การศึกษาเปรียบเทียบการเอื้อประโยชน์ในร่างกายของยาเม็ดนาโพรเซนที่มีจำหน่ายในประเทศไทย

นางสาว อุษา อมรสิริพาณิชย์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต

ภาควิชาเภสัชกรรม

บัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

พ.ศ. 2531

ISBN 974-569-571-8

Comparative Studies of Bioavailability of Naproxen Tablets Commercially Available in Thailand

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A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science in Pharmacy

Department of Pharmacy

Graduate School

Chulalongkorn University

1988

ISBN 974-569-571-8

Thesis Title Comparative Studies of Bioavailability of Naproxen Tablets Commercially Available in Thailand

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อุษา อมรสิริพาณิชย์ : การศึกษาเปรียบเทียบการเอื้อประโยชน์ในร่างกายของยาเม็ดนาโพรเซนที่มีจำหน่ายในประเทศไทย (COMPARATIVE STUDIES OF BIOAVAILABILITY OF NAPROXEN TABLETS COMMERCIALLY AVAILABLE IN THAILAND) อ.ที่ปรึกษา : ผศ. วราภรณ์ สุวกูล, อ.ที่ปรึกษาร่วม : รศ. ดร. อุทัย สุวรรณกูฏ, 123 หน้า.

การวิจัยครั้งนี้มีจุดมุ่งหมายเพื่อศึกษาความสมบูลในร่างกายของยาเม็ดนาโพรเซนตำรับต่าง ๆ ที่มีจำหน่ายในประเทศไทย เทียบกับยาเม็ด Naprosyn^{R} ซึ่งเป็นตำรับต้นแบบที่นำสั่งจากต่างประเทศ โดยทำการศึกษาทั้งในหลอดทดลองและในร่างกาย

การศึกษานอกร่างกายประกอบด้วย การหา ปริมาณตัวยาสำคัญในยาเม็ด ความแข็ง การแตกกระจายตัว และการละลายของยาเม็ดในสารละลายตัวกลางสองชนิด คือ simulated gastric fluid และ simulated intestinal fluid ผลการวิจัยพบว่า ยาเม็ดทุกตำรับมีปริมาณตัวยาสำคัญตามมาตรฐานของ United States Pharmacopoeia XXI ความแข็งของยาเม็ดมีค่าตั้งแต่ 4.52 ± 0.39 ถึง มากกว่า 20 กิโลปอนด์ และมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) ยาเม็ดนาโพรเซนทั้ง 9 ตำรับมีการแตกกระจายตัวภายในเวลา 30 นาที ได้มาตรฐานที่กำหนดใน United States Pharmacopoeia XXI และค่านี้มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) ค่าคงที่อัตราการละลายของยาเม็ดใน simulated gastric fluid และ simulated intestinal fluid มีค่าตั้งแต่ 0.55 ± 0.09 ถึง 2.03 ± 0.35 ต่อชั่วโมง และ 0.76 ± 0.20 ถึง 6.22 ± 1.96 ต่อชั่วโมงตามลำดับ และพบความแตกต่างกันอย่างมีนัยสำคัญทางสถิติของตำรับ B, D, E, H, I และตำรับ B, D, H, I ตามลำดับ เมื่อเปรียบเทียบกับตำรับ A ซึ่งกำหนดเป็นตำรับต้นแบบ

การศึกษาการเอื้อประโยชน์ในร่างกาย กระทำโดยคัดเลือกยาเม็ดจำนวน 5 ตำรับที่มีการละลายแตกต่างกันมาศึกษาในอาสาสมัครชายไทยสุขภาพดีจำนวน 8 คน โดยใช้แบบแผนทดลองข้าม ระดับยาในพลาสมาที่เวลาต่าง ๆ ภายหลังการรับประทานยาเม็ดนาโพรเซนขนาด 250 มิลลิกรัมครั้งเดียว วัดโดยใช้วิธีจำเพาะของไฮเพอร์ฟอร์แมนซ์ลิควิดโครมาโตกราฟี การวิเคราะห์ข้อมูลทางเภสัชจลนศาสตร์ใช้วิธี noncompartment ผลการวิจัยพบว่า การเอื้อประโยชน์ในร่างกายของยาเม็ดนาโพรเซนตำรับต่าง ๆ ที่นำมาศึกษาไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p > 0.05$)

นอกจากนี้ยังพบว่า ความแข็ง การแตกกระจายตัวของยาเม็ดไม่มีความสัมพันธ์กับอัตราการละลายของยาเม็ดในตัวกลางทั้งสองชนิด ($p > 0.05$) และค่าการแตกกระจายตัวกับค่าคงที่อัตราการละลายในตัวกลางทั้งสองชนิดก็ไม่มีความสัมพันธ์กับค่าพารามิเตอร์ทางเภสัชจลนศาสตร์ (AUC_{o}^{∞}, Ka, Cp_{max} T_{max})

ภาควิชา เภสัชกรรม ลายมือชื่อนิสิต .....

สาขาวิชา เภสัชกรรม

ปีการศึกษา 2531 ลายมือชื่ออาจารย์ที่ปรึกษา .....

USA AMORNSIRIPANISH : COMPARATIVE STUDIES OF BIOAVAILABILITY OF NAPROXEN TABLETS COMMERCIALLY AVAILABLE IN THAILAND.
THESIS ADVISOR : ASSIS. PROF. WARAPORN SUWAKUL, M.Sc.,
THESIS CO-ADVISOR : ASSO. PROF. UTHAI SUVANAKOOT, Ph.D. 123 PP.

Naproxen tablets commercially available in Thailand were investigated in order to assess the bioequivalence of the local manufactured brands relatively to the original brand, Naprosyn®. These tablets were evaluated both in vitro and in vivo.

The in vitro studies included the content of active ingredient, hardness, disintegration time and dissolution rates in both simulated gastric fluid and simulated intestinal fluid. The content of active ingredient of all brands were within the range of limitation as specified by the United States Pharmacopoeia XXI monograph. The hardness of tablet ranged from 4.52 ± 0.39 to more than 20 kp., and statistically significant differences among all brands were observed ($p < 0.05$). All nine brands of naproxen tablets met the United State Pharmacopoeia XXI specification for disintegration time, within 30 minutes, however they were statistically significant differences ($p < 0.05$). The dissolution rate constants of these nine brands in simulated gastric fluid and simulated intestinal fluid ranged from 0.55 ± 0.09 to 2.03 ± 0.35 hour^{-1}, and 0.76 ± 0.20 to 6.22 ± 1.96 hour^{-1}, respectively. Statistical results of dissolution rate constants showed significant differences ($p < 0.05$) between brand A and brands B, D, E, H, I in simulated gastric fluid and between brand A and brands B, D, H, I in simulated intestinal fluid.

The bioavailability of five brands of naproxen tablets with differences in dissolution characteristics were studied in 8 Thai healthy male volunteers using a crossover experiment. A single dose of 250 mg. naproxen tablet was orally administered to individual overnight fasted subjects. Plasma naproxen levels were determined by a specifically high performance liquid chromatographic method. Individual plasma-time profile was analyzed according to noncompartmental method. Results showed that no statistically significant differences ($p > 0.05$) in both the rate and the extent of naproxen absorption among the five brands studied were observed. These indicated that the four local manufactured brands of naproxen tablets were bioequivalent to the original brand.

There were no statistically significant linear correlation between hardness, and disintegration time or dissolution rates in both dissolution media of all brands studied ($p > 0.05$). The disintegration time and the in vivo parameters (AUC_o^∞, Ka, Cp_{max}, T_{max}) were not correlated ($p > 0.05$). The dissolution rate constants in both dissolution media and the in vivo parameters (AUC_o^∞, Ka, Cp_{max}, T_{max}) were not significantly correlative as well ($p > 0.05$).

ภาควิชา เภสัชกรรม ..... ลายมือชื่อนิสิต .....

สาขาวิชา เภสัชกรรม .....

ปีการศึกษา 2531 ..... ลายมือชื่ออาจารย์ที่ปรึกษา .....

ACKNOWLEDGEMENTS

I would like to express my profound gratitude to Assistant Professor Waraporn Suwakul and Associate Professor Uthai Suvanakoot for their invaluable supervisions, guidance and encouragement.

My appreciation is also expressed to Associate Professor Duangchit Panomvana Na Ayudhya and Dr. Krisana Kraisintu for their kindness and helpful.

Special thanks is given to Mrs. Sunan Rungsrikansong for her collaboration and helpful advices in HPLC techniques. Sincere thanks are also extended to staffs of Department of Pharmacy and friends for their cooperations.

I am greatly indebted to The Government Pharmaceutical Organization for granting financial support to conduct this project.

Finally, I wish to express my appreciation to my beloved parents, sisters and brothers for their loves, encouragement, understanding, and financial support throughout my study in Chulalongkorn University.

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LIST OF ABBREVIATIONS

°C	=	degree Celcius
%	=	percent
µg	=	microgram
mg	=	milligram
g	=	gram
kp	=	kilopound
µl	=	microlitre
ml	=	millilitre
l	=	litre
nm	=	nanometer
cm	=	centrimeter
rpm	=	revolutions per minute
min	=	minute
hr	=	hour
yr	=	year
AUC_0^∞	=	area under the plasma concentration-time curve
AUMC	=	area under the (first) moment curve
MRT	=	mean residence time
MAT	=	mean absorption time
Ka	=	absorption rate constant
Cp_{max}	=	peak plasma concentration
T_{max}	=	time to peak plasma concentration
$t_{\frac{1}{2}}$	=	half-life