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A review on hepatocyte regenerative potential of Ultra-high diluted *Greater celandine*

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Abstract
Liver disease is still a major health issue because of the lack of a variety of liver-protective medications. In conventional medicine, herbs are used to treat a variety of liver conditions. The hunt for efficient hepatoprotective medications continues in the absence of acceptable treatment for liver problems. Greater celandine used in the treatment of liver disorders like jaundice, gallstones, and gallbladder pain. Although it's a great potent medicine for hepatoprotective activity, it does have its adverse effect of damaging hepatocytes. To avoid the adverse effect and to get the better outcome, the dosage can be tamped down as much as possible. In this review, the methods and outcome of such low dosage is discussed and explained.

Keywords: great celandine, chelidonium majus, hepatoprotective, ultra-high dilution, hepatocyte regeneration

Introduction

Chelidonium majus (family Papaveraceae), or Greater celandine commonly termed rock poppy or swallow-wort, is a herbaceous plant, native to Mediterranean Europe, the subarctic regions of Asia, North America and northwest Africa [1]. Crude extracts as well as purified chemicals from Chelidonium majus show extensive biological effects (anti-inflammatory, antibacterial, anticancer, analgesic, hepatoprotective) that support some of the traditional applications. Chelidonium majus L contains several bioactive alkaloids such as berberine, coptisine, sanguinarine, chelerythrine and chelidonine, all of which show encouraging therapeutic action [2]. Although Chelidonium is used widely for hepatotoxicity, its few compounds have the capability to induce hepatotoxicity in high dosage form, many research has been conducted to find the inducing compound but ended inconclusively [3]. Thus, on diluting the drug in a way without losing its medicinal effect the Hahnemannian's method of ultra-high dilution preparation is used. Ultra-high dilutions of Chelidonium majus extract are reputedly used against different forms of liver disorders including liver cancer [4]. In this review article, an attempt was made to explain the biomolecular effect and pharmacological effect of ultra-high diluted Chelidonium majus.

Chelidonium Majus

Table 1: Taxanomical description [5]

kingdom	*Plantae*
Phylum	*Tracheophyta*
Class	*Magnoliopsida*
Order	*Ranunculales*
Family	*Papaveraceae*
Genus	*Chelidonium L.*
Species	*Chelidonium majus L.*

Fig 1: Chelidonium majus diagram [6]

Fig 2: Chelidonium majus flower [7]

Botanical Description

A rosette of basal leaves grows in the first year of this plant's life. During the second year, this plant grows to approximately 2 feet tall and has branching branches that prefer to spread out. An irritant sap is present in the leaves, which are yellow-orange in colour. The angular, glaucous, and sparsely haired stems are rather stout. The pinnate-pinnatifid or pinnatifid, hairless to largely hairless alternating compound leaves can grow up to 6 inches long and 3 inches wide. The five leaflets or lobes of a compound leaf are typically ovate or obovate in shape. Green and hairless above and pale green and hairless below with strong veins, these pinnatifid leaflets or lobes have secondary lobes and are pinnatifid. Some borders might be dentate or coarsely crenated. The tips of the secondary lobes are round. Compound leaves may have a few hairs on the rachis and petiole. When it comes to flowering stalks, the opposite happens to the compound leaves. Several inches long, the tip of each stalk bears an umbel of 3-8 blooms. Four yellow petals, two sepals, a robust style, and a large number of yellow stamens make up each flower, which measures between 12 and 34 inches across. An inch or so is the pedicel length of each bloom. During the summer months, the flowering period lasts for approximately a month or so. Each of the flower's petals is replaced by an ascending seedpod that grows between 3/4" and 2" long. They have smooth, hairless surfaces and are cylindrical in shape; their exterior surfaces are glaucous and hairless. At certain points throughout the seedpod's maturation, it becomes slightly constrained (torulose). There are little white appendages on the seeds that are ovoid, flattened, and glossy; (elaisomes). This plant reseeds itself in order to grow [8].

Hepatic activity of Chelidonium Majus

Chelidonium majus extract and alkaloid and phenolic fractions from it have been shown to stimulate bile acid-independent flow in isolated perfused rat liver. After 40 minutes, the volume of bile had doubled and the bile acid content had decreased. This impact was not isolated to one of the two portions. Two human trials demonstrated the choleretic action of Chelidonium majus in liver disease patients and healthy volunteers. Intragastrically given hydroethanolic extract with 1.5% total alkaloids as chelidonine improved bile flow [1]. A reduction in the amount of necrotic cells, a prevention of fibrotic alterations, and a drop in transaminase and bilirubin activities were seen in two investigations on rats using ethanolic whole extract. It also showed a protective effect on hepatotoxicity induced by anti-tubercular drugs [9]. Chelidonium majus reduces carbon tetrachloride-induced toxicity in rats. Chelidonium majus treatment decreased necrotic cells, transaminases, and bilirubin activity. In addition, histopathology of liver sections utilising standard scanning and transmission electron microscopy at certain fixing intervals were carefully assessed. The plant extract exhibits anti-tumor, anti-genotoxic, and hepatoprotective characteristics, indicating it might be useful in cancer treatment. To stimulate TNF production in mice, Chelidonium majus activates NF kappa [10]. The protective efficacy of chelidonine, the principal active component of Chelidonium majus, and its PLGA poly incapsulated nanoform (nano-chelidonine) has been tested in cadmium chloride (CdCl2) induced oxidative stress and liver toxicity in mice34. The study found that 30 days of exposure to CdCl2 (1.0 mg/kg body weight twice a week) generated oxidative stress via lipid peroxidation and reactive oxygen species build up (ROS). After CdCl2 exposure, nano-chelidonine significantly reduced lipid peroxidation and oxidative stress while increasing GSH levels. Thus, nano-chelidonine may protect mice from cadmium poisoning [11]. Even though there are many hepatoprotective activity in Chelidonium majus, certain inevitable liver damages in humans has been substantiated by case reports and reviews. Intravascular haemolysis, thrombocytopenia, renal failure, and liver cytolysis were symptoms of haemolytic anaemia caused by oral CM extract use [11].

Pharmacological activity of ultra-high dilution

For ultra-dilutions to be effective, it is necessary to identify plausible ‘non-molecular’ or ‘meta-molecular’ information transmission pathways. The identification of biological targets at multiple levels is an issue in the investigation of how these ultra-high dilutions operate. Low concentrations of active chemicals such as nanoparticles, water clusters, and coherence domains are required for the Ultra-high dilution to take effect. Local molecular interaction and non-linear dynamics are enhanced via Enzyme activation/regulation, gene expression, and cell receptors; Where Enzyme activity occurs through Allosteric activation and Silica nanostructures. Systemic interaction takes place through neuroimmunology where it is targeted biologically by disease dynamics and bioelectricity. Cell response interaction occurs through methods such as Receptor priming, Signal transmission, Stochastic resonance, Neuroimmunology networks, Nonlinearity-chaos, Grotthus-type water chains. An adaptation occurs when an external stimulus is given to networks in the immunological, endocrine, and central nervous system. Small changes may have a big impact on a deterministic system like this one. Rather than relying on just a single signal, the immune response is triggered by a variety of factors that interact with each other synergistically, antagonistically, and via feedback loops. To activate (or reduce) the specific cell activity associated with that particular signal, only a few extracellular molecules or one molecule, or extremely low magnetic fields are needed. To put it another way, this concept suggests that the interaction between an Ultra-high dilute and the cell's membrane produces a cascade of biochemical reactions within the cell that occur from contact with the drug itself. Even gene expression might be affected by such events at the receptor and post-receptor levels [12].

Preparation of Ultra-high diluted chelidonium Majus

Preparation is done as per the Hahnemannian method, where he introduced the ultra-high diluted Chelidonium majus in Materia medica in 1819. Whole plant is collected and turned into coarse powder of 100g and mixture of purified water of 567ml and ethanol of 468 ml are used to prepare the ethanol extract of the Chelidonium majus of 1000ml. The ultra-high dilution is prepared from the raw crude ethanol extract through succussion process known as potentization.[13]where one part of crude drug or preceding potency is added with nine parts of strong alcohol and succussed to obtain the following higher potency. The succussion produces the potency higher with a kinetic force through mechanical jerk done by potentizer machine.

Discussion

Chelidonium majus is a wonderful herbal drug used for many purposes including hepatoprotective action but on prolong usage it can cause hepatocyte damage. The cytotoxicity of the drug must be avoided, so that its whole therapeutic potential is utilized. For such aim to be obtained, the dosage must be lower but the therapeutic action should be amplified. This objective can be achieved by producing the ultra-high dilution of the Chelidonium through Hahnemannian method of potentization. Many theories have been proved in support of the Hahnemannian method and its results have been revised. On following such lower dosage, the organoleptic damage can be avoided and true therapeutic potential of the drug is used for the needful.

Referances

1. Gilca M, Gaman L, Panait E, Stoian I, Atanasiu V. Chelidonium majus– an Integrative Review: Traditional Knowledge versus Modern Findings. *Forsch Komplementmed*,2010:17(5):241-248. doi:10.1159/000321397
2. Nile SH, Wang H, Nile A, *et al*. Comparative analysis of metabolic variations, antioxidant potential and cytotoxic effects in different parts of Chelidonium majus L. Food and Chemical Toxicology,2021:156:112483. doi:10.1016/j.fct.2021.112483
3. Teschke R, Frenzel C, Glass X, Schulze J, Eickhoff A. Greater Celandine hepatotoxicity: a clinical review. Annals of Hepatology,2012:11(6):838-848. doi:10.1016/S1665-2681(19)31408-5.
4. Ulysses Research Foundation, 125, Rash Behari Avenue, Kolkata 700 029, West Bengal, India., Maji AK, Banerji P, Ulysses Research Foundation, 125, Rash Behari Avenue, Kolkata 700 029, West Bengal, India. Chelidonium majus L. (Greater celandine) – A Review on its Phytochemical and Therapeutic Perspectives. Int J Herb Med,2015:3(1):10-27. doi:10.22271/flora.2015.v3.i1.03
5. Registry-Migration.Gbif.Org. GBIF Backbone Taxonomy. Published online 2021. doi:10.15468/39OMEI
6. The pharmacology of chelidonin, A neglected alkaloid of chelidonium, or tetterwort. *JAMA*,1920:75(20):1324. doi:10.1001/jama.1920.02620460022007
7. Celandine Chelidonium Majus Stock Image - Image of celandine, background: 138362643. Accessed December 14, 2021. https://www.dreamstime.com/celandine-chelidonium-majus-greater-isolated-white-background-image138362643
8. Greater Celandine (Chelidonium majus). Accessed December 13, 2021. https://www.illinoiswildflowers.info/weeds/plants/celandine.htm
9. Dutt-Roy R, Kayalvizhi E, Manikandan B, Chandrasekhar M. Hepatoprotective effect of Chelidonium Majus. L extract against antitubercular drugs induced hepatic damage in wistar rats. International Journal of Pharma and Bio Sciences, 2015:6:P677-P681.
10. Biswas SJ, Khuda-Bukhsh AR. Effect of a homeopathic drug, Chelidonium, in amelioration of p-DAB induced hepatocarcinogenesis in mice. BMC Complement Altern Med,2002:2(1):4. doi:10.1186/1472-6882-2-4
11. Pantano F, Mannocchi G, Marinelli E, *et al*. Hepatotoxicity induced by greater celandine (Chelidonium majus L.): a review of the lite-rature, 7.
12. Bellavite P, Marzotto M, Olioso D, Moratti E, Conforti A. High-dilution effects revisited. 2. Pharmacodynamic mechanisms. *Homeopathy*,2014:103(1):22-43. doi:10.1016/j.homp.2013.08.002
13. pharmacopiea chelidonium.pdf.