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PLANT EXTRACTS USED FOR THE CONTROL OF ENDO AND ECTOPARASITES OF LIVESTOCK: A REVIEW OF THE LAST 13 YEARS OF SCIENCE

(Extratos de plantas usados no controle de endo e ectoparasitos de animais de produção: uma revisão dos últimos 13 anos de ciência)

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ABSTRACT - A variety of endo and ectoparasites can affect livestock, causing poor animal performance and low welfare conditions. *Haemonchus contortus* (Trichostrongyloidae), *Rhipicephalus microplus* (Ixodidae), *Cochliomyia* sp. and *Lucilia* sp. (Calliphoridae) are some of the most important parasites to livestock in Brazil and in many other tropical and subtropical countries, where farmers need to be vigilant. Although a constant parasite control uses large-spectrum anthelmintics or synthetic insecticides, giving a timely potent reduction of the infections, they also represent a threat to the lifespan of these compounds due to drug-selected parasites. Thus, the development of plant-based therapies is a solid alternative for standard, agroecological, and holistic farming systems, as well as it is an important ally to combat drug resistant parasite populations. In this article, we discussed the scientific literature on plant extracts, notably hydroalcoholic extract or essential oils, used for the control of the above livestock parasites published in the last 13 years. Our objective was to pinpoint the most important issues for this promising area of research, exploring the potential and the challenges that are facing us by examining more than 150 *in vitro* and *in vivo* studies. Almost all the authors reported positive data from plants or isolates, the most important challenges that were faced during our search were the lack of a proper experimental study design, and the deficiency in the characterization of the plants used. It is our opinion that plant-based products may be a solid choice for parasite control in livestock animals achieving high welfare standards and mitigate farming input (i.e. use of chemicals and their waste into the environment).

Key words: multidrug resistance; organic farming; parasite infections; phytotherapy; ruminants.

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RESUMO - Uma variedade de endo e ectoparasitos pode infectar animais de fazenda causando baixa produtividade e baixa condição de bem-estar. *Haemonchus contortus* (Trichostrongyloidae), *Riphicephalus microplus* (Ixodidae), *Cochliomyia* sp. e *Lucilia* sp. (Calliphoridae) são os parasitos mais importantes para ruminantes no Brasil e em muitos países tropicais e subtropicais, onde produtores devem ficar atentos. Muito embora o controle convencional de parasitos seja constante, usando anti-helmínticos de largo-espectro ou inseticidas sintéticos, permitindo uma eficácia aceitável, isso também representa um risco para a vida útil destes produtos, devido a seleção de parasitos contra as drogas. Assim, o desenvolvimento de medicamentos com extratos de plantas podem ser uma alternativa consistente em sistemas pecuários tradicionais, agroecológicos e holísticos, assim como ser um importante aliado para combater populações de parasitos resistentes. Neste artigo, nós discutimos as pesquisas com o uso de extratos de plantas, notadamente, extratos hidroalcoólicos ou óleos essenciais, usados no controle dos parasitos listados acima, nos últimos 13 anos. Nosso objetivo foi identificar os pontos mais importantes nesta promissora área de pesquisa, buscando os potenciais e os desafios que estão em nossa frente, examinando mais de 150 estudos *in vitro* and *in vivo*. Quase a totalidade dos autores relatou dados positivos com o uso de plantas ou isolados, as maiores dificuldades encontradas durante a pesquisa foi a falta de um desenho experimental correto e caracterização das plantas usadas. É nossa opinião que produtos derivados de plantas podem ser uma alternativa sólida para o controle de parasitos em animais de fazenda, atingindo alto grau de bem-estar animal, mitigando o input negativo das fazendas (ex. uso de químicos e seus desejos no meio ambiente).

Palavras-chave - Fitoterapia; infecções parasitárias; pecuária orgânica; resistência múltipla as drogas; ruminantes.

INTRODUCTION

Livestock production is an important activity worldwide that requires knowledge and the application of modern technologies to be effective and profitable. Welfare conditions of farm animals integrates the health status of livestock and depends on many management strategies that focus in alleviating the imposed stress conditions, i.e. high animal density, contact with infection agents (virus, bacteria, parasites), unbalanced nutrition, and short gestational intervals. In developing countries, particularly those located in tropical and subtropical regions, gastrointestinal nematode infections, acute and chronic), can significantly delay production, decrease revenues and, in extreme cases, be the major cause of death in young animals. In addition, the infestation of living tissues by blowfly larvae and the cattle tick are considered additional problems that affect livestock animals, significantly reducing their performance (Graf et al., 2004; Grisi et al., 2014).

Conventional parasite control against helminths, ticks, flies and myiasis caused by fly larvae depends almost exclusively on the regular usage of broad-spectrum anthelmintics or synthetic insecticide products. The timely potent reduction of the infections by using such drugs represent a major milestone to the livestock industry and are an important factor when setting up any animal health program (Graf et al., 2004). However, the suppressive use of these compounds has caused a threat to the lifespan of these compounds due to the selection of resistant parasite populations (Fortes and Molento, 2013). The use of synthetic antiparasitic drugs also represents a risk to food safety with an unprecedented environmental impact (Ballweber and Baeten, 2012; Beynon, 2012).

Medicinal plants have been used as therapeutic agents in traditional and popular medicine (Khater, 2012; Pavela and Benelli, 2016), and the use of bioactive compounds derived from plants have been investigated as parasiticides in an attempt to be effective against resistant populations, for their relatively low-environmental impact, and for their local availability, improving animal health of distant communities. In South America, a continent with the largest biodiversity on earth, communities hold a valuable traditional knowledge relating the use of medicinal plants (Di Stasi et al., 2002). This vast natural diversity illustrates the potential of the region to have several bioactive products that may be used for the treatment of diseases of humans and animals.

Phytotherapy is being used in large scale parasite control programs in humans (i.e. artemisinin treatment of malaria in Africa and Asia), and may also be a tangible option to fight the alarming drug resistant situation in livestock worldwide. In recent years, efforts have been made towards the application of medicinal plants and their extracts as an alternative or complementary treatment to endo and ectoparasite infections (Khater, 2012; Athanasiadou et al., 2007; Regnault-Roger et al., 2012; Soldera-Silva et al., 2018). However, scientific effectiveness of most plants used as antiparasitic products in laboratory conditions have yet to be confirmed in the field (Molento et al., 2011). Another major issue when applying plant-based extracts as pest control agents is the lack of standardization, which is still considered a limitation to large-scale use (Atanasov et al., 2015). Thus, the investigation and validation of biological properties of plant-derived substances, as well as their chemical characterization, are critical for the scientific endorsement of veterinary phytotherapy field. New technologies are also being developed that will help to unravel the mechanism of action of most of the main isolated compounds and that nanopharmacology should play an important role in the next generation of enterprise (Cruz and Molento, 2015). Lots of obstacles still have to be surpassed to meet the industry demand and all the governmental regulatory steps.

The aim of the present review was to provide up-to-date information on the scientific data from *in vivo* and *in vitro* studies and discuss the biological activity of plant-derived substances against livestock parasites from 2007 to 2019. We looked for the most important issues to this promising area of research, considering their potential and challenges by examining more than 150 articles available at Google Scholar, NCBI/PUBMED, Scielo, Science Direct, Scopus and Web of Science. We used the key words: -parasite scientific name-, plant-base therapy, phytotherapy, livestock, cattle, ruminants, and examined only full articles. More detail information should be looked at the following Tables.

DEVELOPMENT

General characteristics and uses of plant extracts

Phytotherapy products correspond to all preparation, aqueous or hydroalcoholic extracts, syrups and essential oils (EOs), using parts of plants (leaves, stems, roots, flowers, fruits and/or seeds), that may exhibit therapeutic properties. These activities are related to the presence of bioactive compounds, which have distinct chemical characteristics, classified into primary or secondary metabolites (Briskin, 2000). Secondary metabolites, also called special metabolites, are compounds that are biosynthetically derived from the plant's primary metabolism and contain complex structures. These products have also low molecular mass and distinct biological activities (Balandrin et al., 1985).

Although secondary metabolites do not present essential functions in the plants' life cycle, these molecules play an important role to their adaptation to the environment, generating advantages in competition and perpetuation of some species. For example, they may be involved in the pollination process or in the biological defense, acting as chemical defenders against microorganisms, insects, larger predators or even other plants (Balandrin et al., 1985). Most of secondary metabolites can be classified into three chemically distinct groups: terpenoids, synthesized mainly from mevalonic acid or methylerythritol 4-phosphate; phenolic compounds, derived from shikimic or malonic acid; and nitrogen compounds, which are derived from aromatic and aliphatic amino acids (Verma and Shukla, 2015). The products with antiparasitic properties are usually associated with the presence of secondary metabolites, such as EOs, tannins or polyphenols (Khater, 2012; Hoste and Torres-Acosta, 2011).

EOs are a mixture of volatile organic compounds produced by aromatic plants and are found in different organs (i.e., flowers, leaves, stems, seeds, fruits, roots, or bark). These oils are mainly secreted and storedin idioblasts, canals, epidermis cells or glandular trichromes (Bakkali et al., 2008). The extraction EOs can be done by hydrodistillation, steam distillation, dry distillation or others. EOs are liquid, volatile, limpid or rarely colored, lipid soluble and soluble in organic solvents, generally with lower density than water (Stratakos and Koidis, 2016). EO constituents are mainly terpenoids and, to a lesser extent, phenylpropanoids. The plant secondary metabolism is genetically regulated but also strongly influenced by the plant's interaction with biotic and abiotic environmental factors (Verma and Shukla, 2015). Thus, the chemical profile and productivity of EOs and other secondary metabolites can vary according to the type of extraction, climate (i.e. precipitation, temperature, sun exposure), soil composition, plant organ, age and vegetative cycle, circadian rhythm and plant-herbivore interactions, among other factors (Vallad and Goodman, 2004; Pavela and Benelli 2016).

EOs have been widely used against bacteria, virus, fungus, parasites, insects, and in cosmetic applications, especially by pharmaceutical, agricultural and food industries. These compounds exert their activities on insects through neurotoxic effects involving gamma-amino butyric acid (GABA), octopamine synapses and inhibiting acetylcholinesterase (Khater, 2012; Regnault-Roger et al., 2012). EOs are natural in origin and biodegradable, and frequently effective in relatively small quantities. Usually, EOs have an average of 10 to 200 constituents, believed to act in additive and synergy effect. This phyto-complex may also be used to delay insect resistance. EOs often present low toxicity to mammalian cells and are relatively well studied experimentally and clinically. EOs represent a sustainable source of disease control, reducing economic losses, treatment costs and have the possibility to affect resistant parasite populations (Khater, 2012; Regnault-Roger et al., 2012).

Efficacy of plants for the control of *Haemonchus contortus*

Endoparasite infections, especially caused by *H. contortus,* are one of the most important sanitary and economic problems of livestock. Common symptoms include apathy, weight loss, anemia, diarrhea, and even death of young animals. To control these infections, farmers usually use conventional anthelmintic products in preventive programs (Fortes and Molento, 2013). Several alternatives have been suggested to overcome this problem and the use of herbal medicines is in an advanced stage of research, showing promising data (Seddiek et al., 2011; Adenubi et al., 2016; Pavela and Benelli, 2016).

The articles listed in Table 1 suggest that plant extracts that are rich in condensed tannins, flavonoids, or saponins have potent activity against *H. contortus*. On the other hand, several other papers focus on the use of EOs, mainly rich in thymol, carvacrol, geraniol, pulegone and/or eugenol.

Condensed tannins are natural antioxidants used against nematodes and act by reducing the excretion of eggs by decreasing the fertility of female parasites. Lambs infected with endoparasites consuming plants with high tannin contents had a reduction of parasite load (Lisonbee et al., 2009). Flavonoids, on the other hand, can have an indirect effect, since their antioxidant activities can also potentially increase the animals' immune response (Lakshmi et al., 2010). As for the saponins, these compounds are known to interact with collagen proteins from the nematode cuticles, and this interaction is believed to be responsible for their nematotoxic effects (Argentieri et al., 2008).

Efficacy of plants for the control of *Rhipicephalus microplus*

Ticks are the main parasite problem of cattle in most tropical countries, where the infestation by *R. microplus* cause enormous economic impact (Jonsson and Piper, 2007; Molento et al., 2013; Benelli et al., 2016). Due to the lack of up-to-date technical assistance and long-term epidemiological studies, tick control is usually done with the indiscriminate use of commercial synthetic products for both dairy and beef cattle. New technologies are currently being developed for tick control and, among them, microbiological control, breed selection, target selective treatment and the use of plant extracts show the most promising results (Molento et al., 2013; Mapholi et al., 2014; Webster et al., 2015; Adenubi et al., 2016; Pavela and Benelli, 2016). A literature overview on plant-derived products used against *R. microplus* in different *in vitro* tests are showed in Table 2.

Some phenolic compounds found in the phytochemical analyses have significant acaricide effect, however, the mechanism of action of these compounds is still to be established (Krimer-Malesevic et al., 2011). Terpenoids are involved in the defense mechanism of some plants against mites. Terpene-rich methanol extracts of *Hypericum polyanthemun* (millerpertius) at concentrations of 50, 25, 12.5 and 6.25 $mg.ml^{-1}$, obtained, respectively, 100, 96.7, 84.7 and 52.7% mortality of *R. microplus*, 48 h using the larval immersion test (Ribeiro et al., 2007). Hexanic extract of *Piper aduncum* (spiked pepper) presented a LC50 of 9.30 $mg.ml^{-1}$ for larvae and the reduction of tick reproduction (adult immersion test) ranged from 12.48 to 54.22% (Silva et al., 2009). Ribeiro et al. (2010) assessed the acaricidal properties of the EO from *Hesperozygis ringens* on the newly hatched larvae of the cattle-tick using the immersion tests, showing a LC_{50} of 0.260µl/ml. A similar evaluation using the package immersion tests was assessed by Lima et al. (2014), with hexanic extract of *Piper tuberculatum* fruits, where the authors found a LC_{50} of 0.04 mg/ml. The acaricidal efficacy of *Lippia gracilis* EO was assessed against organophosphate-resistant and susceptible strains of *R. microplus* by Costa-Junior et al. (2016), using two genotypes of *L. gracilis* (106 and 201), thymol and carvacrol chemotype, respectively. The thymol chemotype was more effective than the carvacrol, showing a LC_{50} of 1.02mg/ml (Table 1). The EO extracted from *L. triplinervis* shoots was also investigated for acaricidal activity on *R. microplus* (Lage et al., 2012). The authors reported an efficacy of 95.7% using 2.5 mg/ml of EO on newly hatched larvae (larval packet test) (Lage et al., 2012). Likewise, the methanol extract of *Acmella oleracea* showed better results on *R. microplus*, with 98.1% of mortality, using 1.6 mg/ml. More recently, a rare chemotype of *Cinnamomum verum* was studied by Monteiro et al. (2017), demonstrating a LC_{50} of 1.00 mg/ml.

Efficacy of plants for the control of Blowflies

Several flies from Calliphoridae and Cuterebridae families have received considerable attention due to human and animal infestation inducing primary, secondary or facultative myiasis (Papavero and Couri, 2012). Infestation of living tissues mainly by *Cochliomyia hominivorax* causes a loss of US$ 336 million/year in Brazil (Grisi et al., 2014).

Nowadays, conventional control of myiasis depends almost exclusively on synthetic insecticides, representing a major risk to food safety, especially with high residues in meat and milk (Moya-Borja, 2003; Chaaban et al., 2017a). Since 1940, the synthesis of long-acting insecticides has led experts to hope for the control of various diseases caused or transmitted by arthropods or even to eradicate unwanted species. However, the toxicity of synthetic insecticides and the negative effects on human health and the environment, coupled with the development of insecticide resistance, led to a recovery of the interest in low-impact botanical insecticides (Pavela, 2015). The great biodiversity in South America has stimulated the increasing interest on the chemical composition and the biological activity of some native plants. The use of plant extracts in the control of veterinary ectoparasites has increased considerably, owing their popularity mainly with organic farmers and environmentally conscious consumers (Regnault-Roger et al., 2012; Ellse and Wall, 2014). Thus, plant extracts appear as a promising alternative for controlling myiasis (Khater et al., 2011; Callander and James, 2012; Khater, 2014; Shalaby et al., 2015). Table 3 presents the main research using plant extracts against myiasis caused by the larvae of some economically important flies.

Studies with L3 of *C. macellaria* and *L. cuprina* showed that sub-lethal doses of EO interfered with the insects physiological parameters (Chaaban et al., 2017 b, 2019 a,b). Reports on retarded larval growth and changes of physiological parameters at sub-lethal concentrations were also described after treatment of *L. sericata* with fenugreek, celery, radish, and mustard oils (Khater and Khater, 2009). Changes in larvae cuticle necrosis, abnormalities, decrease in motility and adult deformity were also observed using plant extracts (Shalaby et al., 2016; Chaaban et al., 2017a, 2017b).

The wide range of results observed on toxicity studies may be related to the insect life cycle stages, the mechanism of action (i.e. contact and/or ingestion) and the different sensitivity between Diptera species (Callander and James, 2012). The influence of EOs of lettuce (*Lactuca sativa*), chamomile (*Matricaria chamomilla*), anise (*Pimpinella anisum*), and rosemary (*Rosmarinus officinalis*), solubilized in surfactant and distilled water on post-embryonic development of *L. sericata* were evaluated, showing LD_{50}s of 0.57, 0.85, 2.74 and 6.77%, respectively (Khater et al., 2011). The assessment of toxicity in immersion tests with Tween 20 containing 50% EO of *Melaleuca alternifolia* (tea tree), using L3 of *L. cuprina* determined a toxicity rate lower than 50%, demonstrating a greater susceptibility of the 1st and 2nd instar larvae (Callander and James, 2012). The bioefficacy of methanolic extracts of *Azadirachta indica* leaves on the survival and development of myiasis-causing larvae of *Chrysomya bezziana* was assessed by Singh and Kaur (2016). The authors reported a significant toxic effect by the extract, indicating that *A. indica* may be used in controlling the larvae of *C. bezziana*.

The biocontrol of Blowflies by parasitic wasps, nematodes, bacteria, fungi and viruses has been proposed and offers a particularly interesting approach to ectoparasites management (Wall, 2012; Sandeman et al., 2014). However, herbal medicines are in an advanced stage of research, showing promising results, which will be listed below. *In vivo* tests are essential to recommend the exact doses to be applied on animals, however we need large scale studies to determine the real effective concentrations, even including populations that are geographically distant. Despite the increase on studies of plant extracts for myiasis control, some gaps remain to be filled. In Table 3, we note that 52.63% of the papers did not describe which part of the plant were used. Similarly, 89.47% of them did not show the chemical composition of the evaluated plant. Therefore, our opinion is that these data are incomplete, representing an important limitation regarding high-quality scientific information to base alternative forms of treatments for ecto and also to endoparasites of livestock. These limitations are particularly important for all reports and we still have to address this issue to be able to better contribute to the phytotherapy field of science.

Use of individual compounds from plant extracts against parasites of livestock

Determining the *in vivo* or *in vitro* activity of the isolated compounds from plants can bring great advances to parasite control, since it allows their use in specific formulations with maximized efficiency. Such data can be used for the exploration of additive and synergic effects and the exclusion of potential antagonistic compounds present in different plant extracts. In this sense, the evaluation of isolated compounds as parasiticides has been increasing considerably in the last decade (Table 4). The acaricidal activity of b-amino alcohol derivatives of limonene (1-methyl-4-(1-methylethenyl)-2-(4-furfurylamine) cyclohexanol), against *R. microplus* was assessed by Ferrarini et al. (2008). The authors reported 100% larvae mortality at a concentration of 1.25 mg/ml. The toxicity of thymol and carvacrol has also been studied. Thymol has showed a better acaricidal (against *R. microplus*) activity when compared to carvacrol in the larval packet test and larval immersion test (Costa-Junior et al., 2016; Araújo et al., 2016). Likewise, the LC_{50} of 4.46 mg/ml and LC_{50} of 5.50 mg/ml were obtained for carvacrol and thymol, respectively using the adult immersion test. The effects from the interactions of these substances was suggested as a synergic effect in the control of *R. microplus* (Araújo et al., 2016). The acaricidal activity of spilanthol, one of the major chemical constituents of the flowers and leaves of *Acmella oleracea,* was assessed by Cruz et al. (2016). The data revealed a larval mortality of 91.3% from 0.8 mg/ml of this compound (Cruz et al., 2016).

Recent studies showed significant activities of thymol, bromelain, cinnamaldehyde and chlorogenic acid against different life stages of *H. contortus* (Table 4). The inhibitory effect of thymol was assessed on egg hatching by Camurça-Vasconcelos et al. (2007), where the authors found 93.6% of inhibition using 0.62 mg/ml of the isolate. Similarly, the toxicity of cinnamaldehyde was evaluated with the egg hatch test with a LC_{50} of 0.018

mg/ml on *H. contortus* (Katiki et al., 2017), while another study found that 500 µg/ml of chlorogenic acid was enough to cause 100% egg hatch inhibition (Jasso-Díaz et al., 2017). Studies on larval development using individual compounds also presented promising data. Bromelain and the aqueous extract of *Ananas comosus* were studied *in vitro* against *H. contortus*, using the egg hatch test and the larval development test at concentrations of 0.15 and 0.25 mg/ml, exhibiting 99.2 and 100% efficacy, respectively (Domingues et al. 2013). The authors reported that the same substances showed reduced (89 and 42%, respectively), efficacies when running an *in vivo* study.

Challenges and opportunities to the science of phytotherapy

Phytotherapy, as well as herbal medicine/herbalism, and ethnoveterinary, is a regular form of medical science and must be treated so, using all the available technology for its development and distinguished growth. The traditional use of herbs/plants has given rise to a modern discipline, which must comply to scientific standards, not relying in empirical appreciation and old knowledge (Ameh et al., 2010). The World Health Organization – WHO, has given support to the broad use and regulation of herbal medicine, even to the support of clinical trials and the evaluation of their residues (WHO, 2000, 2005, 2007).

Pharmacological activity of plant-derived isolates (effect, persistency, quality, safety/toxic signs, biosynthesis, drug-drug interaction and combination), must be a priority for novel data determinations, as we want to suggest their use in substitution to commercial products. The combination of herbal medicines and commercial products is another great option to fight drug resistant parasites, due to the increase mode of action of the distinctive resulting compound. Some of the studies that were reported in this article shed light into this new research area, determining the composition of plant extracts, and evaluating the toxicity of their individual constituents against livestock parasites (Chaaban et al., 2019). The critical synergic effect between compounds, within and between chemical classes, is another challenge, as the summing effect is dependent of many distinct and fundamental stimuli (i.e. plant phenotypic response, chemical interactions, etc.) (Santos et al., 2018).

An extra perspective is the false impression, from common users, that plant derive products are safer to the environment. Related to this, the risk of host toxic effect is also a major factor to be taken into account, as the skin can be damaged after an overdose of an isolate. Thus, apart from being a real possibility of substitution, some questions have arrived from plant-based products: (1) What are the real concerns if the world decides to go green? (2) What would be the impact of such products? and (3) How can we prepare the consumers to the use of these products judiciously? These questions still need large scale-studies to be elucidated.

On the other hand, there are significant advantages and solid global market opportunities for new ecofriendly products, as holistic farming can mitigate waste products, negative farm inputs and industrial by-products.

CONCLUSIONS

The above listed plant-derived products have demonstrated valuable activity against adult and larvae of *B. microplus*, nematode eggs and larvae and mature larvae of *L. cuprina* and *C. macellaria* at very low concentrations, showing no toxic signs using the *A. salina* model (Sprenger et al., 2015). We believe that plant-based products can be excellent candidates for the development of antiparasitic compounds against livestock parasites.

Nowadays, the demand for safe food-products and healthy animals, have created an opportunity to develop programs for resilient farms, opening a wide opportunity for agroecological commodities. The need to search for natural-product based strategies is also important to confront the problem of drug resistance, creating effective alternatives, which can be used in combination with other management strategies. These products shall be used in associations or rotation programs, reducing the parasite selection pressure and extending the lifespan of all products.

As pointed out in this review, several challenges still must be overcome in order to consolidate the use of plant extracts or isolated components for livestock parasite control. The main limitations are: the standardization of biological tests with plant extracts, toxicity assessment of individual compounds, identification of the mechanisms of action, improvement of product solubility and bioavailability, increase of pharmacological activity, tissue distribution and penetration, protection against physical and chemical degradation, solution stability and the increase of the product shelf-life, drug-drug interaction, overall cost and animal safety.

Furthermore, we think that nanotechnology has emerged as another promising area for the development of products in a wide range of applications (i.e. nanoparticles) (Gunasekaran et al., 2014; Cruz and Molento, 2015; Govindarajan et al., 2016a; Govindarajan et al., 2016b), that could well represent the solution to some of the complex issues raise in this review. Researchers have to face these central problems and provide reliable information to contribute to a safer environment, focusing in improving animal welfare and, at the end of the day, to our own existence.

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