Plants have a significant role in maintaining human health and improving the quality of human life for thousands of years and providing valuables in the form of medicines, beverages, cosmetics and dyes. There exists a plethora of knowledge and information and benefits of herbal drugs in our ancient literature of Ayurvedic and Unani medicine. One of the earliest treatises of Indian medicine, the Charaka Samhita (1000 B.C.) mentions the use of over 2000 herbs for medicinal purpose. Exploration of the chemical constituents of the plants and pharmacological screening may provide us the basis for developing the leads for development of novel agents. In addition, herbs have provided us some of the very important life saving drugs used in the armamentarium of modern medicine. However, among the estimated 250,000-400,000 plant species, only 6% have been studied for biological activity, and about 15% have been investigated phytochemically (Cragg et al., 1997).

Diseases that remain most challenging in today’s healthcare system tend to be complex involving multiple mechanisms, targets and drugs for effective disease management. In contrast to current combination therapies, however, plant based drugs contain a mixture of multiple components thereby saving considerable time and expense (Karnath, 2002). Numerous and diverse classes of natural products have been isolated and their structures characterized in the past century. The elucidation of biological and biochemical mechanisms of natural products with therapeutic action have been invaluable to the efforts of organic and medicinal chemists as tools for deciphering the logic of biosynthesis and as platforms for developing frontline drugs. Natural products and their derivatives have traditionally been the most common source of drugs, and still represent more than 30% of the current pharmaceutical market. Of the 877 small-molecule New Chemical Entities (NCEs) introduced between 1981 and 2002, roughly half (49%) were natural products, semi-synthetic natural product analogues or synthetic compounds based on natural-product pharmacophores, which are an ensemble of steric and electronic features that is necessary to ensure optimal interactions with a specific biological target structure and to trigger or block its biological response. Natural products are still major
sources of innovative therapeutic agents for infectious diseases (both bacterial, parasitic, and fungal), cancer, lipid disorders, and immunomodulation. The complexity of many natural products can limit the scope for making chemical modifications to optimize their therapeutical use and can increase the cost of these drugs. Moreover, the need for a renewable supply of active compounds from biological sources can be an obstacle to large-scale production (Luiz Augusto Basso et al., 2005).

Plants have limitless ability to synthesize aromatic secondary metabolites, important subclasses in this group of compounds include phenols, phenolic acids, quinones, flavones, flavonoids, flavonols, tannins and coumarins. These groups of compounds show antimicrobial effect and serves as plant defense mechanisms against pathogenic microorganisms (Das et al., 2010). Some workers have reported antihelmintic activity in the essential oils of plants (Mali and Mehta, 2008). Many traditional practitioners have claimed that numerous medicinal plants and their formulations can be effectively used for the alleviation of different types of liver and kidney diseases (Vadivu et al., 2008). The importance of natural antioxidants has been clarified by numerous studies which have demonstrated that the consumption of foods rich in such phytochemicals can exert beneficial effects upon human health, possibly by interfering in the processes involved in reactive oxygen and nitrogen species mediated pathologies (Damein et al., 2003). Harmful side effects and weak effectiveness of curative agents in market has made their use limited and the search to find more effective agents continues. Investigation in the plant kingdom culminated in the discovery of many herbal hypoglycemic agents (Tatiya et al., 2011). Discovery of life saving drugs like vinblastine and vincristine from Vinca rosea, for treatment of certain types of cancers including leukemia and Hodkin’s disease have strengthened interest in active principles of medicinal plants (A yatollahi and Malik, 1991). Ginger (Zingiber officinale) is another example of a chemically unstable range of compounds being responsible for the activity and probably acting synergistically (Dubey et al., 2004). These investigations have dual purpose of isolating new medicinally important substances and providing basis of therapeutic studies directed towards the synthesis of drugs modeled on the chemical structure of natural products (A yatollahi and Malik, 1991).
Chemical and pharmacological studies of *Bridelia* species have resulted in the identification of flavonoids, sesquiterpenes, triterpenoids, and phenolic compounds, as well as a wide variety of biological activities including antiamebic, antianemic, antibacterial, anticonvulsant, anti-diabetic, antidiarrhoeal, antihelmintic, anti-inflammatory, antimalarial, antinociceptive, antiviral, and hypoglycemic activities (Ngueyem et al., 2009). Various plants from this family have been investigated for their medicinal properties. *B. retusa* and *B. ferruginea* are known to contain compounds that possess antifungal, anti-inflammatory properties (Jayasinghe et al., 2003; Olajide et al., 2003), the roots and bark of *Bridelia* species have been used for the treatment of headache, abnormal pain, indigestion, astringent, and purgative (Mostafa et al., 2006). Previous studies for *Bridelia* species have reported the occurrence of sesquiterpenes, megastigmane glucosides in *B. glauca* (Sueyoshi et al., 2006), flavonoids in *B. ferruginea* and *B. tomentosa* (Addae-Mensah and Achenbach, 1985; Hui, et al., 2006), phenolic derivatives in *B. ferruginea* *B. retusa* and *B. ndellensis* (Cimanga et al., 1999; Jayasinghe et al., 2003; Mostafa et al., 2006), and triterpenoids in *B. monoica*, *B. tomentosa* and *B. ovata* (Hui and Fung, 1968; Boonyaratavej, 1990; Boonyaratavej et al., 1992) as the chemical constituents, as well as biological activities including snake venom phosphodiesterase-I inhibitory (Mostafa et al., 2006), antibacterial (Ramesh et al., 2001), and antifungal (Jayasinghe et al., 2003) activities. The LD$_{50}$ of the *B. retusa* (EE4965000) administered by i.p. was observed as 1 gm/kg when investigated in mice (CSIR, 1971). Phytochemical analysis has revealed the presence of steroids, triterpenoids, tannins and flavonoids as major constituents by Tatiya et al. (2011). The presence phytoconstituents reported by Banerjee and Kulkarni (2009) includes steroids, carbohydrates, flavanoids, tannins, phenols, glycosides triterpenoids and saponins while absence of alkaloids, reducing sugar, proteins, amino acids, gums and resins were detected. Phytochemical standards analysis of *B. retusa* revealed the presence of bioactive components comprising phenolics, tannins, proanthocyanidin, ellagic acid, mucilage, flavonoids and carbohydrates The acetone exhibited IC$_{50}$ values of 47.20, 110.76, 48.81 44.15 and 50.42 μg/ml, respectively in DPPH (1,1 Diphenyl-2-picrylhydrazyl free radical scavenging activity), ALP (anti-lipid peroxidation effect), hydroxyl, hydrogen peroxide and nitric oxide radical inhibition assays while acetone had effective
reducing power. The results showed that tannins rich fractions of bark had strong antioxidant activity by inhibiting DPPH, ALP, reducing power, hydroxyl radical and hydrogen peroxide and nitric oxide scavenging. These results suggest strong antioxidant potentials of the acetone of *Bridelia retusa* (Tatiya and Saluja, 2010).

In the present, *B. retusa* has been target of investigation for its medicinal properties (Jayasingh *et al*., 2003; Shahid *et al*., 2009; Raja and Srilakshmi, 2010; Tatiya *et al*., 2011). In the type 2 diabetic model rats, the ethanol extract of stem bark of *Bridelia ndellensis* showed an anti-hyperglycemic effect comparable to that of glibenclamide when fed simultaneously with glucose (Sokeng *et al*., 2005). The results of an earlier study suggested that the *Bridelia ferruginea* bark extract had anti-diabetic properties and was thus be useful in the management and treatment of diabetes mellitus (Kolawole *et al*., 2006). The ethanolic extracts of six plants including *Bridelia ovate* showed cytotoxic activity against lung and prostate cancer cell lines (Saetung *et al*., 2005). *B. cambodiana* Gagnep. methanolic extract was found to be cytotoxic against HL-60 cell line (Khiev *et al*., 2009). The methanolic stem bark extract of *B. grandis*, had hypoglycaemic effects in type 2 diabetic mice (Njamen *et al*., 2011). In certain studies carried out using aqueous and alcohol extracts of the bark of *Bridelia retusa* (Linn.) Spreng (Euphorbiaceae) were investigated for acute anti-inflammatory activity in carrageenan-induced rat paw oedema (Mehare and Hatapakki, 2003). Wound healing property of *B. ferruginnea* has been reported with significantly enhanced wound contraction and epithelization (Udegbunam *et al*., 2011). Extract of *Bridelia retusa* leaves was investigated as corrosion inhibitor (Patel *et al*., 2010). The bark of *B. retusa* exhibited variations in their contents of phytocomstituents depending upon the geographical location from where they were collected which was evident and supported from their extractive values and total polyphenol content. The differences in extraction yield and radical scavenging activity may possibly be related to the natural climatic differences which occur over a particular geographical area to be influenced by several climatic factors (Banerjee and Bonde, 2011). A number of factors influence the concentration of the active constituent’s particularly phenolic compounds present in the herbals. Some of the notable factors are time and period of collection, geographical origin and climatic conditions. Sometimes,
the influence of these factors may lead to even absence of active constituents in the same plant collected from different regions, as evidenced by several research reports (Bilia, 2002; Houghton., 1998; Marcus et al., 2002; Banerjee and Bonde, 2011). Therefore, the present investigation was undertaken to elucidate phytochemical and pharmacological investigation of stem bark extract of *Bridelia retusa* S. with emphasis on qualitative phytochemical screening, antimicrobial, antihelminthic, *invivo* antioxidant, hepatoprotective, nephroprotective, antidiabetic and anticancer activity of the bark extracts. Thesis of the present study is divided into five chapters.

I. Phytochemical analysis of extracts of stem bark of *Bridelia retusa* S.

II. Antimicrobial and antihelminthic activity of extracts of stem bark of *Bridelia retusa* S.

III. Amelioration of Carbon tetrachloride induced hepatic and renal disorders in albino mice by extracts of stem bark of *Bridelia retusa* S.

IV. Antidiabetic activity of ethanolic extract of stem bark of *Bridelia retusa* S. in alloxan induced diabetes in albino rats.

V. Anticancer activity of ethanolic extract of stem bark of *Bridelia retusa* S. in Dimethylbenz(a)anthracene (DMBA) induced mammary carcinogenesis in albino rats.

Each chapter has a separate introduction, materials and methods, observations, discussion, summary and conclusion with pertinent literatures of the earlier works. The relevant literature is cited under references, to avoid disruption in the flow of text. Tables, graphs and figures are placed at the end of each chapter.