UNIVERSITI PUTRA MALAYSIA

PHENOL REMEDIATION BY *Ipomoea aquatica Forssk* AND TOXICITY EVALUATIONS ON POST-TREATMENT PLANT EXTRACTS

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By

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Widespread use of phenol in the manufacturing industries and oil refineries resulted in unprecedented phenol leakage into the environment affecting drinking water standards and human health conditions. Phytoremediation was proposed as an environment friendly and cost-effective phenol remediation approach. In this context, *Ipomoea aquatica* Forssk, a native plant commonly found in contaminated sites and has ability to remediate heavy metals, was chosen as the candidate for study. This research aimed to elucidate the oxidative effects, efficiency and mechanisms of phenol remediation by *I. aquatica* Forssk as well as to evaluate the toxicities of the post-remediated plant extracts using *in vitro* and *in vivo* animal model systems. *I. aquatica* Forssk seedlings were subjected to water spiked with 50, 100, 200 and 300 mg/L phenol, respectively. Low phenol concentration produced significantly taller plants (50 mg/L phenol: 101.9 ± 4.4 mm) compared to Control plants (85.2 ± 11.8 mm). At 300 mg/L phenol, plants were stunted, had scars on stems and yellowish leaves with reduced palisade layer and photosynthetic pigments. The tolerance threshold for *I. aquatica* Forssk was recorded as 300 mg/L whereby 50% of the treated plants were dead, while the remaining suffered severe oxidative stress with disrupted membrane integrity (severe electrolyte leakage of 68.0 ± 7.9%). *I. aquatica* Forssk remediated phenol optimally at 100 mg/L with a rate of 2.3 ± 0.0 mg L^{-1} day^{-1}, which was equivalent to removing 273.8 ± 15.3 mg phenol within 14 days. The phenol was degraded through the catechol cleavage pathway with a root peroxidase activity of 118.4 ± 13.0 U/µg protein and catechol production of 2.7 ± 0.0 mg/L. Comparative proteomic analysis showed that *I. aquatica* Forssk exhibited compensatory growth upon exposure to 100 mg/L phenol by mitigating oxidative stress using more antioxidants and metabolising phenol as alternative carbon source in glucose assimilations. Evaluation of the toxicities of the plant extract (using 140 - 500 mg/L) on Zebrafish embryos revealed no fatal toxicities at 320 mg/L as the larvae experienced minor scoliosis and pericardium oedema while LC_{50} of the extract was computed to be 380 mg/L. Likewise, *in vivo* tests on

BALB/c mice with oral administration of 2 000 mg/kg (acute) and 50 - 100 mg/kg/day (sub-acute) plant extracts did not record any mortality or severe toxicity symptoms. The LD_{50} of orally administered extracts was regarded as > 2 000 mg/kg. In accordance to the Globally Harmonised Classification System for Chemical Substances and Mixtures, the data obtained categorised post-remediation *I. aquatica* Forssk plants into Category 5: nontoxic substance. Overall, the data obtained highlights the potential of *I. aquatica* Forssk as a phenol phytoremediator and the treated plants could be used as animal feeds.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

REMEDIASI FENOL OLEH *Ipomoea aquatica* Forssk DAN PENILAIAN KETOKSIKAN EKSTRAK TUMBUHAN PASCA-RAWATAN

Oleh

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Penggunaan fenol yang meluas dalam industri perkilangan dan penapisan minyak mengakibatkan pendedahan fenol ke alam sekitar, dan ianya menyebabkan air minuman tidak boleh diminum dan membahayakan kesihatan manusia. Remediasi fenol dengan tumbuhan telah dicadangkan sebagai cara remediasi fenol yang mesra alam dan kos efektif. Dalam konteks ini, *Ipomoea aquatica* Forssk, tumbuhan yang biasa ditemui di tapak yang tercemar telah dipilih untuk dikaji kerana ianya mempunyai keupayaan untuk menyerap logam berat,. Kajian ini dijalankan untuk menjelaskan kesan oksidatif, kecekapan dan mekanisme remediasi fenol oleh *I. aquatica* Forssk serta untuk menilai toksisiti ekstrak tumbuhan pasca-remediasi dengan model *in vitro* dan *in vivo*. Anak benih *I. aquatica* Forssk telah dirawat dengan air yang mempunyai 50, 100, 200 dan 300 mg/L fenol. Kepekatan fenol yang rendah menghasilkan tumbuhan yang lebih tinggi (50 mg/L fenol: 101.9 ± 4.4 mm) berbanding tanaman Kawalan (85.2 ± 11.8 mm). Pada fenol 200 mg/L, tumbuh-tumbuhan telah terbantut, mempunyai parut di batang dan daun kekuningan dengan lapisan palisade dan pigmen fotosintetik berkurang. Ambang toleransi untuk *I. aquatica* Forssk direkodkan sebagai 300 mg/L di mana 50% daripada tumbuhan yang dirawat telah mati, manakala selebihnya mengalami tekanan oksidatif teruk dengan integriti membran terganggu (kebocoran elektrolit teruk sebanyak 68.0 ± 7.9%). *I. aquatica* Forssk menyerap phenol dengan optimum pada 100 mg/L dengan kadar 2.3 ± 0.0 mg/L/hari, sama dengan penyingkiran fenol 273.8 ± 15.3 mg dalam masa 14 hari. Fenol dihancurkan melalui laluan belahan katekol dengan aktiviti peroksidase 118.4 ± 13.0 U/μg protein dan pengeluaran katekol 2.7 ± 0.0 mg/L. Analisis proteomik perbandingan menunjukkan *I. aquatica* Forssk menunjukkan pertumbuhan pampasan apabila terdedah kepada 100 mg/L fenol dengan mengurangkan tekanan oksidatif dengan antioksidan dan menggunakan fenol sebagai sumber karbon alternatif dalam asimilasi glukosa. Penilaian ketoksikan ekstrak tumbuhan (menggunakan 140 - 500 mg/L) pada embrio Zebrafish tidak megakibatkan

maut pada 320 mg/L walaupun anak ikan mengalami skoliosis dan edema perikardium manakala LC_{50} ekstrak dikira sebagai 380 mg/L. Dalam uji kaji tikus BALB/c, ianya menunjukkan bahawa dengan pemberian oral 2 000 mg/kg (akut) dan 50 - 100 mg/kg/hari (sub-akut) ekstrak tumbuhan tidak mencatat sebarang kematian atau tanda-tanda keracunan teruk. Oleh itu, LD_{50} ekstrak yang diberikan secara oral dianggap sebagai > 2 000 mg/kg. Selaras dengan Sistem Klasifikasi Selaras Global untuk Bahan Kimia dan Campuran, data yang diperolehi mengkategorikan *I. aquatica* Forssk pasca-remediasi ke Kategori 5: bahan tidak bertoksik. Secara keseluruhan, data yang diperolehi menunjukkan potensi tinggi *I. aquatica* Forssk sebagai penyerap fenol dan tumbuhan pasca-remediasi boleh digunakan sebagai makanan haiwan.

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4-AAP	4-Aminoantipyrine
ACN	Acetonitrile
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ATSDR	Agency for Toxic Substances and Disease Registry
BUN	Blood urea nitrogen
EDTA	Ethylenediamine tetraacetic acid
FA	Formic acid
FBA	Fructose-bisphosphate aldolase
FET	Zebrafish embryo acute toxicity test
G3P	Glyceralydehyde-3-phosphate
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase
GGT	Glutamyl transferase
HPLC	High performance liquid chromatography
KEGG	Kyoto Encyclopedia of Genes and Genomes
LC_{50}	Median Lethal Concentration estimated to kill 50% of the test organisms within the test duration
LC-MS/MS	Liquid chromatography tandem mass spectrometry
LD_{50}	Median Lethal Dosage estimated to kill 50% of the test organisms within the test duration.
MDA	Malondialdehyde quantification/content
NO	Nitrite oxide quantification/content
OECD	Organization for Economic Co-operation and Development
PBS	Phosphate buffered saline
PS	Photosystem
ROS	Reactive oxygen species
RuBisCo	Ribulose bisphosphate carboxylase
SOD	Superoxide dismutase
US EPA	U.S. Environmental Protection Agency

CHAPTER 1

INTRODUCTION

1.1 Background study

Phenol is a mono-substituted aromatic alcohol with empirical formula C_6H_6O. It is also referred as hydroxybenzene, carbolic acid or benzenol. At room temperature, pure phenol appears as colourless or pinkish hygroscopic crystals with sickeningly sweet and tarry odour (Bhattacharya *et al.*, 2018). In the past century, phenol was applied to create aseptic condition for surgery as it has alcoholic antiseptic properties (Ibanez *et al.*, 2012). At present, the principal use of phenol is as a precursor to produce phenolic resins. It is broadly applied in oil or coal refineries, and to manufacture plastics, dyes, papers and pharmaceuticals (Lallement *et al.*, 2018). Inappropriate waste management by these refineries and industries had resulted in unprecedented leakages of phenol into the environment, causing severe phenol pollution (Bhattacharya *et al.*, 2018). According to Malaysia Environmental Quality Report 2017, 9.67 metric tonnes of phenolic compounds were disposed from the industries in 2017, causing severe phenol pollution to the extent where drinking water sampled from all states in Malaysia contained phenol levels higher than the 2 µg/L (or 2 ppb) benchmark (Department of Environment, 2018). Due to its poor biodegradability and high water affinity, phenol brings greater risk by contaminating water bodies. Although not strongly acidic, exposure to high concentration of phenol can cause serious health effects such as tissue necrosis and cardiac arrhythmia (Basha *et al*., 2010). Long term contamination may even cause chronic damages such as mutagenicity and carcinogenicity (Huang *et al*., 2014).

There are many technologies currently implemented to clean up phenol polluted sites. For examples, physicochemical methods such as adsorption to activated carbon and chemical oxidation; and biological methods such as biodegradation by bacteria or fungus (Mishra & Kumar, 2017). However, these approaches have drawbacks such as being destructive, expensive, and easily inhibited (Lee & Ong-Abdullah, 2017). Thus, attention was drawn on exploring phytoremediation (using plants as remediator) as an alternative approach to remediate phenol. This approach is relatively cost effective, environment friendly, and generally accepted by society as it is an *in situ* bioprocess with minimal disruption of the environment and ecosystem (Lee *et al.*, 2017).

One of the most crucial traits as a phytoremediator is the capability to survive in severely polluted environments (Suchkova *et al*., 2014). Therefore, *Ipomoea aquatica* Forssk which is a native species in polluted wetlands, drainage channels and marshes was chosen as the phenol phytoremediator candidate in this study. In addition, its potential as a phytoremediator had been widely researched and demonstrated in removing other pollutants, such as excessive

nitrogen (Jampeetong *et al*., 2012), chromium (Chen *et al.*, 2010), cadmium (Hseu *et al*., 2013) and manganese (Dassharma *et al*., 2014).

Phenol was widely demonstrated to cause phytotoxicities as a result of oxidative stress whereby accumulation of reactive oxygen species leads to disrupted membrane integrity and plant death (Ibanez *et al.*, 2012). Therefore, this research aimed to assess the oxidative effects, efficiency and mechanisms of phenol remediation by *I. aquatica* Forssk as well as to evaluate the toxicities of post-remediation tissues through *in vitro* and *in vivo* animal bioassay models. Hypothetically, *I. aquatica* Forssk is capable of degrading phenol into non-toxic metabolites, rendering post-remediation vegetation to be non-toxic and subsequently can be harvested for biofuel production, carbon sequestration or animal feedstock (Batty & Dolan, 2011).

1.2 Objectives

The objectives of present study were:

1. to assess the morphological and histological effects of phenol on *Ipomoea aquatica* Forssk,
2. to assess the concentration-dependent phenol-induced oxidative effects in *I. aquatica* Forssk,
3. to evaluate the ability of *I. aquatica* Forssk to remediate phenol from spiked-water,
4. to identify the up and down-regulated proteins in *I. aquatica* Forssk treated with phenol,
5. to evaluate the embryotoxicity of phenol-treated *I. aquatica* Forssk extracts towards Zebrafish embryos, and
6. to assess the acute and sub-acute oral toxicities of phenol-treated *I. aquatica* Forssk extracts on BALB/c mice.

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LIST OF PUBLICATIONS

Lee, S. Y., & Abdullah, J. O. (2017). Phenol Toxicity and Phytoremediation. *Pertanika Journal of Scholarly Research Reviews*, *3*, 107-118.

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