Clinical Pharmacokinetic of Celecoxib in Healthy Thai Volunteers

Chandhanee Itthipanichpong, MSc*,
Sumana Chompootaweep, MD, MPH*, Supeecha Wittayalertpanya, MSc*,
Wandee Kemsri, BSc*, Nongnuch Thaworn, Msc*,
Pajaree Lilitkarntrakul, MD*, Sithiporn Parikamsil, Bsc*

** Department of Pharmacology, Faculty of Medicine, Chulalongkorn University*

Background: *Celecoxib, a nonsteroidal antiinflammatory drug exhibits its antiinflammatory effect by selective inhibition of cyclooxygenase-2 (COX-2) enzyme. Its efficacy has been accepted for the treatment of arthritic pain with superior gastrointestinal side effect profile compared with other conventional NSAIDs.*
Objective: *To elucidate clinical pharmacokinetic of celecoxib following an oral dose administration.*
Material and Method: *Eighteen healthy Thai male volunteers were enrolled in the present study. Their mean age was 20.94 ± 1.21 years and their mean weight was 63 ± 5.17 kg. They were orally administered 200 mg celecoxib after an over night fasting, serial blood samples were drawn before and at 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8, 10,12, 24 and 48 hours after dosing. Plasma celecoxib was analysed by reversed-phase HPLC.*
Results: *Following a 200 mg celecoxib oral administration, the drug was absorbed into the systemic circulation and reach maximum concentration (T_{max}) within 2.50 ± 1.22 hrs by average with the mean peak concentration (C_{max}) of 686.83 ± 211.35 ng/ml. The extent of absorption (area under the curve, AUC) was approximately 5157.12 ± 1499.46 and 5911.48 ± 1363.51 ng hr/ml for $AUC_{0 \rightarrow t}$ and $AUC_{0 \rightarrow \infty}$ respectively. The apparent volume of distribution (Vd) was found to be 458.93 ± 323.28 L/hr. Celecoxib was eliminated after biotransformation and the metabolites were excreted in both urine and feces. The elimination half-life (t) of celecoxib appeared to be 8.79 ± 5.49 hrs with the apparent clearance (CL) of 35.91 ± 9.85 L. The elimination rate constant for celecoxib obtained from this present study was about 0.11 ± 0.05 hr^{-1}.*
Conclusion: *Pharmacokinetic parameters following an oral dose of 200 mg celecoxib administration were characterized, including C_{max}, T_{max}, Vd, kel, CL, AUC. These parameters reflected absorption, distribution, biotransformation and excretion of celecoxib in healthy Thai volunteers.*

Keywords: *Celecoxib, Pharmacokinetic*

J Med Assoc Thai 2005; 88(5): 632-8
Full text. e-Journal: *http://www.medassocthai.org/journal*

Celecoxib is a nonsteroidal anti-inflammatory drug use for the treatment of several inflammatory and painful conditions eg. osteoarthritis, rheumatoid arthritis. It is the first selective inhibitor of cyclooxgenase-2 (COX-2) available in the market[1]. A reduction of cyclooxygenase-2-dependent prostaglandins, the key mediators for inflammation was found both in vivo and in vitro study.The upper gastrointestinal complication rate in clinical trials was significantly lower for celecoxib than for traditional nonselective NSAIDs (eg. naproxen, ibuprofen) while its therapeutic efficacy was similar to the conventional drugs[1-3]. Therefore, celecoxib is one of the useful alternative NSAIDs for the treatment of osteoarthritis, rheumatotcid arthritis, particularly in patients at high risk of developing gastrointestinal events. Celecoxib is well absorbed and is extensively metabolized in humans, with less than 3% of the dose excreted unchanged in urine and feces. The major route of metabolism appears to be methyl hydroxylation which primarily catalyzed by human liver microsomal CYP2C9[4]. Evidence from literature review demonstrated that there were interethnic differences on drug's pharmacokinetic and may con-

Correspondence to : Itthipanichpong C, Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

tribute to variability to drug response[5,6]. Up to the present there is increasing use of specific COX-2 inhibitor and no clinical pharmalokinetic data has been reported in Thai volunteer? Therefore, the objective of this present study was to characterize the pharmacokinetic parameters of celecoxib after a 200 mg oral dose administration to healthy Thai volunteers.

Material and Method

Subjects and dosages

Eighteen healthy Thai male volunteers between the ages of 18-25 years were administered an oral dose of 200 mg celecoxib. They have been resident in Thailand for at least two generations. They were considered healthy on the basis of their medical history, physical examination, blood chemistry and urinalysis. All volunteers were absent from hypersensitivity to drugs especially drugs in sulfonamide group. Written informed consents were obtained before entering the present study.

Chemicals

The chemical for HPLC analysis was HPLC grade eg. acetronitrile which was purchased from Merck Co Ltd, Germany as well as disodium hydrogenphosphate. Ibuprofen was from BASF Company, Germany.

Analysis of celecoxib in human plasma

For analysis of plasma celecoxib, high performance liquid chromatography technic was used according to a modified method of Schonberger F[7].

Series of standard celecoxib concentration, 3200, 1600, 800, 400, 200, 100, 50 ng/ml were prepared for construction of a calibration curve.

HPLC condition

Mobile phase : 33% 50 mM acetate buffer pH 4.3:67% acetronitrile

Flow rate : 1.2 ml/min

Column : Inertsil ODS-3 C18 silica column, column size 4.6 x 250mm, silica size: 5 μm, porous size: 0.45 μm by GL Sci Inc. Japan

Detector : Fluorescence detector (Excitation: emission wave length was 240:380 nm)

Injection volume : 50 μl

Sample preparations

To 0.5 ml of plasma, 10 μl of internal standard (36.8 μg/ml) was added. After mixing, proteins were precipitated with 1.8 ml acetronitrile. The samples were mixed by vortex and centrifuged at 4,000 rpm for 5 minutes. The supernatant was then transferred and evaporated to dryness with speed vacuum. The residue was dissolved in 500 μl of mobile phase and the solution was centrifuged again at 4,000 rpm for 10 minute. Aliquot of 50 μl of supernate was used for HPLC analysis.

In vivo study

After an overnight fasting, 5 ml of blood samples were drawn from each subject as the baseline control (time 0). Vital signs were also measured before blood samples were drawn for the control purpose. Then the subjects received a single oral dose of 200 mg celecoxib with 200 ml of water. Sixteen aliquot of blood samples (5 ml) were collected in sodium heparin tube before dosing and at 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8, 10, 12, 24 and 48 hours after dosing. Plasma samples were kept at -20°C until drug analysis was performed.

Ethical consideration

The study protocol, consent form, patient information sheet and case report form were approved by the Institutional Ethical Review Committee (Faculty of Medicine, Chulalongkorn University). The present study was carried out in accordance with recommendations of World Medical Association Declaration of Helsinki.

Adverse events monitoring

Adverse events of all volunteers were closely monitored during and a week after study periods. Case report forms were used to record all adverse events encountered by the volunteers.

Data analysis

Pharmacokinetic parameters measurements:

1. Time to reach the maximal concentration (T_{max})

2. Maximal plasma concentration (C_{max})

Both T_{max} and C_{max} were taken from plasma drug concentration profile of each individual.

3. Area under the plasma concentration-time curve from zero to the last quantifiable concentration ($AUC_{0\rightarrow t}$) was calculated using trapezoidal rule

4. Area under the plasma concentration-time curve from zero to infinity ($AUC_{0\rightarrow t}$) is the sum of ($AUC_{0\rightarrow t} + AUC_{t\rightarrow\infty}$ where $AUC_{t\rightarrow\infty}$ (extrapolated AUC from t to infinity) was determined as Ct/kel

5. Half-life ($t_{1/2}$) was calculated from the formula $t_{1/2} = 0.693/kel$

6. Apparent volume of distribution (Vd) was calculated from the formula $Vd = CL/kel$

7. Apparent clearance (CL) was calculated from the formula $CL = F_0 \quad Dose/AUC_{0\rightarrow\infty}$

8. Elimination rate constant (kel) was obtained from the slope of log concentration-time curve in elimination phase

Since there is no clinical data available for oral bioavailability of celecoxib (F_0), thus clearance (CL) in this present study meant CL/F_0 and the apparent volume of distribution (Vd) meant Vd/F_0.

Statistical analysis

All pharmacokinetic parameters were presented according to descriptive statistics; mean $\pm$ standard deviation. ($\bar{x} \pm$ SD), Linear regression and correlation analysis was applied to find the relationship between peak area ratio and celecoxib concentration.

Results

Analytical method validation

In vitro plasma analysis of celecoxib concentration by reversed-phase HPLC using fluorescence detector demonstrated high selectivity. A clear separation of celecoxib peak and ibuprofen peak (internal standard) are shown in Fig. 1. The retention time of celecoxib and ibuprofen was 5.9 and 5.3 min. respectively. Linear relationship between peak area ratio and celecoxib concentration was observed ($r^2 > 0.998$) over 5 orders of magnitude (concentration range from 50-3200 ng/ml, Fig. 2). Recoveries of the analyte varied between 90-110% for high, medium and low concentration. (3200, 800 and 100 ng/ml respectively) The inter-day and intra-day precision were in the acceptable range (%CV < 15%).

In vivo study

All the male subjects who participated in this present study were healthy according to their medical history, physical examination and blood chemistry evaluation (Table 1). Their age ranged from 19-23 years (average 20.94 $\pm$ 1.21, the weight and height ranged from 71.5-54.5 kg and 187-165 cm) (mean weight = 63.00 $\pm$ 5.17 kg, mean height = 173 $\pm$ 6.49 cm). Their body mass indexes were within the normal range (18-24 kg/m^2). The summary of the subject demographic characteristics are shown in Table 1. Each subject completed the study without any adverse events. The mean celecoxib plasma concentration-time profile is demonstrated in Fig. 3, Table 2.

After oral administration of 200 mg celecoxib, an average maximum concentration (C_{max}) was found to be 686 $\pm$ 211.35 ng/ml, while the time to reach peak

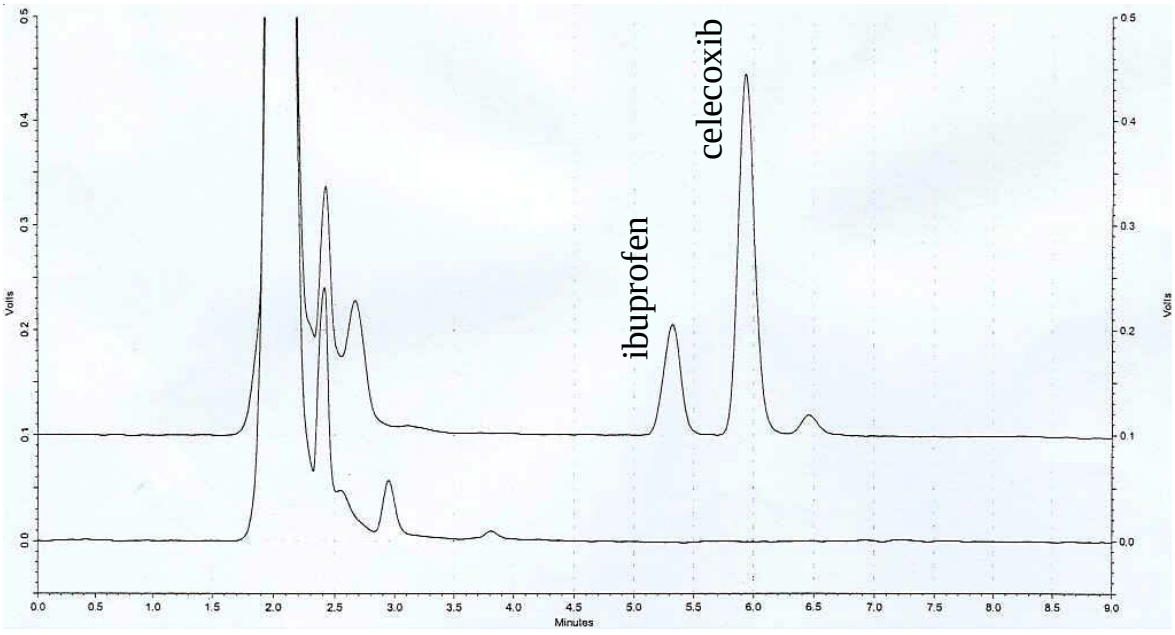

Fig. 1 Representative chromatograms of blank plasma, celecoxib (RT = 5.9) and ibuprofen (internal standard, RT = 5.3 min) of a volunteer

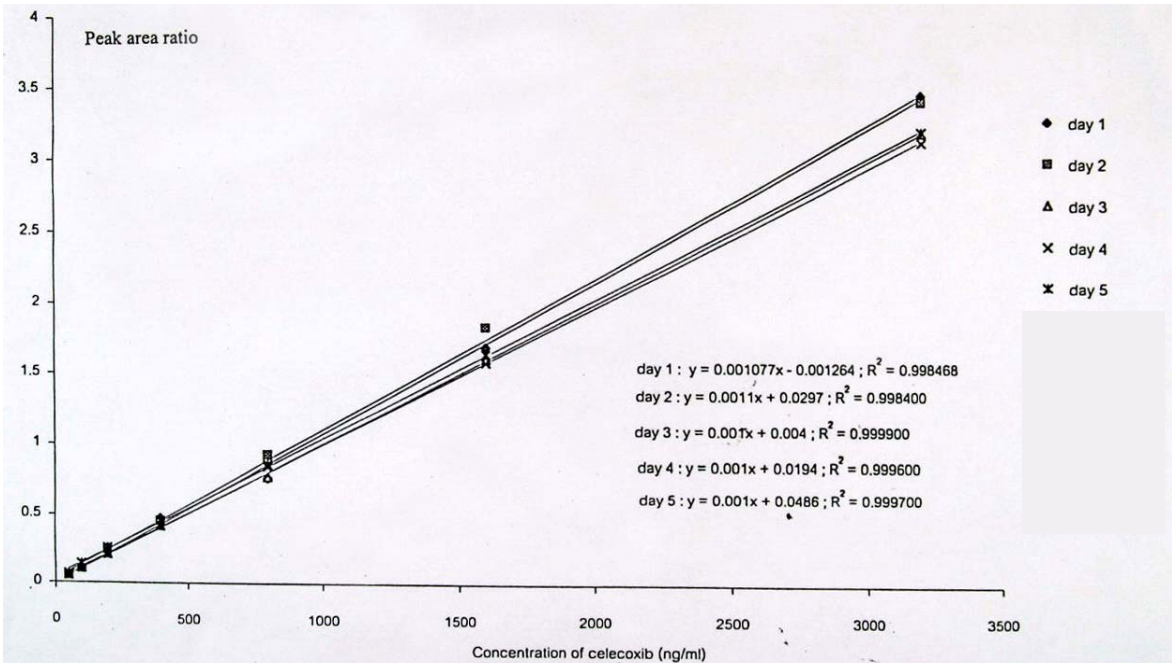

Fig. 2 Standard calibration curve of celecoxib in plasma

plasma concentration (T_{max}) was 2.5 ± 1.27 hrs. The extent of drug absorption which was characterized by area under the plasma concentration-time from zero to infinity ($AUC_{0\rightarrow\infty}$) was shown to be 5911.48 ± 1363.51 ng hr/ml and 5157 ± 1499.49 ng hr/ml for $AUC_{0\rightarrow t}$. The

Table 1. Demographic data of healthy male volunteers participated in study

Subject No.	Sex	Age	Height	Weight	Body mass index (BMI)
1	male	20	169	63	22.06
2	male	20	175	66	21.55
3	male	20	167	61	21.87
4	male	19	165	54.5	20.02
5	male	20	169	71.5	25.03
6	male	20	170	62	21.45
7	male	19	173	62	20.72
8	male	23	185	68	19.86
9	male	23	171	60	20.52
10	male	21	173	59	19.71
11	male	22	168	58	20.55
12	male	21	175	67	21.88
13	male	21	187	70	20.05
14	male	22	180	71	21.92
15	male	21	182	66.5	20.07
16	male	22	171	60	20.52
17	male	21	173	56	18.71
18	male	22	165	58.5	21.48
Mean		20.94	173.22	63.00	20.95
SD		1.21	6.49	5.17	1.43

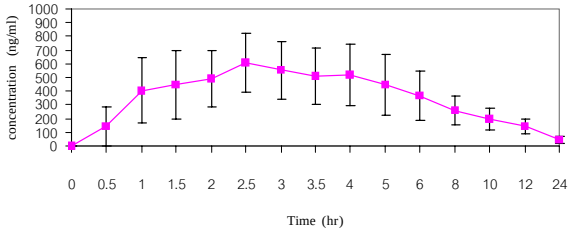

Fig. 3 Mean ± SD plasma celecoxib concentration-time profile following an oral administration of 200 mg celecoxib to 18 healthy male volunteers

mean elimination half-life (t) was 8.79 ± 5.49 hrs. The apparent clearance (CL) of celecoxib in the volunteers was 35.91 ± 9.85 L by average. The apparent volume of distribution (Vd) of approximately 458.93 ± 323.28 L/hr was found in this present study with the mean elimination rate constant of 0.11 ± 0.05 hr^{-1}. All pharmacokinetic parameters described above are shown in Table 3.

Discussion

The discovery of cyclooxygenase-2 (COX-2) enzyme has provided the rationale for the development of a new class of nonsteroidal anti-inflammatory drug (NSAIDs), the selective COX-2 inhibitors, with the aim of reducing the gastrointestinal (GI) toxicity associated with the administration of NSAIDs by virtue of COX-1 sparing[8]. In this present study, the

Table 2. Plasma celecoxib concentration (ng/ml)-time profile following an oral administration of 200 mg celecoxib

	Time (hrs)														
Subject No.	0.5	1	1.5	2	2.5	3	3.5	4	5	6	8	10	12	24	48
1	47.19	205.13	372.54	519.70	663.93	610.09	624.59	759.09	629.65	442.12	376.49	273.89	217.10	47.97	<LOQ
2	562.80	782.28	510.57	639.58	749.75	528.67	506.16	402.94	292.06	235.49	142.62	94.26	66.45	56.84	<LOQ
3	62.31	421.49	240.48	223.77	256.32	246.72	210.65	211.72	183.80	142.41	103.71	114.15	95.32	70.12	<LOQ
4	5.60	20.23	67.99	248.93	556.94	739.20	572.77	630.10	560.97	421.22	297.89	265.07	184.47	54.99	<LOQ
5	195.30	647.04	678.06	655.59	599.45	425.99	346.29	361.42	314.37	285.14	250.28	207.23	177.04	103.42	<LOQ
6	246.88	405.85	400.73	430.52	415.99	335.92	310.34	278.65	197.29	182.91	152.34	103.45	97.90	38.38	<LOQ
7	364.06	493.69	405.81	428.64	382.21	324.63	233.40	206.44	162.90	135.49	133.05	87.72	93.64	50.07	<LOQ
8	69.40	143.85	275.38	499.20	672.58	609.02	726.36	754.99	812.48	575.11	367.74	244.81	158.22	30.43	<LOQ
9	83.80	274.96	229.57	266.46	513.98	606.88	493.21	486.93	410.09	275.92	174.60	111.10	68.58	10.57	<LOQ
10	73.78	259.68	458.48	440.23	676.94	782.22	584.74	611.34	620.49	586.43	402.51	351.94	234.10	64.64	<LOQ
11	41.77	199.75	344.33	321.44	320.95	279.96	303.20	362.04	282.12	238.04	215.62	220.03	194.53	84.48	<LOQ
12	84.75	498.44	826.91	834.19	942.95	822.30	841.06	839.94	624.69	488.07	347.31	231.97	164.67	36.21	<LOQ
13	157.58	368.48	317.54	515.32	1056.62	939.74	891.47	878.41	916.23	803.48	442.11	269.00	169.38	36.42	<LOQ
14	301.18	959.90	1081.21	1020.45	892.55	667.58	558.21	554.10	409.14	346.03	257.03	244.49	115.99	21.43	<LOQ
15	117.69	572.96	565.17	504.89	511.81	381.11	387.24	352.85	383.93	278.01	249.92	204.40	159.62	65.99	<LOQ
16	49.88	416.87	438.41	444.34	389.28	302.97	263.78	254.01	195.14	263.66	155.19	107.21	86.74	8.12	<LOQ
17	94.20	441.50	642.37	610.79	677.94	632.06	663.97	730.95	643.45	511.78	366.73	223.84	132.49	14.15	<LOQ
18	51.23	192.97	180.77	266.26	617.36	666.01	633.49	609.34	380.47	349.14	221.18	167.81	162.78	73.86	<LOQ
Mean	144.97	405.84	446.46	492.79	605.42	550.06	508.39	515.85	445.52	364.47	258.68	195.69	143.28	48.23	
SD	142.63	234.90	245.78	207.96	216.11	206.80	205.42	221.25	224.41	176.95	104.86	77.19	50.60	26.36	

Table 3. Pharmacokinetic parameters (mean ± SD) of celecoxib after an oral administration of celecoxib 200 mg to 18healthy male volunteers

Subject No.	C_{max} (ng/ml)	T_{max} (hours)	$AUC_{0 \rightarrow t}$ (ng.hr/ml)	$AUC_{0 \rightarrow}$ (ng.hr/ml)	$t_{1/2}$ (hr)	K_{el} (hr^{-1})	CL (L/hr)	Vd (L)
1	759.09	4	6492.03	6877.54	5.57	0.1244	29.08	233.76
2	782.28	1	4367.38	5940.83	19.20	0.0361	33.67	932.56
3	421.49	1	2910.74	4924.79	19.91	0.0348	40.61	1166.98
4	739.2	3	5518.40	6007.93	6.17	0.1123	33.29	296.43
5	678.06	1.5	5561.83	7645.00	13.94	0.0497	26.16	526.38
6	430.52	2	3380.90	3922.81	9.79	0.0708	50.98	720.11
7	493.69	1	3234.61	4484.55	17.28	0.0401	44.60	1112.16
8	812.48	5	6254.52	6458.88	4.65	0.1489	30.97	207.96
9	606.88	3	3538.48	3601.41	4.13	0.168	55.53	330.56
10	782.22	3	7132.10	7666.07	5.72	0.1211	26.09	215.43
11	362.04	4	4556.26	5791.77	10.13	0.0684	34.53	504.85
12	942.95	2.5	6940.55	7213.52	5.22	0.1327	27.73	208.94
13	1056.62	2.5	7730.03	7985.07	4.85	0.1428	25.05	175.40
14	1081.21	1.5	6027.81	6151.03	3.99	0.1739	32.51	186.97
15	572.96	1	5007.90	5824.97	8.58	0.0808	34.33	424.94
16	444.34	2	3114.57	3518.59	3.76	0.1844	56.84	308.25
17	730.95	4	6034.17	6105.88	3.51	0.1973	32.76	166.02
18	666.01	3	5025.83	6285.95	11.83	0.0586	31.82	542.95
Mean	686.83	2.50	5157.12	5911.48	8.79	0.11	35.92	458.92
SD	211.35	1.22	1499.46	1363.51	5.49	0.05	9.85	323.28

authors characterized the pharmacokinetic parameters after oral administration of 200 mg celecoxib, the first selective COX-2 inhibitor, in 18 Thai male volunteers. The results of the study demonstrated that celecoxib was well absorbed, reaching peak plasma concentration within 2.55 ± 1.22 hours with the average maximum concentration of 686.83 ± 211.35 ng/ml. Since aqueous solubility of celecoxcib is low at 3 to 7 μg/ml when determined in vitro at pH 7 and at 40°C. pKa of the drug is 11.11, thus, the solubility of the drug is

likely to be low at the physiological pH and it needs more time for dispersion and dissolution of the solid dosage form in the gastrointestinal tract when compared with the oral solution[9]. It was already known that celecoxib was widely distributed in human plasma and the apparent volume of distribution found from the present study was 458.93 ± 323.28 L/hr, suggestion extensive distribution into the tissue. The area under the plasma concentration-time ($AUC_{0 \rightarrow t}$, $AUC_{0 \rightarrow \infty}$), for celecoxib which reflects the extent of drug absorption from time zero to the last quantifiable concentration ($0 \rightarrow t$) and infinity were found to be 5,157.12 ± 1,499.46 and 5,911.48 ± 1363.51 ng hr/ml respectively. Celecoxib is hepatatically metabolized by CYP 2C9 into three inactive metabolites and excreted predominantly by the liver and by renal route to a lesser extent[2,10]. The elimination half-life for celecoxib was 8.79 ± 5.49 hrs with the mean elimination rate constant of 0.11 ± 0.05 hr^{-1} were the result of this present study. It also appeared that the low solubility of celecoxib will prolong absorption process and make elimination half-life more variable[1]. The apparent clearance of celecoxib was approximately 35.91 ± 9.85 L. All pharmacokinetic parameters for celecoxib obtained from the present study mostly complied with other studies, eg. a mean peak plasma concentration (C_{max}) of 705 g/L was reached 2.8 hours (T_{max}) after 200 mg dose in volunteers (n = 36) under fasting conditions[1]. C_{max} and area under the plasma concentration-time curve (AUC) increased in a dose-proportion manner over the therapeutic dose range of 100 to 200 mg. The apparent volume of distribution approximately 400 L in volunteers (n = 24), the mean plasma half-life (t) of celecoxib was 11.2 hours after a single 200 mg dose. The apparent plasma clearance was 27.7 L/hr[11]. A recent study performed in Indian subjects following an oral dose of 200 mg celecoxib revealed that C_{max} was 544.89 ± 273.91 ng/ml, T_{max} was 4 ± 0.88 hr, $AUC_{0 \rightarrow \infty}$ was approximately 4,632.42 ng hr/ml. The elimination half-life (t) was 9.3 ± 3.58 hr. The values for Vd and clearance were 583 + 251 L/kg and 43.14 ± 36.23 L/hr respectively[12]. Racial difference in drug disposition and pharmacokinetic change in the elderly was reported for celecoxib[2]. Interindividual variability in drug response might be a consequence in alteration in drug disposition the data of which needs further investigation.

In conclusion, pharmacokinetic study following 200 mg oral dose of celecoxib was the first report in normal male volunteers. Pharmacokinetic parameters including C_{max}, T_{max}, AUC, Kel, t , Vd and CL were elucidated from this present study.

References

1. Clemett D, Goa KL. Celecoxib. A review of its use in osteoarthritis, rheumatoid arthritis and acute pain. Drug 2000; 59: 957-80.
2. Davies NM, McLachlan AJ, Day RO, Williams KM. Clinical pharmacokinetics and pharmacodynamics of celecoxib a selective cyclo–oxygenase-2 inhibitor. Clin Pharmacokinet 2000; 38: 225-42.
3. Fitz-Gerald GA, Patrono C. The coxibs, selective inhibitors of cyclooxygenase-2. New Engl J Med 2001; 345: 433-42.
4. Tang C, Shou M, Mei Q, Rushmore TH, Rodrigues AD. Major role of human liver microsomal cytochrome P450 2C9 (CYP2C9) in the oxidative metabolism of celecoxib, a novel cyclooxygenase-II inhibitor. J Pharm Exp Ther 2000; 293: 453-9.
5. Johnson JA. Influence of race or ethnicity on pharmacokinetics of drugs. J Pharm Sci 1997; 86: 1328-33.
6. Johnson JA. Predictability of the effects of race or ethnicity on pharmacokinetic of drugs. Int J Clin Pharmacol Ther 2000; 38: 53-60.
7. Schonberger F, Heinkele G, Murdter TE, Brenner S, Klotz U. Simple and sensitive method for the determination of celecoxib in human serum by high-performance liquid chromatography with fluorescence detector. J Chromatograph B 2002; 768: 255-60.
8. Capone ML, Tacconelli S, Sciulli MG, Patrignani P. Clinical pharmacology of selective COX-2 inhibitors. Int J Immunopathol Pharmacol 2003; 16(Suppl 2): 49-58.
9. Paulson SK, Vaughn MB, Tessen SM, Lawal Y, Greask CJ, Yan B, et al. Pharmacokinetics of celecoxib after oral administration in dogs and humans: effect of food and site of absorption. J Pharm Exp Ther 2001; 297: 638-45.
10. Paulson SK, Hribar JD, Liu NW, Hajdu E, Bible RH Jr, Piergies A, et al. Metabolism and excretion of (^{14}C) celecoxib in healthy male volunteers. Drug Metab Dispos 2000; 28: 308-14.
11. GD Searle and Company. Celecoxib prescribing information. Skokie Illinois, 1999; 23.
12. Jayasagar G, Krishna Kumar M, Chandrasekhar K, Madhusudan Rao Y. Influence of rifampicin pretreatment on the pharmacokinetics of celecoxib in healthy male volunteers. Drug Metabol Drug Interact 2003; 19: 287-95.

เภสัชจลนศาสตร์คลินิกของซิลิค็อกซิปในอาสาสมัครไทยสุขภาพปกติ

จันทนี อิทธิพานิชพงศ์, สุมนา ชมพูทวีป, สุพีชา วิทยเลิศปัญญา, วันดี เข็มศรี, นงนุช ถาวร, ปาจรีย์ ลิลิตการตกุล, สิทธิพร ปริกัมศีล

ที่มา: *ซิลิค็อกซิปเป็นยาต้านการอักเสบที่ไม่ใช่สเตียรอยด์ ออกฤทธิ์ยับยั้งการทำงานของเอนไซม์ไซโคลออกซีจีเนส-2 อย่างจำเพาะ ซิลิค็อกซิปเป็นยาที่มีประสิทธิภาพในการลดการอักเสบของข้อ โดยพบอาการไม่พึงประสงค์ต่อทางเดินอาหารน้อยกว่ายาต้านการอักเสบรุ่นเก่า*

วัตถุประสงค์: *เพื่อศึกษาเภสัชจลนศาสตร์คลินิกของซิลิค็อกซิป เมื่อให้ในรูปของการรับประทานในอาสาสมัคร*

วัสดุและวิธีการ: *ภายหลังจากการงดรับประทานอาหารหลังเที่ยงคืน ให้อาสาสมัครชายไทยสุขภาพปกติ จำนวน 18 คน อายุเฉลี่ย 20.94 ± 1.21 ปี น้ำหนักเฉลี่ย 63 ± 5.17 กิโลกรัม รับประทานซิลิค็อกซิป 200 มิลลิกรัม เจาะเลือดอาสาสมัครก่อนการรับประทานซิลิค็อกซิปและภายหลังการรับประทานยาที่เวลา 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8, 10, 12, 24 และ 48 ชั่วโมง ตามลำดับ หาระดับยาซิลิค็อกซิปในเลือดโดยวิธี รีเวอร์ซเฟสโครมาโตกราฟฟี*

ผลการศึกษา: *ภายหลังการรับประทานซิลิค็อกซิป 200 มิลลิกรัม ยาจะถูกดูดซึมเข้าสู่กระแสเลือด โดยระดับยาในเลือดสูงสุด (T_{max}) เกิดในเวลาเฉลี่ย 2.5 ± 1.22 ชั่วโมง และด้วยความเข้มข้นของยาสูงสุดในเลือดเฉลี่ย (C_{max}) 686.83 ± 211.35 นาโนกรัมต่อมิลลิลิตร ปริมาณที่ถูกดูดซึมแสดงเป็นค่าพื้นที่ภาพใต้กราฟ (AUC) มีค่าเฉลี่ย 5157.12 ± 1499.49 และ 5911.48 ± 1363.51 นาโนกรัม.ชั่วโมง/มิลลิลิตร สำหรับ $AUC_{0 \rightarrow t}$ และ $AUC_{0 \rightarrow \infty}$ ตามลำดับการกระจายยาในร่างกาย (apparent Vd) มีค่า 458.93 ± 323.28 ลิตร/ชั่วโมง ซิลิค็อกซิปที่ถูกเปลี่ยนแปลง และขับถ่ายออกจากร่างกายทั้งทางปัสสาวะและอุจจาระโดยมีค่าครึ่งชีวิต ($t_{1/2}$) 8.79 ± 5.49 ชั่วโมง และการขจัดยาออกจากร่างกาย (apparent CL) เป็น 35.91 ± 9.85 ลิตร ค่าคงที่ของการขับยาออกจากร่างกายเป็น 0.11 ± 0.05 ต่อชั่วโมง*

สรุป: *ผลการศึกษาค่าพารามิเตอร์ต่าง ๆ ได้แก่ ค่า C_{max}, T_{max}, Vd, Kel, CL, AUC ของซิลิค็อกซิปภายหลังจากการรับประทานยา บ่งบอกถึงกระบวนการทางเภสัชจลนศาสตร์ ได้แก่ การดูดซึม การกระจาย การเปลี่ยนแปลงยา และการขับยาออกจากร่างกายในอาสาสมัครชายไทยที่มีสุขภาพปกติ*