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DIFFERENT AÇAÍ BY-PRODUCTS IN NANOSTRUCTURED FORMULATIONS: A BRIEF LITERATURE REVIEW[1]

OS DIFERENTES SUBPRODUTOS DE AÇAÍ EM FORMULAÇÕES NANOESTRUTURADAS: BREVE REVISÃO DA LITERATURA

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ABSTRACT

Açaí (*Euterpe oleracea*) is a fruit native to the Amazon rainforest which has several well-known properties. Its by-products have physicochemical limitations and the bioactive substances, specifically the polyphenols, are susceptible to degradation by oxidation during exposure to oxygen, humidity, light, high temperatures and pH alteration. In this context, nanotechnology is related to structures, properties and processes involving materials with dimensions on the nanometer scale, and can be used to overcome these limitations due to the fact that these particles are extensively researched because they offer many advantages over traditional formulations. The aim of this study was to prepare a literature review considering the different by-products of açaí, their biological activities and nanostructured materials to which açaí was complexed. The search was carried out using the Scientific Electronic Library Online (SciELO), PubMed and Web of Science databases, and articles were selected that were written in English, published between 2012 - 2023 and used the descriptors "nano*" AND "açaí" and "nano*" AND "*Euterpe Oleracea*". The studies found showed that the most commonly used nanoformulation was the polymeric nanoparticle and three appeared with the same frequency, namely the metallic nanoparticle, nanoemulsion and nanofiber, while the most exploited by-products are oil, fruit and seeds. Majority of studies also found that açaí by-products nanoformulations are used in the food industry, in the creation of biodegradable materials, in the delivery of pharmaceuticals, and in the area of cosmetology. However, only a small number of studies showed evaluations of biological properties of these products.

Keywords: Nanotechnology, *Euterpe oleracea* Mart., Nanoformulations.

RESUMO

O açaí (Euterpe oleracea) é uma fruta nativa da floresta amazônica que possui várias propriedades bem conhecidas. Em contrapartida, seus subprodutos apresentam limitações físico-químicas e as substâncias bioativas, em especial os polifenóis, são suscetíveis à degradação por oxidação quando expostas a oxigênio, umidade, luz, altas temperaturas e variação de pH. Neste contexto, a nanotecnologia pode ser usada para superar essas limitações. O objetivo desse estudo foi realizar uma revisão de literatura considerando os diferentes subprodutos do açaí, suas atividades biológicas e os materiais nanoestruturados ao qual o açaí foi complexado. A busca foi realizada utilizando as bases de dados Scientific Electronic Library Online (SciELO), PubMed e Web of Science, foram selecionados os artigos que estivessem escritos na língua inglesa, publicados

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entre os anos de 2012 - 2023 e usado os descritores "nano*" AND "açaí" and "nano*" AND "*Euterpe Oleracea*". *Os estudos encontrados demonstraram que a nanoformulação mais utilizada foi a nanopartícula polimérica e três apareceram com a mesma frequência, sendo elas a nanopartícula metálica, nanoemulsão e nanofibra, já os subprodutos mais explorados são o óleo, o fruto e as sementes. Percebeu- se que os subprodutos do açaí são empregados na indústria de alimentos, na criação de materiais biodegradáveis, na entrega de fármacos e na área da cosmetologia. No entanto, um pequeno número de estudos mostrou as avaliações biológicas destes produtos.*

Palavras-chave: *Nanotecnologia, Euterpe oleracea Mart., Nanoformulações.*

INTRODUCTION

The "açaizeiro" tree plays an important socio-economic role in Brazil, especially in the Amazon region located in the north of the country, including the states of Amazonas, Pará, Maranhão, Acre and Amapá. The fruit is commonly used by the local population, who attribute phytotherapeutic effects, such as its action against gastrointestinal problems and coagulation disorders to the fruit pulp, bark and leaves (Miranda *et al*., 2022), (Laurindo *et al*., 2023). In its organic content, açaí has interesting nutrients with high contents of carbohydrates (42.5% ± 3.56), lipids (40.75% ± 2.75), proteins (8.13 g ± 0.63 per 100 g of freeze-dried açaí), as well as vitamins and minerals such as calcium, iron, magnesium and potassium, being also rich in fatty acids such as linoleic acid, oleic acid and palmitic acid (Pantoja; Da Silva, 2022).

Euterpe Oleracea Mart. is the scientific name of the açaí, and due to its rich content of anthocyanins, polyphenols and flavonoids, this fruit has gained importance and aroused the interest of researchers around the world, considering its health benefits, such as the anti-inflammatory, anticarcinogenic and antioxidant capacities, which can perhaps prevent the onset of cardiovascular problems and neurological diseases (Oliveira; Costa; Rocha, 2015). In addition, it has gained popularity in the sports area, due to its protein quality and fiber content, as well as in the cosmetics industry for the development of products to avoid signs of expression associated with skin aging and to prevent dermatological infections (Conceição *et al*., 2017). Furthermore, there is increased research and commercial activiy using other by-products of the fruit, including the seeds, extract, tegument and oil (Vidovix *et al*., 2022; Da Silva *et al*., 2019; Valentim *et al*., 2018; Valério *et al*., 2014). While this fruit boasts numerous functions, there are some limitations that hinder its use and can compromise its effectiveness, such as low solubility in aqueous solutions and instability under different conditions, such as climate and storage conditions (Rabelo *et al*., 2018). Nanotechnology has emerged as a potential tool to overcome these difficulties and limitations (Bayda *et al*., 2020).

Nanotechnology is an area of great development that works with the structuring of objects on an atomic and molecular scale, which enables research, progress, innovation and entrepreneurship (Braga *et al*., 2021; Codevilla, *et al*., 2015). In this regard, this technology can be applied in all industry and service sectors. The union of different types of knowledge based on physics, chemistry, biology, materials science and engineering, computing, among other areas, aims to result in originality capable of contributing to the solution of many problems faced by society (Rajput *et al.*, 2023), which has been revolutionizing and increasing expectations for the improvement of countries and industries.

In this scenario, nanotechnology can be used to overcome the challenges posed by açaí's chemical matrix, as well as being able to control the release of bioactive molecules, increase bioavailability, biocompatibility and protect the chemical matrix against physical and chemical degradation, making it possible to guarantee efficacy or even enhance its pharmacological action, as well as being able to modulate toxicity profiles (Martínez-Ballesta *et al.*, 2018).

Therefore, the aim of this study was to carry out a brief literature review on the main nanostructured systems used to associate/encapsulate different açaí by-products and to evaluate the articles which performed biological activity analysis.

MATERIAL AND METHODS

This study was performed as a narrative literature review. This review used articles indexed in the Scientific Electronic Library Online (SciELO), PubMed and Web of Science databases from journals in different areas of knowledge using the descriptors "nano*" AND "açaí" and "nano*"AND "*Euterpe Oleracea*". Inclusion and exclusion criteria were established for selecting and analyzing the articles. The abstracts of the previously selected articles were checked. If in doubt, the full article was read.

INCLUSION CRITERIA

We selected articles that were not literature reviews, written in English, published between 2012 and 2023, and mentioned the nanostructure used, as well as the type of açaí by-product used.

EXCLUSION CRITERIA

Literature review articles, articles that were not written in English, published before 2012, and that did not include the theme of açaí and nanotechnology or that did not mention the thematic by-product.

RESULTS AND DISCUSSION

A total of 145 articles were found, of which 60 were published in PubMed, 83 in Web of Science and only 2 in the Scientific Electronic Library Online (SciELO). Of this total, 128 articles were excluded based on the exclusion criteria described in the methodology. Thus, 17 articles were selected and analyzed for this review, which are shown in Table 1, including authorship, year of publication, nanostructure, the main objective of each study, the reason for using nanotechnology and whether biological evaluation was performed.

Table 1 - Articles selected for the review, authorship, year of publication, type of nanostructure, their main objectives, reasons for using nanotechnology and biological evaluation.

Author and year of publication	Nanoparticle used	Main goal	Reason for using nanotechnology	Biological assessment
De Souza *et al.*, 2023	Metallic nanoparticle	Develop a green and environmentally safe adsorbent prepared from agro-industrial waste for removing dyes from water, with potential for large-scale application	Adsorption, magnetic susceptibility, non-toxicity, large surface area and high reactivity	Not performed
Sanches *et al.*, 2023	Organogel	Prepare and characterize an açaí oil organogel with hyaluronic acid for topical application to prevent signs of skin aging	Instability and enhancing action	Not performed
Scatolino *et al.*, 2022	Nanofiber	Functionalize açaí cellulose nanofibers with copaiba oil and vegetable tannins to produce films with potential for packaging	Instability, solubility and hydrophobicity	Not performed
Vidovix *et al.*, 2022	Metallic nanoparticle	Investigate an alternative treatment for the adsorption of Triclosan using low-cost adsorbents (soybean hulls and açaí seeds), functionalized with Fe_3O_4 magnetic nanoparticles by the co-precipitation method, establishing economic biotechnology, which could be of great industrial interest	Adsorption and biocompatibility	Not performed
Braga *et al.*, 2021	Nanofiber	To evaluate the physical and mechanical performance of chitosan-based bionanocomposite films reinforced with different fillers of cellulose nanofibrils obtained from açaí (*Euterpe oleracea* Mart.) under two degrees of nanofibrillation	Greater strength, biodegradability, and improved composite performance	Not performed
Sibuyi *et al.*, 2021	Metallic nanoparticle	Synthesize nanoparticles using açaí berry and elderberry extracts and their anticancer properties against prostate and pancreatic cancer cell lines	Instability, fast, environmentally friendly, non-pathogenic, and economical protocol	*in vitro*: pancreatic ductal adenocarcinoma (Panc-1) and prostate carcinoma (PC-3) cells
Contente *et al.*, 2020	Nanoemulsion	Observe the behavior of ketoconazole encapsulated in an açaí oil-based nanoemulsion	Solubility and bioavailability	Not performed
Teixeira-Costa *et al.*, 2020	Polymeric nanoparticle	Encapsulate açaí pulp oil in chitosan/alginate polyelectrolyte complexes, and evaluate the antioxidant capacity of microcapsules as a potential additive for food packaging films	Encapsulation and bioavailability	Not performed

Da Silva *et al.*, 2019	Nanofiber	Develop ultrafine fibers with açaí extract for use as pH sensors with potential application in the food industry	Biocompatibility, modulate the toxic profile and make biodegradable	Not performed
Rosa *et al.*, 2019	Polymeric nanoparticle	Develop nanocapsules loaded with desonide using açaí oil as an oily core	Chemical degradation and photodegradation	*in vitro*: human epithelial cells (HaCaT) and mouse embryonic fibroblasts (3T3)
Rabelo *et al.*, 2018	Nanoemulsion	Protect anthocyanins, phenolic compounds present in açaí fruit and increase their applicability	Instability and chemical degradation	Not performed
Valentim *et al.*, 2018	Nanocellulose	Using lignocellulosic waste from açaí agribusiness to benefit the environment as a precursor material for biomedical applications	Solubility and biodegradable material	Not performed
Gabriel *et al.*, 2017	Polymeric nanoparticle	Investigating the addition of bio-based polyurethane/hydroxyapatite composites as biocompatible scaffolds for numerous tissue engineering applications	Stability and biocompatibility	*in vitro*: human normal lung fibroblasts (MRC-5) *in vivo*: Swiss mice
Monge-Fuentes *et al.*, 2016	Nanoemulsion	Rethink treatment strategies using açaí oil in nanoemulsion as a new photosensitizer for photodynamic therapy used in the treatment of melanoma *in vitro* and *in vivo* experimental models	Bioavailability, hydrophobicity, instability, chemical degradation, and reduction of side effects	*in vitro*: murine fibroblasts (NIH/3T3) and murine melanoma (B16F10) *in vivo*: female C57BL/6 mice
Shim *et al.*, 2016	Polymeric nanoparticle	Enhance the antioxidant activity of açaí berry concentrate by combining it with synthetic antioxidants to explore synergistic effects and improve antioxidant stability by nanoencapsulation	Instability and improve antioxidant performance	Not performed
Valério *et al.*, 2014	Polymeric nanoparticle	Synthesize polyurethane nanoparticles, using isophorone diisocyanate, castor oil and poly(ε-caprolactone) as monomers, containing high amounts of vegetable oils such as açaí oil and crodamol	Hydrophilicity and stability	Not performed
Valério; Araújo; Sayer, 2013	Polymeric nanoparticle	Produce nanoparticles by microemulsion polymerization with isophorone diisocyanate and castor oil, glycerol, and poly (ethylene glycol), with molar masses of 400 and 1000 as monomers, and Tween 80, Span 80 and Lutensol AT 25 as surfactants and açaí oil as stabilizer	Biocompatibility, biodegradability, controlled and targeted delivery of therapeutics	Not performed

Source: Author's construction

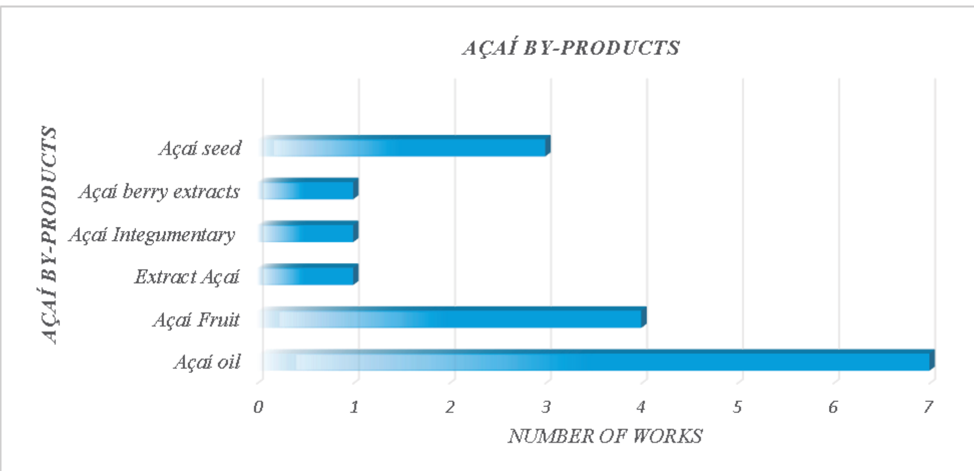
AÇAÍ AND ITS BY-PRODUCTS: POTENTIALS AND LIMITATIONS

The Amazon rainforest biodiversity provides a great source of plant species rich in bioactive compounds and among these, *Euterpe Oleracea* Mart. stands out and has become the target of many research (Lira *et al.*, 2021). Thus, there are various types, ways and benefits of using açaí.

Figure 1 shows the main açaí by-products that were mentioned/used in the 17 studies selected for this review. Among these, the most commonly used was açaí oil, which was the agent of study in 7 scientific articles, followed by the whole fruit, mentioned in 4 publications, and in third place was the açaí seed, which was found in 3 studies . Açaí oils are extracted from oil seeds that have economic, technological and nutritional potential and can be applied in various areas. Among these, the pharmaceutical, cosmetics and food industries are gaining prominence, due to the high content of antioxidant compounds, which gives it a high capacity to fight free radicals, preventing the signs of premature aging, revitalizing the skin, hair and nails (Bomtempo *et al*., 2022). In addition, it is widely suggested that the açaí oil has an anti-inflammatory capacity linked to the inhibition of prostaglandins, significantly reducing edema, granuloma formation, vascular permeability and the number of neutrophils that migrate in peritonitis (Favacho *et al*., 2011). Additionally, açaí oil is abundant in monounsaturated and polyunsaturated fatty acids, which makes it attractive to the food and beverage industries looking for alternatives to make healthier products, as well as being recommended for the prevention of cardiovascular diseases (Nascimento *et al*., 2008). Despite the multiple benefits and potentials reported in the literature, the oil produced from the plant requires further studies in order to safely exploit this bioeconomic capacity, especially with regard to safe and recommended dosages (Marques *et al*., 2016).

Although most of the fruit is made up of the seed, which has efficient adsorption properties, as it is rich in lignin, cellulose and hemicellulose (Vidovix *et al*., 2022), resulting in a large availability of residues in the Amazon region, the whole fruit has also been of scientific interest, as it has nutritional and antioxidant characteristics that contribute to disease prevention. Furthermore, by integrating the açaí pulp, which is rich in carbohydrates, fiber, vitamin E, proteins, minerals and fatty acids, including Omega 6 and 9, into the processing of the fruit, there is a significant increase in energy value when the fruit is consumed (Lobo; Velasque, 2016).

Figure 1 - Açaí by-products used in the selected studies (17 articles in total).



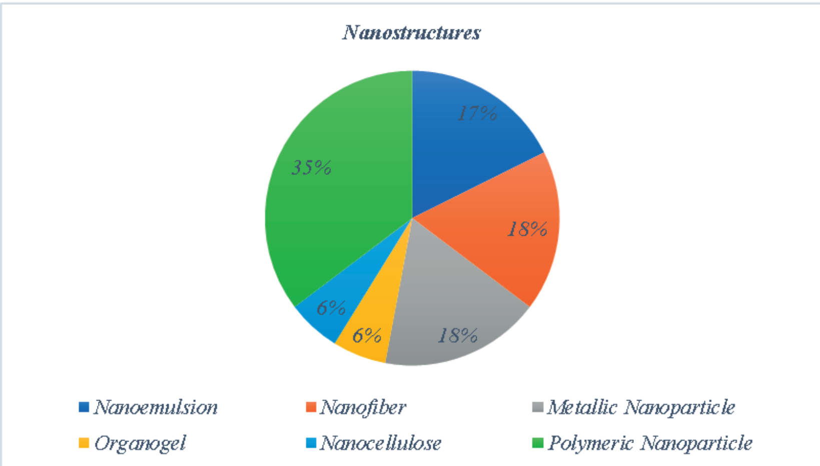
Source: Author's construction

While the açaí fruit's byproducts encompass numerous uses, they also present with limitations for use, since the chemical matrix that makes up such a natural product can suffer degradation effects due to exposure to environmental conditions. This chemical matrix is also quite challenging to work with due to properties in solubility, bioavailability, biocompatibility, which may be avoided through the use of nanotechnology (Rabelo *et al*., 2018; Scatolino *et al*., 2022). In the articles selected for this review, the justification for using nanotechnology is described in Table 1.

NANOSTRUCTURED SYSTEMS CONTAINING AÇAÍ BY-PRODUCTS

Nanotechnology has an innovative edge in multiple areas of knowledge and has been highlighted in numerous areas of science, so it is worth noting that it has useful properties in nutraceutical and pharmaceutical research, as well as improving the absorption of bioactive compounds, protecting them from premature degradation in the body and prolonging their circulation time (Singh *et al*., 2022). Figure 2 shows that polymeric nanoparticles are the nanosystems that appear most frequently in the articles selected for this review.

Figure 2 - Types of nanostructures used in the studies selected for this review.



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Nanofibers

Nanofibers are a category of nanomaterials that are widely produced in laboratories around the world. They play an important role in the evolution of countless areas of technology due to their growing applications, presenting advantages due to their nanometric diameter, such as a high surface area in relation to volume and porosity. Additionally, they are highly sensitive to changes in the surrounding atmosphere, easy to incorporate active compounds and do not require the use of temperatures and pressures, as well as being able to use various natural polymers and biopolymers

(Kuntzler *et al.*, 2018). However, there is an obstacle to producing nanofibers on a commercial scale, as there are a few new technologies with high productivity and cost effectiveness. The established method in the literature is electrospinning, but it requires the use of solvents with dielectric properties and has a low production rate, making it unviable for commercialization, but an alternative to electrospinning is to use the solution blow spinning method. This method allows the production of nanofibers through aerodynamic forces, reducing energy consumption (Monsores *et al.*, 2022).

In the 3 studies involving the production of açaí nanofibers found to compose the review, films were developed for use in the food packaging industry (Scatolino *et al.*, 2022) and biodegradable films for the production industry (Braga *et al.*, 2021). In addition, the innovative study by Da Silva *et al.* (2019) used açaí extract nanofibers to produce colorimetric pH sensors with the aim of demonstrating the quality of perishable food products.

Nanoemulsions

Nanoemulsions are dispersed systems between two immiscible liquids, whose droplets have an average size of less than 200 nm, where there is the preparation of an aqueous and oily phase, using surfactants to obtain stable and homogeneous samples (Chircov; Grumezescu, 2019). Thus, nanoemulsions have unique advantages such as conveying both hydrophilic and lipophilic active ingredients in the same formulation, as well as controlling sensory aspects adapted to the needs of the route of administration for which they are intended (Porto; Almeida; Vicentini, 2020). Nanoemulsions however, are very fragile by nature and minimal signs of destabilization appear easily, which may be related to the nature of the oil phase and another from the addition of polymers. Their stability is also quite sensitive, being highly influenced by changes in temperature, pH and presence of surfactants at high concentrations. (Thakur *et al.*, 2012).

This review found three studies that used nanoemulsions. Contente *et al.* (2020) used a nanoemulsion based on açaí oil to deliver ketoconazole, a lipophilic antifungal drug. Ketoconazole has a wide therapeutic use to treat systemic and superficial mycoses, and açaí oil has fatty acids in its composition that help with skin homeostasis. The nanoemulsion chosen had a polydispersity index (PDI) of less than 0.5, a zeta potential of more than -30 mV and size equal to or less than 200 nm. The inclusion of ketoconazole in the formulation altered the size of the drops, but showed no signs of instability. In this study, it was possible to observe increased absorption of the antifungal by the skin and a reduction in its side effects, demonstrating that açaí oil nanoemulsions can act as an excellent vehicle for antifungals. Another study selected for this literature review, Monge-Fuentes *et al.*, 2016, used nanoemulsions as a carrier for açaí oil applied in photodynamic therapy in the treatment of non-metastatic melanoma, suggesting its use as a photosensitizer with tumor-reducing properties. The nanoemulsion had a PDI of 0.144, a zeta potential of -0.536 mV and a mean diameter of 74 nm.

However, increased studies are needed to identify the components of açaí responsible for these effects. Finally, in Rabelo *et al.* (2018), açaí nanoemulsions were used to evaluate the anthocyanins protection, which are very sensitive to degradation. Improved anthocyanins stability was demonstrated when associated with nanoemulsions, making it more advantageous to the food and pharmaceutical industries.

Polymeric nanoparticle

Polymeric nanoparticles are carrier systems for compounds with a diameter of less than 1 µm (Da Silva Neves, *et al.*, 2022). Nanoparticles must be prepared based on an active ingredient/polymer ratio suitable for achieving high encapsulation efficiency and reduced toxicity. As a rule, the choice of preparation method is determined by the solubility characteristics of the active ingredient (Souto; Severino; Santana, 2012).

Figure 2 shows that polymeric nanoparticles are the most commonly used in studies. This may be due to the ability of these nanoparticles to increase the solubility and stability of bioactive compounds, improve their absorption, protect against premature degradation in the body and prolong their circulation time, demonstrate high absorption efficiency in target cells (or tissue) by preventing premature interaction with the biological environment, improve permeation and retention effect in diseased tissues in addition to better cellular absorption, resulting in decreased toxicity (Codevilla, *et al.*, 2015).

In this review we found 6 studies that used polymeric nanoparticles. Of these studies, 2 included obtaining polyurethane nanoparticles with açaí oil, improving the application of polymers (Valério *et al.*, 2014; Valério; Araújo; Sayer, 2013) and 1 involved the production of polyurethane nanoparticles using the açaí seed to be applied in tissue engineering (Gabriel *et al.*, 2017).

In addition, 3 articles were found that used nanocapsules, a subtype of polymeric nanoparticle, which are vesicular systems in which the drug is confined to a cavity surrounded by a single polymeric membrane, while nanospheres are matrix systems in which the drug is dispersed physically and uniformly (Soppimath *et al.*, 2001). In the study by Shim *et al.* (2016), the efficacy of mixed nanocapsules containing açaí and ascorbic acid was verified, protecting their antioxidant activities, increasing shelf life and bioavailability. Another study tested the photostability of desonide, a corticosteroid used to treat atopic dermatitis, loaded into açaí oil nanocapsules (Rosa *et al.*, 2019). The nanocapsule had a PDI <0.20 and average particle size around 165 and 131 nm, which means homogeneous distribution. And in the study carried out by Teixeira-Costa *et al.* (2020), a nanocapsule based on chitosan and sodium alginate was used to encapsulate açaí pulp oil using polyelectrolyte complexes and showed satisfactory bioactivity, with potential application in food packaging.

Metallic nanoparticles

Metallic nanoparticles are prepared by three different methods: chemical, physical and biological. Chemical synthesis takes place in alcoholic media, microemulsions, via thermal disintegration of metal salts and electrochemical synthesis. The chemical method includes the use of chemical reagents, the physical method uses procedures that involve forces of attraction between particles on a nanometric scale, while the biological method occurs through the reduction of metal ions under the action of plant extracts, essential oils, microorganisms, including bacteria, fungi, yeasts and algae (Guimarães; Amarante; De Oliveira, 2021). Thus, metallic nanoparticles are those produced from a metallic atom if the size definitions prescribed by nanotechnology are respected.

Of the 17 articles selected for this review, 3 included the use of nanoformulations for the production of metallic nanoparticles. One of the studies used iron oxide-based nanoparticles containing soybean hulls and açaí seeds to absorb triclosan from water (Vidovix *et al.*, 2022). Another study aimed to remove dyes from water, but using agro-industrial waste to create a green absorbent (De Souza *et al.*, 2023). Additionally, metallic gold nanoparticles have been used to treat pancreatic and prostate cancer using açaí and elderberry extract (Sibuyi *et al.*, 2021).

Other nanoformulations

In this review there were 2 studies which included the development of nanocellulose and organogels. A highly functionalized surface, a filamentary structure that allows gelling, high porosity, a low coefficient of thermal expansion, optical transparency and interesting self-assembly behaviour are all properties of nanocellulose (Ruiz-Palomero; Soriano; Valcárcel, 2016). Organogels, on the other hand, are interesting because of their thermo-reversibility and because the gelling molecules immobilize large volumes of liquid after self-assembly into a variety of aggregates; however, most of them are composed of gelling agents and organic solvents that are unacceptable from a pharmaceutical point of view/ or untested (Murdan, 2005).

The nanocellulose presented in the work by Valério *et al.* (2014) uses the tegument of *Euterpe oleracea* Mart. to create biphasic ceramics compatible with bone tissue. On the other hand, the organogel containing açaí oil and hyaluronic acid was designed to serve the cosmetics market, idealizing a formulation to prevent skin aging (Sanches *et al.*, 2023).

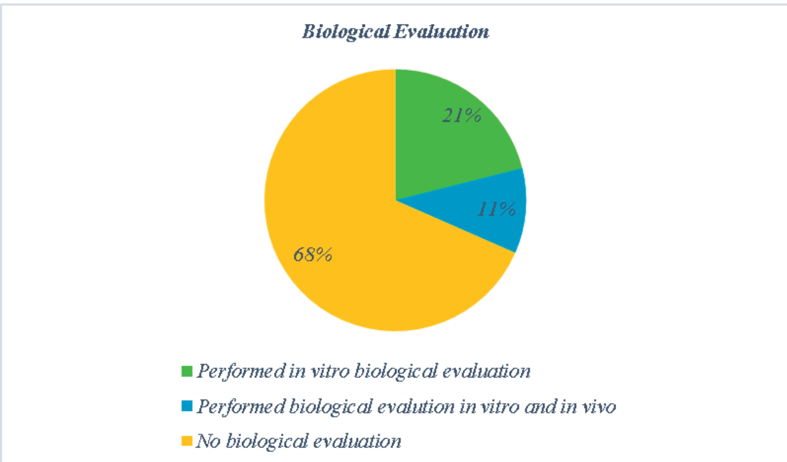
BIOLOGICAL EVALUATIONS OF THE SAFETY AND EFFICACY PROFILES OF NANOTECHNOLOGY-BASED AÇAÍ BY-PRODUCTS

Biological evaluations are necessary in order to avoid cytotoxic effects. Table 1 describes the studies that performed biological evaluations and the experimental model used. Figure 3 shows the analysis of the biological evaluations carried out in the studies selected for this literature review. Nanotoxicology is one of the sub-areas of nanotechnology responsible for assessing the toxic profile of nanoformulations in the biological environment by means of *in vitro* tests using cell cultures and *in vivo* tests using more complex biological systems. According to the graph, only 4 studies (Sibuyi *et al.*, 2021; Rosa *et al.*, 2019; Gabriel *et al.*, 2017; Monge-Fuentes *et al.*, 2016), corresponding to 21% of the 17 articles selected, carried out *in vitro* assessments. Of these, only 2 carried out in vivo tests, totaling 11% of the studies (Gabriel *et al.*, 2017; Monge-Fuentes *et al.*, 2016). The remaining 13 studies did not perform any biological evaluations. It shows the existing lack in terms of studies that consider toxicity analysis as an important step of research development and it serves as an alert to the scientific society.

Sibuyi *et al.* (2021) developed *in vitro* tests with pancreatic ductal adenocarcinoma (Panc-1) and prostate carcinoma (PC-3) cell lines. These cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) and kept in a CO_2 incubator at 37°C. The cytotoxicity test using the 3-4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium bromide (MTT) reagent was performed to check cellular viability after treatments with gold nanoparticles using açaí and elderberry extracts. In the study of Rosa *et al.* (2019), two cell lines were used, human epithelial cells (HaCaT) and mouse embryonic fibroblasts (3T3) to evaluate the açaí oil nanocapsule containing desonide, a cytotoxicity test was analyzed using MTT reagent and phototoxicity using the neutral red dye (NRU) reagent.

In this review, 2 studies were carried out using cell culture and mice to test the efficacy of nanoparticles and nanoemulsions. Gabriel *et al.* (2017) evaluated biological properties *in vitro* using human normal lung fibroblasts (MRC-5) and later *in vivo* Swiss mice. The authors found biocompatible characteristics for application in tissue engineering of polyurethane nanoparticles with açaí seeds. In another study (Monge-Fuentes *et al.*, 2016), two cell lines were used for *in vitro* tests: murine fibroblasts (NIH/3T3) and murine melanoma (B16F10). For the *in vivo* tests, female C57BL/6 mice were used. The obtained results indicated that the nanoemulsion containing açaí oil worked as a photosensitizer in the treatment of non-metastatic melanoma by means of photodynamic therapy.

Figure 3 - Biological evaluation carried out in studies.



Source: Author's construction

CONCLUSION

Among all the studies included in this literature review, a common finding is the açaí fruit and its numerous by-products. These byproducts offer various properties which can be applied to enhance a broad range of nutraceuticals and pharmaceuticals. Açaí oil, açaí fruit and açaí seeds were the most frequently discussed in the studies examined. The açaí oil specifically, was the most popular due to its technological potential and therapeutic properties, demonstrating both positive and negative results in relation to industrial, food, cosmetic and pharmaceutical exploitation. Although, oil formulations still need to be further examined and tested due to lack of adequate evidence in the literature regarding the safety of this bioeconomic capacity. The açaí fruit, on the other hand, stands out for its high fatty acid content and the seed for its efficient adsorption properties. It is essential to encourage new advances in research, development and innovation in the use of açaí, and it is worth emphasizing that Amazonian biodiversity must be conserved due to its economic and environmental importance.

Considering the nanostructures described in the review, it became clear that they are part of a multidisciplinary field, which has been expanding on a large scale. Nanostructures have specific characteristics according to their classification: nanofiber, nanoemulsion, polymeric nanoparticle, metallic nanoparticle, nanocellulose and organogel. Thus, the choice of nanostructure depends on the physical and chemical characteristics of the by-products to be used and the environment in which they will be used. The most commonly studied nanostructure in the studies examined was the polymeric nanoparticle, due to its stability and solubility, improving the absorption and targeting of bioactive compounds. In addition, it was shown that nanofibers and nanocellulose have been widely used in the food industry and in the preparation of biodegradable materials on an industrial production scale. Metal nanoparticles are used to improve the performance of certain compounds in the biological environment. There are only a few studies evaluating the toxicity of these formulations in the biological sphere. Therefore, research investigating the mechanism of nanotoxicology of these formulations is necessary for the safe use of nanomaterials by the population.

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