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The importance of the pet market for the development of new products based on medicinal plants and their derivatives

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The world pet market is currently the fastest growing in the world. The Brazilian Pet Industry Association estimates that the world pet market had a turnover of US $ 124.6 billion in 2018, representing growth of 4.3% in relation to 2017, when the turnover was the US $ 119.5 billion. The United States is the country with the highest sales, accounting for approximately 40.2% of all world sales, followed by Brazil. China now has a share of 3.1% of the world market, while until 2016, it was not among the top 10 worldwide (Abinpet, 2020).

Figure 1 below shows the gross revenue in the percentage of the countries with the highest sales of pet products.

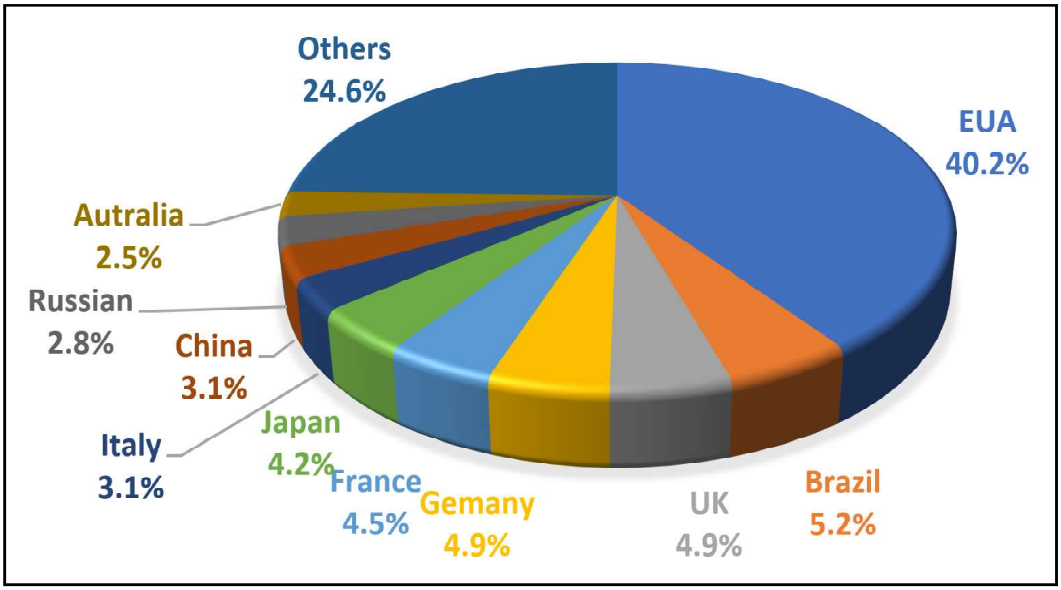

Figure 1: Ten countries with the highest turnover in the pet market, totaling $ 124.6 billion (Abinpet, 2020).

Brazil has the second largest population of pets in the world, reaching approximately 139 million animals, with 54 million dogs, 39.8 million ornamental birds, 23.9 million cats, 19.1 million fish and 2.3 million other animals (Abinpet, 2020).

The growth of the market is accompanied by the rising concern of owners with the health of their animals, both regarding feeding and the use of medicines with less severe side effects, including for the prevention and treatment of infestations by parasites such as fleas and ticks, as well as with public health regarding the transmission of pathogens from animals to humans (Chomel *et al.,* 2011).

In addition to human exposure, medicines administered to pets to control fleas and ticks can be introduced into the wastewater treatment system during the routine bathing of animals, since they are often bathed in residential bathrooms or by professional services where the waste is sent directly to the sewer system (Teerlink *et al.,* 2017).

Fleas (*Ctenocephalides felis* and *C. canis*) and ticks (*Rhipicephalus sanguineus*) transmit diseases to domestic animals, requiring their

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control with chemotoxic agents. However, the agents available in the market are toxic to animals (Mello *et al.,* 2002; Chomel *et al.,* 2011), humans and the environment (Spadotto *et al.,* 2006; Oliveira *et al.,* 2001). Therefore, it is essential to search for substances from natural origins for the control of these ectoparasites, in line with the concept of Unique Health, which has emerged to convey the inseparable union between animal, human and environmental health. In this sense, looking at the whole is essential to ensure high levels of health. Many diseases can be better prevented and combated through integrated action between veterinary medicine, human medicine and other scientific fields.

Fleas and ticks can cause great discomfort to pets, as well as spreading diseases (Esccap, 2018). They can cause allergic reactions of varying intensity, due to the effect of the bite and saliva inoculation, and in large infestations they can cause iron deficiency anemia in young or small animals (Linardi *et al.,*2012; Esccap, 2018). Dogs and cats that are not allergic can be asymptomatic carriers, but in allergic ones, the lesions include papules, crusts, erythema and alopecia, among others (Esccap, 2018; Medleau *et al.,* 2003). Parasitized animals, in an attempt to get rid of fleas, can bite and scratch the skin, pulling out hair and scarifying skin tissues (Linardi, 2012; Esccap, 2018).

The most widely used strategy for the control of insect populations is the administration of insecticides, substances of natural or synthetic origin used to eliminate insects at different stages of their life cycle (Correia *et al.,* 2006; Dos Santos *et al.,* 2020;).

There are several chemical classes available for flea control, such as pyrethroids, organophosphates, carbamates, phenylpyrazoles, nitroguanidines and macrocyclic lactones, which affect the insect's nervous system, as well as growth regulating substances (IGRs - " insect growth regulators"), currently known as arthropod growth regulators (AGRs). These target other organs than those of the neural system, and due to their performance in specific arthropod systems, they are characterized as selective products (Scott *et al.,* 2002; Otranto *et al.,* 2008; Ellse *et al.*, 2014).

Over the years, demands have increased from society for alternative pest control products that do not cause negative impacts on human and animal health, the environment and natural resources (Guimaraes *et al.,* 2014). Although, efficient, synthetic insecticides cause a series of problems, such as environmental contamination, presence of high levels of residues in food, biological imbalance due to the elimination of natural enemies, and the emergence of resistant insect populations (Hernández *et al.,* 1996).

Botanical insecticides are products derived from plant parts, directly through grinding into powder, or derived by extraction with water or organic solvents such as alcohol, ether, acetone, chloroform, *etc.*, or by distillation (Machado *et al.,* 2007). These insecticides have been suggested as potential alternatives to the use of conventional synthetic insecticides, presumably because extracts and essential oils have lesser impacts on human health and the environment (Isman *et al.,* 2011).

The search for such alternatives is attracting rising research interest around the world. A survey carried out in the Elsevier database, covering the last ten years, revealed that studies of natural products applied to veterinary medicine have been growing steeply (Figure 2), including studies of natural products for flea and tick treatment (Figure 3).

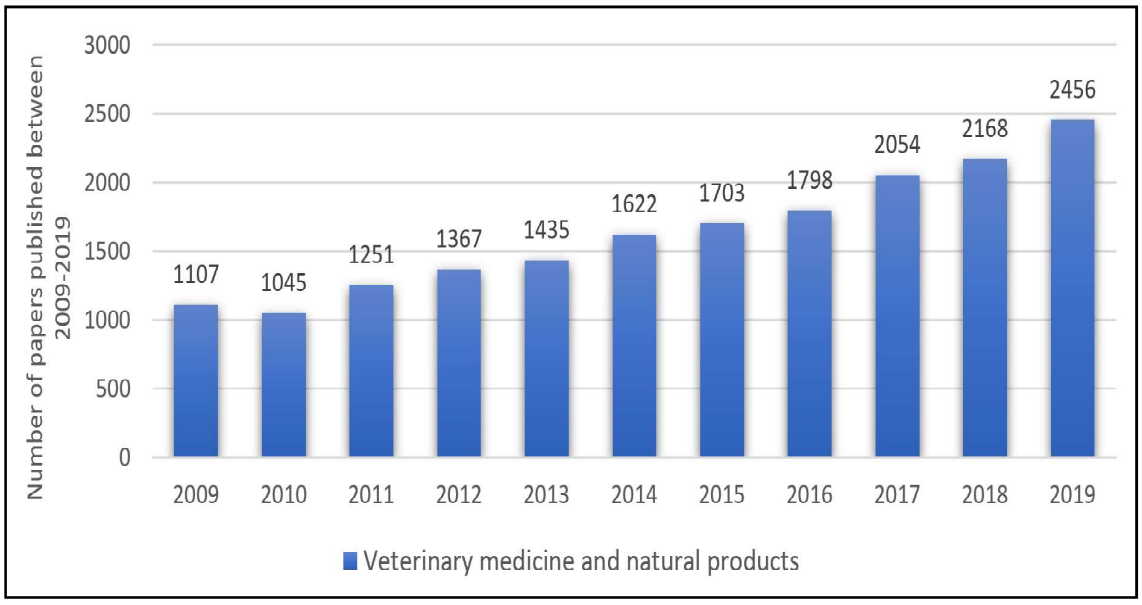

Figure 2: Number of papers published between 2009-2019; keywords veterinary medicine and natural products. Database Science Direct, 2020.

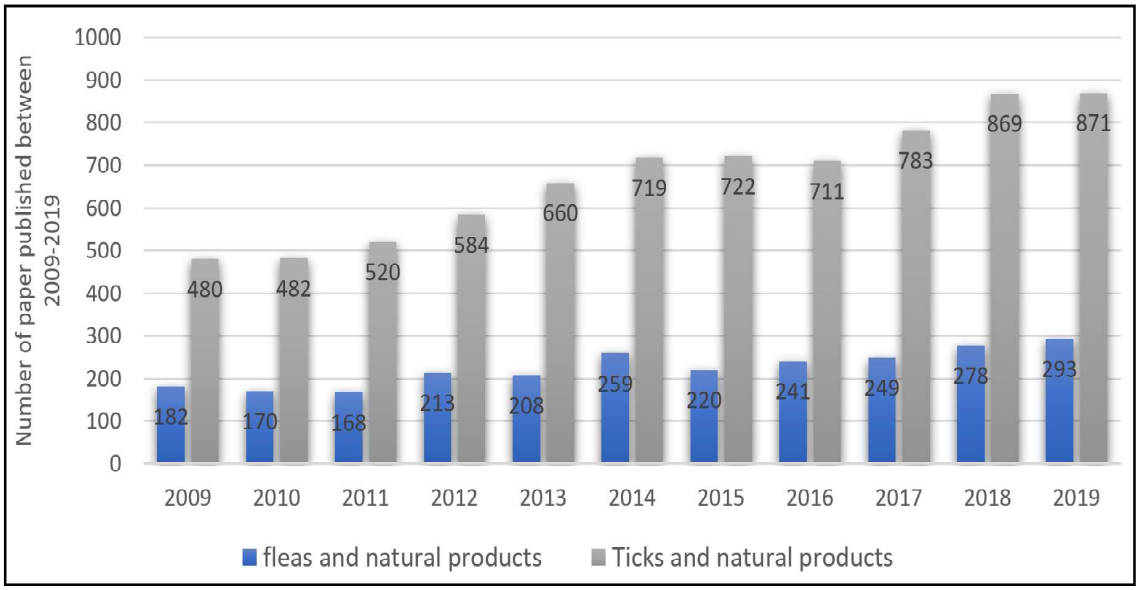

Figure 3: Number of papers published between 2009-2019; keyword's fleas and natural products, and ticks and natural products. Database Science Direct, 2020.

Examples of natural insecticides include pyrethrin (the most important group of natural insecticides), nicotine and rotenone. The known insecticides of synthetic origin belong to the group of chlorinated and phosphorous substances, carbamates, pyrethrin and synthetic pyrethroids (George *et al.*, 2014; Ellse, 2014), among others that have appeared in recent years (Dos Santos *et al.*, 2020).

My team has published several works involving extracts and essential oils of plant species investigating the insecticidal action of these natural products. Some results are presented below in relation to the control of these ectoparasites.

Rosmarinus officinalis L. (Lamiaceae), rosemary, is rich in flavonoids, tannins, terpenes and saponins. The crude extract obtained by maceration in methanol showed activity (95%) *in vitro* at a concentration of 2,500 ppm against adult forms of *Ctenocephalides felis felis*. At the concentrations of 10,000 and 20,000 ppm of crude extract, we observed inhibition rates of 45 and 55%, respectively, against *Rhipicephalus sanguineus* (Batista *et al.,* 2013).

Pilocarpus pennatifolius Lem. (Rutaceae), jaborandi, is a species rich in alkaloids. In a study of this plant, the extract was obtained by exhaustive maceration and the chemical composition was assessed by thin-layer chromatography, followed by colorimetric assays. Dilutions of the extract were prepared in the concentration range between 625 and 20,000 ppm. The results showed that the extract of jaborandi was active *in vitro* in the concentration range tested against ectoparasites, with efficacy values of 35% against *C. felis felis*, 31.82% against *R. microplus* and 59.06% against *R. sanguineus* (Batista *et al.,* 2013a).

Essential oils (EOs) are of great importance for the control of insects and mites. Some studies have reported the efficient action of these products, with high residual effect, which is desired by the herbal industry of products for the treatment of animals (George *et al.,* 2014).

Schinus molle L. is a species that has been extensively studied due to its high yield of essential oils, allowing its action to be evaluated against ectoparasites. Batista *et al.* (2016) showed the effectiveness of extracts and essential oil of this species. In an *in vitro* assay, the non-polar (*n*-hexane) extract showed 100% efficacy (800 µg cm^{-2}; LD_{50} = 524·80 µg cm^{-2}) after 24 and 48 h. Its major compound was lupenone (50·25%). Essential oils from fruits and leaves were evaluated and had 100% efficacy against adult fleas at 800 µg cm^{-2} (LD_{50} = 353·95 µg cm^{-2}) and at 50 µg cm^{-2} (LD_{50} = 12.02 µg cm^{-2}), respectively. However, when evaluated against flea eggs the EO from fruits and leaves was not active against. This was the first study reporting the insecticidal effects of essential oils and extracts obtained from *Schinus molle* against *Ctenocephalides felis felis* (Batista *et al.*, 2016).

In 2019, a study involving the essential oil of the species *Ocimum gratissimum* L. (clove Basil) showed that the components of the oil (mainly eugenol) were active in the control of ticks. The bioassay results showed that *O. gratissimum* essential oil exhibited strong acaricidal activity against *R. sanguineus* (LC_{50}= 6.2 mg ml^{-1}). These results are promising for the development of herbal products to obtain an alternative method of controlling tick larvae while minimizing the use of synthetic products (Ferreira *et al.,* 2019).

EOs from *Alpinia zerumbet* (Pers.) B. L. Burtt & R. M. Sm, *Cinnamomum* spp., *Laurus nobilis* L., *Mentha spicata* L., *Ocimum gratissimum* L. and *Cymbopogon nardus* (L.) Rendle were effective against immature stages and adults of *C. felis felis*. Bioassay results suggested that the method of evaluation was able to perform pre-

screening of the activity of several EOs, including the discriminatory evaluation of flea stages by their LC_{50} values. *Ocimum gratissimum* EO was the most effective in the *in vitro* assays against all flea stages, presenting adulticide (LC_{50} = 5.85 µg cm^{-2}), ovicidal (LC_{50} = 1.79 µg cm^{-2}) and larvicidal (LC_{50} = 1.21 µg cm^{-2}) activities, causing mortality at low doses (dos Santos *et al.,* 2020). *Syzygium aromaticum* essential oil (SAEO) and its major compound eugenol (EG), also produced excellent results against adult fleas and the maturation of eggs into adults of *Ctenocephalides felis felis.* Flea mortality was evaluated 24 and 48 h after exposure. In order to evaluate the inhibition of the maturation of eggs into adults, 10 eggs were exposed to filter paper impregnated with SAEO and EG at the same concentrations used in the pulicidal test, with evaluation performed 30 days after incubation. Untreated fleas were maintained in both studies (control group). The median lethal concentration (LC_{50}) values of SAEO were 5.70 µg cm^{-2} in 24 h and 3.91 µg cm^{-2} in 48 h. The LC_{90} values were 16.10 µg cm^{-2} and 15.80 µg cm^{-2} in 24 and 48 h, respectively. The LC_{50} values regarding the maturation of eggs into adults were 0.30 µg cm^{-2} and the LC_{90} 3.44 µg cm^{-2}. The LC_{50} values of EG were 2.40 µg cm^{-2} in 24 h and 1.40 µg cm^{-2} in 48 h, while the LC_{90} values were 8.10 µg cm^{-2} and 3.70 µg cm^{-2} in 24 h and 48 h, respectively. The LC_{50} against maturation of eggs into adults was 0.10 µg cm^{-2} and the LC_{90} was 0.68 µg cm^{-2} (Lambert *et al.,* 2020).

Nature can be an inexhaustible source of molecules that could act to control ectoparasites from pets. In addition to being mostly biodegradable products with low toxicity, in general, the use process has a low cost.

The phytomedicine is gaining wider acceptance and importance, because it is truly a multidisciplinary area, encompassing several disciplines. In view of the ever increasing amount of awesome research work to be carried in the development of phytomedicines and conventional medicines from plants, a matching increase in the number of good quality, reputed journals is a requirement. In this context, **'Annals of Phytomedicine: An International Journal'** with a commitment to excellence in publishing cutting edge research in all areas of phytomedicine, is a welcome arrival. It is established that a large number of journals devoted to this branch of science, but only few of them publish articles from multidisciplinary areas, thus it a significant addition to the list of the wide-range periodicals on medicinal plants. It is graftying to see that "Annals of Phytomedicine" is catering to the needs of scientists from different closely related disciplines by promoting the publications on plant medicines and specially by inviting the commentaries of stake holders. No doubt, it is a challenging and a difficult job to run such a journal successfully. I am happy to note that 'Annals of Phytomedicine' is already on its way towards accomplishing its mission and reaching its zenith.

Conflict of interest

The author declared that there is no conflicts of interest in the course of conducting the research. The author has final decision regarding the manuscript and decision to submit the findings for publication.

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Biography

Professor Douglas Siqueira de Almeida Chaves was born in 1981 – Mendes, Rio de Janeiro. He Graduated in Pharmacy, master's and doctorate in Chemistry of Natural Products from the Federal University of Rio de Janeiro. Professor Chaves is Associate Professor of Pharmacognosy, Department of Pharmaceutical Sciences, Federal Rural University of Rio de Janeiro/Brazil (UFRRJ). Experience in the Pharmacy area, with emphasis on Chemistry of natural products, acting mainly on the following topics: pharmacognosy, herbal medicines, analytical methods, organic chemistry, chemistry of natural products, phytochemistry, development of products aimed at animal and human health. Professor Chaves has a 15 years' background of teaching and research activities in Pharmacognosy, phytotherapy, development of new phytotherapy and natural products with veterinary importance. He has more than fifty papers in journals of high impact and some chapters of book; associate editor of three journal and referee of several journals such as Industrial Crops and Products, Brazilian Journal of Pharmacognosy, Natural Products Research and others. Professor Chaves published several papers about the chemical composition of essential oil and their activity against insect of veterinary importance. He has some presentations as invited and plenary speaker and has collaboration with research of various countries (Portugal, Poland, Mexico, India, Hungary and Italy). Paper presentation: He has presented more than 70 research papers in various National and International seminars, conferences and symposiums and organized workshops and conferences. Professor of the Pos-graduate Program in Chemistry (PPGQ) and Pos-graduate Program in Veterinary Sciences (PPGCV) at UFRRJ. Currently, Southeast Regional Coordinator of the Brazilian Society of Pharmacognosy and Industrial scientific and technological development fellow of the Special Cooperation Program with the Ministry of Health - COSA. Member of the American Society of Pharmacognosy, Member of the Brazilian Society of Pharmacognosy and Member of the Polish Herbal Committee. Actually, is Head of the Department of Pharmaceutical Sciences. Professor Chaves is working actually in three important projects: Development of phytotherapy from medicinal Cannabis; Herbo Chain: development of an antiviral based in green propolis against SARS-CoV-2; Development of new phytotherapy from *Momordica charantia*.