

Name of the Candidate: Iram Iqbal Hejazi

Name of the Supervisor: Dr. Fareeda Athar

Name of the Co Supervisor: Dr. Sonuchand Thakur

Centre for Interdisciplinary Research in Basic Sciences

Title: Study on the chemotherapeutic potential of plants *Glycyrrhiza glabra* and *Curculigo orchoides*

Abstract

Medicinal plants have been recognized and used throughout human history. Plants produce many chemical compounds having important biological functions, including defence against insects, fungi and herbivores. Chemical compounds in plants mediate their effect on the human body through courses similar to those of conventional drugs. Scientific research is sketching its attention towards naturally-derived combinations and compounds as they are reflected to have fewer toxic side effects paralleled to contemporary treatments such as chemotherapy. The plant kingdom harvests naturally occurring secondary metabolites which are being examined for their antioxidant and anticancer activities. With the success of these plants and their derived compounds that have been developed into essential medications for cancer treatment, new tools are evolving to grow the area more. This study discusses the demand for naturally-derived extracts and compounds from medicinal plants *Glycyrrhiza glabra* Linn and *Curculigo orchoides* Gaertn and their properties which make them targets for potential anticancer treatments.

Plant fractions have been prepared with hexane, chloroform, ethyl acetate, methanol and water and their antioxidant properties are reviewed. Potent antioxidant activity has been well established in both *in vitro* and *in silico* studies which is believed to be responsible for the anticancerous nature of the plant. Results obtained indicate that methanol fraction

of *G. glabra L* exhibited maximum scavenging activity against DPPH and nitric oxide free radicals comparable to standard antioxidant L-AA. Administration of methanol fraction also considerably reduced the malondialdehyde produced due to lipid peroxidation in mammalian liver tissues. Moreover, the levels of antioxidant enzymes SOD, CAT, GST, GPx and GR in the oxidative stress induced tissues were refurbished significantly after treatment with plant's methanol fraction. Moreover, methanol fraction was found to be nontoxic to normal human cell line whereas it inhibited cancer cells HeLa and HepG2 considerably. Apoptosis was established by DAPI fluorescent staining and western blot analysis of pro apoptotic protein caspase-8, caspase-3 and anti-apoptotic protein Bcl-2. There is an up regulation in the levels of pro apoptotic caspase-8 and caspase-3 and down regulation of anti-apoptotic Bcl-2. Furthermore, GC-MS analysis of the methanol fraction revealed the presence of many compounds. *In silico* experiments using Autodock 4.2 tools showed strong affinity of plant compounds towards antioxidant enzymes (proteins) thus validating with the conclusions of antioxidant enzyme assays and establishing a role in cancer pathogenesis. We evaluated antioxidative and anticancerous potential of the plant *Curculigo orchioides Gaertn.* Plant fractions were prepared from dried rhizomes using conventional hot solvent extraction. In vitro antioxidant activity was conducted and active fractions were subjected to GC-MS analysis. Further phytoconstituents were screened and selected on the basis of pharmacokinetic studies using molinspiration online score and Lipinski rule of 5 for drug like characteristics. *In silico* studies using Auto Dock 4.2 tools was performed with preselected antioxidant enzymes downloaded from protein data bank. Furthermore, antioxidant enzyme armory of mammalian tissue was assessed by the selected phytoconstituents (capsaicin and piperine) and cell culture studies on human cancer cell lines HepG2 and HeLa were carried out.