CHAPTER-I

1. INTRODUCTION

The herbal medicines are known to mankind as an oldest form of healthcare system considered to be of great importance among different rural and indigenous communities in many developing countries (Gosh 2003).

People prefer herbal medicines all over the world more than conventional medicines. Plants are always been a major source of drugs and most of the existing drugs which are available at present have been derived from plants directly or indirectly (Dasgupta *et al.* 2013). According to the WHO 2002, in the developing countries about 80% of the population relies solely on traditional medicine for their daily healthcare and in India about 60% of the population living in rural areas use herbal medicines. According to Stickel & Schuppan 2007, the utilization of herbal supplements has increased from 2.5% to 12% during the recent years. The Indian system of traditional medicine is based on Ayurveda, Unani, Siddha, etc., which still provide primary healthcare at large, especially to rural folk (Sharma *et al.* 2012). Around the world, revival of traditional knowledge has gained major importance from conservation perspective as well as sustainable development and search for new formulation or utilization patterns of the plant resources is still on (Pan *et al*. 2013). Traditional medicine system also includes the traditional knowledge, skill and practices truly based on theories as well as experiences of traditional healers/folk communities to sustainably manage their health problems. Many indigenous communities/ traditional healers have their own conventional medicine system with diverse medicinal plants or plant parts and many conventional therapies for untreatable diseases (Sharma *et al.* 2012). A huge number of both wild and cultivated medicinal plants are being used for the cure of various ailments, thus a significant amount of medicinal plants information are available with the traditional healers.

Currently the scenario in America about the improvisation and research on herbal medicine is improving. As reported by Pelkonen *et al.* 2014, in USA, National Center for Complementary and Alternative Medicine (NCCAM) has been funded a sum of US$ 50-128.8 million per annum to complementary and alternative medicines including the herbal medicine. After Asia, Europe is the second largest import/export market of the herbal products (De Vos 2010) and in China alone approximately 100,000 herbal formulae and over 11,000 individual medicinal plants have been documented, which are generally regarded as

rich natural resources for developing new drugs including new type of multi-component drugs (Wang *et al.* 2008; Kuhn & Wang 2008).

Indian forests are rich in medicinal plant species with two mega reserves (Hot spots) of biodiversity (Eastern Himalayas and Western Ghats) having wide spectrum of potential resources of healing properties. The rich diversity of Eastern Himalayan region of India is witnessed by herbs showing potential virtue with regards to hepatoprotective disorders. Traditional Indian system of medicine is therefore well developed due to this richness of bio-resources. More than 7500 plant species are referred in Indian folklore and only about 1700 plant species are mentioned in the documented form of ancient or past literature, out of which only 700 species (approx) have been investigated pharmacologically and chemically (Maiti 2004; Patil & Patil 2010). The turnover of Indian herbal industry is estimated to be around 4000 crore per annum (Nirmal *et al.* 2013; Patil & Patil 2010). The current use of medicinal plant resources on the basis of market signals is however inefficient and inadequate. According to Patil & Patil 2010, nearly 500 plant species are being used by the pharmaceutical industries in India and most of the medicinal plants, especially the medicinal tree species are presently collected from the wild. Recently, utilization of medicinal plants has increased multifold due to ever increasing market of herbal industry.

Liver diseases cause some of the major mortality and morbidity across worldwide. According to estimates made by WHO 2008, prevalence of hepatitis A, B and C virus infection cases is reported to be about 1.4 million, 2 billion and 130-170 million respectively. About 350 million people live with chronic liver infection and almost 6 lakhs and 3.5 lakhs people die every year due to the consequences of hepatitis B (acute or chronic) & hepatitis C respectively (Sharma *et al.* 2012). Thus, impact of the liver disorders on overall population of the world is significant and remains to be one of the severe health problems. Jaundice is not a disease but a symptom which indicate the liver malfunctioning in which yellowing of the skin as well as mucous membranes occurs due to an increased 'bilirubin' a bile pigment in the blood, which is a global concern & most frequent (Fatma & Uphadhyay 2015; Sharma *et al.* 2012). There are various different causes of jaundice *viz*., hepatitis (A, B, C, D, and E), inflammation of the liver, liver cirrhosis, alcoholic liver disease, obstruction of bile ducts, yellow fever, gallstones, typhoid, malaria, haemolytic anaemia, pancreatic cancer, tuberculosis, (Riyaz 1997; Fatma & Uphadhyay 2015; Sharma *et al.* 2012).

Despite of remarkable advancement, the conventional or synthetic drugs used to treat liver diseases are unsatisfactory because they can cause serious long-term side effects

(Velioglu *et al*. 1998; Giacometti *et al*. 2016). It is sometime very difficult to find a protective drug/agents at present for common ailment of liver. Due to lack of reliable hepatoprotective drugs in allopathic system of medical practices, herbs play a significant role in the management of various liver disorders (Sharma *et al.* 2012). A large number of plants and its formulations is known to posses hepatoprotective activity (160 phyto-constituents from 101 different plants) as reported by Handa *et al.* 1986.

1.1 Need for herbal medicine based research

A. Most chronic diseases are not single entities. Instead, mostly there are several etiological factors and multiple mechanisms within numerous molecular pathways (Pelkonen *et al.* 2014). Preventing and treating these major chronic diseases have led to the use of multiple drugs to tackle different targets and various symptoms. It seems that one of the reasons for the less satisfactory success of drug development during the recent decades has been the single-target-single-compound or one-disease-one drug paradigm (Hopkin 2008). Herbal plants have very diverse group of compounds that can solve the problem of single-target-single-compound or one-disease-one drug paradigm (Hopkin 2008).

B. Traditional system of medicine continues to be widely practised on many accounts. Population rise, inadequate supply of drug, prohibitive cost of treatments, side effects of several synthetic drugs and development of resistance to currently used drugs for infectious diseases have led to increased emphasis on the use of traditional herbal medicine/plant materials claim by the traditional healers as a source of medicines for a wide variety of human ailments which otherwise lack scientific validation (Pathare & Wagh 2012).

C. North-East India is the richest reservoir of plant diversity in India with almost 50% of India's total plant diversity (Mao & Hynniewta 2000) and fall under Eastern Himalayan biodiversity hotspots region. Kokrajhar, Assam is one of the gateway to the seven sisters of North-East India (NER). Ethnic communities of Kokrajhar and the other parts of North-East Region of India have always generated, refined and passed on traditional knowledge from generation to generation and still plays a vital role in the daily lives of these people.

D. Due to rapid depletion of bio-resources because of anthropogenic activities and urbanization coupled with improper scientific documentation on herbal medicinal

plants, urgent systematic investigation is required by using biotechnological tools to authenticate and develop new novel drugs from the NE region.

It is reflected that most of the degenerative human diseases have their origin from the deleterious free radical reactions (Florence 1995; Liu *et al*. 2018). Medicinal plants have high contents of natural phyto-constituents viz., polyphenols, flavonoids, terpenoides, tannins, beta-carotene, vitamin C and E etc., which are excellent antioxidants that act as radical scavenger and can prevent incidence of several human disorders (Anderson *et al.* 2001; Alam *et al*. 2013; Ksouri *et al*. 2015). Plant phyto-constituents are chemical compounds that are produced through primary or secondary metabolism by the plants. They play a big role in plant biological system like growth or defence against pathogens (Molyneux *et al.* 2007). Therefore, it is crucial to understand the role of herbal medicines as an alternative to cure liver disorder.

1.2 Research problem and gap

The preliminary work including ground survey & review of essential literature reflected the lack of proper documentary evidence regarding the availability of sufficient scientific work to evaluate the efficacy of candidate medicinal plants used by traditional healer of Kokrajhar to correlate with the efficiency of the same.

1.3 Objectives of the study

The research gap indicated the necessity of such work which can minimise the knowledge gap and boost the utility of candidate plants. Hence the present study is anticipated with the following objectives:

1. To collect and identify traditionally used hepatoprotective medicinal plants by Bodo tribe of Kokrajhar, Assam.
2. To study the *In-vitro* antioxidants property of some hepatoprotective medicinal plants.
3. To study the phytochemical characterization of the candidate medicinal plant by GC-MS analysis.
4. To study *in-vivo* efficacy of the extract on CCl_4 induced hepatotoxicity in rodent model.
5. To study the activity of some specific liver enzymes and histopathological evaluation of the liver & kidney.
6. To understand the *in-vivo* activity of plant bioactive compounds by *in-silico* molecular docking model if any.