CHELIDONIUM MAJUS L. - A REVIEW ON PHARMACOLOGICAL ACTIVITIES AND CLINICAL EFFECTS

Biswas Surjyo Jyoti¹*

¹Department of Zoology, Midnapore College, Midnapore, West Bengal, India-721101
*Corresponding Author: E-mail: surjyo@rediffmail.com

Received: 01/03/2013; Revised: 25/03/2013; Accepted: 30/03/ 2013

ABSTRACT

Chelidonium majus L. (Papaveraceae) is a plant that has been used for centuries in treating many diseases in European and Asian countries. Crude extracts from various parts of the plant contain isoquinoline alkaloids. The alkaloids derived from C. majus have not yet much studied; however, some reports are available on toxicity studies of alkaloids of this plant. In such a scenario there is need for understanding its therapeutic potential and its toxic actions. This review summarizes scientific findings and suggests areas where further research is needed.

KEY WORDS: Chelidonium majus, alkaloids, pharmacology, antioxidant

INTRODUCTION:

*Chelidonium majus* commonly known as swallow-wort, rock poppy or greater celandine belongs to Family-Papaveraceae. This plant is distributed across the globe viz. Europe, Asia, North America and in northwest Africa, particularly in soils rich in nitrogen. The name ‘Chelidonium’ came from Chelidon—a greek word which means swallow bird, as the plant begins to flower when the swallows return. The plant is widely regarded for its therapeutic potential in Western and Asian countries particularly in Chinese traditional medicine and homeopathy. Crude extracts of *C. majus* and isolated compounds exhibit numerous biological activities (Colombo and Bosisio, 1996; Gilca et al., 2010). Though many diseased conditions even today are being treated with *C. majus* both in traditional and homeopathic medical systems but it has some self limitations therefore, its therapeutic efficacy needs critical evaluation. The current review summarizes scientific findings of other investigators on *C. majus* and suggests areas where further investigations/research is needed.

Uses in traditional medicine systems

In many European, Asian and African countries *C. majus* latex was used for bile and liver disorders, for treatment of warts, corns, eczema and solid tumors. It has traditionally being used to treat liver diseases, gastric ulcer, tuberculosis, skin eruptions and oral infections. In Chinese traditional medicine and in homeopathy *C. majus* is used to treat blockage of blood circulation, to relieve pain edema and jaundice.

Phyto-constituents (Figure. 1)

Extracts of Chelidonium has been found to contain three types of benzyl isoquinoline alkaloids viz. protoberberine, protopine, benzophenanthredine. Sanguinarine and chelerythrine are the prominent compounds obtained from roots while coptisine, chelidonine and berberine are obtained from the aerial parts (Colombo and Bosisio, 1996). Other constituents include malic, citric, gentisic, and hydrobenzoic acids. It also contains hydroxycinnamic acid derivatives, sparteine, saponin, carotenoids, chelidocystatin and flavonoids.

PHARMACOLOGICAL ACTIVITIES

Hepatoprotective effects

It has been demonstrated that *Chelidonium majus* favourably modulates carbon tetrachloride induced toxicity in rats. The treatment with *C. majus* considerably reduced the number of necrotic cells and decreased the activities of transaminases and bilirubin (Mitra et al., 1992; Mitra et al., 1996). Biswas et al. (2008) have reported that ethanolic whole plant extract of *Chelidonium majus*, has been tested for its possible anti-tumor, hepatoprotective and anti-genotoxic effects in *p*-dimethylaminoazobenzene (*p*-DAB) induced hepatocarcinogenesis in mice through multiple assays: cytogenetical, biochemical, histological and electron microscopical. Data of several cytogenetical endpoints and biochemical assay of some toxicity marker enzymes at all fixation intervals and histology of liver sections through ordinary,
scanning and transmission electron microscopy at certain fixation intervals were critically analyzed. The results suggest anti-tumor, anti-genotoxic and hepato-protective effects of the plant extract, showing potentials for use in cancer therapy. Chung et al., (2004) demonstrated that C. majus enhances nitric oxide and TNF-α production via NF kappa B activation in mouse.

Effects on enzymes

Mazzanti et al., (2009) reported that there was a significant reduction in glutathione level and SOD activity in liver after high oral dose of C. majus. It was reported by others that C. majus has a strong antioxidant activity as revealed from FRAP assay (Then et al., 2003). Biswas et al., (2008) also reported that LPO and transaminases activity reduced significantly after treatment with C. majus extract against p-DAB induced hepatocarcinogenesis.

Antimicrobial, antiviral and antiparasitic effects

The modulatory effect of C. majus extract against virus was evaluated in various in vitro and in vivo studies C. majus showed antimicrobial effect on gram positive bacteria and on Candida albicans (Lendfeld et al., 1981). Crude extracts of several alkaloids extracted from C. majus exhibited antimicrobial, antiviral and antifungal properties (Lozyuk, 1977; Gerencer, et al., 2006; Parvu et al., 2008; Meng et al., 2009; Monavari et al., 2012). Growth of Alternaria, Aspergillus flavus, Candida albicans, Rhizopus orizae and Scopulariopsis was inhibited by berberine at 10–25 μg/ml concentration (Mahajan et al., 1982). Ma et al., 2000 demonstrated that chelidonine, dihydrochelerythrine and dihydrosanguinarine isolated from C. majus roots have activity against Cladosporium herbarum at 4-10 μg/ml concentration. It has been experimentally proved that compounds 8-hydroxydihydro-sanguinarine, dihydro-sanguinarine, dihydro-chelerythrine, 8-hydroxydihydro-chelerythrine isolated from aerial parts of the plant showed anti-bacterial effect against methicillin resistant Staphylococcus aureus (Zuo et al., 2008).

Alkaloids extract showed antiviral efficacy against human adenoviruses type 5 and 12, herpes simplex virus, and RNA polio virus (Zuo et al., 2008; Horvath et al., 1983; Kery et al., 1987). Zhu and Ahrens (1982) investigated that berberine successfully controlled the intestinal secretion enhanced by E. coli enterotoxin, the effect of which was dose dependent and it may be due to quaternary ammonium group which is responsible for anti-bactericidal property of berberine and protoberberine was found active against reverse transcriptase enzyme of RNA tumor viruses. Chelidocystatin decreases the activity of cysteine proteinases but further in depth research are necessary especially in vivo conditions.

Cardiovascular effects

Sanguinarine has been involved in suppression of angiogenesis by inhibition of VEGF signaling, this has been experimentally proved in pig granulosa cells and in porcine endothelial cells (Basini et al., 2007).

Immuno-modulatory activity

Immuno-modulatory properties of C. majus have been investigated by Song et al., 2002, where he obtained a protein bound to polysaccharide from water extracts of the plant, (CM-Ala) which showed mitogenic activity on spleen, bone marrow cells, it also increased the number of granulocyte macrophage colony forming cells, further it suppressed immune response locally by decreasing epidermal Langerhans cells (Song et al., 2002). It has been demonstrated that C. majus extract improved overall humoral and cellular immunity response and decreased incidence of recurrences of tonsillitis in children (Khmel’nitskaia et al., 1998).

Anti-inflammatory and Analgesic activity

Stylopine is a major component of leaf of C. majus and it suppresses NO and PGE2 production in macrophages by inhibiting iNOS and COX 2 expressions. It has been demonstrated that 5 and 12 lipoygenase were inhibited by sanguinarine and chelerythrine because these enzymes are
involved in leukotriene B₄ and 12 hydroxyeicosatetraenoic acid syntheses. As compared to chelerythrine, sanguinarine showed higher anti-inflammatory activity due to different oxygen electron donating constituents (Lendfeld et al., 1981). It has been reported that C. majus extract increases TNF α production due to NF κB production. It has also been reported that Ukrain induces depolarization of mitochondrial membrane potential and activates caspase in Jurkat T lymphoma cell model (Habermehl et al., 2006).

**Choleretic effects**

Vahlensieck et al., (1995) used phenolic and alkaloid fractions of C. majus for their choleretic activity using perfused rat livers. He demonstrated that total extract induced choleresis i.e. the bile flow was significantly elevated and the amount of the bile was more than double the quantity. Though it was not ascertained which fraction of the extract was responsible for the increased bile flow.

**Effects on reproductive systems**

The feeding of ethanolic extract of C. majus showed that it could combat the spermatotoxic effects to some extent in induced p-DAB induced carcinogenesis. As benzophenanthridine alkaloids have marked nucleophilic properties, they might intercept the reactive metabolites; thereby preventing their attack on nucleophilic sites on DNA, and hence blocking adduct formation (Vavreckova et al., 1996a, b). Further it has been suggested that many enzymatic functions are essential for the normal integrity and function of testis i.e. synthesis, development and maintenance of normal sperm. Therefore, the protective role of C. majus on sperm head could also be attributed to its regulatory effect on protein metabolism and repair activities in the germinal cells (Biswa and Khuda-Bukhsh, 2002).

**Antihyperglycemic and Hypoglycemic activity**

Berberine an isoquinoline alkaloid obtained from C. majus is used widely in China to reduce blood glucose, in type II diabetes. Xuan et al., (2011) reported that berberine inhibits mitochondria function and decreases intracellular ATP in streptozotocin induced diabetes in rats. This leads to a reduction in transcription factors such as FoxO1, SREBP1, and ChREBP. As a result, expression of gluconeogenic genes (PEPCK and G6Pase) and lipogenic gene (FAS) decreases. These molecular changes represent a signaling pathway for improvement of fasting glucose in the berberine treated diabetic rats (Xia et al., 2011).

**Anti-cancer efficacy**

The anti-leukaemic activity of protoberberine alkaloids has been reported and Smekal et al. (1984) demonstrated that sanguinarine intercalates partially as well as totally into the DNA double helix. It has been demonstrated by circular dichroism that the spectrum of DNA is similar to ethidium binding to DNA. C. majus had antiproliferative effect on human keratinocyte cell lines (Vavreckova et al., 1996a, b). Berberine intercalation to DNA might be due to the planes of intercalated molecules which lie parallel to those of purine-pyrimidine pairs. An important constituent berberine has been shown to interact with nucleic acids by various optical methods. It was tested that administration of 350 μg/kg of protopine intraperitoneally inhibited very less regression of Ehrlich carcinoma and application of 50 μg/kg b.w. of chelidonine regressed sarcoma 180 (Sokoloff, 1968). Ukrain™ an anticancer drug whose components include most of C. majus compounds exerts multiple effects on cancer cell lines (Cordes et al., 2003). Several reports have been obtained in both animal and human models regarding anticancer efficacy of Ukrain, against various types of induced stomach carcinogenesis, induced hepatocarcinogenesis, in patients suffering from pancreatic cancer, Kaposi sarcoma (Kim et al., 1997; Biswas and Khuda-Bukhsh, 2002; Lohninger et al., 1996; Gansauge et al., 2002; Ernst and Schmidt, 2005). Chelidonine inhibits telomerase in tumor cells strongly and may provide a basis for probable anticancer agent also this alkaloid arrest mitosis as a result of inhibition of tubulin polymerization and activation of SAPK/JNK pathway.
Central Nervous system

An alkaloid obtained from *C. majus*, thiophosphoric acid has been tested on rodents regarding its action on CNS, it was found that it depresses spontaneous motor activity; it seems to stimulate dopaminergic system and depresses the serotonergic system (Kleinrok *et al.*, 1992).

CLINICAL STUDIES:

Dysentery or gastroenteritis

Ardjah (1991) studied action of celandine on upper abdominal symptoms in human subjects such as cholinergic and spasmolytic effects using panchelidon®. In case of patients with postcholecystectomy 29 patients out of 35 showed clear improvement. A similar study using 21 patients with dyspeptic complaints with alcohol toxic liver parenchyma damage, 20 reported improvement after two weeks of treatment. Limited numbers of clinical studies have been carried out with total extracts in patients with epigastric complications and the sample size was small and definite conclusion could not be ascertained from the study.

Periodontal effects

Benzophenanthridine alkaloids are routinely used for the treatment of periodontal diseases, Boulware *et al.*, (1985) investigated that sanguinaria extract was helpful in lowering of volatile sulphur present in the oral cavity. Southard *et al.*, (1987) reported that benzophenanthridine alkaloids act as an anti-caries thereby preventing tooth decay.

Radioprotective effects

Song *et al.*, 2003 demonstrated that extracts of *C majus* have certain radioprotective effects.

Cytotoxic effects

There were spontaneous reports of adverse drug reactions associated with *C. majus* preparation. Incidences of hepatotoxicity have been reported by several authors (Moro *et al.*, 2002, Kaminsky *et al.*, 2006). It has been reported that *C. majus* showed cytotoxicity towards lymphoma cells and murine cell lines. In some countries Complementary Evaluation Committee recommended that products containing alkaloids obtained from *C. majus* must have a warning label and it should be administered under medical supervision only.

CONCLUSION

We have reported hepatoprotective ability of *C. majus* crude extract and various potencies of it in induced hepatocarcinogenesis. It would be prudent to investigate its constituents singly and in combination, how they modulate pathological changes and which form is more potent or effective. Time of collection of plant materials, place of collection, extraction procedures, and its storage might affect its active compounds both quantitatively and qualitatively. The information summarizes here concerning *C. majus* is intended to serve as a reference to researchers involved in ethnomedicinal research.

ACKNOWLEDGEMENT

Grateful acknowledgements are made to Professor A. R Khuda-Bukhsh, Department of Zoology, University of Kalyani and Dr. Prabir De, Scientist, CCMB, Hyderabad for encouragements.

REFERENCES


