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ESSENTIAL OILS WITH CONTACT INSECTICIDAL ACTIVITY AND ENCAPSULATION METHODS: A LITERATURE REVIEW

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ABSTRACT

Due to the increasing resistance of pests to chemical insecticides and the negative consequences arising from the use of chemicals, such as environmental contamination and health hazards, alternative methods of control need to be studied. In nature, essential oils play an important role in protecting plants as antibacterials, antivirals, antifungals, insecticides, and also against herbivores by reducing their appetite for such plants. Secondary metabolites produced by medicinal or aromatic plants have the capacity for behavioral modification, growth and feeding reduction, besides exerting toxic and sterility effects on insects considered as pests, thus being a control strategy, besides being an alternative to the chemical products available on the market. Thus, the present review aimed to elucidate the use of essential oils in the control of various grain pests by exploring their bioactive compounds and addressing the main methods of encapsulation for the proper storage of these oils.

Palavras-Chave:
Armazenamento
Qualidade
Sustentabilidade

ÓLEOS ESSENCIAIS COM ATIVIDADE INSECTICIDA DE CONTATO E MÉTODOS DE ENCAPSULAMENTO: UMA REVISÃO DA LITERATURA

RESUMO

Devido ao aumento da resistência de pragas a inseticidas químicos e das consequências negativas advindas do uso de produtos químicos como a contaminação do meio ambiente e dos riscos que causam a saúde, métodos alternativos de controle precisam ser estudados. Na natureza, os óleos essenciais desempenham um papel importante na proteção das plantas como antibacterianos, antivirais, antifúngicos, inseticidas e também contra herbívoros, reduzindo seu apetite por tais plantas. Metabólicos secundários produzidos por plantas medicinais ou aromáticas tem capacidade de modificação comportamental, diminuição do crescimento e da alimentação, além de exercer efeito tóxico e de esterilidade em insetos considerados pragas, sendo uma estratégia no controle, além de ser uma alternativa aos produtos químicos disponíveis no mercado. Com isso, a presente revisão teve como objetivo elucidar o uso de óleos essenciais no controle de diversas pragas de grãos, explorando seus compostos bioativos, além de abordar os principais métodos de encapsulamento para o armazenamento adequado desses óleos.

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INTRODUCTION

Plants capable of producing essential oils are classified as either medicinal or aromatic. The production occurs through secondary metabolism, triggered by interactions between the plant and the environment in which it is inserted. Thus, the ecological relationships of these plants are directly related to the biological function of the compounds produced, such as protection against pests, diseases, and herbivory; attraction of pollinators and natural enemies, among others.

The synthesizing and secreting cells can be in the epidermis, cavities, channels, or glandular trichomes of the plant organs. The main physicochemical characteristics of these metabolites are their high volatility and lipophilicity, low molecular weight, and their striking color and odor (SAITO; SCRAMIN, 2000). According to the physicochemical characteristics and the predominant biologically active compounds, they are classified into terpenes, mononoterpenes, sesquiterpenes, and volatile and aromatic phenylpropanoids (BIZZO, 2013). According to Coloma *et al.* (2011), terpenes represent the most abundant class of natural hydrocarbons.

The use of therapeutic properties of essential oils in the alternative control of pests and diseases of agricultural crops has grown widely in recent times (CASALI *et al.*, 2015; OOTANI *et al.*, 2013). Although chemical control is still the most frequent in Brazilian crops, issues such as residual effects on soil, water and food, and genetic mutations that confer resistance to chemical molecules as a result of prolonged use, put pressure on the agrarian sector to seek more sustainable alternatives (HAWKINS *et al.*, 2019).

In general, essential oils represent a small fraction of the plant composition, less than 5% of the plant dry matter, requiring efficient processing. The extraction occurs both from fresh and dried plant organs and can be used by the methods of steam dragging, hydrodistillation, extraction by supercritical CO_2, extraction by organic solvents, or cold pressing. Due to the physicochemical characteristics of these metabolites, there are several variables that interfere with the processing yield, such as the choice of plant, stage of development, harvest time, storage and drying conditions, and the interaction between the solvent and the oil components (RÍOS and RECIO, 2005; YUSOFF, 2011; BARROS, 2014).

However, the high volatility of bioactive components of interest present in essential oils hinders the efficiency of their application in agriculture and the achievement of satisfactory results over time. Given this, encapsulation technologies that allow gradual release have been developed to optimize the use of essential oils in the control of pests and diseases in fields and warehouses (SILVA *et al.*, 2014).

Main bioactive compounds with contact insecticidal activity

In the case of the use of medicinal and aromatic plants in alternative pest control, there are numerous possibilities in the flora with insecticidal action that still need to be better studied (MENEZES, 2005), because for Cosimi *et al.* (2009) and Renault-Roger (1997), essential oils are the most efficient plant insecticides. The active ingredients of botanical insecticides are usually composed of a complex of substances that can act in several ways.

Among the botanical substances with insecticidal activity already known are pyrethrins, rotenone, nicotine, cevadine, veratridine, rianodine, quassinoids, azadirachtin, and volatile biopesticides (ISMAN, 2000). These secondary metabolites of plants with insecticidal effects can act as inhibitors of feeding, hindering growth at any stage of development, in reproduction, by interacting with the insect's integument, causing repellency or promoting death by damage to the central nervous system or in digestive and neurological enzymes (MENEZES, 2005; ISMAN, 2006).

Some research confirms that certain essential oils from plants not only have the ability to repel insects but also have insecticidal action through direct contact or through the airways of insects, i.e., they act on and are absorbed by the chitin and exoskeleton or through the airways (fumigant action), and can thus be useful for the control of pests that attack foodstuffs in warehouses and silos. There are also essential oils that act as an anti-feeding agent, preventing the insects from starting to feed, causing death by starvation. The substances that act by ingestion penetrate the body orally, which is a specific form of action restricted to herbivorous insects, presenting, therefore, little toxicity to humans (MENEZES, 2005).

Another mechanism of action of essential oils with insecticidal activity involves activity on the target organ or molecule. In this case, they act by hindering growth and development, interfering in cellular metabolism (MENEZES, 2005). Its action is associated with the reduction of viability of eggs, nymphs, larvae, and pupae of insects, according to the amount of product used. Reducing the number of eggs and inhibiting oviposition are relevant effects of essential oils since they act directly on insect reproduction, reducing their population (COSTA *et al.*, 2004).

One of the essential factors for substances to have effective action as insecticides is the affinity between them and the chemical structure of the insect, and the ability of the compounds to bind to the lipid layer is essential for the action of the essential oil on insects, since the greater this affinity, the greater the insertion of the essential oil will be, increasing the effectiveness of the treatment (KIM *et al.*, 2003). This type of affinity is used in fumigant treatments, where the insecticide penetrates inside the insect's body and acts as a repellent, affecting biological parameters or interfering in the reproduction of insects.

Among some examples of essential oils with insecticidal action is the citronella oil, present in some aromatic plants, such as lemon grass (*Cymbopogon citratus*, Poaceae) and eucalyptus citriodora (*Eucaliptus citriodora*), being used for the manufacture of repellents against mosquitoes and borrachudos (MENEZES, 2005). Some of the compounds present in these mixtures include camphor-pinene, limonene, citronellol, citronellal, and thymol (NERIO *et al.*, 2009a). According to the studies of Figueiredo, Rocha and Freitas (2018), starting at 15µL of essential oil of mastiff (*Chenopodium ambrosioides L.*) leaves, the insecticidal effect on corn weevil (*Sitophilus zeamais*) is already observed.

Silva and Farias (2020), when studying the insecticidal effects of essential oils of *Cymbopogon citratus* (citronella), *Cymbopogon nardus* (lemongrass) and *Pimenta racemosa* (chili pepper) in the control of *Sitophilus spp.* (Coleoptera: Curculionidae) in bean grains (*Phaseolus vulgaris*) stored under controlled atmosphere, applied two methods (direct and indirect), and found a greater insecticidal effect in the treatment with essential oil of lemon pepper, and the second highest average mortality was presented by the lemongrass oil. These results demonstrate that these two oils are efficient for *Sitophilus spp.* management in the first 72 hours after application.

Kim *et al.* (2003) reported insecticidal activity of five oils on the bean beetle *Callosobruchus chinensis* (L.) and rice beetle *Sitophilus oryzae* (L.). Essential oils of garlic (*Allium scorodoprasm*), pepper (*Capsicum annum*), radish (*Cocholeria aroracia*), mustard (*Brassica juncea*) and cinnamon (*Cinnamomum cassia*) were tested by direct contact by applying them on filter papers that, after dried, were introduced in a flask containing 20 adult individuals from laboratory cultures of these insects. For rice beetle, the essential oils of radish, mustard, and cinnamon caused 100% mortality after the first day of treatment. At a five-times lower dose, the essential oils of mustard, cinnamon, and radish resulted in 100% mortality of the insects on the first day of treatment.

Encapsulation methods for essential oils

The process by which essential oils are stored in a microscopic shell or coating for protection and subsequent release is called encapsulation. This procedure consists of wrapping small particles, a liquid or a gas inside a coating layer or inside a matrix. According Beirão-da-costa *et al.* (2013), this technique allows sensitive structures contained in the essential oil to be protected from inappropriate environmental conditions, such as light, moisture, and oxygen, allowing the conservation of the product, increasing its shelf life and promoting the controlled release of the encapsulated material under predefined conditions.

Encapsulation has the traditional characteristic of not using capsules longer than 3mm. In a general way, the capsules are classified according to their size, with those in the range of 100nm to 1000nm being called microcapsules and those between 1nm and 100nm being considered nanocapsules (SOBEL *et al*., 2014).

The determination of the technology to be used in the encapsulation of oils depends on some variables, such as the physicochemical characteristics of the product, the size of the particles involved, the encapsulating agent, and aspects related to the way the bioactives will be released (AZEREDO, 2005; BURGAIN *et al*., 2011). For Suave (2006), the main difference between the existing encapsulation methods is the type of involvement of the active material by the encapsulating agent, since the relationship between them can be of physical, chemical, or physicochemical nature.

It is also noteworthy that the choice of material for encapsulation of lipophilic compounds, as is the case of essential oils, depends on the physical performance and chemical and surfactant properties (as they are molecules with hydrophilic and hydrophobic regions that can bind to apolar or polar substances) of these oils (VASISHT, 2014). For choices of these materials, it is crucial that during their selection they present fundamental characteristics such as barrier property and film formation.

For the choice of matrix polymers, it is necessary to take into consideration the core material, morphology, particle size distribution, production quantity, budget, and process availability. Sometimes it may be necessary to make adjustments to the initial capsule development design due to unforeseen circumstances such as low availability of material for stability or encapsulation processing. An example is microspheres with a high amount of modified starch, which may be suitable for the use of atomization drying or *spray dryer* processes, making a commercial case for storing the encapsulated essential oil in a vacuum sealed package. Thus, the starch would only be used as a flavor masking matrix component in an encapsulated form. From another perspective, in the complex preservation process, gelatin-based capsules exhibit high core storage capacity when produced by this method (COMUNIAN *et al*., 2017; VASISHT, 2014).

There are two mechanisms for the encapsulation of essential oils, which are divided into two main categories. The first includes chemical methods like interfacial polymerization and molecular inclusion, and the second includes physical methods like spray-drying, spray chilling, freeze-drying, and extrusion, as well as physico-chemical techniques like ionic gelation, complex coacervation, and emulsification (ASBAHANI *et al.,* 2015).

Interfacial polymerization method

The interfacial polymerization method consists of dissolving monomers in a polar organic solvent together with the active ingredient and an oil to form a solution. The solution thus formed is poured slowly, under stirring, into an aqueous phase containing a hydrophilic surfactant. The oil insolubilizes in the presence of water, forming a colloidal dispersion, and the solvent diffuses into the outer aqueous phase. The monomers orient themselves according to their polarity at the oil/water interface, triggering anionic polymerization at the surface of the oil droplets, which leads to the formation of the capsule wall (WATNASIRICHAIKUL *et al.,* 2002).

Although it is a technique still used in interfacial polymerization, some limitations are reported. They use in their composition non-biodegradable and non-biocompatible polymers and promote the formation of toxic residues during the reactions. They may react with the active ingredient during the polymerization reaction in situ and degrade the components in the nanocapsules obtained (QUINTANAR-GUERRERO *et.al.*, 1998). Thus, preformed polymer-based methods, in particular biodegradable polymers, have been employed due to their easy application and low toxicity (QUINTANAR-GUERRERO *et al.*, 2012).

Molecular inclusion method

The molecular inclusion method is a method that occurs at the molecular level, in which a substance that has a hydrophobic character inside and a hydrophilic character on its external surface is used as an encapsulating material. This structure makes it capable of acting as a "host molecule", which, when in contact with the essential oil (host molecule), enables the formation of inclusion complexes (capsules) with several "guest molecules" of reduced polarity and smaller dimensions than the cavities of the host molecule (OLIVEIRA *et al.*, 2009).

β-cyclodextrin (β-CD) has been the most widely used encapsulating material. The mechanism of this process involves the replacement of water molecules from the β-CD cavity by less polar guest molecules, until a dynamic equilibrium is reached, with energy gain (BREWSTER and LOFTSSON, 2007), promoting the stability of the encapsulated agents against hydrolysis, oxidation, and photodecomposition (LOFTSSON and BREWSTER, 1996). The formation of these complexes comes from a geometric arrangement between the "guest molecule" and the "host molecule", as well as from the polarity compatibility between the two (SANTOS and MEIRELES, 2010).

The use of *β*-CD can be an advantageous technique because these compounds have the ability to complex with a large number of hydrophobic compounds, positively alter the physicochemical properties of the material to be encapsulated, are available in large quantities, and the method used is simple and cost-effective (VEIGA *et al*., 2006).

Encapsulation by spray drying

The *spray drying* method of encapsulation is a simple, rapid, commercial, and low-cost method that has been used for the encapsulation of fragrances, oils, flavors, and other heat-sensitive compounds due to the rapid evaporation of the solvent from the droplets. It is one of the oldest encapsulation methods, having originally been used in the 1930s (WILSON and SHAH, 2007).

This technique is based on pumping the solution (oil + encapsulating agent) to the atomizer, where it is sprayed in the form of a mist of droplets (*spray*), to the drying chamber. In this compartment (drying chamber), solvent evaporation occurs (hot air drying), where the liquid droplets are transformed into dry solid particles, which are then collected in the cyclone or other dust collection system, where separation and capture of the encapsulated oil takes place. In other words, in the *spray drying* method of encapsulation, the substance to be encapsulated is homogeneously dispersed or dissolved in an aqueous solution or dispersion containing the encapsulating agent, which is then atomized (to form numerous droplets) in a current of hot air (drying chamber) for subsequent dehydration. In this chamber (drying chamber), evaporation of the solvent occurs, and rapid solidification of the droplets (capsule formation) is achieved.

The encapsulation by *spray drying* allows obtaining the final product without the need to perform washes to separate the microparticles or eliminate solvent residues (AFTABROUCHAD and DOELKER, 1992). The main variables involved in the process are: the inlet and outlet air temperatures; air or carrier fluid flow; temperature and humidity distribution; dwell time; and chamber geometry (KISSEL *et al.*, 2006).

The use of heat can be considered a drawback, capable of affecting the properties of thermosensitive compounds, either the encapsulating agent or the encapsulating agent. However, the high specific surface to volume ratio of the particles promotes rapid evaporation of the solvent. Under these circumstances, the exposure time of the particles to heat is reduced (usually a few seconds), and the core temperature does not exceed 100 °C, which reduces the probability of undesirable changes occurring in thermosensitive compounds (GUINCHEDI and CONTE, 1995).

The type and concentration of the encapsulating agent, the feed rate, and temperature of the system are central aspects in this method, influencing the characteristics of the microparticles (SILVA *et al.*, 2003).

Although most often considered a dehydration process, atomization drying can also be used as an encapsulation method when it retains "active" materials within a protective matrix that is essentially inert to the material being encapsulated (MAHDAVI *et al.*, 2014).

Encapsulation by spray chilling

In the *spray chilling* encapsulation method, the agent to be encapsulated is dispersed or dissolved in the molten encapsulating agent rather than in a solution. Subsequently, this hot dispersion is misted in a cold air stream, forming the microparticles due to the solidification of the encapsulating agent. In other words, the *spray chilling* method of encapsulation is based on the injection of cold air to allow solidification of the particle. Microparticles are produced by a mixture containing the active ingredient (or filler) and the encapsulating agent in droplet form. This mixture is sprayed by an atomizer or sprinkler nozzle and enters a chamber, in which air circulates at a low temperature (CHAMPAGNE; FUSTIER, 2015).

In this technique the solidification of the coating occurs by thermal freezing of the molten encapsulating agent, whereas in the case of *spray drying*, the solidification of the coating is effected by rapid evaporation of the solvent. In other words, the major difference between these two methods is the way the coating solidifies. In addition to this difference with the *spray drying* technique, there is still the fact that this process does not use water or organic solvents, uses less energy and less time in its processing, which translates into considerable advantages for this method.

Encapsulation by lyophilization

The freeze-drying encapsulation method is based on the dehydration of a frozen product by sublimation (direct passage from the solid to the gaseous state), being performed first by a quick freezing of the product followed by sublimation of the ice under vacuum (AZEREDO, 2005). The freeze-drying process can be divided into three steps: quick freezing, primary drying, and secondary drying. Quick freezing is essential for the following steps, since the formation and distribution of pore sizes occurs, which influences the quality of the material. In the primary drying, sublimation occurs (passage from the solid state to the gaseous state directly), and in the secondary drying, the removal of the sublimated moisture occurs (JAYARAMAN; GUPTA,1995).

In this method, a stiffening of the structure occurs by freezing the surface of the material, on which sublimation takes place, which is useful for preventing collapse of the solid matrix after drying. The effect is the formation of a pore that is easily rehydrated with water. Bacterial growth is not viable in the dried material, but they are not exterminated by this type of drying. As there is no water in the medium, the enzyme activities are inactivated after drying, and oxidative or non-oxidative chemical reactions occur in low quantities, bringing very satisfactory results (BOSS, 2004).

Lyophilization can be performed in trays, multi-batch, tunnels, *Vacuum-Spray Freeze Dryers*, continuous and microwave. The choice will depend on the material. This process is widely used in pharmaceuticals (vaccines, antibiotics), biological materials, and foods (meat, coffee, soup, milk), whose organoleptic properties are important and must be preserved. The disadvantage of this process is the high cost, but that can be circumvented by the lack of specific handling and storage of the product in a refrigerated place, especially if it contains high added value (BOSS, 2004).

Extrusion encapsulation

In the extrusion encapsulation method, the encapsulant material + essential oil are mixed and dropped through the orifice of a thin tube or syringe to form micro droplets, the size of which will be dependent on the diameter of the orifice and the speed at which the material exits. Solidification of the coating material can occur by solvent evaporation, solvent diffusion, or chemical reaction (KRASAEKOOPT *et al.*, 2003).

For example, in the case of encapsulant solidification by chemical reaction, calcium chloride ($CaCl_2$) is generally used. After homogenization of the encapsulant material + essential oil, this mixture is extruded drop by drop using a small caliber pipette or a syringe into a solution (calcium chloride ($CaCl_2$)) in which the capsules are formed.

Encapsulation by extrusion is the most popularly employed technique due to its low cost and simplicity, as well as not involving high temperatures (FAVARO-TRINDADE *et al.*, 2011; KENT; DOHERTY, 2014).

Encapsulation by ionic gelation

The encapsulation by ionic gelation uses the ability of anionic polysaccharides (pectin, alginate, carrageenan gum, and gellan gum) to gel in the presence of some ions, such as calcium (BUREY *et al.*, 2008; SILVA *et al.*, 2006). Thus, encapsulation is performed with the ions directly in the polymer solution containing the bioactive product of interest (BUREY *et al.*, 2008).

The ionic gelling reduces the pH of the solution because the Ca+2 ions are released, and following occurs the jelly that surrounds the active compound (PONCELET, 2001). Thus, the concentration of the ionic solution must be adjusted appropriately. Gelling occurs instantaneously where the divalent ions react with the negatively charged biopolymer chains, forming a rigid three-dimensional structure of high water content (HELGERUD *et al.*, 2009; SCHOUBBEN *et al.*, 2010; SMRDEL *et al.*, 2008).

Ion gelation particles can also be prepared by extrusion or atomization. In extrusion, the solution containing the compound of is dripped into an ionic solution by means of a needle, and may be speed controlled or not. By atomization, compressed air is injected, pressing the solution to pass through a hole of controlled size (BUREY *et al.*, 2008; PATIL *et al.*, 2010).

For Patil *et al.* (2010), ionic gelation is a simple technique that does not use high temperatures or organic solvents, which is ideal for encapsulating hydrophobic compounds. However, a limitation of this technology is the fact that the wall of the resulting capsules has a porous structure, allowing low molar mass compounds to escape by diffusion. An alternative to controlling this porosity is to modify the gel structure by mixing it with other biopolymers.

Encapsulation by complex coacervation

In the encapsulation method by complex coacervation, there is the formation of several complexes of biopolymers on the essential oil molecule. From the mixture of two colloids and pH adjustment, the two polymers with opposite charges are phase separated and form solid particles or closed liquid droplets (CHÁVARRI *et al.*, 2010). Coacervation depends on the net charge of the system and is consequently influenced by stoichiometry, structural parameters of the biopolymers, and the conditions of the medium such as pH, ionic strength, temperature, and nature of the reactants.

This technology is used in various segments such as the pharmaceutical, chemical, and food industries. In the case of the food industry, encapsulation is done in bioactive products such as flavorings, oils, and water-soluble active agents such as probiotics (AUGUSTIN; HEMAR, 2009). For some authors, this coacervation technique is complex and presents numerous advantages, such as the versatility of products where it can be applied, control of particle size, the possibility of not using biopolymers or organic solvents, and mild temperatures in processing (ASSIS, ZAVAREZE, PRENTICE-HERNÁNDEZ; SOUZA-SOARES, 2012; MENEZES *et al.*, 2013).

For Meddanha *et al.* (2009), the encapsulation by coacervation has limitations for hydrophilic products, being more indicated for hydrophobic compounds. According to Gouin (2004), this technique has numerous advantages, but in the case of products with low added value, such as some food products, the impact of using the technology on the final price must be considered.

Encapsulation by emulsification

The term emulsion corresponds to the mixture between two immiscible liquids (e.g., water and oil) in which one of them is in the form of fine globules within the other liquid, forming a stable mixture. To maintain this stability, it is necessary to add surfactants, which can be emulsifiers or surfactants, helping to keep this emulsion more homogeneous and moderately stable. The main characteristic of surfactant compounds is their amphiphilic behavior, which enables their interaction with polar and apolar substances. The hydrophobic part binds with apolar substances and the hydrophilic or ionic part with polar substances. Thus, in the emulsification encapsulation method, the capsules are formed from two steps: the dispersion of an aqueous phase inside an organic phase, such as oil + surfactant, resulting in a water-in-oil emulsion; and the solidification of the capsules.

However, emulsification using double emulsion is being widely employed in the encapsulation of oils as it provides better protection for the active ingredients. Emulsions can be water-oil-water (w/o/w) or oil-water-oil (o/w/o). It is noteworthy that emulsification usually results in small-diameter capsules and is easily applied on a large scale (MORTAZAVIAN *et al*., 2007). However, it can produce microcapsules with large variations in size and shape (KENT; DOHERTY, 2014).

CONCLUSIONS

- The biggest obstacle in today's agriculture is the control of pests in an efficient way that is economically viable and associated with reduced environmental damage. One of the main advantages of natural pesticides over synthetic insecticides is the complexity of natural molecules, making it difficult for target insects to acquire genetic resistance. Although the scientific proof of the insecticidal action of plant species is relatively recent, the results are very promising. Given the available literature, it can be seen that the biggest obstacles to the widespread use of essential oils in agriculture are the need to determine the best dosage to be applied and the technologies that circumvent the instability of essential oils.

- Obtaining new commercial natural products is the result of research in different sectors of the industry. According to Saito and Lucchini (1998) and Vendramim and Castiglioni (2000), obtaining vegetable insecticides for use in nature in pest control entails studying the active compounds as well as the synergistic effect between them. chemistry is an allied science in the development of encapsulators that can be used in production field environments or warehouses because they have already allowed molecular modifications and synthesis of compounds with complex structures, minimizing the instability of some natural components (SAITO; LUCCHINI, 1998).

AUTHORSHIP CONTRIBUTION STATEMENT

SILVA, C.S.: Conceptualization, Investigation, Methodology, Project administration, Writing – original draft; **ALBUQUERQUE, C.F.:** Conceptualization, Data curation, Investigation, Methodology, Project administration; **COELHO, A.P.F.:** Data curation, Investigation, Methodology, Project administration, Writing – original draft; **LISBOA, C.F.:** Funding acquisition, Methodology, Project administration, Writing – review & editing; **GONZATTO, M.P.:** Writing – review & editing.

DECLARATION OF INTERESTS

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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