EPPAD Bulletin

Vol 1, Number 1; Sept 4, 2021

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Editor's Note

We are glad to release the first (maiden; inaugural) issue of the Ethiopian Pharmacists and Pharmaceutical Scientists Association in the Diaspora (EPPAD) Bulletin (Vol 1, No 1). ***EPPAD Bulletin*** will be published biannually in September (Fall) and March (Spring). The idea of starting an EPPAD publication was conceived out of the need for EPPAD to inform pharmacists and allied professionals about its activities, share insights on pharmaceutical and health-related topics and provide concise reviews on selected areas of interest. The bulletin is envisioned not as the typical journal-type publication, although in due course it is hoped to evolve into the latter. The editorial team reached a consensus on the content of the bulletin for the foreseeable future, and therefore will entertain articles in the following sections (standing columns):

1. EPPAD News and Highlights
2. Pioneers of Ethiopian Pharmacy
3. Updates on COVID-19
4. Clinical Insights and Pearls

However, in the fast-evolving discipline of pharmacy and related fields, the focus might change in future issues. For the current issue, in the interest of time and in-order to coincide with EPPAD Annual Conference of September 4, 2021, the Editorial Team took it upon itself the task of writing articles. EPPAD leadership have provided a pictures-laden panoramic article highlighting the Association and its activities since its inception. In the Pioneers of Ethiopian Pharmacy section, Ato Aklile walks us on the trails of early days of pharmacy in Ethiopia and highlights the career of the late Dr. Belachew Desta. Dr. Tesfaye Biftu gives a condensed summary of the status of COVID-19 vaccines and therapeutics. It is indeed important to have such a useful write-up within our easy reach as we navigate through the ever-changing face of the virus and the challenges it poses. Dr. Bisrat provides a synopsis of research on an Ethiopian medicinal plant *Veronia amygdalina* (vernacular: ***grawa***) for the treatment of atopic dermatitis and eczema. He gives a detailed background on the pathogenesis of the disease. In this issue, a summary blurb is given on the activities of EPPAD Pharmaceuticals Inc. an offshoot of EPPAD.

Finally, we invite pharmacists and allied professionals to contribute manuscripts for future issues of ***EPPAD Bulletin***. Together, we strive to make this publication a vibrant and participatory medium.

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

EPPAD at a Glance

Who we are:

The Ethiopian Pharmacists and Pharmaceutical Scientists Association in Diaspora (EPPAD) is a non-profit, tax-exempt 501(c)(3) membership association of Ethiopian pharmaceutical professionals in diaspora incorporated in the State of Virginia, USA in September 2018. EPPAD is led by a Board of Directors, which provide overall leadership, guidance, approve annual work plans, and prudent financial management of the Association. Our members include pharmacists, pharmaceutical scientists, other allied professionals and interested institutions.

Mission, Vision and Objectives:

The vision of EPPAD is to promote public health through pharmaceutical care. Its mission is to bring pharmaceutical and allied professionals together to contribute for pharmaceutical manufacturing, pharmacy education, practice, service and scholarship. The objectives of the Association are to create a platform for pharmaceutical professionals in the diaspora to network with each other and enrich their knowledge and skills to be competent professionals in pharmaceutical care in the US through continued education, seminars, and annual conferences. It will also serve as a bridge to connect pharmaceutical professionals of Ethiopian origin working abroad with those working in Ethiopia to promote professional practice, improve access to quality assured, affordable and effective pharmaceutical products and support appropriate policy and regulatory reforms in Ethiopia.

Progress to-date:

Since its inception in 2018, the following table represents some of the key accomplishments of EPPAD:

Summary EPPAD Milestones (Sept 2018 – Sept 2021)		
EPPAD General	EPPAD Board of Directors made of ten members and an Advisor formed	Inception to date
	EPPAD registered as a 501C non-profit organization in the USA	July 2018
	Website, social media accounts such as Facebook, LinkedIn, and Twitter developed	November 2018
	EPPAD has garnered the support of about 200 registered members and several friends of EPPAD	Inception to date
	Pharmaceutical and allied professionals consultative meeting held to deliberate upon EPPAD thematic focus areas	November 2018
	Inaugural Symposium of EPPAD Launched at Ethiopian Embassy Conference Hall in Washington DC	February 2019
	EPPAD post-Covid19 Annual Conference Planned and Conducted at Civic Building Silver Spring	Sept 04, 2021
Education/ Knowledge Exchange	Professional development and guidance meeting to foreign graduates, new graduates, and carrier changing aspirants held	June 2019
	Supply and demand-side survey to identify academic/TA resources in the Diaspora and needs of pharmacy academic and related institutions in Ethiopia with the aim of organizing training/mentoring sessions	June -Dec 2019
	In collaboration with Ethiopian Pharm Association, conducted over 13 virtual seminars on different topics to professionals in Ethiopia and US.	2019/2020
Regulatory/ Policy	Facilitated a consultative meeting for three US EPPAD member team to meet with EFDA in Addis Ababa on mutual collaborations	February 2020
	Supported EFDA to submit an application to EU Medicines Agency for getting Observer Status	September 2019
	Provided laptop computers (pending delivery), PPE materials and Alcoholmeters/jars for enhancing performance at central and regional levels	2019/2020
Philanthropy / Covid19	One-month philanthropy mission to train and support stakeholders/beneficiaries to tackle Covid19 in Ethiopia conducted	August 2019
	Provided Covid19 commodities (PPEs), QA supplies, BP monitors, and Vision Charts provided to the Ministry of Health, Schools of Pharmacy, Community Pharmacies in Ethiopia	April 2020/April 2021
	Provided $3,000 to the Ethiopian Embassy for supporting Covid19 projects in Ethiopia	April 2021
	Provided $1,500 for two charities to support emergency needs such as food and medicine during the Covid19 crisis in Ethiopia.	April 2021
Traditional Medicine	Nine member EPPAD tradition medicine working group (ETMG) formed and SOW developed	2020/2021
	Held several consultative/informational virtual meetings with the representatives of key stakeholders such as the Ethiopian Public Health Institute, The Minsitry of Health, Agricultural Research Institutes, Universities, etc	May 2021
	Reviewed and provided input to discussion around the Traditional Medicine Roadmap, TM Strtaegic Plan and other key documents of the Government.	May 2021

	Drafted an outline for a Manual/Guide for the production of herbal/dietary supplements and a herbal pharmacopoeia in consultaion with key professionals in Ethiopia	July 2021
Investment	Pharmaceutical investment forum in Washington DC held	September 2019
	Supported establishment and registration of EPPAD Pharmaceutical Inc. in Delaware to help in drug manufacturing and import/distribution in Ethiopia	September 2019
	Feasibility study for pharmaceutical manufacturing and Import/Distribution in Ethiopia)	Nov 2019
Sister Organizations	Signed MOU with Ethiopian Pharmaceutical Association (EPA)	December 2019
	Provided BP monitors, Snellen/vision charts, PPE materials etc. through EPA to ten schools of pharmacy	April 2020
	Participated in person and virtually at two EPA Annual Conferences held in Ethiopia	Aug 2019 & 2020
	EPPAD joined hands with pharmacy owners, faith-based organizations, sister associations and others to provide humanitarian support and vaccinations for Covid19 impacted community members in the DMV area.	2020/2021
Funding/ Resource Mobilization	EPPAD mobilized resources for sponsoring its conference, and continuing education initiatives from its membership and sponsors (Howard University, Lion Healthcare Strategies, EPPAD Pharm Inc., RxParadigm)	Inception to date
	EPPAD joined hands with pharmacy owners, faith-based organizations, sister associations and others to provide humanitarian support and vaccinations for Covid19 impacted community members in the DMV area.	May 2021

EPPAD Working Groups

EPPAD has been supporting institutions in Ethiopia with their efforts of improving key challenges in the pharmaceutical sector using its six interest/working groups. These working groups have facilitated knowledge exchange via virtual webinars on multiple pharmacy related topics in collaboration with Ethiopian Pharmaceutical Association (EPA); helped to establish a pharmaceutical company that aims to manufacture safe and quality medicines; and conducted advocacy in policy and policy dialogue with a focus on pharmacy education, traditional medicine, regulatory matters, pharmaceutical waste management, including expiry extensions.

Philanthropy Group

The pharmacy philanthropy group solicits and manages a "pharmacy fund" to implement projects that demonstrate immediate practical outcomes such as scholarship to award/recognize outstanding students; provide financial support for disadvantaged pharmacy students; provide sanitary pads for needy pharmacy female students; offer medicines to welfare groups like Mekedonia senior citizens home, respond to urgent humanitarian needs as appropriate etc.

- Raised about $10,620.00 from its benefactors through direct mail, EPPAD and Gofundme.
- The following charities (Geregesenon Mental Assn, Yewedequtin Ansu, Mary Joy, Kidane Mihiret Youth Assn, Meseret Humanitarian Assn, Muday Charity) benefitted from BP monitors, vision screening charts, Albendazole tablets for mass deworming of 2,000 persons, cash support for emergency needs of two charities and contribution of $3,000 to the Covid19 Fund of the Ethiopian Embassy.
- Ten schools of pharmacies were provided with BP monitors and vision charts to conduct community screening.
- In addition to Covid19 PPE materials, fifty (50) laptop computers donated by USP (awaiting delivery) and one hundred alcoholmeters purchased by EPPAD were provided to EFDA to be distributed to relevant institutions.

Education Group

This working group focuses on human resources development through collaboration with teaching institutions or professional associations in lecturing or availing technical resources to improve knowledge, skills and practice/performance in pharmacy schools in Ethiopia. The members of the groups conducted supply and demand-driven assessment with the aim of mobilizing diaspora experts to provide knowledge exchange initiatives. Coordination in areas actively pursued with the Ministry of Science and Higher Education, Ministry of Health Pharmacy Department/EFDA, the Ethiopian Pharmaceutical Association and twenty public schools of pharmacies in Ethiopia.

Since 2018, the following are some of the accomplishments by the EPPAD Education Group:

- Provided over 13 zoom presentations on various topics including, covid19, AMR, supply chain management, pharmaceutical education, continuous professional development (CPD/CE), traditional medicine, pharmaceutical manufacturing, policy and regulatory etc.
- Provided six month zoom subscription to EPA for conducting other EPA planned webinars

Summary of Webinars Conducted (May 08 – Sept 25, 2020)

	Topic	Date	Participants
EPPAD Webinar 1	Covid19: Implications for Pharmacy Professionals and Pharmacy Services	May 08, 2020	NA
EPPAD Webinar 2	Covid19: Clinical Presentation and Mgt Strategies	May 15, 2020	130
EPPAD Webinar 3	Pharmacy Education & Research During Covid19	May 22,2020	105
EPPAD Webinar 4	Molecular Mechanism of Infection with SARS-Cov-2 & Therapeutic/Vaccine Trials	May 29, 2020	93
EPPAD Webinar 5	Late Stage Clinical Trials, Preparedness for Manufacturing and Access to Covid19 Therapeutics/Vaccines	June 05, 2020	67
EPPAD Webinar 6	Regulatory & Supply Mgt During Covid19: Experiences and Challenges	June 12, 2020	68
EPPAD Webinar 7	Antimicrobial Resistance (AMR) Prevention and Containment in the Era of Covid10	June 19, 2020	44
EPPAD Webinar 8	Covid19 Clinical Presentation & Mgt Strategies with Ethiopia Context	June 26, 2020	37
EPPAD Webinar 9	Opioid in the Era of Covid19	July 24, 2020	NA
EPPAD Webinar 10	Traditional Medicine and Research: Experience and Challenges in Ethiopia	July 24, 2020	NA
EPPAD Webinar 11	Traditional Medicine Education	Aug 28, 2020	NA
EPPAD Webinar 12	Dietary Supplements Regulation in the US	Sept 05, 2020	NA
EPPAD Webinar 13	Transforming Global Health	Sept 25, 2020	NA

Investment Group

EPPAD investment group aimed at creating a platform for bringing together individuals and groups with investment interest, experience, expertise, and resources to the pharmaceutical sector in Ethiopia. In September 2019, this group organized a pharmaceutical investment forum which attracted over sixty participants and conducted feasibility study to engage in socially responsible investment areas including manufacturing of medicines and import/distribution. The group helped establish and register EPPAD Pharmaceutical Inc pharmaceutical company in the State of Delaware. The Business Company will be run by an independent Board of Directors. Based on the premise that the investment environment in Ethiopia is conducive (pharmaceutical industrial park being readied at Klinto in the outskirts of Addis, minimal startup capital with the rest to be accessed through bank loan, tax holidays, etc.), the company has conducted feasibility studies and in the process of establishing a pharmaceutical manufacturing plant in Ethiopia, with a vision to expand in other African countries.

Policy and Regulatory Group

EPPAD members with interest in regulatory and policy areas came together to provide technical assistance in strengthening institutions, improve systems and advocacy in introducing/updating policies, strategies and guidelines in the varies areas in the pharmaceutical sector.

To date, the Working Group has engaged with the Ethiopian Food and Drug Administration to provide support in strengthening EFDA with laptop computers for regional regulatory branch offices, quality assurance equipment - alcoholmeters and jars for hand sanitizers, linking EFDA with the EU Medicines Agency for getting Observer Status and facilitating a consultative visit by three senior members of EPPAD with EFDA in February 2019 and to discuss potential collaborations in the areas of policy, document reviews, institutional capacity, regulatory reforms and system optimization. EPPAD engaged EFDA, MOH, EPSA, Pharmaceutical academics, EPA, and relevant NGO representatives to exchange experiences and information around access to medicines by improving supply chain management and exploring ways to minimize expiry, including promoting expiry extension studies.

Traditional Medicine Group (TMG)

The EPPAD tradition medicine working group is the latest addition to the EPPAD pillars and is formed by professionals interested to contribute to traditional medicine/indigenous knowledge with the aim of serving as a platform to support the promotion of herbal and dietary product development. It will also serve as a bridge to connect professionals working abroad with those working in Ethiopia to promote knowledge exchange, mobilize resources, improve access to current theory and practice, support appropriate policy and regulatory reforms in the traditional medicine sector, and advance the development of quality and tested locally grown herbal products. The Group will work closely with counterpart professionals and institutions in Ethiopia to synergize Traditional Medicine (TM) efforts.

Since its formation, the Group had held several consultative/informational virtual meetings with the representatives of key stakeholders such as the Ethiopian Public Health Institute, The Minsitry of Health, Agricultural Research Institutes, Universities, etc. The Group had provided input in the discussion around the Traditional Medicine Roadmap, and other key documents of the Government. The Group in consultation with key relevant people is in the process of develpoing a manual/Guide for the production of herbal/dietary supplements and a herbal pharmacopoeia.

EPPAD NEWS AND HIGHLIGHTS

Pioneers of Ethiopian Pharmacy

Introduction

It was some 200 years ago that Ethiopian kings approached European governments to introduce the science of modern pharmacy in the country. According to Dr Richard Pankhurst, a French physician, Charles Jacques Poncet, was the first person who brought a "little chest of chemical medicines" to Ethiopia during the time of Emperor Iyasu I in 1699. It can safely be assumed that early hospitals like the Russian Red Cross Hospital in 1896 and its predecessor Menelik II Hospital must have had a pharmacy to serve their patients. King Sahle Selassie and his son Menelik II are said to have a pharmacy at their palaces too. In earnest, Dr Merab founded the first pharmacy in Addis Ababa in 1910, followed by Hakim Zhan in the early 1920s. Since then, there were several pharmacies established by Armenians and Greeks including Brussalian pharmacy: the contributor of this article had the rare opportunity of witnessing the existence of this pharmacy.

Dr. Merab, the personal physician of Emperor Menelik II of Ethiopia, owned the first pharmacy in Addis Ababa

The first half a dozen Ethiopian pharmacists were trained overseas in Lebanon at the American University of Beirut, Europe and USA. They returned to the country to work in the private sector and this group, excepting Lakew Awoke, included Benti Qaano, Berhe Seyoum, Girmai Yoseph, Seyoum Bekele, Elizabeth Berhe, and Seble Feseha. Training of professional graduate pharmacists in Ethiopia started in 1961 with the establishment of the Department of Pharmacy as a unit in the Faculty of Science of the then University College of Addis Ababa.

The first three Ethiopian pharmacists who graduated with a degree of Bachelor of Science (BSc.) in 1964 were Belachew Desta, FissehaTsion Abate, and Laike Gebreselassie. The second batch of graduates included Baro Tumsa, Senay Kefle Yesus and Zewditu Kafil. So much suffices for a taste of the foundation of early pharmacy in Ethiopia.

In this issue of EPPAD Newsletter, one of the first Ethiopian graduates, namely Belachew Desta (PhD) is featured.

Dr. Belachew Desta
Dean; March 1983-July 1991

Belachew Desta, one of the very first three local graduates, got his Bachelor of Science in Pharmacy degree from the then University College of Addis Ababa (UCAA) in 1964. He continued his higher studies at the University of British Columbia in Canada earning a Master of Science degree in 1972 and a PhD degree in Pharmaceutical Sciences in 1982. After graduation, Dr Belachew started his professional career as head of quality control department and production manager at the Ethiopian Drug Manufacturing Company (EDM), the first pharmaceutical plant of the country in 1964. He then went to work as manager at London Pharmacy, one of the early private pharmacies in Addis Ababa.

His academic life started in 1971when he joined the school of pharmacy at HSIU where he played different roles as an Associate Professor, Dean and Researcher (1983-1991). He taught pharmaceutical analysis and drug quality control. He conducted several studies on Ethiopian traditional herbal drugs, and his research outputs in this area were published in peer reviewed journals.

Some of his research included:

- Studies on the toxicity and therapeutic activity of local 33 taenicidal medications
- Anti-fertility activity of 70 medicinal plants
- Antimicrobial activity of 63 medicinal plants
- HPLC analysis of digoxin and digitoxin
- Ethiopian traditional herbal drugs: Potentiality and Appropriate Utilization
- An Evaluation of the USP Dissolution Apparatus

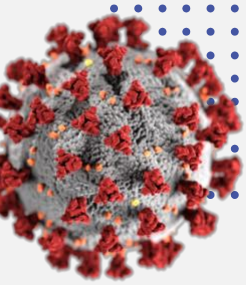
Dr. Belachew is credited for establishing a 5-year pharmacy undergraduate program, upgrading the school to the status of a faculty and strengthening the school by winning project funding from UNDP. He was the first President of the Ethiopian Pharmaceutical Association (EPA) when it was formed forty-seven years ago in 1974, when the contributor of this article happened to be the Secretary at the same time.

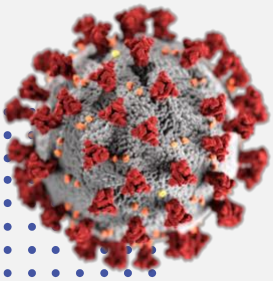
After leaving the University and for two decades thereafter, Dr Belachew ventured into the consultancy field where he became a consultant in drug therapy and herbal medication with operations in Addis and Bahirdar where he recommended to his clientele herbal medications for a variety of diseases.

Dr. Belachew passed away of natural causes in 2021 at the age of 79.

May His Soul Rest In Peace!

By Gabriel Daniel (aka-Aklile G Giorgis)





EPPAD NEWS AND HIGHLIGHTS

RECENT EFFORTS MADE TO DISCOVER & DEVELOP DRUGS TO PREVENT OR TREAT SARS-CoV-2: COVID-19

In this brief review, we will present a short introduction, diagnostic methods, and current efforts to treat COVID-19 using biologics and chemotherapeutic agents.

Introduction:
SARS-CoV-2 is a single-stranded RNA-enveloped virus. The first description of SARS-CoV-2, COVID-19, outbreak was made in December 2019. Now, over 100 million people globally in about 210 countries have been confirmed to have been infected and over two million people have died of COVID-19.

Clinical data
In the United States, there were over 20 million confirmed SARS-CoV-2 infections with >500,000 deaths. The fatality rate in China is estimated to be 4.8%. Spain, Italy, UK, France, Germany, and Turkey each had >2.5 million confirmed infections with mortality rates of 310-1,606 per million. Russia and Iran had 3.9 and 1.4 million confirmed infections and a mortality rate of 512 and 688 per million, respectively. In Brazil, over 9 million confirmed infections have been reported. In Ethiopia, 280,024 confirmed infections and 4,383 deaths have been reported.

Diagnostics
The detection of the viral nucleic acid sequence by PCR analysis is currently the gold standard for diagnosing SARS-CoV-2 infection. Serologic assays for the detection of viral antigens, as well as IgG and IgM antibodies against the viral antigens, have also been developed and used for SARS-CoV-2 infection.

Symptoms
COVID-19 symptoms were observed on different parts of the body including brain, eyes, nose, blood, gastro-intestinal system, lungs, heart, kidney, skin, and the immune system.

Treatment: Biologics
There are over 120 projects globally on SARS-CoV-2 preventive vaccines. These include inactivated virus, viral protein subunits vaccine, messenger RNA (mRNA) vaccine, DNA plasmid, recombinant human adenovirus type 5 (rAd5) or simian adenovirus type 26 (rAd26) expressing SARS-COV-2 spike protein, non-viral replicating vector expressing SARS-CoV-2 protein vaccine and replicating viral vector expressing SARS-CoV-2 protein vaccines.

mRNAVaccines
Moderna and Pfizer-BioNTech's COVID-19 mRNA (BNT162b2) vaccines have been approved by FDA.

Recombinant adenoviral vectors expressing SARS-CoV-2 spike protein/RBD
Several organizations in China, UK, Russia, and the USA developed recombinant adenoviral vectors expressing the COVID-19 genes as vaccines. United Kingdom (Oxford University) has a version (code name AZD1222). Russia has a COVID-19 vaccine (code name Sputnik V) that uses two recombinant adenovirus backbones, with one dose using the rAd5 and the other dose using the rAd26.

Inactivated virus vaccine
Towards the end of 2020, the Chinese health authority announced that inactivated vaccines based on the more traditional vaccine was granted conditional marketing authorization.

Recombinant viral protein vaccines
A recombinant spike protein nanoparticle vaccine (code name NVX-CoV2373, composed of a trimeric full-length spike glycoprotein and their Matrix-M1 adjuvant) was published.

Plasma immunoglobulin and monoclonal antibodies (mAb) and blood plasma therapy
Another potential adjunctive therapy for COVID-19 is the use of convalescent plasma or hyperimmune immunoglobulins. FDA released guidance for an emergency investigational new drug application and screening donors for COVID-19 convalescent plasma on March 24, 2020. Vir Biotechnology has isolated antibodies from patients who survived SARS and teamed with WuXi Biologics. FDA has allowed to use blood plasma from people who recovered from COVID-19.

Anticytokine human monoclonal antibodies
The damage in the lungs and other organs in COVID 19 patients is caused by an amplified immune response and cytokine release. IL-6 appears to be a key driver of this inflammation. Tocilizumab, a mAb IL-6 receptor antagonist alone or in combination has been used in a limited severe COVID-19 cases with early reports of success. Other mAb or immunomodulatory agents in clinical trials include bevacizumab, lenzilumab, and bamlanivimab (LY-CoV555). On 9 November 2020, the FDA issued a limited EUA based on the phase 2 data for the later. Another monoclonal antibody, etesevimab (LY-CoV016), was evaluated in combination with bamlanivimab. On November 21, 2020, few days after the EUA of bamlanivimab was issued, the FDA issued an EUA for casirivimab and imdevimab.

Macrophages, important effector cells for interleukin-6 (IL-6), play an important role in the pathogenesis of COVID-19. Tocilizumab is a humanized IgG monoclonal antibody that can specifically bind to soluble or membrane-bound IL-6 receptors. On February 3, 2021, FDA issued a treatment guideline on tocilizumab and other IL-6 inhibitors. The FDA panel determined that (a) for patients who are within 24 hours of admission to the ICU or who require invasive or noninvasive mechanical ventilation or high-flow oxygen (>0.4 FiO_2/30 L/min of oxygen flow), there are insufficient data to recommend either for or against the use of tocilizumab (or sarilumab, which is also an anti-IL-6) for the treatment of COVID-19, and (b) for patients who do not require ICU-level care or who are admitted to the ICU but do not meet the critical need listed in (a), tocilizumab or sarilumab should not be used apart from a clinical trial setting.

Stem cells therapy
Athersys Inc., Bioscience Institute, and Mesoblast have tested stem cell in COVID-19 patients. In China, stem cell therapy was also evaluated in patients with severe/critical COVID-19 patents.

Treatment: Chemotherapeutics
SARS-CoV-2 has a similar tissue tropism as the SARS virus. It has spike (S) protein that binds to angiotensin-converting enzyme (ACE2) receptor to target cells. After binding to ACE2 receptor, the virus particle uses host cell receptors and endosomes to enter cells. A host type 2 transmembrane serine protease (TMPRSS2) facilitates cell entry via the S protein. Once inside the cell, viral polyproteins are synthesized that encode for the replicase-transcriptase complex. The virus then synthesizes RNA via its RNA polymerase. Structural proteins are synthesized leading to completion of assembly. Viral particles are released. Each of the above viral steps provide potential targets for drug therapy.

Antiviral agents
Remdesivir is a potent RNA-dependent RNA polymerase inhibitor developed in 2014 for the Ebola and Marburg viruses. In late April, Gilead Sciences announced one of its trials had been "terminated" due to low enrollment and the results of that trial had been "inconclusive." A few days later, the company announced that another trial overseen by the National Institute of Allergy and Infectious Diseases "met its primary endpoint." At the same time, another study published in *The Lancet*, reported that participants in the remdesivir clinical trial showed no benefits compared placebo. Despite the conflicting results, the FDA issued an order on May 1, 2020 for the emergency use of remdesivir.

Ribavirin, kaletra, aviifavir, arbidol, umifenovir, and lopinavir–ritonavir were also evaluated. The combination of lopinavir–ritonavir offered no clinical benefit in adult patients with severe COVID-19. In another study, triple combination treatment consisting of interferon-beta-1b, ribavirin, and lopinovir–ritonovir was compared with lopinovir–ritonovir alone (control arm) and showed safety and superior efficacy in alleviating symptoms and shortening the duration of viral shielding and hospital stay in patients with mild-to-moderate COVID-19 symptoms.

Blocking ACE2 receptor or delivering excessive soluble form of ACE2

SARS-CoV-2 exploits the cell entry receptor protein angiotensin converting enzyme II (ACE-2) and DPP4 to access and infect human cells. On April 22, 2020, it was reported that a large, 28-day study done in China showed that hypertensive patients with COVID-19, treated with ACE inhibitors or ARBs was associated with lower risk of mortality compared with ACE inhibitor/ARB nonusers. A drug candidate from Sorrento, STI-4398 (also called COVIDTRAP), a proprietary ACE2 (angiotensin-converting enzyme 2)-Fc fusion protein, acts as a "soluble SARS-CoV-2 virus-binding decoy receptor protein" and binds to the spike protein of the novel coronavirus. Sorrento announced that STI-4398 completely inhibited the novel coronavirus's ability to infect African green monkey kidney epithelial cells (VERO/E6) at low concentration. According to recent (Agust 2020) report from University of East Anglia, England, "COVID-19 patients with high blood pressure who were taking ACEi/ARB medications were 0.67 times less likely to have a critical or fatal outcome than those not taking these medications."

Hydroxychloroquine and Chloroquine & Artemisinin

Chloroquine, an old anti-malarial drug and Hydroxychloroquine inhibit viral entry & endocytosis. Hydroxychloroquine, taken together with the antibiotic azithromycin, appeared to show promising results in a limited, non-peer-reviewed study conducted in France on patients hospitalized with COVID-19. Initially, the FDA issued an emergency use declaration for chloroquine and hydroxychloroquine. A study reported in *The Lancet* later found that the treatments did not appear to help COVID-19 patients hospitalized and instead were associated with heart complications and an increased risk of death. The FDA has now issued a warning and discontinued the study.

Artemisinin was promoted by Madagascar's government as healing coronavirus. The WHO warns, however, that there are no scientific studies yet that prove Artemisinin works.

Camostat mesilate and melatonin

The interaction between host ACE2 and the virus spike protein requires the serine protease TMPRSS2. Camostat Mesilate is a potent serine protease inhibitor. Research on severe acute respiratory syndrome coronavirus SARS-CoV-2 cell entry mechanism demonstrated that SARS-CoV-2 cellular entry can be blocked by camostat mesilate.

University of Kentucky findings published in PLOS Biology revealed that melatonin usage was associated with a nearly 30 percent reduced likelihood of testing positive for SARS-CoV-2.

Glucocorticoids, p38 kinase inhibitors and other anti-inflammatory drugs

Glucocorticoids reduce the excessive host immune attack against the SARS-COV-2-infected cells. On July 17, 2020, the preliminary report of an open-label study on the use of dexamethasone showed that the incidence of death was lower in the dexamethasone group vs usual care group. 67% of the critically ill COVID-19 patients had ARDS. In addition, GEn1E p38 inhibitors may have direct antiviral effects by boosting host-immune response.

Other studies

Famotidine use is associated with reduced risk of intubation in COVID 19 patients. Vitamin D could have a role in suppressing Cytokine Storm,but did not reduce mortality in COVID-19 patients. The cough medicine dextromethorphan could worsen the condition of people infected with the coronavirus. Metformin was significantly associated with reduced mortality in women in observational analyses of claims data from individuals hospitalized with Covid-19. In a study reported in *Cell Press*, and recently by University of Birmingham, the cholesterol-lowering drug, fenofibrate, reduced coronavirus infection by 70%. A study conducted by the University of Maryland School of Medicine published on Oct. 22, 2020, shows patients taking a daily low dose of 81 milligrams aspirin either before being admitted or right after being admitted to the hospital were 43 percent less likely to be put in the intensive care unit, 44 percent less likely to be placed on a ventilator, and 47 percent decrease in the risk of dying from their coronavirus infection.

Summary

Considerable research and development effort have been caried out in the last two years to treat or prevent COVID19 infection. Vaccines have been introduced and shown to save lives. It is likely that therapeutic agents will also be introduced in the coming few years.

(***Editor's Note: this article was written on August 8, 2021. Since figures and other issues regarding COVID-19 change daily and fast, readers are advised to take note of the date of the article***.)

Tesfaye Biftu, PhD
Professor and Director, Institute of Therapeutic Science, Adama University, Ethiopia

EPPAD NEWS AND HIGHLIGHTS

ግራዋ (*Vernonia amygdalina Del.*) for the Management of Eczema, Atopic Dermatitis

Atopic dermatitis is a term interchangeably used with "eczema," since atopic dermatitis is the most common form of eczema. Pruritus (or itch) is one of the biggest problems that people with eczema face. Eczema itch is not "just an itch," it is an intense itching which usually leads to damaged skin barrier because of moisture loss and dry skin, infection, skin lesions, and bleeding. The damaged skin barrier also causes the skin to be more sensitive to external irritants like soaps or household cleaners. The intense itch of eczema can be so bad that it could lead to a repetitive cycle of itching, scratching, and skin barrier damage. Eczema is a very common dermatological illness in Ethiopia. A study done by Kelbore[1] involved a total of 1,704 children with 1,869 new skin diagnoses, of whom 139 (8.2%) had more than one disease. Of these children, 52.4% were males and 44.9% within the age-group 5-10 years. Eczematous dermatitis accounted for the largest group (23.9%, $n = 447$) of skin conditions followed by bacterial infections (21.3%, $n = 398$), fungal infections (18.8%, $n = 351$) and infestations (9.9%, $n = 185$).

Currently there is no known cure for eczema but there are number of medications available in the United States to manage it by relieving itching and prevent new outbreaks. These drug options include over the counter (OTC) medications such as diphenhydramine, chlorpheniramine, cetirizine, etc. Topical options are also available, and include hydrocortisone, medicated OTC shampoos containing ingredients such as ketoconazole, selenium sulfide, coal tar and zinc pyrithione.

There are also number of prescription drugs available for eczema, and it includes topical calcineurin inhibitors (TCIs) that work by stopping certain cells of the immune system from "switching on".

The two TCIs that are available in the United States are tacrolimus ointment and pimecrolimus cream. Biologic drugs are other options and are among the most targeted therapies available today because they essentially use human DNA to treat eczema and other certain diseases at the immune system level. Dupilumab is the only injectable biologic approved for use to manage eczema. It is believed to work by inhibiting two interleukins that contribute to atopic dermatitis, IL-4 and IL-13. Other oral medications that work by modulating the immune system include azathioprine, cyclosporine, methotrexate, and mycophenolate mofetil. However, although these medications are highly effective in slowing down the inflammation, they are expensive, inaccessible to most people in Ethiopia. and have major unwanted side effects and toxicities. Therefore, it is imperative to search for other alternative therapies.

One such therapy is the herb *Vernonia amygdalina* Del known as with its common name, *grawa (ግራዋ)* in Amharic and a bitter leaf in English. The plant has also a variety of other names in different languages. The herb, in addition to its other uses, is one of the herbal treatments promoted for the treatment of eczema. *Grawa* is a small tree of 2-5 m with petiolate leaf of about 6 mm in diameter and elliptic shape. It is green in color and is called bitter leaf because the leaves have a bitter taste[2]. The bitterness can be abated by boiling or soaking in several changes of clean water[3] *Grawa* is commonly found throughout Ethiopia and many other African countries. Phytochemical analysis of the plant leaves showed the presence of anthracene, glycosides, steroids, flavonoids, proteins, carbohydrates, reducing sugars, saponins and tannins.[4] Phytochemical screening of *grawa* also revealed the presence of saponins, sesquiterpenes and flavonoids[5,6].

One of the unique characteristics of the plant is that it is drought-resistant and thrives in humid environments. It has multiple uses including for the management of tonsillitis, epidemic diseases, bacterial infections, cough, bleeding, gastrointestinal problems, tuberculosis, asthma, constipation, oxidative stress, helminthic infections, malarial infections, gastrointestinal disorders, loss of appetite, wounds, thrombi, diabetes mellitus, lipid disorders, and breast cancer[7]. The methanol leaf extract was relatively safe with median lethal dose, $LD_{50} \geq 5000$ mg/kg when single dose was administered orally to mice. *Grawa* leaf extract is also promoted as a potential substitute for hops (ጌሾ) in beer production. In Ethiopia, the plant is commonly used in cleaning the containers used for fermentation purpose. Due to its bitterness, it also used for the control of microbial contamination in beer brewing without affecting the quality of malt, and also to make honey wine called Tej[8].

There are several published journal articles on the positive clinical benefits of *grawa* in many types of illnesses. However, the number of publications is limited when it comes to its efficacy against atopic dermatitis. Ngatu NR et al.[9] conducted an extensive study to determine the efficacy of *grawa* in the treatment of atopic dermatitis, including eczema. In their study, atopic dermatitis-like disease was induced in NC/Nga mice, so as to evaluate the anti-allergic effects of *grawa* (*V. amygdalina*) leaf extracts (VAM). They selected 80 NC/Nga mice and randomly divided them in groups of five or six aqueous extracts (VAM1), methanolic extracts (VAM2), hydrocortisone (HCT), and the normal mice (NORM) groups. They chose NC/Nga strain of mice because these animals have been reported to develop atopic dermatitis-like skin lesions which are similar to humans. Their result shows that HCT, VAM1 and VAM2-pretreated mice showed significantly lower number of scratching behavior episodes ($p< 0.01$). In addition, VAM1, VAM2 exerted a significant inhibitory effect on the development of atopic dermatitis skin symptoms ($p< 0.001$). The authors concluded that their study confirm that VAM extracts prevent and improve atopic eczema dermatitis syndrome in mice.

In addition to their study in mice, the authors also reported a clinical case study of a patient who has been suffering from eczema dermatitis for several months. The patient presented to their clinic with itchy erythematous skin lesions and was treated with the use topical zinc oxide ointment and some topical steroid preparations such as betamethasone dipropionate cream; however, his skin condition did not improve. The patient was then treated with *grawa* (VAM) and he reported that he was relieved from the itch completely within the second week and improved the severity of the disease (EASI = 0.7) on day 21. For more about a year since this treatment, the patient did not develop similar skin condition. The authors concluded that their results suggest that VAM extracts, known as ERK pathway inhibitor, exert prophylactic and curative effects on eczema dermatitis possibly through this pathway inhibition and down-regulation of IgE production.

Ngatu NR, in another publication, also reported the result of their study that enrolled 25 patients with mild to moderate eczematous skin disease[10]. The patients were divided into 4 treatment groups of 5-7 patients (age range: 5-17 years). Within 1-2 weeks of topical treatment, their skin symptoms were completely resolved confirming the anti-itch, anti-inflammatory, and anti-allergic effect of the plant. In these patients, the extract was applied topically and prevented the development of atopic dermatitis.

Ngatu NR also reported a 5-year-old girl case study who developed atopic eczema skin lesions during infancy, diagnosed with psoriasis, which later became recalcitrant despite a long period treatment with some steroid preparations, zinc oxide and local ethnomedicine products[11]. The child suffered with severe lichenification, oozing, swelling and hyperpigmention on large areas of upper and lower limbs and trunk at the time of admission. During the hospital course, she was treated with a twice daily application of 10% *Vernonia amygdalina* extracts. Three weeks later, the authors reported that they noted a marked improvement of eczema area severity index (EASI) and dermatological life quality index (DLQI), with reduction of total serum IgE, eosinophilia and erythrocytes sedimentation rate (ESR). They concluded that *V. amygdalina* leaf extracts could be beneficial as antiallergic agent in humans.

Although the plant is commonly used in Ethiopia, particularly in rural parts of the country for the treatment of eczema dermatitis and psoriasis, not many clinical studies are currently available to make a strong recommendation based on the literature reviewed. Therefore, further clinical studies are needed to determine its safety and efficacy for the management of atopic dermatitis. including eczema and psoriasis.

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EPPAD NEWS AND HIGHLIGHTS

In Other News

EPPAD Pharmaceuticals Inc.

EPPAD Pharmaceuticals was founded by a dedicated group of Ethio-American pharmaceutical experts and other interested individuals who share a common purpose of developing, manufacturing, and distributing quality-assured, affordable medicines for Ethiopian, and broader African market. With imports comprising as much as 70 to 90 percent of drugs consumed in most countries in sub-Saharan Africa, we are dedicated to local productions. EPPAD has studied the market including local measures of feasibility, demand, and investment attractiveness. We will also engage in an import and distribution side of the business where it makes sense.

The company aims to make a meaningful, positive impact on public health that brings meaningful difference to health of the Ethiopian public and others we serve. The company is guided by the following principles: integrity, mutual respect, responsiveness, accountability, collaboration and transparency.

EPPAD Pharmaceuticals Inc. is a Delaware incorporated company. The company is in the process of establishing a Pharmaceutical Manufacturing Plant in Ethiopia. The feasibility study is completed and the field office in Ethiopia is actively operational. The founding members have raised the necessary investment to start the process. Securing land/property, machinery and other resources are in progress. Our hope is to build an exemplary venture of collaboration with economic impact while improving the health standard of people's lives.