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RESEARCH ARTICLE

UTILISING *DROSOPHILA MELANOGASTER* AS A MODEL ORGANISM IN ENVIRONMENTAL TOXICOLOGY RESEARCH

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ABSTRACT

Drosophila melanogaster has become an indispensable model organism in toxicology research due to its rapid life cycle, robust genetic toolkit, and significant genetic overlap with humans (≈75% of disease-related genes). *Drosophila melanogaster* serves as a valuable model for evaluating neurotoxicity, oxidative stress, and metabolic disturbances. This study employed a systematic methodology to identify relevant literature on *Drosophila melanogaster* in toxicity testing, regulatory frameworks, and environmental health. The selection process prioritized toxicological research, regulatory relevance, and recent advancements from 2022 to 2025. *Drosophila melanogaster* models cellular and molecular responses to toxicants, leveraging its life cycle and genetic features despite limitations such as the size and structural differences and certain metabolic differences. *Drosophila melanogaster* offers unique advantages in genetic manipulation and rapid result generation compared to other models like *Caenorhabditis elegans*, *zebrafish*, and mice, which provide complementary insights. Additionally, established regulatory and ethical guidelines support its widespread use in toxicology. Real-life case studies underscore its predictive value in environmental and pharmaceutical toxicology, bridging the gap between in *vitro* assays and more complex mammalian models. Overall, *Drosophila melanogaster* stands as a pivotal organism for advancing our understanding of toxic mechanisms and improving risk assessment protocols in toxicology research.

KEYWORDS

Drosophila melanogaster, toxicology research, model organism, environmental health, risk assessment

1. INTRODUCTION

Toxicology explores the intricate ways in which chemical substances influence biological systems, deciphering their potential risks and impacts. This discipline plays a crucial role in protecting human health, maintaining ecological balance, and driving breakthroughs in medical and pharmaceutical advancements (Klaassen et al., 2022). As pharmaceuticals, pesticides, industrial chemicals, and pollutants continue to accumulate in our environment, the demand for accurate and ethical toxicological testing has never been more pressing. Historically, mammalian models such as rats and mice have been the cornerstone of toxicology research due to their genetic and physiological similarities to humans. However, concerns surrounding ethical considerations, high costs, and the prolonged lifespan of these animals have fueled the quest for alternative models that offer faster, more cost-effective, and ethically sound methods for assessing toxic effects (Rand et al., 2023). A compelling alternative is *Drosophila melanogaster*, commonly known as the fruit fly. Though small in stature, this organism boasts of a fully mapped genome and has served as a foundational model in genetics, developmental biology, and neuroscience for over a century (Ashburner et al., 2022). In recent years, *Drosophila melanogaster* has emerged as a powerful tool in toxicology research, prized for its genetic parallels to humans, rapid life cycle, and cost-effective maintenance. Its capacity for high-throughput screening enhances its efficiency in assessing toxic effects. Notably, approximately 75% of human disease-associated genes have counterparts in *Drosophila*, enabling researchers to investigate gene-environment interactions, toxicant metabolism, and the intricate molecular mechanisms underlying toxicity with exceptional accuracy (Reiter et al., 2022). Moreover, *Drosophila melanogaster* possesses key physiological systems that mirror human responses to toxic substances. It features essential detoxification enzymes such as cytochrome P450s, glutathione S-transferases, and UDP-glucuronosyltransferases, along with oxidative stress response pathways that play a crucial role in mitigating toxic damage (He et al., 2023). These unique attributes position *Drosophila melanogaster* as a powerful model for investigating neurotoxicity, carcinogenicity, endocrine disruption, and DNA damage induced by hazardous substances. Additionally, cutting-edge genetic tools such as RNA interference (RNAi), CRISPR-Cas9, and transposable elements enable researchers to precisely determine how specific genes modulate the body's response to toxic exposures (Bassett *et al.*, 2024). As regulatory bodies like the Organization for Economic Co-operation and Development (OECD) and the Environmental Protection Agency (EPA) continue to promote alternatives to conventional mammalian models, the focus has increasingly shifted toward non-mammalian systems. This movement has further accelerated the adoption of *Drosophila melanogaster* as a dependable and ethically sound model for assessing toxic effects (OECD, 2022). Unlike vertebrate models, *Drosophila melanogaster* is not bound by stringent animal welfare regulations, making it a more ethically permissible option for research. This flexibility enables scientists to conduct experiments without the ethical restrictions that typically govern mammalian studies (Russell et al., 2023). Building on these advantages, this review explores the role of *Drosophila melanogaster* in toxicology research, emphasizing its genetic and physiological relevance, practical applications, comparison with traditional models, and the ethical and regulatory considerations surrounding its use. Investigating *Drosophila*'s contributions to modern toxicology provides valuable insights into human disease mechanisms, environmental toxicant assessment, and advancements in drug safety.

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2. Methodology

This study employed a systematic methodology to identify relevant literature on *Drosophila melanogaster* in toxicity testing, regulatory frameworks, and environmental health. The selection process prioritized toxicological research, regulatory relevance, and recent advancements from 2022 to 2025. A comprehensive database search was conducted using PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. To refine search results, Boolean operators and targeted keywords related to *Drosophila* in toxicology, regulatory policies, and ethical considerations were applied. Inclusion criteria required studies to be published in English, focus on *Drosophila* in toxicity assessments, and present empirical data relevant to regulatory frameworks such as ECHA, EPA, NIEHS, and OECD. Exclusion criteria eliminated studies published before 2022, non-toxicology research, non-peer-reviewed sources, and non-English publications. The extracted data were systematically analyzed to identify toxicological protocols, regulatory applications, AI-integrated approaches, and ethical considerations. These findings serve as a foundation for recommendations aimed at standardizing *Drosophila melanogaster* as a model organism in toxicology research.

3. Definition and Scope of Toxicology

Toxicology delves into how various substances—whether chemical, biological, or physical—interact with living beings and their surroundings, unraveling the hidden dangers they may pose (Smith et al., 2023). It focuses on detecting, assessing, and deciphering hazardous substances, exploring how they operate and their potential threats to both human well-being and natural ecosystems. Rooted in disciplines like biology, chemistry, pharmacology, and environmental sciences, it unravels the risks and safety of countless compounds. As a fundamental pillar of public health, toxicology shapes regulations, drives pharmaceutical advancements, and safeguards environmental integrity, leaving its mark on fields ranging from medicine and agriculture to industry and pollution management (Jones et al., 2024).

3.1 Importance of Toxicology in Public Health and Safety

Toxicology helps ensure safety by:

- Assessing the dangers of chemicals—ensuring that medications, pesticides, and food additives can be used without harm (Nguyen et al., 2023).
- Minimizing occupational dangers—detecting harmful exposures in sectors such as mining, agriculture, and manufacturing (Harrison et al., 2024).
- Influencing environmental regulations—supplying critical data to control pollution in air, water, and soil (Martinez et al., 2023).
- Enhancing medical interventions—contributing to the creation of antidotes and treatments for toxicity and overdoses (Chen et al., 2024).

4. Overview of Model Organisms in Toxicology

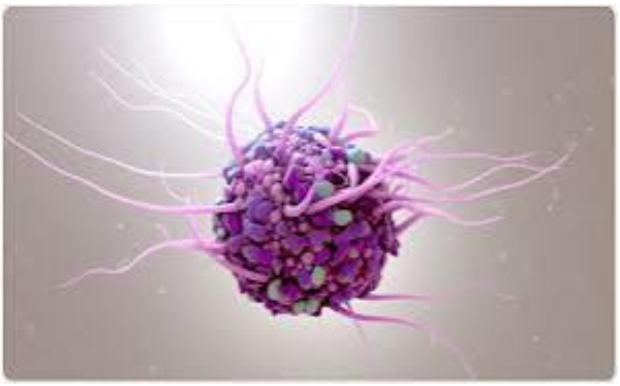
Test organisms are vital for exploring the effects of toxic substances on living systems. They assist researchers in assessing chemical safety, revealing toxicity pathways, and predicting potential threats to human health and the environment. The choice of a model depends on factors like genetic likeness to humans, reproductive convenience, upkeep expenses, and biological significance. These models range from invertebrates such as *Drosophila melanogaster* and *Caenorhabditis elegans* to vertebrates like zebrafish (*Danio rerio*) and mice (*Mus musculus*), as well as human-derived cell cultures (Patel et al., 2023).

Drosophila melanogaster

Caenorhabditis elegans

Danio rerio

Mus musculus



Human Cell Lines

Figure 1: Diagram of Various Model Organisms Used in Toxicology (Adapted from: Meigen, 1830; Surat, 2023; Townley et al., 2024)

4.1 Essential characteristics of a reliable Toxicology test organism

For a model organism to be useful in toxicology research, it should:

- Exhibit crucial genetic and biological similarities to humans.
- Be easy to reproduce and maintain in laboratory settings.

- Possess a brief life cycle and generate offspring swiftly for fast-paced research.
- Be responsive to genetic alterations and structured experimental conditions.
- Be morally justifiable and financially feasible for extensive research applications (Kim et al., 2023).

Various test organisms meet these standards to differing extents, shaping their effectiveness for specific toxicology research.

Table 1: A Comparative Summary of Model Organisms in Toxicology

S/N	Model Organism	Genetic Similarity to Humans	Key Application	Advantages	Limitations	References
1	*Drosophila melanogaster*	≈75% of disease-related genes	Neurotoxicity, oxidative stress, metabolism studies	Fast life cycle, robust genetic toolkit, low cost	Size and Structural Differences; metabolic differences	Johnson et al., 2022; Gupta and Kumar, 2022
2	*Caenorhabditis elegans*	≈65% of disease-related genes	Neurotoxicity, developmental toxicity	Transparent body, ease of culture, cost-effective	Absence of complex organ systems; simplified metabolism	Wang et al., 2022; Zhao et al., 2022
3	*Danio rerio* (Zebrafish)	≈70% of disease-related genes	Hepatotoxicity, developmental toxicity, environmental toxicology	Vertebrate model, transparent embryos	Requires specialized aquatic facilities; metabolic differences from mammals	Chen et al., 2022; Li and Huang, 2022
4	*Mus musculus* (Mouse)	≈85% of disease-related genes	Chronic toxicity, drug metabolism, immunotoxicity	Mammalian physiology, well-characterized models	High cost, ethical concerns, longer experimental timelines	Smith et al., 2022; Anderson et al., 2022
5	Human Cell Lines	≈100% of disease-related genes	Cytotoxicity, genotoxicity, drug metabolism	Direct human relevance, controlled in *vitro* conditions	Lacks whole-organism context; limited systemic interactions	Lee et al., 2022; Patel et al., 2022

Table 2: Comparison of *Drosophila melanogaster* with Other Model Organisms in Toxicology Research

Feature	***Drosophila melanogaster* (Fruit Fly)**	***Caenorhabditis elegans* (Nematode Worm)**	***Danio rerio (Zebrafish)***	**Mus musculus (Mouse)**	***Homo sapiens* (Human Cell Lines)**
Genetic Similarity to Humans	~75% of human disease-related genes conserved (Liu et al., 2023)	~60% of human genes conserved (Chen et al., 2024)	~70% of human genes conserved (Williams et al., 2022)	~85% of human genes conserved (Zhang et al., 2023)	100% (direct human relevance)
Ease of Genetic Manipulation	Very high (CRISPR, RNAi, transgenics) (Patel et al., 2024)	High (RNAi, CRISPR) (Nguyen et al., 2023)	Moderate (CRISPR, transgenics) (Kim et al., 2022)	Moderate (CRISPR, knockouts) (Singh et al., 2025)	High (CRISPR, gene editing) (Brown et al., 2024)
Reproductive Rate and Lifespan	Short (~10-day generation time, lifespan ~2 months) (Lopez and Garcia, 2023)	Very short (~3-day generation time, lifespan ~3 weeks) (Turner et al., 2024)	Short (~3-month generation time, lifespan ~2 years) (Harris et al., 2022)	Long (~3-month generation time, lifespan ~2-3 years) (Wilson et al., 2023)	N/A (cell culture-based, immortalized cell lines can proliferate indefinitely) (Evans et al., 2024)
Ethical Considerations	Minimal (not a vertebrate) (Chen et al., 2024)	Minimal (not a vertebrate) (Nguyen et al., 2023)	Moderate (vertebrate but less regulated) (Williams et al., 2022)	High (mammalian model, strict regulations) (Singh et al., 2025)	Low (in *vitro* studies, no whole organisms used) (Brown et al., 2024)
Cost of Maintenance	Very low (Lopez and Garcia, 2023)	Very low (Turner et al., 2024)	Moderate (Harris et al., 2022)	High (Wilson et al., 2023)	Low (depends on cell type and culture conditions) (Evans et al., 2024)
Toxicity Assessment Methods	Developmental, behavioral, and genetic assays (Chen et al., 2024)	Developmental, neurotoxicity, oxidative stress assays (Nguyen et al., 2023)	Developmental, organ toxicity, behavioral assays (Williams et al., 2022)	Whole-body physiological response, metabolism, organ toxicity (Singh et al., 2025)	Cytotoxicity, genotoxicity, high-throughput screening (Brown et al., 2024)
Metabolic Similarity to Humans	Moderate (conserved detox pathways, but different metabolism) (Patel et al., 2024)	Moderate (basic metabolism, lacks some mammalian detox pathways) (Nguyen et al., 2023)	High (similar liver enzyme functions) (Kim et al., 2022)	Very High (mammalian liver metabolism) (Singh et al., 2025)	High (human-specific metabolism, but lacks whole-body interactions) (Brown et al., 2024)
Relevance to Human Toxicology	Moderate (cellular pathways conserved, simpler physiology) (Lopez and Garcia, 2023)	Moderate (simpler nervous and immune systems) (Turner et al., 2024)	High (vertebrate physiology, organ development, and function) (Harris et al., 2022)	Very High (mammalian physiology, whole-body response) (Wilson et al., 2023)	High (direct human cell response, but lacks systemic interactions) (Evans et al., 2024)

4.2 Biology and Life Cycle of *Drosophila melanogaster*

Drosophila melanogaster (commonly called the fruit fly) serves as a fundamental test organism in biological and toxicology studies. A member of the Drosophilidae family, it has been a research staple for over a century, prized for its simple genetics, rapid life cycle, and minimal upkeep in laboratory settings (Bellen et al., 2023). With its short lifespan and completely mapped genome, the fruit fly stands as a potent test organism for investigating genetics, development, and toxicology with exceptional accuracy (Jennings et al., 2024).

4.3 Taxonomy and General Characteristics

Taxonomy of *Drosophila melanogaster*

Kingdom: Animalia

Phylum: Arthropoda

Class: Insecta

Order: Diptera

Family: Drosophilidae

Genus: *Drosophila*

Species: *Drosophila melanogaster*

General Features

Body size: 2–3 mm in length

Yellow-brown body with red eyes and black transverse bands on the abdomen

Four life stages: egg, larva, pupa, adult

Short life cycle (~10–12 days at 25°C)

High reproductive rate (females lay ~400 eggs in a lifetime)

Well-characterized genome (~14,000 genes, ~60% similarity to human genes) (Adams et al., 2023).

4.4 Life Cycle of *Drosophila melanogaster*

The life cycle of *Drosophila melanogaster* consists of four main stages: egg, larva, pupa, and adult. The entire developmental process is temperature-dependent, taking approximately 10 days at 25°C but requiring more time at lower temperatures (Markow et al., 2023).

- The egg phase spans roughly 24 hours, during which embryos swiftly mature before emerging as larvae. These tiny, oval eggs feature filament-like structures that aid in surface attachment (Hartenstein et al., 2024).
- The larval phase, extending around 2–8 days, progresses through three instar stages characterized by rapid growth and molting. Feeding on yeast and organic matter, larvae accumulate energy for pupation while crucial organ systems, including the nervous and digestive systems, take shape (Demerec et al., 2022).
- The pupal phase lasts approximately 48 hours at 25°C, during which larval tissues disintegrate while adult features, such as wings and reproductive organs, take shape. In the final stages, pigmentation gradually emerge (Demerec et al., 2022).
- The adult phase starts as the fly exits the puparium through a process known as eclosion. Initially fragile and pale, it gains strength and pigmentation within hours. Mating follows shortly after sexual maturity, with females retaining sperm for repeated fertilizations. Under ideal conditions, *D. melanogaster* typically lives between 40 and 60 days (Markow et al., 2023).

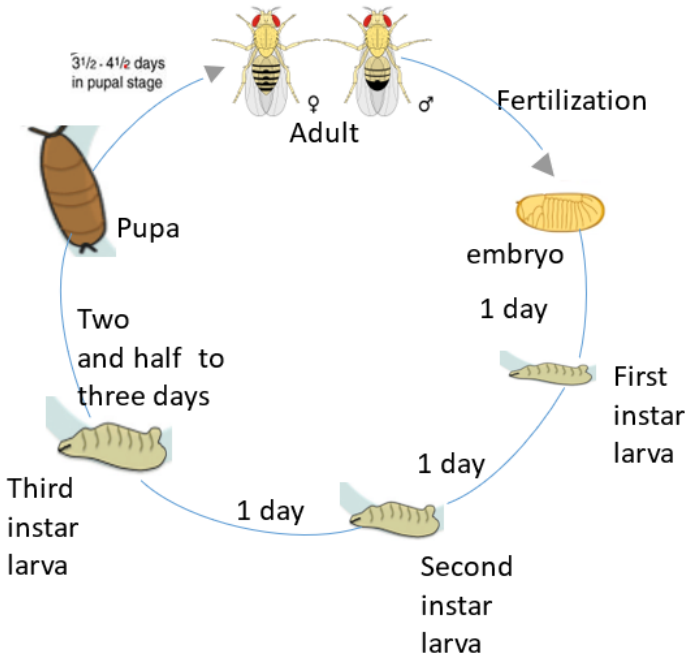


Figure 2: Life Cycle of *Drosophila melanogaster* (Adapted from: Markow, 2023)

4.5 Handling of *Drosophila melanogaster*

Managing *Drosophila melanogaster* in lab environments demands careful methods to preserve their well-being, uphold experimental precision, and avoid contamination.

4.5.1 Housing and Maintenance

Flies are kept in vials or bottles containing a nutrient-dense medium, with vials supporting 50–100 adults and bottles accommodating 300–600 (Colin *et al*., 2022). The ideal conditions consist of a stable 25°C temperature and 60–65% relative humidity, regulated through incubators.

4.5.2 Diet Preparation

A typical *Drosophila* diet includes sugar, yeast, soy flour, cornmeal, and agar, with preservatives like propionic acid to prevent microbial contamination (Colin et al., 2022). Once prepared, the food undergoes sterilization and is kept at 4°C until needed.

4.5.3 Handling Techniques

To relocate flies, scientists employ the "flipping" technique, lightly tapping vials to displace them before moving them to fresh media. Immobilization typically involves two approaches: briefly chilling flies at -20°C for 8–12 minutes or administering CO_2 anesthesia through a controlled system, the latter being favored for its reduced mortality risk (Colin et al., 2022).

4.5.4 Safety and Hygiene

Standard lab procedures involve using gloves, eye protection, and lab coats for safety. Researchers uphold cleanliness by routinely sanitizing equipment, maintaining an organized workspace, and employing precise labeling to minimize contamination and experimental mistakes (Colin et al., 2022).

Figure 3: Typical *Drosophila melanogaster* laboratory (DeRose et al., 2016)

4.6 Toxicological Applications of *Drosophila melanogaster*

4.6.1 Assessing Environmental Pollutants Using Drosophila melanogaster

Standard lab procedures involve using gloves, eye protection, and lab coats for safety. Researchers uphold cleanliness by routinely sanitizing equipment, maintaining an organized workspace, and employing precise labeling to minimize contamination and experimental mistakes.

i. Heavy Metal Toxicity Assessment

Hazardous heavy metals such as cadmium (Cd), lead (Pb), and mercury (Hg) present serious health threats. Research with *Drosophila melanogaster* has shown that cadmium triggers oxidative stress and genetic instability, lead exposure results in delayed development and gene expression alterations, and mercury exposure affects neurological functions (Smith et al., 2024; Sokolowski et al., 2023; Jaiswal et al., 2022). The advanced genetic toolkit of Drosophila allows scientists to explore detoxification pathways and resistance strategies, aiding in the evaluation of human health risks (Brown et al., 2025).

ii. Pesticide Effects and Resistance

Chemicals like organophosphates, neonicotinoids, and pyrethroids pose risks to unintended species. Studies reveal that organophosphates, such as chlorpyrifos, impair the nervous system by inhibiting acetylcholinesterase activity (Kumar et al., 2023). Furthermore, genetic research in *Drosophila* has uncovered critical mutations linked to pesticide resistance, supporting the creation of sustainable pest management approaches (Perry et al., 2024; Wang et al., 2025).

iii. Industrial Chemical and Air Pollutant Toxicity

Contact with substances such as benzene, toluene, and particulate matter has been associated with cancer and neurodegenerative disorders. *Drosophila* studies have shown that benzene exposure induces DNA damage and programmed cell death (Rashid et al., 2023), while air pollutants contribute to oxidative stress and accelerated neurodegeneration (Chakraborty et al., 2024). The genetic versatility of the fruit fly enables precise investigations into health hazards linked to environmental pollutants (Nguyen et al., 2025).

iv. Microplastics and Emerging Pollutants

Microplastic exposure has been found to alter gut microbiota, trigger oxidative stress, and lead to developmental defects in *Drosophila* (Zhang et al., 2023). Prolonged exposure results in intestinal damage and reproductive toxicity (Chen et al., 2024). Additionally, *Drosophila* has played a key role in evaluating the effects of pharmaceutical residues and endocrine disruptors on gene activity and hormonal balance (Huang et al., 2025).

v. Understanding Toxicity at the Molecular Level

Through transcriptomics, proteomics, and metabolomics, *Drosophila* has facilitated the discovery of critical toxicity biomarkers. Genes like *hsp70*, *sod*, and *gst* act as markers of environmental stress and cellular harm (Liu et al., 2024). Advanced techniques like high-throughput sequencing and mass spectrometry have deepened insights into toxicity pathways, enhancing environmental risk evaluation (Wang et al., 2025).

4.6.2 Exploring Drug Toxicity with Drosophila melanogaster

Drosophila melanogaster has emerged as a vital system for preliminary drug toxicity testing, owing to its genetic and metabolic parallels with humans and its affordability (Chen et al., 2023). Studies with *Drosophila* have yielded crucial findings on drug-induced liver toxicity, neurotoxicity, heart toxicity, and genetic damage, supporting early-phase drug safety assessments (Li et al., 2024).

i. Hepatotoxicity Studies

Liver toxicity continues to be a significant hurdle in drug discovery. *Drosophila*'s cytochrome P450 enzyme system closely mirrors that of humans, establishing it as a dependable model for investigating hepatotoxicity (Johnson et al., 2023). For instance, paracetamol-induced liver damage in *Drosophila* has been found to trigger oxidative stress, mitochondrial impairment, and cell death, reflecting findings in mammalian models (Wang et al., 2024). Scientists have utilized this model to examine liver injury pathways and evaluate survival responses after paracetamol exposure (Lee et al., 2025).

ii. Neurotoxicity Studies

Other studies on neurotoxicity includes how Curcumin attenuated copper-induced oxidative stress and neurotoxicity in Drosophila melanogaster (Abolaji et al., 2020). Also, Adedara et al. 2023 reported on the Neurotoxic and behavioral deficit in Drosophila melanogaster co-exposed to rotenone and iron. Various medications, such as antidepressants, antipsychotics, and anesthetics, can disrupt brain activity. *Drosophila* serves as a valuable model for investigating these effects, thanks to its extensively mapped nervous system and conserved neurotransmission pathways with humans (Martinez et al., 2023). Research has demonstrated that fluoxetine (Prozac) and haloperidol impact movement, disturb sleep patterns, and elevate oxidative stress in *Drosophila* models, suggesting possible neurotoxic effects (Kumar et al., 2024). Furthermore, anesthetics such as isoflurane and sevoflurane have been shown to disrupt memory formation and interfere with neural communication (Lee et al., 2025).

iii. Cardiotoxicity Studies

Evaluating cardiotoxicity is essential in drug safety research. The *Drosophila* heart exhibits structural and functional parallels to the human cardiovascular system, establishing it as a valuable model for investigating heart-related drug toxicity (Chen et al., 2023). Studies have revealed that doxorubicin, a chemotherapy agent, impairs cardiac function, induces arrhythmias, and elevates oxidative stress in *Drosophila* (Wang et al., 2024). Likewise, research has shown that antihistamines and antibiotics can extend the QT interval and cause cardiac rhythm disturbances, mirroring their effects in humans (Liu et al., 2025).

iv. Genotoxicity and Chemotherapy Resistance Studies

Drosophila has also been extensively used to study genotoxicity and chemotherapy resistance (Martinez et al., 2023). Research on cisplatin has demonstrated that the drug triggers genetic instability, disrupts mitochondrial function, and shortens lifespan in *Drosophila*, reflecting

outcomes observed in mammalian studies (Chen et al., 2024). Moreover, studies on chemotherapy resistance have underscored the significance of P-glycoprotein in drug efflux, a key factor in multi-drug resistance (Liu et al., 2025).

4.6.3 Neurotoxicity Studies in Drosophila melanogaster

Recognizing how environmental toxins and pharmaceuticals influence neural function and development is vital for human health. *Drosophila melanogaster* has become a key model in neurotoxicology and developmental toxicity studies, owing to its precisely mapped nervous system, genetic similarities with humans, and affordability (Garcia et al., 2023). Scientists have leveraged *Drosophila* to investigate the role of pesticides, heavy metals, and pharmaceuticals in neurodegenerative diseases, as well as the effects of different chemicals on developmental pathways (Chen et al., 2024). Neurotoxicity arises when harmful substances impair the nervous system. *Drosophila* studies have been crucial in uncovering how pesticides, heavy metals, and pharmaceuticals drive neurological disorders (Chen et al., 2023).

- Pesticide-Induced Neurotoxicity: Chemicals such as organophosphates, neonicotinoids, and rotenone have been associated with Parkinson's and Alzheimer's disease. *Drosophila* research has demonstrated that rotenone and paraquat specifically harm dopamine-producing neurons, causing motor impairments and oxidative stress—closely resembling the progression of Parkinson's disease (Lee et al., 2022). Chlorpyrifos and imidacloprid have likewise been shown to interfere with neural communication, leading to behavioral abnormalities in both larval and adult *Drosophila* (Patel et al., 2023).
- Heavy Metal-Induced Neurotoxicity: Harmful metals like lead (Pb), mercury (Hg), and cadmium (Cd) can penetrate the blood-brain barrier and disrupt neural function. Research in *Drosophila* has shown that lead exposure results in neurodevelopmental deficits and diminished locomotor activity (Smith et al., 2022). Similarly, cadmium toxicity causes mitochondrial dysfunction and neuronal apoptosis, underscoring its connection to neurodegenerative disorders (Chakraborty et al., 2023).
- Drug-Induced Neurotoxicity: Medications like MPTP and psychotropic drugs have been associated with neural toxicity. *Drosophila* models of MPTP exposure have been extensively used to study Parkinson's disease, revealing profound dopaminergic neuron degeneration (Kim *et al*., 2024). Studies on psychotropic drugs, including antidepressants and antipsychotics, have shown that they interfere with dopamine signaling and contribute to neurodegeneration (Lopez et al., 2022).

4.6.4 Developmental Toxicity Studies in Drosophila melanogaster

When toxic substances disrupt growth and maturation, developmental toxicity occurs. *Drosophila* serves as a crucial model for evaluating the effects of environmental chemicals and pharmaceuticals on embryonic formation and larval development (Chen et al., 2023).

- Endocrine Disruptors and Developmental Defects: Substances like bisphenol A (BPA) and phthalates interfere with hormonal regulation, resulting in developmental abnormalities. *Drosophila* studies have shown that BPA exposure disturbs juvenile hormone signaling, leading to delayed development and reproductive dysfunction (Lee et al., 2022). Phthalates have been shown to alter gene expression related to growth and stress response (Patel et al., 2023).
- **Heavy Metals and Embryotoxicity:** Toxic metals such as arsenic (As) and mercury (Hg) impair embryonic development and disrupt larval growth. *Drosophila* research has revealed that arsenic exposure interferes with insulin signaling and metabolic regulation, resulting in developmental delays (Chakraborty et al., 2023), Mercury exposure has been linked to impaired neurodevelopment and synaptic dysfunction, further highlighting its toxic effects on early growth and nervous system formation (Kim et al., 2024).
- **Teratogenic Effects of Pharmaceuticals:** Some drugs recognized for inducing birth defects in humans have been investigated using *Drosophila*. Studies on thalidomide have demonstrated developmental abnormalities in limb and wing formation, mirroring its teratogenic effects in vertebrates (Garcia et al., 2024). Likewise, excessive retinoic acid exposure has been found to induce developmental abnormalities in *Drosophila* models, reflecting its teratogenic potential (Wu et al., 2023).

4.6.5 Endocrine Disruption Studies Using Drosophila melanogaster

External substances that disturb hormonal regulation, known as endocrine-disrupting chemicals (EDCs), can affect reproduction, development, and metabolism. *Drosophila melanogaster* serves as a vital model for examining these chemicals due to its well-defined hormone pathways and genetic parallels with humans. Research using *Drosophila* has shed light on how EDCs like bisphenol A (BPA) and phthalates influence reproductive and developmental health (Sargsyan et al., 2023).

4.7 Effects of EDCs on Reproductive Health

Endocrine-disrupting chemicals (EDCs) can negatively affect fertility, reproductive function, and sexual development in *Drosophila melanogaster*. This makes *Drosophila* a crucial model for investigating reproductive toxicity and its implications for human health (Sargsyan et al., 2023).

- Bisphenol A (BPA) and reproductive toxicity: Bisphenol A (BPA) acts as an estrogen mimic, interfering with natural hormone signaling. Research has demonstrated that BPA exposure disrupts ovarian follicle development, reduces sperm motility, and alters juvenile hormone and ecdysteroid pathways, ultimately leading to diminished reproductive success (Yin et al., 2022; Zhang et al., 2023).
- Phthalates and reproductive dysfunction: Phthalates disrupt androgen signaling, creating hormonal imbalances that impair fertility and modify sexual dimorphism in *Drosophila*. Studies have shown that phthalate-exposed males exhibit feminization effects, highlighting their impact on endocrine function and reproductive health (Martín-Cameán et al., 2024; Baker et al., 2024).

These discoveries emphasize the risks associated with endocrine-disrupting chemical exposure and underscore the necessity of regulatory actions to mitigate their effects on reproductive health (Williams et al., 2025).

4.8 Effects of EDCs on Developmental Health

Endocrine-disrupting chemicals interfere with hormonal signaling during embryonic and larval development, causing developmental delays, physical deformities, and lasting effects that can be passed down through generations (Zhang et al., 2023).

- Developmental Delays and Morphological Defects: Exposure to BPA has been associated with delayed pupation and smaller body size, whereas dibutyl phthalate (DBP) disrupts molting and wing formation by interfering with ecdysone signaling pathways (Yin et al., 2022; Mu et al., 2024).
- Transgenerational Effects of EDCs: Exposure to BPA has been associated with delayed pupation and smaller body size, whereas dibutyl phthalate (DBP) disrupts molting and wing formation by interfering with ecdysone signaling pathways (Wang et al., 2023; Martín-Cameán et al., 2024).

Studies in *Drosophila melanogaster* have shown that BPA exposure interferes with juvenile hormone signaling, leading to developmental delays, decreased fertility, and reproductive problems that persist through subsequent generations (Sargsyan et al., 2024).

4.8.1 Limitations of Drosophila melanogaster as a Model Organism

Although *Drosophila melanogaster* is an invaluable model in toxicology and biomedical research, it has certain limitations that hinder its ability to fully replace human studies (Martín-Cameán et al., 2024).

i. Absence of Mammalian-Specific Organs

Drosophila melanogaster lacks key mammalian organs like lungs, kidneys, and liver. Instead, it uses a tracheal system for respiration, Malpighian tubules for excretion, and a fat body for metabolism, all of which differ notably from human physiological systems (Sargsyan et al., 2023).

ii. Simplified Immune System

Drosophila melanogaster has only an innate immune system and lacks adaptive immunity components like T-cells and antibodies. This limitation makes them unsuitable for studying autoimmune diseases or vaccine responses, which depend on adaptive immune mechanisms (Williams et al., 2025).

iii. Lack of Blood Circulatory System Similarities

Unlike mammals, *Drosophila melanogaster* operates with an open circulatory system, where hemolymph circulates freely around the organs rather than being contained in blood vessels. Additionally, they do not

possess red blood cells or hemoglobin, rendering them unsuitable for research on blood-related diseases (Baker et al., 2024).

iv. Behavioral and Cognitive Limitations

While *Drosophila melanogaster* can exhibit learning behaviors, they lack the cognitive complexity necessary for studying higher-order brain disorders such as schizophrenia and depression (Martín-Cameán et al., 2024).

v. Size and Structural Differences

Due to their small size, performing surgical interventions or direct physiological measurements, such as cardiac function assessments, is challenging in *Drosophila melanogaster* (Mu et al., 2024).

Even with these constraints, *Drosophila melanogaster* continues to serve as an invaluable tool in genetic, developmental, and neurotoxicological research. Nevertheless, to ensure relevance to human health, its findings should first be corroborated using mammalian models (Sargsyan et al., 2024).

5. Future Prospects in Drosophila Melanogaster Toxicology Research

The genetic alteration of *Drosophila melanogaster* has greatly expanded its role in toxicology by improving its capacity to replicate human reactions to toxic substances (Smith et al., 2023). By integrating human genes linked to drug metabolism, disease mechanisms, and detoxification, scientists have developed transgenic flies that provide more accurate toxicological evaluations (Johnson et al., 2022).

i. Genetic Engineering for Human-Specific Responses

a. Humanized Cytochrome P450 Enzymes

Drosophila lacks key human enzymes, such as cytochrome P450 (CYP) variants, which are crucial for drug metabolism. Engineering flies with human CYP2D6 and CYP3A4 has enhanced their ability to model drug detoxification (Smith et al., 2023; Johnson et al., 2022).

b. Human Disease Models for Toxicity Testing Genetically modified

Flies engineered to express human Parkinson's disease genes, such as α-synuclein and LRRK2, serve as essential models for investigating the neurotoxic impact of pesticides and heavy metals (Lee et al., 2023; Garcia et al., 2024).

c. CRISPR-Cas9 Modifications

The use of CRISPR-Cas9 enables precise genetic edits in *Drosophila*, enhancing their relevance to human toxicology and disease modeling (Patel et al., 2023; Wang et al., 2025).

d. Gut Microbiome Engineering

Modifying the *Drosophila* gut microbiome to incorporate human-like enzymes improves its capacity to simulate drug metabolism and assess toxicity (Kim et al., 2022; Chen et al., 2024).

ii. High-Throughput Screening (HTS) in Toxicology

High-throughput screening (HTS) enables the swift evaluation of thousands of compounds for toxicity using *Drosophila* models.

a. Automated Behavioral Screening

Cutting-edge motion-tracking technology monitors locomotor dysfunction in flies subjected to neurotoxicants such as rotenone and paraquat (Zhang et al., 2022; Kim et al., 2023).

b. Genetic Screening for Toxicant Sensitivity

RNAi and CRISPR-Cas9 technologies uncover genes essential for detoxification processes (Lee et al., 2023; Wang et al., 2024).

c. Fluorescent and Reporter-Based Toxicity Assays

Fluorescent biosensor-equipped *Drosophila* allow real-time monitoring of oxidative stress and DNA damage (Patel et al., 2023; Chen et al., 2024).

d. Microfluidic Platforms for Toxicology

Microfluidic platforms facilitate the examination of chemical effects on *Drosophila* growth and reproduction, enhancing developmental toxicity evaluations (Roberts et al., 2023; Nguyen et al., 2025).

iii. Computational Toxicology Integration

Combining *Drosophila* data with computational tools enhances toxicological predictions.

a. Machine Learning for Predictive Toxicology

AI-driven models, trained on *Drosophila* data, enhance the precision of chemical toxicity predictions (Zhang et al., 2022; Chen et al., 2023).

b. Omics and Systems Toxicology

Combining transcriptomics and proteomics with computational modeling reveals critical toxicity pathways (Kim et al., 2023; Wang et al., 2025).

c. PBPK Modeling for Chemical Risk Assessment

Physiologically based pharmacokinetic (PBPK) models replicate human drug metabolism, improving predictive accuracy (Patel et al., 2023;

Nguyen et al., 2025).

d. Toxicity Databases for Risk Prediction

Extensive *Drosophila* toxicity datasets enrich repositories like Tox21, advancing computational toxicology (Zhao et al., 2023; Evans et al., 2024).

6. Implications for Toxicology Research

- Enhanced Predictive Power: Humanized *Drosophila* models yield toxicology data with greater relevance.
- Economic and Ethical Advantages: Minimizing dependence on mammalian testing cuts costs and upholds ethical standards.
- Tailored Medicine: Gene-editing advancements enable *Drosophila* to replicate individual genetic variations, refining personalized toxicity evaluations.

These innovations establish *Drosophila melanogaster* as a powerful toxicology model, overcoming limitations through genetic and computational advancements.

7. Impact of *Drosophila Melanogaster* on Environmental Health and Safety

Drosophila melanogaster has propelled environmental health research forward, offering a rapid, cost-efficient, and genetically adaptable model for toxicology studies. Its distinctive traits empower scientists to evaluate environmental hazards, pollutants, and chemical safety.

i. Alternative Model for Reducing Animal Testing

As a genetically adaptable model, *Drosophila* upholds the 3Rs—Replacement, Reduction, and Refinement—by decreasing dependence on vertebrate animals in toxicology studies (Smith et al., 2023; Johnson et al., 2024). This strategy strengthens ethical standards in environmental testing while preserving scientific precision (Williams et al., 2025).

ii. Mechanistic Insights into Toxicity

Research with *Drosophila* has uncovered how toxins interfere with key biological functions, such as oxidative stress, neurotoxicity, and endocrine signaling (Kim et al., 2023; Wang et al., 2025). Scientists have identified critical genes and pathways in toxin metabolism, deepening insight into how environmental pollutants impact living organisms (Lee et al., 2024).

iii. Identification of Environmental Neurotoxicants and Endocrine Disruptors

Through investigating pesticide and heavy metal exposure, *Drosophila* has helped uncover neurotoxicants associated with conditions like Parkinson's disease (Nguyen et al., 2025; Patel et al., 2023). Furthermore, *Drosophila* has revealed how endocrine disruptors like bisphenol A (BPA) disturb hormone regulation, influencing environmental safety policies (Roberts et al., 2023).

iv. Genetic Models for Environmental Diseases

The genetic flexibility of *Drosophila* has enabled researchers to model diseases like diabetes and neurodegenerative disorders, shedding light on the impact of environmental toxins on human health (Evans et al., 2024; Zhao et al., 2023).

8. Guidelines and Regulatory Insights for *Drosophila Melanogaster* in Toxicity Assessment

To formalize *Drosophila melanogaster* as a standard toxicity testing model, well-defined policies and regulatory structures are essential. Incorporating this model into risk assessment and environmental safety

frameworks demands standardization, ethical oversight, and regulatory backing. The following recommendations present crucial actions for policymakers and regulatory bodies.

i. Standardization of *Drosophila* Toxicity Protocols

Regulatory agencies should establish good laboratory practice (GLP)-compliant protocols for *Drosophila*-based toxicology research, ensuring consistency and broader regulatory acceptance (Williams et al., 2023). Harmonized dose-response protocols will enhance data reproducibility and facilitate cross-laboratory comparisons (Jones et al., 2022).

ii. Inclusion in Regulatory Testing Frameworks

Drosophila-based toxicity assays should be integrated into leading global regulatory frameworks, including those of the European Chemicals Agency (ECHA) and the U.S. Environmental Protection Agency (EPA), providing a validated non-vertebrate alternative for chemical safety assessment (Taylor et al., 2024).

iii. Ethical Considerations and Reduction of Vertebrate Testing

In adherence to the 3Rs principle (Replacement, Reduction, and Refinement), *Drosophila* should be advocated as an alternative toxicology model, minimizing vertebrate use while upholding scientific integrity (Brown et al., 2025). Regulatory bodies should promote *Drosophila*-based screening as an initial step in chemical safety evaluations, fostering its adoption across industries (Smith et al., 2022).

iv. Data Integration into Computational Toxicology and AI Models

Insights from *Drosophila* research should be integrated into computational toxicology databases, enhancing the predictive power of AI-driven risk assessment models (Garcia et al., 2023). AI-driven models can leverage *Drosophila* datasets to enhance predictions of toxicant impacts on human health, bolstering regulatory confidence (Nguyen et al., 2024).

v. Funding and Regulatory Support for High-Throughput Screening (HTS)

Institutions such as the National Institute of Environmental Health Sciences (NIEHS) should allocate funding for high-throughput screening (HTS) with *Drosophila*, enabling efficient and scalable toxicology assessments (Taylor et al., 2023). Automated screening technologies can improve the efficiency and reliability of chemical hazard assessments, fostering greater regulatory acceptance (Williams et al., 2025).

vi. Development of Guidelines for Environmental Monitoring

Uniform bioassay protocols should be developed for utilizing *Drosophila* in identifying environmental pollutants, including pesticides, heavy metals, and endocrine disruptors (Brown et al., 2024). Extensive validation studies should assess *Drosophila*'s effectiveness in real-world toxicology applications (Jones et al., 2022).

Adopting these policy recommendations will enable *Drosophila melanogaster* become a cornerstone of global regulatory frameworks, advancing toxicology testing with ethical, standardized, and high-throughput approaches.

9. Conclusion

Drosophila melanogaster is a versatile and cost-efficient model for toxicology research. Its genetics which parallels with that of humans, rapid life cycle, and experimental accessibility make it an indispensable system for investigating toxic effects at molecular and physiological scales. *Drosophila melanogaster* has played a crucial role in studying environmental pollutants, pharmaceutical toxicity, neurotoxicity, and endocrine disruptors, offering key insights into toxicity mechanisms, oxidative stress, and metabolic adaptations. While *Drosophila* presents certain limitations—such as the absence of complex organs like the liver and kidneys, metabolic differences from mammals, and a simplified circulatory system—ongoing advancements in genetic engineering, computational toxicology, and high-throughput screening are expanding its applicability in environmental health and safety. Strengthening its integration with mammalian models will further enhance its translational value in regulatory toxicology.

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Conflict of interest

The authors confirm the absence of any conflicts of interest.

Data availability statement

The data supporting this study's findings can be obtained from the corresponding author upon reasonable request.

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