Introduction

Medicinal plants are proven to be a plausible alternative to synthetic drugs (Kettner *et al*., 2005). There is a relationship between life, disease and plants since the birth of mankind. Plants have been used in the traditional healthcare system from time immemorial, particularly among tribal communities. From the ancient time, human found the use of plants in studying diseases and treatments (Lyons and Pertrucelli, 1987). Over the years, people from the tribal group have developed a great extent of knowledge and experience on the use of plant and plant products as herbal remedies for the treatment of various health problems (Kala, 2005). By their experience, this knowledge of herbal remedies was transferred to generations as folk medicine. The oldest religious book of the World "Rigveda" provides information about the medicinal use of plant "Soma" as a medicinal agent by the Indo-Aryans, which was written between 4000 and 1600 B.C. (Bhattacharjee, 2004). This ethnic knowledge is utilized as worth for exploring the traditional claims scientifically, especially in the field of research and development. The ethnomedicinal plants have received valuable global attention to scientists and researchers from various disciplines such as pharmacology, phytochemistry and clinical studies (Hynniewta and Kumar, 2008).

Around 80% of the total world population of developing countries rely directly or indirectly on medicinal plants for their primary health care (Akerele, 1993). World population uses around 35,000-70,000 species of plants for medicinal, nutraceuticals and cosmetic uses (Kalia, 2005). India has one of the oldest, rich wealth of medicinal plants and most diverse cultural with living traditions associated with the use of medicinal plants. Traditional Indian medicinal system is blessed with different

systems of medication and practices such as Unani, Ayurveda, Siddha and Homeopathy (Gadgil, 1996). Our country is considered to be one of the 12 mega–biodiversity countries of the world found to be rich in plant biodiversities concentrated in various hotspots such as regions of Eastern Himalayas, North East India, Western Ghats and Andaman and Nicobar Islands (Seth and Sharma, 2004). According to Foundation for the revitalization of local health traditions, 2007, of the total 17,500 native plants species 6,000 (34.3%) are known to have medicinal importance in India. In the present scenario, the demands for herbal products are growing exponentially all over the world and major pharmaceutical companies are currently conducting extensive research on plant materials for their potential medicinal value.

In the United States of America, about 8% of the hospitalised patients suffer from the side or adverse effects of synthetic drugs (Philomena, 2011). National Poison Control Centres of the United States does not have any category for side or adverse reactions to herbs in their database. Therefore, people with every passing year come towards the herbal medicine as they believe that, the medicinal plant remedies are free from undesirable of toxic side effects (Kazemipoor *et al*., 2012; Haq, 2004). Botanical misidentification or mislabelling of plant material plays a role in toxic reactions in humans. The unprofessional processing leads to contamination of herbals with microorganisms. The most common error occurs in case of herbal medicines is same vernacular name given to two or more entirely different species. It may create considerable misidentification in the collection of medicinal plants which results in ambiguity. Fungal toxins such as aflatoxin, heavy metals and pesticides are also the huge problem. Safe traditional preparation and standardization of medicinal plants reduce the potential for herbal poisoning (Efferth and Kaina, 2011).

Standardization of herbal medicines is the process of developing the set of standards which includes inherent characteristics or features, constant parameters, qualitative and quantitative values that carry an assurance of authenticity efficacy, quality, safety and reproducibility of the drug (Kunle *et al*, 2012). Production and commercialization of the herbal medicine and natural products in recent years need the assurance of safety, quality and efficacy of medicinal plants and it has become an important issue. The herbal raw material is susceptible to a lot of variation due to several factors like misidentification of the plants, climatic variation (depending on the season of collection), the ecotype, chemotypic and genotypic variations. Conditions during drying and storage, the presence of xenobiotic also affects the quality of herbal drug (Dixit and Yadav, 2008). Standardization of herbal medicine on the basis of pharmacognostical standardization includes collection, botanical identification, macroscopic and microscopic examination, physicochemical parameters and establishment of DNA fingerprint profiles (Ganie *et al*., 2015). It also includes determination of pesticide residue and heavy metal contamination (Patel *et al*., 2006). Phytochemical standardization (qualitative and quantitative) includes (i) preliminary phytochemical testing for the presence of different phytochemical classes, (ii) Quantification of various phytochemical compounds, (iii) Quantification of chemotaxonomic marker compound for standardization, incorporating analytical instrumentation which is more accurate and precise (Pravin *et al*, 2012).

Pharmacological standardization of herbal drugs has been applied to demonstrate the therapeutic efficacy and biological activity. The assays on living animal and on their intact or isolated organs can indicate the effect of the drug or their preparations. These pharmacological assays are important to ensure the safe use and dose estimation for herbal drugs. The use of toxic plant or their ingredients must have been eliminated.

There are recent reports of toxicity which could largely be due to misidentification and overdosing of certain constituents that can be reduced by pharmacological evaluations (Mosihuzzaman and Iqbal, 2008).

Kidneys are vital organ to perform important functions like homeostasis, regulation of the extracellular environment, such as detoxification and excretion of toxic metabolites or drugs (Ferguson *et al*., 2008). Kidneys receive rich blood flow of 25% of resting cardiac output and play an important role in the elimination of many drugs and their metabolites. The kidney is therefore heavily exposed to large concentrations of drugs, metabolites and toxins, making it more vulnerable to drug toxicity, the kidneys are considered to be the major target organ for exogenous toxicants. Drug-induced renal injury contributes up to 25% of all cases of acute renal failure. Chemotherapy or anticancer medicine has been of limited use due to their side effect of nephrotoxicity (Nagai and Takano, 2010; Naughton, 2008; Kohli *et al*., 2000).

Cisplatin (cis-diamminedichloroplatinum [II]) is a platinum coordinated, potent antineoplastic agent commonly used in many solid cancers including testis, ovary, bladder, kidney, lung and head-neck cancers. Its mode of action has been reported to its ability to crosslink with the purine bases on the DNA, causing DNA damage and subsequently inducing apoptosis in cancer cells (Shaloam and Paul, 2014). Nephrotoxicity is the major side effect of cisplatin (Longo *et al*., 2011; Chirinoa and Pedraza, 2009; Kelland, 2007).

There is no specific therapy for acute renal failure, only the supportive care is necessary for renal function restoration. It can only be prevented by avoidance of nephrotoxic substances and maintenance of adequate hydration and perfusion (Hausberg and Schaefer, 2006). Most of the researches are focused on inventing compounds and formulations which could reduce or prevent the negative effects of

drugs causing kidney toxicities. Today, besides many synthesized medication available, large amounts of medicinal plants and their products which can be used as foods or food ingredients still play a key role in the prevention and treatment of different diseases (Jelena *et al*., 2015). Co-administration of various medicinal plants along with chemotherapeutic agent treatments may attenuate its toxicity.

The genus *Exacum* (Gentianaceae, tribe Exaceae) consists of 64 species distributed across palaeotropical regions. Including Africa, Madagascar, Socotra, Himalayas, Arabian Peninsula, India, Sri Lanka, Southern China and Malaysia, and Northern Australia. *Exacum lawii* C.B. Clarke, species of genus *Exacum* is small herb commonly distributed in the Western peninsula, Western coast region of India, Southern part India, Mysore and Coimbatore. It is endemic to Jarandeshwar hill from Satara district, Maharashtra and Western ghat of Karnataka. The majority of species (38 species) found in Madagascar. The second most species-rich area (14 species) is Sri Lanka and the Southern tip of the Indian subcontinent (mainly the Western Ghats), three species found in North India and the Himalayan region. Southern Arabian Peninsula (Dhofar of Oman and nearby Mahrah of Yemen) and the Island of Socotra shared three species. The African continent has only two species *Exacum oldenlandioides* widespread throughout the entire tropical Africa and *Exacum zombense* endemic to the Shire Highlands in Malawi. Two species, *Exacum hamiltonii* and *Exacum teres*, are restricted to the Himalayas, and two species, *Exacum pteranthum* and *Exacum sutaepense*, are limited to the mountainous regions between Burma and Thailand (Yong *et al*, 2005; Linnaeus, 1747a; Linnaeus, 1747b; Struwe *et al*, 2002; Hooker, 1885). The *Exacum lawii* is annual, glabrous, small erect herb rarely reaching 15 cm tall and flowers are bluish-purple. The common name is Law's Persian violet. It is locally known as Lahan chirayata in Maharashtra, Manali in

Malayalam, Marukozhunthu in Tamil. *Majorana hortensis* (Lamiaceae) in Siddha system of medicine has also the common name Marukozhunthu (Murugesa, 1988). The *Exacum lawii* is annual, glabrous, small erect herb rarely reaching 15 cm tall. Flowers are bluish-purple. The whole plant has been used traditionally as the folk remedy for the treatment of kidney disorders and eye diseases (Gamble, 1923; Kirtikar and Basu 1935; Chopra *et al*, 1956).

In the present study, the *Exacum lawii* was selected for the evaluation nephroprotective activity, antibacterial and antifungal activity against ocular infection. To the best of our knowledge, till date, no data is reported on the pharmacognostical study and scientific evaluation of ethno-pharmacological profiles of this the plants. Hence, it is worthwhile and quite pertinent to scientifically explore the unexplored medicinal plant *Exacum lawii*. The main focus of the study was to pharmacognostical standardization and evaluation of its nephroprotective activity using cisplatin-induced toxicity model in rodents and in-vitro human embryonic cell line (HEK-293). The in-vitro antibacterial and antifungal activity against ocular infection were also explored.