Chapter 1
Introduction
1. INTRODUCTION

Ever since the discovery of Human Immunodeficiency Virus (HIV), as the causative agent of Acquired Immuno deficiency Syndrome (AIDS), presently redesignated as HIV-diseases, research activities sprang up multidirectionally to find antiviral agents for AIDS (Sinoussi, 1996). The major targets of active research have been the inhibitors for Reverse transcriptase (RTI), an enzyme involved in the RNA-dependent DNA synthesis of retroviruses, and for the HIV-1 protease, another replicative enzyme involved in the maturation and release of infectious HIV particles. These researches culminated in the discovery of Azidothymidine (AZT) (Robbins, 1993) and Saquinavir (Winslow, 1995). Limited by moderate clinical efficacy when administered as monotherapy regimen and by adverse side effects, RTIs gave way for non-nucleoside RTIs. However emergence of drug resistant variants of HIV for RTIs curtailed their use in anti-HIV treatment. Alternatively it was believed that HIV protease inhibitors singly or in combination with RTIs would prove successful in HIV management. Thus protease inhibitors namely: Saquinavir, Indinavir, Ritonavir and Nelfinavir have been approved. They too could not achieve the desired level of success. (Deeks, 1997)

Since HIV diseases are essentially immuno deficiency diseases, it was hypothesized that in addition to direct intervention against the virus per se, efforts are to be directed to enhance the defence mechanism of the body by identifying the use of immunomodulators like the Interferons, Interleukines etc (Lew et al., 2001). The culmination of these epoch making research and development has been the institution of Highly Active Anti-retroviral treatment (HAART), which includes
a) 2 Nucleoside RT Inhibitor + Non-Nucleoside RTI + PI

b) 2 Nucleoside RTI + 1 Non-Nucleoside RTI

c) 3 Nucleoside RTI

d) 2 Nucleoside RTI + 1 PRI (or)

e) PRI + 1 Non Nucleoside RTI (Yeni, 2002).

Eventhough HAART therapy has dramatically brought down the rate of occurrence of opportunistic infections and increased the man - working hours and longevity of physical well being in HIV-treated individuals, there is an established need to be on continuous HAART therapy without any scope of complete viral clearance and termination of treatment. In addition to the cost burden of such treatment, HAART associated side effects like muscular dystrophies etc (Carpenter et al., 1997) are now considered as impediments against international adoption of HAART therapy in HIV diseases.

With the shift of AIDS epicentres to the developing and under developed world like Asia and Sub-Saharan Africa, there is also a paradigm shift towards exploration of cost effective and safer drugs from the traditional systems of medicine of different countries especially the Chinese systems of medicine. Even the Western world has recognized the value of traditional medicine as Complementary and Alternative Medicine (CAM). Sixty percent of medical colleges in the western countries have begun to teach alternative medicine practices and biomedical research organisations are investing
substantial grants towards investigatory research of these systems of medicines. One of the priority areas has been the search for anti-HIV-1 compounds from natural products of terrestrial and marine origin. Of the several lead potentials seen against HIV, some of them were from extracts of blue green algae like Lyngbya langerheinii, Phormidium tenue, brown seaweed Fucus vesiculosus and green algae Spiruluna platensis (Ayhunie et al., 1998).

The present research is one such attempt to explore anti-HIV drug potentials from 33 Indian Medicinal plants. These plants were selected on the basis of citations in literatures of Indian system of medicine and analysed by adopting internationally acceptable study design for pre-clinical laboratory evaluation of anti-HIV drug potentials from natural products.