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Maximizing Benefits of Traditional and Alternative Medicine in a Modern Era of Pharmacotherapy

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Abstract

Pharmacological benefits of herbal interventions are incontestable and there is widespread use of traditional and alternative medicine across disease conditions and socioeconomic status, on the African continent. While the efficacy of some treatments has been documented, there is a general dearth of information on quality control, potential for drug-drug, and drug-herb interactions. Generating and archiving this information is critical in providing empirical evidence to promote the use of traditional medicine in the modern era of pharmacotherapy. In this review, we provide a historical account of traditional, alternative, and complementary medicine with a focus on Africa. Case studies of clinical use of example products are presented. In addition, we share suggestions towards strengthening and safeguarding the practice of traditional medicine, including evaluating the risk of interactions with conventional drugs, implementation of standardization and quality control measures, to minimize undesirable effects and optimize benefits.

Keywords: Traditional medicine, Alternative medicine, Safety, Efficacy, Pharmacotherapy, Herb-drug interactions

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1. Introduction

Traditional, Complementary, and Alternative Medicine (TCAM) refers to all forms of medical intervention outside conventional practice of medicine. According to the World Health Organization (WHO), TCAM includes use of herbal medicine, supplements, nutraceuticals and such practices as yoga which are based on theories, beliefs and cultures (WHO, 2019). The practice of Traditional Medicine (TM) dates back to antiquity as proven by literature relating to Ayurveda and Traditional Chinese Medicine (Pan et al., 2014; Robinson,

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2006). As such, TM is intricately integrated in the livelihoods and health-seeking behaviors of a huge proportion of the world's population. The knowledge and practice of TM has been passed on from generation to generation via apprenticeship and, lately, through recorded history.

A glimpse at the reported literature clearly demonstrates irrefutable health and medical benefits of TM. For many people, TM provides a quick and cheap access to health care. A considerable proportion of the global population, with some sources stating as high as 80% in Africa, are believed to resort to TM as the first option when they get ill (Ekor, 2013; James et al., 2018; Oyebode et al., 2016). Besides being affordable, TM is embraced by many as it is thought to provide holistic care, targeting not only the symptoms of disease but rather, the root cause of the illness (Ozioma and Chinwe, 2019). In addition to the fact that traditional practitioners are perceived to be more sociable and deeply involved in the day-to-day lives of the local people, use of nature-derived interventions is often associated with better safety and efficacy. This appeal has been further spurred by escalating costs of modern health care and unsatisfactory patient-health worker interactions due in part to stressful working environments and workloads on the part of the healthcare provider (James et al., 2018).

2. Limitations of Conventional Therapy

Conventional Medicine (CM), which gained traction in many countries during the colonial era, is the mainstream form of medical care in most nations. This organized, standardized and referenced source of healthcare has enjoyed support both in terms of research, supply, use and regulation. It is therefore common to find formularies such as essential drug lists and established drug regulatory bodies that control and guide the practice of CM in many countries. On the contrary, such frameworks and support that abound towards CM are sorely lacking with TM. The overreliance on CM has presented financial and economic strain and pressure on the respective countries, most of which are unable to sustain the cost of healthcare and must depend on international donor support and funding. Consequently, reports of stock-outs even on the most basic and essential medicines are frequent occurrences especially in developing countries (Koomen et al., 2019; Nditunze et al., 2015).

Besides, not all medical conditions are amenable to treatment by CM. There is a growing list of existing, emerging, and re-emerging diseases that are refractory to available conventional medications. It has become common for terminally ill patients or those suffering from metabolic and degenerative disorders to either supplement CM with TM or to use TM solely (Mbizo et al., 2018; Peltzer and Pengpid, 2019). On the other hand, unbearable toxicity inflicted by some of the conventional medications has reduced the appeal of such treatments (Ekor, 2013; Welz et al., 2018). This has necessitated the pursuit of alternative forms of medications.

3. The Place of Traditional Medicine in the Modern Era

In the face of limitations of conventional medicines as outlined above and given the enlarging global burden of disease, the need to seek alternative forms of medication is justified. Traditional medicine has been, and continues to be, an attractive source of healthcare to satisfy this need for several reasons as outlined earlier. In addition to proven efficacy with a long-standing history of practice, TM is generally accessible and affordable to many people in Africa and other developing countries. Moreover, it has been generally held that practitioners of TM offer holistic healthcare and are much trusted by the patrons of TM who feel more satisfied with the service. In addition, TM is considered by some to be safer compared to CM. Therefore, despite the astronomical progress in modern pharmaceutical practice, TM still holds a central place in the provision of healthcare. This assertion is supported by the numerous case studies, some of which are presented in this review, indicating utility of TM.

4. Case Studies and Experiences on the Use of TCAM in Africa

Of all therapeutic systems, African TM has been argued to be the oldest and, perhaps, the most assorted. Considered to be the cradle of mankind, Africa has a rich biological and cultural diversity characterized by regional differences in healing practices. In Sub-Saharan Africa, health and healing practices have evolved over three millennia in constant interchange with those of other world regions. Ancient Egyptian medicine shaped the ideas of the civilizations around it including the medicine of classical Greek and Roman Antiquity (Janzen and Green, 2008). The Edwin Smith Papyrus, an ancient textbook on surgery almost devoid of magical

thinking and describes in exquisite detail the examination, diagnosis, treatment, and prognosis of numerous ailments, contains medical information which may date to a time as early as 3000 BC (Breasted, 1930). Imhotep, in the 3rd dynasty, is sometimes credited with being the father of ancient Egyptian medicine and with being the original author of the Edwin Smith Papyrus, describing ailments, cures and anatomical observations.

Before the African continent was open to exploration, settlement, trade and missionary enterprise, Africans relied on their indigenous practitioners. These medicine men had knowledge of herbs and roots and often discovered several effective indigenous drugs. Some of these have been shown to have real therapeutic value in conditions such as intestinal parasitic diseases and diarrhea (Burke-Gaffney, 1968).

One plant that highlights the contribution of African TM to modern medicine is *Catharanthus roseus*, commonly known as the Madagascar periwinkle or basically *Vinca rosea*. Its extensive use in TM globally can be traced way back to Madagascar where it has been utilized for centuries to treat a few diseases and disorders including leukemia, diabetes, sore throat, malaria, eye irritation, wasp stings and microbial infections (Komakech, 2017). In TM, it is commonly used as a bitter tonic, galactagogue, and emetic. Being a source of the anticancer alkaloids, vincristine, and vinblastine (Figure 1), which are too complex to be synthesized in the laboratory, there has been immense interest in this species arising from this therapeutic role (Mahomoodally, 2013; Makunga, 2011; Pereira *et al.*, 2010). Due to its declining population, *Catharanthus roseus* has now been listed as an endangered plant in the Red List of Threatened Species of International Union for Conservation of Nature and Natural Resources (Komakech, 2017).

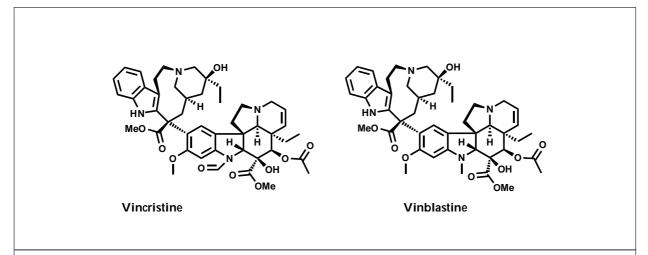


Figure 1: Structures of Anticancer Drugs Vincristine and Vinblastine

5. Prevalence of TCAM Use by Disease Indication

5.1. Malaria and Febrile Illness

In eight studies reporting the use of TCAM for malaria and febrile illness, at least 50% of adults and nearly a quarter of children reported using TCAM (Bakshi et al., 2013; Diallo et al., 2006; Diaz et al., 2013; Eseigbe et al., 2012; Graz et al., 2015; Jombo et al., 2010; Mensah and Gyasi, 2012; Ranasinghe et al., 2015). Among adult populations in Sierra Leone and Ghana, the rates of TCAM product use were as high as 55% (Ranasinghe et al., 2015) and 50.3% (Mensah and Gyasi, 2012) respectively while the rates of use among children in Sierra Leone, as reported by two large-sample-sized studies, was much lower – 22% (Bakshi et al., 2013) and 24.7% (Diaz et al., 2013). Between 2003 and 2013, an increase in rate of TCAM use for uncomplicated malaria was reported in Mali – from 24% to 58% (Graz et al., 2015). In another large-sample-sized study conducted in Mali, half of the patients with complicated malaria were found to use TCAM alone for management of their health compared to 27% in patients with uncomplicated malaria (Diallo et al., 2006). On the other hand, among 33 children with complicated malaria, the rate of TCAM product use was much lower (18.2%) (Eseigbe et al., 2012). In Nigeria, one study reported a TCAM practitioner use prevalence of 49.7% for malaria (Jombo et al., 2010).

5.2. Infertility, Childbirth, Pregnancy, and Abortion

A recent systematic review (James et al., 2018) summarized 18 studies that have reported the prevalence rates of TCAM use for abortion, during pregnancy and childbirth. An average of 48.4% (range = 12-90.3%) of pregnant women were reported to use a TCAM product during pregnancy. When large-sample-sized (Addo, 2008; Duru et al., 2016; Fakeye et al., 2009; Olusanya et al., 2011; Tamuno et al., 2010) and small-sample-sized (Bayisa et al., 2014; Laelago et al., 2016; Malan and Neuba, 2011; Mekuria et al., 2017; Mothupi, 2014; Mureyi et al., 2012; Nergard et al., 2015; Nyeko et al., 2016; Ologe et al., 2008) studies are compared, this rate is consistent. As regards TCAM practitioner service utilization during pregnancy, there is a paucity of literature with only one Zambian (Banda et al., 2007) and Nigerian (Ebuehi and Akintujoye, 2012) study recording the fraction of women seeking the service of a traditional medicine practitioner during their pregnancy (Zambia: 21%; Nigerian: 44.6%). In a study involving 611 Ghanaian women, 11.7% were reported to use TCAM products during childbirth while two large-sample-sized studies in Nigeria recorded 24.1% and 42.5% use of the services of TCAM practitioners by postpartum women during childbirth (Olusanya et al., 2011; Sarmiento et al., 2016). For pregnancy termination, nearly a quarter (22%) of urban Tanzanian women seek assistance from a traditional medicine practitioner compared to 16.9% of their rural counterparts (Rasch and Kipingili, 2009). Although studies on TCAM use for infertility are scanty, one Ugandan study reported high use (76.2%) of herbal medicine among women seeking infertility care (Kaadaaga et al., 2014). Furthermore, among infertile couples in Nigeria, one study reported high (69%) use of TCAM practitioner service (Ola et al., 2008).

5.3. Sexual Health Conditions

In a certain study, 68% of Zambian women were reported to use TCAM to constrict and dry up the vaginal passage before sexual intercourse (Mbikusita-Lewanika et al., 2009) while 56.3% of their Ghanaian counterparts used TCAM to manage gynaecological conditions (Addo, 2008). In a Ugandan study with 224 subjects, 54.9% of patients (male and female) with a wide range of sexually transmitted infections used TCAM (Nuwaha and Muganzi, 2008).

5.4. Cancer, Diabetes, Hypertension, and Asthma

Among hypertensive patients, several studies have reported TCAM use rate of between 19.5% and 67.8% (mean = 27.1%) (Amira and Okubadejo, 2007; Erku and Mekuria, 2016; Hughes *et al.*, 2013; Kretchy *et al.*, 2014; Nuwaha and Musinguzi, 2013; Olisa and Oyelola, 2009; Osamor and Owumi, 2010). Noteworthy, the reported prevalence in the only study that involved a large sample size (n = 500) amongst these was 24% (Olisa and Oyelola, 2009).

For diabetic patients, some recently reviewed studies (James *et al.*, 2018) revealed that Tanzania had the highest prevalence of TCAM use (at 77.1%) (Lunyera *et al.*, 2016) above that of Nigeria (46%) (Ogbera *et al.*, 2010), Guinea (33%) (Baldé *et al.*, 2006) and Kenya (12.4%) (Mwangi and Gitonga, 2014).

In cancer patients, a remarkably high prevalence (65 – 79%) in use of TCAM has been documented in Sub-Saharan African countries such as Nigeria, (Ezeome and Anarado, 2007) Ethiopia (Erku and Mekuria, 2016) and Ghana (Yarney *et al.*, 2013).

In Nigerian asthmatic patients, slightly over 50% of adult (James *et al.*, 2018) and a quarter of paediatric patients (Oshikoya *et al.*, 2008) were reported to use TCAM products.

5.5. HIV/AIDS

There are several studies in literature documenting the use of TCAM products in the treatment of HIV/AIDS in Africa. In a recent study conducted in Cameroon (Mabou et al., 2019), of the 247 people living with HIV, 54.9% declared using in total 70 medicinal plants with 91.3% of users reporting being content with the medicinal plants while unwanted effects were reported in 2 cases only. In another recent cross-sectional survey conducted in Gondar, Ethiopia, of the 360 HIV patients surveyed, nearly three quarters 255 (70.8%) indicated using traditional medicine. The study also found that the most common herbal preparations used were Ginger (*Zingiber officinale*) (47%), Garlic (*Allium sativum L.*) (40.8%) and Moringa (*Moringa stenopetala*) (31.4%) (Haile et al., 2017). Another study was conducted in North-Western Ethiopia almost concurrently with that of Haile and colleagues. In this study, the objective was to assess TCAM use by patients on

antiretroviral therapy (ART) at University of Gondar Comprehensive Specialized Hospital: 43.7% of the 300 participants indicated using TCAM. Spiritual and herbal therapies were the leading forms of TCAM used which constituted 56.5% and 36.6% of the patients respectively. *Nigella sativa* (22.9%) and *Moringa oleifera* (20.8%) were the most frequently used herbal products. Most of the patients (73.3%) using TCAM reported improvement of their conditions (Endale et al., 2017).

Another study conducted on HIV patients in KwaZulu-Natal, South Africa, aimed to assess the use of TCAM prior to the initiation of ART in three public hospitals. Over half (317, 51.3%) of the total number of study participants (n = 618) reported use of TCAM with herbal therapies alone accounting for 29.6% of use (Peltzer et al., 2008). Many other studies have been conducted which involved HIV patients and traditional healers although these involved limited sample sizes. In almost all the studies, over 50% of the HIV-positive study participants were reported to utilize TCAM (Alexio and Precious, 2014; Babb et al., 2007; Kisangau et al., 2011; Langlois-Klassen et al., 2007; Nagata et al., 2011). On the other hand, some studies concluded that traditional healers continue to play a significant role in health promotion in regions where access to modern health care remains a challenge (Mbatha, 2010).

As recently summarized in a review, TCAM use in other conditions such as mental and neurological disorders, musculoskeletal abnormalities, diarrhea, eye diseases, surgical care, infantile colic, tuberculosis, oral health and mycetoma have been reported in Sub-Saharan Africa (James et al., 2018).

6. Evidence from Randomized Clinical Trials in Support of African TM

In one prospective, randomized controlled trial, the efficacy of *Combretum micranthum* (kinkeliba) and *Hibiscus sabdariffa* (bissap) in the form of galenic capsules of plant powder in adult patients with non-complicated hypertension (> 140/90 mm Hg) was assessed (Seck *et al.*, 2017). During four consecutive weeks, 125 patients were randomly allocated to group 1 (kinkeliba leaves 190 mg × 2/day), or group 2 (bissap calyx 320 mg × 2/day), or group 3 (ramipril 5 mg/day) with patient's blood pressure being measured weekly. Over three weeks of treatment, the Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) decreased in all three groups (p < 0.001). At the end of four weeks, 37% [95% CI: 23.6–51.9] of patients in the kinkeliba group, 39% [95% CI: 25.7–54.3] of patients in the ramipril group and 21% [95% CI: 11.7–35.9] of those taking bissap had their blood pressure normalized.

In other studies, the antidiabetic properties of Aspalathus linear is have been evaluated with patents being filed. Aspalathus linearis is a fynbos species endemic in South Africa and is cultivated to produce the well-known herbal tea commonly known as rooibos. Its potential health-boosting properties, most notably, antioxidant activity along with being caffeine-free with low levels of tannins has contributed to its popularity and consumer acceptance worldwide. Rooibos extracts, usually formulated with other ingredients in pill form, are available albeit these have been categorized as dietary supplements. Recent studies have demonstrated the potential of aspalathin (an antioxidant in rooibos) (Figure 2) and selected rooibos extracts as antidiabetic agents (Frank and Dimpfel, 2010; Joubert et al., 2008; Na et al., 2004). In Japan, a patent application for the use of aspalathin in this regard was filed while a placebo-controlled trial application for the use of rooibos extract as an antidiabetic agent was filed (Larsen et al., 2011).

Figure 2: Structures of Aspalathin and Harpagoside

In another example, *Centella asiatica*, a medicinal plant that has been used since pre-historic times, has been studied for its enhancement of cognitive function in a randomized placebo-controlled double-blind trial involving 28 healthy elderly participants. Cognitive performance and mood modulation were evaluated following administration of plant extracts at various doses ranging from 250 to 500 and 750 mg once daily for two months. It was demonstrated that the working memory and the N100 component amplitude of event-related potential were enhanced by the high dose of the extract. Following treatment, self-rated mood was also found to improve. Moreover, 1- and 2-months post-treatment with high doses, *C. asiatica* was suggested to increase calmness and alertness (Wattanathorn *et al.*, 2008).

Clinical trials on the anti-inflammatory, general analgesic (commonly for lower back pain), and antirheumatic effectiveness of the plant *Harpagophytum procumbens* have also been conducted. The plant is native to the red sand regions in the Transvaal of Namibia, Botswana, and South Africa. The San and Khoi peoples, indigenous to Southern Africa, have used it medicinally for centuries if not millennia (Andersen *et al.*, 2004; Gurib-Fakim *et al.*, 2010; Williamson, 2011). Being one of the most highly commercialized indigenous traditional medicines from Africa, it is exported in bulk, mainly to Europe, where it is made into many health products such as topical gels, patches, capsules, tablets, and teas (Mncwangi *et al.*, 2012). In one clinical trial, Harpagophytum extract (WS1351) was administered at two daily doses of 600 and 1200 mg containing 50 and 100 mg of harpagoside (Figure 2) respectively and compared to a placebo to evaluate the former's effectiveness in lower back pain. Included in this randomized double-blind study, which took place over a period of 4 weeks, were subjects (n = 197) with chronic susceptibility to back pain and current exacerbations with intense pain. Of the 183 subjects who completed the study, 6 and 10 in the 600 and 1200 mg treatment arms, respectively, were reported pain-free without using tramadol (rescue pain medication) (Mncwangi *et al.*, 2012).

There are other clinical trials conducted on African traditional medicines to assess their safety and/or effectiveness against other diseases and conditions including dermatological, hepatitis, HIV/AIDS (Handema et al., 2007), malaria (Mesia et al., 2011; Ogwang et al., 2011), respiratory and sickle cell anemia (Wambebe et al., 2001). However, many of the clinical trials seem to have remained unpublished (Willcox et al., 2012).

7. Strengthening TM in a Modern Era of Pharmacotherapy

Despite profound benefits, TM bears its share of limitations and challenges. First and foremost, nature-derived resources run the risk of depletion if not timely and adequately replenished (Nishteswar, 2014). There is therefore the prevailing need to replete the utilized resources to ensure continuity of supplies. Additionally, for some herbal preparations, huge parts of plants are required to achieve the required dose of medication. This presents a challenge with not only sustainability but also the ability to satisfy the medical needs across a large, and constantly enlarging, population (McMullin et al., 2012; Nankaya et al., 2019).

Just as geographical conditions vary across the globe, constituents of medicinal value may vary between species of plants that yield the various active constituents. It has, therefore, been a challenge to standardize the process of preparing the various treatments obtained from nature. Similarly, geographical differences have created a dilemma in harmonizing the procedures involved in processing and preparing the herbal medications (Chawla et al., 2013; Karbwang et al., 2019).

On many occasions, the accuracy of preparing and determining the appropriateness of prescribed doses is the prerogative of the traditional practitioner. As this is dependent upon the experience built over time, it presents a daunting task to the naïve and inexperienced practitioners who are likely to make many errors in their debut into this field.

Perhaps the most besetting issue that has dented the global acceptance of the practice of TM is the concern over its safety and efficacy (Mensah et al., 2019; Moreira et al., 2014; Zhang et al., 2015). Just as with CM and any other form of treatment, the patient needs to be assured that it would do them no harm and that it is efficacious. Some reports indicate that those involved in TM feel that there is no need to subject TM to scrutiny in much the same way that it is conducted in CM (Incayawar et al., 2009). This, in turn, has led to the flourishing of impostors and widespread use of substandard and even harmful products. Besides, poor storage and unchecked preparation procedures has contributed to the safety concerns in the use of TM. In

other cases, practitioners have been criticized for adulterating the purported TM with, among other substances, portions of conventional medicines (Al Lawati et al., 2017; Ching et al., 2012; Posadzki et al., 2013). This, apart from misrepresenting the true composition of the herbal preparation, also poses a risk of drug drug-interactions or increased drug adverse effects for patients who, for example, are not supposed to use a certain medication which has been used as an adulterant.

8. Proposed Framework for Promoting TCAM

The meaningful and satisfactory exploitation of TCAM requires that the practice be conducted within a properly instituted framework. Proactive efforts and conscious steps must be taken to maximize the health care potentials and benefits embedded within TM. Key stakeholders in the healthcare industry: the government, consumers of the products, academic and research institutions, must be involved. Of necessity, the averseness to TM by proponents and patrons of CM must be mitigated. There must be a shift in the mindset, attitudes and perceptions towards TM which must be viewed as an important, legal, and recognized approach, as well as alternative to CM, in seeking and offering health care solutions.

8.1. Partnerships with Traditional Healers and TM Practitioners

A critical step towards achieving wider accessibility and trust in TM is the mending of broken relations, a building of mutual trust and confidence, between TM and CM practitioners. For a long time, the two professions have been on extreme opposite poles regarding their views and approach to healthcare provision (Tiwari et al., 2009). This antagonism has proved counterproductive. Both sides need to appreciate that they complement each other in the quest to provide equitable health care. One way of spearheading this is by fostering partnerships and collaborations between TM and CM practitioners. Strengths and limitations existent between the two sides should be acknowledged and shared (Oliver, 2013). Similarly, successes in the treatment and management of complex disease conditions should be shared across the divide. This can, for example, bring to the limelight a potentially ground-breaking remedy from traditional sources for a disease without current cure and inspire further scientific investigations into the probable mechanisms of action and other pharmacokinetic profiles. The public should be encouraged and facilitated to reach out and seek health care services from either practitioner without fear of reprimand or ridicule.

8.2. Balanced and Objective Media Publicity

Generation and consumption of information, communication and technology is a critical driver in access to healthcare and its acceptability by the general populace. This fact applies to the use of TM as well. Much of the information and reports by various mainstream media outlets, which are often the most trusted by most of the population, appear to show bias against TM. In most cases, TM is depicted as being unsafe and inefficacious even in the absence of extensive and impartial investigations. This indiscriminate reporting has the tendency of leading to misinformation and prejudices by the public who end up shunning what would be a useful resource to them and, possibly, a cheaper option. Prior to the release of such media reports, we recommend that media houses ensure balanced, contextual, and accurate reporting. Towards attaining objective reporting, information could be sought, for example, regarding any known pharmacological activity profile of the herbal preparation, method of use as well as quantities (dosage) and schedule. This way, it may be possible to identify potential reasons for undesired outcomes which, if rectified, may rescue the use of a given product rather than discredit it altogether.

8.3. Creating Databases for Botanical Sources of Medicinal Value

As stated before, TM has been practiced for centuries in traditional African communities and elsewhere, world over. Over the years, knowledge has been passed on from generation to generation and as such, later generations benefited from cumulated experience and conserved folklore knowledge. To propel the practice of TM, information needs to be gathered on the identity and use of various medications. For plants, the species, period of growth, place of growth (soil and rainfall pattern) are critical. These are important especially in the context of replanting natural resources of herbal plants that may be in danger of extinction due to overexploitation. Other related information that requires archiving include mode of harvesting, storage, processing, and administration of the medicinal preparations. In addition to keeping records of the identity of

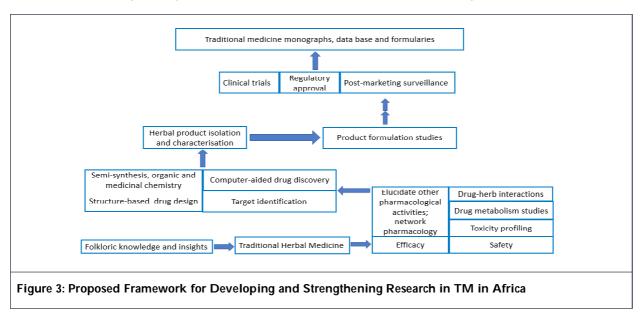
the plant specimens, an account of the procedures for preparing the herbal drug product will help provide future point of reference. Just as with CM where reference books and formularies exist and are regularly updated, equivalent resources for TM should be made available to develop this area of practice.

8.4. Establishment of Research Centers to Conduct Preliminary Analysis

In the modern era of pharmacotherapy, a wider acceptance of TM will require that there be some form of validation regarding the safety and efficacy of the products. This is an appropriate opportunity to involve academic and research institutions. For example, for an herbal preparation acclaimed for its ability to treat diarrhea, appropriate experiments to assess effects of the product on gastrointestinal motility should be conducted. Similar approaches can be made, to the extent possible, to provide some form of scientific basis for reported use of various traditional medicines. We also encourage that experiments be carried out to explore effects of the herbal concoctions on key body systems and tissues to provide empirical insights into any pharmacological effects or toxicities. If this approach is adopted, it has the potential to lead to the discovery of hitherto unreported benefits or potential side effects of the respective herbal preparations.

The screening of biological and pharmacological activities of commonly used herbal preparations in the various global regions should lead to the development of an herbal preparation monograph containing a database of information for future reference. Additionally, studies on toxic effects of herbal medicines should be performed to provide insights into potential adverse effects. For instance, *in vitro* toxicology can be evaluated using a panel of cells to provide an indication of the toxicological profile, range of tolerated doses or concentrations.

A fundamental cause for the unwanted side effects of TM is in their concurrent use with CM. Drug-herb interactions can take place at any of the phases of pharmacokinetics: absorption, distribution, metabolism and excretion (Oga et al., 2016; Singh and Zhao, 2017). Regarding metabolism, the cytochrome P450 superfamily of enzymes, responsible for the biotransformation of most drugs on the market, is a major target for drug-drug interactions through enzyme induction or enzyme inhibition. Enzyme induction can lead to subtherapeutic concentrations and hence therapeutic failure or inefficacy of the victim drug. On the other hand, enzyme inhibition can result in elevated drug levels and toxicity of the victim drug. When the victim drug has a narrow therapeutic index or is associated with lethal adverse effects, drug-drug and drug-herb interactions can be critical. Some of the metabolic drug-drug interaction experiments can be focused towards the key CYP450 enzymes. Through such experiments, the potential TMs to affect the disposition and pharmacokinetics of commonly used prescription or over-the-counter medicines can be determined and appropriate advice given to patients. This information can also be properly curated for inclusion in a software that can be developed in future to predict potential for drug-herb interactions involving commonly used drug classes. The concept of strengthening research and development of TM is depicted in Figure 3.



Additional research on herbal preparations can involve the isolation and elucidation of the structure and identity of phytochemical components. This will assist in further evaluating biological and pharmacological activities of isolated components in comparison with the combined concoction. Depending on the results, isolated components may be found to be more potent than combined fractions. Moreover, the isolated components may lend themselves to chemical modifications via medicinal chemistry strategies to yield improved structural analogues. This has been performed in several areas including in the research on antimalarial quinolines and anticancer drugs such as paclitaxel and vinca alkaloids (Newman and Cragg, 2012; Yuan et al., 2016). The ensuing structure-activity and structure-property relationship trends will allow logical progression of promising series or even investigation of analogues against other diseases of interest. Such prospects are further motivated by the advent of structure-based drug design, an integral part of computeraided drug discovery. The application of these *in silico* tools have the potential to identify novel therapeutic uses of lead compounds identified from nature. Similarly, by browsing through millions of synthetic compounds deposited in drug banks, structure similarity searches can be conducted to expedite drug discovery, pharmacological and toxicological profiling of promising isolated active principles from plants.

When a potential drug lead has been optimized and established to be feasible for therapeutic intervention, it is vital that formulation studies are conducted to select the best drug delivery system. Formulations may assist in further improving the pharmacokinetic profiles of compounds that may be beset by, for example, poor solubility. Furthermore, modifications in the release characteristics can be done to afford sustained release preparations for longer durations of actions, if desired.

8.5. Clinical Trials and Regulatory Aspects

Just as it happens with CM, products from herbal sources should be evaluated empirically through clinical trials. This will ensure that the pharmacological benefits are appropriately curated, and notice made of any undesirable effects. This pragmatic approach can be useful in unravelling benefits that were hitherto unexpected or unrecorded. Changes in biochemical parameters and other body functions can be investigated by measuring specific biomarkers from body matrices.

Regulatory approval of TM and its adoption in the mainstream healthcare services of governments is an important step in weeding out substandard products and quackery. Such legal frameworks can lead to confidence in the use of TM and offer protection of the consumers from harmful substances since, it is expected that these products would have undergone minimum tests for safety and presence of toxic substances such as heavy metals and microbial contamination.

Therefore, the regulation should govern aspects such as the preparation, handling, storage, and administration of the TM. This will ensure that requisite standards are set and upheld. Proper hygiene and sanitation must be central to the regulatory requirements and certification of premises conducting TM. Laws to combat adulteration and counterfeits should be considered to safeguard the public against unscrupulous dealers.

As with CM, herbal product literature inserts should be made a requirement in providing information on the indications, dosage, precautions, adverse effects, and contraindications of respective products. In the WHO Africa region, several countries pledged to promote the use of TM and to facilitate its legislation and regulation (WHO, 2011). Despite promising progress since such a bold declaration was made, room remains for even much more to be accomplished towards implementing the proposals.

8.6. Establishing, Staffing, and Funding of TM Research Centers

Just as with any other drug discovery and research endeavor, promoting the rational use of TM requires a well-supported research team in terms of infrastructure and human resource. Universities and research centers have a critical role to play in moving natural products research to the next level. Typical members of staff will comprise researchers across the spectrum of drug discovery and development including those experienced and interested in natural products research. For the beginning, institutions and countries with underdeveloped TM research can liaise and seek technical support and guidance from other countries like China and Japan who have well established research centers and academic institutions focused on natural products drug research.

The research on TM can be embedded within universities thereby providing an opportunity to induct students into natural products research and enabling them to appreciate the role of TM. Early induction into the role of TM is likely to contribute to the erasing of the skewed thoughts on inferiority of this mode of healthcare as compared to CM. With research exposures to countries which have embraced and developed TM as a vital component of their healthcare provision, this experience should lead to capacity and infrastructure development over time.

Research of any kind requires financial support and TM is no different. For effective research progress in TM, as mentioned earlier, we propose that these activities be embedded within university establishments. One benefit of this approach is that there will be access to intellectual expertise from faculty across the various disciplines that are critical to TM research, drug discovery and development. Moreover, the research can benefit from funding and infrastructural support that is more readily channeled through academic institutions even for resource-constrained countries. When governments are convinced of the role of TM to the health of their people, substantial support in the form of funding for research, can be obtained.

Since TM is recognized globally as a prominent form of health care, there is increasing support in terms of funding for research relating to TM and exploration of potential novel leads for drug discovery. These funding opportunities can provide a further important aspect of financial support to centers researching on TM. Other forms of funding can be accessed through fellowships and scholarships to pursue postgraduate training and research experience in pharmacognosy and TM. With the networks and collaborations that are likely to develop over time, TM centers can evolve to be vibrant research institutions contributing to safe and effective alternative healthcare.

9. Conclusion

In summary, TM has proven indispensable in offering countless medical benefits and solutions. Besides complementing conventional approaches to treatment using classical pharmaceuticals, TM has provided relief where orthodox interventions have failed. Several pharmacological profiles of herbal and other forms of alternative remedies have been demonstrated in preclinical and clinical studies. We have highlighted some examples of herbal-derived products based on TM practice in Africa. With the cost of modern pharmacotherapy being out of reach for many and coupled with the fact that several ailments remain inadequately managed by mainstream xenobiotics, TM is bound to continue playing an important role in the quest for good health. For this reason, it is vital that the safety and efficacy of products originating from TM be established. The practice of TM should be safeguarded by incorporating standardization, regulation and surveillance of the practice and accompanying products. We have also shared an approach towards strengthening research and practice of TM that calls for cooperation and unity of purpose from the various stakeholders including respective governments, academic and research centers as well as proponents of both conventional and traditional medicines. Finally, funding from government and international sponsors is a crucial driver in staging successful drug discovery and development research involving TM given the intensive demand on resources that the field has. This plea is especially urgent for resource-constrained settings in Africa where TM remains inadequately explored for the discovery and development of pharmaceuticals.

Conflicts of Interest

The authors declare no conflict of interest.

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