TABLE OF CONTENTS

ं अभिनाति ।	Dogo
	Page
ACKNOWLEDGEMENT	iii
ABSTRACT (ENGLISH)	v
ABSTRACT (THAI)	vii
LIST OF TABLES	xiii
LIST OF ILLUSTRATIONS	xv
ABBREVIATIONS	xvii
CHAPTER 1 INTRODUCTION	1 0
CHAPTER 2 LITERATURE REVIEWS	5
2.1 Lung cancer in Chiang Mai	5
2.2 Biomarkers	11
2.3 Biomonitoring and health risk assessment	15
2.4 Genetic effect of environmental exposure	16
in human population	
2.5 Chromosomal aberration	19
2.6 Micronucleus test	Ur ₂₄ versity
2.7 Single cell gel electrophoresis (comet assay)	e 27 v e o
CHAPTER 3 MATERIALS AND METHODS	34
3.1 The studied subjects	34
3.2 Chromosomal aberration assay	35

TABLE OF CONTENTS (CONTINUED)

	Page
3.3 Micronucleus Test	37
3.4 Alkaline single cell gel electrophoresis (comet assay)	38
3.4.1 Estimation of internal standard range	39
3.4.2 Detection of DNA damage	40
3.5 Statistical analysis	42
3.6 Health risk assessment	43
CHAPTER 4 RESULTS	44
4.1 The studied populations	44
4.2 Chromosomal aberration analysis	46
4.2.1 Chromosomal aberration endpoints	46
and mitotic indices	
4.2.2 The effects of confounding factors on	47
chromosomal aberrations in total population	
4.2.2.1 Effect of cigarette smoking on	56
chromosome aberration	
4.2.2.2 Effect of chewing of fermented tea	U ₅₆ versity
leaf or betel nut on chromosome aber	rration
4.3 Micronucleus test	59
4.3.1 Micronucleus endpoints and	59
nuclear division indices	

TABLE OF CONTENTS (CONTINUED)

	Page
4.3.2 The effects of confounding factors on	62
micronucleus endpoints in total population	
4.3.2.1 The effects of gender on micronucleus	62
induction	
4.3.2.2 The effects of cigarette smoking on	64
micronucleus induction	
4.4 Single cell gel electrophoresis assay (comet assay)	66
4.4.1 Estimation of internal standard ranges and	66
the exclusion of the outliers	
4.4.2 Detection of DNA damage in Saraphi and	66
Chom Thong populations using three types of blood	i
measured before and after exclusion of the outliers	
4.4.3 The effects of confounding factors	73
on DNA damage using data from PB measured	
before and after exclusion of the outliers	
Copyrigh in total population Chiang Mail U	
4.5 The health risk assessment	76
CHAPTER 5 DISCUSSION	77
CHAPTER 6 CONCLUSION	87

TABLE OF CONTENTS (CONTINUED)

			Page
REFERENC	ES		89
APPENDIX			114
	APPENDIX A	Informed consent and questionnaire form	115
	APPENDIX B	Reagent preparation for chromosomal and	127
		micronucleus tests	
	APPENDIX C	Reagent preparation for comet assay	130
	APPENDIX D	Classification of structural chromosomal	134
		aberration	
	APPENDIX E	Criteria for micronucleus analysis	138
	APPENDIX F	Analysis of DNA damage by comet assay	140
	APPENDIX G	General characteristics of studied populations	141
		in chromosome aberration and micronucleus tes	ts
	APPENDIX H	Studied populations for comet assay	147
	APPENDIX I	Results of chromosome aberration and	153
	ans	micronucleus tests	
	APPENDIX J	Results of DNA damage detects by comet assay	164 Jersity
CURRICUL	UM VITAE		173 Y e o

LIST OF TABLES

Tables		Page
1	The age-standardized incidence rates of new malignant cases	6
	and mortality rates of lung cancer in Chiang Mai	
2	The crude incidence rates of lung cancer in Saraphi and	11
	Chom Thong districts	
3	Chi-square test of confounding factors between Saraphi	45
	and Chom Thong populations	
4	Comparison of chromosome aberrations separated by	48
	gender between studied populations	
5	Types and frequencies of chromosome aberrations	49
	observed in each population	
6	The effect of confounding factors on chromosomal	55
	aberrations evaluated from total population	
7 C O	The basal levels of the percentages of aberrant cells and	J ₁ 57 versity
	aberrations separated by smoking habits between	
	studied populations	

LIST OF TABLES (CONTINUED)

Tables		Page
8	The basal levels of the percentages of aberrant cells	58
	and aberrations separated by chewing habit	
	between studied populations	
9	Comparison of micronucleus induction between	60
	studied populations	
10	The effect of confounding factors on micronucleus	63
	induction evaluated in total population	
11	The basal levels of total MN in 1,000 BN and	65
	% BN with MN separated by smoking habits	
	between studied populations	
12	Electrophoresis runs with the outliers (+) of	70
	internal standards which were outside the accepted ranges	
13	The DNA damage measured by comet assay	71
	compared between two studied populations, using data	7
	from 3 types of blood a) before and b) after exclusion of the	outliers
14 Cor	Comparison of DNA damage detected from	J72 versity
	peripheral blood by comet assay between both studied popul	ations
15	The effect of confounding factors on DNA damage	74
	using data from PB of all subjects, a) before and	
	b) after the exclusion of the outliers	

LIST OF ILLUSTRATIONS

Figures		Page
1	Distributions of a) % aberrant cells and b) % aberrations	50
	of both studied populations	
2	Normal metaphase with 46 chromosomes	51
3	Chromatid-type aberration, gap	51
4	Chromatid-type aberration, break	52
5	Chromatid-type aberration, deletion	52
6	Chromosome-type aberration, gap	53
7	Chromosome-type aberration, break	53
8	Chromosome-type aberrations, acentric and dicentric	54
9	Chromosome-type aberrations, ring and dicentric	54
10	Distributions of a) total MN in 1,000 BN and	61
	b) the percentage of BN with MN of both populations	
11 8	Internal standard for each of the experiments using	68
	untreated isolated lymphocytes and considering	
	three image analysis parameters:	
	a) tail length b) tail intensity and c) tail moment respectively	ervec

LIST OF ILLUSTRATIONS (CONTINUED)

Figures		Page
12	Internal standard for each of the experiments using	69
	irradiated isolated lymphocytes and considering	
	three image analysis parameters:	
	a) tail length; b) tail intensity and c) tail moment respectively	
13	Binucleated cells for micronucleus analysis	138
	(1,000 X magnification)	
14	Binucleated cells with micronuclei	139
	(1,000 X magnification)	
15	The gradual levels of DNA damage from undamaged cell	140
	to totally damaged cell (1,000 X magnification)	

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่ Copyright[©] by Chiang Mai University All rights reserved

ABBREVIATIONS

CA chromosome aberration

BN binucleated cell

MN micronucleus

SD. standard deviation

PB peripheral blood

SPB stimulated peripheral blood

SPB-APC stimulated peripheral blood in a presence of aphidicolin

TL tail length

TI tail intensity

TM tail moment

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่ Copyright[©] by Chiang Mai University All rights reserved