# A Common Feature of Pesticides: Oxidative Stress
# The Role of Oxidative Stress in Pesticide-induced Toxicity

Rasheed O. Sule[a], Liam Condon[a], and Aldrin V. Gomes[a,b*]

[a] Department of Neurobiology, Physiology and Behavior,
[b] Department of Physiology and Membrane Biology
University of California, Davis, Davis, CA 95616

## Supplemental Tables

**Supplemental Table 1. Tissue Toxicity of Pesticides**

| **Pesticide** | **Cardiac Toxicity** | **Kidney Toxicity** | **Liver Toxicity** | **Brain Toxicity** | **Other Organ Toxicity** |
|---|---|---|---|---|---|
| Glyphosate | [1, 2] (Zebrafish (*Danio rerio*)*, and* mammals) | [3-5] (rats and common carp (Cyprinus carpio L.)) | [5, 6] (rats and field lizard podarcis siculus) | [7] (mice) | |
| Atrazine | [8, 9] (mice, African clawed frog) | [10-12] (Piaractus mesopotamicus, quail (Coturnix C. coturnix, Caspian kutum, Rutilus frisii kutum) | [10] (Piaractus mesopotamicus) | [13] (rat) | [14] quails (Coturnix Coturnix coturnix) |
| Metolachlor-S | | | [15] (rat) | | |
| 2,4-dichlorophenoxyacetic acid (2,4-D) | [16, 17] (rats, humans) | [17, 18] (rodents, humans) | [17, 18] (rodents, humans) | [19] (rodents, fish) | |
| Metam | | | [20] (rat) | | |
| Acetochlor | [21] (zebrafish larvae) | | | [22] (zebrafish larvae) | |
| Chloropicrin | | | | | [23] (respiratory, humans) |
| Chlorothalonil | | | [24] (zebrafish (Danio rerio) | | [25] (Ovaries, mice) |
| Pendimethalin | [26] (zebrafish) | [27] (rat) | [27-30] (rat, rainbow trout (Oncorhynchus mykiss), | | [31] (bone marrow, mouse) |

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| | | | Nile tilapia (*Oreochromis niloticus*) | | |
| Ethephon | | [32, 33] (rats) | [34, 35] (rats) | | |
| Mancozeb | | [36] (rats) | [36-38] (rats) | [36, 39] (rats) | [40] (striated muscle, rats) [41] (reproductive organs/rats) |
| Chlorpyrifos | [42-44] (rabbits, rats) | [45-48] (rats, mice) | [46, 47, 49] (rats, mice) | [45, 50] (rats) | |
| Propanil | | [51] (mice) | [51-54] (rats, mice) | | [55] (Thymus/ mice) |
| Dicamba | | | [56] (human) | | |
| Trifluralin | | [57] (rats) | | | |
| Acephate | | [58] (in Vitro/renal tubular cells) | | | [59] (reproductive organs/ male mice) |
| Paraquat | [60-63] (mice) | [64-67] (rats) | [66, 68-71] (rats, mice, lizards, zebrafish) | [72-77] (rat, human, mice, monkey, freshwater fish bryconamericus iheringii) | [78] (esophagus, human) [79] (stomach, small intestine, testes, rat) |
| Glufosinate | | | [80] (fish) | [81, 82] (mice, zebrafish larvae) | |
| Phorate | | | [83] (mice) | | [83] (testis, mice) |
| Dicrotophos | | | | | [84] (blood, rat) |
| Dimethoate | [85, 86] (rats) | [87-89] (rats, mice, fish) | [88-93] (rats, mice, fish) | [91, 93, 94] (rats) | |
| Terbufos | [95] (rats) | | | | |

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| Lindane | [96-98] (rats) | [99-101] (rats, fish) | [99, 100, 102] (rats, fish) | [103, 104] (rats, mice) | |
| Dichlorodiphenoxy-trichloroethane (DDT) | [105] (mice) | | [106] (rats) | | |
| Maneb | | [107-109] (rats, mice, fish) | [108, 110] (mice, fish, zebrafish embryos) | [111] (zebrafish embryos) | |
| Dieldrin | | [112] (rat) | [112] (rat) | [113] (human) | |
| Clothianidin | | [114] (fish) | | [114] (fish) | |
| Chlordane | | | [115] (rats) | | [116] (Thymic atrophy, rats) |
| Pentachlorophenol (PCP) | | | [117, 118] (rats) | | [119] (reproductive organs/fish) |
| Endosulfan | [120-122] (rats) | [123] (mice) | [123] (mice) | [122, 124, 125] (rats, zebrafish) | |
| Zineb | | | [126] (rats) | [126] (rats) | |
| Rotenone | | [127, 128] (rats) | [127, 129, 130] (rats, fish) | [127, 131] (rats, fish) | |
| Ziram | | | | [132] (zebrafish embryos) | |
| Methamidophos | [133] (rats) | [134] (rats) | [134] (rats) | [135] (rats) | |
| Dichlorvos | | [136-139] (rats, mice) | [136, 140, 141] (rats, mice) | [142, 143] (rats) | |
| Tebuconazole | [144, 145] (rats) | [146] (rat) | [145] (zebrafish) | | |
| Triflumuron | | [147] (mice) | [147] (mice) | | |
| Acetamiprid | | [148, 149] (rats, mice) | [149, 150] (rats) | [151, 152] (rats, mice) | |

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| Thifluzamide | | [153] (zebrafish) | [153, 154] (zebrafish) | | |
| Aldicarb | [155] (human) | [155] (human) | [155] (human) | | |
| Propoxur | [44] (rabbits) | | [156, 157] (rats) | [158] (rats) | |
| Methidathion | [159] (rats) | | [160, 161] (rats) | | |
| Diazinon | [162, 163] (rats) | [164, 165] (rats, fish) | [165, 166] (rats, fish) | [167, 168] (rats, mice) | |
| Monocrotophos | [169] (rats) | [170] (fish) | [170] (fish) | [171] (rats) | |
| Aluminum phosphide | [172] (rats) | [172] (rats) | | | |
| Penconazole (triazole) | [173] (rats) | [174] (rats) | | | |
| Imidacloprid (IMI) | | | [175] (fish) | | |
| Fluazifop-p-butyl (FPB) | | [176] (rats) | [176] (rats) | | |
| Nitenpyram | | | [177] (zebrafish) | | |
| Thiacloprid | | | [178] (rats) | | |

**Supplemental Table 2. Signaling Pathways altered by Pesticides**

| Pesticide | Signaling Pathways Involved | Reference |
|---|---|---|
| Glyphosate | Mitochondrial apoptotic signaling pathway | [179], [180] |
| Atrazine | NF-κB signaling pathway | [181] |
| | Apoptosis signaling pathway<br>Nrf2 signaling pathway<br>TNF-α NF-κB signaling pathway | [182] |
| | Nrf2 signaling pathway | [183] |
| | TNF-α NF-κB signaling pathway | [184] |
| | Autophagy and apoptosis pathways | [185] |
| | ER stress-signaling pathway<br>Mitochondrial apoptosis pathway<br>Autophagy pathway | [186] |
| 2,4-dichlorophenoxyacetic acid (2,4-D) | Apoptosis signaling pathway | [187] |
| Acetochlor | MAPK signaling pathway | [188] |
| | Apoptosis signaling pathway | [189] |
| Chloropicrin | Apoptotic signaling pathways<br>MAPK signaling pathway | [190], [191] |
| | ER stress-signaling pathways | [192] |
| Pendimethalin | TNF-α signaling pathway<br>Apoptosis signaling pathway | [27] |
| Mancozeb | Apoptosis signaling pathway | [193], [194] |
| | iNOS and NOX4 signaling pathways | [195] |
| Chlorpyrifos | Apoptosis signaling pathway<br>PKCδ-STAT1 signaling pathway<br>NOX-1 signaling pathways | [196] |
| | IκB/NF-kB signaling pathway | [197] |
| | MAPK signaling pathway | [198] |
| | Apoptosis signaling pathway<br>Increased TLR7 signaling | [199] |

| **Pesticide** | **Signaling Pathways Involved** | **Reference** |
|---|---|---|
| Paraquat | Nrf2 signaling pathway<br>NF-κB signaling pathway | [200] |
| | Apoptosis signaling pathway<br>NF-κB signaling pathway | [201] |
| | ER stress–signaling pathways | [202-206] |
| | PERK signaling pathway | [207] |
| | Nrf2 signaling pathway | [208] |
| | Proteasomal and autophagic Pathways | [209] |
| Permethrin | TLR4-NF-κB signaling pathway | [210] |
| | Nrf2 signaling pathway<br>TLR4-NF-κB signaling pathway | [211] |
| | Nrf2 signaling pathway<br>NF-κB signaling pathway | [212] |
| Deltamethrin | Nrf2 signaling pathway<br>NF-κB signaling pathway<br>Nrf2 signaling pathway | [212],<br>[213] |
| Bifenthrin | MAPK signaling pathway | [214] |
| | TNF-α signaling pathway<br>Flt signaling pathway<br>IL-6 signaling pathway | [215] |

Flt, vascular endothelial growth factor receptor 1 precursor; IL-6, interleukin 6; Nrf2, nuclear factor erythroid 2-related factor 2; TLR4, toll Like receptor 4; ER, endoplasmic recticulum; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; MAPK, mitogen-activated protein kinase; TNF-α, tumor necrosis factor alpha; STAT1, signal transducer and activator of transcription 1; NOX-1, nadph oxidase 1

**Supplemental Table 3. Effects of commonly used Conventional Pesticide Active Ingredients in the Agricultural Market Sector in 2012 on oxidative stress in different tissues.**

| Pesticide | Cell Type/Model System | Concentration /dose | Oxidative stress markers | Reference |
|---|---|---|---|---|
| Glyphosate | Human Skin Keratinocytes HaCaT cells | *10, 25, 50, 100* μM | Increased intracellular ROS levels. Decreased SOD1 expression level. | [179] |
| | Human liver carcinoma (HepG2) cells | 0.5, 2.91, 3.5 μg/mL | Decreased total antioxidant capacity, decreased GPx activity, increased DNA damage. | [216] |
| | Rat heart H9c2 cells | 5 μM, 10 μM | Induced apoptotic cell death. Decreased Bcl-1 expression, increased Bax expression, increased caspases 3/7/9 activity, decreased mitochondrial membrane potential. | [180] |
| | Adult albino male rats (Liver) | 134.95 mg/kg | Increased lipid peroxidation, increased NO level, decreased GSH level, increased TNF-α level. | [217] |
| | *Caenorhabditis elegans* | 2.7%, 5.5%, 9.8% | Increased GST expression, decreased ATP levels, decreased mitochondrial membrane potential. | [218] |
| | *Chlorella kessleri* | 40, 50, 60, 70 mg/L | Increased lipid peroxidation, increased GSH content, increased SOD and CAT activities. | [219] |
| Atrazine (ATR) | Male and female Balb/c mice | 100-400 mg/kg | Increased ROS, increased GSSG activity, and decreased GSH activity. | [181] |
| | Male mice (Liver and kidney) | 78.25 mg/kg | Decreased CAT activity, GST activity, and SOD activity. Decreased intracellular ferric reducing/ antioxidant power. Increased lipid peroxidation. | [220] |
| | Male Wistar rats (Erythrocytes) | 300 mg/kg | Decreased GSH activity. Increased SOD activity, CAT activity, increased GPx activity, and GST activity. | [221] |
| | Adult male Wistar rats (testes and epididymis) | 120, 200 mg/kg | Decreased epididymal CAT activity, decreased GST activity, decreased SOD activity, and increased lipid peroxidation. | [222] |
| | Male Wistar rats | 25 mg/kg | Decreased CAT activity, GSH activity, and SOD activity. Increased lipid peroxidation. | [223] |
| | Adult male albino rats | 300 mg/kg | Decreased CAT activity, GPx activity, GSH activity, SOD activity, and increased lipid peroxidation. | [182] |
| | Female Wistar rats | 5 mg/kg and 125 mg/kg | Decreased CAT activity, decreased GPx activity, increased lipid peroxidation, increased NO level, increased expression of Nrf2 in kidney, decreased expression of HO1 and NQO1. | [183] |
| | Murine microglial cells (BV-2) | 12.5, 25, and 50 μM | Increased intracellular ROS, increased NO and iNOS level, increased *TNF-α and IL*-1β level. | [184] |

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| | Albino rats | 400 mg/kg | Significantly decreased serum/cardiac tissue GSH and TSH levels; significantly increased cardiac tissue HO-1 activity; serum/cardiac tissue GPx and CAT activity, MDA and serum 8-OHdG level altered; significantly decreased cardiac tissue complex I activity. | [224] |
| Metolachlor-S | *Scenedesmus obliquus (green algae)* | 0.1, 0.2, and 0.3 mg/L | Increased ROS generation level, increased SOD and CAT activities. | [225] |
| | *Parachlorella kessleri* (microalga) | 2–200 μg/L | Increased intracellular ROS level, increased antioxidant enzymes (APX, GR, CAT) activities, increased lipid peroxidation. | [226] |
| | Wheat (*Triticum aestivum* L.) | 2.5, 5 mg/L | Increased superoxide anion (ROS) level, increased lipid peroxidation, increased SOD activity, decreased POD activity, decreased CAT and DHAR expression. | [227] |
| 2,4-dichlorophenoxyacetic acid (2,4-D) | *Umbelopsis isabelline (Fungus)* | 100 mg/L | Increased ROS and RNS level, increased lipid peroxidation, decreased CAT activity. | [228] |
| | Pea (*Pisum sativum* L.) | 45.2 μM 22.6 mM | Increased XOD activity, increased SOD, CAT, GPx, APX, and glutathione reductase (GR) activities, increased lipid peroxidation. | [229] |
| | Non-green potato tuber callus | 1-50 μM | Increased CAT, SOD, GR, and GST activities. | [230] |
| | Male 7-week-old Kunming mice | 50, 100, 200 mg/kg | Increased testicular lipid peroxidation, decreased SOD and CAT activities, increased testicular cell apoptosis. | [187] |
| | Goldfish gills, *Carassius auratus* | 1-100 mg/L | Increased lipid peroxidation, increased GSSG content, increased SOD, CAT, and GPx activities. | [231] |
| | *Cnesterodon decemmaculatus* | 252 mg/L | Increased DNA damage, increased CAT, GST, and GSH activities. | [232] |
| | *Acanthospermum hispidum* D.C., Asteraceae weed | 300 μM | Increased lipid peroxidation. | [233] |
| | Rat Cerebellar Granule Cells | 1 mM | Increased ROS generation level, decreased GSH level, decreased CAT activity, increased GPx activity | [234] |
| | Wistar rats | 600 ppm | Increased hepatic lipid peroxidation, decreased CAT, SOD, GPx, and GSH activities. | [235] |

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| | Wistar Albino rats | 5 mg/kg | Increased hepatic lipid peroxidation, increased protein carbonylation, decreased GSH content. Decreased SOD, CAT, GST, and GPx activities in liver. | [236] |
| | Male Wistar rats (Liver) | 15, 75, 150 mg/kg | Increased lipid peroxidation, decreased CAT, GPx, and GR activities, increased/decreased SOD activity. | [237] |
| | Male Wistar Albino rats Plasma, Liver, Kidney, Erythrocytes | 15, 75, 150 mg/kg | Increased lipid peroxidation, decreased SOD, GPx, and CAT activities. | [238] |
| | Male Wistar rats (Liver) | 15, 75, 150 mg/kg | Decreased CAT and GR enzymatic activities. | [239] |
| Metam | Female B6C3F1 mice *Peritoneal macrophages* | 50 µL | Decreased GSH level, upregulation of genes involved in response to oxidant stress. | [240] |
| Acetochlor | *Soil bacteria* | 62 mM and 620 mM | Increased lipid peroxidation, , increased CAT activity at low concentration, decreased CAT activity at high concentration, decreased GR activity. | [241] |
| | *Bufo raddei* tadpole liver | 0.017, 0.034 and 0.068 mg/L | Increased lipid peroxidation, increased DNA damage, decreased total antioxidant capability level. | [242] |
| | Female zebrafish | 1-100 µg/L | Increased plasma ROS level, increased plasma CAT, SOD, and GPx activities. | [243] |
| | Male C57BL/6 mice (testis) | 250, 500, and 1000 mg/kg | Increased lipid peroxidation, decreased SOD activity, decreased GSH activity. | [188] |
| | GC-1 spermatogonia cell | $10^{-4}$ M, 2 × $10^{-4}$ M, 4 × $10^{-4}$ M, 8 × $10^{-4}$ M, and $10^{-3}$ M | Increased cell apoptosis, increased lipid peroxidation, decreased SOD and GSH activities, increased Bax expression and decreased Bcl-2 expression | [188] |
| | Human liver carcinoma cells (HepG2) | 100-400 µM | Increased ROS generation, increased apoptotic cells, decreased antioxidant SOD and GPx activities, decreased mitochondrial transmembrane potential. | [244] |
| | Zebrafish | 50, 100, 200 µg/L | Increased *CAT, GPX, GPX1a, Cu/Zn-SOD and Mn-SOD mRNA levels.* | [189] |

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| Chloropicrin | Primary human corneal epithelial (HCE) cells | 50, 75 μM | Increased apoptotic cell death and DNA damage, increased HO-1 expression, increased lipid peroxidation, increased protein carbonylation. | [190] |
| | Human retinal pigment epithelial cells (ARPE-19) | 1–50 μM | Increased ROS production, increased HO-1 level. | [192] |
| | Human lung epithelial cells (A549) | 1–200 μM | Increased ROS production, increased protein oxidation | [191] |
| Chlorothalonil | *Gill tissues of Pacific oyster (Crassostrea gigas), blue mussels (Mytilus edulis)* | 0.1, 1, and 10 μg/L | Increased lipid peroxidation, increased intracellular GSH level, increased CAT, SOD, GPx, and GR activities. | [245] |
| | *Polychaete Laeonereis acuta* | 0.1, 10, and 100 μg/L | Decreased antioxidant capacity against peroxyl radicals, increased lipid peroxidation. | [246] |
| | *Fish Danio rerio* | 0.1 and 10 μg/L | Gills: Increased ROS level, increased antioxidant capacity against peroxyl radicals (ACAP), increased GST and GCL activities,<br>Liver: Increased lipid peroxidation, increased SOD activity. | [247] |
| | Isolated rat hepatocytes | 1–1000 μM | Increased lipid peroxidation, decreased GSH content. | [248] |
| | *Botryllus schlosseri hemocytes* | 0.1, 1 and 10 μM | Increased apoptotic cells, decreased cytochrome c oxidase activity, decreased GSH activity. | [249] |
| | *Male Wistar rats (Liver)* | 0.1, 0.13, 0.5, 1 mg/kg | Increased 8-OH-2-deoxyguanosine (8-OH-2-DG) level. | [250] |
| Pendimethalin | Fresh water fish, *Channa punctatus* | 0.9, 1.8, and 2.7 mg/L | Increased lipid peroxidation, decreased GSH level, decreased SOD and CAT activities. | [251] |
| | Male Wistar rats (Liver and Kidney) | 62.5, 125 and 250 mg/kg | Increased lipid peroxidation, increased protein carbonylation, decreased GSH level, decreased SOD, CAT, and GST activities, increased oxidative DNA damage. | [27] |
| | Human lymphocytes | 50, 100, 200 μM | Increased ROS level,<br>increased mitochondrial dysfunction, increased apoptosis, increased oxidative DNA damage. | [252] |
| | Rat bone-marrow cells | 12.5, 25, and 50 mg/kg | Increased oxidative DNA damage, increased ROS level, increased lipid peroxidation, increased mitochondrial dysfunction, increased apoptotic cells, decreased CAT activity, decreased GSH level. | [252] |

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| | *Clarias batrachus* (liver) | 0.177, 0.236, 0.355 mg/L | Increased lipid peroxidation, increased SOD and CAT activities. | [253] |
| | Fish *Channa punctatus* (Brain) | 0.5, 0.8 ppb | Increased lipid peroxidation, increased protein carbonylation, decreased GSH level, decreased CAT, GST, and SOD activities. | [254] |
| | Fish *Channa punctatus* (Gills, Liver, Kidney) | 0.5, 0.8 ppb | Increased lipid peroxidation, increased protein carbonylation, decreased GSH and NP-SH level, decreased CAT, GPx, and GST activities. | [255] |
| | Chinese hamster lung fibroblast (V79) cells | 1, 2.5, 5, 7.5, 10, 25, 50, 100, 250, 500 and 1000 µM | Increased ROS level, increased oxidative DNA damage. | [256] |
| Ethephon | Male mice (Spleen and thymus) | 1995 ppm (1/10th oral LD50) | Increased lipid peroxidation, decreased GSH level, decreased CAT and GPx activities, no change in SOD activity. | [257] |
| | 3T3 murine embryonic fibroblast (MEF) cells | 10, 40, 160, 640 µM | Increased ROS production level, increased lipid peroxidation, increased DNA damage. | [258] |
| | Spinach (Spinacia oleracea L.) | 10 mM | Increased CAT, polyphenol oxidase (PPO), peroxidase (POD) activities. | [259] |
| | *Ipomoea cairica* (Linn.) Sweet | 1.4, 7.2 g/L | Increased $H_2O_2$ levels. | [260] |
| | *Schisandra chinensis Turcz*. (*Baill*.) | 1 ppm, 10 ppm | Increased POD activity, decreased PPO activity. | [261] |
| Mancozeb | *Carassius auratus Goldfish blood and gills* | 3, 5 and 10 mg/L | Increased protein carbonylation, increased lipid peroxidation, increased SOD, CAT, GST, and G6PDH activities. | [262] |
| | Carassius auratus Goldfish brain, liver, and kidney | 3, 5 and 10 mg/L | Increased protein carbonylation, increased lipid peroxidation, increased SOD activity in liver and kidney, increased CAT activity in liver, increased GPx activity in liver and kidney. | [263] |
| | *Cassia angustifolia* | 0.1, 0.15, 0.2 and 0.25 % | Increased lipid peroxidation, increased APX, GR, SOD, CAT activities, increased GSH content. | [264] |
| | *Caenorhabditis elegans* | 0.1%, 1.0%,1.5% | Increased $H_2O_2$ levels, increased GST expression, decreased mitochondrial membrane potential, decreased ATP levels. | [265] |
| | *Caenorhabditis elegans* | 0.1%, 7.5%, 15% | Increased $H_2O_2$ levels, increased hydroxyl radicals (·OH) level, decreased mitochondrial membrane potential, increased GST expression. | [266] |

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| | *Drosophila melanogaster* | 5 and 10 mg/mL | Increased lipid peroxidation, increased ROS level, increased CAT and GST activities, decreased SOD activity, decreased GSH level. | [267] |
| | *Rat-1 fibroblasts,* Peripheral blood mononucleated cells (PBMC) | 125, 250, 500 ng/mL | Increased 8-hydroxy-2′-deoxyguanosine (8-OHdG) level, increased ROS level, increased apoptotic cells. | [193] |
| | Male NMRI mice | 50 and 500 mg/kg | Increased lipid peroxidation, increased protein carbonylation, decreased SOD and CAT activities, decreased GSH content, decreased total antioxidant capacity, decreased GPx expression, increased iNOS and NOX4 expression. | [195] |
| | Rat thymocytes | 0.5, 2 and 5 µg/ml | Increased ROS production, increased apoptotic cells, decreased mitochondrial membrane potential, decreased ATP levels. | [268] |
| | *Human Gastric Adenocarcinoma* (*AGS*) cells | 5, 10 µM | Increased ROS level, increased apoptotic cells, decreased mitochondrial transmembrane potential, upregulation of Bax and downregulation of Bcl-2 and Bcl-xL. | [194] |
| Chlorpyrifos | Immortalized murine mesencephalic dopaminergic (N27) cells | 300 nM-300 µM | Increased intracellular ROS generation, increased mitochondrial ROS, decreased mitochondrial membrane potential, decreased GSH level, increased DNA fragmentation, increased caspase-3 activation and proteolytic cleavage of PARP, increased Bax level and decreased Bcl-2 level, increased proteolytic cleavage of PKCδ, increased STAT1 phosphorylation. | [196] |
| | Lund human mesencephalic (LUHMES) cells | 10 nM-100 µM | Increased DNA fragmentation, increased intracellular ROS, decreased mitochondrial membrane potential, and increased caspase-3 activity. | [196] |
| | Human neuroblastoma *SH-SY5Y* cells | 50 µM to 200 µM | Increased intracellular ROS, increased apoptosis, increased TNF-α levels, dysfunction in HO-1 and MnSOD levels. | [197] |
| | Rat adrenal pheochromocytoma (PC12) cells | 25, 50, 100, and 200 µM | Increased apoptotic cells, increased activity of caspase-9 and caspase-3 and cleaved of PARP-1, increased ROS level, increased lipid peroxidation, decreased mitochondrial complex I activity, increased HO-1 level, decreased CuZnSOD and MnSOD levels. | [198] |
| | Rat erythrocytes | 6.75 mg/kg | Decreased SOD activity, GST activity, and CAT activity. Increased lipid peroxidation. | [269] |
| | Male Wistar rats | 4.75 mg/kg | Decreased CAT activity, decreased SOD activity, increased GPx activity, and increased lipid peroxidation. | [270] |

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| | Male Wistar rats (aorta, liver, plasma, and kidney) | 2.5, 5, 25 mg/kg | Increased lipid peroxidation, increased nitration (NO), increased SOD activity. | [271] |
| | Male Swiss albino adult rats | 5, 10, 20, 30 mg/kg | Increased lipid peroxidation, decreased testicular CAT, SOD, and GPx activities, decreased GSH content. | [272] |
| | Adult male Wistar rats | 8 mg/kg | Increased amygdala ROS levels. Increased amygdala and hippocampal NO level. | [273] |
| | Male Wistar rats | 5.4 mg/kg | Increased levels of MDA, SOD and CAT; decreased GPx and GST activities in heart. | [274] |
| | Male Kunming mice | $10^{-5}$ M | Increased lipid peroxidation, increased •OH level, decreased SOD, GPx, and CAT activities, decreased GSH content, increased levels of Bax, Bcl-2, and p53 in splenic B cells. | [199] |
| Metolachlor | Male Wistar rats (Liver) | 400–1000 nmol/mg | Decreased mitochondrial membrane potential. | [15] |
| | *Soil bacteria* | 34 mM and 340 mM | Increased lipid peroxidation, increased CAT activity at low concentration, decreased CAT activity at high concentration, decreased GR activity. | [241] |
| | Lettuce, bean and pea seeds and leaves | 0.2 – 200 μM | Decreased CAT, SOD, and GPx antioxidant enzymatic activities. | [275] |
| Propanil | 8 weeks old male rats | 200 mg/kg | Increased lipid peroxidation, decreased SOD, GPx, and GST activities, decreased GSH level. | [276] |
| | Wistar rats Liver | 100 mg/kg | Increased lipid peroxidation, decreased CAT, SOD, GST, and GSH activities. | [277] |
| | Albino rats Liver | 20 mg/kg | Increased lipid peroxidation, decreased GSH level, decreased CAT activity. | [52] |
| | Common carp (*Cyprinus carpio*) Brain | 2 and 4 mg/L | Increased lipid peroxidation, increased protein carbonylation, decreased GSH level, decreased SOD, CAT activities | [278] |
| Dicamba | Isolated mitochondria from Potato tubers (*Solanum tuberosum)* | 5-30 μmol/mg | Decreased mitochondrial transmembrane potential, inhibited complex II, III, and IV activity. | [279] |
| | Non-green potato tuber callus | 1-50 μM | Increased CAT, SOD, GR, and GST activities. | [230] |
| | *Cnesterodon decemmaculatus* | 410 mg/L | Increased DNA damage, increased CAT, GST, and GSH activities. | [232] |

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| | Isolated mitochondria Arabidopsis | 1 mM | Increased mitochondrial $H_2O_2$ levels. | [280] |
| Trifluralin | Chinese hamster lung fibroblast (V79) cells | 1, 2.5, 5, 7.5, 10, 25, 50, 100, 250, 500 and 1000 µM | Increased ROS level, increased oxidative DNA damage. | [256] |
| | Male Wistar albino rats Kidney, ureter, urinary bladder | 0.8, 2 g/kg | Increased lipid peroxidation, decreased SOD and GPx activities, increased apoptotic DNA fragmentation. | [57] |
| Acephate | *Chlamydomonas mexicana* | 15 mg/L | Increased SOD and CAT activities. | [281] |
| | *Drosophila melanogaster* | 1-6 µg/mL | Increased lipid peroxidation, increased protein carbonylation, increased CYP450, SOD, CAT, and GST activities, increased Hsp70 expression, increased DNA damage. | [282] |
| | *Male albino rats (Plasma and Liver)* | 30 mg/kg | Increased lipid peroxidation, decreased CAT, SOD, and GSH activities, increased GPx activity. | [283] |
| | *Male rats (Erythrocytes)* | 360 mg/kg | Increased lipid peroxidation, decreased GSH content, increased GST and GR activities. | [284] |
| | *Albino rats* | 50 mg/kg | Increased lipid peroxidation, decreased testicular activities of CAT, SOD, and levels of GSH. | [285] |
| | *Human Sperm* | 50, 100, and 200 µg/mL | Increased DNA damage. | [286] |
| | Chinese hamster ovary (CHO-K1) cells | 237.12 µM | Increased GST and GPx activities, increased GSH content. | [287] |
| | Porcine kidney proximal tubule *cell* line (*LLC-PK)* | 2500 ppm | Increased lipid peroxidation, increased $H_2O_2$ accumulation, | [58] |
| Paraquat (PQ) | Human dopaminergic neuroblastoma cells (SK-N-SH) | 0.2, 0.5, 1 mM | Increased cytosolic ROS, increased mitochondrial ROS, increased apoptosis, increased oxidative stress in the mitochondrial matrix, decreased mitochondrial membrane potential, increased free radical formation, increased lipid peroxidation. | [200] |
| | Human IMR-32 neuroblastoma cells | 0.05, 0.1, 0.2 mM | Transcriptional activity driven by ARE and NF-κB activated. | [200] |
| | Rat lung slices | 100 µM–10 mM | Complex I-dependent increased ROS production. | [288] |
| | Rat organotypic midbrain slice cultures | 10–50 µM | Excitotoxic mechanism of ROS production. | [289] |
| | Rat primary mesencephalic cultures | 0.5–1 µM | NADPH oxidase-dependent microglial ROS production. | [290] |

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| | Rat primary mesencephalic cultures | 250 μM | Robust and immediate production of ROS, involvement of mitochondrial complex III and mitochondrial membrane potential in ROS generation. | [291] |
| | Human neural progenitor cells (hNPCs) | 1, 10, 100 μM | Decreased SOD and CAT, increased lipid peroxidation, increased Nrf2, HO-1, and NQO1expression, upregulated Cyt C and caspase-9. | [208] |
| | Human neural progenitor cells (hNPCs) | 0.1, 1, 10, 100 μM | Increased apoptotic cells, increased intracellular ROS, increased caspase-3 activity, increased NF-κB activity, p53 and p21 mRNA expression. | [201] |
| | Human plasma | unknown | Increased lipid peroxidation, decreased plasma antioxidant capacity and plasma SH groups. | [292] |
| | Rat brain mitochondria | 250 μM | Robust and immediate production of ROS, mitochondrial uptake of PQ, involvement of mitochondrial complex III and mitochondrial membrane potential in ROS generation. | [293] |
| | Non-green potato tuber callus | 1-50 μM | Increased CAT, SOD, and GR activities. | [230] |
| Glufosinate | *Amaranthus palmeri* | 560 g/ha | Increased $O_2^-$ and $H_2O_2$ (ROS) level, increased SOD, CAT, APX, and GR activities. | [294] |
| | Horseweed, palmer amaranth, kochia | 560 g/ha | Increased lipid peroxidation, increased $O_2^-$ and $H_2O_2$ (ROS) level, increased SOD, CAT, APX, and GR activities. | [295] |
| | *Chlorella vulgaris* | 10, 20 μg/mL | Increased lipid peroxidation, increased SOD, CAT, and POD activities. | [296] |

**Supplemental Table 4. Effects of most commonly used Organophosphate Insecticide Active Ingredients in the Home and in 2012 on oxidative stress in different tissues.**

| Pesticide | Cell Type/Model System | Concentration/dose | Oxidative stress markers | Reference |
|---|---|---|---|---|
| Phorate | Male Wistar rats (Liver/bone marrow cells) | 0.046, 0.092, 0.184 mg/kg | Increased lipid peroxidation, decreased CAT activity and GSH level, increased intracellular ROS in bone marrow cells, reduced mitochondrial membrane potential in bone marrow, significant cellular DNA damage and apoptosis. | [297] |
| | Human amnion epithelial (WISH) cells | 50-1000 µM | Increased extracellular superoxide anion ($O_2^-$) production, increased intracellular ROS generation, mitochondrial damage. | [298] |
| | Human lymphocytes | 50-500 µM | Increased intracellular ROS generation, decreased mitochondrial membrane potential. | [299] |
| | Calf thymus DNA (ct-DNA) | 1000 µM | Increased 8-Hydroxy-2′-deoxyguanosine (8-oxodG) DNA adduct formation. | [299] |
| Dicrotophos | Renal tubular epithelial cell (LLC-$PK_1$) | 1250 ppm | Increased ROS production, increased lipid peroxidation. | [300] |
| | Human liver carcinoma (HepG2) cells | 25 - 400 µM | Increased DNA damage level. | [301] |
| | Human liver carcinoma (HepG2) cells | 50 µM–200 µM | Increased intracellular ROS production, decreased mitochondrial membrane potential, increased apoptosis. | [302] |
| Dimethoate | Bok choy | 600 g a.i. /ha (applied dose of active ingredient per hectare) | Increased ROS level. | [303] |
| | Rat liver and kidney | *10-30 mg/kg* | Decreased SOD level, increased lipid peroxidation. | [304] |
| | Rat peripheral blood cells | *10-60 mg/kg* | Increased DNA damage and fragmentation, increased apoptosis, decreased mitochondrial membrane potential. | [305] |
| | Human peripheral blood lymphocytes | 40-100 mM | Increased lipid peroxidation, increased protein oxidation, increased SOD and CAT activities. | [306] |
| | *Gammarus pulex* | 10-40 µg/L | Increased lipid peroxidation, decreased GSH level, decreased SOD, CAT, and GST activities. | [307] |

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| | Male Wistar rat liver and brain | 0.6, 6, 30 mg/kg | Increased lipid peroxidation, increased SOD, CAT, GPx, and GR activities, decreased GSH at 30 mg/kg. | [91] |
| | Adult female rats | 0.2 g/L | Increased lipid peroxidation, decreased GPx, SOD, CAT activities activity, decreased GSH level. | [308] |
| | Female Wistar rats (Erythrocytes) | 0.2 g/L | Increased lipid peroxidation, increased protein carbonylation, increased advanced oxidation protein products (AOPP), increased CAT, SOD, and GPx activities decreased GSH level. | [309] |
| | Rat erythrocytes | 0.03 mg/kg | Increased lipid peroxidation, increased SOD and CAT activities, increased total-SH content. | [310] |
| | Freshwater fish *Channa punctatus* (Bloch) | 4.8, 9.6, 14.3 μg/L | Increased lipid peroxidation, decreased SOD activity, increased GSH level, increased DNA damage. | [311] |
| | *Oncorhynchus mykiss* | 0.0735, 0.3675, 0.7350 mg/L | Increased lipid peroxidation, increased SOD and GPx activities. | [312] |
| | *Cyprinus carpio* | 16 and 32 μg/L | Increased lipid peroxidation, increased CAT activity, decreased total antioxidant levels. | [313] |
| Terbufos | Mouse immortalized spermatogonia (GC-1) cells | 50, 100, 200 μM | Increased intracellular ROS production, decreased mitochondrial membrane potential, increased apoptosis, increased DNA damage. | [314] |

**Supplemental Table 5. Table showing additional pesticides that have been documented to cause oxidative stress in different tissues.**

| Pesticide | Cell Type/Model System | Concentration/dose | Oxidative stress markers | Reference |
|---|---|---|---|---|
| Lindane | Thymic cells from C57BL/6 mice | 37.5, 50, 75, 150, 200 μM | PER and lindane mixtures increased SOD activity, had no effect on CAT levels and inhibited GPx and GSH-R specific activities. | [315] |
| | Rats | 100 mg/kg | Increased lipid peroxidation, decreased GSH, SOD, CAT, GPx, and GST activities. | [96] |
| Dichlorodiphenoxy-trichloroethane (DDT) | Human normal liver (HL-7702) cells | *p,p'*-DDT (10, 20, 30 μM) | Increased intracellular ROS. Activated caspase-9, increased Bax and p53 levels, anti-apoptotic gene Bcl-2 downregulated, and increased NF-κB p65 levels. | [316] |
| Maneb | Rat adrenal pheochromocytoma (PC12) cells | 50–1000 ng/ml | Increased GSH and GSSG, altered HO-1 levels. | [317] |
| | Rat primary mesencephalic cultures | 30 μM | ROS generation, mitochondrial uncoupling. | [318] |
| | | 10–120 μM | Decreased ATP levels, mitochondrial dysfunction. | [318] |
| Dieldrin | Rat adrenal pheochromocytoma (PC12) cells | 30–500 μM | Increased ROS, decreased mitochondrial membrane potential and activity, decreased lipid peroxidation, increased DNA fragmentation. | [319] |
| | Rat adrenal pheochromocytoma (PC12) cells | 100μM | Increased 8-oxodGuo levels (created by ROS). | [320] |
| | Rat adrenal pheochromocytoma (PC12) cells | 100-300μM | Increased caspase-3 activity and DNA fragmentation. | [321] |
| | Immortalized mouse nigral clonal (SN4741) cells | 40 μM | Increased ROS, apoptotic cell death | [322] |
| | PC12 cells | 30-100 μM | Increased ROS, apoptotic cell death. | [323] |
| | Immortalized rat mesencephalic clonal (N27) cells | 0-70μM | α-synuclein aggregation, increased DNA fragmentation. | [324] |
| | Primary mouse microglial cultures | 0.1 nM–1 μM | Microglial NADPH-oxidase dependent ROS production. | [325] |

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| | Human THP-1 monocytes | 10 μM, 20 μM | Elevated ROS level, dose-dependent increase in p47$^{phox}$ phosphorylation (necessary to activate NOX2). | [326] |
| | Mice | 3–48 mg/kg | Increased lipid peroxidation. | [327] |
| | Mice | 0.3–3 mg/kg | Decreased GSH, decreased DAT expression, increased α-synuclein, increased cysteinyl-catechol adducts. | [328] |
| Clothianidin | Male Wister rats | 2, 8, and 24 mg/kg | Increased TBARS significantly in testicular tissue, GSH level did not change significantly in all treated groups. | [329] |
| | Male Wister rats | 2, 8, and 32 mg/kg | Significant decrease in the GSH level in the testicular tissue. | [330] |
| Chlordane | Human THP-1 monocytes | 1 μM , 5 μM, and 10 μM *trans*-nonachlor | Elevated ROS level, enhanced superoxide production, dose-dependent increase in p47$^{phox}$ phosphorylation (necessary to activate NOX2). | [326] |
| | Murine macrophage cell J774a.1 | 10 μM *trans*-nonachlor | Increased intracellular superoxide level | [326] |
| | Human HL-60 cell | 1 μM and 10 μM *trans*-nonachlor | Increased intracellular superoxide level | [326] |
| Pentachlorophenol (PCP) | Primary murine splenocytes | 25–100 μM PCP | Increased ROS production, increased apoptosis, decreased mitochondrial membrane potential. | [331] |
| | Primary murine splenocytes | PCP metabolite (12.5–50 μM TCHQ) | Significantly increased ROS production, increased apoptosis, increase in annexin V and PI positive (necrotic cells), decreased mitochondrial membrane potential, ERK activation, increased expression of cleaved caspase-3 and degradation of PARP. | [331] |
| | Murine hepatocytes | 0.03, 0.06, and 0.12% | Increased 8-OHdG levels | [332] |
| | Sprague–Dawley rats | 40 mg/kg PCP | Increased lipid peroxidation | [118] |
| Endosulfan | Human peripheral blood lymphocytes | 0.1, 17 μM | Increased apoptosis | [333] |
| | Human neuroblastoma *SH-SY5Y* cells | 50, 100, 200 μM | Increased intracellular ROS, increased intracellular superoxide anion, decreased specific activities of SOD, CAT, and GPX, | [334] |

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| | | | increased lipid peroxidation, increased expression of NFκB p50. | |
| | Male Wistar rats | 2 mg/kg | Increased SOD, GPx, CAT activities and increased (MDA level) lipid peroxidation. | [122] |
| Zineb | Human neuroblastoma *SH-SY5Y* cells | 50, 100, 200 μM | Increased intracellular ROS, increased intracellular superoxide anion, decreased specific activities of SOD, CAT, and GPX, increased lipid peroxidation, increased expression of NFκB p50. | [334] |
| 1-methyl-4-phenylpyridinium ($MPP^+$) | Human dopaminergic neuroblastoma cells (SK-N-SH) | 0.01–2.5 mM $MPP^+$ | Increased mitochondrial ROS, increased apoptosis, increased oxidative stress in the mitochondrial matrix, decreased mitochondrial membrane potential, increased lipid peroxidation. | [200] |
| | Rat dopaminergic N27 cells | 100–1000 μM | Increased intracellular ROS, increased Nox2 protein expression. | [335] |
| Rotenone | Rat primary mesencephalic cultures | 0.5–30 nM | NADPH oxidase dependent microglial ROS production. | [336] |
| | Human dopaminergic neuroblastoma cells (SK-N-SH) | 0.65–4 μM | Increase mitochondrial ROS, increased apoptosis, decreased mitochondrial membrane potential, increased lipid peroxidation. | [200] |
| Ziram | Human Natural Killer *Cells (NK-92MI)* | 0.125 – 4 μM | Increased apoptosis, increased intracellular levels of active caspases3, 3/7, 8, 9, increased cytochrome-c release and decreased mitochondrial membrane potential. | [337] |
| | Progenitor Leydig cells (PLCs) | 1 – 5 μM | Increased intracellular ROS, increased apoptosis, decreased mitochondrial membrane potential. | [338] |
| Methamidophos | Human Peripheral Blood Mononuclear Cells (PBMCs) | 3 – 20 mg/L | Increased intracellular ROS production, increased lipid peroxidation, decreased GSH level. | [339] |
| Dichlorvos | Adult male Wistar rats | 8.8 mg/kg | Increased amygdala and hippocampal ROS levels. Increased NO level both in amygdala and hippocampus. | [340] |
| | Human erythrocytes | 1 – 100 μM | Decreased SOD, CAT, and GPx activities. Increased lipid peroxidation. | [341] |

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| | Human colon carcinoma (HCT116) cell | 150 – 450 µM | Increased ROS, increased lipid peroxidation, increased DNA damage, decreased mitochondrial membrane potential, increased caspase-3, CAT, and SOD activities. | [342], [343] |
| | Male Wistar rats (Erythrocytes) | 70 mg/kg | Increased lipid peroxidation, increased SOD activity. | [344] |
| | Male albino rats (Brain) | 6 mg/kg | Increased lipid peroxidation, increased protein carbonylation, increased mitochondrial DNA oxidation, increased level of mitochondrial ROS production, decreased mitochondrial glutathione levels and MnSOD activity. | [345] |
| Tebuconazole | H9c2 cardiac cells | 10 – 100 µM | Increased mitochondrial ROS, increased lipid peroxidation, increased apoptosis, decreased mitochondrial membrane potential, increased in Bax/Bcl-2 level, activated caspase-9 and caspase-3. | [346] |
| | Male Wistar rat | 0.9, 9 and 27 mg/kg | Increased lipid peroxidation, protein carbonyl, advanced oxidation protein product (AOPP) levels and DNA damage. Increased renal SOD, CAT, and GPx activities, decreased GSH activity. | [346] |
| Triflumuron | Balb/c mice bone marrow cell | 250 – 500 mg/kg | Increased DNA damage. | [347] |
| | Human colon carcinoma (HCT116) cell | 100, 200, 400 and 600 µM | Increased intracellular ROS, increased lipid peroxidation, increased DNA damage, increased SOD, CAT, and GST activities. Decreased mitochondrial membrane potential | [347], [348] |
| | Human renal embryonic cells (HEK 293) and Human liver carcinoma cells (HepG2) | 50 – 300 µM | Increased intracellular ROS, increased lipid peroxidation, increased Hsp70 levels, increased CAT and SOD activities, decreased mitochondrial membrane potential, increased expression levels of Bax and decreased expression of Bcl-2. | [349] |
| | Male Balb/C mice | 250, 350, and 500 mg/kg | Increased protein carbonyl, increased lipid peroxidation, increased CAT, SOD, GPx, and GST activities. | [147] |
| Acetamiprid | Rat adrenal pheochromocytoma (PC12) cells | 110, 220, and 330 µM | Increased intracellular ROS, increased lipid peroxidation, increased DNA damage, decreased mitochondrial membrane potential. | [350] |

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| | Pancreatic Cell Line AR42J | 1 - 6 mM | Increased DNA damage, decreased GSH level. | [351] |
| | Male and female Wistar rats (Kidney & Liver) | 5.5, 11, and 22 mg/kg | Increased lipid peroxidation, decreased GSH, SOD, CAT, and GPx activities. | [352] |
| | Kumming male mice | 30 mg/kg | Increased MDA and NO concentrations in the testes; reduced the activity of CAT, GPx, SOD; and activated p38. | [353] |
| Thifluzamide | Zebrafish embryos | 0.19, 1.9, 2.85 mg/L | Increased lipid peroxidation, decreased SOD. | [354] |
| Aldicarb | Chinese Hamster Ovary (CHO-K1) cells | Aldicarb 10 µg/mL | Increased lipid peroxidation, decreased GSH activity, increased GR, GPx and GST activities. | [355] |
| | Chinese Hamster Ovary (CHO-K1) cells | Aldicarb sulfone 10 µg/mL | Increased lipid peroxidation, decreased GSH activity, increased GR, GPx and GST activities. | [355] |
| | Chinese Hamster Ovary (CHO-K1) cells | Aldicarb sulfoxide 10 µg/mL | Increased lipid peroxidation, decreased GSH activity, increased GR, GPx and GST activities. | [355] |
| Propoxur | Chinese Hamster Ovary (CHO-K1) cells | 10 µg/mL | Increased lipid peroxidation, decreased GSH activity, increased GR, GPx and GST activities. | [355] |
| Methidathion | Male Wistar rats | 5 mg/kg | Increased lipid peroxidation. | [356] |
| Diazinon | Female Sprague-Dawley rats | 8, 10, 12 and 20 mg/kg | Increased lipid peroxidation, decreased SOD, GPx activities. | [357] |
| | Male Wistar albino rats | 20 mg/kg | A significant increase in cardiac MDA and NO content was observed compared with the control group, but cardiac antioxidants were significantly ($p \leq .05$) decreased. | [358] |
| | Male MFI mice | 16.25 and 32.5 mg/kg | Increased lipid peroxidation, increased protein carbonylation, decreased GSH level, decreased CAT, SOD, GPx, and GR activities. | [359] |
| | Rats | 15 mg/kg | Increased MDA level, lower level of reduced GSH, induction of apoptosis | [163] |
| | Male Wistar rats | 20 mg/kg | Increased level of TNF-α and *8-iso-prostaglandin F*2α | [360] |
| | Wistar albino rats | 335 mg/kg | Increased lipid peroxidation | [361] |

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| Monocrotophos | Wistar rats | 0.36 mg/kg | Cardiac oxidative stress was conferred by accumulation of protein carbonyls, lipid peroxidation and glutathione production. | [169] |
| | Male albino Wistar rats (Liver, Kidney, Spleen, Brain) | 4.5 and 9.0 mg/kg | Increased lipid peroxidation, increased DNA damage. | [362] |
| | Chinese hamster ovary (CHO-K1) cells | 233.58 μM | Increased GPx activity, increased GSH content. | [287] |
| Aluminum phosphide | Male Wistar rats | 12 mg/kg | Elevated ROS and plasma iron levels. Increased Caspase 3 and 9 levels, increased CAT activity. | [363] |
| | Male Wistar rats | 6 and 12 mg/kg | Increased hydroxyl radicals, increased lipid peroxidation, decreased mitochondrial complexes (II, IV and V), decreased mitochondrial membrane potential, increased apoptosis. | [364] |
| Penconazole (triazole) | Male Wistar rats | 67 mg/kg | Increased lipid peroxidation, protein carbonyls and DNA fragmentation in the heart, increased CAT, SOD, and GPx activities, decreased GSH level. | [173] |
| Imidacloprid (IMI) | Chinese hamster ovary (CHO-K1) cells | 0.97– 500 μM | Significant inhibition of the activity of GST, GPx, and GR. | [365] |
| | Male Wistar rats | 40 mg/kg | Significant increase in MDA level, the activities of CAT, and SOD and decreased the activities of GST and total SH. | [366] |
| | Male Wistar rats | 45 and 90 mg/kg | Significantly increased MDA levels and decreased GSH levels and the activities of CAT, SOD, GPx, and GST. | [367] |
| | Male Wistar rats | 45 and 90 mg/kg | Increased MDA content and decreased the activities of SOD, GSH, GPx, and CAT. | [368] |
| | Male Wistar rats | 0.5, 2, and 8 mg/kg | Increased lipid peroxidation and increased apoptosis. | [369] |
| | Wistar rats | 1 mg/kg | Significant increase in NO production in brain. IMI induced the mRNA transcription of iNOS, eNOS, and nNOS in brain and iNOS and eNOS in the liver. IMI significantly increased CAT activity in brain and increased MDA levels in plasma, brain, and liver. XO activity was elevated in liver and | [370] |

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| | | | brain; MPO activity was increased only in the liver. GSH levels were significantly depleted in brain. | |
| | Female Wistar rats | 5, 10, and 20 mg/kg | Significantly increased MDA content and significantly decreased SOD, CAT and GPx activities, and GSH content in ovary. | [371] |
| | Female Wistar rats | 10 µM equivalent to 2.6 mg/100 g | Increased the production of NO levels in liver. MDA increased significantly in liver and plasma. CAT, SOD, and GPx activities responded differently to IMI administration. GSH level was significantly decreased in the liver and brain. | [372] |
| | Female Wistar rats | 5, 10, and 20 mg/kg | Significantly decreased GSH level in liver and the activities of GPx, CAT, and SOD in liver and brain and significantly increased MDA content in brain and kidney. | [373] |
| | Male Swiss albino mice | 14.976 mg/kg | Significantly increased MDA levels, increased CAT, SOD, GPx and GST activities, and decreased GSH level. | [374] |
| | Earthworm *Eisenia fetida* | 0.2, 0.66, 2, and 4 mg/kg | IMI significantly increased ROS level, MDA content, and CAT and peroxidase (POD) activities. | [375] |
| | Honeybees (*Apis mellifera* L.) thorax | 0.7, 2.0 ng/mL | Increased lipid peroxidation, increased GPx, CAT activities | [376] |
| Fluazifop-*p*-butyl (FPB) | Male Wistar rats | 18.75, 37.50, and 75.00 mg/kg | Increased lipid peroxidation, decreased testicular antioxidant status, decreased testicular activities of SOD, CAT, GST and GSH. | [176] |
| | *Acanthospermum hispidum* | 10 µM | Increased lipid peroxidation, increased ROS level, | [377] |
| | *Acanthospermum hispidum* | 5 µM, 10 µM | Increased ROS level, increased SOD, CAT, APx, and GR activities. | [378] |
| | *Acanthospermum hispidum* | 5 µM, 10 µM | Increased lipid peroxidation. | [379] |
| Nitenpyram | Male and female zebrafish (*Danio rerio*) | 0.6, 1.2, 2.5, and 5.0 mg/L | Resulted to DNA damage in the exposed zebrafish livers. SOD and CAT activities were inhibited; ROS production, GST activity, DNA damage, and MDA content increased. | [177] |

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| Thiacloprid | Male Wistar rats | 22.5, 112.5 mg/kg | Significantly decreased CAT, GPx, and GSH, increased lipid peroxidation levels in lymphoid organs and significantly increased total NOx (NO2 and NO3) in polymorphonuclear leukocytes and TBARS levels in all lymphoid organs and the plasma. | [380] |
| | Earthworm *Eisenia fetida* | 1 and 3 mg/kg | Increased DNA damage, inhibited the activities of GST, CAT, SOD, and POD. | [381] |

**Supplemental Table 6. Table showing pesticide tolerable and nontoxic concentrations.**

| Pesticide | Nontoxic concentrations | Reference |
|---|---|---|
| Glyphosate | 10-100 μM induced proliferation and cell growth in Human Skin Keratinocytes HaCaT cells. | [179] |
| | 0.5-2.91 μg/mL induced a slight increase of cell proliferation after treatment in Human liver carcinoma (HepG2) cells. | [216] |
| | 2.7% No significant superoxide and hydroxyl radicals production in *Caenorhabditis elegans*. | [218] |
| | 0.5 - 15 mM had no effects on transmembrane potential (Δψm), no effect on enzymatic activities of mitochondrial respiratory complexes II, III, and IV, and no effect on ATP and ATPsynthase activities in isolated rat liver mitochondria. | [382] |
| Atrazine (ATR) | 5 and 25 mg/kg had no significant increase on blood urea nitrogen (BUN) and creatinine (CREA) levels in female Wistar rats. | [183] |
| Metolachlor-S | 2 μg/L had no effect on cell growth and cell numbers at 48h treatment, it decreased ROS content at 72 h treatment, and decreased lipid peroxidation at 4 h treatment in *Parachlorella kessleri* (microalga). | [226] |
| 2,4-dichlorophenoxyacetic acid (2,4-D | 0.01-0.5μM had no effect on cell growth in non-green potato tuber callus. | [230] |
| | 1-100 mg/L had no effect on protein carbonyl levels in Goldfish gills, *Carassius auratus*. | [231] |
| | 15 mg/kg had no clinical signs of 2,4-D poisoning in Male Wistar rats (Liver) | [237] |
| | 15 mg/kg had no clinical signs of 2,4-D poisoning in Male Wistar rats (Liver) | [239] |
| Acetochlor | 0.017mg/L had no significant increase in lipid peroxidation (MDA content) in tadpole liver. | [242] |
| | 250mg had no effect in the organ/body ratio in lung, spleen, testis in C57BL/6 male mice. | [188] |

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| | 50 μM did not induce any significant cytotoxic effect for 12 h and 24 h in HepG2 cells. 100 μM had no effect on the mitochondrial membrane potential after 24 hr treatment. | [244] |
| Chloropicrin | 10-20 μM had no significant decrease in cell viability of human retinal pigment epithelial (ARPE-19) cells. | [192] |
| | 10 μM had no significant decrease in cell viability of lung epithelial cell line (A549). | [191] |
| Chlorothalonil | 1-5 μM did not induce cytotoxicity (<15% LDH leakage) and lipid peroxidation in isolated rat hepatocytes. | [248] |
| Pendimethalin | 50 μM no effect on mitochondrial membrane potential (Δψm) in human lymphocytes. | [252] |
| | 12.5 mg/kg did not show significant ROS level and had no significant effect on the mitochondrial membrane potential in rat bone-marrow cells. | [252] |
| | 1-25 μM had no effect on cell viability in Chinese hamster lung fibroblast V79 cells. | [256] |
| Ethephon | 10-160 μg/ml significantly increased cell proliferation in 3T3 embryonic fibroblast cells. 10-40 μg/ml had no significant changes in ROS content and lipid peroxidation. | [258] |
| | 3-10 mg/L had no effect on significant effect on the protein carbonylation. 3-5 mg/L had no effect on lipid peroxidation in *Carassius auratus.* | [262] |
| Mancozeb | 5mg/ml had no significant effect on cell viability after 15 days of treatment in Drosophila melanogaster. | [267] |
| | 50mg/kg had no effect on lipid peroxidation in male NMRI mice testes. | [195] |
| Chlorpyrifos | 25 μM had no significant effect on cell viability in SH-SY5Y cells. | [197] |
| | 25 μM had no significant effect on cell viability in PC12 cells and had no effect on cell morphology. | [198] |
| | 2.5 mg/kg had lower MDA level compared to 5 and 10mg/kg exposure in aorta, liver, plasma, and kidney of male Wistar rats. | [271] |
| | 0.1 and 1 μM did not affect cell viability in splenocytes. | [199] |

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| Metolachlor | 100 μM did not affect cell density in *B. stearothermophilus.* | [15] |
| Paraquat | 0.1-10 μM did not affect cell viability in human neural progenitor cells. | [201] |
| Bifenthrin | 5 μM did not affect cell viability in human colorectal HCT-116 cells. | [214] |
| | 5mg/kg had no effect on the body weight of male mice and no obvious signs of poisoning was found. | [383] |
| | 1-5 μM did not affect cell viability in human umbilical vein endothelial (HUVEC) cells. | [215] |
| Malathion | 6 mM had no effect on cell viability and had a mitogenic effect on the growth of human liver carcinoma (HepG2) cells. | [384] |
| Phorate | 0.046mg/kg did not induce lipid peroxidation in rats liver tissue after 14 days exposure. | [297] |
| Dimethoate | 0.6mg/kg did not induce lipid peroxidation in rats liver and brain tissue. | [91] |
| Endosulfan | 50 μM had no significant difference in LDH release (cell viability) in SH-SY5Y cells | [334] |
| Zineb | 50 μM had no significant difference in LDH release (cell viability) in SH-SY5Y cells. | [334] |
| Methamidophos | 3 mg/L did not affect the cell viability in human peripheral blood mononuclear cells. | [339] |
| Dichlorvos | 1 μM did not induce MDA level/lipid peroxidation in erythrocytes. | [341] |
| Acetamiprid | 27.5-55 mg/kg had no clinical signs of toxicity in Wistar rats. No significant decreases in body weight during 13 weeks of treatment. | [352] |
| Imidacloprid | 5-10 mg/kg did not produce any signs of toxicity and mortality during 90 day exposure. | [371] |
| | 0.2 mg/kg had no significant change in ROS level and MDA content during exposure period of 14 days in *Eisenia fetida*. | [375] |

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