Pharmacokinetics and Bioequivalence Study of the Two 20-MG Quinapril Hydrochloride Tablet Formulations in Healthy Thai Male Volunteers

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Objective: *To determine the pharmacokinetics and bioequivalence of two 20-mg quinapril hydrochloride tablet preparations; Quinaril® (The Biolab Ltd, Bangkok, Thailand) as the test and Accupril® as the reference.*
Material and Method: *The present study was a single dose, randomized, two-period crossover design conducted in 24 healthy volunteers under fasting conditions with a 7-day washout period. Serial plasma concentrations of quinapril and its active metabolite quinaprilat up to 24 h after dosing were determined by HPLC with UV detection. The pharmacokinetic parameters were analyzed by noncompartmental analysis and the ANOVA was carried out using logarithmically transformed data of the AUC and C_{max} as well as untransformed T_{max}.*
Results: *There were no significant differences between the two preparations regarding the T_{max} of quinapril and quinaprilat and their median T_{max} were 0.5 h and 1.4 - 1.5 h, respectively. The half-life of quinapril (1.2 h) was faster than quinaprilat (1.8-1.9 h) although the volume of distribution (Vd/F) of quinapril (1.1 L/kg) was larger than quinaprilat (0.3 L/kg), however, its clearance rate (CL/F) was faster when compared to quinaprilat (20-26 ml/min/kg vs. 1.7 ml/min/kg). The mean (90% CI) for the ratios $\frac{Test}{Reference}$ of quinapril were 0.99 (0.89-1.10), 0.99 (0.90-1.09) and 1.01 (0.90-1.14), respectively for AUC_{0-24}, $AUC_{0-\infty}$ and C_{max}. Similarly, the corresponding values for quinaprilat were 0.95 (0.90-1.01), 0.95 (0.90-1.01) and 1.03 (1.00-1.07), respectively. These values were within the bioequivalence range of 0.80 - 1.25, thus, demonstrated the bioequivalence of the two preparations.*
Conclusion: *The results of the present study indicated that the two quinapril HCL preparations are bioequivalent and it can be assumed that they are therapeutically equivalent and exchangeable in clinical practice.*

Keywords: *Pharmacokinetics, Bioequivalence, Quinapril*

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Quinapril hydrochloride is the ethyl ester prodrug of a dicarboxyl-containing angiotensin-converting enzyme (ACE) inhibitor, structurally related to enalapril. The drug is deesterified by hepatic esterase to the principal active metabolite, quinaprilat, which is a potent inhibitor of ACE[1-5]. Quinapril is indicated for the treatment of hypertension and heart failure[3-5]. Metabolic side effects are not encountered during longterm therapy and the drug does not alter plasma concentrations of uric acid or calcium and may improve insulin sensitivity in patients with insulin resistance[1]. The drug also decreases cholesterol and lipid levels in proteinuric renal disease[3-5]. The recommended initial dosage of quinapril is 10 or 20 mg once daily. Following oral administration, quinapril is rapidly absorbed. Its peak plasma concentrations are observed within 1 hour (h)[3-6]. About 38% of an oral dose of quinapril is deesterified to quinaprilat. Conversion of quinapril to

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quinaprilat is reduced in patients with impaired liver function. The peak concentrations of quinaprilat are approximately 2 h post-dose, thereafter, the drug is eliminated by renal excretion[3-6]. The mean elimination half-life of quinapril and quinaprilat are 1 h and 2-3 h, respectively[3]. The pharmacokinetics of quinapril and quinaprilat are linear over a single-dose range of 5-80 mg doses and 40-160 mg in multiple daily doses[3-6]. Serious adverse reactions to ACE inhibitor are rare, and in general, ACE inhibitors are well tolerated.

Recently a generic preparation of quinapril has been manufactured for clinical use. Although the generic and reference preparations contain the same active ingredients, they may be different from each other by manufacturing processes or content of excipients, which may affect the rate and extent of drug absorption. Therefore, the bioequivalence testing is mandated to confirm the bioavailability between the generic and the reference products in human subjects. The rationale behind the concept of bioequivalence is that if two pharmaceutical products provide identical plasma concentration-time profiles, they will exhibit no difference in their efficacy[7]. The objective of the present study was to determine the bioequivalence of a generic quinapril 20-mg tablet formulation with that of the reference, when given as equal dose. Since bioequivalence of two formulations comprised equivalence with respect to the rate and extent of their absorption, the pharmacokinetics parameters were assessed and compared according to the Thai FDA criteria[7].

Material and Method

Subjects

Twenty-four healthy Thai male volunteers aged between 19-40 years old and the body mass index within 18-25 participated in the present study. Volunteers were in good health based on medical history, physical examination, routine blood test including complete blood count with differential count and blood chemistry profiles as well as having a negative screening test for hepatitis B surface antigen, anti-hepatitis-C antibody, and anti-HIV. Volunteers with known contraindication or hypersensitivity to quinapril were excluded as well as those with a known history of drug abuse, alcohol consumption, or cigarette smoking. No drug was allowed 1 month before the study period to avoid the effects of inducing or inhibiting hepatic metabolizing enzyme and the risk of drug interactions. The present study was approved by the Research Ethics Committee of the Chiang Mai University, Thailand and all volunteers signed the informed consent form prior to participating in the present study.

Study drug

Reference product: Accupril® 20 mg tablet [Manufactured by: G□decke Gmbh, Berlin, 79090 Freiburg, Germany, Imported by: Pfizer (Thailand) Limited, Bangkok, Thailand] Lot No. 0211075, Mfd 07/2005, Exp 06/2008.

Test products: Quinaril® 20 mg tablet (The Biolab Ltd, Bangkok, Thailand) Lot No: Q-20-022/FQ-20-003, Mfd 24/11/2006.

Method of drug administration

The present study was a single dose, two-period crossover study. After an overnight fast, each volunteer was assigned to receive a single oral dose of quinapril formulations (either Accupril® or Quinaril®) with 240 ml electrolyte fluid. Water and lunch were served at 2-h and 4-h after the dose, respectively. The wash out period between each treatment was 1 week, thereafter, volunteers were administered the different brand of quinapril formulation in the same manner. Blood samples were collected at pre-dose and at 0.5, 0.75, 1, 1.25, 1.5,1.75, 2,2.25,2.5, 3,4,6, 8,10,12,15 and 24 h post dose. Samples were centrifuged and plasma was stored at -20□C until analysis.

Determination of the plasma quinapril and quinaprilat concentrations

Quinapril, quinaprilat, and internal standard in plasma samples were determined by a high performance liquid chromatography with UV detection[8]. The plasma sample was prepared by solid phase extraction (SPE), using C-2 SPE cartridge and precondition consequentially with methanol, and water. Thereafter, a mixture of 500 ul plasma sample and 40 ul 1 M KH_2PO_4 was loaded to the cartridge and let it free flow. The SPE was washed with 200 ul of 100 mM NaH_2PO_4/2-propanol/methanol (25-3-3, v/v/v) and vacuumed to dryness. The samples were eluted with 1.5 ml chloroform/acetonitril/methanol, (35-60-5, v/v/v), thereafter, evaporated to dryness and reconstituted with 30 ul of mobile phase then injected onto the HPLC system. The chromatographic system consisted of a 150 x 4.6 mm i.d., 5 um C18 reversed phase analytical column with a 10 x 4.0 mm i.d., 5 um C18 guard column. The mobile phases consisted of 10 mM perchloric acid (pH 3.2)/2-propanol/triethylamine (500/101/200, ml-ml-ul)(mobile phase A) and 10 mM perchloric acid (pH 3.2)/2-propanol/methanol/triethylamine (500/89/179/200, ml-ml-ml-ul) (mobile

phase B). The flow rate was 1.0 ml/min while the temperature was 55□C and the column effluents detected at 210 nm. The analytical column was equilibrated with mobile phase A before injected 30 ul of the sample. The mobile phase B was run for 15 minutes then came back to mobile phase A for 20 minutes.

Pharmacokinetic analysis

Maximal plasma concentration (C_{max} ng/ml) and time to reach the C_{max} (T_{max} h) were obtained directly from the raw data. The area under the curve from time zero to the last measured concentration (AUC_{0-24}, ng.h/ml) was calculated by trapezoidal integration. The total area under the curve from time zero to infinity ($AUC_{0-\infty}$, ng.h/ml) was calculated as the sum of AUC_{0-24} and residual area (Ct/*Ke*, Ct as the last measured concentration and *Ke* as the apparent terminal elimination rate, estimated by log-linear regression from the terminal portion of the log-transformed concentration-time plots). Half-life ($t_{1/2}$) was calculated by dividing 0.693 by the *Ke*. The total drug clearance adjusted for bioavailability was calculated by dividing the dose by the AUC. The apparent volume of distribution adjusted for bioavailability (Vd/F) was calculated by dividing the Cl/F by the *Ke*. The pharmacokinetic parameters were determined by non-compartmental analysis by using the TopFit, pharmacokinetic data analysis program for PC (Gustav Fischer Verlag, Stuttgart, Germany)[9].

Statistical analysis[10,11]

An analysis of variance (ANOVA) was performed to determine the statistical differences of pharmacokinetic parameters. Statistical analysis of AUC and C_{max} were performed on the logarithmically (ln) transformed data. The 90% confidence interval (CI) for the ratio of AUC and C_{max} values of the $\frac{\text{Test}}{\text{Reference}}$ were calculated using the equation: 90% CI $(\mu_T-\mu_R) = (\bar{X}_T-\bar{X}_R) \pm t^{v}_{0.1}\sqrt{\frac{2S^2}{n}}$. The antilogarithm of the confidence interval $(\mu_T-\mu_R)$ expressed the bioequivalence as a ratio of the test product and the reference product $[\mu_T/\mu_R]$.

Bioequivalence acceptance criteria

The bioequivalence acceptance criteria required that the 90% CI for the ratio μ_T/μ_R of the $AUC_{0-\infty}$ and C_{max} fell within the interval of 0.8-1.25. Regarding analysis of T_{max},, the bioequivalence range was expressed as untransformed data (absolute difference) and the stipulated bioequivalence range of difference T_{max} [Test-Reference] was $\pm$ 20% of the T_{max} of the reference formulation.

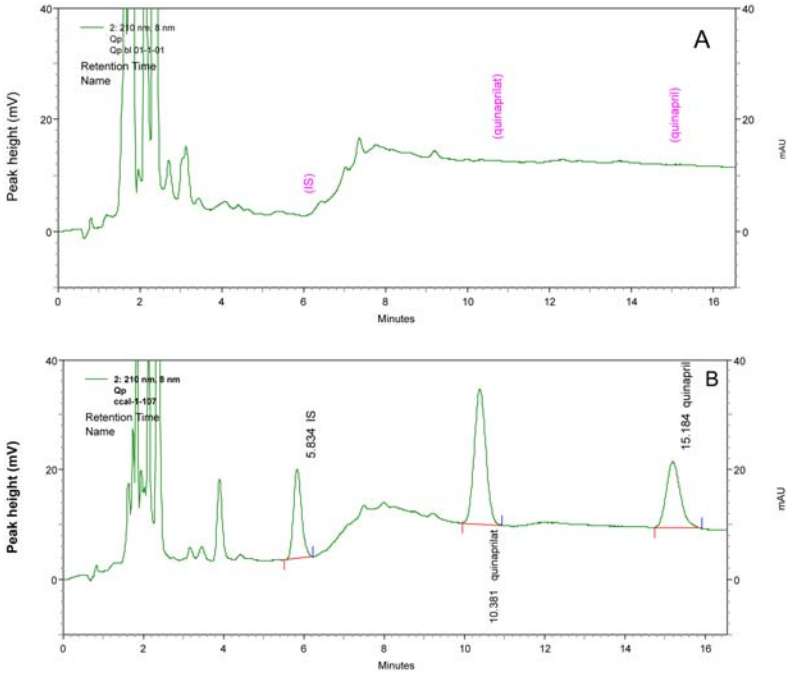

Fig. 1A Chromatogram of blank plasma
Fig. 1B Chromatogram of quinaprilat (1600 ng/ml), quinapril (800 ng/ml) and IS (enalapril), in human plasma

Results

The chromatograms of blank plasma and plasma containing enalapril (IS), 1,600 ng/ml of quinaprilat and 800 ng/ml of quinapril are presented in Fig. 1. The retention time of IS, quinaprilat and quinapril were 5.8, 10.3, and 14.8 minutes, respectively. Calibration curves of the drugs in plasma were linear from 10-800 ng/ml and 20-1600 ng/ml for quinapril and quinaprilat, respectively. Linear regression of concentrations vs. peak height ratios of quinaprilat/IS and quinapril/IS gave coefficients of determination (r^2), which were greater than 0.990. The lower limit of quantization for quinapril and quinaprilat was 10.0 ng/ml and 20.0 ng/ml, respectively. The mean recoveries (%) of IS, quinaprilat and quinapril were 82.32, 76.94 and 80.76, respectively.

The administrations of quinapril in 24 healthy volunteers in the present study were well tolerated and none of any adverse effect including hypotension were reported. The mean plasma concentration-time profiles of quinapril and quinaprilat are depicted in Fig. 2. Table 1 and 2 illustrate pharmacokinetic parameters of quinapril and quinaprilat, respectively, while Table 3

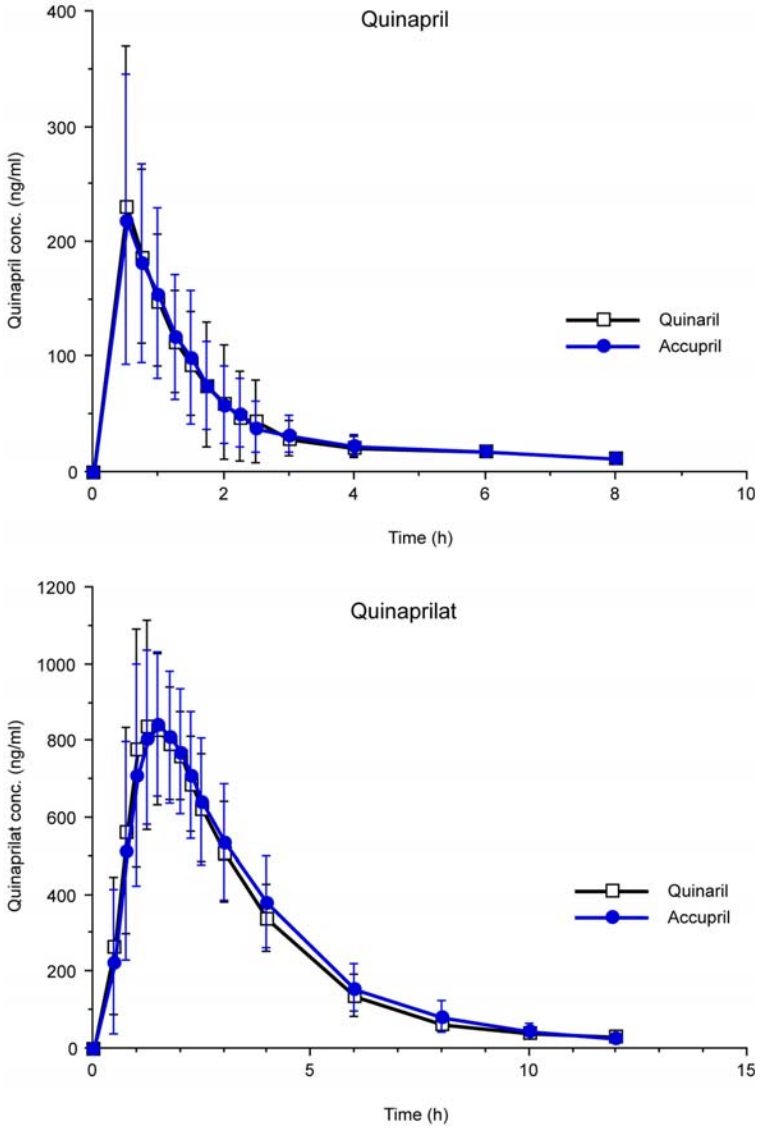

Fig. 2 Mean plasma concentration-time profiles of quinapril and quinaprilat after oral administration of 20 mg Quinaril® (-□-) and Accupril® (-●-) under fasting

Table 1. Pharmacokinetic parameters of quinapril after single oral administrations of 20-mg Quinaril® and Accupril®

Quinaril®	T_{max} (h)	C_{max} (ng/ml)	AUC_{0-t} (ng.h/ml)	$AUC_{0-\infty}$ (ng.h/ml)	$t_{1/2}$ (h)	Vd/F (L/kg)	CL/F (ml/min/kg)
Mean	0.68	261.60	290.36	308.00	1.15	1.10	26.30
SD	0.36	122.06	108.13	111.50	0.33	0.58	31.12
Max	1.75	633.00	549.13	576.49	1.67	3.07	163.76
Min	0.50	108.98	99.87	109.00	0.43	0.48	8.76
Median	0.50						
Accupril®	T_{max} (h)	C_{max} (ng/ml)	AUC_{0-t} (ng.h/ml)	$AUC_{0-\infty}$ (ng.h/ml)	$t_{1/2}$ (h)	Vd/F (L/kg)	CL/F (ml/min/kg)
Mean	0.72	255.87	296.51	314.88	1.15	1.06	19.90
SD	0.32	98.72	121.16	126.20	0.36	0.37	9.37
Max	1.50	456.21	535.16	572.82	1.67	1.82	43.75
Min	0.50	77.52	120.55	136.00	0.36	0.39	8.82
Median	0.50						

Table 2. Pharmacokinetic parameters of quinaprilat after a single oral administrations of 20-mg Quinaril® and Accupril®

Quinaril®	T_{max} (h)	C_{max} (ng/ml)	AUC_{0-t} (ng.h/ml)	$AUC_{0-\infty}$ (ng.h/ml)	$t_{1/2}$ (h)	Vd/F (L/kg)	CL/F (ml/min/kg)
Mean	1.44	931.62	3007.38	3094.28	1.80	0.27	1.77
SD	0.43	199.13	622.04	635.86	0.29	0.06	0.43
Max	2.50	1396.89	4542.39	4654.02	2.50	0.45	3.22
Min	0.75	573.67	1541.33	1634.22	1.26	0.20	1.10
Median	1.38						
Accupril®	T_{max} (h)	C_{max} (ng/ml)	AUC_{0-t} (ng.h/ml)	$AUC_{0-\infty}$ (ng.h/ml)	$t_{1/2}$ (h)	Vd/F (L/kg)	CL/F (ml/min/kg)
Mean	1.49	899.99	3161.24	3243.72	1.90	0.28	1.69
SD	0.40	184.32	708.06	714.57	0.33	0.07	0.38
Max	2.25	1312.96	4834.97	4973.17	2.75	0.49	2.48
Min	1.00	538.56	2276.30	2371.43	1.19	0.16	1.00
Median	1.50						

Table 3. Bioequivalence analysis

PK parameters	Quinapril Mean (90% CI) (BE range 0.80-1.25)	Quinaprilat Mean (90% CI) (BE range 0.80-1.25)
AUC_{0-t}	0.99 (0.89-1.10)	0.95 (0.90-1.01)
$AUC_{0-\infty}$	0.99 (0.89-1.09)	0.95 (0.89-1.01)
C_{max}	1.01 (0.90-1.14)	1.03 (1.00-1.07)
T_{max} difference (h)	(-0.4), (-0.14)-0.07 BE range = $\pm$ 0.14 h	(-0.5), (-0.20)-0.09 BE range = $\pm$ 0.30 h

shows their calculated 90% CI. The median time to reach the maximum concentration (T_{max}) of quinapril for Quinaril® (0.5 h, range 0.5-1.75 h) was similar to that of Accupril® (0.5 h, range 0.5-1.5 h), and the point estimated, (90%CI) for the T_{max} difference of the two preparations [(-0.4), (-0.14)-0.07] were within the bioequivalence range of ± 0.14 (± 20% of T_{max} of the reference) (Table 3). Similar to quinapril, the median T_{max} of quinaprilat for Quinaril® (1.38 h, range 0.75-2.5 h) and Accupril® (1.5 h, range 1.0-2.25 h) were not significantly different and the point estimated, (90% CI) for the T_{max} difference of the two preparations [(-0.5), (-0.20)-0.09] were within the bioequivalence range of ± 0.30. The mean (± SD) of the C_{max}, AUC_{o-t} and $AUC_{o-\infty}$ of quinapril were not significantly different between the two preparations (261.6 ± 122.06 vs. 255.87 ± 98.72 ng/ml, 290.36 ± 108.13 vs. 296.51 ± 121.16 ng.h/ml, and 308.0 ± 111.5 vs. 314 ± 126.2 ng.h/ml). The mean elimination half-lives ($t_{1/2}$, h) of quinapril were 1.15 ± 0.33 (range 0.43-1.67) and 1.15 ± 0.36 (range 0.36-1.67) for Quinaril® and Accupril®, respectively. The average relative bioavailability (F_{rel}) calculated from C_{max}, AUC_{o-24} and $AUC_{o-\infty}$ of Quinaril®/Accupril® was 107.0%, 103.8%, and 102.9%, respectively. Likewise, the mean (± SD) of the C_{max}, AUC_{o-24} and $AUC_{o-\infty}$ of quinaprilat were not significantly different between the two preparations (931.62 ± 199.13 vs. 899.99 ± 184.32 ng/ml, 3007.38 ± 622.04 vs. 3161.24 ± 708.06 ng.h/ml, and 3094.28 ± 635.86 vs. 3243.72 ± 714.57 ng.h/ml). The mean $t_{1/2}$, h of quinaprilat were 1.8 ± 0.29 (range 1.26-2.5) and 1.9 ± 0.33 (range 1.19-2.75) for Quinaril® and Accupril®, respectively. The average relative bioavailability (F_{rel}) calculated from C_{max}, AUC_{o-24} and $AUC_{o-\infty}$ of Quinaril®/Accupril® was 104.3%, 96.9%, and 97.1%, respectively.

Bioequivalence analysis for the active metabolite quinaprilat showed that the 90% CI for the ratios were 0.90-1.01, 0.90-1.01, and 1.00-1.07, respectively for AUC_{0-24}, $AUC_{0-\infty}$ and C_{max}. Similarly, the corresponding values for quinapril were 0.89-1.10, 0.90-1.09, and 0.90-1.14, respectively. Since these values were well within the bioequivalence range of 0.8-1.25, the present study concluded the bioequivalence of the two preparations.

Discussion

In the present study, bioequivalence comparing both the rate and extent of quinapril absorption was investigated in order to assure therapeutic equivalence of the generic product with the innovator. Bioequivalence studies frequently rely on pharmacokinetic parameter measurements such as T_{max}, C_{max} and AUC. The AUC determines the extent of systemic drug absorption or drug bioavailability, whereas T_{max} and C_{max} determine the rate of systemic drug absorption. The two or more formulations will be bioequivalent if there are no significant differences in the rate and extent of drug absorption. Quinapril is a prodrug requiring esterolysis in the liver to yield its active metabolite quinaprilat. With the exception of captopril and lisinopril, all ACE inhibitors are given orally as ethyl esters, because the active acid forms generally have limited bioavailability[1-3]. With reference to the FDA guideline, if the metabolite significantly contributes to the net activity of a drug product and the pharmacokinetic system is non-linear, it is necessary to measure both parent drug and active metabolite concentrations in the plasma and evaluate them separately. However, for quinapril, quinaprilat is responsible for the therapeutic efficacy and the pharmacokinetics of quinapril and quinaprilat are linear over a single-dose range of 5-80 mg dose, bioequivalence based on only quinaprilat is justified. Nonetheless, since the present HPLC method could determine both quinapril and quinaprilate, both products were assayed and assessed for bioequivalence. The determination of quinapril and quinaprilat concentrations in plasma by HPLC with UV detection (HPLC–UV) after solid phase extraction is the most convenient way for the quantification[8]. This method is highly specific and provides a rapid, simple technique suitable for use in routine practice. In addition, the method reveals assay linearity covering wide range of concentrations with good precision, accuracy, and recovery and the LLOQ for quinapril and quinaprilat were 10 ng/ml and 20 ng/ml, respectively. These values were considered sufficient sensitivity for the bioassay because the AUC analysis in the present study showed that the sampling time was adequate and the calculated AUC-extrapolation was less than 20% in all subjects.

Pharmacokinetic study showed that after oral administrations of quinapril HCL, the plasma concentrations of quinapril and quinaprilat increased rapidly. The median T_{max} of the parent drug for both preparations were 0.5 h and were comparable to the values previously reported (0.7-1.4 h)[1-3]. Similarly, the T_{max} of the active metabolite quinaprilat from the test (1.4 h) and the reference (1.5 h) were not significantly different between the two preparations and these values were similar to those previously reported (1.4-2.3 h)[1-3]. The mean volume of distribution (Vd/F) of quinapril (1.1 L/kg) was larger than quinaprilat (0.3 L/kg). The Vd of quinaprilat is comparable to the extracellular water (0.2 L/kg) suggested a more water-soluble of the active

metabolite than the parent compound which is more lipid soluble thereby has larger Vd. The clearance of quinaprilat (CL/F) was slower than that of quinapril (1.7 ml/min/kg VS 20-26 ml/min/kg). The clearance of quinaprilat was similar to the glomerular filtration rate (1.8 ml/min/kg or 120 ml/min), which suggested that the drug was eliminated primarily by renal excretion. Complied with data from a drug monograph, the elimination half-life of quinaprilat increased as creatinine clearance decrease and there is a linear correlation between plasma quinaprilat clearance and creatinine clearance. In contrast to quinaprilat, the clearance of quinapril was similar to those of the hepatic blood flow (1,350 ml/min or 19.3 ml/min/kg) corresponding to the fact that the concentration of quinaprilat was reduced in patients with alcoholic cirrhosis due to impaired deesterification of quinapril. The average half-life, $t_{1/2}$ of quinapril (1.2 h) was faster than those of quinaprilat (1.8-1.9 h) and these values were comparable to those values previously reported (1 h and 2 h for quinapril and quinaprilat, respectively). The reason for the shorter half-life of quinapril is due to a rapid clearance by the liver when compared to the slower renal clearance of quinaprilat although the Vd of quinaprilat is smaller than quinapril.

From the plasma concentration-time profiles, the plasma levels and the AUC of quinaprilat were significantly higher than those of quinapril. The mean C_{max} and $AUC_{0-\infty}$ of quinaprilat were 3.5 times and 10 times higher than those of quinapril, respectively. The inter-subject variability of the AUC and C_{max} for quinapril and quinaprilat were significantly high and the p-values from ANOVA table were < 0.5. These findings were expected since some volunteers may either exhibit extremely high or extremely low values for AUC and C_{max} concentrations of quinapril and quinaprilat. However, the overall coefficient of variation (%CV) estimated from S^2 obtained from the ANOVA for the AUC and C_{max} of quinaprilat (11% and 7%, respectively) were less than those values for quinapril (21% and 24%, respectively) and the power of tests for AUC and C_{max} of quinaprilat and quinapril were > 90% and > 80% for the sample size of 24, respectively[12]. Bioequivalence study showed no significant differences between the test and the reference products regarding the rate and extent of their absorption for both quinapril and quinaprilat. The 90% CI for the ratios of quinapril were 0.89-1.10, 0.90-1.09, and 0.90-1.14, respectively for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max}. The corresponding values for quinaprilat were 0.90-1.01, 0.90-1.01, and 1.00-1.07, respectively. Since these values were well within the bioequivalence range of 0.8-1.25, the present study concluded the bioequivalence of the two preparations.

Conclusion

The present study evaluated the bioequivalence of 20-mg oral formulations of quinapril tablets manufactured by The Biolab Ltd, Bangkok, Thailand (Quinaril®) and the innovator Accupril® (Pfizer Limited) in 24 healthy Thai male volunteers using a randomized, two-way crossover design under fasting conditions. Each volunteer was given both the test and the reference product with a washout period of 1 week. Quinapril and quinaprilat in plasma were measured by HPLC with UV detection. The bioequivalence was compared using the parameter $AUC_{0-t,}$ $AUC_{0-\infty}$ and C_{max} after ln transformed and the 90% CI of these parameters for [Test/Reference] were well within the bioequivalence range proposed by The Thai FDA, thus, the present study demonstrated the bioequivalence of the two preparations.

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การศึกษาเภสัชจลนศาสตร์และชีวสมมูลของยาเม็ดควินาพริลไฮโดรคลอไรด์ขนาด 20 มิลลิกรัม 2 ตำรับ ในอาสาสมัครชายไทยสุขภาพดี

นพมาศ โรจนเสถียร, นยฎา นาเสงี่ยม, บุญเยี่ยม คำสอน, สุกิจ รุ่งอภินันท์, อภิวัฒน์ เจงเจริญ

วัตถุประสงค์: *เพื่อศึกษาเภสัชจลนศาสตร์และชีวสมมูลของยาควินาพริลไฮโดรคลอไรด์ชนิดรับประทานขนาด 20 มิลลิกรัม ในอาสาสมัครชายไทยสุขภาพดี 24 คน โดยอาสาสมัครแต่ละคนจะได้รับยาสามัญควินาพริลไฮโดรคลอไรด์ที่ผลิตในประเทศ และยาต้นตำรับแอคคูพริว โดยวิธีสุ่มไขว้ แบบสองช่วงและสองระยะ เว้นระยะห่างของการศึกษาแต่ละครั้งนาน 1 สัปดาห์ อาสาสมัครจะได้รับยาหลังงดน้ำและอาหารและจะถูกเก็บตัวอย่างเลือดก่อนได้รับยาและหลังจากได้รับยาที่เวลาต่าง ๆ ถึง 24 ชั่วโมง ทำการวิเคราะห์หาระดับยาควินาพริลและควินาพริลแลทซึ่งเป็นตัวยาออกฤทธิ์ ในพลาสมาโดยวิธีโครมาโตกราฟี ชนิดของเหลวสมรรถนะสูงที่เชื่อมต่อกับเครื่อง วัดแสงยูวี นำความเข้มข้นของยาที่เวลาต่าง ๆ มาประเมินหาค่าทางเภสัชจลนศาสตร์และวิเคราะห์ทางสถิติ เพื่อหาชีวสมมูลของยา โดยจะเปรียบเทียบค่าทางเภสัชจลนศาสตร์ระหว่างยาทดสอบและยาต้นตำรับโดยใช้การวิเคราะห์ความแปรปรวน (ANOVA)*

ผลการศึกษา: *พบว่าไม่มีความแตกต่างกันทางสถิติของเวลาที่ความเข้มข้นของยาสูงสุดในเลือดระหว่างยาทดสอบและยาต้นตำรับ ค่ามัธยฐานของเวลาที่ความเข้มข้นของยาสูงสุดในเลือดของยาควินาพริล และควินาพริลแลทมีค่าเท่ากับ 0.5 ชั่วโมงและ 1.4-1.5 ชั่วโมง ตามลำดับ ค่าครึ่งชีวิตของยาควินาพริล (1.2 ชั่วโมง) จะเร็วกว่ายาควินาพริลแลท (1.8-1.9 ชั่วโมง) แม้ว่าปริมาตรการกระจายยาของยาควินาพริล (1.1 ลิตร/กิโลกรัม) จะมากกว่ายาควินาพริลแลท (0.3 ลิตร/กิโลกรัม) แต่อัตราการขจัดยาของยาควินาพริล (20-26 มิลลิลิตร/นาที/กิโลกรัม) จะเร็วกว่ายาควินาพริลแลท (1.7 มิลลิลิตร/นาที/กิโลกรัม) ส่วนค่าเฉลี่ย (ช่วงความเชื่อมั่นร้อยละ 90) ของสัดส่วนของพื้นที่ใต้กราฟที่เวลา 0-24 ชั่วโมง พื้นที่ใต้กราฟที่เวลา 0-อสงไขย และความเข้มข้นสูงสุดของยาในเลือด ระหว่างยาทดสอบ/ยาต้นตำรับของยาควินาพริลมีค่าเท่ากับ 0.99 (0.89-1.10), 0.99 (0.90-1.09) และ 1.01 (0.90-1.14) ตามลำดับ และสำหรับยาควินาพริลแลทมีค่าเท่ากับ 0.95 (0.90-1.01), 0.95 (0.90-1.01) และ 1.03 (1.00-1.04) ตามลำดับ ซึ่งค่าเหล่านี้อยู่ในช่วงค่าชีวสมมูลที่ยอมรับคือ 0.8-1.25 การศึกษาครั้งนี้สรุปได้ว่ายาทั้งสองตำรับมีชีวสมมูลกัน*