

A Review of the Toxicity and Effects of Mancozeb, an Ethylene Bis (dithiocarbamate) Fungicide, on Fish Species

Chijioke Francis^{1*}, Lemuel Angyunwe Samuel¹, Egbuji Jude Victor Ifeanyi², Okolie Vincent Onyinyechi Dominion¹

¹National Biotechnology Research and Development Agency, Arochuku, Abia State, Nigeria

²Caritas University Amorji Nike, Emene, Enugu, Enugu State, Nigeria

*Corresponding author. E-mail: francischijiokepapa@yahoo.com; Phone: +234-8034948912

Received: 28 February 2025 [] Published: 19 March 2025

Mancozeb is widely utilized in Nigeria and globally. It is used to control and eradicate various fungal diseases on agricultural crops such as fruits, vegetables, and cereals. Mancozeb is moderately to highly toxic to fish and non-target organisms. The objective of this literature review is to document the toxicity and effects of Mancozeb, an Ethylene Bis(dithiocarbamate) Fungicide, on Fish Species. Fifteen laboratory studies and two modeling studies were reviewed from literature in which fifteen different Fish Species were investigated. Acute concentration of Mancozeb results in mortality (96 h LC₅₀) while sub-lethal concentration induces multiple lethal changes such as behavioral alteration, haematological (RBCs, WBCs, or plasma), histopathological (kidney, liver, gills, spleen), oxidative stress biomarkers (catalase, glutathione reductase, superoxide dismutase, etc.), genotoxicity, and biochemical parameters (protein, lipids, carbohydrates, moisture content, and ash, etc.). Mancozeb is hydrophobic in nature, but its metabolite ethylenethiourea has the abundant capacity to contaminate groundwater. Continuous misuse of fungicides can enter the aquatic ecosystem and result in harmful effects. Therefore, the use of bio-pesticides should be implemented and encouraged among farmers, especially those residing close to water bodies, to reduce the detrimental effects of fungicides on aquatic fauna and flora. Researchers worldwide should investigate the harmful effects of Mancozeb on several Fish Species and their environment.

Introduction

In recent years, the high rate of increase in human population and the rapid pace of industrialization have created significant pesticide-related problems, particularly in the disposal of wastewaters (Sexana, 2025). Mancozeb, a synthetic ethylene bis(dithiocarbamate) fungicide, belongs to the subclass of carbamate fungicides (Thiruchelvam, 2005; Srivastava and Singh, 2014). It is widely applied to agricultural crops such as vegetables, cereals, and fruits to control and eradicate fungal diseases (Cycon et al., 2010; Paro et al., 2012).

The chemical structure of Mancozeb involves dithiocarbamate groups (–N–C(=S)–S–) (Engels et al., 2011; PubChem, 2021). It is marketed under various trade names, including Manzate®[®], Dithane®[®], Penncozeb®[®], Fore®[®], Roper®[®], and Z-force, both in Nigeria and globally. Mancozeb is a mixture of two compounds with active ingredients, Maneb (manganese) and Zinc, at a ratio of 2:1, respectively (Morgan, 1982; Hayes and Laws, 1991; Thiruchelvam, 2005). It is produced in several forms, such as liquids, dust, wettable powders, water-dispersible granules, and ready-to-use formulations (Thiruchelvam, 2005).

Mancozeb is classified as a contact or broad-spectrum fungicide with preventive activity characteristics and is one of the most widely used agrochemicals on a global scale (Goldoni and Silvia, 2012). Among pesticides, fungicides, insecticides, and herbicides are the most statistically used (Sharma et al., 2019; Maino et al., 2023). However, Mancozeb poses significant toxicological health hazards to animals and humans, including reproductive toxicity, carcinogenicity, and neurotoxicity (Abdelkader et al., 2023). Pesticides like Mancozeb can accumulate in fish and affect human health through bioaccumulation in the food chain (Kamlesh et al., 2024). Concentrations of Mancozeb up to approximately 1.30 µg/L have been detected in aquatic systems (Flores-García et al., 2011).

Exposure of *Clarias gariepinus* juveniles to Mancozeb has been shown to cause histopathological changes (Chijioke et al., 2024), haematological alterations (Francis et al., 2023), and oxidative stress-related changes (Odo et al., 2023). Mancozeb, with a 96 h LC₅₀ value of 410.90 mg/L, is moderately to highly toxic to *Clarias gariepinus* juveniles and should be used with caution (Chijioke et al., 2024). Ecotoxicological investigations are necessary to determine the toxicity and potential risks of such chemicals using various biomarkers in fish to monitor the

Table 1 Results of various toxicity investigations of Mancozeb on Fish Species, identified by literature search

Mancozeb Assay (Acute Toxicity)	Fish Species	Result	References
96 h LC50	<i>Puntius ticto</i>	12.95 mg/L	Sharma et al. (2016)
96 h LC50	<i>Cyprinus carpio</i> Juveniles	8.03 mg/L	Simakani et al. (2018)
96 h LC50	<i>Oreochromis mossambicus</i>	11.68 mg/L	Saha et al. (2016)
96 h LC50	<i>Oncorhynchus mykiss</i>	0.092 mg/L	Atamanalp and Yanik (2003)
96 h LC50	<i>Clarias batrachus</i> Adults	28.58 mg/L	Srivastava and Singh (2013)
96 h LC50	<i>Clarias batrachus</i> Juveniles	14.04 mg/L	Srivastava and Singh (2013)
96 h LC50	<i>Oreochromis niloticus</i>	11.49 mg/L	Ibrahim et al. (2023)
96 h LC50	<i>Clarias gariepinus</i> Juveniles	410.90 mg/L	Francis et al. (2023); Odo et al. (2023)
96 h LC50	<i>Lophiosilurus alexandri</i> Fingerlings	2.29 mg/L	Silvia et al. (2023)
96 h LC50	<i>Danio rerio</i> Adults	11.8 mg/L	Mendes et al. (2024)
96 h LC50	<i>Carassius auratus</i>	9 mg/L	Atamaniuk et al. (2014)
96 h LC50	<i>Channa punctatus</i> Adults	9.5 ppm	Choudhury and Das (2020)
96 h LC50	<i>Channa punctatus</i>	11.56 mg/L	Kumar et al. (2024)
96 h LC50 (48 hours)	<i>Salmo gairdneri</i>	1.85 mg/L	Hejduk and Svobodová (1980)
96 h LC50 (48 hours)	<i>Poecilia reticulata</i>	2.2 mg/L	Hejduk and Svobodová (1980)

quality of aquatic environments (Iyiola et al., 2024; Jesna et al., 2025). Despite its widespread use, there is no comprehensive review on the toxicity and effects of Mancozeb, an ethylene bis(dithiocarbamate) fungicide, on fish species.

The present review aims to provide a detailed analysis of various eco-toxicological aspects of Mancozeb reported in fish, including behavioral, histopathological, haematological, biochemical, and oxidative stress biomarker alterations, as well as other toxic effects.

Behavioral Alterations

Exposure of non-target species to fungicides can alter physiological processes (Zubrod et al., 2019) and induce toxicity that can trigger cell death if thorough detoxification is not applied. Several authors have described the toxicity of Mancozeb to different fish species, particularly in terms of behavioral response alterations.

Francis et al. (2023) and Odo et al. (2023) reported similar behavioral alterations in *Clarias gariepinus* juveniles exposed to Mancozeb concentrations (0.00, 150, 300, 400, 450, 600, and 750 mg/L for 96 h). During the control period of the exposure, normal behavioral responses were observed, and no mortality occurred. However, treatment groups exposed to Mancozeb exhibited physiological and behavioral abnormalities that increased with both duration and concentration. Fish in tanks with higher concentrations of the test chemical displayed faster opercula movement, jerky movements, erratic swimming, skin discoloration, convulsions, hyperactivity, air gulping, hemorrhage, and loss of equilibrium. *Clarias gariepinus* juveniles lost their balance, became exhausted due to respiratory complications, settled at the bottom of the tank, and eventually died. In sub-lethal concentrations, similar behavioral responses were observed, but no mortality was recorded over 28 days.

Saha et al. (2016) reported that *Oreochromis mossambicus* exhibited various behavioral abnormalities when exposed to

Mancozeb. The mortality rate of the treated fish exposed to Mancozeb varied significantly ($P < 0.05$) compared to the control at all concentrations and exposure times. The mortality rate also varied significantly ($P < 0.05$) across exposure times (24, 48, 72, and 96 h) at all doses. Fish showed excessive mucous secretion and hyper-excitability at higher concentrations during 72 and 96 h of exposure. The opercula movement of the fish increased significantly ($P < 0.05$) compared to the control with increasing concentrations but decreased significantly ($P < 0.05$) over time in all treatments.

Simakani et al. (2018) observed behavioral dysfunction in *Cyprinus carpio* exposed to Mancozeb concentrations (0, 0.94, 1.87, 3.73, 7.50, 15, 30, and 60 mg/L) at different intervals (24, 48, 72, and 96 h). The results revealed changes in fish behavior and morphology. At the early stages of exposure, the fish exhibited anxiety and fast swimming, followed by anorexia. Surface swimming, irregular swimming, and loss of balance were observed in the exposed fish. In the sub-acute test, fish were exposed to Mancozeb concentrations (0.00, 1.6, 2.4, and 3.2 mg/L, representing 20%, 30%, and 40% of the 96 h LC50) for one week.

Srivastava and Singh (2013) observed that *Clarias batrachus* fingerlings and adults exposed to Mancozeb concentrations (10, 15, 20, and 25 mg/L) for 24–96 h under laboratory conditions exhibited slow swimming activity, loss of equilibrium, hypo- and hyperactivity, and vertical positioning. Eventually, their activity ceased, and the fish died.

Silvia et al. (2023) investigated the effects of Mancozeb on *Lophiosilurus alexandri* fingerlings exposed to six concentration groups (Control, T1, T2, T3, T4, T5) for 24–96 h. The control, T1, and T2 groups exhibited normal swimming patterns, while higher concentration groups (T3, T4, T5), particularly T4 (4 mg/L of Mancozeb), showed abnormal behavior. Fish scattered around the aquarium, and variations in mortality were observed among the T3, T4, and T5 groups.

Haematological Alterations

Francis et al. (2023) investigated the haematological parameters of *Clarias gariepinus* juveniles exposed to sub-lethal concentrations of Mancozeb (0.00, 20.55, 41.09, and 82.18 mg/L) for days 1, 7, 14, 21, and 28, with a 7-day recovery period. The results showed a significant concentration- and duration-dependent decrease in red blood cell (RBC) count, packed cell volume (PCV), and hemoglobin (Hb), while white blood cell (WBC) count increased. Mean corpuscular hemoglobin (MCH) was not significantly different, whereas mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular volume (MCV) fluctuated. The activities of neutrophils and lymphocytes were not significantly different among treatment groups, while monocytes, basophils, and eosinophils fluctuated. The study concluded that exposure to Mancozeb alters haematological parameters in *Clarias gariepinus* juveniles.

Atamanalp and Yanik (2003) observed haematological alterations in *Oncorhynchus mykiss* exposed to a sub-lethal concentration of Mancozeb (1/2 of LC50 = 1.1 mg/L) at 24-hour intervals for 3 weeks. The results revealed an increase in RBC count and a decrease in WBC count, PCV, MCV, and MCHC.

Shahi and Singh (2014) studied the effects of sub-lethal concentrations of Mancozeb (80% of the 24-hour LC50 value of 7.7 mg/L) on selected haematological parameters of *Clarias batrachus* for one week. They reported that Mancozeb caused a decrease in Hb, MCH, MCHC, RBC count, and WBC count.

Histopathological Alterations

Histopathological analysis is a vital bio-indicator that can be used to determine cellular changes in organs such as the kidney, liver, and spleen (Capkin et al., 2006).

Choudhury and Das (2020) assessed the histopathological damage in the kidney and liver of *Channa punctatus* exposed to concentrations (4 ppm, 6 ppm, 8 ppm, 10 ppm, and 12 ppm) and chronic sub-lethal concentrations (1/3 of the 96 h LC50 = 3 ppm) of Mancozeb for 15 and 30 days. In the control group, the liver showed normal hepatocyte cells, parenchymal cells, and sinusoids. However, several histopathological alterations were observed in the liver of Mancozeb-treated groups, including degeneration of hepatic tissues and the formation of vacuoles after 15 days, which became more prominent after 30 days. The kidney of the control group exhibited intact nephrons and interstitial tissues. In contrast, the Mancozeb-treated groups showed the formation of vacuoles, necrosis of interstitial cells, and shrinkage of Bowman's capsule. After 30 days, the kidney exhibited swelling of renal tubules and hypertrophy of distal convoluted tubules.

Chijioke et al. (2024) investigated severe histopathological changes in the kidney of *Clarias gariepinus* juveniles exposed to sub-lethal concentrations of Mancozeb over 0, 7, 14, 21, and 28 days (with a 7-day recovery period). Necrosis and degeneration of renal tubules, inflammation of the hematopoietic tissue, shrinkage of the tubule lumen, and hemorrhage of kidney cells were observed in groups B (days 7 and 21), A and B (day 14), and B and C (day 28). The liver of control groups showed normal hepatocyte cells, parenchyma cells, and sinusoids, with normal histoarchitecture observed on days 1 and 7. However,

treatment groups exhibited increased lipid-like vacuolation on day 14 (group B) and day 21 (group C). By day 28 (group B), multifocal areas of hepatocellular necrosis with leukocyte infiltration were observed. The spleen showed no histological changes compared to the control from day 1 to 28 (including the 7-day recovery period).

Kumar et al. (2024) investigated histopathological alterations in the gills, liver, kidney, and muscle tissue samples of *Channa punctatus* exposed to Mancozeb concentrations (control, 1.156 mg/L = 1/10th of the 96 h LC50, and 2.312 mg/L = 1/5th of the 96 h LC50). High levels of reactive oxygen species (ROS) and histological alterations such as destruction of gill arches and necrosis were observed. Liver tissue revealed vacuolation, necrosis, and cytoplasmic degeneration in fish exposed to 2.312 mg/L (1/5th of the 96 h LC50). Kidney tissue in the same group showed a reduction in renal tubules, hypertrophy, vacuolation, and elevated ROS effects. Muscle tissue in the 2.312 mg/L group exhibited degeneration and vacuolation.

Silvia et al. (2023) observed histopathological alterations in the liver tissue of *Lophiosilurus alexandri* fingerlings exposed to Mancozeb. Fish in all treatment groups, including the control, showed necrosis, which was more evident in the T5 group (0.8 mg/L of Mancozeb). Inflammatory infiltration was observed in exposed groups, with greater intensity in the T4 group. The control group did not exhibit inflammatory infiltration in the liver.

Biochemical Alterations

Simakani et al. (2018) assessed the impact of sub-lethal concentrations of Mancozeb (0, 1.6, 2.4, and 3.2 mg/L) on the plasma biochemistry of *Cyprinus carpio* after a one-week exposure period. Mancozeb had significant effects on plasma glucose levels, with the highest glucose level observed at the concentration of 3.2 mg/L ($P < 0.05$). Mancozeb concentrations also significantly affected plasma total protein and globulin levels, with the highest and lowest levels observed at 1.6 mg/L and 3.2 mg/L, respectively ($P < 0.05$). Mancozeb exposure significantly affected alanine aminotransferase (ALT) activities, with the highest and lowest activities observed at 1.6 mg/L and 3.2 mg/L, respectively. The lowest plasma aspartate aminotransferase (AST) levels were observed in the 1.6 mg/L and 2.4 mg/L treatment groups, which were significantly different compared to the control group. Mancozeb treatment groups had similar enzyme activities, which were significantly lower than the 3.2 mg/L group ($P < 0.05$).

Srivastava and Singh (2013) investigated the effects of Mancozeb concentrations (40% of the LC50 = 10.86 mg/L) at different intervals (24, 48, 72, and 96 h) on tissues (liver and muscles). Protein levels decreased by 87% and 70% in muscles and liver, respectively, after 72 h. Glycogen levels decreased by 82% and 70% in muscles and liver, respectively, after 24 h, and by 60% in both tissues after 72 h. DNA levels decreased by 80% in muscles and 78% in liver after 24 h, and by 66% in muscles and 64% in liver after 72 h. RNA levels decreased by 78% in muscles and 76% in liver after 24 h, and by 68% in muscles and 65% in liver after 72 h. In terms of enzymatic changes, protease

activity increased in both muscles and liver. Lactate dehydrogenase (LDH) activity increased in muscles and liver after 24 h and continued to increase after 72 h. Succinate dehydrogenase (SDH) activity decreased by 73% and 65% in muscles and liver, respectively, after 24 h, and by 60% in both tissues after 72 h. Glutamic pyruvic transaminase (GPT) activity increased in muscles and liver after 24 h, with the highest increase observed in muscles after 72 h, followed by the liver.

Banaee et al. (2023) reported changes in biochemical parameters in the hepatocytes of zebrafish (*Danio rerio*) after exposure to Mancozeb for 21 days. The results revealed no significant change ($P < 0.005$) in aspartate aminotransferase (AST) activity in fish hepatocytes exposed to Mancozeb (5.5 and 11 $\mu\text{g/L}$). However, when metalaxyl was combined with Mancozeb (5.5 and 11 $\mu\text{g/L}$), AST activity increased. Exposure to metalaxyl (6.5 and 13 mg/L) combined with 11 $\mu\text{g/L}$ of Mancozeb significantly increased alanine aminotransferase (ALT) activity. Gamma-glutamyl transferase (GGT) activity decreased in fish hepatocytes ($P < 0.05$), while lactate dehydrogenase (LDH) activity decreased and alkaline phosphatase (ALP) activity increased compared to the control group. Glycogen content also decreased in the treated groups.

Oxidative Stress Biomarkers Alterations

Odo et al. (2023) investigated oxidative stress alterations in *Clarias gariepinus* juveniles exposed to sub-lethal concentrations of Mancozeb (0.00, 20.55, 41.09, and 82.18 mg/L) sampled on days 1, 7, 14, 21, and 28, with a 7-day recovery period. The study focused on the kidney, liver, and gill tissues. The results showed that changes in oxidative stress parameters, including lipid peroxidation (LPO), catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione reductase (GR), and malondialdehyde (MDA), were concentration- and duration-dependent. Lipid peroxidation significantly increased ($P < 0.05$) on days 21 and 28 compared to the control. CAT activity was not significantly different compared to the control group. SOD activity significantly decreased on days 7, 14, and 21 compared to the control. GPx activity significantly decreased on days 1 and 21 compared to the control, while GR activity significantly increased on days 7 and 21 compared to the control.

Kumar et al. (2024) evaluated the activity of LPO and glutathione (GSH) in the gill, liver, kidney, and muscle tissues of *Channa punctatus* in control and Mancozeb-treated groups (1.156 mg/L = 1/10th of the 96 h LC50 and 2.312 mg/L = 1/5th of the 96 h LC50) after a 96-hour exposure period. The study revealed an enhancement of LPO activity in the gills, liver, kidney, and muscle tissues of the Mancozeb-exposed groups compared to the control, with the highest activity observed in the liver tissues of the 2.312 mg/L group. There was a decrease in GSH activity in the Mancozeb-exposed treatment groups compared to the control, with the lowest GSH content recorded in the 2.312 mg/L group.

Banaee et al. (2023) reported changes in oxidative biomarkers in the hepatocytes of zebrafish (*Danio rerio*) after exposure to Mancozeb for 21 days. The results revealed a significant increase in SOD and CAT activities compared to the control group.

The maximum increase in CAT activity occurred in the hepatocytes of fish exposed to 11 $\mu\text{g/L}$ of Mancozeb. MDA levels also increased significantly ($P < 0.05$).

Atamaniuk et al. (2014) investigated the impact of acute toxicity of Mancozeb concentrations (0.0, 3, 5, and 10 mg/L) after 96 hours on the levels of oxidative stress biomarkers and the antioxidant system in the brain, liver, and kidney of goldfish (*Carassius auratus*). Levels of carbonyl proteins (CP) in the control group were similar in the brain and liver (1.64 ± 0.16 and 1.31 ± 0.24 nmol mg^{-1} protein) but higher in the kidney (3.17 ± 0.53 nmol mg^{-1} protein). Exposure to Mancozeb concentrations (3, 5, and 10 mg/L) caused a significant increase in CP levels in the liver (92% above control) and kidney (98% above control), but did not affect brain CP content. Levels of lipid peroxides (LOOH) in the control group were lowest in the brain (55.5 ± 2.7 nmol gwm^{-1}), almost twice as high in the kidney (94.5 ± 6.1 nmol gwm^{-1}), and highest in the liver (3659 ± 861 nmol gwm^{-1}). Mancozeb exposure had no effect on LOOH in the liver, but the highest concentration (10 mg/L) resulted in a significant increase (44%) in the brain. In the kidney, a 25% increase in LOOH occurred after exposure to 3 mg/L of Mancozeb. Exposure to Mancozeb concentrations (3, 5, and 10 mg/L) induced oxidative stress in all three tissues, as indicated by oxidative damage to proteins and lipids.

SOD activity in control fish was similar in all tissues studied (131 ± 32 and 132 ± 10 U mg^{-1} protein in the brain, liver, and kidney). Exposure to Mancozeb concentrations (5 and 10 mg/L) for 96 hours enhanced SOD activity by 70% in the liver and 37% in the kidney. CAT activity was 7.32 ± 0.52 , 141 ± 18 , and 30 ± 2.3 U mg^{-1} protein in the brain, liver, and kidney, respectively. In the kidney and liver, Mancozeb had no effect on CAT activity at any concentration tested. However, in the liver, treatment with 5 and 10 mg/L enhanced CAT activity by 23% to 52%. GPx activity was lowest in the brain (50.8 ± 4.3 mU mg^{-1} protein) and threefold higher in the liver and kidney (145 ± 17 and 170 ± 19 mU mg^{-1} protein, respectively). A significant increase in GPx activity (49%) was observed in the liver after exposure to the highest concentration of Mancozeb (10 mg/L). GST activities in control fish were 0.71 ± 0.09 , 2.97 ± 0.11 , and 1.13 ± 0.12 U mg^{-1} protein in the brain, liver, and kidney, respectively. Exposure to the highest concentration of Mancozeb (10 mg/L) decreased GST activity in the liver by 23%, but GST activity remained unchanged in other tissues. GR activities were similar in control fish for all three tissues (54.4 ± 2.5 , 39.0 ± 1.9 , and 74.9 ± 3.1 mU mg^{-1} protein in the brain, liver, and kidney, respectively). GR activity decreased in the brain, liver, and kidney (26%, 28%, and 37%, respectively) in a concentration-dependent manner after exposure to Mancozeb concentrations (3, 5, and 10 mg/L). Glucose-6-phosphate dehydrogenase (G6PDH) activity was 19.5 ± 3.0 and 31.0 ± 1.62 mU mg^{-1} protein in the brain and liver, respectively, and much higher in the kidney (134 ± 3.3 mU mg^{-1} protein) of control goldfish. Exposure to Mancozeb concentrations (3, 5, and 10 mg/L) did not affect G6PDH activity in the brain and liver, but a significant decrease (12% to 15%) was observed in the kidney.

Chromosomal Alterations and Carcinogenic Effects (Genotoxicity)

Kuppuswamy and Seetharaman (2020) revealed that the exposure of zebrafish (*Danio rerio*) to Mancozeb could alter the expression of genes involved in brain cell apoptosis. Exposure of *Clarias batrachus* to sub-lethal concentrations of Mancozeb (80% of the 24-hour LC50) after 24, 48, 72, and 96 hours revealed that the number of micronuclei was highest at 48 hours (Shahi and Singh, 2014).

Marques et al. (2016) investigated the DNA and chromosome-damaging potential of Mancozan[®], containing Mancozeb concentrations (0.29 and 2.9 µg/L), in the European eel (*Anguilla anguilla*) after short-term exposure (3 days). The highest concentration of Mancozan[®] affected DNA integrity (comet assay), while the adoption of endonucleases indicated oxidative damage. Chromosomal damage (ENA assay) showed significant effects, revealing the clastogenic and aneugenic properties of Mancozan[®]. The two genetic endpoints were significantly correlated.

Kumar et al. (2024) studied the effects of Mancozeb concentrations (control, 1.156 mg/L = 1/10th of the 96 h LC50, and 2.312 mg/L = 1/5th of the 96 h LC50) after 96 hours. The results revealed a significant ($P < 0.05$) induction in micronucleus (MN) frequency in the gills, liver, and muscles of fish in the Mancozeb-treated groups compared to the control. The highest frequency of MN was observed in the 2.312 mg/L Mancozeb concentration group (1/5th of the 96 h LC50), indicating induced DNA damage.

Banaee et al. (2023) reported the effects of Mancozeb exposure on transcriptional gene levels of detoxification enzymes in zebrafish (*Danio rerio*) after 21 days. The expression of the *cyp1a* gene significantly increased ($P < 0.05$) in the hepatocytes of zebrafish exposed to Mancozeb (5.5 and 11 µg/L). The expression of *Ces2* was up-regulated in the hepatocytes of zebrafish exposed to 11 µg/L of Mancozeb. There was a significant rise in *Ces2* and *cyp1a* mRNA levels in the hepatocytes of zebrafish co-exposed to 11 µg/L compared to the control group. The gene expression of *Ces2* and *cyp1a* was significant ($P < 0.05$) for 11 µg/L of Mancozeb.

Reproductive and Developmental Alterations

Gürol et al. (2020) reported the effects of Mancozeb concentrations (control, 5 ppm, and 7.5 ppm) on the testicular histology of zebrafish (*Danio rerio*) over 5 days. No effects were observed in the testicular histopathology of the control group. However, testicular histopathology increased with concentration and exposure time in the treatment groups (5 ppm and 7.5 ppm). The study revealed degeneration of spermatogenic cells, disorganization of seminiferous tubules, fibrosis, tubular fusions, vacuolization, edema, hemorrhage, reduced spermatogenic cell clusters, decreased sperm count, hypertrophy of spermatocytes, and pyknotic and karyolytic nuclei.

Tzanova et al. (2017) investigated the reproductive impact of Mancozeb on *Oncorhynchus mykiss* fry, focusing on biological parameters such as egg fertilization rate and hatchability rate. The experimental groups revealed that the fertilization rate

of fish eggs in the second group was significantly reduced after artificial insemination. The third group, which utilized a sperm-activating medium, showed significantly improved fertilization. The survival of the yolk sac depended on the quality of eggs obtained from different trout groups.

Respiratory Alterations

Srivastava and Singh (2013) observed dose-dependent respiratory alterations in *Clarias batrachus* fingerlings and adults exposed to Mancozeb concentrations. For fingerlings, concentrations at 24, 48, 72, and 96 hours were 39.80, 37.38, 29.92, and 23.3 mg/L, respectively. For adults, concentrations at 24 to 96 hours were 71.54, 47.28, 33.23, and 28.16 mg/L, respectively. Within 5 to 10 minutes of exposure, the breathing of the fish was affected, and they came to the water-air interface for air gulping, a behavior typical of *Clarias batrachus*, an air-breathing catfish. This was likely due to the effect of Mancozeb on the gills and general metabolism. The toxicity in both fingerlings and adults was time- and dose-dependent.

Morphological Alterations

Simakani et al. (2018) observed morphological alterations in *Cyprinus carpio* exposed to Mancozeb concentrations (0, 0.94, 1.87, 3.73, 7.50, 15, 30, and 60 mg/L) at different intervals (24, 48, 72, and 96 hours). Morphological changes included mucus hypersecretion, body and gill discoloration, scale loss, and hemorrhage on the body and around the operculum.

Morphometric Indices

Odo et al. (2023) investigated morphometric indices such as the condition factor and hepatosomatic index in *Clarias gariepinus* juveniles exposed to Mancozeb. The results revealed no significant difference compared to the control from day 1 to 28 (including a 7-day recovery period).

Physico-Chemical Parameters of Test Water

Several authors reported the physico-chemical parameters of water for different fish species exposed to Mancozeb. According to Simakani et al. (2018), the water quality parameters for *Cyprinus carpio* were within acceptable ranges during the 10-day exposure period: temperature $18.25 \pm 0.21^\circ\text{C}$, pH 7.3 ± 0.35 , dissolved oxygen 7.3 ± 0.4 mg/L, nitrite 1.1 ± 0.12 mg/L, ammonia 0.67 ± 0.1 mg/L, and hardness (CaCO_3) 318 ± 21.12 mg/L.

Odo et al. (2023) stated that the physico-chemical parameters of the test water used for sub-lethal concentrations (0.00, 20.55, 41.09, and 82.18 mg/L) over a 5-week exposure period were as follows: temperature $28 - 32^\circ\text{C}$, pH $7.3 - 12.3$, alkalinity $0.88 - 4.10$, carbon dioxide 12.5 mg/L, and dissolved oxygen $6.6 - 7.8$ mg/L. All parameters were favorable for fish production and survival except for the alkalinity range.

Kumar et al. (2024) reported the physico-chemical parameters of test water used for short-term exposure after 96 h LC50: pH

7.3, temperature 27°C, dissolved oxygen 6.3 mg/L, alkalinity 3.6 mg/L, and hardness 58 mg/L.

Sharma et al. (2016) revealed the physico-chemical parameters of test water used for lethal toxicity exposure after 96 h LC50: temperature 24.3°C, pH 8, dissolved oxygen 3.1 ppm, total dissolved solids (TDS) 0.22, conductivity 0.33, salinity 0.2, and carbon dioxide 0.5/50 ml.

Silvia et al. (2023) reported the following parameters for *Lophiosilurus alexandri* fingerlings exposed to Mancozeb: pH 7.4 ± 0.1, dissolved oxygen 7.3 ± 0.63 mg/L, temperature 24 ± 0.4°C, water conductivity 500 µS/cm, and ammonia 0.05 mg/L.

Conclusion

Mancozeb has been proven to be moderately to highly toxic to fish. Intensive ecotoxicological investigations of Mancozeb on various fish species are necessary to fully understand its impacts and ensure the protection of aquatic ecosystems.

Acknowledgement

I sincerely appreciate my parents, Chief and Lolo Francis Nwosu and Marylyn Brown, for their prayers and encouragement during the preparation of this paper review.

Conflict of Interest

The authors declare no conflict of interest.

Funding

This journal paper was reviewed by Mr. Francis Chijioke and co-authors.

References

- Abdelkader, S. M., Elkhishin, I. A. R., Mesallam, D. I. A., & Abdelwahab, M. M. (2023). Some toxicological health hazards of mancozeb: A review article. *Zagazig Journal of Forensic Medicine and Toxicology*, 21(2), 148–160.
- Atamanalp, M., & Yanik, T. (2003). Alterations in hematological parameters of rainbow trout (*Oncorhynchus mykiss*) exposed to mancozeb. *Turkish Journal of Veterinary and Animal Science*, 27, 1213–1217.
- Atamaniuk, T. M., Kubrak, O. I., Husak, V. V., Storey, K. B., & Lushchak, V. I. (2014). The mancozeb-containing carbamate fungicide tattoo induces mild oxidative stress in goldfish brain, liver, and kidney. *Environmental Toxicology*, 29(11), 1227–1235.
- Banaee, M., Sagvand, S., Sureda, A., Amini, M., Haghi, B. N., Sopjani, M., & Faggio, C. (2023). Evaluation of single and combined effects of mancozeb and metalaxyl on the transcriptional and biochemical response of zebrafish (*Danio rerio*). *Comparative Biochemistry and Physiology Part C: Toxicology and Pharmacology*, 268, 109597. <https://doi.org/10.1016/j.cbpc.2023.109597>
- Capkin, E., Altinok, I., & Karahan, S. (2006). Water quality and fish size affect toxicity of endosulfan, an organochlorine pesticide, to rainbow trout. *Chemosphere*, 64, 1793–1800.
- Chijioke, F., Odo, U. U., Odinakachukwu, N. L., Chinedu, N. O., Anya, C. B., Iyikiti, J. C., Egbuji, J. C., Lemuel, A. S., Odanwu, S. E., Chukwukereze, K. U., Ndubuisi, J. O., Obodo, D. E., & Odo, G. E. (2024). Toxicity of mancozeb on the African catfish *Clarias gariepinus* juveniles kidney, liver, and spleen histoarchitecture. *Journal of Clinical Toxicology*, 14(555), 1–13. <https://doi.org/10.35248/2151-0495.24.14.555>
- Choudhury, R., & Das, P. (2020). Histopathological studies on liver and kidney of *Channa punctatus* (Bloch) exposed to mancozeb-containing pesticide Dithane M-45. *Pollution Research*, 39, 87–91.
- Cycoń, M., Piotrowska-Seget, Z., & Kozdrój, J. (2010). Responses of indigenous microorganisms to a fungicidal mixture of mancozeb and dimethomorph added to sandy soils. *International Biodeterioration and Biodegradation*, 64(4), 316–323. <https://doi.org/10.1016/j.ibiod.2010.03.006>
- Engels, H. W., Weidenhaupt, H. J., Pieroth, M., Hofmann, W., Menting, K. H., Mergenhausen, T., & Uhrlandt, S. (2011). Rubber, 9. Chemicals and additives. *Ullmann's Encyclopedia of Industrial Chemistry*, 11. <https://doi.org/10.1002/14356007.a23.365.pub3>
- Flores-García, M. E., Molina-Morales, Y., Balza-Quintero, A., Benítez-Díaz, P. R., & Miranda-Contreras, L. (2011). Pesticide residues in drinking water of an agricultural community in the state of Mérida, Venezuela. *Investigación Clínica*, 52(4), 295–311.
- Francis, C., Odo, U. U., Ugwanyi, K. C., Egbuji, J. V., Lemuel, A. S., Okpechi, N. J., Ugwu, I. J. A., & Odo, G. E. (2023). Abnormalities in behavioral responses and hematological parameters of African catfish *Clarias gariepinus* juveniles exposed to acute and subchronic effects of mancozeb. *International Journal of Fisheries Studies*, 11(5), 88–98. <https://doi.org/10.22271/fish.2023.v11.i5b.2853>
- Goldoni, A., & Silva, L. B. D. (2012). Potencial mutagênico do fungicida mancozebe em *Astyanax jacuhiensis* (Teleostei: Characidae). *Bioscience Journal*, 28, 297–301.
- Gürol, M. A., Arman, S., & Yönlü, N. D. (2020). Effects of mancozeb on the testicular histology of the zebrafish (*Danio rerio*). *Annales de Limnologie-International Journal of Limnology*, 56(10), 1–5. <https://doi.org/10.1051/limn/2020009>
- Hayes, W. J., & Laws, E. R. (1991). *Handbook of pesticide toxicity, classes of pesticides* (Vol. 3). New York: Academic Press Inc.
- Hejduk, J., & Svobodova, Z. (1980). Acute toxicity of carbamate-based pesticides for fish. *Acta Veterinaria Brno*, 49(3-4), 251–257.
- Ibrahim, R. E., Elbealy, M. A., Salem, G. A., Abdelwarith, A. A., Younis, E. M., Wagih, E., & Rahman, A. N. A. (2023). Acute mancozeb-fungicide exposure induces neuro-ethology disruption, health disorders, and immune-oxidative dysfunction in Nile tilapia (*Oreochromis niloticus*). *Aquatic Toxicology*, 261, 106630. <https://doi.org/10.1016/j.aquatox.2023.106630>
- Iyiola, A. O., Kolawole, A. S., Setufe, S. B., Bilikoni, J., Ofori, E., & Ogwu, M. C. (2024). Fish as a sustainable biomonitoring tool in aquatic environments. In *Biomonitoring of pollutants in the global south* (pp. 421–450). Singapore: Springer Nature Singapore.
- Jesna, P. K., Das, B. K., Sarkar, D. J., Krishnani, K. K., Chadha, N. K., & Hemaprasanth, K. (2025). Assessment of the toxicological effects of cypermethrin nanoformulation on *Hypselobarbus pulchellus* using selected biomarkers: Toxicity of cypermethrin nanoformation. *Fishery Technology*, 62(1). <https://doi.org/10.56093/ft.v62i1.153927>
- Kamlesh, R., Santosh, S., Sudhakar, P., & Sunita, A. (2024). Role of pesticides in biodiversity loss. *International Journal of Bioscience and Biochemistry*, 6(1), 01–03.

- Kumar, M., Mishra, A., Verma, A., Jain, A., Khan, A. A., Dwivedi, S., & Trivedi, S. P. (2024). Assessment of oxidative stress, genotoxicity, and histopathological alterations in freshwater food fish *Channa punctatus* exposed to fungicide, mancozeb. *Journal of Applied Biology and Biotechnology*, *12*(1), 159–164. <https://doi.org/10.7324/JABB.2024.142595>
- Kuppuswamy, J. M., & Seetharaman, B. (2020). Mancozeb exposure at sublethal concentration alters the transcription of the genes related to apoptosis in the adult zebrafish (*Danio rerio*) brain. *Research Journal of Pharmacy and Technology*, *13*(10), 4801–4804.
- Maino, J. L., Thia, J., Hoffmann, A. A., & Umina, P. A. (2023). Estimating rates of pesticide usage from trends in herbicide, insecticide, and fungicide product registrations. *Crop Protection*, *163*(1), 1–7. <https://doi.org/10.1016/j.cropro.2022.106125>
- Marques, A., Rego, A., Guilherme, S., Gaivão, I., Santos, M. A., & Pacheco, M. (2016). Evidences of DNA and chromosomal damage induced by the mancozeb-based fungicide Mancozan® in fish (*Anguilla anguilla* L.). *Pesticide Biochemistry and Physiology*, *133*, 52–58. <https://doi.org/10.1016/j.pestbp.2016.03.004>
- Mendes, E. J., Mazon, S. C., Marsaro, I. B., Hermes, M. E., Sachett, A., Bertinello, K. T., & Siebel, A. M. (2024). Investigation on the mancozeb toxicity in adult zebrafish (*Danio rerio*). *Journal of Toxicology and Environmental Health, Part A*, *87*(15), 616–624. <https://doi.org/10.1080/15287394.2024.2352787>
- Morgan, D. P. (1982). Pesticide studied in man. *Journal of the American Medical Association*, *247*(22), 3140–3140.
- Odo, U., Ebuka, I., Chijioke, F., & Odo, G. E. (2023). Morphometric indices and oxidative stress biomarkers of African catfish *Clarias gariepinus* juveniles exposed to agricultural fungicide mancozeb. *Toxicology and Applied Pharmacology Insights*, *6*(1), 54–64.
- Paro, R., Tiboni, G. M., Buccione, R., Rossi, G., Cellini, V., Canipari, R., & Ceconi, S. (2012). The fungicide mancozeb induces toxic effects on mammalian granulosa cells. *Toxicology and Applied Pharmacology*, *260*(2), 155–161. <https://doi.org/10.1016/j.taap.2012.02.005>
- PubChem. (2021). Mancozeb. Retrieved March 14, 2021, from <https://pubchem.ncbi.nlm.nih.gov/compound/76957227>
- Saha, N. C., Giri, S. K., Chatterjee, N., Biswas, S. J., & Bej, S. (2016). Acute toxic effects of mancozeb to fish (*Oreochromis mossambicus*) and their behavior. *International Journal of Advance Research in Biological Sciences*, *3*, 40–44.
- Saxena, V. (2025). Water quality, air pollution, and climate change: Investigating the environmental impacts of industrialization and urbanization. *Water, Air, and Soil Pollution*, *236*(2), 1–40.
- Shahi, J., & Singh, A. (2014). Genotoxic and haematological effect of commonly used fungicide on fish *Clarias batrachus*. *Journal of Biology and Earth Sciences*, *4*(2), 137–143.
- Sharma, A., Kumar, V., Shahzad, B., Tanveer, M., Sidhu, G. P. S., Handa, N., & Thukral, A. K. (2019). Worldwide pesticide usage and its impacts on ecosystem. *SN Applied Sciences*, *1*, 1–16.
- Sharma, M. R., Mushtaq, S. A., & Allayie, V. H. (2016). Assessment of lethal toxicity of mancozeb and its consequences on the behavior of freshwater fish, *Puntius ticto*. *Journal of International Academic Research for Multidisciplinary*, *4*(2), 132–138.
- Silva, A. L., Albinati, A. C. L., Souza, S. A., Marques, J. V. S., Andrade, I. B. M., Souza, Y. R. C., & Amorim, A. G. (2023). Evaluation of the acute and sublethal toxicity of mancozeb in Pacamã (*Lophiosilurus alexandri*). *Brazilian Journal of Biology*, *83*, e274393. <https://doi.org/10.1590/1519-6984.274393>
- Simakani, P., Abolhasani, M. H., & Hoseini, S. M. (2018). Determination of mancozeb toxicity and biochemical effects in common carp (*Cyprinus carpio*). *International Journal of Aquatic Biology*, *6*(3), 157–161.
- Srivastava, P., & Singh, A. (2014). Potential effects of agricultural fungicide (mancozeb) on fish *Clarias batrachus*. *Research Journal of Biological Sciences*, *9*(4), 129–134. <https://doi.org/10.36478/rjbsci.2014.1>
- Srivastava, P., & Singh, A. (2013). In vivo study of effects of dithiocarbamates fungicide (mancozeb) and its metabolite ethylenethiourea (ETU) on freshwater fish *Clarias batrachus*. *Journal of Biology and Earth Sciences*, *3*(2), 228–235.
- Thiruchelvam, M. (2005). Mancozeb. *Elsevier*, 5–8.
- Tzanova, M., Atanasov, V., Zaharinov, B., Beev, G., Dinev, T., & Valkova, E. (2017). Reproduction impact of mancozeb on rainbow trout (*Oncorhynchus mykiss* W.) and accumulation of its carcinogen metabolite, ethylene thiourea in fish products. *Journal of Central European Agriculture*, *18*(2), 369–387.
- Zubrod, J. P., Bundschuh, M., Arts, G., Brühl, C. A., Imfeld, G., Knäbel, A., & Schäfer, R. B. (2019). Fungicides: An overlooked pesticide class? *Environmental Science and Technology*, *53*(7), 3347–3365.