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Influence of parasitism in dogs on their serum levels of persistent organochlorine compounds and polycyclic aromatic hydrocarbons



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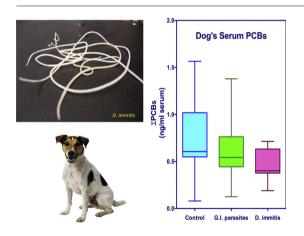
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HIGHLIGHTS

Study exploring the influence of parasitic nematodes in serum levels of POPs.

- D. immitis is strongly associated with lower levels of organochlorine compounds.
- Gastrointestinal parasites are associated with lower levels of PCBs in host dogs.
- A weak relation between parasitism and PAHs levels of the hosts was found.
- The possibility exists that parasitic nematodes could metabolize POPs.

GRAPHICAL ABSTRACT



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ABSTRACT

Persistent organochlorine pollutants (POPs) are toxic chemicals, which accumulate in humans and animals, as only few species have the capability of eliminating them. However, some authors have pointed to the possibility that certain species of invertebrates (i.e. nematodes) could metabolize this type of compounds. As certain species of nematodes act as parasites of vertebrates, this research was designed to explore the influence of some of the most common parasites of the dogs in their serum levels of 56 common POPs. The study included three groups of dogs (n=64), which were prospectively recruited in the island of Gran Canaria (Canary Islands, Spain): a) control animals, non-parasitized (serologically tested negative, n=24); b) dogs tested positive for intestinal parasites and negative for other parasites (n=24); and c) dogs tested positive for heartworm disease (*Dirofilaria immitis*) and negative for other parasites (n=16). The presence of *Dirofilaria immitis* was strongly associated with lower serum levels of a wide range of pollutant in their hosts (PCB congeners 28, 52, 118, 138, 153, and 180; hexachlorobenzene, lindane, aldrin, dieldrin, anthracene and pyrene). We also found an inverse association between the hosts' serum levels of PCBs and intestinal parasites. We did not find any association with DDT or its metabolites, but this might be explained by the recently suggested ability of dogs for the efficient metabolization of these compounds. According to the results of this study certain forms of parasitism would reduce the

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bioavailability of the major classes of POPs in dogs. However, further studies are needed to elucidate whether this phenomenon is due to a competence between parasites and hosts or could respond to a possible capability of parasitic nematodes for the metabolization of these POPs.

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1. Introduction

Persistent organic pollutants (POPs) are toxic chemicals that are generally resistant to degradation in the environment and biota. This group of chemicals is constituted by a high variety of synthetic, lipophilic, persistent and cumulative substances (Safe, 1990). Many POPs come from the production and use of organochlorine compounds, such as organochlorine pesticides (OCPs) and polychlorinated biphenvls (PCBs). Polycyclic aromatic hydrocarbons (PAHs) are ubiquitous environmental pollutants containing two or more fused benzene rings that are produced during the incomplete combustion of organic matter and during human or industrial activities (Guo et al., 2012). Because of their efficient metabolization in most species, strictly speaking, PAHs cannot be considered as POPs, but due to their high prevalence in the environment and their lipophilicity, PAHs are usually considered as POPs (EC, 2004; Lammel et al., 2013). The majority of POPs, such as PCBs and OCPs, are currently banned from use and are no longer produced or used around the world. However, due to their fat solubility and resistance to chemical and biological degradation, ingestion of certain classes of POPs by animals leads to bioaccumulation throughout their lives, generally in the fatty tissues, and to biomagnification in the food chain (Gioia et al., 2014; Safe, 1994).

Some studies have determined the levels of contamination by POPs in dogs, especially with the intention of exploring the possibility of such species of serving as a sentinel of human exposure to POPs (Ali et al., 2013; Ruiz-Suárez et al., 2016), but also in relation with certain pathologies (Sévère et al., 2015). Although there are differences among studies, the most abundant POPs detected in humans have also been those detected in dogs (Kunisue et al., 2005). For certain contaminants, such as DDT and metabolites, relevant differences in concentrations have been described among species (several orders of magnitude lower in dogs than in humans (Ruiz-Suárez et al., 2016)). Therefore, it has been suggested that the dogs (and other canines) could pose the capability of metabolizing some of these recalcitrant environmental pollutant (Hoshi et al., 1998; Ruiz-Suarez et al., 2015; Ruiz-Suárez et al., 2016; Shore et al., 2001).

Since POPs are biomagnified in the food chain, the level of contamination by POPs is mainly determined by dietary habits, in humans (Boada et al., 2014; Luzardo et al., 2013; Rodríguez-Hernández et al., 2015a, 2015b; Vogt et al., 2012) and also in animals (Kunisue et al., 2005; Luzardo et al., 2014; Polischu et al., 2002; Ruiz-Suarez et al., 2015). Therefore, in most vertebrates the continuous exposure throughout life leads to the bioaccumulation of these substances, as to date it has been reported that only few species have the capability of fully eliminating them. The metabolic capacity of organisms to selectively attack certain compounds, leading to either detoxification and elimination or to the formation of toxic metabolites remains to be assessed in deep, but the evidences to date indicate that this capability is very limited. Thus, in the case of PCBs, it has been described that some animals (e.g. marine mammals) pose the enzimatic capability to remove certain types of PCBs via the formation of hydroxy-PCB and other POP metabolites ("reactive intermediates"), and it has been proposed that these intermediates may play an important role in the disruption of certain endocrine processes (Goerke and Weber, 2001; Norstrom, 2002; Ross and Birnbaum, 2001). However, in the vast majority of vertebrates there are only a few major mechanisms of discharging these pollutants, and therefore of reducing the body burden of POPs (mainly breastfeeding (Fernandez-Rodriguez et al., 2015), milking (Luzardo et al., 2012; Pan et al., 2014), or laying eggs (Byer et al., 2015; Luzardo et al., 2013). Moreover, in a recent paper it has been shown that the blood levels of ΣOCPs and ΣPCBs of sick turtles was correlated with the degree of emaciation, indicating a mobilization of lipid soluble contaminants from their site of storage in adipose tissue into the bloodstream. After the hospitalization period in which the turtles received a balanced diet and also supplementation, some of these contaminants, especially PCBs, suffered a fat redistribution effect on their circulating levels, and therefore their bioavailability, were lower. This is, the POPs seem to be redistributed instead of eliminated (Camacho et al., 2014). However, novel factors have been proposed that may have influence on the reduction of plasma levels of POPs (and probably other contaminants). This is the case of parasitism and parasitic diseases. Since some nematodes have been reported to be capable of eliminating certain POPs (such as PCBs) (Schafer et al., 2009), some authors have studied the relation of the presence of parasitic nematodes and the levels of certain contaminants in humans (Henriquez-Hernandez et al., 2015) and other species of vertebrates (Blanar et al., 2009; Brazova et al., 2015; Carreras-Aubets et al., 2012). In those studies, an inverse relationship for some of the studied chemicals has been found.

Dogs are frequently affected by parasitism and therefore might represent a good model to study the abovementioned relationship with contaminants. Many types of parasites can be found in the domestic dog, and parasitic nematodes are among the most prevalent (i.e. gastro-intestinal parasites and dirofilaria heartworms).

Gastrointestinal nematodes are usually spread in feces or during pregnancy or nursing, and cause a serious infection in dogs and puppies (where they can cause fatal illness). These parasites compete for the food of its host and may cause diarrhea and other symptoms. As food is the main source of chemical pollutants this competence would limit the bioavailability of these pollutants for the host. Virtually 100% of dogs (and cats), from well-cared pet dogs to stray animals, have been in contact with parasitic nematodes (ascarids and ancylostomatids) or, at least, are at risk of disease (Traversa, 2012).

On the other hand, the cardiopulmonary disease caused by *Dirofilaria immitis* (heartworm disease) is a zoonotic disease affecting dogs and cats living in temperate and tropical areas throughout the world (Genchi et al., 2005), which is transmitted by different species of culicid mosquitoes (*Culex* spp., *Aedes* spp., and *Anopheles* spp., among others) (Cancrini and Gabrielli, 2007). It is caused by foot-long worms that live in the pulmonary arteries and heart of affected pets, causing severe lung disease, heart failure and damage to other organs in the body. Heartworm disease affects dogs, cats and ferrets, but adult heartworms also live in other mammal species, including wolves, coyotes, foxes, sea lions and—in rare instances—humans (Simon et al., 2012).

The Canary Islands, where this research was done, is a Spanish region, which belongs to the so-called outermost regions of the European Union due to their geographical position outside and far away the European continent. This territory has semitropical climate, which is influenced by the Atlantic trade winds and their proximity to the Western Sahara coast. Besides to the worldwide high prevalence of gastrointestinal parasites, heartworm disease caused by *Dirofilaria immitis* is endemic in these islands, with prevalence in dogs of up to 22.5% (Carretón et al., 2012; Montoya-Alonso et al., 2016).

The aim of this study was to analyze the relationship between nematode parasitism and the circulating levels of persistent and semipersistent organic pollutants of their hosts. For this purpose, we used as experimental model a total of three groups of dogs: two groups of prospectively recruited dogs, from newly diagnosed cases in the

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