Homeopathy, Acupuncture and Phytotherapy in the Veterinary Treatment or Prophylaxis of Diseases in Animals: An Overview of Systematic Reviews

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Abstract

Introduction Complementary and alternative veterinary medicine (CAVM) has been intensively used, and there is currently an increasing demand for a more rigorous approach regarding its clinical effectiveness.

Aims The objectives of this overview were: first, to identify systematic reviews on homeopathy, acupuncture and phytotherapy in veterinary medicine and assess their methodological quality; and second, to map interventions and findings in the treatment or prophylaxis of any medical conditions in any animal species for which high-quality systematic reviews had identified reliable evidence of efficacy or effectiveness in randomized controlled trials (RCTs) or controlled clinical trials (CCTs).

Method The study was an overview of systematic reviews published in the years 2000 to 2022 inclusive. The following databases were used: CAB Abstracts, PubMed and Vet Index, from which the abstracts of 173 articles were extracted, 22 of which were initially included for complete analysis. After excluding 15 studies according to the exclusion/inclusion criteria, 7 review papers were comprehensively analyzed. The review quality was assessed by the Measurement Tool to Assess Systematic Reviews (AMSTAR 2) method. The reported RCTs/CCTs in these reviews were analyzed for their reliability, and the results were classified according to statistical significance and risk of bias.

Results Seven eligible systematic reviews reported studies on dogs, horses, cats, cattle, sheep, goats, swine, rabbits and poultry. The number of primary RCTs/CCTs was 38 for homeopathy, 35 for acupuncture, and 171 for phytotherapy. The AMSTAR 2 evaluation ranked two reviews of veterinary homeopathy as high-quality, in which two placebo-controlled RCTs comprised reliable evidence, one of which reported efficacy of homeopathy as prophylaxis for diarrhea in pigs. The systematic reviews of acupuncture and phytotherapy were all of low quality, preventing formal assessment of their reviewed RCTs/CCTs.

Keywords
- complementary therapies
- randomized clinical trials
- systematic review
- veterinary medicine

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Conclusion Only the systematic reviews of homeopathy were rated of sufficient quality to enable the assessment of reliable evidence within their reviewed RCTs. Contemporary high-quality systematic reviews of clinical trials in each of the three areas of CAVM are required.

Introduction

There is consensus that acquired microbial resistance to drugs renders humans and animals increasingly vulnerable to disease. This problem is not only restricted to the resistance of bacteria, fungi and protozoa, but also includes viruses, and it is associated with losses in animal production and reduced animal welfare.[1–6] In addition, there is a persistent risk of transmission between wild and domestic animals and humans.[7–9] The development of new treatments for infectious and non-communicable diseases has therefore been in increasing demand.[10–13]

Interest in complementary veterinary practices has also grown recently, especially with the development of ethnoveterinary medicine. The latter seeks to use regional resources (medicinal plants) to treat animals and is a field of expertise for improving animal health and welfare associated with traditional and indigenous knowledge. Moreover, it could be a valuable tool for animal production and zoonosis control, especially in developing countries.[14–17] Drugs prepared with plant extracts are multi-component compounds characterized by action on multiple pharmacological targets.[18] They are helpful as a support tool for farm animal treatments. Moreover, some plants have immunomodulatory potential.[11,19–22]

In addition to the interest in systematizing ethno-veterinary medicine,[20,21] other traditional practices are commonly used to treat various diseases.[23] Homeopathy and acupuncture are the most used[24] for companion and production animals and, to a lesser extent, exotic species.[12,25–29] Although such practices are often analyzed as a single set, it is necessary to note that, unlike phytotherapy, homeopathy and acupuncture are based on empirical observations, each with an underlying rationale that differs from Western medicine.[30,31] However, applying scientific methods[11,13,18,32–35] allows for establishing phenomenological features that improve and refine these clinical practices in a way that cannot be easily achieved from their traditions alone.

Those scientific studies have described effects, including gene expression and neuro-immuno-endocrine regulation, based on different mechanisms such as anatomical connections between acupoints and nerve endings, hormesis, cytoskeleton organization, or epigenetic-driven processes.[32–40] Such findings underpin the potential for applying these therapies in ensuring animal welfare, whose growing need has driven the establishment of guidelines and specific legislation in several countries.[25,41,42]

The recent approximation between tradition and science has thus generated a new demand: the need to conduct scientific research to assess the effectiveness and safety of these therapies.[6,22,43–47] For example, the regulation of organic farms states that livestock should be treated preferably with phytotherapeutic products and other complementary therapies. However, scientific publications in this field still need to be made available,[1,21,48] leading to the necessity of using conventional drugs, mainly to treat infections. In 2017, the organic market moved 92 billion Euros globally, which is still growing due to high global demand.[49] The average annual growth of trade in organic products has been over 11% since 2000, a rate much higher than that of non-organic agricultural products. This international demand for organic products will undoubtedly increase further in the coming years. The consumption of such products is often associated with consumer safety and health, along with less social and environmental damage.[50]

In this scenario, it is of considerable importance to search for accurate and elucidative information on the efficacy and effectiveness of such therapies in veterinary medicine (efficacy is the clinical performance shown by tests in which the treatment is evaluated under controlled conditions, while effectiveness is the clinical performance in the "real world"). For this reason, an overview of reviews in this area of veterinary medicine was proposed, considering that such publications occupy the top of the evidence pyramid[51] and cover critical analysis items such as the risk of bias (RoB) in the primary studies. Such aspects are recent demands within complementary veterinary medicine and general veterinary clinical research.[52]

An "overview of systematic reviews" is a type of study that compiles evidence from various intervention reviews to produce an accessible and helpful research summary; thus, reporting the methodological quality of each included review is recommended. According to Pollock and collaborators in 2021[53], "overviews" are an increasingly popular form of evidence synthesis, as they aim to provide "user-friendly" summaries to aid decision-making by managers and professionals without the need to assimilate the results of several, sometimes contradictory, systematic reviews.[53,54]

Aims

The present study aimed to characterize and assess the quality of published systematic or scoping reviews about homeopathy, acupuncture, or phytotherapy (the use of medicinal plants) for the veterinary treatment or prophylaxis of any medical condition in any animal species (primary objective), thus providing overarching information for veterinarians who want to use such practices or for researchers who wish to advance in this field.

For randomized controlled trials (RCTs) and controlled clinical trials (CCTs) within high-quality systematic reviews, a further more focused aim (secondary objective) was to identify reliable evidence in each of veterinary homeopathy, acupuncture and herbal medicine, wherein a relationship (causal or associative) between intervention and clinical outcome had been investigated. Identifying the best examples of such veterinary trials would encourage those same research methods to be followed in future studies.

Methods

A search strategy focused on systematic reviews, scoping reviews and/or meta-analyses was used as a starting point to identify reviews whose original content was controlled trials (randomized or non-randomized). Reviews published from January 2000 to December 2022 inclusive were considered for the overview. No restrictions on animal species were applied.

Data Sources

The search for data on the effectiveness and efficacy of the specified interventions (homeopathy, acupuncture and herbal medicine in veterinary medicine) was carried out by searching for systematic review articles and/or meta-analyses using the databases PubMed, CAB Abstracts, and Veterinary Index. The selection of only systematic review articles (with or without meta-analyses) and scoping reviews was based on a need to obtain evidence of effectiveness with the highest possible reliability based on the evidence pyramid.[51]

In the PubMed database, the results were searched using the following topics: "homeopathy", "acupuncture", "phytotherapy", "medicinal plants", "veterinary", "systematic review", "meta-analysis", "systematic review with meta-analysis", "systematic review", "meta-analysis". In the CAB Abstracts database, the search was based on the following subjects: "homeopathy", "acupuncture", "medicinal plants", "phytotherapy", "veterinary", and "evidence-based research". And in the Veterinary Index database, the defined topics were (in Portuguese) "homeopathy", "acupuncture", "phytotherapy", "medicinal plants", and "veterinary".

Thus, the search strategy was developed by author M.T., who is a librarian and information specialist, and was established as follows:

PubMed

((homeopathy OR phytotherapy OR medicinal plants OR acupuncture) AND (veterinary)) AND (systematic review OR meta-analysis OR systematic review with meta-analysis).

Result: 56 studies.

https://bit.ly/38BJuA3.

CAB Abstracts

((homeopathy OR "medicinal plants" OR acupuncture OR phytotherapy) AND (veterinary)).

Refinements: Item Types = Evidence-Based Research.

Result: 62 studies.

https://bit.ly/2XmSKFZ.

Vet Index (Portuguese)

(tw:(homeopatia OR fitoterapia OR plantas medicinais OR acupuntura)) AND (tw:(veterinária)) AND (tw:(revisão sistemática OR metanálise)).

Result: 55 studies.

https://bit.ly/3BCzOBU.

These databases were chosen due to the increased probability of finding eligible studies among reviews published in languages known to the present group of authors: English and Portuguese were thus selected as suitable languages. The primary literature search was carried out in 2021, with a more recent update for the purposes of the current paper: these surveys resulted in 173 potential systematic reviews (including duplicates) being identified. They were uploaded into the Rayyan digital tool[55] to first screen articles through abstract analysis, removing duplicate items and papers that did not adhere to the inclusion criteria (see below).

Identification of Articles for Complete Data Extraction

The files in RIS and NBIB formats were uploaded to the Rayyan platform by authors M.T. and E.C.M. Among the abstracts resulting from the search, two duplicates were excluded. The remaining abstracts were selected in parallel by two evaluating authors (E.C.M. and L.V.B.), who were blinded so that they could not observe one another's decisions during the analyses. After completing this first analysis, the double-blind mode on the Rayyan platform was removed by M.T., and the differences found were resolved by consensus between E.C.M. and L.V.B.

In short, among the 173 abstracts retrieved from the literature, two were removed due to duplication, and 171 were analyzed in this first screening.

Criteria for Eligibility

In all evaluation phases, the inclusion and exclusion criteria were pre-defined as follows.

Inclusion

- Systematic or scoping review article with or without meta-analysis, even if the nature of the method was not described clearly in the title.
- A review based on effectiveness or efficacy studies in animals, without restrictions regarding the species studied or the nature of the diseases reviewed.
- Published in English or Portuguese, with an abstract in English, during the period January 2000 to December 2022 inclusive.
- Review that includes two or more clinical studies that used homeopathy, acupuncture, or medicinal plants (phytotherapy), even if the review was focused primarily on conventional approaches to a specific condition.
- Review that allows a cause-effect or a clear associative relationship between intervention and clinical outcome to be identified.
- Published as a scientific article in an indexed peer-reviewed journal.

- Treatment and/or prophylaxis was the subject of the review.

Exclusion

- Review published in a format other than systematic, scoping, or meta-analysis.
- Review focused on a specific clinical outcome and included articles reporting various therapeutic approaches, resulting in the reporting of just a single primary study related to homeopathy, acupuncture, or herbal medicine.
- Review with a focus on *in-vitro* research, research on experimental animals (non-clinical approach), or clinical research with no control group.
- Review reporting interventions in which medicinal plants were used in a mixture of plant extracts in such a manner that prevented the assessment of each plant's effects.

The search for reviews was limited to those published no earlier than January 2000 due to the significant upgrade thereafter in methodological quality compared to prior reviews, partly associated with the development of proper metrics to evaluate evidence in systematic reviews.[56–58]

After the preliminary view from the RAYYAN platform, 22 articles were selected for detailed full-text analysis, followed by a new screening and selection according to the inclusion and exclusion criteria. Authors E.C.M., J.K.H., and L.V.B. performed this step. From this second screening, 15 reviews were excluded for the reasons reported in ►**Supplementary File 1** (available online only) and 7 reviews were considered eligible for the main analysis.

Data Extraction and Management

From this second selection, the content of the seven articles considered eligible was compiled into three tabulations: (1) eligible reviews' design, the type of reported trials included and their respective controls, and the species used for treatment or prophylaxis; (2) characterization of eligible reviews according to the quality of review methods employed and whether they included RoB assessment of the primary studies, previously defined by consensus among authors E.C.M., M.T., L.V.B., and J.K.H.; (3) clinical condition and classification of findings from reliable trials extracted from high-quality systematic reviews. The first two tabulations refer to the primary objective of this article, while the third tabulation refers to the secondary objective.

Authors E.C.M. and L.V.B. identified the review papers, characterized the interventions, and analyzed the findings; author N.S. reviewed those extracted data. Aspects related to the quality of the selected reviews were analyzed employing the "level of confidence" criteria proposed in the Measurement Tool to Assess Systematic Reviews (AMSTAR 2) to rate overall confidence in a review's results, and comprising a checklist composed of 16 items (**Box 1**).[56,59] This was a step elaborated by author E.C.M. and revised by J.K.H. In both cases, differences were resolved by consensus.

According to this method, a review presenting weaknesses in none or only one non-critical item is classified as one that can be viewed with "high overall confidence"; a classification "moderate degree of overall confidence" is attributed to a review showing weaknesses in more than one non-critical item; a "low overall confidence level" is attributed to a review showing weaknesses in one critical item; and a "critically low overall confidence" level is assigned to a review showing weaknesses in more than one critical item.[56,59]

We regarded a "high quality" review paper as one whose AMSTAR 2 rating was "high level of confidence". By definition, such a review included an assessment of the RoB per RCT/CCT. Among the quality analyses, item 9 from the AMSTAR 2 checklist was key to assessing whether review

Box 1 Critical and non-critical items from the AMSTAR 2 checklist of 16 items

Critical items for this overview.
2. Did the review article explicitly state that the review methods were established before the review was carried out, and did this justify any significant deviation from the protocol?
4. Did the review authors use a comprehensive literature search strategy?
7. Did the review authors list excluded studies and justify the exclusions?
9. Did the review authors use a satisfactory technique to assess the risk of bias (RoB) in individual studies included in the review?
11. If meta-analysis was performed, did the review authors use appropriate methods for the statistical combination of results?
13. Did the review authors consider the RoB in individual studies when interpreting/discussing the review results?
15. If they performed quantitative synthesis, did the review authors conduct an adequate investigation of publication bias (slight study bias) and discuss its likely impact on the review results?

Non-critical items for this overview.
1. Did the survey questions and inclusion criteria for the review include the PICO components (population, intervention, comparison, and outcome)?
3. Did the review authors explain their selection of study designs for inclusion in the review?
5. Did the review authors perform study selection in duplicate?
6. Did the review authors perform the extraction of duplicate data?
8. Did the review authors describe the included studies in adequate detail?
10. Did the review authors report funding sources for the studies included in the review?
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies, on the meta-analysis or other evidence synthesis results?
14. Did the review authors provide a satisfactory explanation for and discuss any observed heterogeneity in the review results?
16. Did the review authors report any potential sources of conflict of interest, including any funding received for conducting the review?

Abbreviation: AMSTAR, Measurement Tool to Assess Systematic Reviews.

authors used a satisfactory (or any) method to assess the RoB in each of the primary trials included in their review. Naturally, any observational (non-controlled) studies cited in the reviews were not considered.

Classification and Evaluation of Findings

The findings for the intervention–outcome associations in the trials included in a high-quality review were classified herein into five categories: "Positive", "Potentially positive", "Ineffective", "Inconclusive", and "Negative". This classification was adapted from that of others[60,61] but reflected the statistical significance of the reported effects in controlled trials (RCTs or CCTs) that were described by the authors of the original review as "reliable evidence" based on an evaluation of low RoB.

No restriction to the studied clinical findings was applied. The intervention–outcome association described for the main outcome per relevant RCT or CCT included in eligible reviews was classified as follows.

Positive: The presence of statistical significance for the main outcome of the intervention group in relation to a negative control group or equivalence with standard care.[54,62]

Potentially positive: Identification of statistical significance between intervention and negative controls or equivalence with standard treatments, but with insufficient experiments in the same intervention category precluding specific meta-analysis.

Ineffective: The absence of statistical significance between intervention and negative controls or statistical significance in favor of standard care in relation to the tested intervention.

Inconclusive: Identification of inadequate statistical analysis, impairing a definitive conclusion.

Negative: A statistically significantly worse clinical picture with the intervention: that is, only side- or undesirable effects observed after treatment.

Results

The workflow was managed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 diagram[63,64] (►**Fig. 1**). The recovered data from each eligible review were transcribed into a spreadsheet. ►**Table 1** and ►**Table 2** were generated, containing the main information from each review and mentioning relevant aspects of the reported primary clinical trials.

Characterization of Review Studies

Of the seven papers that were eligible for this overview, there were two homeopathy reviews, two acupuncture reviews, and three reviews on phytotherapy or medicinal plants.[1,44,65–69] Almost all review authors declared no conflict of interest, and some declared that there was no funding for the research. All seven selected studies were systematic reviews (no scoping reviews) (►**Table 1**).

The species reported in the review articles were dogs, horses, cats, cattle, sheep, goats, swine, rabbits, and poultry

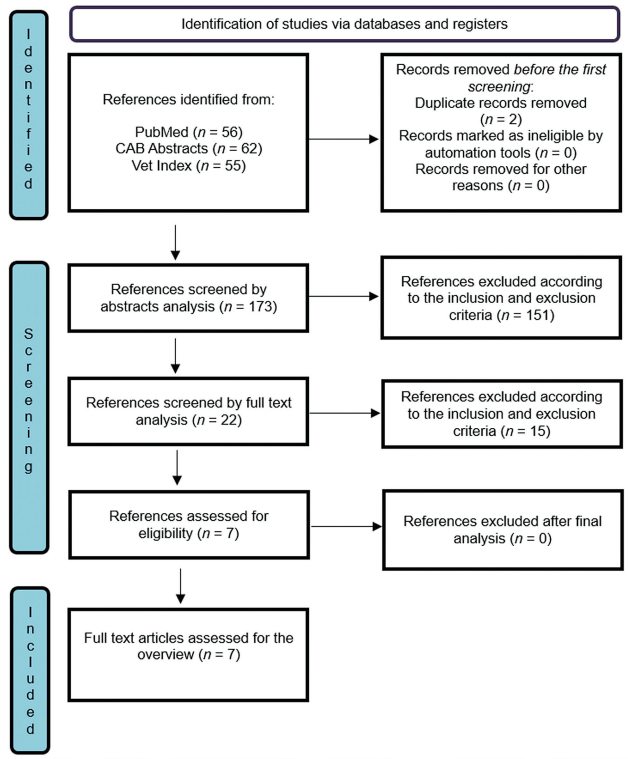

Fig. 1 PRISMA 2020 flow diagram.[63]

(►**Table 1**). Two reviews[1,66] reported further demographic details such as sex, age, breed, or whether these items were described in the primary studies.

The total number of primary articles (RCTs or CCTs) assessed in the reviews was 38 for homeopathy, 35 for acupuncture, and 171 for medicinal plants (►**Supplementary File 2**, available online only).

The countries where the primary studies were carried out included Brazil, China, England, Finland, Germany, India, Italy, Mexico, Netherlands, Norway, Scotland, Sweden, Switzerland, Turkey, and the United States. Four reviews did not report any relevant data on geographic location.

None of the reviews reported the occurrence of adverse effects, regardless of the intervention analyzed: homeopathy, acupuncture, or medicinal plants. However, Farinacci et al[68] included some comments about body weight loss and reducing food intake in phytotherapy studies to treat intestinal diseases in poultry.

The Overall Quality of the Analyzed Reviews

The study design varied according to each category of intervention. In homeopathy reviews, only RCTs were assessed. In acupuncture and phytotherapy studies, CCTs and RCTs were assessed.

Three of the seven eligible review articles assessed RoB[58] of the primary studies: two reviews[44,67] used the Cochrane tool; one review used the Jadad scale[62] adapted for veterinary medicine[66] (►**Table 2**).

According to the scoring system described in the AMSTAR 2 tool,[56] a "high confidence" level was assigned to two of the seven reviews[44,67]; a "critically low confidence" level was

Table 1 Characterization of the selected systematic reviews according to their design, type of reported clinical trials, and respective controls, and species used for treatment and prophylaxis in veterinary medicine, concerning homeopathy, acupuncture, and medicinal plants

First author, year, and reference number	Type of review	Study design of primary references	Type of control	Species reported
Homeopathy				
Mathie & Clausen 2015[44]	Systematic review	RCT	Controlled by other than a placebo	Dairy herds, poultry, swine, canine, equine
Mathie & Clausen, 2014[67]	Systematic review	RCT	Controlled by placebo	Dairy herds, commercial pig and goat farms, canine
Acupuncture				
Dragomir et al 2021[65]	Systematic review	CCT / RCT	Conventional pharmacological or surgery treatments	Canine
Habacher et al 2006[66]	Systematic review	CCT / RCT	Conventional pharmacological or surgery treatments; skin pierced at non-acupoints; no treatment	Equine, canine, swine, and dairy herds (bovine and ovine)
Medicinal plants				
Farinacci et al 2021[68]	Systematic review	CCT / RCT	Against placebo (negative control) or comparative control (pragmatic design)	Poultry
Tamminen et al 2018[69]	Systematic review	RCT	No treatment (7/9 RCTs); comparative control or pragmatic design (2/9 RCTs)	Livestock (bovine, poultry, swine)
Ayrle et al 2016[1]	Systematic review	CCT / RCT	Placebo (negative control); comparative control (pragmatic design)	Livestock (bovine, swine, equine, leporine)

Abbreviations: CCT, controlled clinical trial; RCT, randomized controlled trial.

Table 2 Overall level of confidence in the results of systematic reviews, according to assessment using AMSTAR 2, and the method each review employed to evaluate the risk of bias (RoB: Cochrane or Jadad scale)

Authors and year	AMSTAR 2 assessment: level of confidence	RoB evaluated?
Homeopathy		
Mathie & Clausen, 2015[44]	High	Yes: Cochrane
Mathie & Clausen, 2014[67]	High	Yes: Cochrane
Acupuncture		
Dragomir et al 2021[65]	Critically low	No
Habacher et al 2006[66]	Critically low	Yes: modified Jadad
Phytotherapy		
Farinacci et al 2021[68]	Critically low	No
Tamminen et al 2018[69]	Critically low	No
Ayrle et al 2016[1]	Critically low	No

Abbreviations: AMSTAR, Measurement Tool to Assess Systematic Reviews; RoB, risk of bias.
Note: The assessment of CCTs/RCTs in each review is described in ►**Supplementary File 2** (available online only).

Table 3 Details of AMSTAR 2 evaluation of selected reviews

	AMSTAR 2																
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Overall
Mathie & Clausen 2015																	H
Mathie & Clausen 2014																	H
Dragomir et al 2021																	CL
Habacher et al 2006																	CL
Farinacci et al 2021																	CL
Tamminen et al 2018																	CL
Ayrle et al 2016																	CL

Yes Partial yes No No meta-analysis conducted

Abbreviation: AMSTAR, Measurement Tool to Assess Systematic Reviews (according to Li et al. 2023 (https://doi.org/10.3389/fmed.2023.1196357)). For overall level of confidence: H, high; CL; critically low.

assigned to the five remaining reviews since an average of four critical items per review were unmet. No studies were classified as having a "moderate" or "low" level of confidence.

The AMSTAR 2 evaluation (►**Table 3**) showed the highest occurrence of "Yes" responses in item 1: "Did the survey questions and inclusion criteria for the review include the PICO components (Population, Intervention, Comparison, Outcome)?"; and in item 16: "Did the review authors report any potential source of conflict of interest, including any funding received for carrying out the review?".

On the other hand, the highest occurrence of "No" responses was observed in items 7, 9, 10, 13, and 14. The most critical of those for our overview (items 7, 9, and 13) are related to the criteria used for excluding studies, RoB evaluation, and the consideration of individual studies' RoB in interpreting a review's findings.

Findings from High-Quality Systematic Reviews

Only two of the seven reviews[44,67] were classified as high-quality by the AMSTAR 2 analysis: both those reviews assessed homeopathy interventions, focusing exclusively on RCTs whose control group was either placebo[67] or other than placebo.[44]

In Mathie and Clausen 2015,[44] no trial had sufficiently low RoB to be judged as reliable evidence: 16 of the 20 RCTs had high RoB; the remaining four had uncertain RoB in several domains of assessment; 11 of the 20 articles presented favorable results for homeopathy when compared to the respective controls.

In Mathie and Clausen 2014,[67] two placebo-controlled trials presenting reliable evidence (low RoB) could be highlighted: a prophylactic effect of homeopathic *Escherichia coli* on diarrhea in piglets, which showed a significant improvement favoring homeopathy considering the score and duration of symptoms[70]; and individualized homeopathic treatments for bovine mastitis, which were not statistically different either from placebo or from antibiotics, when the outcomes were evaluated employing scores in a semi-crossover trial design.[71]

Both eligible systematic reviews on veterinary acupuncture were evaluated as poor in the AMSTAR 2 assessment. In Dragomir et al 2021,[65] nine articles were analyzed, but no RoB assessment was reported, precluding any substantial conclusion about efficacy or effectiveness. In Habacher et al 2006,[66] most RCTs and CCTs showed statistical significance favoring acupuncture, though with low scores when using the Jadad scale to assess RoB; by contrast, two RCTs scored 4 on the Jadad scale (►**Supplementary File 2**, available online only) but neither of them had results favoring acupuncture.

Concerning phytotherapy, one of the three systematic reviews reported nine RCTs and their specific findings separately from the observational studies that were also consulted.[69] In the other two reviews, the authors proposed a scoring system based on the differences between verum and control to assess the therapeutic activity of the studied plants in a number of conditions in poultry[68] and in gastrointestinal and respiratory diseases in calves and piglets.[1] However, none of the three eligible reviews presented an RoB evaluation, being thus classified via AMSTAR 2 as low quality and preventing an informed conclusion about the efficacy or effectiveness of phytotherapy on the studied veterinary conditions.

Discussion

The main objective of this overview was to characterize and assess the quality of reviews on veterinary homeopathy, acupuncture and herbal medicine and, secondarily, to highlight the findings of reliable clinical trials that had been identified in high-quality reviews. This initiative was designed to yield good-quality overarching information on the subject for veterinary professionals, researchers and decision-makers. Consequently, the analysis highlighted what still needs improvement regarding systematic reviews and original clinical research methods, and which clinical trials can be presented as good examples for planning further studies on complementary and alternative veterinary medicine (CAVM).

The search period was defined as 2000 to 2022, since the metrics and guidelines for constructing high-quality systematic reviews have been developed only in the last two decades.[72] This kind of overview approach, which focuses on the top of the evidence pyramid, has already been reported by other authors in the domain of human medicine, sometimes presented in a graphical form called an "evidence map"[61,73,74]. For each of the three CAVM interventions that was our focus, as for example in homeopathy,[43,75] the number and heterogeneity of primary studies per review was seen by the original review authors as insufficient to justify specific meta-analysis for each intervention/outcome association.

The methods proposed by Portella et al 2020[60] were adapted herein by evaluating direction of treatment effect per clinical trial per review, using the categories positive, potentially positive, ineffective, inconclusive, or negative, for trials assessed by the original review authors as reliable evidence (low RoB: Cochrane or Jadad). However, a trial with low RoB turns out to be an uncommon finding—even from among our three CAVM reviews that assessed RoB *per se*. For example, in Habacher et al 2006,[66] most studies showed statistical significance between experimental and control groups but with poor scores for RoB. In Mathie & Clausen 2015,[44] no primary study presented sufficiently low RoB to be considered reliable evidence; indeed, six of the 20 RCTs had high RoB. Mathie & Clausen 2014[67] appraised two placebo-controlled RCTs in homeopathy as comprising reliable evidence[70,71]: these can be taken as good examples of RCTs on which to base further studies. A positive finding for homeopathy was observed in one of those two RCTs.[70]

Most reviews on phytotherapy included comprehensive lists of "active" plants, usually presenting antimicrobial or antihelminthic action. However, a clear discrimination between RCTs and CCTs was not observed, and the statistical validity of these findings and/or information on the RoB from primary studies was scanty.[1,68,69] Regarding homeopathy, given the small number of RCTs in a given intervention category with comparable protocols, a comprehensive meta-analysis could be done only when accepting the inevitable clinical and statistical heterogeneity. For instance, a separately published meta-analysis[45] relating to previously reported review data[67] indicated that more low-RoB RCTs were needed to allow conclusive results about any differences between homeopathy and placebo.

The problem of poor methodological quality does not seem exclusive to RCTs of CAVM therapies: given the recent interest of veterinarians in these issues, it is a global problem. According to Sargeant et al,[52] there is still a need for authors, reviewers and journal editors to be supported by guidelines to strengthen the planning, execution and evaluation of clinical trials in veterinary medicine. An example of a policy is the Consolidated Standards of Reporting Trials (CONSORT), initially designed for human research but can be easily transposed to veterinary research. Consequently, improving clinical research methods would impact the quality of the findings and conclusions of future systematic reviews.

Efforts in this direction have been supported recently by two comprehensive articles offering recommendations for high standards of veterinary clinical study methods—both observational studies and randomized trials.[76,77] Following such guidelines would undoubtedly be reflected in assessments of higher quality for clinical studies and subsequent systematic reviews. The assessment of RoB is a mandatory field for protocols registered in the PROSPERO repository of systematic reviews.[78]

A CAVM-related systematic review that was published after our literature search affirms a continuing problem with low-quality clinical trials. The review focused on laser therapy at acupoints specific to musculoskeletal, neurologic, skin and pain conditions described in dogs, cats and horses.[79] These authors also complain of the difficulty of getting reliable conclusions about the effectiveness of this therapeutic practice because the studies presented mainly high or moderate RoB, and the interventions were too heterogeneous to enable meta-analysis.

The most relevant limitation of the current overview is our method of searching for evidence only from RCTs cited in high-quality systematic reviews. Though this approach has the advantage of producing a refined search of very good examples, it also has disadvantages. In this case, the narrowed selection implies the non-inclusion of RCTs that have not yet been the subject of a systematic review. A related limitation is the time since the publication dates of relevant reviews on a given topic, which, in the case of RCTs in veterinary homeopathy, were 2014 and 2015.[44,67]

To gain an understanding of the potential impact of these limitations, a supplementary search was made in Google Scholar, an online search engine for academic publications, to identify any CCTs (published from 2000 up to July 2023) that were not cited in the high-quality reviews included herein. A large number of potentially eligible studies were identified: 37 for homeopathy (►**Supplementary File 3**, available online only); 37 for acupuncture (►**Supplementary File 4**, available online only); 18 for phytotherapy (►**Supplementary File 5**, available online only). The actual number of these RCTs and CCTs that would be eligible for an updated review, and the reliability of their evidence, is currently unknown. There is thus a pressing need for contemporary high-quality systematic reviews in each of these areas of CAVM.

Conclusions

The species reported in a total of seven eligible systematic review articles on CAVM were dogs, horses, cats, cattle, sheep, goats, swine, rabbits, and poultry. The total number of primary articles (RCTs or CCTs) assessed in these reviews was 38 for homeopathy, 35 for acupuncture, and 171 for phytotherapy. Only two of the seven reviews (both on homeopathy) were rated as sufficiently high in quality to justify our consideration of the original clinical trial results: two placebo-controlled RCTs comprised reliable evidence, reporting efficacy as prophylaxis for diarrhea in pigs and ineffectiveness as treatment for mastitis in cattle. The systematic reviews of acupuncture and phytotherapy were rated of insufficient quality to enable the formal assessment of any reliable evidence within the original RCTs or CCTs. Undertaking contemporary high-quality

systematic reviews of clinical trials in each of the three areas of CAVM is a pressing requirement.

Highlights

- The study is an overview of systematic reviews of homeopathy, acupuncture and phytotherapy in veterinary medicine, published from 2000 to 2022.
- Seven articles were eligible for evaluation and analysis, reporting studies on dogs, horses, cats, cattle, sheep, goats, swine, rabbits, and poultry.
- The seven eligible reviews were evaluated using the AMSTAR 2 method.
- Two reviews of RCTs in veterinary homeopathy were evaluated as high quality.
- Efficacy of homeopathy as prophylaxis for diarrhea in pigs was identified from an RCT that comprised reliable evidence.
- The reviews of acupuncture and phytotherapy all possessed low quality.

Supplementary material

Supplementary file 1. Excluded reviews.
Supplementary file 2. List of highlighted CCTs/RCTs from systematic reviews.
Supplementary file 3. Homeopathy: Google Scholar search.
Supplementary file 4. Acupuncture: Google Scholar search.
Supplementary file 5. Phytotherapy: Google Scholar search.

Authorship

This "overview" followed the guidelines on the authorship of scientific articles recommended by the International Committee of Medical Journal Editors.

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Conflict of Interest

None declared.

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