

## FEATURE ARTICLE

### SCIENCE FROM THE THIRD WORLD THE STORY OF ENDOD

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Two Ethiopian scientists, Dr. Aklilu Lemma and Dr. Legesse Wolde-Yohannes received the 1989 Right Livelihood Award. Dr. Aklilu and Legesse received the award in recognition for their work on the molluscicidal plant, Endod (*Phytolacca dodecandra*). The award was shared by a third Ethiopian, Dr. Melaku Worede, for his achievements in establishing the Plant Genetics Resources Centre in Addis Ababa. The award ceremony was held in Stockholm, Sweden on 9<sup>th</sup> December, 1989. Dr. Aklilu Lemma, a parasitologist by training (Sc.D. Johns Hopkins University, 1964) made his first observation in 1964 in the town of Adwa (Northern Ethiopia) where he noted dead snails downstream from where villagers were washing clothes using the soap berry plant, Endod. He was quick to recognize how significant a molluscicidal plant would be to the control of schistosomiasis, a serious and rapidly spreading tropical disease that afflicts 200 - 300 million people with another 400 - 600 million potentially exposed to it, in Africa, parts of the Caribbean and South America and Asia. Dr. Aklilu worked in Ethiopia until 1976 when he moved to the United Nations, working in UNCTSD until 1986 and then at UNICEF first as a senior Adviser on Technology for Health and Development, and in 1988 became the Deputy Director for the newly established UNICEF International Child Development Centre in Florence, Italy. His joining the United Nations at that time gave him an opportunity to continue his advocacy and promotion of Endod amongst different scientific groups and some international organizations. It was the combination of his continuous efforts through this "window to the international community" and the dedicated endeavours of his colleague, Dr. Legesse Wolde-Yohannes, co-winner of the award, to keep the Endod work going in Ethiopia despite severe financial limitations, that enabled them to get to where they are on Endod today.

Dr. Aklilu Lemma presented his acceptance speech on the title "Science from the Third World; The Story of Endod". The following is an adapted version of the speech which he kindly agreed to its publication in the Bulletin of the Chemical Society of Ethiopia.

On 18 June 1990, Dr. Aklilu Lemma was awarded an honorary doctoral degree by the University of Toledo, Ohio, for his work with the United Nations in promoting the transfer of technology to the Third World and for his pioneering studies on Endod.

**Early studies and rationale (1964-70).** Soon after the field experience which unquestionably established that Endod has molluscicidal properties, a number of questions had to be answered. These were: What were the level and diversity of activities of the Endod berries? Are all the different species of snails that transmit schistosomiasis killed by it? What were the effects of organic and inorganic materials on the potency of the berries and what else does it kill?

We found that the sun-dried and crushed berries, when suspended and serially diluted in distilled water, killed all the important species of snails in concentrations ranging from 10 to 25 ppm within 24 hr. The activity was found to remain stable under different physicochemical conditions with little effect on the other flora and fauna of the environment except insect larvae (like mosquitoes), fish and aquatic leeches. Exposure of small mammals to very high doses of Endod solution also proved safe to them. The safety to humans was further substantiated by the fact that people have been using the berries of this plant for centuries as soap! Some of these tests were done using standardized test procedures so that others could easily repeat our work, as indeed they did, and our findings were shortly reconfirmed.

There are alternative molluscicides to Endod, but they come at a very high price. There are safe and effective chemotherapeutic agents for the treatment of schistosomiasis, but people who have been treated in endemic areas become



Aklilu Lemma



Legesse W/Yohannes

re-infected rapidly. Health education and latrine building could help, but this is a long-range prospect tied to a rise in the socio-economic standard of the society as a whole. Therefore the use of molluscicides to eliminate the snails that transmit the disease appears to be the major alternative for the control of schistosomiasis. For ideal control, however, these three approaches should be used concurrently as part of the overall primary health care (PHC) delivery schemes.

Chemicals such as copper sulphate and sodium pentachlorophenate have been used as molluscicides for many decades in Egypt, Sudan and other parts of the world to control schistosomiasis. Recently, however, another more effective compound, the niclosamide ethanamine salt (the ethanamine salt of 5,2'-dichloro-4'-nitrosalicylanilide) called **Bayluscide**, produced by Bayer Co. in West Germany, has been found to be more effective and is currently the only molluscicide recommended by the World Health Organization, (WHO) for global use. But this compound is very expensive (US\$ 25,000 - 30,000 per ton). Partly as a result of this prohibitively high cost, most developing countries, especially those in Africa, are not doing much about controlling this disease. In the meantime, the many well-intentioned agricultural development and water conservation schemes are serving as new reservoir sites for the snails to breed and the disease is spreading rapidly, but silently!

The implications of this phenomenon, as can be readily realized, are very serious. In 1986, at a special WHO expert meeting on plant molluscicides, where potentials of over 1000 different species of plants were assessed by an independent group, Endod was found to be the most promising and most extensively studied of all plant molluscicides known to date.

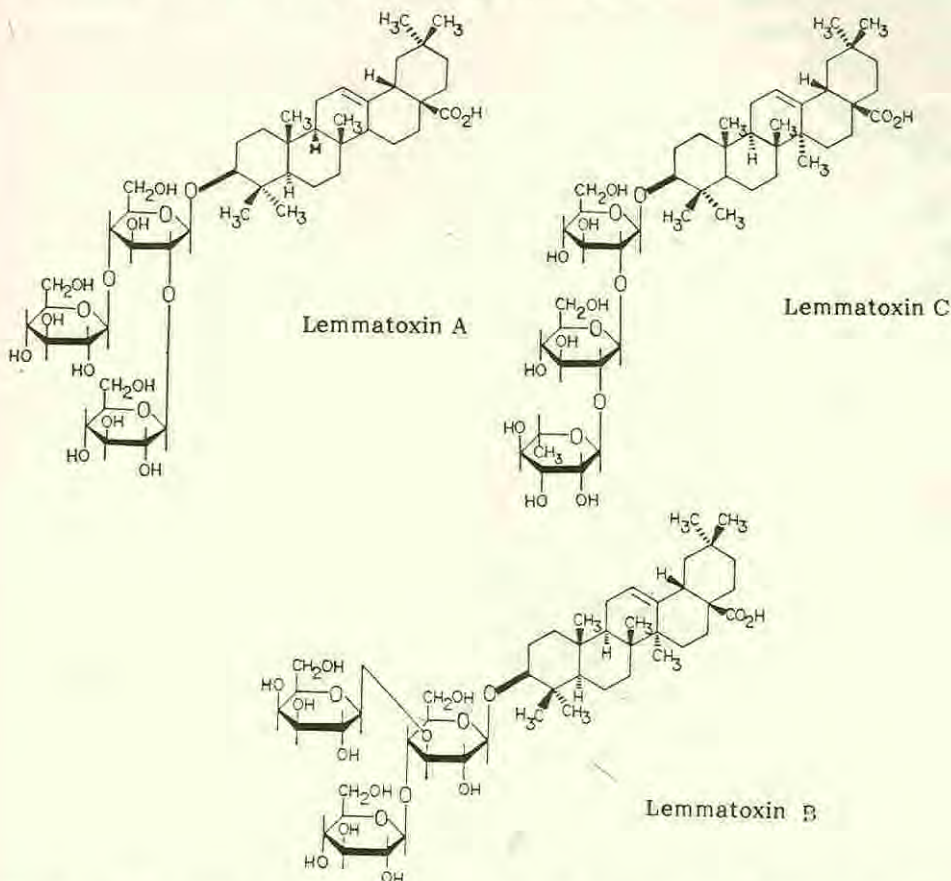
Various extraction procedures to concentrate the active components of Endod have been developed and some even patented. Biosynthetic production of the active principle through the use of Endod tissue (callus) culture systems have also been developed. All these have now been abandoned because of the additional cost they entail and their impracticality for field use.

A concerted effort to develop simple methodologies for the development and safe use of Endod could pave the way for the development of other plant molluscicides that could be used in different countries. Ideally, each country where schistosomiasis is endemic should select and use the equivalent of its own "Endod" for snail control.

As I mentioned earlier, the first ten years, from 1964-74, were the period of our greatest scientific achievements. Most of the studies on the molluscicidal and other properties of Endod were undertaken during these exciting 10 years. Findings were presented at a number of international conferences, and were published in major international publications, including the **Bulletin of the World Health Organization**, in 1970 (Vol. 42, pp. 597-612).

**Chemical and toxicological studies in the U.S.A. (1970-72).** Important chemical and toxicological investigations were undertaken. At the Stanford Research Institute (SRI) in Menlo Park, California, the following studies were conducted: chemical isolation and identification of the active principle, named "lemmatoxin" by Robert Parkhurst, the chemist who did the work; tests that established the nonmutagenic nature of the product with additional studies on the safety of the butanol extract to non-target animals. Other potential uses of Endod were also investigated: its fungicidal properties, its potential as an additive to detergent formulations, as a foaming agent in lightweight concrete preparations, and as a spermicide for possible use in birth control (for which SRI obtained a patent). Further molluscicidal and toxicological studies were undertaken in collaboration with Professor D. Heyneman at the University of California Medical Center in San Francisco. With Professor Andrew Spielman of Harvard School of Public Health, we studied the larvicidal effects of Endod against mosquito larvae, as well as its snail ovicidal (egg-killing) properties and together with

Dr. Barnett Cline of the US Public Health Service in Puerto Rico, we conducted a limited-scale field evaluation of the butanol-extract in natural bodies of water. All these studies have been published in different journals.



**The Adwa trials (1969-74).** During the period of 1969-74, a major five-year project was undertaken by the Institute of Pathobiology staff (Addis Ababa University) in the town of Adwa to control schistosomiasis primarily by the use of locally collected *Endod* to kill the target snails. The project also involved active community participation - a critically important factor.

In short, the results showed that transmission of the disease was significantly reduced from 63% to 33% in the population of 17,000 people. Within this population, among 3,500 children from the ages of 1-6 years, the infection rate fell from 50% to 7% (85% reduction).

These results were presented at the International Conference on Schistosomiasis held in Cairo, Egypt, in 1975 and published in the proceedings of that conference.

**Agrobotanical studies (1976-81).** During 1976-81, the Netherlands Government supported some important agrobotanical studies on *Endod* in Ethiopia. The studies were conducted by Dr. Legesse Wolde Yohannes, and a Dutch scientist, Dr. Charles Lugt. Out of over 500 varieties of *Endod* collected from all over Ethiopia, they cultivated 65 different strains and selected three varieties with especially high molluscicidal potency and high yield of berries.

One of these strains, E-44, has been selected and introduced successfully for cultivation in many African countries including Kenya, Tanzania, Zambia, and Swaziland as well as Brazil and the Philippines. It has also been chosen to serve as the standard "reference" strain of Endod for all chemical, toxicological and field studies.

**The period of obstacles (1981-86).** Following the successful earlier studies, we expected that this period would see the expansion of the agricultural production and large-scale field application and evaluation of Endod in Ethiopia.

For such activities, the Institute of Pathobiology needed financial assistance and the support of international bodies such as the World Health Organization (WHO). However, WHO required further studies to confirm the safety of Endod to humans and the environment before they would give clearance for its wide use. They insisted that the scientific work we had done in Ethiopia and elsewhere be repeated under standardized conditions following "Good Laboratory Practices" (GLP) in internationally recognized institutions - meaning in developed countries.

As a precondition for field evaluation, WHO also required that this biodegradable natural product be subjected to the same rigorous toxicological tests required before any unknown synthetic chemical product can be registered as a pesticide. This, of course, meant the need for substantial financial resources to support such studies in countries with "GLP".

**Fish toxicity.** The only reason given for not allowing field testing of Endod was its toxicity to fish. But this is not unique to Endod. All other molluscicides, including the only molluscicide approved by WHO for global use, the petrochemical byproduct **Bayluscide**, are also known to kill fish at molluscicidal concentrations. But the important point here is that edible fish and disease transmitting snails rarely live in the same habitat. Edible fish normally live in larger bodies of water whereas the snails require slow flowing streams and canals or shallow shores of larger water bodies.

As molluscicides are applied to bodies of water, the fish become irritated and swim rapidly into safer waters. The snails, without such mobility, are the principal targets of the molluscicides. Small fish in shallow waters may be killed by molluscicides, but the fish repopulate from untreated bodies of water upstream, as well as from the egg-masses of the fish, which are not affected by Endod. Furthermore, since Endod is biodegradable, its active principle rapidly decomposes, breaking down into inert and non-harmful material within a few days.

**Traditional use.** From a traditional acceptability point of view, Endod is a typical example of a natural product that has been selected by society through centuries of its safe use for washing clothes. People in the Ethiopian highlands have adopted and cultivated the Endod plant (synonymous with "soap") near their homes, using the berries as a laundering agent for the glistening white cotton shawls, the **shama**, which is characteristic of our culture.

The fish killing property of Endod is also well known and traditionally accepted. In fact, people in rural communities use it as an intoxicant to collect edible fish.

**Overcoming obstacles and present status.** The last few years have seen important breakthroughs that have countered many of the biases and obstacles raised against Endod, and that for so long have kept it in a vicious circle: no funds were made available for the rigorous toxicological tests required before Endod could be officially field tested, and no field tests could be sanctioned until these tests were completed.

As part of the continued fight to break this vicious circle and gain international recognition and support for the study of Endod, I organized the **First International Workshop on Endod, held in 1983 in Lusaka, Zambia**. A large number of concerned scientists and interested Africans attended, with the meeting formally opened by the Prime Minister. It was both a scientifically and personally rewarding meeting for me and my colleagues who have been engaged in Endod studies for many years. It gave us strong moral support, encouragement and a real sense of collegial solidarity. The proceedings of that meeting published in 1984 in book form by Tycooly International Ltd. continue to serve as a consolidated source of useful information on Endod.

A **Second International Workshop was held in Swaziland in 1986**, the proceedings of which were also published in book form with the financial support of UNICEF. By the time of the Swaziland meeting, the Ethiopian Strain E-44 of Endod had been introduced and experimentally studied in a number of countries including Swaziland, Zambia, Zimbabwe, Kenya and Brazil.

In Zambia, Dr. S. Silangwa, a parasitologist at the National Council for Scientific Research, and his colleagues are actively engaged in agronomic studies, and simple extraction and packaging procedures, for the dual use of Endod as a locally producible **molluscicide and detergent**. They are using the locally collected Endod plants and imported (E-44) strains of Endod in some of the 300 hectares of land.

In Swaziland, Prof. L. Makhubu, a natural product chemist with a research grant from USAID, is leading agronomic and chemical studies to determine the growth characteristics of the plant at different altitudes in Swaziland, and to develop technologies for packaging the product for dual purpose as a molluscicide and as a detergent for village level use.

In Zimbabwe, scientists at the Blare Laboratory are also doing studies on the local and imported (E-44) strains of Endod in different communities in the country with some financial support from Denmark (DANIDA). Mr. Jerry Ndamba, one of the members of the team, is doing a Ph. D. thesis on this project through special arrangement with the University of Copenhagen and the Danish Bilharzia Laboratory (DBL).

**The Third International Workshop is being planned for October 1990 in Ethiopia** where Dr. Legesse Wolde-Yohannes and his colleagues at the Institute of Pathobiology at the University of Addis Ababa are continuing their pioneering work on the potential dual use of Endod as a molluscicide and locally producible detergent, with meager financial resources.

Following the workshops in Zambia and Swaziland, the UN Development Programme (UNDP)/UN Fund for Science and Technology for Development, in cooperation with the International Development Research Centre (IDRC) in Canada, convened an **Endod Toxicology Expert Group meeting in New York in February 1986**. The objective of that meeting was to identify and remove the main obstacles against the field application of Endod. A second meeting of the same group was held at the WHO in Geneva in December 1986. This Expert Group developed a procedure for preparing **standard water extracts of Endod (Endod-S)** to be used as the standard material for testing in different laboratories. The group also delineated selected basic toxicological tests to be performed in order to clear Endod for field trials.

IDRC has since commissioned studies towards the basic OECD/Tier I regulatory requirements, including acute mammalian and eco-toxicity studies that are now being performed in Canada, basically repeating what was done several years before, but this time under "Good Laboratory Practices". These studies are expected to be completed in 1990, hopefully paving the way for more extensive field evaluation.

In a parallel and independent initiative, the Finnish International Development Assistance Agency (FINNIDA) is presently planning to fund the remaining

definitive toxicological studies required for the **international registration of Endod as a pesticide**, following established procedures for registering any synthetic chemical product. A coordinating committee has been established to avoid duplication and ensure speedy completion of the required studies. FINNIDA is also planning to provide support for agrobotanical and community-based studies in Zambia on a bilateral assistance basis.

In other developments, scientists in a number of African countries, Brazil, and more recently, the Philippines, are forming an **Endod Technical Cooperation Among Developing Countries (TCDE) Network** and are exchanging seeds and information. They plan to have a newsletter to exchange their research findings and coordinate their work on a regular basis. In the Netherlands, a group of concerned and interested scientists, coordinated by Dr. Charles Lugt in the Hague, have formed a "**Support Endod Group**" that is doing extraction and toxicological evaluation work. In Florence, Italy, an Italian "**Technical Working Group on Endod**" has put together a major project for collaborative agrobotanical studies in Ethiopia and Zimbabwe. They are now trying to obtain some funds for this from the Italian government. Drs. Giovanni Ferrari and Valerio Giannellini at the University of Florence are the prime-movers of this project.

In spite of all these promising initiatives, however, there is still the need for more financial support for the work to be done. The toxicological studies should be completed as soon as possible, to get the clearance and support of WHO and other organizations. The agrobotanical and extraction studies and community involvement strategies need to be sharpened to pave the way for large-scale field studies. If the current turn of positive events continues, and if the necessary financial and intellectual support is obtained from all concerned groups, I believe that by 1992 Endod should be widely used in some African countries. The popularization and cash award (for the research) received from the Right Livelihood Foundation will help in this direction.

**Lessons for the Future.** Thinking beyond Endod, some useful lessons can be drawn from our long experience in the struggle to overcome obstacles and to help promote the future of science and technology in Africa.

We have learned the hard way that the root problems of scientific research in Africa are not only the lack of adequate facilities and funds, but also the biases and reservations of some individuals and organizations in industrialized countries who find it difficult to accept that any good science can come from our part of the world. Even our own government officials who rely on foreign assistance and the advice of such international organizations may be unduly pressured.

Also, except for occasional lip service, little credit is given to the wisdom of traditional societies in their ability to select, over long periods of time, such natural products as Endod for their continued and demonstrably safe use. To modify and redirect this traditionally accepted product for the control of schistosomiasis (whose spread owes much to well-intentioned but epidemiologically disastrous projects designs) has been a major challenge.

Thorough toxicological evaluation should indeed be required of any product before it is used in field conditions. But such evaluation should also include the traditional knowledge of the people about such products. The logic of requiring the same toxicological tests from both a known biodegradable natural product and an unknown synthetic chemical product should be questioned. This also applies to the many traditional herbal medicines which are routinely used by millions of our rural people who cannot afford, or have no access to, modern medicines.

After three decades of post-colonial struggle, hopes and disappointments, I believe that the best future course for Africa is to invest in efforts to build

the endogenous capabilities of its own people. This can be done through raising self-esteem and self-confidence by creating a sense of respect for the wisdom and experience of its own traditional societies, and trained scientists, perhaps through the integrated application of traditional and modern technologies for alleviation of local problems. Future action should also focus on an increased recognition and strengthening of existing African scientists and research and training institutions. Africa's scientific and technological manpower and infrastructure must be increased by many fold. It is only through this type of major efforts that we can promote sustainable and self-reliant development in Africa.

International collaborative and development aid should be more geared towards helping us help ourselves, however slow and frustrating the process may appear, rather than creating increasing dependence, as has been the case so often in the past. Put very simply, development assistance should focus more on teaching us how to fish rather than giving us fish when we are hungry, and then only when our cries are heard throughout the world through the mass-media.

### CONCLUSION

In conclusion, I would like to thank the so many colleagues and organizations, in Africa and elsewhere, who have been our genuine partners in this venture. I would particularly like to acknowledge the continued support and encouragement of the Addis Ababa University, the U.S. Office of Naval Research (O.N.R.), the Stanford Research Institute (S.R.I.), the Netherlands government, IDRC of Canada, DANIDA and FINNIDA, and the United Nations, particularly UNICEF and UNFSTSD. I would also like to take this occasion to thank my wife, who for 25 years has given her unflinching personal and moral support in my studies and struggles for the international recognition of Endod.

Finally, I want to thank the Right Livelihood Society for giving us this opportunity to speak our minds frankly and openly to an audience that can make a difference! May this occasion serve as a major encouragement to the many able Third World Scientists in whose name we would like to accept this Award.