POTENTIALBIOLOGICALAND ANTIMICROBIAN EFFECTSOF THE ESSENTIAL OILOF*Anibarosaeodora*:AREVIEWOF THE LITERATURE

ABSTRACT

Aims: Maptheliteratureinsearchofthemainbiologicalandantimicrobial effectsofthe essentialoil(EO)of*Anibarosaeodora*.
Studydesign: ThisisanintegrativereviewbasedonthePRISMAmethod.
PlaceandDuration ofStudy: CenterforBiologicalandHealthSciencesofaUniversity in theBrazilianAmazon,fromJanuaryto August2022.
Methodology: Asearchwascarriedoutinthemaindatabases, suchasEmbase,Scopus, PubChem, PubMed,LILACS,SciELOandPortalBVS,withthedescriptors consultedinthe MedicalSubjectHeadings(MeSH).
Results:134articleswerefound and,afterapplying theinclusionandexclusion criteria,17 wereselectedforfullanalysis.TheEOof*Anibaroseadora*revealedmainlyantibacterial, antifungal,antiparasiticandantiviralpropertiesandin twostudies,anestheticeffects,without observation ofseriousadverseeventsanddeaths,wereobserved,butthespecificactive compoundwas notidentified.The antibacterialactivityof linalool,the compoundmost presentin*Anibaroseadora*EO,wassignificant.*Anibaroseadora*EOalsoshowedinhibitory andfungicidal potential.Inaddition,Anibaroseadorahadanantidepressanteffect, reducing anhedonia.
Conclusion: TheEOof*Anibarosaeadora*showedpotentialbiopharmacological and microbiological activitiesinpre-clinicalmodels.Linaloolstoodoutasthesubstancewiththe highestconcentration intheEO;however,itisnotyetknownwhetherthiscompoundisthe main active component.Therefore,more studies should be conductedto supportand describethepharmacologicalpotentialof*Anibarosaeadora*EO,leadingtoevidence-based pharmacology.

Keywords:Essentialoils,Anibarosaeodora,Pharmacologicalpotential,Linalool,Pau-rosa

1. INTRODUCTION

Essentialoils(EOs)arecompoundsoriginatingfromthesecondarymetabolismofaromatic plants,withorganolepticproperties. Inthiscontext,EOsstandoutashighlyvolatileandfat-soluble products, composed mainly of low molecular weight substances, such as monoterpenes, sesquiterpenes, phenylpropanoids and esters [1,2,30,31,32], enabling a great biologicalandpharmacologicalpotentialofthesecompounds.
EOsfromtheAmazonregionstandoutfortheirantimicrobial,oxidativeandlow-toxicity properties,aswellastheirimportantroleinprotectingplantcrops.Duetotheseactivities, theyarewidelyusedinvariousindustries,notablyinthepharmacological,food,cosmetics andperfumeryindustries[3].

AmongtheAmazonianspecies,*Anibarosaeodora*[4]standsoutasacandidateforthe productionofessentialoilduetoitslocalcommercialandethnopharmacologicalvaluefor thetreatmentofvariousailments.ThisspeciesbelongstotheLauraceaefamilyandisalso knowninBrazilaspau-rosa,pau-rosa-itaúba,pau-rosamulatinhoandpau-rosa-imbaúba, whileit iscalled*rosewood*intheUnitedStatesandEngland;itisanevergreentree, characteristicof terrafirmeareasandwidelydistributedin the Amazonregion,inthe BrazilianstatesofAcre,Amapá,Amazonas,Pará,RoraimaandintheAmazonianportions ofFrenchGuiana,Venezuela,Peru,SurinameandColombia[5,6]. Therefore,thepharmaceuticalrelevanceofthecompoundspresentintheOEof*Aniba rosaeodora*isofvitalimportancetothescientificcommunityandtosociety.Therefore,this study aimsto map the main biological and antimicrobial effects of *Anibarosaeodora* essentialoil in theliterature.

2. MATERIALANDMETHODS

Thisisanintegrativereview,aimedatgatheringthemostrecentknowledgeonthesubject, so itattemptedto follow the recommendationsand criteriadescribedin the Preferred ReportingItems forSystematicReviewsandMeta-Analyses(PRISMA)[7].Forthispurpose, searcheswerecarriedoutintheEmbase,Scopus,PubChem,PubMed,LILACS,SciELO andBVSPortaldatabases,usingthedescriptors"*Anibarosaeodora*"and"essentialoils"and theirequivalents,previouslyconsultedintheMedicalSubjectHeadings(MeSH).Inthe PubChemdatabase,the searchwas carriedoutonlywith thedescriptor"*Anibarosaeodora*." Inthisway,articlesavailableinfull,inEnglishandPortuguese,publisheduptothedateof thesearch,May13,2022,wereincluded;nofilterswereusedinanysearches. Aftercollectingthearticles,theCovidenceplatformwasusedtohelpsortandselectthe studies,whichtookplaceintwostages:thefirstconsistedofreadingtheabstract,andthe secondofreadingthefullarticle.Therefore,duplicatearticlesandarticlesthatdidnotdeal withtheusesandpropertiesof*Anibarosaeodora*essentialoilinthehealtharea,aswellas literaturereviews,wereexcludedfromthestudy. Afterselection,eacharticlewascategorizedaccordingtoitsmaintopicandthengrouped withotherarticlesonthesametopictofacilitatediscussion.

3.RESULTSAND DISCUSSION

The searchesresultedin 28 studies in Embase, 53 studies in Scopus,15 studies in PubChem and11inPubmed,whileinLILACS,SciELOandPortalBVS5,6and16results werefound,respectively,totaling134studies.Thus,ofthe134articles, 72wereconsidered duplicatesand,afterreadingthetitlesandabstracts,36studieswereexcludedbecausethey wereconsideredirrelevant.Fortheeligibilityanalysis,26studieswereread,ofwhich17 wereselected,asshownin figure1.Table1 summarizesthestudies.

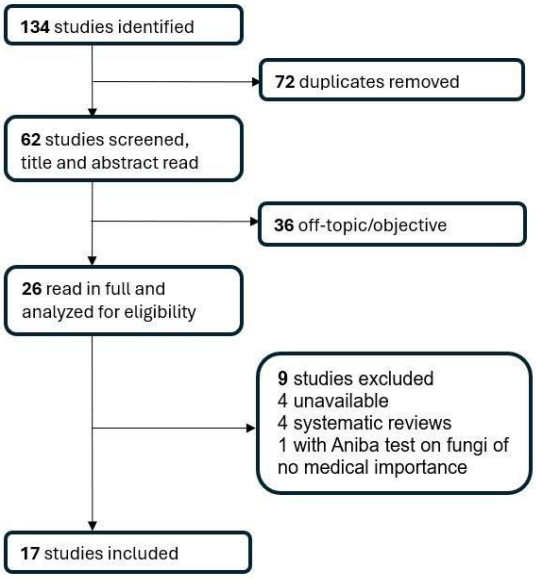

Fig.1.Flowchartofstudyselection.

Table1.Selectedstudiesandmainresultsregardingthebiologicaleffectsof*Aniba rosaeodora*essentialoil.

Referência	Metodologia	Principaisresultados
Alcântara et al.,2010[8]	Quantitative andqualitativestudy ofthemajorcomponents ofthe essentialoilandtheirproperties.	The essential oil of *Anibarosaeodora*showedantioxidant activityandinhibited plateletaggregation.
Baldisserotto etal.,2009[9]	Experimental studyontambaqui fishfarms.	Theessentialoilof*Anibarosaeodora*didnot causedeathinanyoftheanimals andalso showedreductionintheinductiontime forall stagesofanesthesiaasthedoseincreased.
Chao et al., 2000[10]	Experimentalstudywithcultures ofmicroorganisms.	The essential oil of *Anibarosaeodora*showedhighzonesofinhibitio n invitro againstvariouspathogenscompared to44 otheroils,especiallybacterial and fungal, withmoderateefficacyagainstviruses.
daSilvaetal., 2021[11]	Experimental invitrostudyfor antiparasitological, antibacterial andantiplasmodialanalysis.	The essential oil of *Anibarosaeodora*showed moderateactivity against Leishmaniaamazonensisinthe promastigoteform.
deAlmeidaet al.,2009[12]	Experimental studyinmaleswiss albinomice.	The sedativeeffectof*Anibarosaeodora*essential oilwasshown tobedose- dependent andwaspotentiated when administeredtogetherwith pentobarbital.
deSiqueiraet al.,2014[13]	ExperimentalstudyinWistarrats.	Administrationoftheessentialoilintothe inferior venacava of rats at doses of 1 mg/kgand10to20mg/kginduced ashort- andlong-termbradycardic andhypotensive effect,respectively.

de Valois et al.,2001[14]	Aromatherapy treatment for cancerpatients.	Cancerpatients treated witharomatherapy derived from*Anibarosaeodora*experienced animprovementinsymptomssuchaspain.
dosSantoset al.,2018[15]	Experimentalstudyin Wistarrats.	Ratsadministeredtheessentialoilshowed nosignificant differencefromthecontrol group intests toverifyCNSdepression, anxiolyticeffectandshort-term memory alteration. However,therewasasignificant antidepressant effectthroughinteractions withserotoninergicpathways.
Kizaket al., 2018[16]	Experimental study using *Carassiusauratus*(goldfish).	The essential oil of *Anibarosaeodora*showedconsiderableanesthetic activity,and therewasnomortalityamongthespecimens andnoadverseeffectsobserved.
Kohn et al., 2012[17]	Experimental studywith microorganismcultures.	Theessentialoilexhibited anInhibitory Percentage (IP)againstavian metapneumovirus of98%,exertingitseffect by inhibitingviral replication, thus significantlyreducingthecytopathiceffecton thecellsanalyzedinvitro.
Owen et al., 2018[18]	Experimental studywith microorganismcultures.	Thezoneofinhibition (ZI)of*A.rosaeodora*essential oilwassimilartothatoftheother oilsanalyzed (oregano andcumin),butits minimuminhibitoryconcentration (MIC)was higherthanthatofboth,indicating low antibacterial potential.However,the concentrated linaloolextract(themain component oftheoil)showed goodresults, bothin termsofZIandCIM.
Pawar etal., 2006[19]	Experimentalin vitrostudy carried out to test the antimicrobial activityof75essentialoilsagainst *Aspergillusniger*.	Amongtheessential oilstested,*A. rosaeodora*exhibitedoneofthesmallest inhibition zonesof*A.nigerhyphae*(8mm), aswellasalowsporeinhibitionzone(10 mmor50x104)characterized byitslow antifungalpotential.
Rosatoet al., 2010[20]	Inanexperimental study,the authors combined gentamicinand otheressential oils,including*A. rosaeodora*, *invitro*totesttheir antimicrobial activityagainst variousGram-positive andGram-negativebacteria.	Theminimuminhibitoryconcentration (MIC) of*A.roseaodora*rangedfrom0.05to0.1 mg/mLforthevarious bacteria tested,while thefractionalinhibitoryconcentration (FIC) wasbetween0.05and 0.1mg/mL.*Aniba*essential oilobtainedthebestsynergistic associationwithgentamicin, withtheMICof gentamicinreducingfrom4to0.24µg/mL for*Acinobacterbaumanii*.
Sampaio et al.,2012[21]	Thisexperimental study investigateswhether oneof the mechanisms of*A.roseaodora*essential oilisinhibition of adenylate cyclaseactivity, constituting anxiolyticand anticonvulsant effects,using chickenretinasasamodelforthe	At concentrationsof 6 and 17.5 mM, the essential oildidnotinhibittheaccumulation ofcAMPinthecontrol;however, the accumulation of cAMP stimulated by forskolinwasinhibitedbyAnibaessential oil atconcentrations of6and17.5mM.The (-)-linaloolenantiomer wasshowntohavethe greatest biological effect. The authors

	centralnervoussystem(CNS).	suggestthatinhibitionofadenylatecyclase isoneofthecauses oftherelaxing and anticonvulsant effectsoftheessentialoilon theCNS.
Simić et al., 2004[22]	Thisexperimental study investigates the*invitro*antifungal activityoffouressential oilsfrom *Lauraceae*species,including *Anibaroseaodora*. Several fungi weretested, including*Aspergillus niger,Fusarium tricinctum*and *Mucormucedo*.	*Aniba*essentialoilhadthesecondhighest antifungalactivity ofthe four EOs tested, and at a concentration of 0.5-10 µL/mL usingthemacrodilutionmethod,thegrowth ofallthemycromyceteswasinhibited.Ata concentrationof15-20µL/mL,*Aniba*oilwas activeagainstthefungi*Trichodermaviride*, *Aspergillusterreus*and*Aspergillusflavus*. The
Sœuret al., 2011[23]	Experimentalstudyevaluatingthe effectsof*Aniba*essential oilon humansquamous cellcarcinoma A431cells,immortal transformed human keratinocyte(HaCaT) cells,keratinocytes transformed with HPV16E6/E7 andprimary humankeratinocytes(NHEK).	essentialoil of *Aniba*at established concentrationsobtainedkillingactivitieson A431humansquamouscellcarcinomacells andHaCaTcells,whichdidnothappenwith HEK001 transformed keratinocytes and NHEK primaryhumankeratinocytes.Aniba's mechanismswerethe productionofreactive oxygen species, mitochondrial membrane deporalizationand caspase-dependent apoptoticcelldeath.
Teles et al., 2020[24]	Experimentalstudyusingfemale Balb/cmice	The essential oil of *Anibarosaeodora*showed activity againstallthebacterial strains tested, as well as antioxidantand antitrypanosomalactivity.

3.1Anestheticandsedativeeffects

Inoursystematic review,twostudiesanalyzed thepossibleanestheticeffectsof*A. rosaeodora*essentialoilonfish[9,16].Inbothstudies,thepurposeofusinganesthesiawith *A.rosaeodora*wastotransporttheanimals,toreduceagitationandtokeeptheanimals comfortablduringtheprocess;thestudybyBaldisserottoetal.(2018)[9]wascarriedout ontambaquis, whilethestudybyKizaketal.(2018)[16]wascarriedoutonaquarium goldfish. Thus, anesthesiawasinducedinbothstudies,andtheinduction timewasconsidereddose-dependentaccordingto theconcentrationof the essential oil; the recovery time from anesthesiawasonlyconsidered dose-dependent inthestudybyBaldisserottoetal(2018) [16].In general,thestudieshighlightthebiologicaleffectsof*A. rosaeodora*asan anesthetic, withoutadverseeffectsduringrecovery andwithouttheoccurrenceofdeathsinthestudies, whichhasimportantimplicationsfortheuseofthissubstanceintheseanimals,butdoesnot answerquestionsaboutthepossiblemechanismsinvolvedintheinductionofanesthesia, norwhichcompoundpresentintheessentialoilwouldbeprimarilyresponsible forthe effects. Thecurrentliteraturehypothesizes thatthelinaloolcompoundandthemonoterpene components areresponsible fortheanaestheticeffectofA.rosaeodora essentialoil, considering thatEOsrichinlinalool,derivedfromotherplantcompounds, havealsoshown anaestheticeffectsonotherfishspecies[25,26].

In addition,the study byAlmeidaetal.(2009)[12], carried outonalbinomice,evaluatedthe sedative effectsof *A. rosaeodora*when compared with pentobarbital.In thisway, the

responseswere considereddose-dependent,and it is importantto note that when *A. rosaeodora*oil was administeredtogetherwith pentobarbital,sedationwas potentiated, suggestingthatperhaps*A.rosaeodora*oilhasapharmacological targetsimilarto pentobarbital, inpossibleionchannelsthatactinthegeneration ofneuronalelectrical potentials[12],oreveninanantagonisticwaytopentobarbital, whichactivatesGABA receptorstoproduceitspharmacologicaleffects[27].

InthestudybyValoisetal.(2001)[14],patients undergoingcancertreatmentunderwentin-hospitalaromatherapysessions for3yearswithvariousEOs,including*A.rosaeodora*.After thisperiod,aquestionnaire recordedthedifferencesreportedinvarioussymptoms.Pain, tensionandemotionalstressimprovedsignificantly,especiallyinhospitalizedpatients.

InanotherstudybySampaioetal.(2011)[21],theoilwasappliedtopreserved chicken retinas, andtheintracellularconcentrationofcAMPwithandwithouttheadditionofforskolin was measured. There wereno significant changes without the addition, but the concentrationofcAMPwas significantlyreducedwith theaddition,indicatingthattheoilacts onforskolinreceptors,leadingtosedativeandanticonvulsanteffects.

3.2Antioxidanteffect

In thisreview,threestudiesincludedsoughtto elucidatethe antioxidanteffectsof A. rosaeodoraessentialoil[8,23,24].Intheresearchcarriedoutby Alcântaraetal.(2010)[8], itwasshownthattheoil'santioxidantactivitywasassessed byitsabilitytosequesterthe stableradical2,2-diphenyl-1-picrylhydrazyl(DPPH).InthestudybySoeuretal.(2011)[23] to investigatethe involvement of oxidative stress in apoptosis, the oil was tested on apoptotic cells derived from culture medium, together with α-tocopherol, and showed efficacyinincreasingthenumberofviablecellsandreducingtheproportionofapoptotic cells.Finally,theanalysiscarried outbyTelesetal.(2020)[24]foundthattheEOof*A. rosaeodora*andlinalool*invitro*showeddose-dependentantioxidantactivity,demonstrated by thepercentage of inhibition of 2,2-azinobis-(3-ethylbenzothiazoline-6-sulfonicacid) (ABTS). Therefore,accordingtothestudiesselectedandanalyzed,thecompoundstudiedhas varied antioxidantactivityagainstdifferentspeciesoffreeradicals,however,thereisalackof*in vivo*teststobetterelucidatethesecases,aswellasclarityonthemechanismsofaction.

3.3Antidepressanteffect

Regardingtheimportanceofevaluatingtheantidepressantactivityof EO,a studycarriedout byTelesetal.(2020)[24],analyzedthebehaviorofrodentssubmittedtoaninducing protocolofdepressivebehavior,inthedepressiveneurobehavioralteststheoilshoweda positiveaction,since itmanagedtoreduce anhedonia,characterizedbythelackof pleasure ingratifyingstimuli,andhelpedtonormalizethebehaviorof thesespeciesofanimals.

Similarly,anotherincludedstudyevaluatedthepossibleantidepressant effectsofvarious EOsrichinlinalool(>85%concentration) andtheconclusionsandoutcomesfoundare similartothoseofTelesetal.(2020)[24],withareduction inanhedonia,anxiousand depressivebehavior[15].Inaddition, itwasobservedthatlinalool compoundsdidnotcause negativeeffectsontheshort-termmemoryofmurines.

Thesefindingsareimportantconsidering thatthemainantidepressants availableforthe treatmentofdepressivedisorders areselectiveserotoninreuptakeinhibitors,whose efficacy isestablishedincurrentliterature,aswellastheiradverseeffects,such asdecreasedlibido, vomiting,nauseaandheadache, amongothers,headache, amongothers,symptomsthat canleadtodiscontinuationoftreatment[28].Itis necessarytoinvestigatewhetherEOshave biologicallyactivecompoundswithantidepressanteffects,alowprofileofadverseeffects andgreatertolerability,inordertomakethemviabletreatments forvariousdepressive disorders.

3.4Antibacterialeffect

Fourstudieswereincludedwhoseobjectives includedanalyzing theantibacterial properties of*A.rosaeodora*, mainlythroughtheapplicationofEOin*invitro*cultures.Inoneofthese studies,Chaoetal.(2000)[10]checkedthezoneofinhibition ofarangeofoilsagainst various Gram-positiveandGram-negativepathogens,and*A.rosaeodora*oilwasamong the sevenwiththebestresults,especiallyagainst*Alcaligenes faecalis*,whosezoneofinhibition was19mm.

Rosatoetal.(2010)[20]showedasimilar resultagainst various bacteria, especially *Acinetobacterbaumannii*,whencombiningtheantibioticgentamicinwiththeoil,generatinga synergisticeffectthroughtheinteractionofthemonoterpenes withthe30Ssubunitofthe bacterialribosomes.Inastudy usingchromatography,Owenetal.(2018)[18]describedthe biochemicalcompositionoftheoilandfoundthatitismainlycomposedofthemonoterpene linalool,whichalsoturnsouttobethemaincompoundwithanantimicrobialeffect.

In addition,Teles et al.(2020)[24]againidentifiedlinaloolasthemaincomponentof theoil, andclassifieditsMinimumInhibitoryConcentration (MIC)asmoderatebasedontheHoletz etal.(2002)[29]scale,inadditiontoshowingantimicrobialactivityagainstbacterialcultures suchas*Aeromonascaviae*and*Enterococcusfaecalis*,withinhibitionhalosrangingfrom7to 25mm,demonstratingsensitivitytothisoil.

Itcanbeseenthat,ingeneral,*A.rosaeodora*hassignificantantibacterial potentialthrough linalool.However,this potentialis dose-dependentand variablein relation to different bacteria,makingfurtherstudiesnecessarytounderstandtheexactmechanismofactionand itsclinicalapplicability.

3.5Antifungaleffect

Threestudiesevaluatedtheantifungal capacityoftheessentialoil.Amongthese,thestudy byChaoetal.(2000)[10]analyzedthezoneofinhibition(ZI)againstthreefungi,comparing itto43otheroils.Theresultswerepositive,especiallyagainst*Candidaalbicans*(ZI>33 mm),butnotsignificantagainst*Rhizopusoligosporus*(ZI= 2mm).

InthestudybySimićetal.(2004)[22],theinhibitoryandfungicidal potentialoftheoilwas evaluatedusingmacroandmicrodilution inculturesofvariousfungi.Macrodilutionshowed growth inhibitionofallthe variants included,butmicrodilutionrequiredhigher concentrations (15to20µL/mL)toeliminatethemostresistantfungi.

In anotherstudy by Pawar et al. (2006) [19], the efficacy of *A. rosaeodora*against*Aspergillusniger*wasnotsignificant,withcomparativelylowZI ofhyphae(8 mm)andspores (10mm).Thetwomosteffectiveoilswerecloveandlemongrass, whosecompositionis mainlyeugenolandbenzylalcohol,ratherthanlinalool.

3.6Anti-parasiticeffect

Theanti-parasiticeffectwasdemonstrated intwostudiesagainstpathogenicprotozoa.The first,byTelesetal.(2020)[24],demonstrated aneffectagainstvariousformsof *Trypanosoma cruzi*throughlinaloolandthroughtheactivationofnitricoxide-producing macrophages. Theprotozoan*Leishmaniainfantum*alsosufferedananti-parasitic effect throughmitochondrialdysfunctionsinducedbytheoil.

Inturn,thestudybydaSilvaetal.(2021)[11]showedonlymoderateactivityagainst*T. cruzi*,despitetheoilhavingahighselectivityindexagainsttrypomastigotes.

3.7Antiviral effect

Thepossible antiviraleffectof*A.rosaeodora*EOwasinvestigated inascreening study conductedbyKohnetal.(2012)[17];inthestudy,theoilhadantiviralactions,possibly duringthereplicationstage,atconcentrationsof2.5µg/mL, againstavianmetapneumovirus (mPVA).Apartfromtheseconclusions,itisuncertainwhattherealantiviralpotentialofthis plantcompoundis.

3.8Cardiovascularеffect

Thestudyby Siqueiraetal. (2014)[13]wastheonlyoneincludedthatreportedsometypeof cardiovascular impairmentgeneratedbythecompoundsin*A.rosaeodora*oil.The researcherstestedtheeffectsofhypotensionandbradycardiainrats,suggesting thatthe possibleeffectsofthesubstanceoccurthroughvagalreflexesandcholinergicefference. Thepossiblehypotensive effectsareverylikelytooccurduetolinalool,themostabundant compoundin*A.rosaeodora*oil,occurringinconcentrations between86%[8]and91.55% [16], butit cannotbe ruledout that they occur dueto the biologicalactivityof other compoundspresent,such assesquiterpenes,geraniol,alpha-terpineol,amongothers[13]. It isthereforeimportanttocontinue researchingthisessentialoilinordertotrytoestablish,in otherpre-clinicalstudies,whichactiveingredientisresponsibleforthehypotensiveeffect andwhatitspossibleimplicationsareforuse inhumans.

4.CONCLUSION

TheEOof*Anibarosaeodora*hasshowndiverseandimportantbiological,antiparasitic, antifungal, antiviraland antibacterial activities, with promising responses in preclinical models*in vitro*or*in vivo*.However,thereisstilla lackofknowledgeaboutwhichcompounds aredirectlyinvolvedintheeffectsoftheessentialoilandthemechanismsinvolved,including receptors,interactionswithtargetmoleculesandothermolecules.

Itissuggestedthatlinalool,presentinthehighestconcentrationintheessentialoil,isits mainactive compound,butthereisstillalackofevidencetoconfirm thishypothesis,asitis possiblethatcompoundspresent inlower concentrationsalso have potent biologicaleffects. Inaddition,itisessentialtoknowthetargetsofthecompounds, includingtoelucidate possibleadverseeffects.

Thus, thisintegrativereview observedthat the EO of *Anibarosaeadora*has potential biopharmacologicalactivities,buttherearestillfewstudiesinthisarea,which callsformore researchfocusedonisolatingtheactiveprinciplespresentintheoil'scomposition andpre-clinicalresearchthatinvestigatesthephysiologicalandpharmacomicrobiological effectsof thissubstanceingreaterdepth.

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