UNIVERSITI PUTRA MALAYSIA

IMIDACLOPRID RESIDUE IN PADDY, UNPOLISHED AND POLISHED RICE, AND HEALTH RISK ASSESSMENT OF RICE CONSUMPTION IN TANJUNG KARANG, MALAYSIA

RAIHANAH BINTI CHOKELI

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By

RAIHANAH BINTI CHOKELI

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the Degree of Master of Science

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RAIHANAH BINTI CHOKELI

October 2015

Chair : Professor Zailina Hashim, PhD
Faculty : Medicine and Health Sciences

Background: Rice (Oryza sativa L.) by large is staple food consumed and produced by most of the world population including Malaysia. In order to combat from brown planthoppers attack, farmers have used imidacloprid in the paddy fields. However, the used of imidacloprid might give some effect to the population that consume rice. **Objective:** The objective of this study was to evaluate the non-carcinogenic health risks on Tanjung Karang's population (n=552) through rice consumption. **Methodology:** Fifty samples of paddy, unpolished rice and polished rice were collected from paddy fields and milling factory in Tanjung Karang, Selangor and were analysed for imidacloprid residues. The population was divided into 3 age groups which are adult, teenagers and children. Imidacloprid residue analysis in paddy and rice samples was conducted using the simplified and validated QuEChERS (quick, easy, cheap, effective, rugged, and safe) preparation method. Samples were extracted with acetonitrile (ACN) and salts anhydrous magnesium sulphate ($MgSO_4$) and sodium chloride (NaCI) while cleaning was by treating with primary secondary amine (PSA). Imidacloprid residue was quantified with Ultra High Performance Liquid Chromatography (UHPLC) using C18 column and UV detector. The method was validated in term of linearity, range, limit of detection (LOD), limit of quantification (LOQ), precision (repeatability and intermediate precision), and accuracy (recovery). LOD and LOQ and of the method was 0.001 mg/L and 0.003 mg/L, respectively. **Result:** The validated method provides good analytical results wherein the linearity r^2 was 0.9996, recoveries 80−120 % and RSDs <20%. Through of this method, imidacloprid residue was detected in 20%, 14% and 10% of paddy samples, unpolished rice and polished rice, respectively with 4% of the total samples exceeded the MRL. The mean imidacloprid concentration was 0.14 mg/kg in the paddy sample, 0.04 mg/kg in unpolished rice sample and 0.03 mg/kg in polished rice sample. The EDI for adult, adolescent and children were 0.08 mg/kg, 0.03 mg/kg and 0.0002 mg/kg, respectively. HQ value of adult was 1.32 showed that this group was exposed to non-carcinogenic health risk through rice consumption. **Conclusion:** The result of analysis showed that imidacloprid residues were present in paddy and rice samples originate from Tanjung Karang paddy cultivation area. Imidacloprid was detected in mostly in paddy samples compared to brown rice and white rice, respectively with 4% of the total samples exceeded the Malaysian Residue Level (MRL). This indicates that routine monitoring of

this contaminants in food items is required to prevent, control and reduce the contamination and to minimize health risks. This research has provided important information on imidacloprid residues contamination on local paddy and rice for the first time.

Keywords: Imidacloprid, QuEChERS, Health Risk Assessment, UHPLC-UV

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
sebagai memenuhi keperluan untuk Ijazah Master Sains

IMIDACLOPRID DALAM PADI, BERAS YANG TIDAK DIGILAP DAN BERAS YANG DIGILAP SERTA PENILAIAN RISIKO KESIHATAN PENGGUNAAN BERAS PADA PENDUDUK TANJUNG KARANG, MALAYSIA

Oleh

RAIHANAH BINTI CHOKELI

Oktober 2015

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Pendahuluan: Beras (Oryza sativa L.) adalah makanan ruji yang digunakan dan dihasilkan oleh kebanyakan penduduk di dunia termasuk Malaysia.Dalam usaha untuk memerangi daripada serangan bena perang ke atas padi, petani telah menggunakan imidacloprid di sawah padi. Walau bagaimanapun, penggunaan imidacloprid mungkin dapat memberi sedikit kesan kepada mereka yang makan nasi. **Objektif:** Tujuan kajian ini adalah untuk menilai risiko kesihatan bukan karsinogen terhadap penduduk di Tanjung Karang (n = 552) melalui penggunaan beras. **Metodologi:** Lima puluh sampel padi, beras tidak digilap dan beras digilap telah dikumpulkan dari sawah padi dan kilang di Tanjung Karang, Selangor.Sampel tersebut telah dianalisis untuk mengetahui kandungan sisa imidacloprid. Populasi kajian telah dibahagikan kepada 3 kumpulan umur iaitu dewasa, remaja dan kanak-kanak. Analisis sisa imidacloprid dalam sampel padi dan beras telah dijalankan menggunakan kaedah QuEChERS (cepat, mudah, murah, berkesan, lasak, dan selamat).Sampel telah diekstrak dengan menggunakan asetonitril (ACN), garam magnesium sulfat kontang ($MgSO_4$) dan natrium klorida (NaCI) manakala pembersihan dilakukan menggunakan primary secondary amina (PSA). Sisa imidacloprid telah diukur dengan Ultra High Performance Liquid Chromatography (UHPLC) menggunakan kolum C18 dan pengesan UV. Kaedah ini telah disahkan dalam tempoh kelinearan, pelbagai, had pengesanan (LOD), had kuantifikasi (LOQ), ketepatan (kebolehulangan dan ketepatan perantaraan), dan ketepatan (pemulihan). Bacaan LOD dan LOQ adalah 0.001 mg / L dan 0.003 mg / L. **Hasil kajian:** Kaedah di dalam kajian ini disahkan memberikan hasil analisis yang baik di mana kelinearan r^2 adalah 0.9996, pemulihan 80-120% dan RSDs <20%. Melalui kaedah ini, sisa imidacloprid dikesan dalam 20%, 14% dan 10% daripada sampel padi, beras tidak digilap dan beras digilap dengan 4% daripada jumlah sampel melebihi MRL. Kepekatan imidacloprid min adalah 0.14 mg / kg dalam sampel padi, 0.04 mg / kg dalam sampel beras tidak digilap dan 0.03 mg / kg dalam sampel beras digilap. EDI bagi populasi orang dewasa, remaja dan kanak-kanak adalah 0.08 mg / kg, 0.03 mg / kg dan 0.0002 mg / kg.Nilai HQ dewasa adalah 1.32 menunjukkan bahawa

kumpulan ini telah terdedah kepada risiko kesihatan bukan karsinogen melalui penggunaan beras. **Kesimpulan:** Hasil analisis menunjukkan bahawa terdapat sisa imidacloprid di dalam padi dan beras sampel yang diperoleh dari kawasan penanaman padi Tanjung Karang. Imidacloprid dikesan di dalam kebanyakan sampel padi berbanding beras perang dan beras putih, masing-masing dengan 4% daripada jumlah sampel melebihi Tahap Sisa Baki Malaysia (MRL). Ini menunjukkan bahawa pemantauan rutin bahan cemar ini dalam barangan makanan diperlukan untuk mencegah, mengawal dan mengurangkan pencemaran dan untuk mengurangkan risiko kesihatan. Kajian ini telah menyediakan maklumat penting mengenai pencemaran sisa imidacloprid pada padi tempatan dan beras buat kali pertama.

Kata Kunci: Imidacloprid, QuEChERS, Penilaian Risiko Kesihatan, UHPLC-UV

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Thank you

I certify that a Thesis Examination Committee has met on 16 October 2015 to conduct the final examination of Raihanah bt Chokeli on her thesis entitled "Imidacloprid Residue in Paddy, Unpolished and Polished Rice, and Health Risk Assessment of Rice Consumption in Tanjung Karang, Malaysia" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

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LIST OF ABBREVIATIONS

a.i.	Active Ingredient
ACN	Acetonitrile
ADI	Acceptable Daily Intake
AOAC	Association Of Official Agricultural Chemists
ARD	Acute Reference Dose
BDL	Below Detection Limit
BERNAS	Beras Nasional
CDC	Centers For Disease Control
CODEX	Codex Alimentarius Commission
DOA	Department Of Agriculture
EDI	Estimated Daily Intake
EFSA	European Food Safety Authority
EU	European Union
FAO	Food And Agriculture Organization
FDA	Food And Drug Administration
FFQ	Food Frequency Questionnaires
GAP	Good Agricultural Practice
GC	Gas Chromatography
GDP	Gross Domestic Product
HQ	Hazard Quotient
IADA	Integrated Agricultural Development Area
IUPAC	International Union Of Pure And Applied Chemistry
kg/ha	Kilogram Per Hectare
LC	Liquid Chromatography
LC_{50}	Lethal Concentration Of Half Population
LC–MS/MS	Liquid Chromatography-Tandem Mass Spectrometry
LD_{50}	Lethal Dose
LOAEL	(Lowest Observed Adverse Effect Level)
LOD	Limit Of Detection
LOQ	Limit Of Quantification
MANS	Malaysian Adult Nutrition Survey

mg/kg	Milligram per kilogram
$MgSO_4$	Magnesium Sulfate
MOH	Ministry Of Health
MRL	Maximum Residue Limit
nAChR	Nicotinic Acetylcholine Receptors
NaCl	Sodium Chloride
NOAEL	No-Observed Adverse Effect Level
OC	Organochlorines
Organophosphates	(Op)
PPM	Part Per Million
PSA	Primary Secondary Amine
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, And Safe)
RfD	Reference Doses
RSD	Relative Standard Deviation
S/N	Signal-To-Noise
SF	Safety Factors
UF	Uncertainty Factors
UHPLC-UV	Ultra High Performance Liquid Chromatography (UHPLC) With Ultra Violet Detector
USDA	United States Department Of Agriculture
USEPA	United State Environmental Protection Agency
WHO/FAO	World Health Organization/ Food And Agriculture Organization

CHAPTER 1

INTRODUCTION

Rice (*Oryza sativa L.)* by large is staple food consumed and produced by most of the world population ranking third after wheat and maize (Akinbile et al., 2011). China and India yield an approximate of 332 million tonnes of rice amounting to almost 50% and 89% of the world's cereal and harvested rice production respectively (Laborte et al., 2012). In Malaysia, the rice production is in the 25th place with the total production of 2.4 million tonnes. The national average rice production in the country is only 3.0 tons per hectare (Akinbile et al., 2011). Rice are grown mainly in eight granaries of the Peninsular Malaysia making it the most valuable plantation produced nationally after rubber and palm oil. About 300 500 hectares in Malaysia Peninsular is devoted to rice production (Food and Agriculture Organisation, 2002).

About one-third of the agricultural productions are maximized using various types of pesticides (Liu et al., 2002). Chemical use is the most common pest control method currently. According to Sondhia, (2014), two million metric tons of pesticides used by 1.8 billion people engage in agriculture annually onto only 25% of the land area worldwide (Alavanja, 2009). From Figure 1.1, herbicides (47.5%) is a highly used pesticides compared to insecticides (29.5%), fungicides (17.5%) and others (5.5%).

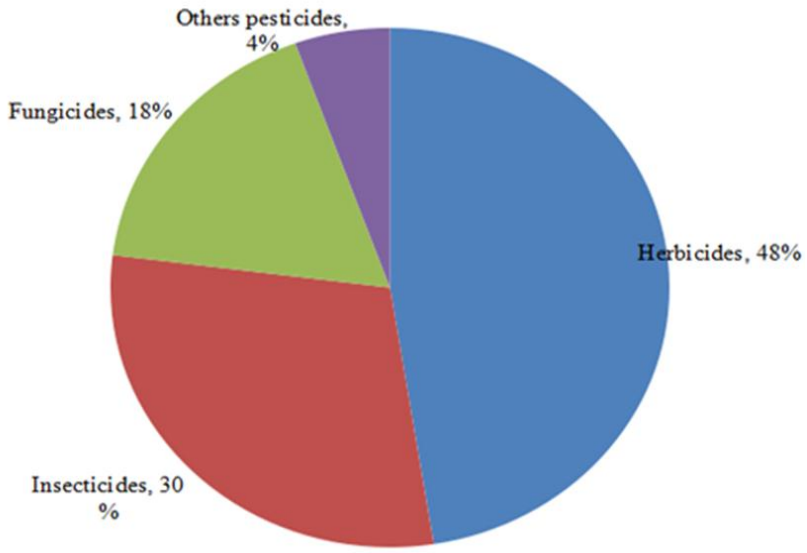


Figure 1.1: Worldwide consumption of pesticides
(Source: De et al., 2013)

Furthermore, the study conducted by Cai, (2008) found that without the usage of agrichemical like pesticides, the production of fruits, vegetables and cereals would reduced to 78%, 54% and 32%, respectively. Zhang et al., (2011) stated four main concerns of pesticide usage around the world: (1) a lot of countries manufacture and utilized illegal harmful pesticides to date; (2) high exposure of pesticides to produces such as rice, cotton and vegetables to fulfill the food demand; (3) lack of enforcement to effectively regulate pesticides application which results in the consumption of unqualified pesticides, and lastly (4) the pesticide residue standard were not implemented effectively. Pesticide residues data in most of the Asian country shows that agriculture products namely cereals, fruits and vegetables are the major dietary source of consumers contaminated with pesticide residues (Wanwimolruk et al, 2012). The increasing rate in food demand from the ever-growing trend of the world population growth can also contribute to the excessive and uncontrollable usage of pesticides in agricultural setting. Human exposure towards pesticide residues through the food, among other things, is of significant concern to everyone from the local authorities, researchers, producers, as well as consumers (Curbelo et al., 2012).

Oryza sativa, the variety of rice that is a staple with highest production worldwide after maize (Harrisson et al., 2002) is consumed in particular at the West Indies and Asian regions. In Malaysia, rice is a crucial part of the nation's diet. Although wheat and livestock are slowly gaining influence in Malaysian food consumption pattern, rural people especially still favors rice. Per capita consumption of rice constituted about 11 percent (82 kilograms) nationwide over the total estimation around 2.3 million tons annually (Shamsudin et al., 2008). The use of pesticides is essential in crop protection during growth, storage and transportation which leads to the improvement in agricultural activities in twentieth century (Mohan et al., 2010). In consequence, food was contaminated extensively due to the arbitrary and imprudent use of pesticides that have begun to receive much attention from many organizations because these residues are found in food commodities that may be hazardous to human health (Jayashree and Vasudevan, 2007).

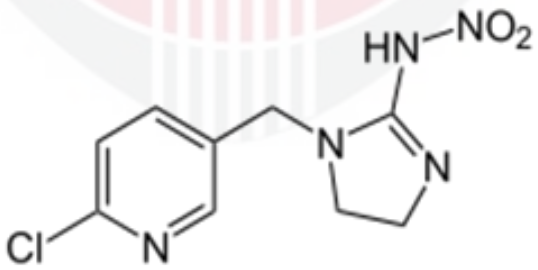


Figure 1.2: Imidacloprid – chemical structure

Imidacloprid, 1-(6-chloro-3-pyridinyl) methyl)-N-nitro-2-Imidazolidinimine), with Malaysia commercial name Confidor is a systemic insecticide and categorized under neonicotinoids (Figure 1.2). Neonicotinoids (a class of chemicals) insecticides are human-made derived from an alkaloid component, nicotine occurring naturally in tobacco plant (Tomizawa and Casida, 2005). Worldwide, it is used in massive amount as insecticides. It acts differently from the current pesticides by adhering to nicotinergic receptors as an agonist on the postsynaptic membrane (Fishel, 2005). Therefore, disturbing the stimulus delivery in the insect's body mechanism and obstructing the above-mentioned neuronal tract in specific. Acetylcholine, a crucial neurotransmitter accumulates leading to paralysis and eventually death of the pest's. It works through the exposure by touch as well as via stomach activity. Imidacloprid is classified as a toxicity class II, which from the scale of I to IV, I is being classified as the top-level, by the Environmental Protection Agency (EPA) and labeled with the "Warning" signal word. Expected symptoms after high level exposure are lethargy, muscle twitch, cramps and weakness. The Lethal Dose (LD_{50}) is 131 and 450mg/kg for mice and rats, respectively. Airborne concentration of more than 69 and 5323 mg/meters cubed air in aerosol and dust forms respectively are fatal to half of the tested animal (LC_{50}). As supported by study done by Fishel (2005) that imidacloprid has been considered as safe and non-sensitive to eyes and skin.

In farming, imidacloprid is commonly utilized for insect's monitoring. It is powerful for managing dangerous pest species including aphids, whiteflies, thrips, scales, psyllids, plant bugs, leafhoppers, planthoppers . A study done by Jaun, (2008) reported that 50.7% of paddy farmers in (Department of Irrigation and Drainage Malaysia) IADA Barat Laut Kuala Selangor including Kampung Sawah Sempadan is using insecticide imidacloprid (Confidor) as one of their pesticides mixture in spraying activities; also lambda-cylothrin (Karate), Lufenuron (Match) and Chlorpyrifos + cypermethrin (Nurelle) with 45.8%, 43.8% and 33.3% concentration respectively.

In this study, it is more focusing on insecticide residue namely Imidacloprid in paddy and rice, planted in Selangor Darul Ehsan. Monitoring of imidacloprid residue in paddy and rice sample was combined with data of rice consumption of Tanjung Karang residential to estimate the potential non-carcinogenic health risk.

1.2 Problem Statements

Although pesticides is effective in crop protection, its usage affect the environment as well as consumers in the case of the presence of pesticides residues in edible rice products (Darko and Akoto, 2008). Exposure to pesticides can always occur during the paddy cultivation process. Basically, some of the pesticides are used to keep pests from attacking food in order to preserve the crops. These compounds have been shown to be toxic to both humans and environment because they are hormone mimickers which are carcinogenic, mutagenic, teratogenic and besides having the ability to persist in the soil (Hamilton et al., 2004). Depending on their chemical characteristics, these compounds may migrate into the grain particularly rice.

The contamination of rice by chemical hazards like pesticides residues has become an alarming worldwide public health concern as people demand for food that are high quality, nutritious and safe for consumption, high-quality. It is indispensable to control the use of pesticides and minimize contamination because of its high consumption by

people (Munshi et al., 2011). According to US EPA findings, pesticides residue should only be present on the outer layer and eliminated during grain milling, mostly in by products such as bran and husk. However, a number of prior studies have been executed analyzing the distribution of contaminants in irrigated rice milling, especially in the inner part of this grain (Kapoor et al., 2012; Chen et al., 2009; Kaushik et al., 2009).

Monitoring of pesticide contamination in food products such as rice is very important. Being an essential alimentary source throughout the world, the quality of rice should not be compromised by the presence of any chemical contamination like pesticide residues. Sometimes, contamination in the rice is due to illegal or non-scientific use of pesticide at the time of early cultivation process until the harvest. Pesticide residues although in negligible amount or in traces are harmful to human (Munshi et al., 2011).

1.3 Study Justification

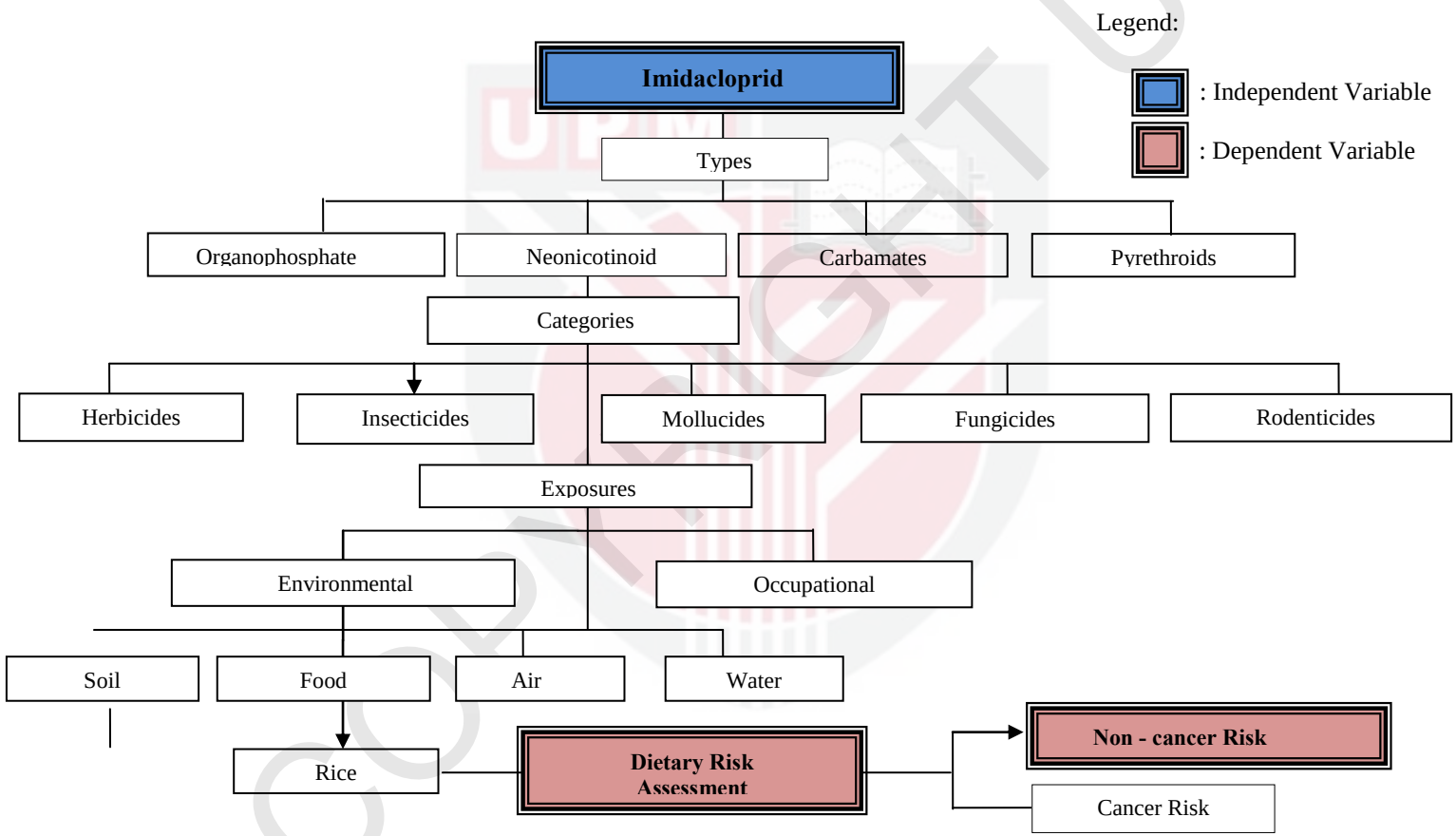
Basically, an estimated half of the human population represented by almost 3.0 billion Asians feed on the rice. Thus this daily consumption which provides up to 80 percent calories needs to be of healthy and standard quality. According to the Malaysian Dietary Guidelines, National Coordinating Committee on Food and Nutrition (2010), it states that we, the Asian population must to take 6 to 11 servings a day from carbohydrate sources such as in the bread, cereal, rice and pasta group. Recently, through the Malaysian Adult Nutrition Survey (MANS) in 2012, it is reported that 97% of the nation have an average of 2½ plates of *nasi putih* (cooked rice) twice daily (Norimah et al., 2008).

It clearly shows that most of the Malaysian population consumes rice in their daily life. Thus, this study is expected to prove that our rice contain permissible level of pesticide residue and do not pose any risk to the consumer. The health risk assessments were evaluated through the Hazard Quotient (HQ) for non carcinogenic risk.

1.4 Study contribution

There are still a limited number of studies referring to neonicotinoids in terms of potential hazard to human health especially in Malaysia. Therefore, this dissertation is aimed to provide data and fill the knowledge gap about the pesticides residue level in Selangor's rice production. Furthermore, its impact on human health in term of non carcinogenic risks for long term consumption of local rice would be estimated through the study. Nonetheless, the residue data is only focused on imidacloprid insecticides as the popular usage among paddy farmers. In addition, findings from this study would also provide a baseline value for pesticide contamination in our rice production and its impacts to human health. This type of data also can be used as the recommendations for the responsible management or authorities in order to control the usage of pesticides in the field. Moreover, in Malaysia, there is no data of health risk assessment on imidacloprid residue in paddy and rice yet. In view of this, this study has contributed the publication of this issue in order to understand more on health risk assessment through the local rice consumption among three different populations.

1.5 Conceptual Framework



1.6 Definition of Term

1.6.1 Conceptual definition

Imidacloprid

A pesticide is any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest. Pests can be insects and insect-like organisms, mice and other vertebrate animals, unwanted plants (weeds), or fungi, bacteria and viruses that cause plant diseases. Though often misunderstood to refer only to insecticides, the term pesticide also applies to herbicides, fungicides, and various other substances used to control pests (Lehotay et al., 2005).

Method validation

The process used to confirm the analytical procedure employed for a specific test is suitable for its intended use. Results from method validation can be used to judge the quality, reliability and consistency of analytical results; it is an integral part of any good analytical practice (Kalra, 2011).

Health Risk Assessment

According to the Report of a Joint FAO/WHO Consultation (2005), health risk assessment through dietary intake was calculated using food consumption data on the concentration of chemical residue found in food. The resulting dietary exposure estimate was then compared with the relevant toxicological or nutritional reference value for the food chemical of concern.

1.6.2 Operational definition

Imidacloprid

Imidacloprid insecticide came from neonicotinoid class found in the paddy, brown and white rice samples has been selected to be analyzed in this study is extracted using QuEChERS method and analyzed through UHPLC-UV.

Method Validation

Method validation is a process that verifies if an analytical procedure matches the laboratory and instrument condition for the intended analysis. To ensure data credibility in the quantitative residue analyses, sample preparation was thoroughly validated considering parameters like recovery, precision (relative standard deviation), determination coefficient (R^2), linearity, detection limit and quantification limit. In this study, method was validated following the established European Union guidelines on quality control procedures for pesticide analysis (European Union, 2007).

Health Risk Assessment

In this study, the risk assessment through dietary intake was calculated on the imidacloprid exposure through rice consumption. The assessment was evaluated

through the Hazard Quotient (HQ) for non carcinogenic effects to estimate the health risk of those who were exposed to imidacloprid from rice ingestion in their daily meal.

1.7 Research Objectives

1.7.1 General Objective

To determine the imidacloprid residue concentration in paddy and rice as well as the Dietary Health Risk Assessment among the Tanjung Karang's population, Selangor, Malaysia.

1.7.2 Specific Objectives

1) To optimize and validate the QuEChERS method prior the analysis of sample using UHPLC - UV.

2) To determine and compare the concentration of imidacloprid residue in samples from 3 different stages of rice processes (paddy, brown rice and white rice).

3) To determine the rice consumption pattern (ingestion rate) among three different age group (children, adolescent and adult).

4) To estimate and compare the Estimated Daily Intake (EDI) of imidacloprid residue through the white rice consumption among the three groups of Tanjung Karang's population

5) To determine and compare the Hazard Quotient (HQ) for imidacloprid residue in white rice consumptions among the three groups of Tanjung Karang's population

1.7.3 Hypothesis

1) There is a significant difference between the imidacloprid residue concentration in three different types of rice samples

2) There is a significant difference in the Estimated Daily Intake (EDI) for imidacloprid residue through the white rice consumption among the three groups of Tanjung Karang's population

3) There is a significant difference in Hazard Quotient (HQ) for imidacloprid residue in white rice sample between the three groups of Tanjung Karang population.

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