Journal of Sustainability Science and Management
Volume 18 Number 6, June 2023: 149-160
eISSN: 2672-7226

SUSTAINABLE BIOREMEDIATION OF ACETAMINOPHEN USING BACTERIA: A REVIEW

GEORGE HAIKAL, N. K. K[1], RAZALI, I. A[1], WAN HANAFI, W. N.[1], GERALDI, A.[2,3], NI' MATUZAHROH[2,3], FATIMAH[2,3], AND TAY, C. C[1,4]*

[1]Faculty of Applied Science, Universiti Teknologi MARA, 40450 Shah Alam, Selangor, Malaysia. [2]Department of Biology, Faculty of Science and Technology, Universitas Airlangga, 60115 Surabaya, Indonesia. [3]Research Centre for Bio-Molecule Engineering, Universitas Airlangga, 60115 Surabaya, Indonesia. [4]myBioREC, Faculty of Civil Engineering, Universiti Teknologi MARA, 40450 Shah Alam, Selangor, Malaysia.

**Corresponding author: taychiay@uitm.edu.my, taychiay@gmail.com*
Submitted final draft: 29 March 2023 *Accepted: 8 April 2023* http://doi.org/10.46754/jssm.2023.06.013

Abstract: Acetaminophen is a common antipyretic and analgesic pharmaceutical contaminant and has become one of the most emerging contaminants in the environment. Bioremediation is the suitable method to degrade acetaminophen as it is sustainable, mimics nature and is low-cost. The bioremediation of acetaminophen is performed by identifying the bacterial characteristics and the source of the bacteria involved in the degradation of acetaminophen. Based on this review study, gram-negative bacteria showed the highest efficiency in degrading acetaminophen by *Pseudomonas aeruginosa* strain HJ1012 and *Cupriavidus necator* with an efficiency of 99% and 100%, respectively. In addition, synergistic or antagonistic interaction among bacteria in mixed culture is a gap of study. The findings from the previous study showed that the optimum conditions are pH 7.0, temperature ranges between 30–40 °C, and a poor culture medium of minimal salt solution. Furthermore, the study sheds light on enzyme involvement and characterisation of acetaminophen degradation pathways toward less harmful intermediates are addressed in order to achieve sustainable development goals through environmental security and health safety. These identified research gaps offer fundamental knowledge and shed insight into upcoming mechanism and application studies.

Keywords: Acetaminophen, bacteria, interaction, medium, pathway.

Introduction

Nowadays, pharmaceutical compounds have been utilised for various medicinal purposes, especially for humans and animals. Pharmaceutical compounds reach the environment through treated wastewater discharge, animal waste runoff and sewer lines (Patneedi *et al.*, 2015). Due to incomplete removal or improper disposal, the presence of pharmaceutical compounds in the aquatic system adversely influences the aquatic ecosystem and thus raises significant concerns.

Acetaminophen is a common antipyretic and analgesic pharmaceutical contaminant that has become one of the emerging contaminants in the environment. The concentrations of acetaminophen are usually in the range of ng/L to mg/L levels (Żur *et al*., 2018a). Wu *et al*. (2012) stated that acetaminophen had caused severe ecological consequences, although it was not highly persistent in the environment. Acetaminophen transforms into several metabolites, such as benzoquinone and hydroquinone. These metabolites are toxic to the aquatic ecosystem. Thus, acetaminophen should be removed to protect the environment (Żur *et al*., 2018b).

The conventional methods used for removing pharmaceutical compounds are physical and chemical. However, these methods are not the desirable option for removing pharmaceutical compounds due to the high operational cost and the generation of secondary pollutants. Biological methods are chosen to remove pharmaceutical compounds because the methods are sustainable mimic nature and have low operation costs (Edrees *et al.,* 2017). Bioremediation is a biological method that

converts contaminants into less harmful forms. *In-situ* and *ex-situ* bioremediation are the two types of bioremediation processes. *In-situ* bioremediation is the treatment of contaminated substances at the same location, whereas *ex-situ* bioremediation involves the removal of contaminated substances at different places from the original contaminated site (Kumar *et al.,* 2018). Biosparging, biostimulation, bioventing and bioaugmentation are examples of *in-situ* bioremediation, meanwhile land farming and composting are examples of *ex-situ* bioremediation. In bioremediation, bacteria, fungi and algae degrade toxic compounds (Vidali, 2001).

Bioremediation for Acetaminophen

Bioremediation degrades or transforms contaminants into less toxic forms by using microorganisms and their enzymes (Abatenh *et al*., 2017). In bioremediation, microorganisms, include algae, fungi and bacteria have been utilised to degrade pharmaceutical contaminants (Shabani *et al*., 2021). This is because microorganisms excrete enzymes that facilitate the utilisation of environmental contaminants and removal of contaminants (Abatenh *et al*., 2017).

Table 1 shows the advantages and disadvantages of using microorganisms in bioremediation. Algae is an autotroph that can grow in harsh environments, including severe temperatures and pH. In contrast to heterotrophic microorganisms, algae development is unaffected by nutrient depletion (Fu *et al*., 2016). However, the drawback of algae for bioremediation is low survival rates when drastic changes occur (Silva *et al*., 2019).

Fungi have been known for the ability to use intracellular and extracellular oxidative enzymes to convert a wide spectrum of recalcitrant compounds, which is resistant to microbial attack (Silva *et al*., 2019). According to Table 1, mycelial fungi have a physiology and colonisation strategy that enable them to resist unexpected changes in pH. It also efficiently breaks down complex organic molecules, despite their long growth cycle and low survival rate (Anastasi *et al*., 2013).

Bacteria have an amazing ability to multiply, contributing to their fast growth rate (Table 1). For example, *E. coli*, under ideal conditions, can double its population every 20 minutes (Allen & Waclaw, 2018). The ability to perceive its environment and respond to external stimuli is crucial for bacterial development and survival.

Table 1: Types of microorganisms used in bioremediation for acetaminophen

Microorganisms	Advantages	Disadvantages	References
Algae • *Chlorella vulgaris* • *Lessonia nigrescens* Bory • *Macrocystis integrifolia* Bory	• Can grow in very harsh environmental conditions	• Low survival rate • Degradation of contaminants with limited coverage	Silva e*t al*. (2019)
Fungi • *Trametes versicolor* • *Aspergillus niger* • Mucor hiemalis	• Degrade complex organic compounds efficiently • Tolerate a wide pH range	• Low survival rate • Long growth cycle	Silva e*t al*. (2019)
Bacteria	• High survival rate • Widely diverse organisms • Faster growth	• The scope of the application is limited	Coelho *et al*. (2015)

The availability of nutrients for development, secondary metabolites, and other microbes are examples of stimuli (Waters *et al*., 2005). Coelho *et al*. (2015) mentioned that bacteria have a higher survival rate than algae and fungi when exposed to high contaminant levels, resulting in high degradation performance. This suggests bacteria is a potential degrader for pharmaceutical contaminants.

Bacteria for Bioremediation of Acetaminophen

The structure of bacteria cell membranes plays a role in their ability to degrade organic micro-pollutants and serves as selective barriers between the cell interior and the outer side (Fisher & Mobashery, 2020). Organic contaminants can get through the cytoplasmic membrane and impair the physiological activities of the membrane. To mitigate the negative effects and accumulation in cells, bacteria had to evolve adaption mechanisms (Murínová & Dercová, 2014). The fluidity of the membrane and the ratio of the bilayer to non-bilayer phospholipids, as well as toxic chemical efflux, protein repair processes, and contaminant degradation, are all maintained through cell adaptation.

Furthermore, bacteria develop biofilms that are embedded with extracellular polymeric substances. Such condition increases their protection against harsh environmental conditions, which increase their access to hydrophobic impurities or specialised contaminants degrading enzymes (Edrees *et al*., 2017). The efficiency of gram-positive and gram-negative bacteria in degrading acetaminophen is shown in Table 2.

Generally, gram-negative bacteria showed higher efficiency in degrading acetaminophen at 79.40 – 100% compared to gram-positive bacteria 86.90–97% (Table 2). This may be due to gram-negative cell walls made up of thin layers of peptidoglycan that can absorb many foreign substances and convert them into less toxic products (*Żur et al*., 2018a).

Additionally, most studies only focus on utilising one gram-negative or gram-positive bacteria to degrade acetaminophen. To improve the understanding and efficiency of acetaminophen degradation, comparing the performance of gram-positive and gram-negative bacteria degrade acetaminophen in a proposed study is critical.

Many studies on acetaminophen biodegradation have been reported using single pure cultures of acetaminophen-degrading bacteria, as shown in Table 2. However, relatively few experimental studies have been reported on acetaminophen biodegradation using mixed microbial cultures (Dionisi, 2014). Findings from Zhang *et al*. (2013), *Stenotrophomonas* sp. strain f1 and *Pseudomonas* sp. strains f2 and fg-2 were grown and completely degraded acetaminophen at concentrations of 400 mg/L in mixed cultures with acetaminophen as the sole carbon, nitrogen, and energy source. Thus, a synergistic interaction of the consortium derived from the acetaminophen-degrading mixed culture boosts acetaminophen degradation significantly. In addition, mixed microbial cultures are widely perceived as having the potential to be effective at biodegrading recalcitrant substances (Kim *et al*., 2009). However, there is a gap in the study to further insight into the synergistic and antagonistic interaction among bacteria in mixed culture.

Table 2 shows that the sources of the gram-positive and gram-negative bacteria obtained were from sludge samples. The aromatic compounds are abundant in wastewater treatment plant influents, and the bacteria in the sludge samples are adapted to decompose aromatic compounds. As a result, microorganisms from this source are expected to degrade acetaminophen efficiently.

Factors Affect Bioremediation of Acetaminophen Using Bacteria

Bioremediation is affected by several factors, including the presence of a microbial population capable of degrading acetaminophen and environmental conditions such as temperature, pH and medium (Vidali, 2011). As stated by *Żur et al*. (2018a), the value of pH influences acetaminophen degradation because it affects

Table 2: Gram-positive and gram-negative bacteria efficiency in degrading acetaminophen

Bacteria Type	Bacteria Name	Source of Bacteria	Concentration of Acetaminophen (mg/L)	Efficiency (%)	References
Gram-positive bacteria	*Bacillus drentensis* strain s1	Sludge sample	300	95.10%	Chopra and Kumar (2020)
	Enterococcus faecium	Sludge sample	200	86.90%	Palma *et al*. (2021)
	Corynebacterium nuruki	Sludge sample	200	97.00%	Palma *et al*. (2021)
Gram-negative bacteria	*Pseudomonas* sp. STB2	Sludge sample	3000	79.40%	Abdullah (2018)
	Pseudomonas aeruginosa strain HJ1012	Sludge sample	2200	99.00%	Hu *et al*. (2013)
	Cupriavidus necator	Sludge sample	400	100%	Wei *et al*. (2011)

microbial cell shape, activity, and membrane characteristics. Meanwhile, temperature affects the rate of most biochemical reactions in the bioremediation process (Das & Chandran, 2011). Medium plays an important role in stimulating the growth of certain bacteria that utilise acetaminophen as a source of energy and food thus bioremediation takes place (Kram & Finkel, 2015).

The value of pH affects the biosorption and toxicity of contaminants by changing the surface cells ionisation (*Żur et al*., 2018a). According to Wolski *et al*. (2006), the surface of bacterial cells becomes negative at higher pH values, resulting in alterations in the electrostatic interaction between pharmaceutical contaminants and biomass surface, thus influencing biodegradation performance. According to Xagoraraki *et al*. (2008), the production of the protonated form (ROH) of acetaminophen has been found at lower pH, whereas acetaminophen occurs as phenolate (RO^-) form in an alkaline environment. In a laboratory experiment, a lower degradation of acetaminophen was observed at pH values greater than 8.0 or lower than 6.0. It was determined that the suggested optimum conditions for pH were at 7.0, where the highest acetaminophen degradation occurred.

Temperature affects bacterial physiology and enzymatic reaction and thus plays a crucial role in degradation processes (*Żur et al*., 2018a). The rate of most biochemical reactions is affected by temperature, and the rate of reactions doubles with an increase of every 10 ***°C.*** Bacterial membranes became more rigid at lower temperatures, resulting in greater viscosity of membrane phospholipids, meanwhile membrane transport was usually inhibited at higher temperatures by the denaturation of membrane-associated proteins (*Żur et al*., 2018a). Although bacteria can survive in these extreme conditions, the ideal temperature should be maintained for the best growth and reproduction (*Żur et al*., 2018a). Das and Chandran (2011) stated that the optimum temperature for the degradation of acetaminophen was between 30-40°C.

Rich and poor culture mediums are two different types of medium. Bushnell Hass Medium and Trypticase Soy Broth are examples of the rich medium. Meanwhile, the mineral salt solution is a poor medium lacking essential

nutrients (Kram & Finkel, 2015). As shown in Table 3, the Bushnell Haas Medium showed higher efficiency of 95.10% in the degradation of acetaminophen than Trypticase Soy Broth with an efficiency of 89% in degrading acetaminophen. A rich culture medium contains all essential nutrients and enables the bacteria to grow rapidly (Akay & Tezel, 2020). As for the poor culture medium study, bacteria in mineral salt solution such as *Pseudomonas aeruginosa* strain HJ1012, *Pseudomonas moorei* KB4 strain and *Delftia tsuruhantensis* degraded acetaminophen with the efficiency of 99%, 100%, 97%, respectively. Kram and Finkel (2015) state that a poor medium lacks nutrients. The bacteria in the Mineral Salt Solution break down the complex molecules to become the source of carbon and energy for growth and survival. There are limited studies comparing the types of mediums used for degrading acetaminophen.

Acetaminophen Degradation Pathway by Bacteria

To provide a realistic design of the biodegradation system for acetaminophen, the metabolic pathway must be investigated to understand harmful intermediates, their accumulation, and their final products. There are several pathways and different intermediates involved in the degradation of acetaminophen. Figure 1 illustrates the metabolic degradation pathway of acetaminophen by *Bacillus drentensis* strain s1. According to Chopra and Kumar (2020), the conversion of 4-aminophenol to hydroquinone is expected to be the primary degradation pathway for acetaminophen biodegradation by bacteria. Acetaminophen was transformed to 1, 4-benzenediol or hydroquinone via the hydroquinone pathway. During catalysis by amidohydrolase, the amino group of acetaminophens was substituted by a hydroxyl group, resulting in hydroquinone. Hydrolytic enzymes catalysed the hydroxylation of acetaminophen during degradation, releasing acetamide to generate hydroquinone. It was then converted into 2-isopropyl-5-methylcyclohexanone and oxalic acid (Chopra & Kumar, 2020).

Another pathway of acetaminophen degradation was proposed by Zhang *et al*. (2012). Figure 2 shows the acetaminophen degradation pathway. In the first stage, an amidohydrolase catalyses the acetate release from acetaminophen and converts to 4-aminophenol, which is subsequently ring fissioned and the amino group replaced by a hydroxyl group to yield hydroquinone. Following that, a hydrolytic enzyme catalyses the initial hydroxylation of acetaminophen to form hydroquinone with the release of acetamide, which is then converted into oxamic acid. Some strains converted aminophenol to the equivalent 1, 4-benzenediol or hydroquinone molecules. Attempts to isolate and identify acetamide and oxamic acid, on the other hand, were unsuccessful.

Table 3: Medium used in degrading acetaminophen

Parameters	Bacteria	Medium	Efficiency	References
Rich Medium	*Bacillus drentensis* strain s1	Bushnell Haas Medium	95.10 %	Chopra and Kumar, 2020
	Pseudomonas sp. STB3	Tryptic Soy Broth	89 %	Edrees *et al*., 2018
Poor Medium	*Pseudomonas aeruginosa* strain HJ1012	Minimal Salt Solution	99 %	Hu *et al.,* 2013
	Pseudomonas moorei KB4 strain	Minimal Salt Solution	100 %	Żur *et al*., 2018b
	Delftia tsuruhantensis	Minimal Salt Solution	97 %	De Gusseme e*t al*., 2011

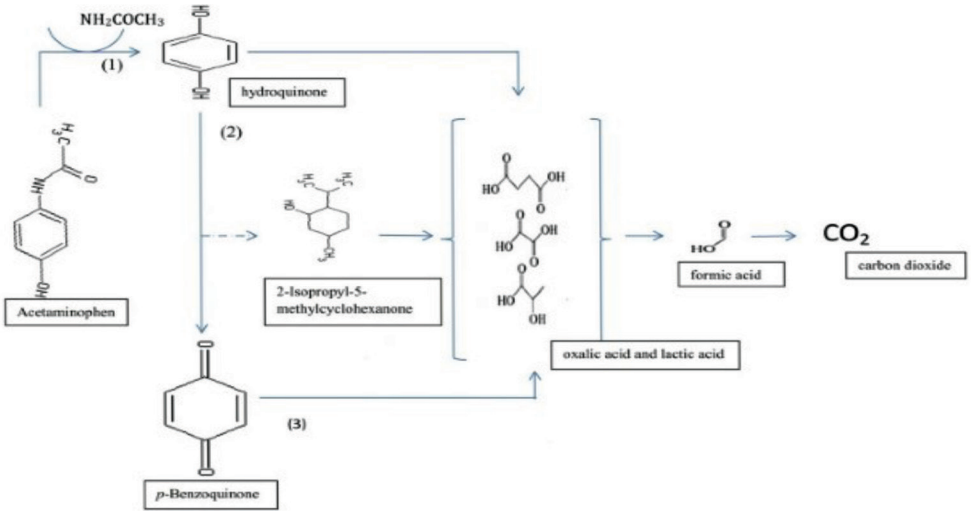


Figure 1: *Bacillus drentensis* strain s1 metabolic pathway for acetaminophen degradation (Chopra & Kumar, 2020)

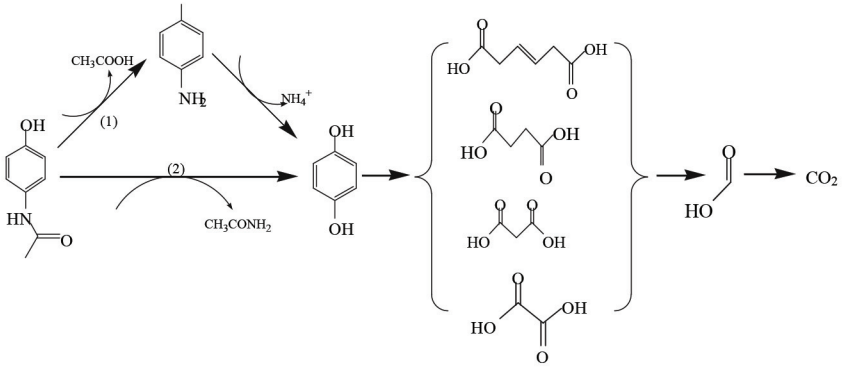


Figure 2: Acetaminophen degradation pathway (Zhang *et al*., 2012)

Both proposed pathways are similar in identifying the two primary acetaminophen degradation intermediates, 4-aminophenol and hydroquinone. Moreover, both pathways share similar final products: formic acid and carbon dioxide. The differences between these two pathways are, in the first pathway, suggested by Chopra and Kumar (2020), 2-isopropyl-5-methylcyclohexanone and oxalic acid were identified meanwhile in the second pathway, suggested by Zhang *et al*. (2012), attempts at isolating and identifying oxamic acid and acetamide failed. Besides quinones, oxalic acid also is a toxic compound when the concentration is high (Schuler *et al*. 2021). There has been limited research on the metabolic pathways of acetaminophen biodegradation, and they are still poorly characterised. Furthermore, there is a lack of research on acetaminophen degradation, including a study of the specific activity of enzymes involved in the pathways of acetaminophen degradation. Aside from that, research needs to focus on initiating a pathway that produces less harmful intermediates to overcome toxicity issues.

Enzyme for Degradation of Pharmaceutical Contaminants

In general, the performance of degradation is evaluated through removal percentage. There is a lack of studies on the degradation rate of pharmaceutical compounds due to the involvement of many factors and

complex processes. The degradation rate of pharmaceutical contaminants is usually influenced by the concentration of contaminants and the amount of catalyst present. In this context, the amount of catalyst refers to the number of organisms capable of metabolising the contaminants and the number of enzymes produced by each bacterium (Abatenh *et al*., 2017). In addition, environmental factors also may contribute to a variation in the rate of degradation.

Enzymes increase the speed of a reaction by lowering the activation energy of molecules (Ruggaber & Talley, 2006). Enzymes like oxidoreductase (laccase and peroxidase) and hydrolases (lipase and haloalkane dehalogenase) are involved in bioremediation. The list of enzymes involved in bioremediation, producing microorganisms and their functions are shown in Table 4.

Oxidoreductases are a class of enzymes that absorb electrons from molecular oxygen and catalyse the oxidation/reduction reaction. Due to the ability to oxidise resistant pollutants, several researchers have widely investigated oxidoreductase enzymes in recent years. Table 5 shows the examples of oxidoreductase enzymes involved in the bioremediation of acetaminophen.

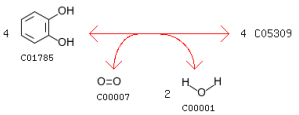
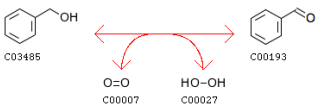
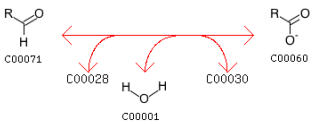
Oxidoreductases are enzymes produced by bacteria, fungi, and plants capable of eliminating natural and artificial pollutants (Okino-Delgado *et al.,* 2019). Based on Table 5, the bacteria that produce laccase, oxygen oxidoreductase, aldehyde oxidoreductase and manganese peroxidase are *Pseudomonas*, *Pseudomonas aeruginosa*, *Desulfovibrio desulfuricans* ATCC 27774, and *Bacillus velezensis*, respectively. Each enzyme has its reaction for the bioremediation of acetaminophen. Laccases, aldehyde oxidoreductase and manganese peroxidase, are widely used for the bioremediation of a wide range of industrial pollutants (Chandra & Chowdhary, 2015; Saikia *et al*., 2022). While research on enzymatic activities of oxygen oxidoreductase is rarely discussed.

Laccases are multi-copper oxidoreductases that can oxidise various aromatic compounds (Varga *et al.,* 2019). Laccases use molecular oxygen as an electron acceptor to catalyse the oxidation of different aromatic compounds, especially compounds with electron-donating groups of phenols (OH) into free radicals (Silva *et al.,* 2019; Chandra & Chowdhary, 2015). Laccase is a "green catalyst" because it only produces water as a by-product (Kumar & Chandra, 2020). In addition, laccases are

Table 4: Enzymes involved in bioremediation, producing microorganisms and their functions

Enzyme Classification	Example	Producing Microorganism	Functions
Oxidoreductase	Laccase	*Bacillus*	Aromatic compounds have a cleave ring that reduces one molecule of oxygen in water, resulting in the formation of free radicals (Arregui *et al*., 2019)
	Peroxidase	*Pseudomonas sp.*	After the oxidation of organic molecules, catalyse reduction reactions in the presence of peroxides like hydrogen peroxide (H_2O_2) and generate reactive free radicals (Bansal & Kanwar, 2013).
Hydrolases	Lipase	*Burkholderia*	Triglycerol is broken down into glycerol and fatty acid, useful in polyaromatic hydrocarbon degradation and wastewater treatment (Sharma *et al*., 2019).
	Haloalkane dehalogenases	*Pseudomonas pavonaceae*	It breaks the carbon-halogen bonds in halogenated compounds and converts them into non-toxic forms (Satpathy, 2021).

Table 5: Example of oxidoreductase enzyme produced by bacteria

Example of enzyme	Producing Microorganism	Reaction	References
Laccase	*Pseudomonas*		Chandra and Chowdhary (2015)
Oxygen oxidoreductase	*Pseudomonas aeruginosa*		(Entsch and Ballou, 1989)
Aldehyde oxidoreductase	*Desulfovibrio desulfuricans* ATCC 27774		Kozono *et al.* (2020)
Manganese peroxidase	*Bacillus velezensis*		Al-Dhabi *et al.* (2021)

suitable catalysts for the bioremediation of acetaminophen due to the stability of bacterial laccases under varied pH, temperature, organic solvents and salt concentrations (Arregui *et al.,* 2019).

Oxygen oxidoreductase, also known as alcohol oxidase (Veteikytė *et al*., 2013). Oxygen oxidoreductase uses molecular oxygen to oxidise primary aromatic alcohol into aromatic aldehyde, producing hydrogen peroxide as a by-product (*KEGG enzyme: 1.1.3.7*). By providing insight into the pathways and mechanisms, this enzyme has the potential to bioremediate aromatic compounds of acetaminophen. However, a minimal study has been conducted on oxygen oxidoreductase.

Aldehyde oxidoreductases are members of the xanthine oxidase family (Fourmond, 2018). According to Koehler *et al*. (1996), a wide variety of aliphatic and aromatic aldehydes are specific substrates for aldehyde oxidoreductase. Aldehyde oxidoreductase uses water molecules to oxidise aldehyde to carboxylic acid, which then enters the Krebs cycle (Fetzner, 2000). Fourmond (2018) mentioned that aldehyde oxidoreductase oxidises a variety of aldehydes. However, their physiological substrates and functions are commonly unspecified.

Manganese peroxidase, also known as Mn (II): hydrogen-peroxide oxidoreductase, is ubiquitous (Zdarta *et al*., 2018). Manganese peroxidase uses hydrogen peroxide to oxidise Mn^{2+} into Mn^{3+} and produce water, thus completing the catalytic cycle of MnP. These ions then combine with anions of dicarboxylic acids to form chelate complexes and enter the Krebs cycle (Khatoon *et al*., 2017). According to Hofrichter (2002), the capability of MnP enzymes is proved by their products; the chelated Mn^{3+} ions, which act as charge-transfer mediators, attack phenolic compounds. Manganese peroxidase is an eco-friendly enzymatic activity that bioremediates pharmaceutical compounds into non-toxic forms and cleans the environment (Saikia *et al*., 2022).

In conclusion, enzymes play an important role in the bioremediation of acetaminophen. The demand for these enzymes in the biotechnological sector has increased in recent years due to their being environmentally friendly. Therefore, these

enzymes are recommended as catalysts for the bioremediation of acetaminophen.

Conclusion

This review highlights the bioremediation of acetaminophen by using bacteria. It is found that gram-negative bacteria have higher efficiency than gram-positive bacteria in degrading acetaminophen. However, only a few studies compare the effectiveness of gram-positive and gram-negative bacteria as well as bacteria interactions in mixed culture in the degradation of acetaminophen. The source of bacteria was a significant factor in improving the efficiency of degrading acetaminophen. Most of the bacteria used in the review study were isolated from sludge samples in wastewater treatment plants as bacteria evolved and adapted to environmental changes. The findings of this review show that the optimised conditions for acetaminophen degradation are pH 7.0, temperature 30–40 *°C, and the poor culture medium* minimal salt solution. Bacteria degrade complex molecules to provide carbon and energy for bacteria growth and survival. This review also addresses gaps of study on the characterisation and enzyme in the degradation pathway that produce less toxic intermediates and achieve a sustainable environment and human health safety.

Acknowledgements

The authors would like to acknowledge UiTM for providing a research facility and Airlangga Tahun 2020, grant scheme with contract number: 427/UN3.14/PT/2020 and UiTM 600-TNCPI/PBT 5/3 (038/2020).

References

Abatenh, E., Gizaw, B., Tsegaye, Z., & Wassie, M. (2017). The role of microorganisms in bioremediation-A review. *Open Journal of Environmental Biology*, *2*(1), 038-046.

Abdullah, Q, Y., Edrees, W. H., Al-Kaf, A. G., & Naji, K. M. (2018). Biodegradation of paracetamol by native bacterial strains isolated from Yemeni pharmaceutical wastewater plant in Sana'a". *Chronicles of Pharmaceutical Science*, *2*, 512-522.

Akay, C., & Tezel, U. (2020). Biotransformation of Acetaminophen by intact cells and crude enzymes of bacteria: A comparative study and modelling. *Science of the Total Environment*, *703*, 134990.

Akhtar, N., & Mannan, M. A. ul. (2020). Mycoremediation: Expunging environmental pollutants. *Biotechnology Reports*, *26*, e00452. https://doi.org/10. 1016/j.btre.2020. e00452

Allen, R. J., & Waclaw, B. (2018). Bacterial growth: A statistical physicist's guide. *Reports on Progress in Physics*, *82*(1), 016601.

Anastasi, A., Tigini, V., & Varese, G. C. (2013). The bioremediation potential of different ecophysiological groups of fungi. In *Fungi as bioremediators* (pp. 29-49). Berlin, Heidelberg: Springer.

Arregui, L., Ayala, M., Gómez-Gil, X., Gutiérrez-Soto, G., Hernández-Luna, C. E., Herrera de los Santos, M., Levin, L., Rojo-Domínguez, A., Romero-Martínez, D., Saparrat, M. C., Trujillo-Roldán, M. A., & Valdez-Cruz, N. A. (2019). Laccases: Structure, function, and potential application in water bioremediation. *Microbial Cell Factories*, *18*(1), 200. https://doi.org/10.1186/s12934-019-1248-0

Chandra, R., & Chowdhary, P. (2015). Properties of bacterial laccases and their application in bioremediation of industrial wastes. *Environmental Sciences: Processes and Impacts*, *17*(2), 326-342. https://doi.org/10.1039/C4EM00627E

Chopra, S., & Kumar, D. (2020). Characterization, optimization, and kinetics study of acetaminophen degradation by Bacillus drentensis strain S1 and wastewater degradation analysis. *Bioresources and Bioprocessing*, *7*(1), 1-18.

Coelho, L. M., Rezende, H. C., Coelho, L. M., de Sousa, P. A., Melo, D. F., & Coelho,

N. M. (2015). Bioremediation of polluted waters using microorganisms. *Advances in Bioremediation of Wastewater and Polluted Soil*, *10*, 60770.

Das, N., & Chandran, P. (2011). Microbial degradation of petroleum hydrocarbon contaminants: An overview. *Biotechnology Research International*, *2011*.

De Gusseme, B., Vanhaecke, L., Verstraete, W., & Boon, N. (2011). Degradation of acetaminophen by Delftia tsuruhatensis and Pseudomonas aeruginosa in a membrane bioreactor. *Water Research*, *45*(4), 1829-1837.

Dionisi, D. (2014). Potential and limits of biodegradation processes for the removal of organic xenobiotics from wastewaters. *ChemBioEng Reviews*, *1*(2), 67-82.

Edrees, W. H. A., Abdullah, Q. Y. M., Al-Kaf, A. G., & Naji, K. M. (2017). A review on comparative study between the physicochemical and biological processes for paracetamol degradation. *Universal Journal of Pharmaceutical Research*, *2*, 12.

Entsch, B., & Ballou, D. P. (1989). Purification, properties, and oxygen reactivity of P-hydroxybenzoate hydroxylase from pseudomonas aeruginosa. *Biochimica Et Biophysica Acta (BBA) - Protein Structure and Molecular Enzymology*, *999*(3), 313-322. https://doi.org/10.1016/0167-4838(89)90014-9

Fetzner, S. (2000). Enzymes involved in the aerobic bacterial degradation of N -heteroaromatic compounds: Molybdenum hydroxylases and ring-opening 2,4-Dioxygenases. *Naturwissenschaften*, *87*(2), 59-69. https://doi.org/10.1007/s001140050011

Fisher, J. F., & Mobashery, S. (2020). Constructing and deconstructing the bacterial cell wall. *Protein Science*, *29*(3), 629-646.

Fourmond, V. (2018). Direct electrochemistry of molybdenum and tungsten enzymes. *Encyclopedia of Interfacial Chemistry*, 477-488. https://doi.org/10.1016/b978-0-12-409547-2.13354-2

Fu, W., Chaiboonchoe, A., Khraiwesh, B., Nelson, D. R., Al-Khairy, D., Mystikou, A., & Salehi-Ashtiani, K. (2016). Algal cell factories: Approaches, applications, and potentials. *Marine Drugs*, *14*(12), 225.

Hofrichter, M. (2002). Review: Lignin conversion by manganese peroxidase (MNP). *Enzyme and Microbial Technology*, *30*(4), 454-466. https://doi.org/10.1016/s0141-0229(01)00528-2

Hu, J., Zhang, L. L., Chen, J. M., & Liu, Y. (2013). Degradation of paracetamol by Pseudomonas aeruginosa strain HJ1012. *Journal of Environmental Science and Health, Part A*, *48*(7), 791-799.

Khatoon, N., Jamal, A., & Ali, M. I. (2017). Polymeric pollutant biodegradation through microbial oxidoreductase: A better strategy to safe environment. *International Journal of Biological Macromolecules*, *105*, 9-16. https://doi.org/10.1016/j.ijbiomac.2017.06.047

Kim, Y. M., Ahn, C. K., Woo, S. H., Jung, G. Y., & Park, J. M. (2009). Synergic degradation of phenanthrene by consortia of newly isolated bacterial strains. *Journal of Biotechnology*, *144*(4), 293-298.

Koehler, B. P., Mukund, S., Conover, R. C., Dhawan, I. K., Roy, R., Adams, M. W., & Johnson, M. K. (1996). Spectroscopic characterization of the Tungsten and iron centers in aldehyde ferredoxin oxidoreductases from two hyperthermophilic archaea. *Journal of the American Chemical Society*, *118*(49), 12391-12405. https://doi.org/10.1021/ja962197u

Kozono, I., Hibi, M., Takeuchi, M., & Ogawa, J. (2020). Purification and characterization of molybdenum-containing aldehyde

dehydrogenase that oxidizes benzyl maltol derivative from pseudomonas nitroreducens SB32154. *Bioscience, Biotechnology, and Biochemistry*, *84*(11), 2390-2400. https://doi.org/10.1080/09168451.2020.1799749

Kram, K. E., & Finkel, S. E. (2015). Rich medium composition affects Escherichia coli survival, glycation, and mutation frequency during long-term batch culture. *Applied and Environmental Microbiology*, *81*(13), 4442-4450.

Kumar, A., & Chandra, R. (2020). Ligninolytic enzymes and its mechanisms for degradation of lignocellulosic waste in environment. *Heliyon*, *6*(2), e03170. https://doi.org/10.1016/j.heliyon.2020.e03170

Kumar, V., Shahi, S. K., & Singh, S. (2018). Bioremediation: An eco-sustainable approach for restoration of contaminated sites. In *Microbial Bioprospecting for Sustainable Development* (pp. 115-136). Singapore: Springer.

Murínová, S., & Dercová, K. (2014). Response mechanisms of bacterial degraders to environmental contaminants on the level of cell walls and cytoplasmic membrane. *International Journal of Microbiology*, *2014*.

Okino-Delgado, C. H., Zanutto-Elgui, M. R., do Prado, D. Z., Pereira, M. S., & Fleuri, L. F. (2019). Enzymatic bioremediation: Current status, challenges of obtaining process, and applications. *Microorganisms for Sustainability*, 79-101. https://doi.org/10.1007/978-981-13-7462-3_4

Palma, T. L., Magno, G., & Costa, M. C. (2021). Biodegradation of paracetamol by some gram-positive bacterial isolates. *Current Microbiology*, 1-13.

Patneedi, C. B., & Prasadu, K. D. (2015). Impact of pharmaceutical wastes on human life and environment. *Rasayan Journal of Chemistry*, *8*(1), 67-70.

Saikia, S., Yadav, M., Hoque, R. A., & Yadav, H. S. (2022). Bioremediation mediated by manganese peroxidase – An overview. *Biocatalysis and Biotransformation*, 1-13. https://doi.org/10.1080/10242422.2022.2113517

Schuler, E., Demetriou, M., Shiju, N. R., & Gruter, G. J. M. (2021). Towards sustainable Oxalic Acid from CO2 and biomass. *ChemSusChem*, *14*(18), 3636-3664.

Shabani, M., Pontié, M., Younesi, H., Nacef, M., Rahimpour, A., Rahimnejad, M., & Khelladi, R. M. B. (2021). Biodegradation of acetaminophen and its main by-product 4-aminophenol by Trichoderma harzianum versus mixed biofilm of Trichoderma harzianum/Pseudomonas fluorescens in a fungal microbial fuel cell. *Journal of Applied Electrochemistry*, *51*(4), 581-596.

Silva, A., Delerue-Matos, C., Figueiredo, S. A., & Freitas, O. M. (2019). The use of algae and fungi for removal of pharmaceuticals by bioremediation and biosorption processes: A review. *Water*, *11*(8), 1555.

Varga, B., Somogyi, V., Meiczinger, M., Kováts, N., & Domokos, E. (2019). Enzymatic treatment and subsequent toxicity of organic micropollutants using oxidoreductases - A review. *Journal of Cleaner Production*, *221*, 306-322. https://doi.org/10.1016/j.jclepro.2019.02.135

Veteikytė, A., Aštrauskaitė, M., Gruškienė, R., Tekorienė, R., & Matijošytė, I. (2013). Secondary alcohol oxidase activity identified in genus of pseudomonas isolated from the oil polluted soil. *Biocatalysis and Agricultural Biotechnology*, *2*(2), 89-95. https://doi.org/10.1016/j.bcab.2012.11.005

Vidali, M. (2001). Bioremediation. An overview. *Pure and Applied Chemistry*, *73*(7), 1163-1172.

Waters, C. M., & Bassler, B. L. (2005). Quorum sensing: Cell-to-cell communication

in bacteria. *Annu. Rev. Cell Biology Development Biology*, *21*, 319-346.

Wei, F., Zhou, Q. W., Leng, S. Q., Zhang, L. L., & Chen, J. M. (2011). Isolation, identification and biodegradation characteristics of a new bacterial strain degrading paracetamol. *Environmental Science*, *32*(6), 1812-1819.

Wolski, E. A., Murialdo, S. E., & Gonzalez, J. F. (2006). Effect of pH and inoculum size on pentachlorophenol degradation by Pseudomonas sp. *Water SA*, *32*(1), 93-97.

Wu, S., Zhang, L., & Chen, J. (2012). Paracetamol in the environment and its degradation by microorganisms. *Applied Microbiology and Biotechnology*, *96*(4), 875-884.

Xagoraraki, I., Hullman, R., Song, W., Li, H., & Voice, T. (2008). Effect of pH on degradation of acetaminophen and production of 1, 4-benzoquinone in water chlorination. *Journal of Water Supply: Research and Technology—AQUA*, *57*(6), 381-390.

Zdarta, J., Meyer, A. S., Jesionowski, T., & Pinelo, M. (2018). Developments in support materials for immobilization of oxidoreductases: A comprehensive review. *Advances in Colloid and Interface Science*, *258*, 1-20. https://doi.org/10.1016/j.cis.2018.07.004

Zhang, L., Hu, J., Zhu, R., Zhou, Q., & Chen, J. (2013). Degradation of paracetamol by pure bacterial cultures and their microbial consortium. *Applied Microbiology and Biotechnology*, *97*(8), 3687-3698.

Żur, J., Piński, A., Marchlewicz, A., Hupert-Kocurek, K., Wojcieszyńska, D., & Guzik, U. (2018a). Organic micropollutants paracetamol and ibuprofen—toxicity, biodegradation, and genetic background of their utilization by bacteria. *Environmental Science and Pollution Research*, *25*(22), 21498-21524.

Żur, J., Wojcieszyńska, D., Hupert-Kocurek, K., Marchlewicz, A., & Guzik, U. (2018b). Paracetamol–toxicity and microbial utilization. Pseudomonas moorei KB4 as a case study for exploring degradation pathway. *Chemosphere*, *206*, 192-202.