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Ecotoxicity studies of Metformin

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ABSTRACT

Metformin is a biguanide antihyperglycemic agent. Metformin is considered an antihyperglycemic drug because it lowers blood glucose concentrations in type II diabetes without causing hypoglycemia. Metformin is a widely prescribed and used antidiabetic drug. But Metformin now possesses an environmental concern due to the various environmental threats. It is a commonly detected drug in various aquatic environments. It is not highly bioaccumulative in fish; metformin can be taken up by plants and aquatic organisms and may be metabolized into Guanylurea (GUU). Some studies indicate that GUU, a transformation product of metformin, can be even more toxic than metformin itself. Metformin and GUU have been shown to cause toxic effects on aquatic organisms, including neurotoxicity, endocrine disruption, and the production of reactive oxygen species (ROS). Metformin can disrupt the function of acetylcholinesterase in aquatic organisms.Metformin also affects the growth and reproduction of small aquatic organisms.It has been determined that certain microorganisms, like *Pseudomonas putida* and *Aminobacter sp.,* may possess enzyme pathways that allow them to break down GUU. Therefore, they have to be utilized anywhere GUU is found in larger concentrations. It is necessary to investigate several techniques, such as biodegradation, adsorption, and improved oxidation processes, for extracting Metformin from wastewater. It is necessary to develop strategies to improve the biodegradation of GUU and Metformin, such as discovering, improving and employing microbial strains.

Key words: *Metformin, Ecotoxicity, Guanylurea.*

Introduction

The chemical name of Metformin is 1,1-dimethylbiguanide hydrochloride. The molecular formula is $C_4H_{11}N_5$•HCl. It has a molecular weight of approximately 165.63 g/mol. It appears as a white to off-white crystalline solid. It is freely soluble in water and practically insoluble in acetone, ether, and chloroform. The pKa value is about 12.4 (National Center for Biotechnology Information, 2025).

Metformin is a biguanide antihyperglycemic agent. Metformin is considered an antihyperglycemic drug because it lowers blood glucose concentrations in type II diabetes without causing hypoglycemia. It is commonly described as an "insulin sensitizer" leading to a decrease in insulin resistance and a clinically significant reduction of plasma fasting insulin levels. Another well-known benefit of this drug is modest weight loss, making it an effective choice for obese patients with type II diabetes (Lund *et al.,* 2007) (Viollet *et al.,* 2012).

Metformin increases the ability of cells to uptake glucose by improving their insulin sensitivity. It also works by decreasing the amount of glucose made by the liver and decreasing the absorption of glucose from the intestine (Carmen Pope, 2024).

Metformin is a widely prescribed and used an-

(Assistant Professor)

tidiabetic drug. But Metformin now possesses an environmental concern due to the various environmental threats.

- Metformin is a commonly detected drug in various aquatic environments; including wastewater, surface water, and drinking water owing to its incomplete metabolism in the human body and is eventually disposed in wastewater.
- The high level of Metformin in environmental water clearly indicated a rise in the diabetic population and prescription rates.
- It is excreted intact in nature, leading to its persistent presence in environmental water.
- It is not highly bioaccumulative in fish; Metformin can be taken up by plants and aquatic organisms and may be metabolized into Guanylurea (GUU).
- Metformin and its byproduct GUU have been detected in various countries, with concentrations ranging from a few nano grams per liter to micrograms per liter.
- Some studies indicate that GUU, a transformation product of Metformin, can be even more toxic than Metformin itself.
- Metformin and GUU have been shown to cause toxic effects on aquatic organisms, including neurotoxicity, endocrine disruption, and the production of reactive oxygen species (ROS).
- Metformin can disrupt the function of acetylcholinesterase in aquatic organisms.
- Metformin also affects the growth and reproduction of small aquatic organisms.
- Studies have shown that metformin can cause oxidative stress, genotoxicity, and morphological alterations in fish.
- The Predicted Environmental Concentration (PEC)/Predicted No Effect Concentration (PNEC) ratio of 0.093 corresponds to the phrase 'Use of the substance has been considered to result in insignificant environmental risk.

(Unax Lertxundi, *et al.*, 2023),(Zheng, *et al.*, 2024), (Lei Dong *et al.*, 2024), (Astra Zeneca, 2023)

(Jürg Oliver Straub *et al.*, 2019), (He Y, Zhang, *et al.*, 2022), (Aline Andrade Godoy, *et al.*, 2018)

Conclusion and Discussion

Type II diabetes is treated with Metformin, an antihyperglycemic medication. Metformin is becoming more prevalent in the ecosystem, particularly in aquatic environments, as a result of diabetic patients' usage and growing numbers. The environment does not easily biodegrade Metformin. In aquatic environments, it changes mostly into Guanylurea (GUU), which is then capable of additional biodegradation. It has been determined that certain microorganisms, like *Pseudomonas putida* and *Aminobacter* sp., may possess enzyme pathways that allow them to break down GUU. Therefore, they have to be utilized anywhere GUU is found in larger concentrations (Eliane Papa Ambrosio-Albuquerque *et al.*, 2021)

It is necessary to investigate several techniques, such as biodegradation, adsorption, and improved oxidation processes, for extracting Metformin from wastewater. It is necessary to develop strategies to improve the biodegradation of GUU and Metformin, such as discovering, improving and employing microbial strains (Lei Dong *et al.*, 2024),

To create comprehensive mineralization methods for Metformin and its byproducts, more study is required. Overall, even though Metformin may not pose a significant environmental danger at this time, continued research and monitoring are essential to address the possibility of ecotoxicity and endocrine disruption, especially given its growing use and the demand for more efficient wastewater treatment techniques.

Conflict of Interest- None

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