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Carbendazim toxicity and environmental fate: A critical review of mechanisms, impacts, and future research priorities

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Abstract

Carbendazim (Methyl (1H-1,3-benzimidazol-2-yl)carbamate), a widely used systemic benzimidazole fungicide, represents a significant environmental and toxicological concern due to its persistence in ecosystems and documented reproductive and developmental toxicity. This comprehensive review integrates current knowledge on carbendazim's toxicological mechanisms across multiple biological systems, including mammalian, avian, aquatic, and terrestrial organisms, with particular emphasis on its molecular basis of action through tubulin binding and the consequences of disrupted microtubule dynamics. Critical analysis reveals significant inconsistencies in reported toxicity thresholds across studies, likely attributable to methodological variations, species-specific sensitivity, and impurity profiles in technical-grade formulations. Regarding environmental fate, carbendazim demonstrates moderate persistence in soil (6–12 months half-life) but greater persistence in water systems (2–25 months), with degradation occurring primarily through microbial metabolism and photochemical pathways. This review identifies important knowledge gaps, including incomplete characterization of metabolite toxicity, limited field-based exposure studies, mixture toxicity scenarios, and the potential for bioaccumulation through food chains. Emerging evidence suggests that certain degradation products may exhibit comparable or even greater toxicity than the parent compound, necessitating revised risk assessment protocols. Integration of advanced mechanistic studies with standardized comparative approaches and field-relevant exposure scenarios is essential for developing robust regulatory frameworks and bioremediation strategies. The review underscores the need for urgent re-evaluation of maximum residue limits, particularly in dietary staples in regions with intensive carbendazim application.

Keywords: Carbendazim; Benzimidazole fungicide; Toxicity; Environmental fate; Bioremediation

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1. Introduction

Carbendazim is a systemic benzimidazole fungicide that has been extensively employed in global agriculture for over four decades to control a broad spectrum of fungal diseases, including those caused by *Septoria*, *Fusarium*, and *Sclerotinia* species (Bai et al., 2024). Its primary mechanism of action involves binding to β-tubulin and inhibiting microtubule polymerization. This mode of action makes it effective in both protective and curative applications across a wide range of crop systems, including cereals and ornamental plants (Lu et al., 2004a). The widespread utilization of carbendazim reflects its agronomic efficacy and cost-effectiveness; however, this intensive application pattern has resulted in significant environmental accumulation and persistent contamination of soil, water, and food systems (Zhou et al., 2023).

Global production and use of carbendazim remain substantial across many agricultural regions, particularly in developing countries such as India, China, and several nations in Africa and South America, despite regulatory restrictions in the European Union, the United States, Canada, and Australia (Rama et al., 2014). This regulatory divergence highlights major knowledge gaps and varying international risk assessment frameworks. The presence of more than 20 carbendazim-based fungicide formulations, including both original products and generic variants, further complicates the toxicological profile, as technical-grade active ingredients from different manufacturers often contain distinct impurity profiles that can markedly influence toxicological outcomes (Egorova et al., 2022).

Increasing evidence of carbendazim's harmful effects on non-target organisms and ecosystems has intensified scientific concern (Olaseni et al., 2025). Reported impacts include irreversible male infertility, teratogenicity, embryolethality, mutagenicity, potential carcinogenicity, and endocrine-disrupting activity, issues that warrant thorough scientific evaluation and integration (Sharma et al., 2022). Furthermore, the environmental persistence of carbendazim and its metabolites, combined with potential bioaccumulation through food chains, creates scenarios for chronic human and environmental exposure that warrant comprehensive assessment (Zhou et al., 2023).

This review offers a critical, evidence-driven integration of current knowledge on carbendazim toxicity and environmental fate, drawing on mammalian, avian, aquatic, and terrestrial studies, alongside detailed assessments of both abiotic and biotic degradation pathways. It examines toxicological mechanisms across molecular, cellular, and organismal levels, evaluates inconsistencies within the existing literature, explores possible sources of variation in reported outcomes, and identifies major knowledge gaps that warrant further investigation.

The primary aims of this review are to:

- integrate multidisciplinary evidence on carbendazim toxicity across diverse biological systems and endpoints;
- critically assess and clarify conflicting findings within the published literature;
- provide a comprehensive account of environmental fate and degradation pathways, including metabolite formation;

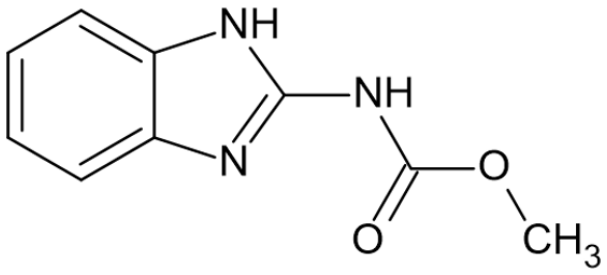

Figure 1: Chemical structure of carbendazim fungicide.

- identify and quantify key uncertainties and unresolved research questions.

2. Carbendazim: Chemical Properties and Mode of Action

2.1. Chemical Structure and Physicochemical Properties

Carbendazim has the molecular formula $C_9H_9N_3O_2$ and a molecular weight of 191.19 g/mol. Its structure contains a benzimidazole ring with a carbamate methyl ester substitution (Figure 1), a configuration that imparts systemic behavior and broad biological activity (PubChem, 2025). Key physicochemical parameters that shape its environmental fate and toxicological profile include an aqueous solubility of approximately 8–10 mg/L at 20 °C; a vapor pressure of 0.5–1.5 $\times$ 10^{-6} Pa at 20 °C, indicating negligible volatilization; an octanol–water partition coefficient (log K_{ow}) of 1.48–1.61, categorizing the compound as moderately lipophilic; and a dissociation constant (pK_a) of 4.2. These attributes collectively determine soil sorption dynamics, mobility in aquatic systems, and potential for biological accumulation. The moderate lipophilicity indicates a capacity for uptake into lipid-rich tissues and possible bioconcentration, although the reported log K_{ow} values imply that its bioaccumulation potential is lower than that of strongly hydrophobic contaminants (PubChem, 2025).

2.2. Mechanism of Toxicity

The primary molecular mechanism of carbendazim toxicity involves its direct interaction with β-tubulin (Figure 2), the core structural component of eukaryotic microtubules (Yenjerla et al., 2009). Carbendazim binds β-tubulin with a dissociation constant (K_d) of approximately 42.8 ± 4.0 μM in mammalian systems, reflecting a moderate binding affinity (Zhou et al., 2016). This interaction occurs at or near the colchicine-binding site and inhibits microtubule polymerization, reducing microtubule dynamic instability by nearly 50% at 10 μM *in vitro* (Zhou et al., 2016). As a result, cells in the S/G_2 phases fail to progress through mitosis, leading to metaphase arrest, accumulation at the G_2/M checkpoint, and eventual apoptotic or necrotic cell death (Zhou et al., 2016).

At the cellular level, the toxic effects arising from carbendazim–tubulin interactions extend well beyond mitotic inhibition. Microtubules constitute essential elements of cellular structure and function, supporting intracellular transport through kinesin- and dynein-mediated motor activity, forming the structural basis of cilia and flagella, contributing to transcriptional regu-

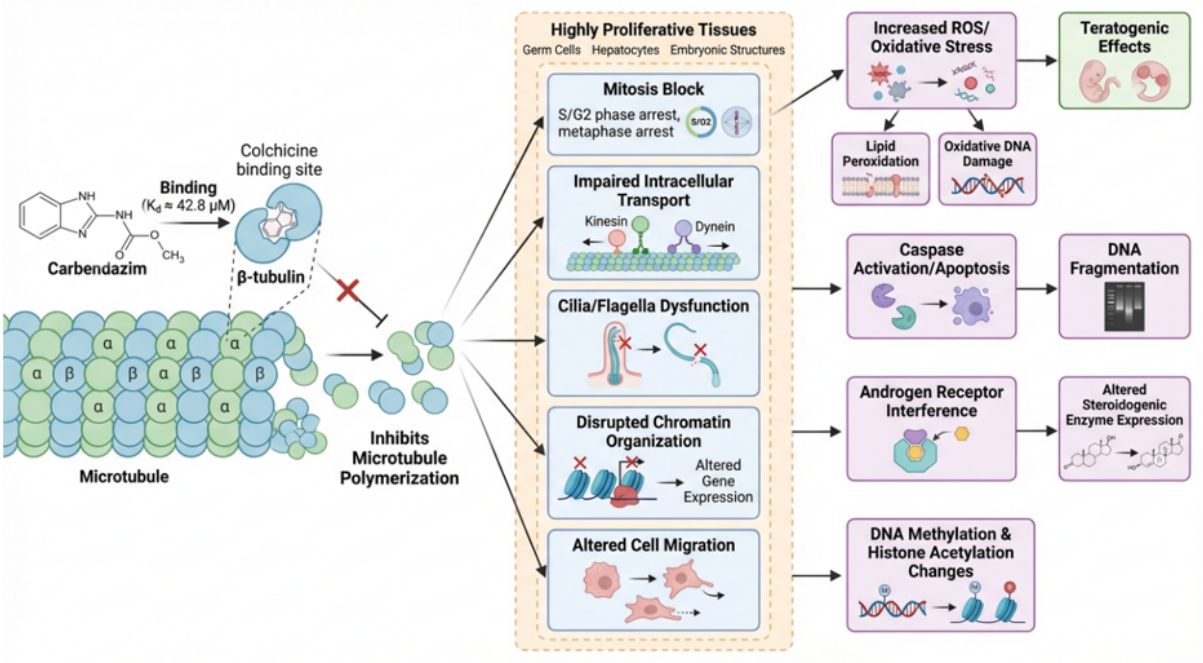

Figure 2: Mechanistic overview of carbendazim toxicity.

lation through chromatin organization, and guiding cell migration and morphogenesis during development (Campion et al., 2012). Disruption of these microtubule-dependent processes by carbendazim interferes with a wide range of cellular functions, with particularly pronounced effects in highly proliferative tissues such as germ cells, hepatocytes, and developing embryonic structures (Correa et al., 2002).

Additional mechanisms of carbendazim toxicity, increasingly supported by recent mechanistic studies, include: (1) the generation of reactive oxygen species (ROS), reflected in elevated lipid peroxidation and oxidative stress biomarkers across multiple cellular and animal models; (2) the induction of apoptosis through caspase activation and associated DNA fragmentation; (3) endocrine-disrupting activity mediated by interactions with androgen receptors and alterations in steroidogenic enzyme expression; and (4) potential epigenetic modifications, including changes in DNA methylation and histone acetylation (Jiang et al., 2015). The oxidative stress pathway appears particularly important in developmental toxicity, as ROS-driven perturbations of developmental gene expression and signaling pathways may contribute to teratogenic outcomes independent of direct microtubule inhibition (Pitchika et al., 2024).

3. Carbendazim Toxicity

3.1. Mammalian Toxicity

3.1.1 Acute, Subchronic, and Chronic Toxicity

Acute oral toxicity studies in rats demonstrate median lethal dose (LD_{50}) values ranging from 1,379 to 1,662 mg/kg body weight, classifying carbendazim as moderately toxic via the oral route (AICIS, 2022). The relatively broad range in reported LD_{50} values likely reflects varia-

tion in technical-grade formulation purity, particularly regarding impurity profiles, which substantially influence acute toxicity outcomes. Intraperitoneal administration yields lower LD_{50} values (200–300 mg/kg), suggesting enhanced bioavailability through this route and supporting a toxicokinetic, rather than intrinsic toxic potency, explanation for route-dependent differences (Selmanoğlu et al., 2001).

Subchronic and chronic toxicity studies identify the liver, kidney, and reproductive organs as primary target tissues. A 28-day dietary study in rats receiving up to 800 mg/kg carbendazim reported hepatic hypertrophy, fatty infiltration, and dose-dependent histopathological changes (Mantovani et al., 1998). Renal effects include tubular dilation, protein accumulation, and in higher-dose regimens, acute tubular necrosis (Mantovani et al., 1998). Notably, these hepatic and renal effects demonstrate dose-dependent reversibility upon cessation of exposure, suggesting functional rather than irreversible organ damage in subchronic scenarios (Mantovani et al., 1998).

Thyroid, adrenal, and testicular tissues also exhibit toxicological sensitivity to chronic carbendazim exposure. Relative weight increases in thyroid and adrenal glands have been documented at doses of 200–400 mg/kg over 56-day periods (Mantovani et al., 1998). Testicular effects—described in detail in Section 3.1.2—represent the most consistent and toxicologically significant finding in mammalian toxicity studies, with documented changes in spermatogenesis evident at doses as low as 25–50 mg/kg in certain experimental protocols (Yu et al., 2009).

Substantial inter-study variability in reported NOAEL (no observed adverse effect level) and LOAEL (lowest observed adverse effect level) values complicates risk characterization. NOAEL values ranging from 10 mg/kg to $>$100 mg/kg have been reported for developmental endpoints depending on species, strain, experimental protocol, and timing of exposure (Iso et al., 2025; Mantovani et al., 1998). This $\sim$10-fold variability likely reflects: (1) species-specific sensitivity differences, particularly between rats, rabbits, and hamsters; (2) methodological variations in dose administration (gavage vs. dietary); (3) genetic differences in metabolic capacity between inbred and outbred strains; and (4) critical window sensitivity during developmental exposure periods. Additionally, technical-grade formulation purity substantially influences NOAEL/LOAEL designations; studies employing analytical-grade carbendazim typically report higher NOAEL values compared to those utilizing technical-grade material containing manufacturing byproducts (Iso et al., 2025).

3.1.2 Reproductive and Developmental Toxicity

Carbendazim exhibits profound reproductive toxicity in male mammals, characterized by dose- and duration-dependent reductions in testis weight, sperm concentration, sperm motility, and fertility (Lu et al., 2004a). Histopathological examination reveals degenerative changes in seminiferous epithelium, including sloughing of germ cells, multinucleate giant cells, Sertoli cell damage, and altered spermatogenic cell populations (Kadalmani et al., 2002; Nakai et al., 2002; Nakai and Hess, 1994). Crucially, these changes demonstrate reversibility upon cessation of exposure, though extended exposure periods may result in partially irreversible changes to testicular tissue (Nakai et al., 2002; Nakai and Hess, 1994).

The mechanism of carbendazim-induced male reproductive toxicity involves complex interactions with androgen signaling pathways. Seminal studies demonstrated that pretreatment with flutamide, an androgen receptor antagonist, completely prevented reproductive and developmental toxicity induced by carbendazim, despite carbendazim not directly agonizing androgen receptors (Lu et al., 2004a). Subsequent mechanistic investigations revealed that carbendazim induces dose-dependent increases in androgen receptor concentration in testis and epididymis, and competes for androgen receptor binding *in vitro* with nanomolar affinity, exhibiting androgenic rather than antiandrogenic properties (Lu et al., 2004a). This paradoxical androgenic activity from a compound that produces reproductive toxicity highlights the complexity of endocrine mechanisms; excessive androgenic signaling may overwhelm normal feedback regulation and developmental processes, producing pathological outcomes (Lu et al., 2004a).

Developmental toxicity from prenatal carbendazim exposure manifests distinctly in male versus female offspring. Pregnant rats exposed to 200 mg/kg carbendazim during the critical period of urogenital differentiation (gestational days 0–20) produce male offspring exhibiting testicular and epididymal atrophy (Hsu et al., 2011). Female offspring from similarly exposed dams display marked developmental defects including incomplete uterine horn development, enlargement of the urethra, absence of vagina, and inappropriate induction of seminal vesicles, phenomena collectively indicating altered sexually dimorphic development with an androgen-dependent shift toward male phenotypic characteristics (Hsu et al., 2011). These effects appear specific to high-dose, brief exposure regimens; chronic, lower-dose prenatal exposure may produce subtler alterations to reproductive tract development (Lu et al., 2006).

Postnatal developmental toxicity encompasses broader phenotypic alterations. Early postnatal survival is reduced, with significant mortality documented on postnatal days 1 and 21 following prenatal maternal exposure (Lu et al., 2006). Growth retardation, delayed sexual maturation, and persistent alterations to hypothalamic–pituitary–testicular (HPT) axis function have been documented in offspring from prenatally exposed dams (Lu et al., 2006). The involvement of HPT axis disruption suggests mechanisms extending beyond local gonadal effects to include central nervous system endocrine regulation, a critical consideration in interpreting developmental toxicity effects.

A notable inconsistency in the reproductive toxicity literature concerns the apparent dose–relationship between acute, high-dose exposures and chronic, lower-dose exposures. High-dose, brief exposure (single dose or 28-day regimen) at 200–400 mg/kg produces severe reproductive effects including irreversible male infertility and marked teratogenicity (Lu et al., 2004a). However, certain dietary studies at lower doses (25–50 mg/kg/day for 56 days) also produce histopathological testicular changes yet demonstrate reversibility (Lu et al., 2006). A critical interpretation is that teratogenic effects appear dose- and timing-dependent, with sensitive developmental windows during urogenital differentiation particularly critical, whereas postnatally acquired toxicity demonstrates greater reversibility. Additionally, inconsistencies between prenatal and postnatal exposure studies may reflect differing susceptibility windows and developmental plasticity; prenatal exposure during critical differentiative periods produces irreversible phenotypic changes, whereas postnatal functional toxicity may be more reversible

if the fundamental developmental framework is established.

3.1.3 Genotoxicity and Carcinogenicity

Carbendazim exhibits genotoxic potential through multiple endpoints. The Ames bacterial mutagenicity test shows contradictory results; analytical-grade carbendazim exhibits no mutagenic activity in *Salmonella typhimurium* strains with or without metabolic activation (Egorova et al., 2022), whereas technical-grade formulations demonstrate pronounced mutagenic effects, particularly in TA98 strain (Egorova et al., 2022). This critical discrepancy indicates that impurities in technical-grade formulations, rather than carbendazim itself, may constitute the primary genotoxic hazard (Egorova et al., 2022).

Mammalian *in vivo* genotoxicity testing reveals clear evidence of clastogenic and aneugenic activity. The micronucleus assay in CD-1 mice demonstrates dose-dependent increases in micronuclei frequency in bone marrow erythrocytes (Egorova et al., 2022; Sarrif et al., 1994), a marker of chromosomal aberrations and aneuploidy. The mechanism appears directly linked to tubulin binding—disruption of microtubule dynamics during mitosis impairs proper chromosome segregation, producing numerical and structural chromosome abnormalities (Egorova et al., 2022).

Regarding carcinogenicity, the epidemiological and experimental evidence presents a complex, partially contradictory picture. Early EPA classification (1989) designated carbendazim as a possible human carcinogen (Group C) (McCarroll, 2002). This classification was based primarily on hepatic tumor development in CD-1 and Swiss mice exposed to high-dose carbendazim (approximately 800–1,000 mg/kg/day)—doses substantially exceeding occupational exposure scenarios (Mo et al., 2022; Zhang et al., 2023). However, recent experimental carcinogenicity studies in CBA mice strain, considering impurity profiles, failed to demonstrate statistically significant increases in tumor incidence compared to controls, with spontaneous tumor incidence appearing within normal ranges for the strain (Nguyen et al., 2025). These contradictory findings suggest that: (1) tumor induction may be strain-specific, with certain inbred lines exhibiting exaggerated response compared to others; (2) technical-grade formulation quality may influence tumorigenicity; and (3) dose–response relationships may demonstrate non-linear characteristics with tumor induction only above certain threshold exposures.

3.2. Avian Toxicity

Limited but significant evidence indicates reproductive and developmental toxicity in avian systems. A study examining carbendazim effects in Japanese quail (*Coturnix coturnix japonica*) magnum (reproductive tract) documented severe degenerative changes in luminal and glandular epithelial cells including pyknotic nuclei, dilated endoplasmic reticulum, swollen mitochondria, and abundant vacuoles and lysosomes (Kimaro et al., 2013). These morphological alterations, attributed to cytoskeletal disruption from carbendazim toxicity, posed potential threats to reproductive function and egg production (Kimaro et al., 2013). The conserved mechanism across avian and mammalian systems, tubulin-mediated disruption of cell division and cellular architecture, suggests that avian species represent relevant indicators of carbendazim hazard,

yet this remains an understudied compartment.

3.3. Aquatic Toxicity: Fish and Invertebrates

3.3.1 Fish Toxicity

Acute toxicity studies in fish reveal species- and endpoint-dependent variation. Early LC_{50} (lethal concentration for 50% of population) values for rainbow trout (*Oncorhynchus mykiss*) were reported as 370 μg/L (Cuppen et al., 2000), while acute toxicity to other fish species demonstrated greater resistance, with LC_{50} values in the range of 1–5 mg/L (Cuppen et al., 2000). This heterogeneity likely reflects differences in water chemistry, temperature, fish size, and acclimation status.

Chronic exposure studies in food-fish species are limited but revealing. A recent study examining *Channa striata* (snakehead fish) exposed to carbendazim concentrations of 1.05 and 1.10 μg/L (5% and 10% above permissible limits) for 96 hours documented significant hematological changes including dose-dependent reduction in red blood cell count, hemoglobin level, and packed cell volume, coupled with increased white blood cell count and poikilocytosis (Dubey and Kumar, 2025). Genotoxicity, assessed via micronucleus assay, showed significant increases in micronuclei frequency, indicating DNA damage (Dubey and Kumar, 2025). Histopathological examination revealed degenerative changes in liver, kidney, and muscle tissues (Dubey and Kumar, 2025). Behavioral alterations included hyperactivity, gulping (indicative of respiratory distress), abnormal skin pigmentation, and excessive mucus secretion (Dubey and Kumar, 2025).

The marked sensitivity of certain fish species to carbendazim, particularly at concentrations only marginally above regulatory permissible limits (1.0 μg/L), indicates inadequate safety margins in current standards. The occurrence of genotoxic effects at these ecologically relevant concentrations suggests that standard acute LC_{50}-based risk quotients may substantially underestimate environmental hazard. The apparent disconnect between acute LC_{50} values (μg/L to mg/L range) and chronic genotoxic/histopathological effects (single μg/L range) indicates that standard toxicity testing protocols may fail to capture sensitive sublethal and chronic endpoints relevant to ecosystem protection (Dubey and Kumar, 2025).

3.3.2 Aquatic Invertebrate Toxicity

Daphnia magna, a keystone freshwater invertebrate, exhibits toxicological sensitivity to carbendazim. Traditional acute immobilization tests report 48-h EC_{50} (median effective concentration) values of approximately 460 μg/L (Silva et al., 2023), indicating moderate acute toxicity. However, recent multigenerational studies reveal substantially greater concern. Exposure to ecologically relevant concentrations (5 μg/L) across 12 generations induced genome-wide transcriptional alterations, with differential expression patterns in genes involved in reproductive physiology, defense mechanisms, and stress response pathways (Silva et al., 2023). Notably, this concentration (5 μg/L) represents the NOEC for reproduction in *Daphnia* (Silva et al., 2023).

Mechanistically, carbendazim disrupts tubulin polymerization in *Daphnia* cells, impairing microtubule-dependent processes including oogenesis, embryogenesis, and molting (Silva et al., 2023). The multigenerational character of observed effects suggests that: (1) carbendazim disrupts epigenetic programming across generations; (2) chronic low-dose exposure produces cumulative cellular damage; or (3) adaptive responses to carbendazim stress are genomically encoded but only partially protective (Silva et al., 2023).

A critically important observation involves synergistic toxicity in binary mixtures. When carbendazim was combined with other pesticides, DNA damage assessments revealed synergistic rather than additive effects, principally in *Daphnia* but with implications for field scenarios where pesticide mixtures are routinely encountered (Silva et al., 2015).

The aquatic invertebrate toxicity data reveal a substantial disconnect between acute lethality-based endpoints and chronic, sublethal endpoints. The relevance of chronic, low-dose exposure at concentrations documented in environmental monitoring (5–30 μg/L in contaminated surface waters) to *Daphnia* populations warrants serious consideration; reproductive disruption and genomic stress may produce population-level consequences that exceed those predicted from acute LC_{50} values. Furthermore, the documented synergistic toxicity with co-occurring pesticides indicates that risk assessment based on single-chemical toxicity substantially underestimates environmental hazard in realistic agricultural scenarios.

3.4. Terrestrial Toxicity: Soil Organisms

Carbendazim exhibits high acute toxicity to earthworms, with 14-day LC_{50} values of approximately 8.6 mg/kg dry soil in *Eisenia fetida* (Huan et al., 2016). This classification as "highly toxic" to earthworms reflects the fundamental mechanism of carbendazim toxicity; earthworms depend critically on microtubule dynamics for neuromotor function, cell division in growth tissues, and reproductive processes. Field-scale surveys document that carbendazim application at agricultural rates produces earthworm population declines persisting for weeks to months post-application (Huan et al., 2016).

Carbendazim also alters soil microbial community structure and function. Exposure to carbendazim suppresses microbial biomass, reduces enzyme activity (particularly cellulase and phosphatase), and produces shifts in bacterial community composition toward more carbendazim-tolerant genera including *Pseudomonas* and *Bacillus* (Chauhan et al., 2023). These ecotoxicological changes to soil communities potentially disrupt nutrient cycling, decomposition processes, and soil structure maintenance—ecosystem services critical to agricultural productivity and environmental quality (Chauhan et al., 2023).

4. Environmental Fate and Degradation Pathways

4.1. Environmental Occurrence and Distribution

Carbendazim has been widely detected across diverse environmental compartments worldwide. Surface waters in agricultural regions show concentrations ranging from 0.01 μg/L in minimally contaminated systems to 214 ng/L in heavily agricultural areas; urban streams in the

Brazilian Amazon documented mean concentrations of 214 ng/L in 80% of samples tested (Rico et al., 2022). Groundwater in agricultural regions similarly shows contamination; European monitoring documented detectability in groundwater at various sites (Acayaba et al., 2021). Soil samples from intensively cultivated regions contain carbendazim residues at concentrations up to 0.5–1.0 mg/kg in heavily treated fields (Mu et al., 2023). Foodstuff monitoring, particularly in China and India where carbendazim application restrictions are minimal, documents persistent residues in cereals, vegetables, and other staple crops, with concentrations in certain samples approaching or exceeding maximum residue limits (Bhandari et al., 2019; Wang et al., 2024).

A particularly concerning finding involves detection of carbendazim in household dust and drainage systems in urban areas, indicating non-occupational, diffuse exposure pathways (Wang et al., 2019). This finding implies that dietary and non-dietary exposure routes may collectively constitute substantial population exposure in regions with intensive carbendazim application.

4.2. Abiotic Degradation Pathways

4.2.1 Hydrolysis

Carbendazim hydrolysis in aqueous solution proceeds via pH-dependent mechanisms. The documented half-life for hydrolysis at neutral pH ranges from 25 weeks to 6 months, representing moderate chemical stability (Boudina et al., 2003). At elevated temperatures, hydrolytic degradation increases; this thermal dependence suggests potentially higher degradation rates in tropical agricultural regions. The primary hydrolytic product is 2-aminobenzimidazole (2-AB), formed through ester cleavage and loss of methanol (Boudina et al., 2003).

The physicochemical properties and toxicological potential of 2-AB warrant particular attention. Early literature suggested that 2-AB represented a benign degradation product; however, recent investigations reveal that 2-AB retains toxicological activity and demonstrates persistence comparable to, or exceeding, carbendazim in certain aquatic environments (Thiaré et al., 2015). This represents a critical knowledge gap with regulatory implications, as risk assessments have typically focused on the parent compound carbendazim, potentially underestimating total hazard arising from its degradation products.

4.2.2 Photodegradation

Carbendazim undergoes pH- and dissolved oxygen-dependent photochemical degradation in aqueous solution, with documented half-lives for photolysis ranging from 42 to 175 days depending on light intensity, wavelength, and water chemistry (Boudina et al., 2003). Under simulated sunlight (290–490 nm), carbendazim remains stable for 166 hours under sterile, neutral pH conditions (Boudina et al., 2003). The relatively slow photochemical degradation rate implies that carbendazim contamination in aquatic environments represents a persistent photochemical target.

The primary photodegradation product identified is 2-aminobenzimidazole (2-AB), although additional minor photoproducts, including hydroxylated derivatives, have been characterized

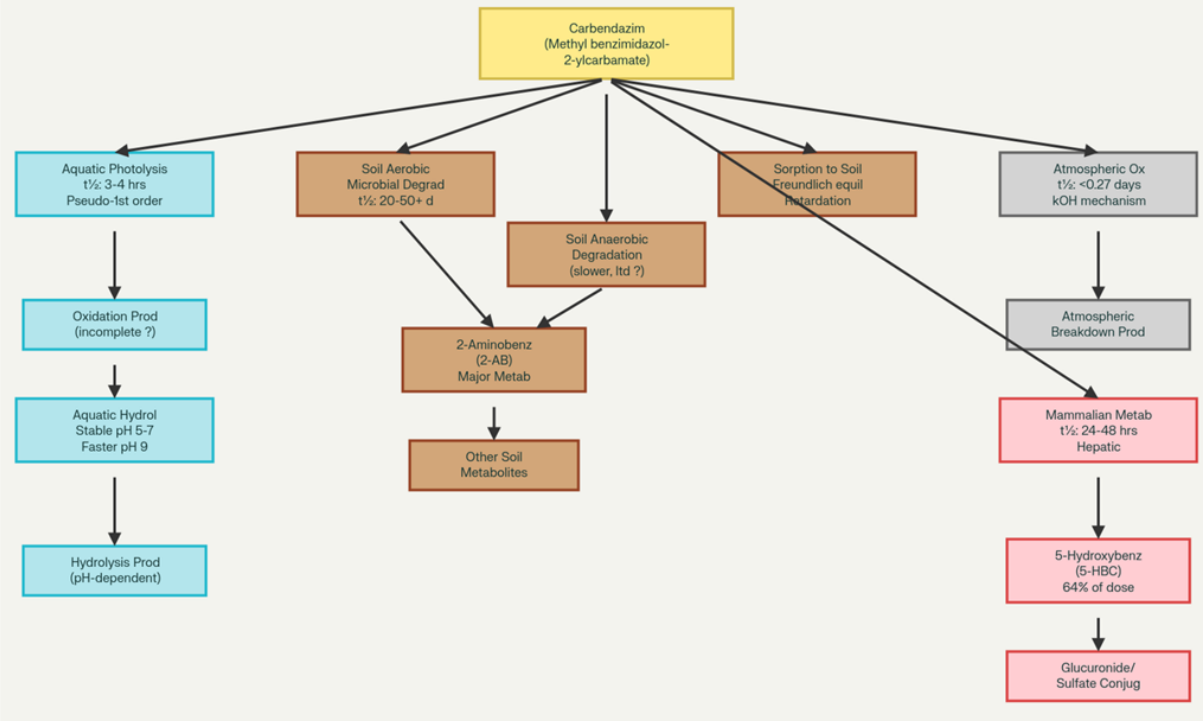

Figure 3: Carbendazim degradation pathways in flowchart.

(Boudina et al., 2003). Photochemical degradation pathways appear to proceed via hydroxyl radical-mediated oxidation mechanisms following photogeneration of reactive species. Critically, photodegradation rates decrease substantially in natural waters with high dissolved organic carbon content, indicating that humic substances may physically shield carbendazim from photochemical transformation (Boudina et al., 2003).

Photodegradation is associated with reduced overall toxicity; photoproducts exhibit diminished phytotoxicity and acute toxicity relative to the parent compound in certain bioassays (Jornet et al., 2013). However, this observation does not guarantee overall risk reduction, as the persistence and toxicological properties of 2-AB remain incompletely understood.

4.2.3 Atmospheric Degradation

The atmospheric half-life of carbendazim is extremely short, approximately < 0.27 days, due to rapid reactions with atmospheric hydroxyl radicals, with a rate constant $k_{\mathrm{OH}} > 60 \times 10^{-12}$ cm^3 molecule^{-1} s^{-1} (Mazellier et al., 2003). This suggests that volatilized carbendazim is rapidly oxidized in the atmosphere, producing secondary organic products. However, the agricultural use pattern of carbendazim (soil and foliar application rather than intended volatilization) indicates that atmospheric degradation represents a minor pathway in the overall environmental fate budget.

4.3. Biotic Degradation: Soil and Aquatic Systems

4.3.1 Microbial Degradation Mechanisms

Microbial degradation represents the predominant environmental transformation pathway for carbendazim under natural conditions (Figure 3). Multiple bacterial genera possess carbendazim-degrading capacity, including *Bacillus*, *Pseudomonas*, *Rhodococcus*, *Sphingomonas*, and *Aeromonas* (Zhou et al., 2024). Different bacterial isolates from soil and aquatic environments exhibited varied carbendazim-degrading efficiencies, as summarized in Table 1.

Table 1: Bacterial species examined under different experimental conditions and their corresponding carbendazim degradation efficiencies

Bacterial species	Experimental condition	Degradation efficiency
Klebsiella oxytoca (wild strain)	MSM supplemented with 30 mg/L carbendazim	Growth and degradation observed (Alvarado-Gutiérrez et al., 2020)
Flavobacterium johnsoniae	Same as above	Growth and degradation observed (Alvarado-Gutiérrez et al., 2020)
Stenotrophomonas maltophilia	Same as above	Growth and degradation observed (Alvarado-Gutiérrez et al., 2020)
Rhodococcus sp. D-1	MS medium; carbendazim (50 ppm), 200 rpm, 30 °C	97.33% degradation within 2 days (Bai et al., 2017)
Achromobacter sp. GB61	M9 MS media supplemented with 100 mg/L carbendazim	76.2% degradation (optimized conditions) (Bhandari et al., 2022)
Rhodococcus qingshengii djl-6	500 mg/L carbendazim in soil sample	93% degradation within 14 days (Chuang et al., 2021)
Pseudomonas sp. CBW	MS medium + 1.0 and 10 mg/L carbendazim; 30 °C, 150 rpm	87.1% (1 mg/L) and 99.1% (10 mg/L) degradation after 3 days (Fang et al., 2010)
Rhodococcus sp. djl-6	M9 medium supplemented with 100 mg/L carbendazim	55.56% degradation in one day (Jing-Liang et al., 2006)
Pseudomonas sp. CT-VT7	MM + 200 mg/L carbendazim; 200 rpm, 6 days	Approximately 90% degradation after 6 days (Le et al., 2017)
Rhodococcus jialingiae djl-6-2	100 mg/L carbendazim; 30 °C, 160 rpm	94% degradation within 60 h (Wang et al., 2010)
Rhodococcus sp. CX-1	MSM supplemented with 100 mg/L carbendazim	9.54% degradation within 1 h (Long et al., 2021)

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Bacterial species	Experimental condition	Degradation efficiency
Bacillus subtilis	MS media supplemented with 10 µg/mL carbendazim	75.7–95.2% degradation after 15 days (Salunkhe et al., 2014)
Mycobacterium sp. SD-4	MSM supplemented with 50 mg/L carbendazim	90% degradation within 72 h (Zhang et al., 2017)
Nocardioides sp. SG-4G	MSM supplemented with 40 µM carbendazim	Complete degradation within 5 h (Pandey et al., 2010)
Brevibacillus sp. C17	MS media supplemented with 100 mg/L carbendazim	87.25% degradation within 36 h (Kanjilal et al., 2018)
Achromobacter sp. GB61	Minimal broth, soil and soil slurry systems	Up to 81.98% (broth), 83.2% (soil), 86% (slurry) degradation (Negi et al., 2014)
Bacillus licheniformis JTC-3	MS media supplemented with 10 mg/L carbendazim	73.2% degradation within 24 h (Panda et al., 2017)
Pseudomonas putida djl-1B	Applied to spinach, celery, and rape crops	CBZ half-lives: 30.53 h (celery), 25.11 h (spinach), 22.75 h (rape) (Ye, 2015)
Bacillus pumilus NY97-1	MS medium + 10–300 mg/L carbendazim	Up to 90.07% degradation at 300 mg/L (Zhang et al., 2009)
Stenotrophomonas sp.	MS medium + 250 µg/mL carbendazim; 21 days	68.9% degradation (Santos et al., 2017)
Chryseobacterium sp. JAS14	MSM / soil + 200 mg/L carbendazim	Complete degradation within 4–9 days (Silambarasan and Abraham, 2020)
Aeromonas caviae JAS15	MSM / soil + 200 mg/L carbendazim	Complete degradation within 4–9 days (Silambarasan and Abraham, 2020)
Streptomyces sp. (CB1)	Minimal salts medium + 1000 mg/L carbendazim	$59.04 \pm 3.86\%$ degradation in 7 days (Singh et al., 2019)
Bacillus subtilis (CB2)	Same as above	$65.69 \pm 2.82\%$ degradation in 7 days (Singh et al., 2019)
Pseudomonas aeruginosa (CB3)	Same as above	$73.73 \pm 6.10\%$ degradation in 7 days (Singh et al., 2019)
Rhizobium leguminosarum (CB4)	Same as above	$55.44 \pm 1.76\%$ degradation in 7 days (Singh et al., 2019)

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Bacterial species	Experimental condition	Degradation efficiency
Bacillus subtilis subsp. *stercoris* (KACC 15590)	M9 minimal medium + 250 mg/L carbendazim	Negligible degradation (Song and Hwang, 2024)
Bacillus velezensis HY-3479	M9 minimal medium + 250 mg/L carbendazim	76.99% degradation at 48 h (Song and Hwang, 2024)
Ralstonia sp. (strain 1-1)	CBZ medium with and without yeast extract	19.16% degradation without yeast extract; 95.96% with yeast extract (Zhang et al., 2005)
Rhodococcus erythropolis djl-11	MSM containing 1000 mg/L carbendazim	Complete mineralization within 72 h (Zhang et al., 2013)

Final degradation products and toxicity

The primary breakdown products of carbendazim identified in the sources are 2-aminobenzimidazole (2-AB) and 2-hydroxybenzimidazole (2-HB) (X. Zhang et al., 2013). Shit et al. (2025) also stated that 2-HB further degraded into 1,2-diaminobenzene then catechol and these products are further mineralized to non-toxic end products like CO_2 and H_2O, the intermediate toxicity of 2-AB and 2-HB is a concern. Zhou et al. (2023) mention that 2-AB is a highly toxic substance that could inhibit cell proliferation. However, Panda et al. (2017) reported that 2-hydroxybenzimidazole, the metabolic end-product in their study, showed no zone of inhibition in toxicity tests, suggesting it was non-toxic. Silambarasan and Abraham (2020) found that phytotoxicity and cytogenotoxicity of carbendazim were reduced after biodegradation, indicating a detoxification process. Therefore, while the initial breakdown products may still possess some level of toxicity, the overall process of microbial degradation aims to reduce the environmental impact by eventually mineralizing carbendazim into less harmful substances.

4.3.2 Environmental Persistence: Soil Systems

Soil persistence of carbendazim exhibits substantial variability, with reported half-lives ranging from 6 to 12 months in bare soil under temperate conditions (Singh et al., 2016). This variability reflects: (1) soil physicochemical properties (pH, organic matter content, soil type); (2) microbial community composition and biomass; (3) environmental temperature and moisture regimes; (4) co-application with other pesticides that may inhibit or promote microbial degradation; and (5) initial carbendazim concentration and application method.

Soil adsorption characteristics influence bioavailability and persistence. Carbendazim exhibits moderate to low soil adsorption, with documented Freundlich adsorption coefficient values varying substantially across soil types (Muhamad et al., 2011). The moderately mobile nature of carbendazim indicates potential for downward leaching into groundwater, particularly in soils with low organic matter and in coarse-textured (sandy) soils. Soil pH influences both adsorption and degradation; acidic soils demonstrate enhanced carbendazim persistence, while neutral to alkaline soils show enhanced microbial degradation (Muhamad et al., 2011).

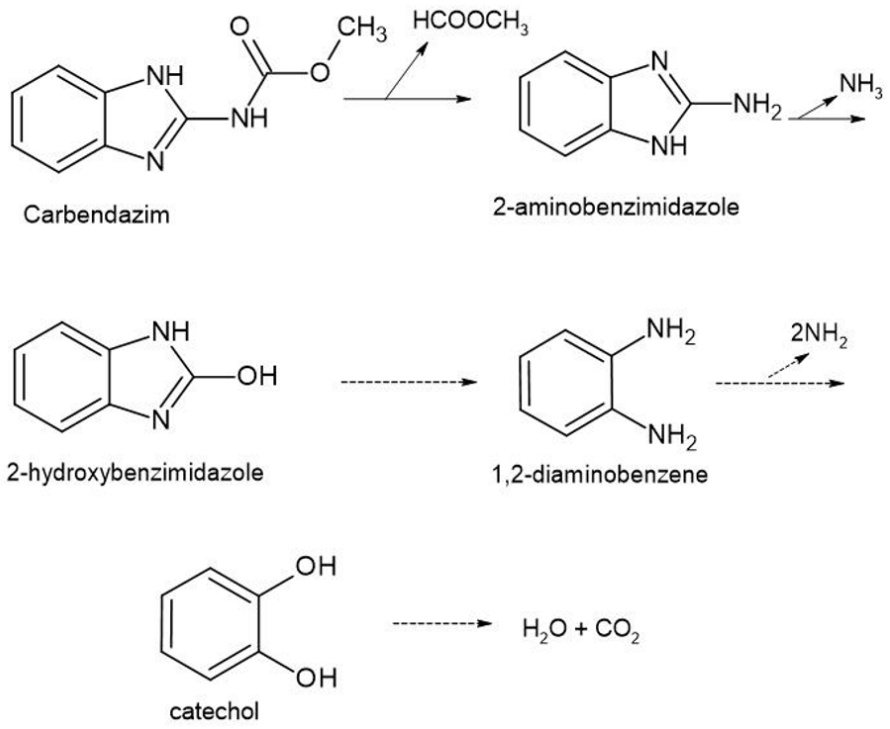

Figure 4: Proposed degradation pathway of carbendazim.

4.3.3 Environmental Persistence: Aquatic Systems

Aquatic persistence of carbendazim exceeds terrestrial persistence substantially, with half-lives of 2–25 months documented in various aquatic systems (Cuppen et al., 2000). This extended aquatic half-life reflects: (1) reduced microbial degradation capacity compared to soil systems (aquatic microbial communities are often less adapted to pesticide degradation than soil communities); (2) reduced photochemical degradation due to water column shading and dissolved organic matter; (3) sorption to suspended particulates and sediments reducing bioavailability to microorganisms; and (4) lower temperature in deep water bodies reducing metabolic rates (Cuppen et al., 2000).

5. Knowledge Gaps, Uncertainties, and Critical Research Needs

5.1. Mechanistic and Exposure Gaps

Despite existing knowledge on carbendazim's toxicity, significant gaps remain in understanding its underlying mechanisms and long-term effects. Emerging evidence points to epigenetic alterations, specifically DNA methylation and histone modifications, contributing to developmental issues (Sharma et al., 2022). However, the reversibility, heritability, and transgenerational impact of these changes are largely uncharacterized, posing critical regulatory challenges. Furthermore, carbendazim's neurotoxic and immunotoxic effects are substantially understudied, with current research focusing primarily on reproductive and liver toxicity (Lu et al., 2004b; Ma et al., 2023). Crucially, the consequences of chronic, low-dose exposure, which better re-

flects real-world scenarios, remain largely unknown, particularly concerning bioaccumulation, delayed adverse outcomes, critical developmental vulnerabilities, and dose–response relationships.

5.2. Inconsistencies and Understudied Areas

Inconsistencies in toxicological data complicate hazard assessment. A notable discrepancy exists between the genotoxicity of carbendazim's analytical standard and its technical-grade formulation. This suggests that manufacturing impurities, rather than carbendazim itself, may be responsible for genotoxic effects, implying that quality improvements could mitigate this risk. Discrepancies in carcinogenicity across different mouse strains point to species-specific metabolic differences and genetic predispositions, indicating that carbendazim's carcinogenic potential might not be a universal mammalian property. Additionally, research on carbendazim's toxicity in amphibians, reptiles, soil microorganisms, and sediment-dwelling organisms is sparse. The environmental impact of carbendazim's mixtures with other pesticides is also poorly understood, with early findings suggesting synergistic toxicities that could lead to an underestimation of risks in current assessments. Finally, while bioremediation strategies are being explored, their field-scale efficacy, long-term sustainability, and cost-effectiveness require further investigation, alongside the validation of novel physical and chemical remediation methods.

5.3. Critical Research Needs

Systems-Level Mechanistic Toxicology Beyond Classical Targets: Future research must move beyond tubulin-binding paradigms by integrating multi-omics approaches (transcriptomics, metabolomics, epigenomics) across tissues, life stages, and exposure durations. Such systems-level studies are essential to uncover novel toxicity pathways, identify sensitive biological networks, and define critical windows of susceptibility that are currently invisible to conventional toxicological frameworks.

Epigenetic and Transgenerational Risk Characterization: A major unresolved gap lies in understanding whether carbendazim induces heritable epigenetic alterations. Rigorous investigation of DNA methylation, histone modification, and chromatin remodeling—and their persistence across generations—is crucial to redefine developmental and reproductive risk, particularly under low-dose and chronic exposure scenarios.

Comprehensive Metabolite Profiling and Toxicity Integration: Risk assessment remains incomplete without systematic structural and toxicological characterization of all major degradation products. Priority should be given to intermediate metabolites with environmental persistence. Establishing structure–activity relationships and incorporating metabolite toxicity into hazard quotients will significantly strengthen regulatory realism and environmental relevance.

Field-Realistic Exposure and Mixture Toxicity Studies: Laboratory toxicity data must be aligned with environmental reality through field-relevant exposure assessments, including chemical mixtures, spray drift, runoff, and dietary pathways. Research focusing on commonly co-applied agrochemicals and food-chain transfer will substantially improve ecological and

human health risk extrapolation.

6. Conclusion

Carbendazim presents an ongoing ecotoxicological enigma, characterized by an incompletely defined hazard profile that extends beyond the parent compound to its suite of transformation products and metabolites. While the primary mechanism of action, microtubule disruption via β-tubulin binding, is conserved across taxa, secondary pathways involving oxidative stress and endocrine disruption through androgen receptor antagonism introduce significant complexity to hazard characterization and risk assessment frameworks. Environmental fate studies underscore concern, revealing greater persistence in aquatic ecosystems (half-life of 2–25 months) compared to terrestrial environments (6–12 months), fostering chronic exposure scenarios likely underestimated by current regulatory paradigms. The formation of degradation products, particularly 2-aminobenzimidazole (2-AB) and 2-hydroxybenzimidazole (2-HB), represents a critical knowledge deficit, as risk assessments predominantly focus on the parent compound, potentially overlooking cumulative or synergistic toxicities.

Inconsistencies in toxicological data, notably genotoxicity and carcinogenicity discrepancies between analytical standards and technical-grade carbendazim, alongside strain-dependent carcinogenicity variations, suggest that impurity profiles and methodological heterogeneity significantly influence reported endpoints. These uncertainties highlight the potential for hazard mitigation through refined manufacturing processes. The synergistic toxicity observed in pesticide mixtures further amplifies environmental risks, indicating that single-chemical assessments inadequately reflect realistic agricultural exposures. The dearth of field-based, chronic low-dose exposure studies critically limits our understanding of long-term environmental consequences. Divergent global regulatory approaches reflect both philosophical differences and disparities in accessing robust mechanistic toxicological information, necessitating a harmonized, evidence-driven approach. Future research imperatives include comprehensive degradation product characterization, standardized international testing, realistic field exposure assessments, investigation of epigenetic and neurotoxicological endpoints, and the development and validation of *in situ* remediation technologies. The substantial remaining knowledge gaps strongly support stringent regulatory actions, emphasizing the need for precautionary measures and accelerated research to safeguard ecological integrity.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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