CHAPTER 3  OBJECTIVES OF THE PROPOSED STUDY

3.1. Aim of the study

Using non-toxic chemical substances is regarded as a promising alternative for the prevention and treatment of human cancer. Moreover, from the literature survey it is clear that employment of polyphenols in combination with chemotherapy regimens can possibly improve the therapeutic efficacy and reduce the side effects of chemotherapy. However, the precise underlying molecular mechanisms remain largely unknown. In this regard, the polyphenol ferulic acid which is rich in dietary sources may act as a sensitizer and protector of chemotherapy.

The aim of the present study is to characterize the chemosensitizing and chemoprotective effects of the dietary polyphenol ferulic acid on cisplatin chemotherapy in different cancer cell lines, normal cells and animal models.

3.2. Objectives

The objective of the current study is to provide insights into the cellular, biochemical, histological and molecular basis of the potentiating effects of ferulic acid on cisplatin chemotherapy in human cervical cancer (in vitro) and Dalton’s lymphoma (in vitro and in vivo), with an emphasis on its ability to regulate cell proliferation and apoptosis.

The specific objectives of the present study are,

- To evaluate the synergistic effect of FA and cisplatin on the cytotoxicity of the cervical cancer cell lines, HeLa and SiHa
- To determine intracellular reactive oxygen species (ROS on FA and/or cisplatin treat on cervical cancer cells
• To find out the alteration in the levels of cellular antioxidants and lipid peroxidation on FA and/or cisplatin treated cells
• To examine the morphological changes during apoptosis in FA primed cisplatin treated cancer cells
• To study the early stages of apoptosis by determining the mitochondrial membrane potential changes on FA and/or cisplatin treated cervical cancer cells
• To find out the effect of FA pretreatment on the changes in nucleus and DNA by examining nuclear condensation and DNA damage in cisplatin treated HeLa and SiHa
• To determine the effect of FA and/or cisplatin on the expression of signaling proteins such as caspase 3, caspase 9, Bcl-2 and p53 which are involved in apoptosis
• To demonstrate the enhancing effect of FA in cisplatin treatment on cytotoxicity, antioxidant and lipid peroxidation status in Dalton’s lymphoma cell lines
• To find out the protective effect of FA over cisplatin therapy on normal cells
• To investigate the antitumor and chemoprotective effects of FA and/or cisplatin combination in Dalton’s lymphoma induced solid tumor and ascitic tumor model in mice.

3.3. **Work design**

The present work was designed to carry out in 5 phases:

• Phase I: *In vitro* studies on the sensitizing effects of FA on cisplatin in cervical cancer cell lines (HeLa and SiHa)
• Phase II: Sensitizing effects of ferulic acid on cisplatin in Dalton’s lymphoma cell lines *in vitro*
• Phase III: Protective effect of FA in cisplatin treatment in normal human lymphocytes

• Phase IV: *In vivo* studies to study the potentiation of the antitumor activity of cisplatin by FA in Dalton’s lymphoma induced solid tumor in Swiss albino mice

• Phase V: *In vivo* studies on chemoprotective effect of FA on cisplatin treated Dalton’s lymphoma induced ascitic tumor on Swiss albino mice.