

Bioactivity of the specie *Annona coriacea*: A systematic review**Bioatividade da espécie *Annona coriacea*: Uma revisão sistemática**

DOI:10.34119/bjhrv3n4-263

Recebimento dos originais: 03/07/2020

Aceitação para publicação: 18/08/2020

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ABSTRACT

The araticum (*Annona coriacea* Mart.) is a tree of the Annonaceae family with great distribution in the northern Cerrados of the State of Piauí. Several species of this family have medicinal use and demonstrate some biological activities that have already been experimentally proven such as antihelminthic, antimalarial, antimicrobial, antinociceptive, antiprotozoal, insecticidal, parasiticidal and antioxidant activities due to the presence of acetogenins. The objective of this study was to carry out a scientific and technological prospection of the *Annona coriacea* plant related to tickcidal activity. The scientific bases used were; *PubMed*, *ScienceDirect* and *Web of Science* and the technological databases include; EPO, WIPO, USPTO, DII, LATIPAT and INPI, with the following keywords: *Annona coriacea*, *Annona coriacea* and tickcidal, *Annona coriacea* and acaricide and *Annona coriacea* and biocide, all articles published in the last decade and without temporal cut for patent registration being counted. We found 156 articles and 17 patents, most of them dealing with medicinal use and chemical composition of the plant. The study showed that there is interest in the plant studied, but there is a wide field to carry out studies on technological innovation and development of new products, as in the area of tickcidal products.

Keywords: Annonaceae, tick, phytochemistry, phytotherapy, natural product.

RESUMO

O araticum (*Annona coriacea* Mart.) é uma planta arbórea da família Annonaceae com grande distribuição nos Cerrados Setentrionais do Estado do Piauí. Diversas espécies desta família têm uso medicinal e algumas atividades biológicas já foram comprovadas experimentalmente como as atividades antihelmíntica, antimalárica, antimicrobiana, antinociceptiva, antiprotozoária, inseticidas, parasiticidas e antioxidante devido às acetogeninas. O objetivo deste estudo foi realizar uma prospecção científica e tecnológica da planta *Annona coriacea* relacionada com a atividade carrapaticida. As bases científicas foram *PubMed*, *ScienceDirect* e *Web of Science* e as tecnológicas EPO, WIPO, USPTO, DII, LATIPAT e INPI, com as palavras-chave: *Annona coriacea*, *Annona coriacea* e carrapaticida, *Annona coriacea* e acaricida e *Annona coriacea* e biocida, sendo computados todos os artigos publicados na última década e sem recorte temporal para o registro de patentes. Foram encontrados 156 artigos e 17 patentes, a maioria abordando uso medicinal e composição química da planta. O estudo mostrou que existe interesse pela planta estudada, contudo há um campo vasto para execução de estudos de inovação tecnológica e desenvolvimento de novos produtos, como na área de carrapaticidas.

Palavras-chave: Annonaceae, carrapato, fitoquímica, fitoterápico, produto natural.

1 INTRODUÇÃO

Annona coriacea Mart., popularly known as araticum, is an arboreal species with great distribution in the Northern Cerrados of the State of Piauí (Sousa et al. 2013). It is a fruit of the Annonaceae family, as well as the pinecone (*A. squamosa*) and the graviola (*A. muricata*) (Ribeiro et al. 2000).

Regarding the biodiversity composition of chemical substances, this family is characterized by the presence of terpenoids (mainly diterpenes), alkaloids derived from isoquinolines, phenolic acids, tannins, flavonoids, steroids, aromatic and benzene substances, catechins, proanthocyanidins,

carbohydrates, lipids, proteins, lactones, vitamins, carotenes, saponins, besides essential oils, whose composition is predominantly of monoterpenes and sesquiterpenes (Luna 2006, Lima 2007, Silva et al. 2009, Reis 2011).

Pharmacological and phytochemical studies using species of annonaceae have largely intensified due to the discovery of acetogenins, extremely bioactive secondary metabolites, exclusive to this family, which have been considered as important alternatives for the development of antitumor drugs (Leite 2009, Rupprecht et al. 1990).

Regarding the biological activities of *A. coriacea*, it has been used in traditional medicine due to its analgesic, anti-inflammatory, antiprotozoan, antioxidant, antiproliferative, anticholinergic, antinociceptive and antifungal properties (Sousa et al. 2007, Toledo et al. 2011, Siqueira et al. 2011, Benites et al. 2015, Formagio et al. 2015, Sousa et al. 2011, Sousa et al. 2012, Silva et al. 2012).

In China, some annonaceae are widely cultivated and used as insecticides and parasiticides (Chen et al. 2004). There are proven anthelmintic, antimalarial, antimicrobial, antinociceptive, antiprotozoal, pesticide and antioxidant activities due to acetogenins (Alali et al. 1999, Gripp et al., 2020, Julian-Loeza et al. 2011). Thus, considering the reports in the literature and emphasizing its parasiticide potential, the species in question is known to be an antiparasitic agent, which is still unsatisfactory. In this sense, due to its wide use in folk medicine and some of its scientifically verified actions, the phytochemical study of araticum extract on ticks is relevant, since they cause damage to bovine performance due to their spoiling, mechanical and toxic actions (Fraga et al. 2003).

The *Rhipicephalus (Boophilus) microplus* is an ectoparasite of great economic impact in cattle raising in Brazil because it can cause losses such as: reduction of the productive and reproductive performance of dairy cattle herd, reduction of the production yield, reduction of the quality of animal hide, and loss of animal weight and milk production (Gomes et al. 2011, Santos and Vogel 2012), which leads to economic losses to producers, by reducing the income related to the animal and increased expenses with products for the control of this parasite.

Currently, the chemical control of ticks is characterized by the progressive increase in the number of strains resistant to the main acaricides used and, consequently, by the increase in the frequency of application (Furlong et al. 2007), which causes two major problems: the accelerated development of resistance to the active ingredient and the residues in products of animal origin, which has caused great concern to society and government agencies (Leal et al. 2003).

In this perspective, plants are important sources of substances having different chemical structures with different activities against arthropods (Sousa et al. 2008), which drive the development of research on new control practices such as the use of medicines based on plant extracts.

In view of the above, it is believed that with regard to scientific and technological prospection, research that shows the properties already described for *Annona coriacea*, with special focus on its antiparasitic activity, represent a valuable tool, because they constitute systematic means of scientific information that are fundamental in guiding the development of new technologies (Machado et al. 2014).

In this context, the objective of the present study was to carry out a scientific and technological prospection of plant *A. coriacea* related to tickcidal activity, in order to analyze the number of patent applications filled in each country, through national and international innovation and technology data bases, as well as to describe the profile of scientific production of this species.

2 MATERIALS AND METHODS

The prospective study was carried out in november 2019 based on the search of patent applications and scientific articles on the species *Annona coriacea*, as well as its relationwith tickcidal activity. The following keywords were used: *Annona coriacea*, *A. coriacea* and tickcidal, *A. coriacea* and acaricide and *A. coriacea* and biocide. The scientific bases used were *PubMed*, *ScienceDirect* and *Web of Science*. In this stage, only research articles published in the last 10 years that displayed these descriptors in their titles and/or abstracts were selected. Duplicate articles found in the same database and/or in more than one of the databases used, were excluded.

The *European Patent Office* (EPO), *World Intellectual Property Organization* (WIPO), *United States Patent and Trademark Office* (USPTO), *Derwent Innovations Index®* (DII), Latin American Patent database (LATIPAT) and database of the Brazilian National Institute of Industrial Property (INPI) were used for the technological databases. Prospection was carried out through search, collection and treatment of data in patent documents between the years 1963 and 2019.

The program Microsoft Excel version Windows 10®was used for data analysis.

3 RESULTS AND DISCUSSION

3.1 SCIENTIFIC PROSPECTION

Concerning *Annona coriacea* species, the initial search with this descriptor in *PubMed* gave rise to (58) associated results, 64 in *Science Direct* and 31 related articles in *Web of Science*. However, with regard to tickcidal activity, 1 article was found in the *PubMed* database and 2 articles in the *Web of Science* database using the following descriptors: *Annona coriacea* and acaricide and *Annona coriacea* and biocide (Table I).

TABLE I: Number of scientific articles published in PubMed, ScienceDirect and Web of Science databases, by keywords.

Keywords	PubMed	ScienceDirect	Web of Science
Annona coriacea	58	64	31
Annona coriacea and tickcide	0	0	0
Annona coriacea and acaricide	1	0	1
Annona coriacea and biocide	0	0	1

Through the scientific bases used in this study, a total of 156 articles were computed for the species studied. The search strategy and selection of the researched articles were described through the PRISMA flowchart (Figure 1). Of the total number of articles identified in the databases, after reading the title and abstract and, when necessary, the text itself, some were excluded by duplication, because it is a book chapter or because the species itself was not cited in the text. As well as those who approached the species in a botanical, ecological, genetic, morphological and chemical context, besides those who reported other biological activities, other than the tickcidal activity. Those in which the species was cited only in the references and those in which the authors mentioned the species only in their discussion, but not related to the tickcidal activity, were also removed resulting in the eligibility of only 4 articles for discussion, all found in the *Web of Science* database (Table II).

Figure 1. PRISMA flow diagram.

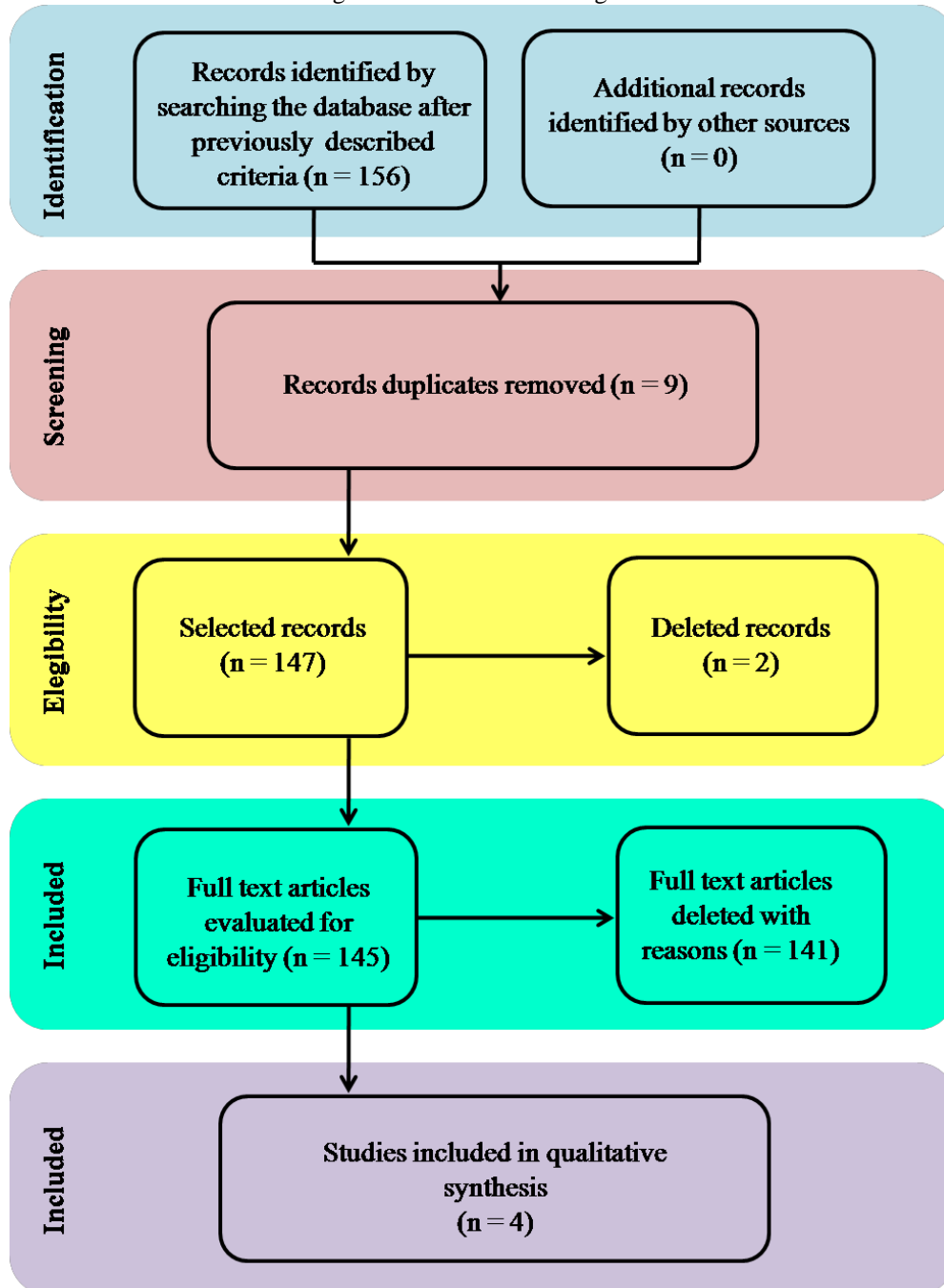
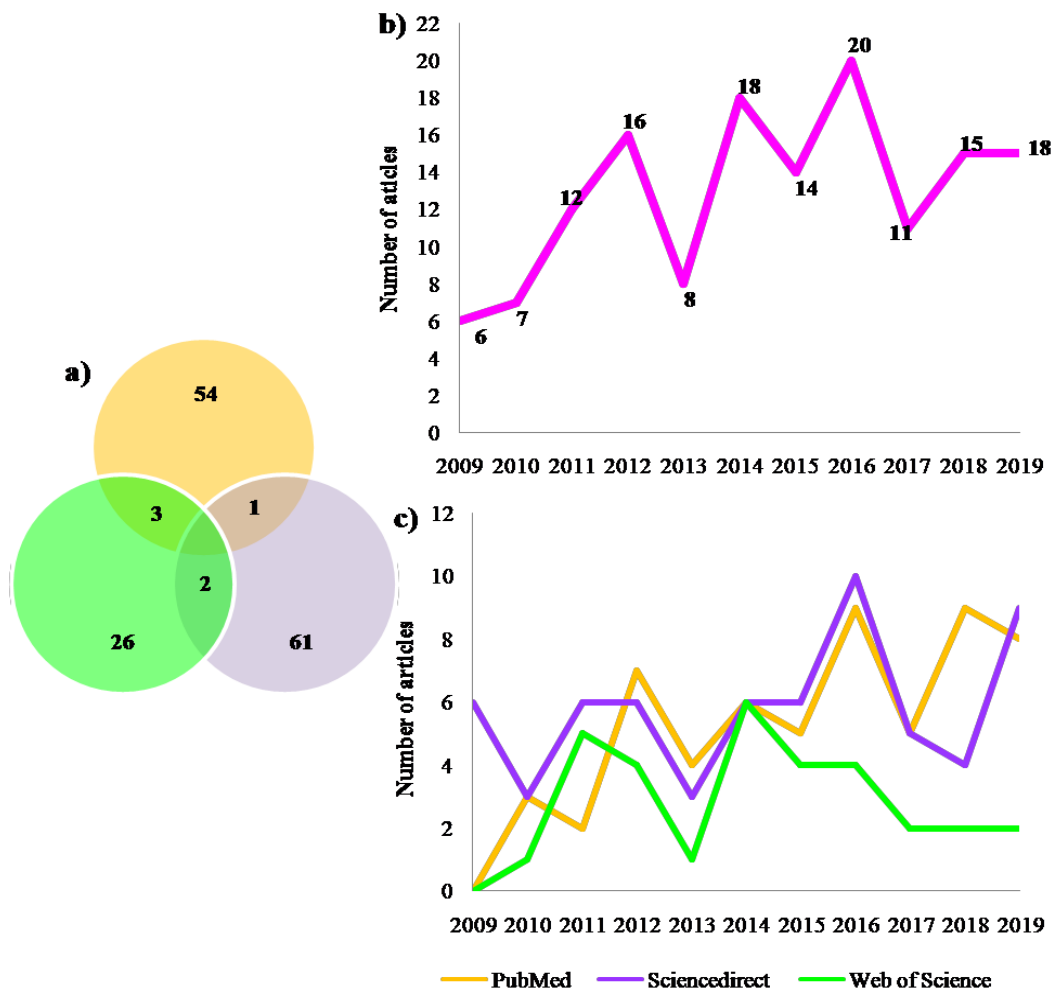


TABLE II: Publications on tickcidal activity found in *Web of Science* database, 2009-2019.

Author/Year	Title	Arthropod	Objective	Periodical	Principal Results
Alves et al. 2015	Acaricidal activity of Annonaceae fractions against <i>Tetranychus tumidus</i> and <i>Tetranychus urticae</i> (Acari: Tetranychidae) and the metabolite profile of <i>Duguetia lanceolata</i> (Annonaceae) using GC-MS	Mite	Select soluble fractions in dichloromethane with acaricide activity, coming from methanolic extracts of annonaceous species.	Semina: Ciências Agrárias	Among the soluble fractions in dichloromethane, only that coming from the bark of the stem of <i>D. lanceolata</i> caused a reduction in the survival of females of <i>T. tumidus</i> , but without ovicidal activity. Activity regarding <i>T. urticae</i> was also found. The analysis of the metabolite profile of the <i>D. lanceolata</i> stem bark fraction by means of GC-MS suggested that the major constituents are 2,4,5-trimethoxystyrene and trans-asarone.
Carneiro et al. 2013	Biocide activity of <i>Annona coriacea</i> seeds extract on <i>Rhodnius neglectus</i> (Hemiptera: Reduviidae)	Insect	To evaluate the biocidal activity of the ethanolic extract of <i>Annona coriacea</i> seeds in nymphs and adults of <i>Rhodnius neglectus</i> (Chagas disease vector).	Revista de Biologia Tropical	<i>A. coriacea</i> extract was able to disrupt the development of nymphs and adults of <i>R. neglectus</i> , with a mortality rate higher than 90%, 36% and 100%, in the highest concentrations, respectively. There was also inhibition of moulting in nymphs, lower reproductive capacity in females, food deterrence, and morphological changes in nymphs and adults.
Freitas et al. 2014	Effects of Methanolic Extracts of <i>Annona</i> Species on the Development and Reproduction of <i>Spodoptera frugiperda</i> (J.E. Smith) (Lepidoptera: Noctuidae)	Insect	Report the effect of methanol leaf extracts from <i>Annona dioica</i> , <i>Annona cacans</i> and <i>Annona coriacea</i> on the development and reproduction of <i>Spodoptera frugiperda</i> .	Neotropical Entomology	<i>A. coriacea</i> leaf extract decreased larval survival, interrupted pupal development and affected weight gain of <i>S. frugiperda</i> . <i>A. dioica</i> also affected the survival of larvae, but its effects were more pronounced at the adult stage, as fecundity, fertility, egg hatching and embryonic development were severely affected. Extracts of <i>A. cacans</i> leaves had no effect on <i>S. frugiperda</i> . Extracts of leaves of <i>A. dioica</i> and <i>A. coriacea</i> showed higher content of flavonoids and phenols, respectively. Our results indicated that both <i>A. dioica</i> and <i>A. coriacea</i> have the potential for development of botanical insecticides.
Costa et al. 2012	Morphological Changes in the Midgut of <i>Aedes aegypti</i> L. (Diptera: Culicidae) Larvae Following Exposure to an <i>Annona coriacea</i> (Magnoliales: Annonaceae) Extract	Insect	Describe the morphological changes that occur in the middle intestine of the third instar <i>Aedes aegypti</i> L. (Diptera: Culicidae) after treatment with a methanolic extract of <i>Annona coriacea</i> (Magnoliales: Annonaceae).	Neotropical Entomology	Insects exposed to the extract demonstrated intense and destructive cytoplasmic vacuolization in columnar and regenerative intestinal cells. The apical surfaces of columnar cells exhibited cytoplasmic protrusions oriented toward the lumen, suggesting that these cells could be involved in apocrine secretory processes and/or apoptosis.

Figure 2 (a, b, c) shows the evolution of publications in the scientific databases related to the term *Annona coriacea*, being possible to observe an increase in publications in the last 10 years, with emphasis on the year 2016, which has 13.79% of articles. This trend is related to the versatility of araticum's applications in different areas of research, such as medicine, pharmacology, chemistry, botany, entomology and agriculture. November 2019 already has a significant portion of articles (12.41%), and this result is superior to that of the year 2018, which shows the growing interest of the research groups for the species object of this study.

Figure 2. Results obtained for the scientific search for the term "*Annona coriacea*" in *PubMed*, *ScienceDirect* and *Web of Science* (a) and Annual evolution of publications referring to the term "*Annona coriacea*" in the aforementioned scientific bases, general (b) and individual (c).

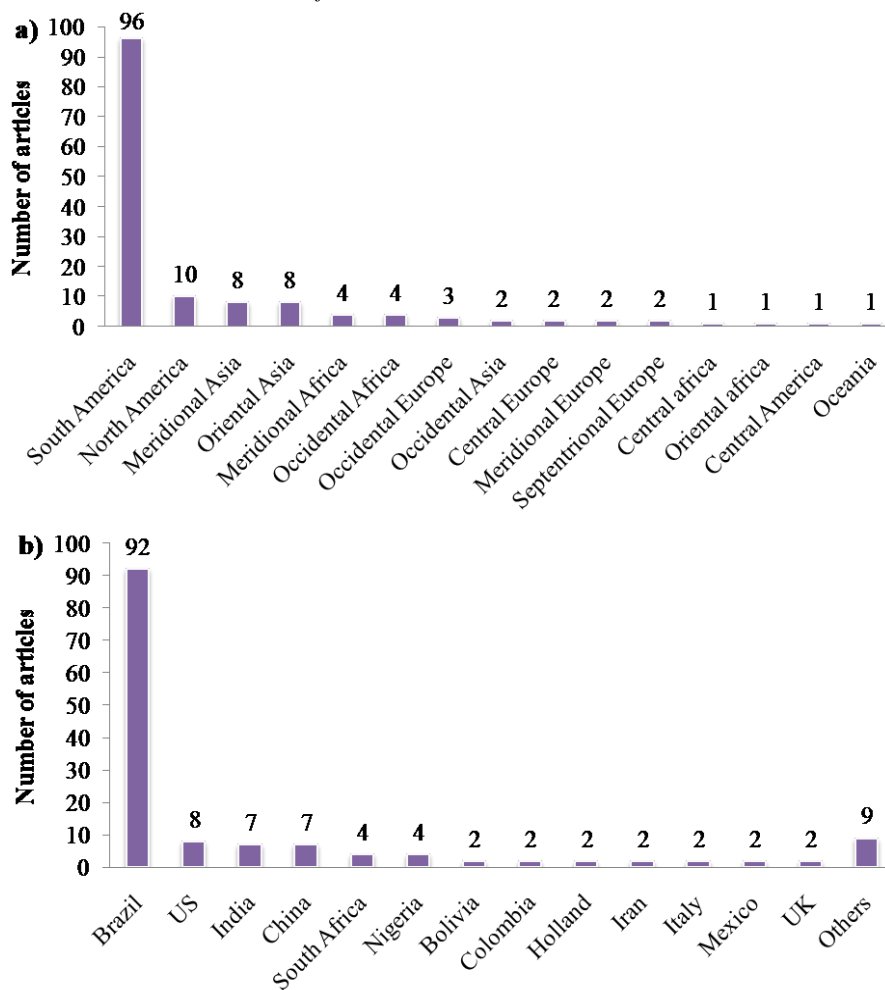


The development of scientific research on the species studied, point out American and Asian countries as the authors of number of publications, especially Brazil (South America), which stands out in 1st place, with a total of 92 publications reported between 2009 and 2019, followed by the

United States (North America), with 8 papers and China (East Asia) and India (South Asia), with 7 studies, each, occupying the second, third and fourth place in this order (Figure 3 a, b).

The profile of the studies varied widely, with the highest number of publications referring to medicinal potential (Table III). Among the pharmacological activities described are cytoprotective (Júnior et al. 2016), antiproliferative and anticholinesterase (Formagio et al. 2015), antidiarrheal (Araújo et al. 2014, Lozano et al. 2014), anticoagulant (Ribeiro et al. 2017), antimicrobial (Toledo et al. 2011), antiophidic (Ribeiro et al. 2014, Saraiva et al. 2015), anti-inflammatory (Sousa et al. 2014, Sousa et al. 2012, Sousa et al. 2011), antioxidant (Novaes et al. 2019, Benites et al. 2015), diuretic (Magalhães et al. 2019), phytotoxic (Novaes et al. 2016), hepatotoxic (Nascimento et al. 2012), antinociceptive (Sousa et al. 2012, Sousa et al. 2011) and antiprotozoal (Siqueira et al. 2011). These studies promote the emergence of new drugs as an alternative to pharmacotherapy.

Figure 3. Distribution of scientific articles by world region (a) and country of origin (b), referring to the term “*Annona coriacea*” in *PubMed*, *ScienceDirect* and *Web of Science* databases.



In public health, arboviruses have been a cause of great concern all over the world, most of them transmitted by hematophagous arthropods, where mosquitoes of the *Culex* and *Aedes* genera represent are the most dangerous to human health, however, other arboviruses are transmitted by sand flies and ticks (Weaver and Reisen 2010). In this scenario, insecticide applications with relevance to health were addressed, such as the use of extracts to induce morphological changes in the middle intestine of *Aedes aegypti* larvae (Costa et al. 2012), as well as the ethanolic extract of seeds, which was able to disturb the development of nymphs and adults of *Rhodnius neglectus* (Hemiptera: Reduviidae), host of *Trypanosoma cruzi* (Carneiro et al. 2013), besides the leaf extract that decreased the survival of the larvae, interrupted the development of the pupae and affected the weight gain of *Spodoptera frugiperda*, which indicates that this species can be used in development of botanical insecticides (Freitas et al. 2014). However, few studies reported the tickcidal effects of the *Annona coriacea* plant.

TABLE III: Evaluation of studies that presented some biological activity found in *PubMed*, *ScienceDirect* and *Web of Science*, 2009-2019.

Author/ Year	Title	Parte da Planta	Indicação Terapêutica	Principais Resultados
Júnior et al. 2016	Chemical Characterization and Cytoprotective Effect of the Hydroethanol Extract from <i>Annona coriacea</i> Mart. (Araticum)	leaves	cytoprotective	The results obtained in this study show that HEAC presents cytoprotective activity on the strains tested in vitro and may also exert an antagonistic effect when associated with aminoglycosides, reinforcing the need for caution in the combination of natural and pharmaceutical products.
Formagio et al. 2015	In vitro biological screening of the anticholinesterase and antiproliferative activities of medicinal plants belonging to Annonaceae	leaves, floral chapters and seeds	antiproliferative and anticholinesterase	In general, the results indicated that <i>Annona crassiflora</i> and <i>A. coriacea</i> extracts have antiproliferative and anticholinesterase properties, which opens new possibilities for alternative pharmacotherapeutic drugs.
Araújo et al. 2014	Evaluation of the anti-mycobacterium tuberculosis activity and in vivo acute toxicity of <i>Annona sylvatic</i>	leaves	antidiarrhea	Tea from <i>Annona coriacea</i> leaves is used to control diarrhea.
Lozano et al. 2014	The apparency hypothesis applied to a local pharmacopoeia in the Brazilian northeast	leaves	antidiarrhea	Tea from <i>Annona coriacea</i> leaves is used to control diarrhea.
Ribeiro et al. 2017	Ethnobotanical study of medicinal plants used by Ribeirinhos in the North Araguaia microregion, Mato Grosso, Brazil	stem bark	anticoagulant	The bark of the stem of <i>Annona coriacea</i> is macerated and used against thrombosis.
Toledo et al. 2011	Antimicrobial and cytotoxic activities of medicinal plants of the Brazilian cerrado, using Brazilian cachaça as extractor liquid	leaves	antimicrobial	Antimicrobial activity was demonstrated for <i>Annona coriacea</i> specie, where the CE obtained from it showed better activity against the promastigote form of <i>Leishmania amazonensis</i> (IC ₅₀ = 175 g/ml). None of the extracts showed toxicity against human erythrocytes.
Ribeiro et al. 2014	Promising medicinal plants for bioprospection in a Cerrado area of Chapada do Araripe, Northeastern Brazil	leaves and stem bark	antiophidic	The leaves or bark of the stem of <i>Annona coriacea</i> are used against snake bite, applied on the affected part of the body.
Saraiva et al. 2015	Plant species as a therapeutic resource in areas of the savanna in the state of Pernambuco, Northeast Brazil	root	antiophidic	<i>Annona coriacea</i> root is used against snake bite by ingestion or poultice.
Souza et al. 2014	Ethnopharmacology of medicinal plants of carrasco, northeastern Brazil	leaves	anti-inflammatory	Tea from the leaves of <i>Annona coriacea</i> is indicated against depurative dermatitis.
Novaes et al. 2019	Comparing antioxidant activities of flavonols from <i>Annona coriacea</i> by four approaches	leaves	antioxidant	Of the eleven flavonols isolated from the leaves, two response patterns of glycosylated flavonols in antioxidant assays were observed: (i) quercetin and its derivatives were the most active antioxidant compounds in PPHD and FRAP assays; and (ii) derivatives of isomarnetin had higher or similar antioxidant activities than derivatives of quercetin in ABTS + and ORAC assays.

Magalhães et al. 2019	Medicinal plants of the Caatinga, northeastern Brazil: Ethnopharmacopeia (1980–1990) of the late professor Francisco José de Abreu Matos	leaves	diuretic	Annona coriacea leaf tea is used as a diuretic to combat nervousness and urinary infection. The study demonstrated a new approach in ethnopharmacology, mapping the therapeutic potential of Caatinga species.
Novaes et al. 2016	Biological activities of Annonaceae species extracts from Cerrado	leaves and stems	phytotoxic	The strongest phytotoxic activities were detected for extracts of <i>Annona coriacea</i> and <i>Xylopia aromatica</i> . These extracts also inhibited the growth of <i>Urochloa decumbens</i> (Stapf) R. D. Webster. The extracts of <i>A. coriacea</i> were also very toxic to the shrimp nauplii. Among the four species, <i>X. aromatica</i> and <i>A. coriacea</i> exhibited strong biological activities and the results may be useful in agricultural fields in Brazil. These extracts have also been promising for the isolation and identification of valuable commercial metabolites.
Benites et al. 2015	Contents of constituents and antioxidant activity of seed and pulp extracts of <i>Annona coriacea</i> and <i>Annona sylvatica</i>	fruit pulp and seeds	antioxidant	<i>Annona coriacea</i> seed extracts demonstrated a moderate antioxidant effect with free radical sequestering activity of 31.53% by the DPPH test, 51.59% by the β -carotene bleaching method and 159.50 μ M trolox/g extract in the ABTS assay. The hydromethanolic extract of <i>A. coriacea</i> displayed a high content of total phenol (147.08 \pm 4.20 mg of GAE/g extract) and flavonoid (131.18 \pm 2.31 mg of QE/g extract). This indicated that the antioxidant activity of the extracts was related to the content of these constituents.
Nascimento et al. 2012	Investigation of the toxic potential of crude ethanol extract of <i>Annona coriacea</i> (<i>araticum</i>) seeds in acute exposed mice	seeds	hepatotoxic	The results suggest hepatotoxic effects of the raw extract of <i>Annona coriacea</i> seeds, but without damage to the brain and kidneys in this experiment, showing a toxic potential for this species, as for the Annonaceae family.
Sousa et al. 2012	Pharmacological effects of two polar fractions from <i>Annona coriacea</i> Mart in animal models	leaves	antinociceptive and anti-inflammatory	The results show that fractions of <i>Annona coriacea</i> have antinociceptive and anti-inflammatory effects, supporting the use of this plant in folk medicine.
Sousa et al. 2011	Pharmacological Effects of the Hexane and Dichloromethane Fractions from <i>Annona coriacea</i> Mart. (Annonaceae) Leaves	leaves	antinociceptive and anti-inflammatory	The results show that <i>Annona coriacea</i> has antinociceptive and anti-inflammatory effects, supporting the use of this plant in folk medicine.
Siqueira et al. 2011	Chemical constituents of the volatile oil from leaves of <i>Annona coriacea</i> and in vitro antiprotozoal activity	leaves	antiprotozoan	The volatile oil showed anti-Leishmania and trypanocidal activity against promastigotes of four species of leishmania and trypomastigotes of <i>Trypanosoma cruzi</i> , and was more active against <i>Leishmania (L.) chagasi</i> (IC50 39.93 μ g/mL) (IC 95% 28.00-56.95 μ g/mL).

A study on the acaricidal activity of Annonaceae fractions against *Tetranychus tumidus* and *Tetranychus urticae* (Acari: Tetranychidae) was performed with the objective of selecting soluble fractions in dichloromethane with acaricidal activity, however, in this study, species of the genus *Annona* were not active against *T. tumidus* and *T. urticae* (Alves et al. 2015), although other studies report that acetogenin, a secondary metabolite exclusive to this botanical family, exert acaricidal activity (Lümmem 1998), indicating that this result may have been different from what is reported in the literature due to the different methodologies used to obtain metabolites.

With regard to emerging diseases, a certain study reports the identification of a better antiparasitic activity of *Acoricea* extract against the promastigotes forms of *Leishmania amazonensis*, when compared to the extracts of *Curatella americana*, *Sclerolobium aureum* and *Plathymenia reticulata* (Toledo et al. 2011), as well as the essential oil of the leaves, which showed antileishmaniasis and trypanocidal activity against promastigotes of four species of *Leishmania* and trypanostigotes of *Trypanosoma cruzi*, showing more active against *Leishmania (L.) chagasi* (Siqueira et al. 2011).

Several current problems involving health, agribusiness, sustainability and environmental impact are caused by the use of synthetic insecticides. For problems of this nature, studies with plant products that serve as vector controllers are necessary, which is the case with the species *A. coriacea*.

3.2 TECHNOLOGICAL PROSPECTION

In the technological prospection, the number of patent applications filed in the following databases: EPO, DII, USPTO, WIPO, LATIPAT and INPI, was evaluated according to the terms used, and the patent registration was verified only in the DII, WIPO and INPI databases, when searching for the descriptors "*Annona coriacea*" and "*Annona coriacea and biocide*", in the title and/or abstract of patent, totaling 17 registrations (Table IV). These results serve as an alert to the national scientific community, since only five registrations were made in the national database, and only four reported on species of annonaceae, which makes new research and development of products related to this botanical family relevant.

TABLE IV: Number of patents filed with technology banks, EPO, DII, USPTO, WIPO, LATIPAT and INPI by keywords.

Keywords	EPO	DII	LATIPAT	WIPO	USPTO	INPI
<i>Annona coriacea</i>	0	1	0	10	0	5
<i>Annona coriacea</i> and tickcide	0	0	0	0	0	0
<i>Annona coriacea</i> and acaricide	0	0	0	0	0	0
<i>Annona coriacea</i> and biocide	0	0	0	1	0	0

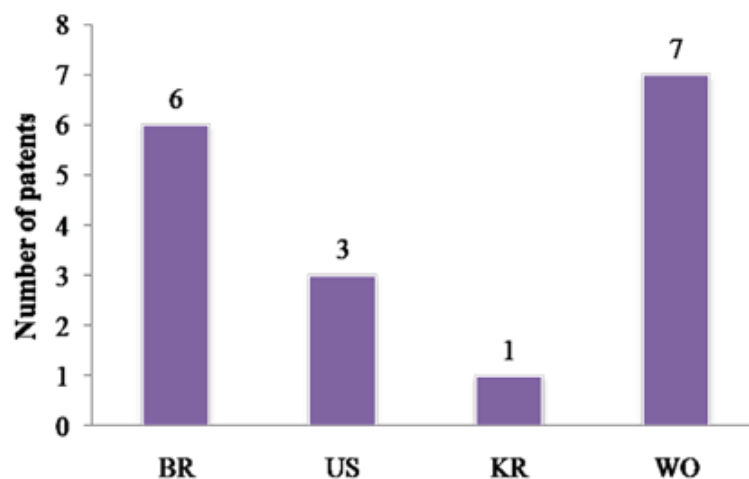
However, of the total number of patents, only one patent was located in the WIPO base that had contained a term relating the specie of study with tickcidal activity and this patent was once again present among those found for the descriptor "*Annona coriacea*", in this technological base. One of the patents found in the INPI database, did not cite the *Annona coriacea* specie, nor any other species of the same family. After reading and evaluation, it was verified that three patents were concerned with the same innovation, but filed in different countries and a duplicate registration for the same country. Considering the exclusion of these five patents, patent registrations were reduced to 12.

Concerning this refined number of patents, four reported the species *Annona coriacea*, three the species *A. muricata* and two the species *A. squamosa*. A record for *A. vepretorum* also occurred and three patents address various species of the genus *Annona* spp. in their context.

Patent registrations in general are small in number when compared to scientific publications. But still, there was a growing interest in the species *Annona coriacea*, because in 2014, there was an increase in the number of patent registrations, which corroborates the years of higher scientific production (Table V). It is important to remember that between the date of patent filing until the date of publication, there is a period of 18 months of secrecy in Brazil, and this time may vary for other countries.

With regard to the protection of products and/or processes related to araticumby means of patents, Brazil (BR) is first, followed by the United States (US), while Korea, appears with only one patent document. Patent registration at the WIPO (WO) base surpasses Brazil, adding up to seven patent applications for registration. This usually occurs "because the same patent is filed in different offices and also in the WIPO database" via the Patent Cooperation Treaty (PCT) (Costa et al. 2014) (Figure 4).

Figure 4. Patent applicant countries for the species *Annona coriacea* Mart. BR = Brazil; JP = Japan; KR = Korea; US = United States; WO = Patent Cooperation Treaty (PCT).



According to the international classification of patents, of the 12 applications for registration, some are mainly found in Section A (Human Needs), in the A61K Classification, which deals with preparations for medical, dental or hygienic purposes, as well as in the A23L Classification, which refers to food, food products or non-alcoholic beverages, not covered by subclasses A21D or A23B-A23J; their preparation or treatment, for example, cooking, modification of nutritional qualities, physical treatment; conservation of food or food products in general, followed by Section C, on Chemistry and Metallurgy, with the majority in the C12N Classification, which refers to microorganisms or enzymes; their compositions; propagation, conservation, or maintenance of microorganisms; genetic engineering or mutations and culture media; as well as in the C11D Classification, which deals with detergent compositions; use of isolated substances as detergents; soap or soap manufacturing; resin soaps and glycerol recovery, and finally, Section B, which deals with processing and transportation operations, which constitute in the B01F Classification, the understanding of mixture as the agitation of a single material (Figure 5).

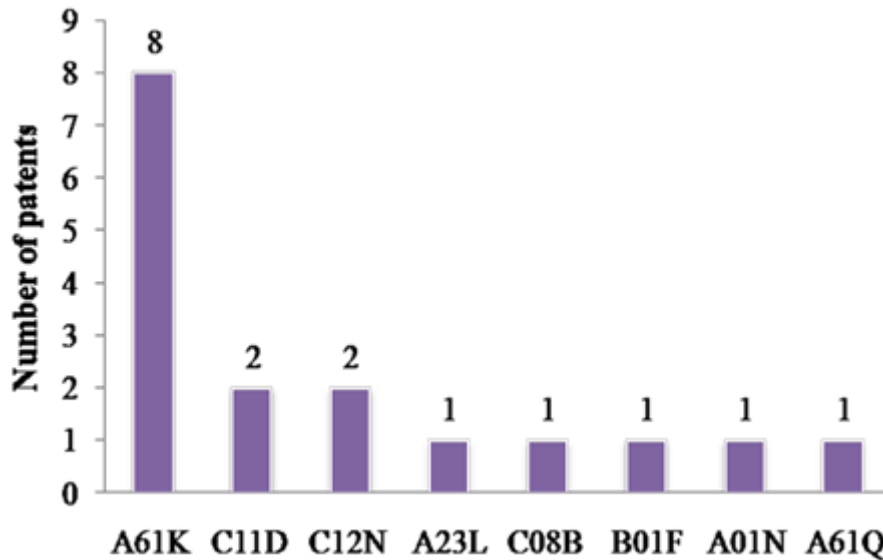
TABLE V: Patents with technological applications for the species *Annona coriacea* Mart. deposited with DII, INPI and WIPO.

Patente number	IPC	Inventor	Title	Inovação	Deposit year	Publication year
BR201106468-A2 Souza et al. 2015	A23L 001/064 A23L 001/068	SOUZA MARTIM SILVA	Food product comprises bitter ginger extract, araca-boi, soursop, camu-camu, cupuassu and mapati	The food product comprises bitter ginger extract (Zingiber zerumbet), araca-boi (<i>Eugenia stipitata</i>), soursop (<i>Annona coriacea</i> Mart.), camu-camu (<i>Myrciaria dubia</i>), cupuassu (<i>Theobroma grandiflorum</i>) and mapati (<i>Pourouma cecropiifolia</i>). The food product has high content of vitamin C, good rheological characteristics and preservatives characteristics by using Amazonian fruits, and improved texture and taste in mouth during consumption, and improves life quality.	2011	2015
US20160312153 A1 Hüffer et al. 2016a KR1020160101078 A Hüffer et al. 2016b WO2015091160 A1 Hüffer et al. 2015	C11D 3/00 C08B 31/18 C11D 3/22 (+12)	HÜFFER MARCOS DETERING	Modified polysaccharide for use in laundry detergent and for use as anti-greying agent	The present invention relates to a modified polysaccharide obtainable by a process comprising the step of treating a polysaccharide with gaseous or liquid SO ₂ , a laundry detergent composition comprising said modified polysaccharide, the use of said modified polysaccharide to increase whiteness of a washed fabric, the use of said modified polysaccharide as anti-greying agent in aqueous laundry processes, the use of said modified polysaccharide as a rheology modifier for homecare applications and the use of said modified polysaccharide in the manufacture of a liquid laundry composition. Further aspects of the invention are a method for preparing a laundry detergent composition comprising said modified polysaccharide. (<i>Annona coriacea</i> Mart.)	2014	2016/2015
US20160263013 A1 Brownell et al. 2016 WO2015066352 A1 Brownell et al. 2015	A61K 8/97 A61Q 19/08 A61K 8/49 (+4)	BROWNELL; CHU; CORNELIUSEN; HONG; HWANG; HYUN; JIA; JIAO; KIM; LEE; LEE; NAM; OH; YIMAM	Skin Care Compositions and Methods of Use Thereof	In brief, the present disclosure is directed to compounds and compositions useful for skin care, body slimming and reducing cellulite, including stereoisomers, pharmaceutically or dermatologically acceptable salts, tautomers, and prodrugs of the disclosed compounds, and to related methods for tightening and improving firmness of sagging skin, improving skin tone, improving skin elasticity, reducing water retention for smoother and tighter skin, and reducing fat deposits in cutaneous tissues. (<i>Annona spp.</i>)	2014	2016-2015
WO2015000064 A1 Evans and Evans 2015	A61K 31/085 A61K 31/015 A61K 36/00 (+2)	EVANS; EVANS	Composition for treating pain and/or inflammation comprising eugenol and beta-caryophyllene	A novel pharmaceutical composition is provided comprising beta--caryophyllene or a functionally equivalent derivative, analogue or pharmaceutically acceptable salt thereof, and eugenol or a functionally equivalent derivative, analogue or pharmaceutically acceptable salt thereof. The composition is useful to treat pain and/or inflammation. (<i>Annona squamosa</i> L.)	2014	2015

WO2014154814 A1 Ranf et al. 2014	C12N 5/00 C09K 8/035 C12N 9/38	RANFT; NAVICKAS; SIGGEL; ASSMANN; BALDENIUS; PETERS; STEIDEL; BENKERT	Method for blocking permeable zones in oil and natural gas bearing subterranean formations by in-situ xyloglucan degalactosylation	A method for treating an oil and/or natural gas bearing subterranean formation penetrated by at least one well bore, comprising the steps of (a) providing an aqueous well treatment formulation (A) which comprises (A1) a xyloglucan having an average molecular weight (M_w) of from 200 000 to 1 500 000 Da, (A2) an enzyme preparation comprising β -galactosidase being capable of removing galactose from xyloglucan, and (A3) optionally one or more additives; (b) injecting said aqueous well treatment formulation into at least one well bore penetrating the oil and/or gas bearing subterranean formation; and (c) gelling of said aqueous well treatment formulation effected by partial degalactosylation of the said xyloglucan; thereby blocking highly permeable zones in the oil and/or natural gas bearing subterranean formation. (<i>Annona coriacea</i> Mart.)	2014	2014
WO2010111745 Wolf 2010	A61K 8/97 A61K 31/375 A61Q 5/00 A61Q 19/02 A61Q 19/08	WOLF	Compositions and methods for increasing vitamin c uptake into cells and methods for retarding skin ageing, lightening skin and modulating hair colour	The present invention relates to compositions comprising extracts from plants of the Combretaceae family and the use thereof in methods for increasing the uptake of vitamin C into cells. The invention also relates to methods for treating and/or retarding skin ageing, and further relates to a method for lightening skin and modulating hair colour. (<i>Annona spp.</i>)	2010	2010
US20020132021 Raskin and Poulev 2002	A61K 35/78 A01H 3/00 C12Q 1/02 C12Q 1/18 G01N 33/50	RASKIN; POULEV	Elicited plant products	The present invention is directed to a method of eliciting chemical compounds in plants. The process of the present invention may be employed for commercial production of desired compounds. The commercial production of such compounds can be accomplished in an aqueous medium containing an elicitor. The elicitor can be any elicitor, including for example, chemical elicitors such as acetic acid, which has demonstrated promising activity in inducing and improving compounds having therapeutic activity. The plants or plant parts of the invention can be specifically grown or maintained for the purpose of recovering compounds therefrom. In a preferred embodiment, the plant is grown hydroponically or aeroponically. In a particularly preferred embodiment, the roots are harvested in a manner such that the plant remains alive and can grow new roots for future harvesting and recovery of additional compounds. The invention also provides a method of identifying an agent exuded from or onto a plant surface having therapeutic activity. (<i>Annona spp.</i>)	2001	2002
WO2014154806 A1 Wang et al. 2014	C12N 5/00 C09K 8/035	WANG; NAVICKAS; RANFT; BOYKO;	Process for preparing partially degalactosylated xyloglucan	A method for treating an oil and/or natural gas bearing subterranean formation penetrated by at least one well bore, comprising the steps of (a) providing an aqueous	2014	2014

		WENZKE; ASSMANN; BALDENIUS; KRENNRICH; SIGGEL	and its use for oilfield applications	treating formulation which comprises a treating composition, comprising partially degalactosylated xyloglucan having a galactose removal ratio of at least 0.40, based on the total number of β -D-galactopyranosyl residues of xyloglucan; and (b) injecting said aqueous treating formulation into at least one well bore penetrating the oil and/or gas bearing subterranean formation; thereby blocking highly permeable zones in the oil and/or natural gas bearing subterranean formation. (<i>Annona coriacea</i> Mart.)		
BR 10 2012 026697 0 A2 Moraes-Filho et al. 2018	A61K 36/185 A61K 127/00 A61P 35/00	MORAES FILHO; OLIVEIRA; FERREIRA; SANTOS; MORAES	Herbal medicine formulated from a standardized acetonic extract obtained from the leaves of <i>Annona muricata</i> .	The present invention indicates that the acetone extract of <i>Annona muricata</i> leaves exhibit little toxic action and significant tumor growth inhibitory activity, both in model of Walker 256 carcinosarcoma in rats, and in Sarcoma 180 model in mice.	2012	2018
BR 10 2016 029177 1 A2 Matos et al. 2018	A61K 36/185 A61P 3/10	MATOS; FONTANA; SILVA	Extraction process of soursop seed oil (<i>Annona muricata</i> L.) and the product obtained	The present invention concerns an extraction process to obtain crude oil using as raw material seeds of soursop (<i>Annona muricata</i> L.) with potential for pharmacological and biotechnological use and application. More specifically, the process involves the fractioning and obtaining of the liquid fraction of the oil, where the said oil presents a reduced quantity/concentration of acetogenins, thus indicating toxic action, which can be used in models for evaluation of biological properties, with immunomodulatory effects, and also as an active agent for the treatment of diabetes mellitus type 1.	2016	2018
BR 10 2017 003197 7 A2 Santana Neto et al. 2018	B01F 3/10 A61K 31/185 A61K 47/40	SANTANA NETO; RIBEIRO; IMBROINISE; SILVA; BARROS	Method of production of microstructures and nanocapsules of cyclodextrin containing oil from <i>Annona vepretorum</i> Mart.	The present invention deals with the method of production of nanocapsules consisting of β -cyclodextrin in spherical and cylindrical formats containing <i>Annona vepretorum</i> oil, aiming at increasing the anti-inflammatory, antibiotic and antitumor activity.	2017	2018
BR 102018008313-9 A2 Basílio Júnior et al. 2019	A01N 65/08 A01N 25/28 A01P 7/02 A01P 7/04	BASÍLIO JÚNIOR; TRINDADE; MACIEL; LEMOS; SANTANA; ARAÚJO; SILVA; FIGUEIROA; MORAIS	Microemulsified insecticide / acaricide formulation by spray dryer of <i>Annona squamosa</i> and <i>Annona muricata</i>	The present invention is characterized by the development of a microencapsulated natural product by spray drying based on hexane seed extract of <i>Annona squamosa</i> (pine cone) and ethanolic extract of <i>Annona muricata</i> (soursop), developed from biodegradable polymers such as starch, maltodextrin gelatin and aerosil, which presents an insecticidal / acaricidal action of homogeneous, continuous and gradual release of the active principle with lethal and sublethal action.	2018	2019

Figure 5. Patents filed with technology banks by international classification code.



Among the documents examined, the patent of Basílio Júnior et al. (2019), classified A01N 65/08, dealing with biocides, repellents or attractants to pests or plant growth regulators containing material obtained from algae, lichen, bryophyte, multicellular plants or fungi or extracts thereof and A01N 25/28, refers to biocides, pest repellents or attractants or plant growth regulators, characterized by their forms or their inactive ingredients or their methods of application, substances to reduce the harmful effect of the active ingredients on non-pest organisms, in coated particulate form, microcapsules, being reported to Arthropodicides / Acaricides (A01P 7/02) and Arthropodicides / Insecticides (A01P 7/04); discusses the development of a microencapsulated natural product by spray drying based on hexane seed extract of *Annona squamosa* (pine cone) and ethanolic extract of *Annona muricata* (sour sop), formulated from biodegradable polymers, with homogeneous insecticidal / acaricidal action, continuous and grading of the active principle with lethal and sublethal action. Thus, this patent corroborates the purpose of this research, since the species used by the authors are annonaceae, as well as the target organisms being arthropods.

Thus, it is possible to infer, through the analysis of the patents developed for the species *Annona coriacea* that the number of patents registered is not very significant, since this species exhibit several secondary metabolites with various promising physiological effects (Almeida et al. 2015).

4 CONCLUSION

Considering the consulted databases, the importance of the *Annona coriacea* species is prominent and this species can be used in technological innovation studies and development of new

products, increasing the knowledge about the species and providing data that will contribute to its understanding, besides valuing biodiversity and the preservation of the species and its environment.

ACKNOWLEDGMENTS

The authors are thankful to Boris Timah Acha for reviewing the English language in this manuscript. This paper was not funded. Foundation for Research Support of Piauí State /Coordination for the Improvement of Higher Education Personnel – FAPEPI/CAPES [Nº 006/2018].

AUTHOR CONTRIBUTIONS

SRS: Bibliographic review research; Elaboration, writing and revision of the manuscript. FCF, JRSJ, AAJFC, DRJF and LCCN: Contribution to concept and design of the study and critical review of the manuscript. RRSF and RNL: contribuiu pesquisando material bibliográfico e processamento de dados.

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