pubvet
MEDICINA VETERINÁRIA E ZOOTECNIA
ISSN 1982-1263
https://doi.org/10.31533/pubvet.v18n02e1544

Alternative approaches for treating canine otitis externa caused by *Malassezia pachydermatis*: Review and recommendations

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Abstract. *Malassezia pachydermatis* is a fungal pathogen that often leads to dog dermatitis and ear infections. The current treatment for otitis externa, which involves antifungal, antibiotic, and glucocorticoid drugs, faces challenges due to drug resistance and pet owners' compliance with prolonged treatment. This review delves into alternative treatment methods beyond conventional antifungal drugs and provides recommendations for their practical use. These methods include phytotherapies, chemical substances, drug repositioning, ear cleaners, alternative administration methods, and therapeutic diets. Further research, clinical trials, and comparative studies are needed to validate the efficacy of these alternative treatments and incorporate them into clinical practice. By implementing these methods, traditional treatment protocols can be optimized, drug resistance can be minimized, and the management of *M. pachydermatis* otitis externa in dogs can be improved, following the One Health approach that promotes prudent antimicrobial use.

Keywords: Alternative treatments, antimicrobial resistance, *Malassezia pachydermatis*, otitis externa

Abordagens alternativas para tratamento da otite externa canina causada por Malassezia pachydermatis: Revisão e recomendações

Resumo. *Malassezia pachydermatis* é um patógeno fúngico que frequentemente causa dermatites caninas e infecções de ouvido. O tratamento atual para otite externa, que envolve medicamentos antifúngicos, antibióticos e glicocorticoides, enfrenta desafios devido à resistência aos medicamentos e à adesão dos donos de animais de estimação ao tratamento prolongado. Esta revisão investiga métodos de tratamento alternativos além dos medicamentos antifúngicos convencionais e fornece recomendações para seu uso prático. Esses métodos incluem fitoterapias, substâncias químicas, reposicionamento de medicamentos, limpadores de ouvido, métodos alternativos de administração e dietas terapêuticas. Mais pesquisas, ensaios clínicos e estudos comparativos são necessários para validar a eficácia destes tratamentos alternativos e incorporá-los na prática clínica. Ao implementar estes métodos, os protocolos de tratamento tradicionais podem ser otimizados, a resistência aos medicamentos pode ser minimizada e o tratamento da otite externa por *M. pachydermatis* em cães pode ser melhorado, seguindo a abordagem One Health que promove o uso prudente de antimicrobianos.

Palavras-chave: Tratamentos alternativos, resistência antimicrobiana, *Malassezia pachydermatis*, otite externa

Introduction

The *Malassezia* genus includes 18 yeast species that depend on lipids. It is widely known for its involvement in skin conditions in humans and animals. Among these species, *Malassezia pachydermatis* is a significant cause of fungal dermatitis and otitis in dogs (Guillot & Bond, 2020; Puig et al., 2017). This yeast species naturally inhabits the skin microbiota of domestic animals such as cats and dogs. It colonizes areas, including the external auditory canals, anal sac, rectum, and vagina (Bensignor & Grandemange, 2006; Korbelik et al., 2018). However, under certain predisposing conditions, *M. pachydermatis* can transition from a harmless commensal to a pathogenic state, causing diseases (Logas, 1994).

Otitis externa is a common condition caused by *M. pachydermatis* that can lead to various clinical symptoms (Gheller et al., 2017; Souza et al., 2021; Yamamoto et al., 2010). These symptoms may include head shaking, pruritus, pain, otorrhea, erythema, edema, crusts, desquamation, and secretions (Gheller et al., 2017). It is worth noting that infections caused by *M. pachydermatis* are often identified by a distinct yellow to brownish ceruminous discharge and a dark, foul-smelling exudate (Campbell et al., 2010; Puig et al., 2019). The pathogenesis of this fungal infection is complex. It involves an inflammatory response influenced by predisposing and perpetuating factors (Karlapudi, 2017). These factors disrupt the normal balance within the auditory canal, facilitating the yeast's pathogenic transformation.

Canine otitis externa caused by *M. pachydermatis* is diagnosed through a thorough history and clinical examination (Maginn, 2016). However, accurate diagnosis requires cytological examination (Angus, 2004; Graham-Mize & Rosser Junior, 2004; Kashif et al., 2016). While fungal culture is the gold standard for diagnosis, it is not commonly used in routine clinical practice, unlike antifungal susceptibility testing (Hurtado-Suárez et al., 2016; Puig et al., 2019). The standard treatment protocol for otitis externa in dogs usually involves the topical application of a combination of drugs, such as an antifungal, an antibiotic, and a glucocorticoid, into the external ear canal (Bensignor & Grandemange, 2006; Rosychuk, 1994). Ear cleaners are also often used to enhance drug penetration and clinical outcomes (Maginn, 2016; Martino et al., 2016; Nuttal, 2010).

The effectiveness of various therapies in treating external otitis is being questioned due to their potential disadvantages. Antibiotics and glucocorticoids, commonly used in this treatment, may not effectively target the *M. pachydermatis* bacteria, which can render the treatment ineffective and even harmful (Bensignor & Grandemange, 2006; Maginn, 2016; Noli et al., 2017; Shaw, 2016; Velegraki et al., 2015). Recent studies have also highlighted the emergence of drug-resistant isolates of *M. pachydermatis* (Collignon & McEwen, 2019; McEwen & Collignon, 2018). Given that otitis externa requires a prolonged course of treatment, it is crucial to ensure that dog owners follow the treatment plan to prevent refractory cases (Maginn, 2016; Noli et al., 2017).

Clinicians face challenges finding effective treatments for *M. pachydermatis*-induced external otitis in dogs. As a result, they are exploring various alternative treatment methods, including phytotherapy and drug repositioning (Bismarck et al., 2020; Chan et al., 2018a; Ebani et al., 2020). This study aims to review these alternative methods, focusing on treatments other than traditional antifungal drugs. This review's findings will present a comprehensive list of considerations and recommendations for employing these alternative therapeutic approaches.

Review criteria

For this review, we used ScienceDirect and MEDLINE/PubMed databases to search for studies related to "canine Malassezia external otitis" from January 2000 to February 2023. We focused on using specific keywords such as "dog" or "canine," "Malassezia," "external," and "otitis." To ensure scientific rigor and relevance, we only included peer-reviewed and original studies written in English.

To ensure a focused review on the targeted subject, we set exclusion criteria to omit literature reviews, theses, book chapters, and studies on other dermatological diseases. The detailed selection process demonstrates the methodical screening and article selection stages, enhancing the review's transparency (Figure 1).

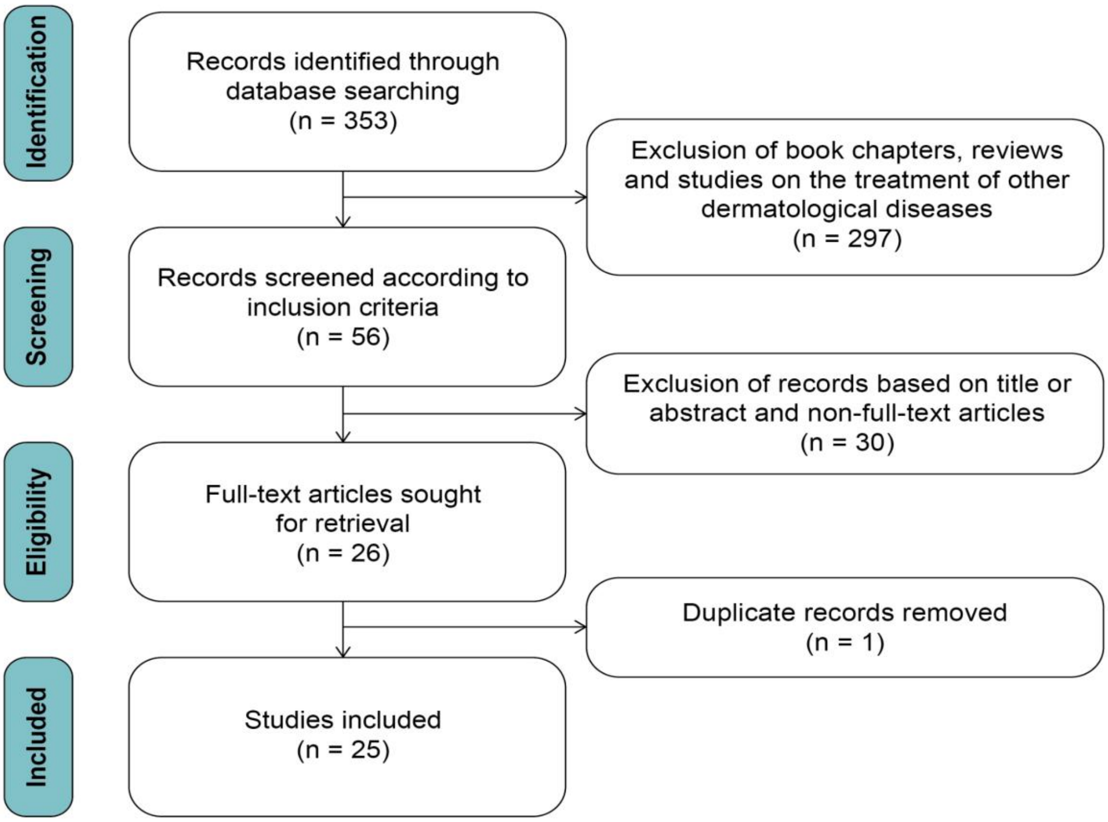

Figure 1. Flowchart of article selection

Treatment alternatives for *M. pachydermatis* otitis

Recent years have seen significant advancements in alternative treatments for otitis externa caused by *M. pachydermatis* in dogs (Bismarck et al., 2020; Cafarchia et al., 2014; Chan et al., 2018a; Cole et al., 2007; Corona et al., 2021; Di Cerbo et al., 2016; Ebani et al., 2020; Mason et al., 2013), to help veterinarians in their routine. The search strategy for this review revealed several articles, summarized in Table 1. These studies provide practical methods to reduce the incidence of drug resistance, encourage the rational use of antimicrobial drugs, and present successful cases of treating this pathology (Guillot & Bond, 2020). Figure 2 illustrates the different treatment alternatives identified by the articles included in this study.

Table 1 Data compiled from the studies on the treatment alternatives for external otitis caused by *Malassezia pachydermatis* in dogs

Reference	Alternative therapy	Animals and/or isolates	Outcome
	Phytotherapy		
Bismarck et al. (2020)	EOs of angelica root, cinnamon leaf, clary sage, garlic clove, coriander seed, fennel, lavadin super, fine lavender, lemon, lemongrass, manuka, Indian melissa, neroli, oregano, palmarosa, ravintsara, pink geranium, tea tree, thyme, thyme linalool, thyme thymol 19% and winter savory	Fifteen clinical isolates	Winter savory, lemongrass, oregano, palmarosa, and cinnamon leaf EOs demonstrated the best antifungal activities
Ebani et al. (2020)	Commercial EOs of oregano, savory, and thyme tested alone and in combination	Five clinical isolates	The three EOs showed antifungal activity. The savory EO alone showed the greatest activity. The mixture of the three EOs did not generate better results than the isolated oils
Moulari et al. (2007)	*Harungana madagascariensis* leaf ethyl acetate extract	One isolate	The extract showed antiseptic and antimicrobial activity
Nardoni et al. (2017)	Essential oil blend: grapefruit 0.5%, clary sage 0.5%, basil 0.5%, rosemary 1% (Mix 1), lemon 1%, clary sage 0.5%, rosemary 1%, roman chamomile 0.5% (Mix 2), clary sage 1%, rosemary 1%, lavandin 1% (Mix 3), lemon 1%, rosemary 0.5%, grapefruit 1%, roman chamomile 0.5% (Mix 4), and roman chamomile 1%, grapefruit 0.5%, thyme 0.5%, lavandin 1% (Mix 5)	Ten clinical isolates (*in vitro*) and 25 dogs with otitis externa (*in vivo*)	*In vivo*: Only mixtures 1 and 2 had satisfactory results. *In vitro*: Mixtures 1 and 3 inhibited fungal growth at the 50% EO dilution; Mixtures 4 and 5 at the 75% EO dilution, while Mixture 2 at the 25% EO dilution showed the lowest MIC

Table continuation 1 on the next page…

Table continuation 1

Reference	Alternative therapy	Animals and/or isolates	Outcome
	Phytotherapy		
Puigdemont et al. (2021)	Pomegranate extract as an ear cleanser + oral prednisone	Fifteen dogs with otitis externa	Topical treatment containing corticosteroids and natural antimicrobial agents reduced clinical signs and controlled yeast overgrowth
Sim et al. (2019a)	Cinnamon EO and its phenolic component, cinnamaldehyde	Twenty clinical isolates	Cinnamon EO and its phenolic compound showed a fungicidal effect
Sim et al. (2019b)	Thyme EO and its phenolic component thymol, and the EO of oregano and its phenolic component carvacrol	Twenty clinical isolates	The EOs and their respective phenolic compounds showed fungicidal activity
Vercelli et al. (2021)	A commercial product containing EOs of tea tree, serpillus, dalmatian sage, common eucalyptus, rosemary, macadamia, as well as fine lavender and sunflower as active compounds and sunflower seed oils, isopropyl myristate, and isopropyl adipate as a blend of triglycerides as excipients.	One clinical isolate and 12 dogs with acute otitis externa	*In vitro* assays demonstrated a fungicidal effect of the product. In addition, remission of clinical signs after administration was observed in most dogs
	Chemical substances		
Cafarchia et al. (2014)	A solution containing a killer peptide	Sixteen dogs with otitis externa (*in vivo*) and their respective 16 strains (*in vitro*)	The synthetic peptide had an antifungal effect, and the animals' clinical signs improved. Furthermore, the study indicated a dosage for reestablishing the microbiota
Corona et al. (2021)	Lactoferricin, a synthetic peptide derived from milk protein	Forty clinical isolates from dogs and 10 isolates from cats	The 20% lactoferricin solution showed a greater antifungal effect compared to the 13.3% dilution and other serial dilutions
Henselm et al. (2009)	Miconazole potentiated with a commercial chelating agent (Tricida®)	Twenty dogs with recurrent chronic external otitis (*in vivo*) and 31 isolates from the ears of these animals (*in vitro*)	Tricida® + miconazole showed antifungal activity. Potentiated miconazole was more effective in reducing cytology scores compared to regular miconazole. However, there was no difference between the two substances in the reduction of clinical signs
Lee et al. (2022)	Atmospheric cold plasma alone and in association with 0.02%, 0.2%, and 2% chlorhexidine	One clinical isolate	Atmospheric cold plasma showed antifungal activity from 5 min onwards at a power of 50 W and a synergistic effect when combined with 0.02% and 0.2% chlorhexidine solutions
Nakano et al. (2005)	β-thujaplicin	Fifty-one clinical isolates	β-thujaplicin showed antifungal activity
Nakano et al. (2006)	β-thujaplicin	Thirty-one dogs diagnosed with otitis externa	β-thujaplicin improved the clinical signs of 11 dogs, as well as decreased the yeast count in ear canal cytology
Siemieniuk et al. (2018)	Association of oxythiamine with ketoconazole and hydrogels formed with this mixture	Sixty-five clinical isolates and one CBS 7925 strain	Isolated oxythiamine showed inferior fungicidal properties compared to ketoconazole. The combination exhibited strong synergism *in vitro*. In addition, the hydrogels showed stronger bioadhesiveness due to the addition of the combination of oxythiamine and ketoconazole
	Drug repositioning		
Chan et al. (2019)	Non-antibiotic adjuvants: N-acetylcysteine, Tris-EDTA and disodium-EDTA	Twenty clinical isolates	The three adjuvants showed antifungal activity
Chan. et al. (2018a)	Narasin (coccidiostat)	Twenty clinical isolates	Narasin demonstrated an antifungal effect only in high concentrations (>128 µg/mL)
Chan et al. (2018b)	Monensin (ionophore)	Twenty-one clinical isolates	Monensin demonstrated low antifungal activity
	Ear cleaners		
Cole et al. (2007)	Commercial ear cleaner containing tromethamine, EDTA, and benzyl alcohol potentiated with the addition of 1% ketoconazole	Nineteen clinical isolates and one ATCC 14522 strain	The enhanced cleaner was more effective compared to regular ear rinse
Marrero et al. (2017)	Ear cleaner composed of hydrogen peroxide compared to three commercial ear rinses	Forty clinical isolates	Hydrogen peroxide at 1.5% showed greater antifungal activity compared to commercial cleaners. The effectiveness of those on the market was confirmed
Mason et al. (2013)	Commercial ear cleaners: Cerumaural®, CleanAural Dog®, Epi-Otic®, MalAcetic Aural®, Otoclean®, Otodine®, Sancerum®, Surosolve®, TrizUltra™ + Keto	Fifty clinical isolates	The ear rinses with the greatest antifungal activity were TrizUltra™ + Keto, Epi-Otic®, Sancerum®, CleanAural Dog®, and MalAcetic Aural®. Otodine® and Surosolve® also worked but with less efficacy

Table continuation 2 on the next page…

Table continuation 2

Reference	Alternative therapy	Animals and/or isolates	Outcome
	Ear cleaners		
Swinney et al. (2008)	Commercial ear cleaners: Sancerum®, Epi-Otic®, CleanAural Dog®, CleanAural Cat®, Otoclean®, MalAcetic Otic®, Malacetic HC®, Triz Plus®, TrizEDTA®.	One clinical isolate	Cleanural Dog® ear cleaner demonstrated the greatest antifungal efficacy. Among the rest, only the ear rinses: Sancerum®, Triz Plus®, Epi-Otic®, Otoclean® and MalAcetic Otic® showed antifungal activity in dilutions of up to 1/4
	Alternative administrations		
Blake et al. (2017)	A single dose of a commercial product, Otic Solution®, which contains florfenicol, terbinafine, and mometasone furoate	One hundred and eighty-three dogs with otitis externa	Clinical cure was achieved in the majority of dogs that received Otic Solution®. The dose of terbinafine in this new formulation was found to be effective
Pinchbeck et al. (2002)	Pulse administration of itraconazole oral solution at a dosage of 5 mg/kg, PO, every 24 h for two consecutive days, without receiving treatment for the following five days. Repeating the cycle for 21 days, totaling six doses of the medication	Twenty dogs with dermatitis or external otitis	The experimental treatment had similar clinical results to the conventional one
	Diet		
Di Cerbo et al. (2016)	Nutraceutical diet that contains hydrolyzed fish proteins, rice carbohydrates, *Melaleuca alternifolia*, *Tilia chordata*, *Allium sativum*, *Rosa canina*, zinc, and omega 3/6 (1:0.8 ratio)	Thirty dogs with chronic otitis externa	The nutraceutical diet provided rapid relief of clinical signs

EOs, essential oils; MIC, minimum inhibitory concentration; PO, oral administration.

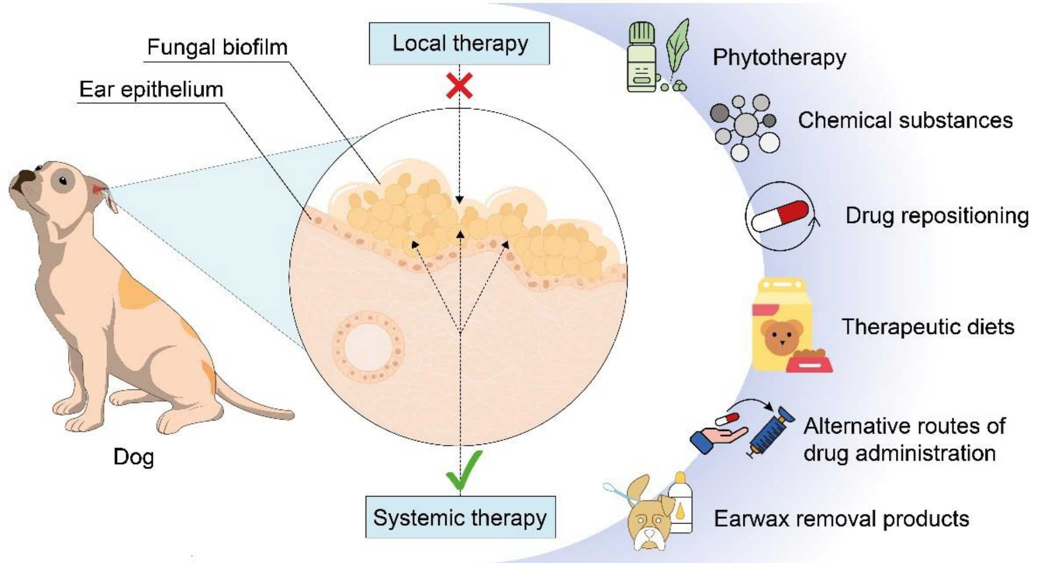

Figure 2. Alternative treatment options against *Malassezia pachydermatis* otitis externa in dogs.

Phytotherapies

Essential oils (EO) and their phenolic components have been evaluated in eight studies with promising results. Most studies have shown their antifungal activity (Bonin et al., 2020; Dutra et al., 2019; Matos et al., 2021). These compounds exhibit antibacterial and anti-inflammatory properties. These properties can help reduce clinical signs and can be used in mixed infections (Bismarck et al., 2020; Moulari et al., 2007; Nardoni et al., 2017; Puigdemont et al., 2021; Sim et al., 2019a; Sim et al., 2019b; Vercelli et al., 2021).

The antifungal activity of 22 EOs was evaluated in an *in vitro* study. Results showed that sausage leaf, oregano, lemongrass, palmarosa, and cinnamon oils were effective against *M. pachydermatis* (Bismarck et al., 2020). Another study found that *Harungana madagascariensis* leaf extract was active against *M. pachydermatis*, *Staphylococcus intermedius*, and *Pseudomonas* species (Moulari et al., 2007). In an *in vivo* study, pomegranate extract and oral prednisone were as effective as conventional treatment and significantly reduced clinical signs (Puigdemont et al., 2021). Phenolic components like carvacrol and thymol derived from oregano and thymol oil demonstrated fungicidal activity and more potent antimicrobial properties than their EOs (Sim et al., 2019a).

Similarly, cinnamon bark EO and its phenolic compound cinnamaldehyde also showed promising antimicrobial potential against *M. pachydermatis* (Sim et al., 2019b). A combination of essential oils was effective against clinical isolates of *M. pachydermatis*. Two of the five mixtures tested – one containing *Citrus paradisi*, *Salvia sclarea*, *Ocimun basilicum*, and *Rosmarinus officinalis*, and the other composed of *Citrus limon*, *S. sclarea*, *R. officinalis*, and *Anthemis nobilis* caused a reduction in clinical signs when used on patients (Henselm et al., 2009). A commercial product containing EOs from several plants was effective *in vitro*, improved clinical signs, and restored fungal homeostasis in the ear of most treated dogs (Vercelli et al., 2021). Finally, three other commercial products based on oregano, savory, and thyme EOs were investigated separately and evaluated in a mixture. The savory oil alone demonstrated the best result, which presented lower minimum inhibitory concentrations than the other two oils tested and the mixture of the three. The combination of oils did not produce more pronounced antimicrobial activity compared to the other two isolated natural compounds. Nonetheless, all substances tested, including those combined, demonstrated antifungal activity against isolates from dogs with otitis externa (Ebani et al., 2020).

Chemical substances

Medicinal chemistry is a fascinating field that helps search for new therapeutic substances and alternative medicines. It can be used to treat various conditions, including canine otitis externa caused by *M. pachydermatis*. Depending on their properties, chemical compounds may serve as adjuvants, synergists, or antifungal substances (Cafarchia et al., 2014; Corona et al., 2021; Henselm et al., 2009; Lee et al., 2022; Nakano et al., 2005; Siemieniuk et al., 2018).

Research studies have evaluated the effectiveness of various substances and techniques in treating dogs with otitis caused by the yeast *M. pachydermatis*. For instance, Cafarchia et al. (2014) found that a synthetic peptide showed antifungal activity in dogs with otitis, reducing clinical signs and yeast counts in cytological evaluation. Another study found that a peptide derived from milk protein, lactoferricin, exhibited antifungal activity against *M. pachydermatis in vitro* (Corona et al., 2021). In addition, the natural monoterpenoid β-thujaplicin was found to have antimicrobial activity against *M. pachydermatis* in both *in vitro* and *in vivo* studies (Nakano et al., 2005, 2006).

Henselm et al. (2009) evaluated the antimicrobial activity of miconazole and the chelating agent Tricida, both alone and in combination. The two drugs showed good activity against *M. pachydermatis* strains *in vitro*, with the combination being more effective in reducing the yeast count in cytological analysis than the antifungal drug alone. However, tests in dogs demonstrated that the reduction in clinical signs was not significant for the combination compared to miconazole alone.

Another study evaluated the efficacy of oxythiamine and ketoconazole against strains of *M. pachydermatis* isolated from dogs. The results showed a strong synergistic effect due to the cumulative actions of the same metabolic pathway and different mechanisms of action of the compounds. Additionally, when applied topically in an animal model, a hydrogel formulation containing this combination revealed promising characteristics such as drug delivery capacity and increased bioadhesiveness, allowing for the reduction of the ketoconazole concentration (Siemieniuk et al., 2018).

A cold atmospheric plasma was also evaluated against isolates of *M. pachydermatis* from canine otitis externa. The study showed effectiveness over long exposure times (5 minutes) and high powers (50 W). Furthermore, a synergistic effect was associated with 0.02% or 0.2% chlorhexidine solutions (Lee et al., 2022).

Drug repositioning

Drug repositioning is a promising option for treating otitis externa caused by *M. pachydermatis* in dogs, as it eliminates the need to develop new molecules, thereby reducing costs and speeding up research (Chan et al., 2019; Chan et al., 2018a; Chan et al., 2018b).

In a study, the coccidiostat narasin exhibited antifungal properties at high concentrations (Chan et al., 2018b). However, the ionophore monensin modulated the rumen microbiota and did not demonstrate promising results (Chan et al., 2018a). In a separate study, two chelating agents and a mucolytic agent were tested as adjuvant therapies and showed good inhibitory activity against *M. pachydermatis* isolates.

Furthermore, Chan et al. (2019) reported the antimicrobial activity of Tris-ethylenediaminetetraacetic acid (EDTA) and EDTA disodium against *M. pachydermatis*, but more fungal isolates are required to establish the therapeutic efficacy.

Ear cleaners

The treatment of otitis externa is usually accompanied by ear cleaners, particularly in cases of chronic otitis (Nuttall, 2016). The development of ear cleaners and the evaluation of their efficacy have been increasing to improve the clinical effectiveness of existing therapeutic protocols (Blake et al., 2017; Cole et al., 2007; Marrero et al., 2017; Mason et al., 2013).

Mason et al. (2013) evaluated the *in vitro* antimicrobial activity of nine ear cleaners against 50 *M. pachydermatis* isolates, with most formulations showing favorable results. A commercial ear cleaner was also tested *in vitro* in the presence or absence of 0.1% ketoconazole. A significant reduction in *Malassezia* growth was consistently observed when ketoconazole was present (Cole et al., 2007). As observed, the composition of commercial cleaners should be considered when assessing their effectiveness, as they may have specific targeting properties. Swinney et al. (2008) observed that antimicrobial activity will likely increase with isopropyl alcohol, parachlorometaxylenol, and a low pH. Furthermore, an *in vitro* study using hydrogen peroxide as an ear cleaner indicated more significant yeast inhibition than three commercial ear cleaners (Marrero et al., 2017).

Alternative administration

Malasseziosis requires a long-term therapeutic approach and demands attention from owners. However, poor adherence to the therapy is often observed, which leads to high rates of drug resistance and chronicity of the disease (Noli et al., 2017). To improve adherence by dog owners and prevent medication stockpiling, studying and evaluating alternative administration routes is recommended. Also, avoid using medications without veterinary advice (Blake et al., 2017; Pinchbeck et al., 2002).

A clinical trial evaluated the effectiveness of a single topical dose of a commercial product containing florfenicol, terbinafine hydrochloride, and mometasone furoate applied locally in treating canine otitis externa. The product showed clinical improvement in 73% of the cases (Blake et al., 2017; Pinchbeck et al., 2002). Another study compared the efficacy of daily therapy with ketoconazole (5 mg/kg, orally) to a pulse administration regimen for two consecutive days per week for three weeks. Both protocols showed similar effectiveness. Although the alternative treatment was less effective than usual, it could be a potential salvage therapy (Pinchbeck et al., 2002)

Therapeutic diet

Food has therapeutic properties that include anti-inflammatory and antioxidant activities, as reported by research (Glos et al., 2008). Probiotics have been shown to improve the health of fur in animals and can also be used in humans to alleviate conditions like dandruff, where *Malassezia* can be one of the triggers. Thus, dietary management can be an effective tool in treating canine otitis externa caused by *M. pachydermatis*, as it is beneficial for treating other veterinary dermatological diseases (Di Cerbo et al., 2016; Glos et al., 2008). In an *in vivo* study, a nutraceutical diet consisting of hydrolyzed fish proteins, rice carbohydrates, *Melaleuca alternifolia*, *Tilia cordata*, *Allium sativum*, *Rosa canina*, zinc, and omega 3/6 was evaluated for its efficacy in treating dermatological issues. The study found that this diet significantly reduced the main clinical signs of the dermatological presentation. However, the number of *M. pachydermatis* yeast cells in cytology showed a slight reduction compared to animals that received the standard diet (control group) (Di Cerbo et al., 2016).

Key remarks and recommendations

1) Researchers interested in using alternative therapeutic approaches to treat *M. pachydermatis* otitis externa are challenged with various options. The choice of the most suitable option depends on the severity of the disease and on the availability of the method to be employed. Some important considerations can be drawn from the studies reviewed here. Below, we provide a list of key points and suggestions to be considered when embarking on an exploration of this exciting frontier;

2) Phytotherapies: Eight studies have explored the potential of essential oils and their phenolic components in treating various infections. These studies have shown that these compounds possess antifungal, antibacterial, and anti-inflammatory properties, which can significantly reduce clinical signs. Moreover, these treatments have shown promise in mixed infections. Further research is needed to understand the potential of these phytotherapy treatments;
3) Chemical Substances: Medicinal chemistry provides a variety of chemical compounds that can function as alternative treatments. Synthetic peptides, natural monoterpenoids, and drug combinations have all shown promising results in combating *M. pachydermatis*. However, the efficacy of these compounds in transitioning from *in vitro* to *in vivo* settings remains a significant challenge, requiring further investigation;
4) Drug Repositioning: When treating otitis externa, drug repositioning can be a cost-effective alternative. Narasin, a coccidiostat, has shown potential antifungal activity at high concentrations but can also be toxic. Additional research is required to validate its therapeutic efficacy. Furthermore, further exploration of chelating agents and mucolytic agents is needed.
5) Ear Cleaners: When managing otitis externa, choosing ear cleaners is crucial. It is essential to carefully consider the composition of commercial ear cleaners, as specific components, such as isopropyl alcohol and low pH, can enhance antimicrobial activity. Choosing the correct formulation is essential to improve treatment outcomes. Hydrogen peroxide shows promise as an effective ear cleaner, and there should be encouragement for developing new ear cleaners.
6) Alternative Administration: Owners may find it easier to comply with administering medication to their pets if alternative methods are offered, such as single topical doses or pulse regimens. These methods could also be helpful in situations where standard treatments have failed. Modifying the usual treatment protocols may be necessary if the effectiveness of alternative methods is proven. Additionally, developing new substances may raise questions about the effectiveness of conventional treatments.
7) Therapeutic Diet: Otitis externa can be treated with dietary management. Nutraceutical diets containing certain ingredients have shown promise in reducing clinical symptoms but have little effect on reducing yeast cells. Further research is required to improve dietary strategies for this condition.

Conclusions

One Health approach recommends the prudent use of antimicrobial agents, given the worldwide concerns with antimicrobial resistance. Among the articles included in this study, phytotherapy was the most extensively studied area. Various natural substances were evaluated for therapeutic use against otitis externa caused by *M. pachydermatis* in dogs. Subsequently, the prospecting of new active compounds from synthetic chemical substances was widely undertaken. Drug repositioning has also been shown to have a significant impact as a therapeutic option, as ear cleaners combined with standard treatment and even different dosages and diets with therapeutic potential.

These alternative approaches have shown promise in reducing clinical signs and addressing the growing issue of drug resistance. Further exploration and validation through clinical trials and comparative studies are essential to facilitate their integration into clinical practice. In this quest for alternative treatments, the goal is to enhance the well-being of canine patients and refine and optimize traditional treatment protocols.

Statements and Declarations

Funding

The authors thank the Brazilian agencies Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for providing research grants.

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Author contributions

Roger F. Gomes, Alexandre M. Fuentefria, and Regis A. Zanette were responsible for the study conception and design. Data collection was performed by Roger F. Gomes. The first draft of the manuscript was written by Manoela A. M. Mace and Roger F. Gomes. Manuscript revision was performed by Erico S. Loreto, Alexandre M. Fuentefria, and Regis A. Zanette, and all authors read and approved the final manuscript.

Data Availability

All data generated during this study are included in this published article.

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Histórico do artigo:
Recebido: 1 de dezembro de 2023
Aprovado: 18 de dezembro de 2023