ABSTRACT

Cancer cells differentiate themselves from normal cells in diminished expression of L-asparagine. Hence, they are not capable of producing L-asparagine, and mainly depend on the L-asparagine from the circulating plasma pools. Supplementation of L-asparaginase results in continuous depletion of L-asparagine. Under such environment, cancerous cells do not survive. This phenomenal behavior of cancerous cells was exploited by the scientific community to treat neoplasias using L-asparaginase. This enzyme is also a choice for acute lymphoblastic leukemia, lymphosarcoma and in many other clinical relating to tumour therapy in combination with chemotherapy.

For an asparaginase to be ideally suited for use in antineoplastic therapy, it should satisfy certain criteria. The organism that is selected should produce the asparaginase in high yield, and it should be capable of being grown in large quantities on a simple and inexpensive medium. The procedures developed for purification of the enzyme should be as rapid and simplified as possible, providing pure enzyme in high yield. The purified enzyme should have long term stability on storage, maximal activity at a physiological pH and a Km for substrate below the concentration of the substrate in the blood. The thesis includes six chapters as follows.

Chapter 1 provides general background for understanding baseline research in the area of the selected topic and provides the information about L-asparaginase as an antitumor drug, Treatment with L-asparaginase, Side effects of administration of bacterial L-asparaginase, Resistance to L-asparaginase, and the need for alternative source of L-asparaginase.
Chapter 2 described review of some of the important work carried out in the field of the topic of research. It includes review of sources of L-asparaginase, pharmacology and biochemical aspects of the enzyme and production of L-asparaginase.

Chapter 3 is specifically dedicated to the proposed research methodology used in the research work. It includes the strategy employed for production, statistical design for media optimization purification of L-asparaginase, Characterization of purified L-asparaginase, In silico protein structure modeling, active binding site evaluation and Protein docking. Clinical application which includes, Studies on antitumor effect of L-asparaginase using tumour cell lines, Comparison of antineoplastic activity of L-asparaginase with routine antitumour drugs.

Chapter 4 includes the results of the experiments with appropriate justification and discussion.

Chapter 5 includes the conclusion and future scope of the work.