Bioactivity Evaluation and Phytochemical Characterization of *Pajanelia longifolia* (Willd.) K. Schuman (Bignoniaceae)

Chapter 1

General Introduction
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The use of medicinal plants in the treatment and prevention of disease is not new. Plant kingdom has served a prolific source of many new drugs, food additives, flavours, etc. and as a matter of fact that about 25% of drugs available have their origin from plants (Fabricant and Farnsworth, 2001). For centuries, natural products and medicine have been closely related through the use of traditional medicine and natural poisons (Butler, 2004). Plant extracts contain vast source of organic molecules that have intrinsic bioactivities on physiology and metabolism. Phytochemical studies of plant extract for detecting the presence of different metabolites like alkaloids, terpenoids, saponin, tannin, etc. is considered the first step in identifying the medicinal value of the plant in drug discovery efforts. One of the important breakthrough in drug discovery from natural sources was bioactivity guided fractionation and continual improvement in the screening formats. In addition to this, reagent production, data management, etc. has been one of the mainstay in this regard (Butler, 2004). The importance of natural products in medicine has recently been reviewed by several workers (Newman et al., 2000; 2003; Chan-Bacab and Peña-Rodriguez, 2001; Schwikkard and Heerden, 2002; Kohen and Carter, 2005; Paterson and Anderson, 2005; Balunas and Kinghorn, 2005; Jones
et al., 2006; Chin et al., 2006; Dixon et al., 2007; Fraga, 2007; Connolly and Hill, 2008; Li et al., 2009).

The process of drug discovery is complex. It is an inter-disciplinary pursuit of biochemistry, life sciences, pharmacology and clinical science. Over a period of 25 years from 1981 to 2006, natural products have produced significant number of new drugs and drug leads (Newman et al., 2007). The analysis of the drugs developed from 1981 to 2002 showed that natural product derived drugs comprises of 28% of all new chemical entities launched in the market (Newman et al., 2002). About 24% of new chemical entities were either synthetic or natural mimic compounds based on studies of pharmacophores related natural products (Chin et al., 2006). The combined percentage, i.e., 56% of all new chemical entities indicated that natural product played an important role in discovery of new drug and leads compounds. Grifo et al. (1997) suggested that out of 150 prescription drugs in United States, 84 fell into the category of natural products or related drugs. The drugs have been prescribed predominantly as analgesic, anti-allergic, cardiovascular and anti-microbial in nature. It has been opined that about 87% of all categorized human diseases can be cured by drugs of natural product origin, however, there is no introduction of natural product
derived drugs for seven categories like anesthetic, antihistamine, anxiolytic, chelator, antidote, diuretic and hypnotic since 1981 to 2000 (Newman et al., 2002; Chin et al., 2006). About 79% antibacterial drugs have been traced to have natural product origin and became available in United States and worldwide (Butler, 2004).

Terrestrial plants, especially higher plants have long history of use in curing diseases. Several reviews and reports have been published in this regard, however, least emphasis have been given to traditional medicine as a source of new drugs (Fabricant and Farnsworth, 2001). Researches have been carried out on natural products, which are used in traditional system of medicine and many new bioactive and novel compounds have been isolated and characterized. Mahjoub et al. (2005) isolated and characterized a new bioflavonoid and an isobiflavonoid from Rhus tripartium, a medicinal plant from Tunisia. Jhao et al. (2005) reported phenanthraquinone, Bahuhinione from Chinese medicinal plant Bauhinia variegate L. The crude extract of its stem showed anti-tumor activity on human myeloid leukemia K562 cells (Jhao et al., 2005). This is an example of bioactivity guided isolation of natural product. Ma et al. (2005) isolated two new saponins from the bud of Aralia elata (Miq.) Seem. The root bark of the plant is used in Chinese traditional
medicine system for treatment of rheumatism and diabetes. The roots of *Symlocos chinensis*, an ethnomedicinal plant is used in China for treatment of cough, fever and malaria. Zhao and Yu (2005) have isolated two new triterpenoid saponins from the ethanolic and butanolic extract of the root, which have shown significant anti-tumor activity. Luo *et al.* (2005) have isolated two new triterpenoid saponins from *Sarcandra glabra*. *Aristolochia cretica*, a Greek medicinal plant is used in treatment of arthritis, snake bite, fever and pruritus. Georgopoulou *et al.* (2005) isolated a new sucrose ester, Acretoside from the root of the plant. However, no bioactivity of the compound was reported. Likewise, several new compound have been reported from many traditionally used medicinal plants. The current drug discovery from higher plants is mainly based on bioactivity guided isolation methods. Though many plant derived drugs are under clinical trials, about 23 new drugs of natural product origin have been launched in the market since 2000 till 2005, most of them being used in the treatment of cancer, neurological disorders, genetic disorders, diabetes, etc. (Chin *et al.*, 2006). Plants are the most common source of samples for evaluation of high-throughput screens of natural products. There are about 250,000 plant species in this world. Their distribution is not random and thus the chemistry of different plant families known to differ significantly. It
is, therefore, expected that large variety of compounds are yet to be isolated and characterized.

The human genome project has unshared a new era of post genomic scientific research and biomedical applications. Recent advances in disciplines like biology, chemistry, pharmacology, computer aided drug designing and not the least, Ethnobotany and their integration has changed the face of drug discovery research. It has no doubt facilitated the translation of vast information of human body in developing target oriented drugs.

Drug discovery is a complex and generally starts with the identification of a compound that binds to a target or show efficacy in a simple computer screen (Lang et al. 2007). The molecules that show good affinity are called "hits". The next step is to identify a compound with attractive medicinal and pharmaceutical property, e.g., low toxicity and sufficient aqueous solubility to be orally active. Such compounds are often called "lead". Generally hits are identified by screening while leads are developed from chemical synthesis. Screening involves large number of compounds either of natural product origin or synthesized (synthetic compounds) or even from the databases that can be examined for biological activity. Enzyme targets are generally used for screening
and best compounds are moved forward in a process aimed at modifying their chemical structure to improve potency, specificity and \textit{in vivo} activity while lowering toxicity and side effects. Synthetic methods include combinatorial chemistry and library synthesis (Lang \textit{et al.}, 2007).

In the present investigation, \textit{Pajanelia longifolia} (Willd). K. Schuman, an ethnomedicinal plant of Southern Assam has been selected for isolation and characterization of natural products, evaluation of biological activity (anti-microbial and hepatoprotective) and \textit{in silico} approaches to study drug likeliness and drug receptor interaction of the isolated compounds.