

APPENDICES



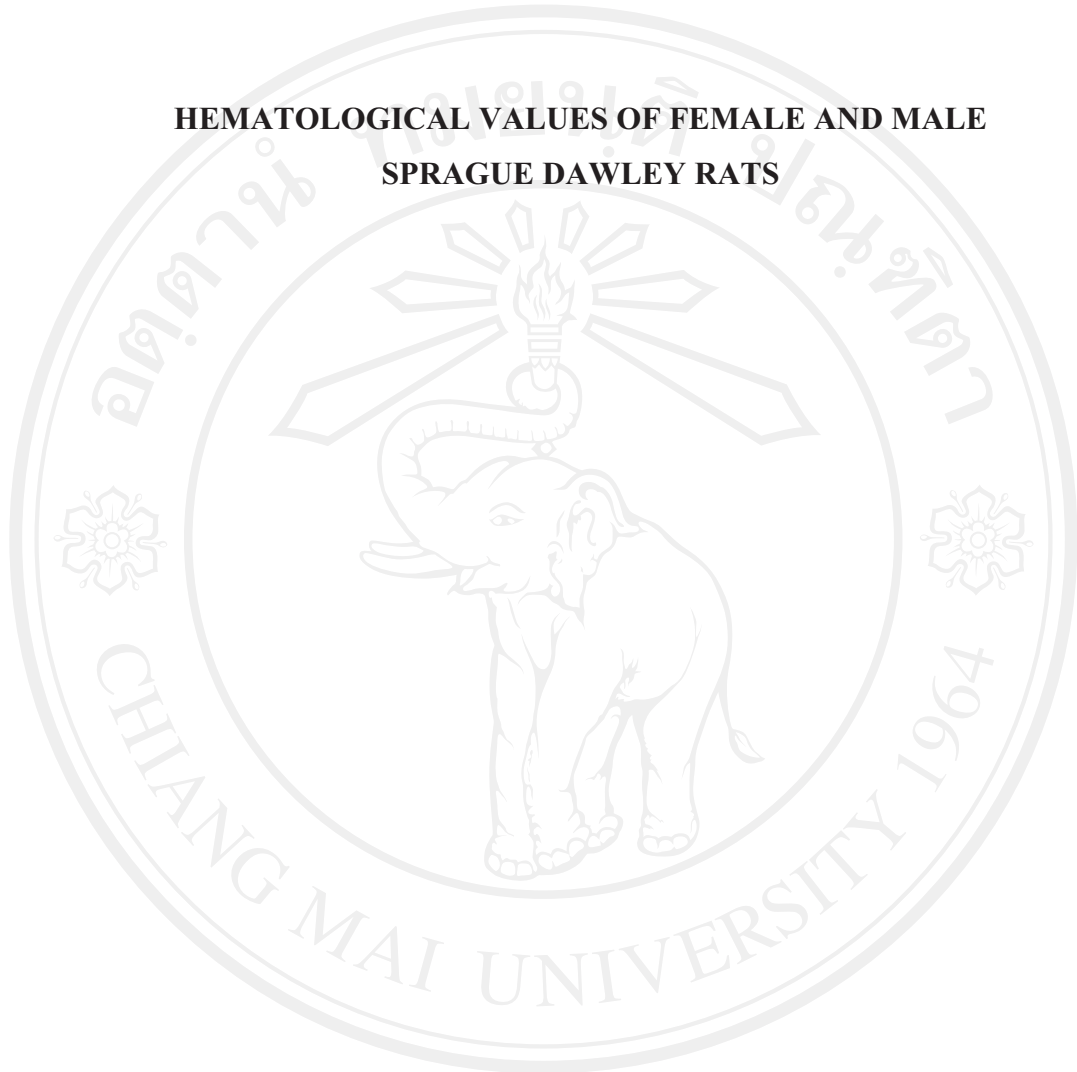
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APPENDIX A

**HEMATOLOGICAL VALUES OF FEMALE AND MALE
SPRAGUE DAWLEY RATS**



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Table 30 Hematological values of female Sprague Dawley rat in the Facility of National Laboratory Animal Centre, Mahidol University

Parameter	4 wks	6 wks	8 wks	10 wks	12 wks	Retired breeder
Red blood cell ($\times 10^6/\mu\text{l}$)	5.2 - 6.4	6.0 - 7.1	7.1 - 7.7	7.2 - 8.3	7.8 - 8.7	7.4 - 8.7
Hemoglobin (g/dl)	11.4 - 13.9	13.0 - 14.7	14.7 - 15.6	14.7 - 16.2	15.2 - 16.9	15.1 - 16.8
Hematocrit (%)	33.8 - 41.2	37.7 - 41.2	42.0 - 44.2	39.8 - 45.2	41.0 - 46.2	41.2 - 45.4
Mean corpuscular volume (fl)	61.0 - 68.0	56.9 - 63.8	56.2 - 59.4	52.1 - 57.0	51.1 - 53.7	50.7 - 57.7
Mean corpuscular hemoglobin (pg)	20.8 - 23.4	20.2 - 22.5	19.8 - 21.2	19.2 - 20.9	18.4 - 19.9	18.5 - 20.5
Mean corpuscular hemoglobin concentration (g/dl)	33.0 - 35.5	33.8 - 37.1	34.8 - 36.1	35.3 - 37.7	35.7 - 37.7	35.5 - 38.6
Platelet ($\times 10^5/\mu\text{l}$)	7.51 - 11.79	7.03 - 13.85	7.39 - 12.14	8.06 - 13.91	6.39 - 13.46	7.10 - 11.50
White blood cell ($\times 10^3/\mu\text{l}$)	1.6 - 6.0	4.3 - 9.9	5.2 - 12.5	5.4 - 11.6	4.6 - 10.9	2.9 - 8.3
Neutrophil (%)	5.0 - 22.0	3.0 - 16.0	3.0 - 15.0	5.0 - 26.0	8.0 - 25.0	14.0 - 31.0
Lymphocyte (%)	78.0 - 95.0	81.0 - 95.0	83.0 - 96.0	71.0 - 94.0	72.0 - 92.0	66.0 - 85.0
Monocyte (%)	0.0 - 2.0	0.0 - 3.0	0.0 - 2.0	0.0 - 4.0	0.0 - 4.0	0.0 - 3.0
Eosinophil (%)	0.0 - 1.0	0.0 - 2.0	0.0 - 1.0	0.0 - 2.0	0.0 - 2.0	0.0 - 1.0
Basophil (%)	0	0	0	0	0	0

Table 31 Hematological values of male Sprague Dawley rat in the Facility of National Laboratory Animal Centre, Mahidol University

Parameter	4 wks	6 wks	8 wks	10 wks	12 wks	Retired breeder
Red blood cell ($\times 10^6/\mu\text{l}$)	5.6 - 6.7	6.5 - 7.1	6.8 - 7.8	7.2 - 7.7	7.2 - 8.2	7.2 - 8.9
Hemoglobin (g/dl)	11.7 - 13.9	13.7 - 15.1	14.4 - 17.1	14.6 - 15.7	14.6 - 16.0	15.7 - 18.3
Hematocrit (%)	35.9 - 40.4	37.8 - 41.6	37.6 - 43.0	38.0 - 41.7	37.2 - 42.0	42.5 - 51.9
Mean corpuscular volume (fl)	59.7 - 66.7	56.9 - 59.8	53.8 - 57.8	51.7 - 55.0	50.6 - 53.3	55.6 - 61.5
Mean corpuscular hemoglobin (pg)	19.8 - 23.0	20.4 - 21.9	8.9 - 22.9	19.5 - 21.3	19.3 - 21.1	20.1 - 22.1
Mean corpuscular hemoglobin concentration (g/dl)	32.4 - 35.5	35.4 - 37.5	34.2 - 40.5	36.5 - 39.4	36.9 - 39.8	35.1 - 37.4
Platelet ($\times 10^5/\mu\text{l}$)	6.00 - 9.88	6.54 - 12.73	7.07 - 11.89	6.84 - 10.22	6.39 - 9.66	6.01 - 10.11
White blood cell ($\times 10^3/\mu\text{l}$)	2.0 - 5.3	4.1 - 9.4	2.9 - 11.1	3.7 - 8.5	3.2 - 9.0	3.1 - 12.4
Neutrophil (%)	4.0 - 18.0	2.0 - 19.0	3.0 - 16.0	5.0 - 19.0	3.0 - 33.0	4.0 - 60.0
Lymphocyte (%)	82.0 - 96.0	79.0 - 98.0	82.0 - 96.0	79.0 - 94.0	66.0 - 97.0	38.0 - 90.0
Monocyte (%)	0.0 - 3.0	0.0 - 7.0	0.0 - 6.0	0.0 - 4.0	0.0 - 7.0	0.0 - 10.0
Eosinophil (%)	0.0 - 2.0	0.0 - 1.0	0.0 - 3.0	0.0 - 3.0	0.0 - 3.0	0.0 - 20
Basophil (%)	0	0	0	0	0	0

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Table 32 Hematological references values of female Sprague Dawley rat

Parameter	Reference 1		Reference 2					
	11 wks	18 wks	3-5 wks	7-11 wks	12 wks	16-24 wks	49-84 wks	91-105 wks
Red blood cell ($\times 10^6/\mu\text{l}$)	7.79 \pm 0.33	8.09 \pm 0.43	5.19 \pm 0.61	7.05 \pm 0.38	7.14 \pm 0.63	7.60 \pm 0.34	7.46 \pm 0.43	7.27 \pm 0.40
Hemoglobin (g/dl)	16.5 \pm 0.5	15.7 \pm 0.5	11.0 \pm 0.8	14.8 \pm 0.6	14.7 \pm 0.7	15.2 \pm 0.7	14.5 \pm 0.7	14.5 \pm 0.8
Hematocrit (%)	41.8 \pm 0.16	41.2 \pm 0.19	37.4 \pm 2.0	45.6 \pm 1.6	45.3 \pm 2.0	46.0 \pm 1.5	45.1 \pm 1.8	44.7 \pm 2.2
Mean corpuscular volume (fl)	54 \pm 1.3	51 \pm 1.2	72.5 \pm 5.3	64.9 \pm 3.5	63.8 \pm 4.8	60.4 \pm 2.3	60.4 \pm 2.4	61.5 \pm 2.4
Mean corpuscular hemoglobin (pg)	21.1 \pm 0.8	19.4 \pm 0.7	21.4 \pm 1.7	21.0 \pm 1.4	20.7 \pm 1.7	19.9 \pm 0.9	19.5 \pm 0.9	20.0 \pm 0.9
Mean corpuscular hemoglobin concentration (g/dl)	39.2 \pm 1.3	38.2 \pm 1.2	29.5 \pm 1.3	32.3 \pm 0.9	32.4 \pm 1.0	33.0 \pm 1.1	32.1 \pm 0.9	32.5 \pm 0.8
Platelet ($\times 10^5/\mu\text{l}$)	10.60 \pm 1.60	8.97 \pm 1.42	10.38 \pm 2.54	11.35 \pm 2.02	11.12 \pm 1.35	11.39 \pm 2.58	9.80 \pm 1.87	11.20 \pm 2.20
White blood cell ($\times 10^3/\mu\text{l}$)	11.9 \pm 4.6	11.4 \pm 3.8	7.43 \pm 2.96	12.48 \pm 2.69	11.46 \pm 2.57	9.81 \pm 1.79	8.37 \pm 2.01	7.42 \pm 1.62
Neutrophil (%)	9.2 \pm 4.3	10.7 \pm 7.9	14.2 \pm 4.9	15.4 \pm 6.0	12.1 \pm 6.8	15.4 \pm 4.5	23.6 \pm 8.6	28.4 \pm 7.2
Lymphocyte (%)	87.6 \pm 5.4	86.7 \pm 8.0	82.3 \pm 5.4	82.0 \pm 6.6	84.8 \pm 8.3	81.3 \pm 5.1	71.6 \pm 9.3	66.4 \pm 7.5
Monocyte (%)	2.2 \pm 2.0	1.3 \pm 1.3	3.2 \pm 3.2	1.5 \pm 1.4	2.0 \pm 2.5	2.3 \pm 1.6	2.8 \pm 2.1	3.0 \pm 1.5
Eosinophil (%)	1.0 \pm 1.1	1.3 \pm 1.3	0.3 \pm 0.5	0.9 \pm 0.5	1.1 \pm 0.9	1.2 \pm 1.1	1.8 \pm 1.4	1.9 \pm 1.5
Basophil (%)	0	0.07 \pm 0.26	0	0.06 \pm 0.17	0	0.08 \pm 0.19	0.05 \pm 0.23	0.17 \pm 0.35

Reference: 1) Leonard R, Ruben Z. Hematology Reference Values for Peripheral Blood of Laboratory Rats. Lab Ani Sci. 1986; 36(3): 277-281.

2) Feldman BV, Zinkl JG, Jain NC. Schalm's veterinary hematology. 5th ed. Philadelphia: Lea & Febiger, 2000. 1277p.

Table 33 Hematological references values of male Sprague Dawley rat

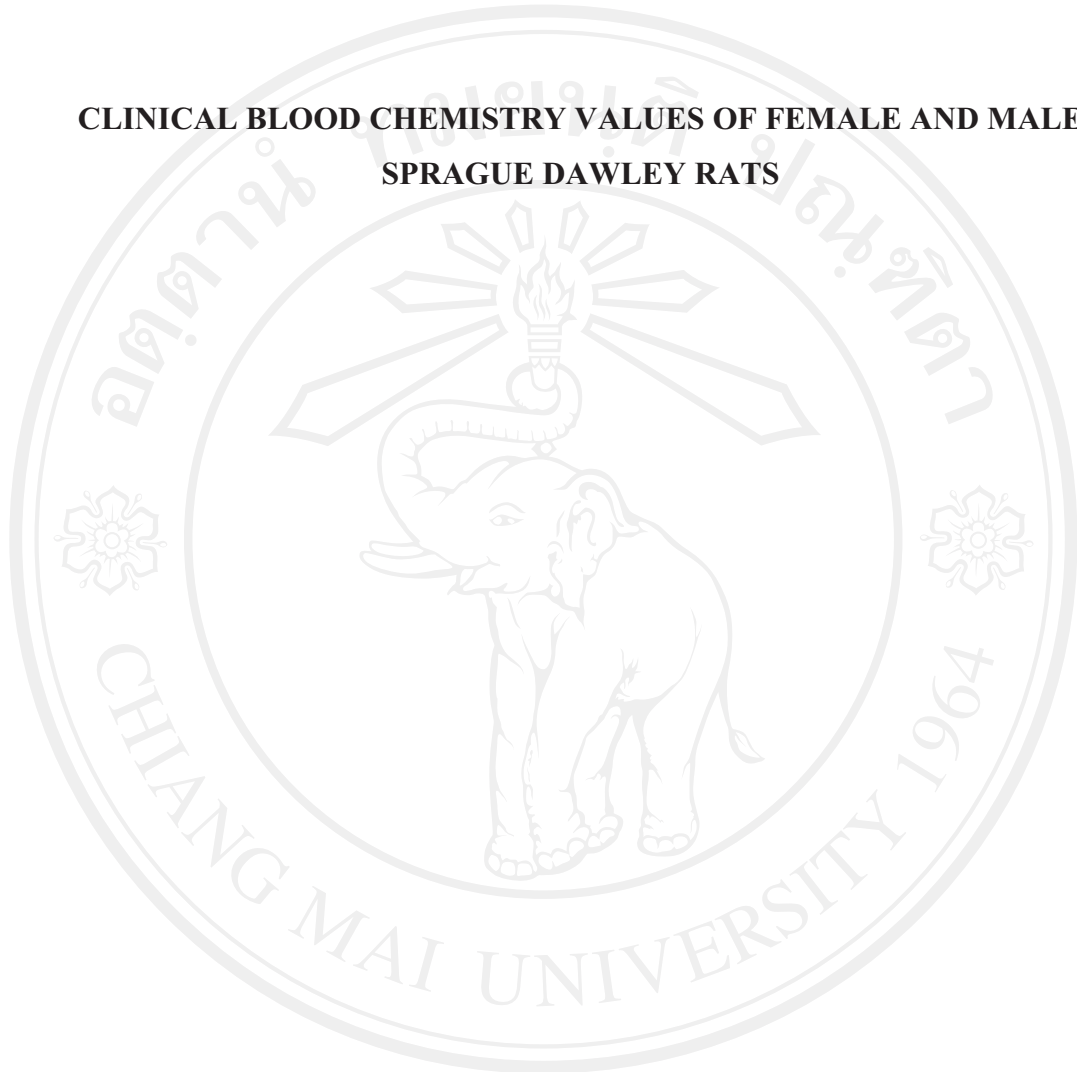
Parameter	Reference		2					
	11 wks	18 wks	3-5 wks	7-11 wks	12 wks	16-24 wks	49-84 wks	91-105 wks
Red blood cell ($\times 10^6/\mu\text{l}$)	7.99 \pm 0.36	8.54 \pm 0.51	5.19 \pm 0.61	7.05 \pm 0.38	7.14 \pm 0.63	7.60 \pm 0.34	7.46 \pm 0.43	7.27 \pm 0.40
Hemoglobin (g/dl)	16.3 \pm 0.6	15.9 \pm 0.8	10.8 \pm 0.8	14.6 \pm 0.6	15.4 \pm 1.1	15.3 \pm 0.6	15.0 \pm 0.9	15.1 \pm 1.0
Hematocrit (%)	42.5 \pm 0.17	41.2 \pm 0.20	36.6 \pm 2.4	46.6 \pm 1.8	48.7 \pm 2.2	48.1 \pm 1.9	47.1 \pm 2.6	46.5 \pm 1.6
Mean corpuscular volume (fl)	54 \pm 1.6	50 \pm 1.7	72.2 \pm 3.8	66.6 \pm 5.0	61.3 \pm 2.3	56.4 \pm 2.4	57.6 \pm 3.4	56.3 \pm 3.3
Mean corpuscular hemoglobin (pg)	20.3 \pm 0.9	18.7 \pm 1.1	20.9 \pm 1.1	20.9 \pm 1.6	19.4 \pm 1.2	17.9 \pm 1.0	18.3 \pm 1.1	18.3 \pm 1.6
Mean corpuscular hemoglobin concentration (g/dl)	39.2 \pm 1.3	38.2 \pm 1.2	29.4 \pm 0.9	31.3 \pm 0.9	31.6 \pm 1.5	31.8 \pm 0.9	31.9 \pm 1.2	32.4 \pm 1.6
Platelet ($\times 10^5/\mu\text{l}$)	10.66 \pm 0.71	8.78 \pm 1.10	11.73 \pm 2.61	10.51 \pm 2.78	0.98 \pm 1.83	10.31 \pm 2.01	11.08 \pm 1.93	11.79 \pm 2.57
White blood cell ($\times 10^3/\mu\text{l}$)	14.8 \pm 3.5	12.1 \pm 2.9	8.34 \pm 2.90	12.46 \pm 3.51	15.26 \pm 3.54	11.98 \pm 3.11	11.59 \pm 2.27	15.08 \pm 13.3
Neutrophil (%)	12.0 \pm 3.6	9.6 \pm 4.8	14.4 \pm 4.5	13.7 \pm 3.9	16.0 \pm 5.6	20.1 \pm 5.6	25.3 \pm 7.3	31.3 \pm 6.4
Lymphocyte (%)	83.6 \pm 5.6	88.2 \pm 5.4	81.9 \pm 5.5	83.6 \pm 4.1	81.5 \pm 5.7	77.3 \pm 6.0	70.6 \pm 8.0	61.9 \pm 6.9
Monocyte (%)	3.9 \pm 2.4	1.5 \pm 1.6	2.9 \pm 1.7	2.0 \pm 1.3	1.5 \pm 1.4	1.4 \pm 1.0	2.3 \pm 1.8	5.0 \pm 2.7
Eosinophil (%)	0.5 \pm 0.8	0.6 \pm 1.2	0.4 \pm 0.7	0.7 \pm 0.7	0.8 \pm 0.7	1.0 \pm 0.9	1.6 \pm 1.2	1.3 \pm 0.9
Basophil (%)	0	0	0.02 \pm 0.10	0.04 \pm 0.13	0.05 \pm 0.15	0.13 \pm 0.24	0.10 \pm 0.31	0.04 \pm 0.13

Reference: 1) Leonard R, Ruben Z. Hematology Reference Values for Peripheral Blood of Laboratory Rats. Lab Ani Sci. 1986; 36(3): 277-281.

2) Feldman BV, Zinkl JG, Jain NC. Schalm's veterinary hematology. 5th ed. Philadelphia: Lea & Febiger, 2000. 1277p.

APPENDIX B

**CLINICAL BLOOD CHEMISTRY VALUES OF FEMALE AND MALE
SPRAGUE DAWLEY RATS**



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Table 34 Clinical blood chemistry values of female Sprague Dawley rat in the Facility of National Laboratory Animal Centre, Mahidol University

Parameter	4 wks	6 wks	8 wks	10 wks	12 wks	Retired breeder
Glucose (mg/dl)	63.5 – 91.7	73.6 – 122.0	86.8 – 122.8	87.3 – 141.7	83.1- 133.9	114.4 – 162.9
BUN (mg/dl)	10.2 – 20.9	13.6 – 23.2	14.2 – 20.0	13.6 – 19.9	13.9 – 21.5	14.9 – 30.7
Creatinine (mg/dl)	0.37 – 0.50	0.46 – 0.58	0.50 – 0.61	0.51 – 0.70	0.50 – 0.65	0.55 – 0.70
Total protein (g/dl)	5.01 – 5.84	5.50 – 6.26	5.89 – 6.86	5.82 – 6.91	5.79 – 6.57	5.95 – 7.48
Albumin (g/dl)	3.80 – 4.40	4.10 – 4.50	4.10 – 4.70	4.10 – 4.90	4.00 – 4.70	3.90 – 4.50
Total bilirubin (mg/dl)	0.04 – 0.11	0.01 – 0.08	0.05 – 0.13	0.05 – 0.12	0.06 – 0.18	0.04 – 0.13
AST (U/l)	115 – 255	90 – 157	89 – 142	78 – 127	78 – 154	80 – 203
ALT (U/l)	27 – 43	23 – 53	22 – 37	20 – 41	21 – 50	24 – 66
Alkaline phosphates (U/l)	203 – 302	117 – 223	77 – 197	64 – 98	55 – 86	39 – 89

Table 35 Clinical blood chemistry values of male Sprague Dawley rat in the Facility of National Laboratory Animal Centre, Mahidol University

Parameter	4 wks	6 wks	8 wks	10 wks	12 wks	Retired breeder
Glucose (mg/dl)	36.2 – 86.4	71.5 – 186.8	93.1 – 142.3	80.3 – 156.7	91.3 – 136.5	97.8 – 157.5
BUN (mg/dl)	10.2 – 18.7	12.9 – 18.1	12.1 – 22.2	10.6 – 18.5	13.2 – 21.8	12.2 – 20.2
Creatinine (mg/dl)	0.35 – 0.50	0.42 – 0.52	0.41 – 0.60	0.46 – 0.65	0.46 – 0.55	0.51 – 0.66
Total protein (g/dl)	4.86 – 5.60	5.50 – 6.26	5.89 – 6.86	5.82 – 6.91	5.79 – 6.57	5.95 – 7.48
Albumin (g/dl)	3.80 – 4.40	4.10 – 4.50	4.10 – 4.70	4.10 – 4.90	4.00 – 4.70	3.90 – 4.50
Total bilirubin (mg/dl)	0.04 – 0.11	0.01 – 0.08	0.05 – 0.13	0.05 – 0.12	0.06 – 0.18	0.04 – 0.13
AST (U/l)	115 – 255	90 – 157	89 – 142	78 – 127	78 – 154	80 – 203
ALT (U/l)	27 – 43	23 – 53	22 – 37	20 – 41	21 – 50	24 – 66
Alkaline phosphates (U/l)	203 – 302	117 – 223	77 – 197	64 – 98	55 – 86	39 – 89

Table 36 Clinical blood chemistry references values of rats

Parameter	Taconic (www.taconic.com/healthr/hematology/sdheme.htm)				University of Minnesota
	6 wks		10-12 wks		
	Male	Female	Male	Female	
Glucose (mg/dl)	249.0 ± 69.2	250.4 ± 71.8	120.7 ± 26.5	186.1 ± 64.0	50 – 160
BUN (mg/dl)	19.6 ± 2.6	20.4 ± 2.6	21.1 ± 1.8	22.3 ± 2.8	10 – 21
Creatinine (mg/dl)	1.4 ± 0.6	1.2 ± 0.7	1.3 ± 0.1	1.3 ± 0.1	0.5 – 1
Total protein (g/dl)	8.2 ± 1.4	7.6 ± 1.2	6.3 ± 0.2	6.4 ± 0.4	5.6 – 7.6
Albumin (g/dl)	3.7 ± 0.1	4.1 ± 1.1	3.4 ± 0.2	3.6 ± 0.1	3.8 – 4.8
Total bilirubin (mg/dl)	0.5 ± 0.2	0.6 ± 0.2	0.2 ± 0.1	0.2 ± 0.2	0.2 – 0.5
AST (U/l)	340.3 ± 58.2	301.3 ± 90.2	332.0 ± 58.0	316.8 ± 47.6	
ALT (U/l)	73.0 ± 24.7	79.3 ± 16.3	78.1 ± 14.8	62.6 ± 23.1	35 – 80
Alkaline phosphates (U/l)	266.5 ± 51.1	171.0 ± 28.4	196.4 ± 52.8	137.6 ± 28.1	16 – 50

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APPENDIX C

DOSE TRANSLATION

For testing new drugs, the most appropriate species for assessing human risk is determined and then followed by toxicology studies. The K_m factor, body weight (kg) divided by body surface area (m^2), is used to convert the mg/kg dose used in a study to an mg/ m^2 dose. The K_m values based on average body surface area calculations for human, baboon, dog, monkey, rabbit, guinea pig, rat, hamster, and mouse (Reagan-Shaw *et al.*, 2008). According to Thai Herbal Pharmacopoeia (THP), the fruit of *P. emblica* is categorized in a group of expectorant, laxative with secondary astringent and antiscorbutic agents and it is recommended for a usage of crude plant material at 6-12 g/day or 100-200 mg/kg/day, the average weight of Thai adult is about 60 kg (Department of Medical Sciences, Ministry of Public Health, 2000). For evaluation of chronic toxicity, the animal dosage of crude plant material for rats can be calculated by the following formula (Reagan-Shaw *et al.*, 2008):

$$\begin{aligned}\text{Animal dose (mg/kg)} &= [(\text{human dose (mg/kg)} \times \text{human } km) / \text{animal (rat) } km] \\ &= [(100 \times 37) / 6] \\ &= 616.67 \text{ mg/kg}\end{aligned}$$

The average yield of crude extract is 8.76%. The dose of crude water extract of *P. emblica* is about 54.02-108.04 mg/kg. So the doses of 300, 600 and 1,200 mg/kg/day crude water extract were set for the experimentation, which are equivalent to 2.8-22.2 times of the normal human dose (crude plant material).

VITA

NAME Miss Kanjana Jaijoy

DATE OF BIRTH 28 March 1977

INSTITUTION ATTENDED

1. Dara Academy School, Chiang Mai, Thailand: Certificate of Mathayom VI
2. Faculty of Nursing, Payap University, Chiang Mai, Thailand: Bachelor of Nursing Science
3. Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand: Master of Science (Pharmacology)

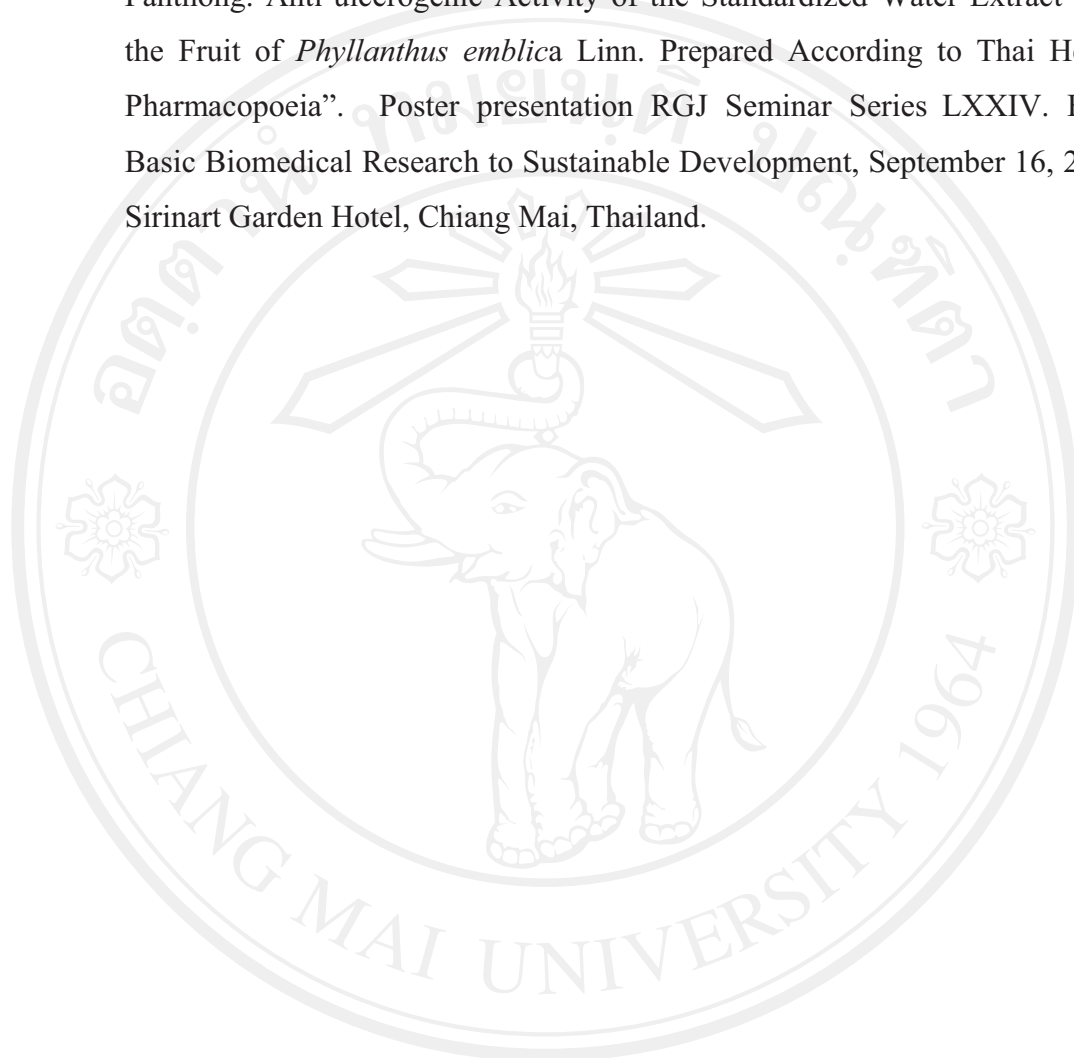
PUBLICATION

1. Jaijoy K, Soonthornchareonnon N, Lertprasertsuke N, Panthong A, Sireeratawong S. Acute and chronic oral toxicity of standardized water extract from the fruit of *Phyllanthus emblica* Linn. IJARNP 2010; 3(1):48-58.
2. Jaijoy K, Soonthornchareonnon N, Panthong A, Sireeratawong S. Anti-inflammatory and analgesic activities of the water extract from the fruit of *Phyllanthus emblica* Linn. IJARNP 2010; 3(2):28-35.

POSTER PRESENTATION

1. Kanjana Jaijoy, Seewaboon Sireeratawong, Noppamas Soonthornchareonnon, Ariyaphong Wongnopphavich, Siriwan Ongchai, Natthakarn Chiranthanut, Parirat Khonsung, Chaichan Sangdee, Ampai Panthong. Anti-inflammatory, Analgesic, Chondroprotective Activities and Toxicity of the Standardized Water Extract from the Fruit of *Phyllanthus emblica* Linn. Prepared According to Thai Herbal Pharmacopoeia". Poster presentation RGJ-Ph.D Congress XI, Research Towards Sustainability, April 1-3, 2010; Jomtien Palm Beach Hotel & Resort Pattaya, Chonburi, Thailand.

2. Kanjana Jaijoy, Seewaboon Sireeratawong, Noppamas Soonthornchareonnon, Natthakarn Chiranthanut, Parirat Khonsung, Chaichan Sangdee, Ampai Panthong. Anti-ulcerogenic Activity of the Standardized Water Extract from the Fruit of *Phyllanthus emblica* Linn. Prepared According to Thai Herbal Pharmacopoeia”. Poster presentation RGJ Seminar Series LXXIV. From Basic Biomedical Research to Sustainable Development, September 16, 2010; Sirinart Garden Hotel, Chiang Mai, Thailand.



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