Research in the use of enzymes as therapeutic agents mark a recent advancing trend in biomedicines. Some very exciting advances include attempts dealing with enzyme replacement in genetic disorders, nutrient or metabolite depletion in cancer therapy, enzymatic alteration of cell surface for immunotherapy, management of autoimmune and other noninfectious inflammatory diseases, use of enzymes and proteins to promote or inhibit blood clotting, and enzyme replacement for digestive disorders.

Much work has been done in this area of research for cancer therapy, subsequent to the discovery of Kidd (1953) that the enzyme L-asparaginase in guinea pig serum was the responsible factor for regression of a murine lymphoma (Broome, 1961 and 1963). Mashburn and Wriston (1964) found an L-asparaginase produced by Escherichia coli to be as effective an antitumour agent as that of the guinea-pig serum. The intense oncolytic effect of the enzyme against a spontaneously occurring canine lymphosarcoma drew attention to asparaginase as a
possibly useful drug in clinical medicine (Old et al., 1967; Macewen et al., 1981; Jeglum et al., 1988). On successful clinical application the enzyme L-asparaginase has become a standard drug for treatment of acute lymphoblastic leukemia (Dolowy et al., 1966; Hill et al., 1969; Grundman and Getten, 1970; Creutziz et al., 1980; Koza et al., 1981; Stein et al., 1982; Winkler et al., 1983; Sanchetee et al., 1985; Vecchi et al., 1986; Martell and Jacobs, 1987; Buchanan et al., 1987; Van et al., 1989).

Asparaginases are found in diverse sources in nature, including bacteria, yeasts, molds, plants and vertebrates. The enzymes derived from microorganisms are the major source of the enzymes for practical clinical use. However, all the asparaginases are not clinically useful. Those derived from E. coli (Mashburn and Wriston, 1964; Jaffe et al., 1971; Haskell et al., 1972; Roberts et al., 1976; Durden and Distasio, 1980, 1981). Erwinia carotovora (Wade et al., 1968; Distasio and Niederman, 1976; Wileman et al., 1986), Citrobacter freundii (Distasio et al., 1976; Davidson et al., 1977 a) and Vibrio succinogenes (Distasio and Niederman, 1976) have been shown to be potentially therapeutically useful. A fungal L-asparaginase produced by Aspergillus terreus has been reported with antitumour activity (DeAngeli, 1970), but it was not put in clinical use.
L-Asparaginase is characterised to degrade L-asparagine into L-aspartic acid and ammonia in a hydrolytic reaction. This causes a rapid depletion of serum asparagine, an exogenous supply of which, is required for the growth of certain tumours (Boyse et al., 1967; and Patterson et al., 1969; and Wileman et al., 1986). Certain lymphoid tumours in animals and man are the most sensitive neoplasms. The L-asparaginase is effective against more than fifty neoplasms of the mouse, three of the rat, and spontaneous canine lymphosarcomas. In man the most responsive disease to asparaginase therapy is acute lymphocytic leukemia. Treatments for solid tumours e.g. lung cancer and melanoma with asparaginase therapy were without significant effects. Nevertheless, the single most important contribution of asparaginase has been the practical demonstration of an enzyme induced selective nutritional deficiency for certain tumour cells as compared with normal cells. It is now known that tumour cells acquire essentiality for some of the non-essential amino acids as well. Depletion caused in their amounts circulating in serum results in decreasing tumour cell proliferation to effect tumour regression. Use of amino acid degrading enzymes for the chemotherapy of cancer has recently developed as a very promising concept in cancer treatment research.

Current studies of its mechanism of action have suggested more research into the molecular modification
and modulation of this enzyme to preserve or enhance its catalytic activity and to increase its permeation into tumour cells while minimizing its toxic effects (O'Driscoll et al., 1975; Karsakevich et al., 1987; Shpurnka et al., 1988; Ho et al., 1988). These researches clearly show the need for new L-asparaginases which should possess an abundant source, ease in purification, storage stability over long terms, low Km value for L-asparagine, the minimal to no immunogenicity, and an independent nature for chemotherapy so that a combination therapy is not required.

With this aim present study was carried out to obtain some new L-asparaginases from potential fungal isolates, to characterise them biochemically and immunologically, and to evaluate their tumouricidal activity under laboratory trials. Work done on L-asparaginases produced by Aspergillus terreus, Cladosporium cladosporioides and Cladosporium oxysporum represents this thesis.
Studies on amino acid degrading enzymes, for both the essential and non-essential amino acids, represent an important approach in chemotherapy for cancer (Holcenberg, 1981; and Roberts, 1981). It has been established that the tumour cells develop an increased demand for certain amino acids, and in this respect some of the otherwise non-essential ones like asparagine, glutamine and arginine may become essential for these cells (Knox et al., 1969; Weber, 1974; Reitzer et al., 1976; and Holcenberg, 1981). Any system of treatment with drugs must, therefore, include one such enzyme in the schedule of drug administration. Acute lymphocytic leukemia in children and some adults has been treated with L-asparaginase in combination of vincristine and prednisone, as well as some other pharmaceuticals (Sutow, 1976; Trueworthy et al., 1978; and Chessels and Cornbleet, 1979).

Intensive research for L-asparaginase has been carried out among microorganisms and other higher forms.