METAGENOMIC CHARACTERIZATION OF BACTERIAL COMMUNITY IN HYPERSALINE LAKE TUZ FOR HALOGENATED POLLUTANTS DEGRADATION

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DEDICATION

This thesis is dedicated to my husband, Mr. (Prince) Oyewusi Abdulfatai Olarenwaju Ajadi for his support and unconditional love.

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ABSTRACT

The use of microbes to degrade pollutants is the prevailing, low-cost green technology to treat different kinds of polluted environments. As a result of the unethical dumping of industrial effluents into these environments, many naturally existing hypersaline areas are becoming progressively polluted. This study, therefore, aim to evaluate microbial diversity, characterize novel pollutants degrading-bacteria from hypersaline Lake Tuz in Turkey and conduct *in-silico* assessment of dehalogenase gene. In this study, metagenomics analysis was done using 16S rRNA amplicon sequencing. Bacteria identification was performed using 16S rRNA amplification and whole genomic sequencing. The study also includes assessment and interaction of dehalogenase (DehH2) gene in respect to salt tolerance with pollutants haloacetates, haloacids and chlorpyrifos, by substrate docking, MD simulation and MM-PBSA. In the present study, metagenomic analysis revealed that Firmicutes, Fusobacteria and Proteobacteria were the most abundant phyla and functional genes related to adaptation and bioremediation potential. The isolated *Bacillus subtilis* strain H1 and *Bacillus thuringiensis* strain H2 were capable of degrading haloalkanoic acids, haloacetates and chlorpyrifos. Strains H1 and H2 were optimally utilized 2,2-dichloropropionic acid (2,2-DCP), 2,3-dichloropropionic acid (2,3-DCP), L-2-chloropropionic acid (L-2-CP), D-2-chloropropionic acid (D-2-CP), 3-chloropropionic acid (3CP), monochloroacetate (MCA), trichloroacetate (TCA) and organophosphate (chlorpyrifos) as their carbon source under similar growth conditions (pH 8.0, 30 ◦C), except the latter preferred a higher concentration of halogenated compound (30 mM) as well as salinity (35%). Dehalogenase from strain H2 (DehH2) was found belongs to Group II dehalogenase with a 63.71% sequence identity to PH0459 haloacid dehalogenase of hyperthermophilic *Pyrococcus horikoshii* OT3 (PDB ID 1X42). The MD simulations revealed that haloacids and haloacetates were preferentially degraded by the DehH2 (−6.3 to −4.7 kcal/mol and −3.3 to −4.6 kcal/mol) at 35 % NaCl and without NaCl respectively, through three or four hydrogen bonds to the catalytic triad, Asp125, Arg201, and Lys202. Data of MD simulation corroborated earlier molecular docking results, in which the complexes were observed to reach equilibrium at short period of time RMSD (~ 0.13 – 0.189 nm) and have the

minimum number of fluctuations (0.05 – 0.25 nm). The MM-PBSA calculations revealed that haloacetates and haloacids gave the lowest free binding energies (ΔGbinding) (– 45.14 to – 7.62 Kcal/mol). The exception was chlorpyrifos in which RMSD (~ 0.295 to unstable), RMSF values (0.05 – 0.59 nm) were the largest, while chlorpyrifos was unable to spontaneously bind to DehH2 (+180.57 kcal/mol) at both salinity conditions (35% and 0% NaCl). Whole genomic sequencing analysis such as Multi locus sequence alignment (MLSA), average nucleotide identity (ANI) and core genome phylogenetic analysis re-identified *Bacillus thuringiensis* H2 as *Bacillus megaterium.* Several genes involved in pollutants degradation and adaptation are found in the genome sequence. Based on the findings, it was apparent that hypersaline Lake Tuz inhabit novel pollutant-degrading bacteria which could be used for wastewater treatment.

ABSTRAK

Penggunaan mikroorganisma untuk mengurangkan pencemaran merupakan teknologi hijau yang kosnya adalah rendah untuk merawat pelbagai bahan cemar alam sekitar. Hasil daripada perbuatan yang tidak beretika semasa pembuangan bahan sisa industri dipersekitaran, kawasan tinggi garam menjadi semakin tercemar. Oleh itu, kajian ini adalah untuk menilai kepelbagaian mikroorganims dan mencirikan bakteria novel dari Tasik Tuz di Turki yang berkepekatan tinggi garam untuk penilaian*in-silico* gen dehalogenase Dalam kajian ini, analisis metagenomik dilakukan melalui penjujukan 16S rRNA amplikon. Pengenalpastian bakterium telah dikaji menggunakan amplifikasi 16S rRNA dan penjujukan genomik. Kajian ini juga menilai interaksi dehalogenase (DehH2) dengan kehadiran garam dan bahan pencemar seperti asid haloalkanoik, haloasetat dan klorofiros dengan menggunakan kaedah pengikatan/interaksi enzim-substrat, simulasi MD dan MM-PBSA. Dalam kajian ini, analisis metagenomik mendedahkan fila terbanyak yang mempunyai gen berfungsi dengan adaptasi dan berpotensi terhadap bioremediasi adalah dari Firmikutes, Fusobakteria dan Proteobakteria. *Bacillus subtilis* stren H1 dan *Bacillus thuringiensis* strain H2 mampu untuk mendegradasi asid haloalkanoik, haloasetat dan klorofiros. Strain H1 dan H2 memanfaatkan secara optima asid 2,2-dikloropropionik (2,2-DCP), 2,3-dikloropropionik (2,3-DCP), L-2-kloropropionik (L-2-CP), D-2-kloropropionik (D-2-CP), 3-kloropropionik (3CP), monokloroasetat (MCA), trikloroasetat (TCA) dan organofosfat (klorofiros) sebagai sumber karbon dalam keadaan pertumbuhan yang sama (pH 8.0, 30 ◦C), kecuali strain H2 yang lebih sesuai terhadap kepekatan tinggi bahan cemar berhalogen (30 mM) serta tahap kemasinan tinggi (35%). Gen DehH2 adalah dalam kumpulan II dehalogenase dengan kesamaan identiti 63.71% kepada dehalogenase haloasid PH0459 dari *Pyrococcus horikoshii* OT3 hipertermofilik (PDB ID 1X42). Simulasi MD mendedahkan bahawa haloasid dan haloasetat merupakan pilihan yang terbaik untuk didegradasi oleh DehH2 (−6.3 hingga −4.7 kcal/mol) dan −3.3 kepada −4.6 kcal/mol) pada kepekatan 35 % NaCl dan tanpa NaCl masing-masing, melalui tiga atau empat ikatan hidrogen kepada triad pemangkin, Asp125, Arg201, dan Lys202. Data simulasi MD mengesahkan keputusan interaksi molekul substrat dan protein yang terdahulu, di mana komplek tersebut diperhatikan mencapai keseimbangan dalam tempoh masa yang singkat RMSD (~ 0.13 – 0.189 nm) dan mempunyai bilangan turun naik minimum (0.05 – 0.25 nm). Pengiraan MM-PBSA menunjukkan bahawa haloasetat dan haloasid memberikan nilai tenaga ikatan bebas terendah (ΔGbinding) (– 45.14 hingga – 7.62 Kcal/mol). Pengecualian pada klorofiros di mana RMSD (– 0.295 kepada nilai tidak stabil), RMSF (0.05 – 0.59 nm) adalah nilai yang terbesar, manakala kloeofiros tidak dapat mengikat secara spontan terhadap DehH2 (+180.57 kcal/mol) pada kedua-dua keadaan kepekatan garam (35% dan 0% NaCl). Melalui analisa penjujukan genomik seperti jajaran jujukan pelbagai lokus (MLSA), purata identiti nukleotida (ANI) dan analisa filogenetik genomik teras telah mengenal pasti semula *Bacillus thuringiensis* H2 sebenarnya adalah *Bacillus megaterium.* Beberapa gen yang terlibat dalam degradasi bahan cemar dan adaptasi telah dijumpai di dalam jujukan genom tersebut. Berdasarkan penemuan ini, adalah jelas bahawa Tasik Tuz yang berkepekatan garam tinggi mengandungi pelbagai bakteria novel yang berupaya mendegradasi bahan cemar yang boleh digunakan untuk merawat air sisa.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

2,2-DCP	-	2,2-dichloropropionic acid
2,3-DCP	-	2,3-dichloropropionic acid
L-2-CP	-	L-2-chloropropionic acid
D-2-CP	-	D-2-chloropropionic acid
3CP	-	3-chloropropionic acid
MCA	-	Monochloroacetate
TCA	-	Trichloroacetate
PCR	-	Polymerase Chain Reaction
MD	-	Molecular Dynamic
MM-PBSA	-	Molecular Mechanics-Poisson Boltzmann Surface Area
RMSD	-	Root-Mean Square Deviation
RMSF	-	Root-Mean Square Fluctuation
ATB	-	Automated Topology Builder
MLSA	-	Multi Locus Sequence Alignment
ANI	-	Average Nucleotide Identity
BLAST	-	Basic Local Alignment Search Tool
DNA	-	Deoxyribonucleic Acid
MEGA 7	-	Molecular Evolutionary Genetics Analysis Software
16S rRNA	-	16 Subunit Ribosomal Deoxyribonucleic Acid
GROMACS	-	GROningen Machine for Chemical Structure
DehH2	-	Dehalogenase from *Bacillus* sp. H2
PDB	-	Protein Data Bank
3D	-	Three-dimensional
SOPMA	-	Self-Optimized Prediction Method with Alignment
D or Asp	-	Aspartate
E or Gly	-	Glutamate
EC	-	Enzyme commission number
GRAVY	-	Grand average of hydropathy
QIIME	-	Quantitative Insights Into Microbial Ecology
NF	-	Nanofiltration

PGAP	-	Prokaryotic Genomes Annotation Pipeline
RAST	-	Rapid Annotation using Subsystem Technology
WGS	-	Whole Genome Sequencing
ONT	-	Nanopore Technologies
OTUs	-	Operational Taxonomic Units
ASVs	-	Amplicon Sequence Variants
ANOVA	-	Analysis of Variance
ID	-	Identification
TG	-	Tuz Gölü
K or Lys	-	Lysine
R or Arg	-	Arginine

LIST OF SYMBOLS

kg	-	Kilogram
%	-	Percent
kJ	-	Kilojoule
Da	-	Daltons
kDa	-	Kilodaltons
cal	-	Calorie
kcal	-	Kilocalorie
mM	-	Millimolar
°C		Degree Celsius
K		Kelvin
Φ		Phi
Ψ		Psi
Å		Armstrong
ΔG		Gibbs energy
ns		Nanosecond
pI		Isoelectric point
nm		Nanoometre
ps		picosecond
mol		Molar
pH		Potential of hydrogen
h		Hour
min		Minute
NaOH		Sodium hydroxide
HCl		Hydrochloric acid
rpm		Revolution per minute
KH_2PO_4		Monopotassium sulphate
$MgCl_2.6H_2O$		Magnesium chloride hexahydrate
K_2HPO_4		Dipotassium sulphate
$(NH_4)_2SO_4$		Ammonium sulphate
NaCl		Sodium chloride

$MgSO_4.7H_2O$	Magnesium sulphate heptahydrate
w/v	Weight per volume percentage
U/g	Unit per gram
g	Gram
µmol	Micromole
$CaCl_2.2H_2O$	Calcium chloride dihydrate
s	second
U/ml	Unit per ml
$NaH_2PO_4.2H_2O$	Monosodium sulphate
$MgSO_4$	Magnesium sulphate
$MnSO_4.4H_2O$	Manganese sulphate tetrahydrate
$ZnSO_4.H_2O$	Zinc sulphate monohydrate
$CoCl_2.6H_2O$	Cobalt chloride hexahydrate
$FeSO_4.7H_2O$	Iron sulphate heptahydrate
v/v	Volume percentage per 100 ml volume

LIST OF APPENDICES

CHAPTER 1

INTRODUCTION

1.0 Background of study

The extensive utilization of harmful organic compounds and the subsequent rise in pollutant concentrations in the environment are as a result of rapid industrialization, an increase in population, military activities, changed agricultural practices and urbanization practices. Environmental contamination owing to natural and anthropogenic causes is increasing day by day. 'Pollutants' are referred to as any unwanted chemical substance introduced into the environments. Lethal effects of these chemicals led to 'pollution', a process by which a resource (man-made/natural) is often rendered unsuited for use by humans. Categories of pollutants found in waste materials includes petroleum oil, hydrocarbons, halogenated hydrocarbons, nitroaromatic compounds, organophosphorus compounds, solvents, pesticides and heavy metals. These pollutants are released into the environment per annum and contributing to environmental pollution due to its rigorous uses. Some of them may be produced by living organisms or formed during abiogenic processes (Gribble, 2003), natural production of persistent halogenated organic compounds is thought to be far lower than industrial production. Although these harmful halogenated organic compounds are formed locally, their environment spread is global. The strong carbon-halogen bonds and non-reactive substituents may be responsible for persistent halogenated organic compounds' recalcitrance (Gribble, 2003).

Industrial Accident owing to human failures and activities involving deliberate waste discarding result in more than 90% of oil pollution (Stolecka and Rusin, 2021; Iqbal *et al.*, 2021). Dispersion of contaminants have been found to have impact on soils, air, marine and fresh water. Halogenated organic compounds such as Haloacids [2,2-dicloropropionic acid (2,2-DCP) as an active ingredient of DALAPON, 2,3-dichloropropionic acid (2,3-DCP), $_{D,L}$-2-chloropropionic acid ($_{D,L}$-2CP), 3-

chloropropionic acid (3CP)], haloacetate [like monochloroacetate (MCA), dichloroacetate (DCA), trichloroacetate (TCA)] are one of the most common types of chemicals found in the environment. Because of their use in agriculture, dry cleaning and degreasing agents, as well as their widespread accidental and deliberate release into the environments, organohalogens are major groundwater contaminates (Harrison, 2015). Their use and misuse in industry and agriculture result in a considerable amount of these compounds being released into the environment, resulting into widespread dispersal and, in certain cases, unwanted situations, such as environmental contamination. The influence of the halogen substituents on the chemistry of halogenated organic compounds is profound in several ways (Bidleman *et al.,* 2020). The carbon-halogen bond has a relatively high polarity in general. The addition of a halogenated diminishes the compounds' water solubility while increasing their lipid solubility (Hansen, 2019). Many of these recalcitrant compounds are not only persistence in the environment, but also difficult to metabolise in living organisms, posing a variety of chronic ecotoxicity hazards, including endocrine disruption and negative effects on the reproductive and immune systems (Tiwari *et al.,* 2019).

Little attention has been drawn to contamination and biodegradation of extreme environments while many polluted environments present high pressure or high salinity, extreme acidic or alkaline pH, high or low temperature (Zhang *et al.,* 2021; Liu *et al.,* 2021). More than 30 years ago the anthropocentric term "extremophile" was introduced to describe any organism capable of living and growing under extreme conditions that is particularly hostile to human and majority of the known microorganisms. Extremophilic microorganisms (extremophiles) are modified naturally to thrive in such aggressive environments. Microbes living in extreme habitats are characterized by strong selective physico-chemical properties such as salinity, temperature, pH, radiation, low concentration of dissolved oxygen and nutrients as well as existence of these toxic compounds are the main factors that are constantly increases the harshness of the extreme environments. There extreme environments signify an interesting source of bacteria diversity and metabolic activities with exciting biotechnological capability (Prakash and Chandra, 2020; Tang, 2020). Microbes inhabiting such environments are referred to as "extremophiles" showing metabolic and physiological adaptations to their environmental situations.

For instance, they may have usual enzymes that allow them to adapt to extreme situations (Gunde-Cimerman *et al.,* 2020; Pátek *et al.,* 2021).

The marine/hypersaline habitat is regarded as mostly unexploited source for the detection of a novel kinds of enzyme/genes. However, extremophilic microbes like halophiles have been slightly utilized in biotechnological activities with a little exemption such as dehalogenases (Giovanella *et al.,* 2020). Moreover, emphasized on the huge diversity of bacteria, their application in bioremediation, osmoadaptation ability and metabolic capability to produce compatible solutes, and halophilic enzymes, has led to conclude that microbes are most preferred agents for clean-up polluted environments compared to cost-intensive physical and chemical techniques such as burying, combusting, extracting soil vapor, soil washing and dispersion (Xu *et al.,* 2013; Ferronato and Torretta, 2019).

Very few fractions of the potent microbes involved in biodegradation can be cultured by using standard laboratory agar medium and in many cases these abundant taxa are the one that cannot be cultured in the laboratory even though most samples are dominated by some species (Seymour, 2014; Molina-Menor *et al.,* 2021). Currently genome analysis such as metagenomics have launched new possibilities for exploring the new pollutants degrading genes and their regulatory features from both cultivable and uncultivable microbes from environment (Weigold *et al.,* 2016; Mukherjee *et al.,* 2017; Imperato *et al.,* 2019). However, the study of pollutant-degrading microbes, identifying their genetic, and biochemistry, adaptation strategies as well as developing techniques for their use have led to a crucial human endeavour. Advancement in complete genome sequencing technique is offering an increase and better understanding on how microbes conduct pollutant degradation and environmental adaptation at genetic levels. Although, various complete genome of many distinct pollutant-degrading bacteria has been revealed, investigation on genetic basis of pollutant degradation (especially regulatory function of haloacid dehalogenases) and environmental adaptation to the environments are yet to be clarified or still at infancy.

With rapid advancement of high-throughput sequencing, and genomics techniques such as metagenomics has enabled large-scale microbial community analysis and become a competent approach to examine the ability of certain microbes in various environments. This method helps to examine the complex microbial community structure and allow screening of a functional and beneficial potential of the environments (Li *et al.,* 2020; Ruiz et al, 2021). The application of genome sequencing methods can be primarily classified into amplicon sequencing, shotgun metagenomics, single-cell genomic sequencing and whole-genome sequencing of cultured microbes according to the problems they need to be solved. Whole Genome Sequencing (WGS) is one of the mightiest means for regaining the genetic and metabolic diversity found in microbes. Nevertheless, many microbes evade cultivation (Rappé and Giovannoni, 2003; Ruiz et al, 2021), making complete genome less appreciated using traditional approaches. However, in other to conquer this challenge metagenomics and single-cell genomics are two methods that provide access to microbial genomes without the need of cultivation. Sequencing all DNA from a bulk sample, known as metagenomic, has become a powerful approach where hundred and sometimes thousands of genomes can be extracted from an environmental sample (Doud *et al.,* 2020; Kumar *et al.*, 2021).

The hostile environments (like hypersaline Tuz Gölü lake) which host a considerable diversity of extremely halophilic and halotolerant bacteria was studied to provide unparalleled opportunities to understand the genetic response of microbial communities to adapt to its original environmental condition and at the same time utilising pollutants haloacids [such as 2,2-dicloropropionic acid (2,2-DCP) as an active ingredient of DALAPON, 2,3-dichloropropionic acid (2,3-DCP), D,L-2-chloropropionic acid (D,L-2CP), 3-chloropropionic acid (3CP)], haloacetate [like monochloroacetate (MCA), dichloroacetate (DCA), trichloroacetate (TCA)] and organophosphate compounds (chlorpyrifos) as a carbon sources and a model toxic chemicals for pollutant degradation. Halogens such as chlorine are cycled through transformation of inorganic halide into organohalogen compounds and vice versa which may pose challenges to our health. There is evidence that these reactions are microbiologically driven, but the key enzymes and groups of microorganisms involved are not well studied. To uncover the diversity, pollutant encoding genes involved in

degradation and adaptation genes in hypersaline Lake Tuz, current investigation was carried out.

1.1 Problem Statement

Many naturally occurring hypersaline environments are increasingly threatened by environmental pollution as the result of unscrupulous dumping of industrial effluents into these ecosystems. It was estimated that 5% of industrial effluents are saline and hypersaline which could potentially increase the concentration of solutes in affected water bodies. Also, due to the complexity, toxicity, persistence and ubiquitous distribution spreading of some synthesized halogenated compounds in such environments, they had threatened the health and living quality of living organisms on earth and post health challenges on human health. Also, given the evidence that many microbes resist being cultured. The bacteria that can be grown in the laboratory are only a small fraction of the total diversity that exists in nature.

Herein, this study proposes to provide information on the bacterial diversity of Tuz Gölü lake water and revealed halophilic bacteria capable of degrading pollutants as well as their adaptation potentials. Their utilization of using bacterial for removing pollutants from environments may prove useful in alleviating the current problem of water pollution associated with the current practice of dumping industrial waste in the water. Based on literature, the hypersaline Lake Tuz can serve as the source hypersaline pollutants degrading microbial agents. However, the lake is lacking knowledge on the microbial population of the hypersaline Lake Tuz dehalogenase-producing bacteria. Also, information on their mutually inclusive adaptations to both salinity and pollutants degradation capabilities at the enzymatic and genomic level are not fully understood. Hence, studies on the versatility of bacterial to resolve these issues deserve scientific and commercial considerations.

1.2 Aim of Research

This research was aimed in using metagenomic, protein in-silico and genomic studies to reveal dehalogenase-producing bacteria isolates for effective bioremediation of organohalides polluted environments.

1.3 Research objectives

The objectives of the research are:

(a) To determine the metagenome of bacterial population in Tuz Gölü lake.

(b) To isolate and characterize halophilic bacterial capable of degrading halogenated organic compounds (haloacids, haloacetates) and chlorpyrifos.

(c) To assess putative dehalogenase gene and carry out the in-silico assessment to predict and explain the three-dimensional structure of dehalogenase in relation to its salinity-stability and pollutants degradation.

(d) To evaluate the complete genome of a single dehalogenase-producing bacterium.

1.4 Scopes of Study

Water sample was collected aseptically from the shallow shores (average depth 0.2 m) of the halogen-contaminated hypersaline lake Tuz Gölü, near the Van area in Turkey. Firstly, bacteria diversity was done by DNA extraction, followed by amplification of 16S amplicon gene utilizing universal forward and reverse primer, then followed sequencing and bioinformatic analysis utilizing several bioinformatics tools and finally PICRUSt tool was used to predict the metagenomic function on the 16S amplicons data sets.

Next, isolation and characterization of dehalogenase-producing bacterial using minimal media supplemented with various carbon sources such as 2,2-DCP, 2,3-DCP, $_{D,L}$-2CP, 3CP, MCA, TCA, and chlorpyrifos. Two bacterial strains were isolated and further identified through morphological, molecular (16S rRNA sequencing) and biochemical methods. Growth experiments and biodegradation potential were performed by checking the effects of various concentrations of carbon sources, salinity, temperature, and pH on bacterial growth as well as determining the release of chloride ion during dehalogenation processes at 24 h interval over 5 days.

The study then analysis the full sequence of dehalogenase gene from the isolated bacterial species using primers from group I and II dehalogenases. Although, the study could only manage to amplify only group II dehalogenase from one of the bacterial. Then, primary sequence and structural analysis as well as in-silico method via molecular dynamic simulation and substrate docking of halotolerant dehalogenase enzyme was analysis using several computer technologies as a tools to provide a structural insight into the molecular binding processes between dehalogenase enzyme and substrate used (2,2-DCP, 2,3-DCP, $_{D,L}$-2CP, 3CP, MCA, TCA, and chlorpyrifos) in relation to salinity-stability and substrate degradation.

Finally, the complete genome of one of the bacterial was sequenced at the GenSeq SDN BHD (Malaysia). The draft genome was generated using Nanopore MinION and Illumina platforms (MiSeq). Then the de-novo assembly was done using SPAdes v3.12.0, followed by hybrid genome assembly using Unicycler v0.4.7. The genome sequence generated was annotated using the NCBI Prokaryotic Genomes Annotation Pipeline (PGAP) and Rapid Annotation using Subsystem Technology (RAST server). The programs tRNAscanSE and RNAmmer were used for tRNA and rRNA gene prediction. A circular genomic map for genome of strain H2 was created using CGView Server.

1.5 Significance of Study

Little is known about dehalogenase enzyme-producing bacteria from the hypersaline condition. Therefore, by studying the genomic functions and bacterial diversity using genomic/metagenomic approach will reveal unique characterization of all genes related to metabolic activities and bioremediation capacities and inborn stability in highly saline environment. The study revealed the bacteria diversity of the lake which reveal unique features of microbes harbouring in the ecosystem. This study discovered of dehalogenase-producing bacteria from hypersaline habitat, and this will facilitate the removal of pollutants. In addition, genome information on metabolic activities and bioremediation capabilities of bacterium in highly saline environments will contribute to the knowledge of enzyme – and metabolite tailoring in other microorganism. This could provide better alternatives for bioremediation of contaminated marine/hypersaline water bodies. In this context, microbial prospecting may prove as one of the better alternatives for bioremediation of contaminated water bodies. Pertinently, degradation ability of pollutant-degrading bacterial in hypersaline conditions requires specialized cellular genes involved in the process. Such information using genomic/metagenomic approach seems to be lacking at the moment.

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LIST OF PUBLICATIONS

- **Published paper.**

- **Oyewusi, H. A**., Abdul Wahab, R., Edbeib, M. F., Mohamad, M. A. N., Abdul Hamid, A. A., Kaya, Y., & Huyop, F. (2021). Functional profiling of bacterial communities in Lake Tuz using 16S rRNA gene sequences. Biotechnology & Biotechnological Equipment, 35(1), 1-10.
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- **Oyewusi, H. A**., Wahab, R. A., & Huyop, F. (2020). Dehalogenase-producing halophiles and their potential role in bioremediation. Marine Pollution Bulletin, 160, 111603.
- **Oyewusi, H. A**., Huyop, F., & Wahab, R. A. (2020). Molecular docking and molecular dynamics simulation of *Bacillus thuringiensis* dehalogenase against haloacids, haloacetates and chlorpyrifos. Journal of Biomolecular Structure and Dynamics, 1-16.
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- **Oyewusi, H. A**., Huyop, F., Wahab, R. A., & Hamid, A. A. A. (2021). In silico assessment of dehalogenase from *Bacillus thuringiensis* H2 in relation to its salinity-stability and pollutants degradation. *Journal of Biomolecular Structure and Dynamics*, 1-15.

- **Accepted paper.**

- **Habeebat Adekilekun Oyewusi**, Roswanira Abdul Wahab, Fahrul Huyop. A review on enzymatic response to salt stress and metagenomic analysis of adaptation protein in hypersaline environment. journal of tropical life science.

- Paper under review

- **Habeebat Adekilekun Oyewusi**, Fahrul Huyop and Roswanira Abdul Wahab, Genomics investigation and *in silico* analysis of functional haloacid degrading genes (L-2-haloacid dehalogenases) of *Bacillus* strain H2 isolated from hypersaline Lake Tuz (Turkey). Gene Reports.