# A Study on the Pharmacokinetics of Chlorzoxazone in Healthy Thai Volunteers

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***Background:*** *Chlorzoxazone (CHZ), a centrally acting skeletal muscle relaxant, is metabolized to 6-hydroxychlorzoxazone (6-OH-CHZ) by CYP2E1. CHZ can be used as an in vivo probe of CYP2E1 activity in patients with liver diseases. Pharmacokinetics of CHZ in Thai subjects should be studied for application to Thai patients.*
***Objective:*** *The purpose of the present study was to determine clinical pharmacokinetics of CHZ and 6-OH-CHZ.*
***Material and Method:*** *Ten healthy Thai volunteers were included. After an overnight fasting, the volunteers were orally administered 400 mg CHZ and serial blood samples were collected at 0 (predose), 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, and 8 hours after dosing. Plasma CHZ and 6-OH-CHZ were assayed by reversed-phase high-performance liquid chromatography (HPLC) with UV detector. The pharmacokinetic parameters including maximum concentration ($C_{max}$), time to reach maximum concentration ($T_{max}$), area under the concentration-time curve ($AUC_{0-8}$ and $AUC_{0-\infty}$), elimination half-life ($t_{1/2}$), elimination rate constant ($K_{el}$), oral clearance (Cl), and volume of distribution (Vd) were determined.*
***Results:*** *CHZ was absorbed into systemic circulation with time to reach maximum concentration ($T_{max}$) of 2.00 $\pm$ 0.82 hrs and maximum concentration ($C_{max}$) of 7.15 $\pm$ 2.09 μg/ml. It was metabolized to 6-OH-CHZ with $T_{max}$ of 3.05 $\pm$ 1.17 hrs and $C_{max}$ of 1.77 $\pm$ 0.50 μg/ml. The extent of CHZ absorption (area under the concentration-time curve, AUC) was 25.47 $\pm$ 7.11 and 27.52 $\pm$ 8.05 μg.hr/ml for $AUC_{0-8}$ and $AUC_{0-\infty}$, respectively. The $AUC_{0-8}$ and $AUC_{0-\infty}$ of 6-OH-CHZ were 7.32 $\pm$ 2.21 and 8.50 $\pm$ 2.78 μg.hr/ml, respectively. The elimination rate constant ($K_{el}$) was 0.48 $\pm$ 0.10 and 0.40 $\pm$ 0.13 $hr^{-1}$ for CHZ and 6-OH-CHZ, respectively. The elimination half-life ($t_{1/2}$) was 1.49 $\pm$ 0.32 and 1.95 $\pm$ 0.73 hours for CHZ and 6-OH-CHZ, respectively. Oral clearance (Cl) and volume of distribution (Vd) of CHZ was found to be 15.77 $\pm$ 4.81 (L/hr) and 33.13 $\pm$ 9.75 L, respectively.*
***Conclusion:*** *An oral dose of 400 mg CHZ was used to probe for the pharmacokinetic characteristics of this drug in Thai volunteers. Those parameters reflected absorption, distribution, and elimination of CHZ in healthy Thai volunteers.*

***Keywords:*** *Chlorzoxazone, Pharmacokinetics*

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Chlorzoxazone (CHZ) is a centrally acting skeletal muscle relaxant[1,2]. It acts primarily at the level of the spinal cord and subcortical areas of the brain where it inhibits multisynaptic reflex arcs involved in producing and maintaining skeletal muscle spasm of varied etiology. The clinical result is a reduction of the skeletal muscle spasm with relief of pain and increased mobility of the involved muscles[3]. Another mechanism of CHZ is to inhibit degranulation of mast cells, subsequently preventing the release of histamine and slow-reacting substance of anaphylaxis (SRS-A), mediators of type I allergic reactions. CHZ may also reduce the release of inflammatory leukotrienes. In

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addition, CHZ may act by inhibiting calcium influx[4]. A previous report showed that the drug is rapidly absorbed from the gastrointestinal tract[5]. Onset of therapeutic activity is observed within 1 hour, with a duration of action of approximately 6 hours[6].

CHZ is almost exclusively metabolized by CYP2E1 to a single major metabolite, 6-hydroxychlorzoxazone (6-OH-CHZ), which is rapidly glucuronidated and eliminated by the kidney[7]. CHZ exists in the unchanged form in plasma but is not generally found (< 1% of a dose) in urine, whereas 6-OH-CHZ is predominantly present in both plasma and urine as a glucuronide conjugate[1]. CHZ selectivity to CYP2E1 as well as its good safety record makes the drug a suitable *in vivo* probe of CYP2E1 activity in humans[8]. It is now used as an indicator of exposure to organic solvents, and to monitor liver function before and after transplantation as well as the severity of liver disease, mainly alcoholic liver disease[9]. Racial and ethnic differences in drug metabolism, on the basis of genetic or environmental factors, have become increasingly important[10]. However, no clinical pharmacokinetic data are reported in Thai population. The pharmacokinetics of CHZ in healthy Thai volunteers should be studied for proper application to the patients. Therefore, the aim of the present study was to determine the pharmacokinetic parameters of CHZ in healthy Thai volunteers. The pharmacokinetics of the main metabolite of CHZ, 6-OH-CHZ, was also investigated.

## Material and Method

### *Volunteers*

Ten healthy Thai volunteers (4 male and 6 female) participated in the present study. All of the volunteers were judged healthy on the basis of medical history, physical examination, and laboratory test including liver function tests. They were nonsmokers. They were not taking any medications and had abstained from alcohol use for 1 week prior to the studies. They were enrolled in the present study after each had given written informed consent. The protocol was approved by the Institutional Ethical Review Committee of Faculty of Medicine, Chulalongkorn University.

### *Chemicals*

CHZ tablets (Maselax®, 200 mg) were obtained from the Thai Japan Laboratories Co., LTD. Standards of CHZ, 3-aminophenyl sulfone (internal standard) and β-glucuronidase (Type G0751) were purchased from Sigma. 6-OH-CHZ was purchased from Ultrafine Chemicals (Manchester, UK). HPLC grade acetonitrile and diethyl ether were purchased from Merck.

### *Drug administration*

After an overnight fasting, the volunteers were administered 400 mg CHZ orally. Breakfast and lunch were given at 2 hours and 4 hours after the dose, respectively. Serial blood samples (5 ml each) were obtained from an arm vein at the following intervals: 0 (pre-dose), 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6 and 8 hours after drug administration. The samples were collected in sodium citrate tubes, centrifuged, and the separated plasma was stored at -20$^{O}$C until analysis for CHZ and 6-OH-CHZ concentrations.

### *Method validation*

Method for CHZ and 6-OH-CHZ analysis was validated following Guidance for industry: Bioanalytical method validation (U.S. Department of Health and Human Series FDA, CDER, CVM. May 2001, BP)[11].

### *Sample preparation*

Plasma CHZ and 6-OH-CHZ were determined by a modification of a reversed-phase high-performance liquid chromatography (HPLC) assay as described previously by Frye et al[1] and Mishin et al[12].

### *Instruments and HPLC conditions*

The HPLC column was a $C_{18}$ reversed-phase column (250 x 4.6 mm I.D., particle size 5 μm). The mobile phase was composed of phosphoric acid (0.5%, pH 3.5): acetonitrile (70:30, v/v) and the flow rate was 0.8 ml/min. 50 μl sample aliquots were injected onto the column. The absorbance of the eluent was monitored by UV detector at 287 nm.

### *Data analysis*

Maximum concentration ($C_{max}$) and time to reach the maximal concentration ($T_{max}$) for CHZ and 6-OH-CHZ were evaluated for each patient. The area under the concentration-time curve $(AUC)_{CHZ(0-8)}$ and $AUC_{6\text{-}OH\text{-}CHZ(0-8)}$ were determined by trapezoidal rule. $AUC_{CZX(0-\infty)}$ was calculated by the sum of $AUC_{0-8}$ and $C_{last}$ / $K_{el}$, $C_{last}$ was the 8-hour concentration. $K_{el}$ is the elimination rate constant estimated from the slope of log concentration-time curve in elimination phase. An elimination half-life ($t_{1/2}$) for CHZ and 6-OH-CHZ were calculated from the ratio of 0.693 / $K_{el}$. Oral clearance (Cl) for CHZ was calculated from the dose / $AUC_{0-\infty}$ ratio. An apparent volume of distribution (Vd) was calculated from Cl / $K_{el}$ ratio.

All pharmacokinetic parameters were presented as mean ± standard deviation (SD) and range in the text and table and as mean ± standard error of mean (SEM) in the figure.

**Results**

The present method used for determination of CHZ and 6-OH-CHZ in plasma showed high sensitivity with clear separation of peak of CHZ, 6-OH-CHZ, internal standard and any endogenous substances (Fig. 1). The least-squares regression analysis gave a mean linear correlation coefficient of $r^2 = 0.9999$ and 0.9989 for CHZ and 6-OH-CHZ, respectively. The intra-day and inter-day of low, medium and high concentrations were in the acceptable range (%CV < 15%). The accuracy of low, medium and high concentrations were within the acceptable limit 85-115%.

The mean ± SD and range of demographic data of all volunteers are presented in Table 1. The volunteers were aged 26 - 38 years (33.80 ± 4.85 years), weighed 41-70 kg (57.60 ± 7.93 kg), and had a height of 150.0-175.0 cms (160.0 ± 0.09 cms). Their body mass indices (BMI) were within the range of 18-25 kg / $m^2$. The clinical laboratory data of all volunteers were presented as mean ± SD with ranges shown in Table 1. They were in good health with normal liver and renal function.

All volunteers completed the study with no adverse events observed following CHZ administration. CHZ was rapidly absorbed with the maximum levels of CHZ reached within 1 to 3 hours in most volunteers, presented by $T_{max}$ of 2.00 ± 0.82 hours, and the mean maximum concentration ($C_{max}$) of CHZ was 7.15 ± 2.09 μg/ml. CHZ was rapidly metabolized to 6-OH-CHZ with the peak concentration of 6-OH-CHZ ($C_{max}$) 1.77 ± 0.56 μg/ml, and $T_{max}$ of 3.05 ± 1.17 hours. Representative mean concentration-time profiles of

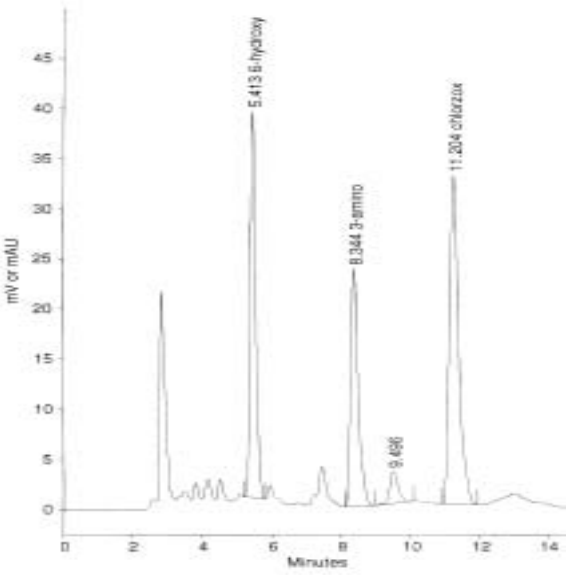


**Fig. 1** Chromatograms of standard 6-OH-CHZ, internal (3-aminophenyl sulfone) and CHZ in plasma sample with the retention times of 5.4, 8.3 and 11.2 min, respectively

CHZ and 6-OH-CHZ are shown in Fig. 2. The area under the concentration-time from 0 to 8 ($AUC_{0-8}$) was 25.47 ± 7.11 and 7.32 ± 2.21 μg.hr/ml for CHZ and 6-OH-CHZ, respectively, and area under the concentration-time from 0 to infinity ($AUC_{0-\infty}$) was 27.52 ± 8.05 and 8.50 ± 2.78 μg.hr/ml for CHZ and 6-OH-CHZ, respectively. The $K_{el}$ values calculated from slope of elimination phase of CHZ and 6-OH-CHZ were 0.48 ± 0.10 and 0.40 ± 0.13 $hr^{-1}$, respectively. The elimination half-life ($t_{1/2}$) was 1.49 ± 0.32 and 1.95 ± 0.73 hours for CHZ and 6-OH-CHZ, respectively. Oral clearance (Cl) and apparent volume of distribution (Vd) of CZX appeared to be 15.77 ± 4.81 (L/hr) and 33.13 ± 9.75 L, respectively.

**Table 1.** Demographic and Clinical laboratory data of 10 healthy Thai volunteers enrolled in the study

| | Mean ± SD | Range |
|---|---|---|
| Age (years) | 33.80 ± 4.85 | 26-38 |
| Weight (kg) | 57.60 ± 7.93 | 41-70 |
| Height (cm) | 160.00 ± 0.09 | 150.0-175.0 |
| Body mass index (BMI) (kg / $m^2$) | 22.56 ± 2.20 | 18.22-25.25 |
| Glucose (Normal, 70-110 mg/dl) | 88.30 ± 7.44 | 77-100 |
| Creatinine (Normal, 0.5-2.0 mg/dl) | 0.74 ± 0.22 | 0.5-1.1 |
| SGOT (Normal, 0-38 U/L) | 21.20 ± 5.51 | 14-28 |
| SGPT (Normal, 0-38 U/L) | 17.80 ± 9.02 | 9-37 |
| Alkaline phosphatase (Normal, 39-117 U/L) | 63.50 ± 13.17 | 44-93 |

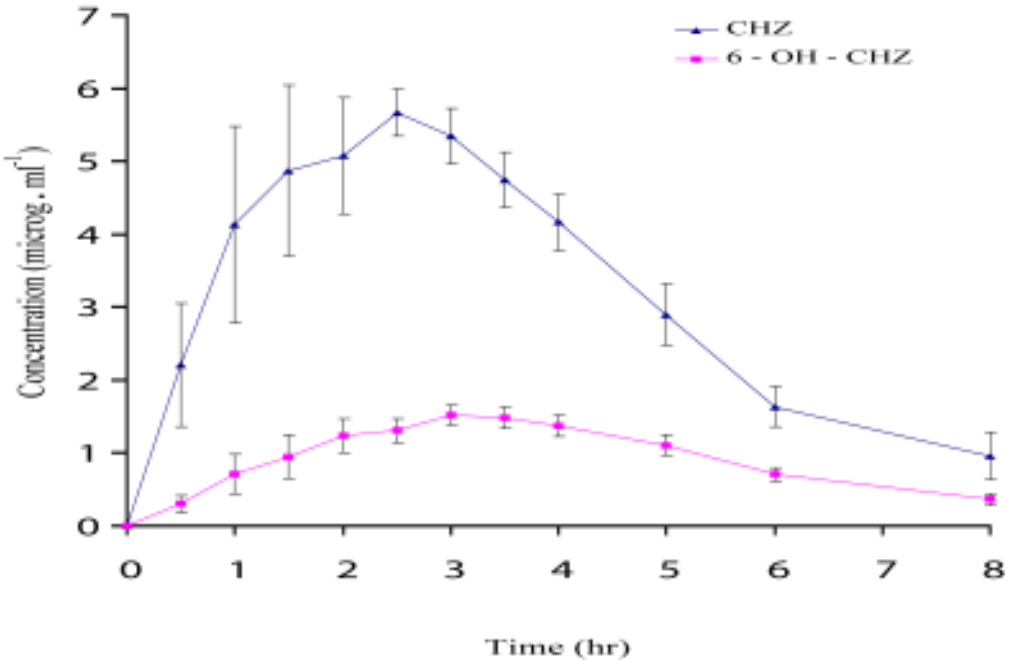


**Fig. 2** Mean (± SEM) plasma concentration-time profiles of CHZ and 6-OH-CHZ (n = 10)

All pharmacokinetic parameters of CHZ and 6-OH-CHZ are presented in Table 2.

## Discussion

The result of the present study demonstrated that CHZ was well tolerated. No adverse event was detected. It has already been known that maximum concentration ($C_{max}$) and the time to reach the maximum concentration ($T_{max}$) show the involving the rate of drug absorption. The present results showed that CHZ was rapidly absorbed with time to reach peak concentration within 2 hours. The area under the concentration time-curve (AUC) is a parameter indicating the extent of drug absorption into systemic circulation. The $AUC_{0-\infty}$ of CHZ determined from the present study was 27.52 ± 8.05 μg.hr/ml. Other parameters indicated that CHZ had a short elimination half-life ($t_{1/2}$), high clearance (Cl) and large volume of distribution (Vd).

A comparison of pharmacokinetic parameters of CHZ between healthy Thai volunteers and other ethnic volunteers is shown in Table 3. $T_{max}$ of CHZ in healthy Thai volunteers was equal to that of healthy Japanese volunteers. The elimination half-life ($t_{1/2}$) of CHZ in healthy Thai volunteers (1.49 ± 0.32 hours) was slightly longer than that of healthy Japanese volunteers (1.09 ± 0.20 hours) and healthy American

**Table 2.** Pharmacokinetic parameters of CHZ and 6-OH-CHZ in 10 healthy Thai volunteers

| Pharmacokinetic parameters | CHZ | | 6-OH-CHZ | |
|---|---|---|---|---|
| | Mean ± SD | range | Mean ± SD | range |
| $C_{max}$ (μg/ml) | 7.15 ± 2.09 | 9.89-4.91 | 1.77 ± 0.50 | 2.78-1.01 |
| $T_{max}$ (hr) | 2.00 ± 0.82 | 3.00-1.00 | 3.05 ± 1.17 | 5.00-1.50 |
| $AUC_{0-8}$ (μg.hr/ml) | 25.47 ± 7.11 | 34.16-15.70 | 7.32 ± 2.21 | 10.63-4.88 |
| $AUC_{0-\infty}$ (μg.hr/ml) | 27.52 ± 8.05 | 39.44-16.58 | 8.50 ± 2.78 | 12.14-5.25 |
| $K_{el}$ ($hr^{-1}$) | 0.48 ± 0.10 | 0.62-0.34 | 0.40 ± 0.13 | 0.59-0.21 |
| $T_{1/2}$ (hr) | 1.49 ± 0.32 | 2.01-1.12 | 1.95 ± 0.73 | 3.32-1.17 |
| Cl (L/hr) | 15.77 ± 4.81 | 24.13-10.14 | - | - |
| Vd (L) | 33.13 ± 9.75 | 51.98-19.85 | - | - |

**Table 3.** Comparison of pharmacokinetic parameters of CHZ in healthy Thai, Japanese and American volunteers

| Pharmacokinetic parameter | Thai $\overline{X} \pm$ SD (400 mg CHZ) n = 10 | Japanese[13] $\overline{X} \pm$ SD (250 mg CHZ) n = 20 | American[6] $\overline{X} \pm$ SD (500 mg CHZ) n = 10 |
|---|---|---|---|
| $T_{max}$ of CHZ (μg/ml) | 2.00 ± 0.82 | 2.1 ± 1.0 | - |
| $T_{1/2}$ of CHZ (hr) | 1.49 ± 0.32 | 1.1 ± 0.2 | 1.09 ± 0.20 |
| $T_{1/2}$ of 6-OH-CHZ (hr) | 1.95 ± 0.73 | - | 1.28 ± 0.23 |
| Cl of CHZ (L/hr) | 15.77 ± 4.81 | 13.0 ± 4.5 | 13.92 ± 4.98 |

volunteers (1.10 ± 0.2 hours). Similarly, $t_{1/2}$ of 6-OH-CHZ in healthy Thai volunteers (1.95 ± 0.73 hours) was longer than that of healthy Japanese volunteers (1.28 ± 0.23 hours). Oral clearance (Cl) of CHZ in healthy Thai (15.77 ± 4.81 L/hr) was slightly higher than that of healthy Japanese volunteers (13.92 ± 4.98 L/hr) and healthy American volunteers (13.0 ± 4.5 L/hr). CHZ is almost exclusively metabolized by CYP2E1 to 6-OH-CHZ[7]. Racial and ethnic differences in drug-metabolizing ability associated with genetic or environmental factors are well recognized[10]. Therefore, racial and ethnic differences in drug metabolism and inter-individual variability may be the reasons for the differences in the pharmacokinetics of CHZ in healthy Thai, Japanese and American volunteers.

CHZ can be used as a selective *in vivo* probe of CYP2E1 activity in humans[14,15]. It is now used to monitor liver function before and after transplantation and the severity of liver disease[9]. The present study yielded pharmacokinetic data of CHZ and 6-OH-CHZ in healthy Thai volunteers. The data of $T_{max}$ of CHZ and 6-OH-CHZ with the range of 1 to 3 hr may suggest the appropriate time point to monitor the level of 6-OH-CHZ/CHZ ratio that is used to indicate CYP2E1 activity in the patients with liver diseases.

In conclusion, pharmacokinetic characteristics of 400 mg oral dose of CHZ were reported in healthy Thai volunteers. These parameters reflected absorption, distribution, and elimination of CHZ. The data may be applied for clinical use in Thai patients.

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**References**

1. Frye RF, Stiff DD. Determination of chlorzoxazone and 6-hydroxychlorzoxazone in human plasma and urine by high-performance liquid chromatography. J Chromatogr B Biomed Appl 1996; 686: 291-6.
2. Lucas D, Berthou F, Girre C, Poitrenaud F, Menez JF. High-performance liquid chromatographic determination of chlorzoxazone and 6-hydroxychlorzoxazone in serum: a tool for indirect evaluation of cytochrome P4502E1 activity in humans. J Chromatogr 1993; 622: 79-86.
3. The comprehensive resource for physicians, drug and illness information. Available from: http://www.rxmed.com/b.main/b2.pharmaceutical/b2.1.monographs/CPS-%20Monographs/CPS-%20(General%20Monograpl. Dec, 2004.
4. Drug bank: chlorzoxazone. Available from: http://redpoll.pharmacy.ualberta.ca/drugbank/cgi-bin/getCard.cgi?CARD=APRD00308.txt. Oct, 2005.
5. Leclercq I, Horsmans Y, Desager JP. Estimation of chlorzoxazone hydroxylase activity in liver microsomes and of the plasma pharmacokinetics of chlorzoxazone by the same high-performance liquid chromatographic method. J Chromatogr A 1998; 828: 291-6.
6. Wang Z, Hall SD, Maya JF, Li L, Asghar A, Gorski JC. Diabetes mellitus increases the in vivo activity of cytochrome P450 2E1 in humans. Br J Clin Pharmacol 2003; 55: 77-85.
7. Dreisbach AW, Ferencz N, Hopkins NE, Fuentes MG, Rege AB, George WJ, et al. Urinary excretion of 6-hydroxychlorzoxazone as an index of CYP2E1 activity. Clin Pharmacol Ther 1995; 58: 498-505.
8. Ernstgard L, Warholm M, Johanson G. Robustness of chlorzoxazone as an in vivo measure of cytochrome P450 2E1 activity. Br J Clin Pharmacol 2004; 58: 190-200.
9. Tanaka E, Terada M, Misawa S. Cytochrome P450 2E1: its clinical and toxicological role. J Clin Pharm Ther 2000; 25: 165-75.
10. Poland RA, Lin KM, Nuccio C, Wilkinson GR.

Cytochrome P450 2E1 and 3A activities do not differ between Mexicans and European Americans. Clin Pharmacol Ther 2002; 72: 288-93.
11. U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Veterinary Medicine (CVM). Guidance for Industry: Bioanalytical Method Validation. May 2001, BP.
12. Mishin VM, Rosman AS, Basu P, Kessova I, Oneta CM, Lieber CS. Chlorzoxazone pharmacokinetics as a marker of hepatic cytochrome P4502E1 in humans. Am J Gastroenterol 1998; 93: 2154-61.
13. Kim RB, Yamazaki H, Chiba K, O'Shea D, Mimura M, Guengerich FP, et al. In vivo and in vitro characterization of CYP2E1 activity in Japanese and Caucasians. J Pharmacol Exp Ther 1996; 279: 4-11.
14. Kramer I, Dalhoff K, Clemmesen JO, Loft S, Poulsen HE. Comparison of chlorzoxazone one-sample methods to estimate CYP2E1 activity in humans. Eur J Clin Pharmacol 2003; 59: 775-8.
15. Emery MG, Fisher JM, Chien JY, Kharasch ED, Dellinger EP, Kowdley KV, et al. CYP2E1 activity before and after weight loss in morbidly obese subjects with nonalcoholic fatty liver disease. Hepatology 2003; 38: 428-35.

## เภสัชจลนศาสตร์ของคลอซอกซาโซนในอาสาสมัครคนไทยสุขภาพดี

**นันทพร พรมพิลา, สุพีชา วิทยเลิศปัญญา, ปิยะวัฒน์ โกมลมิศร์**

***ภูมิหลัง:*** *คลอซอกซาโซนเป็นยาคลายกล้ามเนื้อ ออกฤทธิ์ต่อระบบประสาทส่วนกลาง ถูกเปลี่ยนแปลงได้ด้วยเอนไซม์ไซโตโครม พี450 2อี1 ไปเป็น 6-ไฮดรอกซีคลอซอกซาโซน สามารถใช้ตรวจวัดการทำงานของเอนไซม์ไซโตโครม พี450 2อี1 ในผู้ป่วยโรคตับได้ ข้อมูลเภสัชจลนศาสตร์ของคลอซอกซาโซนในคนไทยควรจะได้รับการศึกษาก่อนที่จะนำไปประยุกต์ใช้กับผู้ป่วยคนไทย*

***วัตถุประสงค์:*** *เพื่อศึกษาเภสัชจลนศาสตร์ของคลอซอกซาโซน*

***วัสดุและวิธีการ:*** *ศึกษาในอาสาสมัครคนไทยสุขภาพดีจำนวน 10 ราย หลังจากงดรับประทานอาหารหลังเที่ยงคืน ให้อาสาสมัครรับประทานยาคลอซอกซาโซนปริมาณ 400 มิลลิกรัม เจาะเลือดอาสาสมัครก่อนรับประทานยาและหลังจากรับประทานยาที่เวลา 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6 และ 8 ชั่วโมง ตามลำดับ วิเคราะห์หาระดับคลอซอกซาโซนและ 6-ไฮดรอกซีคลอซอกซาโซนในพลาสมาด้วยวิธี high-performance liquid chromatography (HPLC) โดยใช้ UV detector เป็นเครื่องตรวจวัด คำนวณค่าเภสัชจลนศาสตร์ต่าง ๆ ได้แก่ ความเข้มข้นสูงสุดของยา ($C_{max}$) ระยะเวลาที่ยามีความเข้มข้นสูงสุด ($T_{max}$) พื้นที่ใต้กราฟของความเข้มข้นของยากับเวลา ($AUC_{0-8}$ และ $AUC_{0-\infty}$) ค่าคงที่ในการขจัดยาออกจากร่างกาย ($K_{el}$) ค่าครึ่งชีวิต ($t_{1/2}$) อัตราการขจัดยา (Cl) และปริมาตรการกระจายตัวของยา (Vd)*

***ผลการศึกษา:*** *คลอซอกซาโซนถูกดูดซึมเข้าสู่กระแสเลือด โดยมีระดับยาในเลือดสูงสุด ($T_{max}$) ที่เวลาเฉลี่ย 2.00 $\pm$ 0.82 ชั่วโมง ค่าความเข้มข้นของยาในเลือดสูงสุด ($C_{max}$) เฉลี่ย 7.15 $\pm$ 2.09 ไมโครกรัมต่อมิลลิลิตร คลอซอกซาโซนถูกเปลี่ยนแปลงไปเป็น 6-ไฮดรอกซีคลอซอกซาโซน โดยระดับ 6-ไฮดรอกซีคลอซอกซาโซนในเลือดสูงสุดที่เวลาเฉลี่ย 3.05 $\pm$ 1.17 ชั่วโมง และมีค่าความเข้มข้นในเลือดสูงสุดเฉลี่ย 1.77 $\pm$ 0.50 ไมโครกรัมต่อมิลลิลิตร ปริมาณคลอซอกซาโซนที่ถูกดูดซึมแสดงได้ด้วยพื้นที่ใต้กราฟ (AUC) มีค่าเฉลี่ย 25.47 $\pm$ 7.11 และ 27.52 $\pm$ 8.05 ไมโครกรัม.ชั่วโมงต่อมิลลิลิตร สำหรับ $AUC_{0-8}$ และ $AUC_{0-\infty}$ ตามลำดับ พื้นที่ใต้กราฟของ 6-ไฮดรอกซีคลอซอกซาโซนมีค่าเฉลี่ย 7.32 $\pm$ 2.21 และ 8.50 $\pm$ 2.78 ไมโครกรัม.ชั่วโมงต่อมิลลิลิตร สำหรับ $AUC_{0-8}$ และ $AUC_{0-\infty}$ ตามลำดับ ค่าคงที่อัตรา การขจัดยาออกจากร่างกาย ($K_{el}$) ของคลอซอกซาโซนและ 6-ไฮดรอกซีคลอซอกซาโซนมีค่าเฉลี่ย 0.48 $\pm$ 0.10 และ 0.40 $\pm$ 0.13 ต่อชั่วโมง ตามลำดับ ค่าครึ่งชีวิต ($t_{1/2}$) ของคลอซอกซาโซนและ 6-ไฮดรอกซีคลอซอกซาโซนมีค่าเฉลี่ย 1.49 $\pm$ 0.32 และ 1.95 $\pm$ 0.73 ชั่วโมง ตามลำดับ อัตราการขจัด (Cl) และปริมาตรการกระจายตัว (Vd) ของคลอซอกซาโซนเฉลี่ย 15.77 $\pm$ 4.81 ลิตรต่อชั่วโมง และ 33.13 $\pm$ 9.75 ลิตร ตามลำดับ*

***สรุป:*** *การรับประทานยาคลอซอกซาโซนปริมาณ 400 มิลลิกรัม ให้ข้อมูลทางเภสัชจลนศาสตร์ ซึ่งข้อมูลเหล่านี้ ได้แสดงถึงลักษณะการดูดซึม การกระจายตัว และการขจัดของยาคลอซอกซาโซนในอาสาสมัครคนไทยสุขภาพดี*