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Corresponding author:
Maureen Nanziri Mayanja

mayanja66@yahoo.com

Author Affiliation:
College of Veterinary Medicine, Animal Resources and Biosecurity, Makerere University

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Conflicts of interest:
None declared.

Effectiveness of Ethnoveterinary Medicinal Plants of Eastern Africa in Control of Livestock Pests or Disease Pathogens: A Systematic Review

Mayanja, NM[1]; Nalubega, R[2]; Kinengyere, AA[3]; Collins, AG[4]; Ocan, M[5]; and Tabuti, JRS[6].

Review question / Objective: **a) What is the current state and distribution of evidence on medicinal plants for ethnoveterinary practice in livestock keeping communities in Eastern Africa? b) What evidence exists about the pharmacological activities and effectiveness in control of livestock pests or disease pathogens, of ethnoveterinary medicinal plants accessible to the drylands of Eastern Africa?**
Information sources: **An initial search will use the EBSCO Discovery Service and subsequently, main consideration will be made for search systems and platforms that access databases covering disciplines of Health and Agricultural Sciences including: Pubmed, Web of Science, Embase, EBSCOhost, and ProQuest. Google scholar will be used as a Web search engine to identify relevant literature. Sources of unpublished studies to undergo conventional subject searching will include the open access System for Information on Grey Literature in Europe (OpenSIGLE); Makerere Institutional Repository (MakIR) and Electronic Repository of the Addis Ababa University. Other grey literature sources will be reports from scientific research groups or government agencies such as Consultative Group for International Agricultural Research (CGIAR) and International Livestock Research Institute (ILRI).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 September 2022 and was last updated on 07 May 2023 (registration number INPLASY202290006).

INTRODUCTION

Review question / Objective: **a) What is the current state and distribution of evidence on medicinal plants for ethnoveterinary practice in livestock keeping communities in Eastern Africa? b) What evidence exists about the pharmacological activities and effectiveness in control of livestock pests or disease pathogens, of ethnoveterinary**

medicinal plants accessible to the drylands of Eastern Africa?

Rationale: Medicinal plants are those that possess therapeutic properties or exert beneficial pharmacological effect on the human or animal body (Namdeo, 2018). Ethnoveterinary medicine has been defined by different authors (Dzoyem et al., 2020; Wanzala et al., 2005), but Imrie (2005) simply described it as the study of veterinary folk medicine, which in turn is the use of plants and traditional methods for treating animals. According to Feyera, Mekonnen, Wakayo, and Assefa (2017), in Ethiopia 95% of traditional livestock remedies are prepared from plants. Ethnoveterinary medicine is one of the affordable and accessible methods for controlling livestock pests and diseases especially in pastoral communities living in hard-to-reach drylands. It can also be an alternative to the conventional medicines, which are increasingly not responding due to growing pathogen and parasite resistance.

Global interest in Ethnoveterinary Medicinal practices has increased in the last decade, leading to extensive work especially in Africa; Asia; North and South America; as well as Europe (Chakale, Mwanza, & Aremu, 2021). Research on ethnoveterinary medicinal plants varies in relation to their utility and applicability in ruminants as well as stage of development for on-farm use. The planned review is intended to unravel such evidence. A preliminary search of PROSPERO, International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY) and the Cochrane Database of Systematic Reviews was conducted and no current or underway systematic reviews or scoping reviews on the topic were identified. The objective of this systematic review is to assess the extent of the literature about effectiveness of ethnoveterinary medicinal plants, in Eastern Africa, in the prevention and treatment of pests or diseases of livestock. Livestock, in this context, is taken to mean farm animals, except poultry. The output may guide scientific research into ethnoveterinary plant items that may be developed for sustainable use by livestock keeping communities in the drylands of Eastern Africa.

Condition being studied: Pharmacological activity of traditional medicinal plants on ruminant pests, ailments, or disease pathogens.

METHODS

Search strategy: The authors are cognizant of the fact that there are problems in indexing and abstract content, making it difficult to devise a sensitive and exhaustive search strategy (Papaioannou, Sutton, Carroll, Booth, & Wong, 2009). Concepts and themes may be poorly defined, ambiguous or variability exists in their indexing in various publications, more than one strategy is thus planned.

One of the strategies to be employed is the "Contact with Experts" and will involve at least two reviewers with knowledge in ethnoveterinary medicinal plants to identify key papers. A compilation of relevant and authoritative articles, termed "pearls", will be made ready for use in the subsequent search. Another strategy will be Traditional or Citation Pearl Growing (TPG). Pearl growing involves taking a 'pearl' article and using its characteristics such as index terms and keywords in an iterative process of searching (Papaioannou et al., 2009). As described by Schlosser, Wendt, Bhavnani, and Nail-Chiwetalu (2006), TPG will be done by noting how the 'pearls' compiled earlier are indexed, in only one database, in terms of keywords and quality filters. Those index terms will then be applied and a search for other relevant articles will be done in a single database. Any new index terms found in articles identified in the new search will be added - to retrieve more articles of the same kind. An iterative process of searching the selected database will continue until a repeat of the search with additional index terms yields no further entries.

Subsequently, a three-step strategy will be followed to locate published, unpublished studies and gray literature and may be updated towards the end of review. In the first phase, an initial limited search using the EBSCO Discovery Service will be

undertaken. From identified articles on the topic free-text words in the title and abstract will then be analysed and, together with all index terms identified during TPG, used to develop a full search strategy. This search strategy will be followed in the process of searching subsequent databases.

In the second phase, a conventional subject search will be applied across all published and unpublished databases or sources starting with PUBMED. However, given that some items like subject headings and fields are database specific, the search strategy, including all identified keywords and index terms, will be adapted for each included database, information source and academic search systems. This conventional subject search will be the principal technique entailing the development of a search strategy around terms relevant to the PICOS framework and to the index terms identified during the first stage of this search process. These terms will be in combination with Boolean and Proximity operators; Truncation; Wildcard characters; Synonyms and acronyms of text words, limiters and quality filters where found relevant. To bring key concepts together, the search terms within a single element of the PICOS framework will be combined using the Boolean operator "OR" while those among one or more elements will be combined using "AND" with appropriate brackets included. Search strings combining all different elements of the PICOS framework will be adjusted based on the requirements of each database. The search for each of the selected databases will initially involve use of a combination of terms and keywords, free terms and their derivatives or synonyms as well as any relevant index terms that may be identified during preliminary phases of the search. The proposed systematic review will be conducted in reference to, among others, the Joan Brigg's Institute methodology for reviews (Aromataris & Munn, 2020).

Participant or population: Ethnoveterinary medicinal plants that are used in of control of livestock pests or diseases will be considered.

Intervention: Medicinal plants have been tested for pharmacological activities including antibacterial, antifungal, anthelmintic; acaricidal; antioxidant, antimycobacterial, anti-inflammatory and cytotoxicity (Kumsa and Hagos (2020), Kalayou et al. (2012), Eguale, G.Tilahun, Gidey, and Mekonnen (2006)). Studies of ethnoveterinary medicinal plant pharmacological activity and effectiveness on livestock pests, ailments and disease pathogens will be considered.

Comparator: n/a.

Study designs to be included: This systematic review will consider both experimental and quasi-experimental evaluation studies that report positive outcomes; in-vivo and in-vitro assays and phytochemical composition assessment. Qualitative studies that focus on ethnoveterinary medicinal plant use including, but not limited to qualitative description and action research, will be considered.

Eligibility criteria: Studies done on plant items not indigenous to or inaccessible within the Eastern African region will be excluded. Publications with a temporal boundary of publications from 1995 forward will be considered. This period is considered based on Wanzala et al. (2005), who noted that a sizeable body of published literature and annotated bibliography abstracting on ethnoveterinary medicine exists since 1996.

Information sources: An initial search will use the EBSCO Discovery Service and subsequently, main consideration will be made for search systems and platforms that access databases covering disciplines of Health and Agricultural Sciences including: Pubmed, Web of Science, Embase, EBSCOhost, and ProQuest. Google scholar will be used as a Web search engine to identify relevant literature. Sources of unpublished studies to undergo conventional subject searching will include the open access System for Information on Grey Literature in Europe (OpenSIGLE); Makerere Institutional Repository (MakIR)

and Electronic Repository of the Addis Ababa University. Other grey literature sources will be reports from scientific research groups or government agencies such as Consultative Group for International Agricultural Research (CGIAR) and International Livestock Research Institute (ILRI).

Main outcome(s): Potential of ethnoveterinary medicinal plant to control or cause complete destruction of livestock pests and disease pathogens. Evidence of healing livestock ailments.

Data management: The search will be accurately documented and reproducible; all identified citations will be collated and uploaded into Endnote software (version 20.2.1.15749 for Windows, Thomson Reuters, New York). An EndNote file will initially be created for each database searched; all the files will then be merged into a single file and duplicates will automatically be removed. Searches will undergo an examination for duplicate publications; patterns of publication over time, by type of publication, country of origin and the sector in which the reflective account took place as a means of data extraction.
The authors whose full texts papers cannot be accessed by the numerous internet-based sources used, will be requested to provide them through their emails. Reasons for exclusion of sources of evidence at full text that do not meet the inclusion criteria will be recorded and reported in the review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion, or with an additional reviewer/s. The results of the search and the study inclusion process will be reported in full in the final review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses – PRISMA revised flow diagrams for original reviews (Page et al., 2021). This will indicate the number of included and excluded studies and the corresponding reasons for exclusion.

Quality assessment / Risk of bias analysis: The search will be accurately documented and reproducible; all identified citations will be collated and uploaded into Endnote software (version 20.2.1.15749 for Windows, Thomson Reuters, New York). An EndNote file will initially be created for each database searched; all the files will then be merged into a single file and duplicates will automatically be removed. Searches will undergo an examination for duplicate publications; patterns of publication over time, by type of publication, country of origin and the sector in which the reflective account took place as a means of data extraction.
The authors whose full texts papers cannot be accessed by the numerous internet-based sources used, will be requested to provide them through their emails. Reasons for exclusion of sources of evidence at full text that do not meet the inclusion criteria will be recorded and reported in the review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion, or with an additional reviewer/s. The results of the search and the study inclusion process will be reported in full in the final review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses – PRISMA revised flow diagrams for original reviews (Page et al., 2021). This will indicate the number of included and excluded studies and the corresponding reasons for exclusion.

Strategy of data synthesis: A draft data extraction tool will be developed based on the insights on choice of data extraction tools, by Elamin, Flynn, Bassler, Briel, and Pablo Alonso-Coello (2009), and revised as necessary during the process of extracting data from each included evidence source. Modifications will be detailed in the review. Using that developed tool, data will be extracted from papers included in the review by two or more independent reviewers. The data extracted will include specific details about the population, intervention, concept, outcome, setting, study methods and key findings relevant to the review questions. Any disagreements

that arise between the reviewers will be resolved through discussion, or with an additional reviewer. If appropriate, authors of papers will be contacted to request missing or additional data, where required.

Subgroup analysis: n/a.

Sensitivity analysis: n/a.

Language restriction: Searches will be restricted to English or French language publications.

Country(ies) involved: Authors are specifically from Uganda, which lies astride the equator in Eastern Africa. The review considers studies relevant to the Eastern Africa countries including Uganda, Kenya, Tanzania, Ethiopia, Burundi, Eritrea, Rwanda, Somalia, Somaliland and Djibouti.

Keywords: Farm animals; Pharmacological activity; Phytochemical composition; Phytomedicinal.

Dissemination plans: Guided by a commentary by Pieper and Rombey (2020), that identified and characterised current options to prospectively register a systematic review, this protocol is registered in the open access International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY) registry. This registry explicitly mentions acceptance of systematic review protocols assessing interventions and animal studies.

Contributions of each author:

Author 1 - Mayanja Nanziri Maureen - MNM - Provided Team leadership, technical expertise on review processes and drafted protocol for editing by team members.
Email: mayanja66@yahoo.com
Author 2 - Nalubega Rebecca - RN - Read through several drafts and provided content expertise on ethnoveterinary medicinal plants.
Email: drnalubegar@gmail.com
Author 3 - Kinengyere Annet Alison - AAK - developed the final search strategy, run the searches reviewed the protocol.
Author 4 - Atuheire Grace Collins - CGA – Guidance on statistical and other analysis as will be deemed necessary in the review process.
Email: atuheirecollinsgrace@gmail.com
Author 5 - Ocan Moses - MO – Expert advisor on systematic review and evidence synthesis.
Author 6 - Tabuti RS. John - JT – Content Expert for ethnoveterinary medicinal plants and practice.
Email: jtabuti@gmail.com

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APPENDIX I SEARCH STRATEGY FOR PROQUEST CENTRAL

abstract((Ethnoveterinary plants OR ethnoveterinary medicinal plants OR Indigenous medicinal plants OR ethnomedical plants OR medicinal plants OR combined aqueous herbal extract* OR leaf extract* OR cattle disease* herbal remed* OR traditional cattle medicine OR folk medicine OR herbal remed* OR herbal preparation OR tincture OR essential oils OR phytochemical OR phytogenic OR tannins OR alkaloids OR flavonoids OR polyphenols OR phenols OR terpenoids OR terpenes OR carotenoids OR glycosides)) AND abstract((Antimicrobial OR anthelmintic OR antiparasitic OR antinematodal OR antinematode OR antimycoplasm* OR antiviral OR anti-tick OR repellent OR acaricidal properties OR Acaricidal activity OR Anti-tick activity OR bioacaricidal activity OR acaricidal OR bactericidal OR antibacterial effect OR antibacterial activit* OR antibacterial properties OR wound healing activit* OR antioxid* OR anti-inflam* OR cytotoxicity OR cytotoxic OR toxicity OR phytoparasiticidal OR phytotherapy OR "Biodegradable parasiticide" OR in vitro antimicrobial activit* OR "in vitro anthelmintic" OR phytochemical properties OR phytochemistry OR Immune response OR Adjuvants OR Immunomodulatory OR Ethnomedicines OR Phytochemicals OR ethnomedical AND ethnoveterinary OR Pharmacological activity OR Ethnopharmocolog* OR Larvicidal OR anti rickettsial OR anti babesial OR antileishmanial OR anti-trypanosomal activity OR antiprotozoal OR antiviral OR "anti-rift valley fever virus" OR antidiarrheal OR "analgesic activity" OR "antipyretic activity" OR antinociceptive)) AND abstract(((pests OR disease pathogens OR infectious OR infections OR outbreaks OR ailment*) AND (Livestock OR ruminants OR

cattle OR goats OR sheep OR camel OR farm animals OR herd OR bovine OR calves OR beef cattle OR dairy cattle OR porcine OR ovine))) AND abstract((Eastern Africa OR Uganda OR Eastern Africa drylands OR Kenya OR Tanzania OR Ethiopia OR Burundi OR Ethiopia OR Eritrea OR Rwanda OR Somalia OR Somaliland OR Djibouti))