CHAPTER III

RESULTS

In vitro studies

1. The content of active ingredient

The mean content of gemfibrozil in brand A and brand B were presented as the percent labelled amount in the Table 2 to be 96.60 ± 1.13% (mean ± SD) and 99.08 ± 1.59%, respectively. There were no statistically significant differences in the percent of gemfibrozil between brand A and B at significant level of 0.05 ($p>0.05$).

2. Uniformity of dosage units

Amount of gemfibrozil contained in each capsule of both brand A and brand B shown in Table 3, lied within the range of 93.11 to 99.20% and 93.44 to 99.81%, respectively. The percentage relative standard deviation of brand A and brand B were 1.97 and 2.04 , respectively. The mean amount of both brand A and brand B were 97.20 ± 1.91% and 97.04 ± 1.98%, respectively. There were no statistically signficant differences in the term of percentage of gemfibrozil between brand A and B at significant level of 0.05 ($p>0.05$).

3. Disintegration

The results disintegration time data of gemfibrozil was depicted in Table 4. The mean disintegration time of gemfibrozil capsule for brand A and brand B were 5.26 ± 0.13 minutes and 5.30 ± 0.14 minutes, respectively , in which no statistically significant differences were observed at significant level of 0.05 ($p>0.05$).

4. Dissolution

As present in Table 5 , the percent of gemfibrozil dissolved at 45 minutes in each capsule of both brand A and brand B lied within the range of 90.66 to 99.51% and 87.87 to 98.89%, respectively and the mean percent of gemfibrozil dissolved for brand A and brand B were 96.04 ± 3.48% and 94.44 ± 3.88% , respectively. No statistically significant differences of gemfibrozil dissolved was observed between brand A and brand B at significant level of 0.05 ($p>0.05$).

In Vivo Studies

1. Bioanalytical method validation

1.1 Accuracy

The accuracy of the method for analysing gemfibrozil in serum was determined in term of the percentage of recovery as shown in Table 6. The recovery values were not dependent upon concentration ($p>0.05$). Therefore, the mean recovery representing the accuracy of method was calculated to be 96.05%.

1.2 Precision

The precise for analysing gemfibrozil in serum samples at the same day or at the different day can be demonstated in the term of relative standard deviation (RSD) or the percent coefficient of variation (%CV). As shown in Table 7 and 8, the RSD values of the series of calibration concentration for intra-day and inter-day were in the range of 2.35 to 8.14 and 3.32 to 18.31, respectively. According to the acceptable criteria for the precision validation, It is stated that the acceptable RSD value for any concentration in analysis should not more than 15 excepted the concentration at LOQ, the RSD value can be extended to not more than 20. Therefore , this analytical method is precise enough to be used in analysis of gemfibrozil in serum sample.

1.3 Sensitivity

The lowest limit of quantitation (LOQ) for the analysis of gemfibrozil was determined to be 0.05 μg/ml (n = 5 , RSD = 8.35).

1.4 Selectivity and specificity

The selectivity of the method was proven to be specificity only for gemfibrozil and internal standard as shown in Figure 3 [A] ,[C] and [D]. The retention times of gemfibrozil and internal standard were 9.2 and 5.4 minutes , The retention time observed were similar in either standard solution or spiked serum or serum sample obtained from subject that administered gemfibrozil. Additionally, no interferring endogenous substances in human serum was observed at gemfibrozil or internal standard peak in the chromatogram as shown in Figure 3 [B] ,[C] and [D]. For the serum sample from subject administered gemfibrozil (Figure 3 [D]),

it is noticeable that there were at least two metabolite peaks eluting before internal standard. The content of metabolites varied during sampling time schedule for both the chromatogram from brand A and brand B administration as illustrated in Appendix D.

1.5 Linearity

The calibration curve for the spiked gemfibrozil in human serum was linear over the concentration range of 0 - 48 μg/ml. The curve was constructed in Figure 4. By using linear regression analysis, the represent linear calibration curve equation was

$$y = 0.0657 x + 0.02$$

Where, y is the peak area ratio between gemfibrozil and internal standard , x is concentration of gemfibrozil in serum.

2. The stability study of gemfibrozil in serum at -20 °C

The mean concentration of gemfibrozil in serum at concentrations of 3.0 , 12.0 and 24.0 μg/ml (n=3) were separately plotted against the storage time as shown from Figure 5 to Figure 7. The correlation between gemfibrozil concentration and time was very poor in which the correlation coefficient (r) for concentrations 3.0, 12.0 and 24.0 μg/ml were determined to be 0.1014, 0.2125, 0.0594 , respectively. This confirmed the stability of gemfibrozil in serum up to 42 days without any noticeble decomposition.

3. Characterization of subjects

Selected subjects with the age ranged between 18 and 39 years, body weight and height of 46-68 kg and 155-174 cm , respectively, were selected for this study. They were all passed the physical examination. The physical characteristic and laboratory results of each subject were presented in the Appendix B. All of these data fully confirm the appropriate condition of volunteer using as subject for this study.

4. Pilot study

The serum gemfibrozil concentration-time profiles of subject 01P, 02P, 03P and 04P were depicted from Figure 8 to Figure 11, respectively. From the profiles, the time to peak serum gemfibrozil concentration (Tmax) can be clearly observed and the exponential decline on the elimination phase of drug were properly defined. The time to peak serum gemfibrozil concentration (Tmax) were 1.25-2.00 hours and the peak serum gemfibrozil concentration (Cmax) were 36.19-48.99 μg/ml.

All four volunteer in pilot study did not show any adverse side effects during experiment. In the addition , the complete data of serum analysis of gemfibrozil from pilot study also proved the benefit of assay methodology used.

5. Bioavailability study

5.1 Serum gemfibrozil level

Individual serum gemfibrozil concentration-time profile of brand A and B were depicted from Figure 12 to Figure 23 and their data were fully presented in Appendix C. The concentration-time profiles of

gemfibrozil from each subject displayed the similar pattern in such the way that after reaching the peak concentration, the serum gemfibrozil level declined rapidly within first seven hours and then slowly declined. Comparative of mean serum concentration-time profile of brand A and B gemfibrozil was depicted in Figure 24.

5.2 Pharmacokinetic analysis

5.2.1 Compartmental analysis

By RSTRIP program , all of the data presented that gemfibrozil exhibits the one-compartment model except the data from subject A11 that the two-compartment model was more appropriated .

The pharmacokinetic parameters of gemfibrozil in Thai male subjects calculating from compartmental method were summarized in Table 9-12. The average value of absorption rate constant (Ka) , the elimination rate constant (Ke) , peak serum concentration (Cmax), the time to peak serum concentration (Tmax) , the area under the concentration-time curve ($AUC_{0-\infty}$), the area under the first moment curve ($AUMC_{0-\infty}$), the elimination half-life ($T_{1/2}$) and the mean residence time (MRT) were 0.8415 ± 0.1819 hr^{-1} , 0.6307 ± 0.1353 hr^{-1}, 28.32 ± 9.211 μg/ml , 1.81 ± 0.334 hrs, 106.09 ± 23.529 μg/ml.hr , 305.29 ± 85.041 μg/ml.hr^2 , 1.15 ± 0.227 hr and 2.91 ± 0.560 hr , respectively.

5.2.2 Noncompartmental analysis

The area under the concentration-time curve ($AUC_{0-\infty}$), the area under the first moment curve ($AUMC_{0-\infty}$) , and the mean residence time (MRT) of gemfibrozil calculated from the MKMODEL were presented

in Table 14. The mean values of $AUC_{0-\infty}$, $AUMC_{0-\infty}$ and the MRT of gemfibrozil in Thai male subjects following administration of 600 mg gemfibrozil single dose were 108.93 ± 23.028 μg/ml.hr , 344.27 ± 85.255 $\mu g/ml.hr^2$ and 3.18 ± 0.457 hr , respectively.

5.2.3 The appropriate compartmental model for gemfibrozil in Thai

As presented in Table 15, the $AUC_{0-\infty}$ calculating from compartmental and noncompartmental methods were 106.09 ± 23.529 μg/ml.hr and 108.93 ± 23.028 μg/ml.hr, respectively in which no statistically significant difference were observed at significant level of 0.05.

5.2.4 Relative bioavailability of gemfibrozil between brand A and B

The pharmacokinetic parameters of gemfibrozil in Thai subjects were established in Table 16 to 19. The mean peak serum gemfibrozil concentration (Cmax) for brand A and B were 39.65 ± 9.402 μg/ml and 39.06 ± 10.25 μg/ml , respectively. The mean time to peak serum gemfibrozil concentration (Tmax) were 2.06 ± 0.355 hr for brand A and 1.92 ± 0.358 hr for brand B. The mean absorption rate constant (Ka) were 0.8351 ± 0.1869 hr^{-1} and 0.8478 ± 0.1765 hr^{-1} and the mean area under the concentration-time curve were 113.94 ± 18.232 μg/ml.hr and 103.92 ± 26.037 μg/ml.hr for brand A and brand B , respectively. No statistically significant difference of these values were observed between brand A and B ($p>0.05$). The relative bioavailability was calculated to be 1.09 or 109 %. The pharmacokinetic parameters affecting bioavailability of gemfibrozil were summarized in Table 20.

Table 2 Content of active ingredient of two brands gemfibrozil (n=3)

brand	n	percent labelled amount	percent labelled amount (mean ± SD)	RSD
A	1	95.33	96.60 ± 1.138	1.18
	2	97.52		
	3	96.96		
B	1	97.52	99.08 ± 1.593	1.61
	2	100.7		
	3	99.01		
unpaired t-test			NS (p=0.09)	

Table 3 Dosage form uniformity of gemfibrozil capsules

capsule No.	percent of gemfibrozil	
	brand A	brand B
1	93.11	97.43
2	98.99	97.63
3	98.07	98.02
4	96.37	98.37
5	98.82	93.89
6	98.07	93.44
7	99.20	97.57
8	96.82	99.81
9	97.38	96.41
10	95.19	97.87
mean	**97.20**	**97.04**
SD	**1.91**	**1.98**
RSD	**1.97**	**2.04**
unpaired t-test	**NS (p=0.86)**	

Table 4 Disintegration data of two brands gemfibrozil

capsule No.	disintegration time (min)	
	brand A	brand B
1	5.16	5.36
2	5.33	5.05
3	5.08	5.36
4	5.41	5.47
5	5.38	5.33
6	5.20	5.25
mean	**5.26**	**5.30**
SD	**0.13**	**0.14**
RSD	**2.52**	**2.69**
unpaired t-test	**NS (p=0.59)**	

Table 5 Dissolution data of two brands gemfibrozil capsule

capsule No.	percent of gemfibrozil dissolved at 45 minutes	
	brand A	brand B
1	99.35	94.69
2	95.01	96.09
3	93.92	92.37
4	99.51	87.87
5	97.80	98.89
6	90.66	96.71
mean	**96.04**	**94.44**
SD	**3.48**	**3.88**
RSD	**3.62**	**4.11**
unpaired t-test	**NS (p=0.47)**	

Table 6 The recovery of spiked gemfibrozil in serum (n=3)

concentration gemfibrozil spiked (μg/ml)	recovery of gemfibrozil analysed (%)			percent recovery of gemfibrozil (mean ± SD)	RSD
	1	2	3		
3	102.0	93.78	87.52	94.44 ± 7.262	7.69
16	82.28	105.6	103.4	97.39 ± 13.21	13.6
32	90.44	95.22	103.3	96.32 ± 6.495	6.74
analysis of variances (ANOVA)				**F_{cal} = 0.075** **$F_{0.05}$ (2,6) = 5.14**	
statistic significance				**NS (p=0.93)**	
grand total mean of recovery (%)				**96.05**	

Table 7 Intra-day precision for gemfibrozil analysis in serum (n=3)

concentration (μg/ml)	peak area ratio (mean ± SD)	RSD
0.05	0.0340 ± 0.0028	8.14
0.5	0.0666 ± 0.0044	6.59
3.0	0.2553 ± 0.0060	2.35
6.0	0.4183 ± 0.0113	2.70
12.0	0.9061 ± 0.0364	4.02
24.0	1.6449 ± 0.0638	3.88
48.0	3.1141 ± 0.1546	4.96

Table 8 Inter-day precision for gemfibrozil analysis in serum (n=10)

concentration (μg/ml)	peak area ratio (mean ± SD)	RSD
0.05	0.0258 ± 0.0047	18.31
0.5	0.0599 ± 0.0083	13.92
3.0	0.2265 ± 0.0197	8.68
6.0	0.4154 ± 0.0245	5.89
12.0	0.8377 ± 0.0793	9.47
24.0	1.5743 ± 0.0841	5.34
48.0	3.1333 ± 0.1040	3.32

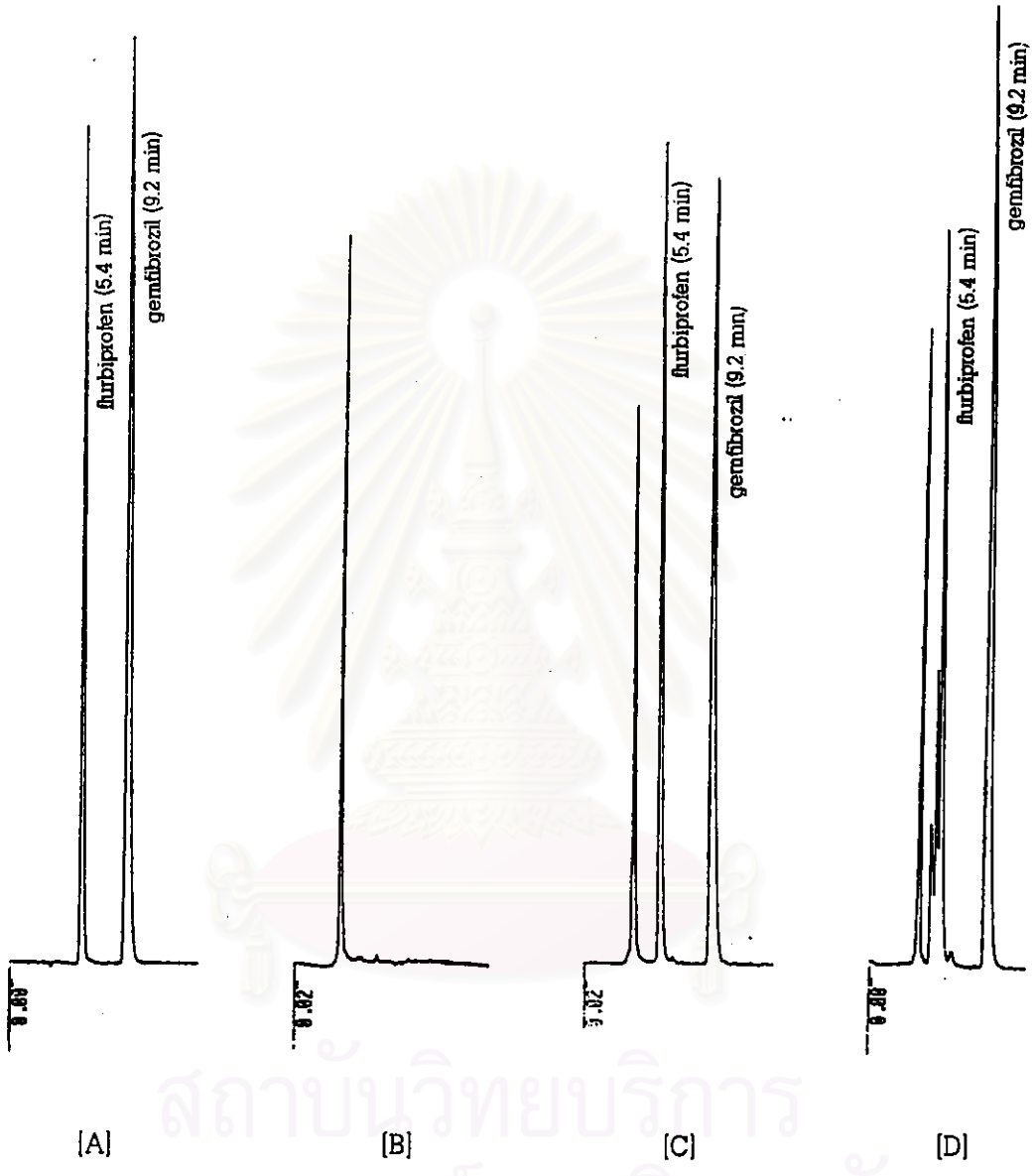

Figure 3 Chromatograms of serum extracts, A = standard solution, gemfibrozil 24 µg/ml B = blank serum ; C = spiked serum, gemfibrozil 24 µg/ml ; D = serum sample 2.5 hr after a 600 mg oral dose of gemfibrozil

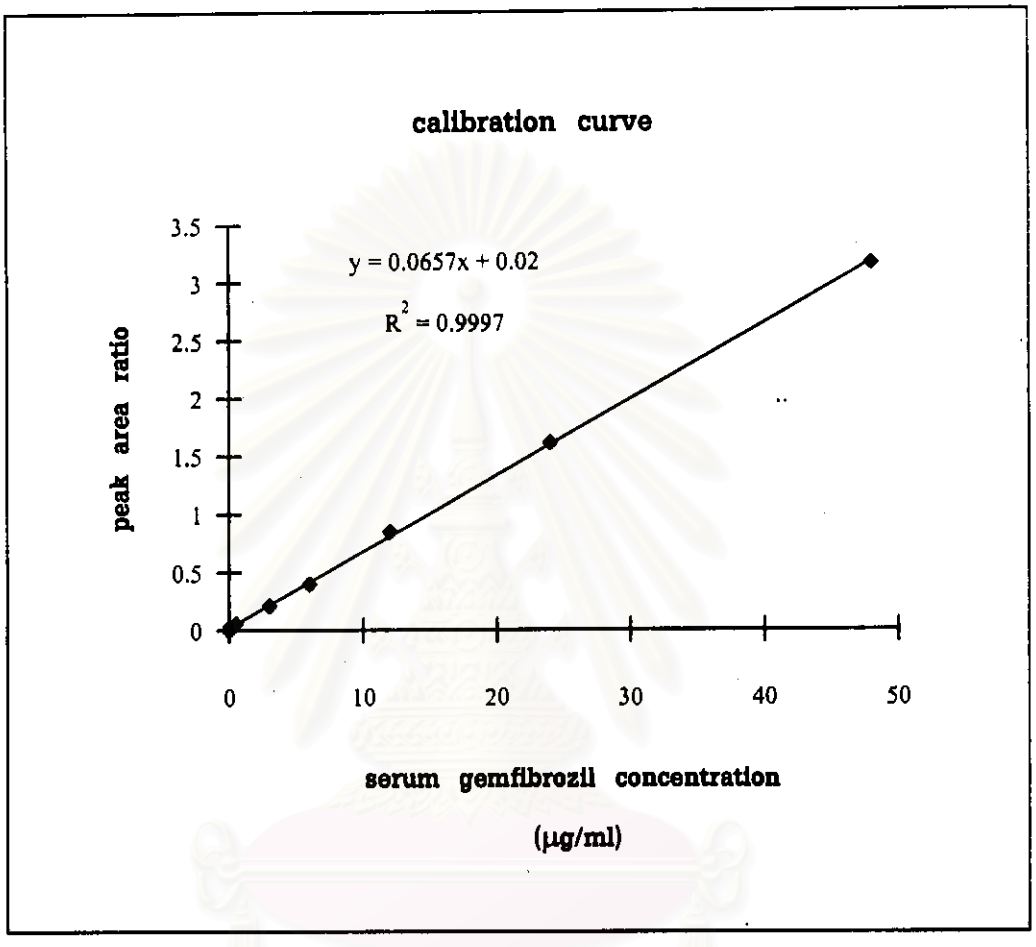

Figure 4 Representation calibration curve for estimation of gemfibrozil in human serum

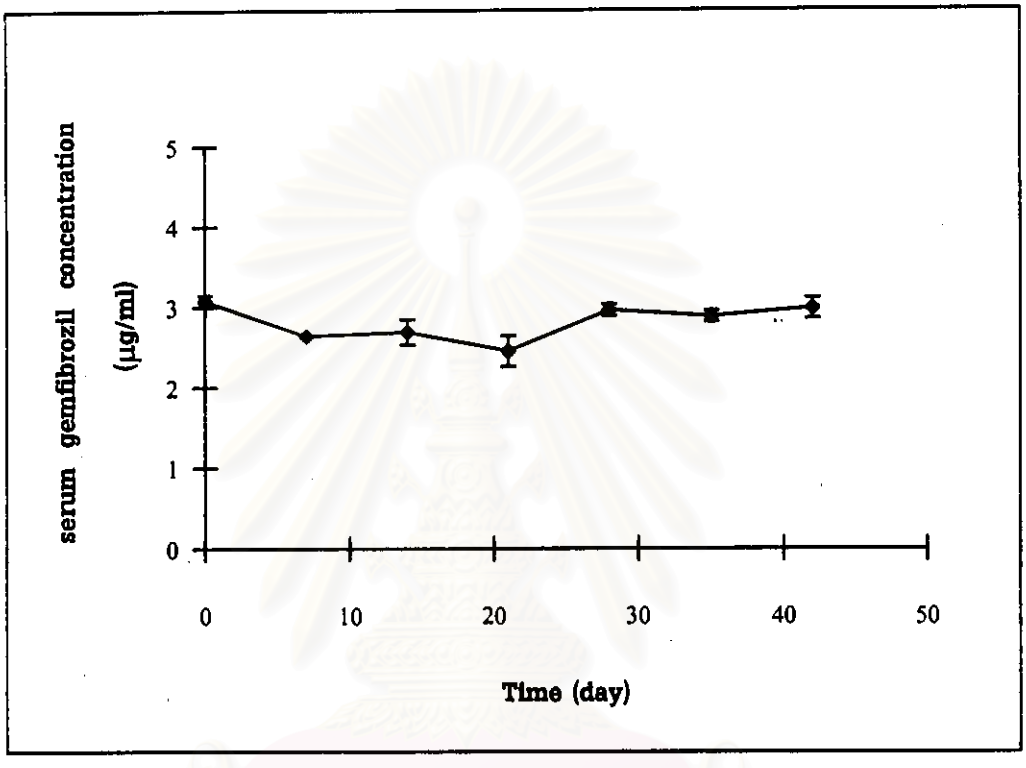

Figure 5 The relationship between mean concentration of spiked serum gemfibrozil concentration of 3 µg/ml (n = 3) and time up to 42 days ; r = 0.1014 (vertical line indicated standard deviation)

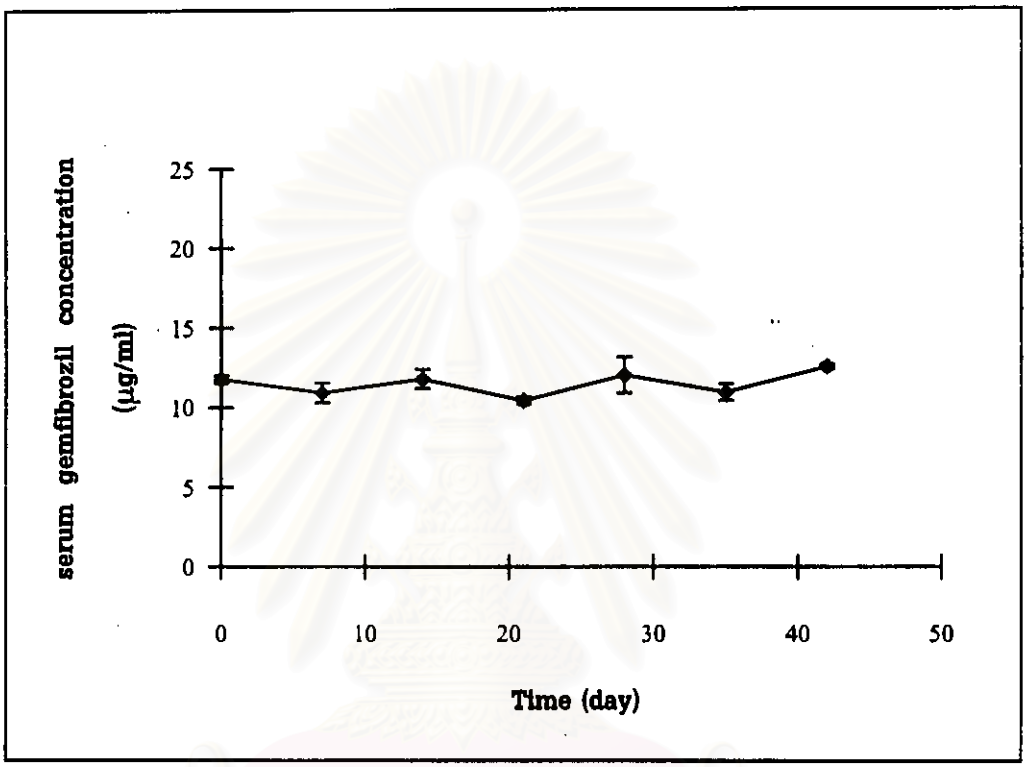

Figure 6 The relationship between mean concentration of spiked serum gemfibrozil concentration of 12 µg/ml (n = 3) and time up to 42 days ; r = 0.2125 (vertical line indicated standard deviation)

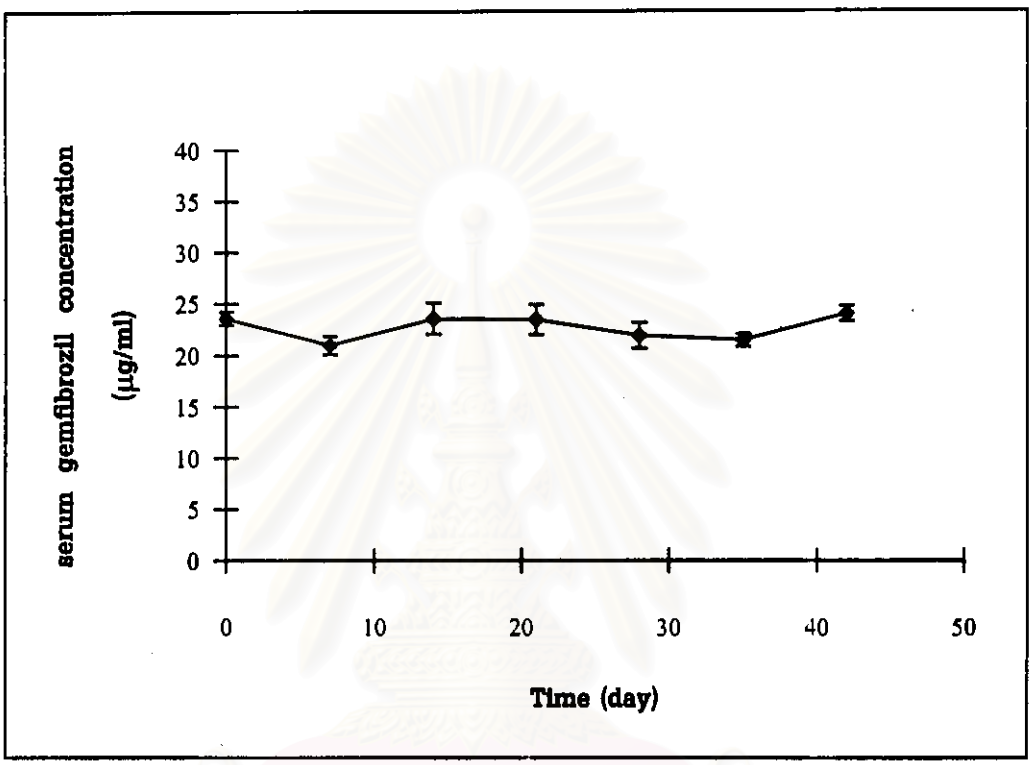

Figure 7 The relationship between mean concentration of spiked serum gemfibrozil concentration of 24 µg/ml (n = 3) and time up to 42 days ; r = 0.0594 (vertical line indicated standard deviation)

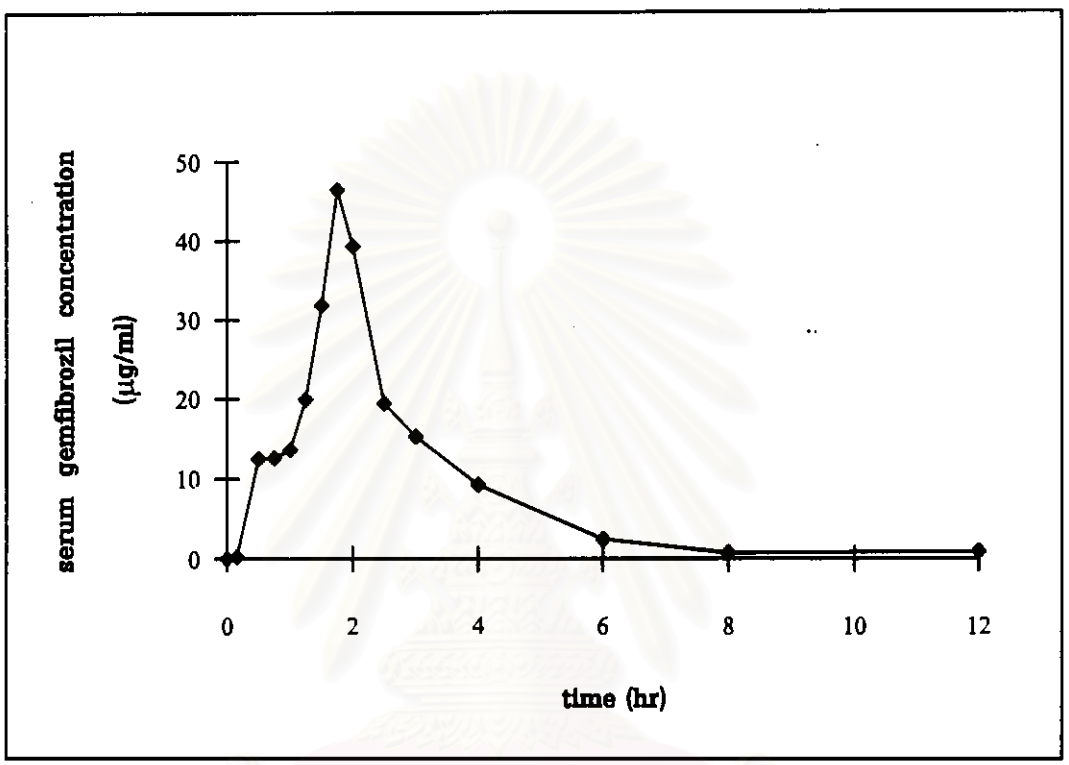

Figure 8 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A) to subject 01P in pilot study

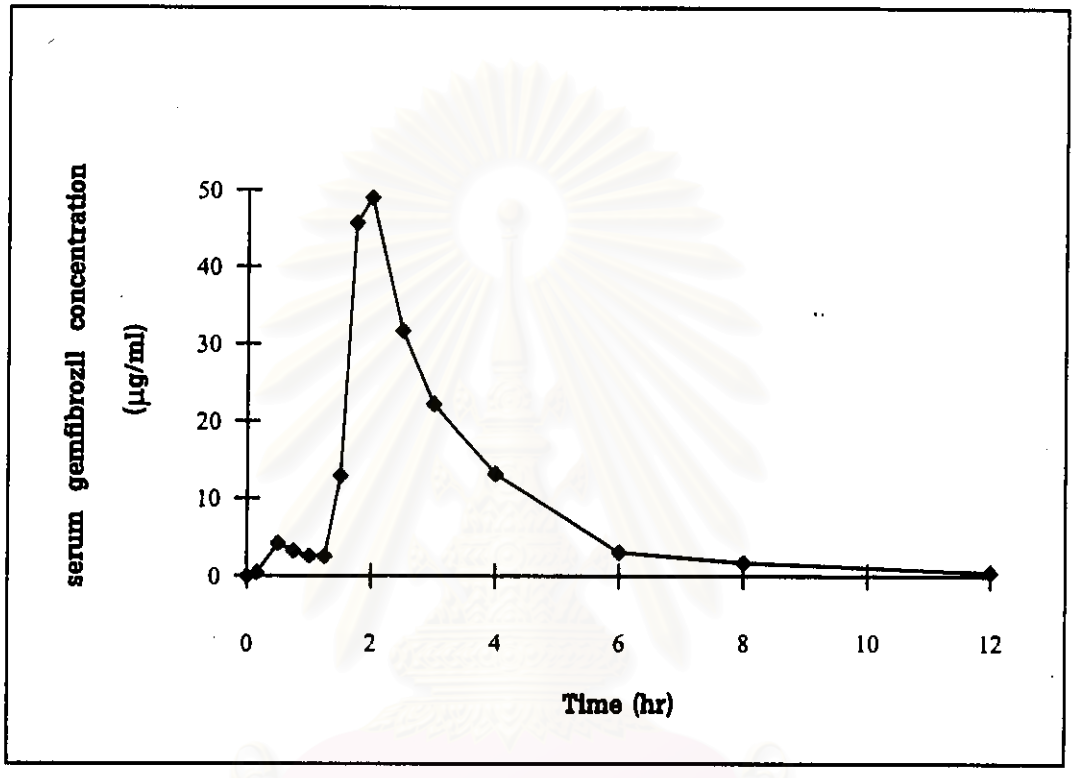

Figure 9 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A) to subject 02P in pilot study

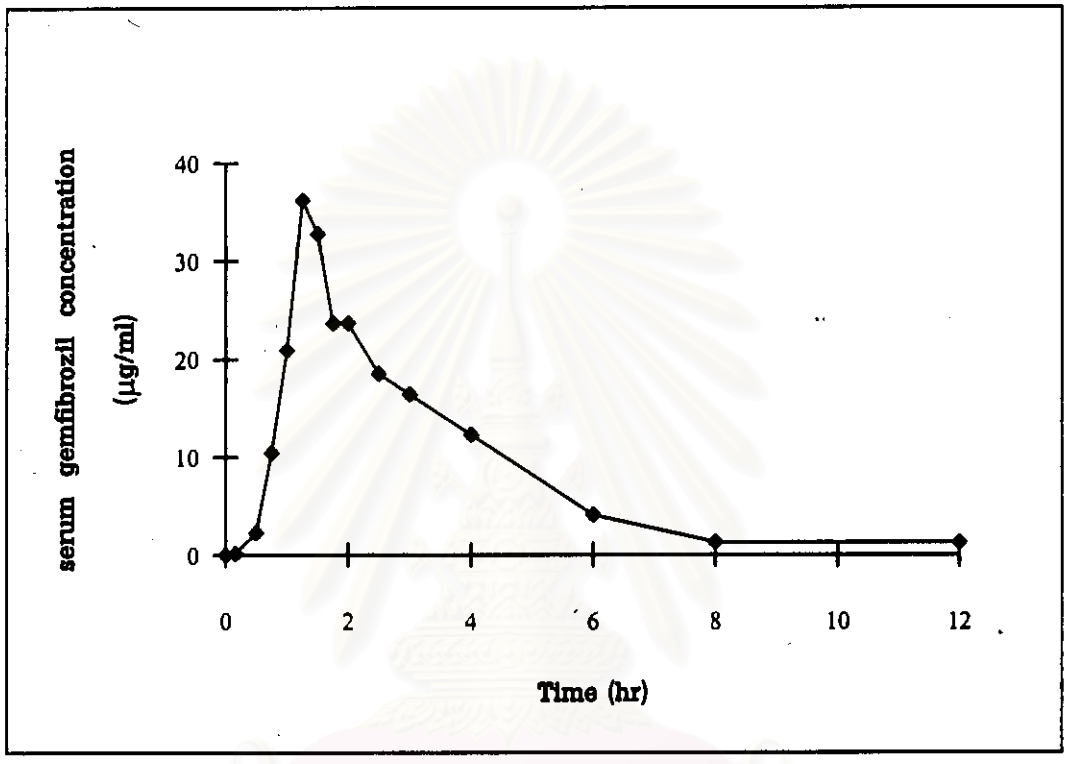

Figure 10 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand B) to subject 03P in pilot study

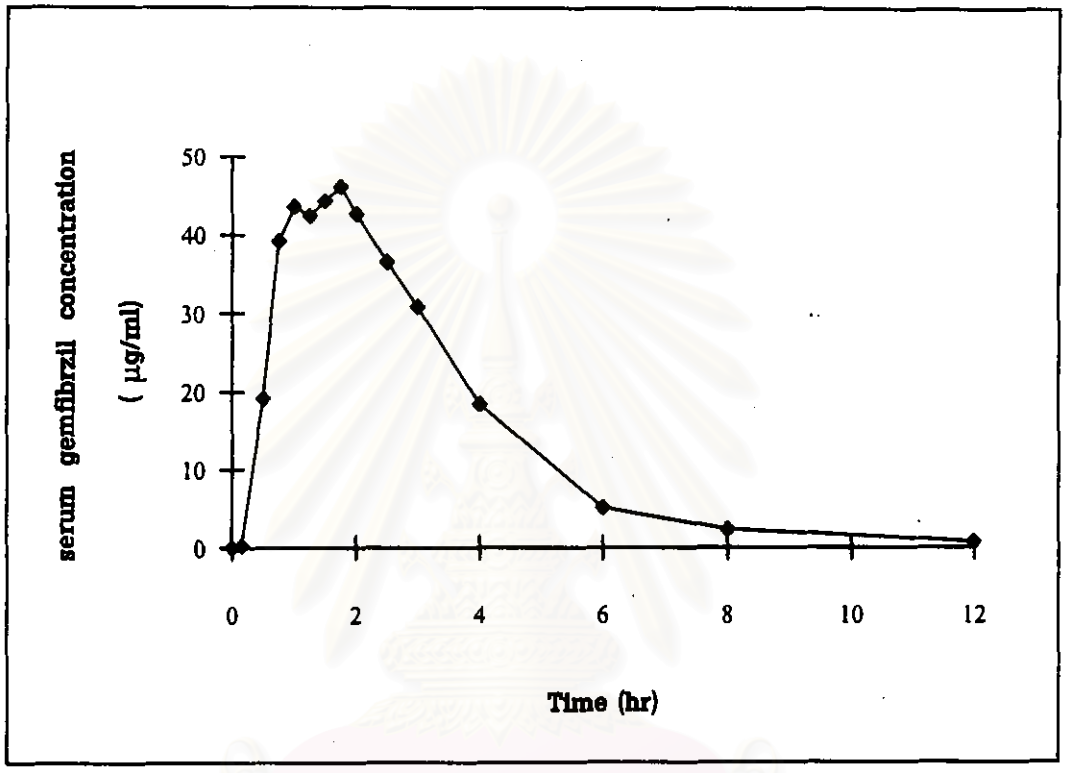

Figure 11 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand B) to subject 04P in pilot study

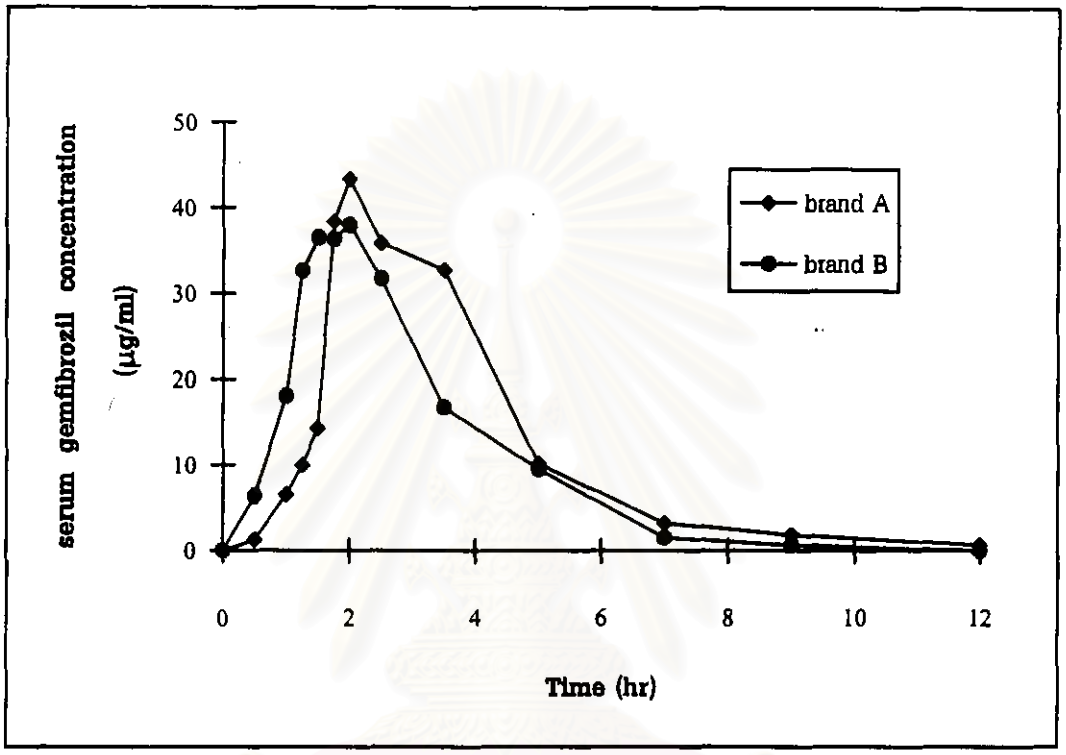

Figure 12 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 01

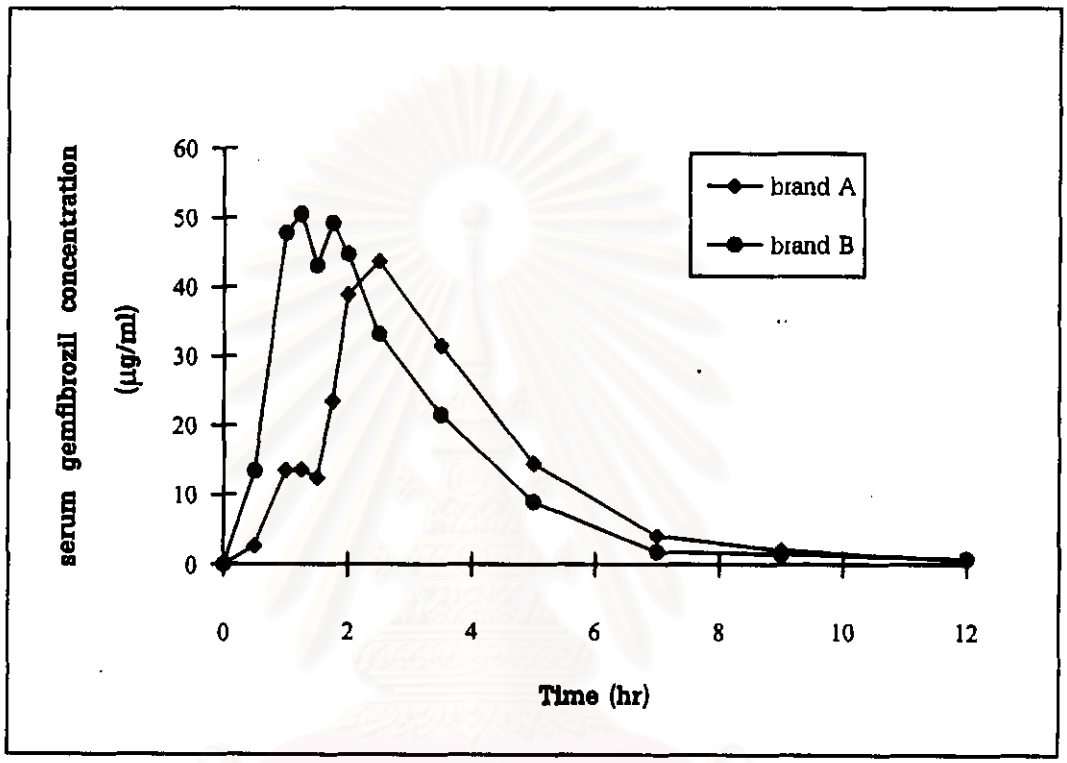

Figure 13 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 02

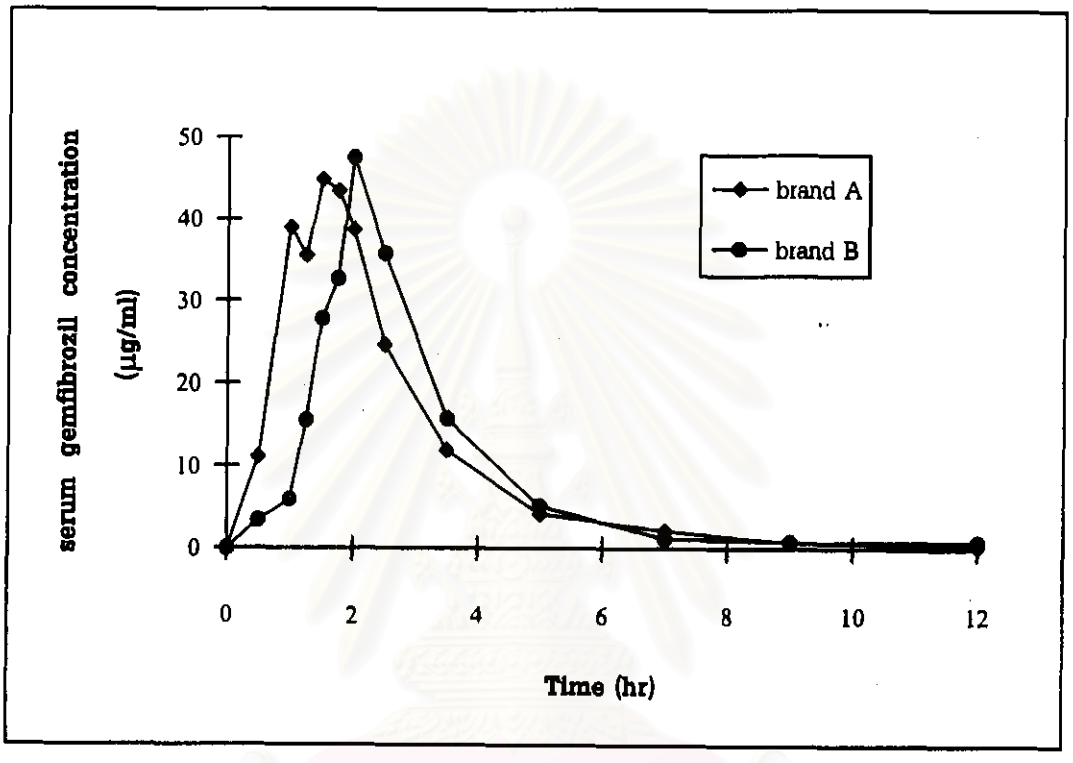

Figure 14 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 03

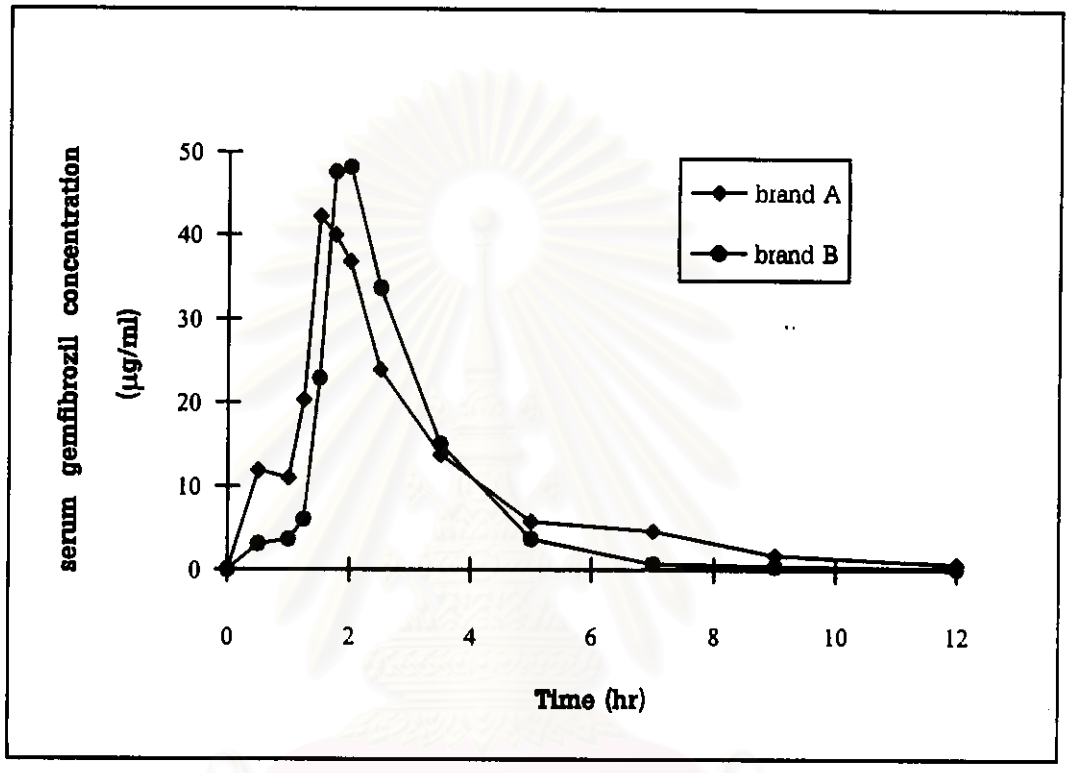

Figure 15 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 04

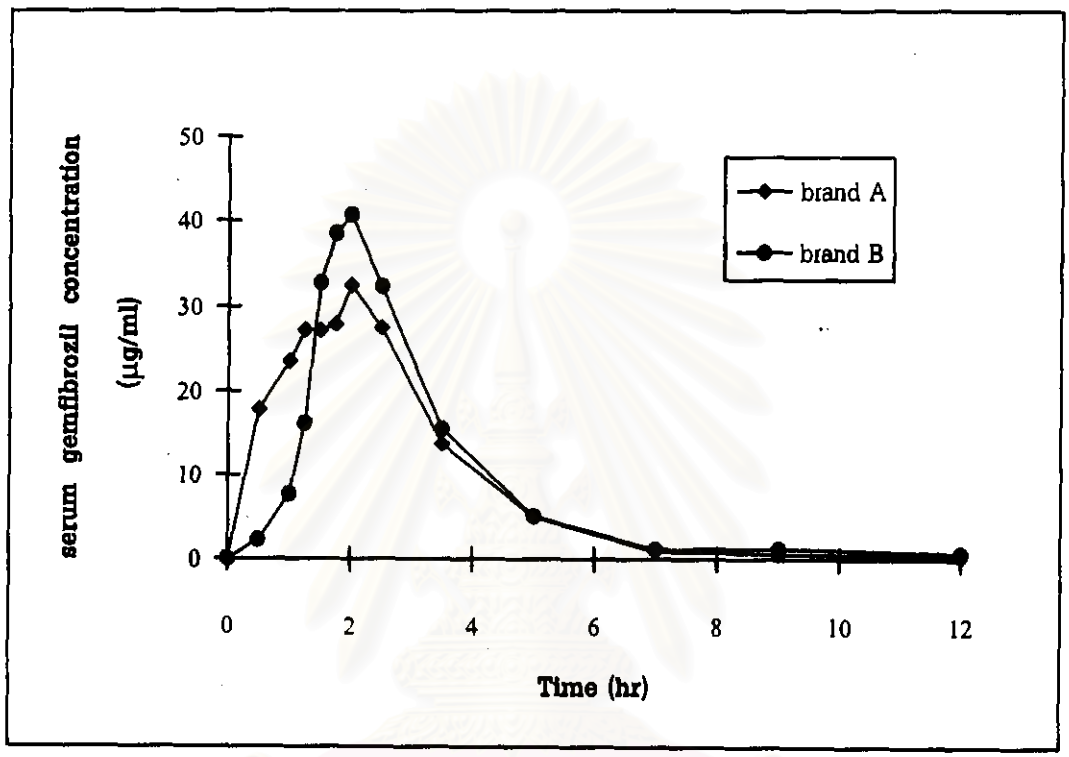

Figure 16 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 05

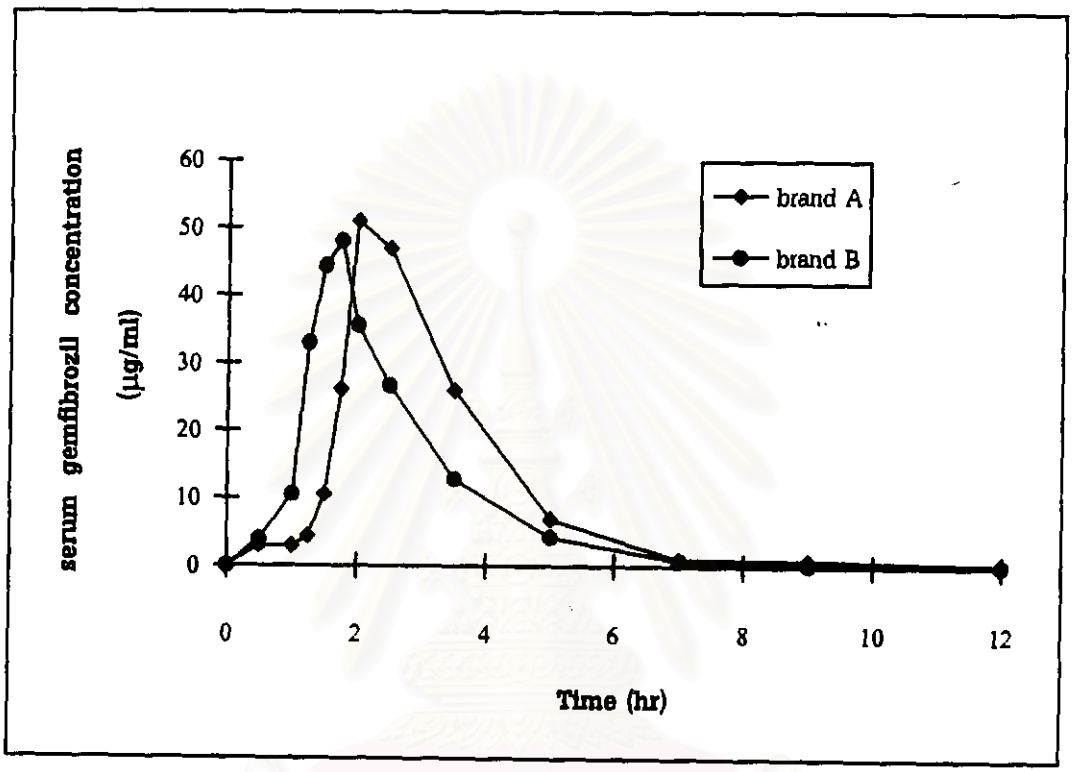

Figure 17 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 06

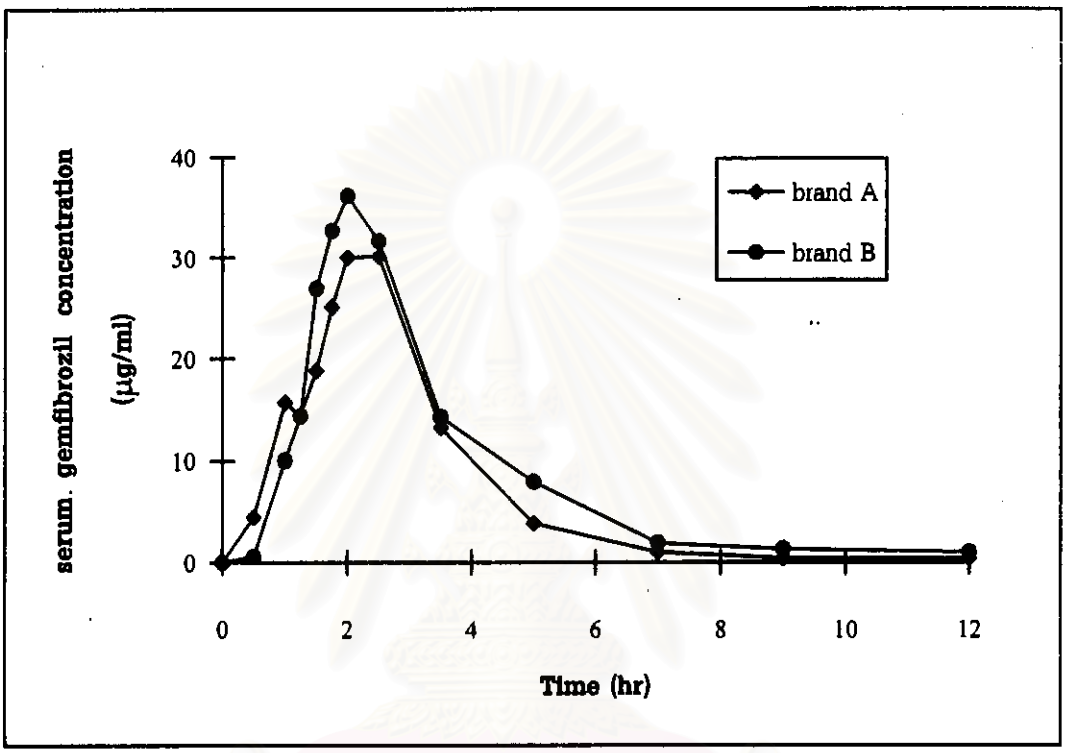

Figure 18 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 07

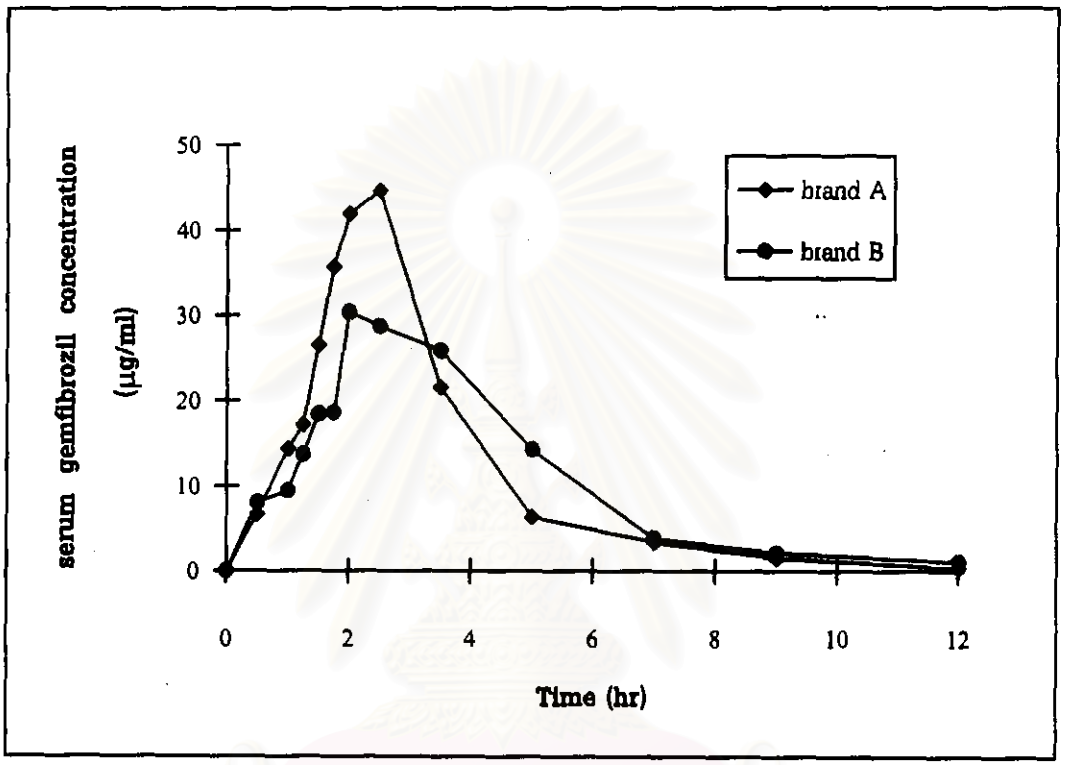

Figure 19 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 08

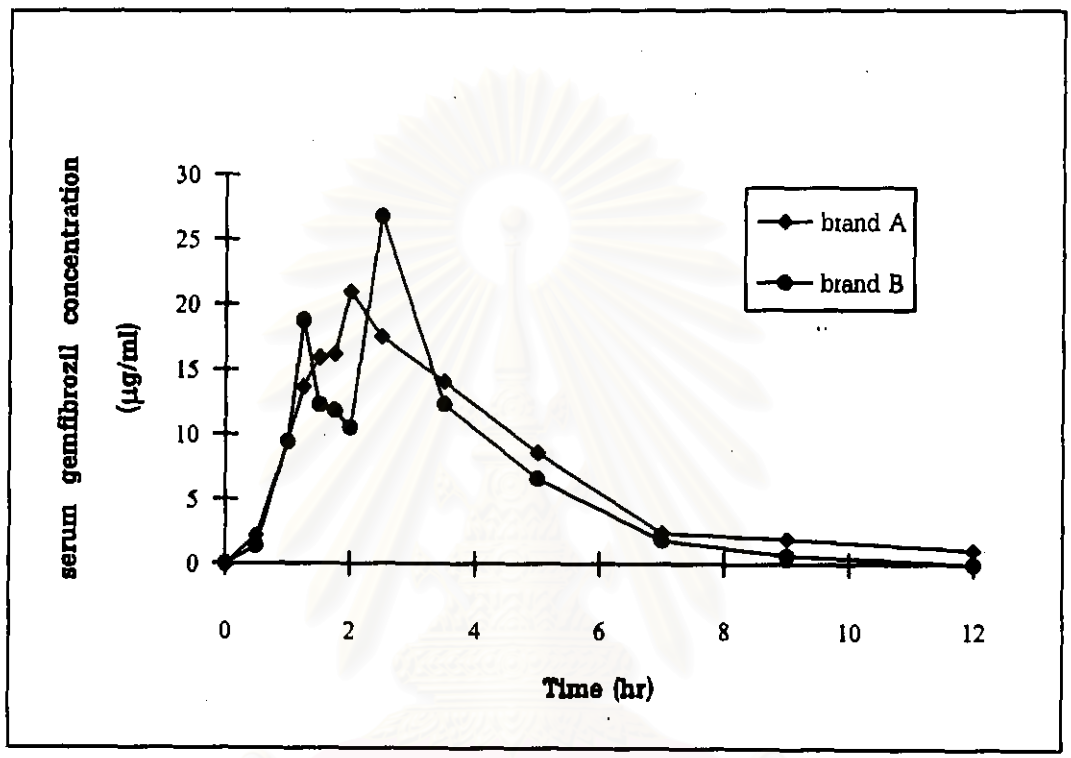

Figure 20 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 09

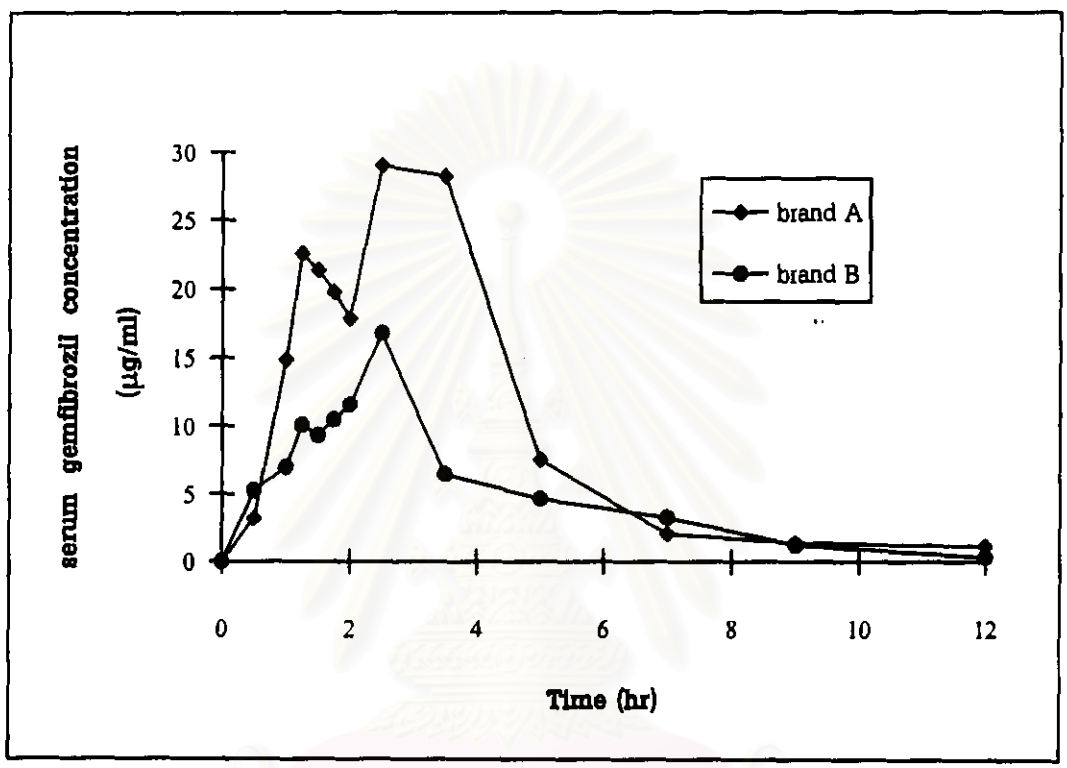

Figure 21 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 10

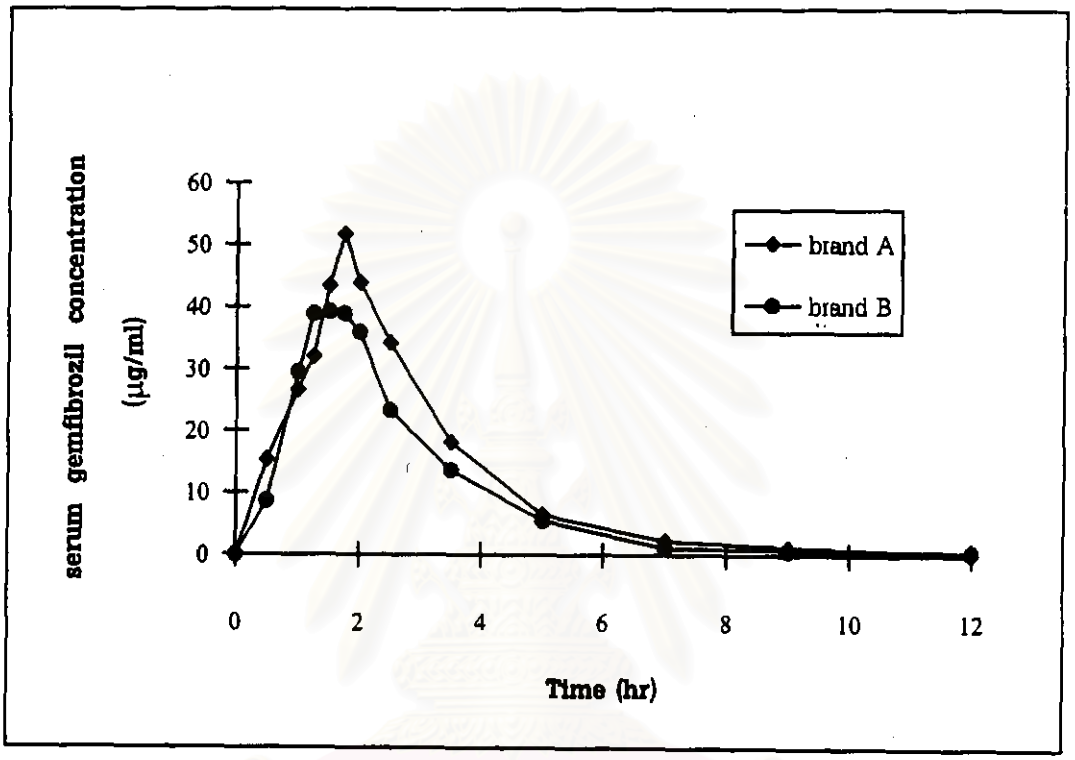

Figure 22 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 11

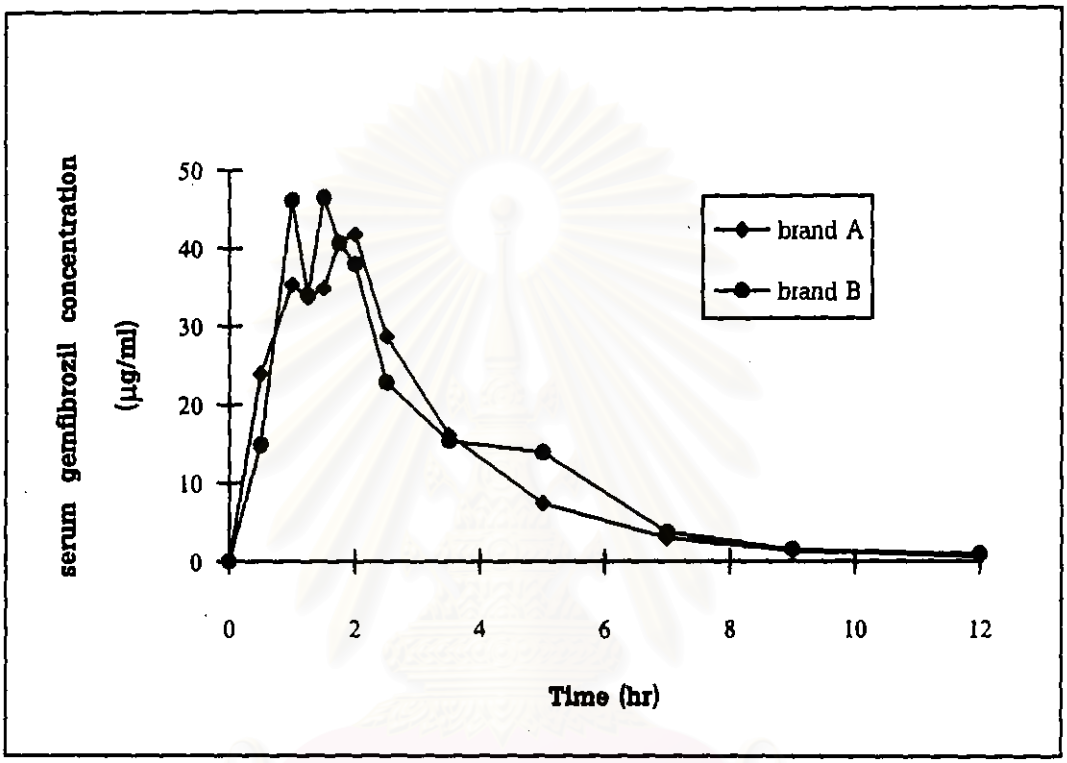

Figure 23 The serum concentration-time profile following single oral dose of 600 mg gemfibrozil (brand A and brand B) to subject 12

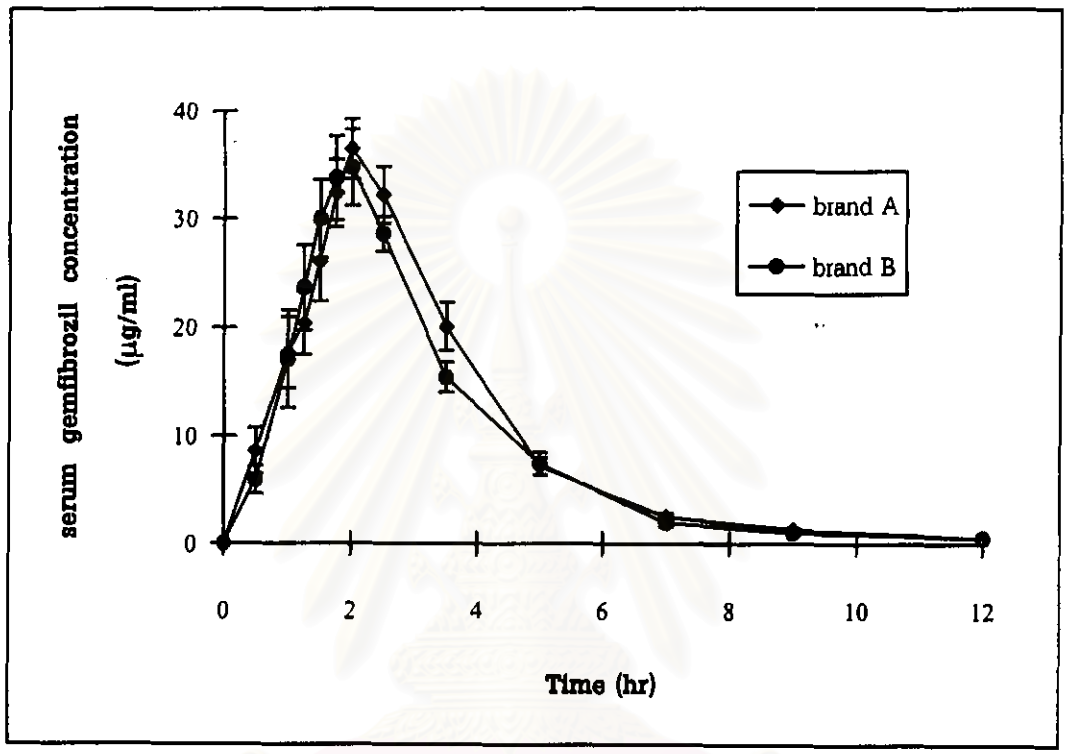

Figure 24 Comparative mean serum concentration-time profile from 12 subjects following single dose of 600 mg brand A and B gemfibrozil (vertical line indicate standard error of mean)

Table 9 Pharmacokinetic parameters ; Ka , Ke , of gemfibrozil obtained from RSTRIP program following 600 mg single oral administration of brand A and brand B gemfibrozil capsule.

N	Ka (hr^{-1})	Ke (hr^{-1})
A01	0.5953	0.5130
A02	0.6214	0.4686
A03	1.3057	0.8672
A04	0.9149	0.5674
A05	0.9413	0.6291
A06	0.6342	0.5263 ..
A07	0.9237	0.6382
A08	0.8384	0.5388
A09	0.6950	0.5094
A10	0.7811	0.5032
*A11	0.9097	0.8605
A12	0.8607	0.6876
B01	0.8641	0.7012
B02	1.0783	0.8565
B03	0.8189	0.6087
B04	0.6489	0.7188
B05	0.8857	0.5950
B06	0.9511	0.8116
B07	0.7830	0.6094
B08	0.5818	0.4529
B09	0.8488	0.5431
B10	0.5711	0.4570
B11	1.1627	0.8822
B12	0.9799	0.5901
mean	**0.8416**	**0.6307**
SD	**0.1819**	**0.1353**

* follow two compartmental model

Table 10 Pharmacokinetic parameters ; Cmax , Tmax , of gemfibrozil obtained from RSTRIP program following 600 mg single oral administration of brand A and brand B gemfibrozil capsule.

N	Cmax (μg/ml)	Tmax (hr)
A01	27.65	2.36
A02	25.23	2.31
A03	42.38	1.34
A04	27.19	1.72
A05	28.19	1.29
A06	16.86	2.29
A07	22.49	1.72
A08	29.72	1.91
A09	17.68	2.13
A10	23.51	2.01
*A11	40.00	1.54
A12	36.94	1.37
B01	34.85	1.73
B02	49.37	1.41
B03	24.80	1.91
B04	21.00	2.02
B05	29.19	1.90
B06	30.77	1.61
B07	26.86	1.97
B08	22.57	2.30
B09	14.01	1.91
B10	11.05	2.01
B11	38.31	1.41
B12	39.12	1.34
mean	**28.32**	**1.81**
SD	**9.211**	**0.334**

* follow two compartmental model

Table 11 Pharmacokinetic parameters ; $AUC_{0-\infty}$, $AUMC_{0-\infty}$, of gemfibrozil obtained from RSTRIP program following 600 mg single oral administration of brand A and brand B gemfibrozil capsule.

N	$AUC_{0-\infty}$ (μg/ml.hr)	$AUMC_{0-\infty}$ (μg/ml.hr^2)
A01	136.26	494.49
A02	127.96	478.98
A03	109.78	210.67
A04	104.55	298.54
A05	100.92	267.62
A06	79.258	274.52
A07	80.532	213.36
A08	122.17	372.46
A09	81.426	277.02
A10	103.59	338.48
*A11	131.42	318.08
A12	131.10	342.97
B01	122.15	315.59
B02	140.26	293.85
B03	96.199	275.53
B04	83.643	245.26
B05	110.74	311.17
B06	95.394	217.83
B07	106.24	310.03
B08	120.15	471.80
B09	57.012	172.15
B10	59.031	232.53
B11	103.48	206.29
B12	142.84	387.83
mean	**106.09**	**305.29**
SD	**23.529**	**85.041**

* follow two compartmental model

Table 12 Pharmacokinetic parameters ; MRT , half-life , of gemfibrozil obtained from RSTRIP program following 600 mg single oral administration of brand A and brand B gemfibrozil capsule.

N	MRT (hr)	half-life (hr)
A01	3.63	1.35
A02	3.74	1.48
A03	1.92	0.80
A04	2.86	1.22
A05	2.65	1.10
A06	3.46	1.32
A07	2.65	1.09
A08	3.05	1.29
A09	3.40	1.36
A10	3.94	1.38
*A11	2.42	0.81
A12	2.61	1.01
B01	2.58	0.99
B02	2.10	0.81
B03	2.86	1.14
B04	2.93	1.07
B05	2.81	1.17
B06	2.28	0.85
B07	2.92	1.14
B08	3.93	1.53
B09	3.02	1.28
B10	3.27	1.52
B11	2.00	0.79
B12	2.72	1.17
mean	**2.91**	**1.15**
SD	**0.560**	**0.227**

* follow two compartmental model

Table 13 Pharmacokinetic parameters ; Cmax , Tmax , obtained from noncompartmental analysis by MKMODEL program following 600 mg single oral administration of brand A and brand B gemfibrozil capsule.

N	Cmax (μg/ml)	Tmax (hr)
A01	43.36	2.00
A02	43.70	2.50
A03	44.86	1.50
A04	42.25	1.50
A05	32.48	2.00
A06	50.97	2.00
A07	30.13	2.50
A08	44.59	2.50
A09	20.93	2.00
A10	29.01	2.50
A11	51.72	1.75
A12	41.77	2.00
B01	37.97	2.00
B02	50.47	1.25
B03	47.49	2.00
B04	48.22	2.00
B05	40.69	2.00
B06	48.03	1.75
B07	36.20	2.00
B08	30.35	2.00
B09	26.75	2.50
B10	16.80	2.50
B11	39.30	1.50
B12	46.47	1.50
mean	**39.35**	**1.99**
SD	**9.420**	**0.364**

Table 14 Pharmacokinetic parameters ; $AUC_{0-\infty}$, $AUMC_{0-\infty}$, MRT , obtained from noncompartmental analysis by MKMODEL program following 600 mg single oral administration of brand A and brand B gemfibrozil capsule.

N	$AUC_{0-\infty}$ (μg/ml.hr)	$AUMC_{0-\infty}$ (μg/ml.hr^2)	MRT (hr)
A01	129.80	483.42	3.72
A02	141.33	518.65	3.71
A03	111.44	288.61	2.59
A04	108.85	368.13	3.38
A05	99.190	273.38	2.76
A06	111.74	349.13	3.12
A07	81.109	239.06	2.95
A08	123.25	396.08	3.21
A09	82.875	358.77	4.33
A10	115.24	379.36	3.29
A11	130.02	354.64	2.73
A12	132.46	380.56	2.87
B01	111.87	311.98	2.79
B02	149.80	414.13	2.76
B03	100.34	327.81	3.27
B04	90.050	249.60	2.77
B05	103.77	306.62	2.95
B06	93.774	240.59	2.69
B07	99.850	364.06	3.65
B08	125.85	482.20	3.83
B09	67.642	217.14	3.21
B10	55.056	211.34	3.84
B11	107.07	281.26	2.63
B12	141.97	465.90	3.26
mean	**108.93**	**344.27**	**3.18**
SD	**23.028**	**85.255**	**0.457**

Table 15 Comparative of $AUC_{0-\infty}$ determinations between the compartmental and noncompartmental analysis by student's t-test

N	$AUC_{0-\infty}$ (μg/ml.hr)	$AUC_{0-\infty}$ (μg/ml.hr)
A01	136.26	129.80
A02	127.96	141.33
A03	109.78	111.44
A04	104.55	108.85
A05	100.92	99.190
A06	79.258	111.74
A07	80.532	81.109
A08	122.17	123.25
A09	81.426	82.875
A10	103.59	115.24
*A11	131.42	130.02
A12	131.10	132.46
B01	122.15	111.87
B02	140.26	149.80
B03	96.199	100.34
B04	83.643	90.050
B05	110.74	103.77
B06	95.394	93.774
B07	106.24	99.850
B08	120.15	125.85
B09	57.012	67.642
B10	59.031	55.056
B11	103.48	107.07
B12	142.84	141.97
mean	**106.09**	**108.93**
SD	**23.529**	**23.028**
t-test	**NS (p=0.68)**	

Table 16 Peak serum concentration (Cmax) observed directly from serum concentration-time data for 12 subjects following 600 mg single oral administration of two brands gemfibrozil capsule.

subject No.	Cmax (μg/ml)	
	brand A	**brand B**
01	43.36	37.97
02	43.70	50.47
03	44.86	47.50
04	42.25	48.22
05	32.48	40.70
06	50.97	48.03
07	30.13	36.20
08	44.60	30.35
09	20.93	26.75
10	29.01	16.80
11	51.72	39.30
12	41.77	46.47
mean	**39.65**	**39.06**
SD	**9.402**	**10.25**
unpaired t-test	**NS (p=0.89)**	

Table 17 Time to peak serum concentration (Tmax) observed directly from serum concentration-time for 12 subjects following 600 mg single oral administration of two brands gemfibrozil capsule.

subject No.	Tmax (hr)	
	brand A	brand B
01	2.00	2.00
02	2.50	1.25
03	1.50	2.00
04	1.50	2.00
05	2.00	2.00
06	2.00	1.75
07	2.50	2.00
08	2.50	2.00
09	2.00	2.50
10	2.50	2.50
11	1.75	1.50
12	2.00	1.50
mean	**2.06**	**1.92**
SD	**0.355**	**0.358**
unpaired t-test	**NS (p=0.35)**	

Table 18 Absorption rate constant (Ka) of gemfibrozil following single oral dose of 600 mg of two brands gemfibrozil capsules.

subject No.	Ka(hr^{-1})	
	brand A	**brand B**
01	0.5953	0.8641
02	0.6214	1.0783
03	1.3057	0.8189
04	0.9149	0.6489
05	0.9413	0.8857
06	0.6342	0.9511
07	0.9237	0.7830
08	0.8384	0.5818
09	0.6950	0.8488
10	0.7811	0.5711
11	0.9097	1.1627
12	0.8607	0.9799
mean	**0.8351**	**0.8478**
SD	**0.1869**	**0.1765**
unpaired t-test	**NS (p=0.83)**	

Table 19 Area under the concentration-time curve ($AUC_{0-\infty}$) calculated according to noncompartmental analysis from 12 subjects following 600 mg single oral administration of two brands gemfibrozil capsule.

subject No.	$AUC_{0-\infty}$ (μg/ml.hr)	
	brand A	brand B
01	129.80	111.87
02	141.33	149.80
03	111.44	100.34
04	108.85	90.050
05	99.190	103.77
06	111.74	93.774
07	81.109	99.850
08	123.25	125.85
09	82.875	67.642
10	115.24	55.056
11	130.02	107.07
12	132.46	141.97
mean	**113.94**	**103.92**
SD	**18.232**	**26.037**
unpaired t-test	**NS (p=0.31)**	

Table 20 Comparative pharmacokinetic parameters affecting bioavailability of brand A and brand B gemfibrozil capsules

parameters	value (mean ± SD)		unpaired t-test*
	brand A	brand B	
Cmax (μg/ml)	39.65 ± 9.402	39.06 ± 10.249	NS
Tmax (hr)	2.06 ± 0.355	1.92 ± 0.358	NS
Ka (hr^{-1})	0.8351 ± 0.1869	0.8478 ± 0.1765	NS
$AUC_{0-\infty}$ (μg/ml.hr)	113.94 ± 18.232	103.92 ± 26.037	NS
relative bioavailability = 1.09 or 109 %			

* at significant level of 0.05