2. SCOPE AND OBJECTIVES
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Although great advancements have been made in the treatment and control of cancer progression, significant deficiencies and room for improvement still remain. Further, the majority of cancer chemotherapeutics severely affect the hosts' normal cells (Mascarenhas et al., 1994).

Plants have been the basis of traditional medicine systems that have existed for thousands of years specially in countries such as China (Chang and But, 1986) and India (Kapoor, 1990). These plant-based systems continue to play an essential role in healthcare even today. Further, several modern drugs have been derived from plants sources. Well-known examples of plant-derived modern drugs and lead compound are Morphine, Vinblastine and Vincreistine, Quinine, Artemisinin, Camptothecin, Topotecan, Irinotecan (Kingston, D., 2011).

Cancer is one of the most dreaded diseases of the 20th century and spreading further with increasing incidence in the 21st century. In the United States, it accounts for 25% of the deaths presently. Today multidisciplinary scientific investigations are being carried out to combat this disease, but a perfect cure is yet to be brought into the world of medicine. In recent years, a greater emphasis has been given towards research on complementary and alternative medicine that deals with cancer management. Several studies have been conducted on herbs under a multitude of ethnobotanical grounds. Ayurveda, a traditional Indian medicine, has been successful from very early times in preventing or suppressing various tumors.

In recent years, drug discovery efforts to harness novel anticancer targets with potential to provide more selective and safe anticancer drugs have advanced significantly. There is excitement today in the field of cancer drug discovery. As the first generation of these new agents enters clinical trials it remains to be seen whether the present optimism will
be confirmed. The occurrence of different novel targets in different cancers means that therapy will have to be tailored according to individual cancer target profiles. Cocktails of these agents may also be required in some cases for optimal therapy. Further, these new anticancer agents are not cytotoxic but rather cytostatic and have to be administered over long periods of time to be effective. These agents, therefore, should have minimal toxicity. In cases of aggressive cancers, these agents may have to be combined with conventional cytotoxic agents initially to reduce tumor burden. It is also being contended that the present models and the end points that are used to evaluate the preclinical and clinical efficacy of newer compounds may not be appropriate because these models were developed for the old cytotoxic paradigm of cancer chemotherapy.

Reactive oxygen species (ROS) and Reactive nitrogen species (RNS) of free radicals that are formed in the body as a consequence of normal metabolic reactions, exposure to ionizing radiations and by the influence of many xenobiotics, have been indicated as the cause for several diseases like cancer, heart diseases, aging, etc. In this context, antioxidants have an important role in biological systems. They are emerging as prophylactic and therapeutic agents. These are agents which scavenge free radicals and prevent the damage caused by them. Several antioxidants of plant origin have been experimentally proved and used as effective protective agents against free radical mediated toxicity.

The use of natural products has been contemplated as of exceptional value in the control of cancer (Suffness et al., 1990). Furthermore, the search for new sources of biologically active compounds is important for the discovery of new drugs for the treatment of cancer. Currently there is, therefore, considerable scientific and commercial interest in the continuing discovery of newer anticancer agents from natural product sources (Kinghorn, 2004). A myriad of plants products exist that have shown very promising anti-cancer
properties *in vitro*, but are yet to be evaluated. Further intensive investigations are, therefore, required to determine the efficacy of these plant products in treating cancers.

Several members of the genus *Ipomoea* are widely used in folk medicine all over the world specially as powerful cathartics (Shellard et al., 1961). Pharmacological studies have reported antimicrobial (Vallette, et al.,1938; Carlson, et al., 1948), analgesic (Bhargav, et al., 1978), spasmogenic (Matin, et al.,1969), spasmolytic (Gupta, et al., 1967; Iyer, et al., 1974), hypotensive (Matin, et al., 1969; Rakhit, et al.,1958), insecticidal (Canonica, et al.,1972) and psychotomimetic effects (Heacock, et al.,1975 ) on medicinal plants belonging to the genus *Ipomoea*. 4-Ipomeanol, a pneumotoxic furan derivative isolated from *Ipomoea batatas* (Convolvulaceae), has been clinically evaluated as a lung-cancer-specific antineoplastic agent. Chemical investigations indicate indole alkaloids (Chao, et al., 1973) and resin glycosides (Wagner et al., 1974) are the most common constituents in the family convolvulaceae. *Ipomoea obscura* plant leaves are used as an application to apthous affections after toasting, powdering and boiling with ghee and in admixture with the leaves of *Argyreia mollis* used for sores. Some reports (Van Jaarsveld et al., 2006) indicate that *Ipomoea batatas* contains abundant beta carotene that can reduce the incidence of certain cancer and coronary heart disease in humans (Gester, H., 1993; Ziegler, R. G. 1989). Some resin glycosides from *ipomoea batatas* have been claimed to show cytotoxic activity (Bah, et al., 1997). The plant has also been reported to be helpful in metastasis inhibition (Cardenas, et al., 2004). *Ipomoea species thus seems to have the potential for isolating newer leads/drugs for anticancer activity.*

The objective of the present investigations was, therefore, to evaluate *Ipomoea leari*, a medicinal plant belonging to genus of *Ipomoea* for its antioxidant and anticancer activity. *Ipomoea leari* was selected for the study in view of the several ethnomedical and
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Chemosystemic information reported on this plant (The wealth of India; Bhakuni, et al., 1969). It was proposed to screen the successive extracts and the isolated compound(s) for their *in vitro* antioxidant and anticancer activities using standard procedures. The active extracts and compounds isolated were also proposed to be screened for their *in vivo* anticancer activity.

The objectives of the present investigation are,

- to prepare successive extracts from the plant, *Ipomoea leari*.
- to isolate phytoconstituents from these extracts and their characterization by spectral and other methods,
- to screen the extracts and the isolated compounds for their antioxidant activity by using *in vitro* methods,
- to screen the extracts and the isolated compounds for cytotoxic and anticancer activity by using *in vitro* methods,
- to screen the potent plants extracts and the isolated compounds for their *in vivo* anticancer activity,
Plan of work

Investigations were proposed to be carried out with the following plan of work;

(i) Collection and authentication of plant material

(ii) Pharmacognostical studies
   a. Evaluation of quality of raw materials
   b. Anatomical studies

(iii) Preparation of successive extract of n-hexane, chloroform, ethyl acetate and hydromethanolic(1:1) solvents of *Ipomoea leari*

(iv) Phytochemical studies of the extracts
   - Qualitative phytochemical analysis of the extracts
   - Quantitative estimation of total phenols and flavonoids content
   - Isolation and characterization of the isolated compounds

(v) Biological studies of the extracts

   **Antioxidant activity**

   - *In vitro* antioxidant studies of the extracts and the isolated compounds
     a. DPPH radical scavenging assay
     b. Hydrogen peroxide scavenging assay
     c. Nitric oxide radical scavenging assay
     d. Reducing power assay
     e. Scavenging of hydroxyl radical by p-NDA method
     f. Scavenging of ABTS radical cation assay
   
   - *In vivo* antioxidant studies of the active extract and biochemical estimation of CAT, SOD and LPO.
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**Anticancer activity**

- *In vitro* cytotoxicity of the extracts and the isolated compounds
- Short term toxicity studies using ascitic tumor cells
- Long term toxicity studies using established cell cultures
- *In vivo* anticancer studies of the active extracts and isolated compounds by,
  a) Effect on DLA induced ascitic tumor model
  b) Effect on EAC induced ascitic tumor model
  c) Effect on DLA induced solid tumor model

**Plant profile and review of literature**

*Ipomoea leari* Knight ex Paxton

**Family:** Convolculaceae

**Synonyms:** Ipomoea congesta, Ipomoea indica

**English name:** Ivy-leaf morning glory, Blue dawn flower

**Form:** Vine

**Flowers:** Flowers with blue to purplish petals and softly hairy to almost hairless green segments (sepals) outside the petals. Flowers are most of the year.

**Origin:** Origin of the plant is uncertain, but it is widespread throughout the tropical world.

**Description:** Twining perennial vine with stems to more than 7 m long hairy. Leaves with blade ovate in outline, 4–17 cm long, 3–16 cm wide, base heart-shaped, margins entire to deeply 3-lobed; leaf stalk 2–18 cm long. Inflorescence axillary, 2–many-flowered. Capsule globe-shaped, about 10 mm wide, with 3 chambers.
**Distinguishing features:** Distinguished by sepals 1.5–2.5 cm long, gradually tapering to a point; flower funnel-shaped, 5–8 cm long, 6.5–8 cm wide, with paler mid-petal bands and pink to whitish tube inside.

Blue Dawn Flower is a morning glory vine with a striking purple-blue color flowers. The flowers open in the morning and fade to magenta in the evening. Blue Dawn Flower is a perennial with heart-shaped or 3-lobed leaves and with flowers produced daily from a dense clustered inflorescense. Blue Dawn Flower is commonly found at hill stations like Nainital and Mussoorie, scrambling over fences and over woody plants, often to their detriment. It is also found in south India. It has been described as troublesome if left unchecked. But it is delight when in flower. This plant can produce hundreds a fragile flowers everyday and since it works on a 24 hour cycle it can leave a messy carpet below. The flowers are dark blue in the morning to purple/magenta at noon and pink in the evening. It is useful as a cover for waste lands and embankments.
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**Ethnopharmacological information**: The root is reported to be used by the Mundas for dysentery (The wealth of India).

Jagat et al., have isolated a new glycoside, Ipolearoside from *Ipomoea leari* and showed that the glycoside has significant anticancer activity against Walker carcinosarcoma 256 in rats (Jagat et al., 1973).

Ram prakash et al., in their review of anticancer and antiviral activities of Indian medicinal plants, have reported anticancer activity for *Ipomoea leari* (Ram prakash et al., 1990).

Bhakuni et al., have reported the screening of three hundred Indian medicinal plants for their biological activity and indicate that *Ipomoea leari* has significant anticancer activity (Bhakuni et al., 1968).