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# Pesticide Exposure Risks to Chiropteran Species and the Impacts on Emerging Zoonotic Diseases

*Sarah Hooper and Sybill Amelon*

## Abstract

Neonicotinoids have been in the spotlight in the pollinator community as they persist in the soil, have high water solubility, and have been associated with negative health implications on insect pollinators. The risk of new novel pesticides, including neonicotinoids, to bats are largely unknown. Bats have unique physiology as they are the only mammals capable of true and sustained flight, and have physiological adaptations including echolocation and torpor which under current protocols for acute and chronic toxicity studies in birds and terrestrial animals are not assessed. Due to these characteristics, some have argued that bats may serve as important bioindicators for ecosystem health and pesticide use. This chapter will focus on pesticides, and discuss the increased risk of exposure, morbidity, and mortality of bats species due to their unique physiology and natural life history. Special emphasis will be on potential increased risk of zoonotic disease transmission in bats exposed to emerging contaminants that suppress their immune system or cause increased biological stress.

**Keywords:** bats, chiroptera, contaminants, ecotoxicology, insectivorous bats, frugivorous bats, mammals, pesticides, pesticide exposure, toxicology, viral diseases of bats, zoonotic diseases

## 1. Introduction

Pesticides refer to a broad range of chemicals designed to control target organisms such as insects (insecticides), plants (herbicides), and other organisms (e.g. fungicides and algicides). While judicious use of pesticides can be beneficial, there is always a risk that non-target organisms will be affected. For some compounds, the widespread negative side-effects on non-target organisms outweigh the benefits of use. The classic examples of such compounds are DDT and other organochlorides. In the early 1960s, Rachel Carson published the book *Silent Spring*, which captured the public's attention on the widespread detrimental effects that organochlorides caused in the avian population such as embryotoxicity, eggshell thinning, and severe population declines [1, 2]. As a result of her work, DDT and other organochlorides were banned in the US beginning in the early 1970s with other developed countries following suit [1, 3].

Since the banning of organochlorides, new compounds have arisen to take their place such as neonicotinoids—the most widely used insecticides in the world with over 25% market share [4, 5]. Neonicotinoids have been in the spotlight in the pollinator community as they persist in the soil, have high water solubility, and have been associated with negative health implications on pollinators [5, 6]. The risk of these newer pesticides, including neonicotinoids, to bats are largely unknown, because required pesticide risk assessment schemes for birds and mammals have been deemed inadequate to assess the risk to bats [7].

This chapter will explore the how the natural life history of bats and their physiologic adaptations (e.g. echolocation, torpor and true, sustained flight [8]) increases their risk of oral, dermal, and inhalation exposure to pesticides. Understanding how Chiropteran ecology and physiology contribute to an increased risk of pesticide exposure is critical for several reasons. 1) Bats suffering from anthropogenic stressors such as environmental pollutants are at increased risk of immunosuppression—meaning an increase in the production and shedding of viruses [9, 10]. 2) Bats serve as important bioindicators for pesticide use and eco-system health [11]—meaning the utilization of bats as bioindicators may be key to predicting emerging and re-emerging zoonotic diseases as recent zoonotic disease outbreaks have been closely interlinked to ecosystem health [12].

## 2. Worldwide pesticide use and registration of pesticides

Worldwide, 3.5 million tons of pesticides were applied to farmland in 2020 [13, 14]. This is likely an underestimate, as the data was obtained from a selection of different databases—some of which are limited in their scope. For instance, one database used, the United States Geological Service (USGS) Pesticide National Synthesis Project, is a database that tracks agricultural pesticide use in the United States. In 2015, this database discontinued recording pesticides used in seed treatment applications [15]. The primary use of neonicotinoids are seed treatments [5], therefore neonicotinoids use is greatly underestimated in the United States, the second largest consumer of pesticides per the Food and Agriculture Organization of the United Nations (FAO) [16]. Additionally, many databases exclude non-agricultural pesticide products used by consumers (i.e. for home use and lawn/garden use), therefore true worldwide pesticide use is difficult to estimate.

Before a pesticide can be sold to consumers, each country undertakes a review process to validate the chemical is safe for nontarget species and efficacious. Typically, this process is allocated to governmental agencies (e.g., the Environmental Protection Agency (EPA) in the United States and the Europe Food Safety Authority (EFSA) in the European Union), or a government appointed board (e.g. The Pesticides and Toxic Chemicals Control Board in Saint Kitts and Nevis). While toxicology and ecotoxicological assessments vary by each country, the minimum requirements for most ecotoxicological studies must "(1) quantify the magnitude of acute mortality caused by the application, (2) determine the existence and extent of reproductive impairment in nontarget species from the application, and (3) determine the extent to which survival is influenced" [7, 17].

To fulfill these objectives, the study designs classically focus on obtaining the $LD_{50}$, the lethal dose for 50% of a group of experimental animals; $LC_{50}$, the lethal concentration in air or water that kills 50% of the experimental animals during a specific time period; and no-observed-effect-level (NOEL), the highest concentration of the substance at which no adverse effects are observed in the experimental animals. The experimental animals used to obtain the ecotoxicological data must be a species that is similar to those found in the desired application area. Typically

rats (e.g. *Rattus norvegicus*) serve as the representative species for terrestrial mammals, the northern bobwhite (*Colinus virginianus*) or another quail species for an upland game bird, the mallard duck (*Anas platyrhynchos*) for waterfowl, and the house sparrow (*Passer domesticus*) or zebra finch (*Taeniopygia guttata*) for passerines [7, 17, 18]. Bats are classified as a terrestrial mammal for ecotoxicology testing purposes, and therefore are represented by rats, an r-selected species [19] without the physiological adaptations such as highly vascularized wings or echolocation.

## 3. Chiropteran life history, ecology, and physiological adaptations

### 3.1 Overview of bat diversity and ecological services

The order Chiroptera contains more than 1400 species—equating to over 1 in every 5 mammals is a bat [20]. Chiropteran species were previously divided into two suborders, Megachiroptera and Microchiroptera based upon morphological and behavior data. The suborder Megachiroptera consists of approximately 166 species, all belonging to the family Pteropodidae, whose diet consist of fruit, nectar, or pollen [20]. Seventeen other families compose the suborder Microchiroptera, the majority of which consume insects [20]. These suborders are still routinely used by some scientists and biologists. However, new molecular biology findings combined with morphological and behavior data have led researchers to propose two new suborders of bats, Yinpterochiroptera and Yangochiroptera, which do not coincide with the previous subordinal classification [21].

Chiroptera are critical to ecosystem health as they provide critical ecosystem services such as arthropod suppression, seed dispersal, and pollination on every continent except Antarctica [20, 22]. However, some ecosystems are at risk of degradation due to more than a quarter of the world's bat species facing the threat of extinction [23]. Additionally, over half of the species are facing population declines or have unknown population statuses further jeopardizing ecosystem health [23, 24].

Bat population declines are frequently attributed to habitat loss, White-nose Syndrome, wind energy, and more recently climate change [23, 25]. Pesticide exposure and pollutants are less recognized for causing population declines due to the lack of Chiropteran specific ecotoxicological studies. The few studies that are published directly link population declines to dermal contact and oral ingestion of pesticides [26–30].

### 3.2 Foraging ecology and diet

Nearly all bat species are nocturnal, with dusk and a few hours before dawn being their most active foraging times. Foraging strategies are diverse and are dependent upon the diet and the individual species morphological characteristics. The feeding behavior of bats who consume primarily fruit, frugivorous bats, are based upon their body size, dentition, and skull/jaw morphology [31]. Nectivorous bats, those whose diet consumes of primarily nectar, select flowers based upon their digestive capacity, lingual (tongue) morphology, and possibly metabolic rate [32, 33]. Relatively little is known about fishing bats, or piscivorous bats, who consume fish prey. It has been suggested that skull morphology, body size, wing morphology, and acoustic properties dictate piscivorous bats dietary niche partitioning [34, 35]. There is a lack of information on dietary morphological adaptations for the 3 sanguinivorous bat species who are obligate blood feeders.

Most is known about insectivorous bat species, those who consume insects, because most Chiropteran species fall within this category. Wing morphology, body

size, and echolocation strategies influence which insect species are preyed upon [36]. For example, the aerial hawking species botta's serotine (*Eptesicus bottae*) have an average body mass of 8.9 ± 1.3 grams (adult males and nonreproductive females), broad wings with an average wingspan of 27.3 ± 1.8 mm and an average wing area of 12.6 ± 6.7 cm$^2$ [37, 38]. *E. bottae* fly around 5.7 meters per second and their echolocation calls allow them to detect large prey up to 21 meters away with an echo delay of one wing beat [38]. With these morphological characteristics helping to dictate their diet, DNA metabarcoding studies have revealed they consume primarily insects from the orders Auchenorrhyncha, Coleoptera, Lepidoptera, Heteroptera, and Hymenoptera [37].

By consuming agricultural pests as part of their diet, insectivorous bats are highly valued by farmers. Presently there is no worldwide estimate of the economic value of the ecological services provided by bats; however, researchers in the US have estimated that insectivorous bats provide roughly $22.9 billion dollars per year in natural pest control services to US crops [39]. Due to the high foraging activity around agricultural areas and active consumption of pests that are targeted by insecticides, nearly all of the Chiropteran ecotoxicology studies focus on insectivorous species [30].

The majority of bat species in agricultural areas actively forage over fields at night with an increase in activity at dusk or dawn due to the increased activity of crepuscular insects [40]. Due to the recognition of pesticides affecting bee health, current guidelines for pesticide applicators are to apply pesticides at dusk, dawn and late at night while pollinator activity is low to non-existent in order to avoid pollinator mortality [41].

The application of pesticides at the height of bat activity, directly increase the risk of inhalation exposure of the droplets and vapors created during pesticide applications [7]. By flying through the spray clouds when foraging over agricultural fields or the vapors along the field margins, there is an increased risk of dermal exposure as well as an increased risk of oral exposure through the consumption of prey coated during the application process. Additionally, the lights used during dusk or night application may increase bat activity of non-light aversive species due to the attraction of insects to the lights [42].

It is plausible that frugivorous and nectivorous bat species also experience a similar increase in risk to pesticide exposure especially in intensively managed orchards. Because there is only a single study documenting organochlorine pesticide in a nectivorous bat species, the lesser long-nosed bat (*Leptonycteris sanborni*), [43] and no studies, other than manipulative experimental exposure studies, on frugivorous bats [30] it is difficult to assess their exposure risk. Whereas there are numerous records of organochlorine, organophosphate, and other pesticide residues found in deceased insectivorous species indicating that pesticide exposure is occurring and can be linked to mortality [30].

### 3.3 Roosting ecology

Due to recent estimates of the economic value insectivorous bats (e.g. see [39]), the agricultural industry and general public have begun recognizing the valuable natural pest control services provided by insectivorous bats. This recognition has resulted in some farmers attempting to attract bats by placing bat houses near fields or leaving untouched treelines with adequate roosting structures such as tree cavities or flaking bark [7, 44, 45].

Depending upon the species, some bats may also use farmland buildings such as barns or stables, or even roost on farm homes made of brick that contain shallow cracks [46] or under shutters based upon the authors' personal observations. With

roost locations located within or adjacent to crops where pesticides are applied, bats within these roosts are at increased risk of inhalation and dermal exposure from pesticide drift [47] especially those roosting on exterior walls of buildings.

While bats are within their day roosts, they exhibit a variety of activities (e.g. parturition, nursing, torpor, and grooming) depending upon the sex and season. All these activities increase the risk of exposure. For instance, grooming could result in the increased risk of oral exposure if the roost is contaminated through pesticide drift or if bats where in direct contact with the pesticides during the application process. These roosts tend to be continuously habited for weeks to months and many are reutilized each year [48] leading to the potential for continuous long-term exposure if the roosts are contaminated. Bats also utilize night roosts in order to conserve energy, avoid predators, digest consumed food, to exchange information and for social interactions [49]. These night roosts have similar increased risks if they are in areas exposed to pesticide drift.

Some species select caves to roost for hibernation or may utilize them throughout the year. By crawling on cave walls and drinking from underground water sources, they are at risk of dermal and oral exposure because cave sediments, groundwater, and drip water samples in surveyed areas have all been reported to contain a variety of organochlorines and other pesticide metabolites [50–53].

## 3.4 Drinking

Bats are unable to obtain enough water through their diet, and so must rely upon drinking to meet daily needs. In addition to drinking potentially contaminated karst water, bats also drink from tailing ponds which can be high in cyanide, heavy metals, and occasionally pesticides depending upon the location of the mining operation [53]. Within the agricultural setting, bats have been observed to drink from irrigation canals, small ponds, and water troughs with the latter two often containing pesticides from overland flow [53] and thereby increasing the risk of oral exposure.

## 3.5 Reproduction

It is generally believed that bats reproduce once per year with most species giving birth to 1 pup or occasionally twins (e.g. big brown bat, *Eptesicus fuscus*) [54]. The exception to this is bats belonging to the genus Lasiurus who can give birth to up to four pups. For more detailed information on the reproductive biology of bats see [54].

Actual pesticide exposure risks to pups is difficult to assess. Two older studies assessing banned organochlorine pesticides such as DDE documented maternal transfer and resulted in offspring mortality [55, 56]. There is only a single study assessing reproductive effects for a commercially available fungicide, tebuconazole. This study coated papaya with the manufacturer's recommended application concentration of tebuconazole. When great fruit-eating bats (*Artibeus lituratus*) consumed the fruit, testicular and epididymal histomorphological changes were observed, suggesting that the fungicide tebuconazole may impact reproductive capacities in males [57]. Unfortunately, reproductive females were not evaluated.

Despite the lack of studies on contaminants in actively reproducing female bats and/or their offspring, it is probable that pups can be exposed in utero based upon numerous studies in humans and other mammals documenting placental transfer of commonly sold pesticides including neonicotinoids [58–60]. Furthermore, because pesticides and their metabolites are often detected in mammalian milk [61–63], pups are likely exposed to pesticides for approximately 3–4 weeks after birth while nursing.

## 4. Chiropteran physiology

### 4.1 Skeletal morphology and flight

Unique skeletal system and integumentary system adaptations combined make bats the only mammals capable of true, sustained flight. Chiropteran species have a strong axial skeleton with non-pneumatized, marrow-filled long bones and elongated metacarpal bones and phalanges [64]. A bilayered 1–2 cell thick epidermis (e.g. <s10 μm in the epauletted fruit bat, *Epomophorus wahlbergi*) separated by a non-distinct dermis or hypodermis form the extremely thin wing membrane. Within the non-distinct dermis there are highly vascularized connective tissues [65]. Collagen and elastic fibers within the connective tissues serve as "fingerprints" that can be used to identify individuals [66] and are responsible for providing the mechanical strength needed for flight [65, 66].

The wings may serve additional purposes other than flight. The thin, and highly vascularized wing tissue has been suggested to allow diffusion of oxygen and carbon dioxide between the environment and the vasculature, thereby contributing to a bat's total gas exchange [65]. Wing membranes are essential to thermoregulation [67] and also water exchange [8, 65]. These adaptations allowing water and gas exchange through the wing membrane could also increase the risk of dermal absorption of pesticides—especially considering the wing membrane of bats accounts for up to 85% of a bat's total body surface [65].

When bats fly, it is energetically expensive, especially since bats flap continuously rather than glide [36]. To meet this energy demand, food intake is high. When foraging each night, frugivores consume up to 2.5 times their body weight in fruit [68], insectivores consume up to 1.3 times their body weight in insects [7], and some nectivorous species consume nectar from 80 to 100 flowers each night [69]. With high food consumption, there is an increased risk of oral exposure to all bat species.

### 4.2 Torpor

Torpor or heterothermic responses are "facultative, reversible decreases in metabolic rate and body temperature in response to environmental cues" [70]. All species of bats may select to employ daily torpor, the lowering of their body temperature set point, respiratory rate, and metabolic rate for a single circadian cycle or a portion of a circadian cycle [49, 71] to help offset the high metabolic and thermoregulatory costs [71]. Hibernating species may engage in multi-day torpor bouts which can save them up to 99% of their daily energy requirements [72]—allowing them to survive winter when food availability is reduced [71].

Throughout hibernation (multi-day torpor), bats use white adipose tissue as their primary fuel source [73]. When arousing from torpor, especially multi-day torpor bouts, they may engage in passive rewarming which can reduce arousal costs by 50% or more [74]. Even with passive rewarming, torpor arousal is still energetically demanding and bats must mobilize a portion of their brown adipose tissue to generate heat [73].

During the fall, when hibernating bats are developing large fat stores, the risk of oral exposure to pesticides increases as they consume a greater amount of prey. Concurrently, lipophilic (fat soluble) pesticide residues are stored within the adipose tissue (see Table 1 in [30] for studies which measured pesticides in Chiropteran adipose tissue) as a large portion of pesticides, especially within the insecticide class, are lipophilic [75]. Hibernating bats may be at risk of continuous lipophilic pesticide exposure as bats mobilize their white adipose tissue. During arousal the rapid mobilization of brown adipose tissue may cause an increased risk of a sudden large dose of lipophilic pesticides to be released.

### 4.3 Echolocation

It is a common myth that bats are blind, as in fact they have color vision and may be sensitive to UV light [76]. The majority of species within the Pteropodidae family (Old World Fruit bats such as flying foxes), use their acute vision to perceive their environment and forage for food rather than rely upon echolocation. Whereas bats in the other families are believed to use echolocation as the primary way to forage and navigate through their environments [77]. When these species echolocate, they produce high frequency sounds or tongue clicks [78]. Their auditory system processes the echoes and enables the 3D perception of the object and the spatial location of the object. For more detailed information on the adaptive sonar behavior of bats and echolocation auditory mechanisms see [77, 79].

Echolocation has been suggested to contribute to the global success of a wide range of bat species [78]. While echolocation may not increase a bats risk to pesticide exposure, it can be negatively affected by sublethal concentrations of pesticides [80].

### 4.4 Other considerations for reference species

At sublethal doses, the neonicotinoid imidacloprid suppresses the expression of genes related to echolocation (e.g. FOXP2) [80], interferes with the spatial memory [81], and leads to inflammation and mitochondria dysfunction-related apoptosis [80]. This type of ecotoxicological data suggests that using mammals who do not have echolocation capabilities may need to be reassessed as a reference species for bats.

Other considerations for reference species selection should consider that other mammals do not have the physiological adaptations described above. Additionally, rats, the most commonly used reference species, have a relatively short lifespan of 3 years or less in a laboratory or pet setting, with the average lifespan of a wild rat being less than 1 year [82]. Free-ranging bats live much longer with some species living for at least 32 years based upon recapturing banded individuals [83]. The longer lifespans of bats put them at increased risk of bioaccumulation of pesticides and other contaminants such as heavy metals.

## 5. Zoonotic disease risks

It is estimated that over 60% of newly emerging diseases are zoonotic with approximately 3 out of every 4 diseases being the result of spillover from wildlife [84, 85]. Due to the ongoing worldwide pandemic COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), bats are often cited by the media and some scientists as the source of this zoonotic disease as well as other zoonotic viral diseases such as Ebola [86]. COVID-19 is an emerging infectious disease but at the time of this writing there is no evidence it is a zoonotic disease [87].

A zoonotic disease, or zoonosis, is defined by the World Health Organization as "any disease or infection that is naturally transmissible from vertebrate animals to humans [88]". While the origin of SARS-CoV-2 remains unknown [89], there is no evidence that bats serve as the reservoir of the virus. This is because a reservoir is "a population, species or community assemblage of different species in a given geographic area in which a microorganism naturally occurs and is indefinitely maintained" [86]. Since SARS-CoV-2 has not been detected in any bat species, they cannot serve as reservoirs of the virus [86]. The miscommunication seems to originate from the misunderstanding of a report of a newly identified coronavirus circulating within intermediate horseshoe bats (*Rhinolophus affinis*) which exhibits

96% similarity to SARS-CoV-2 virus [90]. This newly identified coronavirus is suggested to be the ancestral origin of the SARS-CoV-2 virus [90], but it is not the same virus that is causing the COVID-19 pandemic. For a complete review on effective communication regarding zoonotic diseases and the terminology commonly misunderstood and miscommunicated in relation to bats see [86].

While COVID-19 may not be a zoonotic virus, bats do serve as the reservoir for other zoonotic viruses such as rabies and Nipah virus [86]. When new zoonotic diseases arise, they are most often the result of a spillover event from bats or other wildlife reservoir species to humans or another mammalian host [10, 91].

Spillover events are complex processes and are rare [9]. When spillover events do occur, there must be a "perfect storm" or a situation where several factors need to be present for the spillover event to occur. Two of those factors, pathogen shedding and environmental conditions, are discussed below. For an extensively detailed description of all potential factors see Plowright et al. 2015 [92].

Before describing these factors, it must be noted that the immune system of bats is not well understood. The limited research conducted on Chiropteran immune systems verify there is much diversity among species (e.g. the interferon gene locus is contracted in the black flying fox (*Pteropus alecto*) whereas expanded in the Egyptian fruit bat (*Rousettus aegyptiacus*) [93–95]). While this diversity exists, their immune systems uniformly appear to allow chronic/latent viral infections where the host remains asymptomatic and viral shedding does not occur. This benign virus-host relationship is more commonly recognized as the Susceptible-Infectious-Latent-Infectious (SILI) hypothesis [10].

The SILI hypothesis suggests that when bats are stressed by physiological and/or environmental stressors, the virus(es) can reactivate due to a suppression of the host's immune system [10]. These viruses may remain nonpathogenic within bats, but the reactivation of the viruses results in viral shedding [10]. Viral shedding leads to an increased risk of spillover events as these viruses may cause severe disease in other mammals [86, 96].

Anthropogenic changes such as urbanization and high human population density are known physiological and environmental stressors to bats due to the loss, degradation and/or fragmentation of suitable habitats [97]. While these anthropogenic stressors are well studied, there are few experimental studies assessing if pesticides and other pollutants are sublethal stressors as most Chiropteran contaminant studies are observational.

Pesticides are classified as stressors in other mammalian species as they are known to cause oxidative stress, genotoxic effects, and suppress the immune system [98–101]. Two studies conducted in the fruit bat *A. lituratus* measured oxidative stress when exposed to fruit sprayed with the organochlorine insecticide endosulfan and the pyrethroid insecticide deltamethrin. The metabolism of the pesticides increased the generation of reactive oxygen species (ROS) including nitric oxide and hydrogen peroxide leading to liver morphological changes [102] and oxidative damage to both liver and the pectoral muscle [102, 103]. Since fruit bats are believed to be highly resistant to oxidative stress in part due to the high level of antioxidants in their diet [104], this finding is significant. Especially since it is well established that chronically increased oxidative stress leads to a variety of pathophysiological conditions [105] and directly alters the immune system [106]. It is unknown if increased oxidative stress leads to increased viral shedding, thereby increasing the risk of zoonotic disease and should be evaluated in future studies.

Oxidative damage has been shown to induce genotoxicity when humans have been exposed to some contaminants such as lead and toluene [107, 108]. Two commonly employed genotoxicity tests are the micronucleus test and the comet assay. The micronucleus test assesses chromosomal damage (see [109] for detailed review

of the technique) while the comet assay detects a wide array of DNA damage such as DNA strand breaks (single and double stranded) and incomplete excision repair (see [110] for detailed review of the technique).

Micronucleus tests conducted in the insectivorous bat species, Parnell's mustached bat (*Pteronotus mexicanus*), documented that *P. mexicanus* roosting in caves surrounded by agriculture and foraging over pesticide treated fields, had a higher number of micronuclei than bats roosting and foraging in areas where no more than 15% of the surrounding land-use was agriculture [111]. Another study assessing micronuclei and other nuclear abnormalities in insectivorous, frugivorous, and nectivorous bats discovered that nectivorous bats did not have any significant nuclear changes in agricultural or urban areas [112]. Frugivorous and insectivorous bats however did have significantly higher micronuclei in urban and agricultural areas with other nuclear changes such as binucleated cells being commonly observed in urban areas [112]. A third study assessing genotoxicity using the comet assay documented that banana bats, *Neoromicia nana*, foraging over South African waste water treatment plants containing pesticides and other pollutants had significantly higher DNA damage compared to bats foraging at reference sites within Umdoni Park [113]. All three studies are limited from the perspective that none measured actual pesticide concentrations in tissues or bodily fluids (e.g. urine). Although it cannot be solely concluded that the genotoxic effects were truly from pesticide exposure, research in other mammalian species documents a clear link between pesticide exposure and induced genotoxicity [99]. This fact identifies along with the three Chiropteran studies suggesting pesticide exposure can induce genotoxic changes, highlights a large research need for assessing if pesticides are genotoxic to bats and if it leads to viral shedding via immunosuppression mechanisms.

Although there are few studies measuring the ecotoxicological effects of pesticides on bat species, the available studies show that some species suffer oxidative damage, genotoxic changes, and mortality. This suggests that compounding anthropogenic stressors, including environments with heavy pesticide use, may cause environmental conditions to become favorable for a spill-over event to occur by causing physiological stress in insectivorous and frugivorous bats. This compounded physiological stress may result in viral reactivation and viral shedding by suppressing bats' unique immune system. Because bats sustain a high viral load and are phylogenetically close to humans, the risk of zoonotic disease transmission from spill-over events is greatest from bats compared to other species [114].

## 6. Conclusions

Ecotoxicological studies in wildlife species use rats as the reference species for terrestrial wildlife, including bats. With over 1400 bat species, and unique morphological characteristics such as highly vascularized wing membranes composing up to 85% of their body surface and unique physiology such as echolocation [20, 59], species lacking these characteristics (e.g. rats) may not be adequate when assessing effects of pesticide exposure.

Bats natural life history combined with these unique adaptations leads to the increased risk of pesticide exposure. Due to their high risk of exposure, bats can serve as important bioindicators for both pesticide use and ecosystem health [11]. Early detection of zoonotic diseases may be possible by monitoring ecosystem health through bioindicators such as bats [11, 12], because unhealthy ecosystems exert physiological and environmental stressors. These stressors, including pesticides, may lead to a spillover event where a wildlife species immune system becomes suppressed and pathogen shedding becomes possible [9, 10, 91, 92].

## Conflict of interest

The authors declare no conflict of interest.

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