

## RISK PROFILE

# *Chelidonium majus extract*

CAS No. 84603-56-3

Date of reporting 04.06.2012

### Content of document

|   |   |
|---|---|
| 1. Identification of substance                      | 1 |
| 2. Uses and origin                                  | 1 |
| 3. Regulation                                       | 2 |
| 4. Relevant toxicity studies                        | 3 |
| 5. Exposure estimates and critical NOAEL/NOEL       | 3 |
| 6. Other sources of exposure than cosmetic products | 3 |
| 7. Assessment                                       | 4 |
| 8. Conclusion                                       | 4 |
| 9. References                                       | 5 |

### 1. Identification of substance

|                                  |  |
|----------------------------------|--|
| <b>Chemical name (IUPAC):</b>    | Chelidonium majus  |
| <b>INCI</b>                      | CHELIDONIUM MAJUS EXTRACT  |
| <b>Synonyms</b>                  | Celandine extract  |
| <b>CAS No.</b>                   | 84603-56-5   |
| <b>EINECS No.</b>                | 283-257-3  |
| <b>Molecular formula</b>         | Not applicable   |
| <b>Chemical structure</b>        | See Council of Europe 2008 for structural formulas for the more important alkaloids.   |
| <b>Molecular weight</b>          | Not applicable   |
| <b>Contents (if relevant)</b>    | Chelidonium Majus Extract is an extract of the leaves and aerial parts of the Celandine, <i>Chelidonium majus</i> L., Papaveraceae. Like other members of the Papaveraceae (poppy) family, <i>Chelidonium majus</i> L. contains alkaloids as its main active compounds. The alkaloids are regarded as poisonous. The leaves and roots contain 0.2-2.8 % alkaloids. The alkaloids found in greatest quantity is chelidonine, berberine, allocryptopine, coptisine, magnoflorine, sparteine, chelerytrine, sanguinarine and protopine. |
| <b>Physiochemical properties</b> | Not available.   |

## 2. Uses and origin

|             |  |
|-------------|--|
| <b>Uses</b> | <p>➤ <b>Cosmetic products:</b></p> <p><i>Functions according to:</i></p> <ul style="list-style-type: none"><li>○ CosIng database<br/>“Antidandruff” – Helps control dandruff (CosIng [online]).</li><li>○ Other<br/>Chelidonium majus extract is used in cosmetics for its antidandruff properties. The extract is also used in hand creams, cream for sensitive skin and after-shave cream (Council of Europe, 2008).</li></ul> <p><i>Frequency of use</i><br/>A total of 6 products and 24 products showed up in a search at Codecheck.info and EWG’s Skin Deep, respectively. See below for the distribution of the products among the different product categories.</p> <p><u>EWG’s Skin Deep:</u><br/>Anti-aging face cream (3 products)<br/>Around-eye cream (1 product)<br/>Conditioner (2 products)<br/>Face cleanser (2 products)<br/>Face cream (4 products)<br/>Hair styling (1 product)<br/>Shampoo (4 products)<br/>Skin whitening cream (2 products)<br/>Tanning oil/cream (5 products)</p> <p><u>Codecheck.info:</u><br/>Hair styling (3 products)<br/>Shampoo (3 products)</p> <p>(EWG’s Skin Deep [online]; Codecheck.info [online]).</p> <p><i>Concentrations being applied</i><br/>Not known</p> <p>➤ <b>Medicinal products/applications</b><br/>Chelidonium majus extracts have been shown to stimulate production of bile and pancreatic digestive enzymes in human studies, and are therefore frequently prescribed to treat gastric and biliary disorders (Council of Europe, 2008).</p> <p>The extract has been reported to exhibit antiviral, anti-inflammatory, anti-tumor and antimicrobial properties (Council of Europe, 2008).</p> <p>It has been claimed that the extract help with psoriasis and warts (Council of Europe, 2008).</p> <p>➤ <b>Food</b></p> |
|-------------|--|

|   |  |
|---|--|
|   | No data available.   |
| <b>Origin</b><br>Natural (exo /endo)<br>Synthetic | Natural, plant-derived.<br>Water, ethanol and propylene glycol can be used as extracting agents (Then et al., 2000). |

### 3. Regulation

|                          |                              |
|--------------------------|------------------------------|
| <b>Norway</b>            | No regulation <sup>1</sup> . |
| <b>EU</b>                | No regulation.               |
| <b>Rest of the world</b> | No regulation.               |

### 4. Relevant toxicity studies

|   |   |
|---|---|
| <b>Absorption</b><br>Skin<br>GI tractus   | Skin and GI tractus: not data available   |
| <b>Distribution</b><br><b>Metabolism</b><br><b>Excretion</b>                                    | No data available.  |
| <b>Local toxic effects</b><br>Irritation<br>Sensitivity   | Skin irritation: The extract causes irritation and blisters.<br><br>When applied to the skin, the raw plant juice causes irritation, and even vesication. And it has long been known as a caustic for the removal of warts. The juice – or an extract - also has an effect on corns and calluses (Council of Europe, 2008). There are several reports about production of contact dermatitis (BODD, Etxenagusia MA <i>et al</i> , 2000).  |
| <b>Systemic toxic effects</b><br><br>Acute<br><br><br><br><br><br><br><br><br><br>Repeated dose | Existing studies on the systemic toxic effects of <i>Chelidonium majus</i> extract is limited.<br><br>Several in vitro studies show cytotoxicity of several of the individual alkaloids on carcinoma cell lines (Council of Europe, 2008). Ethanol extracts of <i>Chelidonium majus</i> show cytotoxicity on human lymphoblastoid Raji cells, suppressing cell growth at concentrations of 10 and 50 µg/ml (Spiridonov et al., 2005).<br><br>Anecdotally, skin poisoning has resulted from handling the crushed plant (Holisticonline).<br><br>No available data.<br><br>No available data. |

<sup>1</sup> The Norwegian medicinal products agency considered *Chelidonium majus* extract a medicinal remedy. Because of that up till 2008 topical products containing the substance were considered medicines – meaning a topical product containing it were automatically classified a medicine. This regime has since been lifted.

|   |  |
|---|--|
| Mutagenicity /genotoxicity                | No available data.<br><br>No teratogenicity effects have been seen after use of Chelidonium majus extract (Council of Europe, 2008). |
| Carcinogenicity                           |  |
| Reproductive toxicity /<br>teratogenicity |  |

## 5. Exposure estimate and critical NOAEL / NOEL

|                                   |   |
|-----------------------------------|---|
| <b>NOAEL/NOEL critical</b>        | There is not sufficient data to set a NOAEL/NOEL value.                               |
| <b>Exposure cosmetic products</b> | There is not sufficient information to calculate the exposure from cosmetic products. |
| <b>Margin of Safety (MoS)</b>     | The Margin of Safety can not be calculated.   |

## 6. Other sources of exposure than cosmetic products

|  |   |
|--|---|
| <b>Food stuffs</b>   | No data.  |
| <b>Pharmaceuticals</b>                                       | The usual daily dose is 12 to 30 mg of its active ingredients, which equals to 2-4 g of the extract (Council of Europe, 2008).  |
| <b>Other sources</b>   | No data.  |
| <b>Adverse side effects - from uses other than cosmetics</b> | There are several reports of hepatotoxicity in humans after treating gastric and biliary disorders with Chelidonium majus extract (Benninger J et al., 1999; Moro PA et al., 2009; Teschke R et al., 2011). |

## 7. Assessment

The Council of Europe assessed the safety of use of Chelidonium majus extract in cosmetics in 2008, and concluded that the available data are insufficient to support the safety of Chelidonium majus extract for use in cosmetic products (Council of Europe, 2008). It was also stated that a dermal 28-day study to establish a NOEL/NOAEL and a skin penetration study are needed, and that the extraction method should be standardised to ensure minimal variability. In addition, information about the use concentrations is necessary to calculate the exposure from cosmetics.

Applied to the skin the extract is strongly irritation and may cause contact dermatitis. Extracts show pronounced hepatotoxic properties. Indications are the toxic alkaloids are taken up in the body to some extent when the plant juice (roots) come in contact with the skin.

## 8. Conclusion

In conclusion, because of the skin irritation effect, the hepatotoxicity and the very scarce information about the systemic toxicity otherwise we propose to prohibit the use of the Chelidonium majus extract in all cosmetics products.

## 9. References

Benninger J, Schneider HT, Schuppan D, Kirchner T, Hahn EG. Acute hepatitis induced by greater celandine (*Chelidonium majus*). *Gastroenterology*. 1999 Nov;117(5):1234-7.

Council of Europe. Active ingredients used in cosmetics: safety survey. Council of Europe Publishing. Strasbourg, March 2008.

Etxenagusia MA et al, Contact dermatitis from *Chelidonium majus* (greater celandine). *CONTACT DERMATITIS*; 43; 1; 47; 2000 Jul

Moro PA, Cassetti F, Giugliano G, Falce MT, Mazzanti G, Menniti-Ippolito F, Raschetti R, Santuccio C. Hepatitis from Greater celandine (*Chelidonium majus* L.): review of literature and report of a new case. *J Ethnopharmacol*. 2009 Jul 15;124(2):328-32.

Spiridonov NA, Konovalov DA, Arkhipov VV. Cytotoxicity of some Russian ethnomedicinal plants and plant compounds. *Phytother Res*. 2005 May;19(5):428-32.

Then M, Szentmihályi K, Sárközi A, Illés V, Forgács E. Effect of sample handling on alkaloid and mineral content of aqueous extracts of greater celandine (*Chelidonium majus* L.). *J Chromatogr A*. 2000 Aug 11;889(1-2):69-74.

Teschke R, Glass X, Schulze J. Herbal hepatotoxicity by Greater Celandine (*Chelidonium majus*): causality assessment of 22 spontaneous reports. *Regul Toxicol Pharmacol*. 2011 Dec;61(3):282-91.

**Online:**

BODD: Botanical Dermatology Database: [www.bodd.cf.ac.uk/BotDermFolder/BotDermA/ARAL.html](http://www.bodd.cf.ac.uk/BotDermFolder/BotDermA/ARAL.html)

Codecheck © 2011. Available at: <http://www.codecheck.info/> (accessed 1<sup>th</sup> December 2011).

CosIng, European Commission, Health and Consumers, Cosmetics. Available at: <http://ec.europa.eu/consumers/cosmetics/cosing/> (accessed 1<sup>th</sup> December 2011).

EWG's Skin Deep © Cosmetic Safety Database. Environmental Working group. Available at: <http://www.ewg.org/skindeep/> (accessed 1<sup>th</sup> December 2011).

Holisticonline Available at; [http://www.holisticonline.com/Herbal-Med/\\_Herbs/h213.htm](http://www.holisticonline.com/Herbal-Med/_Herbs/h213.htm)