

**CHALLENGES AND OPPORTUNITIES OF THE UGANDAN TRADITIONAL
HERBAL MEDICINE SECTOR**

ABSTRACT

The use of herbal medicine products worldwide and in Uganda is on the rise and there is much-renewed interest in their use because of the belief that they are safe. However, this belief is not backed up by credible scientific research for many products in Uganda. Almost all herbal products produced locally in Uganda have no scientific proof for their claimed safety and efficacy for the treatment of the various conditions they are claimed to treat example; covid-19, HIV, hypertension, erectile dysfunction, and others. There is an urgent need to quickly improve and enforced research on the local products in order to realise the economic benefits which could be lying hidden in them and put a ban on adulterated products from being sold to the public. This review was conducted in order to determine the challenges and opportunities in the Traditional Herbal Medicine sector in Uganda. It was found out that enormous challenges face the Traditional Medicine sector in Uganda including; lack of research on products available for use, claims of one product treating multiple conditions, adulteration of products with established Pharmaceutical drugs and no stringent regulations on registration of products. However, a lot of opportunities were also noted available for exploitation to develop the sector further. Collaboration with local Universities to speed up research using the Reverse Pharmacology approach⁽¹⁾ on the available products, strictly enforcing regulation on product registration and exploiting the reverse Pharmacology approach to study the local products, aggressive and intentional investment in basic research infrastructures and speeding up Clinical Trials on

products found to be safe and effective could allow the realisation of the benefits which could be hidden in the local Traditional Medicine products.

Key Words: Challenges, Opportunities, Traditional Medicine, Uganda

1.0 INTRODUCTION

The use of Herbal Medicinal products for the treatment of various conditions and infections has been practiced for as many years as humans have existed and a bigger percentage of the world's population believes in it (2, 3). Although the majority of people tend to think that Herbal Medicine products are safe, many are also known to be toxic and there is a lot of concern about the safety and efficacy of many herbal products (4). With renewed and increasing interest in Herbal Medicine products and the wide market available, there is a growing need to regulate the sector to ensure only safe and effective products are made available for use. Many research conducted and reported by National Drug Authority (NDA) have frequently indicated adulteration of many products in Uganda which seems an intentional act by the product owners (5-9). All involved in patient care using modern Medicine thus needs to know the effects of the commonly used herbal medicinal products **taken by the population** in areas where they operate to avoid dangerous interactions **with the allopathic drugs** from occurring as their use is deeply rooted in mankind's history(3, 10). For toxic products that can be used in specified manners, their toxicity needs to be well defined through well-conducted scientific research and data made available. **The NDA guidelines 1.5.3 titled "Category 3 Traditional Medicines", sub-section 3A and 3B requires all Herbal Medicine products available in the market for commercial purpose to have research data available on them. This is not the case for many products available on the Ugandan market, mostly the local products** (11). In Uganda just like in many other Countries in the world, several Traditional Medicine products are available for sale to the public to manage several conditions and most importantly with many claims of cure and complete safety. Currently, there are 234 local Herbal products notified to NDA and about 163 products from other countries in Uganda by 24 June, 2022, our monitoring of the NDA website since 2018 indicates a tremendous increase in the number of products notified to NDA from 64 in 2018, 163 in 2020 and now 234

by June 2022. Conversely, herbal products from other countries have also been growing in the list from 123 in 2018 to 163 in 2022 with products from many countries now available. It's important to note that most of the products from other Countries available in the Ugandan market actually have a similar type here in Uganda, a case in point being the China Green Tea which has been studied for the effects of their polyphenols and found to lower the levels of Low-Density Lipoproteins (LDL) in people with hyperlipidemia, effects on prostate cancer, and several other conditions (12-14). The China Green Tea however, is not listed on the Uganda National Drug Authority website as an herbal product. The challenge here thus is that we are buying green tea products from other countries and yet Uganda too produces a lot of green tea which can be developed to this level. There is an opportunity in this case to change this trend in favour of Uganda.

The World Health Organisations Strategy for Traditional Medicine states that, the responsibility of ensuring the safety of a population from traditional medicine products, be it locally produced or imported, rest with National Regulatory Bodies because there are no universally agreed on mechanism for regulation of Traditional Medicine products Internationally compared to conventional Medicine products (15). This, therefore, implies that each Country must put in place strong measures for Herbal Medicine Regulation. Many Countries may have laws but are not enforced and this is where Uganda is as well. In this current review, a search was conducted on all the products listed on the Ugandan NDA website, both local and International, and also looked back to previous discussions made with the team at NDA on the way forward. The best development noted was the initiation of Clinical Trials on locally produced Herbal Medicine Products; Covidex and UBV-01N. Success or failure resulting from these two trials will bring valuable lessons on how to deal with successive trials and further research on other locally

produced Herbal Medicine products in the future. More so, it has already opened the way for the modernization of Uganda's Traditional Medicine sector into producing products of modern standards which can be accepted in other Countries as well.

2.0 METHOD

Literature search on products listed on the National Drug Authority Website was conducted for all products for evidence of publication, indicating either safety or efficacy (animal study or Clinical trial) study on the Herbal Medicine products. All product that were not listed on the NDA website were not considered. Searches were made on Google, Google scholar and PubMed. Search terms included; safety, efficacy and name of the local or International product listed. Products found on Google were further subjected to search on Google scholar and PubMed for any further evidence of scholarly articles on them.

3.0 RESULTS

The number of products which were found listed on the Ugandan National Drug Authority website at the time are presented below.

Table 1. Number and origin of various products listed in Ugandan NDA website by 24th June 2022

Sn	Country of origin	Number of products
1	Uganda	234
2	India	109

3	Pakistan	32
4	Belgium	5
5	Thailand	4
6	Bangladesh	3
7	Singapore	3
8	Jordan	2
9	Kenya	2
10	Indonesia	1
11	Egypt	1
12	United States of America	1
Total number		397

Table 1 shows that of the 397 human herbal products listed in the Uganda National Drug Authority websites as of 24 June 2022, local products were 234 and 163 products were International Herbal Medicine products.

Out of the 234 local products only one product Artavol® was found with publication on its efficacy on animal models. Two products Covidex and UBV-01N were listed for clinical trials while the rest of the local products has no information on scientific proof of efficacy and safety or clinical trial.

4.0 DISCUSSIONS:

It was found out that many International products had scientific publications available on them (16-32) while one local product Artavol® had publications on its malaria prophylactic effects

(33, 34) and two were undergoing clinical trials (Covidex and UBV-01N). Rest of the local products listed had no scientific publications available on them. For example, a study on cystone, a herbal remedy for treatment of urolithiasis originating from outside Uganda found out that it was 66.6% effective when compared to the placebo (35). Evecare, a product marketed for management of haemorrhoids was found to be 87% effective in a trial (36). The majority of the International Herbal products available in the Ugandan market are from India (109) followed by Pakistan (32). It's interesting to note that Herbal Medicine product research including Clinical Trials in India started way back in the 1960s while in Uganda, only 1 product has been studied clinically with available publication on it's efficacy (37, 38) and in laboratory animals(33) and 2 are currently undergoing Clinical Trials. About the local products sold in Uganda, the following challenges were noted; most only underwent phytochemical screening as a basis for their notification and yet the presence of a phytochemical in a product does not guarantee their claimed safety or efficacy, there are many studies that have reported cases of adulterations (5-9) which makes these products a threat to those who may already be taking the same drugs as many people use herbal medicines concurrently with the conventional drugs (8, 39-43). The notion that one product treats almost everything as it's a common practice for those advertising herbal medicine products, most products don't have scientific proof of efficacy and safety either alone or when used concurrently with other products. Because of these, the products can only be sold and used locally and not by everyone as some people do not trust them. The products cannot be exported to other Countries and thus the economic benefit which could be realised from their sales is limited, and the preparation of products sometimes are not standardised. Although there are many challenges, there are also windows of opportunities worth exploiting in order to develop the herbal medicine sector to International standards. NDA has started to accept product

notification and later on registration as was noted in a discussion with the NDA staff, Scientist are now available though not in big numbers to help conduct safety and efficacy studies on traditional medicine products at (NCRI, Pharmbiotrac at MUST, Makerere University etc). Some of the products may be very effective and need scientific backing so that benefits could be accrued from them by the product owners. To achieve the required success, there is a need for formalization of; Collaboration between the Scientists and Traditional Medicine Practitioners with effective products, a Mechanism for signing Non-Disclosure Agreements (NDA) between the Scientists and the Traditional Medical Practitioners which are enforceable, Registration of the available Scientists to conduct safety and efficacy studies by NDA so that such Scientists can take responsibilities for the outcome of their studies, Enforcing the publication of results of studies or submission to NDA if publication not allowed due to secrecy/Intellectual Property issues, Products should be tested for acute toxicity, sub-acute and most importantly teratogenicity effects and for products which are to be taken long time, sub-chronic and chronic toxicity studies can be warranted. These research must be conducted by using the OECD so that such results can be acceptable to many Regulatory Bodies. This would make it easy to export safe and efficacious Herbal Medicine products from Uganda to other Countries. To realise this goal, research Institutions must focus aggressive investment on research infrastructures to allow for thorough conduct of safety and efficacy studies on the local Herbal products available and those originating from other Countries for the purpose of validation.

There is always demands for results for Clinical Trial in humans for some of these products in different Countries where they may gain recognition. This however, is normally very expensive considering the requirements for conducting Clinical Trial and enormous expenses in preclinical studies which has limited new drug discovery in recent times (44). The opportunity with

Traditional Medicine product on the other hand is that, such can be easily conducted through a Reverse Pharmacology approach, a process commonly referred to as the Clinic to laboratory approach other than the laboratory to the Clinic approach in the classical Pharmacology process of drug discovery(45-47). Reverse pharmacology refers to the process where Traditional Medicine products already in wide use by the population can be Clinically studied by making observations of those undergoing treatment and conducting important investigations before initiation of treatment, during treatment, and after treatment in order to ascertain evidence of efficacy and safety while the product is being used based of the Traditional Methods (1, 45, 48, 49) . This process only allows those products with proven efficacy and safety during such traditional treatment, combined with scientific investigations to be selected for further scientific development, reducing the chances of failure of the product. The Reverse Pharmacology is thus a drug discovery process that starts with human trials and ends with human trial (50).

With lots of renewed interest and uptake of Herbal Medicine products, National Regulatory Bodies should take advantage of ensuring that every product to be registered is tested for safety, efficacy and must be of good quality. Efforts can also be made to ensure that those with reasonable data on safety and efficacy at basic research levels can be Clinically tried to generate more data on safety and efficacy. This can be done through partnership with Universities that have capacities to conduct such studies. In many Universities, research is being conducted at various levels. Through collaboration, efforts can be directed at evaluating products listed on the National drug authority website for their claimed efficacy.

For products which are already in much use, the Reverse Pharmacology approach can be applied in the evaluation of their safety and efficacy. For those claimed to treat bacterial infections, their effects can easily be determined in laboratories that routinely conduct culture and sensitivity

testing to determine their in-vitro efficacy. The biggest opportunity, in this case, will be the creation of locally safe and efficacious products, the creation of job opportunities through the value chains of such products, and the generation of revenue from both local and International sales of efficacious products.

5.0 Conclusion

The various challenges which face Herbal Medicine sector in Uganda include; low research, adulterations and many unsubstantiated claims on a single product. However, there are opportunities that can be exploited locally using the Reverse Pharmacology approach to drug development. The local products can easily and quickly be developed for local use and export through the Reverse Pharmacology approach. For this to be possible, the responsible authorities such as National Drug Authority, Ministry of Science, Technology and Innovation, Ministry of Health and National Bureau of Standards in Uganda and their counterparts in other African Countries can take this approach carefully to help their respective local herbal industries grow to International standard. This is possible because most of these products are already being consumed by the population in large quantities and it makes sense to use scientific methods to study those already using the products to learn about their safety and efficacy. Dose escalation studies can then be conducted after carefully evaluating the safety and efficacy of equivalent current doses and other higher doses in Animal models as a method for refining the efficacy of the available products.

Aggressive investment in basic research infrastructures, conducting Clinical Trials to allow for effective evaluation of the safety and efficacy of Herbal Medicine products produced locally is

the key to improving its uptake and realization of the economic benefit which could be hidden, in the Ugandan Traditional Medicine Sector.

REFERENCES.

1. Willcox ML, Graz B, Falquet J, Diakite C, Giani S, Diallo D. A “reverse pharmacology” approach for developing an anti-malarial phytomedicine. *Malaria Journal*. 2011;10(1):1-10.
2. Adhikari PP, Paul SB. History of Indian traditional medicine: a medical inheritance. *HISTORY*. 2018;11(1).
3. Dubick MA. Historical perspectives on the use of herbal preparations to promote health. *The Journal of Nutrition*. 1986;116(7):1348-54.
4. Jamshidi-Kia F, Lorigooini Z, Amini-Khoei H. Medicinal plants: Past history and future perspective. *Journal of herbmed pharmacology*. 2018;7(1).
5. Abuga KO. Adulteration of herbal preparations. *East and Central African Journal of Pharmaceutical Sciences*. 2021;24(1):1-2.
6. Dumba K, Kwiringira W, Namukobe J, Ntale M. Identification and Analysis of Adulterants in Aphrodisiac Herbal Medicines Sold by Private Herbal Clinics, Pharmacies and Herbal Drug Shops in Kampala, Uganda. *East and Central African Journal of Pharmaceutical Sciences*. 2021;24(1):3-14.
7. Kwesiga V, Ekeocha Z, Byrn S, Clase K. Compliance to GMP guidelines for Herbal Manufacturers in East Africa: A Position Paper. 2021.
8. Seden K, Kamoga R. Patient safety in Uganda. *Global Patient Safety: Routledge*; 2018. p. 190-204.
9. TWAWEBWA SW. FACULTY OF MEDICINE DEPARTMENT OF PHARMACEUTICAL SCIENCES: MBARARA UNIVERSITY OF SCIENCE AND TECHNOLOGY; 2015.
10. Ang-Lee MK, Moss J, Yuan C-S. Herbal Medicines and Perioperative Care. *JAMA*. 2001;286(2):208-16.
11. The “Professional Guidelines for Regulation of Local Traditional/Herbal Medicines for Human and Veterinary Use in Uganda, Doc. No. DAR/GDL/033, Revision No. 0.”, (2022).
12. Lee T-M, Charng M-J, Tseng C-D, Lai L-P. A double-blind, randomized, placebo-controlled study to evaluate the efficacy and safety of sta-2 (green tea polyphenols) in patients with chronic stable angina. *Acta Cardiologica Sinica*. 2016;32(4):439.
13. Mak JC. Potential role of green tea catechins in various disease therapies: progress and promise. *Clinical and Experimental Pharmacology and Physiology*. 2012;39(3):265-73.
14. Miyata Y, Shida Y, Hakariya T, Sakai H. Anti-cancer effects of green tea polyphenols against prostate cancer. *Molecules*. 2019;24(1):193.
15. World Health Organization. WHO traditional medicine strategy: 2014-2023: World Health Organization; 2013.
16. Bhushan SV, FAIS M, Bhushan A, Kale A. GANGRENE OF THE LEFT INDEX FINGER ON APPLICATION OF AMRUTANJAN PAIN BALM. 2018.
17. Bostandjiev R, Mitra S. clinical evaluation of tentex forte and Himcolin cream in the treatment of functional erectile dysfunction. *Med Update*. 2004;11:47-51.

18. Chuan-ji L, Shao-jun W, Jian-wu H. Clinical Application and Efficacy Assessment of MEBO Scar Lotion. *The Chinese Journal of Burns Wounds & Surface Ulcers*. 2002;03.
19. Demarin V, Kes VB, Trkanjec Z, Budišić M, Pašić MB, Črnac P, et al. Efficacy and safety of Ginkgo biloba standardized extract in the treatment of vascular cognitive impairment: a randomized, double-blind, placebo-controlled clinical trial. *Neuropsychiatric disease and treatment*. 2017;13:483.
20. Dwivedi VK, Chaudhary M. Comparative wound healing efficacy of ampuicare and becaplermin in diabetic rat. *African Journal of Pharmacy and Pharmacology*. 2012;6(12):883-92.
21. Ebrahimi M, Bakhshayeshi S, Heshmat R, Shahbazi S, Aala M, Peimani M, et al. Post marketing surveillance on safety and effectiveness of ANGIPARS in treatment of diabetic foot ulcers. *DARU Journal of Pharmaceutical Sciences*. 2015(1):45-9.
22. Gharibdoost F, Faezi ST, Khorram Khorshid H, Kamali K, Solaymani-dodaran M, Chaman R. Efficacy and safety of ANGIPARS for the treatment of skin manifestations of scleroderma: a phase 2 clinical trial. *Rheumatology Research*. 2016;1(1):3-9.
23. Kenzale R, Shaikh F, Sathaye S. Evaluation of hepatoprotective effect of polyherbal formulation-Livomyn. *Int J Res in Pharmaceutical Sci*. 2011;2(3):338-43.
24. Kooy Fvd. Reverse pharmacology and drug discovery: *Artemisia annua* and its anti-HIV activity. *Artemisia annua-Pharmacology and Biotechnology*: Springer; 2014. p. 249-67.
25. Kumar AA, KP RK. ANXIOLYTIC PROFILE OF A POLYHERBAL DRUG MENTAT. 2013.
26. Loguercio C, Festi D. Silybin and the liver: from basic research to clinical practice. *World journal of gastroenterology: WJG*. 2011;17(18):2288.
27. Mohammed F, Ansam N. Clinical efficacy of Diabecon in treatment of type 2 diabetes mellitus, in newly diagnosed diabetic patients and in those on drug treatment (Glibenclamide and Metformin) in Erbil Governarate-Kurdistan Region/Iraq. *Al-Mustansiriyah Journal for Pharmaceutical Sciences*. 2013;13(1).
28. Prakash T, Kulkarni K. Koflet lozenges in the treatment of sore throat. *The Antiseptic*. 2001;98(4):124-7.
29. Preeti Dubey M, Bhandari PR. Clinical Evaluation of M2 Tone in Adolescent Menstrual Disorders.
30. Ranjana M, Misra D. Evaluation of the Efficacy of V-Gel in Vaginitis and Cervicitis. *The Indian Practitioner*. 2001;54(9):645-9.
31. Saodekar M, Anjekar C. Clinical trial with Gasex and Diarex for bowel preparation. *PROBE*. 1982;21(2):101-4.
32. Zobeiri M, Parvizi F, Rahimi R, Heydarpour F, Sheikhan HR, Navabi J, et al. Efficacy and safety of Hemoheal cream in patients with hemorrhoids: a randomized double-blind placebo controlled clinical trial. *Journal of Traditional Chinese Medicine*. 2021;41(2):301.
33. Amany M, Ajayi CO, Natukunda B, Agaba AG. Prophylactic Effects of ARTAVOL® on Plasmodium berghei Infected Mice. *East Africa Science*. 2021;3(1):58-66.
34. Martin A, Clement OA, Bernard N, Francis W, Alice B, Rose N, et al. Assessment of the immunomodulatory activity of Artavol® aqueous extract in Plasmodium berghei infected mice. *African Journal of Pharmacy and Pharmacology*. 2022;16(5):79-89.
35. Kumaran MS, Patki PS. Evaluation of an Ayurvedic formulation (Cystone), in urolithiasis: A double blind, placebo-controlled study. *European Journal of integrative medicine*. 2011;3(1):23-8.

36. Gupta P. The efficacy of *Euphorbia prostrata* in early grades of symptomatic hemorrhoids--a pilot study. *European review for medical and pharmacological sciences*. 2011;15(2):199-203.
37. Lutgen P. *Artemisia* Plants: A Deadly Weapon Against Tropical Diseases. *Int J Clin Res Trials*. 2016;1(108):2.
38. Lutgen P. Prophylaxis with *Artemisia Annu*a is very efficient: the role of chelators. *Pharm Pharmacol Int J*. 2017;5(5):00138.
39. Hughes GD, Aboyade OM, Clark BL, Puoane TR. The prevalence of traditional herbal medicine use among hypertensives living in South African communities. *BMC complementary and alternative medicine*. 2013;13(1):1-8.
40. Karungi C, Asiimwe P, Ssentongo C, Tuhaise SP, Oloro J. Effects of Herbal Medicine Use on Adherence to Conventional Anticancer Drugs. 2020.
41. Moreira DdL, Teixeira SS, Monteiro MHD, De-Oliveira ACA, Paumgartten FJ. Traditional use and safety of herbal medicines. *Revista Brasileira de Farmacognosia*. 2014;24:248-57.
42. Poppenga RH. Herbal medicine: potential for intoxication and interactions with conventional drugs. *Clinical techniques in small animal practice*. 2002;17(1):6-18.
43. Tulunay M, Aypak C, Yikilkan H, Gorpelioglu S. Herbal medicine use among patients with chronic diseases. *Journal of intercultural ethnopharmacology*. 2015;4(3):217.
44. Saxena A. Reverse pharmacology: a new approach to drug development. *Innoriginal: international journal of sciences*. 2015.
45. Dutta S, Banerjee S, Kumar S, Jain A. Reverse pharmacology: A science redefining drug discovery. *European Journal of Biomedical and Pharmaceutical Sciences*. 2019;6:245-9.
46. Patwardhan B, Mashelkar RA. Traditional medicine-inspired approaches to drug discovery: can Ayurveda show the way forward? *Drug discovery today*. 2009;14(15-16):804-11.
47. Patwardhan B, Vaidya AD. Natural products drug discovery: accelerating the clinical candidate development using reverse pharmacology approaches. 2010.
48. Raut AA, Chorghade MS, Vaidya AD. Reverse pharmacology. *Innovative Approaches in Drug Discovery*. 2017:89-126.
49. Saeidnia S, R Gohari A, Manayi A. Reverse pharmacognosy and reverse pharmacology; two closely related approaches for drug discovery development. *Current pharmaceutical biotechnology*. 2016;17(11):1016-22.
50. Arulsamy A, Kumari Y, Shaikh M. Reverse pharmacology: fast track path of drug discovery. *Pharm Pharmacol Int J*. 2016;4(3):00077.