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ที่มีจำหน่ายในประเทศไทย



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BIOAVAILABILITY OF DOXYCYCLINE CAPSULES

COMMERCIALY AVAILABLE IN THAILAND

MISS SOMSRI RIENNIYOM

A Thesis Submitted in Partial Fulfillment of the Requirements
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สมศรี เจริญนิยม : การเอื้อประโยชน์ในร่างกายของยาแคปซูลดอกซีไซคลินที่มีจำหน่าย
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การวิจัยครั้งนี้มีจุดมุ่งหมายเพื่อเปรียบเทียบความสมมูลในร่างกายของยาแคปซูลดอกซีไซคลิน
ขนาด 100 มิลลิกรัมที่ผลิตในประเทศกับผลิตภัณฑ์ต้นแบบ (ไวบรามัยซิน) โดยจะมีการประเมินคุณภาพทั้ง
ในหลอดทดลองและในร่างกาย

การศึกษาในหลอดทดลองได้ทดสอบการแตกกระจายตัวและการละลายของยาดอกซีไซคลิน
แคปซูลทั้งหมด 8 บริษัท ที่ทำการศึกษานี้เข้ามาตรฐานของ เกล็ดซ์ตัวรับสหรัฐอเมริกา

แคปซูลดอกซีไซคลิน 4 บริษัท ซึ่งมีค่าคงที่อัตราการละลายต่าง ๆ กัน ได้ถูกเลือกมาศึกษา
ถึงการเอื้อประโยชน์ในร่างกายโดยใช้อาสาสมัครชายไทย 20 คน ที่มีสุขภาพสมบูรณ์ และมีอายุระหว่าง
18-24 ปี รับประทานยาแคปซูลดอกซีไซคลิน 100 มิลลิกรัม 1 เม็ดต่อบริษัท หลังจากอดอาหารตลอดคืน
และจะได้รับยาแคปซูลบริษัทอื่นถัดไปทุก 2 สัปดาห์ แบบแผนการรับประทานยาเป็นแบบการทดลองอย่าง
ข้ามสมบูรณ์ ตัวอย่างเลือดจะถูกเก็บก่อนรับประทานยา และหลังรับประทานยาทันทีจนถึง 33 ชั่วโมง
ตัวอย่างพลาสมาถูกแยกออกทันที เพื่อนำไปหาปริมาณดอกซีไซคลิน โดยใช้วิธีไฮเพอร์ฟอร์แมนซ์ลิควิด
โครมาโตกราฟี ผลปรากฏว่า ยาดอกซีไซคลินแคปซูลต้นฉบับ มีปริมาณยาที่ถูกดูดซึมน้อยกว่ายาบริษัท
อื่น ๆ อีก 3 ตัวรับที่ผลิตในประเทศ แต่อัตราเร็วในการดูดซึมไม่แตกต่างกัน

การศึกษานี้พบว่าเวลาในการแตกกระจายตัว กับค่าคงที่อัตราการละลายไม่มีความสัมพันธ์
เชิงเส้นกันอย่างมีนัยสำคัญทางสถิติที่ระดับความเชื่อมั่น 95% ทำนองเดียวกันเวลาในการแตกกระจายตัว
และค่าคงที่อัตราการละลายก็ไม่มีความสัมพันธ์เชิงเส้นอย่างมีนัยสำคัญที่ระดับความเชื่อมั่น 95% กับ
พารามิเตอร์ทางเภสัชจลนศาสตร์ (AUC_0^t , AUC_0^∞ , และ C_{pmax})

ค่าเฉลี่ยของระดับยาสูงสุดในพลาสมาอยู่ระหว่าง 1.53 ถึง 2.15 ไมโครกรัมต่อมิลลิลิตร
ส่วนเวลาที่พบระดับยาสูงสุดในร่างกายมีค่าตั้งแต่ 1.55 ถึง 2.25 ชั่วโมง ค่าครึ่งชีวิตของดอกซีไซคลิน
ในคนไทยโดยเฉลี่ยคือ 15.09 (12.88 ถึง 16.67) ชั่วโมง ซึ่งค่าดังกล่าวนี้ใกล้เคียงกับค่าที่มี
รายงานไว้ในวารสารต่างประเทศ

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SOMSRI RIENNIYOM : BIOAVAILABILITY OF DOXYCYCLINE CAPSULES
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This research study was proposed to compare the rate and extent of absorption of the local manufactured brands of 100 mg doxycycline capsules relative to the original brand, Vibramycin[®], according to both the in vitro and in vivo results. The disintegration time and dissolution rate of doxycycline capsules were determined from the in vitro studies. All eight brands studied met the United State Pharmacopoeia XXI specification.

Four brands of doxycycline capsules which showed the differences in their dissolution rate constants were selected for bioequivalent study in 20 Thai healthy male volunteers, age ranged from 18 to 24 years. The 100 mg single dose of doxycycline capsule from four selected brands was administered to individual overnight fasted volunteer following a complete crossover design. Blood samples of every subject were collected before the administration of a drug and immediately after drug administration up to 33 hours. Plasma samples were separated and doxycycline levels were determined using a high performance liquid chromatographic technique. The innovator's product (brand A) significantly ($p < 0.05$) showed the lower of extent of doxycycline absorption than those from the local manufactured products (band B, C, D) while the rate of drug absorbed into the body was not different.

There were no statistically significant linear correlation between the disintegration time and the dissolution rate constants. Also no correlation between the in vitro and the in vivo parameters (AUC_0-t , AUC_0^∞ and C_{pmax}) were observed ($p > 0.05$).

The mean peak plasma doxycycline concentrations were ranged from 1.53 to 2.15 $\mu\text{g/ml}$ and the time to peak plasma level ranged from 1.55 to 2.25 hours. The mean biological half-life of doxycycline in Thai male was 15.09 (12.88-16.67) hours which was similar to the other previously reported.

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ABBREVIATIONS

g	gram
ml	millilitre
min	minute
mg	milligram
μ g	microgram
μ l	microlitre
kg	kilogram
cm	centrimetre
IV	intravenous
mv	millivolt
μ m	micrometre
mm	millimetre
id	internal diameter
M	Molar
HPLC	High Performance Liquid Chromatography
$^{\circ}$ C	degree celcius
rpm	revolutions per minute
nm	nanometre
S.D.	Standard Deviation
hr.	hour
conc.	concentration
Cpmax	peak plasma level
Tmax	Time to peak plasma level
Ka	Absorption rate constant
AUC $_{0}^{\infty}$	area under the plasma concentration time curve
t $_{0}$	lag time
SGOT	Serum Glutamic Oxaloacetic Transaminase
SGPT	Serum Glutamic Pyruvic Transaminase
SEM	Standard error of the mean