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A Quick Review of the Effects of *Chelidonium majus* L and Its Active Components on Health and Disease Treatment

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Abstract

Background: Using herbs for the treatment of diseases has a long history. *Chelidonium majus* from the family of Papaveraceae is one of the best-known and most widely used herbs in traditional medicine. The aim of this study was to review studies related to *Chelidonium majus* active components, as well as its therapeutic and toxic effects on body tissues.

Methods: This short overview was done by searching several databases including Magiran, Iran medex, IranDoc, SID, Medlib, Web of Science, Scopus, PubMed, Science Direct and Google Scholar. All articles that met the inclusion criteria were studied and evaluated.

Results: The presence of various compounds in the plant such as alkaloids, flavonoids, and opioid derivatives, as well as its ability to produce nitric oxide (NO) and tumor necrosis factor (TNF) and its multiple capabilities in affecting the activities of various body tissues in hepatic, renal, neurological, reproductive and hormonal systems have made it a leading plant in the listofmedicinalherbs.The levels of the active compounds in the plant are influenced by the location, altitude and ambient temperature of its growing area and harvest time, a fact which partly justifies the controversial reports on the effects of this extract on body tissues.

Conclusion: Because of the multiplicity and diversity of its active ingredients, *Chelidonium maj*us has the potential to be used for the treatment and control of hard to treat diseases (HTDS). However, it is recommended to do more studies on its mechanism and its possible adverse effects.

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Introduction

The use of medicinal plants has a long history. Today, due to a common belief that medicinal plants have no side effects, they are increasingly welcomed. This positive view on medicinal herbs has paved the way for their entering into the market without any prior standard toxicology tests. However, the fact is that there are many reports on the toxicity of some plants including *Chelidonium majus* (1, 2).

Chelidonium majus, commonly known ascelandine or greater celandine is a medicinal plant from the family of

Papaveraceae. Its other names are tetterwort, nipplewort, and swallow wort (3, 4). This plant is widely found all over the world including Europe, North Africa, South America, Asia, and in particular in northern Iran. It grows mainly in nitrogen-rich soils (2). *Chelidonium majus* has been used in folk medicine as a diuretic, choleretic drug, analgesic especially in abdominal pain, peptic ulcer and menstrual pain and also as a spasmolytic, anti-inflammatory and anti-tumor agent. It has been also used for promoting diuresis in oedema and ascites, treating jaundice and relieving cough and hypnotic effects. It has been used to treat liver diseases, gallstones, ulcers and skin diseases such as warts, papillomas, and nodules too (1, 2). It is also used as a pain killer, as well as an anti-virus, anti-bacterial, anti-fungal, and anti-protozoa agent (2-5).

In contrast, some studies suggest hepatic and renal toxic properties for the extract -an issue that requires further toxicological research (6). However, due to the active ingredients and pharmacological effects of this plant, hopefully many diseases will be cured by using its compounds in near future. Thus, this study was done to review the literature on the effects of the extract of *Chelidonium maj*us on different body organs in different databases.

Materials and Methods

The present study is a review of existing information on the *Chelidonium majus L*. All relevant documents published during the time period of 2006-2016 were reviewed.

*Chelidonium maj*us was used as the keyword and relevant materials published in journals, Persian and English books, theses and reports on medicinal plants and traditional medicine were reviewed. A total of 48 publications that provided information about the use of *Chelidonium majus L.* in the treatment of various ailments were reviewed. Pertinent literature was searched in different electronic databases (ISI Web of Science, MEDLINE, Science Direct, Scopus, Embase, Magiran, Iran medex, IranDoc, SID, Medlib and Google Scholar). We considered only original works on medicinal plants, including those that cited the plant species referred to as *Chelidonium majus L*, with botanical identification correctly described according to the Missouri Botanical Garden (http://www.tropicos.org). We do not claim to have included every existing information source about traditional uses of *Chelidonium majus L.* and we have focused on information easily accessible to researchers.

The Chemical Compounds of the Extract

The extract of *Chelidonium majus* contains various alkaloid compounds such as protopine, benzophenanthredine, chelerrytherine, sanguinarine, isochelidonine, coptisine, chelidonine and berberine. The last three components, especially coptisine, are abundantly found in the aerial parts of the plant. Salts of calcium, magnesium, aluminum and resin and mucilage are available in the plant as well (2,5). The chromatographic studies on the plant in different parts of northern Iran showed that the levels of isoquinoline alkaloids in the plant are directly related to the altitude and inversely related to the temperature at which the plant is growing. The greatest accumulation of alkaloid compounds in the plant occurs in spring (7).

In addition, temperature, time, place of collection, methods of extraction and storage may affect the amount of active ingredients in the plant. Studies have showed that the plant seeds contain lectin while it is not found in other parts of the plant like flowers, leaves, stems, roots and sap (8). *Chelidonium majus*, also, contains acids such as malic, citric, caffeic, coumaric, gentisic, and hydroxy benzoic acid. Among its other compounds one can refer to saponin, carotenoids, flavonoids and hydroxycinnamic acid derivatives (2, 9).

The Effects of the Extract of *Chelidonium majus* on Liver and Kidney Functions

Studies on the effects of *Chelidonium majus* extract on the liver toxicity induced by carbon tetrachloride showed that the extract could reduce the levels of hepatic enzymes and necrotic liver cells (9). In Biswas et al. study, this plant extract was effective in the treatment of liver cancer and it increased NO and TNF-α. Moreover, its phenolic compounds and alkaloids increased the flow of bile (2,9). Despite the above studies, some reports indicated that the extract of the plant has toxic effects on some tissues such as the liver. Zarei and colleagues showed that daily oral administration of the plant extract at a dose of 400 mg/kgbw increased the level of aspartate aminotransferase (AST), albumin and creatinine in hypercalcemic rats. It seems that the plant extract, especially at high doses, has toxic effects on the liver and kidneys (1). Some other studies have implied side effects and liver toxicity of the plant, too and in some countries it is obligatory to put warning labels on the alkaloid products derived from *Chelidonium majus* (10).

In the study conducted by RUPASRI DUTT-ROY et al. on the hepatoprotective effect of the plant when used together with anti-TB drugs of rifampicin (RIF) and isoniazid (INH),which are associated with liver damage, it became clear that the levels of AST, alanine aminotransferase (ALT) and bilirubin total increased in the group that received the extract at a dose of 100mg/kgbw., but in the group which received the extract at a dose of 500mg /kgbw., the levels of total bilirubin and ALT decreased while the level of AST increased (11). The decreased levels of ALT and bilirubin can partially justify the stabilization of cell membranes as well as the reconstruction of tissue damage resulting from the use of INH and RIF. In the mentioned study, the necrotic cells also decreased which were resulted from the antioxidant properties of the plant exerted through the increased activity of catalase and superoxide dismutase, as well as inhibiting the lipid peroxidation in the liver (12, 13).

Yılmaz and colleagues showed that using *Chelidonium majus* extract at doses of 100 and 200 mg/kgbw, in rats with carbon tetrachloride- induced hepatotoxicity, decreased AST, ALT and total bilirubin compared to the group which only received carbon tetrachloride. But, it increased the levels of these factors compared to the control group (12).

Ukrain is a synthetic drug based on the alkaloids present in *Chelidonium majus* which exerts anti-cancer properties through mitochondrial death pathway. It has no major side effects; however, in some cases liver damages have been reported (13). Several contradictory results have been reported on the effect of the extract of this plant on the liver which might be due to the factors affecting the plant's active

components such as temperature, time and place of collection, the storage methods and extraction procedures.

The ethanol extract of *Chelidonium majus* is still widely used in traditional medicine to treat liver diseases. Biswas and et al, by using scanning techniques and electron microscopy, showed that in rats with liver tumors, *Chelidonium majus* had anti-tumor, anti-genotoxic and hepatoprotective effects. They have concluded that this plant has the potential to treat cancer (9). *In vivo* studies have shown that the alkaloids in *Chelidonium majus* such as chelerythrine, sanguinarine, berberine, coptisine, protopine and allocryptopine inhibit mitochondrial respiratory enzymes such as NADH dehydrogenase through the liver and suppress the succinate dehydrogenase (4). There are reports on the potential liver damage as a result of consuming *Chelidonium majus* in several European countries; even though, the relationship between these two has not been definitely established yet (14).

Some studies have shown that the intake of cadmium causes nephron toxicity and renal dysfunction in mice. The oral administration of methanol extract of *Chelidonium majus* could return the kidney weight, adjust serum electrolytes, urea, creatinine, urinary excretion of electrolytes and resulted in urine volume adjustment (4, 15).

The Effect of *Chelidonium majus* Extract on the Pituitary-thyroid Axis

In Zarei and et al study, the alcoholic extract of *Chelidonium majus* reduced the concentration of thyroid hormones (16). Flavonoids belong to a group of natural substances with variable phenolic structures which share their main feature of having high antioxidant properties. So, with this mechanism the plant is probably effective in reducing blood lipids (17, 18). The active alkaloid ingredients available in *Chelidonium majus* easily pass through cell membranes and are able to react with cell components such as cytoskeleton tubulin protein. Alkaloids also inhibit the synthesis of cholesterol and therefore they decrease the plasma concentration of cholesterol (1, 19).

In Aqababa H, et al. study, the plant extract reduced thyroid hormones and increased TSH. Presumably, the presence of flavonoids inhibited the activation and release of thyroperoxidase and consequently reduced the amount of thyroid hormones. Flavonoids reduce thyroid hormone levels through inhibiting the activation of type I deiodinase enzyme as well as preventing the organification of tyrosine in thyroid cells. Studies showed that compounds like flavonoids, through inhibiting catechol-O-methyl transferase (COMT), could increase thyrotropin-releasing hormone (TRH), leading to an increase in the synthesis and secretion of TSH (17).

The Effect of *Chelidonium majus* Extract on Reproduction and Prolactin Hormone

In a study on the effect of extracts of the aerial parts of Chelidonium *majus* on the lipid profiles, prolactin and pituitary-gonadal axis in hypercholesterolemic rats, *Chelidonium majus* extract could reduce cholesterol, triglycerides and testosterone, while it increased prolactin and gonadotrophin levels (19). One way to adjust the level of gonadotrophin is through testosterone negative feedback loop (20). In the mentioned study, as the level of testosterone decreased, the gonadotrophin levels increased reasonably. One

of the reasons for prolactin increase is the presence of endogenous opioid derivatives (18,19).

On the one hand, *Chelidonium majus* belongs to the family of *Papaveraceae* that contains compounds of morphine and opioids, papaverine, codeine, etc. which exert their effect through opioid, dopamine, benzodiazepines and cholinergic neurotransmitters (2, 21). On the other hand, the effects of the extracts of the plants with alkaloids (including *Chelidonium majus*) on hepatitis and fibrosis have been already confirmed which significantly increase ALT and AST (22,23). The *Chelidonium majus* extract probably reduces the amount of cholesterol by increasing prolactin (19) and also it decreases the amount of testosterone by reducing the activity and the number of mitochondria (24).

Researchers have found that high doses of the extract of *Chelidonium majus* reduce glutathione (GSH) and SOD activities in rats (24, 25). Glutathione peroxidase as an antioxidant protects sperms in the testes and if it is reduced, it may result in infertility. This enzyme prevents the destruction of DNA in sperm cells and sperm generating cells (25). The administration of sanguinarin, as an alkaloid derived from *Chelidonium majus*, caused DNA damage in some cells of the bone marrow. Thus, the lowered testosterone level seems reasonable. *Chelidonium majus* extract also increased the production of nitric oxide (NO) and increased the production of tumor necrosis factor alpha (TNF-α) (26) and it has been reported that NO increases the secretion of gonadotropins, enhances sperm motility and induce secretion (20).

This plant extract could diminish the spermatoxic effects of the cancer induced by dimethylaminoazobenzene (P-DAB). Benzophenanthridine alkaloids have nucleophilic properties, and they can react with the active metabolites and prevent them from attacking nucleophilic sites in DNA and in this way they prohibit the production of wastes. In addition, it has been suggested that many enzymatic activities are necessary for the development and maintenance of sperms. Thus, the protective role of *Chelidonium majus* extract in sperm tract induces regulatory effect on protein metabolism and repairs activity of the germinal cells (2).

The Effect of *Chelidonium majus* Extract on Lipid Profiles

In a study about the effect of the extracts of aerial parts of *Chelidonium majus* on lipid profiles in hypercholesterolemic rats, decreased cholesterol and triglycerides level shave been reported (19). Berberine as an alkaloid is one of the active components of *Chelidonium majus* that can be effective in the prevention of coronary artery disease and possibly in reducing total cholesterol levels (27, 28). It has been recently reported that berberine could reduce cholesterol with a mechanism different from statins. Co-administration of statins and berberine is more effective in lowering the cholesterol level. Berberine facilitates the excretion of cholesterol through increasing the production of a receptor in the liver that binds to cholesterol. Also, the alkaloid compounds present in the plant might be involved in inhibiting the production of cholesterol (29).

The Hypoglycemic and Antihyperglycemic Effects of *Chelidonium majus* Extract

In China, berberine has been widely used for lowering blood sugar in diabetes type II. According to Xia X et al berberine can inhibit mitochondrial function and ATP within

cells in STZ-induced diabetic rats. This leads to a reduction in the transcription factors such as SREBP-1 and FoxO1. As a result, the expression of gluconeogenesis gene and lipogenic gene is reduced. The molecular changes represent a signaling way to improve blood sugar in diabetic rats treated with berberine (2, 30).

The Effect of *Chelidonium majus* Extract on Enzymes

In Mazzanti et al. study, the activity of SOD and glutathione levels in the liver reduced after the intake of high doses of *Chelidonium majus* extract (24). Some other researchers have also reported that the plant has strong antioxidant properties (2, 15).

The Effect of the Extract on Immune System

Song et al., in studying the effect of *Chelidonium majus* extract on the immune system, showed that there is a protein bonded to a polysaccharide in the aqueous extract of the plant which has mitogenic activity in the spleen and bone marrow and increases the number of granulocyte-macrophage colony-forming cells (4). In addition, it reduces the local immune response in the epidermal langerhans cells. So, it was proved that the plant extract increases the cellular and humoral adaptive immune responses and reduces the chance of recurrence of tonsillitis in children (2, 29).

According to some previous studies, *Chelidonium majus* extract inhibits the production of inflammatory mediators and improves the cellular and humoral immune system as wells as the performance of the tonsils. *Chelidonium majus* extract increases NO and TNF-α production in macrophages in combination with interferon-gamma. Recently, an alkaloid called 6-acetonyl-5,6-dihydrosanguinarine has been identified in *Chelidonium majus* extract that increases the production of inflammatory cytokines, including interleukin 6 and 8, and TNF-α in dendritic and macrophages cells (5, 31). In a previous study,6-Acetonyl-5,6-dihydrosanguinarine (ADS) isolated from *Chelidonium majus* started the production of pro-inflammatory cytokines through ROS-JNK/ERK-NFκB signaling pathway and consequently the extract induced inflammatory cytokines as a positive immune modulator (31). In a study done by Gupta SL et al, *Chelidonium majus* showed enhancing and moderating effects on the immune system that it is probably due to sanguinarine, the alkaloid presents in the plant extract that stimulates phagocytic activity and promotes the protective responses (32).

The Analgesic and Anti-inflammatory Effects of *Chelidonium majus*

Stylopine as one of the main components of the plant inhibiting INOS and cyclooxygenase-2 prevents the production of nitric oxide and prostaglandin E_2 in macrophages. Lipoxygenase is inhibited by chelerythinesinguinar in because this enzyme is involved in the synthesis of leukotriene B_4 and hydroxicosatetranoic acid. The anti-inflammatory activity of sanguinarine is more than that of chelerythrine. *Chelidonium majus* extract has been reported to increase the production of TNF-α through making NF kβ (2).

In traditional medicine, *Chelidonium majus* has been used for the treatment of many infectious diseases. In an *in vivo* study, the extract significantly reduced itching and serum levels of IgE, TNF-α and IL-4 in mice with atopic dermatitis

(33). Several important components such as stylopine, chelidonine, 8-hydroxydihydro sanguinarine, chelerythrine, sanguinarine isolated from the plant have strong inhibitory effect on the production of nitric oxide, prostaglandin E_2, interleukin 6 and β1, induction of cyclooxygenase 2 expression of iNOS and TNF-α in macrophages (4, 34).

In vivo studies also showed that anguinarine and chelerythrine benzophenanthridine, present in the extract, reduce carrageenan-induced paw edema. Also, they showed that sanguinarine has an anti-inflammatory potential higher than that in chelerythrine (4). *Chelidonium majus* extract had anti-arthritic potential in rats with the arthritis induced by collagen (35). It has been proven that the extract of *Chelidonium majus* inhibits the mentioned model through reducing the production of TNF-α, IL-6, IFN-gamma, T and B cells, immunoglobulins G and M and increasing the proportion of regulatory T cells (4).

Recently, Tail-flick studies in mice have revealed that the extracts of *Chelidonium majus* and Chelidonine have more analgesic effect than aspirin (36, 37). Molecular studies showed that *Chelidonium majus* extract inhibits the ionic currents activated by gamma-aminobutyric acid (GABA) and those activated by glutamate in neurons of the gray matter area. This mechanism is proposed to explain the important role of *Chelidonium majus* extract as a pain relief (4).

Mikolajczaket al., in their study on the analgesic and anti-inflammatory effects of the aqueous extract of *Chelidonium majus* with and without protein, showed that the protein-containing extract produced substances with morphine-like analgesic effect which created anti-inflammatory effects as well. The exact mechanism of this effect is still unclear (38).

Anti-Alzheimer Effects of *Chelidonium majus*

Acetylcholine is one of the important neurotransmitters in transferring messages from neurons to muscles which in Alzheimer's disease is broken down by acetylcholinesterase. The ethanol extract of the aerial parts of *Chelidonium majus* strongly inhibits this function of the enzyme. Several alkaloids isolated from the roots and aerial parts of *Chelidonium majus* such as 6-ethoxydihydrochelerythrine, 6-ethoxydihydrosanguinarine, 8-hydroxydihydrochelerythrine, 8-hydroxydihydrosanguinarine, sanguinarine, chelidonine, chelerythrine and berberine decrease the activity of acetylcholinesterase and butyrylcholinesterase (4,39).

Antispasmodic and Anticonvulsant Effects of *Chelidonium majus*

The aqueous extract of *Chelidonium majus* and its active components induced expansion in the ileum contraction caused by acetylcholine and barium in guinea pig. The alkaloids of chelidonine and protopine might have caused this expansion. Another study showed that coptisine and caffeoylmalic available in the extract have anti-spasmodic properties too (4).

Anti-ulcer Activity of *Chelidonium majus*

Studies have shown that the extract of *Chelidonium majus* is effective in the treatment of irritable bowel syndrome and, in a dose-dependent manner; it provides anti-ulcer effects through reducing the amount of acid secretion and releasing leukotrienes and increasing the secretion of mucin and prostaglandins E_2. Studies also show that in mice with ulcerative colitis, chelidonic acid in *Chelidonium majus* a

control the inflammation by inhibiting the production of IL-6, TNF-α, cyclooxygenase-2 and hypoxia inducing factor (HIF-1α) (4, 38).

Anti-cancer Activity of *Chelidonium majus*

In vitro and *in vivo* studies on anti-cancer properties of *Chelidonium majus* have shown that its isolated compounds such as chelidonine, sanguinarine, chelerythrine, and protopine have strong effects on pancreatic and colon cancerous cells, while they have modest cytotoxic effects in breast cancer. Crude ethanol extract of the herb and its oil-free extract also have a moderate to strong cytotoxic effects on pancreatic adenocarcinoma cells. In mice treated with cm- 2b, metastasis significantly decreased compared with the control group while this effect was not seen in Ukrain. *Chelidonium majus* extract could not affect the weight of the primary tumor, either (14). In whole, it can be said that the extract of *Chelidonium majus* has strong anti-tumor effects, particularly on pancreatic tumors (40). *Chelidonium majus* extract induces apoptosis by caspase activation through MAPK signal pathways independent of NF-κB in human epidermal carcinoma cells (41). Studies on the anticancer properties of four different plants showed the cytotoxic activity in four species decreased from *Echinophora-platyloba* to *Ferulago angulata*, *Chelidonium majus L*, and *Salvia officinalis L*, respectively. So, isolating its antitumor ingredients can be helpful for cancer treatment (42).

Deljanin et al. showed that extract of *Chelidonium majus* had a time- and dose-dependent increasing cytotoxic effect on all six lines of human tumor cell. The extract promoted cell cycle stop phase and apoptosis. Therefore, it can be a good medicinal plant with anti-tumor effects and cytotoxic mechanisms which can be used alongside with conventional chemotherapy to prevent metastasis (43).

Havelek and colleagues studied the effect of chelidonine on the cancerous blood cells and showed its effect as potential inducer of cell death in cancer cells, especially leukemic cells (44). The results indicated that the antiproliferative activity of the ethereal extract of *Chelidonium majus* on the human tumor cell line is much more than its aqueous extract. Results also showed that the effects of *Chelidonium majus* extract depended on its concentration and polarity. The anti-proliferation activity of the ethereal extract is probably due to its higher levels of lipophilic substances that pass through the cell membrane easily. Alkaloids react inside cells. They react with proteins, DNA and lipids (45).

Antioxidant Activity of *Chelidonium majus*

In vitro studies indicate that *Chelidonium majus* extract has antioxidant properties (46). Phytochemical analysis shows that its antioxidant capacity is dependent on its alkaloid content (3). *In vitro* studies showed that polyphenols in the extract of the plant (roots, stems, leaves and seeds) eliminated different free radicals such asperoxyl radicals, hydroxyl, superoxide, hypochlorite, hydrogen peroxide and singlet oxygen (47). The antioxidant effect of the plant is exerted through up-regulation of FOXO3 transcription factors and original antioxidant enzymes including catalase and manganese superoxide dismutase (48).

In a study, the secondary metabolites content and antioxidant activity of the plant in its various stages of growth (early stages of flowering, maturity stage of flower and fruit

setting stage) were studied and it was found that the highest concentration of phenolic content was in the completion stage of leaf production. The highest concentration of flavonoids was in the early stages of flowering and the highest antioxidant level was at the start of leaf production. So, it can be concluded that concentrations of secondary metabolites in the plant depend on the plant's growth stage (49).

The ischemia-reperfusion courses cause severe and destructive damages in distant organs. Kocak et al showed that intraperitoneal administration of Ukrain reduced the lung damage resulting from pulmonary ischemia-reperfusion in rats which might be due to its antioxidant and anti-inflammatory properties (50).

Antimicrobial and Anti-parasitic Activities of *Chelidonium majus*

The alkaloids in *Chelidonium majus* inhibit trichomonasvaginalis. The alkaloid sanguinarine, also causes deformity and loss of protozoa (4). The ethanol extract of *Chelidonium majus* has anti-parasitic activity against dactylogyrus which is related to benzophenanthridine alkaloid (51). The alkaloid extract of *Chelidonium majus* has antiviral activity against a variety of viruses. The crude extract of *Chelidonium majus* inhibits the growth and development of herpes simplex virus type 1 (52). In addition to the previously mentioned activities of the crude extracts of *Chelidonium majus*, it could inhibit the activity of AIDS virus type 1 (HIV-1) which is due to the sulfate glycosaminoglycan in the extract. In vitro studies showed that benzophenanthridine alkaloid fractions of the various parts of the plant have antiviral activity against herpes simplex virus type I (HSV-1) and adenovirus type 5 and 12. The alkaloids *in Chelidonium majus* such as berberine and chelidonine inhibit the reverse transcriptase enzyme in HIV-1 virus (4).

Both the aqueous and methanol extracts of *Chelidonium majus* significantly inhibited Fusarium species such as F. culmorum, F. graminearum, F. oxysporumcubense and F. solani (4, 53). In addition, the compounds isolated from *Chelidonium majus* including Q by l8- hydroxyl dihydrosanguinarine, 8-hydroxydihydrochelerythrine, dihydrosanguinarine, dihydrochelerythrine, sanguinarine and chelerythrine have strong antifungal activity against drug-resistant fungi (53, 54). Chelerythrine and the combination of chelerythrine and sanguinarine have anti-fungal properties against trichophyton strains, microsporumcanis, epidermophytonfloccosum and aspergillus fumigates (4). Recent studies showed that alkaloids benzophenanthridine, sanguinarine and chelerythrine alkaloids strongly inhibited alternaria alternate, curvularialunata, pyriculariaoryza, F. solani, valsamali, F. oxysporum sp. niveum and F. oxysporum f. sp. vasinfectum (54, 55).

Cytotoxic Effects of *Chelidonium majus*

Despite the fact that *Chelidonium majus* has been extensively used in traditional and modern medicine, the researchers have reported that the plant has undesirable side effects in animals and humans. It is reported that the use of latex *Chelidonium majus* strongly stimulates the lining of the mouth, throat, stomach and intestines, and when applied directly on the skin, it may cause skin irritation, blisters and allergic contact dermatitis (4).

Drug Interactions

Many people use synthetic and chemicals drugs together with herbal ones. Sometimes, these plants and their compounds may interfere with those medications and may cause side effects. There is not enough information about drug interactions; however, several reports indicated that some of the active ingredients of the plant could interfere with some drugs through affecting cytochromeP_{450} enzymes (4, 55).

Conclusion

The extract of *Chelidonium majus* has been widely used in traditional and modern medicine with many therapeutic potential and some side effects; however, its effects on the liver are controversial and need further investigations. This might be partly related to the factors affecting the amounts of its compounds such as temperature, time, location, methods of extraction and storage as well as the part of the plant which is used to prepare the extract.

Chelidonium majus is considered to be a valuable herb due to the presence of variety and potent alkaloids and bioactive agents. The demonstration of cytotoxic effects in animal and human samples indicates the potential effects of this plant on stopping the growth of cancer cells and microorganisms.

Although the beneficial effects of *Chelidonium majus* on improving the function of immune systems, antioxidants and anti-inflammatory suggest its beneficial effects in various tissues and systems, there are still many concerns about its potential toxic effects on tissues such as liver.

The existence of multiple ambiguities about the effects of this plant makes it necessary to perform further and detailed studies to obtain more accurate and transparent responses about the exact functions of this magic plant.

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