2.0 REVIEW OF LITERATURE

There is evidence of herbs having been used in the treatment of diseases and for revitalizing body systems in Indian, the Egyptian, the Chinese, the Greek and the Roman civilizations. Plants have a vast potential for their use as curative medicine. In India, medicinal plants are widely used by all sections of people both directly as folk medicines in different indigenous systems of medicine like Siddha, Ayurveda and Unani and indirectly in the pharmaceutical preparations (Srinivasan et al., 2001). India has about 4.5 million plant species and among them, several thousands have been claimed to possess medicinal properties against human diseases. Although traditional medicinal healers have used medicinal plants for treatment of ailments for hundreds of years, there has always been a lingering question in scientific circles about their therapeutic efficacy. As a consequence, the pharmacological activity of many medicinal plants has been studied, even though the vast majority of medicinal plants remain to be studied for their phytochemical components and pharmacological effects.

2.1 Plants with antimicrobial activity

The use of plant extracts and phytochemicals, both with known antimicrobial properties, are of great significance to therapeutic treatments (Nagesh and Shanthamma, 2009). Extracts of plants were used for the treatment of various diseases and this forms the basis for all Indian systems of Medicine. However, this area is not much developed when compared to modern system of medicine, mainly because of the lack of scientific documentation in this field (Kalimuthu et al., 2010).
Mostly the pharmacological activity of medicinal plants resides in its secondary metabolites which are comparatively smaller molecules in contrast to the primary molecules such as proteins, carbohydrates and lipids. These natural products provide clues to synthesize new structural types of antimicrobial and antifungal chemicals that are relatively safe to man (Kalimuthu et al., 2010).

The effect of plant extracts on bacteria has been studied by a large number of researchers in different parts of the world (Reddy et al., 2001; Ateb and Erdo, 2003). Agarry et al., (2005) have shown the potent antimicrobial activities of the gel and leaf of Aloe vera against a wide range of bacteria and fungi. Bearberry and cranberry juice have been used to treat urinary infections while plant species such as lemon balm, garlic and tea tree are described as broad-spectrum antimicrobial agents (Rios and Recio, 2005).

Mathabe et al., (2006) reported that methanol, ethanol, acetone and hot water extracts from different plant parts (leaves, roots, bark and stem rhizome), of Indigofera daleoides, Punica granatum, Syzygium cordatum, Gymnosporia senegalensis, Ozoroa insignis, Elephantorrhiza elephantina, Elephantorrhiza burkei, Ximenia caffra, Schotia brachypetala and Spirostachys africana showed remarkable antibacterial activity against Vibro cholera, Escherichia coli and Staphylococcus aureus, Shigella species and Salmonella typhi.

Crude extracts of some well known medicinal plants are used to control plant pathogens (Kubo et al., 1981). Many species of Acacia caesia are found to have diverse phytochemical compounds having medicinal
properties (Lee et al., 2000). The antibacterial activity of methanol extract and its petroleum ether, chloroform and ethyl acetate fractions from the root bark of Akanda (*Calotropis gigantea*) were investigated by Ashraful et al., (2008).

The methanol extracts of forty nine different plant extracts were screened for antifungal activity, out of which forty three plant extracts exhibited varying degrees of inhibition activity against the fungi (Varaprasad et al., 2009). Antibacterial activities of aqueous and methanol extracts of some medicinal plants reported by Girish and Satish, (2008) against some human pathogenic bacteria showed the methanol extracts had wider range of activity on these organisms than the aqueous extracts, which indicates that the methanol extracts of all selected plants may contain the active components.

Senthilkumar and Reetha, (2009) reported that methanol extract of *Aegle marmelos* and *Cassia auriculata* extract showed higher antibacterial activity to a group of bacterial pathogens. The functions of triterpene saponin in plants for its antimicrobial, fungicidal, antibacterial, antiviral, analgesic, anti-inflammatory, antitumor, cytotoxic, immunostimulant, antihelmintic, expectorant and antitussive activities, have been known for many years (Hostettmann and Marston, 1995).

*In vitro* anti-bacterial activity of a glycoside, phenyl ethyl β-D-glucopyranoside from the plant *Sida rhombifolia* was studied by Ekramul et al., (2002) and showed that it had significant anti-bacterial activity against most of the tested bacteria.
In vitro antifungal activity of saponins from Tribulus terrestris L. against Candida albicans, C. glabrata, C. parapsilosis, C. tropicalis and Cryptococcus neoformans were studied using microbroth dilution assay and reported that saponins had significant antifungal activity by weakening the virulence of C. albicans and killing fungi by destroying the cell membrane (Zhang et al., 2006).

The compounds isolated from Verbascum lasianthum and V. pterocalycinum mutense were evaluated for their in vitro antifungal activity by TLC bioautographic assay and the triterpenoid saponins, were found to exhibit potent in vitro antifungal activity against Colletotrichum acutatum, C. fragariae and C. gloeosporioides. Some saponins and phenylethanoid glycosides possessed a dose-dependent antimicrobial activity against several bacteria and fungi (Zhang et al., 2006).

Mandal et al., (2005) investigated the potent antimicrobial activity of two triterpene saponins isolated from the funicles of Acacia auriculiformis against various pathogenic organisms. Flavonoids may act through inhibiting cytoplasmic membrane function as well as by inhibition of DNA gyrase and β-hydroxyacyl-acyl carrier protein dehydratase activities (Cushnie and Lamb, 2005; Zhang et al., 2008).

A phytochemical like isoflavone genistein was able to change cell morphology (formation of filamentous cells) and inhibited the synthesis of DNA and RNA of Vibrio harveyi (Ulanowska et al., 2006). It has been suggested that terpenes promote membrane disruption, coumarins cause
reduction in cell respiration and tannins act on the membranes of microorganism as well as bind to polysaccharides or enzymes promoting inactivation (Ya et al., 1988; Chung et al., 1998; Cowan 1999).

2.2 Plants with Antioxidant potentials

In recent years much attention has been devoted to natural antioxidant and their association with health benefits. Plants are potential sources of natural antioxidants and produce various antioxidative compounds that have therapeutic potentials. Antioxidant-based drug formulations are used for the prevention and treatment of many complex diseases.

The aqueous, methanol and ethanol extracts of Melissa officinalis, Matricaria recuttia and Cymbopogan citrates were found to possess DPPH scavenging activity (Pereira et al., 2009). The alcohol–water extract of Ichnocarpus frutescens leaves possessed 1, 1-diphenyl-2-picrylhydrazyl radical and superoxide anion radical scavenging activity (Kumarappan et al., 2007). The methanol extracts of leaves and flowers of Lippia alba exhibited very significant DPPH radical scavenging activity compared to the standard antioxidant ascorbic acid (Ara and Nur, 2009). The methanol extract of Manikara zapota showed strong activity on scavenging DPPH radical, which implicated an essential defence against the free radicals (Kaneria et al., 2009). The hot water extract of Perilla frutescens stalk showed moderate DPPH radical scavenging abilities than the leaf and seed extracts (Chou et al., 2009).

The methanol extract of Helichrysum plicatum has been reported to have antioxidant activity using two in vitro methods, namely DPPH and β-carotene linoleic acid assays (Tepe et al., 2005). Vinay et al., (2010) have
reported a high radical scavenging activity in the stem of *Kigelia* followed by leaf of *Hibiscus, Gemelia* and *Kigelia*. Piao *et al.* (2004) reported the DPPH radical-scavenging activity in furano coumarins and its correlation with the number of phenolic hydroxyl groups present in their structures.

The essential oils of *Myrtus communis* contained compounds such as 1, 8-cineole and methyl eugenol that showed considerable DPPH scavenging activities (Dukic *et al.*, 2010). Siddhuraju and Becker (2007) have reported the antioxidant and free radical scavenging activities of processed cowpea seed extracts, wherein the DPPH radical and ABTS cation radical scavenging activities were correlated with the ferric reducing antioxidant capacity of the extracts. The antioxidant activity of the aqueous extracts of the leaves of *Bauhinia forficata* and *Cissus sicyoides* were determined using several different assay systems, namely (ABTS) decolorization, superoxide anion radical (O$_2^-$) scavenging and myeloperoxidase activity (Khalil *et al.*, 2008).

The methanol extract of *Annona squamosa* and *Sapium macrocarpum* showed two times more DPPH scavenging activity than the commercial antioxidant butylated hydroxyl anisole (Ruiz *et al.*, 2008). An aqueous extract from *Choerospondias axillaries* showed a potent scavenging effect on DPPH (Wang *et al.*, 2008). Methanol extract of bark, fruits and leaves of *Ficus microcarpa* exhibited excellent ABTS scavenging activity (Ao *et al.*, 2008). The scavenging effect of *Andrographis paniculata* was demonstrated against DPPH and ABTS showing its ability to convert unpaired electrons to paired ones (Tripathi and Kamat, 2007).
A crude aqueous extract of *Chlorophytum borivilianum* has been shown to scavenge DPPH free radicals and decrease TBARS, revealing that it is a promising anti-stress agent as well as a potential antioxidant (Kenjale *et al.*, 2007). Desai *et al.*, (2008) reported the free radical scavenging potential of the aqueous extract of roots of *Baliospermum montanum* by DPPH and nitric oxide (NO) scavenging assay which showed a high concentration-dependent free radical scavenging activity.

An aqueous extract from *Choerospondias axillaries* showed a potent scavenging effect on DPPH (Wang *et al.*, 2008). The antioxidant and antibacterial properties of the acetone and methanol extracts from leaves and roots of *Sansevieria hyacinthoides* were investigated. The leaves extract at 1 mg/ml exhibited over 80% DPPH activity, while acetone and methanol extracts from the roots at 0.75 mg/ml showed 91.4 and 92.8% DPPH scavenging activity (Aliero *et al.*, 2008).

### 2.3 Plants with anticancer properties

Plant derived compounds, in particular have a special place in anti-cancer therapy, and some of the new chemotherapeutic agents currently available for use in a clinical setting include paclitaxel, vincristine, podophyllotoxin and camptothecin (Gerzon, 1980; Kinghorn and Balandrin, 1993). Due to lack of effective drugs, cancer is a fatal disease rating the top three cause of death. Many of the chemotherapeutic agents sold for the treatment of cancer are highly expensive, mutagenic, carcinogenic and teratogenic and marrow inhibition limits their applications (Kumarappan *et al.*, 2007). Therefore the quest for effective anti-cancer drug is an active research field.
The search for anticancer agents from plants dates back to 1947, when the cytotoxic properties of podophyllotoxin from *Podophyllum peltatum* were detected (Kelly and Hartwell, 1954). The discovery of the anticancer properties of vinblastine and vincristine from *Cataranthus roseus* soon followed (Noble *et al*., 1958) and gave the impulse for wide range of investigations of plant extracts and plant derived compounds for possible anticancer activity. Similar useful drugs like diterpene taxol obtained from plant *Taxus brevifolia* (Suffness 1987), pyridocarbazole alkaloid ellipticine from *Ochrosia elliptica* and pyrrolo (3,4-β)-quinoline alkaloid camptothecin were obtained from *Camptotheca acuminata* (Hamburger *et al*., 1991).

Plants belonging to *Apocynaceae* are reported to have anticancer properties. Flavonoids have been shown to possess antimutagenic and anticarcinogenic activity (Kuroda and Hara, 1999; Babu *et al*., 2003). The methanol extract of the fruits of *Solanum Nigrum* was evaluated for the anticancer activity on the *HeLa* cell line. The cytotoxicity of *Solanum nigrum* on *HeLa* cell was evaluated by the SRB assay and MTT assay. The methanol extract of these drug showed greater activity on *HeLa* cell line and little activity on *Vero* cell line, indicating *Solanum Nigrum* can be used as anticancer agent (Sanjay *et al*., 2009).

The extracts from *Atractylodes lancea*, *Kaempferia galangal*, *Zingiber officinal*, *Piper chaba*, *Mesua ferrea*, *Ligusticum sinense* and *Mimusops elengi* exhibited promising activity against the cholangio carcinoma CL-6 cell line with survival of less than 50% at the concentration of 50 μg/ml. Among these, the extracts from *Atractylodes lancea*,
Kaempferia galangal, Zingiber officinale, Piper chaba and Mesua ferrea showed potent cytotoxic activity against Hep-2 cell (Wiratchanee et al., 2010).

Branchlets and berries of Juniperus foetidissima and J. sabina were evaluated by MTT assay against three tumor cell lines (Hela, KB, MDA-MB-468), using ELISA at 540 nm. Extracts of male branchlets of J. foetidissima and berries extract of J. sabina were cytotoxic against Hela cell line (Hojjat et al., 2009).

### 2.4 Plants that induce apoptosis

Apoptosis is vital process for maintenance of homeostasis and eradication of damaged cells. There are many chemopreventive agents, which result in cancer cell death by induction of apoptosis. The methanol extract of Indigofera tinctoria on HCT 116 cells determined by cell viability, DNA fragmentation and comet assay showed that these extracts had an antiproliferative effect on HCT 116 cells via apoptosis (Magesh et al., 2009). Chloroform extract of Epipremnum pinnatum produced significant growth inhibition against T-47D breast carcinoma cells and analysis of cell death mechanisms indicated that the extract elicited both apoptotic and non-apoptotic programmed cell deaths (Lan et al., 2007).

The study of action of willow (Salix safsaf) extract on two types of tumours, Ehrlich ascites carcinoma cells (EACC) and acute myeloid leukemia (AML) showed an increase in DNA fragmentation and expression of p53 protein in tumor cells (Zahran et al., 2005). The cytotoxicity and mechanisms of action of three Hypoxis species on HeLa, HT-29 and MCF-7 cancer cell lines and peripheral blood mononuclear cells (PBMCs) showed
the activity of caspase-7 in two cell lines and DNA fragmentation in all three cancer cell lines (Boukes and Venter, 2011).

A crude aqueous *Sutherlandia frutescens* whole plant extract induced cytotoxicity in neoplastic cells (cervical carcinoma) and CHO (Chinese Hamster Ovary cells) cell lines which was confirmed by DNA fragmentation patterns and flow cytometric analysis (Chinkwo, 2005). A 549 human lung cancer cells exposed to ethanol extract of *Dunaliella salina* showed significant DNA fragmentation (Sheu *et al.*, 2008).

Inagaki *et al.*, (2007) demonstrated that a compound purified from the ethyl acetate extract of black soyabean vinegar induced DNA fragmentation and the development of apoptotic bodies in U937 cancer cells. *Duchesnea indica* phenolic fraction significantly inhibited SKOV-3 cell proliferation and markedly induced apoptosis by characteristic nuclear DNA fragmentation (Peng *et al.*, 2009).

Clitocine, a natural biologically active substance isolated from the mushroom *Leucopaxillus giganteus*, induced DNA fragmentation (Ren *et al.*, 2008). Agarwala *et al.*, (2010) demonstrated the cytoprotective potential of mangiferin, against mercury chloride induced toxicity in HepG2 cell line using DNA fragmentation as an index. A progressive increase in fragmented DNA was also observed in oesophageal cancer cells (TE-2) treated with the natural antioxidant gallic acid, which was isolated from the fruits of a medicinal Indonesian plant (Faried *et al.*, 2007).

DNA fragmentation was observed in human breast cancer cells treated with cajanol, a novel anticancer agent from pigeonpea (*Cajanus*
roots. The fragmented DNA ladder in d-gal-treated mice was inhibited by troxerutin, a naturally occurring bioflavonoid (Luo et al., 2010). Ethanol extract of 29 *Sophora moorcroftiana* seeds significantly inhibited SGC-7901 (gastric cancer) cell proliferation and induced apoptosis by characteristic nuclear DNA fragmentation (Ma et al., 2006).

Akbar et al., (2011) reported the anticancer properties of aqueous extract of *Artemisia vulgaris, Cichorium intybus, Smilax glabra, Solanum nigrum* and *Swertia chirayta* against various human cancer cell lines and the results showed that these plants cause induction of apoptosis in cancer cells as measured by internucleosomal DNA fragmentation and caspase-3 activation.

Montririttigri et al., (2008) reported the anticancer activity of the pure constituent isolated from *Stephania venosa* tuber on human ovarian cancer cells (SKOV3). DNA fragmentation and caspase activation studies showed that this plant could significantly inhibit the treated tumour cell proliferation and cause cells death via apoptosis.

### 2.5 Scope of *Sansevieria roxburghiana*

The medicinal properties of *Sansevieria* species are well documented. According to Van Wyk et al., (2000) *Sansevieria* species consists of many sapogenins, of which ruscogenin is the most common, and is commercially used as an anti-inflammatory agent and venotonic. A steroidal saponin was isolated from the leaves of *S. cylindrica*. Its structure was established as (D-glucopyranosyloxy)-22-hydroxyfurost-5-en-3-yl 12-
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\(O\)-(6-deoxy-L-mannopyranosyl)-15-\(O\)-(6-deoxy-L-manno pyranosyl) D-glucopyranoside, showed anti-inflammatory activity. The steroidal saponin showed no haemolytic effects in the \textit{in vitro} assays and demonstrated inhibition of the capillary permeability activity (Antunes \textit{et al.}, 2003).

Studies by Ikewuchi \textit{et al.} (2010) report that the phytochemical screening of \textit{S. liberica} leaves revealed the presence of alkaloids, carotenoids, flavonoids (catechins and flavones), phytates, saponins and tannins. A study of the steroidal constituents of the leaves of \textit{S. hyacinthoides} led to the isolation of 25\$-ruscogenin and a natural

pregnane, 1\textbeta, 3\textbeta-dihydroxy-5, 16-pregnadien-20-one (Marcella \textit{et al.}, 1996).

To provide a rationale for the use of the plant in fever and inflammatory disorders, ethanol extract of \textit{S. trifasciata} was found possess moderate dose-dependent analgesic effect on the various pain models used (Sunilson \textit{et al.}, 2009).
A study by Olivia Case, (2005) reported that S. *personii* showed better antibacterial activity when compared to S. *aethiopica* and S. *hyacinthoides*. Hot extract of S. *personii* were mostly antiinflammatory, compared to cold extracts, which were pro-inflammatory.

Aliero *et al.*, (2008) suggested the potential of leaves and rhizomes of S. *hyacinthoides* as a source of natural antioxidant and antimicrobial agent against both Gram positive and Gram negative bacteria.

‘Murva’, a drug used in Ayurveda, contains three different species of Sansevieria. A study on this drug by Joy *et al.*, (2008) showed that out of three species, S. *roxburghiana* showed the most effective antibacterial, anti-inflammatory and antipyretic activity. Joanne Bero *et al.*, (2009) reported that the dichloromethane extract of the leaves of S. *liberica* showed moderate antiplasmodial activity. The leaves and twigs extracts of S. *guineensis* from Guatemala showed antiplasmodial activity (Franssen *et al.*, 1997).

The sedative and anticonvulsant activities of the roots of S. *liberica* have been studied by Adeyemi *et al.*, (2007). The Igbo ethnic group of Eastern Nigeria uses the leaf extracts of S. *trifasciata* in the treatment of convulsions, feverish headaches, headaches, pains, respiratory disorders and also uses as an antibacterial agent (Agoha *et al.*, 1976). It was found that the bioactive compounds identified account for the therapeutic properties of the leaves of S. *trifasciata* (Ogukwe *et al.*, 2004). An analgesic property of S. *trifasciata* was studied by Sunilson *et al.*, (2009).
The *in vitro* antifungal activity of an aqueous extract of *S. zeylanica* against clinical isolates of *Trichophyton rubrum*, *T. mentagrophytes*, *Microsporum audouinii*, *Epidermophyton floccosum*, *Candida albicans*, *Aspergillus flavus*, *A. niger* and *A. fumigatus* was investigated by Onah *et al.*, (1994). All isolates were inhibited by *S. zeylanica* extract.

Rhizome of *S. roxburghiana* are used as purgative, febrifuge and in the treatment of gonorrhoea, heart-diseases, leprosy, fever, cough, piles, asthma, tuberculosis and dysuria (Saraswathy *et al.*, 2007).

Antitumour activity of *S. roxburghiana* rhizome against Ehrlich ascites carcinoma in mice was studied by Haldar *et al.*, (2010) and showed that *S. roxburghiana* rhizome exhibited remarkable antitumour activity in Swiss mice that is plausibly attributable to its augmenting endogenous antioxidant mechanisms.

Though there are various reports on the biological activity of the genus *Sansevieria*, reports on the medicinal properties of *S. roxburghiana* is fragmentary. Considering the vast potentiality of *S. roxburghiana* as a source for various ailments, the present study is done to screen for antibacterial, antifungal, antioxidant and anticancer activity of *S. roxburghiana*. The potentiality of this plant as an antimicrobial, antioxidant and anticancer agent will be an added credit to the pharmaceutical industry.