2.1. *Cephalotaxus griffithii*

The genus *Cephalotaxus* (Plum Yew) belongs to the family Cephalotaxaceae, is a member of coniferales. Cephalotaxaceae is a monogeneric family and has seven species namely, *C. oliveri*, *C. fortunei*, *C. griffithii*, *C. alpina*, *C. harringtonii*, *C. nana* and *C. hainanensis* (Lang et al., 2013). "Cephalotaxus" means "head-yew," from the Greek "kephale" for head and the botanical name "taxus" for the yew genus. "Head-yew" refers to the flowering structures that are borne in tight clusters or "heads" and to its needles, which resemble those of yew. *Cephalotaxus* was once an integral part of the prehistoric, indigenous flora of both North America and Asia. This genus has long since disappeared in North America and is now seriously endangered in Asia (Lang et al., 2011). In Asia, the plant is distributed in India, Japan, Korea, south, central, and eastern China, Hainan, Taiwan, Burma, Laos, and parts of Vietnam. (Kim, 1995; Lang et al., 2013) (Figure 2.1. and 2.2.).

*Cephalotaxus* trees have been used as timber, firewood and ornament. The seeds have also been used as an illuminant for paintings in Japanese tradition (Abdelkafi and Nay, 2012). *Cephalotaxus* has been used in traditional Chinese medicine for the treatment of human malignant tumors, rheumatism, dyspepsia, abdominal distension and the like (Editorial Board of China Herbal, 1999). The bark and leafy branches of *Cephalotaxus fortunei* have also been reported to be used in traditional Chinese medicine as immunosuppressant and antineoplastic agent (Cisowski et al., 2005). The genus *Cephalotaxus* has received a great level of scientific interest as it contains ingredients having anticancer activity especially alkaloids and terpenoids (Abdelkafi
and Nay, 2012). Recently, homoharringtonine (HHT) an alkaloid isolated from C. harringtonia was approved by USFDA for the treatment of adult patient with chronic myeloid leukemia (http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm325895.htm). Apart from anticancer property, flavonoids isolated from Cephalotaxus were found to possess antioxidant (Bae et al., 2007) and osteoblast differentiation stimulating activity (Lee et al., 2006).

Figure 2.1. Distribution of C. oliveri, C. griffithii, C. alpina, C. harringtonii. (Adapted from Lang et al., 2013)

Cephalotaxus griffithii Hook. f., commonly known as Griffith's plum yew is a shrub or small tree and found up to an altitude of 2000 m and is distributed in North East India, western Sichuan province in China, and Myanmar (Shankar, 2008). In North
East India, it is distributed in Mishmi Hills, Arunachal Pradesh, Manipur and Nagaland (Shankar, 2008). So far, only two phytochemical analyses from *C. griffithii* have been attempted. Kamil et al. (1982) isolated and characterized six flavonoids and Phutdhawong et al. (2002) reported 22 volatile compounds identified through GC-MS analysis from the hydrodistillation oil of the needles of *C. griffithii* growing in Thailand, with α-pinene (58.5%), caryophyllene (11.7%), β-pinene (4.2%), myrcene (3.5%) and limonene (3.1%) as the major components.

*Figure 2.2. Distribution of C. nana, C. hainanensis and C. fortunei* (Adapted from Lang et al., 2013)
2.2. *Oroxylum indicum*

*Oroxylum indicum* (L.) Benth. ex Kurz commonly called as midnight horror, tree of Damocles, Indian caper, Indian trumpet flower or Indian trumpet tree is a small to medium sized deciduous tree. It is distributed in India, Sri Lanka, Malaysia, China, Thailand, Philippines and Indonesia (Anonymous, 1972). In India, the tree is growing in North-East regions, Himalayan foothills, Eastern and Western Ghats (Bennet et al., 1992). It is found up to an altitude of 1200 m mainly in the river banks or slopes of the hills (Chauhan, 1999).

2.2.1. Ecology

*Oroxylum indicum* lives in relationship with the actinomycete *Pseudonocardia oroxyli* present in the soil surrounding the roots (Gu et al., 2006).

2.2.2. Traditional use

*Oroxylum indicum* is an important folklore medicine and played an immense role in health care and prevention of diseases in many Asian countries (Kirtikar and Basu, 1996). Each part of this plant possesses medicinal value. The root bark is a well known tonic and astringent, and is used in fever, diarrhoea, dysentry, bronchitis, intestinal worms, leucoderma, asthma, inflammation, anal troubles, rheumatism (Parrotta, 2001) stomatitis, nasopharyngeal cancer and tuberculosis (Khare, 2004; Bhattacharje, 2005). Tender fruits and seeds are refreshing and stomachic and used as expectorant, purgative and bitter tonic (Khare, 2004; Bhattacharje, 2005). Dried seed powder is used by women to induce conception. The seeds are ground with fire soot and the paste is applied to the neck for quick relief of tonsil pain. The seeds are used in traditional
Indian Ayurvedic medicine, included in famous tonic formulations such as *Chyawanprash* (Singh and Chaudhary, 2011). Leaves are used as stomachic, carminative and flatulent. Leaf decoction is given in treating rheumatic pain, enlarged spleen (Khare, 2004), ulcer, cough, and bronchitis. Mature Fruits are acrid, sweet, antihelmintic, and stomachic. They are useful in pharyngodynia, cardiac disorders, gastropathy, bronchitis, haemorrhoids, cough, piles, jaundice, dyspepsia, smallpox, leucoderma and cholera (Warrier, et al., 1995). Bark decoction is taken for curing gastric ulcer and a paste made of the bark powder is applied for mouth cancer, scabies and other skin diseases. The medicated oil of *O. indicum* in sesame oil base instilled into ears mitigates the pain in otitis (Chauhan, 1999; Warrier et al., 1995).

2.2.3. *Phytochemistry*

*O. indicum* leaves are reported to contain flavonoids namely baicalein (5,6,7-trihydroxy flavone), chrysin (5,7-dihydroxy flavone) (Chen et al., 2003; Chen et al., 2005), scutellarein, anthraquinone and aloe-emodin, (Singh and Chaudhary, 2011; Dey et al., 1976), and their glycosides baicalein 7-O-glucoside, baicalein-7-O-diglucoside (Yuan et al., 2008a) baicalin (baicalein-7-glucuronide), scutellarin (scutellarein-7-glucuronide) (Chen et al., 2003; Chen et al., 2005), chrysin-7-O-glucuronide, chrysin-diglucoside and irridoids (Yuan et al., 2008a). The leaves were also found to contain quercetin-3-o-α-L-arabinopyranoside, 1-(2-hydroxyethyl) cyclohexane-1, 4-diol, apigenin (Yuan et al., 2008b)

Stem bark contains ellagic acid (Hari et al., 2010), chrysin, oroxylin-A, scutellarin, baicalein (Chen et al., 2003; Maitreyi et al., 2008), 5-hydroxy 8-methoxy 7-o-β-D-glucopyranuronosyl flavones (Maitreyi et al., 2008), stig mast-5-en-3-ol (Nair and
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Joshi, 1979), pratensol (Polya, 2003), 3-(4-hydroxy phenyl) 2-propenoic acid (DNP on CD-ROM, Version 9:2 Copyright) and flavonoid 3,4’,5,7-tetrahydroxy-flavonol (Kaisarul et al., 2009), 5-hydroxy 4’,7-dimethoxy flavones(Bays and Finch, 1990), 7-o-methyl chrysin (Kumar et al., 1999), dihydrooroxylin-A, methyl-3,4,5-trihydroxy-6-(5-hydroxy-6-methoxy-4-oxo-2-phenylchroman-7-yloxy)-tetrahydro-2H-pyran-2-carboxylate, 5-hydroxyl-7-methoxy-2-(2-methoxy-6-(3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yloxy)phenyl)-4H-chromen-4-one (Hari et al., 2010).

Root of *O. indicum* is reported to contain 2, 5-dihydroxy-6, 7-dimethoxy flavone and 3,7,3’-5’-tetramethoxy-2-hydroxy flavone. (Kawsar et al., 2003). Root bark contain chrysin, scutellarin-7-rutinoside, weak acids, traces of alkaloids (Subramaniam and Nair, 1972), sitosterol, galactose, baicalein, biochanin-A, ellagic acid, oroxylin-A (Dalal and Rai, 2004) and 5,7-dihydroxy-6-methoxy flavone (Zaveri et al., 2008). The fruits pods are reported to contain oroxylin A, chrysin, baicalein, a triterpene carboxylic acid and ursolic acid (Roy et al., 2007). Seeds contain oils and flavonoids such as chrysin, oroxylin A, baicalein, baicalein-7-O-diglucoside (Oroxylin B), baicalein-7-O-glucoside, apigenin (Tomimori et al., 1988), terpenes, alkaloids, saponins (Bhattacharje and Das, 1969), tetuin, the 6-glucoside of baicalein, benzoic acid and fatty acids (Chen et al., 2003; Chen et al., 2005). A new flavone glucuronide-oroxindin and chrysin-7-O-diglucoside were also isolated.

Fruits are reported to contain oroxylin A, chrysin and ursolic acid (Jiwajinda et al., 2002), aloe-emodin (Kupchan and Karim, 1976). The seed oil contains caprylic, lauric, myristic, palmitic, palmotoleic, stearic, oleic and linoleic acids (Kapoor, 2001).
2.2.4. Pharmacological properties

2.2.4.1. Antimicrobial activity

*Oroxylum indicum* is reported to possess antimicrobial activity. The stem bark extract of methanol, ethyl acetate, and ethanol were shown to possess antibacterial activity against gram positive and gram negative bacteria viz. *Bacillus subtilis*, *E. coli*, and *Pseudomonas aeruginosa* (Das and Choudhury, 2010). Further, three fractions, obtained from methanolic stem bark extract namely hexane, carbontetreachloride and chloroform extracts were found to possess antibacterial and antifungal activity (Kaisarul et al., 2009).

2.2.4.2. Antioxidant Activity

Many researchers have shown that *Oroxylum indicum* possessed antioxidant activity (Kalaivani and Mathew, 2009; Mishra et al., 2010; Kumar et al., 2010). In a comparative study among nine different plants revealed that *Oroxylum indicum* stem bark showed the highest antioxidant activity by inhibiting lipid-peroxidation ($IC_{50}$ -0.08 $\mu g/ml$) (Siriwatanametanon et al., 2010). Further, antioxidant potential of methanolic extracts among different parts of *Oroxylum indicum* indicated that leaves and root bark extracts showed maximum radical scavenging activity than stem bark, stem and fruit extract (Mishra et al., 2010).

2.2.4.3. Anticancer activity

Methanolic and aqueous extract of stem bark of *Oroxylum indicum* have shown cytotoxic activity against MDA-MB-435S and Hep3B cell lines *invitro* (Kumar et al.,
Evaluation on the anticancer potential of 11 plants used in Bangladeshi folk medicine found that extract of *Oroxylum indicum* showed the highest toxicity on all tumor cell lines tested, with an IC$_{50}$ of 19.6 µg/ml for CEM, 14.2 µg/ml for HL-60, 17.2 µg/ml for B-16 and 32.5 µg/ml for HCT-8 (Costa-Lotufo et al., 2005). In another comparative antiproliferative study among nine plants, it was found that *Oroxylum indicum* stem bark extract stood second in inducing cell death of HeLa cells (Siriwatanametanon et al., 2010).

### 2.2.4.4. Antiinflammatory Activity

The root bark of *Oroxylum indicum* has been shown to inhibit inflammation in carrageenan induced rat paw oedema and cotton pellets induced chronic inflammation rat models (Maitreyi and Sunita, 2010). Leaves of *Oroxylum indicum* have also been found to possess antiinflammatory activity against carrageenan induced rat paw oedema (Upaganlawar et al., 2009).

### 2.2.4.5. Analgesic activity

The butanol extract of root bark of *Oroxylum indicum* was reported to show analgesic activity in tail flick and acetic acid induced writhing response models (Maitreyi and Sunita, 2010).

### 2.2.4.6. Hepatoprotective activity

Leaf, stem bark and root bark of *Oroxylum indicum* have been shown to possess hepatoprotective activity against carbon tetrachloride induced hepatotoxicity in rats (Tenpe et al., 2009; Bichitra et al., 2011; Ahad et al., 2012).
2.2.4.7. *Nephroprotective Activity*

The ethanolic extract of roots and chrysin isolated from roots of *Oroxyllum indicum* has shown protective effect against cisplatin-induced renal injury in rats (Adikay S et al., 2011a; Adikay S et al., 2011b).

2.2.4.8. *Antihyperlipidemic Activity*

*Oroxyllum indicum* root bark extract has been shown to reduce cholesterol, total triglycerides, LDL-C, VLDL-C levels and increase in the levels of HDL-C in cholesterol induced hyperlipidemic albino Wistar rat model (Shetgiri et al., 2010).

2.2.4.9. *Immunomodulatory Activity*

The root bark butanol fraction of *Oroxyllum indicum* has been shown to increase immune response in rats in response to sheep red blood cells (Zaveri et al., 2006).

2.2.4.10. *Gastro protective activity*

The root bark of *Oroxyllum indicum* has been shown to protect against ethanol induced gastric mucosal damage in rats (Zaveri and Jain, 2007).