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The family Didelphidae as a host of zoonotic pathogens
La familia Didelphidae como hospedero de patógenos zoonóticos

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The family Didelphidae has often been associated with transmission cycles of zoonotic diseases, such as Leishmaniasis and Chagas disease. In this work, we review the scientific literature published from 1994 to 2024 on studies of the family Didelphidae and its pathogens. Of the 5 terrestrial genera of the family Didelphidae analyzed, 86 % reported *Didelphis* as a host of various pathogens. In this genus, a larger number of pathogen groups have been reported, including bacteria, viruses, nematodes, fungi, and helminths, as well as protozoa that cause Chagas and Leishmaniasis diseases. *Didelphis albiventris* and *D. virginiana* are the species with the highest number of pathogen species documented to date (12 and 9, respectively). This information highlights the importance of understanding the role of the family Didelphidae in zoonotic cycles, considering that several species of the family have adapted to anthropized environments.

Key words: *Didelphis*; marsupials; opossums; synanthropic; zoonoses.

La familia Didelphidae ha sido frecuentemente asociada a ciclos de transmisión de enfermedades zoonóticas, por ejemplo, Leishmaniasis y Chagas. En este trabajo se realizó una revisión de la literatura científica publicada de 1994 a 2024 sobre estudios realizados en la familia Didelphidae y sus patógenos. Los resultados mostraron que, de los 5 géneros terrestres analizados de la familia Didelphidae, el 86 % reportaron a *Didelphis* como hospedero de diversos patógenos. En este género se han reportado mayor número de grupos, incluyendo la presencia de bacterias, virus, nematodos, hongos y helmintos, además de los protozoarios que provocan las enfermedades de Chagas y Leishmaniasis. *Didelphis albiventris* y *D. virginiana* son las especies en las que más patógenos se han documentado hasta el momento (12 y 9, respectivamente). Esta información destaca la importancia de comprender el papel de la familia Didelphidae en los ciclos zoonóticos, considerando que varias especies de la familia se han adaptado a los ambientes antropizados.

Palabras clave: *Didelphis*; marsupiales; sinantrópico; zarigüeyas; zoonosis.

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Zoonotic diseases (ZDs) are caused by pathogens such as viruses, bacteria, protozoa, helminths, or fungi found initially in wild species and that reach human populations through their interaction with them (Plowright *et al.* 2017; Ellwanger and Chies 2021). Increased exposure to these pathogens is driven by climate change, pollution, land-use changes, and human incursions into wild systems during food gathering, hunting, or logging (Rahman *et al.* 2020; Morand and Lajaunie 2021; Choo *et al.* 2023; Tumelty *et al.* 2023).

The family Didelphidae comprises about 95 species of marsupials distributed in the Americas (Gardner 2019) and is recognized for including species that host various zoonotic parasites (Jansen *et al.* 2010; Bezerra-Santos *et al.* 2021; Bitencourt and Bezerra 2022). This is relevant because zoonotic diseases are expanding their distribution range (Kilpatrick and Randolph 2012; Han *et al.* 2016), and several didelphid species can establish populations in rural, semi-urban, and urban areas (Costa-Neto *et al.* 2019; Simioni *et al.* 2022). This makes didelphids one of the main hosts in the life cycles of pathogens that cause zoonotic diseases (Ávila-Jiménez *et al.* 2024).

The genus *Didelphis* has attracted considerable interest in the scientific community because pathogens that affect human populations have been documented in this genus; for example, the protozoan *Trypanosoma cruzi,* which transmits Chagas disease (Robertson 1929). This work aims to review the scientific literature on the family Didelphidae as a host of pathogens that cause zoonotic diseases.

A literature review was carried out using the Scopus and Web of Science search engines. The search included articles published in the past 30 years (1994–2024) because molecular techniques have improved since the 1990s, making it possible to document the presence of pathogens in mammals accurately. Although protozoa have been documented in the Didelphidae family since the early 20th century, such as *Trypanosoma* or *Leishmania*, defining 1994 as the lower limit of the search does not exclude the documentation of these or other parasites that were already diagnosed previously through direct observation in blood or using immunological tests. The search included the following words: zoonotic, disease, emerging (and their equivalent words in Spanish) with 5 of the main terrestrial genera of the family Didel-

phidae: *Didelphis*, *Caluromys*, *Philander*, *Chironectes*, *Lutreolina*, and the arboreal genus *Marmosa*. These genera were selected because they have been documented to include synanthropic species. From each study found, the locality where the work was conducted was extracted to determine the region where most of the research is being performed on the subject. The results were captured on a map of the Americas in QGIS version 3.22 (QGIS 2021). In addition, a cloud of words that appeared most frequently in the studies was constructed. This analysis was limited to the 50 most frequent words to make this representation as concise as possible. The analyses were carried out in RStudio (R Core Team 2022), with the support of the bibliometrix library (Aria and Cuccurullo 2017) and wordcloud2 (Lang and Chien 2018).

The literature search showed that 73 studies have been carried out on pathogens in the family Didelphidae between 1994 and 2024 (Table 1). The countries where most research has been carried out are Brazil (43 % of studies), the USA (30 %), and México (11 %), while Panamá and Venezuela are the countries with the lowest scientific production, with 3 and 2 studies, respectively (Figure 1). In general, there is an increasing trend in the number of publications per year, with 2020, 2022, and 2023 standing out as the years with the highest production (Figure 2a). In México, the Universidad Autónoma de Yucatán is the academic institution with the highest number of publications on the subject (Figure 2b).

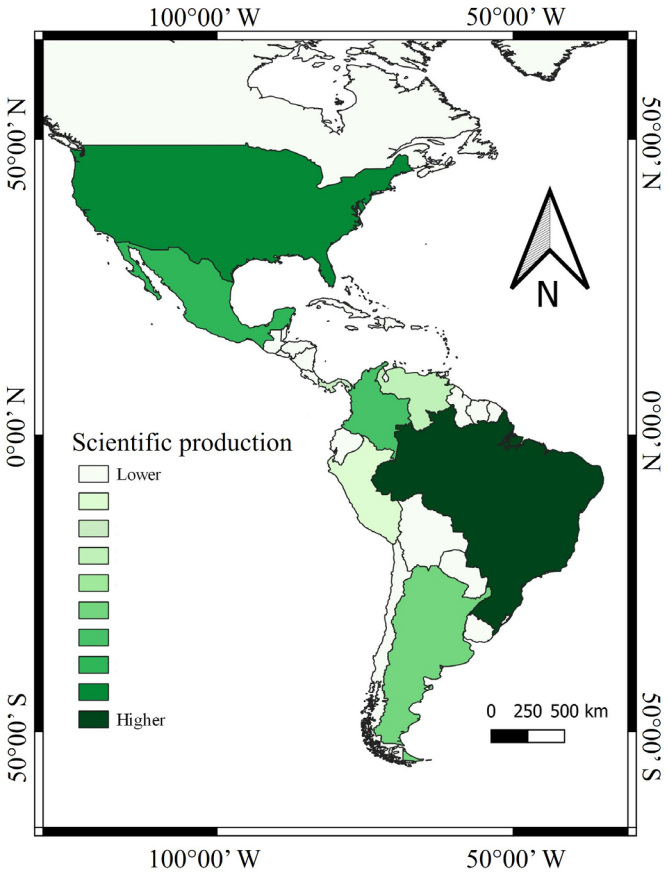

Figure 1. Geographic distribution of the annual production of scientific articles on the family Didelphidae and its pathogens in the Americas.

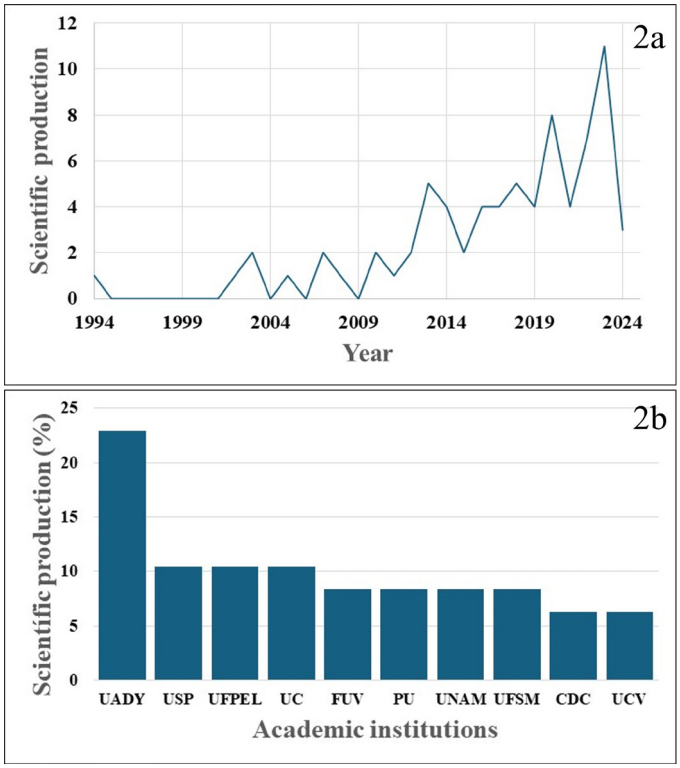

Figure 2. Annual production, 2a) and main academic institutions, 2b) that have conducted scientific research on the family Didelphidae and its pathogens in the Americas. UADY = Universidad Autónoma de Yucatán; USP = University of São Paulo; UFPEL = Federal University of Pelotas; UC = University of California; FUV = Federal University of Vicosa; PU = Purdue University; UNAM = Universidad Nacional Autónoma de México; UFSM = Federal University of Santa Maria; CDC = Center for Disease Control and Prevention; UCV = Universidad Central de Venezuela.

According to the cloud, the words most frequently reported are *Trypanosoma cruzi*, zoonosis, opossum, Chagas disease, and *Didelphis virginiana* (Figure 3). A reference to public health also appears in this word cloud, although less frequently. In total, 27 pathogens carried by the family Didelphidae have been documented. Of these, 33 % correspond to helminths, 33.3 % to bacteria, 18 % to protozoa, 7.4 % to ectoparasites, 3.7 % to fungi, and 3.7 % to viruses (Table 1). Ninety-six percent of pathogens have been identified at the species level and 4 % at the genus level. Pathogens have been documented in *Didelphis albiventris, D. aurita, D. marsupialis, D. virginiana, Marmosa mexicana, Monodelphis domestica, Lutreolina crassicaudata, Philander frenatus*, and *P. oposum*. Of all the species with pathogen records, *D. albiventris* and *D. virginiana* have the highest number of pathogen species recorded (12 and 9 species, respectively), while only 1 pathogen species has been recorded in *M. mexicana, M. domestica, L. crassicaudata, P. frenatus,* and *P. oposum* (Table 1). *Didelphis albiventris* and *D. virginiana* are also the species with the highest diversity of pathogen groups, including nematodes, protozoa, bacteria, helminths, and fungi (Table 1).

Didelphids have been studied historically as potential hosts of zoonotic agents (Bezerra-Santos *et al.* 2021). The countries with the highest scientific production on the subject in the past 30 years are Brazil, the United States, and México, while scientific production for Central American

Table 1. Pathogens documented in species of the family Didelphidae.

Species	Pathogen agent	Taxonomic group	References
Didelphis albiventris	*Angiostrongylus cantonensis*	Nematode	Vielmo *et al.* (2022)
	Babesia sp.	Protozoon	Perles *et al.* (2023)
	Ctenocephalides felis	Siphonapter	Lignon *et al.* (2023)
	Ehrlichia canis	Bacterium	Bertão-Santos *et al.* (2023)
	Helminths	Helminth	Vielmo *et al.* (2022)
	Helicobacter sp.	Bacterium	Cardia-Caserta *et al.* (2023)
	Leishmania sp.	Protozoon	Lima *et al.* (2013); Cutolo *et al.* (2014); Ratzlaff *et al.* (2023)
	Leptospira borgpetersenii	Bacterium	Jorge *et al.* (2012)
	Paracoccidioides brasiliensis	Fungus	Richini-Pereira *et al.* (2008)
	Toxoplasma gondii	Protozoon	Richini-Pereira *et al.* (2016)
	Trichinella spiralis	Nematode	Castaño-Zubieta *et al.* (2014)
	Trypanosoma cruzi	Protozoon	Tenório *et al.* (2014); Zitelli *et al.* (2021)
Didelphis aurita	*Hepatovirus A*	Virus	Carneiro *et al.* (2018)
	Leishmania sp.	Protozoon	Ratzlaff *et al.* (2023)
	Nematodes and trematodes	Nematode, Platyhelminth	Teodoro *et al.* (2019)
	Intestinal parasites	Platyhelminth, Nematode	Teodoro *et al.* (2019); Bezerra-Santos *et al.* (2020a); Bezerra-Santos *et al.* (2020c); Alonso *et al.* (2024)
	Trichinella sp.	Nematode	Jurkevicz *et al.* (2022)
Didelphis marsupialis	*Anaplasma phagocytophilum*	Bacterium	Rojero-Vázquez *et al.* (2017)
	Babesia sp.	Protozoon	Calchi *et al.* (2023)
	Bartonella sp.	Bacterium	Calchi *et al.* (2023); Rojas-Jaimes and Valle-Mendoza (2023)
	Borrelia puertoricensis	Bacterium	López *et al.* (2023)
	Leishmania sp.	Protozoon	Schallig *et al.* (2007); Ávila-Jiménez *et al.* (2024)
	Leptospira sp.	Bacterium	Haro *et al.* (2021)
	Toxoplasma gondii	Protozoon	Bezerra-Santos *et al.* (2020b)
	Trypanosoma cruzi	Protozoon	Travi *et al.* (1994); Ramírez *et al.* (2013); Roque *et al.* (2013); Cantillo-Barraza *et al.* (2015); de Buhr *et al.* (2018); Bilheiro *et al.* (2022); Pineda *et al.* (2022); Tineo-González *et al.* (2023)
Didelphis virginiana	*Anaplasma phagocytophilum*	Bacterium	Rojero-Vázquez *et al.* (2017)
	Ectoparasites	Siphonapters, Mites	Castellaw *et al.* (2011); Canto-Osorio (2020); Glebskiy *et al.* (2022); Ferreira *et al.* (2023)
	Leptospira sp.	Bacterium	Richardson and Gauthier (2003); Grimm *et al.* (2020); Helman *et al.* (2023)
	Rickettsia sp.	Bacterium	Dzul-Rosado *et al.* (2021); Blanton *et al.* (2022)
	Salmonella enterica	Bacterium	Ruiz-Piña *et al.* (2002); Haro *et al.* (2021)
	Toxoplasma gondii	Protozoon	Suzán and Ceballos (2005); Houk *et al.* (2010); Horta *et al.* (2016); Torres-Castro *et al.* (2016)
	Trypanosoma cruzi	Protozoon	Hodo and Hamer (2017); Vandermark *et al.* (2018); Kramm *et al.* (2019); Zecca *et al.* (2020)
	Intestinal parasites	Platyhelminths, Nematodes	Aragón-Pech *et al.* (2018); Ruiz-Piña *et al.* (2002)
	Paragonimus mexicanus	Platyhelminth	García-Márquez *et al.* (2010)
Marmosa mexicana	*Trypanosoma cruzi*	Protozoon	Haro *et al.* (2021)
Monodelphis domestica	*Babesia* sp.	Bacterium	Calchi *et al.* (2023)
Lutreolina crassicaudata	*Strongyloides* sp.	Nematode	Cardia *et al.* (2016)
	Toxoplasma gondii	Protozoon	Richini-Pereira *et al.* (2016)
Philander frenatus	*Toxoplasma gondii*	Protozoon	Zitelli *et al.* (2021)
Philander opossum	*Trypanosoma cruzi*	Protozoon	Roque *et al.* (2013); Haro *et al.* (2021)

countries such as Nicaragua, Belize, and Honduras were not documented in the search carried out. This may be due to the difficulties in obtaining funds for research in the latter countries (Ríos and Herrero 2005). However, these findings could be biased since the search used only 2 search engines. Future studies should contemplate identifying the regions with the highest and lowest scientific production using other massive search engines, such as Google Scholar, during the documentation phase.

On the other hand, Didelphidae is one of the most abundant mammal families in the Americas, with a distribution that ranges from South America to the United States (Ceballos 2014). This wide distribution contributes to a greater dispersal of zoonotic diseases (Bezerra-Santos *et al.* 2021; Choo *et al.* 2023). In the family, *Didelphis* is the genus in which the relationship with its pathogens has been studied most intensely (Table 1). This highlights some information gaps regarding other genera of didelphids genera with a broad distribution, such as *Philander.* The genus *Didelphis* has been recognized as an important host group of protozoa, bacteria, viruses, and helminths (Bezzerra-Santos *et al.* 2021). Its role as host is particularly relevant as it is synanthropic and constantly interacts with domestic animals and human populations (Guzman-Marin *et al.* 2016; Guimarães

et al. 2022; Rojas-Sánchez *et al.* 2023). This underlines the importance of implementing a detailed management program in anthropized environments to avoid threatening their populations while reducing their potential impact on public health, given their role as hosts of zoonotic pathogens (Zepeda-Espinosa *et al.* 2019; Cáceres *et al.* 2020). The genus *Didelphis* is a host of the etiological agents of Chagas disease and Leishmaniasis, classified as diseases of poverty frequently associated with areas lacking urban infrastructure (Ghorbani and Farhoudi 2017). Likewise, permanent efforts are being made to contain intestinal diseases caused by helminths, as they can cause anemia and death, mainly in children, in several regions of the Americas (Lustigman *et al.* 2012). It is worth highlighting that zoonoses have impacts not only at the health level but also in the socioeconomic context and human development in general (Narrod *et al.* 2012).

Although the conservation status of most species in the Didelphidae family is Least Concern according to the International Union for Conservation of Nature (IUCN 2024), further research is needed to better understand the ecological dynamics of this group and its pathogens, particularly its association with the human population (de Oliveira-Carneiro *et al.* 2019; Bezerra-Santos *et al.* 2021; Ávila-Jiménez *et al.* 2024). Additionally, screening tests should be performed on rescued or relocated animals to start monitoring this family in cities and clarify its importance in the transmission cycles of zoonotic diseases.

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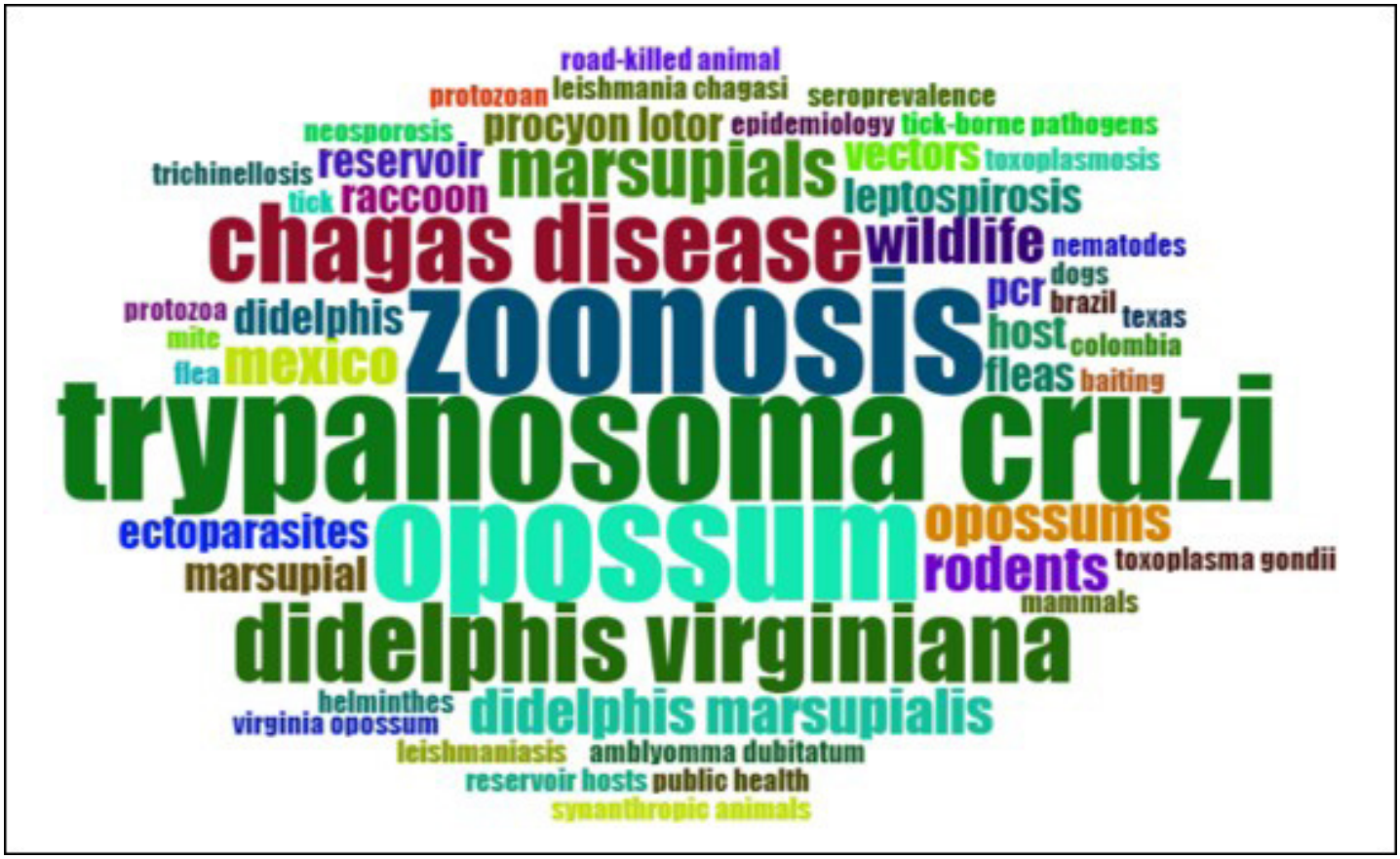

Figure 3. Cloud of the words most frequently cited (largest) and least frequently cited (smallest) in the scientific publications analyzed.

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