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FORMATION OF POLYCYCLIC AROMATIC HYDROCARBONS AND HETEROCYCLIC AMINES IN GAS-GRILLED HONEY-SPICES MARINATED BEEF SATAY

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By

NOR HASYIMAH BINTI AHMAD KAMAL

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Chair : Prof. Jinap Selamat, PhD
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Polycyclic aromatic hydrocarbons (PAHs) and heterocyclic amines (HCAs) are cooking toxicants that have been associated with elevated malignancy risk due to consumption of grilled red meat. They are simultaneously generated in satay due to high temperature grilling process. The objectives of this study were: a) To determine the effects of temperature on simultaneous formation of PAHs and HCAs in gas-grilled beef satay, b) To evaluate the effects of honey-spices marination on simultaneous formation of PAHs and HCAs. Unmarinated samples were used as control. Fifteen PAHs were determined using high performance liquid chromatography with fluorescence detection method (HPLC-FLD) and nine HCAs were quantified using liquid chromatography tandem-mass spectrometry (LC-MS/MS) with gradient programme. Solid-phase extraction (SPE) method was used for sample clean-up. The natural precursors in raw beef satay samples were analysed to reflect on the formations of PAHs (fats) and HCAs (free amino acids, sugars, and creatinine). For the first objective, beef satay were grilled at 150°C, 200°C, 250°C, 300°C, 350°C. The lowest concentrations of PAHs and HCAs were significantly (P<0.05) generated at 150°C as the formation of PAHs and HCAs increased simultaneously with temperatures. Benzo[a]pyrene were detected in all samples and increased markedly at 300°C and 350°C. The sums of 4 PAHs (PAH4) in marinated beef satay at 300°C and 350°C exceeded maximum level in Commission Regulation (EU) 2015/1125. Significant reductions of polar and non-polar HCAs, except 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) were detected in marinated beef satay across all temperatures. The second objective of this study used two different honey-spices (*Apis mellifera* honey-spices and *Trigona sp.*honey-spices) marinades at grilling temperature of 150°C, 250°C, and 350°C. The formation of PAHs (marinated beef satay) and HCAs (control) were the highest (P<0.05) at 350°C. The most prominent PAHs were phenanthrene (24.61–84.36 ng/g) and fluoranthene (10.00–36.52 ng/g) while HCA was 9H-pyrido[4,3-b]indole (2.67–393.89 ng/g). Both honey-spices marinations significantly (P<0.05) reduced naphthalene, fluorene, and pyrene (PAHs), and 2-amino-9H-pyrido[2,3-b]indole, 1-methyl-9H-pyrido[4,3-b]indole, and 9H-pyrido-[4,3-b]indole (HCAs) in gas-grilled beef satay across all temperatures. However, 2-amino-3,7,8-

trimethylimidazo[4,5-f]quinoxaline (7,8-DiMeIQx) were not detected in any marinated samples. Partial least squares regression (PLSR) revealed significant positive correlations among precursors (raw beef satay samples) with PAHs and HCAs, respectively. Overall, it is concluded that overall formation of fifteen PAHs and nine HCAs simultaneously in gas-grilled beef satay samples increased with grilling temperatures. Formation of PAHs revealed inverse quantitative profiles in contrast with HCAs in marinated beef satay. Honey-spices marination prior to grilling reduced the formation of HCAs; on the contrary, do not present the same effect in the production of PAHs in grilled beef satay.

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

PEMBENTUKAN HIDROKARBON AROMATIK POLISIKLIK DAN AMINA HETEROSIKLIK DALAM SATE DAGING GAS-PANGGANG PERAP MADU-REMPAH

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Polisiklik aromatik hidrokarbon (PAHs) dan heterosiklik amina (HCAs) adalah bahan toksik masakan yang dikaitkan dengan peningkatan risiko malignan berikutan pengambilan daging merah yang dipanggang. Mereka dihasilkan secara serentak dalam sate akibat proses memanggang yang bersuhu tinggi. Objektif kajian ini adalah: a) Untuk menentukan kesan suhu pada pembentukan PAHs dan HCAs dalam sate daging gas-panggang, b) Untuk menilai kesan perapan madu-rempah pada pembentukan PAHs dan HCAs. Sampel yang tidak diperap digunakan sebagai kawalan. Lima belas PAHs dikuantifikasi dengan menggunakan kromatografi cecair prestasi tinggi dengan kaedah pengesanan pendarfluor (HPLC-FLD) dan sembilan HCAs dikira menggunakan kromatografi cecair-spektrometri jisim (LC-MS / MS) dengan program kecerunan. Kaedah pengekstrakan fasa pepejal (SPE) digunakan untuk pembersihan sampel. Prekursor semulajadi dalam sampel sate daging mentah telah dianalisis untuk mencerminkan pembentukan PAHs (lemak) dan HCAs (asid amino bebas, gula, dan kreatinin). Bagi objektif pertama, sate daging dipanggang pada 150°C, 200°C, 250°C, 300°C, 350°C. Kepekatan terendah bagi PAHs dan HCAs adalah signifikan (P<0.05) pada 150°C memandangkan pembentukan PAHs dan HCAs meningkat secara serentak dengan suhu. Benzo[a]pirina dikesan dalam semua sampel dan meningkat dengan ketara pada 300°C dan 350°C. Jumlah 4 PAHs (PAH4) dalam sate daging perap yang dipanggang pada 300°C dan 350°C melebihi tahap maksimum dalam Peraturan Suruhanjaya (EU) 2015/1125. Pengurangan ketara HCAs polar dan bukan polar, kecuali 2-amino-1-metil-6-fenilimidazo(4,5-b)piridina (PhIP) dikesan dalam sate daging perap pada semua suhu. Objektif kedua kajian ini menggunakan dua perapan madu-rempah berbeza (madu *Apis mellifera*-rempah dan madu *Trigona sp*.-rempah) pada suhu 150°C, 250°C, dan 350°C. Pembentukan PAHs (sate daging perap) dan HCA (kawalan) yang tertinggi adalah signifikan (P<0.05) pada suhu 350°C. PAHs yang paling ketara adalah fenantrena (24.61–84.36 ng/g) dan fluorantena (10.00–36.52 ng/g) manakala HCA ialah 9H-pirido-[4,3-b]indola (2.67–393.89 ng/g). Pengurangan ketara (P<0.05) diperolehi bagi naftalena, fluorena, dan pirena (PAHs), dan 2-amino-9H-pirido[2,3-b]indola (AαC), 1-metil-9H-[4,3-b]indola, dan 9H-pirido-[4,3-b]indola

(HCA) bagi sate daging panggang pada semua suhu. Walau bagaimanapun, 2-amino-3,7,8-trimetilimidazo[4,5-f]kuinoksalina (7,8-DiMeIQx) tidak dikesan dalam mana-mana sampel sate daging perap. Regresi kuasa dua terkecil separa (PLSR) menunjukkan korelasi signifikan positif antara prekursor (sampel daging sate mentah) dengan PAHs dan HCAs. Secara keseluruhan disimpulkan bahawa pembentukan lima belas PAHs dan sembilan HCAs secara serentak dalam sampel sate daging gas-panggang meningkat mengikut suhu memanggang. Pembentukan PAHs menunjukkan profil kuantitatif songsang berbanding dengan HCAs dalam sate daging yang diperap. Perapan madu-rempah sebelum memanggang menunjukkan kesan pengurangan ke atas pembentukan HCAs; namun sebaliknya tidak menunjukkan kesan yang sama bagi PAHs dalam sate daging.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

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Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

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LIST OF ABBREVIATIONS

4,8-DiMeIQx	2-amino-3,4-8-trimethylimidazo[4,5-f]quinoxaline
7,8-DiMeIQx	2-amino-3,7,8-trimethylimidazo[4,5-f]quinoxaline
Ace	acenaphthene
Acy	acenaphthylene
Ant	anthracene
AαC	2-amino-9H-pyrido[2,3-b]indole
ANOVA	analyses of variance
AOAC	Association of Official Analytical Chemists
ATSDR	Agency for Toxic Substances and Disease Registry
BaA	benz[a]anthracene
BaP	benzo[a]pyrene
BbF	benzo[b]fluoranthene
BghiP	benzo[g,h,i]perylene
BkF	benzo[k]fluoranthene
CO_2	carbon dioxide
CH_4	methane
Chr	chrysene
DAD	diode array detector
DBahA	dibenzo[a,h]anthracene
DiMeIQx	2-amino-3, 4, 8-trimethylimidazo[4,5-f]quinoxaline
DNA	deoxyribonucleic acid
EFSA	European Food Safety Authority
EU	European Union
Fl	Fluorine

Fla	fluoranthene
GC-MS	gas chromatography–mass spectrometry
H_2O	water
H_2S	hydrogen sulfide
Harman	1-methyl-9H-pyrido-[4,3-b]indole
HCAs	heterocyclic amines
HMW	high molecular weight
HPLC	high performance liquid chromatography
HPLC-FLD	high performance liquid chromatography with fluorescence detection
IARC	International Agency for Research on Cancer
Ind	indeno[1,2,3-cd]pyrene
IQ	2-amino-3-methyl-3H-imidazo[4,5-f]quinolone
IQx	2-amino-3-methyl-3H-imidazo[4,5-f]quinoxaline
LC-MS/MS	liquid chromatography tandem mass spectrometer
Lex	excitation light
Lem	emission light
LMW	low molecular weight
LOD	limit of detection
LOQ	limit of quantification
MA	marinated gas-grilled beef satay with *Apis mellifera* honey-spices marination
MeAαC	2-amino-3-methyl-9H-pyrido[2,3-b]indole
MeIQ	2-amino-3,4-dimethyl-3H-imidazo[4,5-f]quinolone
MeIQx	2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline
MMW	medium molecular weight
MT	marinated gas-grilled beef satay with *Trigona sp.* honey-spices

	marination
NaOH	sodium hydroxide
Nap	naphthalene
ND	not detected
Norharman	9H-pyrido-[4,3-b]indole
NTP	National Toxicology Program
PAHs	polycyclic aromatic hydrocarbons
Phe	phenanthrene
PhIP	2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine
PLSR	partial least square regression
PRS	propyl sulfonic acid strong cationic
Pyr	pyrene
ROS	reactive oxygen species
SCF	Scientific Community on Foods
SPE	solid-phase extraction
UHPLC	ultra-high performance liquid chromatography
US EPA	United States Environmental Protection Agency
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

1.1 Research background

Red meats are the excellent food sources with high biological value proteins, omega-3 polyunsaturated fatty acids and conjugated linoleic acids, vitamins (vitamins B6, B12, and D), and other micronutrients which provide high energy densities (Laskowski et al., 2018). Thus, thermal food processing is used to produce microbiologically safe foods including raw meats with optimal organoleptic properties and minimise the amount of potentially harmful substances. Hence, raw meats turned to be more appetizing with changes in texture, appearance, flavour, and chemical properties as a result from the alteration of protein structures and other added ingredients (Ferguson, 2010; Jägerstad & Skog, 2005). However, cooking toxicants are incidentally incorporated as by-products during food processing at high temperatures, which potentially cause adverse health effects if present in large amounts. The exposure risks however vary among individuals depending on dietary habits and differences in cooking practice (Gibis, 2016; Jägerstad & Skog, 2005).

Polycyclic aromatic hydrocarbons (PAHs) being the ubiquitous environmental pollutants are also generated during thermal food processing such as grilling. The production of carcinogenic compounds in grilled meat is not only accounted by the formation of polycyclic aromatic hydrocarbons (PAHs), which were detected in 1963 (Jägerstad & Skog, 2005). Since 1977, much interest was also focused on another class of food-borne toxicants termed as heterocyclic amines (HCAs) (Gibis, 2016). These cooking toxicants simultaneously present especially in the charred parts of proteinaceous muscle meat such as beef when heated at high temperatures (grilling) for a period of time. HCAs showed extremely high mutagenic potency using the Ames test, 100 to 100 000 times higher than PAHs although PAHs were shown to be the major mutagens on a mass basis (Alomirah et al., 2011; Ferguson, 2010; Gooderham et al., 2001).

Anthropogenic PAHs are produced from variety of incomplete combustion meanwhile food seems to be the major dietary route of PAHs exposition (Alaejos & Afonso, 2011). PAHs generally exists in cooking oil fumes, smoked foods, and foods cooked at high temperature; composed mainly of compounds consisting of three or more fused benzene rings without any acyclic groups (Adeyeye, 2018; Jägerstad & Skog, 2005). The mechanism of formation of PAHs is not well understood, but two principal pathways (pyrolysis and pyrosynthesis) are considered to be involved. High temperature grilling mainly appears as the major route of generating PAHs in meats compared to other cooking methods. Knize et al. (1997) concluded that open flame grilling enhances the formation of PAHs. Consumption of grilled and charred meats increases an individual's exposure to PAHs (Pirsaheb et al., 2020; Wenzl et al., 2006; Jägerstad & Skog, 2005).

Cooking methods greatly influence the formation of HCAs as the concentration of HCAs in food is usually found within the low range of nanogram/gram (ng/g). HCAs are classified in 2 groups: thermic HCAs (100°C to 300°C) and pyrolytic HCAs (> 300°C). Potent HCAs are formed during heat treatment via Maillard reaction (Alaejos & Afonso, 2011; Cheng et al., 2007). HCAs are created within the muscle meats as a result of reactions between amino acids (building blocks of proteins) and creatine (a chemical found in muscle) during thermal exposure (high temperature cooking). HCAs are found most concentrated in the meat juices. Apart from cooking method, the formation of HCAs is also dependent on temperature and heating conditions used (Gibis, 2016).

PAHs and HCAs have been evaluated by the International Agency for Research on Cancer (IARC) on the risk of cancers which has come to the conclusion that several of these food-borne toxicants are possibly or probably carcinogenic to humans. Benzo[a]pyrene (BaP) is classified as carcinogenic to humans (Group 1), and some of other PAHs as probably carcinogenic or possibly carcinogenic. Eight of the HCAs the most abundant 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx) and 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) as possible human carcinogens (Group 2B) and 2-amino-3-methylimidazo[4,5-f]quinoline (IQ) as a probable human carcinogens (Group 1) (Viegas et al., 2012; Alaejos & Afonso, 2011). Frequent dietary intake high in PAHs may induce foregut tumours and lung tumours. Epidemiologic studies found the relationship of HCAs (particularly the tryptophan pyrolysis products) to several types of cancer (pancreas, breast, and colon) in humans (Gibis, 2016; Alaejos & Afonso, 2011).

1.2 Significance of study

PAHs and HCAs are considered as dietary risk factor for human cancer due to the capability of PAHs and HCAs to form on proteinaceous muscle foods during ordinary cooking practices even at low parts-per-billion (ppb), hence implies frequent exposure to the general public. Moreover, grilled foods are gaining popularity not only at home but in the restaurants as well. Satay is an example of popular grilled meat (beef or chicken) in many Southeast Asian countries (Malaysia, Indonesia, Thailand, Singapore) and even in some European countries such as Holland (Farhadian et al., 2012). Due to the increasing popularity, it is a great concern that grilled meat (including satay) may pose a risk to the population.

This study determined simultaneous formation of PAHs and HCAs in gas-grilled beef satay since their occurrence and mitigation strategies in grilled foods are still a challenge as the available studies simultaneously highlighting both of the concomitant mutagens (PAHs and HCAs) in satay are still scarce. Moreover, PAHs and HCAs concentrations in beef satay subjected to temperatures higher than conventional grilling temperatures (200°C) or using different grilling methods than charcoal grilling have not been fully investigated which creates a knowledge gap.

The marinating ingredients including spices and other condiments used in marination of the grilled meat leads to variations in the total PAHs and HCAs generated in grilled meat (Pirsaheb et al., 2020). There are extensive ingredients are used for marination of satay which varies according to different food vendors (Wu et al., 1997). Continuous possible innovations of interventions towards reducing PAHs and HCAs simultaneously in grilled satay is indeed a major research area to work out (Singh et al., 2016). Therefore, the potential effects of honey-spices marination on formation of both, PAHs and HCAs simultaneously is definitely worthy as concerns are raised on consumers' health risks on grilled meat (Irnanda et al., 2012).

1.3 Research hypotheses

There are two hypotheses for this study as follows:

H1: Grilling temperatures affect the formation of both, PAHs and HCAs in gas-grilled beef satay.

H2: Marination reduces the simultaneous formation of PAHs and HCAs in gas-grilled beef satay.

1.4 Research objectives

The objectives of this study are:

1. To determine the effects of temperature on simultaneous formation of PAHs and HCAs in gas-grilled beef satay

2. To assess the effects of honey-spices marination on simultaneous formation of PAHs and HCAs.

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