

# **UNIVERSITI PUTRA MALAYSIA**

# MULTICLASS EMERGING ORGANIC POLLUTION AND ASSOCIATED RISKS IN THE KLANG RIVER ESTUARY IN MALAYSIA

TUAN MOHAMAD FAUZAN TUAN OMAR

FPAS 2019 3



## MULTICLASS EMERGING ORGANIC POLLUTION AND ASSOCIATED RISKS IN THE KLANG RIVER ESTUARY IN MALAYSIA

By

# TUAN MOHAMAD FAUZAN TUAN OMAR

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfillment of the Requirements for the Degree of Doctor of Philosophy

November 2018

#### COPYRIGHT

All material contained within the thesis, including without limitation text, logos, icons, photographs and all other artwork, is copyright material of Universiti Putra Malaysia unless otherwise stated. Use may be made of any material contained within the thesis for non-commercial purposes from the copyright holder. Commercial use of material may only be made with the express, prior, written permission of Universiti Putra Malaysia.

Copyright © Universiti Putra Malaysia

P 1/10/14 1000801182

EPAS 2019 3

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

### MULTICLASS EMERGING ORGANIC POLLUTION AND ASSOCIATED RISKS IN THE KLANG RIVER ESTUARY IN MALAYSIA

By

#### TUAN MOHAMAD FAUZAN TUAN OMAR

#### November 2018

#### Chairman Faculty

: Professor Ahmad Zaharin Aris, PhD : Environmental Studies

The occurrence, distribution and sources of multiclass emerging organic contaminants (EOCs) in the environmental matrices (estuarine water, sediment and biota) from Klang River estuary were examined. The targeted EOCs for this assessment were endocrine disrupting compounds (bisphenol A, 4-OP, 4-NP, E2, E1 and EE2), organo phosphorous pesticides (quinalphos, chlorpyrifos, diazinon) and pharmaceutically active compounds (primidone, sulfamethoxazole, dexamethasone, diclofenac, amoxicillin, progesterone, testosterone). Analytical methods of quantification for determination of multiclass EOCs were developed for three components of environmental matrices, namely estuarine water, sediment and biota matrices. The developed analytical methods were validated for linearity, extraction efficiency (% recovery), precision, method detection limit as well as matrix effects. Satisfactory optimization were achieved for the developed analytical methods with extraction efficiency between 51 to 126%, as well as excellent linearity (r > 0.991) and precision (%CV < 20). Results from this field study showed that prevalent contamination of Klang River estuary by EOCs with several compounds such as diclofenac, bisphenol A, progesterone, estrone and amoxicillin were predominantly detected in the three environmental matrices. For estuarine water samples, bisphenol A was the compound mostly detected, contributed about 54.77% of total concentration followed by amoxicillin (39.17%), estrone (2.16%) and diclofenac (1.67%). The highest concentration of EOCs in surface water samples was found in BPA at 597.30 ng/L, followed by amoxicillin at 102.31 ng/L. While for sediment samples, bisphenol A was the highest concentration detected at 16.84 ng/g followed by diclofenac (13.88 ng/g) and estrone (12.47 ng/g). The percentage of contribution (% of total concentration) is in order of bisphenol A (49.68%), diclofenac (16.19%), progesterone (10.37%) and E1 (9.25%). As for biota matrices, diclofenac (10.76 ng/g) was detected at the highest concentration in fish samples, while progesterone (9.57 ng/g) was the highest concentration found in the molluscs. Principal component analysis (PCA) has successfully extracted four principle components, revealing that the sources of EOCs in the estuary originated from water/waste treatment plants, medical waste discharges,

industrial pollution and aquaculture/livestock activities. Estimation of human health risk assessment, calculated as hazard quotient (HQ) were less than 1, suggesting the consumption of fish and mollusc from Klang River estuary will not pose any health risk to the consumers. Meanwhile, environmental risk assessment, expressed as risk quotients (RQs) for all targeted compounds were also less than 1 for the three test species (phytoplankton, zooplankton and fish) evaluated. Hence, the targeted EOCs have not indicated significant risks to the ecosystem during the current assessment. Nonetheless, result from this field assessment is an important finding for pollution studies in Malaysian tropical coastal ecosystems particularly for organic micro-pollutant EOCs and can also serve as a baseline database for future reference.

Keywords: Emerging organic contaminants; Klang River estuary; environmental risk assessment; health risk assessment; coastal ecosystem

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

#### PENCEMARAN PELBAGAI KELAS ORGANIK YANG BARU MUNCUL DAN RISIKO-RISIKO BERKAITAN DENGANNYA DI MUARA SUNGAI KLANG, MALAYSIA

Oleh

#### TUAN MOHAMAD FAUZAN TUAN OMAR

November 2018

#### Pengerusi : Profesor Ahmad Zaharin Aris, PhD Fakulti : Pengajian Alam Sekitar

Kejadian, taburan dan sumber pencemaran sebatian organik EOC pelbagai kelas dalam matriks alam sekitar (air, sedimen, ikan dan moluska) di muara Sungai Klang telah diperiksa. Sebatian EOC yang disasarkan untuk kajian ini adalah pengganggu endokrin fenolik (bisfenol A, 4-OP, 4-NP), racun perosak organo fosforus (quinalfos, klofirifos, diazinon), hormon estrogenik (E2, E1, EE2) dan sebatian aktif farmaseutikal (primidon, sulfametosazol, desametason, diklofenak, amoksisilin, progesteron, testosteron). Kaedah analisis untuk penentuan EOC pelbagai kelas telah dibangunkan untuk tiga komponen matriks alam sekitar, iaitu air muara, sedimen muara dan biota. Kaedah analisis yang telah dibangunkan ini telah disahkan untuk kelinearan, kecekapan pengekstrakan (% pemulihan), ketepatan, had pengesanan, serta kesan matriks. Pengoptimuman kaedah analisis adalah memuaskan dengan peratusan kecekapan pengekstrakan bagi semua matriks adalah diantara 51% - 126%, kelinearan melebihi r>0.991 dan pekali variasi (CV) bagi ketepatan adalah tidak melebihi <20%. Hasil daripada penilaian lapangan ini menunjukkan pencemaran EOC di muara Sungai Klang dengan beberapa sebatian seperti diklofenak, bisfenol A, progesteron, estron dan amoksisilin dikesan pada ketiga-tiga matriks alam sekitar tersebut. Bagi sampel air muara, bisfenol A merupakan sebatian yang paling banyak dikesan, mewakili 54.77% kepekatan keseluruhan diikuti oleh amoksisilin (39.17%), estron (2.16%) dan diklofenak (1.67%). Kepekatan sebatian bisfenol A yang dikesan dalam sampel air muara adalah pada 597.30 ng/L, diikuti oleh amoksisilin pada 102.31 ng/L. Manakala, bagi sampel sedimen muara, kepekatan bisfenol A (16.84 ng/g) adalah yang paling tinggi dikesan, diikuti oleh diklofenak (13.88 ng/g) dan estron (12.47 ng/g). Sebatian bisfenol A mewakili sebanyak 49.68% kehadiran di dalam sampel sedimen muara diikuti oleh diklofenak (16.19%), progesteron (10.37%) dan estron (9.25%). Bagi matriks biota, diklofenak (10.76 ng/g) dikesan pada kepekatan tertinggi dalam sampel ikan, manakala progesteron (9.57 ng/g) merupakan kepekatan tertinggi yang hadir dalam siput paya bakau. Analisis prinsipal komponen (PCA) telah berjaya mengenalpasti empat

komponen utama, menunjukkan sumber-sumber EOC di muara adalah berasal dari loji rawatan air/sisa, pelepasan sisa perubatan, pencemaran industri dan aktiviti akuakultur/ternakan. Anggaran penilaian risiko kesihatan manusia, dikira sebagai darjah bahaya (HQ) kurang dari 1, menunjukkan pengambilan ikan dan siput paya bakau dari muara Sungai Klang sebagai sumber makanan tidak akan menimbulkan risiko kesihatan kepada pengguna. Sementara itu, penilaian risiko alam sekitar, dinyatakan sebagai darjah risiko (RQs) untuk semua sebatian yang disasarkan juga kurang daripada 1 untuk tiga spesies ujian (fitoplankton, zooplankton dan ikan) yang telah dinilai. Oleh yang demikian, pencemaran EOC tidak menunjukkan risiko yang ketara kepada ekosistem semasa penilaian dilakukan. Walau bagaimanapun, hasil daripada penilaian lapangan ini adalah penemuan penting bagi kajian pencemaran ekosistem pantai tropika Malaysia terutamanya untuk kajian bahan pencemar EOC mikro organik dan boleh dijadikan pangkalan data asas bagi rujukan masa hadapan.

Kata kunci: pencemaran organik baru muncul; muara Sungai Klang; penilaian risiko alam sekitar; penilaian risiko kesihatan; ekosistem pantai

#### ACKNOWLEDGEMENTS

Alhamdulillah, praise upon Allah this work had been completed. First of all I would like to thank my academic adviser, Prof. Dr. Ahmad Zaharin Aris and members of supervisory committee, Prof. Dr. Fatimah Md. Yusoff and Prof. Dr. Shuhaimi Mustafa for constant guidance, motivation, encouragement and support upon accomplishing this work. I am very thankful to have been given a chance to gain some of your knowledge and experience and I am sure this will be benefited me in my future career.

Special thanks to member of Hydrogeology Lab, Hanisah Mohmad Nasir, Wee Sze Yee, Nur Afifah Hanun Ismail, Nur Nasyitah Sobihah Mohd Nasri, Nur Farhana Mokhtar for the help during sampling and laboratory work. It is indeed an enjoyable moment working with all of you and I am definitely will miss the team especially when we are out for sampling work. To big family of Prof AZA Hydrochemistry Lab, Encik Anuar Sefie (NAHRIM), Encik Zahidi Hamzah (JMG), Dr. Shah Cristiani Azhar (UPM), Puan Nordiani Sidi (UPM) and Dr. Looi Ley Juen (UPM), thank you for your constant support and motivation.

Lastly, my lovely thanks extended to my family, especially bonda Raja Jamaiah Raja Ahmad and my mother-in-law, Engku Samsiah Engku Yusuf for the prayer and doa, and always behind me for whatever I am doing. To my dearest wife, Azrilawani Ahmad thank you for your understanding throughout this PhD journey and no words can describe how grateful I am to have you as my pillar of support. To my wonderful children, Firhana Azzalea, Firhan Afeef and Fitriya Annisa, walid love all of you so much.

Special dedication to ayahanda Tuan Omar Raja Senik, thanks for shaping me to what I am now. Till we meet in *jannah*, Insyaallah.

## TABLE OF CONTENTS

			Page
ABST	RACT		
ABST	RAK		iii
ACKN	NOWLE	DGEMENTS	v
APPR	OVAL		vi
DECL	ERATI	ON	viii
LIST	OFTAB	LES	vin
LIST	OF FIG	URES	vvi
LIST	OF ABB	BREVIATIONS	xix
СНАР	TER		
1	GENH	ERAL INTRODUCTION	1
	1.1	Background of study	1
	1.2	Problem statement	3
Same and the standards	1.3	Objectives of study	4
TIOSUY .DM MBMB	1.4	Scope of study	4
in Akuakultur	1.5	Significance of study	4
li Pertenian	1.6	Research framework	5
Serdang, Selangor	1.7	Thesis outline	5
2	LITE	RATURE REVIEW	7
	2.1	Physico-chemical properties of targeted emerging organic	
		contaminants (EOCs)	7
		2.1.1 Endocrine disrupting compounds (EDCs)	7
		2.1.2 Pesticides	9
		2.1.3 Pharmaceutically active compounds (PhACs)	11
	2.2	Analytical challenges for determination of EOCs in	
		environmental and biota matrices	14
		2.2.1 Sample handling, storage and preservation	14
		2.2.2 Optimization of parameters for LC MS-MS and GC	
		MS analyses	18
		2.2.3 Analytical methods for aqueous and solid	
		environmental samples	32
		2.2.4 Analytical methods for biota samples	33
	2.3	Occurrence and levels of EOCs in environmental and biota	
		matrices	35
	2.4	Sources and fate of EOCs in the ecosystem	39
	2.5	Environmental and human health risk assessment	41
3	MATI	ERIALS AND METHODS	45
	3.1	Sampling area	45
	3.2	Chemicals, standards and materials	48
	3.3	Sample collection and pre-treatment	48
		3.3.1 Estuarine water samples	48
		3.3.2 Sediment samples	48

	3.3.3 Biota samples	49
3.4	Extraction and clean-up	49
	3.4.1 Extraction and clean-up for estuarine water sample	49
	3.4.2 Extraction and clean-up for sediment sample	51
	3.4.3 Extraction and clean-up for biota sample	51
3.5	LC MS-MS Analysis	54
3.6	Quality assurance/Quality control	54
3.7	Statistical analysis	55

	ANIC	CONTAMINANTS (EOCs) THE
ENVI	RONME	INTAL MATRICES
4.1	Introdu	uction
4.2	Materi	ials and methods
	4.2.1	Chemicals, standards and materials
	4.2.2	Extraction and clean-up for estuarine water sample
	4.2.3	Extraction and clean-up for sediment sample
	4.2.4	Extraction and clean-up for biota sample
	4.2.5	LC MS-MS Analysis
1.3	Result	s and discussion
	4.3.1	Optimization of LC MS-MS analysis
	4.3.2	Optimization of extraction and clean-up for
		estuarine water samples
	4.3.3	Optimization of extraction and clean-up for solid
		environmental samples
	4.3.4	Optimization of extraction and clean-up for biota
		matriaga
		maurices
1.4	Conclu	usion
4.4	Conclu	ision
4.4 E <b>ME</b> I	Conclu RGING	ORGANIC CONTAMINANTS IN TROPICAL
EME	Conch RGING STAL	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY.
EME COAS	Conclu RGING STAL AYSIA:	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY, OCCURRENCE, SOURCES AND
EME COAS MAL ENVI	Conch RGING STAL AYSIA: RONME	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY, OCCURRENCE, SOURCES AND ENTAL RISK
4.4 EME COAS MAL ENVI 5.1	Conche RGING STAL AYSIA: RONME Introdu	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY, OCCURRENCE, SOURCES AND ENTAL RISK action
4.4 EME COAS MAL ENVI 5.1 5.2	Conclu RGING STAL AYSIA: RONME Introdu Materi	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY, OCCURRENCE, SOURCES AND ENTAL RISK action als and methods
EME COAS MAL ENVI 5.1 5.2	Conclu RGING STAL AYSIA: RONME Introdu Materi 5.2.1	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY, OCCURRENCE, SOURCES AND INTAL RISK action als and methods Chemicals, standards and materials
EME COAS MAL ENVI 5.1 5.2	Conclu RGING STAL AYSIA: RONME Introdu Materi 5.2.1 5.2.2	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY, OCCURRENCE, SOURCES AND INTAL RISK action als and methods Chemicals, standards and materials Sample collection and pre treatment
4.4 EME COAS MAL. 5.1 5.2	Conche RGING STAL AYSIA: RONME Introdu Materi 5.2.1 5.2.2 5.2.3	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY, OCCURRENCE, SOURCES AND ENTAL RISK action als and methods Chemicals, standards and materials Sample collection and pre treatment Sample extraction and clean-up
EME COAS MAL ENVI	Conche RGING STAL AYSIA: RONME Introdu Materi 5.2.1 5.2.2 5.2.3 5.2.4	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY, OCCURRENCE, SOURCES AND ENTAL RISK action als and methods Chemicals, standards and materials Sample collection and pre treatment Sample extraction and clean-up LC MS-MS Analysis
4.4 EME COAS MAL ENVI 5.1 5.2	Conche RGING STAL AYSIA: RONME Introdu Materi 5.2.1 5.2.2 5.2.3 5.2.4 5.2.5	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY, OCCURRENCE, SOURCES AND ENTAL RISK action als and methods Chemicals, standards and materials Sample collection and pre treatment Sample extraction and clean-up LC MS-MS Analysis Quality assurance (OA) and quality control (OC)
4.4 EME COAS MAL ENVI 5.1 5.2	Conche <b>RGING</b> <b>STAL</b> <b>AYSIA:</b> <b>RONME</b> Introdu Materi 5.2.1 5.2.2 5.2.3 5.2.4 5.2.5 5.2.6	ORGANIC CONTAMINANTS IN TROPICAL WATER OF KLANG RIVER ESTUARY, OCCURRENCE, SOURCES AND ENTAL RISK action als and methods Chemicals, standards and materials Sample collection and pre treatment Sample extraction and clean-up LC MS-MS Analysis Quality assurance (QA) and quality control (QC) Environmental risk assessment (ERA)

	5.2.5	Quality assurance (QA) and quality control (QC)
	5.2.6	Environmental risk assessment (ERA)
5.3	Results	s and discussion
	5.3.1	Physicochemical characteristics of surface estuarine water
	5.3.2	Occurrence and level of PhACs and EDCs in surface waters of Klang River estuary

	5.3.3	Correlation between target compounds and physicochemical properties of estuarine water	
	5.3.4	samples and possible pollution sources Environmental risk assessment of PhACs and EDCs	87
		in the surface estuarine waters	88
5.4	Conclus	sion	89
	21-12-1		
OCC	URRENC	E, DISTRIBUTION AND SOURCES OF	
COA	CTAL C	SEDIMENT OF ANTHDODOCENICALLY	
IMD	CTED K	I ANC DIVED ESTUADY MAI AVSIA	04
6 1	Introdu	LANG RIVER ESI UARI, MALAISIA	94
6.2	Matorio	la and mathada	94
0.2	6 2 1	Chamicala, standards and materials	90
	6.2.1	Chemicals, standards and materials	90
	6.2.2	Sample collection	90
	6.2.5	LC MS MS analysis	90
	6.2.4	$\Omega$	90
62	0.2.5 Deculta	quality assurance (QA) and quality control (QC)	90
0.5	6 2 1	Occurrence and level of EOCs in estuaring addiment.	90
	0.5.1	Occurrence and level of EOCs in estuarme sediment	06
	622	Source of EOCs pollution in addiment of Klang	90
	0.3.2	Source of EOCS ponution in sediment of Klang	100
61	Canalu	River estuary	109
0.4	Conciu	sion	111
000	UDDENC	E AND LEVEL OF EMERCING ORGANIC	
CON	TAMINA	NT IN FISH AND MOLILISC FROM KLANC	
DIVE	D ESTU	APV MALAVSIA AND ASSESSMENT ON	
HUM	IAN HEAT	TH PISKS	112
7 1	Introdu	ction	112
7.1	Materia	ls and methods	115
1.2	7 2 1	Standards, chemicals and materials	115
	7.2.1	Sampling sites sample collection and pre treatment	115
	7.2.2	Extraction and clean up	115
	7.2.3	LC MS MS Analysis	115
	7.2.4	$\Omega_{\rm relity}$ assurance $(\Omega \Lambda)$ and quality control $(\Omega C)$	115
	7.2.5	Quality assurance (QA) and quality condition (QC)	115
7.2	7.2.0 Deculta	and discussion	115
1.5	7 2 1	Optimization of analytical method for biota samples	110
	7.3.1	Optimization of analytical method for blota samples	116
	732	Occurrence and concentration of FOCs in fish	110
	1.3.2	samples	116
	722	Occurrence and concentration of FOCs in manarova	110
	1.5.5	spail	124
	731	Estimation of human health risk	124
7.4	Conchu	sion	129

8	SUM	MARY AND RECOMMENDATIONS FOR FUTURE	C
	RESE	EACRH	132
	8.1	Summary	132
	8.2	Recommendation for future research	134
REFER	ENCE	ES	135
APPENI	DICES	S	162
BIODA'	ГА ОН	F STUDENT	167
LIST O	F PUB	BLICATIONS	168

## LIST OF TABLES

Table		Page
2.1	Physical-chemical properties of targeted endocrine disrupting compounds (EDCs)	10
2.2	Physical-chemical properties of targeted organophosporous pesticides	10
2.3	Physical-chemical properties of targeted pharmaceutically active compounds (PhACs)	13
2.4	Storage and preservation techniques for emerging organic contaminants in environmental and biota matrices	16
2.5	LC-MS-MS parameters and sample treatments for emerging organic contaminants in aqueous and solid environmental samples	20
2.6	LC MS-MS parameters and sample treatments for emerging organic contaminants in biota matrices	23
2.7	Gas Chromatography Mass Spectrometry (GC-MS) parameters and sample treatments for emerging organic contaminants in aqueous and solid environmental samples	25
2.8	GC MS parameters and sample treatments for emerging organic contaminants in biota matrices	28
2.9	Important parameters for consideration during method development	30
2.10	Occurrences and levels of EOCs in environmental samples	37
2.11	Occurrences and levels of EOCs in biota samples	38
2.12	Environmental risk assessment of emerging organic pollutants in the aquatic ecosystem	43
2.13	Human health risk assessment of emerging organic pollutants from consumption of edible marine and freshwater biota	44
3.1	Coordinate and description of sampling locations	46
3.2	Analytical setup for instrumentation analysis	55
4.1	Optimization of source dependent parameters for the developed compounds	61

4.2	Method performances for determination of multiclass EOCs in the artificial seawater samples	64
4.3	The application of Soxhlet as an extraction technique for environmental organic contaminants in various types of sediment samples	68
4.4	Extraction efficiency, matrix effect, method detection limit, and linearity of the targeted EOCs in sediment sample optimized in this study	69
4.5	Extraction efficiency (% recovery), method detection limit and linearity of multiclass EOCs in sediment samples	70
4.6	Extraction efficiency, matrix effect, method detection limit and linearity of the targeted compounds optimized for biota matrices	72
5.1	Physico-chemical paramaters analysed for the surface water of Klang River estuary	80
5.2	Concentration of endocrine disrupting compounds (EDCs) and pharmaceutically active chemicals (PhACs) in surface water samples analysed from Klang River estuary	82
5.3	Correlation analysis of parameters analysed in the surface waters of Klang River estuary	90
5.4	Principal component loadings of variables analysed from surface waters of Klang River estuary	91
5.5	Risk quotient (RQ) of endocrine disrupter and pharmaceutically active compounds in surface water samples for three different test species (phytoplankton, zooplankton and fish)	92
6.1	Physico-chemical characteristic of sediment samples collected from Klang River estuary	98
6.2	Concentration of emerging organic pollutants in sediment samples collected from Klang River estuary	99
6.3	Correlation coefficient of emerging organic contaminants, TOC and sediment particle size based on Kendall's tau-b analysis	108
7.1	Emerging organic contaminants in fish species, <i>A. thalassinus</i> and <i>P. anea</i> from Klang River estuary	118
7.2	Emerging organic contaminant in mangrove snails, N. lineata from Klang River estuary	126

# LIST OF FIGURES

Figure		Page
1.1	Research framework for study on emerging organic pollution and risk assessment of Klang River estuary ecosystem	6
2.1	Chemical structure of 4-octylphenol	8
2.2	Chemical structure of bisphenol A	8
2.3	Chemical structure of 17a-ethynyl estradiol	8
2.4	Chemical structure of estrone	8
2.5	Chemical structure of 17β-estradiol	8
2.6	Chemical structure of 4-nonylphenol	8
2.7	Chemical structure of quinalphos	11
2.8	Chemical structure of chlorpyrifos	11
2.9	Chemical structure of diazinon	11
2.10	Chemical structure of diclofenac	12
2.11	Chemical structure of testosterone	12
2.12	Chemical structure of progesterone	12
2.13	Chemical structure of dexamethasone	12
2.14	Chemical structure of sulfamethoxazole	12
2.15	Chemical structure of primidone	12
2.16	Chemical structure of amoxicillin	12
2.17	Analytical strategies for determination of EOCs in environmental and biota matrices	31
2.18	Sources and pathways of emerging organic pollutants in the ecosystem	40
3.1	Map show (a) peninsular Malaysia and (b) sampling points at Klang River estuary denoted by $S1 - S12$	47

3.2	Flow process for determination of pharmaceutical compounds in the surface coastal water	50
3.3	Analytical procedure for the analysis of multiclass EOCs in the Klang estuarine sediment	52
3.4	Analytical procedure for analysis of multiclass EOCs in biota sample	53
4.1	Fragmentation pattern of estrone in Q1MS scan and product ion scan	60
4.2	Chromatographic separation for positive ionization mode compounds	62
4.3	Chromatographic separation for negative ionization mode compounds	63
4.4	Percentage of recoveries for targeted EOCs in biota matrices evaluated at two spiking concentration	73
4.5	Matrix effect of analytical method developed for biota sample	74
5.1	Concentration profile of emerging organic contaminants in surface water of Klang River estuary	84
5.2	Distribution pattern of (a) primidone (b) sulfamethoxazole (c) dexamethasone (d) testosterone (e) diclofenac (f) amoxicillin (g) progesterone (h) $17\beta$ -estradiol (i) estrone and (j) bisphenol A in surface water samples of Klang River estuary. S1-S12 indicate sampling station	85
5.3	Occurrence of emerging organic contaminants (EOCs) in the surface coastal water of Klang River estuary	86
5.4	Risk quotient of emerging organic contaminants (EOCs) in surface water of Klang River estuary calculated for phytoplankton, zooplankton and fish	93
6.1	Boxplot showing the concentration of (a) primidone (b) testosterone (c) diazinon (d) amoxicillin (e) diclofenac (f) E2 (g) E1 (h) BPA (i) EE2 (j) 4-OP and (k) progesterone in sediment of Klang River estuary	101
6.2	Occurrence of emerging organic contaminants (EOCs) in the sediment of Klang River estuary	105
6.3	Concentration profile of emerging organic contaminants in sediment of Klang River estuary	106
6.4	Distribution pattern of emerging organic pollutants in sediment of Klang River estuary	107
6.5	The bi-plot of principle component loadings of variables analysed from surface sediment of Klang River estuary after varimax rotation	110

7.1	Occurrence of emerging organic contaminants in sea catfish, A. thalassinus from Klang River estuary	121
7.2	Occurrence of emerging organic contaminants in croaker, <i>P. anea</i> from Klang River estuary	121
7.3	Distribution pattern of endocrine disrupting compounds in fish species, A. thalassinus and P. anea from Klang River estuary	122
7.4	Levels and distribution pattern of EOC in mangrove snails, <i>N. lineata</i> from Klang River estuary	128
7.5	Occurrence of emerging organic contaminants (EOCs) in mangrove snails, <i>N. lineata</i> from Klang River estuary	129
7.6	Hazard Quotient (HQ) for consumption of fish and mollusc contaminated with bisphenol A, diclofenac and progesterone	130
7.7	Health risk assessment of emerging organic pollutants from the consumption of edible biota from different part of the world	131

# LIST OF ABBREVIATIONS

ng/L	nano gram per litre
ng/g	nanogram per gram
pg/g	pictogram per gram
EE2	17α-ethynyl estradiol
E2	17β-estradiol
E1	estrone
EOCs	emerging organic contaminants
EDC	endocrine disrupting compound
OPPs	organophosphate pesticides
PhACs	pharmaceutically active chemicals
4-OP	4-octylphenol
4-NP	4-nonylphenol
BPA	bisphenol A
LC MS-MS	liquid chromatography mass spectrometry-mass
	spectrometry
Na <sub>2</sub> -EDTA	tetrasodium ethylenediamine-tetraacetate dehydrate
PTFE	polytetrafluoroethylene
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, Safe
MeOH	methanol
MeCN	acetonitrile
Al <sub>2</sub> O <sub>3</sub>	aluminium oxide
USEPA	United States Environmental Protection Agency
MRM	multiple reaction monitoring
MTBE	methyl tert butyl ether
NH4OH	ammonium hydroxide
PCA	principal component analysis
ppt	part per trillion
RQ	risk quotient
HQ	hazard quotient
MEC	measured environmental concentration
PNEC	predicted no effect concentration
OA	quality assurance
òc	quality control
USDA	United States Department of Agriculture
LC50	lethal concentration
EC50	effective concentration
EU	European Union
SPE	solid phase extraction
PPCPs	pharmaceutical and personal care products
EDI	estimated daily intake
EFSA	European Food Safety Authority
TDI	tolerable daily intake
MAE	microwave assisted extraction
UAE	ultrasonic assisted extraction
PLE	pressurised liquid extraction
LLE	liquid-liquid extraction
LUL	inquite inquite extraction

SPME	solid phase micro extraction
GPC	gel permeation chromatography
Primi	primidone
Sulfa	sulfamethoxazole
Dexa	dexamethasone
Diaz	diazinon
Tes	testosterone
Proges	progesterone
Chlor	chlorpyrifos
Quina	quinalphos
Amox	amoxicillin
Diclo	diclofenac
APPCI	atmospheric photoionization pressure chemical
	ionization
NP <sub>n</sub> EO	nonylphenol polyethoxylates
NP <sub>1</sub> EC	nonylphenol monoethoxycarboxilic acid
OP <sub>1</sub> EC	octylphenol monoethoxycarboxilic acid

#### **CHAPTER 1**

### **GENERAL INTRODUCTION**

#### 1.1 Background of study

Emerging organic contaminant (EOC) consists various classes of chemical compounds such as naturally produced compounds including natural estrogens, natural androgens and phytoestrogen, as well as a wide range of industrial chemicals including synthetic hormones, polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls, dioxins, phenolic xenoestrogens, pharmaceuticals and personal care products (PPCPs) and pesticides. These chemical contaminants have been detected in various environmental matrices at low level of concentrations, as low as part per trillion (ppt) level. Numerous studies have reported on the occurrence of EOCs in different types of environmental matrices as reported by Omar et al. (2013), when they detected concentration of dioxins between 1.910 WHO-TEQ pg/g to 3.305 WHO-TEQ pg/g in soil samples collected at selected Malaysian oil palm plantations. A study by Kuch & Ballschmiter, (2000) reported trace concentration of bisphenol A ranged from 4.8 ng/L to 10 ng/L in Sewage Treatment Work (STW) effluents and 0.5 ng/L to 14 ng/L in samples of river water. Phenolic endocrine disrupting compounds such as nonylphenol and octylphenol were detected in the ranged of 6 ng/g to 640 ng/g in sediment samples collected at Tokyo Bay as reported by Isobe et al. (2001). In the same study, Isobe et al. (2001) also reported concentrations of nonylphenol and octylphenol in the Tokyo metropolitan river water. The concentrations for both compounds in the river water were detected in the range between 0.01 ng/L to 1.08 ng/L. Emerging organic pollutants were also detected in Duoro River estuary, Portugal when Ribeiro et al. (2009) reported the presence of industrial pollutant (nonylphenol, octylphenol and bisphenol A) and phytoestrogens (daidzein, genistein and biochanin A) in the river water samples analysed. Bisphenol A was detected up to 10.7 ng/L, daidzein (888.4 ng/L), genistein (197.4 ng/L) and biochanin A (191.4 ng/L).

The pathway of these pollutants in the environment is mainly through wastewater effluent from sewage treatment plants, municipal treatment plants, hospital effluents and from livestock discharge (Sumpter and Jobling, 1995; Ying et al. 2002; Raman et al. 2004; Hutchins et al. 2007). Raman et al. (2004) evaluated estrogen content in animal waste and reported that 17 $\alpha$ -estradiol, estrone and 17 $\beta$ -estradiol were major estrogen compounds contained in the waste samples collected. Hutchins et al. (2007) analysed effluents and suspended solid samples from lagoons that were affected by animal waste discharged and identified that estrone, 17 $\alpha$ -estradiol, 17 $\beta$ -estradiol and estrone were among EOCs present in the samples analysed.

The occurrence of EOCs such as synthetic estrogenic hormones and pharmaceutical compounds in the aquatic environment have received much attention as these compounds have been detected in various aquatic compartments such as water,

sediments and biota due to their high bioactivity, ubiquitous nature, toxicity and persistence in the environment (Aris et al. 2014). These pollutants have become a major problem in aquatic ecosystems because of high resistance to degradation and their tendencies to absorb organic matter, accumulate in sediment and concentrate in biota. Emerging pollutants such as estrogenic hormones were reported in water, sediment and biota by a number of researchers. Kuch et al. (2001) detected the presence of estrogenic hormone in river waters and effluents from sewage treatment work plants. Mean concentration for estrogenic hormones in STW effluents reported in their study was 1.4 ng/L while mean concentration for river water was 0.80 ng/L. Another study by Baronti et al. (2000) also reported the presence of estrogenic hormone in activated sludge treatment plants and in the receiving river water. They evaluated six treatment plants and the range of concentration was from 0.30 ng/L to 6.8 ng/L. Ribiero et al. (2009) conducted a monitoring on the level of EE2 in Douro River estuary, Portugal and they detected the concentration of EE2 in the range from below the detection limit (<18 ng/L) to 101.9 ng/L.

(2008) summarized that EOCs compound can bioaccumulate and Mazotto et al. biomagnify in aquatic organisms. Bioaccumulation study performed with an endobenthic freshwater oligochaete lumbriculus variegatus suggested that this organism has the potency to accumulate high amount of conjugated EOCs compounds (Liebig et al. 2005). A similar suggestion was also reported by Dussault et al. (2009) when they carried out bioaccumulation study of EOCs compounds in benthic invertebrates Chrinomus tentans and Hyalella azteca. Emerging organic contaminants (EOCs) are very toxic to a large number of exposed organisms. Robinson & Hellou, (2009), reported that EOCs such as estrogenic hormones and pharmaceutical compounds can affect the endocrine system of organism at concentration levels as low as nanogram per litre. A study by Andrew et al. (2010) concluded that exposure to a certain amount of estrogenic hormones could induced vitellogenin (VTG) production in the adult Sydney rock oyster, Saccostrea glomerata. VTG induction was also observed in adult male and female carps. Cyprinus carpio when certain dose of estrogenic hormones experimentally injected into these fishes (Sole et al. 2000). VTG has been proven as a useful biomarker for determining the estrogenicity of certain chemicals in aquatic organisms (Sumpter and Jobling, 1995).

Based on previous literatures, emerging pollutants have been ubiquitously detected in various matrices from different geographical origins, indicating global contamination of these compounds in the environment. Toxicity studies carried out on different test species showed evidence of bioaccumulation and biomagnification as well as intersex changes in aquatic organisms when exposed to trace concentrations of emerging organic compounds. Thus, due to adverse effect of these compounds to the ecosystem, extensive study should be conducted to understand the behaviour and effects of these compound in the environment.

#### 1.2 Problem statement

Emerging pollutants such as endocrine disrupting compounds (EDCs), pharmaceutically active compounds and pesticides residues have generated wide attention by scientific and legislative communities in the recent decade because of their widespread presence in the environment and their ability to interfere with the hormonal systems. The ubiquitous presence of these pollutants particularly EDCs in the environment may pose a significant impact to the ecosystem and human health. Research shows that these compounds can disrupt the endocrine system of organism at concentrations as low as nanogram per litre (ng/L). Exposure to EDCs generates additional effects, such as alterations in male and female reproduction and changes in neuroendocrinology, behavior, metabolism and obesity, prostate cancer, thyroid and cardiovascular endocrinology. Endocrine disrupting compounds (EDCs) when absorbed in the body can increase and decrease normal hormone levels, mimic the body's natural hormone and alter the natural hormone production. This interruption in hormonal system may regulate metabolic activity in cells including cancer cells as well as proliferation of cancer and tumor progression. Therefore, due to various health consequences arising from the presence of EDCs, comprehensive research should be carried out for better understanding the behavior and effects of these pollution in the ecosystem as well as the exposed organisms in the environment.

Klang River has been classified as one of the polluted river in Peninsular Malaysia (Huang et al. 2015). It is situated at the heart of Greater Kuala Lumpur and Klang Valley (GKL & KV) and flowing through densely populated areas (estimated 8.0 million population as of 2018) such as Kuala Lumpur and Damansara, as well as industrial areas such as in Petaling Jaya and Shah Alam. The length of the river is approximately 120 km starting from upper catchment in Gombak district to the lower catchment in Klang district and the river ended in the estuary known as Klang River estuary. The total catchment area of Klang River covers an area of 1288 km<sup>2</sup> and most of this river basin has been developed for various purposes such as residential, commercial, industrial, utilities and squatter. Those activities along the basin have contributed to the deterioration of water quality gradually from upstream (class IIB-suitable for body contact and recreational purposes) to downstream (class III-unsuitable for touch and recreational purposes), with numerous pollution sources entering the river either from point source or non point source. The major sources of pollution in the Klang River basin have been identified to be originated from domestic waste, industrial area as well as sewage treatment plant and these pollution are expeted to end up in the estuary if no proper management of waste at the upper and middle cathment area. Based on report by Department of Irrigation and Drainage, in the Klang Valley alone, an estimated 50-60 tons of wastes end up in the river system daily. Hence, due to the socio-economic importance of Klang River estuary the the local community, a comprehensice assessment involving monitoring and risk analysis should be carried out for better protection of ecosystem as well as human population within this estuary.

#### 1.3 Objectives of study

- 1. To optimize and validate methods for determination of EOCs in aqueous and solid environmental matrices, as well as biota samples.
- 2. To determine the level, occurence distribution pattern of EOC pollutant in the environmental (water, sediment) and biota matrices collected from the Klang River estuary.
- To elucidate the potential sources of EOC contamination in the Klang River estuary ecosystem.
- 4. To analyse the environmental and human health risks associated with the presence of EOC in the Klang River estuary ecosystem.

#### 1.4 Scope of study

Environmental emerging organic pollutants have been widely reported as a potential carcinogenic threat to human population. Release of EOCs to the environmental compartment have been extensively monitored and studied. Scientific and legislative communities have given significant attention to the presence of EOCs in the environment, particularly because of their potential adverse effect on human health and aquatic ecosystems. Review of related studies on EOCs in tropical regions has divulged the significant levels of these compounds in environmental and biota matrices due to domestic, agricultural and industrial wastes discharged. However, research on the environmental risk assessment of these compounds in the Malaysian coastal ecosystem has not been extensively investigated and reported. This research attempts to identify and characterize emerging pollutants in the selected polluted ecosystem focusing on Klang River estuary by integrating analytical method development, monitoring, and risk assessment approaches. This study focuses on the distribution of emerging organic pollutant in environmental compartment such as estuarine water and sediment. Biota samples such as fish and mollusk were also analyzed to study the occurrence and level of EOCs in these matrices at the sampling areas. This is to observe the occurrence and distribution of EOCs in sediment, water and aquatic biota that can lead to better understanding of inter-relationship between the studied matrices.

#### 1.5 Significance of study

This study aim to establish a database for EOCs that can be further used for the purpose of environmental and human health risk assessment. It was noted that there was lack of database describing risk assessment for EOCs particularly for priority pollutants such as phenolic EDCs, estrogenic hormones and pharmaceutical compounds in the Malaysian coastal ecosystem. Therefore, risk assessment analysis for various EOCs particularly for compounds which have not yet been reported should be undertaken for better protection of environmental and human health population from these carcinogenic compounds. Outcome from this study will be useful for regulatory bodies in proposing better preventive measures for controlling carcinogenic pollutants entering environmental ecosystem. Outputs from this study also provide a breakthrough on method development particularly for marine environmental matrices and establishment of database, as well as evaluation of risk assessment for selected EOCs in the anthropogenically impacted Klang River estuary.

## 1.6 Research framework

The research framework for study on the emerging pollution and risk assessment of EOC in the Klang River estuary ecosystem is depicted in Figure 1.1.

## 1.7 Thesis outline

This thesis is organized into eight chapters as following:

- i) Chapter 1 provides a general introduction for this study such as background of study, problem statement, scope of study, significant of study as well as research framework.
- ii) Chapter 2 reviews of previous literature covering several aspects such as physicochemical properties of targeted emerging organic pollutants, analytical challenges for determination of EOCs in the environmental matrices, occurrence and level of EOCs in environmental and biota matrices, sources and fate, and environmental and human health risk assessment.
- Chapter 3 describes material and methods such as sampling area, chemical and material used, sample collection and treatment, extraction and clean up, LC MS-MS analysis, quality assurance and quality control as well as statistical analysis.
- iv) Chapter 4 discusses on the optimization of analytical methodologies covering optimization for LC MS-MS analysis as well as for extraction and clean-up techniques of aqueous, solid and biota matrices.
- v) Chapter 5 discusses the presence, occurrence and sources of EOCs in the surface water of the Klang River estuary, and the risk of EOCs to this ecosystem.
- vi) Chapter 6 looks into the occurrence, distribution and potential sources of EOCs in the sediment of Klang River estuary ecosystem.
- vii) Chapter 7 discusses on the occurrence and level of EOCs in the biota samples collected from Klang River estuary and human health risk associated with the presence of EOCs in the those matrices.
- viii) Chapter 8 provide a summarynof thesis and recommendation for future research.



Figure 1.1 : Research framework for study on emerging organic pollution and risk assessment of Klang River estuary ecosystem

9

### REFERENCES

- Adeel, M., Song, X., Wang, Y., Francis, D., & Yang, Y. (2016). Environmental impact of estrogens on human, animal and plant life: A critical review. *Environment International*, 99, 107–119.
- Adeogun, A. O., Onibonoje, K., Ibor, O. R., Omiwole, R. A., Chukwuka, A. V., Ugwumba, A. O., & Arukwe, A. (2016). Endocrine-disruptor molecular responses, occurrence of intersex and gonado-histopathological changes in tilapia species from a tropical freshwater dam (Awba Dam) in Ibadan, Nigeria. Aquatic Toxicology, 174, 10–21.
- Agusa, T., Kunito, T., Sudaryanto, A., Monirith, I., Kan-Atireklap, S., Iwata, H., & Tanabe, S. (2007). Exposure assessment for trace elements from consumption of marine fish in Southeast Asia. *Environmental Pollution*, 145(3), 766–777.
- Agusa, T., Kunito, T., Yasunaga, G., Iwata, H., Subramanian, A., Ismail, A., & Tanabe, S. (2005). Concentrations of trace elements in marine fish and its risk assessment in Malaysia. *Marine Pollution Bulletin*, 51(8–12), 896–911.
- Aktar, W., Sengupta, D., & Chowdhury, A. (2009). Impact of pesticides use in agriculture: Their benefits and hazards. *Interdisciplinary Toxicology*, 2(1), 1–12.
- Ali, N.E., Ho C. S., Mokhtar, K., Talmizi, N. M., Saleh, A. A. (2018). Solid waste management in Shah Alam city residential area, *Journal of Sustainability Science and Management*, 13, 211-227.
- Alexander, H. C., Dill, D. C., Smith, L. W., Guiney, P. D., & Dorn, P. (1988). Bisphenol A: acute aquatic toxicity. *Environmental Toxicology and Chemistry*, 7(1), 19-26.
- Al-Odaini, N. A., Zakaria, M. P., Yaziz, M. I., & Surif, S. (2010). Multi-residue analytical method for human pharmaceuticals and synthetic hormones in river water and sewage effluents by solid-phase extraction and liquid chromatography-tandem mass spectrometry. *Journal of Chromatography A*, 1217(44), 6791–6806.
- Al-Odaini, N. A., Zakaria, M. P., Yaziz, M. I., Surif, S., & Abdulghani, M. (2013). The occurrence of human pharmaceuticals in wastewater effluents and surface water of Langat River and its tributaries, Malaysia. *International Journal of Environmental Analytical Chemistry*, 93(3), 245-264.
- Al-Qaim, F. F., Abdullah, M. P., Othman, M. R., Latip, J., & Zakaria, Z. (2014). Multiresidue analytical methodology-based liquid chromatography-time-of-flightmass spectrometry for the analysis of pharmaceutical residues in surface water and effluents from sewage treatment plants and hospitals. *Journal of Chromatography A*, 1345, 139–153.

- Alvarez-Muñoz, D., Huerta, B., Fernandez-Tejedor, M., Rodríguez-Mozaz, S., & Barceló, D. (2015). Multi-residue method for the analysis of pharmaceuticals and some of their metabolites in bivalves. *Talanta*, 136, 174–182.
- Anastassiades, M., Lehotay, S. J., Stajnbaher, D., & Schenck, F. (2003). Fast and easy multiresidue method employing acetonitrile extraction/partitioning and dispersive solid-phase extraction for the determination of pesticide residues in produce. *Journal of AOAC International*, 86(2), 412–431.
- Andrew, M. N., Dunstan, R. H., & Macfarlane, G. R. (2010). Exposure to 17αethynylestradiol causes dose and temporally dependent changes in intersex, females and vitellogenin production in the Sydney rock oyster, *Ecotoxicology*, 19, 1440–1451.
- Amin, B., Ismail, A., Arshad, A., Yap, C.K., Kamarudin, M.S., A comparative study of heavy metal concentrations Nerita lineata from the intertidal zone between Dumai Indonesia and Johor Malaysia, J. Coastal Develop.10 (2006) 19-32.
- Asante, K.A, Takahashi, S., Itai, T., Isobe, T., Adu-kumi, S., Subramanian, A.,... & Tanabe, S. (2013). Occurrence of halogenated contaminants in inland and coastal fi sh from Ghana: Levels, dietary exposure assessment and human health implications. *Ecotoxicology and Environmental Safety*, 94, 123–130.
- Arditsoglou, A., & Voutsa, D. (2012). Occurrence and partitioning of endocrinedisrupting compounds in the marine environment of Thermaikos Gulf, Northern Aegean Sea, Greece. Marine Pollution Bulletin, 64(11), 2443–2452.
- Aris, A. Z., Shamsuddin, A. S., & Praveena, S. M. (2014). Occurrence of 17αethynylestradiol (EE2) in the environment and effect on exposed biota: a review and effect on exposed biota: a review. *Environment International*, 69, 104–119.
- Aziz, A., Agamuthu, P., & Fauziah, S. H. (2018). Removal of bisphenol A and 2, 4-Ditert-butylphenol from landfill leachate using plant-based coagulant. Waste Management & Research, 36(10), 975-984.
- Azzouz, A., & Ballesteros, E. (2016). Determination of 13 endocrine disrupting chemicals in environmental solid samples using microwave-assisted solvent extraction and continuous solid-phase extraction followed by gas chromatography mass spectrometry, *Analytical and Bioanalytical Chemistry*, 408(1), 231–241.
- Baker, D. R., & Kasprzyk-Hordern, B. (2011). Critical evaluation of methodology commonly used in sample collection, storage and preparation for the analysis of pharmaceuticals and illicit drugs in surface water and wastewater by solid phase extraction and liquid chromatography-mass spectrometry. *Journal of Chromatography A*, 1218(44), 8036–8059.

- Baronti, C., Curini, R., D'Ascenzo, G., Di Corcia, A., Gentili, A., & Samperi, R. (2000). Monitoring natural and synthetic estrogens at activated sludge sewage treatment plants and in a receiving river water. *Environmental Science and Technology*, 34(24), 5059–5066.
- Basheer, C., Lee, H. K., & Tan, K. S. (2004). Endocrine disrupting alkylphenols and bisphenol-A in coastal waters and supermarket seafood from Singapore. *Marine Pollution Bulletin*, 48(11–12), 1161–1167.
- Bashir, F. A., Shuhaimi-Othman, M., & Mazlan, A. G. (2012). Evaluation of trace metal levels in tissues of two commercial fish species in Kapar and Mersing coastal waters, peninsular Malaysia. *Journal of Environmental and Public Health*, 2012, 1-10.
- Bayen, S., Estrada, E. S., Juhel, G., Kit, L. W., & Kelly, B. C. (2016). Pharmaceutically active compounds and endocrine disrupting chemicals in water, sediments and mollusks in mangrove ecosystems from Singapore. *Marine Pollution Bulletin*, 109(2), 716–722.
- Bayen, S., Zhang, H., Desai, M. M., Ooi, S. K., & Kelly, B. C. (2013). Occurrence and distribution of pharmaceutically active and endocrine disrupting compounds in Singapore's marine environment: Influence of hydrodynamics and physicalchemical properties. *Environmental Pollution*, 182, 1–8.
- Bean, T. G., Rattner, B. A., Lazarus, R. S., Day, D. D., Burket, S. R., Brooks, B. W., & Bowerman, W. W. (2018). Pharmaceuticals in water, fish and osprey nestlings in Delaware River. *Environmental Pollution*, 232, 533–545.
- Belfroid, A., van Velzen, M., van der Horst, B., & Vethaak, D. (2002). Occurrence of bisphenol A in surface water and uptake in fish: evaluation of field measurements. *Chemosphere*, 49(1), 97-103.
- Berandah, F.E., Yap, C.K., & Ismail, A., (2010) Bioaccumulation and distribution of heavy metals (Cd, Cu, Fe, Ni, Pb and Zn) in the different tissues of Chicoreus capucinus lamarck (Mollusca: Muricidae) collected from Sungai Janggut, Kuala Langat, Malaysia. Environment Asia, 3 (1), 65-71.
- Bergman, Å., Heindel, J. J., Kasten, T., Kidd, K. A., Jobling, S., Neira, M., & Woodruff, T. J. (2013). The impact of endocrine disruption: A consensus statement on the state of the science. *Environmental Health Perspectives*, 121(4), 104–106.
- Berlioz-Barbier, A., Baudot, R., Wiest, L., Gust, M., Garric, J., Cren-Olivé, C., & Buleté, A. (2015). MicroQuEChERS – nanoliquid chromatography – nanospray – tandem mass spectrometry for the detection and quanti fi cation of trace pharmaceuticals in benthic invertebrates. *Talanta*, 132, 796–802.

- Berlioz-Barbier, A., Vauchez, A., Wiest, L., Baudot, R., Vulliet, E., & Cren-Olivé, C. (2014). Multi-residue analysis of emerging pollutants in sediment using QuEChERS-based extraction followed by LC-MS/MS analysis. *Analytical and Bioanalytical Chemistry*, 406(4), 1259–1266.
- Bhandari, R. K., Deem, S. L., Holliday, D. K., Jandegian, C. M., Kassotis, C. D., Nagel, S. C., & Rosenfeld, C. S. (2014). Effects of the environmental estrogenic contaminants bisphenol A and 17 a -ethinyl estradiol on sexual development and adult behaviors. *General and Comparative Endocrinology*, 214, 195–219.
- Biel-Maeso, M., Baena-Nogueras, R. M., Corada-Fernández, C., & Lara-Martín, P. A. (2018). Occurrence, distribution and environmental risk of pharmaceutically active compounds (PhACs) in coastal and ocean waters from the Gulf of Cadiz (SW Spain). Science of the Total Environment, 612, 649–659.
- Bowden, J. A., Colosi, D. M., Mora-montero, D. C., Garrett, T. J., & Yost, R. A. (2009). Evaluation of derivatization strategies for the comprehensive analysis of endocrine disrupting compounds using GC/MS. *Journal of Chromatographic Science*, 47, 44–51.
- Brits, M., de Vos, J., Weiss, J. M., Rohwer, E. R., & de Boer, J. (2016). Critical review of the analysis of brominated flame retardants and their environmental levels in Africa. *Chemosphere*, 164, 174–189.
- Bueno, M. J. M., Gomez, M. J., Herrera, S., Hernando, M. D., Agüera, A., & Fernández-Alba, A. R. (2012). Occurrence and persistence of organic emerging contaminants and priority pollutants in five sewage treatment plants of Spain: Two years pilot survey monitoring. *Environmental Pollution*, 164, 267–273.
- Buszka, P. M., Yeskis, D. J., Kolpin, D. W., Furlong, E. T., Zaugg, S. D., & Meyer, M. T. (2009). Waste-indicator and pharmaceutical compounds in landfill-leachate-affected ground water near Elkhart, Indiana, 2000-2002. Bulletin of Environmental Contamination and Toxicology, 82(6), 653-659.
- Cai, Q. Y., Mo, C. H., Wu, Q. T., Zeng, Q. Y., & Katsoyiannis, A. (2007). Occurrence of organic contaminants in sewage sludges from eleven wastewater treatment plants, China. *Chemosphere*, 68(9), 1751-1762.
- Can, Z. S., Firlak, M., Kerç, A., & Evcimen, S. (2014). Evaluation of different wastewater treatment techniques in three WWTPs in Istanbul for the removal of selected EDCs in liquid phase. *Environmental Monitoring and Assessment*, 186(1), 525–539.
- Carmona, E., Andreu, V., & Picó, Y. (2014). Occurrence of acidic pharmaceuticals and personal care products in Turia River Basin: From waste to drinking water. Science of the Total Environment, 484(1), 53-63.

- Casatta, N., Mascolo, G., Roscioli, C., & Viganò, L. (2016). Tracing endocrine disrupting chemicals in a coastal lagoon (Sacca di Goro, Italy): Sediment contamination and bioaccumulation in Manila clams. Science of the Total Environment, 514, 214-222.
- Cerqueira, M. B. R., Guilherme, J. R., Caldas, S. S., Martins, M. L., Zanella, R., & Primel, E. G. (2014). Evaluation of the QuEChERS method for the extraction of pharmaceuticals and personal care products from drinking-water treatment sludge with determination by UPLC-ESI-MS / MS. *Chemosphere*, 107, 74–82.
- Céspedes, R., Lacorte, S., Ginebreda, A., & Barceló, D. (2008). Occurrence and fate of alkylphenols and alkylphenol ethoxylates in sewage treatment plants and impact on receiving waters along the Ter River (Catalonia, NE Spain). *Environmental Pollution*, 153(2), 384–392.
- Chen, H., Liu, S., Xu, X. R., Liu, S. S., Zhou, G. J., Sun, K. F., ... & Ying, G. G. (2015). Antibiotics in typical marine aquaculture farms surrounding Hailing Island, South China: occurrence, bioaccumulation and human dietary exposure. *Marine pollution bulletin*, 90(1-2), 181-187.
- Cheng, W. H., & Yap, C. K. (2015). Potential human health risks from toxic metals via mangrove snail consumption and their ecological risk assessments in the habitat sediment from Peninsular Malaysia. *Chemosphere*, 135, 156–16.
- Chiou, C. T., & Kile, D. E. (2000). Contaminant sorption by soil and bed sediment; is there a difference? (No. 087-00). US Geological Survey,.
- Combalbert, S., Pype, M. L., Bernet, N., & Hernandez-Raquet, G. (2010). Enhanced methods for conditioning, storage, and extraction of liquid and solid samples of manure for determination of steroid hormones by solid-phase extraction and gas chromatography-mass spectrometry. *Analytical and Bioanalytical Chemistry*, 398(2), 973–984
- Corrales, J., Kristofco, L. A., Baylor Steele, W., Yates, B. S., Breed, C. S., Spencer Williams, E., & Brooks, B. W. (2015). Global assessment of bisphenol a in the environment: Review and analysis of its occurrence and bioaccumulation. *Dose-Response*, 13(3), 1–29.
- Dean, J. R. (2013). *Environmental Trace Analysis*. (J. R. Dean, Ed.) (first ed.). Chichester, UK: John Wiley & Sons, Ltd.
- de Castro-Català, N., Kuzmanovic, M., Roig, N., Sierra, J., Ginebreda, A., Barceló, D., ... Muñoz, I. (2016). Ecotoxicity of sediments in rivers: Invertebrate community, toxicity bioassays and the toxic unit approach as complementary assessment tools. *Science of the Total Environment*, 540, 297–306.
- DeLorenzo, M. E., & Fleming, J. (2008). Individual and mixture effects of selected pharmaceuticals and personal care products on the marine phytoplankton species Dunaliella tertiolecta. Archives of Environmental Contamination and

Toxicology, 54(2), 203-210.

- Deng, W., Li, N., Zheng, H., & Lin, H. (2016). Occurrence and risk assessment of antibiotics in river water in Hong Kong. *Ecotoxicology and Environmental* Safety, 125, 121-127.
- Dévier, M. H., Labadie, P., Togola, A., & Budzinski, H. (2010). Simple methodology coupling microwave-assisted extraction to SPE/GC/MS for the analysis of natural steroids in biological tissues: Application to the monitoring of endogenous steroids in marine mussels Mytilus sp. Analytica Chimica Acta, 657(1), 28–35.
- Diao, P., Chen, Q., Wang, R., Sun, D., Cai, Z., Wu, H., & Duan, S. (2017). Phenolic endocrine-disrupting compounds in the Pearl River Estuary: Occurrence, bioaccumulation and risk assessment. Science of the Total Environment, 584– 585, 1100–1107.
- Dobor, J., Varga, M., Yao, J., Chen, H., Palkó, G., & Záray, G. (2010). A new sample preparation method for determination of acidic drugs in sewage sludge applying microwave assisted solvent extraction followed by gas chromatography-mass spectrometry. *Microchemical Journal*, 94(1), 36–41.
- Dorne, J. L. C. M., & Fink-Gremmels, J. (2013). Human and animal health risk assessments of chemicals in the food chain: Comparative aspects and future perspectives. *Toxicology and Applied Pharmacology*, 270(3), 187–195.
- Dussault, B., Balakrishnan, V. K., Borgmann, U., Solomon, K. R., & Sibley, P. K. (2009). Bioaccumulation of the synthetic hormone 17α-ethinylestradiol in the benthic invertebrates Chironomus tentans and Hyalella azteca, *Ecotoxicolgy and Environmental Safety*, 72, 1635–1641.
- EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs: Executive summary. EFSA Journal, 13(1):3978, 23 pp. doi:10.2903/j.efsa.2015.3978.
- Escher, B. I., Baumgartner, R., Koller, M., Treyer, K., Lienert, J., & McArdell, C. S. (2011). Environmental toxicology and risk assessment of pharmaceuticals from hospital wastewater. *Water Research*, 45(1), 75–92.
- European Union (2003) Technical Guidance Document on Risk Assessment (Part II), European Chemicals Bureau.
- European Commission, Commission Decision (EC) No 657/2002 of 12 August 2002 of implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results, Official Journal of the European Union L221, 2002, pp. 8–36.

- European Commission, 2006. Commission Regulation (EC) No 1881/2006 of 19 December 2006 of setting maximum levels for certain contaminants in foodstuffs. Official Journal of the European Union L364 (2006) 29-30.
- European Medicines Agency (EMA), 2003. Diclofenac: Summary report-committee for veterinary medicinal products, EMEA/MRL/885/03-FINAL, accessed from http://www.ema.europa.eu.
- Fang, T. Y., Praveena, S. M., Aris, A. Z., Ismail, S. N. S., & Rasdi, I. (2019). Quantification of selected steroid hormones (17β-Estradiol and 17α-Ethynylestradiol) in wastewater treatment plants in Klang Valley (Malaysia). *Chemosphere*, 215, 153-162.
- Ferrara, F., Fabietti, F., Delise, M., & Funari, E. (2005). Alkylphenols and alkylphenol ethoxylates contamination of crustaceans and fishes from the Adriatic Sea (Italy). *Chemosphere*, 59(8), 1145–1150.
- Ferreira, A. M. C., Möder, M., & Laespada, M. F. (2011). Stir bar sorptive extraction of parabens, triclosan and methyl triclosan from soil, sediment and sludge with in situ derivatization and determination by gas chromatography-mass spectrometry. *Journal of Chromatography A*, 1218(25), 3837-3844.
- Forget-Leray, J., Landriau, I., Minier, C., & Leboulenger, F. (2005). Impact of endocrine toxicants on survival, development, and reproduction of the estuarine copepod Eurytemora affinis (Poppe). *Ecotoxicology and Environmental Safety*, 60(3), 288-294.
- Fowler, P. A., Bellingham, M., Sinclair, K. D., Evans, N. P., Pocar, P., Fischer, B., ... O'Shaughnessy, P. J. (2012). Impact of endocrine-disrupting compounds (EDCs) on female reproductive health. *Molecular and Cellular Endocrinology*, 355(2), 231–239.
- García-Galán, M. J., Díaz-Cruz, M. S., & Barceló, D. (2011). Occurrence of sulfonamide residues along the Ebro river basin. Removal in wastewater treatment plants and environmental impact assessment. *Environment International*, 37(2), 462–473.
- Gatidou, G., Thomaidis, N. S., Stasinakis, A. S., & Lekkas, T. D. (2007). Simultaneous determination of the endocrine disrupting compounds nonylphenol, nonylphenol ethoxylates, triclosan and bisphenol A in wastewater and sewage sludge by gas chromatography mass spectrometry, *Journal of Chromatography A*, 1138, 32–41.
- Gatidou, G., Vassalou, E., & Thomaidis, N. S. (2010). Bioconcentration of selected endocrine disrupting compounds in the Mediterranean mussel, Mytilus galloprovincialis. *Marine Pollution Bulletin*, 60(11), 2111–2116.
- Gaw, S., Thomas, K. V., & Hutchinson, T. H. (2014). Sources, impacts and trends of pharmaceuticals in the marine and coastal environment. *Phil. Trans. R. Soc. B*, 369(1656), 20130572.

- Gheorghe, A., van Nuijs, A., Pecceu, B., Bervoets, L., Jorens, P. G., Blust, R., & Covaci, A. (2008). Analysis of cocaine and its principal metabolites in waste and surface water using solid-phase extraction and liquid chromatography-ion trap tandem mass spectrometry. *Analytical and Bioanalytical Chemistry*, 391(4), 1309–1319.
- Gineys, N., Giroud, B., & Vulliet, E. (2010). Analytical method for the determination of trace levels of steroid hormones and corticosteroids in soil, based on PLE/SPE/LC-MS/MS. Analytical and Bioanalytical Chemistry, 397(6), 2295– 2302.
- Gomes, R. L., Avcioglu, E., Scrimshaw, M. D., & Lester, J. N. (2004). Steroid-estrogen determination in sediment and sewage sludge: A critique of sample preparation and chromatographic/mass spectrometry considerations, incorporating a case study in method development. *TrAC - Trends in Analytical Chemistry*, 23(10– 11), 737–744.
- Gong, J., Ran, Y., Chen, D. Y., & Yang, Y. (2011). Occurrence of endocrine-disrupting chemicals in riverine sediments from the Pearl River Delta, China. *Marine Pollution Bulletin*, 63(5-12), 556-563.
- Gong, J., Ran, Y., Chen, D., Yang, Y., & Ma, X. (2009). Occurrence and environmental risk of endocrine-disrupting chemicals in surface waters of the Pearl River, South China. *Environmental Monitoring and Assessment*, 156(1-4), 199-210.
- Gong, J., Ran, Y., Chen, D., Yang, Y., & Zeng, E. Y. (2012). Association of endocrinedisrupting chemicals with total organic carbon in riverine water and suspended particulate matter from the Pearl River, China. *Environmental Toxicology and Chemistry*, 31(11), 2456–2464.
- González-Mariño, I., Quintana, J. B., Rodríguez, I., & Cela, R. (2010). Determination of drugs of abuse in water by solid-phase extraction, derivatisation and gas chromatography-ion trap-tandem mass spectrometry. *Journal of Chromatography A*, 1217(11), 1748–1760.
- Gorga, M., Insa, S., Petrovic, M., & Barceló, D. (2014). Analysis of endocrine disrupters and related compounds in sediments and sewage sludge using on-line turbulent flow chromatography – liquid chromatography – tandem mass. *Journal of Chromatography A*, 1352, 29–37.
- Granados-Galván, I. A., Rodríguez-Meza, D. G., Luna-González, A., & González-Ocampo, H. A. (2015). Human health risk assessment of pesticide residues in snappers (Lutjanus) fish from the Navachiste Lagoon complex, Mexico. *Marine Pollution Bulletin*, 97(1–2), 178–187.
- Gros, M., Petrović, M., Ginebreda, A., & Barceló, D. (2010). Removal of pharmaceuticals during wastewater treatment and environmental risk assessment using hazard indexes. *Environment International*, 36(1), 15–26.

- Gu, Y., Yu, J., Hu, X., & Yin, D. (2016). Characteristics of the alkylphenol and bisphenol A distributions in marine organisms and implications for human health: A case study of the East China Sea. *The Science of the Total Environment*, 539(1239), 460–469.
- Guitart, C., & Readman, J. W. (2010). Critical evaluation of the determination of pharmaceuticals, personal care products, phenolic endocrine disrupters and faecal steroids by GC/MS and PTV-GC/MS in environmental waters. Analytica Chimica Acta, 658, 32–40.
- Guo, F., Liu, Q., Qu, G., Song, S., Sun, J., Shi, J., & Jiang, G. (2013). Simultaneous determination of five estrogens and four androgens in water samples by online solid-phase extraction coupled with high-performance liquid chromatographytandem mass spectrometry. *Journal of Chromatography A*, 1281, 9–18.
- Hajeb, P., Jinap, S., Ismail, A., Fatimah, A. B., Jamilah, B., & Abdul Rahim, M. (2009). Assessment of mercury level in commonly consumed marine fishes in Malaysia. Food Control, 20(1), 79–84.
- Haris, H., & Aris, A. Z. (2015). Distribution of metals and quality of intertidal surface sediment near commercial ports and estuaries of urbanized rivers in Port Klang, Malaysia. *Environmental Earth Sciences*, 73(11), 7205–7218.
- He, X., Deng, M., Wang, Q., Yang, Y., Yang, Y., & Nie, X. (2016). Residues and health risk assessment of quinolones and sulfonamides in cultured fish from Pearl River Delta, China. Aquaculture, 458, 38-46.
- Heberer, T. (2002). Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data. *Toxicology Letters*, 131, 5–17.
- Heberer, T., Reddersen, K., Mechlinski, A. (2002). From municipal sewage to drinking water: fate and removal of pharmaceutical residues in the aquatic environment in urban areas. *Water Science & Technology*, 46, 81–88.
- Hecker, M., & Hollert, H. (2011). Endocrine disruptor screening: Regulatory perspectives and needs. *Environmental Sciences Europe*, 23(1), 1–14.
- Hernando, M. D., Mezcua, M., Fernández-Alba, A. R., & Barceló, D. (2006). Environmental risk assessment of pharmaceutical residues in wastewater effluents, surface waters and sediments. *Talanta*, 69, 334–342.
- Hoppe-Jones, C., Oldham, G., & Drewes, J. E. (2010). Attenuation of total organic carbon and unregulated trace organic chemicals in U.S. riverbank filtration systems. *Water Research*, 44(15), 4643–4659.
- Hu, R., Zhang, L., & Yang, Z. (2008). Picogram determination of estrogens in water using large volume injection gas chromatography-mass spectrometry. *Analytical* and Bioanalytical Chemistry, 390(1), 349–359.

- Huang, Y. F., Ang, S. Y., Lee, K. M., & Lee, T. S. (2015). Quality of water resources in Malaysia. In *Research and Practices in Water Quality*. InTech.
- Huerta, B., Rodríguez-Mozaz, S., & Barceló, D. (2012). Pharmaceuticals in biota in the aquatic environment: analytical methods and environmental implications. Analytical and Bioanalytical chemistry, 404(9), 2611-2624.
- Huerta, B., Jakimska, A., Gros, M., Rodriguez-Mozaz, S., & Barcelo, D. (2013). Analysis of multi-class pharmaceuticals in fish tissues by ultra-highperformance liquid chromatography tandem mass spectrometry. *Journal of Chromatography A*, 1288, 63–72.
- Hutchins, S. R., White, M. V., Hudson, F. M., & Fine, D. D. (2007). Analysis of lagoon samples from different concentrated animal feeding operations for estrogens and estrogen conjugates. *Environmental Science and Technology*, 41(3), 738–744.
- Islas-Flores, H., Gómez-Oliván, L.M., Galar-Martínez, M., Colín-Cruz, A., Neri-Cruz, N., & García-Medina, S. (2013). Diclofenac-induced oxidative stress in brain, liver, gill and blood of common carp (Cyprinus carpio), *Ecotoxicology and Environmental Safety*, 92, 32–38.
- Ismail, N.A.H., Wee, S. Y., & Aris, A. Z. (2018). Bisphenol A and alkylphenols concentrations in selected mariculture fish species from Pulau Kukup, Johor, Malaysia, *Marine Pollution Bulletin*, 127, 536–540.
- Isobe, T., Nishiyama, H., Nakashima, A., & Takada, H. (2001). Distribution and behavior of nonylphenol, octylphenol, and nonylphenol monoethoxylate in Tokyo metropolitan area: Their association with aquatic particles and sedimentary distributions. *Environmental Science and Technology*, 35(6), 1041– 1049.
- Isobe, T., Serizawa, S., Horiguchi, T., Shibata, Y., Managaki, S., Takada, H., ... & Shiraishi, H. (2006). Horizontal distribution of steroid estrogens in surface sediments in Tokyo Bay. *Environmental Pollution*, 144(2), 632-638.
- Jakimska, A., Huerta, B., Bargańska, Ż., Kot-Wasik, A., Rodríguez-Mozaz, S., & Barceló, D. (2013). Development of a liquid chromatography-tandem mass spectrometry procedure for determination of endocrine disrupting compounds in fish from Mediterranean rivers. *Journal of Chromatography A*, 1306, 44-58.
- JECFA (2000). Evaluation of Certain Veterinary Drug Residues in Food. Fifty-Second Report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series 893.
- Jiang, J. J., Lee, C. L., & Fang, M. D. (2014). Emerging organic contaminants in coastal waters: Anthropogenic impact, environmental release and ecological risk. *Marine Pollution Bulletin*, 85(2), 391-399.

- Jiang, L., Hu, X.L., Yin, D.Q., Zhang, H.C., Yu, Z.Y. (2011). Occurrence, distribution and seasonal variation of antibiotics in the Huangpu River, Shanghai, China. *Chemosphere*, 82, 822-828.
- Jobling, S., Nolan, M., Tyler, C. R., Brighty, G., & Sumpter, J. P. (1998). Widespread sexual disruption in wild fish. *Environmental Science and Technology*, 32(17), 2498–2506.
- Jones, O. A. H., Voulvoulis, N., & Lester, J. N. (2002). Aquatic environmental assessment of the top 25 English prescription pharmaceuticals. *Water Research*, 36(20), 5013–5022.
- Jonkers, N., Sousa, A., Galante-Oliveira, S., Barroso, C. M., Kohler, H. P. E., & Giger, W. (2010). Occurrence and sources of selected phenolic endocrine disruptors in Ria de Aveiro, Portugal. *Environmental Science and Pollution Research*, 17(4), 834–843.
- Kabir, E. R., Rahman, M. S., & Rahman, I. (2015). A review on endocrine disruptors and their possible impacts on human health. *Environmental Toxicology and Pharmacology*, 40(1), 241–258.
- Kaklamanos, G., Theodoridis, G., & Dabalis, T. (2009). Determination of anabolic steroids in muscle tissue by liquid chromatography-tandem mass spectrometry. *Journal of Chromatography A*, 1216(46), 8072–8079.
- Kasprzyk-Hordern, B., Dinsdale, R. M., & Guwy, A. J. (2008). The effect of signal suppression and mobile phase composition on the simultaneous analysis of multiple classes of acidic/neutral pharmaceuticals and personal care products in surface water by solid-phase extraction and ultra performance liquid chromatogra. *Talanta*, 74(5), 1299–1312.
- Ke, X., Wang, C., Zhang, H., Zhang, Y., & Gui, S. (2015). Characterization of estrogenic receptor agonists and evaluation of estrogenic activity in the sediments of Liaohe River protected areas. *Marine Pollution Bulletin*, 100(1), 176–181.
- Keshavarzifard, M., Zakaria, M. P., & Sharifi, R. (2017). Ecotoxicological and Health Risk Assessment of Polycyclic Aromatic Hydrocarbons (PAHs) in Short-Neck Clam (Paphia undulata) and Contaminated Sediments in Malacca Strait, Malaysia. Archives of Environmental Contamination and Toxicology, 73(3), 474–487.
- Keshavarzifard, M., Zakaria, M. P., Hwai, T. S., Mustafa, S., Vaezzadeh, V., Magam, S. M., ... & Abootalebi-Jahromi, F. (2014). Baseline distributions and sources of polycyclic aromatic hydrocarbons (PAHs) in the surface sediments from the Prai and Malacca Rivers, Peninsular Malaysia. *Marine Pollution Bulletin*, 88(1-2), 366-372.

- Kim, S. D., Cho, J., Kim, I. S., Vanderford, B. J., & Snyder, S. A. (2007). Occurrence and removal of pharmaceuticals and endocrine disruptors in South Korean surface, drinking, and waste waters. *Water Research*, 41(5), 1013–1021.
- Klečka, G.M., Staples, C.A., Clark, K.E., van der Hoeven, N., Thomas, D.E., Hentges S.G., (2009). Exposure analysis of bisphenol A in surface water systems in North America and Europe. Environmental Science & Technology, 43 6145-6150.
- Klosterhaus, S. L., Grace, R., Hamilton, M. C., & Yee, D. (2013). Method validation and reconnaissance of pharmaceuticals, personal care products, and alkylphenols in surface waters, sediments, and mussels in an urban estuary. *Environment International*, 54, 92–99.
- Kolpin, D. W., Furlong, E. T., Meyer, M. T., Thurman, E. M., Zaugg, S. D., Barber, L. B., & Buxton, H. T. (2002). Pharmaceuticals, hormones, and other organic wastewater contaminants in US streams, 1999–2000: A national reconnaissance. *Environmental Science and Technology*, 36(6), 1202-1211.
- Kuch, H. M., & Ballschmiter, K. (2001). Determination of endocrine-disrupting phenolic compounds and estrogens in surface and drinking water by HRGC-(NCI)-MS in the picogram per liter range. *Environmental Science and Technology*, 35(15), 3201-3206.
- Kuch, H. M., & Ballschmiter, K. (2000). Determination of endogenous and exogenous estrogens in effluents from sewage treatment plants at the ng/L-level. Fresenius' Journal of Analytical Chemistry, 366(4), 392-395.
- Kumar, V., Nakada, N., Yasojima, M., Yamashita, N., Johnson, A. C., & Tanaka, H. (2009). Rapid determination of free and conjugated estrogen in different water matrices by liquid chromatography-tandem mass spectrometry. *Chemosphere*, 77(10), 1440–1446.
- Kuster, M., Azevedo, D. A., López de Alda, M. J., Aquino Neto, F. R., & Barceló, D. (2009). Analysis of phytoestrogens, progestogens and estrogens in environmental waters from Rio de Janeiro (Brazil). Environment International, 35(7), 997-1003.
- Labadie, P., & Hill, E. M. (2007). Analysis of estrogens in river sediments by liquid chromatography-electrospray ionisation mass spectrometry. Comparison of tandem mass spectrometry and time-of-flight mass spectrometry. *Journal of Chromatography A*, 1141(2), 174–181.
- Langford, K. H., & Thomas, K. V. (2009). Determination of pharmaceutical compounds in hospital effluents and their contribution to wastewater treatment works. *Environment International*, 35(5), 766–770.
- Lara-Martin, P. A., Gómez-Parra, A., & Gonzalez-Mazo, E. (2006). Simultaneous extraction and determination of anionic surfactants in waters and sediments. *Journal of Chromatography A*, 1114(2), 205-210.

- Latorre, A., Lacorte, S., & Barceló, D. (2003). Presence of nonylphenol, octyphenol and bisphenol a in two aquifers close to agricultural, industrial and urban areas. *Chromatographia*, 57(1-2), 111-116.
- Lee, Y. J., Lee, S. E., Lee, D. S., & Kim, Y. H. (2008). Risk assessment of human antibiotics in Korean aquatic environment. *Environmental Toxicology and Pharmacology*, 26(2), 216–221.
- Lehotay, S. J., Son, K. A., Kwon, H., Koesukwiwat, U., Fu, W., Mastovska, K., ... Leepipatpiboon, N. (2010). Comparison of QuEChERS sample preparation methods for the analysis of pesticide residues in fruits and vegetables. *Journal* of Chromatography A, 1217(16), 2548–2560.
- Leong, K. H., Benjamin Tan, L. L., & Mustafa, A. M. (2007). Contamination levels of selected organochlorine and organophosphate pesticides in the Selangor River, Malaysia between 2002 and 2003. *Chemosphere*, 66(6), 1153–1159.
- Leong, Y. H., Gan, C. Y., & Majid, M. I. A. (2014). Dioxin-like polychlorinated biphenyls, polychlorinated dibenzop-dioxins, and polychlorinated dibenzofurans in seafood samples from Malaysia: Estimated human intake and associated risks. Archives of Environmental Contamination and Toxicology, 67(1), 21–28.
- Li, Z., Xiang, X., Li, M., Ma, Y., Wang, J., & Liu, X. (2015). Occurrence and risk assessment of pharmaceuticals and personal care products and endocrine disrupting chemicals in reclaimed water and receiving groundwater in China. *Ecotoxicology and Environmental Safety*, 119, 74–80.
- Lin, B.-L., Tokai, A., & Nakanishi, J., (2005). Approaches for Establishing Predicted-No-Effect Concentrations for Population-Level Ecological Risk Assessment in the Context of Chemical Substances Management. *Environmental Science and Technology*, 39, 4833-4840.
- Liebig, M., Egeler, P., Oehlmann, J., & Knacker, T. (2005). Bioaccumulation of 14C-17α-ethinylestradiol by the aquatic oligochaete Lumbriculus variegatus in spiked artificial sediment. *Chemosphere*, 59(2), 271-280.
- Liu, D., Wu, S., Xu, H., Zhang, Q., Zhang, S., Shi, L., ... & Cheng, J. (2017). Distribution and bioaccumulation of endocrine disrupting chemicals in water, sediment and fishes in a shallow Chinese freshwater lake: Implications for ecological and human health risks. *Ecotoxicology and Environmental Safety*, 140, 222-229.
- Liu J., Wang, R., Huang, B., Lin, C., Wang, Y., & Pan, X. (2011). Distribution and bioaccumulation of steroidal and phenolic endocrine disrupting chemicals in wild fish species from Dianchi Lake, China. *Environmental Pollution*, 159, 2815-2822.

- Liu, R., Zhou, J. L., & Wilding, A. (2004). Microwave-assisted extraction followed by gas chromatography-mass spectrometry for the determination of endocrine disrupting chemicals in river sediments. *Journal of Chromatography A*, 1038(1-2), 19-26.
- Llorca, M., Farré, M., Eljarrat, E., Díaz-Cruz, S., Rodríguez-Mozaz, S., Wunderlin, D., & Barcelo, D. (2017). Review of emerging contaminants in aquatic biota from Latin America: 2002–2016. Environmental Toxicology and Chemistry, 36(7), 1716–1727.
- Looi, L. J., Aris, A. Z., Wan Johari, W. L., Md. Yusoff, F., & Hashim, Z. (2013). Baseline metals pollution profile of tropical estuaries and coastal waters of the Straits of Malacca. *Marine Pollution Bulletin*, 74(1), 471–476.
- Loos, R., Hanke, G., Umlauf, G., & Eisenreich, S. J. (2007). LC-MS-MS analysis and occurrence of octyl- and nonylphenol, their ethoxylates and their carboxylates in Belgian and Italian textile industry, waste water treatment plant effluents and surface waters. *Chemosphere*, 66(4), 690–699.
- Loutfy, N., Fuerhacker, M., Tundo, P., Raccanelli, S., & Ahmed, M. T. (2007). Monitoring of polychlorinated dibenzo-p-dioxins and dibenzofurans, dioxin-like PCBs and polycyclic aromatic hydrocarbons in food and feed samples from Ismailia city, Egypt. *Chemosphere*, 66(10), 1962–1970.
- Magi, E., Di Carro, M., & Liscio, C. (2010). Passive sampling and stir bar sorptive extraction for the determination of endocrine-disrupting compounds in water by GC-MS. Analytical and Bioanalytical Chemistry, 397(3), 1335–1345.
- Mailler, R., Gasperi, J., Chebbo, G., & Rocher, V. (2014). Priority and emerging pollutants in sewage sludge and fate during sludge treatment. Waste Management, 34(7), 1217–1226.
- Managaki, S., Murata, A., Takada, H., Tuyen, B.C., & Chiem, N.H. (2007). Distribution of macrolides, sulfonamides, and trimethoprim in tropical waters: ubiquitous occurrence of veterinary antibiotics in the Mekong Delta. *Environmental Science* & Technology, 41, 8004-8010.
- Manickum, T., & John, W. (2014). Occurrence, fate and environmental risk assessment of endocrine disrupting compounds at the wastewater treatment works in Pietermaritzburg (South Africa). Science of the Total Environment, 468–469, 584–597.
- Manning, T., Roach, A., Edge, K., & Ferrell, D. (2017). Levels of PCDD/Fs and dioxinlike PCBs in seafood from Sydney Harbour, Australia. *Environmental Pollution*, 224, 590–596.
- Matéjićek, D. (2011). On-line two-dimensional liquid chromatography-tandem mass spectrometric determination of estrogens in sediments. *Journal of Chromatography A*, 1218(16), 2292–2300.

- Matamoros, V., Rodríguez, Y., & Albaigés, J. (2016). A comparative assessment of intensive and extensive wastewater treatment technologies for removing emerging contaminants in small communities. *Water Research*, 88, 777–785.
- Matuszewski, B.K., Constanzer, M.L., & Chavez-Eng, C.M. (2003). Strategies for the assessment of matrix effect in quantitative bioanalytical methods based on HPLC-MS/MS. *Analytical Chemistry*, 75, 3019-3030.
- Mazotto, V., Gagne, F., Marin, M. G., Ricciardi, F., & Blaise, C., (2008). Vitellogenin as a biomarker of exposure to estrogenic compounds in aquatic invertebrates: A review. *Environment International*, 34, 531-545.
- McClellan, K., & Halden, R. U. (2010). Pharmaceuticals and personal care products in archived U.S. biosolids from the 2001 EPA national sewage sludge survey. *Water Research*, 44(2), 658–668.
- Minguez, L., Pedelucq, J., Farcy, E., Ballandonne, C., Budzinski, H., & Halm-Lemeille, M. P. (2016). Toxicities of 48 pharmaceuticals and their freshwater and marine environmental assessment in northwestern France. *Environmental Science and Pollution Research*, 23(6), 4992-5001.
- Minh, T. B., Leung, H. W., Loi, I. H., Chan, W. H., So, M. K., Mao, J. Q., ... Richardson, B. J. (2009). Antibiotics in the Hong Kong metropolitan area: Ubiquitous distribution and fate in Victoria Harbour. *Marine Pollution Bulletin*, 58(7), 1052–1062.
- Mita, L., Bianco, M., Viggiano, E., Zollo, F., Bencivenga, U., Sica, V., ... Mita, D. G. (2011). Bisphenol A content in fish caught in two different sites of the Tyrrhenian Sea (Italy). *Chemosphere*, 82(3), 405–410.
- Mohamed, S., Nagaraj, G., Chua, F. H. C., & Wang, Y. G. (2000). The use of chemicals in aquaculture in Malaysia and Singapore. In: J.R. Arthur, C.R. Lavilla-Pitogo, & R.P. Subasinghe (Eds.) Use of Chemicals in Aquaculture in Asia : Proceedings of the Meeting on the Use of Chemicals in Aquaculture in Asia 20-22 May 1996, Tigbauan, Iloilo, Philippines (pp. 127- 140). Tigbauan, Iloilo, Philippines: Aquaculture Department, Southeast Asian Fisheries Development Center.
- Mohamad, A., Azlan, A., Razman, M.R., Ramli, N.A., & Latiff, A.A., (2013). Polychlorinated biphenyls (PCBs) concentration in demersal fish and shellfish from West Coast of Peninsular Malaysia. Journal of Food Agriculture and Environment, 11, 1094-1098.
- Mok, W. J., Senoo, S., Itoh, T., Tsukamasa, Y., Kawasaki, K. I., & Ando, M. (2012). Assessment of concentrations of toxic elements in aquaculture food products in Malaysia. *Food Chemistry*, 133(4), 1326–1332.
- Montuori, P., Aurino, S., Nardone, A., Cirillo, T., & Triassi, M. (2015). Spatial distribution and partitioning of organophosphates pesticide in water and sediment from Sarno River and Estuary, Southern Italy. *Environmental Science*

and Pollution Research, 22(11), 8629-8642.

- Moon, H. B., Kim, H. S., Choi, M., Yu, J., & Choi, H. G. (2009). Human health risk of polychlorinated biphenyls and organochlorine pesticides resulting from seafood consumption in South Korea, 2005–2007. Food and Chemical Toxicology, 47(8), 1819-1825.
- Moon, H., Yoon, S., Jung, R., & Choi, M. (2008). Wastewater treatment plants (WWTPs) as a source of sediment contamination by toxic organic pollutants and fecal sterols in a semi-enclosed bay in Korea, *Chemosphere*, 73, 880–889.
- Moreno-González, R., Rodríguez-mozaz, S., Huerta, B., Barceló, D., & León, V. M. (2016). Do pharmaceuticals bioaccumulate in marine molluscs and fish from a coastal lagoon ? *Environmental Research*, 146, 282–298.
- Mortazavi, S., Bakhtiari, A. R., Sari, A. E., Bahramifar, N., & Rahbarizadeh, F. (2013). Occurrence of endocrine disruption chemicals (Bisphenol A, 4-nonylphenol, and octylphenol) in muscle and liver of, Cyprinus carpino common, from Anzali Wetland, Iran. Bulletin of Environmental Contamination and Toxicology, 90(5), 578–584.
- Muñoz, I., Martínez Bueno, M. J., Agüera, A., & Fernández-Alba, A. R. (2010). Environmental and human health risk assessment of organic micro-pollutants occurring in a Spanish marine fish farm. *Environmental Pollution*, 158(5), 1809– 1816
- Naji A., & Ismail A. (2012). Sediment quality assessment of Klang Estuary, Malaysia. Aquatic Ecosystem Health and Management, 15, 287–293
- Nakada, N., Tanishima, T., Shinohara, H., Kiri, K., & Takada, H. (2006). Pharmaceutical chemicals and endocrine disrupters in municipal wastewater in Tokyo and their removal during activated sludge treatment. *Water Research*, 40(17), 3297–3303
- Nasir, N.N.M., Azlan, A., Razman, M.R., Ramli, N.A., & Latiff, A.A. (2011) Dioxins and furans in demersal fish and shellfish from regions in west coast peninsular Malaysia. *Journal of Food Agriculture and Environment*, 9, 72–78
- Nasrabadi, T., Bidhendi, G. N., Karbassi, A., Grathwohl, P., & Mehrdadi, N. (2011). Impact of major organophosphate pesticides used in agriculture to surface water and sediment quality (Southern Caspian Sea basin, Haraz River). Environmental Earth Sciences, 63(4), 873–883
- Nassef, M., Matsumoto, S., Seki, M., Kang, I. J., Moroishi, J., Shimasaki, Y., & Oshima, Y. (2009). Pharmaceuticals and personal care products toxicity to Japanese medaka fish (Oryzias latipes). Journal of the Faculty of Agriculture, Kyushu University, 54(2), 407-411.

- Nie, M., Yan, C., Dong, W., Liu, M., Zhou, J., & Yang, Y. (2015). Occurrence, distribution and risk assessment of estrogens in surface water, suspended particulate matter, and sediments of the Yangtze Estuary. *Chemosphere*, 127, 109–116
- Nie, Y., Qiang, Z., Zhang, H., & Adams, C. (2009). Determination of endocrinedisrupting chemicals in the liquid and solid phases of activated sludge by solid phase extraction and gas chromatography-mass spectrometry. *Journal of Chromatography A*, 1216(42), 7071–7080
- Niemuth, N. J., & Klaper, R. D. (2015). Emerging wastewater contaminant metformin causes intersex and reduced fecundity in fish. *Chemosphere*, 135, 38–45
- Nieto, A., Borrull, F., Pocurull, E., & Marcé, R. M. (2008). Determination of natural and synthetic estrogens and their conjugates in sewage sludge by pressurized liquid extraction and liquid chromatography-tandem mass spectrometry. *Journal of Chromatography A*, 1213(2), 224–230
- Núñez, M., Borrull, F., Fontanals, N., & Pocurull, E. (2015). Determination of pharmaceuticals in bivalves using QuEChERS extraction and liquid chromatography-tandem mass spectrometry. *Analytical and bioanalytical chemistry*, 407(13), 3841-3849.
- Nurulnadia, M. Y., Koyama, J., Uno, S., Kito, A., Kokushi, E., Bacolod, E. T., & Chuman, Y. (2014). Accumulation of endocrine disrupting chemicals (EDCs) in the polychaete Paraprionospio sp. from the Yodo River mouth, Osaka Bay, Japan. *Environmental Monitoring and Assessment*, 186(3), 1453–1463
- Oliveira, T. S., Murphy, M., Mendola, N., Wong, V., Carlson, D., & Waring, L. (2015). Characterization of Pharmaceuticals and Personal Care products in hospital effluent and waste water influent/effluent by direct-injection LC-MS-MS. Science of the Total Environment, 518-519, 459-478
- Omar, T. F. T., Ahmad, A., Aris, A. Z., & Yusoff, F. M. (2016). Endocrine disrupting compounds (EDCs) in environmental matrices: Review of analytical strategies for pharmaceuticals, estrogenic hormones, and alkylphenol compounds. *TrAC* -*Trends in Analytical Chemistry*, 85, 241–259.
- Omar, T. F. T., Kuntom, A., & Latiff, A. A. (2013). Dioxin/furan level in the Malaysian oil palm environment. *Sains Malaysiana*, 42(5), 571–578
- Omar, T.F.T., Aris, A.Z., Yusoff, F.M., & Mustafa, S. (2017). An improved SPE-LC-MS/MS method for multiclass endocrine disrupting compound determination in tropical estuarine sediments, *Talanta*, 173, 51–59.
- Omar, T.F.T., Kuntom, A., Latiff, A.A. (2014). Assessment of dioxins and dioxin-like polychlorinated biphenyls in the palm oil supply chains. *Quality Assurance and Safety of Crops and Foods, 6,* 369-376.

- Ort, C., Lawrence, M. G., Rieckermann, J., & Joss, A. (2010). Sampling for pharmaceuticals and personal care products (PPCPs) and illicit drugs in wastewater systems: Are your conclusions valid? A critical review. *Environmental Science and Technology*, 44(16), 6024–6035.
- Pan, H., Geng, J., Qin, Y., Tou, F., Zhou, J., Liu, M., & Yang, Y. (2016). PCBs and OCPs in fish along coastal fisheries in China: Distribution and health risk assessment. *Marine Pollution Bulletin*, 111(1-2), 483-487.
- Pemberthy, D., Quintero, A., Martrat, M. G., Parera, J., Ábalos, M., Abad, E., & Villa, A. L. (2016). Polychlorinated dibenzo-p-dioxins, dibenzofurans and dioxin-like PCBs in commercialized food products from Colombia. *Science of the Total Environment*, 568, 1185–1191.
- PEMSEA and Port Klang ICM National Demonstration Project. 2005. Port Klang Initial Risk Assessment. PEMSEA Technical Report No.13, 96p. Global Environment Facility/United Nation Development Programme/International Maritime Organization Regional Programme on Building Partnership in Environmental Management for the Seas of East Asia (PEMSEA), Quezon City, Philippines, and Port Klang Integrated Coastal Management National Demonstration Project, Selangor Water Management Authorities (LUAS), Shah Alam. Selangor, Malaysia.
- Peng, X., Wang, Z., Yang, C., Chen, F., & Mai, B. (2006). Simultaneous determination of endocrine-disrupting phenols and steroid estrogens in sediment by gas chromatography-mass spectrometry. *Journal of Chromatography A*, 1116(1-2), 51-56.
- Pereira, A. M. P. T., Silva, L. J. G., Meisel, L. M., Lino, C. M., & Pena, A. (2015). Environmental impact of pharmaceuticals from Portuguese wastewaters: Geographical and seasonal occurrence, removal and risk assessment. Environmental Research, 136, 108–119.
- Petrovic, M., Fernández-Alba, A. R., Borrull, F., Marce, R. M., Mazo, E. G., & Barceló, D. (2002). Occurrence and distribution of nonionic surfactants, their degradation products, and linear alkylbenzene sulfonates in coastal waters and sediments in Spain. *Environmental Toxicology and Chemistry*, 21(1), 37–46.
- Pharmaceutical Services Division Ministry of Health Malaysia. Malaysian Statistics on Medicine 2011- 2014. Kuala Lumpur 2017.
- Philip, J. M., Aravind, U. K., & Aravindakumar, C. T. (2018). Emerging contaminants in Indian environmental matrices e A review. *Chemosphere*, 190, 307–326.
- Pico, Y. (2013). Ultrasound-assisted extraction for food and environmental samples. *TrAC Trends in Analytical Chemistry*, 43, 84-99

- Pojana, G., Gomiero, A., Jonkers, N., & Marcomini, A. (2007). Natural and synthetic endocrine disrupting compounds (EDCs) in water, sediment and biota of a coastal lagoon. *Environment International*, 33(7), 929–936.
- Praveena, S. M., Lui, T. S., Razak, S. Q. N. A., & Aris, A. Z. (2016). Occurrence of selected estrogenic compounds and estrogenic activity in surface water and sediment of Langat River (Malaysia). *Environmental Monitoring and* Assessment, 188(7), 442.
- Praveena, S. M., Shaifuddin, S. N. M., Sukiman, S., Nasir, F. A. M., Hanafi, Z., Kamarudin, N., ... & Aris, A. Z. (2018). Pharmaceuticals residues in selected tropical surface water bodies from Selangor (Malaysia): Occurrence and potential risk assessments. *Science of The Total Environment*, 642, 230-240.
- Raman, D. R., Williams, E. L., Layton, A. C., Burns, R. T., Easter, J. P., Daugherty, A. S., & Sayler, G. S. (2004). Estrogen content of dairy and swine wastes. *Environmental Science and Technology*, 38(13), 3567–3573.
- Ramaswamy, B. R., Kim, J. W., Isobe, T., Chang, K. H., Amano, A., Miller, T. W., & Tanabe, S. (2011). Determination of preservative and antimicrobial compounds in fish from Manila Bay, Philippines using ultra high performance liquid chromatography tandem mass spectrometry, and assessment of human dietary exposure. *Journal of Hazardous Materials*, 192(3), 1739–1745
- Raza, M., Zakaria, M. P., Hashim, N. R., Yim, U. H., Kannan, N., & Ha, S. Y. (2013). Composition and source identification of polycyclic aromatic hydrocarbons in mangrove sediments of Peninsular Malaysia: indication of anthropogenic input. *Environmental Earth Sciences*, 70(6), 2425-2436.
- Ribeiro, C., Tiritan, M. E., Rocha, E., & Rocha, M. J. (2009). Seasonal and spatial distribution of several endocrine-disrupting compounds in the Douro River estuary, Portugal. Archives of Environmental Contamination and Toxicology, 56(1), 1–11
- Robinson, B. J., & Hellou, J. (2009). Biodegradation of endocrine disrupting compounds in harbour seawater and sediments. *Science of the Total Environment*, 407(21), 5713–5718.
- Ronan, J. M., & McHugh, B. (2013). A sensitive liquid chromatography/tandem mass spectrometry method for the determination of natural and synthetic steroid estrogens in seawater and marine biota, with a focus on proposed Water Framework Directive Environmental Quality Standards. *Rapid Communications* in Mass Spectrometry : RCM, 27(7), 738–746.
- Sabik, H., Gagné, F., Blaise, C., Marcogliese, D. J., & Jeannot, R. (2003). Occurrence of alkylphenol polyethoxylates in the St. Lawrence River and their bioconcentration by mussels (Elliptio complanata). *Chemosphere*, 51(5), 349– 356.

- Saeed, T., Al-Jandal, N., Abusam, A., Taqi, H., Al-Khabbaz, A., & Zafar, J. (2017). Sources and levels of endocrine disrupting compounds (EDCs) in Kuwait's coastal areas. *Marine Pollution Bulletin*, 118(1–2), 407–412.
- Sakai, N., Shirasaka, J., Matsui, Y., Ramli, M. R., Yoshida, K., Ali Mohd, M., & Yoneda, M. (2017). Occurrence, fate and environmental risk of linear alkylbenzene sulfonate in the Langat and Selangor River basins, Malaysia. *Chemosphere*, 172, 234–241.
- Salgueiro-González, N., Turnes-Carou, I., Viñas-Diéguez, L., Muniategui-Lorenzo, S., López-Mahía, P., & Prada-Rodríguez, D. (2015). Occurrence of endocrine disrupting compounds in five estuaries of the northwest coast of Spain: Ecological and human health impact. *Chemosphere*, 131, 241–247.
- Salvia, M.-V., Cécile, C.-O., Wiest, L., Baudot, R., & Vulliet, E. (2014). Comparison of Two Analytical Methods for the Determination of Traces of Veterinary Antibiotics and Steroid Hormones in Soil Based on Pressurised Liquid Extraction (PLE) and Quick, Easy, Cheap, Effective, Rugged, Safe (Modified-Quechers) Extraction. *Pharmaceutica Analytica Acta*, 5(9), 1–9.
- Salvia, M. V., Vulliet, E., Wiest, L., Baudot, R., & Cren-Olivé, C. (2012). Development of a multi-residue method using acetonitrile-based extraction followed by liquid chromatography-tandem mass spectrometry for the analysis of steroids and veterinary and human drugs at trace levels in soil. *Journal of Chromatography* A, 1245, 122–133.
- Sánchez-Avila, J., Bonet, J., Velasco, G., & Lacorte, S. (2009). Determination and occurrence of phthalates, alkylphenols, bisphenol A, PBDEs, PCBs and PAHs in an industrial sewage grid discharging to a Municipal Wastewater Treatment Plant. Science of the Total Environment, 407(13), 4157–4167.
- Sanchez-Prado, L., Garcia-Jares, C., & Llompart, M. (2010). Microwave-assisted extraction: Application to the determination of emerging pollutants in solid samples. *Journal of Chromatography A*, 1217(16), 2390–2414
- Sanderson, H., Johnson, D. J., Reitsma, T., Brain, R. A., Wilson, C. J., & Solomon, K. R. (2004). Ranking and prioritization of environmental risks of pharmaceuticals in surface waters. *Regulatory Toxicology and Pharmacology*, 39(2), 158-183
- Sanderson, H., Johnson, D. J., Wilson, C. J., Brain, R. A., & Solomon, K. R. (2003). Probabilistic hazard assessment of environmentally occurring pharmaceuticals toxicity to fish, daphnids and algae by ECOSAR screening. *Toxicology letters*, 144(3), 383-395
- Sangster, J. L., Oke, H., Zhang, Y., & Bartelt-Hunt, S. L. (2015). The effect of particle size on sorption of estrogens, androgens and progestagens in aquatic sediment. *Journal of Hazardous Materials*, 299, 112–121.

- Santarelli, G. A., Migliorati, G., Pomilio, F., Marfoglia, C., Centorame, P., D'Agostino, A., ... & Aprea, G. (2018). Assessment of pesticide residues and microbial contamination in raw leafy green vegetables marketed in Italy. Food Control, 85, 350-358.
- Santhi, V. A., Hairin, T., & Mustafa, A. M. (2012). Simultaneous determination of organochlorine pesticides and bisphenol A in edible marine biota by GC-MS. *Chemosphere*, 86(10), 1066–1071.
- Santhi, V. A., & Mustafa, A. M. (2013). Assessment of organochlorine pesticides and plasticisers in the Selangor River basin and possible pollution sources. *Environmental Monitoring and Assessment*, 185(2), 1541–1554.
- Santhi, V. A., Sakai, N., Ahmad, E. D., & Mustafa, A. M. (2012). Occurrence of bisphenol A in surface water, drinking water and plasma from Malaysia with exposure assessment from consumption of drinking water. Science of the Total Environment, 427-428, 332-338.
- Santos, J. L., Aparicio, I., & Alonso, E. (2007). Occurrence and risk assessment of pharmaceutically active compounds in wastewater treatment plants. A case study: Seville city (Spain). *Environment International*, 33(4), 596-601.
- Santos, L. H. M. L. M., Gros, M., Rodriguez-Mozaz, S., Delerue-matos, C., Pena, A., Barceló, D., & Montenegro, M. C. B. S. M. (2013). Contribution of hospital effluents to the load of pharmaceuticals in urban wastewaters : Identification of ecologically relevant pharmaceuticals. *Science of the Total Environment*, 461– 462, 302–316.
- Sany, S. B. T., Salleh, A., Sulaiman, A. H., Sasekumar, A., Rezayi, M., & Tehrani, G. M. (2013). Heavy metal contamination in water and sediment of the Port Klang coastal area, Selangor, Malaysia. *Environmental Earth Sciences*, 69(6), 2013– 2025.
- Saravanabhavan, G., Helleur, R., & Hellou, J. (2009). GC-MS/MS measurement of natural and synthetic estrogens in receiving waters and mussels close to a raw sewage ocean outfall. *Chemosphere*, 76(8), 1156–1162.
- Selvaraj, K. K., Shanmugam, G., Sampath, S., Joakim Larsson, D. G., & Ramaswamy, B. R. (2014). GC-MS determination of bisphenol A and alkylphenol ethoxylates in river water from India and their ecotoxicological risk assessment. *Ecotoxicology and Environmental Safety*, 99, 13–20.
- Shareef, A., Angove, M. J., & Wells, J. D. (2006). Optimization of silylation using Nmethyl-N-(trimethylsilyl)- trifluoroacetamide, N,O-bis-(trimethylsilyl)trifluoroacetamide and N-(tert-butyldimethylsilyl)-N-methyltrifluoroacetamide for the determination of the estrogens estrone and 17α-ethinylestradi. *Journal of Chromatography A*, 1108(1), 121–128.

- Sibali, L. L., Okonkwo, J. O., & McCrindle, R. I. (2013). Determination of selected phthalate esters compounds in water and sediments by capillary gas chromatography and flame ionization detector. *Journal of Environmental Science and Health, Part A*, 48(11), 1365-1377.
- Sifakis, S., Androutsopoulos, V. P., Tsatsakis, A. M., & Spandidos, D. A. (2017). Human exposure to endocrine disrupting chemicals: effects on the male and female reproductive systems. *Environmental Toxicology and Pharmacology*, 51, 56–70.
- Simon, E., Lamoree, M. H., Hamers, T., Weiss, J. M., Balaam, J., De Boer, J., & Leonards, P. E. G. (2010). Testing endocrine disruption in biota samples: A method to remove interfering lipids and natural hormones. *Environmental Science and Technology*, 44(21), 8322–8329.
- Sodré, F. F., Pescara, I. C., Montagner, C. C., & Jardim, W. F. (2010). Assessing selected estrogens and xenoestrogens in Brazilian surface waters by liquid chromatography-tandem mass spectrometry. *Microchemical Journal*, 96(1), 92– 98.
- Søeborg, T., Frederiksen, H., & Andersson, A. M. (2012). Cumulative risk assessment of phthalate exposure of Danish children and adolescents using the hazard index approach. *International Journal of Andrology*, 35(3), 245–252.
- Solé, M., Porte, C., & Barcelo, D. (2000). Vitellogenin induction and other biochemical responses in carp, Cyprinus carpio, after experimental injection with 17αethynylestradiol. Archives of environmental contamination and toxicology, 38(4), 494-500.
- Stasinakis, A. S., Mermigka, S., Samaras, V. G., Farmaki, E., & Thomaidis, N. S. (2012). Occurrence of endocrine disrupters and selected pharmaceuticals in Aisonas River (Greece) and environmental risk assessment using hazard indexes. *Environmental Science and Pollution Research*, 19(5), 1574-1583.
- Storelli, M. M. (2008). Potential human health risks from metals (Hg, Cd, and Pb) and polychlorinated biphenyls (PCBs) via seafood consumption: Estimation of target hazard quotients (THQs) and toxic equivalents (TEQs). Food and Chemical Toxicology, 46(8), 2782–2788.
- Stumpf, M., Ternes, T. A., Wilken, R.-D., Rodrigues, S. V, & Baumann, W. (1999). Polar drug residues in sewage and natural waters in the state of Rio de Janeiro, Brazil. *The Science of the Total Environment*, 225, 135–141.
- Sumpter, J. P., & Jobling, S. (1995). Vitellogenesis as a biomarker for estrogenic contamination of the aquatic environment. *Environmental Health Perspectives*, 103(SUPPL. 7), 173–178.
- Sun, K., Jin, J., Gao, B., Zhang, Z., Wang, Z., Pan, Z., & Zhao, Y. (2012). Sorption of 17α-ethinyl estradiol, bisphenol A and phenanthrene to different size fractions of soil and sediment. *Chemosphere*, 88(5), 577–583.

- Sun, L., Yong, W., Chu, X., & Lin, J.-M. (2009). Simultaneous determination of 15 steroidal oral contraceptives in water using solid-phase disk extraction followed by high performance liquid chromatography-tandem mass spectrometry. *Journal of Chromatography. A*, 1216(28), 5416–5423.
- Tanoue, R., Nomiyama, K., Nakamura, H., Hayashi, T., Kim, J. W., Isobe, T., & Tanabe, S. (2014). Simultaneous determination of polar pharmaceuticals and personal care products in biological organs and tissues. *Journal of Chromatography A*, 1355, 193–205.
- Tavakoly Sany, S. B., Hashim, R., Rezayi, M., Salleh, A., Rahman, M. A., Safari, O., & Sasekumar, A. (2014). Human health risk of polycyclic aromatic hydrocarbons from consumption of blood cockle and exposure to contaminated sediments and water along the Klang Strait, Malaysia. *Marine Pollution Bulletin*, 84(1–2), 268– 279.
- Taweel, A., Shuhaimi-Othman, M., & Ahmad, A. K. (2013). Assessment of heavy metals in tilapia fish (Oreochromis niloticus) from the Langat River and Engineering Lake in Bangi, Malaysia, and evaluation of the health risk from tilapia consumption. *Ecotoxicology and Environmental Safety*, 93, 45–51.
- Teh, C.B.S., Talib J. (2006). Soil physics analyses volume 1. Universiti Putra Malaysia Press, Kuala Lumpur, Malaysia.
- Ternes, T. A. (1998). Occurrence of drugs in German sewage treatment plants and rivers1. *Water Research*, 32(11), 3245-3260.
- Ternes, T. A., Andersen, H., Gilberg, D., & Bonerz, M. (2002). Determination of estrogens in sludge and sediments by liquid extraction and GC/MS/MS. *Analytical Chemistry*, 74(14), 3498–3504.
- Terzic, S., & Ahel, M. (2011). Nontarget analysis of polar contaminants in freshwater sediments in fl uenced by pharmaceutical industry using ultra-high-pressure liquid chromatography e quadrupole time-of- fl ight mass spectrometry. *Environmental Pollution*, 159(2), 557–566.
- Thomaidi, V. S., Stasinakis, A. S., Borova, V. L., & Thomaidis, N. S. (2016). Science of the Total Environment Assessing the risk associated with the presence of emerging organic contaminants in sludge-amended soil: A country-level analysis. Science of the Total Environment, 548–549, 280–288.
- Thompson, M., Ellison, S.L.R., Wood, R. (2002). Harmonized guidelines for singlelaboratory validation of methods of analysis. Pure Appl. Chem. 74:835-855.
- Tiwari, M., Sahu, S. K., & Pandit, G. G. (2016). Distribution and estrogenic potential of endocrine disrupting chemicals (EDCs) in estuarine sediments from Mumbai, India. *Environmental Science and Pollution Research*, 23(18), 18789–18799.

- Tri, T. M., Anh, H. Q., Tham, T. T., Quy, T. Van, Long, N. Q., Nhung, D. T., & Minh, T. B. (2016). Distribution and depth profiles of polychlorinated dibenzo-pdioxins, polychlorinated dibenzofurans, and polychlorinated biphenyls in sediment collected from offshore waters of Central Vietnam. *Marine Pollution Bulletin*, 106, 341–346.
- US Environmental Protection Agency, (2011). Estimation Program Interface EPI, Suite, Version. Environmental Protection Agency, Office of Pollution Prevention and Toxic's, Washington, DC, USA.
- US EPA, 1994. Method 1613, Revision B: Tetra-through Octa-Chlorinated Dioxins and Furans by Isotope Dilution HRGC/HRMS, US EPA Press, Washington, DC.
- USEPA, 1994. Method 8290: Polychlorinated dibenzodioxins and polychlorinated dibenzo furans by high resolution mass chromatography/high resolution mass spectrometry, Revision 0, US Environmental Protection Agency, Washington, DC.
- USEPA, 2007. Method 1694: Pharmaceuticals and personal care products in water, soil, sediment, and biosolids by HPLC/MS/MS.
- Vaezzadeh, V., Zakaria, M. P., Bong, C. W., Masood, N., Mohsen Magam, S., & Alkhadher, S. (2017). Mangrove Oyster (Crassostrea belcheri) as a Biomonitor Species for Bioavailability of Polycyclic Aromatic Hydrocarbons (PAHs) from Sediment of the West Coast of Peninsular Malaysia. Polycyclic Aromatic Compounds, 6638, 1–16.
- Van De Steene, J. C., & Lambert, W. E. (2008). Comparison of matrix effects in HPLC-MS/MS and UPLC-MS/MS analysis of nine basic pharmaceuticals in surface waters. Journal of the American Society for Mass Spectrometry, 19(5), 713-718.
- Vanderford, B. J., Mawhinney, D. B., Trenholm, R. A., Zeigler-Holady, J. C., & Snyder, S. A. (2011). Assessment of sample preservation techniques for pharmaceuticals, personal care products, and steroids in surface and drinking water. Analytical and Bioanalytical Chemistry, 399(6), 2227–2234.
- Vandermeersch, G., Lourenço, H. M., Alvarez-Muñoz, D., Cunha, S., Diogène, J., Cano-Sancho, G., & Robbens, J. (2015). Environmental contaminants of emerging concern in seafood--European database on contaminant levels. *Environmental Research*, 143, 29–45.
- Vazquez-Roig, P., Segarra, R., Blasco, C., Andreu, V., & Picó, Y. (2010). Determination of pharmaceuticals in soils and sediments by pressurized liquid extraction and liquid chromatography tandem mass spectrometry. *Journal of Chromatography* A, 1217(16), 2471–2483.
- Verlicchi, P., Galletti, A., Petrovic, M., & BarcelÓ, D. (2010). Hospital effluents as a source of emerging pollutants: An overview of micropollutants and sustainable treatment options. *Journal of Hydrology*, 389(3–4), 416–428.

- Verlicchi, P., & Zambello, E. (2016). Predicted and measured concentrations of pharmaceuticals in hospital effluents. Examination of the strengths and weaknesses of the two approaches through the analysis of a case study. Science of the Total Environment, 565, 82–94.
- Wang, H., Zhou, X., Zhang, Y., Chen, H., Li, G., Xu, Y., & Ding, L. (2012). Dynamic microwave-assisted extraction coupled with salting-out liquid-liquid extraction for determination of steroid hormones in fish tissues. *Journal of Agricultural and Food Chemistry*, 60(41), 10343–10351.
- Wang, J., Dong, M., Shim, W. J., Kannan, N., & Li, D. (2007). Improved cleanup technique for gas chromatographic-mass spectrometric determination of alkylphenols from biota extract. *Journal of Chromatography A*, 1171(1-2), 15– 21.
- Wang, L., Ying, G., Zhao, J., Yang, X., Chen, F., Tao, R., & Zhou, L. (2010). Occurrence and risk assessment of acidic pharmaceuticals in the Yellow River, Hai River and Liao River of north China. *Science of the Total Environment*, 408(16), 3139– 3147.
- Weber, A. A., Moreira, D. P., Melo, R. M. C., Vieira, A. B. C., Prado, P. S., da Silva, M. A. N., & Rizzo, E. (2017). Reproductive effects of oestrogenic endocrine disrupting chemicals in Astyanax rivularis inhabiting headwaters of the Velhas River, Brazil. Science of the Total Environment, 592, 693-703.
- Wee, S. Y., & Aris, A. Z. (2017). Ecological risk estimation of organophosphorus pesticides in riverine ecosystems. *Chemosphere*, 188, 575–581.
- Wee, S. Y., Omar, T. F. T., Aris, A. Z., & Lee, Y. (2016). Surface Water Organophosphorus Pesticides Concentration and Distribution in the Langat River, Selangor, Malaysia. *Exposure and Health*, 8(4), 497–511.
- Wenzel, A., Böhmer, W., Müller, J., Rüdel, H., & Schröter-Kermani, C. (2004). Retrosperctive Monitoring of Alkylphenols and Alkylphenol Monothoxylates in Aquatic Biota from 1985 to 2001: Results from the German Environmental Specimen Bank. *Environmental Science and Technology*, 38(6), 1654–1661.
- Wu, J., Qian, X., Yang, Z., & Zhang, L. (2010). Study on the matrix effect in the determination of selected pharmaceutical residues in seawater by solid-phase extraction and ultra-high-performance liquid chromatography-electrospray ionization low-energy collision-induced dissociation tandem mass spectrometry. *Journal of Chromatography A*, 1217(9), 1471-1475.
- Xu, E.G.B., Liu, S., Ying G.-G., Zheng, G.J.S., Lee, J.H.W., & Leung, K.M.Y. (2014). The occurrence and ecological risks of endocrine disrupting chemicals in sewage effluents from three different sewage treatment plants, and in natural seawater from a marine reserve of Hong Kong. *Marine Pollution Bulletin*, 85, 352-362.

- Xu, W.H., Zhang, G., Zou, S.C., Ling, Z.H., Wang, G.L., & Yan, W. (2009). A preliminary investigation on the occurrence and distribution of antibiotics in the Yellow River and its tributaries, China. *Water Environment Research*, 81, 248-254.
- Yahaya, N. (2007). Solid Waste Management in Malaysia, Keynote Address, Waste to Wealth, International Conference and Exhibition 2007, Kuala Lumpur.
- Yamamoto, F. Y., Kupsco, A., & Ribeiro, C. A. O. (2017). Vitellogenin levels and others biomarkers show evidences of endocrine disruption in fish species from Iguaçu River - Southern Brazil, *Chemosphere*, 186, 88–99.
- Yan, C., Yang, Y., Zhou, J., Liu, M., Nie, M., Shi, H., & Gu, L. (2013). Antibiotics in the surface water of the Yangtze Estuary: Occurrence, distribution and risk assessment. *Environmental Pollution*, 175, 22–29.
- Yap, C. K., & Cheng, W. H. (2013). Distributions of heavy metal concentrations in different tissues of the mangrove snail nerita lineata. Sains Malaysiana, 42(5), 597-603.
- Ying, G. G., Kookana, R. S., & Ru, Y. J. (2002). Occurrence and fate of hormone steroids in the environment. *Environment International*, 28(6), 545–551.
- Yu, Y., & Wu, L. (2012). Analysis of endocrine disrupting compounds, pharmaceuticals and personal care products in sewage sludge by gas chromatography-mass spectrometry. *Talanta*, 89, 258–263. https://doi.org/10.1016/j.talanta.2011.12.023.
- Zakaria, M. (2017). Use of antimicrobial agents in veterinary medicine in Malaysia. 2nd OIE Information Seminar for Praticing Veterinatians: Combating AMR (Kuala Lumpur, Malaysia).
- Zakaria, M. P., Geik, K. H., Lee, W. Y., & Hayet, R. (2005). Landfill leachate as a source of polycyclic aromatic hydrocarbons (PAHs) to Malaysian waters. *Coastal Marine Science*, 29(2), 116-123.
- Zhang, C. (2007). Fundamentals of environmental sampling and analysis. John Wiley & Sons.
- Zhang, L. P., Wang, X. H., Ya, M. L., Wu, Y. L., Li, Y. Y., & Zhang, Z. L. (2014). Levels of endocrine disrupting compounds in South China Sea. *Marine Pollution Bulletin*, 85(2), 628-633.
- Zhang, X., Gao, Y., Li, Q., Li, G., Guo, Q., & Yan, C. (2011). Estrogenic compounds and estrogenicity in surface water, sediments, and organisms from Yundang Lagoon in Xiamen, China. Archives of Environmental Contamination and Toxicology, 61(1), 93-100.

- Zhang, Z. L., Hibberd, A., & Zhou, J. L. (2006). Optimisation of derivatisation for the analysis of estrogenic compounds in water by solid-phase extraction gas chromatography-mass spectrometry. *Analytica Chimica Acta*, 577(1), 52-61.
- Zheng, B., Liu, R., Liu, Y., Jin, F., & An, L. (2015). Phenolic endocrine-disrupting chemicals and intersex in wild crucian carp from Hun River, China. *Chemosphere*, 120, 743–749.
- Zhou, L. J., Ying, G. G., Zhao, J. L., Yang, J. F., Wang, L., Yang, B., & Liu, S. (2011). Trends in the occurrence of human and veterinary antibiotics in the sediments of the Yellow River, Hai River and Liao River in northern China. *Environmental Pollution*, 159(7), 1877–188.
- Zou, S., Xu, W., Zhang, R., Tang, J., Chen, Y., & Zhang, G. (2011). Occurrence and distribution of antibiotics in coastal water of the Bohai Bay, China: Impacts of river discharge and aquaculture activities. *Environmental Pollution*, 159(10), 2913–2920.
- Zuo, Y., Zhang, K., & Lin, Y. (2007). Microwave-accelerated derivatization for the simultaneous gas chromatographic-mass spectrometric analysis of natural and synthetic estrogenic steroids. *Journal of Chromatography A*, 1148(2), 211-218.

#### **BIODATA OF STUDENT**



Tuan Mohamad Fauzan Tuan Omar was born on 22<sup>th</sup> February 1983 in Temerloh, Pahang. He received his early education at Sekolah Kebangsaan Kampung Pek (Machang), Maahad Syamsul Maarif (Lelaki), Machang and Maahad Muhammadi (Lelaki), Kota Bharu, Kelantan. After completing his foundation of science at Pusat Asasi Sains Universiti Malaya (PASUM-2003), he continued his highest education at Universiti Malaysia Terengganu (UMT), where he obtained his bachelor degree in Analytical and Environmental Chemistry (2006) and Universiti Sains Malaysia (USM) for his Master of Science (2012). In 2015, he received scholarship from Ministry of Higher Education under MyBrain 15 to pursue PhD study in the field of Environmental Quality and Conservation at Faculty of Environmental Studies, Universiti Putra Malaysia.

Tuan Mohamad Fauzan has more than 10 years working experience in both private and government sector, having started his career as a quality control chemist at Chemical Company Malaysia (CCM) Duopharma Biotech in 2006 after graduation. He then joined Malaysian Palm Oil Board (MPOB) as a Research Officer from 2007 until 2015.

His research interest is on the analytical chemistry specializing on the analytical method development using high end instrumentation techniques such as Gas Chromatography Mass Spectrometry, Liquid Chromatography Mass Spectrometry, Inductively Coupled Plasma Mass Spectrometry and various other instrumentation techniques. He has a wide experience in analyzing contaminants in food and environmental matrices which he gained during working period in MPOB and also for his PhD research. He also involved in the implementation of MS ISO 17025 in the Pesticide Residue Laboratory, MPOB and was appointed as Deputy Technical Manager for the lab. His research profile can be viewed at Scopus (ID:

57189709490);Researchgate\_(https://www.researchgate.net/profile/Tuan\_Fauzan\_Tan\_Omar); OrCiD (https://orcid.org/000-0002-8175-2436) and can be contacted at tmfauzan1612@gmail.com.

#### LIST OF PUBLICATIONS

#### Journal (Published)

- Omar, T.F.T., Aris, A.Z., Yusoff, F.M., Mustafa, S. 2018. Risk assessment of pharmaceutically active compounds (PhACs) in the Klang River estuary, Malaysia, *Environmental Geochemistry and Health*, https://doi.org/10.1007/s10653-018-0157-1, Q1, Impact factor = 2.994.
- Omar, T.F.T., Aris, A.Z., Yusoff, F.M., Mustafa, S. 2018. Occurrence, distribution, and sources of emerging organic contaminants in tropical coastal sediment of anthropogenically impacted Klang River estuary, Malaysia, *Marine Pollution Bulletin*, 131, 284-293, Q1, Impact factor = 3.146.
- Omar, T.F.T., Aris, A.Z., Yusoff, F.M., Mustafa, S. 2017. An improved SPE-LC MS/MS method for multi-class endocrine disrupting compound (EDC) determination in tropical estuarine sediment, *Talanta*, 173, 51-59, Q1, Impact Factor = 4.162.
- Omar, T.F.T., Ahmad, A., Aris, A.Z., Yusoff, F.M. 2016. Endocrine disrupting compounds (EDCs) in environmental matrices: Review of analytical strategies for pharmaceuticals, estrogenic hormones, and alkylphenol compounds, *TrAC-Trends in Analytical Chemistry*, 85, 241–259, Q1, Impact Factor = 8.442.

#### Journal (Submitted)

Omar, T.F.T., Aris, A.Z., Yusoff, F.M., Mustafa, S. Occurrence and level of emerging organic contaminant in fish and mollusk from Klang River estuary, Malaysia and assessment on human health risk, submitted to Environmetal Pollutionunder revision.

### Proceeding (Oral presentation)

- Tuan Fauzan Tuan Omar, Ahmad Zaharin Aris, Nor Farhanna Mokhtar, Hanisah Mohmad Nasir, 2015. Presence of Endocrine Disrupting Compounds (EDCs) in domestic effluents of Klang Valley, Malaysia, Oral presentation, UNU-GIST Joint Programme Symposium, 11-12 November 2015, Marco Polo Ortigas, Manila, the Phillipines.
- Tuan Fauzan Tuan Omar, Ahmad Zaharin Aris, Fatimah Md. Yusoff, Shuhaimi Mustafa, 2018. Presence of emerging organic contaminants in fish and mollusc from Klang River estuary, Malaysia and assessment on human health risk, Oral presentation, 11<sup>th</sup> Society of Environmental Toxicology and Chemistry (SETAC) Asia Pacific 2018, 16-19 September 2018, EXCO Daegu, Republic of Korea.



# **UNIVERSITI PUTRA MALAYSIA**

# STATUS CONFIRMATION FOR THESIS / PROJECT REPORT AND COPYRIGHT

ACADEMIC SESSION : \_\_\_\_\_

# TITLE OF THESIS / PROJECT REPORT :

# NAME OF STUDENT : \_\_\_\_\_

I acknowledge that the copyright and other intellectual property in the thesis/project report belonged to Universiti Putra Malaysia and I agree to allow this thesis/project report to be placed at the library under the following terms:

- 1. This thesis/project report is the property of Universiti Putra Malaysia.
- 2. The library of Universiti Putra Malaysia has the right to make copies for educational purposes only.
- 3. The library of Universiti Putra Malaysia is allowed to make copies of this thesis for academic exchange.

I declare that this thesis is classified as :

\*Please tick (v)



(Contain confidential information under Official Secret Act 1972).

(Contains restricted information as specified by the

RESTRICTED

CONFIDENTIAL



OPEN ACCESS

organization/institution where research was done).

I agree that my thesis/project report to be published as hard copy or online open access.

This thesis is submitted for :



Embargo from\_\_\_\_\_ until \_\_\_\_\_ (date)

(date)

# Approved by:

(Signature of Student) New IC No/ Passport No.: (Signature of Chairman of Supervisory Committee) Name:

Date :

Date :

[Note : If the thesis is CONFIDENTIAL or RESTRICTED, please attach with the letter from the organization/institution with period and reasons for confidentially or restricted.]