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In This Edition

Editor's Note

As EPPAD is getting close to holding its annual conference in Rockville, Maryland on December 3, 2022, we are releasing this issue of the *Bulletin*, Volume 2, Number 2. It has indeed been a busy year for the Association. In this issue, various articles are presented. In the News and Highlights section, trip reports compiled by EPPAD Board members Dr. Bisrat and Ato Aklile are presented, following their respective recent visits to Addis Ababa. During their trips, they had fruitful discussions with counterparts and colleagues in Ethiopia. In this section, Dr. Bisrat also writes an interesting account of Howard University College of Pharmacy 2022 PharmD graduates against an historical background of this institution.

In the Pioneers of Ethiopian Pharmacy section, the careers of two professionals are profiled. The inspiring and illustrious career of Professor Tsige Gebremariam is indeed exemplar of the profession and a model that rising pharmacists can emulate. His stellar performance in teaching, research and administration is testimony to the versatile nature of the profession of pharmacy. Ms Heran Gerba of EFDA has also been profiled in this issue. Her impressive career trajectory buttressed by hard work is equally appealing. Ms Heran's achievements in the regulatory arena is beyond compare.

This issue carries manuscript contributions from Dr. Bisrat Hailemeskel and coauthors, Drs. Worku Abebe and Fekadu Fullas. Bisrat and co-authors provide current knowledge on the *Moringa* plant, drawn from recent studies. Worku provides a unique approach to select Ethiopian spices in their mechanistic roles in the endothelial system and weaving this aspect into possible therapeutic benefits. In his article, Fekadu shares his broader view on African medicinal plants and highlights the role played by important plants from southern and eastern Africa, including Ethiopia.

In future issues, we will try to strike a balance between articles in drug therapy areas and other diverse aspects of health. We encourage pharmacists and pharmaceutical scientists to be part of our journey by contributing manuscripts as we strive to improve the quality and coverage of the *Bulletin*.

We hope you enjoy reading this issue.

Fekadu Fullas, PhD

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

(Senior editors: Profs Tesfaye Biftu, Bisrat Hailemskel and Ato Aklile G. Giorgis; Layout editor: Dr. Pawlose Ketema)

EPPAD News and Highlights

Notes from Gabriel Daniel's Trip to Ethiopia (April/May 2022)

Gabriel travelled for three weeks beginning April 14, 2022 to Ethiopia with the objective of:

1. Delivering donated laptops to EFDA
2. Conducting feasibility study for supporting wheelchair production as cottage industry and
3. Meeting with key stakeholders on these and other EPPAD related activities including EPPAD collaboration in herbal pharmacopeia development as a component of the Road Map.

Meeting with the Ministry of Health

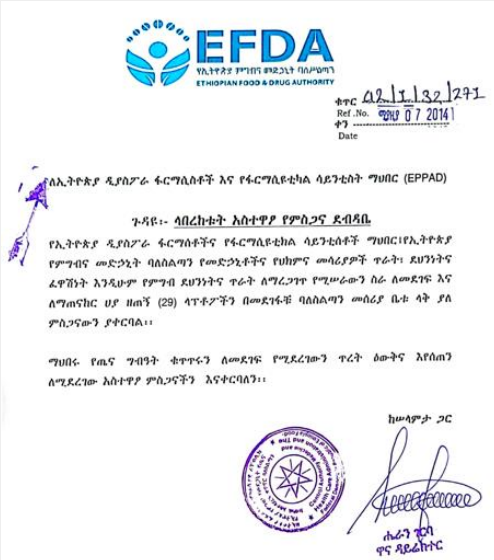
Gabriel met with the State Minister of Health HE Dr. Seharla Abdullah and Mr. Kedir Seid Advisor to the state minister at the Ministry of Health in the presence of Ms Ehtemariam Shambel who heads the traditional medicines group of the MOH.

The meeting with the State Minster was to introduce EPPAD, what it stands for, what it has accomplished so far. The meeting also focused on the wheelchair pilot initiative EPPAD is exploring to help with as well as brief the state minister on the progress of the EPPAD Traditional medicine working group.

The Minster was supportive of the pilot project and promised to assist as appropriate. Regarding the traditional medicine Gabriel briefed the Minster about EPPAD's Traditional medicine group and that it has been working closely with the MOH and in the process of collaborating with the Ministry in the implementation of aspects of the TM Road Map which includes development of a herbal pharmacopoeia.

Donation of Laptops to the Ministry of Health

Gabriel hand carried thirty new laptops (one of which was missing on transit) donated by EPPAD Pharma's Chairman Ambaw Bellete and delivered to FDA. This was a promise fulfilled by an earlier visit made to the FDA by a team of EPPAD Pharma which was on a mission to follow up the effort of setting a pharmaceutical manufacturing plant in Ethiopia. The handing over of the donation was made to Ms Heran Gerba the general manager of EFDA in her office in the presence of Ambaw Bellete and Berhane Mewa who happened to be present in the country. Ms. Heran was very appreciative of the donations and promised to put them to use at the regional EFDA branches who need modern technology to perform their regulatory tasks. EFDA recognized and thanked EPPAD by giving certificate of donation.



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CERTIFICATE
Of ACKNOWLEDGMENT

This certificate is provided

TO Ethiopian Pharmacists and Pharmaceutical Scientists Association in the Diaspora (EPPAD)

for the donation of twenty-nine (29)Laptop Computers for the strengthening the capacity of Ethiopian Food and Drug Authority in supporting mission of safeguarding our people from unsafe food and health products.

April 15, 2022
DATE

EFDA

SIGNATURE
Heran Gerba
Director General

Photo of certificate of acknowledgement and a group shot of EPPAD and EFDA team after the event

Feasibility Study for Wheelchair Production Pilot Project

The main mission of Gabriel's travel was to conduct a quick determination if setting up a pilot project to produce wheelchairs as a cottage industry is feasible and possible. Gabriel visited several facilities in Addis Ababa that are involved in the production of wheelchairs, crutches, walkers, canes etc.

Pictures of wheelchairs (source: Wikipedia)

The facilities visited include both the existing Ethiopian Prosthetic and Orthotic Training

Workshop located around St. Paul hospital and the new location around General Wingate school. This facility that has provided services for over seven decades produces wheelchairs, canes, walkers, crutches, back support bands, neck collars etc. With the high demand for such appliances, the government is in the process of modernizing and expanding the services.

Selam Children's Village/TRIAF located in Kotebe area and involved in custom production of different appropriate technologies including wheelchairs was visited to identify potential collaborators. It was learned Cheshire Ethiopia with main facility in Menagesha is involved in productions of wheelchairs and other mobility enhancing tools and services. This can be another resource the project can collaborate with.

The feasibility study included looking at the availability of the basic equipment/tools and materials to kick off the project. Gabriel visited shops in Addis to conduct a survey of the market for key basic equipment and materials and found out that most are locally available. Personnel working in the visited workshops indicated their willingness to volunteer and provide hands on training.

The other key aspect that the visit looked at was identifying a facility that can be a beneficiary and collaborator. Based on the track record and experience in assisting socially disadvantaged groups in Ethiopia with main operations in Addis Ababa, an organization called "Mecedonia Home for the Elderly and Mentally Disabled" is proposed as a starting institution. Gabriel met with the leadership of Mecedonia and was informed about their readiness to be part of this initiative. It has the space and trainable persons who can house and manage the project with initial support and collaboration with EPPAD.

The next step in this project is to work on a memorandum of understanding (MOU) and provide the startup resources and guidance for launching the pilot project.

Photo Gallery of Workshop products from the Trip

Production and Training Workshop of POC: Orthotic products made locally (crutches, walkers, neck collars, back support…)

About EPPAD Philanthropy

EPPAD Philanthropy is one of the five thematic groups of EPPAD established to coordinate support for implementation of projects that have social impact on different areas in Ethiopia.

Past activities implemented with financial contribution from EPPAD members included direct support to critical need areas to realize immediate practical responses.

Beginning in late 2019, EPPAD Philanthropy implemented several start-up projects in Ethiopia.

- In August 2019, after a visit to eight charities provided deworming for over 2,000 persons, provided distributed and demonstrated the use of digital blood pressure monitors and Snellen's charts for vision screening to six of the charities including the Ethiopian Pharmaceutical Association (EPA) which was provided with the screening tools to conduct community awareness and screening during pharmacy days.
- During the height of Covid-19, EPPAD provided Covid prevention commodities (PPEs), QA supplies like alcohol meter for monitoring of the quality of hand sanitizers to the Ministry of Health, Schools of Pharmacy, and Community Pharmacies.
- EPPAD provided $3,000 to the Ethiopian Embassy for supporting Covid 19 projects in Ethiopia.
- Provided $1,500 for two charities to support emergency needs such as food and medicine during the Covid-19 crisis in Ethiopia.

EPPAD Board Member Visit to Ethiopia

During his June 2022 visit to Addis Ababa, EPPAD Board member Dr. Bisrat Hailemeskel held fruitful discussions with Ethiopian Pharmaceutical Association (EPA) officers on areas of potential collaboration between the two Associations. The areas included: co-celebrating the yearly EPA-initiated yearly "**Ethiopian Pharmacists Day**"; EPPAD helping with EPA's project to establish an "**African consortium of pharmacy associations"** that is similar to the International Pharmaceutical Federation (FIP); collaborating in areas of continuing education program series, scholarship programs, holding regular joint EPPAD Board and EPA Board meetings; EPPAD supporting EPA in its efforts to establish a consortium of over 20 pharmacy schools in Ethiopia. They also exchanged collaborative ideas in different areas. In the future, EPPAD Bulletin will carry stories as some of the ideas materialize.

EPPAD News and Highlights

One in Five of the 2022 graduates from Howard College of Pharmacy were Ethiopian-Americans

Contributed by by Bisrat Hailemeskel, Pharm.D., ABAAHP, RPh. College of Pharmacy, Howard University; 2300 4th Street, N.W., Washington, DC 20059)

It with a great pleasure and honor to report that a total of 30 pharmacists graduated with a Doctor of Pharmacy degree this year from Howard University College of Pharmacy. Of these, 20 percent (1 in 5) were Ethiopian-Americans. Three of the graduates were in the top 5 highest ranking group receiving multiple high achievement awards from the College. Interestingly, the majority of the graduates were female (over 66 percent), with two them ranking in the top four of the graduating class.

Howard University (HU) has had a long relationship with Ethiopia starting at least as far back as the 1930s. Dr.Melaku E. Bayen 1892-1932 E.C. (1900-1940 G.C.) was the first Ethiopian medical doctor to complete his education at HU in 1935. About a decade later in 1945, Emperor Haile Selassie also received an honorary degree from HU. Since then, many Ethiopians and Eritreans graduated from various colleges within the University. One of the many reasons many Ethiopians join Howard is because the Washington DC metro area is home to the largest Ethiopian population outside of Ethiopia, and Amharic is one of six official languages in the city.

HU was founded in 1867 as a private research university and is comprised of 13 schools and colleges. Students pursue more than 140 programs leading to undergraduate, graduate, and professional degrees. One of these colleges with consistent highest number of Ethiopian graduates is the College of Pharmacy. The College has been in existence for more than 150 years providing a traditional and non-traditional Doctor of Pharmacy degree program besides its Master's, Ph.D., and joint Degree programs. Currently, HU is the only college of pharmacy in the greater Washington, DC area.

Over the years, particularly since the 1970's, many Ethiopians received their pharmacy degree from HU and have been working in various areas, including small private companies as well as to high federal government positions. As a professor of clinical pharmacy for the past 20 plus years at Howard, I have witnessed that almost 10-25% of the pharmacy graduates were Ethiopian-Americans for many years in a row. This year's achievement is no different than the past.

In most of my recent tenure years, I have noticed trend that many graduates proceed attend industry fellowship, specialty residency, and other post-doctoral training after graduation. Overall, about 30 percent of Howard pharmacy students pursue industry or a regulatory affairs career; 30 percent pursue community positions; and more than 20 percent pursue graduate school, own a business, or work in a hospital or with managed care companies.

Photo taken in front of Addis Ababa University, Black Lion Hospital (from left to right; Drs. Delbi Hussein, Lauren Latten, Bisrat Hailemeskel, Iman Ahmed, Alemseged Ayele, and Pawlose Ketema)

About a decade or so ago, the College also established an international rotation site in Ethiopia in collaboration with Addis Ababa University, School of Pharmacy, by sending students for their elective rotations to work at Black Lion Hospital. Many students benefited from this rotation while enjoying visits with their families and friends. The 2022 graduates, like the previous years, are also high achieving students engaged in various leadership positions and participating in multiple national and international professional and scientific organizations.

A few years ago, pharmacists in the Washington D.C.-Maryland-Virginia (DMV) metropolitan area re-established an association under EPPAD with the goal to promote pharmacy education, pharmaceutical services and to serve be a bridge between the diaspora and beneficiary groups in Ethiopia.

Although pharmacists have been playing a key role in the health care system worldwide, the recent pandemic further increased their clinical roles in administering COVID-19 tests, childhood vaccines, and COVID-19 vaccines. This is a critical time for the profession to grow and produce more graduates. To witness more Ethiopian pharmacy graduate from HU is significant in that it benefits them individually, but also in the long run will indirectly perhaps benefit the people in Ethiopia.

A photo taken at one of the annual conferences held in the Washington, DC metropolitan area showing some of the members at the conference.

Pioneers of Ethiopian Pharmacy

Prof. Tsige Gebre-Mariam

This third issue of EPPAD Bulletin is featuring Prof Tsige Gebre Mariam whose contribution in pharmaceutical academia and research deserve special recognition. Professor Tsige Gebre-Mariam is a founding member and the current elected President of the Ethiopian Academy of Sciences. He is Professor of Pharmaceutics and Drug Delivery at the School of Pharmacy, College of Health Sciences (CoHS), Addis Ababa University (AAU).

He has served as the Dean of the School of Pharmacy, Vice President for Graduate Studies and Research of AAU and led the Graduate Program Expansion (2004-2009). His Research interest include Synthesis of starch-based nanoparticles as nanodrug carriers; Transdermal and dermal drug delivery; Controlled drug release; Development of phytomedicines, alternative native starches, celluloses and derivatives from local resources. He has hands on experience in Formulation studies, Development of pharmaceutical excipients, Controlled drug release, In-vitro bioequivalence studies, Current good manufacturing practices, Process validation, Development of phytomedicines, Drug supply management. Prof. Tsige has published extensively.

He is a recipient of several awards, fellowships and recognitions including the Prestigious Georg Forster Research Award (2016); Life Time Best Researcher Award; and Dedicated Long Years of Service Award, School of Medicine Golden Jubilee, CoHS (2014); AAU Outstanding Faculty Award for Excellence in Academic Leadership, Teaching, Research and Community Services (2013); Humboldt Ambassador Scientist (2009-2015); Certificate of Recognition and Gold Medal for Outstanding Services to the Profession of Pharmacy in Ethiopia, Ethiopian Pharmaceutical Association (EPA) (2011); Alexander von Humboldt Fellowship; AAU Golden Jubilee Research Award (2000); Certificate of Recognition and Gold Medal for Research, EPA (2000).

Ethiopian Academy of Sciences
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Photo of the current office of EAS

About the Ethiopian Academy of Sciences (EAS

It took nearly five decades to realize the dream of the late Dr. Aklilu Lemma and his colleagues in the 1960s to lay the groundwork for the Academy of Sciences.

The Ethiopian Academy of Sciences (EAS) is a nonprofit and non-governmental organization established to promote a culture of scientific inquiry and creativity and the pursuit of excellence and scholarship in the sciences among Ethiopians. The Academy aims to advance the development of all the sciences, including the natural

sciences, mathematics, the health sciences, agricultural sciences, engineering, social sciences and humanities, fine arts and letters. EAS was established in 2010 with 49 Fellows, was recognized by Act-of-parliament in 2013 with Proclamation No. 783/2013. To date, EAS comprises 184 Fellows, 70 Associate Fellows and 1 Honorary Fellow, all of whom have made outstanding contribution to the expanding knowledge in their respective fields. Professor Demissie Habte, a pediatrician and former dean of medicine at Addis Ababa University and a World Bank health specialist, is the first elected president of EAS. The Academy is housed in the magnificent historic residence of the late Blaten Geta Hiruy Wolde Selassie, where the Blaten Geta Hiruy Memorial Art Center is also located.

Pioneers of Ethiopian Pharmacy

Ms. Heran Gerba

This third issue of EPPAD Bulletin is also featuring Ms. Heran Gerba whose contribution in the regulatory and policy development is nothing short of stellar. Ms. Heran Gerba is the Director-General for the Ethiopian Food and Drug Authority – EFDA (formerly the Ethiopian Food, Medicine and Healthcare Administration and Control Authority – FMHACA) of the Federal Democratic Republic of Ethiopia since 2018.

Ms. Heran is the sixth head of the regulatory office after Hailu Guade, Baro Tumsa, Eshetu Wondemagegnehu, Haile Selasie Bihon and Yehulu DenekewMs. Heran earned a Bachelor's degree in Pharmacy and a Master's degree in Pharmaceutical Analysis & Quality Assurance from Addis Ababa University School of Pharmacy.

During her seventeen years in the regulatory sector, she served in a wide variety of positions, including as a physicochemical and pharmaceutical microbiology analyst, head of a physicochemical division, senior physicochemical analyst, and team coordinator for the pharmaceutical microbiology section, and as "Good Manufacturing Practice" inspector, Senior Medicine Dossier Assessor and as a Deputy Director-General for four years.

As Director General of EFDA since 2018, Ms Heran has demonstrated strong leadership and contributed significantly to key milestones in different areas.

Notable among these include:

- In 2019, under her leadership, *"The Proclamation to Provide for Food and Medicine Administration 1112/2019"* was enacted to effect regulatory transformation in Ethiopia with the establishment the Ethiopian Food and Drug Administration to safeguard the health and safety of patients, users, and other persons by regulating and controlling foods, drugs, cosmetics, and tobacco products and medical devices.

- Proclamations enacted for context-specific tobacco and alcohol control regulation, to enforce and create smoke-free environment (use and prohibition of any tobacco product in any part of all indoor public places, workplaces, and on all means of public transport), increased tobacco taxation and regulate graphic health warnings

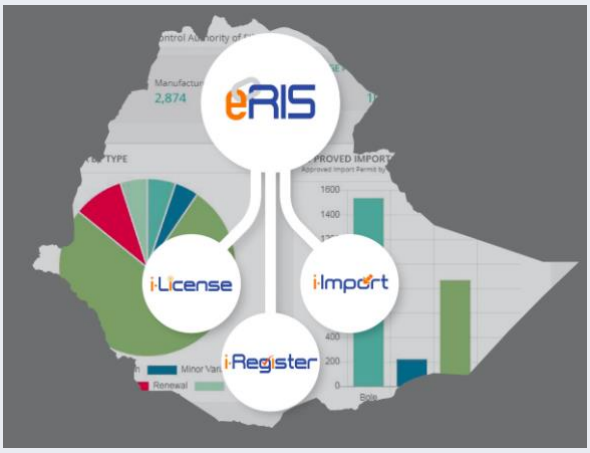
Her leadership role at FDA in regulating tobacco has earned her a recognition with the 2021 "World No Tobacco Day" Award of WHO for her efforts in tobacco control. Ms Heran is one of the six awardees selected for this year from the WHO Africa region. Ms Heran Gerba is the fifth awardee from Ethiopia.

She is also recognized for her effort on tobacco with the 2021 Judy Wilkenfeld Award for International Tobacco Control Excellence.

- EFDA under its role to regulate health products has a vision to become a center of excellence in Africa and for that it has sustained its medicine and condom quality control laboratory ISO 17025 accreditation. And in the year 2022 EFDA got a new ISO 17020 accreditation for Medicine Facility Inspection.
- Development of electronic Regulatory Information System (eRIS), an open source, locally developed and maintained software system that ensures that EFDA can maintain an unbroken chain for online licensing, registration, and import request and approval process. EFDA can track medicines all the way from international (or local) suppliers to the ports, to the Ethiopian Pharmaceutical Supply Agency's (EPSA's) warehouses and finally to each clinic across the country.

About Electronic Regulatory Information System (eRIS)

The Ethiopian Food and Drug Administration (EFDA) oversees the market authorization and import permit approval for both medical and food products for a wide variety of vendors from multiple countries using the Electronic Regulatory Information System (eRIS). Now applicants and EFDA officers can use online, web-based applications to manage the licensing, registration, and import application process. This has dramatically increased processing efficiency and transparency and facilitated unbroken chain of information – from application to port.



The eRIS has the following components:

i-License allows importers, exporters, wholesalers, and manufacturers to apply for certificate of competency and for EFDA authorities to approve these applications online.

i-Inspect allows EFDA to inspect importers, exporters, wholesalers, and manufacturers online using ODK collect as a supporting application to fill checklists offline and upload to i-Inspect and i-License. It also helps manufacturers to request cGMP inspection applications online. EFDA utilizes i-Inspect as a tool to speed up the inspection process.

i-Register allows importers to apply for market authorization approval to register products in Ethiopia for import and for EFDA staff to review and approve the applications.

i-Import allows importers to apply for and receive permits to import medicines &medical devices, dossier evaluation and online interface to help the application process without the limitation to location.

i-Clearance allows importers to apply pre-shipment document review &physical assessment through eSW and receive document verification & port release for medicines and medical devices online.

i-Verify, a health product tracking app, gives regulators and the general public real-time checking of the validity of a product at any stage in the supply chain. Using this service, the agency and the public can report illegal, defective, or counterfeit products on the market and identify whether the drug or food item is purchased through proper channel or contraband, check validation period and import permit dates.

The Endothelium In Health And Disease: Potential Benefits Of Spices

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OBJECTIVE

Studies conducted during the past several decades have led to the discovery of the endothelium as a crucial organ for the regulation of the cardiovascular system and the recognition that its dysfunction is a key pathological condition associated with a number of risk factors that can affect the functions of almost all organs of the body. With this appreciation, efforts have been made more recently directed towards the prevention and treatment of endothelial disorders. The aim of this article is to briefly review the endothelium in health and disease and also describe the endothelial effects of spices commonly used in Ethiopia.

THE ENDOTHELIUM

Overview

The endothelium is a single layer of flat, polygonal endothelial cells constituting the inner cellular lining of the arterial, venous, capillary, and lymphatic systems. As such, it is in direct contact with the blood/lymph and circulating cells, while forming a physical barrier from adjacent tissues. The endothelium is considered one of the largest endocrine organs in the body, with an estimated mass of 1 kg and surface area of 100 m^2 for an adult person (1). Besides serving as a semipermeable barrier, endothelial cells also play a dynamic role in various physiological processes that enable them to maintain multi-organ health and homeostasis. More specifically, the endothelium is a major player in the regulation of blood hemostasis, vascular tone, immunology, inflammation, angiogenesis, reactive oxygen species, and metabolism, among others (1,2). Of particular interest related to the regulation of vascular tone is the formation of nitric oxide (NO) in endothelial cells from L-arginine precursor by the enzyme, NO synthase (eNOS). Besides causing vasodilation as its major action, NO plays an important role as a regulator of blood hemostasis (coagulation), inflammation, free radical formation, leukocyte adhesion, and vascular smooth muscle migration and proliferation (1,2). It is thus predictable that alterations of one or more of the above actions may cause endothelial dysfunction and its adverse consequences.

Endothelial dysfunction

Different factors of both endogenous and exogenous origins have been identified as triggers of endothelial dysfunction. These include, among others, inflammatory mediators, oxidative stress, modified/oxidized lipid products, certain drugs, and risk factors like aging, smoking, unhealthy diets, physical inactivity, irradiation, air pollution and stress (1,2). As a result of these triggering mechanisms, multiple overlapping layers of endothelial dysfunction have been observed, including hyper-permeability, inflammation, leukocyte adhesion, eNOS uncoupling, altered endothelial cell metabolism, increased oxidative stress, vasoconstriction (and/or decreased endothelium-dependent vasorelaxation), loss of antithrombic activity, injury and cell death, senescence/apoptosis, and endothelial-to-mesenchymal transition. It should, however, be reiterated that while endothelial dysfunction is more of a composite of these dysfunctional features, impaired vasodilation is considered a major part of the dysfunction (1,2).

Diseases associated with endothelial dysfunction

The components of dysfunction of the endothelium mentioned above are often associated with multiple commonly encountered diseases, such as

atherosclerosis, hypertension and stroke, diabetes, peripheral arterial disease, metabolic syndrome (obesity, insulin resistance), chronic kidney disease, pre-eclampsia, Alzheimer's disease, COVID-19, and many others (1,2). Whereas these diseases have a link to endothelial dysfunction, at least some of them may also lead to the development of endothelial dysfunction, thereby creating a vicious circle and worsening the disease situations. Given the short duration of time since the emergence COVID-19, it is interesting and instructional to note that infection of endothelial cells with SARS-CoV-2 has been seen to cause at times severe dysfunction of the endothelium followed by a myriad of events that include apoptosis, coagulation/thrombosis, inflammation, angiogenesis, vasoconstriction, vascular leakage and abnormal cell metabolism (1,2). With these manifestations, some investigators regard CODID-19 as a disease of the endothelial cells.

Drugs and other forms of interventions against endothelial dysfunction

Different clinically used pharmacotherapies, such as lipid-lowering, antihypertensive, antidiabetic drugs, antioxidants, anti-inflammatory drugs and bradykinin receptor agonists have been demonstrated to counter endothelial dysfunction as part of their clinical benefits (1,2,3). Along with the use of statins, vitamin C, anticoagulants, tocilizumab, dexamethasone, SGLT2i and adrecizumab, there are also other types of useful therapies for COVID-19-induced endothelial dysfunction. Moreover, the use of some natural products, dietary interventions and other forms of therapies have been implemented to prevent cardiovascular diseases by targeting endothelial dysfunction.

ENDOTHELIAL EFFECTS OF SPICES

Spices are a category of herbal products primarily used for flavoring foods and beverages. They are also commonly used as medicines and food preservatives, among other uses. From combinations of spices, condiments are prepared to enhance the flavors of spices. Being rich in certain phytochemicals, many spices have bioactivity of marked relevance, enabling them to produce noticeable effects on various biological systems. In this regard, spices have been reported to produce analgesic, antitumor, hepatomodulatory, hypolipidemic, anthelmintic, antibacterial, antidiabetic, antihypertensive, anticoagulant, antioxidant, anti-inflammatory, and other effects (4,5,6). In addition to being endowed with unique/district bioactive ingredients, species may also contain other constituents of nutritional as well as medicinal relevance, and these include vitamins, minerals, amino acids, and fibers.

It is believed that spices have been used in Ethiopia for centuries. Recent reports show that Ethiopia produces more than 50 different spices, and as such it is considered one of the top ten countries in the world where spices are used heavily (6,7). Spices in Ethiopia are consumed on a regular basis as basic food components and for a variety of other purposes including for prevention and treatment of various diseases. Readers are referred to a book authored by Fekadu Fullas for additional information on this and related topics (7). As research on spices progresses, new information in the field will continue to emerge. As pointed out earlier, in this paper, the possible endothelial effects of spices that are commonly used in Ethiopia are briefly reviewed in order to ignite interest to further explore their potential as therapeutic agents.

Cinnamon (*Cinnamomum zeylanicum*, Qerefa, Carafu)

Research findings have elucidated that cinnamon has beneficial effects against cardiovascular diseases at least in part via protection of the endothelium due to its antioxidant, anti-inflammatory, lipid-lowering and antithrombotic properties, among others (7,8,9,10). Consistent with this, using animal models in other studies, the active ingredient of cinnamon, cinnamaldehyde, has been demonstrated to enhance endothelium-dependent vasorelaxation by activating Nrf2-mediated antioxidant responses (8,9,10). The antioxidant and anti-inflammatory effects of cinnamon have also been established in several other studies in connection to other related issues (10).

Chili pepper (Cayenne pepper/*Capsicum annum*, Berbere)

Capsaicin is the major active ingredient of chili pepper that makes the spice relevant in a number of aspects. At the basic level, capsaicin has been shown to activate eNOS and result in increased production of NO from endothelial cells, while reducing formation of reactive oxygen species (7,9,10,11). These effects are mediated via stimulation of endothelial capsaicin receptors and influx of calcium. This observation is a clear manifestation of increased endothelial function and physiological processes that are dependent on it. Further research has also proved that the endothelial-dependent vasorelaxation induced by moderate doses of capsaicin is more beneficial for the long-term regulation of blood pressure (9,10,11).

Fenugreek (*Trigonella foenum-graceum*, Abesh, Halbata)

There are only a few studies that directly investigate the effect of fenugreek of the endothelium (7,12). It has been shown recently that fenugreek and its major active ingredient, diosgenin, cause enhanced endothelium-dependent vasorelaxation of isolated aortas obtained from high-fat and high-sugar fed male rats for six weeks. This effect of these substances was associated with their antioxidant activities. In another study, the administration of fenugreek to old N-Mari rats resulted in improvement in endothelial function together with normalization of LDL, VLDL and total cholesterol levels. The fact that fenugreek is endowed with several antioxidant and anti-inflammatory constituents can also provide indirect evidence for its beneficial effect against endothelial dysfunction and disorders related to it (12).

Garlic (*Allium sativum*, Nech shenkurt, Qullabbiiadii)

There are different lines of evidence for the beneficial of garlic and its constituents on endothelial health. In early 2000, using experimental animals and cell models, garlic extracts, due to their antioxidant and anti-inflammatory components have been shown to improve endothelial dysfunction and NO production. These findings were accompanied by decreased LDL oxidation, inflammation and the development of atherosclerosis (7,13,14,15). In humans, garlic supplementation also attenuated/prevented lipid oxidation, oxidative stress, inflammatory mediators, atherosclerosis and endothelial cell damage (13,14,15). Additional human studies also showed short-term treatment with aged garlic extracts improves endothelial functions in men with cardiovascular diseases treated with aspirin and a statin (13,14,15). Regarding treatment of obesity and diabetes, while garlic extract favorably modified endothelial biomarkers associated with human obesity, its component allicin was found to improve endothelium-dependent NO production in diabetic patients by enhancing the expression and/or activity of eNOS in coronary artery endothelial cells (13,14.15). These studies, together with others, generally provide support that improved endothelial function contributes to the health benefits of garlic consumption at least in relation to obesity and diabetes.

Ginger (Zingiber officinale**, Zengbil/gingebel)**

Traditionally, ginger is believed to have several medicinal values, and there is evidence supporting at least some of the traditional claims. Regarding its effect on the endothelium, one study has shown that ginger extract has antioxidant activity against superoxide anion production by porcine coronary artery endothelial cells (7,14,15,). This effect of ginger was linked to enhanced endothelium-dependent arterial vasorelaxation, leading to the conclusion garlic exerts vasoprotective effects and free radical-scavenging activities. The proposed bioactive constituents for these effects of ginger include 6-gingerol and 6-shogaol, which are more directly involved in the prevention of oxidative stress, inflammation and angiogenesis-related processes in vascular endothelial cells (14,15).

Onion (*Allium cepa*, Qey shenkurt, Nech)

Research has revealed that dietary flavonoids in onion reduce the risk of cardiovascular events, particularly quercetin, which has a potent antioxidant activity (7,13,15). This has been proved in part by in vitro experiments in which quercetin improved endothelial function associated with atherosclerosis.

This observation was subsequently complemented by the findings that onion-rich diet improves endothelial dysfunction by reducing some of the risk factors linked to the development of atherosclerosis (13,15). Chronic use of onion extract also ameliorated postprandial endothelial dysfunction induced by maltose in healthy men, further suggesting the benefit of the spice for improving cardiovascular health. Similarly, the administration of onion extract to hypertensive and fructose-fed insulin-resistant rats reduced oxidative stress and VCAM-1 expression, while increasing eNOS activity along with improvement of cardiovascular and metabolic activities (14,15). These results, once again, provided evidence for the antioxidant and anti-inflammatory properties of onion, which, to a certain extent, are also shared by other closely related spices, like garlic and turmeric. Not only the edible part of onion that is therapeutically useful, but also extracts from outer peels of onion have been demonstrated to improve endothelial function, along with boosting the levels of circulating endothelial progenitor cell (EPC) in healthy overweight and obese individuals (14,15). Consistent with these improvements, the administration of red onion juice to dutasteride-treated rats was observed to improve erectile dysfunction (ED) towards control level by inducing enhanced relaxant responses in corpus cavernosum tissues. From these observations, it was suggested that red onion juice could have a restorative effect on ED and endothelium-dependent relaxation subsequent to dutasteride treatment of patients (15,15).

Turmeric (*Curcuma longa*, Erd)

There are studies suggesting the protective role of turmeric on the endothelium (7,17,18). The primary constituent involved in this action of turmeric is curcumin. The mechanisms for the positive endothelial effects of turmeric/curcumin include (a) enhancement of endothelial-mediated vasorelaxation together with increased NO production and antihypertensive responses, (b) antioxidant activity through the reduction of reactive oxygen species and induction of scavengers of free radicals, and (c) anti-inflammatory effects caused by a reduction of various inflammatory-mediator molecules. Because of these beneficial multifunctional properties of turmeric/curcumin, the spice is believed to have significant therapeutic potential for conditions related to endothelial dysfunction (17,18).

CONCLUSION

The endothelium is considered a major mediator of vascular homeostasis through at least its vasodilator, anti-inflammatory, anticoagulant and other properties. Endothelial dysfunction is a common early stage of most cardiovascular disorders and related diseases. Among the different endothelial-derived mediators, NO has a critical role in the regulation of endothelial function. Certain physiological and pathological processes including aging, obesity and diabetes are also linked to endothelial dysfunction, which can be improved by variety of interventions such as lifestyle changes, and drug and natural product utilization. Within the natural product and dietary intervention groups, with the availability of the necessary information, the use of spices appears to be attractive for several various reasons, including acceptability, safety and availability. In this paper, seven spices that are commonly used in Ethiopia are reviewed primarily to help attract attention for future research consideration and product development. As the information gathered here is incomplete, further research is needed to fill the gaps, including identification of the mechanisms of action of the spices, particularly in relation to environmental influencing factors that can possibly affect the characteristics of the spices and the consuming local population.

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Moringa: The Super Food and Nutritional Supplement

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Moringa oleifera (Mo) has been a center of many recent researchers and conference topics. In this paper, an in-depth recent literature search is done to review the most common and resent advances in the health benefits of the plant. Mo is a tree that grows widely in many subtropical and tropical regions of the world. It is grown commercially in many areas including India, Africa, South America, Central America, Mexico, Hawaii, Asia, and Southeast Asia. (Stohs & Hartman, 2015). A literature search was performed via Medline and Scopus databases for articles discussing research on Mo and the many uses of this plant. However, this thorough search failed to reveal data on pricing and market availability of Moringa. There is scant research on herbal supplement sales data in various regions of the world in general. One article discussed the supply of medicinal plants in village markets in northern Peru (Bussmann et al, 2007). Unfortunately, Moringa was not discussed in this paper. There was another research article, again not involving Moringa, on the cost comparison of purified isoflavonoid products in Washington State (Chua et al, 2004). Thus, in an attempt to help provide this important sales information on the popular herbal supplement Mo, data was collected on the availability and pricing of this herbal supplement in the greater Washington D.C., Maryland, and Virginia region of the United States. It is hoped that this study will help to pique interest in medicinal plants and their marketing aspects and generate further studies in the future.

Mo has been long used in traditional medicine for its many medicinal properties including anti-inflammatory, antioxidant, and antimicrobial characteristics. The most commonly used parts of the Mo plant are the leaves either in powder form or as aqueous or alcoholic leaf extracts. Other parts of the plant including seed pods, stems, bark, roots, and oil extracts of the seeds are also often used. (Lunyera et al., 2016).

The Mo plant has many health benefits. The plant is used as an important super food nutraceutical and is cultivated and harvested in many parts of the world. The dried leaves have a crude protein content of 30 percent and contain 19 amino acids. The leaves have the following mineral contents: calcium, phosphorus, magnesium, potassium, sodium, sulfur, zinc, copper, manganese, iron, and selenium. There are seventeen fatty acids, with alpha-linolenic acid having the highest concentration. Vitamin E, carotenoids, ascorbic acid, flavonoids, and phenolics are also found in the leaves. The amino acids, fatty acids, vitamins, and minerals show a desirable nutritional balance (Moyo et al, 2011). The Mo plant is a rich source of many bioactive compounds and incorporating Mo in the diet can improve the nutritional status of nursing mothers and help to combat malnutrition and iron deficiency anemia among children. (Arora et al., 2021). A study was done aimed at exploring the effects of Mo leaves supplementation on the Quality of Life of HIV-positive adults in Nigeria. The study found that Mo leaves increased the physical, psychological, level of independence, and social relationship domains of a survey on Quality of Life as compared to placebo. It was concluded that Mo leaves can be used to improve treatment outcomes by improving nutritional intake and Quality of Life in People Living with Human Immunodeficiency Virus in resource-constrained settings (Gambo et al, 2021).

Mo also shows many health benefits as an herbal medicine nutritional supplement. The leaf part of the plant is most commonly used. The Mo supplement is taken in the form of leaf powder, tablets, or aqueous, alcoholic, or oleaginous leaf

extracts. Mo has been shown to express anti-inflammatory properties. Chronic inflammation may lead to chronic inflammatory associated diseases such as arthritis, colitis, diabetes, and cancer. (Kou et al, 2018; Bhatelia et al 2014). Inflammatory cytokines, such as tumor necrosis factor-alpha, and interleukin-1-beta can upregulate prostaglandin E-2 and nitic oxide thus enhancing the activity of inducible NO synthase, microsomal Prostaglandin synthase-1, and cyclooxygenase-2 in target cells and thus increasing inflammation. Mo has been shown to inhibit the production of tumor necrosis factor-alpha and interleukins in response to stimulated human macrophages, and also inhibit the expression of Re1A, a gene in nuclear factor signaling during inflammation. (Kooltheat N. et al, 2014; Kou et al., 2018).

A number of studies have demonstrated the antioxidant properties of Mo. A study of aqueous extract of Mo leaves using in vitro systems showed the free radical scavenging ability of Mo, and also its ability to inhibit oxidative damage to DNA (Singh et al., 2009). The aqueous leaf extract was shown to exhibit the most antioxidant activity and to have the highest concentrations of phenolic, flavonoid, and ascorbic acid antioxidants. (Stohs and Hartman, 2015). Another study by Siddhuraju and Becker showed that Mo leaf samples from three different agroclimatic origins have very high free radical scavenging activity (Siddhartha & Becker, 2003). Here, these naturally occurring antioxidant compounds decrease oxidative damage in tissues by scavenging harmful free radicals and by cell enhancement. (Razis et al, 2014).

Many studies also show the anti-microbial properties of Mo. A study on the control of coliform bacteria detected from diarrhea-associated patients showed that the organic leaf extracts of Mo exhibited a remarkable antibacterial effect against the tested bacterial pathogens including Escherichia coli, *Shigella dysenteriae*, and Salmonella species (Rahman et al., 2010). Another study showed the antibacterial activity of bark extracts of Mo against Staphylococcus aureus, *Citrobacter freundi*, Bacillus megaterium, and *Pseudomonas fluorescens* (Zaffer et al., 2014).

There was a study done using paper disks soaked in aqueous and ethanolic Mo leaf extracts to determine the susceptibility of gram-positive and gram-negative bacteria. While some of the gram-negative bacteria showed resistance, the Mo leaf extract-soaked disks were most efficient and showed good inhibition against *Staphylococcus aureus*, *Vibrio parahaemolyticus*, *Enterococcus faecalis*, and *Aeromonas caviae* (Peixoto, 2011).

An additional study carried out in Mekelle, Ethiopia evaluated the antimicrobial capability of Mo leaf ethanol extract. The extract exhibited good antibacterial activity against *Pseudomonas aeroginosa*, *Proteus vulgaris*, *Bacillus subtilis*, *Staphylococcus epidermidis*, and *Streptococcus mutans* (Amabye & Firehiwot, 2016).

There was also a study done by Singh and Tafida in Nigeria on the antibacterial activity of Mo leaf extracts against *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. The aqueous, ethanol, and methanol extracts all exhibited large zones of inhibition against each of these bacteria (Singh & Tafida 2013).

A review of the safety of the nutritional supplement Mo and untoward effects show Mo to be a very safe herbal medicine. Based on human, animal, and in vitro studies, various preparations of Mo leaves including aqueous and organic extracts appear to be exceedingly safe at the doses commonly utilized (Stohs & Hartman, 2015).

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African Traditional Medicine: Prospects-A Bird's Eye View*

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Background:

Africa has a huge potential for developing traditional medicine (TM), which is deeply ingrained in indigenous culture. Unlike in the West, it is the first line of defense against diseases in rural areas where most people live. About 70-80% of the continent's population use TM for their healthcare needs. In this short note, *in lieu* of a detailed article, some features of this important healthcare modality are highlighted.

1. Why care about traditional medicine in Africa?

There are many reasons: (a) most of the population use it; (b) it is accessible and affordable; (c) it is deep-rooted in indigenous culture and people believe in it; (d) a good number of the practices may work for the intended purpose; (e) it can be a source of modern drugs and (f) if developed, it can potentially produce foreign currency earnings for African countries.

2. Resources (the size of African flora)

It is estimated that about 45,000 plant species exist in the continent, of which 33% (15,000) are endemic. Overall, about 4,000 plants are used for medicinal purposes. However, many of the medicinal plants have not been researched for constituent profiles and biological (therapeutic) properties. Therefore, there is room for a lot of research.

3. Some examples of prominent African medicinal plants

(a) The Madagascan periwinkle (*Catharanthus roseus*): In the late 1950's and early 1960's, Gordon Svboda at Eli Lilly (USA) discovered two compounds: vincristine and vinblastine, which were later approved by FDA for treating childhood leukemia. This discovery spurred a surge for further search of medicinally useful compounds from plants.

(b) The sea hare (*Dollabela* marine species) from the Indian Ocean, off the island of Mauritius: George Pettit and co-workers at Arizona State University (ASU) in 2004 isolated compounds called dolastatins. A derivative of Dolastatin 10, conjugated to a monoclonal antibody [so-called antibody drug conjugate (ADC)], was approved by FDA in 2019 for the treatment of certain types of lymphomas and leukemia.

(c) The African bush willow (*Combretum cafrum*) from South Africa: In 1982, Pettit at ASU discovered from this plant agents called combretastatins. Combretastatin A-4 phosphate was approved by FDA and European Medicines Agency (EMA) as an orphan drug for treating thyroid cancer.

(d) *Maytenus serrata* from Ethiopia (locally known as *attat* or *qoqoba*): In the 1970's, the National Cancer Institute in the USA was screening tropical plants for anti-cancer activities, and for possible development as medicines. This plant was one of the many that were studied. A potent compound maytansine was obtained from the plant, but it lacked specificity and was toxic. Many years later, it was synthetically modified to a compound called emtansine and eventually coupled to a monoclonal antibody. Today, KADCYLA® (ado-trastuzumab emtansine) is used in oncology practice for early and later stages of metastatic breast cancer.

4. Intellectual Property Rights (IPR)

IPR is a thorny problem when it comes to product development in Africa and in the South in general.

The matter seems to have improved a little bit over the years. Cases in point in the past were: the slimming (weight-reducing) agent P57 from the plant *Hoodia* from Southern Africa, Devil's Claw (*Harpagophytum procumbens*) from South Africa for a variety of ailments, the Ethiopian endod plant (*Phytolacca dodecandra*) for the prevention of schistosomiasis, the plant *Swartzia madagascariensis* from Zimbabwe for candida (fungal) infection. Companies and universities in the West (North) took the plants as well as the information to make fortunes in some cases, without adequate compensation and benefit sharing with the indigenous people.

The Way Forward

South-South collaboration in research and development of traditional medicine is the right approach to adopt for extracting benefits that come out of research. For example, within the African continent, institutions such as the Natural Products Research Network for Eastern and Central Africa (NAPRECA), Western African Network of Natural Product Research Scientists (WANNPRESS), African Laboratory for Natural Products (ALNAP), etc. can help as collaborative centers for such endeavors among African nations. Similar approach can also be adopted in other South-South collaborations. The prospects of traditional medicine in Africa appear to be enormous.

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3. Product Information: KADCYLA® (ado-trastuzumab emtansine). Genentech, Inc. A Member of the Roche Group 1 DNA Way South San Francisco, CA 94080-4990 U.S.; 2022.

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