have shown that *S. haematobium* is more common in West Africa than *S. mansoni* (Ogunnowo, 1990). *S. haematobium* is transmitted in Nigeria by *B. globosus* and *B. truncatus* (Adewunmi *et al.*,1990b, 1991b, 1993). *B. globosus* infected with mammalian cercariae were detected in some of these Human Water Contact Sites. The lack of consistency in the transmission pattern regarding seasonality and focality of transmission makes a thorough knowledge on the transmission pattern essential for the incorporation of community-based focal molluscicide with *Tetrapleura tetraptera* into the integrated approach to control of schistosomiasis morbidity in our ecological complex and highly endemic area.

The cercariae of schistosomes of veterinary important paramphistomes and those of the species of *Fasciola* are produced by *Bulinus* species and *Lymnaea* species respectively. The incidence of *Fasciola gigantica* in some of the inhabitants around the Erinle dam is an indication that fascioliasis could be prevalent in Nigeria (Adewunmi *et al.*, 1993). Some Prosobranchs such as *Potadoma* species and *Melanoides* species (Adewunmi *et al* 1996; Adewunmi and Olorunmola, 1998) are intermediate hosts of *Paragonimus uterobilateralis* of man and blood parasites of birds and mammals respectively (Frandsen and Christensen, 1984). Some of these snails could be developed as potential biological control agents against schistosomiasis transmitting snails.

III. Natural environment markers

Freshwater snails can be used as a sensitive and useful indicators of environmental pollution caused by heavy metals in Nigeria (Adewunmi *et al.*, 1996). We analysed the accumulation of copper, lead and cadmium in *Biomphalaria pfeifferi, Bulinus globosus, Lanistes libycus, Lymnaea natalensis, Potadoma moerchi, Melanoides tuberculata, Gabiella africana, Pila ovum* and *Bellamya* species collected from man-made dams and rivers in parts of Ondo and Osun states, Nigeria using a flameless atomic absorption spectrophotometer. Metal concentrations varied widely among snail species and sites while seasonal changes in metal concentrations occurred in some locations. Snails accumulate metals over a period of time. Because of this integrating monitoring ability of these snails, the data represent the average metal concentration of their habitats (Adewunmi *et al.*, 1996).

We recognise the economic, social and health importance of some tropical diseases such as trypanosomiasis (Adewunmi and Uzoukwu, 1979),

schistosomiasis (Adewunmi and Sofowora, 1980,Adewunmi *et al.* 1990b, 1991b and 1993) and helminthiasis (Adewunmi *et al.* 1993) by carrying out basic epidemiological investigations on them. The results provide the necessary data that could be used in the control of these diseases. The results also indicate that research is needed in the search for appropriate tools for controlling these diseases. Hence the search for anti-infective agents from medicinal plants is appropriate. Many plants and animals serve as sources of food, pharmaceutical or industrial products. For example, about 25.0 % of medicines are of direct plant origin and this percentage could be as high as 50.0 % if one takes into consideration products which have been slightly modified (CTA, 1994).

Plant anthelmintics

Over 74.0 % of the 119 drugs with known chemical structures were discovered by chemists attempting to identify the chemical substances in plants used in traditional medicine (Farnsworth, 1988). Hundreds of plants have been screened against helminths but many of them were on plant nematodes (Muller and Borger, 1940; Veech, 1982). However, the powdered root of Agrimony (*Agrimonia pilosa*, Rosaceae) used to expel tapeworms contained Agrimophol in its buds with anthelmintic activity on *Taenia solium in vitro*. The efficacy of agrimophol in clinical trials gave an overall cure of 95.0 %. Cucurbitine, an amino acid isolated from pumpkin seeds (*Cucurbita moschata*) effectively expelled cestodes: *T. hydatigena, T. pisiformis* and *Diphyllobothrium mansoni* with no signs of toxicity other than vomiting at high doses. Agrimophol and cucurbitine were also found to be active against *S. japonicum* both *in vitro* and *in vivo* (You *et. al.*, 1982).

We found that the aqueous extract of *Calliandra portoricensis* (Jacq) Benth was effective against *Toxocara canis* in dogs (Adewunmi and Akubue, 1981) but with no effect on *Ancylostoma caninum* and *Hymenolepis diminuta* of the dog and rat respectively. We were encouraged by the antischistosomal activity of *Zingiber officinale* on *S. haematobium* infected school children (Kucera *et al.* 1975) and its strong antihelminthic activity against *Ascaris lumbricoides in vitro* (Raj, 1974), to investigate the antischistosomal activity of the plant's extracts and its active components on the infectivity of *S. mansoni* and *S. bovis* miracidia and cercariae. Tables 1 and 2 show the summary of the effects of the active components of two plants on the infectivity of the larval stages of these schistosomes. Gingerol (5.0 µg/ml) isolated from *Z. officinale* abolished the infectivity of *S. mansoni* miracidia and cercariaea in *B. glabrata* and mice respectively (Adewunmi *et al.* 1990d). This indicates that gingerol could be useful in the control of schistosomiasis by its effect on different stages of the parasite. We found similar activity in the extracts of *Tetrapleura tetraptera* and aridanin isolated from the plant on different stages of *S. mansoni* and *S. bovis*. Aridanin (0.25µg/ml) and the water extract reduced the production of cercariae

by snails and also produced profound reduction in worm recovery of mice infected with pretreated cercariaea of *S. mansoni* and *S. bovis* (Adewunmi and Furu, 1989).

Table 1: Pretreatment effect of natural products

Drug	Concentration (µg/ml)	Surviving Snails (%)	Snails shedding cercariae (%)
S. mansoni			
Aridan	25	90	30
Aridanin	0.5	100	0
Gingerol	5	90	0
Control	0	100	100
S. bovis			
Aridan	25	100	20
Aridanin	0.5	100	10
Control	0	100	100

Table 2: Pretreatment effect on infection of mice

Drug	Concentration (µg/ml)	Surviving Snails (%)	Schistosomes recovery (%)
S. mansoni			
Aridan	25	100	100
Aridanin	0.5	100	31
Gingerol	5	100	0
Control	0	100	100
S. bovis			
Aridan	25	100	17
Aridanin	0.5	100	9.8
Control	0	100	100

Molluscicide screening

Molluscicides are important in the control of schistosomiasis. I joined the service of the university of Ife (now Obafemi Awolowo university) as a Resaerch Fellow grade II on December 1, 1977 after about 2½ years' of teaching and research experience at the university of Nigeria, Nsukka. During the First quarter of 1978, Dr. Abayomi Sofowora (Professor Sofowora) directed that I should start work on the project titled "Anti-parasitic activities ofNigerian medicinal plants". This began with the establishment of a snail colony of *Bulinus globosus* and screening of Nigerian medicinal plants for molluscicidal activities in the Drug Research Unit (DRU). In 1979, we attended a conference in Nairobi (trip sponsored by OAU/STRC and the University of Ife) where I presented the first results of our laboratory screening of 181 plant extracts which represented 106 species in 41 Families. This was published in *Planta medica* (Adewunmi and Sofowora, 1980). At the time of going to press, we have screened different parts of Nigerian medicinal plants (leaves, flowers, fruits, stem-barks and roots) representing 121 species in 48 Families and 206 pure compounds for molluscicidal properties. Some of these plants were found to be active (Table 3). They include the root of *Rauvolvia caffra*, the stem and root of *Bombax costatum*, the fruits of *Dialium guineense* and *T. tetraptera*, the *leaves* of *Parkia clappertoniana, Morinda lucida, Rothmania whitefieldii, Xiris anceps, Ximenia americana* and *Dysoxylum lenticellare*, and the root and stem of *Combretum* species. The suitability of having molluscicidal activity only in the roots and stems (see Table 3) depends primarily on their rate of growth, potency and amount of labour involved in digging up the roots (Kloos and McCullough, 1982). These authors suggested that plants endowed with regenerative fruiting parts and seeds should be given preference because they are more easily harvested transported and processed.

Table 3: Active molluscicidal plants

Plant	Plant part
Apocyanaceae	
Rauvolfia caffra	root
Asclepiadaceae	
Cryptostegia grandiflora	stem
Bombacaceae	
Bombax costatum	stem
Bombax costatum	root
Caesalpiniaceae	
Dialium guineense	fruit
Combretaceae	
Combretum ghasalense	stem
Combretum ghasalense	root
Terminalia mollis	root
Euphorbiaceae	
Bridelia atroviridis	stem
Jatropha gossypiifolia	fruit
Meliaceae	
Dysoxylum lenticellare	leaves
Mimosaceae	
Acacia dudgeoni	stem-bark
Dichrostachys glomerata	leaves
Tetrapleura tetraptera	fruit
Calliandra portoricensis	root
Leguminosae	
Parkia clappertoniana	leaves
Ochnaceae	
Lophira alata	leaves
Olacaceae	
Ximenia americana	leaves
Rhamnaceae	
Maesopsis eminii	root
Rosaceae	
Acioa barteri	stem
Acioa rudattisii	stem
Rubiaceae	
Morinda lucida	leaves
Rothmania whitfieldii	stem
Verbenaceae	
Vitex oxycuspis	stem
Xyridaceae	
Xyris anceps	leaves
Zingeberaceae	
Zingiber officinale	rhizome
Zygophyliaceae	
Balanites aegyptiaca	fruit

Active molluscicidal components

Chemical investigations were also carried out on some of these promising molluscicides (Table 3). This led to the chemical isolation and identification of the active coumarins heliettin and imperatorin on *B. globosus* from the roots of *Clausena anisata* (Willd.) Oliv. (Rutaceae) (Adesina and Adewunmi, 1985). The LC_{50}sof heliettin and imperatorin were 4.26 and 4.0 mg/L respectively. I was sponsored by the International Foundation for Science, Stockholm in 1985 to attend a conference on Alkaloids and Anthraquinones of African Medicinal Plants in Addis Ababa, Ethiopia. My interaction with Prof. F.D. Monache at this symposium led to our studies (Adewunmi and Monache, 1989) on the molluscicidal activity of some synthetic and natural coumarins. The molluscicidal activity exhibited by the coumarins depended on the nature of the substituents and the ring system. A reduction of the furan ring led to a progressive reduction of the molluscicidal activity of the coumarins [see 3 , α,α dimethyllyl) psoralen vs isoangenomalin and chalepin].

74 of the 98 alkaloids examined for molluscicidal activity were found to be active at various concentrations (Adewunmi *et al.*, 1989b). 31 of these alkaloids gave 100% kill to *B. glabrata* snails at a concentration of 5.0 mg/L. The most active of this group are dicentrine, solanine and solanidine which produced 50% mortality at a concentration of 1.0 mg/L. The molluscicidal activity shown by this group is less than that of Bayluscide (Niclosamide) which kills the snails at lower concentrations.

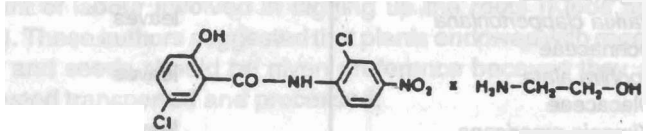

Figure 1. The chemical structure of Bayluscide

However, the molluscicidal action of this group of alkaloids are similar to some natural saponin containing plant molluscicides such as *T. tetraptera*, *Phytolacca dodecandra* and *Swartzia madagascariensis* (Mailard *et al.*, 1989). These are several times more potent than virgili[illegible]on and Hostettmann, 1985). The methanolic extract of the leaves of *Dysoxylum lenticellare* produced 100% mortality to *B. glabrata* at 100 mg/L while that of the stem produced 60% mortality (Adewunmi and Aladesanmi, 1988). The highest molluscicidal activity was recorded with 3-epi-2,18- dimethoxyschelhammericine and lowest in lenticellarine isolatedfrom the leaves (Aladesanmi *et al.*, 1988), a decrease which may be due to the disruption of the homoerythrina skeleton (Aladesanmi and Adewunmi, 1990). An increase in the methoxy groups increased the

molluscicidal activity of the alkaloids whilst the disruption of the carbon skeleton decreased activity. The molluscicidal activity of the extract from *D. lenticellare* is therefore suggested to be due to ferrubietolide and its congeners (Aladesanmi and Adewunmi, 1995).

The ethanol extract of *Zingiber officinale* exhibited weak molluscicidal activity with 20% mortality against *B. glabrata* (Adewunmi *et al.*, 1990b). This confirmed the weak molluscicidal activity reported earlier for the methanolic extract with 20% mortality against *B. (P.) globosus* (Adewunmi and Sofowora, 1980). Gingerol and shogaol isolated from *Z. officinale* exhibited 100% mortality against *B. glabrata* at a concentration of 5.0 ppm.

Five anthraquinones, an anthraquinolmethyl ether (oruwal) and an irridoid ferulate (oruwacin) isolated from the leaves of *Morinda lucida* were found to be molluscicidal to the schistosomiasis and fascioliasis transmitting snails: Bulinus *(P.) globosus*, *B. rohfsii, Biomphalaria pfeifferi* and *Lymnae natalensis* (Adewunmi and Adesogan, 1984). Oruwacin, the most active compound was lethal to the various snail species at LC_{90} of 1.30-5.30 mg/L. We had the impression that the discovery of the molluscicidal activity of anthraquinones was significant and hoped that we could obtain better activity with known anthraquinones. Rubiadin-1.methyl ether and 2-methyl anthraquinones had potent molluscicidal activity.

During the course of our laboratory screening, the extract of the leaves of *Parkia clappertoniana* showed molluscicidal activity against *B. pfeifferi*. At a concentration of 25.0 ppm, 2-hydroxy-

3,7,8,4,5-pentamethoxy flavone gave 80% mortality to *B. glabrata*snails (Lemmich et al., 1996). Adewunmi et al. (1987b) used the molluscicidal active component obtained from *Polygonum senegalensis*, as the basis for the synthesis of chalcone compounds some of which are very potent against *B. glabrata* but the epoxides had little or no activity.

Definitive screening

Definitive screening and comprehensive laboratory screening were carried out on extracts from *Tetrapleura tetraptera* (Aridan), *Calliandra portoricensis* (Ule or Tude), *Jatropha gossypiifolia* (lapalapa pupa) and *Morinda lucida* (Oruwo). In November, 1980, I attended the Tenth International Congress on Tropical Medicine and Malaria, in Manila, the Philippines,(trip sponsored by the University's Learned Conferences Fund) where results of some definitive laboratory and field studies on *T. tetraptera* and *C. portoricensis* were presented. The results of these have been published in international journals. The molluscicidal activity of *J. gossypiifolia* (LC_{50} = 11.55 - 16.24 mg/L) was stable over a wide range of pH and after ultra-violet irradiation but the activity was reduced by presence of minerals in natural waters and physico-chemical

absorption of faecal preparation (Adewunmi and Marquis, 1980). Molluscicidal evaluation of *Jatropha curcas* and other *Jatropha* species had been carried out (Yasuraoka *et al.*, 1980, El-Kheir and EL-Tohami, 1979, Adewunmi and Marquis, 1980). The aqueous extract of *J. curcas* was found to be harmless to fish at molluscicidal concentrations (Yasuraoka *et al.*, 1980). In the Philippines, the extract of *J. curcas* was found to have molluscicidal effect on *Lymnaea amicularia rubiginosa*, an intermediate host of *Fasciola* species (GTZ, 1995). *Jatropha* oil can be used as diesel oil (fuel) and for making soap. The oil has insecticidal activity which has been conclusively demonstrated onthe larvae of the sorghum pests such as *Sesamia calamitis, Buseola fusca* and *Eurytylus immaculatus* and on the larvae of the tobacco moth, *Mandura sexta* (GTZ, 1995).

The molluscicidal potency of the ethanolic extract of *C. portoricensis* was not affected by the inactivating effect of hydrogen ions (pH 4.2 - 4.9 and pH 6.8 - 9.0), and the inactivating effect of organic matter. However, ultra-violet irradiation with a peak at 366.0 nm for 8 hours' duration, and minerals in water slightly affected the molluscicidal activity of the extract. The high piscicidal activity of the extract is a disadvantage (Adewunmi and Marquis, 1981a).

Oruwacin isolated from the leaves of *Morinda lucida* was molluscicidal against *B. (Phyopsis) globosus, B. rohfsii, B. pfeifferi and L. natalensis* (LC_{50} = 1.50 - 5.30 mg/L). Its molluscicidal activity was reduced by ultra-violet light, faecal matter and pH. It was however, not toxic to mosquito larvae, tubifex worms and did not affect the germination of cowpeas and maize (Adewunmi and Adesogan, 1984).

We also studied the effects of some physico-chemical factors and some other factors on the molluscicidal property of *Tetrapleura tetraptera*. The molluscicidal activity of *T. tetraptera* [LC_{50} = 2.01 (1.94 - 2.65 mg/L)] was very potent. Minerals in natural waters and ultra-violet light had no effect on the molluscicidal activity of this molluscicide but organic matters like faecal preparation and alkaline pH decreased its activity by about 2.8 times while its activity was increased by almost 3.0 fold (Adewunmi and Marquis, 1981b) in acidic media.

The molluscicidal activity of the methanolic extract of *T. tetraptera* was reported by Adewunmi and Marquis (1981b). The activity seemed to be linked to triterpenoid saponins andcoumarinic compounds (Adesina *et al.*, 1980). A mono-N-acetylglycoside of oleanolic acid (=3-hydroxyolean-12en-28-oic acid), aridanin was isolated and identified from *T. tetraptera* (Adesina and Reisch, 1985). Activity guided fractionation of the methanolic extract of the fruits of *T. tetraptera* Taub. (Mimosacea) afforded 5 saponins A - E (Figure 2),

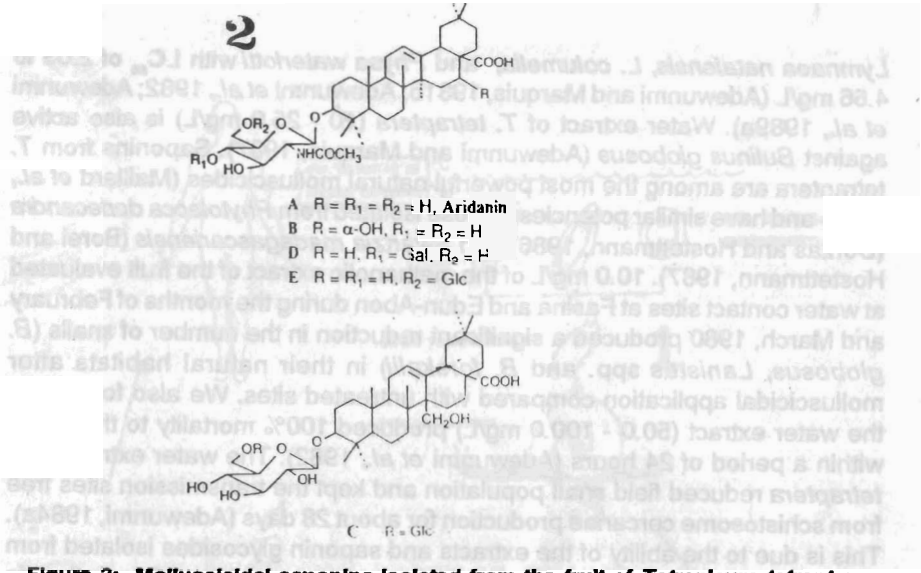

Figure 2: Molluscicidal saponins isolated from the fruit of *Tetrapleura tetraptera*

some of which exhibited strong molluscicidal activity against *B. glabrata*. Saponins A, B, D and E (Figure 2) killed *B. glabrata* snails within 24 hours at concentrations of 2.5, 5.0 and 20.0 ppm. Aridanin was molluscicidal at a concentration of 20.0 ppm. Glycosylation of aridanin increased the toxicity of the saponins to *B. glabrata* snails (Maillard *et al.*, 1989). A monodesmosidic diglycoside of the rare sapogenin 27-hydroxyolean-12(13)-en-28-oic acid (saponin C) exhibiting a weak molluscicidal activity (<40.0 ppm) against *B. glabrata* was isolated from the fruit of *T. tetraptera*, and from previous observations it was thought that the C-27 oxidation of the aglycone is responsible for its low activity (Maillard *et al.*, 1992). Two glycosides reported earlier by our group were also isolated from the stem bark of *T. tetraptera* (Ngassapa *et al.*, 1989). A sulphated triterpene , echinocystic-3-O-sodium sulphate (reported in 1992 by our group) was isolated from the stem-bark of the plant. This compound was not molluscicidal at 20.0 mg/L (Ngassapa *et al.*, 1993). Monodesmosidic saponins (with glycoside chain in position 3) are active against snails while the bidesmosidic (with glycoside chain in positions 3 and 28] are inactive (Domon and Hostettmann, 1984).

Efficacy of *Tetrapleura tetraptera*

Molluscicides are used to kill snails that serve as intermediate hosts for schistosomes and other trematodes. The molluscicidal activity of the methanolic extracts of the leaf, leaf-stalk, stem-bark, root-bark and fruit of *T. tetraptera* varies between 1.50 and 3.16 mg/L indicating the presence of molluscicidalactivity in all parts of the plant. The methanolic extract of *T. tetraptera* is effective against freshwater snails such as *Bulinus globosus*,

Lymnaea natalensis, L. columella, and *Physa waterlotti* with LC_{50} of 2.03 to 4.56 mg/L (Adewunmi and Marquis, 1981b; Adewunmi *et al.*, 1982; Adewunmi *et al.*, 1989a). Water extract of *T. tetraptera* (10 - 25.0 mg/L) is also active against *Bulinus globosus* (Adewunmi and Marquis, 1987). Saponins from *T. tetraptera* are among the most powerful natural molluscicides (Maillard *et al.*, 1989) and have similar potencies to those isolated from *Phytolacca dodecandra* (Dorzas and Hostettmann, 1986) and *Swartzia madagascariensis* (Borel and Hostettmann, 1987). 10.0 mg/L of the methanolic extract of the fruit evaluated at water contact sites at Fasina and Edun-Abon during the months of February and March, 1980 produced a significant reduction in the number of snails (*B. globosus, Lanistes* spp. and *B. forskalii*) in their natural habitats after molluscicidal application compared with untreated sites. We also found that the water extract (50.0 - 100.0 mg/L) produced 100% mortality to the snails within a period of 24 hours (Adewunmi *et al.*, 1982). The water extract of *T. tetraptera* reduced field snail population and kept the transmission sites free from schistosome cercariae production for about 28 days (Adewunmi, 1984a). This is due to the ability of the extracts and saponin glycosides isolated from the plant to interrupt schistosome transmission at two other points in the life cycle of the schistosome (Adewunmi and Furu, 1989). This interruption is possible at the infecting stage of snails by miracidia and the infection stage of man by cercariae (see Figure 3,). The cercaricidal effect of aridanin and the water extracts of *T. tetraptera* has not been evaluated under field conditions. The effective utilization of this product as a cercaricidal agent will be highly useful in the control offascioliasis which is the cause of economic loss to farmers and in the control of dermatitis caused by cercariae of *Trichobilharzia ocellata*. Dermatitis caused by *T. ocellata* cercariae is the cause of economic loss in the recreation industry in Europe and America.

The calculated IC50s of aridanin on freshly laid to one-day-old eggs, 3-day-old eggs and 5-day-old eggs of *B. glabrata* are 5.81 mg/L, 7.30 mg/L and 16.24 mg/L respectively (Adewunmi, 1991b). This indicates the poor ovicidal action of aridanin. This poor ovicidal activity could be overcome by multiple treatments timed to kill the adult and juvenile snails in the control of schistosomiasis (Adewunmi, 1984b).

A joint schistosomiasis research project, carried out by our group and the Danish Bilharziasis Laboratory between 1988 and 1989 in southwestern Nigeria provided data by which it was possible to relate snail recovery from potential transmission sites to the presence or absence of *T. tetraptera*. The presence of *T. tetraptera* around transmission sites appeared to be the most important limiting factor for the presence of snails. Water extracts of *T. tetraptera* (40.0 - 120.0 mg/L) produced molluscicidal activity against *B. globosus* and *L. natalensis* at Esinmirin and Fasina (Adewunmi *et al.*, 1990c). The results indicate that the planting of *T. tetraptera* along water courses has potential for the local control of schistosomiasis.

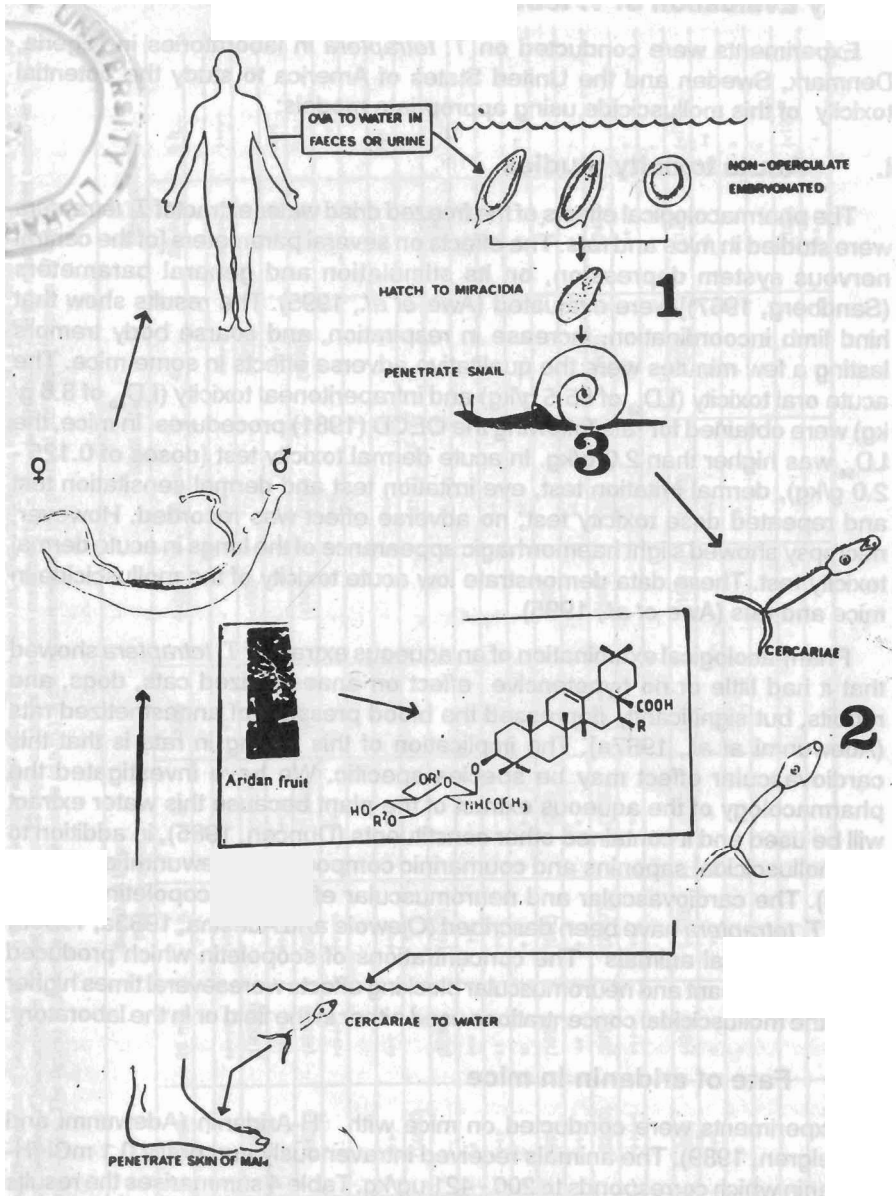

Figure 3: Interruption of the transmission of schistosomiasis by extracts and aridanin isolated from *Tetrapleura tetraptera*. Points 1 - 3 denote interception stages in the development of schistosomes

Safety Evaluation of *T. tetraptera*

Experiments were conducted on *T. tetraptera* in laboratories in Nigeria, Denmark, Sweden and the United States of America to study the potential toxicity of this molluscicide using appropriate models:

I. Acute toxicity studies

The pharmacological effects of the freezed dried water extractof *T. tetraptera* were studied in mice and rats. The effects on several parameters [of the central nervous system depression, on its stimulation and general parameters (Sandberg, 1967)] were evaluated (Awe *et al.*, 1995). The results show that hind limb incoordination, increase in respiration, and coarse body tremors lasting a few minutes were the qualitative adverse effects in some mice. The acute oral toxicity (LD_{50} of 55.5 g/kg) and intraperitoneal toxicity (LD_{50} of 8.6 g/kg) were obtained for rats following the OECD (1981) procedures. In mice, the LD_{50} was higher than 2.0 g/kg. In acute dermal toxicity test (doses of 0.125 - 2.0 g/kg), dermal irritation test, eye irritation test and dermal sensitation test and repeated dose toxicity test, no adverse effect was recorded. However, necropsy showed slight haemorrhagic appearance of the lungs in acute dermal toxicity test. These data demonstrate low acute toxicity of the molluscicide in mice and rats (Awe *et al.*, 1995).

Pharmacological examination of an aqueous extract of *T. tetraptera* showed that it had little or no hypotensive effect on anaesthetized cats, dogs, and rabbits, but significantly depressed the blood pressure of anaesthetized rats (Adewunmi *at al.*, 1987a). The implication of this finding in rats is that this cardiovascular effect may be species specific. We have investigated the pharmacology of the aqueous extract of the plant because this water extract will be used and it contained other constituents (Duncan, 1985), in addition to the molluscicidal saponins and coumarinic compounds (Adewunmi and Furu, 1988). The cardiovascular and neuromuscular effects of scopoletin isolated from *T. tetraptera* have been described (Ojewole and Adesina, 1983a, 1983b) in experimental animals . The concentrations of scopoletin which produced cardiodepressant and neuromuscular blocking effects wereseveral times higher than the molluscicidal concentrations used either in the field or in the laboratory.

II. Fate of aridanin in mice

Experiments were conducted on mice with ^{3}H-Aridanin (Adewunmi and Appelgren, 1989). The animals received intravenously and orally 0.1 mCi ^{3}H-Aridanin which corresponds to 200 - 421 ug/kg. Table 4 summarises the results of the radiolabelled aridanin. in laboartory mice. The survival times for males, females and pregnant female mice varied between 5 minutes and 4 days. In mice intravenously injected with the radiolabelled compound, ^{3}H-Aridanin was

Table 4: Tissue distribution of radioactivity from ^{3}H-Aridanin in mice after different time intervals after intravenous injection of a single dose corresponding to 200 - 421 µg/kg. The relative degree of blackening in different organs after 22 days' exposure has been measured by a microdensitometer and the measurement scored as +, ++, +++, ++++, and +++++. The figures in parenthesis show the results (d.p.m.) of the measurements of the punched out pieces from the 60 um sections.

Tissue or fluid	Survival time Female mice						Male mice						Pregnant mice	
	5 min.	20 min.	1 h.	4 h	24 h	4 days	20 min.	4 h	20 min	4 h
Intestinal cont.	+	+++++	+++++	+++	++	-	+++++	+++++	+++++	+++++
	(1500)	(190000)		(144570)	(6349)	(<100)		(55254)		
Liver	-	++++	++++	++++	-	-	+++	++++	++++	++++
	(48000)	(46120)	(45786)	(15640)	(341)	(<100)	(8090)	(31957)	(13528)	(22041)
Gall bladder	-	+++++	+++++	++++	-	-	+++		+++	++++
Kidney, medulla	+++	+++	+++	+	-	-	+++		++++	+++
	(14500)						(4107)			
Kidney, cortex		(6280)	(4117)	-	-	-			(4695)	
Ovary	++	+++	++	-	-	-	++	++	+++	
Bone marrow	+++	++	++	+	-	-	++	+	++	++
Muscle	+	+	+							
	(997)	(1093)	(552)	(254)	-	(1337)	-	-	-	-
Blood	++++	++	+	+	-	-	++	+	++	+
	(22000)	(3850)	(2467)	(1532)	(451)	(2550)	(350)	(3450)	(2141)	
Lung	+++++	++++	++	+	-	-	++	++	+++	+
Brain	-	-	-	-	-	-	-	-	-	-
Spleen	++	+	+	+	-	-	++	+	++	+
	(350)	(492)	(<100)	(<100)	(<100)	(<100)	(<100)	(<100)	(<100)	(<100)
Pituitary	+	+	+	+	-	-	+	+	++	+
Foetus									-	-
									(<100)	(<100)
Placenta									+++	+

rapidly taken up in the kidney and liver. Its elimination - mainly through the faeces and to a lesser extent through the urine - was rapid. About 40.0% of the total Aridanin was excreted after 24 hours. No specific retention in any tissue was observed after 24 hours and aridanin did not pass the placenta barrier in pregnant mice. After oral administration to mice, most of the labelled aridanin was found in the intestinal contents indicating a very poor absorption. The results showed that a rapid uptake and disappearance and low oral uptake of aridanin in a non-target mammal make this molluscicide a suitable candidate to be tested in field studies.

III. Short-term toxicity studies

The following studies were perfomed with the water extract of *T. tetraptera* on rats and the domestic fowl upto a period of 4 weeks: In Male and female rats (Awe *et al.,* 1995), the 28-day oral gavage testing indicated that daily treatment with the molluscicide had no effects. This represents a 28-day no observable adverse effect. Similarly, in domestic fowls (using 5.0 mg, 20.0 mg and 40.0 mg/kg), no significant effect was observed on oxygen, carbondioxide tension, and haematocrit values such as the packedcell volume, haemoglobin, blood cell values and growth of the birds (Olubunmi *et al.,* 1986).

Iv. Long-term toxicity studies

Mice orally dosed with the methanolic extract (10 - 1000.0 mg/L) of Aridan over a period of 3 months showed no apparent toxic symtoms (Adewunmi and Marquis, 1981b).

v. Special Investigations

Mutagenic potential of aridanin and water extract of *T. tetraptera* was investigated in the Ames test (Ames *et al.,* 1975). No mutagenic effects occurred in *Salmonella typhimurium*, strains TA 97, TA 98 and TA 100 regardless of the presence or absence of a metabolising system (Adewunmi *et al.,* 1991a). However, in a forward mutation assay utilising *S. typhimurium* TM 677, methanolic extracts of the stem-bark was found to be mutagenic in the absence of a metabolising activating system (S-9). An MeoH extract of the fruit exhibited weak mutagenic activity only in the presence of S-9. The stem-bark saponin isolates, aridanin and other saponins were not mutagenic, either with or without metabolising activation (Ngassapa *et al.,* 1993).

Aridanin and water extract of *T. tetraptera* had no influence on cell proliferation and neither induced chromosomal aberrations nor sister chromatid exchanges in Chinese hamster ovary cells cultured *in vitro* (i.e. no genotoxic effect; Adewunmi *et al.,* 1991a).

Effect on other organisms

There is considerable interest in determining the effect of molluscicides on aquatic fauna, as benthic and planktonic species provide an important link in the ecological food chain leading to larger animals such as fish (Andrews *et. al.,* 1983). Studies of the effects of Aridan on some non-target organisms were carried out.The methanolic extract of *T. tetraptera* is toxic to fish (*Tilapia nilotica*, LC_{50} = 0.35 mg/L; *T. galilae*, LC_{50} = 0.44 mg/L) (Adewunmi *et al.,* 1982). Every molluscicide including Bayluscide (Figure 1) is known to kill fish at molluscicidal concentrations. This extract had no apparent toxic effect on the growth of *Lycopersicum esculentum* (tomato plant). Results of our current investigations on cowpeas, maize, sorghum, rice and soya beans showed that the molluscicide is not toxic to them at molluscicidal concentrations (unpublished results). Long-term studies are required on economically important plants. The effects of the water extract of *T. tetraptera* and other molluscicides on *Hydra magnipapillata*, the brine shrimp, *Artemia salina*, *Anopheline* larvae, tadpoles (*Bufo regularis*) and leeches were investigated. The results show that the molluscicides were toxic to *H. magnipapillata*, tadpoles and the leech. Concentrations of the water extract of *T. tetraptera* that were toxic to *Artemia salina* are 31-50 times the molluscicidal concentrations. Similarly, high concentrations of the molluscicides are also required to produce toxic effects on mosquito larvae (Gebremedhin *et al.,* 1994) and earthworms. The leech is a predaceous aquatic animal on snails. But the leech is also a pest to villagers at Erinle dam where they feed on the blood of fisher men and the villagers bathing or washing clothes at the shores of the dam. The lethal action of the water extract of *T. tetraptera* on the leech is turned to an advantage.

Mode of Action studies.

We labelled Aridanin with ^{3}H and studied its distribution in mice and snails by whole body autoradiography and liquid scintillation at the Swedish University of agricultural Sciences, Uppsala (Adewunmi and Appelgren, 1989). It was demonstrated that *B. glabrata* took up appreciable amount of the molluscicide throughtheir exposed body (Adewunmi and Appelgren, 1989). ^{3}H-Aridanin was concentrated by the tissues of the snail. The snail was able to concentrate radioactivity in its tissues 1075 times that of the snail medium (Table 5).This indicates that the molluscicidal action of Aridanin could be due to intoxication. Gross histopathological changes consisting of a swelling of the epithelium covering the headfoot and lining of the gut were observed in three snail species (*B. globosus, Physa waterlotii* and *B. glabrata*) as a result of the exposure of aridan - an effect that could be an accumulation of fluid in the snail tissues (Adewunmi and Ogbe, 1986). The effects of aridanin and serotonin were tested on the rhythmicity of the intestinal smooth muscles of *B. glabrata* snails. Verapamil, lanthanum, and cyproheptadine inhibited the actions of aridanin, suggesting a calcium-dependent action of aridanin on the gut tissue of the snail (Adewunmi *et al.,* 1990a).

Table 5: Excretion/recovery of ^{3}H-Aridanin in snails

Tissue	Concentration in control snails in d.p.m./g. snail tissue	Percentage of total uptake of control snails Recovery time in hours				
		1 (n=5)	4 (n=5)	12 (n=5)	24 (n=5)	48 (n=5)
Foot	259 x 10^4	3.42(1.7)	2.43(1.9)	1.01(0.3)	1.56(1.7)	0.87(0.4)
Gastrointest.tract	460 X 10^4	10.98(6.8)	4.84(2.7)	1.84(1.6)	2.04(1.9)	2.04(1.9)
Hepatopancreas	675 X 10^4	4.33(2.6)	1.61(1.2)	0.79(0.4)	0.76(0.2)	0.93(0.3)
Ovotestis 32 x 10^4	1.46(1.1)	0.93(0.8)	0.43(0.2)	4.16(5.9)	3.11(1.6)	
kidney	1247 x 10^2	25.40(23.9)	2.82(1.9)	3.58(3.1)	4.47(4.3)	6.77(5.6)
Reproductive tract	282 x 10^4	1.05(0.79)	0.31(0.1)	0.34(0.1)	0.56(0.6)	0.29(0.2)
Total		42.33	12.94	8.01	9.6	14.01
Total in d.p.m	2956 x 10^4	1251 X 10^4	283 X 10^4	237 X 10^4	284 X 10^4	414 X 10^4
Ratio of radioactive uptake/g snail tissue (Without shell)/ml of snail medium	1075	455.1	139.1	86.1	103.2	150.6

Aridanin is a saponin. The effect of saponins on cell membranes was reviewed by Duncan (1985), who concluded that the bulk of evidence appears to favour the proposal that the action of saponins could be due to saponin-cholesterol complex formation in relation to membranolysis and the general biocidal activity of saponins. Kwan *et al.* (1988) concluded that the effect of saponin on several cell membrane properties are consistent with the skinning effect of saponins on smooth muscle membranes. Saponin at a concentration of 50 mg/L can be used for the chemical skinning of cardiac muscles (Endo and Kitazawa, 1978). If skinning of any membrane is achieved, the cell will allow the entry of any ion or even a macromolecule (Ohtsuki *et al.*, 1978), so that the membrane potential can thus be completely abolished. The very low concentrations of aridanin employed in these studies and the fact that aridanin exerts its effects at sublethal concentrations suggests that aridanin-inducedpertubation of membrane may be related to its molluscicidal activity (Adewunmi and Marquis, 1981b), its reduction of the growth and egg production

of *B. glabrata* and *L. columella* (Adewunmi *et al.*, 1989a), and its reduction of the carbohydrate and protein content of *B. glabrata* (Adewunmi *et al.*, 1988). The reduction in the growth and egg production of these snails [also produced by low concentrations of the extracts of *Bridelia atroviridis* (Adewunmi *et al.*, 1982)] has been suggested to be due to an influence on carbohydrate and protein metabolism of the snails. The specific uptake of ^{3}H-Aridanin in the snail hepatopancreas and in the ovotestis indicates that the reduction in the growth, egg production, glycogen, and protein contents produced by chronic exposure to low concentrations of aridanin (Adewunmi *et al.*, 1988) could be due to the toxic effects of aridanin on the ovotestis and hepatopancreas (Adewunmi and Appelgren, 1989). The vesicular cells are probably the site of glycogen storage (Pan, 1958). The toxic effect on the vesicular cells could affect glycogen stores (Adewunmi and Appelgren, 1989), which snails use as reserve, an amount that depends on seasonal, nutritional or reproductive factors (Emerson, 1965). The results also show that the metabolism of aridanin in the snail is different from that of the mouse because the Rf- values of ^{3}H-Aridanin detected in the mouse are lower than those detected in the snail. The initial accumulation in, and rapid disappearance of ^{3}H-Aridanin from the liver and the kidney of the mouse are related to excretion. But in the snail, the high-retention of radioactivity in the hepatopancreas and the kidney (non-extractable) points to a possible toxic influence rather than reflecting an excretory process. Aridanin and total saponin extracts from *T. tetraptera* in low concentrations caused damage to the nuclei, mitochondria, alteration to the general celloutline and, to the basal lamina (GKSS supported project with the University of Hamburg). The ratio of the digestive cells to the crypt cells was inverted with an increase in the number of secretory cells and a decrease in the number of digestive cells (Bode *et al.*, 1996). The autolytic action of aridanin and saponins could be related to the pore-forming action (surface active property of the saponins) of *T. tetraptera*.

Other Potential uses of *T. tetraptera*

The following activities of *T. tetraptera* can be exploited for the benefit of mankind

(i). Extracts obtained from *T. tetraptera* exhibited significant anti-ulcer activity confirming its ethnomedical use in the management of gastro-intestinal disorders especially stomach ulceration (Noamesi *et al.*, 1992).

(ii). Alcoholic and water extracts of *T. tetraptera* inhibited the growth of *Staphylococcus aureus* (Salako *et al.*, 1990).

(iii). The extracts from *T. tetraptera* exhibited anticonvulsant activity which could be linked to their ability to depress the central nervous system (Akah and Nwambie, 1993).

(iv). The emulsifying property of the extracts from *T. tetraptera* has been demonstrated (Olaifa *et al.*, 1993). (v). The ethanol extracts and saponins from the stem-bark of *T. tetraptera* exerted an inhibitory effect on luteinizing hormone released by pituitary cells (El Izzi *et al.*, 1990) suggesting its use as a contraceptive agent.

(vi). The nutritional quality of the dry fruit of *T. tetraptera* used as spice, was assessed. The fruit shell, fruit pulp and seed contained varying amounts of nutrients such as protein, lipids and minerals, which were comparable and some were even higher than popular spices such as red pepper, onion, curry and ginger (Essien *et al.*, 1994). In eastern parts of Nigeria, fruits are used to prepare soups for mothers from the first day ofdelivery to prevent postpartum contraction (Nwawu and Akah, 1986). It is used in the preparation of pepper soup in southern parts of Nigeria. The fruits also contain cinnamic acids, caffeic acid and carbohydrates (Adesina , 1982). The latter two of these components are common in most spices.

Molluscicides are crucial for controlling schistosomiasis. Bayluscide Is the only molluscicide recommended by the WHO. The annual health budget of Nigeria is less than one US dollar per person while a metric ton of this molluscicide is about 2.5 million Nigerian Naira. Thus, this molluscicide is expensive. In the United States of America, chemical pesticides were used in the control of the Mediteranean fruit fly during the summer of 1997 (New Horizon, VOA, July, 18, 1997). There is therefore no justication for us in not supporting the use of a plant derived molluscicides such as *T. tetraptera* which can easily be biodegraded in the environment.

Conclusion

The last few years have seen some local and international collaborations been expended on the development of *T. tetraptera* as a potential molluscicide. The lecture I presented during the award of the Oritsejolomi fellowship and medal award ceremony at the university of Ibadan on September 1, 1997 (Adewunmi, 1997) raised some questions concerning the developmnt of *T. Tetraptera* in the very near future: (i). Can we develop molluscicides of natural origin that would be lethal to the intermediate hosts snails at nano- and pico-concentrations? (ii). Can we develop more specific miracides and cercaricides than aridanin at very low concentrations that will be effective in knocking off these larval stages of schistosomes? It is desirable that this would be more friendly with the environment. Modification of the structure of aridanin could make it more effective. Glycosylation increased themolluscicidal activity of aridanin (Maillard *et al.*, 1989). (iii). Can we develop molluscicides targeted at specific receptor sites in the snail tissues which would be different from that of the non-target organisms? (iv). Do we need to go through thorough toxicological evaluation required of any unknown chemical product before it is used in field conditions? "The logic of requiring the same toxicological tests from both a

known biodegradable natural product and unknown synthetic product should be qur ›ned" (Lemma, 1990). (v). How can we carry out interruption on schistosomiasis transmission at different types of water contact sites effectively ? Methods are required which would be effective in the delivery of molluscicides in schistosomiasis control. An effective molluscicide with miracidal and cercaricidal activities, which is, effective and properly delivered at human contact sites should have significant effect on schistosomiasis transmission.

Mr. Vice-Chancellor, Sir, These questions are still valid today. In addition: (a). Government should fund collaborative research in our universities to achieve these objectives and aspirations. (b). In 1983, the Scientific Working Group on Plant Molluscicides of the World Health Organization (this author was a member) met in Geneva and provided Guidelines in a book (WHO, 1987). The National Schistosomiasis Research Committee (I was the National Coordinator) and the National Schistosomiasis Control Programme of the Federal Ministry of Health organised two Symposia which recommended integrated control of schistosomiasis. These recommendations are not implemented yet. Integrated control of schistosomiasis is the approach most likely to succeed: It should include chemotherapy of infected patients, snail control with *T. tetraptera*, health education and improved hygienic conditions. We believe that the development of a low-cost molluscicide from *T.tetraptera* can make a major contribution to such an integrated programme. (c). We (our research group) believe that this low-cost molluscicide can drastically reduce the incidence and intensity of schistosomiasis in Nigeria. (d). We believe that the plant can be exploited on the basis of its biological properties (spice, detergent, fuel, pesticide). (e). We believe that biotechnological tools can be used (as we approach the new millenium) to improve the specific toxicity of aridanin and/or the active components of *T. tetraptera*. This is because with proper manipulation of molecular markers in the study of the plant genetic diversity and genetic engineering to modify genetic inheritance, new varieties of the plant can be created which could not be achieved by natural means. The following is achievable through biotechnological techniques: (i). Development of micropropagation facilities, (ii). Development of commercial production of *in-vitro* plants, and (iii).The use of cloning by somatic embryogenesis which is far more powerful in terms of productivity than micropropagation. (iv). Possibility of enriching its biological properties by genes introduced through *Bacillus thuringiensis* or other suitable agents, for example, a plant can be made more toxic to insect pests (CTA, 1996). Active support is therefore needed and should be given to this programme to finalize research on this plant which offers so much potential biological properties especially in the area of schistosomasis control.

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