EPPAD Bulletin

Vol 3, Number 1 March 2023

Official Biannual Publication of the Ethiopian Pharmacists and Pharmaceutical Scientists Association in the Diaspora (EPPAD)

Published in Springfield, VA - USA

Manuscripts to the Bulletin can be sent to our email address: @ info@eppad.org

In This Edition

Editor's Corner

We are delighted to bring this issue of ***EPPAD Bulletin*** to you (Vol 3, No. 1). EPPAD Annual Conference was held last year on December 3, 2022. In *EPPAD News and Highlights* section, a pictorial depiction of the conference is presented. Also in this section, news coverage about the admission of Ethiopian Food and Drug Authority (EFDA) in the European Pharmacopoeia Commission as an observer is highlighted. EPPAD played a role in the early stages of this endeavor by helping in the writing of the application. In the *Pioneers of Ethiopian Pharmacy* section, Ato Gabriel Daniel eloquently writes a historical review on how the system of pharmaceutical supplies in Ethiopia evolved over the years starting with the Central Medical Store (CMS) to the current Ethiopian Pharmaceutical Supply Agency (EPSA). He provides details on this important aspect of pharmacy. He further mentions key pharmacists who played leading roles and left their own imprints in this area.

In this issue, various articles in diverse areas of pharmacy are included. In the *Clinical Highlights and Review Articles* section, various authors contributed manuscripts. Most of the articles were based on presentations at the 2022 EPPAD Conference. Some clinical insights are provided by Dr. Pawolse Ketema on the zoonotic disease monkeypox (mpox). He describes the clinical presentations, signs and symptoms, transmission, and vaccine treatment options for this rare infection. Drs. Moa and Tesfaye Biftu cover emerging gut hormone-directed therapies related to Parkinson's disease, Alzheimer's and other complications. The article also deals with, among others, modalities for restoring the gut flora, such as using fecal transplants/pills, prebiotics and postbiotics.

Dr Asfaw Debella writes about Ethiopian traditional medicine and the research and business opportunities this practice provides. He provides a broad background of Ethiopian traditional medicine and cites several examples of medicinal plants used as home remedies and gives a concise tabulation of their preparation, uses, chemistry and their diverse pharmacological properties. Dr. Amare Ayalew of Debreberhan University, under a title "Marketing of Traditional Medicine in Ethiopia," focuses on various formulations that the university has developed. He gives background literature, and his effort exemplifies how educational institutions, such as Debereberhan University, can step out of the silos and confines of academia and get involved in modernizing traditional medicine.

EPPAD Bulletin Editorial Team believes that readers can appreciate and learn from the stories and scientific articles covered in this issue.

Fekadu Fullas, PhD

Editor- in-chief, ***EPPAD Bulletin***

EPPAD News and Highlights

The annual EPPAD Conference was successfully held at the Hilton Hotel in Rockville, Maryland on December 3, 2022. The conference was a hybrid-type meeting with several attending in-person at the site, and many others via zoom mainly from Ethiopia. A total of about 40 people participated. Coordinators of EPPAD Working Groups gave condensed reports of various activities which were accomplished during 2022. Professor Tilahun Adera presented a keynote lecture. He also happened to be the recipient of the 2022 EPPAD Research and Development Award. Other recipients in the respective categories were Professor Ariaya Hymete (Pharmacy Faculty), Misrak Lissanu (Leadership Achievement), EPPAD Pharmaceuticals Inc (Social Responsibility), and Dr. Mende Sorato (Pharmacy Practice). CE lectures were delivered by Drs Pawlose Ketema and Tesfaye Tefera. Other papers, many of which are included in this issue of the Bulletin, were presented. The ambiance and camaraderie were evidently palpable throughout the conference and particularly at the networking session, as captured in the pictures below.

Continuing Education (CE) presentations

Award presentations

Some of the live and zoom participants of the conference.

A collage of shots at the networking session of the Conference.

EFDA Granted Observer Status at the European Pharmacopoeia Commission

The Ethiopian Food and Drug Agency (EFDA) collaborated with the Ethiopian Pharmacists and Pharmaceutical Scientists Association in the Diaspora (EPPAD) to develop an application for an observer ship status on the European Pharmacopoeia Commission. The process that started in late 2020 culminated with the European Pharmacopoeia Commission granting observer status to the EFDA during its 174th session (November 2022). This decision demonstrates the dynamism of the European Pharmacopoeia, which now has 31 observers from around the world, in addition to its 40 members (39 European states and the European Union). Ethiopia joins six other African countries, the USA and WHO in this status.

This status allows EFDA representatives to participate in the scientific work of the European Pharmacopoeia Commission and other activities of the European Directorate for the Quality of Medicines and HealthCare (EDQM), so as to benefit from the EDQM's experience in the field of medicinal products for human and veterinary use, to exchange with experts from European and international licensing authorities and inspectorates, and to take part in the work on the development of international quality controls for medicines and the methods of analysis used.

About The European Pharmacopoeia (Ph. Eur.) Commission and EFDA

The European Pharmacopoeia (Ph. Eur.) Commission is the decision-making body of the European Pharmacopoeia and is responsible for the elaboration and maintenance of its content, including the evaluation of proposals for inclusion, revision or suppression of monographs and general chapters.

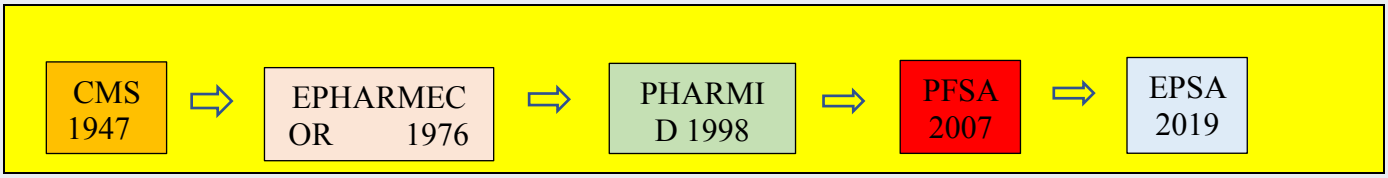
The European Pharmacopoeia Department (EPD) is responsible for the Secretariat of the European Pharmacopoeia (Ph. Eur.) and for preparing the texts of the European Pharmacopoeia (Ph. Eur.) with the relevant groups of experts. To elaborate the Ph. Eur., the EPD works with a network of over 800 experts with an extensive scientific background in different disciplines and from all over Europe and beyond. The Ph. Eur. Commission, the governing body of the Ph. Eur., holds three sessions per year to formally adopt not only the Ph. Eur. texts, but also its work program and to appoint Ph. Eur. experts.

The Ethiopian Food and Drug Administration (EFDA) is a semi-autonomous regulatory agency of The Federal Democratic Republic of Ethiopia mandated to promote and protect the public health by ensuring safety and quality of products and health service. EFDA sets standards and provides regulatory oversight for the registration, quality control, manufacturing, clinical trials, importation, distribution, marketing, information, pharmacovigilance, labeling, prescription, and dispensing of medicines, foods, supplies and medical devices, including licensing and inspection of pharmaceutical professionals and related establishments.

Pioneers of Ethiopian Pharmacy

The Ethiopian Pharmaceutical Supply Services from 1947 to Now

Prepared by Gabriel Daniel (Aklile G Giorgis) - March 2023



The main aim of the Ethiopian Pharmaceuticals Supply Service (EPSS) is to improve the continuous availability of safe and effective health commodities at an affordable price in a sustainable and timely manner. EPSS has evolved to where it is today through five iterations (graphics above) under the leadership of twelve general managers.

The history of the Ethiopian Pharmaceuticals Supply Service begins with the early days of Emperor Haile Selassie with the establishment of the **Central Medical Store (CMS)** about 75 years ago as a public pharmaceutical import, warehousing, and distribution agency of the Ministry of Health in Addis with a branch in Asmara, Eritrea. The history before what is recorded here is something left to us in the future to dig deep and find the history of the earlier days of the supply system. The first location of CMS was the old warehouses, presumably constructed/used by Italian occupiers in the Pasteur Institute compound (now the Ethiopian Public Health Institute – EPHA) in Gullelle in western part of Addis Ababa.

The General Managers during the times of CMS, known to the writer, include Tsehaye Hadgu, Lakew Awoke and Getahun Tadewos (Getahun also oversaw the transition from CMS to EPHARMECOR). In 1976, the military government of Ethiopia (*Derg*) under Colonel Mengistu Haile Mariam decided to create a new supply system with a socialist orientation which resulted in the establishment of the **Ethiopian Pharmaceutical Corporation (EPHARMECOR).** EPHARMECOR was mandated to manage and operationalize the supply services by bringing the central medical store (CMS), the sole government manufacturing plant EPHARM, and all nationalized domestic and international importing private enterprises under the Corporation. These privatized businesses were organized under a branch called Central (Teklehaimanot) Branch managed by technical managers that continued to serve the private sector. To ensure access to quality assured, affordable medicines, EPHARMECOR had dozens of private community pharmacies all around Addis Ababa. The government gave the nationalized residential compound of the late Ras Mesfin Sileshi Djote to EPHARMECOR as the new headquarters (with the original residence of the late Ras Mesfin still the main administrative office-seen in the picture) and warehousing compound that met the security needs and expansion potentials of the agency. The compound currently has several professionally designed blocks for the different product categories it stores and distributes. The steady plunge in EPHAMECOR's capital and the subsequent weakened supply compounded with the period's political partisanship necessitated another restructuring which came during the period of the transitional government of Meles Zenawi in 1994.

The transitional government allocated a significant budget to bridge the pharmaceutical gap and restructured EPHARMECOR into a new organization called **Pharmaceutical and Medical Supplies Importer and Wholesale Distributor (PHARMED).** PHARMED continued with the works of its predecessor. The in-coming Ethiopian People's Revolutionary Democratic Front (EPRDF) advanced free market economy as part of its developmental state model and subsequently privatized the nationalized enterprises. PHARMED was once again re-established with reformed vision, mission, and goals in 2007 under proclamation No. 553/2007 bearing the name **"Pharmaceutical Fund and Supply Agency (PFSA).**

It was during the next several years that a robust re-engineering process was initiated to modernize the logistics, information, and supply chain management systems commensurate with the high demand of quality and efficient services. This helped respond to the supply management needs of expanded health facilities, HIV/AIDS programs funded by the US President's Emergency Plan for AIDS Relief (PEPFAR), Covid-19, and other emergency programs. The supply chain activities were complemented with initiatives that promoted rational use of medicines as a continuum of supply chain. In addition to the products PFSA procures, the Agency also handled the storage and distribution of more than 70 program commodities, and the products included medical equipment, medicine, medical supplies, laboratory reagents etc. donated by development partners.

To manage these high-volume, high-cost commodities professionally and efficiently, PFSA focused on infrastructure, human and information system development projects. A total of 19 modern modular warehouses were constructed at the center and branches all over the country, with location selection based on geographic accessibility to health facilities. This has increased the Agency's warehousing capacity to 305,910 m3 from the 16,760 m3 that was initially available. The government, with support from USAID funded supply chain and pharmaceutical management system partners such as John Snow's DELIVER Project; Management Science of Health's (MSH) Rational Pharmaceutical Management, (RPM), SPS, SIAPS, SCMS projects; Chemonics' Global Health Supply Chain Management (GHSC-PSM) project, developed and implemented the Pharmaceutical Logistic Master Plan (PLMP) in 2005, subsequently adding the Integrated Pharmaceutical Logistics System (IPLS) and Rational Drug Use (RDU) aspects of the service.

Ethiopian Pharmaceuticals Supply Agency (EPSA) procures almost 70% of all the medicines consumed in Ethiopia. EPSA procurement increased from US$ 27 million in 2007 to US$ 500 million in 2018 and was projected to reach about $1 billion in 2022.

Under the current government, PFSA has once again changed its name at the beginning of the 2019 to **"Ethiopian Pharmaceuticals Supply Agency (EPSA),** however, without changing proclamation 553/2007.

Currently, EPSA is acting as the epicenter of public pharmaceutical supply affairs in the country. The head office procures and distributes pharmaceuticals, medical supplies, medical equipment, and laboratory reagents from local and international manufacturers to its nineteen hubs that in turn reach over 5,000 medical facilities located in all corners of the country. It coordinates and oversees a wide network of clusters and its operations that comprise a mix of warehouses and office locations throughout Ethiopia.

Name	*Year Established*	*Duration*	*General Managers*	*Location*
CMS	***1947***	***(29 yrs)***	***Tsehaye Hadgu*** ***Lakew Awoke*** ***Getahun Tadewos***	***EPHI/Pasteur Institute Compound***
EPHARMECOR	***1976***	***(22 yrs)***	***Getahun Tadewos*** ***Atnafu Tariku*** ***Laike Gebre Sellassie*** ***Berhanu Zeleke*** ***Tesfaye Degefu***	***EPHARMECOR*** ***(Ras Mesfin Compound- Opposite St. Paulos Hospital)***
PHARMID	***1998***	***(8 yrs)***	***Getahun Tadewos*** ***Girma Bedasso***	
PFSA	***2007***	***(12 yrs)***	***Hailesellasie Bihon*** ***Meskele Lera*** ***Lokko Abraham MD***	
EPSA	***2019***	***to Present***	***Abdulkedir Gelegelo***	

Acknowledgements: *We thank the following people who, in one way or the other, had a stake in the operation of these iterations of the Ethiopian Pharmaceutical Supply Services and provided with information to fill missing links. (Tesfaye Degefu, Jeregna Qennaa, Hailu Tegegnework, Negusu Mekonnen, Million Abebe, Zenebech WM, Hailu Tadeg, and Workineh Getahun).*

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Return of the Pox: The Case Against Monkeypox

Pawlose Ketema, PharmD, BCPS, BCIDP
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Monkeypox is a rare zoonotic disease belonging to the Poxviridae family. It was first described in the late 1950's as pox-like disease in cynomolgus monkeys. While there were sporadic outbreaks, the disease was largely limited to zoonotic animals until it was first identified in the Democratic Republic of Congo in a 9-month-old child. Monkeypox cases were largely limited to central and West Africa, and cases seen outside of these two regions were largely linked to travel and importation of animals harboring the virus. Although there are two distinct clades, Central African Clade and West African Clade, the genomic variation is less than 1%. The outbreak thus far has largely affected African countries, until a series of outbreaks were reported in May 2022. As of February 2023, there have been 85,922 global cases, with U.S. cases surpassing 30,000 cases. During this current outbreak, the World Health Organization (WHO), proposed a name transition from monkeypox to mpox, citing racial and stigmatizing language observed in some communities. Transmission of mpox varies between endemic and nonendemic areas. In endemic areas transmission, it largely occurs via zoonotic animal reservoirs into humans, while in nonendemic areas, transmission largely occurs via human travel or the importation of infected animals. Infection from mpox is characterized by prodromal symptoms including fever, headaches, chills, malaise, lymphadenopathy, and rash. Although this clinical presentation may mimic other types of orthopox virus infections, the presence of lymphadenopathy and rash are hallmark signs of mpox infection. The rash usually appears in five stages: macules, papules, vesicles, pustules, and scabs. While these lesions could occur at any site, in the current outbreak, it was mostly noted to affect the mouth, genital, and anorectal areas. The presence of lymphadenopathy is also a major distinguishing factor from smallpox, as infection with the smallpox virus does not produce lymphadenopathy.

According to the Centers for Disease Control and Prevention (CDC), there are available vaccines both for pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) as well as treatment options in patients with mpox virus. Treatment of mpox is indicated in patients with severe disease, defined as a hemorrhagic disease, severe lymphadenopathy, involvement of multiple organ systems, immunocompromised, pediatrics, and patients with conditions affecting skin integrity. On the other hand, the Advisory Committee on Immunization Practice (ACIP) has recommended certain individuals receive PrEP and/or PEP using the two available vaccines. Currently, there are four treatment agents including Tecovirimat, Brincidofovir, Vaccinia Immune Globulin Intravenous, and Cidofovir. Tecovirimat was initially approved in 2018 under the designation of Material Threat Countermeasure Priority Review Vouchers for the treatment of human smallpox disease. Since its initial approval, there have been documented cases of its use in the management of smallpox and disseminated ocular infections with cowpox in immunocompromised patients. Tecovirimat works by inhibiting protein p37 which inhibits viral transmission. It is formulated as both oral and intravenous and has a weight-based dosing strategy. Common side effects with oral tecovirimat include headache, nausea, and abdominal pain, while IV formulations are associated with infusion site pain, swelling, erythema, extravasation, and headache. Its use for the treatment of mpox is under the CDC Expanded-Access Investigational New Drug (EA-IND) and obtained through the national stockpile. Other agents listed above have largely been listed as

options or in the case of brincidofovir have been recommended for use in conjunction with tecovirimat in patients with severe disease or those at high risk for progression to severe disease. The two available vaccines for PrEP and PEP include ACAM2000 and JYNNEOS. Unlike ACAM2000, JYNNEOS contains a replication-deficient modified vaccinia virus strain and is therefore associated with a lower risk of adverse effects and is indicated for immunocompromising conditions. Notably, ACAM2000 was used to help eradicate smallpox virus, but since then it has largely fallen out of favor due to the number of block box warnings including myocarditis, and pericarditis as well as a contraindication in immunocompromising conditions.

Mpox continues to pose a significant challenge with limited therapeutic options. While most identified cases have been self-limiting, there have been documented morbidity and mortalities associated with mpox. In suspected mpox cases, prompt initiations of vaccines and therapeutics are essential in preventing the progression to severe disease.

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Emerging Therapy
The Gut-brain Links and the Microorganisms in Our Body*

Moa Biftu (PharmD) and Tesfaye Biftu (Ph.D.)

BACKGROUND

The gut is the body's largest sensory organ with a surface area over one hundred times that of the skin. We often talk about "*butterflies in our stomach*," a "*gut-wrenching experience*," or "*going with our gut*" to express our feelings. Now, we are beginning to learn that there is a complex interaction between various nerve signals, gut hormones and the bacteria that live in our digestive system (the gut microbiota). Almost all the neurotransmitter serotonin is produced in the gut. The gut has more nerve cells than the spinal cord and the immune system. This includes the enteric nervous system **(ENS)** that controls digestion, the swallow reflex, release of enzymes to break down food, and blood flow to manage nutrient absorption and elimination. The **ENS** communicates with our central nervous system **(CNS)** using peptides and electrical signals, and it triggers emotional changes for people with irritable bowel syndrome (**IBS**) and functional bowel problems such as constipation, diarrhea, bloating, pain, and upset stomach.

The brain affects the stomach and intestines. On the other hand, a person's stomach or intestinal distress can also cause anxiety, stress, or depression. The gut-brain axis is a bidirectional communication system between the two. For example, the thought of eating releases digestive juices before food arrives in the stomach. Therefore, the brain and the gastrointestinal (GI) system are intimately connected. This occurs with hormonal circuits and neurotransmitters in response to various stimuli.

The vagus nerve is part of this network and serves as the primary neural link to transmit signals back and forth between the gut, the CNS and the other organs.

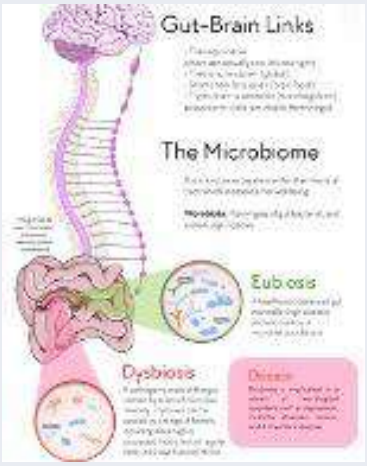
The ENS consists of millions of neurons that help to modulate this communication.

TECHNOLOGIES USED TO UNDERSTAND THE GUT-BRAIN LINK

Recently developed single cell sequencing technology has been used to help understand the function of every specialized cell type in the various compartments of the gut-brain axis. Circuit tracing techniques enable an understanding of how these cells communicate with each other. Optogenetics and chemo genetics, either with light or genetically engineered biological tools, activate the individual cell types to unveil the physiology.

VAGUS NERVE ELECTRICAL STIMULATION TREATMENTS (VNS)

The vagus nerve can be stimulated electrically or by hormones, meditation, exercise, massage, music, laughter, and acupuncture. An electrical device that activates the vagus nerve has been approved as a treatment for migraines, epilepsy, cluster headache and refractory depression. There's also evidence that such systems could be used to treat Parkinson's disease (PD) and autism.



Gut-Brain Axis and Microbiota

GUT HORMONE TARGETED TREATMENTS

Gut hormones are secreted by enteroendocrine cells in the stomach, pancreas, and the small and large intestine. They control various functions and at times act as neurotransmitters and neuromodulators in the central and peripheral nervous systems. The gut hormones can be divided into the gastrin–cholecystokinin, secretin, somatostatin and motilin families.

Ghrelin is a peptide hormone released from the stomach and liver and is often referred to as the "hunger hormone". Treatments with ghrelin agonist can be used to treat anorexia and loss of appetites in cancer patients. Ghrelin blocking treatments are under investigation for obesity. ***Glucose-dependent insulinotropic polypeptide*** (GLP-1) and **glucose dependent insulinotropic polypeptide** (GIP) have acute effects on food intake. ***Oxyntomodulin*** plays a role in controlling acid secretion and satiation. Other gut hormones include ***cholecystokinin, gastrin, secretin, vasoactive intestinal polypeptide (VIP), chromogranin A, enkephalins, enteroglucagon, galanin, leptin, motilin, neuropeptide Y, neurotensin, pancreatic polypeptide, peptide YY, somatostatin, substance P and trefoil peptides*.**

Metabolic disorders

Gut brain communication is essential for gastrointestinal function. The vagus nerve controls aspects of eating. There are around two dozen highly specialized cell types in the vagus nerve, and these can be specifically targeted in the gut to avoid off target toxicity associated with systemic exposure. Hormones that modulate the feeling of fulness and glucose control are well understood.

Obesity is one of the main underlying causes of chronic diseases in the United States and increasingly so in the rest of the world. Currently, there are injectable therapies that produce between 10 to 20% weight loss with diet and exercise. Diabetes and/or obesity drugs that mimic the action of glucagon-like peptide 1 include: Dulaglutide (weekly), Exenatide extended release (weekly), Exenatide (twice daily), Semaglutide (weekly), Liraglutide (daily), Lixisenatide (daily), Semaglutide (taken by mouth once daily) and tirzepatide (weekly).

Emerging science focused on enhancing barrier function in the gut could be helpful in inflammatory bowel disease and other diseases, such as celiac disease, that affect the intestinal lining. There are no approved therapeutics for the treatment of barrier malfunction.

Parkinson's disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder. Medications, such as pramipexole and ropinirole, that increase or substitute for dopamine have been used for the treatment of PD. The gut microbiota produces neurotransmitters or regulate host biosynthesis of neurotransmitters. These neurotransmitters regulate neural signaling in the ENS and vagal nerve to control brain function. Researchers have reported that α-synuclein is able to diffuse from the intestinal tract to the brain via the vagus nerve, supporting the hypothesis that PD pathogenesis may begin in the GI.

MICROBIOTA BASED THERAPY

Liver disease

Gut flora affects the pathogenesis of hepatic encephalopathy (HE). Lactulose, the most used standard therapy, works in part by altering gut flora to decrease ammonia production and absorption. Lactulose also serves as a "prebiotic" ingredient, encouraging the growth of endogenous bacteria. Gut flora therapy also improves uremia in hemodialysis patients.
Improvements in HE is reported by using the number connection test (NCT) and a simple neurophysiologic test, brainstem auditory evoked potential (BAEP) to monitor changes in participants taking either placebo, fermentable fiber, or fermentable fiber plus a probiotic compound.

Cancer

Bacteria, viruses, fungi, and other microbes naturally found in the gut can influence treatment

response either positively or negatively. Gut microbiome can shape how patients with cancer respond to immunotherapy and certain communities of microbes are associated with a better response to cancer treatment. It may be beneficial to alter the microbiome to make treatment more effective.

Fecal microbiota transplants (FMT), taking stool from one healthy patient to another patient, has shown a beneficial effect by promoting healthy bacteria that are able to fight infections, such as *Clostridioides difficle* (*C. diff)*. Infection with *C. diff* can overtake the gut after antibiotic therapy causing life-threatening diarrhea. *Clostridioides difficle* occurs in up to one-third of patients. A defining aspect of recurrent *C. diff* is the lack of diversity in the gut microbiota of those infected. Fecal microbiota transplants, or "poop pills," from healthy donors can restore the gut microbiome diversity in patients with *C. diff* and help clear the infection. This treatment is now the standard of care for patients with recurrent *C. diff*. Alternatively, a mixture or consortia of microbes could be manufactured and administered as a pill. Recently, an oral microbiome therapy, made from a consortium of microbes, was used in a Phase III trial to treat recurrent *C. diff*.

Alzheimer's and neurodegenerative diseases

With age, the beneficial gut microbiota are lost due to factors such as diet, sedentary lifestyle, sleep deprivation, circadian rhythms, and oxidative stress, which in turn affects normal brain function via the brain-gut microbiota **(BGM)**. Several recent reviews and publications indicate that the gut microbiome is responsible for a variety of aging and neurological processes which can be used as potential targets for anti-aging interventions. Understanding the interaction between aging, gut microbiome, neurodegenerative diseases will lead to discovery of ways to delay aging and combat neurodegenerative diseases such as Alzheimer's.

ROLE OF NUTRITION TO IMPROVE GUT MICROBIOTA

It is estimated that 1-3% of our weight is due to microorganisms that reside in or on our body. Our gut carries trillions of bacteria and other organisms living inside the small and large intestines, known as the microbiota or intestinal flora. Microbiota affects our digestion, ability to absorb nutrients, immune system, brain performance, and mood.

Probiotics in Fermented Foods

One way to take care of our intestinal flora is by eating fermented foods, which have been part of the human diet for centuries, and positively influence health in many ways. Fermented foods increase overall gut microbiota diversity and reduce key markers of inflammation, promoting intestinal health. Examples of fermented foods are: ***injera, kimche, plain Greek yogurt, sauerkraut, kefir, natto, kombucha, vegetable brine drinks, and fermented miso***. Injera, a fermented bread from Ethiopia, is made from teff. *Teff* is a superfood with high sources of minerals and vitamins that can boost the immune system.

Prebiotics

Prebiotics are not digested but are fermented in the small bowel, leading to positive effects by increasing the number of beneficial bacteria in the colon and favoring the absorption of minerals such as calcium, iron, magnesium, and zinc. Prebiotics also help with constipation and inflammatory bowel disease.

According to a 2019 article from the National Library of Medicine*, "Prebiotics exert a remarkable influence on human health, which makes them alluring and attractive agents to improve the quality of human life."*

Prebiotics are found naturally in many types of fibrous foods such as vegetables, fruits, and legumes. Examples of foods that contain high levels of prebiotics are ***garlic, onion and leek, bananas, oats and barley, Jerusalem artichoke, asparagus, chicory root, dandelion greens, flaxseeds, cocoa powder, apples, legumes (beans, lentils, and peas), seaweed, wheat bran, jicama root, konjac root and burdock root***.

Processed Foods & Artificial Sweeteners

Sucralose, aspartame and saccharin are reported to interfere with microbiome diversity and hinder the

body's ability to absorb blood sugar. Emulsifiers in processed foods may also destroy the protective layer of mucus in the intestine and interact with microbiota resulting in low-grade inflammation. This in turn can lead to increased body fat and associated metabolic effects such as impaired fasting glucose, high triglyceride levels, and low HDL cholesterol levels.

SUMMARY

Currently, the targets for drugs used to treat diverse diseases are enzymes, receptors, and ion channels. In the future, understanding of the effects of nutrients (food), electrical stimulation and the microbiota in our body, will add additional safe and effective methods to treat diseases.

**Disclaimer: None of the discussions in this article are suggestions to treat any disease. Consult your doctor for any health problems mentioned in the article.*

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Development of Traditional Medicine for the healthcare and its potential for business opportunity

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Summary

Traditional Medicine has been in existence even before the advent of modern medicine. Traditional medicine appears to be the source of healthcare particularly among the rural majority communities of Africa due to its intrinsic qualities, unique and holistic approaches as well as its accessibility and affordability. Complementary and alternative medicine is becoming popular in developed or industrialized countries with alarmingly increasing prevalence of chronic diseases due to aging societies, urbanization, unhealthy eating habits, obesity and lack of physical activity. In the Ethiopian context, a large segment of the population relied for centuries on a system of traditional or indigenous healthcare for treating various ailments. Traditional medicine could contribute a significant role in healthcare through research and development efforts of multidisciplinary experts in integrated manner. Medicinal plants that originate from traditional medicine lore are also obviously an alternate candidate commodities or products as income source and improving the livelihood for the community. It could also contribute to the national economy through export of raw or processed medicinal plants for earning foreign currency in order to exploit the potential of traditional medicine. Therefore, there is a need for partnership, collaboration and concerted efforts for research, development, and promotion of traditional medicine.

Introduction

Traditional and modern systems of medicine were developed by different philosophies. They look at health, diseases, and causes of diseases in different ways. These differences bring different attitudes ranging from complete rejection of traditional medicine by modern medicine to parallel existence of traditional medical practitioners with little communication over patient care (Leonti and Casu, 2013; Enioutina, *et al* 2020). Ethiopia has a rich history of traditional medicine and indigenous knowledge practices. Traditional remedies originated from locally grown plants, animal products and minerals. Traditional medicine is an integral part of the local culture that is affordable and accessible even when there is demonstrably efficient and less costly alternative modern health care. This is often linked to its multi-ethnic and cultural diversity coupled with the various physical environment that fosters an array of unique flora and fauna (Pankhurst, 2001; Fullas, 2012).

The knowledge on Ethiopian traditional medicine were mainly orally based, and information on healing practice were passed down by practicing healers from generation to generation, often with considerable secrecy. However, many written documents exist, such as the very earlier of medico religious texts written in Ge'ez "Metshafe. Faws" and "Metshafe Medhanit" in the mid-17th century. In Ethiopia, traditional health practitioners are categorized as herbalist-healers (Kitel betash), spiritual or faith-based healers and bone settlers (waggesha). In addition to this knowledgeable household members, in many cases mothers, use home-based remedies prepared from medicinal plant products for family healthcare (Debella *et al*., 1999; Asfaw, 2001; Fassil, 2003; Gedif and Hahn., 2003; Birhan and Teklehaymanot, 2011; Lulekal *et al*., 2013)

Traditional medicine has a significant role in the primary health care delivery in Ethiopia. where 80% of human and 90% of livestock population depend on indigenous medicine similar to many developing countries particularly that of Sub-Saharan African countries. A great variety of medicinal plants are used for livestock diseases, particularly by the pastoral and agro-pastoral communities. Livestock have economic benefits through providing milk, meat, skin and manure, and remain marginal due to the prevailing livestock diseases. Animal health problems are among the principal bottlenecks for poor livestock performance and cause high economic losses, particularly for poor farmers (Mesfine and Lemma, 2001; Fassil, 2003; Mussema, 2006).

Medicinal plants play a significant role in primary healthcare delivery in Ethiopia and about 880 species of

medicinal plants distributed in different agroclimatic zones of the country have been used in the traditional health care system of the treatment of numerous ailments (Edwards *et al*., 2000; Hedberg and Persson, 2006 and 2009). This emphasizes the importance of systematic conservation of medicinal plants, documentation of associated traditional knowledge and promotion of research (Kelbessa *et al* 2000; Demissie, 2001; CBD, 2008; Abdella and Sultan, 2018). Although much effort has been undertaken in the research, development and promotion of traditional medicine in Ethiopia, there are still some difficulties and challenges for maximizing the proper utilization of traditional medicine (Abebe, 2001). Some of the challenges and gaps include poor partnerships and collaboration among the research communities, public and private sectors in research and development, promotion as well as production of traditional medicine. Therefore, the need for strengthening collaboration and partnership is highly emphasized for research and development, and that could also facilitate the production of validated traditional medicines in industries, registration, and market availably of medicinal products. This will maximize the potential benefit of traditional medicine in the healthcare in addition to providing the opportunity for commercialization of the products and export promotion. This review is to give an insight on Ethiopian traditional medicine and some medicinal plants used for traditional claimed ailments with scientific evidences for potential development.

Method

The methodological approach is an electronic literature database search conducted using Web of Sciences, AJOL and Pubmed besides reviewing Ethiopian science and medical journals. The key terms used to search the literature were "Traditional medicine" and "Medicinal plants." The inclusion criteria for the compiled information were publications, review articles and proceedings of conferences on traditional medicine of Ethiopia, development and promotion of Ethiopian traditional medicine and publications during 1999 to 2021.

Result and Discussion

Medicinal plants widely used as traditional remedies

Most of the Ethiopian population, especially the rural community, relies on traditional medicine, particularly on medicinal plants for the treatment of various ailments such as malaria, diarrheal diseases, skin infections, diabetes, hypertension, etc. that have public health importance. Among the documented medicinal plants, the most commonly employed plants by traditional healers and as home remedies in caring family members include *Ocimum lamifolium*, *Withania sommenifera*, *Vernonia amygdalina*, *Eucalyptus globules*, *Ruta chalepensis*, *Allium sativum*, *Lepidium sativum*, *Hagenia abyssinica*, *Calpurnia aurea*, *Croton macrostachyus*, Ajua remota/ Ajuga integofera, Genius lotoides, justicia schimperiana, *Moringa stenopetala*, *Nigella sativum*, *Aloe species*, *Plumbago zeylinica*. Various studies were undertaken in different parts of these medicinal plant species used for different ailments. Accordingly, some medicinal plants commonly employed by the community indicated in Table 1.

Medicinal plant growth forms and parts for preparation

The plant growth forms medicinal plants constitute trees, shrubs, herbs, climbers. Herbs were the major medicinal plants used by the community for human treatment followed by shrubs and trees. The plant parts used for medicine preparation by healers are variable. Healers most commonly use fresh specimens from commonly available plants to prepare remedies for their patients since the constituents are not lost before use compared to dried ones. The traditional medicines harvested for preparation of the remedies are leaves, roots, barks, seeds, fruits, stems, flowers, barks or latex. Most remedies were prepared from leaves and roots parts of the medicinal plants compared to other plant parts. The main reasons that many traditional healers used the leaf parts compared to others for remedial preparation is due to easy accessibility and for preventing the plant from extinction (Getnet, *et al*., 2016; Birhanu *et al*., 2015). The pharmacological treatment of disease with the use of herbs known many years ago Schulz *et al*., 2001). since folk healing commonly employ herbs as part of tradition globally. Medicinal plants products have become more widely available commercially, especially in developed countries. In some countries such as Germany, herbal medicines are sold as phytomedicine and subject to the safety, efficacy, and quality as well as rigorous manufacturing standards, this is not so everywhere. By contrast, in the USA most herbal products in the marketplace are marketed and regulated as dietary supplements, a product category that does not require pre-approval of products based on any of these criteria (Schulz *et al*., 2001).

Production and commercialization of validated traditional medicines have paramount importance to properly utilize the untapped national resources for the health benefit besides the economy significance through job creation, improving income source for the rural community by cultivating medicinal plants and supply of raw materials for production, etc. In the Ethiopian context, a guideline was prepared by Ethiopian Food and Drug Authority (EFDA) which was endorsed following the consultative meeting of stakeholders. The guideline could promote the production and commercialization of traditional medicinal products that are scientifically validated to ensure safety and efficacy (EFDA., 2021)

Currently, some five medicinal plants such as *Plumabago zelanica*, *Withania somnifera*, are exported in processed form following the permission received by Ethiopian Biodiversity Institute (EBI) considering access benefit sharing. (EBI report, personal communication). Medicinal plants are commonly sold in most open markets like any other commodities. The remedies are usually sold to the public together with other materials such as spices, salt and other food items in open markets and in places such as roadsides, and near churches or mosques. Medicinal plant vendors, who are not necessarily traditional healers, are involved in the trade of traditional medicine. An increase in the trade of traditional remedies and the services of traditional medicine in cities can be also observed by advertisements using signboards. Advertisements play a major role in informing communities of the skills of healers. For instance, in Addis Ababa's Merkato the largest open market in Ethiopia, various kinds of traditional medicines are available including those used for medico-religious purposes. More women than men are involved as sellers of traditional medicine but male and female traditional healers practice in similar proportions in rural areas (Fassil, 2003; Kloos *et al*., 2014).

In large towns, considerable quantities of fresh or dried medicinal plants and spices are sold by vendors. Many of these plants are supplied by commercial harvesters and sold to turban traders or herbalists mainly women. The commercialization of traditional medicines in towns leads to the replacement of traditional healers by medicinal plants vendors who are not necessarily traditional healers in handling the trade of traditional medicines. Vendors sell traditional medicines just like any other items that are used as household remedies and clients use them in their homes. With increasing commercialization and income generation capacity of traditional medicine, the increment in the number of healers led to the emergence of quacks or fake healers, particularly in large cities like Addis Ababa. In fact, it is very difficult to distinguish between real and quack healers as there are no clear standard guidelines to evaluate traditional healing knowledge. Such healers have great influence in healers' associations in many countries.

This tends to create a challenge by regulators and impede research collaboration in the validation of traditional remedies due to challenges to distinguish quack healers, lack of trust and integrity in the service. This could create difficulties for the integration of traditional medical systems with modern medical systems as recommended by WHO (Kloos *et al*., 2014). Efforts being undertaken by woreda health offices within regional health bureaus to register healers, screen knowledgeable and genuine ones for subsequent registering healers and facilitation of the practice of traditional healers through community participation following the guideline issued by Ethiopian Food and Drug Administration (EFDA) formerly EFMHACA (EFMHACA (now EFDA), 2014).

In addition to the provision of health care services by traditional healers to communities, there is also a tradition of self-care in the homes using medicinal plants obtained from traditional medicine vendors and medicinal plants grown in home gardens. Home treatment is usually the first action taken in the event of an illness. Some of the most widely used home -based traditional medicines in the Ethiopian highlands are *feto* (*Lepidium sativum*), *haregresa* (*Zehneria scabra*), *bahir zaf* (*Eucalyptus spp*), *tena adam* (*Ruta chalepensis*), *damakesse* (*Ocimum spp*), *dingetegna* (*Taverniera abyssinica*), *gizawa* (*Withania somnifera*), *kosso* (*Hagenia abyssinica*), *enkoko* (*Embelia schimperi*), *Kebericho* (*Echinops kebericho*) and metere (*Glinus lotoides*) (Fassil, 2003, Kloos et al., 2014**).**

The Government of Ethiopia is committed through issuing policy and regulation, strategy and supporting research work on traditional medicine for the promotion and eventual integration of traditional medicine into the formal health care system (Abebe, 2001; Kassaye *et al.*, 2006; MoH, 2019, EFDA, 2014 and 2021). Realizing the popularity of Ethiopian traditional medicine, efforts should be strengthened through partnership, collaboration for documentation of indigenous knowledge, research and development, conservation, production, and commercialization of scientifically validated traditional remedies by all stakeholders to maximize the potentials of traditional medicine.

Table 1. Some examples of medicinal Plant species, their parts and use in traditional medicine.

Local name	Scientific names	Traditional use	Parts used	Preparation & administration	Pharmacology, chemistry	Habits
Dengetega	*Taverniera abyssinica* A.Rich	To relieve sudden pain, generalized pain, fever	Roots	The roots are chewed and juice swallowed	Formononetin and afformosin (isoflavonids) as major constituents. Anagesics, antipyretic, antispasmodic	Herb
Netch shinkurt	*Allium stivum* L	Diarrhea, Common cold, malaria	Leaves, cloves	For diarrhea via pounded & boiled leaves For common cold, the cloves grounded infused in tea or milk. For malaria grounded clove mixed with honey and swallowed	Allicin, fibrolytic activity,	Herb
Haleko; Shiferaw	*Moringa stenopetala* (E.G. Baker) Cufod	Diabetes, asthma, hypertension,		Leaves as tea infusion, soup	Rutin major constituent and other flavonoids. Rich in vitamin C & A, Calcium. Various literature reported anti-hyperglycemic, antihypertensive & nutritional values	Tree
Nech-bahirzaf	*Eucalyptus globules* Labill	for influenza & common cold,	leaves	Leaves are placed in boiling water and the steam inhaled	Cineol major constituent. Reported as antibacterial, analgesic & febrifuge	Tree
Kosso	*Hagenia abyssinica* (Bruccie) T. E. Gmel	Tape worm and other intestinal worms	Flowers		Phloroglucinol (Kosin glycosides) major constituents, flavonoids. Antioxidant and anti-proliferative effect, anthelmintic	**Tree**
Tikur azmud	*Nigella sativa* L.	For cough, asthma, muscular pain	seeds	Roasted and grounded seeds placed in boiled water for drink.	Thymoquinone as major constituent. Fixed oils (arachidonic, stearic,	Herb

				Grounded roasted seed mixed with honey and eaten	oleic , palmitic oils as major) Reported to be appetite stimulant & liver tonic, diuretic, antibacterial and skin disorder	
Amira; Mertse	*Plumbago zeylanica* L	For gonorrhea, kola kusel and ulcer	Root	Grounded root placed in boiled water or tella for drink.	Plumbagin (major) and other naphtoquinones. Reported to have broad spectrum antibacterial effect, antineoplastic	Herb
Gizawa	*Withania somnifera* L. Dunal	For malaria	Leaves	Powdered leaves placed in boiled water or tella for drink	Withanoides and withaferins major constituents besides Alkaloid (anaferine, anhygrine), saponins Anti-malarial, anti-inflammatory, anti-diabetic properties	Herb
Enkoko	*Embelia schimperi* Vatke	Tape worm and other intestinal worms	Seeds	Powdered seeds placed in boiled water for drink. Grounded seed mixed with honey and eaten	Embelin and aegicerin as major constituent. Anthelmintic, antibacterial, antifertlity, fungal infestation, anti-inflammatory	Herb

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Marketing of Traditional Medicine in Ethiopia

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Introduction

Traditional medicine, an art of treatment practices, strategies, knowledge, and beliefs including plant-, animal-, and mineral-based medicines, spiritual therapies, manual techniques, and workouts applied singularly or in combination to treat, identify, and prevent illnesses or uphold the well-being. Since ancient times, humans have been using natural products, such as plants, animals, microorganisms, and oceanic organisms, in remedies to prevent or treat illnesses. (Belachew et al. 2021). Recently, there has been an increasing tendency to go back to nature in search of new medicines. To facilitate this, a great deal of effort has been made to compile information on natural products worldwide, and as a result, many ethnic-based traditional medicine databases have been developed. In Ethiopia, there are more than 80 ethnic groups, each having their indigenous knowledge on the use of traditional medicine (Bultum et al 2019).

Globally, up to 70,000 estimated species of aromatic and medicinal plants are found (Farnsworth and Soejarto, 1991). The number of medicinal and aromatic plant species varies in different countries because of agro-ecology which determines exactly the number of all medicinal and aromatic plant species used globally. The increasing global demand for aromatic and medicinal products accelerated conservation, cultivation, and marketing of the plants. Thus great attention was given to collection, maintenance, production, and processing and utilization technologies of those endemic and exotic aromatic plants (Banjaw 2016).

Ethiopia is rich in biodiversity with presence of rich plant diversity. There is no organized cultivation of plants species for medicinal purposes in Ethiopia except few aromatic species. The reason for this is that the quantities of medicinal and aromatic plants traded are very small, and there is no organized large scale value addition and processing (Bekele, 2007). On the other hand in Ethiopia, the cultivation practices being practiced by smallholder farmers is not improved and the technique is highly based on the knowledge that passed from generations and as a result production level is low (Tsegaye and Tasisa 2020). So far with little effort of integration and modernization of traditional medicine, the medicinal plants have continued to be the most affordable and easily accessible source for the treatment of several human and livestock ailments in Ethiopia (Netsanet et al. 2020).

Hence Debre Berhan University is aimed at first to document knowledge of aromatic and medicinal plants which have been used by the traditional healers for different purposes. Secondly in-situ and ex-situ conserving strategies of the plants are implemented and third integrating with modern science to have different bioactive formulation for multipurpose.

Global and Ethiopia Trends of Herbal Medicine

Most of the population inhabiting developing countries are still dependent on herbal medicine to meet their health needs. There is global revival in use of herbal drugs/phytochemicals for various purposes, i.e., in medicine, nutraceuticals and cosmeceuticals. As advanced medical aids are not

easily available around the globe, the World Health Organization (WHO) also advocates the use of herbal medicine and other traditional remedies having proven safe and effective. According to a report, worldwide turnover of herbal medicines is nearly around US$ 90 billion and is constantly expanding at an annual rate of 10–15%. However it is estimated that by the year 2030 the value will reach to approximately US$ 6 trillion (Sharad and Ankita 2018).

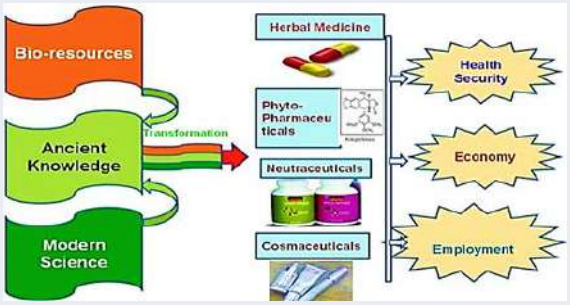

Fig. 1 Herbal drug: opportunities in the twenty-first century

The trade and use of traditional medicines are increasingly receiving attention from policy makers, health officials, social scientists, and environmentalists due to the medicines‟ role as supplementary and alternative medicines as well as social and economic support systems (Diederichs 2006). Ethiopians were recently estimated to buy traditional medicine on average 6.1 times a year from market vendors, plant collectors, and shops (Mander et al. 2006).

Fig 2: Medicine vendors in the Etan Terra area of the Merkato in June 2014 Photo by H. Kloos, Asfaw et al (2014)

Fig 3: Medicine vendors in the Etan Terra area of the Merkato in 1973 Photo by H. Kloos Asfaw et al (2014)

Fig. 2 and Fig.3 show how the old way of commercializing traditional medicine is practiced. Fig. 4 depicts various oil products sold at Afri Herbal and Soap business in Addis Ababa.

Fig 4: https://et.loozap.com/afri-herbal-oil-and-soap-addis-ababa/14926787.html (accessed March 2/2022)

Some of the initiatives which have been undertaken by Debre Berhan University to commercialize aromatic and medicinal plants for different purposes and ex-situ conserving strategies of the plants for keeping sustainability of the work and then

integrating with modern science to have different bioactive formulation for multipurpose are shown below in Fig. 5 and 6.

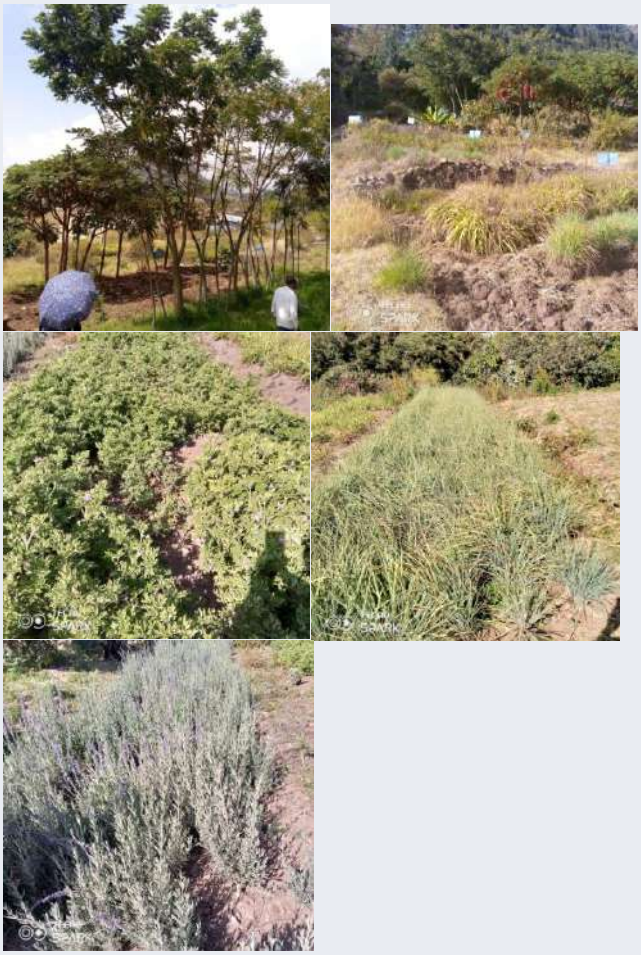

Fig 5. Nursery site of Debre Berhan University for cultivation and conservation of Aromatic and Medicinal Plants
Photo by Amare Ayalew

Fig 6. Debre Berhan University: Some of herbal formulations
Photo by Amare Ayalew

Registration of traditional medicine guideline by World Health Organization for commercialization

Four categories of traditional medicines, based on their mode of preparation, the indication, and extent of the development of the traditional medicine relative to the traditional remedy used, are thus distinguished as set out below by WHO a category two traditional medicine is one that is widely used in the community but has a commercial possibility. It is characterized as follows:

- Traditionally used in a given locality and very well known by the local population, both in terms of composition and treatment.
- The formulation is well known, and its preparation is according to traditional methods.
- Safety and efficacy are justified by a long period of use.
- It is available to local people free of charge.
- However, if a category two medicine were to go on the market, it would have to meet the general minimum requirements for the registration of traditional medicines.

The strategy of the WHO Traditional Medicine (TM) Strategy 2014–2023 was developed in response to the World Health Assembly resolution on traditional medicine (WHA62.13) (1). The goals of the strategy are to support Member States in:

- harnessing the potential contribution of TM to health, wellness and people centered health care.
- promoting the safe and effective use of TM by regulating, researching, and integrating TM products, practitioners and practice into health systems, where appropriate

This strategy is the key on traditional medicine for developing country like Ethiopia for commercialization and integrating of traditional medicine.

Conclusion

Ethiopia has diverse biodiversity among those aromatic and medicinal plants are very crucial for herbal medicine preparation using their bioactive ingredients besides their cosmetic and detergents application. For the purpose of commercialization, the herbal material formulation should be checked for their quality, safety and efficacy which are important criteria set by WHO.

Hence higher institutions like Debre Berhan University should perform integration of the traditional medicine with the modern science for ease of usage and commercialization.

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