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The use of homeopathy in veterinary medicine: a systematic review

O uso da homeopatia na medicina veterinária: uma revisão sistemática

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Highlights _

Most articles lack randomized-controlled methodology. There were more clinical (eight) than prophylactic (six) studies found. Selected articles discussed eight species, with diseases being the main focus. Same species and methodology research on homeopathy is encouraged.

Abstract _

Although its use remains controversial, homeopathy has been proposed as an integrative approach alongside conventional medicine. This systematic review aimed to validate the use of homeopathy in veterinary using randomized controlled trials as the gold standard methodology. We performed a broad bibliographic search on the use of homeopathy in veterinary medicine published between 2016 and 2023, following the prerequisites and protocol established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Cochrane Training. All searched studies were excluded if they did not fit the chosen methodology. Studies were identified based on their data and passed through a selection process. The selected studies were then assessed for risk of bias. The initial database search yielded 161 documents. Of these, 126 studies were excluded because they were not within the scope of the review, either by title or abstract. In total, 35 articles remained and underwent a data extraction process followed by study selection. Due to its methodologies, many studies with high sampling densities, encompassing numerous species and diseases, were not included in this review. Eight articles met the requirements of the present study. The articles predominantly focused on diseases, which may be attributed to the fact that treating such diseases makes it easier to validate the use of homeopathics in veterinary medicine, rather than solely employing it for prevention, as observed

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in the majority of the outcomes. Only four studies exhibited an overall low risk of bias. There is a scant number of robust evidence for veterinary homeopathy. With that, further randomized controlled trials involving the same species are warranted to valitade its use; the limited number of articles did not allow us to conduct a meta-analysis. This systematic review illustrates the need for a better description of the methodologies used in these studies.

Key words: Integrative veterinary medicine. Randomized controlled trials. Clinical treatment. homeopathic products. Prophylactic treatment.

Resumo _

Embora seu uso permaneça controverso, a homeopatia tem sido proposta como uma abordagem integrativa ao lado da medicina convencional. Esta revisão sistemática teve como objetivo validar o uso da homeopatia na medicina veterinária utilizando ensaios clínicos randomizados como metodologia de referência. Uma ampla pesquisa bibliográfica foi realizada em busca de estudos publicados entre os anos de 2016 e 2023, seguindo os pré-requisitos e protocolos estabelecidos pelo Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) e treinamento Cochrane. Estudos foram excluídos caso não se enquadrassem na metodologia escolhida. Os trabalhos foram identificados com base em seus dados e passaram por um processo de seleção. Estudos selecionados foram então avaliados quanto ao risco de viés, sendo que a busca inicial no banco de dados resultou em 161 documentos. Desses, 126 foram excluídos porque não estavam dentro do escopo da revisão, seja pelo título ou resumo. No total, 35 artigos permaneceram e passaram por um processo de extração de dados seguido da seleção. Devidos às suas metodologias, muitos estudos com altas densidades amostrais, abrangendo inúmeras espécies e doenças, não foram incluídos nesta revisão. Oito artigos atenderam aos requisitos da revisão. Os trabalhos focaram predominantemente em doenças, o que pode ser atribuído ao fato de que tratar tais doenças facilita a validação do uso de homeopáticos na medicina veterinária, ao invés de empregá-los exclusivamente para prevenção, como observado na maioria dos resultados. Apenas quatro artigos apresentaram, em geral, um baixo risco de viés. Há um número escasso de evidências positivas robustas para a homeopatia veterinária; mais ensaios clínicos randomizados envolvendo a mesma espécie são necessários para validar o seu uso. O número limitado de artigos não permitiu a condução de uma metanálise, sendo que essa revisão sistemática destaca a necessidade de uma melhor descrição das metodologias utilizadas nesses estudos.

Palavras-chave: Medicina veterinária integrativa. Ensaios clínicos randomizados. Tratamento clínico. Produtos homeopáticos. Tratamento profilático.

Ciências Agrárias

Introduction _

Homeopathy is a specific therapy that stimulates sick organisms to react to diseases and presents three fundamental principles: similarity, individualization, and dilution/ dynamisation (Teixeira, 2011; Hahnemann, 1980). The medication is chosen in accordance with the symptoms pertaining to a particular case. Hence, the etiologic factors, development of the disease, form of illness, concomitant circumstances, and symptoms of the patient are considered when seeking a specific treatment effect (Weiermayer et al., 2020). Homeopathy has the additional benefit of preventing the aforementioned residues from being detected into animal products (Braccini et al., 2019).

However, the situation involves constant doubt owing to the premise of homeopathy, which is to individualize the patient treatment and understand that priority should be placed on curing the patient, as opposed to concentrating on the pathology (Souza, 2002). But, in the case of epidemiological diseases, an entire herd of farm animals can be considered as a single individual and, therefore, treated with the same homeopathic medicinal product (HMP). This approach eliminates the potential placebo effect, particularly as HMPs are often administered to farm animals without direct contact. In both human and veterinary medicine, certain clinical conditions may necessitate the use of only one or a few appropriate HMPs, such as in cases referred to as genus epidemicus (Camerlink et al., 2010; Gaertner et al., 2023).

Research and clinical reports evaluating homeopathy in the field of veterinary medicine can be cited in several areas such as animal behavior (Feitosa et al., 2013), animal production (Souza et al., 2012; Lewandowski et al., 2019; Lobreiro, 2007; Santa Rita et al., 2016), chronic conditions (Mathie et al., 2010), and specific clinical treatments (Defiltro et al., 2020; Figueiredo et al., 2018; Klocke et al., 2010; Rodrigues de Almeida et al., 2008). Previous reviews involving randomized and controlled studies on the subject and their effectiveness have assessed the risk of bias associated with each study (Doehring & Sundrum, 2016; Mathie et al., 2012, 2014). One of the bestknown studies in the field of veterinary homeopathy was reported by Mathie & Clausen (2015a), which followed the methods described by the Cochrane Institute for Systematic Reviews (Clarke & Horton, 2001), and evaluated studies published until 2013. The single meta-analysis done for this study shows evidence for the effectiveness of veterinary homeopathy compared to placebo. Animal studies may provide more insight than placebos, because even if the particular effects of homeopathic remedies are dismissed, studying the treatment could contribute to a fresh comprehension of aspects related to the natural resolution of diseases and placebo effects (Hektoen, 2005).

Therefore, considering the further elucidation of the findings already documented in the literature up to the current moment, the aim of this study was to validate the utilization of homeopathic medicines in veterinary medicine by assessing randomized controlled trials (RCTs) published between 2016 and 2023, while also evaluating bias for study design and outcome through a systematic review.

Materials and Methods _____

All studies included in this review were evaluated by the ethics committees of their respective institutions. Furthermore, all the studies were approved for the use of animals in their research. This study followed the prerequisites and protocol established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2016) and Cochrane Training (Higgins et al., 2023).

Search strategy

The aim of this study was to examine the published literature and identify the largest number of studies related to the use of homeopathy in veterinary medicine. The search for studies in electronic databases was conducted between November 2022 and February 2023.

The bibliographical search inclusion criteria were as follows: studies reporting domestic and/or production animals; having clinical or prophylactic applications; written in English, German, or French; published in a journal between 2016 and 2023; and available in the PubMed, Science Direct, and Carstens-Stiftung HomVet CR databases. The search strategy keywords were as follows: "veterinary" OR "domestic animals" OR "animal production" OR "dog" OR "cats" OR "swine" OR "ovine" OR "caprine" OR "bovine" OR "fish" OR "chicken" OR "homeopathy" OR "randomized". The authors arranged the keywords in the databases accordingly to what they considered most effective for locating and distinguishing articles, thereby preventing excessive repetition. The number of studies on homeopathy, according to the search strategy in each database, is described below.

PubMed: homeopathy AND animal production (12 results), homeopathy AND domestic animals (three results), homeopathy AND dogs (eight results), homeopathy AND cats (three results), homeopathy AND swine (three results), homeopathy AND bovine (11 results), homeopathy AND ovine (seven results), homeopathy AND caprine (one result), homeopathy AND caprine (one result), homeopathy AND fish (10 results), homeopathy AND chicken (two results), homeopathy AND veterinary (68 results), homeopathy AND randomized AND veterinary (11 results).

Science Direct: homeopathy AND animal production (838 results), homeopathy AND domestic animals (178 results), homeopathy AND dogs (176)results). homeopathy AND cats (356 results), homeopathy AND swine (72 results), homeopathy AND bovine (230 results), homeopathy AND ovine (25 results), homeopathy AND caprine (26 results), homeopathy AND fish (422 results), homeopathy AND chicken (139 results), homeopathy AND veterinary (356 results), homeopathy AND randomized AND veterinary (138 results).

For the Carstens-Stiftung HomVet CR database, which focuses simply on homeopathic veterinary medicine, no search keys were selected. From the list of 456 available articles, we obtained 36 articles from 2016 to 2018, which was the last year of update from the platform.



In total, 161 articles were identified. All the identified studies were analyzed by both the main researchers involved in this study. From the 161 studies, 65 were "excluded by title," meaning that studies which contained "humans," "plants," a nonhomeopathic active ingredient, "in vitro," disease induction, general reviews, case reports, surveys, letters, and books explicit written on their titles were removed from the database. Because there were still a large number of studies and most of the titles did not contain the criteria for exclusion, their abstracts were read. Using the same exclusion criteria as those excluded by title, another 61 articles that did not meet the objectives of this systematic review were removed. For both exclusion criteria, the two researchers compared their responses to validate them. Wildlife and aquatic animals, which were not species considered in the inclusion criteria, were not excluded if studies involving such species were found. Finally, a total of 35 articles were subjected to full data extraction.

Data extraction

The extraction process comprised the identification of the study's research design and publication, which were divided into two parts. Part one consisted of the following technical parameters: article title, first author, year of publication, DOI, published journal, journal Scimago ranking, article research platform, keywords used, and article language. The second part of the extraction scrutinized information about the methodology, describing the following parameters: studied species, randomization method, studied condition, intervention (clinical or prophylactic), control group (placebo or other-than-placebo), administration (individual or non-individual), sample size, primary homeopathic agent, homeopathic dynamization, duration of experiment, main outcome, and main outcome result (positive or negative). If the aforementioned parameters were not found in the articles, they were considered absent. These absences were treated as nonexistent data in the selection process.

It is important to notice that, for intervention. two team members independently reviewed the articles and agreed to the classification. A study was defined as clinical when the homeopathic product was selected for a given individual or herd based on their shown symptoms, clinical signs, and previous non-working treatments, and prophylactic when they aimed to optimize the production of an animal, prevent the onset of a disease (still without clinical signs), or were an observational run-in-phase (Frei et al., 2005; Von Ammon & Kösters, 2016).

Study selection

Previously identified articles were selected. This process, adapted from PRISMA (Moher et al., 2016), consisted of six questions that mainly assessed the type of methodology employed in the study, which characterized the searched records as potentially eligible for systematic review. The questions were based on two possible responses: yes or no. Articles were selected or excluded based on the responses to each question (Table 1).



Table 1Exclusion criteria utilized for study selection

Question	Desired answer
Is the study an RCT?	Yes
Is there a placebo control group?	Yes
Was the homeopathic treatment compared with an OTP or an allopathic treatment?	No
Does the dynamization used follow the standards of conventional homeopathy?a	Yes
In case of clinical studies, were the animals infected or the disease induced?	No
Is the article an original paper published by a peer-reviewed journal?	Yes

^a X = decimal dilution; C, CH, K, CK = centesimal dilution; M = millesimal dilution (Adler et al., 2005; Homeopathy, 2023). OTP: other-than-placebo treatment.

Among the 35 studies considered for inclusion in this review, only eight met the aforementioned selection criteria.

Assessment of risk of bias

The Cochrane tool (RoB 2) was used to assess the risk of bias for randomized controlled trials (Higgins et al., 2023). Bias was assessed as a judgment (high risk, low risk, or some concerns) of individual elements from five domains (randomization process, intended intervention, missing outcome, measurement of outcome, and selection of reported result). Reflecting on the appropriate 'Study Design and Setting'', we rated the risk of bias for each trial across all five domains and used the following classification:

• Low risk of bias: The study was judged to have a low risk of bias in all domains.

• **Some concerns:** The study is judged to raise concerns in at least one domain for this result, but there is no high risk of bias in any domain.

• **High risk of bias:** The study is judged to have a high risk of bias in at least one

domain for this result, or the study is judged to have some concerns for multiple domains in a way that substantially lowers confidence in the result.

Studies classified as "low risk" were considered good articles, therefore meaning that methodoly was well explained, the experiment was well conducted, and homeopathy could be used to solve their main problem if main outcome results were positive. The authors also considered that articles classified as "some concerns" that scored "low risk" in the randomization, intervention, and outcome domains could be considered good articles.

Results and Discussion ____

Articles published between 2016 and 2023 that involved the use of homeopathy as an intervention for animals were included in our database. The initial search using the selected keywords yielded 161 documents; English was the most used language (n = 139). Of these, 126 articles that did not meet the scope of the review were excluded either by title (n = 65) or abstract (n = 61), following

our exclusion criteria (Supplementary tables 1 and 2).

The 35 remaining articles underwent data extraction. A description of these studies is provided in Table 2, and their complete bibliographic details are presented in Supplementary Table 3. To better identify the studies used, records were numbered using the letter A (for articles). The searches ranged from A1 to A35. It became evident that a significant portion of the studies did not comply with the desired methodology for review, resulting in these studies undergoing a selection process. Among the 35 studies, 11 were excluded because they did not use randomized trials, which was the primary criterion of the research. As randomized controlled studies are the gold standard for ascertaining the efficacy and safety of a treatment (Akobeng, 2005, pp. 840-844), this systematic review highlights as its main point the need for researchers to consider this methodology when testing homeopathic products.3.

After applying the other selection criteria, the following articles were excluded: 13 studies that did not report a placebo control group, eight studies that compared homeopathic to an other-than-placebo (OTP) or antibiotics treatment, seven studies that did not present accurate homeopathic dynamization, eight studies that induced diseases in their clinical trials, and seven studies that were not peer-reviewed original papers. Some articles were excluded based on two or more criteria. After exclusion, eight were included in this review (Table 3). Six species were studied, indicating that there have been advancements in the field of homeopathy in recent years and that there has been an increased number of homeopathic trials involving a larger variety of animals (e.g., insects and aquatic animals). This indicates that research in the field of veterinary homeopathy is growing and gaining traction in the scientific community, especially as organic stock breeders prioritize phytomedicine and homeopathic methods to control diseases (Regulation (EU) 2018/848). Its application could also combat the indiscriminate use of conventional residue-producing veterinary drugs that can lead to the contamination of food products as well as the overuse of antimicrobials (Figueiredo et al., 2018). In addition, Saxton (2007) stated that research involving only companion animals, such as dogs, suffered disapproval from critics of homeopathy, as studies were too small, mainly not controlled, and that their positive results were not due to homeopathic treatment but simply involved an animal that was already improving. Conversely, Mathie et al. (2012) reported that the minimal number of research involving single animals, such as dogs and horses can be attributed to two factors: the difficulty associated with attaining a good sample size (n) of animals, and the deterrence associated with the participation of tutors in scientific trials. Most of the deterrence associated with the participation of tutors is justified on account of the "worry" that they experience with reference to the welfare of the animals in scientific research. Hektoen (2005) stated that animal welfare needs to be considered in relation to all studies involving placebo or no intervention, even if interesting and valuable knowledge can be derived from such studies. It is imperative that all owners of animals and researchers comprehend the same, so that researchers can offer informed consent with reference to the trial and acquire a larger sample size.

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de Barros2010FlyRCTLavae productionPopylacioPaceboNor-individual1.200Continnyiourax8 CHJaguezesti2021PigRCTDevelopmentPopylacio·Nor-individual180Medicago sativa15 CHJaguezesti2020Rets·InstailluellePipylacioPinebooNor-individual100Medicago sativa15 CHJaguezesti2020PigRCTInstaillueClinicalPiaceboIndividual30Medicago sativa15 CHJaguezesti2020PigRCTInstaillueClinicalPiaceboIndividual30Medicago sativa30 CHJaguezesti2020PigRCTRecoveryPopylacioPineboIndividual30Arrica montana30 CHJaguezesti2020PigRCTPipylacioOTPIndividual30Arrica montana30 CHVendi2020PigRecoveryPopylacioOTPIndividual30Arrica montana30 CHVendi2021PigRCTPipylacioOTPIndividual30Arrica montana30 CHVendi2021PigRecoveryPopylacioPineboIndividual30Arrica montana30 CHVendi2021PigPigPipylacioPipylacioPipylacioPipylacioPipylacio70 Pipylacio70 PipylacioVendi2021PigPipylacioPipylacio	A23	Rosero- García	2019	Fish	RCT	Immune response	Prophylactic	Placebo	Non-individual	100	Passival	30 CH	ı
DargD201FigRCTDevelopmentProhylactic·Non-individual180Medicago sativa15 CHJaguezeski2020Rats·InstituluelikProphylacticPaceboNon-individual1006060Balbueno2020DogRCTHeart failueCinicialProphylacticPiaceboIndividual30Crategus6 CHBalbueno2020DogRCTHeart failueCinicialProphylacticPiaceboIndividual30Crategus6 CHWendt2022DogRCTRecoveryProphylacticPionelio30Minicianal30Minicianal30Wendt2022DogRCTDevelopmentProphylacticPionelioMinicianal30Minicianal30Wendt2022DigRCTDevelopmentProphylacticPionelioMinicianal30Minicianal30Wendt2022DigRCTDevelopmentProphylacticPionelioMinicianal30Minicianal30Wendt2022DigRCTDevelopmentProphylacticPianelioMinicianal30Minicianal30Wendt2023DigRCTPienelioPionelioPionelioPionelio30Minicianal30Wendt2029DigFistPionelioPionelioPionelioPionelio30MinicianalWendt2016FistPioneli	A24	de Barros	2019	Fly	RCT	Larvae production	Prophylactic	Placebo	Non-individual	1,200	Cochliomyia hominivorax	8 CH	I
Jaguezeki202Rats·Intestinal healthProphylacticPlaceboNon-individual40Ethinacea anguetifoia6CHBalbuero202DogRC1HeartfailueClinicalPlaceboIndividual30Cratagus6CHTavagin2022PigRC1RecoveryProphylacticPlaceboIndividual30Cratagus6CHWendt2022PigRC1RecoveryProphylacticPloteboIndividual30Cratagus30CHWendt2022PigRC1RecoveryProphylacticProphylacticProphylacticPlotebo307CHWendt2022PigRC1RecoveryProphylacticOTPIndividual30Arrica montana30CHWendt2016RC1RecoveryProphylacticPlaceboIndividual50Arrica30CHWendt2016FileProProphylacticPlaceboIndividual30Arrica30CHWendt2016FileProProphylacticPlaceboIndividual30Arrica30CHWendt2016FileProProphylacticPlaceboIndividual30Arrica30CHWendt2016PlaneProvensyProphylacticPlaceboPlaceboIndividual30Arrica30CHWendt2016PlaneProvensyProphylacticPlaceboPlaceboPlaceboNon-Individual <td>A25</td> <td>Dang</td> <td>2021</td> <td>Pig</td> <td>RCT</td> <td>Development</td> <td>Prophylactic</td> <td>ı</td> <td>Non-individual</td> <td>180</td> <td>Medicago sativa</td> <td>15 CH</td> <td>I</td>	A25	Dang	2021	Pig	RCT	Development	Prophylactic	ı	Non-individual	180	Medicago sativa	15 CH	I
Balbuero2020DogRCTHeartaiureClicialPlaceboIndividual30Crategus6CHTravagin2022DogRCTRecoveryProphyteticPaceboIndividual30Arrica montana30CHWendt2022PigRCTDevelopmentProphyteticProphyteticProphyteticProphytetic7CH30CHWendt2022PigRCTDevelopmentProphyteticProphyteticProphyteticNon-individual80Arrica montana30CHWendt2016CatRCTDevelopmentCrinicalOTPIndividual80Arrica30CHWendt2018CatRCTPainClinicalOTPIndividual80Arrica30CHWažačni2016FishVRecoveryProphyteticPraceboIndividual300Arrica30CHWažačni2016FishVDevelopmentProphyteticProphyteticProphyteticProphytetic30CHWažačni2016FishVDevelopmentProphyteticProphyteticProphyteticProphytetic30CHWažačni2016FishVDevelopmentProphyteticProphyteticProphyteticProphytetic7CHWažačni2016FishVDevelopmentProphyteticProphyteticProphyteticProphytetic7CHWažačni2016FishVDevelopmentProphytetic <td>A26</td> <td>Jaguezeski</td> <td>2020</td> <td>Rats</td> <td>ı</td> <td>Intestinal health</td> <td>Prophylactic</td> <td>Placebo</td> <td>Non-individual</td> <td>40</td> <td>Echinacea angustifolia</td> <td>6 CH</td> <td>ı</td>	A26	Jaguezeski	2020	Rats	ı	Intestinal health	Prophylactic	Placebo	Non-individual	40	Echinacea angustifolia	6 CH	ı
TavaginTota 20DogRCTRecoveryProphylacticDecko and OTPIndividual30Arricamontana30CHWendt202PigRCTDevelopmentProphylacticVenindividual30Non-individual307 CHWendtigues2016CatRCTDevelopmentOTPNon-individual50Nice ateria7 CHWodrigues2016CatleRCTPainClinicalOTPIndividual50Nice ateria30 CHWadzón-2018CatleRecoveryProphylacticProphylacticProphylacticProphylacticNon-individual50Nice ateria30 CHWadzón-2016Fish-DevelopmentProphylacticProphylacticProphylacticProphylacticNon-individual30 CHWadzón-2016Horse-LamenessClinical-Individual30Wadzón-2016Horse-LamenessClinicalNon-individual30Wadzón-2016HorseClinicalNon-individual30Wadzón-2016NelseProphylacticProphylacticNon-individual30Wadzón-2016NelseProphylacticProphylacticProphylacticNon-individual30 </td <td>A27</td> <td>Balbueno</td> <td>2020</td> <td>Dog</td> <td>RCT</td> <td>Heart failure</td> <td>Clinical</td> <td>Placebo</td> <td>Individual</td> <td>30</td> <td>Crataegus</td> <td>6 CH</td> <td>120 days</td>	A27	Balbueno	2020	Dog	RCT	Heart failure	Clinical	Placebo	Individual	30	Crataegus	6 CH	120 days
Wendt 202 PigRCTDevelopmentProphylactic \cdot Non-individual80Siliceatera7CHRodrigues 2016 CatRCTPainCincialOTPIndividual50Anica30CCoelho 2018 DogRCTRecoveryProphylacticPlaceboIndividual50Nuxvonica6CHSuäzöönia 2016 Fish \cdot DevelopmentProphylacticPlaceboNon-individual300 \cdot 31CHSuäzönia 2016 Horse \cdot LamenessClinical \cdot Individual300 \cdot 31CHSuäzönia 2016 Horse \cdot LamenessClinical \cdot Individual300 \cdot 31CHSuäzönia 2016 Horse \cdot LamenessClinical \cdot Individual300 \cdot 30CHSuäzönia 2016 Neule \cdot DevelopmentProphylacticPlaceboNon-individual30 \cdot 30CHSuäzönia 2016 Neule \cdot LamenessClinical \cdot Individual30 \cdot \cdot \cdot Suäzönia 2016 Neule \cdot LamenessClinical \cdot Non-individual \cdot \cdot \cdot \cdot \cdot Suäzönia 2016 Neule \cdot Non-individual \cdot Non-individual \cdot \cdot \cdot \cdot \cdot \cdot Suäzönia 2016 Neule \cdot Non-i	A28	Travagin	2022	Dog	RCT	Recovery	Prophylactic	Placebo and OTP	Individual	30	Arnica montana	30 CH	ı
RodriguesCateRCTPainClinicalOTPIndividual50Arnica30CCoelho2018DogRCTRecoveryProphylacticPlaceboIndividual50Navonica6CHSuässögiu2016Fish-DevelopmentProphylacticPlaceboNon-individual300-31CHCayado2016Horse-DevelopmentProphylacticPlaceboNon-individual300-31CHCayado2016Horse-LamenessClinicalIndividual300-31CHSuässöniu2016Horse-LamenessClinicalIndividual300-31CHSuässöniu2016Horse-LamenessClinicalIndividual300Noscatelli2016Bei-ResistanceProphylacticPlacebo and OTPNon-individual15 <td< td=""><td>A29</td><td>Wendt</td><td>2022</td><td>Pig</td><td>RCT</td><td>Development</td><td>Prophylactic</td><td>ı</td><td>Non-individual</td><td>80</td><td>Silicea terra</td><td>7 CH</td><td>ı</td></td<>	A29	Wendt	2022	Pig	RCT	Development	Prophylactic	ı	Non-individual	80	Silicea terra	7 CH	ı
Coelho2018DogRCTRecoveryProphylacticPlaceboIndividual-Nux vonica6CHMazón-2016Fish-DevelopmentProphylacticPlaceboNon-individual300-31CHCayado2016Horse-LamenessClinical-Individual15Aconitum30CHSMazón-2016Horse-LamenessClinical-Individual15Aconitum30CHSMazón-2016Nolusk-DevelopmentProphylacticPlacebo and OTPNon-individual15Aconitum30CHMoscatelli2016Bei-DevelopmentProphylacticPlacebo and OTPNon-individualMoscatelli2016Bei-ResistanceProphylactic-Non-individual24Plosphorus30CH	A30	Rodrigues	2016	Cat	RCT	Pain	Clinical	ОТР	Individual	50	Arnica	30 C	I
Wazón- Suástegui2016Fish-DevelopmentProphylacticPlaceboNon-individual300-31CHCayado2016Horse-LamenessClinical-Individual15Aconitum30CHSuástegui2016Nolusk-LamenessClinical-Individual15Aconitum30CHMoscatelli2016NelPevelopmentProphylacticPacebo and OTPNon-individualMoscatelli2016Bee-ResistanceProphylactic-Non-individual24Phosphorus30CH	A31	Coelho	2018	Dog	RCT	Recovery	Prophylactic	Placebo	Individual	ı.	Nux vomica	6 CH	ı
Cayado 2016 Horse - Lameness Clinical - Individual 15 Aconitum 30 CH Mazón- súástegui 2016 Mollusk - Development Prophylactic Placebo and OTP Non-individual - - - Moscatelli 2016 Bee - Resistance Prophylactic - Non-individual 24 Phosphorus 30 CH	A32	Mazón- Suástegui	2016	Fish	I	Development	Prophylactic	Placebo	Non-individual	300	,	31CH	30 days
Mazón Contracted de moltusk - Development Prophylactic Placebo and OTP Non-individual -	A33	Cayado	2016	Horse	I	Lameness	Clinical	I	Individual	15	Aconitum	30 CH	I
Moscatelli 2016 Bee - Resistance Prophylactic - Non-individual 24 Phosphorus 30 CH	A34	Mazón- Suástegui	2016	Mollusk	I	Development	Prophylactic	Placebo and OTP	Non-individual	T		I.	21 days
	A35	Moscatelli	2016	Bee	I	Resistance	Prophylactic	I	Non-individual	24	Phosphorus	30 CH	1 year



intervention; ADM: administration format.

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) N p(H)	N (P)e final Nf	Conditiong	homeopathic agent	Dilution	Duration	Main outcome	outcome results
194	70 9	92 162	Disease	Escherichia coli	200 C	1 year 6 months	Recovery time	Negative
16	0	8 16	Disease	Graphites	30 C	1 year	Papilloma regression	Positive
40	19 1	9 38	Disease	Sarcode thyroidinum	30 C	21 days	T4 levels	Negative
24	12 1	2 24	Disease	Rhipicephalus (Boophilus) microplus	30 CH	1 year	Control of R. (B.) microplus	Negative
96	69 2	2 91	Production	Salvia officinalis	9 CH	2 years	Bone mineralization	Positive
430		2 398	Immunity	Passival	30 CH	I	Health status	Positive
1200		00 1200	Production	Cochliomyia hominivorax	8 CH	I	Myiasis treatment	Positive
30	20 1	0 30	Disease	Crataegus	6 CH	120 days	Heart rate	Positive
le fact I numbe nimals	that the a er of anim for the plá	rticle does n als for the pla acebo treatm	ot provide su icebo treatme ent; ^f total fina	ch an identifica ent; ° total initial al number of ani	tion or doe number o mals; ^g Co	es not make f animals; d nditions ada	e it clear. ^a Initia final number o apted as 'produ	al number of f animals for ction' refers
	and the second se	19 1 19 1 12 1 69 2 316 8 316 8 900 30 20 30 aumber of anim- mals for the plat	9 9 9 9 19 19 38 12 12 24 69 22 91 69 22 91 316 82 398 300 300 1200 20 10 30 fact that the article does no umber of animals for the planals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no umber of animals for the place that the article does no unber of animals for the place that the article does no unber of animals for the place that the article does no unber of animals for the place that the article does no unber of animals for the place that the article does no unber of animals for the place that the article does no unber of animals for the place that the article does no unber of animals for the place that the article does no unber of animals for the place that the article does no unber of animals for the place that the article does no unber of animals for the place that the article does no unber of animals does n	19 19 38 Disease 19 19 38 Disease 12 12 24 Disease 69 22 91 Production 316 82 398 Immunity 900 300 1200 Production 20 10 30 Disease fact that the article does not provide suumber of animals for the placebo treatment. ¹ total find	19 19 38 Disease Craphics 19 19 38 Disease Sarcode 12 12 24 Disease (Boophilus) 13 12 24 Disease (Boophilus) 69 22 91 Production Officinalis 316 82 398 Immunity Passival 900 300 1200 Production Cochliomyia 20 10 30 Disease Crataegus fact that the article does not provide such an identifical umber of animals for the placebo treatment; fotal final number of ani Initial	191938Diseaseoriginate30 C191938DiseaseSarcode $30 C$ 121224Disease(Boophilus) $30 CH$ 692291Production $officinalis$ $9 CH$ 31682398ImmunityPassival $30 CH$ 9003001200Production $officinalis$ $8 CH$ 201030DiseaseCochliomyla $8 CH$ and the article doesProductionCochliomyla $8 CH$ and the article doesNotationCochliomyla $8 CH$ and for the placebo treatment; fotal final number of animals; $9 CO$ $Moninivorax6 CH$	191938DiseaseContinue30 C1 year121224DiseaseSarcode30 CH1 year121224Disease(Boophilus)30 CH1 year692291Productionofficinalis30 CH1 year31682398ImmunityPassival30 CH2 years9003001200ProductionCochliomyia8 CH-201030DiseaseCrataegus6 CH120 daysfact that the article does not provide such an identification or does not makeanimals of chainals of continions addition8 cHall for the placebo treatment; fotal final number of animals; $^{\circ}$ Conditions additionaddition8 cH120 days	19 19 38 Disease Graphics 30.C 1 days 12 12 24 Disease Rhipicephalus 30.CH 1 year 12 12 24 Disease (Boophilus) 30.CH 1 year 13 16 22 91 Production Salvia 9.CH 2 years 316 82 398 Immunity Passival 30.CH - 900 300 1200 Production Cochliomyia 8.CH - 900 300 1200 Production Cochliomyia 8.CH - 20 10 30 Disease Crataegus 6.CH - 20 10 30 Disease Crataegus 6.CH -

to articles that explored animal development and performance; 'disease' refers to articles that explored mastitis, papillomatosis, hyperthyroidism, and heart failure; and 'immunity' refers to articles that explored animals' immune response. 5 5 S

Summary of findings of the selected studies

Table 3





Three conditions were observed between trials, with none assessed in more than one study from the same species. This shows that the type of article intervention was another important aspect of this review, and defining a study as clinical or prophylactic can affect the results, especially in the case of an RCT in which the corroborative support of well-controlled studies relates to efficacy and valuable data (Spieth et al., 2016). Articles that addressed the topic of diseases such as mastitis were categorized under the clinical category, whereas articles that used homeopathy in relation to an animal's enhanced performance or as an immune response mediator were categorized under the prophylactic treatment category. Fewer conditions were observed in the articles included in this systematic review than in previous reviews on homeopathy (Doehring & Sundrum, 2016; Mathie et al., 2012, 2014; Mathie & Clausen, 2015b). However, it is

important to note that the search period for studies in previous reviews was longer (1984-2015) than that of this study (2016-2023). Other database overviews (Clausen & Albrecht, 2010) have also presented more clinical conditions; however, non-RCTs were included in these reviews. This shows the need to continue research in this field to demonstrate constant changes in the number of conditions that can be treated homeopathically, the number of possible homeopathic treatments, and the efficacy of these homeopathic treatments in the veterinary field in general.

Following the PRISMA guidelines (Moher et al., 2016), a flowchart showing the total number of publications identified and the number of publications filtered at each stage of the selection process from the systematic review was created for better visualization (Figure 1).



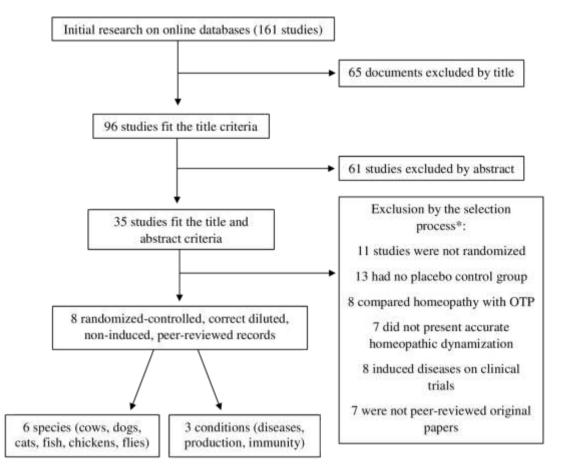


Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart illustrating search, exclusion criteria, data extraction, and article selection and categorization.

* Some articles were excluded by two or more criteria.

When analyzing the title and abstract exclusion criteria (Supplementary tables 1 and 2), a large number of published articles were excluded, as they were case reports and not experiments. Thus, a considerable number of studies with greater sampling densities encompassing a large number of species and diseases could not be included in this review because of the study mode. Experiments, unlike case studies, can be categorized under quantitative research, as they provide statistically significant data as well as an objective, empirical approach (Institute for Work & Health [IWH], 2016), and could bring more significance for the usage of this alternative medicine between veterinarian scientific communities. Adding to that, the absence of validated research on the efficacy of homeopathy through the lack of randomized studies in veterinary medicine complicates the acceptance of this alternative approach as significant, despite



evidence of positive outcomes. Table 4 provides the details of the risk of bias for each of the eight studies. There were no domains with 'high risk' scores. The domain with the most 'some concerns' score was II (intended intervention) in four of the eight studies. This score was given to articles in which the participants were aware of the intervention groups or there was no information on whether there were deviations from intended interventions because of trial context. All domains eventually had 'low' scores. Of the eight, four studies had a low overall risk of bias, and none had the same main outcome, but all involved diseases (Table 3). The ones that presented positive outcomes had dogs as experimental animals, and they were treated individually. These findings imply that homeopathy may be more effective when tailored to specific symptoms, aligning with Hahnemann's "Law of Similars" (Weiermayer et al., 2020). The ones that presented negative outcomes had cows and cats as experimental animals, and although only one of these used the non-individulized type of homeopathy, which could be pointed as one

of the causes for less efficacy, the outcomes measured, number of animals tested, and other variables may have influenced results (Lüdtke & Rutten, 2008). Regarding those classified as 'some concerns', none met the previously mentioned criteria designed by the researchers. This shows the importance of a well-written methodology, which demonstrates good rigor, reliability, and credibility of the research (Bhaskar & Manjuladevi, 2016). Also, in order to have different 'low risk' studies with comparable interventions, the homeopathy used in the studies needs to comply with "homeopathic best care" and should be thoroughly reported in order to be replicable. Additionally, to ensure the quality of randomized controlled trials (RCTs), sufficient resources are necessary. This includes а proficient research team, preferably within an academic research setting, and independent financial support. Further to this, the need for an academic research environment for quality assurance is to be emphasized. This shows the importance of evaluating the quality assessment of the studies.

Table 4

Risk of bias assessments for selected studies	
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ID	First author	Year	I	II	111	IV	V	Bias*
A2	Ebert	2016	Low	Low	Low	Low	Low	Low Risk
A7	Raj	2020	Low	Low	Low	Low	Low	Low Risk
A8	Bodey	2017	Low	Low	Low	Low	Low	Low Risk
A9	Figueiredo	2018	SC	SC	SC	Low	SC	High Risk
A19	Canello	2016	Low	SC	Low	Low	Low	SC
A24	Rosero-García	2019	Low	SC	Low	Low	Low	SC
A25	de Barros	2019	Low	SC	Low	Low	Low	SC
A28	Balbueno	2020	Low	Low	Low	Low	Low	Low Risk

* Overall risk of bias judgment. I: randomization process; II: intended intervention; III: missing outcome; IV: measurement of outcome; and V: selection of reported results. SC: some concerns.

As we were not able to perform a meta-analysis, we could not confirm the efficacy of homeopathy for any of the studies. Thus, in future research, to demonstrate treatment use and efficacy, it will be important to perform several studies that involve the same conditions and species for comparison. While this systematic review specifically included articles employing placebo control, a comparison with the effectiveness of allopathic agents was not pursued. Nevertheless, RCTs with placebo control are seen as "gold standard" for assessing the efficacy of medical interventions. Undoubtedly, evaluating homeopathy using this design is essential, although many RCTs may not represent typical homeopathic care. Consequently, researchers have devised a method to assess the model validity of homeopathic treatment in RCTs, and its utilization in subsequent reviews of homeopathic literature is strongly encouraged (Mathie et al., 2016).

Conclusion _____

In conclusion, although homeopathic products have been used, it is still not possible to validate their use in veterinary medicine because of the low number of trustworthy studies. Moreover, reliable studies yield controversial results, with both positive and negative outcomes. Further experiments involving the same species that follow a randomized controlled trial methodology are warranted. This systematic review also illustrates the need for a better description of the methodologies of the studies, which can affect their bias.

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