AFRICAN TRADITIONAL MEDICINE FOR THE PREVENTION OF COVID-19 PANDEMIC AMONG STUDENTS OF FCE-ABEOKUTA, OGUN STATE

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Abstract: *The coronavirus disease 2019 (COVID-19) pandemic is caused by an infectious novel strain of coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which was earlier referred to as 2019-nCoV. The respiratory disease is the most consequential global public health crisis of the 21st century whose level of negative impact increasingly experienced globally has not been recorded since World War II. Up till now, there has been no specific globally authorized antiviral drug, vaccines, supplement or herbal remedy available for the treatment of this lethal disease except preventive measures, supportive care and non-specific treatment options adopted in different countries via divergent approaches to halt the pandemic. However, many of these interventions have been documented to show some level of success particularly the traditional medicine while there is paucity of well reported studies*

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on the impact of the widely embraced Traditional African Medicines (TAM) adopted so far for the prevention, management and treatment. The paper provided a holistic report on evidence-based antiviral and promising anti-SARS-CoV-2 properties of African medicinal plants based on silico evidence, in vitro assays and in vivo experiments *alongside the available data on their mechanistic pharmacology. This review exercise may lend enough credence to the potential value of African medicinal plants as possible leads in anti-COVID-19 drug discovery through research and development.*

Keywords: *African, Traditional, Medicine, Prevention, Covid-19 Pandemic.*

Introduction

The current pandemic threatening the global community, a highly communicable viral infection otherwise known as Coronavirus disease 2019 (COVID-19), is caused by the Severe Acute Respiratory Syndrome Coronavirus two or SARS-CoV-2 (Chan et al., 2020). The sudden emergence of the disease was first noticed in Wuhan city, China, East Asia (Chan Chang,Kok,Zhu,Chu,To & Yuan, 2020). Social distancing, hand washing, alcoholic disinfectants or hand sanitizers, isolation/quarantine, travel restrictions, wearing of face mask, community containments and partial or total lockdown (World Health Organization, 2020) have continued to remain effective non-pharmaceutical preventive measures.

Despite all the divergent efforts to halt the spread and mortalities associated with COVID-19, the

devastating micro-enemy has continued to spread causing more deaths and a lot of socio-economic implications. While most of the affected countries in Europe and America are relying solely on orthodox drugs, South-East Asia and in particular, China where the COVID-19 pandemic appear to have originated, has adequate documentation of successful outcomes following the integration of Traditional Chinese Medicine (TCM) with orthodox medicines in COVID-19 management (Chang,Kok,Zhu,Chu, To & Yuan, 2020).

Interestingly, overwhelming literature evidence suggests that China and neighboring Asian territories practice a robust age-long traditional medicine system that has been favorably integrated with the western medicine; the TCM-western system of healthcare was therefore adopted to combat the earlier outbreak of SARS-CoV in Guangdong, China in 2002 leading to the reported defeat of the epidemic(Ling,2019). Top among the well documented herbal recipes and formulations used as adjuvants alongside western medicines during the time included San Ren Tang, Yin Qiao San, Ma Xing Shi Gan Tang, Gan Lu Xiao Du Dan, and Qing Ying Tang, a polyherbal formulation containing many indigenous plants. In addition, Hong Kong has documented the traditional application of Sang Ju Yin and Yu Ping Feng San, *Isatis tinctoria* L. (Brassicaceae) and *Scutellariabaicalensis* Georgi (Lamiaceae), for prophylactic use among health workers against SARS-CoV infection (Hensel,Bauer,Heinnidu,Spiegler,Keyser & Henpel, 2020). Following the reported success with the use of herbal adjuvants during the previous outbreaks of viral infections in China, the outbreak of SARS-CoV2 received an immediate authorization of integral Traditional Chinese, western medicines to treat

COVID-19. This means Traditional Chinese Medicine - TCMs (mainly plant-based) were co-administered with western drugs as adjuvants.

However, in Africa, the use of phytomedicines which is also referred to as herbal medicine or phytotherapy is well embraced in different Pan African territories where 80–90% of its rural populations rely on traditional medicines (mainly plant-based) for primary healthcare (Elujoba, Odeleye & Ogunyemi, 2005). The extensive use of the predominantly plant-derived traditional medicine in Africa otherwise referred to as Traditional African Medicine has been described to be associated with African socio-economic and socio-cultural endowments (Elujoba, Odeleye & Ogunyemi, 2005). For this reason, the WHO has continued to sensitize African Member states toward the integration of TAM into their health system (Mahomoodally, 2013) as the body recognizes the relevance of traditional, complementary and alternative medicine to Africa which has a long history of TAM and knowledgeable indigenous practitioners. For instance, there has been an unprecedented use of phytomedicines in Africa following the outbreak and global spread of COVID-19 pandemic, a situation which has been compounded by lack of authorized medicines that are effective, affordable and accessible to the populations coupled with a relatively weak African health sector (WHO, 2020).

Coincidentally, available evidence from Africa Center for disease Control and Prevention (Africa CDC) suggests that the African continent is the last to be hit by the viral pandemic and least affected continent whose mortality rate (2.1%) until July 21, 2020 was less than half of the reported global mortality (5%) rate. Hence,

despite the vulnerability of the African continent, it accounts for only 5% of the globally reported cases of COVID-19. While several factors may be attributable to this seeming positive trend, the near absolute dependence on the obvious potentials of the African medicinal plants for COVID-19 management may not be ruled out. As a malaria endemic region, the Sub-Saharan Africa often co-administer herbal remedies alone or combined with orthodox drugs as adjuvants and many of these plant-based medicines have since been informally repurposed by various users for COVID-19 prevention and symptomatic management as simple home remedies. Unlike the Traditional Chinese Medicine, there is a paucity of well reported studies on the impact of the widely embraced TAM adopted so far for the prevention, management and treatment of COVID-19.

What is Coronavirus (Covid-19)?

Coronavirus disease is a transferable disease brought about by a recently identified virus. This virus is a pandemic disease, brought about by the serious intense respiratory condition. COVID-19 is contacted through the different respiratory tracts, for example, the mouth and the nostrils, and attacks the human respiratory organs. On January 30, 2020, the World Health Organization (WHO) announced that this outbreak had constituted a public health emergency of international concern (Yang, 2020). The novel coronavirus was initially named 2019-nCoV and officially as severe acute respiratory syndrome coronavirus 2 (SARSCoV-2). As of February 26, COVID-19 has been recognized in 34 countries, with a total of

80,239 laboratory-confirmed cases and 2,700 deaths (WHO 2020).

COVID-19 Pandemic: The Role of Traditional Medicine

Traditional medicine has played a huge role in the treatment of several diseases. Currently, medicinal plants such as Artemisia annua are being considered as possible treatments for COVID-19, but they should be tested for efficacy and possible side effects. At present, the WHO is working with some research institutions around the world to select traditional medicine products with potential use for the treatment of COVID-19 after being investigated for clinical efficacy and safety. The WHO has been working with countries to ensure the safe stand most effective use of traditional medicines, and it will continue to give support in exploring the benefits of traditional medicines in the prevention, control, and treatment of infections (WHO, 2020).

Traditional medicines need to be robustly investigated to avoid putting the lives of people in danger during the period of this pandemic and beyond (WHO, 2020). In China, scientists and doctors have recommended using Traditional Chinese Medicine (TCM) as a cure for COVID-19. During the Severe Acute Respiratory Syndrome (SARS) epidemic, TCM was effective in the treatment of infected people. The Chinese Government has ordered the use of TCM herbs to treat COVID-19 patients. It was reported that about 85% of COVID-19 patients with treatment of TCM and regular medication. Research shows that TCM herbs have antiviral ingredients. The potential contribution of TCM to health and well-being has been highlighted in

the WHO global report on Traditional and Complementary Medicine (Ling, 2019). The TCM remedies for COVID-19 are even being sent to some countries such as Italy, Iran, etc. as international aids. However, scientists from other countries claim that it is dangerous to support therapies that have yet to be proven safe and effective.

A report released by the WHO stated that efforts are underway to discover the treatment for COVID-19. However, caution must be taken against misinformation, especially on social media, about the effectiveness of certain remedies. A warning was released by the WHO regarding a COVID19 treatment called COVID Organics (CVO) announced by the Madagascar government that started to deliver the medicine to other African countries such as Equatorial Guinea, Guinea-Bissau, etc. A virtual meeting was held by the WHO with African traditional medicine experts few days after the announcement of CVO by Madagascar government, and the slammed of UN health agency by the Madagascar president for not endorsing CVO as a potential treatment of COVID-19. However, the WHO called for clinical trials of CVO and warned against the self-medication (Yang, 2020).

In most of the areas with weak health systems and institutions, people are nervously hunting for ways to protect themselves from COVID-19. In some counties like Vietnam, Cambodia, Indonesia, Malaysia, Thailand, Philippines, etc., numerous s remedies (such as drinking boiled lemongrass, drinking boiled garlic juice, swabbing nose with garlic juice, coconut oil, jamu drink, tong sui, kariyat, etc.) are circulating ,more especially on the Internet, YouTube, and Facebook. In the current world, the internet is found to be a source of misinformation.

Many reports around the world claim the use of traditional medicine in the treatment of COVID-19. Several media reports claim that traditional medicines in combination with modern drugs are being used to treatCOVID-19 patients in some parts of the world. Nevertheless, as of now, there is no concrete scientific evidence to support the use of traditional medicine in the treatment and management of COVID-19.

Medicinal Plants of African Origin with Antiviral Activities

Africa, with one of the richest cultural heritage in the traditional application of plants in healthcare, is endowed with a vast plant biodiversity (Dzoyem, Ishikalange & Kuete, 2013). An estimated 68,000 plant species have been reported to grow within the continent, over half (35,000) of which are endemic to Africa.

The peculiar diversity and uniqueness of climatic, soil, rainfall and environmental factors have encouraged the growth of an extensive plant diversity, endemism and great variation in indigenous plants across the entire region. The proximity, accessibility and abundance of African medicinal plant resources may have informed their amazing acceptability and popularity by African populations for meeting primary healthcare needs (Neuwinger, 2000) especially during emergency scenarios as in COVID-19.

Diverse plants, with their isolated products and derivatives with antiviral properties including alkaloids, flavonoids, phenolic compounds, terpenes, polysaccharides and polypeptides, have been reported (Ling, 2019). As nature's biological laboratories containing hundreds and thousands of bioactive metabolites, African medicinal plants abundantly

accumulate photochemical markers and defense compounds of chemotaxonomic significance in different plant families. This variation in bioactive chemical markers in different plants has facilitated and justified the use of some plants in some families more often than others following their superior efficacy for conditions they are meant to treat in Traditional African Medicine (TAM) including viral outbreaks.

The antiviral properties and immuno-modulatory activities of these compounds can be utilized in the prevention, treatment and management of COVID-19, which till date awaits effective, safe, affordable and accessible treatment options. The efficacy of some plants and derived photochemical of African origin have been established following their potential to interfere with the replication and transcription machinery of some causative agents of viral infections (Mathomoodall, 2019). Documented antiviral potency of these medicinal plant extracts justifies their selection for further studies as potential agents for prophylactic administration or potential therapeutic intervention against COVID-19. However, an in-depth and rigorous analysis of their efficacy and safety using internationally acceptable protocols is germane during clinical trials prior to healthcare utilization.

Therapeutic Potentials of African Plants

Africans may lack access to western repurposed drugs that are now used to manage COVID-19 in developed countries, but they have unlimited access to medicinal plants which can be standardized for effective and safe use. These tropical plants accumulate both primary and secondary metabolites with a broad range

of *in silico*, *in vitro* and *in vivo* activities including antiviral properties. Many of the antiviral primary metabolites such as polysaccharides and antiviral proteins accumulated in African plants reported in this review have not attracted much research attention and exploitation in antiviral drug discovery. Even of more scientific interest are the highly stable low molecular weight peptides known as cysteine-knot peptides among which, cyclotides are most stable due to their continuous circular configuration, low molecular weight, abundance, sequence variability, oral bioavailability, target specificity, low *in vivo* toxicity and wide distribution in plants families including Violaceae, Rubiaceae, Fabaceae, Curcubitaceae and Solanaceae (Mathomoodally, 2013).

The hydrophobic nature of these interesting peptides appears to be very important for their activity against enveloped viruses. Antiviral Kalata B1 and B8 have been isolated from an indigenous plant *Oldenlandiaaffinis* (Roem and Schult) DC. (Rubiaceae) used in Traditional African Medicine to aid delivery in Central Africa and as an ant malarial herb in Nigeria; cyclotide-rich aqueous extract of *Oldenlandiaaffinis* DC represent a potential multi target peptide drug candidate that awaits scientific investigation against COVID-19. However, phytomedicines containing antiviral Kalata B1 may be contraindicated in pregnancy (Nevwinger, 2000) and more useful during the late stage of hyper-inflammation observed in COVID-19 owing to the immunosuppressant activity of Kalata B1. Meanwhile, the therapeutic potentials of these peptides still lack clinical evidence to support the interesting *in vitro* and *in vivo* findings.

Exploring and exploiting medicinal plants for antiviral activity should be premised on the demonstration of prophylactic and/or therapeutic efficacy at an optimal amount in metabolic fluid. Similarly, plants and their bioactive metabolites have been shown to modulate immunological activities making them suitable candidates for biological response modifiers with the potential to alleviate symptoms and prevent death associated with infectious viral outbreak (Ling, 2019). Therefore, the Africa Centers for disease Control and Prevention (Africa CDC) has provided standard guidelines for Member States when herbal remedies or medicines are proclaimed or developed in their countries (Africa CDC, 2020).

Since the global R and D community is relentlessly working on getting an effective treatment to stop the COVID-19 pandemic, symptomatic management of the viral symptoms and Prevention of infection through divergent approaches should be encouraged. For instance, evidence-based and documented scientific publications on the antiviral and immune modulatory potentials of African plants could provide some clues on prevention and management of COVID-19.

Developing Potential anti-COVID-19 Herbal Medicines

The popular school of thought tends toward the discovery of a single metabolite specific for one macromolecular target. However, modern medicine via the formulation of multi-component medications containing two, three, or more active components is increasingly accepting the limits of the single-molecule

hypothesis. Such multi-component medications are of special importance in anti-infective therapies, and in fact have become the obligatory standard of management in malaria, a protozoan infection, tuberculosis a bacterial infection, and acquired immune deficiency syndrome a viral infection. The overarching aim is to employ the combined drug compounds to target multiple macromolecular targets.

Such multi-component systems natively form a core aspect of plant-derived preparations which range from crude extracts, to carefully design fractional combinations, and to lower extent pure natural products. Since most component active principles exist in lower amounts than found in mainstream pharmaceuticals, toxicities from these preparations are generally rarer especially when prepared using properly validated quality assurance processes or following some local preparation methods. Additionally benefit results from the presence of multiple natural products capable of modulating multiple aspects of the biochemical process of interest, a property that is of special interest in antiviral and ant malarial management. Interestingly, some of these botanicals have been suggested to produce strong biological effects even at the low concentrations at which they are present in herbal preparations (Nevwinger, 2000). Together with their beneficial ability to prevent resistance development, herb-based preparations should preferably form a core component of the search for treatment of the current COVID-19 pandemic.

Since the pharmacy dynamic effects resulting from herb-based preparations eventually depend on the component principles interacting with biological macromolecules, their successful use also depends

critically on pharmacokinetics. With respect to the pharmacokinetics of herbal products, the simultaneous presence of multiple structurally distinct natural products in the same preparation presents a definite layer of challenge not seen with single compound pharmaceuticals but that is often of clinical significance (Mathodally, 2013). Each natural product present in such multi-component preparations possess physicochemical attributes that are often divergent such that it is hardly realistic to describe the overall pharmacokinetics based on a single natural product however significant such compound may be. Instead, it is sometimes more prudent to define these parameters for the bulk product based on an all-or-none basis rather than merely trying to extrapolate the properties from data derived for individual natural products.

This was aptly demonstrated in a 2013 study showing the strong CYP3A4-inhibiting activity of an African herbal preparation NIPRD-AM1 with ant malarial activities (Ling, 2019). NIPRD-AM1 was developed in Nigeria and found to be responsible for diminishing by half the enzymatic activity of the cytochrome P450 enzyme, but following co-administration with metronidazole it was reported to exert no effect on the metabolic disposition of the drug (Ling,2019) It is certainly not inconceivable to expect to find present individual natural products with varied effects on the hepatic enzymes in such herbal formulations as NIPRD-AM1; it is however the overall effect of the mixture that is of practical importance for quality assurance as well as for clinical applicability especially involving the analysis of interference with different metabolizing enzymes and with the absorption process of drugs that are likely to be co-administered.

Absorption and bioavailability profiling is challenging for herbal mixtures, partly because existing mathematical models can only suitably describe single drug molecules. The AUC and bioavailability for example, are referenced against measured systemic concentrations of individual drugs and can only describe one drug substance at a time. This however is not to downplay the importance of equivalent means of profiling herb-based preparations. In fact, many natural products are associated with deficient molecular properties compromising solubility, membrane permeation and thus absorption and bioavailability. This is however not surprising since the evolutionary process that emerged the natural products inside plants is isolated from processes within the human biological system where a fine balance of molecular features is often required for receptor interaction. Natural products present in plants have no such evolutionary imperative beyond the functions natively played in their host plants. Therefore, a good number of natural products with good *in vitro* biological profiles have been reported with suboptimal physicochemical properties.

Interestingly both the pharmacological potency and poor absorption properties of the component natural products are closely tied with their complex chemical structures. Polyphenols are a class of phyto chemicals whose immune modulatory properties can be useful in herbal preparations for COVID19. They are however often characterized by poor absorption and deactivation by gastric conditions (Dzoyem,Ishikalange & Kuete,2013). In the same category is the group of curcuminoids whose antiviral, anti-inflammatory and antioxidant properties should ordinarily qualify as viable components of anti-COVID19 treatment.

A positive aspect of the use of herb-based preparations in pharmacotherapy is the observation that the derivable pharmacological benefits often emanate from multiple constituent natural products that are sufficiently structurally diverse and yet related to permit the modulation of varied and yet related biochemical processes. It is crucial to point out that the anti-coronavirus activities identified for these natural products were obtained by *in vitro* experiments often involving enzyme-based inhibition assays against isolated viral enzymes. In the absence of biological membranes and the complexity associated with in vivo systems, pharmacokinetics is thus unlikely to constitute any real challenge.

On the other hand, had these natural products or their multi-component herbal preparations been tested in *in vivo* situations, they might have been thought to lack the anti-coronavirus activities with which they have been credited. Pharmacokinetic factors and experimental design are thus crucial considerations in the identification of potent anti-SARS-CoV2 herb-based products, and it is recommended that testing should in the first stages employ enzyme-based assays while physicochemical/pharmacokinetic liabilities can later be remedied by employing appropriate formulation techniques.

Conclusion and Recommendations

Based on the discussion of this paper, it was provided in a holistic report on evidence-based on antiviral and promising anti-SARS-CoV-2 properties of African medicinal plants can cure different kinds of disease and this has made African medicine a potential

curative indigenous medicine that can be used to prevent COVID-19 pandemic in Nigeria and other countries of the world. Evidence has shown that, most of the herbs prepared by experts in African continent are active and can be used to prevent different chronic diseases in Africa, therefore, it is evidential that, African medicine has potential to cure and heal different kinds of chronic diseases, including COVID-19 pandemic.

The sustainable use of medicinal plant resource in Africa should encourage their purpose driven cultivation for use in African ethno medicine as well as for production of evidence-led phytomedicines. The establishment of requisite programmme for medicinal plant resource utilization and conservation of endemic African plants are opportunities for future studies. Therefore, future research should focus on an in-depth scientific investigation to demystify the bioactive component and establish chemical fingerprint for such complex herbal phytomedicines and mechanistically study them for an evidence-rooted and verifiable plant-derived medicines with potential for COVID 19 management.

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