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Potential Biological and Antimicrobian Effects of the Essential Oil of *Aniba rosaeodora*: A Review of the Literature

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aims: Map the literature in search of the main biological and antimicrobial effects of the essential oil (EO) of *Aniba rosaeodora*.
Study Design: This is an integrative review based on the PRISMA method.

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Place and Duration of Study: Center for Biological and Health Sciences of a University in the Brazilian Amazon, from January to August 2022.
Methodology: A search was carried out in the main databases, such as Embase, Scopus, PubChem, PubMed, LILACS, SciELO and Portal BVS, with the descriptors consulted in the Medical Subject Headings (MeSH).
Results: 134 articles were found and, after applying the inclusion and exclusion criteria, 17 were selected for full analysis. The EO of *Aniba roseadora* revealed mainly antibacterial, antifungal, antiparasitic and antiviral properties and in two studies, anesthetic effects, without observation of serious adverse events and deaths, were observed, but the specific active compound was not identified. The antibacterial activity of linalool, the compound most present in *Aniba roseadora* EO, was significant. *Aniba roseadora* EO also showed inhibitory and fungicidal potential. In addition, *Aniba roseadora* had an antidepressant effect, reducing anhedonia.
Conclusion: The EO of *Aniba rosaeadora* showed potential biopharmacological and microbiological activities in pre-clinical models. Linalool stood out as the substance with the highest concentration in the EO; however, it is not yet known whether this compound is the main active component. Therefore, more studies should be conducted to support and describe the pharmacological potential of *Aniba rosaeadora* EO, leading to evidence-based pharmacology.

Keywords: Essential oils; Aniba rosaeodora; pharmacological potential; linalool; pau-rosa.

1. INTRODUCTION

Essential oils (EOs) are compounds originating from the secondary metabolism of aromatic plants, with organoleptic properties. In this context, EOs stand out as highly volatile and fatsoluble products, composed mainly of low molecular weight substances, such as monoterpenes, sesquiterpenes, phenylpropanoids and esters [1,2,3,4,5], enabling a biological and pharmacological potential of these compounds. EOs from the Amazon region stand out for their antimicrobial, oxidative and low-toxicity properties, as well as their important role in protecting plant crops. Due to these activities, they are widely used in various industries, notably in the pharmacological, food, cosmetics and perfumery industries [6].

Among the Amazonian species, *Aniba rosaeodora* [7] stands out as a candidate for the production of essential oil due to its local commercial and ethnopharmacological value for the treatment of various ailments. This species belongs to the Lauraceae family and is also known in Brazil as pau-rosa, pau-rosa-itaúba, pau-rosa mulatinho and pau-rosa-imbaúba, while it is called rosewood in the United States and England; it is an evergreen tree, characteristic of terra firme areas and widely distributed in the Amazon region, in the Brazilian states of Acre, Amapá, Amazonas, Pará, Roraima and in the Amazonian portions of French Guiana, Venezuela, Peru, Suriname and Colombia [8,9].

Therefore, the pharmaceutical relevance of the compounds present in the OE of *Aniba rosaeodora* is of vital importance to the scientific community and to society. Therefore, this study aims to map the main biological and antimicrobial effects of *Aniba rosaeodora* essential oil in the literature.

2. MATERIALS AND METHODS

This is an integrative review, aimed at gathering the most recent knowledge on the subject, so it attempted to follow the recommendations and criteria described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [10]. For this purpose, searches were carried out in the Embase, Scopus, PubChem, PubMed, LILACS, SciELO and BVS Portal databases, using the descriptors "*Aniba rosaeodora*" and "essential oils" and their equivalents, previously consulted in the Medical Subject Headings (MeSH). In the PubChem database, the search was carried out only with the descriptor "*Aniba rosaeodora*." In this way, articles available in full, in English and Portuguese, published up to the date of the search, May 13, 2022, were included; no filters were used in any searches.

After collecting the articles, the Covidence platform was used to help sort and select the studies, which took place in two stages: the first consisted of reading the abstract, and the second of reading the full article. Therefore, duplicate articles and articles that did not deal with the uses and properties of *Aniba rosaeodora* essential oil in the health area, as well as literature reviews, were excluded from the study.

After selection, each article was categorized according to its main topic and then grouped with other articles on the same topic to facilitate discussion.

3. RESULTS AND DISCUSSION

The searches resulted in 28 studies in Embase, 53 studies in Scopus, 15 studies in PubChem and 11 in Pubmed, while in LILACS, SciELO and Portal BVS 5, 6 and 16 results were found, respectively, totaling 134 studies. Thus, of the 134 articles, 72 were considered duplicates and, after reading the titles and abstracts, 36 studies were excluded because they were considered irrelevant. For the eligibility analysis, 26 studies were read, of which 17 were selected, as shown in Fig. 1. Table 1 summarizes the studies.

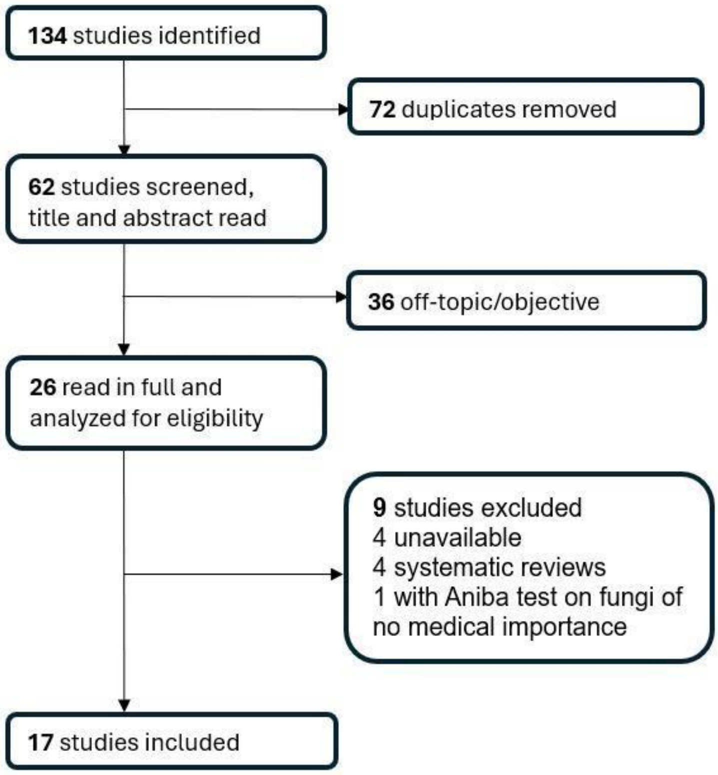

Fig. 1. Flowchart of study selection

Table 1. Selected studies and main results regarding the biological effects of *Aniba rosaeodora* essential oil

Referência	Metodologia	Principais resultados
Alcântara et al., 2010 [11]	Quantitative and qualitative study of the major components of the essential oil and their properties.	The essential oil of *Aniba rosaeodora* showed antioxidant activity and inhibited platelet aggregation.
Baldisserotto et al., 2009 [12]	Experimental study on tambaqui fish farms.	The essential oil of *Aniba rosaeodora* did not cause death in any of the animals and also showed reduction in the induction time for all stages of anesthesia as the dose increased
Chao et al., 2000 [13]	Experimental study with cultures of microorganisms.	The essential oil of *Aniba rosaeodora* showed high zones of inhibition in vitro against various pathogens compared to 44

Referência	Metodologia	Principais resultados
		other oils, especially bacterial and fungal, with moderate efficacy against viruses.
da Silva et al., 2021 [14]	Experimental in vitro study for antiparasitological, antibacterial and antiplasmodial analysis.	The essential oil of *Aniba rosaeodora* showed moderate activity against Leishmania amazonensis in the promastigote form.
de Almeida et al., 2009 [15]	Experimental study in male swiss albino mice.	The sedative effect of *Aniba rosaeodora* essential oil was shown to be dose-dependent and was potentiated when administered together with pentobarbital.
de Siqueira et al., 2014 [16]	Experimental study in Wistar rats.	Administration of the essential oil into the inferior vena cava of rats at doses of 1 mg/kg and 10 to 20 mg/kg induced a short- and long-term bradycardic and hypotensive effect, respectively
de Valois et al., 2001 [17]	Aromatherapy treatment for cancer patients.	Cancer patients treated with aromatherapy derived from *Aniba rosaeodora* experienced an improvement in symptoms such as pain
dos Santos et al., 2018 [18]	Experimental study in Wistar rats.	Rats administered the essential oil showed no significant difference from the control group in tests to verify CNS depression, anxiolytic effect and short-term memory alteration. However, there was a significant antidepressant effect through interactions with serotoninergic pathways.
Kizak et al., 2018 [19]	Experimental study using *Carassius auratus* (goldfish).	The essential oil of *Aniba rosaeodora* showed considerable anesthetic activity, and there was no mortality among the specimens and no adverse effects observed
Kohn et al., 2012 [20]	Experimental study with microorganism cultures.	The essential oil exhibited an Inhibitory Percentage (IP) against avian metapneumovirus of 98%, exerting its effect by inhibiting viral replication, thus significantly reducing the cytopathic effect on the cells analyzed in vitro.
Owen et al., 2018 [21]	Experimental study with microorganism cultures.	The zone of inhibition (ZI) of *A. rosaeodora* essential oil was similar to that of the other oils analyzed (oregano and cumin), but its minimum inhibitory concentration (MIC) was higher than that of both, indicating low antibacterial potential. However, the concentrated linalool extract (the main component of the oil) showed good results, both in terms of ZI and CIM.
Pawar et al., 2006 [22]	Experimental in vitro study carried out to test the antimicrobial activity of 75 essential oils against *Aspergillus niger*.	Among the essential oils tested, *A. rosaeodora* exhibited one of the smallest inhibition zones of *A. niger hyphae* (8 mm), as well as a low spore inhibition zone (10 mm or 50 x 104) characterized by its low antifungal potential.
Rosato et al., 2010 [23]	In an experimental study, the authors combined gentamicin and other essential oils, including *A. rosaeodora*, *in vitro*	The minimum inhibitory concentration (MIC) of *A. roseaodora* ranged from 0.05 to 0.1 mg/mL for the various bacteria tested, while the fractional inhibitory concentration (FIC)

Referência	Metodologia	Principais resultados
	to test their antimicrobial activity against various Gram-positive and Gram- negative bacteria.	was between 0.05 and 0.1 mg/mL. *Aniba* essential oil obtained the best synergistic association with gentamicin, with the MIC of gentamicin reducing from 4 to 0.24 μg /mL for *Acinobacter baumanii*.
Sampaio et al., 2012 [24]	This experimental study investigates whether one of the mechanisms of *A. roseaodora* essential oil is inhibition of adenylate cyclase activity, constituting anxiolytic and anticonvulsant effects, using chicken retinas as a model for the central nervous system (CNS).	At concentrations of 6 and 17.5 mM, the essential oil did not inhibit the accumulation of cAMP in the control; however, the accumulation of cAMP stimulated by forskolin was inhibited by Aniba essential oil at concentrations of 6 and 17.5 mM.The (-)-linalool enantiomer was shown to have the greatest biological effect. The authors suggest that inhibition of adenylate cyclase is one of the causes of the relaxing and anticonvulsant effects of the essential oil on the CNS.
Simić et al., 2004 [25]	This experimental study investigates the *in vitro* antifungal activity of four essential oils from *Lauraceae* species, including *Aniba roseaodora*. Several fungi were tested, including *Aspergillus niger, Fusarium tricinctum* and *Mucor mucedo*.	*Aniba* essential oil had the second highest antifungal activity of the four EOs tested, and at a concentration of 0.5-10 μL/mL using the macrodilution method, the growth of all the mycromycetes was inhibited. At a concentration of 15-20 μL/mL, *Aniba* oil was active against the fungi *Trichoderma viride*, *Aspergillus terreus* and *Aspergillus flavus*.
Sœur et al., 2011 [26]	Experimental study evaluating the effects of *Aniba* essential oil on human squamous cell carcinoma A431 cells, immortal transformed human keratinocyte (HaCaT) cells, keratinocytes transformed with HPV16 E6/E7 and primary human keratinocytes (NHEK).	The essential oil of *Aniba* at established concentrations obtained killing activities on A431 human squamous cell carcinoma cells and HaCaT cells, which did not happen with HEK001 transformed keratinocytes and NHEK primary human keratinocytes. Aniba's mechanisms were the production of reactive oxygen species, mitochondrial membrane deporalization and caspase-dependent apoptotic cell death.
Teles et al., 2020 [27]	Experimental study using female Balb/c mice	The essential oil of *Aniba rosaeodora* showed activity against all the bacterial strains tested, as well as antioxidant and antitrypanosomal activity

3.1 Anesthetic and Sedative Effects

In our systematic review, two studies analyzed the possible anesthetic effects of A. rosaeodora essential oil on fish [12,19]. In both studies, the purpose of using anesthesia with A. rosaeodora was to transport the animals, to reduce agitation and to keep the animals comfortable during the process; the study by Baldisserotto et al. [12] was carried out on tambaquis, while the study by Kizak et al. [19] was carried out on aquarium goldfish. Thus, anesthesia was induced in both studies, and the induction time was considered dosedependent according to the concentration of the essential oil; the recovery time from anesthesia was only considered dose-dependent in the study by Baldisserotto et al. [12]. In general, the studies highlight the biological effects of A. rosaeodora as an anesthetic, without adverse effects during recovery and without the occurrence of deaths in the studies, which has important implications for the use of this substance in these animals, but does not answer questions about the possible mechanisms involved in the induction of anesthesia, nor which compound present in the essential oil would be primarily responsible for the effects. The current literature hypothesizes that the linalool compound and the monoterpene components are responsible for the anaesthetic effect of A. rosaeodora essential oil, considering that EOs rich in linalool, derived from other plant compounds, have also shown anaesthetic effects on other fish species [28,29]. In addition, the study by Almeida et al. [15], carried out on albino mice, evaluated the sedative effects of A. rosaeodora when compared with pentobarbital. In this way, the responses were considered dose-dependent, and it is important to note that when A. rosaeodora oil was administered together with pentobarbital, sedation was potentiated, suggesting that perhaps A. rosaeodora oil has a pharmacological target similar to pentobarbital, in possible ion channels that act in the generation of neuronal electrical potentials [15], or even in an antagonistic way to pentobarbital, which activates GABA receptors to produce its pharmacological effects [30].

In the study by Valois et al. [17], patients undergoing cancer treatment underwent inhospital aromatherapy sessions for 3 years with various EOs, including A. rosaeodora. After this period, a questionnaire recorded the differences reported in various symptoms. Pain, tension and emotional stress improved significantly, especially in hospitalized patients.

In another study by Sampaio et al. [24], the oil was applied to preserved chicken retinas, and the intracellular concentration of cAMP with and without the addition of forskolin was measured. There were no significant changes without the addition, but the concentration of cAMP was significantly reduced with the addition, indicating that the oil acts on forskolin receptors, leading to sedative and anticonvulsant effects.

3.2 Antioxidant Effect

In this review, three studies included sought to elucidate the antioxidant effects of A. rosaeodora essential oil [11,26,27]. In the research carried out by Alcântara et al. [11], it was shown that the oil's antioxidant activity was assessed by its ability to sequester the stable radical 2,2-diphenyl-1-picrylhydrazyl (DPPH). In the study by Soeur et al. [26] to investigate the involvement of oxidative stress in apoptosis, the oil was tested on apoptotic cells derived from culture medium, together with α-tocopherol, and showed efficacy in increasing the number of viable cells and reducing the proportion of apoptotic cells. Finally, the analysis carried out by Teles et al. [27] found that the EO of A. rosaeodora and linalool in vitro showed dose-dependent antioxidant activity, demonstrated by the percentage of inhibition of 2,2-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS).

Therefore, according to the studies selected and analyzed, the compound studied has varied antioxidant activity against different species of free radicals, however, there is a lack of in vivo tests to better elucidate these cases, as well as clarity on the mechanisms of action.

3.3 Antidepressant Effect

Regarding the importance of evaluating the antidepressant activity of EO, a study carried out by Teles et al. [27], analyzed the behavior of rodents submitted to an inducing protocol of depressive behavior, in the depressive neurobehavioral tests the oil showed a positive action, since it managed to reduce anhedonia, characterized by the lack of pleasure in gratifying stimuli, and helped to normalize the behavior of these species of animals.

Similarly, another included study evaluated the possible antidepressant effects of various EOs rich in linalool ($> 85\%$ concentration) and the conclusions and outcomes found are similar to those of Teles et al. [27], with a reduction in anhedonia, anxious and depressive behavior [18]. In addition, it was observed that linalool compounds did not cause negative effects on the short-term memory of murines.

These findings are important considering that the main antidepressants available for the treatment of depressive disorders are selective serotonin reuptake inhibitors, whose efficacy is established in current literature, as well as their adverse effects, such as decreased libido, vomiting, nausea and headache, among others, headache, among others, symptoms that can lead to discontinuation of treatment [31]. It is necessary to investigate whether EOs have biologically active compounds with antidepressant effects, a low profile of adverse effects and greater tolerability, in order to make them viable treatments for various depressive disorders.

3.4 Antibacterial Effect

Four studies were included whose objectives included analyzing the antibacterial properties of A. rosaeodora, mainly through the application of EO in in vitro cultures. In one of these studies, Chao et al. [13] checked the zone of inhibition of a range of oils against various Gram-positive and Gram-negative pathogens, and A. rosaeodora oil was among the seven with the best results, especially against Alcaligenes faecalis, whose zone of inhibition was 19 mm.

Rosato et al. [23] showed a similar result against various bacteria, especially Acinetobacter baumannii, when combining the antibiotic gentamicin with the oil, generating a synergistic effect through the interaction of the monoterpenes with the 30 S subunit of the bacterial ribosomes. In a study using chromatography, Owen et al. [21] described the biochemical composition of the oil and found that it is mainly composed of the monoterpene linalool, which also turns out to be the main compound with an antimicrobial effect.

In addition, Teles et al. [27] again identified linalool as the main component of the oil, and classified its Minimum Inhibitory Concentration (MIC) as moderate based on the Holetz et al. [32] scale, in addition to showing antimicrobial activity against bacterial cultures such as Aeromonas caviae and Enterococcus faecalis, with inhibition halos ranging from 7 to $25 \mathrm{~mm}$, demonstrating sensitivity to this oil.

It can be seen that, in general, A. rosaeodora has significant antibacterial potential through linalool. However, this potential is dose-dependent and variable in relation to different bacteria, making further studies necessary to understand the exact mechanism of action and its clinical applicability.

3.5 Antifungal Effect

Three studies evaluated the antifungal capacity of the essential oil. Among these, the study by Chao et al. [13] analyzed the zone of inhibition (ZI) against three fungi, comparing it to 43 other oils. The results were positive, especially against Candida albicans (ZI > 33 mm), but not significant against Rhizopus oligosporus ($\mathrm{ZI}=2 \mathrm{~mm}$).

In the study by Simić et al. [25], the inhibitory and fungicidal potential of the oil was evaluated using macro and microdilution in cultures of various fungi. Macrodilution showed growth inhibition of all the variants included, but microdilution required higher concentrations (15 to $20 \mu \mathrm{L} / \mathrm{mL}$) to eliminate the most resistant fungi.

In another study by Pawar et al. [22], the efficacy of A. rosaeodora against Aspergillus niger was not significant, with comparatively low ZI of hyphae ($8 \mathrm{~mm}$) and spores ($10 \mathrm{~mm}$). The two most effective oils were clove and lemongrass, whose composition is mainly eugenol and benzyl alcohol, rather than linalool.

3.6 Anti-parasitic Effect

The anti-parasitic effect was demonstrated in two studies against pathogenic protozoa. The first, by Teles et al. [27], demonstrated an effect against various forms of Trypanosoma cruzi through linalool and through the activation of nitric oxide-producing macrophages. The protozoan Leishmania infantum also suffered an anti-parasitic effect through mitochondrial dysfunctions induced by the oil.

In turn, the study by da Silva et al. [14] showed only moderate activity against T. cruzi, despite the oil having a high selectivity index against trypomastigotes.

3.7 Antiviral Effect

The possible antiviral effect of A. rosaeodora EO was investigated in a screening study conducted by Kohn et al. [20]; in the study, the oil had antiviral actions, possibly during the replication stage, at concentrations of 2.5 µg/mL, against avian metapneumovirus (mPVA). Apart from these conclusions, it is uncertain what the real antiviral potential of this plant compound is.

3.8 Cardiovascular Effect

The study by Siqueira et al. [16] was the only one included that reported some type of cardiovascular impairment generated by the compounds in A. rosaeodora oil. The researchers tested the effects of hypotension and bradycardia in rats, suggesting that the possible effects of the substance occur through vagal reflexes and cholinergic efference.

The possible hypotensive effects are very likely to occur due to linalool, the most abundant compound in A. rosaeodora oil, occurring in concentrations between 86% [11] and 91.55% [19], but it cannot be ruled out that they occur due to the biological activity of other compounds present, such as sesquiterpenes, geraniol, alpha-terpineol, among others [16]. It is therefore important to continue researching this essential oil in order to try to establish, in other pre-clinical studies, which active ingredient is responsible for the hypotensive effect and what its possible implications are for use in humans.

4. CONCLUSION

The EO of *Aniba rosaeodora* has shown diverse and important biological, antiparasitic, antifungal, antiviral and antibacterial activities, with promising responses in preclinical models in vitro or in vivo. However, there is still a lack of knowledge about which compounds are directly involved in the effects of the essential oil and the mechanisms involved, including receptors, interactions with target molecules and other molecules.

It is suggested that linalool, present in the highest concentration in the essential oil, is its main active compound, but there is still a lack of evidence to confirm this hypothesis, as it is possible that compounds present in lower concentrations also have potent biological effects. In addition, it is essential to know the targets of the compounds, including to elucidate possible adverse effects.

Thus, this integrative review observed that the EO of Aniba rosaeadora has potential biopharmacological activities, but there are still few studies in this area, which calls for more research focused on isolating the active principles present in the oil's composition and preclinical research that investigates the physiological and pharmacomicrobiological effects of this substance in greater depth.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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