

Traditional medicines for COVID-19: perspectives from clinical pharmacologists

Getnet Yimer¹, Edmund Ekuadzi², Pius Fasinu³, Andreia Cristina de Melo⁴, and Goonaseelan Pillai⁵

¹The Ohio State University

²Kwame Nkrumah University of Science and Technology

³Campbell University College of Pharmacy and Health Sciences

⁴INCA Brazilian National Cancer Institute

⁵CP Plus Associates

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Abstract

There has always been high interest in the use of traditional medicines for COVID-19 from early in the course of the pandemic. Significant advances in the science of ethnopharmacology has helped to introduce chemical entities identified from natural sources into modern medicine. However, the wider integration of natural products into the modern drug discovery process will require enhanced collaboration among different stakeholders including the pharmaceutical industry, academic research units, regulatory bodies, ethics review committees, local, regional, continental and international organizations. Revisiting this topic holds promise of benefit for both the current and future pandemics.

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Authors:

Getnet Yimer, Edmund Ekuadzi, Pius Fasinu, Andreia Cristina de Melo, Goonaseelan (Colin) Pillai

Affiliations:

Department of Pharmacology, University of Cape Town, South Africa

Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, Kwame Nkrumah University of Science and Technology (KNUST), Ghana

Global One Health initiative, The Ohio State University, Columbus, OH, USA.

Division of Clinical Research, Brazilian National Cancer Institute, INCA, Rio de Janeiro, Brazil

Department of Pharmaceutical Sciences, College of Pharmacy and Health Sciences, Campbell University, North Carolina, USA

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Abstract

There has always been high interest in the use of traditional medicines for COVID-19 from early in the course of the pandemic. Significant advances in the science of ethnopharmacology has helped to introduce chemical entities identified from natural sources into modern medicine. However, the wider integration of natural products into the modern drug discovery process will require enhanced collaboration among different stakeholders including the pharmaceutical industry, academic research units, regulatory bodies, ethics review committees, local, regional, continental and international organizations. Revisiting this topic holds promise of benefit for both the current and future pandemics.

Background

While the timelines for vaccine discovery and clinical development are remarkable and unprecedented, at the time of writing, there is no known pharmacological cure for SARS-Cov-2 infection. In addition to the plethora of investigations into conventional therapies, it is also noteworthy that there has always been high interest in the use of traditional medicines for COVID-19 from early in the course of the pandemic. The dismally slow rate of vaccine access for low- and middle-income countries (LMICs) has galvanised healthcare practitioners and scientists to re-visit both conventional and traditional medicines.

China and countries in Africa have long histories of use of traditional and herbal medicine in the treatment and prevention of human and animal diseases¹. In many communities, traditional medicine is an important contributor to primary health care building on a longstanding cultural acceptability in its use²⁻⁴. In Africa, anecdotal estimates are that they have been used for >80% of illness at least once. Most individuals who provide traditional medicine therapy are highly respected in their community. In some instances, this trust is linked with religion and steeped in culture and tradition. In addition, accessibility, availability and affordability of herbal medicines often makes them a preferred choice over conventional therapies. Even practitioners of modern medicine would find it difficult to deny the confidence that their patients have in traditional medicine and the relief that they afford in some circumstances.

Significant advances in the science of ethnopharmacology has helped to introduce single chemical entities, in contrast to composite natural product source, into modern medicine⁵. Indeed, many of the natural products that have been developed into modern therapeutics have come from plants⁶.

In presenting our views as clinical pharmacologists, we acknowledge our bias in having been trained in conventional drug use, but highlight our respect for the potential role of traditional medicines in the current-, and future pandemics. Our purpose is to invite comment, critique, and alternate viewpoints.

There is international and government support for traditional medicines

There is a high level of political and leadership acceptability - partly because of the push by the public, long standing anecdotal evidence of effectiveness and the desperate scramble to find cures for the COVID-19 pandemic. In Africa, while acknowledging the need to be cautious about misinformation and disinformation about their effectiveness, the World Health Organization, Africa CDC and the African Union Commission for Social Affairs have issued statements welcoming traditional medicines for COVID-19. This has included endorsement of a protocol for Phase III clinical trials of herbal medicines and the establishment of data and safety monitoring boards for the clinical trials.

Can conventional Research and Development methods align with traditional medicine?

A large number of modern-day therapies have had their documented origins in natural products. These include the popular antimalarial drugs, quinine and artemisinin from *Cinchona* and *Artemisia* species respectively; the heart failure treatment, digoxin from *Digitalis species*; the important pain relief agents codeine and morphine from *Papaver* species; anticancer drugs vincristine and vinblastine from *Catharanthus roseus* and the pre-surgery medication, atropine from *Atropa belladonna* ⁷.

At first blush, the conventional science-based approach to identifying new therapies seems incongruent with the process by which traditional medicine is practiced. African traditional medicine provides holistic treatment. The techniques often derive from the understanding of the aetiology of disease, as conceived by the practitioners: herbalists, traditional birth attendants, bone setters, diviners, faith healers and spiritualists. Their belief that diseases may be caused by spiritual and esoteric causes as well as physical and psychological causes⁸. Following diagnosis, a treatment usually consisting of a polyherbal remedy is prescribed. In some cases, individual compounds are responsible for the reputed pharmacological effect. However, in many cases, the observed pharmacological effects is due to a mixture of different compounds as well as the holistic approach of the practitioner.

As scientists, we recognize the benefit of traditional medicine but have been trained to seek standards, procedures and investigations that would provide confidence in short and long-term safety and efficacy claims that align with our own preconceptions of specific safety and efficacy metrics. This raises a number of questions to be considered:-

Can claims of efficacy be described with the scientific methods that are already available for conventional R&D? Could safety claims be under-written by the tests that are already available for new chemical entities? What could be the social, economic and political readiness if there is a need to strictly follow the procedures required by conventional science? What would be the impact on the established trust and usage by the communities who depend primarily on traditional medicine? How could orthodox and traditional healthcare practitioners mutually learn from each other to benefit their common patient base?

The integration of African natural products into the modern drug discovery process will require enhanced collaboration among different stakeholders including the pharmaceutical industry, academic research units, regulatory bodies, ethics review committees, local, regional, continental and international organizations. This aligns with the compromise process that some experts have promoted to facilitate the integration of traditional and orthodox medicine by recognizing claims of efficacy, and then attempting to collect as much clinical experience data as possible, while moving backwards through laboratory evaluations, preclinical experiments, and targeted clinical studies based on the learnings (see Table 1). We realize that these are big asks and suggest that assessments might be prioritized for those traditional therapies that are widely used or have popular support, and that the goal should be to support evaluation in clinical trials.

{INSERT TABLE 1 HERE}

We conducted an informal assessment of the COVID-19 clinical trials registered on <https://www.covid-trials.org/> and noted that several traditional medicines are being examined in clinical trial settings across the world. The therapies under investigation comprised a diverse slate ranging from honey, plant products formulated into dosage forms through to a large number of Chinese Traditional Medicines. We were especially encouraged to note a trend towards study designs that would increase confidence in the study outcomes such as blinding processes and randomisation of participants to the interventions. However, we acknowledge that the rigour and requirements of clinical trials are likely to be unaffordable for most investigators and countries, but suggest that the approach outlined in Table 1, while expediting the process, might inform future research and future pandemic preparedness.

What can be done ?

General principles:

- The need for mutual respect and partnership between modern and traditional medicine and both groups should aim to be complementary with each other and not competitive.

- The overall goal should be to emphasize safety while establishing evidence of efficacy and quality assurance of approved products
- Any intervention (whether a conventional or a traditional medicine) should not damage the processes and efforts to contain the pandemic and protect public health
- Any intervention should not delay provision of supportive or more aggressive care for the individual patient where indicated
- Promote dialogue among stakeholders including industry, funders, academia, policymakers and traditional medicine practitioners and herbalists.
- Facilitate exchange of information and success from different countries, including avoiding redundancies

For policymakers, herbalists and the community at large:

Publicize the existence of the rich knowledge and data on traditional medicine and acknowledge the need for proper documentation and validation

Ensure that, while there is a room to expedite the process, there is no shortcut and hence the need to follow all applicable due diligence to ensure safety of the products

For Ethics committee and regulatory agencies:

- Safety is a high priority, even during a pandemic, and will impact current and future efforts
- Expedite processes, allow adaptability of studies, without compromising all requirements
- Promote the scientific approach with its insistence on evidence generation

Conclusion: We are optimistic that there is an opportunity to revolutionize the way we collaborate with traditional medicines and its practitioners. A strong and deliberate collaboration among the various stakeholders – traditional healers, scientists, government, and academia can usher in a new paradigm with informed and safe use of traditional remedies for the current and future pandemics.

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