Endogenous Pharmaceutical Innovation in the Era of COVID-19: Epistemological perspectives from Benin and South Africa

Ogundiran Soumonni
Wits Business School
and
Aimé Sègla
Université d'Abomey-Calavi

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Endogenous Pharmaceutical Innovation in the Era of COVID-19

Epistemological perspectives from Benin and South Africa

Ogundiran Soumonni* and Aimé Sègla**

Abstract

The COVID-19 pandemic represents an epochal shock to global health and economic systems that has highlighted, more than ever, the need for innovative responses to safeguard the very survival of persons and communities as a first-order priority. As such, what the global crisis signalled was that the overwhelming focus on economic growth and development had to be significantly curtailed in order to address the much more ominous public health challenge. Thus, a moral dilemma presented itself as the first one to address, which required ethical knowledge to help make judgements about. A second-order problem, though equally urgent and still of relevance, emerged: What knowledge is available to tackle the novel disease itself from both the public health and medicinal points of view. Questions, such as the following, were the subject of intense controversies in public forums across the world: What kind of knowledge is valid? Whose knowledge claims are reliable? Which institutions are sufficiently trustworthy to certify the efficacy of various proposed solutions? Are alternatives to these worth considering? In this paper, we first clarify the nature of these "ethico-epistemological" problems in the African context by leaning on the historically informed theoretical paradigm of endogenous development. From this vantage point, we highlight some of the recent methodological controversies both within synthetic (or allopathic) medicine and in contrast with phytomedicine (or plant-based medicine), which is often based on culturally embedded medicine. We clarify key semantic ambiguities that further obfuscate such debates and consequently propose a conceptual framework that could help reveal potential pathways for anchoring endogenous innovation in the delimited domain of the pharmaceutical industry. Finally, we apply our framework to Benin and South Africa and reflect on the implications of our analysis for endogenous pharmaceutical innovation in Africa beyond the COVID-19 era.

Keywords: endogenous innovation, pharmaceutical innovation, epistemology, innovation systems, COVID-19, Africa

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* Wits Business School, University of the Witwatersrand, South Africa; diran.Soumonni@wits.ac.za
** Université d'Abomey-Calavi, Benin & Max-Planck Institute, Germany; a_s_aime@yahoo

1. Introduction

The main objective of this paper is to present some of the main epistemological controversies that have arisen during the COVID-19 pandemic and to reflect on those as a basis for proposing a theoretically informed conceptual framework that could better inform policy interventions to advance pharmaceutical innovation in Africa. In particular, we underscore the contested nature of various knowledge claims of having a proven treatment globally and attempts in selected African countries to propose possible solutions of their own. While people across the world have been implored to comply with emerging governmental regulations, which were said to have been informed by expert advice, it quickly became clear that all experts were not in agreement with the measures. These scientific controversies consequently spilt out into popular discourse in an atypical manner.

However, the moral predicament that accompanied the global pandemic, namely that between wealth accumulation and the preservation of human lives, required ethical knowledge to help make judgements about it. In the Southern African context, for instance, one of the key axioms of Ubuntu philosophy in general, and with respect to "traditional African medicine" in particular, *"feta kgomo o tshware motho"* (preserving the life and dignity of a human being must supersede the accumulation of wealth) in the sePedi language, offers us a clear ethical direction (Ramose, 2005). Additionally, serious contestations relating to the validity of the very knowledge bases and methodological approaches from which various solutions have been proposed have been no less contentious. They, therefore, underscore the need to better understand the status of the know-how available in Africa, clarify ambiguous terminology about it, and identify the extent to which it could contribute to worldwide efforts to significantly mitigate the impact of the pandemic.

One of the most widespread controversies emerged around the announcement of a cure for COVID-19 by Didier Raoult, a prominent French microbiologist and expert in "drug repositioning", who declared that a combination of the anti-malarial hydroxychloroquine and the antibiotic azithromycin could cure the disease (Sayare, 2020). Raoult's claims in the media and in a scientific article in March 2020, were by May of the same year prominently rejected by a subsequently retracted article in the prestigious medical journal, The Lancet, which claimed that based on randomised clinical trials, there was no association between using either chloroquine or hydroxychloroquine (HCQ) on the one hand, and health benefits to COVID-19 patients on the other (Mehra, et al., 2020). Thus, while discrediting the scientific basis for the efficacy of HCQ on methodological grounds and even suggesting that it was harmful, the US-based researchers, Mehra, et al. (2020), later withdrew their article in response to charges that they had used a suspicious and unverifiable dataset.

This type of epistemological debate also played itself out in the Global South, with respect to proposed treatments based on natural or herbal medicines, as opposed to synthetic pharmaceutical treatments, suggesting an irreconcilable fault line between them. However, a Chinese researcher from the Department of Traditional Medicine at Zhejiang University warned in The Lancet that despite an official announcement of the approval of three widely used herbal medicines to treat COVID-19 symptoms in April 2020, such drugs carried their

own risks and should therefore not be used without sufficiently rigorous scientific testing (Yang, 2020). That public statement in favour of scientific rigour by a Chinese natural medicine researcher need not be seen as either ad hoc or exceptional, however. It may instead be better understood through the observation by Hwang (2020) that China has a fairly well-integrated medical system, whereas South Korea's is strictly bifurcated between "traditional medicine" and "Western" medical health services.

In Africa, the media prominently featured claims by the president of Madagascar that the Artemisia plant-based medication, COVID Organics (CVO), has strong healing properties. The Cameroonian Archbishop of the city of Douala, Samuel Kleda, reported a successful treatment based on a herbal mixture that targets associated respiratory ailments, and South Africa assembled its best scientific minds to direct its response to the pandemic (Tangwa & Munung, 2020). The Malagasy case, in particular, generated a lot of controversies, in part, because of the confrontational style of the country's president in the face of what he viewed as an international dismissal of African knowledge and because of the perception by many public commentators of the implausibility of medicinal treatment for the virus coming from an impoverished country. In contrast, the posture of Samuel Kleda, who has studied herbal medicines for three decades, was much more modest. He sought to clarify the difference between his healing approach, which helps to eliminate or alleviate symptoms, and that of a conclusive cure, thereby calling for collaboration with scientific researchers and other health experts to ensure greater efficacy (Sina, 2020). In a similarly inclusive vein, South Africa's president called for complementary efforts with "traditional medicine" to fight the pandemic in his Heritage Day speech in September 2020, stating the following:

> *"In as much as we join the international community and search for diagnostics and therapeutics, we are also looking at the real and important contribution indigenous knowledge systems, particularly traditional medicine can play in improving the life outcomes of our people." (RSA, 2020).*

It is important to note, however, that historical evidence suggests that what is widely characterised as two distinct traditions of medicine actually have a more intertwined record than is generally recognised by observers, and concerning epidemics, in particular. In a recent book, the Pulitzer Prize-winning African American author, Isabel Wilkerson, revived the memory of Onesimus, an enslaved African, who told his captor of an inoculation procedure against smallpox in his native West Africa that saved 97.5% of the 240 people who adopted it during a similar epidemic in Boston, Massachusetts, in 1721 (Wilkerson, 2020). Unfortunately, even though this method became the basis for standard vaccinations in the US, Wilkerson notes that Onesimus was neither compensated for his contribution nor even freed from his status of enslavement, thereby highlighting the grossly unethical dimension of this medical knowledge transfer from Africa to America. These initial insights are intended to frame the broad contours of the epistemological challenge for endogenous innovation in the pharmaceutical industry that we discuss in subsequent sections.

2. Background

As indicated in the abstract, two premises ground our study. The first is the moral challenge that the pandemic presented with respect to the preservation of human life vis-à-vis wealth accumulation. Secondly, the pandemic led the public to raise important epistemological questions about available knowledge resources to resolve the health crisis, which have serious implications for the role of endogenous innovation in the pharmaceutical industry. In other words, an ethical imperative rather than an economic one takes precedence in our use of the endogenous innovation concept. It is nevertheless critical to briefly clarify the concept of pharmaceutical innovation to better appreciate the ethico-epistemological considerations thereof.

A classification scheme provided by Djellal and Gallouj (2005) subdivides medical innovation into three subgroups, namely: 1) biomedical or bio-pharmacological innovation, which includes novel medicines and pharmaceutical substances; 2) technological systems that offer healthcare and biological analysis; 3) "soft", "invisible", or intangible medical innovation involving therapeutic strategies, care protocols, etc. The first subgroup, bio-pharmacological innovation, may further be based on either synthetic medicine (also labelled "conventional" or "orthodox" medicine) or phytomedicine (or plant-based medicine). However, Iwu (2002) provides the useful clarification that the related term, phytopharmaceuticals, refers to chemically isolated plant substances that are usually treated like their synthetic equivalents by most governments, which is not necessarily the case for other phytomedicines, whose active ingredients are exclusively contained in plant materials or extracts that may result in polyvalent therapeutic action.

Although the study, identification, standardisation, quality control, and production of phytomedicines have become the explicit focus of the growing domain of pharmacognosy within pharmaceutical science (Dhami, 2013), the implicit inference is that the process of drug discovery in synthetic medicine is well established. However, in a study about the means by which medical expertise progresses, Nelson, et al. (2011) demonstrated that while many biomedical scientists believe that increased scientific research (learning by searching) leads to improvements in practice, such expected scientific breakthroughs are empirically relatively rare. Conversely, they argue, learning by doing and using in clinical practice, as well as the cumulative observation of physicians and patients over time, are sometimes more significant sources of medical innovation than can be obtained via either in vitro (test tube) research or animal research, or even exclusively through randomised clinical trials, which are considered to be the highest benchmark for evaluating the effectiveness of a new intervention. Phrased differently, even though the scientific paradigm and the practice paradigm are interrelated, it is not unusual for a high degree of scientific understanding to have little bearing on practice, and conversely, that ongoing practices may be acknowledged as being effective, but with minimal scientific understanding as to exactly why (Nelson, et al., 2011).

An argument for the relative importance of the practice paradigm vis-à-vis the scientific paradigm in producing useful knowledge in the context of the pandemic underpinned the epistemological claims made by the French microbiologist, Didier Raoult. Indeed, in an early

multiple-authored paper of his in March 2020, the authors claimed a 100% success rate in treating patients with both HCQ and azithromycin, based on a single-arm protocol (rather than the more rigorous double-blind testing against a placebo), but issued a proviso in the conclusion, arguing that the context of the pandemic temporarily justified publishing the findings despite the small sample size of 36 patients and other methodological shortcomings (Gautret, et al., 2020). A detailed, 10-point rebuttal was subsequently published by the Dutch clinical epidemiologist, Frits Rosendaal, who argued that even if the study had been based on an uncontrolled case series of patients who were treated, the failure to unequivocally establish the effectiveness of the clinical treatment or to present its adverse effects rendered the conclusions both unjustified and negligent (Rosendaal, 2020).

Beyond the methodological shortcomings relative to the ideal practice, of which he was well aware, Raoult insisted in the face of intense criticism that many significant achievements in health had never been validated by stringent randomised controlled trials (R.C.T.s) and that it would be unethical to deny a drug whose effectiveness was "visible" to ill patients (Sayare, 2020). Nevertheless, by July 2020, a number of French doctors and patients, as well as a group that represents 500 infectious diseases specialists, filed professional misconduct complaints against Raoult, accusing him of continuing to promote the HCQ/azithromycin combination despite its potentially deleterious side effects and the lack of sufficiently rigorous clinical trials to substantiate its benefits (AFP, 2020).

That contestation within the broad scope of synthetic medicine is important to reflect upon because several African countries, such as Benin and Burkina Faso, began clinical trials to establish the relative efficacy between the HCQ/azithromycin combination and a phytomedicine, Apivirine, developed by a Beninese researcher, with Burkina Faso indicating its ability to produce 200,000 tablets of HCQ per day, depending on the outcome of the tests (Nabaloum, 2020). In response to a number of proposed African medicinal solutions, however, a Burkinabé epidemiologist wrote an article in the widely circulated continental news magazine, Jeune Afrique, challenging the president of Madagascar, as well as the Beninese inventor of Apivirine, to publish the results of their trials rather than relying on rhetoric to make their respective cases due to the risk of diffusing highly toxic medicines (Kouanda, 2020).

Thus, epistemological debates about a highly specialised field, contemporary medicine, were prominently thrust into the public eye in a manner that is seldom witnessed. Nevertheless, given that a large proportion of Africans straddle between synthetic and culturally embedded medicine due to the cost-prohibitive access to the former on the one hand, and greater social ease with the latter on the other hand, a keen appreciation for the epistemological questions of the type enumerated above are of contextual relevance.

3. Main focus of the paper

In this section, we first seek to clarify some semantic ambiguities with respect to terms that are used in different ways in the literature, to provide a greater degree of precision in how

we operationalise the concepts in our paper. We then propose a conceptual framework that offers a way of understanding the various components and interrelationships that make up endogenous innovation as it applies to our topic of investigation. Third, we present the findings of two mini-case studies, which then underpin some recommendations that could help guide the activities of policymakers and other practitioners in a more evidentiary manner.

3.1. Issues, controversies, problems

Our starting point is to clarify commonly used, but often conceptually vague, terminology that relates to scientific knowledge in general, medical knowledge in particular, and the manner in which they are grounded in ethical principles. To begin with, the terms "indigenous knowledge" or "traditional knowledge" are typically used in contrast with "modern" or "Western" knowledge. However, Hountondji (1994) has argued that this bifurcation is unsatisfactory because it suggests a radical separation between the old and the new and reflects a barely masked assumption of a priority of Western cultures over the supposedly static, undifferentiated, and ultimately marginalised non-Western ones. Furthermore, in the face of continuing interactions over long periods of time, it is rarely clear when "indigenous" knowledge becomes "modern" and vice versa. It is in large measure, to circumvent and overcome this ambiguity, that we choose to employ the terms "endogenous knowledge" and "endogenous innovation" that we have already referred to, and that will be made clearer below.

From the point of view of what is commonly understood to be "modern science", Nelson (1974) assessed the extent to which the "indigenous science community" in latecomer economies had a significant role in technology adaptation and ultimately technological leadership. Richard Nelson, therefore, clearly considers domestic "modern" scientists to simultaneously be "indigenous" scientists who exist even in "less developed countries" and whose R&D efforts, beyond their techno-economic benefits, could be seen as a way to influence scientific values in a given country. From this vantage point, the nomenclature of "indigenous knowledge" applies both to the community that operates outside of Western-style institutions (themselves originally influenced by non-Western traditions) and those that operate within it.

A practical experience relayed by Abayomi Sofowora, the highly regarded author of the pedagogical book, "Medicinal plants and traditional medicine in Africa" (first published in 1982), is highly instructive in this regard. A long-time professor of pharmacy and a high-level advisor to the World Health Organization (WHO), he recalled an applicant for a prestigious academic post at an elite national university in Nigeria who repeatedly referred to other Nigerians with considerable knowledge of medicinal plants outside the academic setting as "indigenous", to the great annoyance of the selection panel (Sofowora, 2010). That particular response conveys Sofowora's view that competence and belonging to two different epistemic communities by a person from a given locale does not make him or her any more or any less "indigenous". It also reflects our perspective that the interaction between them is a fruitful basis for endogenous knowledge.

3.1.1. Epistemological perspectives on endogenous knowledge

The eminent South African philosopher Mogobe Ramose has famously demonstrated that the philosophy of Ubuntu/Botho is consistent with its cognate concepts in the remainder of Southern Africa and in much of the African continent. With respect to medicine, in particular, we lean on his insight that the term *"bongaka"* in sePedi, seTswana, and seSotho refers to the medical institution that informs the morally binding nature of the conduct between the doctor and the patient in African cultural settings (Ramose, 2005). In Ramose's assessment, it is first based on the acknowledgement that human life and integrity must prevail over wealth generation (usually symbolised by a metaphysical ritual), and only after does the prescription of an appropriate herbal medicine proceed. He, therefore, draws the compelling conclusions that in the African philosophical understanding under consideration, positivist or "value-free" conceptions of both law and economics are rejected in favour of establishing harmony between the physical and the psychic/communal dimensions. This perspective consequently has implications for the diagnosis and treatment of diseases, as well as the overall organisation of medical practice (Ramose, 2005).

Another study of plural medical systems in mid-20th century Bechuanaland (present-day Botswana) by the medical historian, Julie Livingston, emphasises the "productive misunderstandings" that arose from the encounter between the culturally-based medical system and the one introduced in the colonial context (Livingston, 2007). However, we find her account of the significant innovation that continued to occur in Tswana medicine due to the expansion of its own biomedical epistemology to account for evolving phenomena to be more compelling from an integrative point of view. It is useful to note parenthetically in this regard that two extant private firms in the contemporary city of Gaborone in Botswana, named Bongaka Pharmaceuticals and Bongaka Health Care, may be predominantly based on synthetic medicine, but their names simultaneously capture the holistic concept of "healing", as understood in the surrounding socio-cultural and linguistic setting. With respect to plant-based drug development initiatives in neighbouring South Africa (to which this cultural understanding extends itself), the STS scholar, Geri Augusto, uses the notion of "transepistemic research" to offer persuasive conceptual and strategic direction for mutual cognitive acknowledgement, complementary understanding, and identification of shared interests between two seemingly distinct knowledge traditions (Augusto, 2005, p. 201).

Furthermore, this perspective finds a strong echo as the basis of the concept of "endogenous development" that was most ably and comprehensively articulated by the late, preeminent historian from Burkina Faso, Joseph Ki-Zerbo. In an important book that he edited in 1992, entitled *"La natte des autres: Pour un développement endogène en Afrique"*, Ki-Zerbo stressed the significance of drawing from a historically and culturally based knowledge heritage in order to help address present-day challenges, but in critical exchange with more recent knowledge, both locally generated and adopted from elsewhere (Ki-Zerbo, 1992). Among the chapters in the book are three dedicated to medicine (Gbodossou, 1992; Hodouto, 1992; Sawadogo, 1992), including one on the creation of a centre for the "judicious integration" of conventional and culturally based, holistic approaches to medicine by the Beninese medical doctor, Erick Gbodossou, who is equally trained in both traditions.

With respect to the quest for effective knowledge, irrespective of traditions, however, it is useful to refer to Louis Pasteur, the celebrated 19th-century French microbiologist, chemist, and inventor (of vaccines, among other inventions), who famously stated in 1888 that "Science has no nationality because knowledge is the patrimony of humanity, the torch which gives light to the world". While Pasteur may have been referring to a particular conception of scientific rationality, his cross-cutting statement was suggestive of deference to the validity of knowledge rather than to the national origins of its holder. Nevertheless, the renowned 20th-century Austrian philosopher of science, Paul Feyerabend, would go much further in 1975, chastising some of his fellow European philosophers for their gratuitous use of the term "Voodoo" [sic] as the quintessential antithesis of science, stating that:

> *"Nobody knows it, everybody uses it as a paradigm of backwardness and confusion. And yet Voodoo [sic] has a firm though still not sufficiently understood material basis, and a study of its manifestations can be used to enrich, and perhaps even to revise, our knowledge of physiology." (Feyerabend, 2010, p. 30)*

The contemporary relevance of this discourse, from the perspective of the holders of this African-derived knowledge system in Haiti and in the specific context of the current COVID-19 pandemic, is highly noteworthy. Given the inadequacy of the public health system in the small Caribbean country, many communities turned to their Vodun priests and priestesses for preventative and medicinal natural herbal remedies. In a widely circulated investigation by Reuters, these knowledge holders are reported to have converted their temples into isolation centres in which their treatments were administered (Paultre & Sanon, 2020).

A study of a similar context on the African side of the Atlantic by the noted Beninese historian, Élisée Soumonni, provides the insight that while healing practices and ritual ceremonies in culturally embedded medical systems are connected, several European commentators on the smallpox pandemic that occurred in 19th-century Benin only emphasised rituals, thereby "mistaking form for content" (Soumonni, 2012, p. 39). In the context of COVID-19, the archaeologist Akinwumi Ogundiran proposes a revisitation of how, over a millennium of managing the smallpox disease, the Yoruba of West Africa (present in modern-day Nigeria, Benin, Togo, Sierra Leone, and the Diaspora in the Americas) incorporated sacred groves that could serve as isolation centres against epidemics into their ancestral urban planning (Ogundiran, 2020). Furthermore, Sègla (2015) describes the process of smallpox inoculation in greater detail and presents evidence to suggest that the process of vaccination in general, though incorporated into initiation ceremonies, had been known to the Yoruba at least since 500 AD.

More specifically, however, Soumonni (2012) points out that metaphysical/physical correspondences are known among the knowledge-holders and draws our attention to the original 1967 publication of an impressive, though non-exhaustive, compilation of 3,529 Yoruba medicinal plants by the French anthropologist, Pierre Verger, entitled *"Awọn ewé ọsanyin: Yoruba medicinal leaves"*. In consulting an expanded version of that work, we note that not only did Verger (1997) assign Latin-based scientific names to the specimens (based on analyses done in African and European laboratories), there were also multiple Yoruba

names for some of the individual species or combinations of plants, depending on their diverse uses.

Beyond the medical knowledge heritage described above, there is a substantial amount of information relating to an African contribution to global medicine from time immemorial. In discussing the origins of Western medicine, for example, Newsome (2007) provides evidence that some of the earliest medical writings in the Nile Valley in antiquity, which subsequently heavily influenced Ancient Greece, such as the Edwin Smith papyrus and the Ebers papyrus, did include religious commentary, but were certainly replete with details about herbal pharmacology, intestinal disease, dermatology, obstetrics, and physical diagnosis that are consistent with "objective and scientific medicine". Finch (2007) further presents proof of medical skill in other parts of the continent that were comparable to that of the West at the same time. For instance, Banyoro surgeons, primarily in modern-day Uganda, were observed performing Caesarean sections in 1879 (published in the Edinburgh Medical Journal in 1884); and the Zulu in modern-day South Africa had precise knowledge of the uses of at least 700 medicinal plants, some of which were subsequently adopted in the Western pharmacopoeia.

In his review of a book on "native" African medicine among the Mano of present-day Liberia, the pioneer African American historian, Carter G. Woodson, underscored the study's finding that the Mano society's medical practitioners distinguished between rational treatments of diseases and metaphysical rites, despite instances in which both were used simultaneously (Woodson, 1941). These Mano "traditional doctors" had a clear knowledge of anatomy and physiological processes and had developed an effective system of quarantine for smallpox, which involved isolating patients in a "sick bush" (Finch, 2007).

It is therefore not surprising that in a medical historical study of eight 19th-century European-trained West African medical doctors, Adeloye (1974) reported that three of them (Africanus Horton, Obadiah Johnson, and Sodeinde Leigh-Sodipe) wrote successful theses on the basis of their documentation and classification of extant medical knowledge in their region of origin. A fourth doctor, Oguntola Sapara, used his own financial resources and spent time investigating West African herbal medicine, and used that knowledge to help in the fight against local epidemics such as smallpox, tuberculosis, and the bubonic plague that emerged in the early 20th century (Adeloye, 1974). Likewise, the Black South African medical doctor, William Anderson Soga, qualified in Glasgow, Scotland, in 1883, and subsequently praised the effectiveness of "traditional medicine" in treating fractures, but was also critical of what he considered to be the unscrupulous behaviour of some "traditional diviners" (Mayosi, 2015, p. 636).

The cursory presentation above of culturally embedded African scientific medicine across the length and breadth of the continent, in both ancient and relatively recent times, is intended to demonstrate that it cannot arbitrarily be divorced from "modern" medicine as though the latter were alien to Africa. Thus, while accepting the pluralistic basis of knowledge, including the metaphysical, historical, cultural, and more instrumental scientific dimensions, our specific interest in this paper is in articulating the epistemological foundations of endogenous knowledge for innovation, which are also plural. Said differently, in this paper, we are more interested in the content of embodied knowledge in

a manner that is potentially transferable across cultures and epistemic communities in interaction than merely in its symbolic form.

3.1.2. Epistemological perspectives on endogenous innovation

Given our clarification of "endogenous knowledge" in the previous section, we now extend it to the notion of "endogenous innovation" as a conceptual framework that had already been anticipated in Ki-Zerbo's theory of endogenous development and combine it with insights from the contemporary innovation systems framework. In fact, Gu and Lundvall (2006) have used the term "endogenous innovation", from a systemic point of view, in connection with China's aspiration to "harmonious development", which they argue is rooted in its ancient contributions to global science and technology, as well as its Confucian philosophical heritage. Our use of the term is analogous to this sense, although more substantively grounded in historical and philosophical perspectives on innovation than were presented in their article. Consequently, our approach can be understood as bringing the more critically oriented social studies of science and technology (STS) outlook together with the more programmatically driven innovation studies approach to bear on present-day COVID-19 challenges in Africa.

Nevertheless, irrespective of whether we are referring to endogenous knowledge that is primarily culturally embedded or that which mainly emerges from the dominant global mode, the challenge of endogenous innovation in relation to pharmacology and medicine remains daunting. In her study of a South African start-up pharmaceutical company, iThemba Pharmaceuticals, that unsuccessfully sought to undertake drug discovery based on "mainstream" synthetic chemistry, rather than the "bioprospecting" of botanical knowledge, Pollock (2019) succinctly summed up the endogenous innovation challenge as follows:

> "*What if South Africa were to become a prominent place not just of raw materials, test subjects, and end users but of the basic science of pharmaceutical knowledge making? Synthesizing Hope is unusual in combining attention to global health and attention to postcolonial science, two spheres that are not often thought about together. In global health literature, scientists working in postcolonial contexts like Africa receive scant attention. Most global health research assumes that rich countries are the main, if not unique, source of knowledge making and that this knowledge flows "south" (Pollock, 2019, p. 1).*

Likewise, an earlier study by Foster (2017) on the Hoodia plant, which is well known to the San people of Southern Africa, underscored the extended negotiations among the knowledge-holding communities, the Council for Scientific Research (CSIR) of South Africa, and international companies with respect to patenting, benefit-sharing, and other concerns. However, that attempt at endogenous innovation through an interaction between different knowledge traditions and among diverse actors was not successful either. While the books by Anne Pollock and Laura Foster shed enlightening insights in relation to the tensions associated with endogenous pharmaceutical innovation from a humanistic, STS perspective, we proceed to map out, in a more explicitly policy-relevant manner, potential pathways to the viable attainment of that aspiration.

3.2. Conceptual framework: endogenous pharmaceutical innovation

In this section, we present a theoretically informed conceptual framework that is intended to explicitly elucidate some of the pathways that could engender an innovative and locally relevant yet competitive pharmaceutical industry in Africa in the short, medium, and long term. The main theoretical paradigms that we weave together are innovation systems, pharmaceutical innovation, and endogenous development. Informed by these perspectives, we propose the three main dimensions of our framework below.

3.2.1. Endogenous technological innovation

In this dimension, we elevate the technological component of innovation with respect to the capabilities of domestic firms and organisations in the pharmaceutical industry. We begin with the importance of scientific knowledge, in particular, to the long-term growth and development of the industry, which is consistent with the insights of endogenous growth and endogenous innovation in the neoclassical economics tradition, as well as in the evolutionary economics and innovation system approaches. This general acknowledgement has been demonstrated, for instance, by Nelson and Romer (1996), using examples from agricultural biotechnology. We, therefore, use the term "original innovation" to refer to the novel scientific knowledge derived from laboratory-based R&D, and that represents one key contribution to the progress of medical know-how (Nelson, et al., 2011).

We also use it in reference to the type of knowledge acquired in an explicitly African cultural and linguistic setting, but which is acknowledged to be highly specialised, such as "traditional doctors" who have specific expertise as botanists with a deep and expansive knowledge of the effectiveness, toxicity, preparation, and dosage of medicinal plants (Sofowora, 2010). It is notable that in his preface to Sofowora's book (published in both English and French), the equally pioneering Beninese professor of pharmacy, Edouard Adjanohoun, lamented the fact that despite their abundance (200,000 out of 300,000 identified plant species are in the Global South), the only medicinal plants that African students were being taught about were those that had been featured in textbooks from industrialised countries (Adjanohoun, 2010). Adjanohoun, therefore, called for greater resources to be directed toward related teaching and research on this rich plant heritage in Africa.

The next component of endogenous technological innovation is termed "secondary innovation", which Wu and Li (2015) refer to as the sequential process by which firms in "latecomer" economies first acquire mature production or manufacturing capabilities and progressively upgrade their technological capabilities, but with the primary intention of closing the gap in productivity with those countries that frequently capture market opportunities based on knowledge at the frontiers of science. However, given that a treasure trove of knowledge that is required for pharmaceutical innovation has been accumulated in many parts of the Global South and Africa, in particular, over centuries and even millennia, we consider that long-term effort at exploration, experimentation, and application to be consistent with the notion of original innovation. Based on this premise, the uni-directional, forward-looking "catch up" basis for secondary innovation becomes bi-directional in our conceptual framework for the reasons below.

In the first instance, as Lee, et al. (2018) point out, catching-up firms can only develop successful domestic brands by overcoming steep challenges in the face of incumbents' positions in the relevant global value chain. The difficulty at upgrading is even more severe in the pharmaceutical industry due to the much more stringent patenting that is a result of the significant R&D investment costs by dominant firms, which are typically on the order of five times more than in other manufacturing industries (2 to 3% of revenues in the latter versus 10 to 20% for pharma), as well as to prevent the relative ease of imitation, according to Scherer (2010). Hwang (2020) further corroborates the argument that given the strong hierarchy by leading pharmaceutical firms in the global value chain (GVC), very few latecomer firms have been competitive on the basis of their domestic innovation in synthetic medicines and that phytomedicines, therefore, offer a window of opportunity to decouple the home-grown industry from the GVC on the basis of its local knowledge and demand. This possibility offers a basis for our proposed bi-directionality.

In the African context, a study on herbal medicine in Ghana by Essegbey and Awuni (2016) demonstrates that its practitioners are primarily located in the informal or popular sector, but are gradually registering their enterprises, improving their manufacturing processes, and upgrading their quality assurance levels. According to the authors, intellectual property protection is generally informed by social norms of secrecy, and when formal, it is limited to trademarks, partly because the standards of technological capabilities for patenting are too stringent for most local enterprises to meet (Essegbey & Awuni, 2016). However, if further supported, as in the GVC-related example above, this also represents an opportunity to build manufacturing capabilities based on original, culturally embedded phytomedicinal knowledge.

We now introduce a third component of the endogenous technological innovation dimension, termed "tertiary innovation", which has been used to explain the innovative deployment of existing products and services in the context of the green energy industry (Soumonni & Ojah, 2021). Tertiary innovation can also be likened to learning by doing and using in clinical practice, which according to Nelson, et al. (2011), includes an evaluation-selection process involving not only formal randomised clinical trials but also a multiplicity of other dynamic evaluation methods that ultimately contribute to the development of new treatments, and to fundamental biomedical understanding.

To illustrate the relevance of the sub-categories above to the development of phytomedicines, which are produced by extracting, purifying, concentrating, fractionally distilling, or subjecting plant materials to similar physical or biological processes, the three generations identified by Okigbo and Mmeka (2006) are a useful guide, namely: 1) the first in which botanical plants are used in mainly unprocessed form; 2) the second in which pure molecules are extracted to be used as therapeutic agents, e.g. quinine; and 3) the last in which the formulation of medicines is based on randomised, double-blind clinical trials and toxicological studies. While each subsequent generation reflects a greater degree of scientific precision, it is important to note that all three have their independent search (original innovation), production (secondary innovation), and innovative diffusion models (tertiary innovation).

For synthetic medicine, a much more recently published set of commentaries led by the president of the International Union of Immunological Societies, the Kenyan immunologist, Faith Osier, provides us with a glimpse of the technological capabilities that the 15 represented countries have deployed in responding to the pandemic (Osier, et al., 2020). Each of the countries' immunologists worked closely with public health officials, epidemiologists, clinicians, and other experts, to better understand and manage the new disease. At the level of tertiary innovation, which mainly required the rapid deployment of adopted technologies, all countries embarked on a vibrant public information campaign, most boosted their testing capacity, a few (namely Cuba) had highly effective track and trace programs, and many specifically reported undertaking clinical research to better understand the local dynamics of the disease (e.g. Senegal and South Africa). The existence of manufacturing plants for the production of vaccines (e.g. Brazil) and the ability to develop immunological diagnostics would then represent characteristics of secondary innovation, while the development of new preventive medicines, immunotherapeutics (including human monoclonal antibodies), and vaccines would represent original innovation capabilities (e.g. China and Cuba) (Osier, et al., 2020).

3.2.2. Epistemic pharmaceutical communities

In the second dimension of our conceptual framework, we adopt the notion of "epistemic communities", which has been found to be relevant to health policy by Löblová (2018) in its reference to actors across society who have expertise in a given domain, and organise themselves around their shared knowledge, normative principles, notions of validity, and common policy objectives. While our use of the term overlaps with the more widely known "communities of practice", we nevertheless employ the former because of our emphasis on the high degree of professional competence, critical self-awareness, and intentional networking to achieve joint objectives. In the first instance, we identify the epistemic community whose activities revolve around synthetic medicine, whether as medical doctors, public health researchers, pharmacists, pharmaceutical researchers, or policymakers, etc. With respect to South Africa's pharmaceutical industry, for example, the arena is characterised by Suleman and Gray (2017) as consisting primarily of formal public and private sector actors engaging in the acquisition and distribution of generic and imported medicines. This constitutes for us the relevant cluster from which the synthetic medicine epistemic community emerges.

Secondly, in his contribution on medicinal plants to Joseph Ki-Zerbo's seminal book on endogenous development in Africa, Sawadogo (1992) reported the manner in which he had assembled anthropologists, sociologists, ethnobotanists, and culturally embedded doctors in order to select and harvest certain widely utilised medicinal plants (tertiary innovation). His laboratory research team subsequently extracted their active ingredients, developed appropriate dosages, investigated their effects on physiological functions with the aim of scaling up the production of the phytomedicines (secondary innovation), and finally, sought to engage in fundamental research for a more rigorous understanding of complex phenomena that had not yet been explained (original innovation) (Sawadogo, 1992). We, therefore, identify these actors across disciplines as forming another epistemic community that revolves around phytomedicine.

Thirdly, we identify a “transepistemic” community that is informed by common aims between different traditions (in our case, the synthetic and phytomedicinal approaches) whose actors jointly develop innovation models and are keenly conscious of the epistemological challenges that may impede the desired equitable outcomes (Augusto, 2005). It is also consistent with the notion of “transdisciplinarity” in the endogenous development framework, which according to Laleye (1992), invites dispersed knowledge holders from different horizons to be willing to subordinate some of their discipline-centric preferences (without sacrificing freedom of critique) to sharpened solidarity with respect to resolving fundamental societal challenges. In this regard, we cite PROMETRA International (research, education, and advocacy organisation on “African traditional medicine” headquartered in Dakar, Senegal), which collaborates with the well-respected and historically African American Morehouse School of Medicine in Atlanta, USA (Braithwaite, et al., 2020; Gbodossou, 1992). Their integrative research on preventive and complementary solutions has made promising interventions during the Ebola epidemic and the ongoing COVID-19 pandemic (MSM, 2021; PROMETRA, 2021).

We should note, however, that the basis for this hybridity is a reflexive and critical complementarity between them, rather than a static or deontological (rule-based) knowledge regime. Sofowora (2010), for instance, is of the view that the rationale for illnesses is the main difference between the two approaches to medicine, with culturally embedded medicine often attributing this to spiritual or metaphysical causes as much as to physical causes, while synthetic medicine focuses primarily on the physical dimension and to a lesser extent, psychological complications. Abayomi Sofowora nonetheless concedes that even certain practices that may initially appear to be arbitrary (e.g. plucking medicinal leaves at different times of the day) are actually consistent with established scientific findings that demonstrate the variation of secondary metabolytes in some plants, or changes in composition in others, during the course of the same day.

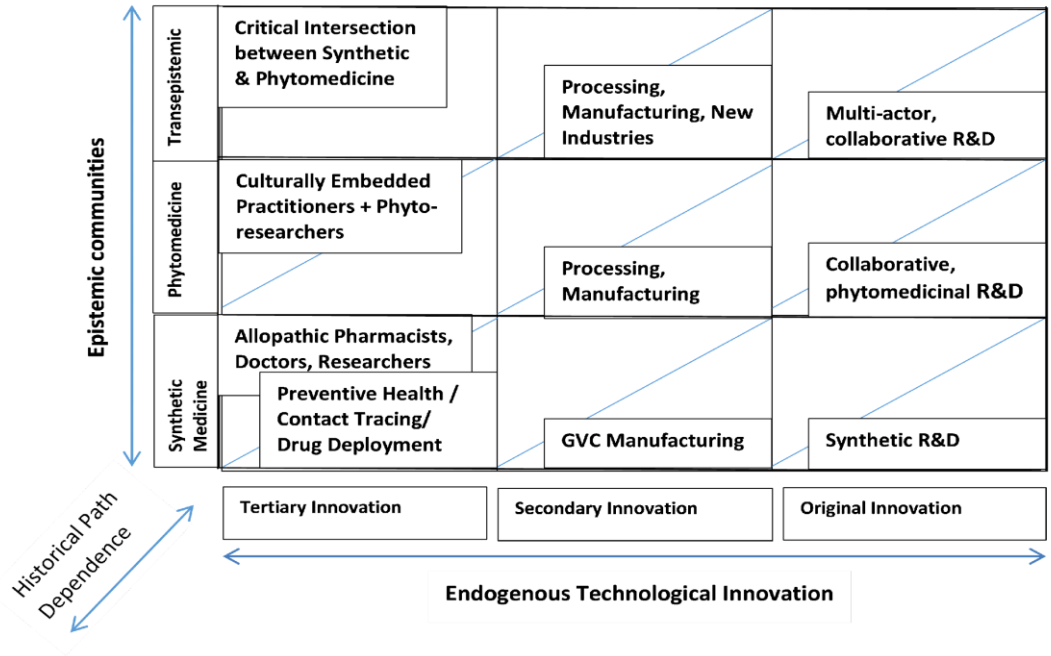
On the other hand, Tangwa (2007) argues that patients who consult practitioners of culturally embedded medicine typically do so only after they have exhausted well-known home remedies and that most such practitioners rely on herbal plants, whereas any need for specific spiritually based healing, per se, is relatively unusual. Godfrey Tangwa, a bioethicist, therefore challenges the type of comparison of “Western Scientific Medicine” (allopathic or synthetic medicine) and “African Traditional Medicine” (culturally embedded medicine) that insists that the latter should be subordinated to the former without rigorously ascertaining what the bases for their complementarity might be. However, he points out that while in medical research, a promising drug can only be validated on rigorous, methodological grounds, medical therapy (whether culturally based or allopathic) is governed by an ethical standard that prioritises the health of the patient. This ethos may then justify the use of a promising drug that is yet to be conclusively proven, on humanitarian grounds (Tangwa, 2007).

For his part, Ogungbemi (2007) contends that to the extent that esoteric or supernatural claims are made by certain practitioners of culturally embedded medicine, or conversely, if practitioners of allopathic medicine categorically dismiss their counterparts in the former

group, then such attitudes would be unproductive. Citing an example of a clinic in Bulawayo, Zimbabwe, in which allopathic doctors referred patients to their culturally embedded doctors for psychosomatic disorders and behavioural problems, Segun Ogungbemi, a philosopher, thus concludes that when those who have knowledge of curative and preventive medicine are open to dialogue and critique, then the potential for contributing to healthcare is magnified.

Thus, outlooks on the manner in which synthetic medicine and phytomedicine might be jointly used in practice range from sympathy with culturally embedded medicine but subject to scientific verification (Sofowora), to opposition to the establishment of any type of what Augusto (2005) calls "cognitive hierarchy" (Tangwa and Gbodossou), to a rejection of the esotericism of culturally embedded medicine on the grounds that it is anachronistic (Ogungbemi). As can be seen, these epistemological perspectives by experts in their respective fields do not fall along disciplinary lines but are based on their judgement of the relative strengths and weaknesses of the two main approaches. Our explication of the first two dimensions of our framework is depicted in Figure 1 below, with each of the nine boxes depicting possible pairs of a type of technological innovation and a given epistemic community that could use it to achieve a desired innovative outcome.

Figure 1: Conceptual framework: Endogenous Pharmaceutical Innovation.



Source: Authors' own.

The most appropriate paths (boxes), or various combinations of paths, that could enable the achievement of collective goals in a given society are then informed by historical path dependence, which we proceed to discuss in the third dimension.

3.2.3. Historical path dependence

Although having diverse interpretations in the policy theory literature, our use of the term "path dependence" is consistent with the proposition by Ingram, et al. (2007) that policies toward politically powerful target groups will be highly favourable if they have a positive social construction, but less explicit if they are viewed negatively ("contenders"). On the other hand, politically weak target groups that benefit from a positive social construction ("dependents") will get positive rhetorical support, but only minimal or modest substantive support, while weak groups that have a negative social construction ("deviants") tend to be burdened with a disparate proportion of policy-backed sanctions (Ingram, et al., 2007). Therefore, an understanding of the degree of political power that the epistemic groups that we proposed have, as well as the way in which they are typically viewed by policymakers, can serve as predictors of the degree of support (substantive or rhetorical) or sanction that they ultimately receive.

For example, herbal medicine and associated therapeutic practices in Africa were long characterised as being "retrograde" during colonial rule, and later, by the health community based on synthetic medicine (Okigbo & Mmeka, 2006). However, through the efforts of pharmaceutical researchers and gradual recognition by various governmental bodies and international organisations such as the WHO, phytomedicine has received official recognition as having the potential to help meet the shortfall in the delivery of health services by the state and private sector. Thus, plant medicine has moved from the position of a "deviant" that is explicitly sanctioned to a "dependent" that is accepted to varying degrees but remains politically weak.

Nonetheless, our use of the term "historical path dependence" is intended to go beyond the preliminary, though valuable assessment of its use in the social construction framework. It underscores the need to have a more rigorous epistemological engagement between the "subordinated" or "defeated" substantive knowledge of politically weak epistemic communities and the justificatory claims of those that are powerful. This approach is specifically informed by the historically grounded imperative of endogenous development, which we have already defined in subsection 3.1.1., but is now more specifically applied to the first two dimensions of our framework.

With respect to endogenous technological innovation, Ki-Zerbo (1992) supports the view that it can be inspired by restoring in the younger generation the inventive spirit that drove the development of magnificent accomplishments in ancient times and further deepened by reviving the old foundations of that knowledge. Nevertheless, he insists that one should not confuse the "traditional" in the sense that it merely ought to be "preserved" or remain unexamined, with the "endogenous", which implies the capacity to adopt and improve upon extant knowledge, in particular, that which is embedded in African languages, cultures, and values, through contemporary scientific R&D and related methods.

The conceptual elucidation of the otherwise loosely used terms in quotation marks above is emblematic of one of the pillars of the endogenous development theoretical framework by Ki-Zerbo (1992), namely, a selective epistemological secession from dominant paradigms

that may employ words with normatively and teleologically charged meanings. To further buttress the point, the words "traditional" and "orthodox" are synonymous in the English language (as they are in French). Yet, the former is widely used to refer to culturally embedded medicine, while the latter refers to allopathic medicine. This leads us to the crucial question posed by Tangwa:

> "*In what sense can a system on which only 20% of a population depends for their healthcare needs be considered as 'mainstream' while that on which more than 80% depends, and have depended for centuries, be considered as unconventional/unorthodox?" (Tangwa, 2007, p. 48).*

Likewise, the terms "native", "indigenous", "modern", "conventional", and so on are not necessarily neutral, and their use may vary widely depending on a given author's own presuppositions. This, in large measure, explains why we have opted for the theoretically grounded term "endogenous" that happens to be much more widespread in the French-speaking literature but which enables us to explicitly grapple with the dynamics of interaction among diverse knowledge traditions across space and time.

Beyond this call for terminological and semantic caution, however, the detailed study of epistemic tensions regarding the knowledge of plants in the 17th and 18th century Cape region (in what is now South Africa) by Augusto (2007) draws our attention to a number of crucial insights that can enable us to bridge the apparent impasse. One is her usage of the concept of "cognitive injustice" to demonstrate the manner in which the overwhelming majority of flora and fauna, that had been identified and classified by Khoikhoi, Sankwe, and Nguni-speaking societies, were appropriated by European naturalists who typically bestowed their personal names (in Latinised form) on the plants.

Another is the notion of "epistemic openness", which Geri Augusto uses to show how certain persons from groups such as the Malay, Surinamese, Akan (from present-day Ghana and Côte d'Ivoire), and the BaKongo (from modern-day DRC, Republic of Congo, and Angola), who found themselves enslaved in the Cape, brought with them ethnobotanical knowledge that they drew upon and exchanged with others in their new environment. She also points out that products like tobacco, thought of as medicinal plants or as valuable drugs, were brought to the Cape from the Caribbean by Dutch colonists (Augusto, 2007). Augusto (2017) also reminds us that tobacco was one of the quintessential "plants of bondage" that were cultivated by subjugated Africans and Native Americans. Nevertheless, the imposition of this plant never succeeded at deterring the survival of desirable food and medicinal plants, whether camouflaged on plantations ("limbo plants") or grown in maroon communities ("liberation flora") throughout the Americas (Augusto, 2017).

Given the temporal and spatial scale of the knowledge flows described above, a very recent and epistemologically significant COVID-19-related innovative effort on the Caribbean Island of Guadeloupe, which has generated widespread excitement in the French-speaking parts of the Caribbean and African world, more generally, is therefore of high relevance to our study as well. On February 11, 2021, the Caribbean pharmacist and doctor of pharmacognosy, Henry Joseph, announced that in collaboration with another

Guadeloupean former NASA research chemist, Damien Bissessar, he had demonstrated that specific molecules from extracts of *"l'herbe à pic"* in French or *"zèb a pik"* in Guadeloupean Creole (Neurolaena lobata), an endemic plant on the island, could block the reproduction of RNA viruses in general, and the coronavirus in particular, in a living organism (Trésor, 2021).

Dr Joseph, an innovator and researcher of medicinal plants for 32 years, and director of Phytobôkaz Laboratories, already holds patented solutions that demonstrate the effectiveness of *l'herbe à pic* (Neurolaena lobata) for treating infections by RNA viruses such as the rhinovirus (responsible for head colds), myxoviruses, a group that includes influenza viruses, the Dengue virus, as well as several protozoan parasites (Joseph, 2006). Of additional pertinence to us is Joseph's insistence that what he explicitly calls the clinical observations that were carried out by his ancestors, who had been "legally" prohibited from practising medicine of any kind in 1799, are the basis for his contemporary research (AJ+, 2021; Trésor, 2021). Expressing gratitude for the "clandestine" transmission of this knowledge from generation to generation, Henry Joseph affirms an epistemic identity with his forebears. His worldview is, therefore, consistent with the onto-triadic structure of being in Ubuntu philosophy (that is, the living, the living dead, and the yet to be born) and conserves its core principles with respect to medical care (Ramose, 2005).

3.3. Empirical methodology: mini-case studies

In this section, we present a concise overview of the methodological approach that we employ to better ground our conceptual framework empirically. Our primary methods of data collection included in-depth semi-structured interviews, unstructured interviews in professional settings, questionnaires, and relevant documentary evidence.

In total, we communicated in-depth with ten experts (five each from South Africa and Benin) with deep professional and experiential knowledge about the COVID-19 pandemic (see Table 1 below). This dialogical information was then triangulated using credible media reports, patents, and results of laboratory trials. The main findings of our investigations in Benin and South Africa are now described in the illustrative rather than exhaustive mini-cases below. They primarily address the various dimensions of our conceptual framework but also highlight expressed perspectives that may depart from it.

Table 1: Key expert knowledge resource persons.

	South Africa	Benin
1.	Pharmaceutical industry executive	Pharmacist and innovative entrepreneur
2.	Medical doctor and infectious diseases researcher	Immunologist and cellular biologist (Member – Ministry of Higher Education and Research Committee on COVID-19)
3.	Biotechnology research scientist	Research scientist in applied microbiology and pharmacology

4.	Culturally embedded phytomedicine practitioner	Sociologist, entrepreneur, and phytomedicine manufacturer
5.	Medical doctor and occupational health specialist	Forensic doctor and public health specialist

Source: Authors' own.

3.3.1. South Africa

South Africa has demonstrated its strong technological capabilities during the pandemic, particularly in terms of keeping abreast of international developments, adapting them to national conditions, and contributing meaningfully to global research efforts in various health-related domains. For instance, the genomic sequencing capability that led to the identification of the 501Y.V2 variant by the genomics team based at the KwaZulu-Natal Research Innovation and Sequencing Platform (KRISP), which is part of South Africa's genomic surveillance network (KRISP, 2021), represents higher-order technological capabilities that are unusual in Africa. Initially reported in South Africa on December 18, 2020, this variant and others, according to Abdool Karim and de Oliveira (2021), have the ability to evade natural and vaccine immunity, thereby making it crucial to suppress the replication of viruses both through public health initiatives and through equitable vaccine distribution.

The innovative efforts described above can be thought of as preventive rather than curative interventions, but they are critical for strengthening the resilience of the healthcare system and can therefore be characterised as tertiary innovation. With respect to core pharmaceutical innovation, we also found evidence of good tertiary innovation capabilities, that is, implementing the base technologies in the arena, such as testing, storage, and dispensing vaccines and other globally available medicines. Vaccine distribution initially began slowly, partly due to rapidly changing variants in the virus, but subsequently picked up pace during the "third wave" of the pandemic.

In terms of secondary innovation, however, we found that South Africa used to have strong domestic manufacturing and production capabilities, but only a few major ones have been left standing, including Aspen, Adcock Ingram, and Novartis, which primarily manufacture generic medicines. The Biovac Institute, a biopharmaceutical company that was deliberately established in partnership with the South African government to develop domestic capabilities in vaccine manufacturing, was characterised as having lost its competitiveness over the years, despite its strong beginnings.

However, the political will to revive Biovac has been reignited in the current context. On March 2, 2021, a partnership among the Wits/South African Medical Research Council (SAMRC) Antiviral Gene Therapy Research Unit (AGTRU), the Wits Commercial Enterprise, and Biovac was announced. Its purpose is to build the skills required to manufacture viral vector-based vaccines, a highly specialised alternative to conventional vaccines, that can also be deployed against COVID-19 in South Africa (Wits, 2021). The explicit strategic intent to spur a technological catch-up effort was also articulated in the communiqué by the CEO

of Biovac, Dr Morena Makhoana, who expressed the view that it was important for South Africa to ultimately acquire the capability to manufacture vaccines across the entire value chain, based on its original, R&D-based innovation, as opposed to importing active pharmaceutical ingredients (API) (Wits, 2021). On July 21, 2021, Reuters reported that Biovac had signed a "finish and fill" agreement with Pfizer and BioNTech to manufacture 100 million doses of their mRNA–based COVID-19 vaccine every year as of 2022 (Erman, et al., 2021). Aspen was also reported to be implementing a similar agreement with Johnson & Johnson in relation to its viral vector-based vaccine.

With respect to phytomedicines, while our research interlocutors welcomed the favourable reference to "indigenous knowledge systems" in the president's Heritage Day Speech, they differed on the level of expectation that they had of it. The culturally embedded medical practitioner, who acquired expertise in medicinal plants based on familial and lineage ties, as well as through well-structured training programs in South Asia, was of the view that the proclamation was more nominal than substantive. This was based on the individual's professional experience, observation, and considered judgement that the medical establishment generally "looks down" on "indigenous knowledge" practitioners and that the cost of getting various tests run by government laboratories are prohibitive for most fellow practitioners. On the other hand, a research scientist with expertise in phytomedicine thought that the president's announcement, in conjunction with analogous statements from the Ministry of Higher Education, Science, and Innovation, clearly suggested that the initiative in favour of culturally embedded medicine would indeed rise to the top of the national agenda.

In relation to epistemic communities, despite the use of the more widespread terminology to refer to themselves and others, we did find a very close identification between the two sub-groups of the phytomedicinal epistemic community. They view themselves as allies, with the professional scientists providing a source of institutional support and legitimacy for the culturally embedded knowledge holders. Conversely, the culturally embedded practitioners give the research scientists a strong sense of connection with their common cultural roots, as well as an opportunity for the latter to contribute the contemporary scientific techniques acquired to improve upon age-old practices in a manner that could be beneficial to rural and grassroots communities.

Nonetheless, it is important to underscore a nuance that we did not originally anticipate in our framework. Our culturally embedded medical interlocutor actually holds a bachelor's degree in social sciences from an English-medium university. Thus, although unknown to each other, a hypothetical interaction between them would likely generate an even closer familiarity between them than our constructs might suggest if understood too rigidly. Both participants' views on the importance of intellectual property were also revealing. The practice among culturally embedded medical practitioners is to share information about the various herbal plants, although the specific preparation was generally only disclosed to close-knit family members and associates. However, once they reached out to research scientists with contemporary technological know-how, they were willing to divulge their preparation procedures in exchange for intellectual property protection in the form of trademarks and possibly, patents.

Our engagement with the synthetic medicine epistemic community yielded some valuable insights as well. A practising medical doctor and occupational health specialist informed us that during the first wave of the pandemic, the individual had used chloroquine as a prophylactic, which was well known from childhood, and later, the hydroxychloroquine/azithromycin/Zinc combination. The individual speculated that pending further investigation, it seemed likely that infection was avoided by taking those drugs, especially given that all the other medical staff in the unit had been infected. A second interlocutor, a medical doctor and infectious diseases expert, nevertheless refuted this view. Citing the peer-reviewed scientific literature, the individual argued that a mere association between variables should never be mistaken for causality and that in the absence of evidence from the most rigorous clinical trials, there was still no known cure for the virus. There are promising treatments, however, such as monoclonal antibody therapy, which is still experimental and extremely expensive, and a more affordable early treatment based on inhaled budesonide (Ramakrishnan, et al., 2021).

An executive in the synthetic pharmaceutical industry, however, expressed immense sympathy for "common sense" prevention to strengthen immunity, including plant-based medicine that is embedded in cultural practices but rejected alleged associations between a given drug or genetic predisposition and resistance to COVID-19. In the final analysis, the individual stated, "I am a science guy". To further emphasise the value of phytomedicine, our participant drew our attention to the "Svalbard Global Seed Vault", which was established by the Norwegian government in 2008, ostensibly to preserve the genetic diversity of plants, with the capacity to store more than four million seed samples in mountain caverns. Nevertheless, the industry executive pointed out that these kinds of genetic banks are of great interest to the pharmaceutical industry and that there may only be relatively few known medicinal plants that are yet to be mapped because of their potential to boost the profitability of the industry.

The transepistemic community that we conceptualised in our framework is therefore delicate to identify in practice. This is because, on the one hand, there is a common interest in medicinal plants between the synthetic medicine community and the phytomedicine community. But on the other hand, one subset of the synthetic community shares values with the latter regarding its potential for the collective good (whether on ecological or developmental grounds), while the other subset seeks to appropriate its potential rewards in an exclusive manner. It is only the subset with shared values that can be considered to be members of a transepistemic community, however.

3.3.2. Benin

Relative to South Africa and other hard-hit countries globally, Benin has been much less impacted by the pandemic, although its effects are still palpable. Some hypotheses that our research participants gave to this effect were the relative youth of the population and the notion that people in the tropical regions of Africa are constantly exposed to various pathogens, which may have strengthened their immunity in the face of COVID-19. Others suggested that the better ventilated, somewhat claustrophobic housing preferences (e.g. fewer self-contained apartments) may have helped. All our participants agreed, however, that these were merely speculative and did not amount to controversies.

With respect to endogenous technological innovation, tertiary innovation on the basis of robust contact tracing and testing was characterised as being relatively low. Despite an agreement among the member states of the Economic Community of West African States (ECOWAS) to standardise the cost of a single test at the equivalent of $US 50 (roughly the same in South Africa) and to commit some of those revenues to a common vaccine fund, the cost in Benin ranged from $US 90 to $US 135 (Fraternité, 2021). Furthermore, the communication of data relating to the trajectory of the infection rate was erratic, and as such, there was a general lack of confidence in the reliability of data communicated by the state, despite the higher than average costs of testing for international entry and exit.

Conversely, however, the quarantine and treatment centres for those infected were reported to be more effective than those in the conventional health system. This was attributed to the efforts of dedicated medical personnel who arose to meet the new challenge. With respect to more central pharmaceutical considerations, our research participants in public health and in the pharmaceutical industry reported that hydroxychloroquine was the basis of the official protocol for treating COVID-19 patients in Benin, even after the drug had lost governmental endorsement in France and in the European Union, more generally. We would therefore characterise the state-driven tertiary innovation capabilities as being weak, but the overall level in the country is medium due to its compensation by the conscientiousness of medical professionals.

In relation to plant-based medicines, a researcher on the biochemistry of natural bioactive substances reminded us that they have always been part of the popular, primary health system (i.e. outside the state) and confirmed that they are being relied upon again during the pandemic, both as preventives and as treatments. The individual informed us that a plant known as Glycyrrhiza glabra L. (Fabaceae), typically known under the common name, liquorice, had been shown in a number of recent research publications to have strong anti-viral and immunoregulatory properties and to alleviate many symptoms of COVID-19. Our participant asserted that Benin's rich biodiversity boasted several medicinal plants with abundant secondary metabolites that have desirable anti-viral properties. Based on those, the individual's laboratory had produced three formulations that were currently being tested, and others had been proposed by culturally embedded practitioners in its network. While these products are already being used in society in a pragmatic manner, robust clinical evaluation on patients still needs to be undertaken. These efforts correspond to attempts at original innovation in close collaboration with culturally embedded knowledge holders.

Another of our interlocutors, a professional pharmacist and co-founder of a pharmaceutical start-up company, described himself as straddling between culturally embedded medicine and synthetic medicine. In order to justify the positionality between these two, the individual quoted an African adage that may be translated in the following manner: "it is from the end of an old rope that one knits a new one". Along with the forensic doctor and public health specialist, both suggested that while culturally embedded medicine may help to identify effective medicinal plants, contemporary scientific techniques should help to further specify them with respect to dosage, efficacy, and safety, and in alignment with the guidelines of international regulatory bodies. Based on this premise, the pharmacist and

another researcher attested to having sufficient technical capability to scale up their pharmaceutical solutions (secondary innovation) but said that they were obliged to raise their own funding, which then undermined their ability to afford intellectual property protection and finance clinical trials.

An important debate relating to a phytomedicine named Apivirine in Benin, which was reported to have demonstrated anti-viral properties against the COVID-19 virus, has implications for properly identifying epistemic communities. The medicine, which is based on the extract of the plant, Dichrostachys glomerata, often used in spices, has already been approved by the European Patent Office (EPO) (Agon & Kinnoudo, 2008). Apivirine was subsequently repurposed for its potential efficacy in the context of the COVID-19 pandemic. It should be noted that one of its inventors, the pharmaceutical innovator and founder of the enterprise, Dr Valentin Agon, was the first place winner of the prestigious Innovation Prize for Africa in 2016 for his patented, low-cost, anti-malarial phytomedicine, Api-Palu, thereby demonstrating the possibility of this technological know-how being used for inclusive innovation (Soumonni, 2016).

However, Apivirine became the subject of some controversy in the context of COVID-19 because of the lack of recognition in Benin and inconsistent support that the medicine received from authorities in Burkina Faso, where it was being tested against hydroxychloroquine. Two of our university-based research participants were sympathetic to phytomedicine but expressed the view that well-established national and international protocols for testing medicines should simply be the arbiter for this particular drug. On the other hand, a public health expert expressed some suspicion that larger interests were at play, which sought to undermine African-derived solutions. Likewise, another researcher perceived a reluctance from dominant international bodies to endorse more inclusive pharmaceutical solutions. Our pharmacist interlocutor thought that political will was ultimately necessary to promote such potentially innovative products until they were eligible for more rigorous testing. Thus, all of the participants were transepistemic in principle, but they each stated their perceived pre-conditions for a fruitful interaction among actors.

3.4. Solutions and recommendations

Based on our investigation of epistemological controversies and varied perspectives that have come to the fore during the current pandemic, we have proposed a conceptual framework that enables an improved understanding of the dynamics of endogenous pharmaceutical innovation. The framework can consequently highlight several potential pathways and combinations thereof (corresponding to the nine pairs or boxes in Figure 1) for directing pharmaceutical innovation toward transformative change in Africa. Although we brought an etic (or outsider) perspective to pharmaceutical innovation, strictly speaking, the participation of the subject matter experts in our study helped us make much better sense of our own reading of the specialised literature that has a more outward orientation. We are therefore able to propose the following policy-relevant recommendations:

1. Semantic and terminological attention
   The widespread terms “indigenous” or “traditional” knowledge in contradistinction with “modern” knowledge are overwhelmingly used in a colloquial manner that tends to lack conceptual rigour. The term phytomedicine (or plant-based medicine), on the other hand, covers a range from the use of botanical plants in an unprocessed form, to the extraction of pure molecules from them, to the formulation of medicines that can be subjected to controlled clinical trials. Similarly, synthetic medicine may cover a range from very mature medicines (e.g. paracetamol and chloroquine) that are fairly easily manufactured locally to frontier R&D solutions like viral vector vaccines. We, therefore, recommend that policy actors use, or at least, include such more precise categories in order to preserve the credibility of pharmaceutical innovators relative to the national and international scientific communities.

2. Substantive revision of existing policies
   Beyond the terminological considerations above, there are also epistemological implications for the development and revision of broadly related policies. Our use of the concepts of endogenous knowledge and endogenous innovation is deliberately intended to emphasise a more critical, dialogical, and interactive approach to knowledge generation across multiple grammars of science and across cultures but while being grounded in a given society’s history. We, therefore, propose that if not terminologically, then substantively and more importantly, such concepts should be incorporated by researchers and policymakers who are working to better shape pharmaceutical innovation dynamics in Africa, both during the current pandemic and beyond.

3. Platforms for communities of practice
   More programmatically, epistemic communities with shared assumptions, commitments, and overlapping subject matter expertise should be encouraged to deepen the knowledge that its various members have. For instance, the dearth of knowledge of medicinal plants in conventional textbooks used in Africa can be compensated for by a more intensive engagement with culturally embedded knowledge holders. Simultaneously, the latter would benefit from the availability of contemporary scientific techniques to investigate their efficacy in the face of emerging maladies. Such outcomes should be scrupulously documented and diffused with the support of policy actors. The same should be done for the synthetic epistemic community, as well as with respect to upgrading its average level of technological capabilities. Robust platforms for transepistemic interaction should also be promoted, especially in relation to challenges that are only partially addressed by one main community or the other. As such, a complementary and symbiotic relationship should be more deliberately nurtured and systematised in connection with the community of practice.

4. Political resources for weaker actors
   We found that in South Africa, practitioners of phytomedicine benefit from a positive social construction by high-level policymakers but may be seen as dependents because of their weak political influence. Their social construction in Benin may be seen as ambivalent, although phytomedicine, even if not necessarily valorised, is widespread in

the country. In the two countries, the phytomedicine epistemic community should be more deliberate about mobilising valuable resources and gaining political recognition, both from state and non-state actors, such that their activities can achieve greater scale. One way to do that is to form advocacy coalitions to increase awareness about the scientific basis of phytomedicine as well as its cross-cutting social, cultural, economic, and environmental benefits.

5. Boost pharmaceutical manufacturing capabilities
   With respect to synthetic medicine, South Africa has demonstrated strong technological capabilities (especially world-class scientific competencies) during the COVID-19 pandemic. Policy-relevant actors in this industry should revive the stagnating innovation capabilities and strive for global competitiveness in those areas in which it has notable expertise. South African pharmaceutical firms with manufacturing capabilities (secondary innovation) should therefore leverage the scientific know-how in the country (e.g. original innovation in vector viral vaccines) in the medium term, that is, beyond "finish and fill" agreements with dominant multinational firms. They should also take advantage of the positive image that the country has achieved in the scientific community as a way to further boost their own credibility. The Beninese medical doctors tasked with managing COVID-19 patients also demonstrated a high level of competence and commitment in administering the existing solutions available to them. That cadre of professionals should seek stronger international linkages, particularly with other African countries such as South Africa, in order to deepen the endogenous capabilities in the continent. Both countries should further expand the manufacturing of generic medicines, but with a view to upgrading such capabilities with respect to producing novel medicines, whether synthetic or phytomedicinal. While Beninese pharmaceutical innovators are much less likely to be globally competitive in the short term, they could nevertheless take on some of the more mature and relatively inexpensive and environmentally benign segments of that industry. This would strengthen the industrial base and reduce the costs of excessive importation. One of our research participants indicated efforts in that vein through the establishment of a start-up company.

6. Establish an inclusive and innovative division of labour
   Our findings suggest that a transepistemic community exists in both countries, that is, actors in synthetic medicine who are sympathetic to phytomedicine and vice versa.
   - However, the inclusive dimension of the health care challenge should be elevated so that innovative activities in phytomedicine, for instance, are further incentivised, even if their products are temporarily classified as health foods, while more rigorous upgrading and testing are being done. This would be consistent with the more inclusive orientation of South Africa's 2019 White Paper on Science, Technology and Innovation. It would also prioritise collective human dignity over material wealth for a few, which is one of the core ethical tenets of Ubuntu philosophy that finds resonance across Africa and beyond. Furthermore, the notion of inclusion need not be limited to the distribution of benefits but should begin with the knowledge contribution to innovation itself.
   - In addition, a division of labour is desirable in which one epistemic community refers patients to the other based on a keen appreciation of the relative

strengths and weaknesses of their knowledge bases. It would also apply within epistemic communities whereby some actors may have a deep knowledge of medicinal plants or preventive measures but may not have access to more contemporary techniques to improve their efficacy and vice versa. Innovation policymakers and managers should therefore develop and work to implement policies that leverage these intersecting and complementary communities as a resource as opposed to reinforcing (even if inadvertently) silos that may be excessively rigid. Likewise, innovators, entrepreneurs, community groups, civil society organisations, researchers, linguistic, and cultural communities, and public officials, both within and across borders, should be encouraged to elevate knowledge-based considerations in their various critical deliberations (See sub-sections 3.2.2. and 3.2.3 for concrete examples). In this manner, numerous spaces and possibilities for constructive interaction can be identified, which should contribute to the endogenous innovation imperative in the pharmaceutical industry, in particular. Our conceptual framework offers clear pathways to this end, especially when epistemological controversies appear to obfuscate the fundamental societal issues at stake.

4. Future directions

The ongoing debate at the World Trade Organization on whether intellectual property rules should be weakened to allow lower and middle-income countries to gain access to the know-how to manufacture vaccines underscores the imperative of strengthening innovation capabilities in Africa. As such, a follow-up to this study would be to look more closely at the intellectual property dimensions of both phytomedicine and synthetic medicine with respect to acceptable socio-economic and health outcomes, as well as "inclusive catch-up" with a desired standard of well-being. Another would be to identify and investigate in-depth case studies of unique and exemplary pharmaceutical organisations that can serve as models of endogenous pharmaceutical innovation for transformative innovation in Africa.

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DSI/NRF/Newton Fund Trilateral Chair in
Transformative Innovation, the 4IR and
Sustainable Development (UJ-TRCTI)
JBS Park, 69 Kingsway Ave, Auckland Park
Johannesburg, 2092

General enquiries:
Telephone: 011 559 1792
E-mail: nabilanm@uj.ac.za
Website: www.uj.ac.za