Review Article

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

ABSTRACT

Aims: Mapthelitratureinsearchofthemainbiologicalandantimicrobial 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], enabling a great biologicalandpharmacologicalpotentialofthesecompounds.
EOsfromtheAmazonregionstandoutfortheirantimicrobial,oxidativeandlow-toxicity properties,aswellastheirimportantroleinprotectingplantcrops.Duetotheseactivities,

they are widely used in various industries, notably in the pharmacological, food, cosmetics and perfumery industries [3].

Among the Amazonian species, *Aniba rosaeodora* [4] 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 [5,6].

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. MATERIAL 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) [7]. 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 figure 1. Table 1 summarizes the studies.

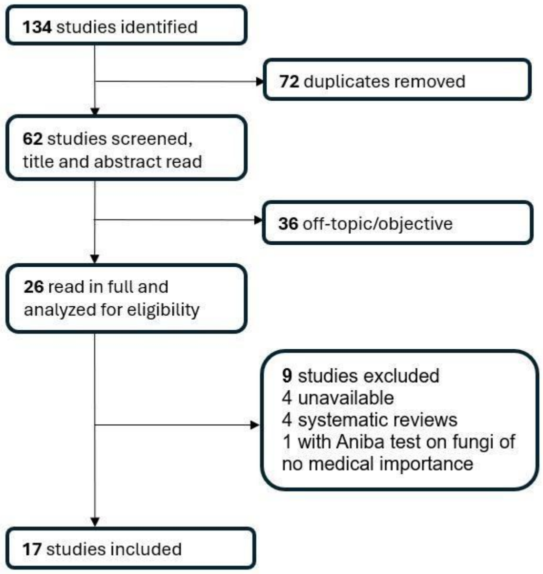

Fig.1.Flowchartofstudyselection.

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*showedhighzonesofinhibition 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*showedconsiderableanesth eticactivity,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 mechanismswereproductionofreactive oxygen species, mitochondrial membrane deporalizationand caspase-dependent apoptoticcelldeath.
Teles et al., 2020[24]	Experimentalstudyusingfemale Balb/cmice	The essential oil of *Anibarosaodora*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 comfortableduringtheprocess;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].IntheresearchcarriedoutbyAlcântaraetal.(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

RegardingtheimportanceofevaluatingtheantidepressantactivityofEO,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.

3.8Cardiovasculareffect

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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