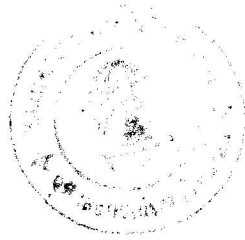


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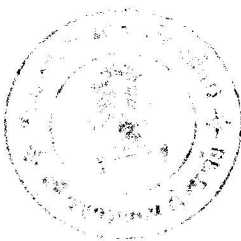
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SYNTHESIS OF PEPTIDES AS POTENTIAL PROTEASE
INHIBITORS FOR ANTIARTHRITIS AND ANTIEMPHYSEMA



MISS JONGKOLNEE JONGARAMRUONG

A Thesis Submitted in Partial Fulfillment of the
Requirements

for the Degree of Master of Science

Department of Chemistry

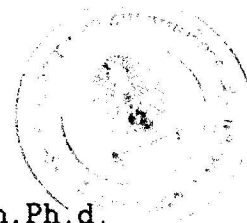
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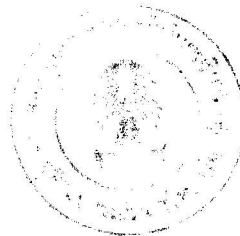
พิมพ์ต้นฉบับบทคัดย่อในภาษาอังกฤษในกรอบสี่เหลี่ยมนี้เพียงแผ่นเดียว

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งานวิจัยนี้ได้ทำการสังเคราะห์เปปไทด์ หรืออนุพันธ์ของกรดอะมิโน จำนวน 13 ตัว ซึ่งทั้งหมดนี้
เป็นสารใหม่ที่ยังไม่เคยมีผู้ใดสังเคราะห์มาก่อน เปปไทด์ที่สังเคราะห์ได้ทำให้ริสฤทธิ์โดยการตกผลึกหลายครั้ง
และแยกโดยคอลัมน์โครมาโทกราฟี ตรวจสอบความบริสุทธิ์ของสารสังเคราะห์โดยวิธีทินแลร์โครมาโทกราฟี
เอชพีแอลซี (HPLC) และการวิเคราะห์หาองค์ประกอบของธาตุในสารประกอบ ทำการพิสูจน์สูตรโครงสร้าง
โดยวิธีอินฟราเรดสเปกโทรสโกปี โปรตอน และคาร์บอน-13 นิวเคลียร์แมกเนติกเรโซแนนซ์สเปกโทรสโกปี

จากการทดสอบสมบัติในการยับยั้งเอนไซม์กลุ่มเซรีนโปรตีเอส ในสภาวะที่เหมาะสม พบว่าสาร
สังเคราะห์ทุกตัวเป็นตัวยับยั้งที่ดีสำหรับทริพซินและโคโมทริพซิน แต่สำหรับอิลาสเตสแสดงฤทธิ์ที่ต่ำมาก จน
ไม่สามารถทำการทดสอบกับตัวยับยั้งที่สังเคราะห์ได้

สรุปได้ว่าสารสังเคราะห์ทั้งหมดไม่สามารถออกฤทธิ์อย่างเฉพาะเจาะจง จึงไม่อาจนำมาใช้เป็น
สารต่อต้านโรคไขข้อ และสารต่อต้านโรคเอดส์ในคนได้



ภาควิชา เคมี
สาขาวิชา เคมีอินทรีย์
ปีการศึกษา 2535

ลายมือชื่อนิสิต สมบัติ รุ่งเรือง
ลายมือชื่ออาจารย์ที่ปรึกษา C 7
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม

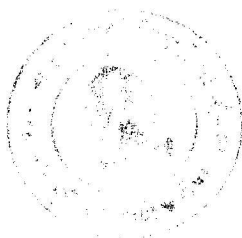
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In the course of this research work, a series of 13 peptides or amino acid derivatives were synthesized. All of the synthetic peptides were novel. These synthetic compounds were purified by fractional recrystallization and column chromatography. The purity of the final compounds was confirmed by thin-layer chromatography, high performance liquid chromatography and elemental analysis. The structure elucidation was performed by infrared spectroscopy, proton and carbon-13 nuclear magnetic resonance spectroscopies.

The enzyme inhibition activities of the synthetic compounds were tested with serine proteases in the optimum conditions. It was found that all the synthetic compounds were good inhibitors against trypsin and chymotrypsin. However, the elastase showed so low activity that it was impossible to be tested with the synthetic compounds.

In conclusion all the synthetic peptides were not specific inhibitors and they could not be used for further testing in treatment of antiarthritis and antiemphysema in human.



ภาควิชา.....เคมี

สาขาวิชา.....เคมีอินทรีย์

ปีการศึกษา.....2535

ลายมือชื่อนิสิต.....

ลายมือชื่ออาจารย์ที่ปรึกษา.....

ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....

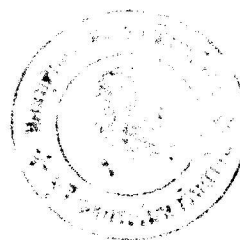
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LIST OF ABBREVIATIONS

Abs	absorbance
Ar	aromatic
BAPNA	N-benzoyl-DL-arginine- <i>p</i> -nitroanilide
BOC	tertiary butyloxycarbonyl
b. p.	boiling point
br.	broad
BZ	benzoyl
calc'd	calculated
°C	degree celcius
cm	centimeter
d	doublet
DMSO	dimethyl sulfoxide
Fig.	Figure
g	gram
HEPES	N-2-hydroxyethylpiperazine-N-2-ethanesulfonic acid
HLE	human leukocyte elastase
Lit	literature
m	multiplet
M	mole per liter or molar
mg	milligram
min	minute
mL	milliliter
mm	millimeter
mM	millimolar
mmole	millimole

m.p.	melting point
M _r	relative molecular weight
nm	nanometer
ppm	parts per million
P	phenylalanine
q	quartet
R _f	rate of flow in chromatography
s	singlet

Suc-Ala-Ala-Pro-Phe-*p*NA

Succinyl-Alanine-Alanine-Proline-Phenylalanine-
paranitroanilide

t	triplet
T	tyrosine
THF	tetrahydrofuran
TLC	thin layer chromatography
V	valine
Z	carbobenzoxy