3. Aims and Objectives
PART A:

The use of terrestrial plants for chemoprophylaxis is being practiced by cultures all over the world. In India, a therapy called Ayurvedic medicine and traditional Chinese medicine makes use of plant parts and their products as central dogma of the medical system. The very philosophy of Ayurveda revolves around ‘prevention’. However, irrespective of the validity of these methods, roughly 79% of world's population and approximately 600 million people in India rely on traditional folklore medicine to some extent. Undoubtedly, natural products represent a rich and untapped resource for the discovery of drugs with potential application for preventing and/or treating contemporary diseases. The huge diversity of plant species leads to the expectation that many therapeutic worthwhile compounds remain undiscovered. Random screening of these compounds is not an effective approach as the National Cancer Institute failed to find a compound with clinical anti-cancer activity among 114,000 plant extracts from 35,000 species. The use of folk beliefs and traditional healers as a short cut to the discovery and isolation of pharmacologically active compounds has been a productive approach.

So in the present investigation we selected some plants like *Withania somnifera, Piper longum* that are used in Ayurveda, *Hippophae rhamnoides* used in Chinese traditional system of medicine. *Decalepis hamiltonii* taken in food in several parts of Karnataka, is a blood purifier and *Micrococcus paniculata* is used by the folklore in Goa to cure jaundice. So the aim of the present study is to assess the chemopreventive potential of these plants using skin and stomach tumor as the model systems. Their effect on the activity of the xenobiotic metabolizing enzymes (Phase I and phase II) and antioxidant enzymes (SOD, catalase, GPX, GR) has been studied as they play an important role in the metabolism of carcinogens. The following studies have been performed.

1. Effect on the carcinogen induced tumorigenesis.
   a. Benzo(a)pyrene induced forestomach papillomagenesis in Swiss albino mice
   b. DMBA induced skin papillomagenesis in Swiss albino mice.

2. Effect of plant materials on the induction of
   a. Phase I enzymes- Cytochrome P50, Cytochrome b5, Cytochrome P450 reductase, Cytochrome b5 reductase
b. Phase II enzymes- Glutathione S-transferase, DT-diaphorase
c. Antioxidant enzymes- Superoxide dismutase, Catalase, Glutathione peroxidase, Glutathione reductase
d. Lipid peroxidation levels and lactate dehydrogenase

3. To differentiate the normal and tumor tissues histologically

The plants selected for the study include-
1. *Hippophae rhamnoides* (Seabuckthorn)
2. *Withania somnifera* (Ashwagandha)
3. *Piper longum* (Pipli)
4. *Decalepis hamiltonii* (Makaliberu in kanada)
5. *Micrococcus paniculata* (Aelu or asola in Konkini)

**PART B:**

In this present study we tried to investigate the activity of a few transcription factors that may be involved in oncogenesis, antioncogenesis and oxidative stress as described in literature. The transcription factors selected for studies are

1. Nuclear factor kappa B (NF-kB)
2. Interferon Regulatory factor-1 and 2 (IRF-1 and IRF-2).

The purpose of investigating the activities of the above given transcription factors is to observe how their activity changes upon the administration of chemopreventive modulators and carcinogens to animals. The logic in selecting the above transcription factors is that NF-kB is upregulated due to oxidative stress and many chemopreventive agents can downregulate its activity. IRF-1 is antioncogenic factor. So in our studies we tried to find out the effect of one of the plants that showed chemopreventive potential in our investigation on the activities of NF-kB and IRF-1.