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This thesis is based on the following papers, which are referred to in the text by their Arabic numbered.

1	El-Seedi, H.R., Abd El-Wahed, A. , Khalifa, S.M., Ali, H.B., Kita, M., Kigoshi, H., Alajlani, M., Backlund, A., Göransson, U. and Verpoorte, R. Chemistry, chemical property space, activity and synthesis of macrocyclopeptide alkaloids. <i>Journal Natural Products</i> , 2017. Accepted. IF= 3.662
2	Hesham R. El-Seedi , Aida A. Abd El-Wahed , Bassem Y. Sheikh, Shaden A. M. Khalifa, Aamer Saeed, Ufuk Koca-Caliskan, Mohammad F. A-Ajmi, Rob Verpoorte. Bee venom composition; unraveling the biodiversity and the potential biological activities. Chapter for published by Elsevier Science Publishers, The Netherlands (Accepted)

Conferences and posters

1. Medical Congress 2013 - Pain and Pain from 12 -13 November, 2013, **Stockholm** Waterfront Congress Centre.
2. Nordic Natural Products conference (NNPC): "Natural Products Research - Past, Present & Future" 15th - 16th June 2015, **Visby**, Sweden with one poster.
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Author's contribution

Participated in the planning experiments, reviewing the literature, chemical analysis, evaluation, and writing.

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Abbreviations

ACN	Acetonitrile
ACPs	Anti-cancer Peptides
Ala	Alanine
AMPs	Anti-microbial Peptides
ANN	Artificial Neural Network
Api m 2	Hyaluronidase
Api m 3	Acid Phosphatase
Api m 5	Dipeptidylpeptidase IV
Api m 7	CUB Serine Protease
Arg	Arginine
Asn	Asparagine
Asp	Aspartic Acid
BV	Bee Venom
BOC	<i>t</i> -Butoxycarbonyl
Fmoc	9-Fluorenylmethyloxycarbonyl
CNS	Central Nervous System
Cys	Cysteine
Da	Dalton
DA	Discriminant Analysis
DCM	Dichloromethane
DIPEA	Diisopropylethylamine
DMF	<i>N,N</i> -Dimethylformamide
DMSO	Dimethyl Sulfoxide
E-value	Expect Value
ESI-MS	Electrospray Ionization-Mass Spectrometry
EtOH	Ethanol
FA	Formic Acid
FDA	Food and Drug Administration
FD	Fluorescein Diacetate
FMCA	Fluorometric Microculture Cytotoxicity Assay
Gln	Glutamine
Glu	Glutamic Acid
Gly	Glycine

HBTU	<i>N,N,N',N'</i> -Tetramethyluroniumhexafluorophosphate
His	Histidine
HIV-1	Human Immune Deficiency Virus 1
HPLC	High Performance Liquid Chromatography
HSV-1	Herpes Simplex Virus 1
IARC	International Agency for Research on Cancer
IC ₅₀	Inhibitory Concentration 50%
Ile	Isoleucine
LC-MS	Liquid Chromatography-Mass Spectrometry
Leu	Leucine
LMW	Low Molecular Weight
Lys	Lysine
NPs	Natural Product
μM	Micromolar
<i>m/z</i>	Mass-To-Charge Ratio
MALDI	Matrix-Assisted Laser Desorption/Ionization
MCD	Mast Cell Degranulating
Met	Methionine
MICs	Minimum Inhibitory Concentrations
MRJPS	Major Royal Jelly Proteins
MS	Mass Spectrometry
MS-MS	Mass Spectrometry-Mass Spectrometry
MW	Molecular Weight
PBS	Phosphate Buffered Saline
Phe	Phenylalanine
PLA2	Phospholipase A2
Pro	Proline
QTOF-MS	Quadrupole Time-Of-Flight- Mass Spectrometry
RF	Random Forest
RJ	Royal Jelly
RT	Room Temperature
S-S bond	Disulfide Bond
Ser	Serine

SI	Survival Index
SPPS	Solid Phase Peptide Synthesis
SVM	Support Vector Machines
TFA	Trifluoroacetic Acid
Thr	Threonine
TIPS	Trimethylsilylisopropane
Trp	Tryptophan
TSB	Tryptic Soy Broth
Tyr	Tyrosine
Val	Valine
WHO	World Health Organization

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Summary

The work present in this thesis was carried out mainly at the Division of Pharmacognosy, Department of Medicinal Chemistry, Faculty of Pharmacy, Uppsala University, Sweden, Division of Clinical Pharmacology, Uppsala University Hospital, Sweden, a laboratory of Natural Products Chemistry, Department of Chemistry, Faculty of Science, EL-Menoufia University, Egypt and Department of Bee Research, Plant Protection Research Institute, Agricultural Research Centre, Egypt.

This study focus in isolation, characterization and identification for bioactive peptide (s) from royal jelly (RJ) and bee venom (BV), in addition to synthesis of secapin and royalisin from BV and RJ, respectively.

Specific objectives of this study were:

- Biologically evaluate for RJ and BV as antimicrobial and anticancer agents, respectively.
- Isolation and structure elucidation of bioactive peptide(s) from RJ and BV.
- Synthesis of bioactive peptide of secapin and royalisin from BV and RJ, respectively.

The work carried out in this thesis had been summarized in the following chapters:

Chapter 1:

1. In this part, it is focus on cancer, antimicrobial diseases and role of natural products in cure of these diseases. Additionally, some current drugs from nature sources as anticancer and antimicrobial.
2. Gives overview on bee products, their ingredients which act as anti-microbial and anti-cancer activities, finally we focused on RJ and BV as source for bioactive peptide(s).

Chapter II: Materials, and methodology

This included the materials and reagents were used in addition to the instruments and databases. The chapter is divided into three parts:

The 1st part: Isolation and identification for bioactive peptide from RJ as anti-microbial.

The 2nd part: Isolation and determination for bioactive peptide from BV as anti-cancer.

The 3rd part: Includes synthesis of secapin and royalisin using solid phase peptide synthesis (SPPS).

Chapter III: Results and discussion

Part 1: Enzymatic hydrolyzate for RJ was performed by trypsin with the high yield 51.6%. Forty three peptides were identified using a combination of mass spectrometry and bioinformatics. Hydrolyzate proteins were fractionation using high pressure liquid chromatography (HPLC) into 14

fractions. Six fractions shown antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans*. Bioassay guided isolation for RJ_F11 leads to isolation and structure elucidation of three peptides ((RJHP_1, 2, 3) using RP-HPLC. The peptides were eluted at R_t 32, 36 and 31.5 min, respectively. The amino acid sequence were HPARFENFDDVNFR, VFHPLLKHHQVMNC DK and LLTFDLTTSKLLK, respectively. The molecular weight for isolated peptides were 1762.85, 1945.78 and 1491.31 Da, respectively. The most active peptide was RJHP_3 (MIC_{100} was 216, 108, and 216 $\mu\text{g/ml}$), respectively compared with melittin (MIC_{100} : 5.17, 7.12, 1.78 and 2.2 $\mu\text{g/ml}$) towards *E. coli*, *P. aeruginosa* and *S. aureus*, respectively.

Part 2: Isolation for four peptide from BV including two new peptides, in addition to melittin, and Mast Cell Degranulating (MCD). The cytotoxic activity of the four peptides were evaluated by FMCA assay, with five different cancer cell lines. Melittin and HF6 peptides were exert promise results as cytotoxic against cancer cell lines (IC_{50} for U-937 GTB, RPMI 8226/s, PRMI 8226/Dox40, CCRF CEM, CEM/ VM-1 at 1.3, 1.1, 1.4, 1.7 and 2.0 μM), respectively, and for melittin while HF6 has IC_{50} at 2.5, 1.8, 2.1, 1.9 and 2.1 μM , respectively.

Part 3: Include the synthesis of two peptides; secapin and royalisin from BV and RJ, respectively by SPPS.