General Summary

Isolation and Biotransformation of Some Biologically Active Natural Products

This study included four parts:

Part I

Phytochemical study of *Nerium oleander* L. roots

Chapter 1

Preliminary Phytochemical Screening

The preliminary phytochemical screening revealed the presence of carbohydrates and/or glycosides, sterols and/or triterpenes and cardenolides

Chapter 2

Chemical investigation of pet. ether extract

This afforded the following compounds:

1- Luepol acetate
2- Oil fraction was analyzed through GC.
3- Triterpene mixture consists of lupeol, α-amyrin and β-amyrin
4- β-sitosterol
Chapter 3

Chemical investigation of methylene chloride extract

This afforded the following compounds:

1- 2,4-di-hydroxy-acetophenone
2- Uzarigenin (14β-hydroxy-5α-card-20(22)-enolide.
3- 3-epi-digitoxigenin.
4- Odoroside-H.
5- 3β-O-(β-D-digosyl)-14β-hydroxy-5α-card-20(22)-enolide.
6- 3β-O-(β-D-digosyl)-14β-hydroxy-5α-card-20(22)-enolide.
7- Strospeside (Gitoxigenin-3-O-β-D-digitaloside).
8- β-sitosterol 3-glucoside.

Chapter 4

Chemical Investigation of Dia-ion Fraction

This afforded the following compounds:

1- Uzarigenin-3-O-β-D-glucopyranosyl- (1→4)- O-β-D-digitalopyranoside.
3- 3β- O –(4-gentiobiosyl-D- digitalopyranoside)- 14β-hydroxy-16α-acetoxy-5β-card-20(22)-enolide.
4- 3β- O-(4-gentiobiosyl-D-diginopyranoside)-14β-hydroxy-5α-card-20(22)-enolide.

Part II

Phytochemical study of *Boswellia carterii* Bird. to isolate major compounds for biotransformation and biology

This study resulted in isolation of:

1- Incensole (1, 12-epoxy-3,7-cembradien-11-ol).
2- 3α-acetoxy-tirucall-8, 24-dien-21-oic acid.

Part III

Biotransformation

This part includes the microbial transformation of two compounds, odoroside-H and uzarigenin by *Cunninghamella echinulata* NRRL 1382. This micro-organism converted both compounds into 7β-hydroxy derivatives.

Part IV

Integrated biological study

This part include several assays which are integrated with molecular docking study.
1- Anti-quorum sensing activity:
Twenty three plant extracts were evaluated for their anti-quorum sensing activity. The most promising plant extract was *Myoporum laetum* leaves especially methylene chloride fraction. Two major compounds were isolated from this fraction, namely, tricin and chrysoeriol, but unfortunately, they have no anti-quorum sensing. On the other hand, the anti-quorum sensing of *Nerium oleander* fractions have no anti-quorum sensing activity. While the assessment of this activity for isolated compounds, we found that compound NOC1 has good activity as anti-quorum sensing.

2- ABTS antioxidant assay: was performed on various isolated compounds and it confirmed that, phenolic compounds as flavonoids have higher antioxidant activity than steroid or triterpenes. Human antioxidant enzyme (PDB code: 3MNG) was used for molecular docking.

3- Cytotoxicity by Ehrlich Ascites in vitro Assay: was performed on isolated compounds. It was found that compound NOC2 and its microbial metabolite NOC2M22 have nearly the same cytotoxic effect. The virtual screening for isolated compounds using molecular docking on two important targets as: Carbonic anhydrase II (CAII) and protein kinase CK2, 3-acetoxy-tirucallic acid was found to be the best fitting
General Summary

for all CAII crystal structures. While for protein kinase CK2, β-sitosterol-3-O-glucoside, NOP1 and tirucallic acid derivatives could be considered as good inhibitors for protein kinase CK2, through docking studies.

4- Cytotoxic Activity of Incensole and 3-acetoxy-tirucallic acid adopting Sulphorhodamine-B (SRB) assay. This assay was performed on prostate carcinoma (PC3) and breast carcinoma (MFC7) and showed that incensole has best IC 50% for both cell lines. This experimental study was supported by docking studies for incensole and 3-acetoxy-tirucallic acid on crystal structures of future targets for anti-cancer therapy.

5- Cardioprotective Effect of Oleogumresin from Boswellia carterii Birdwood. This study revealed the mild cardioprotective effect of oleogum resin against isopernaline induced myocardial infarction.

6- Evaluation of Anti-diabetic potential of Incensole by Experimental and Docking studies. In this study, evaluation of the anti-diabetic effect of incensole against STZ-induced diabetes was done. The experimental and docking studies revealed the beneficial effect of incensole in comparison with standard anti-diabetic drug, glibenclamide.