






**COMMENTARY**

# Traditional medicines for COVID-19: Perspectives from clinical pharmacologists

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There has 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 have 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 amongst the pharmaceutical industry, academic research units, regulatory bodies, ethics review committees and local, regional, continental and international organizations. Revisiting this topic holds promise of benefit for both the current and future pandemics.

**KEYWORDS**

COVID-19, herbalists, natural products, traditional medicines

## 1 | 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 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 galvanized healthcare practitioners and scientists to re-visit both conventional and traditional medicines.

Countries in Africa have a long history of using traditional and herbal medicine in the treatment and prevention of human and animal diseases.<sup>1</sup> In many communities, traditional medicine is an important contributor to primary health care building on a longstanding cultural acceptability in its use<sup>2–4</sup> with anecdotal estimates of 80–90% of rural populations relying on plant-based traditional medicines for this purpose.<sup>5</sup> During the Ebola Virus Disease outbreak of 2014–2016, Balde et al. documented several recipes of herbal therapies, however, none were studied in conventional clinical trials.<sup>6</sup> 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 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.

There is a high level of political and leadership acceptability for African traditional medicines—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.

Significant advances in the science of ethnopharmacology has helped to introduce single chemical entities, in contrast to composite

natural product source, into modern medicine.<sup>7</sup> 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*; anti-cancer drugs vincristine and vinblastine from *Catharanthus roseus*; and the pre-surgery medication, atropine from *Atropa belladonna*.<sup>8</sup>

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

## 2 | CAN CONVENTIONAL PHARMACEUTICAL RESEARCH AND DEVELOPMENT METHODS BE APPLIED TO TRADITIONAL MEDICINE?

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

- Can claims of efficacy and safety be underwritten by the scientific methods that are already available for conventional drug research and development?
- What are the potential social, economic, political and community usage implications if traditional medicine is required to strictly follow the procedures required by conventional science?
- How could modern and traditional healthcare practitioners learn from each other to benefit their common patient base?

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 aetiology of disease, as conceived by the practitioners: herbalists, traditional birth attendants, bone setters, diviners, faith healers and spiritualists. Their belief is that diseases may be caused by spiritual and esoteric causes as well as physical and psychological triggers.<sup>9</sup> 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.

The integration of African natural products into the modern drug discovery process will require enhanced collaboration among the pharmaceutical industry, academic research units, regulatory bodies, ethics review committees and local, regional, continental and international organizations. This aligns with the compromise process that

some experts<sup>10,11</sup> have promoted to facilitate the integration of traditional and orthodox medicine by firstly 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. We realize that these represent formidable ambitions and suggest that assessments might be prioritized for those traditional therapies that are widely used or have popular support and evaluate these in clinical trials. Recent reviews of African natural products that have therapeutic potential for COVID-19 provide useful starting points.<sup>5,12</sup>

We conducted an informal assessment of the COVID-19 clinical trials registered on <https://clinicaltrials.gov> and <https://pactr.samrc.ac.za> (accessed on 31 May 2021) to identify the characteristics of studies involving African traditional medicines. Our search identified 10 clinical trials in Egypt, Ghana, Kenya, Nigeria, Sudan and Togo. At the time of our search, all the trials were listed as either “recruiting” or “not yet recruiting,” thus eventual trial execution and dissemination of the results is uncertain. Notwithstanding the succinct and often incomplete nature of the entries on these registries, we were encouraged to note hospital-based studies and study processes that might increase confidence in the trial outcomes, for example, blinding, randomization and comparisons to standard of care. 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 research for future pandemics.

## 3 | RECOMMENDATIONS

### 3.1 | General principles

- Dialogue and information exchange between modern and traditional medicine should be based on mutual respect and aim to be complementary rather than competitive.
- The overall goal should be to emphasize safety while establishing evidence of efficacy and quality assurance of approved products.
- Population level interventions (whether a modern or a traditional medicine) should not damage the processes and efforts to contain the pandemic and protect public health
- Individual patient level interventions should not delay provision of supportive or more aggressive care where indicated

### 3.2 | For practitioners and users of traditional medicine

- Publicize the existence of the rich knowledge and data on traditional medicine and advocate for proper documentation and validation
- Acknowledge and participate in the review processes and due diligence that would ensure efficacy, safety and quality of the products

**TABLE 1** Proposed approach to integrate African natural products into modern drug discovery paradigms

↓ Engage community, practitioners and leaders	Continuously assess existing beliefs and information
↓ Natural products library	Collect and store natural product extracts and pure compounds and systematically record key features in a searchable database
↓ Lead identification	Screen natural product extracts <sup>a</sup> or pure compounds against a cellular, tissue or animal model to identify “hits,” that is, promising compounds for further study
↓ Lead optimization	Conduct further studies in pharmaceuticals, pharmacology using pharmacokinetic and toxicology models to identify promising candidates with favourable absorption, permeability, efficacy <sup>b</sup> and safety <sup>b</sup> characteristics
↓ Preclinical development	Conduct pre-clinical safety studies on the identified lead compounds or natural product extracts to determine safe starting doses for clinical trials

<sup>a</sup>The natural product extract has to be standardized based on an active constituent or group of active constituents.<sup>9,10</sup>

<sup>b</sup>Experience with conventional therapies suggests that while the parent drug might be important for efficacy, the safety signals are often driven by the metabolites or additives.

### 3.3 | For ethics committees, regulatory agencies and policymakers

- Safety is a high priority despite the urgency posed by the pandemic—any compromise sets dangerous precedents for future efforts
- Review the bureaucracy and expedite current processes without compromising on core requirements
- Promote the scientific approach to evidence generation

## 4 | CONCLUSION

We are optimistic that there is an opportunity to revolutionize the way we collaborate with traditional medicines and its practitioners. A cohesive and purposeful collaboration among 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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### COMPETING INTERESTS

GY, EE, PF and ACM have no disclosure relevant to this publication. GP is a consultant to the Bill & Melinda Gates Foundation on capacity development for global health.

### AUTHOR CONTRIBUTIONS

GP and GY conceptualized this study. GP, EE and PF conducted the literature search and review of trial registries. GY, EE, PF, ACM and GP wrote, reviewed and approved all drafts of the manuscript.

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