INPLASY PROTOCOL

Corresponding author:
Maureen Nanziri Mayanja

mayanja66@yahoo.com

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

Review Stage at time of this submission: The review has not yet started.

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]; Tabuti, JRS[3]; Atuheire, CG[4].

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: 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 also be considered. In addition, systematic reviews that meet the inclusion criteria will be considered.

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: 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. 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). However, 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. Increasing evidence strongly suggests that Ethnoveterinary practices have the potential to improve livestock health in Sub-Saharan Africa (McLachlan et al., 2019). Oyda (2017) noted that Ethnoveterinary practices have retained their popularity in South Africa, and their use is rapidly spreading in the rest of Africa. Ethno-veterinary 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. Ethnoveterinary medicine can also be a possible alternative to the conventional medicines which are increasingly not responding due to growing pathogen and parasite resistance. According to Feyera, Mekonnen, Wakayo, and Assefa (2017), in Ethiopia 95% of traditional livestock remedies are prepared from plants. The planned review is intended to unravel such evidence which may guide scientific research into sustainable development of ethnoveterinary plant items for use, especially by livestock keeping communities in the drylands of Eastern Africa. Livestock is taken to mean, farm animals, except poultry. 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 control of livestock pests or disease pathogens.

Condition being studied: This review is to establish evidence of Effectiveness (of such pharmacological activity of traditional medicinal plants) on livestock ruminant pests or disease pathogens.

METHODS

Search strategy: This protocol has been developed with reference to the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol – PRISMA-P 2015 outlined by Moher et al. (2015). The proposed systematic review will be conducted in reference to, among others, the Joan Brigg's Institute methodology for reviews (Aromataris & Munn, 2020). The current 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 search 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 thus be made ready for use in the subsequent search.

The next search 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 the Scopus as 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 Scopus 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. The Peer Review of Electronic Search Strategies (PRESS) 2015 Evidence-Based Checklist, as given by McGowan et al. (2016), will be used as a guide to prepare a strategy that will result in a comprehensive search with minimal errors. This primary search strategy will be subjected to peer review.

In the second phase, a conventional subject search will be applied across all published and unpublished databases or sources. 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. Evidence from the systematic evaluation and comparison of search and retrieval qualities of academic search systems by Gusenbauer and Haddaway (2020), has been considered in proposing the following search systems and platforms. Main consideration will be made to search those that access databases covering disciplines of Health and Agricultural Sciences including: Embase, Pubmed, ProQuest, ScienceDirect, EBSCOhost and Web of Science. Other platforms and databases to be searched are CAB Direct, African Journals Online (AJOL), Directory for Open Access Journals (DOAJ), Semantic Scholar, JSTOR, Research4Life (Hinari, AGORA, OARE, GOALI, ARDI) and Worldwide Science.

Sources of unpublished studies to undergo conventional subject searching will include: DATAD Repository, Networked Digital Library of Theses and Dissertations, Makerere Institutional Repository (MakIR) and Electronic Repository of the Addis Ababa University. In addition, grey literature sources will include Consultative Group for International Agricultural Research (CGIAR); technical reports from scientific research groups or government agencies such as National Agricultural Research Organisations (NARO) found in Eastern Africa; International Livestock Research Institute (ILRI) and the open access System for Information on Grey Literature in Europe (OpenSIGLE). Google scholar will be used as a Web search engine to identify relevant literature.

In the third stage of the search process, ancestry searches will be done by using the reference listing from all studies that will have been identified for critical appraisal, by the various methods, to locate additional studies. Any relevant articles that will not have shown up in in the electronic data base subject search will be added to the overall search yield. The 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. For example:

o "Ethnoveterinary plants in Eastern Africa" OR "ethnoveterinary plants in control of livestock pests or diseases in Eastern Africa".

o "(Livestock) AND Eastern Africa AND (ethnoveterinary control of livestock pests or diseases)"

o "(ruminants, cattle, goats, sheep, camel) AND East* Africa AND (ethno* use in livestock pests and diseases)"

o "(Ethnoveterinary plants) AND (Pharmacological activity)"

o "(Ethnoveterinary plants) AND (Effectiveness)"

o "(antimicrobial OR anthelmintic OR acaricidal OR antiparasitic) AND (activity of ethnoveterinary plants)"

o "(antioxid* OR anti-inflam* OR cytotox*) AND (activity of ethnoveterinary plants)".

Participant or population: This review addresses issues about ethnoveterinary medicinal plants. Ethnoveterinary medicinal practices involve the use of plants and in Eastern Africa, some pastoralists prefer traditional medicinal plants to modern medical system for their livestock (Obakiro et al., 2020). However, 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. This review addresses issues about ethnoveterinary medicinal plants. Ethnoveterinary medicinal practices involve the use of plants however, 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.

Intervention: Many plants are 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)). This review is to establish evidence of such pharmacological activity on livestock (ruminant) pests or disease pathogens.

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 also be considered. In addition, systematic reviews that meet the inclusion criteria will be considered.

Eligibility criteria: Studies done on items not indigenous to or not accessible within the Eastern African region will be excluded.

Information sources: 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 also be considered. In addition, systematic reviews that meet the inclusion criteria will be considered.

Main outcome(s): The review intends to provide evidence of the potential for ethnoveterinary medicinal plants to control or cause complete destruction of pests or disease pathogens.

Data management: Following the search, all identified citations will be collated and uploaded into Endnote software (version X8.0.1 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.

Following a pilot test, titles and abstracts will then be screened by at least two or more independent reviewers for assessment against the inclusion criteria for the review. Potentially relevant sources will be retrieved in full and their citation details imported into the JBI SUMARI review management software (Munn et al., 2019).

The full text of selected citations will be assessed in detail against the inclusion criteria by two or more independent reviewers. 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. 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.

Quality assessment / Risk of bias analysis: Standard checklists of quality assessment criteria, including those from the Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information - JBI SUMARI (Munn et al., 2019) will be used to appraise studies.

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: Uganda is located in East Africa and lies astride the equator.

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

Dissemination plans: Guided by a commentary by (Pieper & Rombey, 2020), that identified and characterised current options to prospectively register a systematic review, this protocol will be registered in the open access INPLASY registry. This registry explicitly mentions acceptance of systematic review protocols assessing interventions and animal studies.this protocol will be registered in the open access INPLASY registry. This registry explicitly mentions acceptance of systematic review protocols assessing interventions and animal studies.

Contributions of each author:
Author 1 - Maureen Nanziri Mayanja - Provided Team leadership, technical expertise on review processes and drafted protocol for editing by team members.
Email: mayanja66@yahoo.com

Author 2 - Rebecca Nalubega - Read through several drafts and was the content expert on ethnoveterinary medicinal plants. Email: drnalubegar@gmail.com

Author 3 - John R. S. Tabuti - Reviewed final drafts and provided content expertise on ethnoveterinary practice. Email: jtabuti@gmail.com

Author 4 - Collins Grace Atuheire - Provision of statistical and other analysis as will be deemed necessary. Email: atuheirecollinsgrace@gmail.com

References: Chakale, M. V., Mwanza, M., & Aremu, A. O. (2021). Ethnoveterinary knowledge and biological evaluation of plants used for mitigating cattle diseases: A critical insight into the trends and patterns in South Africa. Frontiers in Veterinary Science, 891.

Dzoyem, J. P., Tchuenteu, R. T., Mbarawa, K., Keza, A., Roland, A., Njouendou, A. J., & Assob, J. C. N. (2020). Ethnoveterinary medicine and medicinal plants used in the treatment of livestock diseases in Cameroon. In Ethnoveterinary Medicine (pp. 175-209): Springer.

Eguale, T., G.Tilahun, Gidey, M., & Mekonnen, Y. (2006). In Vitro Anthelmintic Activities of Four Ethiopian Medicinal Plants Against Haemonchus Contortus. Pharmacology online, 3, 153-165.

Elamin, M. B., Flynn, D. N., Bassler, D., Briel, M., & Pablo Alonso-Coello, P. J. K., Gordon H. Guyatt, German Malaga, Toshiaki A. Furukawa, Regina Kunz, Holger Schünemann, Mohammad Hassan Murad, Corrado Barbui, Andrea Cipriani, Victor M. Montori. (2009). Choice of data extraction tools for systematic reviews depends on resources and review complexity. Journal of Clinical Epidemiology, 62(5), 506-510. Retrieved from https://doi.org/10.1016/j.jclinepi.2008.10.016

Gusenbauer, M., & Haddaway, N. R. (2020). Which academic search systems are suitable for systematic reviews or meta-analyses? Evaluating retrieval qualities of Google Scholar, PubMed, and 26 other resource. Research Synthesis Methods, 11, 181-217. doi:10.1002/jrsm.1378

McGowan, J., Sampson, M., Salzwedel, D., Cogo, E., Foerster, V., & Lefebvre, C. (2016). PRESS Peer Review of Electronic Search Strategies: 2015 guideline statement. Journal of Clinical Epidemiology, 75, 40-46.

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., & Mark Petticrew, P. S., Lesley A Stewart and PRISMA-P Group. (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Systematic Reviews, 4(1). Retrieved from http://www.systematicreviewsjournal.com/content/4/1/1

Wanzala et al (2005). Ethnoveterinary medicine: a critical review of its evolution, perception, understanding and the way forward. Livestock Research for Rural Development 17(11).