

Study of Chemotherapeutic Potential of Medicinal Plants viz. Myrtaceae Family and Their Anticancer Activity

Keywords: *Callistemon viminalis*, *Callistemon lanceolatus*, GC/MS, STAT3, apoptosis, cell cycle, δ -Opioid receptor, farnesyl transferase

Interest in traditional medicines is not new but has been spurred in recent years by methodological advances in ethanobotanical and pharmacological studies. On practical ground herbal medicines beset with problems like misleading botanical identification, adulteration, variability in application of common standardization procedures and above all limited studies towards ascertaining the correct origin of the drug. Hence, scientific evaluation of herbal drugs with promising therapeutic use is very much essential. The observation, identification and experimental investigation of the ingredients and the therapeutic effects of indigenous drugs are all interdisciplinary field of research. Based on the extensive medicinal claims of the plants, the current research work was carried out in order to scientifically evaluate the folklore claims and to explore the unexplored phytochemical constituents since no scientific investigations has been made on anticancer activity in these two plants *Callistemon viminalis* and *Callistemon lanceolatus*.

The present thesis comprises of five chapters. The **first chapter** deals with the general introduction including literature of the work done in the area of cancer and defines the objective of the investigation.

The **second chapter** deals with the antioxidant and anticancer compounds present in the *C. viminalis* leaves extracts and its anticancer activity against liver cancer cell lines by inhibiting STAT3 protein. Presence of phenolic and flavonoid content in **ELE** and **MLE** extract of *C. viminalis* might be responsible for the DPPH scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, nitric oxide scavenging and reducing power ability.

Molecular docking results revealed that the hydrophobic and hydrogen bond interactions are the main force for binding of compounds of extracts **ELE** and **MLE** with the SH2 domain of STAT3. Moreover, our results is suggesting the **ELE** and **MLE** extracts reduces the cell proliferation against liver cancer cell lines by inhibiting of STAT3 protein and can be successfully exploited in the herbal formulation of cancer chemoprevention and chemotherapy.

The **third chapter** deals with the antioxidant and anticancer compounds present in the *C. lanceolatus* leaves extracts and its anticancer activity against liver cancer cell lines by inhibiting STAT3 protein. Presence of phenolic and flavonoid content in **ELE** and **MLE** extract of *C. lanceolatus* might be responsible for the DPPH scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, nitric oxide scavenging and reducing power ability. The results of our research revealed that **ELE** and **MLE** extracts of *C. lanceolatus* are better sources of antioxidants.

Molecular docking results revealed that the hydrophobic and hydrogen bond interactions are the main force responsible for binding of compounds present in **ELE** and **MLE** extracts with the SH2 domain of STAT3. Moreover, our results are suggested that **ELE** and **MLE** extracts reduces the cell proliferation against liver cancer cell lines by inhibition of STAT3 and can be successfully exploited in the herbal formulation of cancer chemoprevention and chemotherapy.

The **fourth chapter** describes *C. viminalis* contain some compounds that can be used as possible δ -Opioid receptor (DOR) and farnesyl transferase (FT) protein inhibitors, on the basis of extensive docking experiments corroborated with biological activity spectrum results. However, molecular docking and biological activity spectrum study are the one way of estimating the activity of the molecules involved. Hence, further study could prove this compound to be a probable anti-inflammatory and anti-cancer drug. With these encouraging results, all compounds can be further explored for structural modification and detailed investigations to arrive at possibly newer potent agents with better therapeutic activity and mechanistic details.

The **fifth chapter** describes anticancer compounds from *C. lanceolatus* derived natural compounds and its anticancer activity against cervical cancer cell lines by inhibiting STAT3. To identify STAT3 inhibitors from *C. lanceolatus* derived natural compounds like cyanidin-3,5-diglucoside, kaempferol-3-o- β -d-galactopyranoside and quercetin-3-o-(2''-o-galloyl)- β -d-galactopyranoside by molecular docking studies were carried out. Molecular docking results revealed that the hydrophobic, hydrogen bond and π - π interactions are the main forces for binding of compounds with the SH2 domain of STAT3.

C. lanceolatus derived natural compounds reduced the STAT3 mRNA expression and increased the p53 mRNA expression, as confirmed by RTPCR and also reduced the STAT3 protein expression and increased the p53 protein expression, as confirmed by Western blot. Moreover, our results suggests that the *C. lanceolatus* derived natural compounds reduces the cell proliferation against cervical cancer cell lines by inhibiting of STAT3 protein and can be successfully exploited in the herbal formulation of cancer chemoprevention and chemotherapy.