



INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Malathion Toxicity- A Review

Preeti Tirkey¹ and Malabika Sikdar²

Ph.D. Research Scholar¹ Associate Professor²

Department of Zoology

Dr. Harisingh Gour Vishwavidyalaya (A Central University), Sagar (M.P.)

Abstract-

Fish are extremely sensitive to alterations in their aquatic habitat. They are referred to be the bio-indicator species to monitor water contamination as a result. Due to its strong insecticidal properties, minimal toxicity to mammals, low persistence, and quick biodegradation in the ecosystem, organophosphate pesticides are frequently used among other types of pesticides in intensive agricultural practices to protect crops from numerous pests and illnesses. Exposure to by metabolism damage, which sporadically results in the fish's demise. One of the earliest organophosphate insecticides, malathion ($C_{10}H_{19}O_6PS_2$) is still widely employed as a dust, emulsion, and vapor to control a variety of insect pests in a variety of environments. One of the insecticides that has been the subject of the most research, malathion, may cause a number of important alterations in fish. The goal of this study is to review the toxicological effects of the organophosphate pesticide Malathion on fish, including hematological parameters, physical parameters, biochemical parameters, behavioral changes, neurotoxic effects, histopathological alterations, respiratory responses, bioaccumulation, and chromosomal changes.

Keywords- Malathion, Fish, Ecosystem, Insecticides.

Introduction-

Pesticides are widely used around the world to boost agricultural yield with low labor and in less time. Different types (insecticides, herbicides, fungicides, bactericides etc.) and classes (organophosphorus, organochlorine, pyrethroids etc.) of pesticides are employed in agricultural fields, homes, and industries for very long, based on the target species and their efficacy against them (Ullah et al., 2018). Pesticides lead to water bodies from different sources including runoffs from agricultural fields, industrial effluents, and domestic wastes. These pesticides directly affect the aquatic flora and fauna by leading to different toxicological effects/endpoints and indirectly

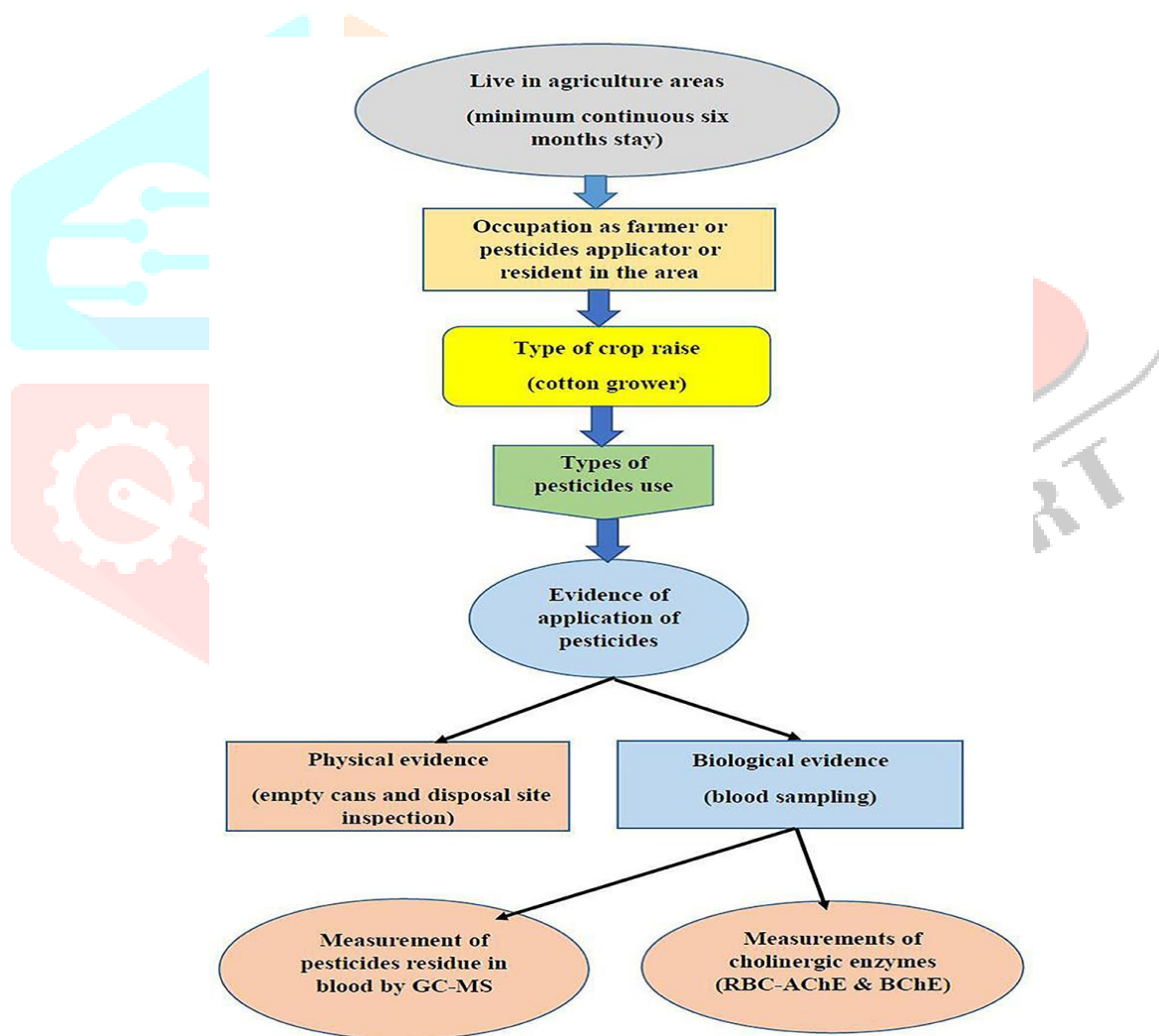
affect human health upon the use and consumption of the water or the edibles from these water bodies such as fish that bio-accumulated these pesticides (Cerejeira et al., 2003). The cellular and biochemical responses of fish are widely assessed for investigating the potential risks associated with the aquatic pollutants (Lakra and Nagpure, 2009). The liver stands out among these organs as the direct target of pollutants, the detoxification center, and the organ with the greatest potential for clearly indicating pathological and physiological changes, even at the most minute scale and in response to extremely low concentrations of pollutants.

OPs are in use since very long, such as Malathion is in use since the 1950s, therefore these pesticides are present in almost every water body and ecosystems. These are up take by aquatic organisms from the ambient water, sediments, food, and particulate matters suspended in the water column (Patil and David, 2009). Therefore, the modern toxicology and current knowledge are mostly based on toxicological studies involving aquatic organisms. These organisms are employed as model systems for assessing the basic processes contributing to cellular damage, tissue injury, free radicals protection, and physiological alterations including aging, different diseases/disorders, and genotoxic effects (Volodymyr, 2011).

Malathion is a earliest and broad spectrum insecticides which is widely used for agricultural and non-agricultural purposes. It is used directly in the water bodies for killing mosquitoes larva. The concentration of Malathion reported from realistic environment varies in different ranges such as 0.008–0.012 µg/L (rivers joining the Chesapeake Bay), up to 0.16 µg/L (urban streams), and up to 15 µg/L (Colorado wetland) (Fordham et al., 2001; Webb and Crain, 2006). Some studies reported severely threatening and very higher concentrations of Malathion (8.12 µg/L to 105.2 µg/L) in water samples from various sites (Karmakar et al., 2016). There is a wealth of well-researched information about the harmful effects of malathion available online as a result of the unfavourable effects of malathion in many model species. OPs are of intense environmental concern since very long due to their poor biodegradability and hydrolyzation. The concern is elevated by the efficient absorbance, and rapid redistribution and disposal of the organophosphorus compounds to various organs of the exposed organisms, interfering membranes' dependent processes such as nerve conductance, plasma membrane, and enzymatic activities (Karaoz et al., 2002). The liver was selected for the study, as it is one of the main organs, performing a wide variety of body functions such as maintaining the internal environment, the flow of nutrients, controlling the metabolism of fats, proteins, and carbohydrates, detoxification etc. Moreover, the liver was selected as the target organ for evaluating Malathion induced toxic effects on account of being a center for lipid and glucose homeostasis, and enzymes production (Lasram et al., 2015). The purpose of the current research is to investigate the genotoxic potential of malathion in rat Sprague-Dawley peripheral blood leukocytes and bone marrow cells. As toxicological end-points, DNA damage, mitotic index (MI), and chromosomal aberrations (CAs) were used. These endpoints were chosen in light of the fact that the assays used in bone marrow for identifying chromosome aberrations and DNA damage in peripheral blood leukocytes are highly sensitive, quick, affordable, and simple to carry out.

Mode of action-

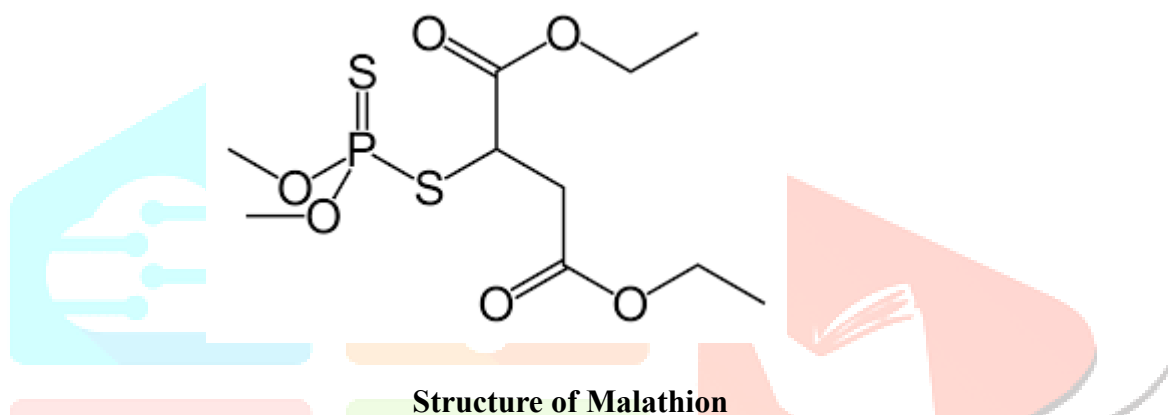
Malathion is a nonsystemic acaricide and insecticide with contact, gastrointestinal, and respiratory effects and low mammalian toxicity. The molecule degrades quite quickly in the environment, therefore the residual effect is minimal. Less than a week is the half-life in soil, water, and plants. By using different formulation technologies, the residual impact can be prolonged. After being absorbed by the target organ, the pro-insecticide malathion is bioactivated by oxidative desulfuration to the cholinesterase inhibitor (ChEI) malaoxon. Mammals convert malathion through metabolic activation (oxidation) to malaoxon, which has the ability to block cholinesterase enzymes in the body's blood, brain, and nervous tissue. In animals, little malaoxon is produced in vivo from malathion. This explains its low mammalian toxicity together with its quick metabolism by detoxifying enzymes (carboxyesterases and glutathione transferases). There are different ways of the assimilation of malathion in the environment is shown in the following process.



This the pathway through which Malathion work in the environment

Basic chemical and physical characteristics-

At room temperature, malathion is a colourless to pale yellow liquid with a distinctive odour and a relative density of 1.23g/ml at 20°C. It begins to degrade at 174°C and has a freezing point lower than 220°C. Malathion is categorized as generally nonvolatile because of its low vapour pressure (4.5 10⁴ Pa at 25°C) and high aqueous solubility (148.2 mg/l in water at 25°C) (Henry's law constant: 1.01 10³ Pa m³ /mol). According to its octanol-water partition coefficient (log Pow^{2.748}), malathion is comparatively lipophilic. Malathion is hydrolyzed more quickly when the pH rises. Malathion's hydrolysis half-life is 11.8 hours at pH 9 and 25 degrees Celsius, compared to pH 5. Aqueous photolysis had to be conducted at pH 4 to minimize hydrolysis. The half-life of malathion for photolysis is 93 days (sensitized) and 156 days (non-sensitized). Malathion has a flash point of 173 2°C and is not explosive under normal conditions of storage and use. It does not have oxidizing or reducing properties.



Malathion metabolism-

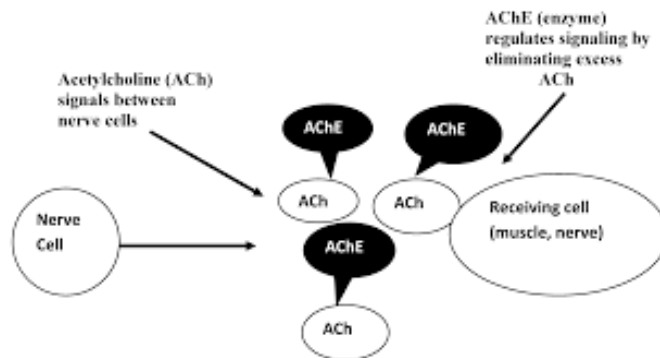
Malathion is rapidly metabolized in mammals as well as in plants and the environment. Details of rates and routes of metabolism have been published in a review (Roberts and Hutson, 1999), with considerably more unpublished information from regulatory reviews cited in the text. The metabolic pathways in mammals, plants, and the environment are broadly similar, with a major metabolic process being hydrolysis of ester bonds of malathion to form malathion monocarboxylic acid (MMCA) and malathion dicarboxylic acid (MDCA). These acids are further broken down into low-molecular-weight molecules, some of which are naturally occurring. Oxidation to malaoxon is a very modest pathway, but significant in mechanism of action and toxicity. Mainly in urine and to some extent in feces as mono- and dicarboxylic acids and other metabolites. More details on the absorption, distribution, metabolism, and excretion (ADME) studies on malathion are given later. Proposed metabolic pathways for Malathion. Numerous crops, including cotton, lettuce, lucerne, and wheat, have been used to study the metabolism of the pesticide malathion in plants.

Plants extensively metabolise malathion, which results in the incorporation of radiolabeled carbon into the organic components of plants. Each crop matrix examined contained unchanged malathion. Malaoxon, isomalathion, diethyl maleate, monoethyl maleate, diethyl mercaptosuccinate, MDCA, MMCA, diethyl methylthiosuccinate, diethyl fumarate, desmethyl malathion, and tetraethyl dithiodisuccinate are among the identified metabolites that make up less than 10% of the total radioactive residue (TRR). In one instance, 12.8% of the TRR in lettuce contained MMCA. Some of the radioactive residues were identified as organic acids and sugars, proving radioactivity incorporation into the TCA cycle (tricarboxylic acid cycle). Other naturally occurring plant components, such as the cell wall fractions of starch, protein, pectin, lignin, hemicellulose, and cellulose, were also contaminated with radioactivity. The metabolic process in plants produces MDCA by deesterifying parent malathion. These acids are further broken down into low-molecular-weight molecules, some of which are naturally occurring. Oxidation to malaoxon is a very modest pathway, but significant in mechanism of action and toxicity

Malathion exposure to humans-

Given the variety of uses for malathion, there are numerous ways that people could be exposed to it. For agricultural use, exposure may happen during application at several phases, specifically during formulation mixing and equipment loading. It is obvious that these exposures can be reduced to a minimum by using practical protective equipment and adhering to label directions. Baker et al. (1978) reported more than 2800 cases of poisoning in Pakistan in July 1976 due to the use of malathion products (three different preparations were used) in a malaria prevention program. Using a brand with the highest concentration of isomalathion, RBC cholinesterase was decreased by an average maximum of 45%. Workers who reported headaches, impaired vision, or vomiting had considerably lower cholinesterase levels. Overall, there was a good correlation between the isomalathion content of the three utilised products and the decline in cholinesterase activity.

In vivo animal experiments revealed a link between the products' isomalathion content and the decrease of cholinesterase activity. During the investigation, improper labour procedures that exposed large amounts of skin tissue were commonly seen. The study's authors came to the conclusion that the products' negligent and incorrect use during mixing, loading, and spraying, as well as the fact that two of the three items had higher levels of malathion, were to blame for the study's amount and severity of malathion poisoning. People entering previously treated areas again may also be exposed to malathion. In-depth investigation has been conducted on the potential exposure to malathion residues in treated fields in the United States by the Agricultural Re-entry and Outdoor Re-entry Exposure Task Forces. All the pesticide-induced changes, inhibition of acetylcholinesterase (AChE), the enzyme involved in terminating the action of the neurotransmitter acetylcholine (AChE is most often studied (Singh and Kumar 2000). . The literature available put forth by several workers (Singh and Kumar 2000; Parma de Croux et al. 2002) explain the inhibition of AChE in different organisms during pesticide exposure.



Effects of malathion seen in animals for toxicological studies-

Malathion enters the body fast, undergoes biotransformation, and is subsequently promptly expelled. Mono- and dicarboxylic acids of malathion are largely excreted in urine and to a lesser amount in faeces after elimination. In the tissues, malathion or its metabolites do not build up. In rats of both sexes, ¹⁴C was rapidly and extensively eliminated following low (40mg/kg BW) or large (800mg/kg BW) oral doses of ¹⁴C malathion. The administered dose was eliminated in the urine in an amount of 76–88% and in the faeces in an amount of 7–11%. Within 12 hours, about 80% of the low-dosage group's dose was excreted in urine. At this point, high-dosage males only excreted roughly 48% of the whole dose, and high-dose females only excreted roughly 67%.

More than 90% of the total starting dosage in both sexes was excreted cumulatively (0-72h) through both urine and faeces at both dose levels. Malathion pretreatment had no impact on the excretion profile.

Conclusions:

Malathion has been used as an insecticide with a variety of applications for approximately 50 years. During this time, its toxicology has been extensively studied and reported. Because malathion exhibits low mammalian toxicity and it has been shown that relevant impurities may enhance toxicity, it is essential that the impurity profile of malathion used in toxicity studies is known. Malathion is a pro-insecticide, and the necessary bioactivation to malaoxon results in a delay in which other metabolic reactions take place. Consequently, the formation of MMCA and MDCA dominates its metabolism in mammals. The inhibition of AChE activity is the malathion effect that is most sensitive, with RBC AChE being more sensitive than brain AChE. This result was seen in rats, mice, dogs, and people. Malathion does not harm nerves permanently. Mild clinical toxicity symptoms typically appear at higher dosage levels. Effects at low doses are negligible or nonexistent. Malathion has no negative effects on reproduction and is not genotoxic in vivo. At high dosage levels, pup weights were somewhat lowered. Most regulatory authorities have chosen RBC AChE as the endpoint for use in risk assessment because of its sensitivity to malathion exposure, protecting other endpoints of concern.

Acknowledgment:

Author gratefully acknowledge the Supervisor and HOD, Department of Zoology, Dr. Harisingh Gour Vishwavidyalaya, Sagar, Madhya Pradesh for providing infrastructure and experimental facility and also for Non-NET UGC fellowship.

Conflicts of Interest:

There is no conflict of interest.

REFERENCES

- Ali, D., Nagpure, N. S., Kumar, S., Kumar, R., Kushwaha, B., & Lakra, W. S. (2009). Assessment of genotoxic and mutagenic effects of chlorpyrifos in freshwater fish *Channa punctatus* (Bloch) using micronucleus assay and alkaline single-cell gel electrophoresis. *Food and Chemical Toxicology*, 47(3), 650-656.
- Ambrus, A., Hamilton, D. J., Kuiper, H. A., and Racke, K. D. (2003). Significance of impurities in the safety evaluation of crop protection products. *Pure Appl. Chem.* 75, 937-973.
- Baker, E., Warren, M., Zack, M., Dobbin, R., Miles, J., Miller, S., Alderman, L., and Teeters, W. (1978). Epidemic malathion poisoning in Pakistan malaria workers. *Lancet* 1(8054), 31-34.
- Cerejeira, M. J., Viana, P., Batista, S., Pereira, T., Silva, E., Valério, M. J., ... & Silva-Fernandes, A. M. (2003). Pesticides in Portuguese surface and ground waters. *Water research*, 37(5), 1055-1063.
- Luo, W., Phung, D., Tran, T., Gupta, S., Rana, S., Karmakar, C., ... & Berk, M. (2016). Guidelines for developing and reporting machine learning predictive models in biomedical research: a multidisciplinary view. *Journal of medical Internet research*, 18(12), e323.
- Lasram, M. M., Dhoub, I. B., Annabi, A., El Fazaa, S., & Gharbi, N. (2015). A review on the possible molecular mechanism of action of N-acetylcysteine against insulin resistance and type-2 diabetes development. *Clinical biochemistry*, 48(16-17), 1200-1208.
- Kallappa Patil, V., & David, M. (2009). Hepatotoxic potential of malathion in the freshwater teleost, *Labeo rohita* (Hamilton). *Veterinarski arhiv*, 79(2), 179-188.
- Karaoz, E., Gultekin, F., Akdogan, M., Oncu, M., & Gokcimen, A. (2002). Protective role of melatonin and a combination of vitamin C and vitamin E on lung toxicity induced by chlorpyrifos-ethyl in rats. *Experimental and Toxicologic Pathology*, 54(2), 97-108.
- Roberts, T. R., and Hutson, D. H. (1999). "Metabolic Pathways of Agrochemicals, Part 2, 364." Royal Society of Chemistry, Cambridge, UK.

Sheorey, P. R., Loui, J. P., Singh, K. B., & Singh, S. K. (2000). Ground subsidence observations and a modified influence function method for complete subsidence prediction. *International Journal of Rock Mechanics and Mining Sciences*, 37(5), 801-818.

Ullah, S., Akhtar, P., & Zaefarian, G. (2018). Dealing with endogeneity bias: The generalized method of moments (GMM) for panel data. *Industrial Marketing Management*, 71, 69-78.

Umetsu, N., Grose, F. H., Allahyari, R., Abu-El-Haj, S., and Fukuto, T. R. (1977). Effect of impurities on the mammalian toxicity of technical malathion and acephate. *J. Agric. Food Chem.* 25(4), 946–953.

Volodymyr, T., Vasylyshyn, N., & Yuriy, H. (2011). The Behavior Investigation of Systems with Electropolymerization of Heterocyclic Compounds and Simultaneous Chemical Surface Polymerization. *Journal of Materials Science and Engineering*, 5(4), 462-467.

Webb, C. M., & Crain, D. A. (2006). Effects of ecologically relevant doses of malathion on developing *Xenopus laevis* tadpoles. *Bios*, 77(1), 1-6.

