



UNIVERSITI PUTRA MALAYSIA

***DETERMINATION OF BLOOD CHOLINESTERASE,
NEUROBEHAVIORAL PERFORMANCE AND GENETIC DAMAGE DUE
TO ORGANOPHOSPHATE EXPOSURE AMONG MALE COCOA
FARMERS IN PAHANG AND PERAK, MALAYSIA***

NORSYAZWANI BINTI MOHAMMAD

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By

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**Thesis Submitted to the School of Graduate Studies, Universiti Putra
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Doctor of Philosophy**

January 2022

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in
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January 2022

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Cocoa plantation farmers in Malaysia are continually being exposed to Organophosphate (OP) insecticide. Chlorpyrifos (group II) is an example of OP used in cocoa farms, and this chemical categorized as a moderately hazardous substance that may cause severe health effects to the plantation workers such as effects to the neurological system, reproductive system, hormonal changes and development of cancer. There are approximately 12,839 workers which is inclusive of cocoa farmers working with cocoa centre and independent smallholder cocoa farmers in Malaysia who are working in the cocoa plantations sector with the breakdown of 4,881 workers in Sabah, 5,613 workers in Sarawak and 2,345 (18.3%) workers in the Peninsular Malaysia. Cocoa farmers are considered at-risk for exposures to OP insecticides from activities such as mixing, spraying, cleaning, loading and disposal process at the workplace. It is imperative for studies to be implemented to find out how the exposure of cocoa farmers to OP pesticides may impact their health and safety, as there are currently no data available and focusing on that. Hence, the study was performed to assess the acute and chronic health effects among male cocoa farmers in Perak and Pahang, Malaysia over the period of exposure to OP in cocoa plantation. The blood cholinesterase level and neurobehavioral performance were used as indicators to determine the acute health effects, while genetic damage assessment was further conducted to determine the chronic health effects of the substance. This is a cross-sectional study among the male cocoa farmers who are working in the fields at the Cocoa Research and Development Centre in Jengka, Pahang and Bagan Datuk, Perak, Malaysia. This study is divided into three interlinked sub-studies: namely i) sociodemographic and occupational background distribution of respondents, ii) evaluation of OP exposure level, and iii) analysis of health effects linked to the OP exposure. A simple randomized method was applied in recruiting male cocoa farmer

respondents (n=102). In Sub-study I, a structured questionnaire was administered to obtain individual, residential and occupational information. In Sub-study II, blood samples were collected via finger prick technique to evaluate acute OP exposure via determination of cholinesterase level. Calculations to estimate the intensity level of insecticide exposure were performed by using information obtained in sub-study 1 and used in an established algorithm. In Sub-study III, Neurobehavioral Core Test Battery (NCTB) was used to measure the neurobehavioral performance. NCTB is one of the test batteries that are designed to assess the neurobehavioral performances on the human nervous system to assess effects due to neurotoxic chemicals exposures. There are seven subtests of NCTB which were included in this study. Buccal epithelial cell samples (n=97) were swabbed to identify genetic damage from chronic exposure to OP through comet and micronuclei (MN) assays. The average age of cocoa farmers was at 36.54 ± 9.93 years old. The most common health symptoms facing by cocoa farmers were burning sensation in the face (57.8%), dizziness (51%), skin rashes and fatigue (38.2%), and headache and coughing (32.4%). In Sub-study II, the median (interquartile range, IQR) estimation for intensity level of OP exposure among the cocoa farmers was 15.60 (16.0), with 52% of them were categorized as having a low-intensity level. The mean (SD) of blood cholinesterase levels among cocoa farmers group was 87.01 (13.15) in percentage which corresponding with the normal range. About 7.8% of cocoa farmers had abnormal levels. OP exposure had given poor performance on motor functionality and manual dexterity of cocoa farmers. In logistic regression, factors such as length of tenure showed statistically significant contribution to the performance on visual-motor speed (adjusted odds ratio (AOR) 0.18, 95% confidence interval (CI), 0.05-0.66) and motor steadiness (AOR 0.14; 95%CI, 0.04-0.54). In comparison, the age variable was contributing significantly to the reporting of manual dexterity performance (AOR 0.11; 95%CI, 0.01-1.01). In Sub-study III, the comet tail length values ranged between 12.06 and 35.27 μm (mean: 22.63 μm), whereas the percentage of DNA in the tail ranged between 16.79% and 53.69% (mean: 33.82%). Cocoa farmers reported an average MN frequency (per 1000 cells) with 8.51 ± 3.99 . Meanwhile, the blood cholinesterase level (odds ratio (OR) -0.12, 95% confidence interval (CI), -0.20- (-0.66), $p < 0.01$ and OR -0.13; 95%CI, -0.23- (-0.04), $p < 0.01$), smoking duration (OR -0.23; 95%CI, -0.43- (-0.02), $p < 0.05$), and appropriate personal protective equipment (PPE) (OR -10.14; 95%CI, -17.55- (-2.72), $p < 0.01$), were among the significant predictive factors that contributed to 13% of the comet assay formation (e.g. comet tail length and the percentage of DNA in the tail). On the other hand, approximately 20.8% of MN frequency variation were explained by age (OR 0.10; 95%CI, -0.01-0.20), $p < 0.05$), BMI (OR 0.26; 95%CI, 0.09-0.43), $p < 0.01$), smoking habit (OR 5.19; 95%CI, 2.07-8.32), $p < 0.01$) and smoking duration (OR -0.23; 95%CI, -0.37-(-0.08), $p < 0.01$) among the cocoa farmers. In summary, the cocoa management has established good labour practices and guidelines for cocoa farmers to follow when handling pesticides. This is evidenced by the fact that majority of cocoa farmers had normal blood cholinesterase levels despite being constantly exposed to OP as part of their work. Most of them were slightly exposed to pesticides, but some of them showed poor motor functionality and manual dexterity. There are other factors might contribute to poor motor functionality and manual dexterity such as the environment, genetics and their lifestyle. This study suggests that the neurobehavioral assessments and genetic damage measurements conducted have provided insight into the need for early

detection and screening of minor exposures to OP in cocoa farmers. The management need to provide necessary chemical-resistant PPE to cocoa farmers such as nitrile glove and respirator with filter. Besides there are also necessary to implement periodically monitoring health risk among cocoa farmers in the future.

Keywords: Organophosphate, blood cholinesterase level, health symptom, neurobehavioral performance genetic damage, cocoa farmers



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

PENENTUAN TAHAP KANDUNGAN ENZIM KOLINESTERASE DALAM DARAH, PRESTASI TINGKALAKU NEURO DAN KEROSAKAN GENETIK DISEBABKAN OLEH PENDEDAHAN RACUN ORGANOFOSFAT DALAM KALANGAN PEKEBUN KOKO LELAKI DI PAHANG DAN PERAK, MALAYSIA

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Pekebun koko yang bekerja di ladang koko di Malaysia, secara berterusan telah terdedah kepada racun serangga organofosfat (OP). *Chlorpyrifos* (kumpulan II) merupakan salah satu contoh OP yang digunakan di ladang koko, dan bahan kimia ini dikategorikan sebagai bahan berbahaya sederhana yang boleh menyebabkan kesan kesihatan yang teruk kepada pekebun koko seperti kesan kepada system saraf, system pembiakan, perubahan pada hormon penyakit kanser. Terdapat kira-kira 12,839 pekerja yang bekerja dalam sektor perladangan koko termasuk pekebun koko yang bekerja di pusat dan pekebun kecil yang mempunyai tanaman persendirian koko iaitu 4,881 orang pekerja di Sabah, 5,613 orang pekerja di Sarawak dan 2,345 (18.3%) orang pekerja di Semenanjung Malaysia. Pekebun koko berisiko untuk terdedah kepada racun serangga OP daripada aktiviti seperti membancuh racun, menyembur racun, membersihkan peralatan semburan dan proses pelupusan di tempat kerja. Kajian ini penting untuk dilaksanakan bagi mengetahui bagaimana pendedahan pekebun koko kepada racun serangga OP boleh memberi kesan kepada kesihatan dan keselamatan mereka, kerana data tersebut masih tiada direkodkan pada masa ini. Oleh itu, kajian ini dilakukan untuk menilai kesan kesihatan akut dan kronik dalam kalangan pekebun koko lelaki di Perak dan Pahang, Malaysia sepanjang tempoh mereka terdedah kepada OP di ladang koko. Tahap kolinesterase darah dan prestasi neurobehavioral digunakan sebagai penunjuk untuk menentukan kesan kesihatan akut, manakala penilaian kerosakan genetik selanjutnya dijalankan untuk menentukan kesan kesihatan kronik akibat daripada penggunaan racun OP tersebut. Kajian ini menggunakan kaedah hirisan lintang dalam kalangan pekebun koko lelaki di Pahang dan Perak, Malaysia yang bekerja di ladang di Pusat Penyelidikan dan Kemajuan Koko di Jengka, Pahang dan Bagan Datuk, Perak, Malaysia. Kajian ini

dibahagikan kepada tiga subkajian yang saling berkaitan: iaitu i) taburan latar belakang sosiodemografi dan pekerjaan responden, ii) penilaian tahap pendedahan OP, dan iii) analisis kesan kesihatan yang dikaitkan dengan pendedahan OP. Kaedah rawak mudah digunakan untuk pemilihan responden (n=102). Sub-kajian I menggunakan soalan selidik berstruktur (n=102) untuk mendapatkan maklumat individu, penempatan dan pekerjaan. Bagi sub-kajian II pula, sampel darah diambil melalui teknik *finger prick* untuk menilai pendedahan OP melalui penentuan tahap kolinesterase. Pengiraan untuk menganggarkan tahap intensiti pendedahan racun serangga dilakukan dengan menggunakan algoritma yang sah dengan mendapatkan maklumat yang diperloehi dalam sub-kajian I. Dalam sub-kajian III, *Neurobehavioral Core Test Battery (NCTB)* digunakan untuk mengukur prestasi tingkah laku neuro. NCTB ialah salah satu bentuk ujian yang direka untuk menilai prestasi tingkah laku neuro pada sistem saraf manusia untuk menilai kesan akibat pendedahan bahan kimia neurotoksik. Terdapat tujuh sub-ujian NCTB yang dimasukkan dalam kajian ini. Sampel sel pipi (n=97) diambil untuk mengenal pasti kerosakan genetik daripada pendedahan kronik kepada OP melalui ujian komet dan mikronukleus (MN). Purata umur pekebun koko dalam kajian ini ialah 36.54 ± 9.93 tahun. Simptom kesihatan yang paling biasa dikaitkan dengan pendedahan racun serangga dalam kalangan pekebun koko adalah rasa bahang panas di bahagian muka (57.8%), pening (51%), ruam pada kulit dan keletihan (38.2%), serta batuk dan sakit kepala (32.4%). Dalam sub-kajian II, anggaran median (julat antara kuartil, IQR) untuk tahap intensiti pendedahan racun perosak dalam kalangan peladang koko adalah 15.60 (16.0), di mana 52% daripada mereka telah dikategorikan sebagai mengalami tahap intensiti yang rendah.

Min (SP) tahap kandungan enzim kolinesterase dalam darah kalangan pekebun koko adalah 87.01 (13.15) peratus dan dikategorikan dalam julat yang normal. Sebanyak 7.8% pekebun koko mengalami tahap kandungan enzim kolinesterase dalam darah yang tidak normal. Pendedahan OP telah memberikan prestasi yang lemah pada kefungsi motor dan ketangkasan pergerakan dalam kalangan pekebun koko. Bagi regresi logistik pula, faktor seperti jangka masa bekerja telah menunjukkan secara statistik memberi sumbangan signifikan kepada prestasi kelajuan moto visual (*adjusted odds ratio (AOR)* 0.18, 95% *confidence interval (CI)*, 0.05-0.66) dan kefungsi motor (*AOR* 0.14; 95% *CI*, 0.04-0.54). Bagi pembolehubah umur pula, ianya memberi sumbangan signifikan kepada prestasi ketangkasan pergerakan (*AOR* 0.11; 95% *CI*, 0.01-1.01). Dalam Sub-kajian III, *comet tail length* (μm) mempunyai nilai antara 12.06 dan 35.27 μm (min: 22.63 μm), manakala peratusan *DNA in tail* (%) mempunyai nilai antara 16.79% dan 53.69% (min: 33.82%). Petani koko melaporkan purata frekuensi MN (setiap 1000 sel) dengan 8.51 ± 3.99 . Manakala, tahap kolinesterase dalam darah (*odds ratio (OR)* -0.12, 95%, *confidence interval (CI)*, -0.20- (-0.66), $p < 0.01$ dan *OR* -0.13; 95% *CI*, -0.23- (-0.04), $p < 0.01$), tempoh merokok (*OR* -0.23; 95% *CI*, -0.43- (-0.02), $p < 0.05$), dan peralatan perlindungan diri (PPE) yang sesuai (*OR* -10.14; 95% *CI*, -17.55- (-2.72), $p < 0.01$), adalah antara faktor ramalan penting yang signifikan menyumbang kepada 13% dalam pembentukan ujian komet seperti *comet tail length* dan peratusan *DNA in the tail*. Selain itu, sebanyak 20.8% variasi frekuensi MN telah dijelaskan mengikut umur (*OR* 0.10; 95% *CI*, -0.01-0.20), $p < 0.05$), BMI (*OR* 0.26; 95% *CI*, 0.09-0.43), $p < 0.01$), tabiat merokok (*OR* 5.19; 95% *CI*, 2.07-8.32),

$p < 0.01$) dan tempoh merokok ($OR -0.23$; $95\%CI, -0.37-(-0.08)$, $p < 0.01$) dalam kalangan pekebun koko. Secara ringkasnya, pihak pengurusan koko telah mewujudkan amalan kerja dan garis panduan yang baik untuk diikuti oleh pekebun koko semasa mengendalikan racun perosak. Ini terbukti apabila majoriti pekebun koko mempunyai tahap kolinesterase darah yang normal walaupun sentiasa terdedah kepada OP sebagai sebahagian daripada kerja mereka. Kebanyakan mereka terdedah sedikit kepada racun perosak, tetapi sebahagian daripada mereka menunjukkan kelemahan pada fungsi motor dan ketangkasan pergerakan. Selain itu, terdapat faktor lain yang menyumbang kepada kelemahan pada fungsi motor dan ketangkasan pergerakan seperti persekitaran, genetik dan gaya hidup. Kajian ini mencadangkan bahawa penilaian tingkah laku neuro dan ukuran kerosakan genetik yang dijalankan telah memberikan gambaran tentang keperluan untuk pengesanan awal dan pemeriksaan pendedahan kecil kepada OP dalam kalangan pekebun koko. Pihak pengurusan perlu menyediakan PPE kalis bahan kimia kepada pekebun koko seperti sarung tangan jenis nitril dan alat pernafasan dengan penapis. Selain itu, pemantauan risiko kesihatan juga perlu dilaksanakan secara berkala dalam kalangan pekebun koko pada masa hadapan.

Kata kunci: Organofosfat, tahap kandungan enzim kolinesterase dalam darah, simptom kesihatan, prestasi tingkah laku neuro, kerosakan genetik, pekebun koko

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LIST OF ABBREVIATIONS

| | |
|-------|---|
| ACh | Acetylcholine |
| AChE | Acetylcholinesterase / Blood cholinesterase |
| AHS | Agricultural Health Study |
| BMI | Body mass index |
| CA | Chromosomal aberration |
| CABI | CAB International |
| CDC | Centres of Disease Control and Prevention |
| CPD | Cocoa pod borer |
| DDT | Dichlorodiphenyltrichloroethane |
| DNA | Deoxyribonuclei acid |
| DOA | Department of Agriculture |
| GDP | Gross domestic product |
| IMP | Industrial Master Plan |
| IQR | Interquartile range |
| MCB | Malaysia Cocoa Board |
| mL | Millilitre |
| MN | Micronuclei |
| MyGAP | Good Agricultural Practice |
| NAP | National Agricultural Policy |
| NCTB | Neurobehavioral Core Test Battery |
| OCs | Organochlorines |
| OP | Organophosphate |
| OPs | Organophosphates |
| OSHA | Occupational Safety and Health Act |
| PBS | Phosphate buffer solution |
| PON1 | Paraoxonase 1 |

| | |
|---------------|---|
| PPE | Personal protective equipment |
| RNA | Ribonucleic acid |
| ROS | Reactive oxygen species |
| RR | Response rate |
| SCE | Sister Chromatic Exchange |
| SCGE | Single-Cell Gel Electrophoresis |
| SD | Standard deviation |
| SPSS | Statistical Package for the Social Science |
| US | United States |
| USECHH | Use and Standard of Exposure of Chemicals Hazardous to Health |
| USEPA | United States Environmental Protection Agency |
| UV | Ultraviolet |
| WHO | World Health Organization |
| μL | Microlitre |
| μm | Micrometer |

CHAPTER 1

INTRODUCTION

1.1 Research Background

Cocoa or *theobroma cacao* is a tropical lowland crop that grows best in areas with the maximum and minimum annual average temperatures of 30 to 32 degrees Celsius and 18 to 21 degrees Celsius, respectively, in addition to with an annual rainfall level of between 1500 mm and 2000 mm (Berbiye, 2014). Cocoa is among the earliest crops introduced into tropical countries, such as Nigeria, Ivory Coast, Cameroon, Ghana, and other West African countries during the 19th century (Idris et al., 2013). These countries produced sweets from the fruits of cocoa and therefore becoming important cocoa exporting countries between 1954 and 1969 (Idris et al., 2013).

In Malaysia, the cocoa plantation has been introduced as commercial crops since the 1950s. Since then, the cocoa industry grows continuously and is now becoming the third major commodity crop in Malaysia, after oil palm and rubber (Azhar & Lee, 2004). Up to this time, Dato' Sri Dr. Mohd Uzir Mahidin, Chief Officer, Department of Statistics Malaysia, reported that these three commodity crops are still a major contributor to the Malaysian economy, increasing from RM115.5 billion in 2019 to RM118.6 billion in 2020 (Department of Statistics Malaysia [DOSM], 2021). Nowadays, Malaysia is the second-largest cocoa grinder in Asia and the eighth largest in the world, behind Cote d'Ivoire, Netherland, Indonesia, Germany, United States, Ghana, and Brazil (Bernama, 2021). The estimated total size of Malaysian cocoa plantations is about 16,000 hectares, with Sarawak having the largest plantation total surface area of 6,860 hectares. The second-largest plantation of 5,780 hectares is located in Sabah, while the rest of Peninsular Malaysia has a total area of 2,370 hectares (Malaysia Cocoa Board [MCB], 2018). The cocoa plantation is an economy generating activity, contributing RM5.55 billion to the nation's export revenue in 2018, accounting for RM1.44 billion or 0.1 percent of the gross domestic product (GDP) of Malaysia (MCB, 2018).

Cocoa is a delicate and sensitive crop. Thus, cocoa farmers need to carry out some precautions to protect these crops from harsh environments, pests, and diseases. Mirids and Cocoa Pod Borer (CPD) are major insect pests that pose serious threats to global cocoa productivity and yield (International Cocoa Organization, 2015). Although the use of non-chemical means to combat pests is recommended for health and other reasons, the use of a certain quantity of chemicals, in the form of pesticides, such as herbicides, insecticides, fungicides, and fertilizer, is unavoidable for the effective management of cocoa plantations (Afrane & Ntiamoah, 2011). In fact, pesticides are not a modern invention and have been existing and used for many years. A large number of synthetic

pesticides were presented and developed in the market since the middle 1940s (Bolognesi et al., 2011; Ortiz-Hernandez et al., 2013; Zhang, 2018). Since then, the development and usage of pesticides have been continuously and extensively expanded in both the developed and developing countries from across the globe (Benedetti et al., 2013; Zhang et al., 2011).

World Health Organization (WHO) has defined pesticides as “*Chemicals compounds that are used to kill pests, including insects, rodents, fungi and unwanted plants (weeds)*”. Other agencies, such as the United States Environmental Protection Agency or US EPA, have defined pesticides as “*Any substances or mixture of substances intended for preventing, destroying, repelling, regulating or controlling the pests*”. These chemical substances can be divided into many groups, including the herbicides group for destroying weeds and unwanted vegetation, insecticides used for controlling the variety of insects, fungicides as prevention measures for molds and mildew growth, and rodenticides for the killing of rats, mice, and other species of rodents (Abubakar et al., 2020; Kapka-Skrzypczak et al., 2011; Zacharia, 2011).

The importance of pesticides in the agricultural sector is undeniable because it is an effective solution for the pest management and controls in agricultural production. The application of these pesticides has greatly reduced the number of insects, pests, diseases, and weeds, thus substantially increases crops yields and economic activities (Abubakar et al., 2020). However, the continuous application and reliance on pesticides in the agricultural sectors can pose serious implications for both environmental and human health risks. These threats is a key problem in a number of studies, especially since the book *Silent Spring* was published in 1962 by Rachel Carson (Abubakar et al., 2020; Aktar et al., 2009; Bernardes et al., 2015; Kim et al., 2016; Mahmood et al., 2016; Özkara et al., 2016; Zacharia, 2011). She has described how the Dichlorodiphenyltrichloroethane (DDT) insecticides entered the food chains and are accumulated in the fatty tissues of animals, including human beings. DDT later causes cancers, as well as damages to the human genes (Abubakar et al., 2020; Damalas, 2009; Fosu-Mensah et al., 2016; Özkara et al., 2016). Apart from that, Carson went on to explain that DDT and other pesticides used continuously for weeks and months to kill insects remained toxic in the environment, even after these pesticides were diluted by rainwater, and continued to contaminate the food supplies (Carson, 2002). Carson then concluded that the use of pesticides was potentially toxic to other organisms, including humans, and it is also affecting the environment.

Agricultural farmworkers are among the high-risk group exposed to pesticides through their daily activities of spraying, mixing, and loading pesticides at the workplace (Aktar et al., 2009; Bernardes et al., 2015). Farm children and infants who grow up near agricultural farmland also have a higher probability of developing adverse health effects when compared to children with minimal or zero exposures to pesticides (How et al., 2014; Lockman et al., 2015). Apart from the agricultural setting, the production and formulators workers from the

manufacturing settings are also at risk for the possibility of pesticide poisoning since they handle various types of chemicals, including raw materials, toxic solvents, and inert carriers in the production of pesticides (Aktar et al., 2009).

As discussed previously, pesticides enter the human body through dermal contact, inhalation, or ingestion (Kapka-Skrzypczak et al., 2011). Skin is the largest organ in the body; therefore, it is the most susceptible exposure site for liquid and airborne chemicals. Additionally, the absorption through the skin can occur simultaneously and rapidly if there are cuts or wounds on the skin (Kapka-Skrzypczak et al., 2011). Besides, pesticides can affect the respiratory system via inhalation and absorption routes, specifically during the carrying or handling of pesticides since the chemical substances in use are volatile and easily absorb into the human body (WHO, 2008).

In terms of occupational exposure, Nordin et al. (2002) explained that the oral or ingestion routes are often the main pathways of exposures caused by poor hygienic practices, such as not washing hands before eating and drinking, smoking or chewing tobacco during the handling of pesticides, mistaking pesticide for food or drink, and splashing pesticides into the mouth through carelessness or accidental incidents. Another important factor in pesticide exposure is intentional pesticide ingestion, a common method for self-harm reported in the rural developing world (Gunnell et al., 2007).

Pesticides have a variable effect on human health. The effects may be acute, thus appear in days and are immediate, or the effects may take months or years to develop, and hence are called chronic or long-term effects (Arshad et al., 2016; Mahmood et al., 2016; Marcelino et al., 2019). Acute effects of pesticide exposures include headache, stinging of the eyes and skin, irritation of the nose and throat, the appearance of the rash and blisters on the skin, diarrhea, abdominal cramp, nausea and vomiting, blurred vision, and very rarely death. In short, the exposure is not severe enough for the affected individual to seek medical attention (Mahmood et al., 2016).

Chronic effects of pesticides are often lethal and may not appear even after many years. These are long term effects that cause damages to multiple organs, such as the detrimental effects to the neurological system (e.g., loss in balance and memory) (Binukumar & Gill, 2011), reproductive systems by affecting the capabilities of hormonal metabolism levels in males and females (Aiassa, 2018; Simaremare et al., 2020). Besides, past studies have indicated and associated the long term effects of pesticides with the development of cancers (Alavanja et al., 2013; Kim et al., 2016; Vivien et al., 2013), as well as the damages to the liver and lungs, in addition to might cause blood diseases such as leukaemia and lymphoma (Kim et al., 2016; Mahmood et al., 2016).

After numerous states had banned and restricted the use of DDT (Abubakar et al., 2020; Aktar et al., 2009), the introduction to other synthetic insecticides, such as organophosphate (OP), continues to rise in the period of 1960s. In the 1970s, the carbamate insecticides were revealed, then followed by pyrethroid insecticides in the 1980s (Leemans et al., 2019). However, OP pesticides are still thriving and have now become one of the predominant insecticides used worldwide (Aktar et al., 2009).

The OP insecticide is designed to kill insects and other pests through the inhibition of the enzyme acetylcholinesterase (AChE) mode of action. AChE is essential for the regulation of the nervous system within organisms. Hence, the OP might lead to the eventual death of insects by irreversibly preventing nervous conduction. Besides, OP also affects the human nervous system in a similar mechanism (Damodaran, 2014; Moretto, 2014; Perry et al., 2020; Suratman et al., 2015). The acute effects of OP are well investigated by the researchers (Perry et al., 2020). In addition, short-term symptoms due to low doses of OP exposure may include headaches, salivation, inability to concentrate, weakness, tiredness, nausea, diarrhea, and blurred vision. Meanwhile, higher doses of exposure can lead to respiratory paralysis and death (El-Zaemey et al., 2013; Perry et al., 2020).

Apart from the AChE inhibition pathway, in addition to obstructing and interfering with other neurochemical functions like a neurotransmitter in humans, the OP chemicals also can induce reactive oxygen species (ROS) and contribute to the development of oxidative stresses. These stresses subsequently affect the synthesis of Deoxyribonucleic acid (DNA), Ribonucleic acid (RNA), and protein (Hundekari et al., 2013; Marcelino et al., 2019; Sosa et al., 2013; Ubaid ur Rahman et al., 2020). Damaged DNA and the division of cells with un-repaired damages may lead to mutations and chromosomal instability in individuals who are exposed to anticholinesterase agents (Basu, 2018). Thus, biological markers for OP exposures, like AChE inhibition and effects due to OP exposures, have been developed to measure the genetical changes in exposed humans (Basu, 2018; Jiang et al., 2019; Sosa et al., 2013; Yu et al., 2016).

About 12,839 workers (cocoa farmers and independent smallholders) in Malaysia working in the cocoa plantation sector, including 4,881 workers in Sabah, 5,613 workers in Sarawak, and 2,345 (18.3%) workers in Peninsular Malaysia. The cocoa industry has been consolidated into one organisation, the Malaysian Cocoa Board (MCB), to ensure continued growth of cocoa activities. This organisation has four coordinated centres known as the Cocoa Research and Development Centre located in Sabah and Sarawak, while the centres for Peninsular Malaysia are located in Jengka, Pahang and Bagan Datuk, Perak.

Cocoa farmers working in these four centres are responsible for cocoa plantation maintenance and production, including pesticide handling, which includes activities such as mixing, spraying, cleaning, and disposing of empty pesticide

containers. In addition to handling pesticides, they also performed various field activities such as spreading fertiliser, pruning excess cacao branches, picking and drying ripe cacao fruit, clearing plantations of unwanted grass and bush growth, and many other agricultural activities. They were labourers who worked outdoors for eight hours five days a week, as opposed to an independent smallholder cacao farmer who worked only part-time.

Pesticides are the best alternative solution used in other agricultural sectors, including cocoa plantations, for pest and disease control. However, regular and indiscriminate use of pesticides can have serious consequences for cocoa farmers. In Malaysia, there are currently no data on how cocoa farmers' exposure to pesticides can affect their health and safety. Previous studies had stated that the predominant health effects among cocoa farmers in Nigeria were eye irritation, skin irritation, dizziness, respiratory problems, and stomach cramps, which often occurred during and after chemical use (Aminu et al., 2020; Isah et al., 2020; Ogunjimi & Farinde, 2012; Raimi, 2021). In addition, a study by Sosan et al. (2008) demonstrated that residues of the insecticide diazinon (organophosphates) were detected in the blood of 42 out of 76 cocoa farmers in southwestern Nigeria. Another study by Sosan et al. (2010) found that 8 out of 76 cocoa farmers in southwestern Nigeria had chronic OP insecticide poisoning because their AChE activities had decreased by 30% compared to baseline data (baseline data were collected in 2005). Isah et al. (2020) had mentioned that cocoa farmers who are frequently exposed to large and continuous amounts of pesticides have the potential to cause DNA damage. However, review of the observations revealed that no studies had been conducted to assess DNA damage in cocoa farmers in Nigeria.

From the above, there is limited documented information on pesticide exposure, safety measures, and work habits of cocoa farmers using pesticides in Malaysia and internationally. Therefore, this study can be a preliminary study in Malaysia to determine the health effects of pesticides on cocoa farmers.

1.2 Problem Statement

Up to February 2021, nearly 3,300 active pesticide substances have been registered in Malaysia, according to the Department of Agriculture (DOA). Insecticides alone have covered around 600 units (Malaysia, 2008), followed by OP insecticide is widely used, followed by carbamate, and pyrethroids. However, the total amount of pesticides used is expected to increase continuously year by year, in line with the increasing agricultural areas and the need to provide high-yielding food and crops productions to meet the economic and population demands.

Recent data suggested that the use of pesticides in cocoa farms is estimated used of pesticides in a season (3 months) is 25.93 litres and for insecticides is

about 4.53 litres (including OP insecticide (chlorpyrifos) about 1.6 litres) in 3 months for one hectare (Malaysia Cocoa Board [MCB], 2016). Cocoa farmer working in the field at Cocoa Research and Development Centres are responsible for maintaining 4 hectares of cocoa field with about 200 - 5000 cocoa trees (MCB, 2016). Thus, the cocoa plantation workers in Malaysia are continually being exposed to OP, as this is the most common insecticide used to kill and control pests in cocoa farms. The active ingredient of OP is chlorpyrifos (group II), an example of insecticides containing moderately hazardous substances that are dangerous, toxic, and can cause severe effects to the human health, used in the cocoa farms (WHO, 2019).

In 2019, approximately 13000 workers (cocoa farmers and independent smallholders' farmers) from the cocoa plantation sector in Malaysia (unpublished Malaysia Cocoa Industry Report, 2019) were being continuously exposed to these types of insecticides as part of occupational exposures. Insecticides sprayed onto the cocoa trees may affect the workers as the spread of insecticides will directly be in contact with the applicators. In view of this, the cocoa farmers are considered as a vulnerable and at-risk group that receives the greatest exposure to the OP insecticides, such as through mixing, spraying, cleaning, loading, and transporting activities at the workplace. During field observation and face-to-face interview, some cocoa farmers did not wear gloves and masks when mixing chemicals. Tasks involves mixing pesticide and water in the ratio indicated on the label in the tank of the equipment. During the mixing process, cocoa farmers could inhale the fumes of the pesticide because they were not wearing PPE. Another cocoa farmer was smoking and drinking a mineral bottle about 10 metres from the mixing area. Another problem was that some of them wanted to smoke after spraying and then took off their gloves to wash their hands. The possibility of exposure to hazardous chemicals is probably very high because workers do not use proper protective measures or hygiene practises. The possibility of exposure to hazardous chemicals is likely to be severe, as there is no proper protection or hygienic practices among the workers. Thus, a detailed understanding of OP exposure and safe handling of pesticides among cocoa farmers are essential for drawing firm conclusions about the potential health effects.

The legislation requirement specified in the Occupational Safety and Health Act 514 1994 (Use and Standard of Exposure of Chemicals Hazardous to Health) Regulation 2000 in Malaysia has made it mandatory that the workers who are exposed to OP must undergo routine medical surveillance of cholinesterase activity in red blood cells and plasma. However, upon investigation from an interview session with the Director of Cocoa Plantation and Research Centre in Jengka, Pahang and Bagan Datuk, Perak, it was found that no such medical surveillance programs have been implemented to the 13 000 workers registered under the Malaysian Cocoa Board. This is one of the points that need to be highlighted in this study. In addition, this study is expected to draw the attention of top management, cocoa authorities, and governments to the chronic adverse health effects of the use of OP in farming populations and to highlight the important issues that require regular medical monitoring of cocoa farmers.

Regarding worker safety, employers have provided some training on the proper and safe use of pesticides, the use of personal protective equipment (PPE), and basic chemical handling skills, but these trainings may not be sufficient because farmers may not fully understand the importance and purpose of these trainings. Regarding PPE provisions, employers have provided latex gloves to protect hands from dermal exposure to pesticides, but it has been noted that some PPE is not appropriate because it is the type of hand protection commonly used in medical or industrial settings. Instead, the use of chemical-resistant gloves is a must, especially when there is a risk of contact with chemical pesticides. This is a great concern because by considering the high volume and percentage of pesticides used in the plantation fields, it is expected that the workers who worked without adhering to the proper Occupational Safety and Health procedures and wearing protective equipment may have been exposed to the high number of pesticides.

Past studies that estimate the extent exposures of workers to pesticides are lacking among the population of cocoa farmers. Similar studies conducted in Malaysia were focusing on paddy farm workers (Baharuddin et al., 2011; Hamsan et al., 2018; How et al., 2014) and palm oil workers (Kuntom et al., 2007), the workers from the two main agricultural commodities since many years. As such, evidence in the literature detailing the high amount of pesticide exposures occurring among the farming or plantation workers in Malaysia and its subsequent health effects are mostly referring to the three types of agricultural commodities. Furthermore, the requirements from the pesticides regulation should be conducted among the cocoa farmers because a recent study has shown that the paddy farmers who are occupationally exposed to OP in Malaysia had shown inhibition of blood cholinesterase levels that were significantly associated with the potential chromosomal and DNA strands breakages (Hamid et al., 2016; Ishak et al., 2015; Vivien et al., 2013). In view of this issue, there are limited numbers of research on the occupational pesticide exposures of cocoa farmers.

Moreover, those dealing directly or indirectly with OP are at the most risk of overexposure, but the symptoms can be difficult to be recognized, since most of the occupational poisoning cases were under-reported, as these cases were either not properly presented to the healthcare facilities or the cases presented were incorrectly recorded (Kamaruzaman et al., 2020). As a result, biomarkers are extremely important and useful for further and proper diagnosis of OP exposure in individuals, especially among farmers.

The National Institute for Occupational Safety and Health (NIOSH) in the United States had established the Sentinel Event Notification System for Occupational Risk (SENSOR) for the pesticide database surveillance program. A total of 13 states participated in the SENSOR pesticide program. From the database, it was reported that 1,343 cases of acute pesticide-related illnesses from insecticide exposure were reported from 1998 to 2011. Approximately 22.3% of the cases were due to organophosphates.

Therefore, the research question arises on whether the OP insecticides used in cocoa plantations might relatively decrease the AChE levels among cocoa farmers and leading to neuromuscular dysfunction, with additional risks to develop genetic damage that may increase their susceptibility to cancer development. This research question is crucial since, so far, there is a limited reliable database that is focusing on pesticide-related illnesses in Malaysia. Then, it is the responsibility of the government and the employers to take this issue as a challenge in order to protect their farmers against the risks of pesticide usage.

1.3 Study Justification

Organophosphate exposure can cause both acute (short-term) and chronic (long-term) health effects, which can occur months or years after exposure. Acute health effects include watery eye, rashes, nausea, tingling, dizziness and diarrhoea. While cancers, birth defects, reproductive dysfunction, immunotoxicity, neurological and development dysfunction are examples of known chronic effects.

Through the participation of cocoa farmers in the measurement of blood cholinesterase level, analysis of genetic damages, and neurobehavioral performances on the use of OP insecticides, the government and cocoa board will be able to have a baseline assessment of the health statuses among the farmers. Hence, the safety precautions or other implementations regarding health and performances can take place efficiently. Furthermore, the results from this study will be used as the baseline data on OP insecticides exposures among a selected group of agricultural workers.

Since there is evidence showing that the exposure to these pesticides among the cocoa farmers is not being assessed and monitored, thus the results obtained from this fundamental study will become useful for the cocoa board to assist any policy and for the standard work procedure makers to understand the risks of pesticides exposures toward the farmers' health. The collected data can be used as references to control any further exposures of pesticides and to develop guidelines or amend the existing guideline so that these guidelines can be used to reduce the health hazards among the farmers in the future.

If adverse health effects associate with pesticide exposures can be controlled among farmers, their labour productivity can also be increased while ensuring the sustainability of cocoa production in the market. The results of this study can also contribute to the planning and establishment of a monitoring system for pesticide exposure in other agricultural sectors.

Furthermore, this fundamental study may serve as a starting point to conduct health hazards evaluations among the farmers, since there is no specific research or study on the consequences of pesticides exposures to the farmers' health, considering the articles published in the Malaysia Cocoa Journal (Navies et al., 2015). The Cocoa Journal collection focuses only on physiology, strategy, and technology to sustain cocoa production. In addition, the statistical data on the MCB's website only provides information on cultivated areas, cocoa bean production by region, cocoa prices, and export and import of cocoa products. Thus, this study can provide basic data for the government and Malaysia Cocoa Board to develop various strategies and policies crucial towards the health performances of cocoa farmers which could minimize human exposure to pesticides.

By identifying the health risks posed by pesticides to cocoa farmers, implementation of appropriate on-farm pesticide management can be initiated, which is important so that effective health programs can be planned and targeted to the most vulnerable populations. In addition, the government can develop new tools or techniques to predict the potential hazards of pesticides or improve current pesticide formulations toward safer formulations so that the health risk to other populations, especially the young generation, can be minimized.

1.4 Conceptual Framework

Figure 1.1 shows the conceptual framework in the study by conducting exposure assessments (blood cholinesterase level) and effects assessments (neurobehavioral performance and genetic damage in buccal epithelial cells), and lastly highlight the potential risk factors characterize the effects from the OP exposure.

Past studies have proven that the farmers are the most prominent subjects routinely being exposed to pesticides, as compared to other occupations (Benedetti et al., 2018; Perry et al., 2020). The farmers' exposures to pesticides mainly occur during the preparation (mixing), and the application of the pesticides spray solution, followed by during cleaning the pesticides spraying equipment (Damalas & Koutroubas, 2016; Farahat et al., 2003; Kachaiyaphum et al., 2010; Robson et al., 2009; Śpiewak, 2001). Farmers are also exposed to pesticides even when they are not performing these activities, as the exposures can arise from being near to pesticide storage, touching pesticides-contaminated clothes, lack of hygienic practice, or by living near to the farm.

Pesticides can enter the human body in three common ways: (1) through the skin (direct contact), (2) mouth (ingestion), and (3) lungs (inhalation). The dermal and inhalation routes of entries are typical and common routes of pesticides exposures experienced by farmers (Damalas & Koutroubas, 2016). Dermal absorption may occur from splashes and spills when handling pesticides, but the

degree of hazards depends on the toxicity and the duration of exposures (Baldi et al., 2006; Macfarlane et al., 2013).

The inhibition of AChE is one of the most effective measurements for OP exposure (Elerseck & Filipič, 2011; Hashmi & Khan, 2011; Kapka-Skrzypczak et al., 2011). The level of AChE (enzyme activity) was assessed from finger-prick blood sample (10 μ l) is used as a biomarker of exposure to evaluate the internal dose level of OP exposure among the study populations. Besides, when the AChE is inhibited by an OP, an excess of acetylcholine (a neurotransmitter that stimulates the muscle movements) occurs, and this causes the muscles to move excessively, therefore can lead to nerve failure (Mackenzie Ross et al., 2010; Perry et al., 2020; Takahashi & Hashizume, 2014). In other words, the drop in AChE levels leads to muscle contractions or spasms, which in turn lead to a reduction in neurological performance.

Besides, the decreasing blood cholinesterase level demonstrated a significant association with the increased oxidative stresses through the generation of ROS among the farmers who were exposed to OP (Kapka-Skrzypczak et al., 2011; Vivien et al., 2013). Further generations of ROS levels are associated with the damages to nucleic acids and induced chromosomal breakages. These damages due to the chronic exposure to OP can later develop into higher cancer risk (Alavanja et al., 2013; Bonassi et al., 2007; Kaur et al., 2011; Kawaguchi et al., 2010; Vivien et al., 2013). Hence, two genetic risk assessments assays were carried out with the buccal epithelial cells, i.e., micronuclei assay and comet assay which were used as biomarker of effects from exposure to OP exposure.

The risk factors, such as individual, residential and occupational parameters, are also investigated in order to characterize these risks with neurobehavioral performances and genetic damage in the population studied.

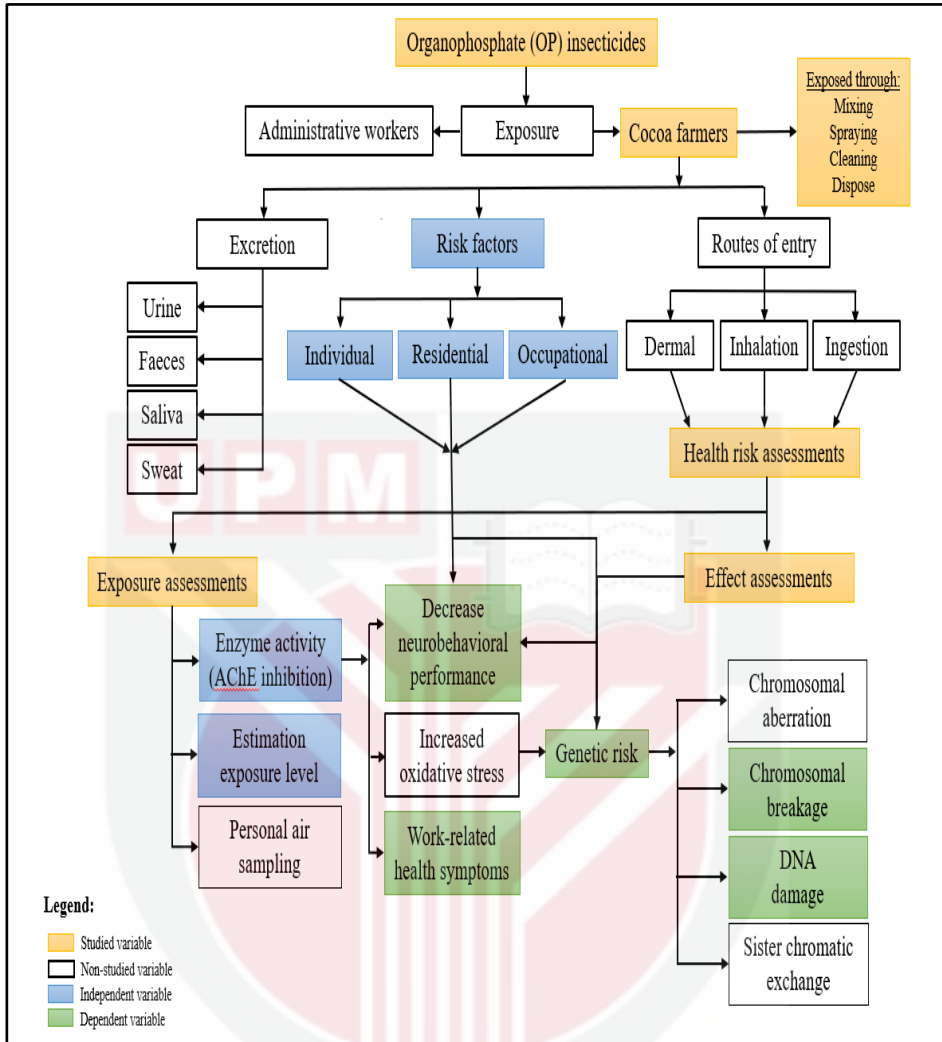


Figure 1.1: Conceptual framework for the present study

1.5 Research Question

In general, this study consisted of three sub-studies, namely i) sub-study I: sociodemographic and occupational background distribution of respondents, ii) sub-study II: evaluation of organophosphate (OP) exposure level, and iii) sub-study III: analysis of health effects linked to the organophosphate (OP) exposure. All of the sub-studies would be linked to answer the following research questions.

1.5.1 Sub-study I: Sociodemographic and Occupational Background Distribution of Respondents

- a. What is the proportion of individual, residential and occupational characteristics among male cocoa farmers in Pahang and Perak?
- b. What are the common work-related health symptoms facing among male cocoa farmers after handling (spraying) organophosphate?

1.5.2 Sub-study II: Evaluation of Organophosphate (OP) Exposure Level

- a. What is the estimation of intensity level due to OP exposure among male cocoa farmers by using validated algorithm formula calculation?
- b. What are the levels of blood cholinesterase among male cocoa farmers due to

1.5.3 Sub-study III: Analysis of Health Effects Linked to the Organophosphate (OP) Exposure

- a. Does the exposure to OP pose any abnormal risk related to neurobehavioral performance and genetic damage to the male cocoa farmers in Pahang and Perak?
- b. What are the predicted of potential risk factors that influence the neurobehavioral performance and formation of genetic damage to male cocoa farmers?

1.6 Objectives

1.6.1 General Objectives

The study was performed to assess the acute and chronic health effects among male cocoa farmers in Perak and Pahang, Malaysia over the period of exposure to OP in cocoa plantation. The blood cholinesterase level and neurobehavioral performance were used as indicators to determine the acute health effects, while genetic damage assessment was further conducted to determine the chronic health effects of the substance.

1.6.2 Specific Objectives

1.6.2.1 Sub-study I: Sociodemographic and Occupational Background Distribution of Respondents

- a. To determine the proportion of individual, residential and occupational characteristics among the male cocoa farmers.
- b. To identify the work-related health symptoms due to organophosphate handling reported among the male cocoa farmers.

1.6.2.2 Sub-study II: Evaluation of Organophosphate (OP) Exposure Level

- a. To estimate the intensity levels of OP exposure among the male cocoa farmers.
- b. To determine blood cholinesterase levels among the male cocoa farmers.

1.6.2.3 Sub-study III: Analysis of Health Effects linked to the Organophosphate (OP) Exposure

- a. To analyse neurobehavioral performance and genetic damage (e.g., micronuclei and comet assays; tail length and the percentage of DNA in the tail) among the male cocoa farmers.
- b. To determine the relationship between blood cholinesterase level with neurobehavioral performance and genetic effects (micronuclei assays and comet assay) among the male cocoa farmers.
- c. To determine the relationship between potential risk factors with selected neurobehavioral performance and genetic effects (micronuclei assays and comet assay) among cocoa farmers

1.7 Hypothesis

- a. Cholinesterase level among male cocoa farmers may be in abnormal range.
- b. Neurobehavioral performance level among male cocoa farmers may be poor.
- c. Genetic damage in buccal cells among male cocoa farmers may be present.

1.8 Definition of Variables

1.8.1 Conceptual Definition

a) Organophosphate (OP)

OP is defined as organic phosphorus compound that is also derivative of phosphoric acid (Martin-Reina et al., 2017). The general structure of OPs is $O=P(OR)_3$, a central phosphate molecule with alkyl or aromatic compounds which can be considered as esters of phosphoric acid (Elersek & Filipič, 2011; Johnstone, 2006). The use of OP chemicals remains widespread in the agricultural industry due to their high spectrum efficacy (English et al., 2016). Common OP compounds used in agriculture are parathion, malathion, chlorpyrifos, and dichlorvos. The main mechanism of OP is blocking the enzyme acetylcholinesterase and subsequently causing nervous damages that result in the death of an insect.

b) Biomarker of Exposure to OP

A biomarker of exposure referred to as the measured compartment or a fluid-form of chemicals, its analyte or the product excreted from the interaction between chemical exposed with the target molecule. Biomarker of exposure to OP are used to estimate the exposure and risk information on the specified chemical exposure in the individuals body including metabolites in blood and urine, enzymatic changes that are detected by using blood components, exhaled air, hair or nails, sweat, and tissues (Kapka-Skrzypczak et al., 2011).

c) Neurobehavioral Performance

The nervous system of a human consists of mood, cognitive and psychomotor abilities (WHO, 1986). The presence of OP can cause damages to the human nervous system due to the inhibition of AChE. This inhibition leads to uncontrolled neurotransmitter (also known as acetylcholine), an important signal that is crucial to transmitting electrical pulse between the nerve cells (Čolović et al., 2013; Sapbamrer & Nata, 2014; Strelitz et al., 2014).

d) Genetic damage

Genetic damage can be used as an indicator or as a biomarker to determine the exposure effects. The assays to measure the genetic damage were applied previously in evaluating the early adverse health effects attributed to the exposures of genotoxic agents among the studied population (Da Silva et al., 2012; Hamid et al., 2016; Intranuovo et al., 2018; Vivien et al., 2013). Genetic damage is cell abnormalities that can be found either in the form of micronuclei (MN), comet assay, sister chromatic exchange (SCE), and chromosome

aberration (CA) (Wang et al., 2010). Genetic damage can be measured by using biological samples, such as buccal epithelial cells (Marcelino et al., 2019; Torresbugarín et al., 2014; Vivien et al., 2013) and human peripheral lymphocytes (Benedetti et al., 2013; Da Silva et al., 2012; Intranuovo et al., 2018).

e) Farmers

Farmers are referred to as the persons who are working in the agricultural sector. They are producing a variety of food products for human and animal consumption. Farmers are the most vulnerable group of workers that are at high risk of contracting acute adverse effects, like pesticide poisoning (Hamsan et al., 2017; Marcelino et al., 2019).

1.8.2 Operational Definition

a) Organophosphate (OP)

According to MCB, active ingredients of chlorpyrifos from OP (group II) are the common type of insecticide used in cocoa plantations to protect the cocoa fruits from insects. Insecticides sprayed to the cocoa trees can affect the workers, as the applicators are directly in contact with the insecticides during insecticide spraying. The possibility of exposure to hazardous chemicals is severe, especially if the workers are not wearing proper protection or practicing proper hygiene practices.

b) Biomarker of Exposure to OP

In this study, an enzyme activity (inhibition of AChE) as an indicator of biological response was used as an internal marker for OP exposure. The inhibition of AChE activity in the central and peripheral nervous systems is considered and known to be the main mechanism of OP toxicity (Kapka-Skrzypczak et al., 2011). Capillary blood from fingertips (10µl) was collected to measure the level of blood cholinesterase activity in the cocoa farmers. The blood cholinesterase test kit (Lovibond, AF267; Tintometer Ltd. UK) was used to measure the exposure levels or AChE activities in the blood samples collected from the respondents. This particular test kit uses the colorimetric principle to analyse the normal breakdown process of acetylcholine. In principle, the accumulation of acetylcholine in the blood specimens causes colour changes (Vivien et al., 2013).

c) Neurobehavioral Performance

In this study, Neurobehavioral Core Test Battery (NCTB), developed by World Health Organization (WHO), was used to detect the neurobehavioral performances effects among the study groups. The seven subtests, such as the Digit Span, Benton Visual, Digit Symbol, Santa Ana, Pursuit Aiming, Trail Making, and Simple Reaction Time test, were conducted as neurobehavioral assessments in this study.

d) Genetic damage

Genetic damage was measured through comet and micronuclei (MN) assays by using buccal epithelial cells which collected from the cocoa farmers. Comet assay known as Single-Cell Gel Electrophoresis (SCGE), is a fast and effective way to measure DNA damage (Gyori et al., 2014; Kawaguchi et al., 2010; Nandhakumar et al., 2011). This assay is carried out by using comet analysis software that screens the captured images. In this study, the DNA damage was determined by estimating the comet tail length (μm) and the percentage of DNA in the tail (Gyori et al., 2014). MN assay can become a biological indicator by monitoring the presence of MN for chromosomal breakage. Falck (2014) defined the MN as small additional nuclei that are formed during mitosis, possibly due to chromosome lagging and failure to be included in the nuclei of the formed daughter cell. Individuals with a high frequency of MN formation in their cells are having a high risk of developing cancer (Bonassi et al., 2007).

e) Farmers

Male cocoa farmers who were registered and worked in the fields at the Cocoa Research and Development Centre in Jengka, Pahang, and Bagan Datuk, Perak were selected as the respondents in the study. Both of the selected locations are identified as the main cocoa centre in Peninsular Malaysia. The work tasks of cocoa farmers include fertilization, pruning excess cocoa branches, picking ripe cocoa, and cleaning the cocoa field area, and these farmers usually spend eight hours working in the outdoor tasks for five days per week. On the other hand, cocoa farmers from independent smallholding farms, as well as those who registered and worked part-time, were excluded from this study.

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