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Reply to letter to the editor

Response to comment on article, doi.org/10.1016/j.fct.2018.12.055

This letter is in response to the comment on article (doi: 10.1016/j.fct.2018.12.055) by Dr. Małgorzata Kalemba-Drożdż, who expresses concerns related to our paper "Are wild and cultivated flowers served in restaurants or sold by local producers in Denmark safe for the consumer?" published in Food Chemical and Toxicology (doi: 10.1016/j.fct.2018.07.007).

The focus on our review is flowers eaten as food in the European Union. The objection that the paper should include culinary uses outside Europe in e.g. Asia and the Middle East or the use of plant material (of e.g. *Epilobium angustifolium*) in herbal teas or alcohols are out of the scope of our review. Further, the use of *Galium verum* in cheese manufacturing was due to its believed milk-coagulating effects and not for coloring or food as such (Brøndegaard, 1987).

As also described in the section on methods, we included peer-reviewed publications in English using three bibliographic databases in addition to an extensive Danish ethnobotanical work by Brøndegaard (Brøndegaard, 1987), toxicological textbooks in English, German and Danish and toxicological reports from the Danish Poison Centre. However, the European Union has 24 official and working languages and it would have be an impossible task to include papers in all native languages on ethnobotanical use, but we have included ethnobotanical surveys on plant use in European countries including Poland, Switzerland, Cyprus, Czech Republic, Slovakia, Estonia, Sweden, Spain, Portugal, Italy, and the Mediterranean area as a whole. In fact, the ethnobotanical surveys on plant use in Poland included three written by prof. Łukasz Łuczaj (Łuczaj, 2008, 2010; Łuczaj and Szymanski, 2007). According to Dr. Kalemba-Drożdż, the culinary context (cookbooks etc.) should be included in the assessment of novel food status and food safety of the flowers, however we have decided to provide the scientific material for the national authorities or EU Commission to decide whether a use as food is safe and is significant enought to not being novel.

As stated in our discussion, and also mentioned by Dr. Kalemba-Drożdż, the amount of plant material which potentially causes toxicity is important to consider. Occasional use of flowers of *Viola tricolor* or *Tropaeolum major* flowers as decorations of cakes seemingly does not cause toxic effects, but as illustrated by the referral to a Danish cookbook, the creativity among chefs and cookbook writers is high and include e.g., recipes where wild flowers are the major part of salad and not just decorations. Further, some constituents e.g., pyrrolizidine alkaloids are potential harmful even in small amounts especially if consumed on a regular basis, as also discussed. As stated in the section on methods, our estimations of safe human intake are rough estimates (e.g., not taking toxicological assessment factors into account). Additionally, we find it important to flag potential health concerns in subgroups of consumers when relevant, e.g., salicylic acid sensitive subgroups.

For the discrepancy between the lists published by the German Federal Office of Consumers Protection and Food Safety (BVL) and the Danish Veterinary and Food Administration regarding *Viola tricolor*, we suggest that Dr. Kalemba-Drożdż contacts the risk managers in the Danish Veterinary and Food Administration directly.

The historic use of *Tropaeolum* flowers since 1600s is described in our paper, whereas the use of the seeds and leaves are out of the scope of this paper. The significant reduction of foetal and placental weights in rats following administration of benzyl isothiocyanate (Adebiyi et al., 2004) is considered an adverse effect of potential obstetric importance, not necessarily linked to pre- and post-implantation fetal loss and thus not a controversy. In the study by Adebiyi et al., a no adverse effect level (NOAEL) for reduced placental weights in rats after treatment with benzyl isothiocyanate could not be established thus a safe edible amount was not possible to calculate.

Regarding *Calendula officinalis*, an experiment by Sabir et al., showed a significant increase in damage frequency in the Comet assay at the highest dose, (Sabir et al., 2015) as seen in the results of the paper, however if you only read the abstract, you may end with the same conclusion as Dr. Kalemba-Drożdż. The overall finding by Ramos et al. (1998) was negative using the Ames test on extracts of *Calendula officinalis*. Therefore, we come to the overall conclusion that "experimental data suggest no genotoxic or developmental effects".

In our section concerning *Chrysanthemum coronarium* L. we clearly state, that "the content of camphor in the flowers does not give rise to health concerns since an adult may eat more than 3 kg fresh flowers (…) before the maximum limit for acute toxicity of camphor is exceeded." However, due to limited phytochemical data and insufficient toxicological data no safe amount of flowers for consumption could be established. Thus, other potential toxic compounds could be present.

We invite Dr. Kalemba-Drożdż to read our paper once more in detail.

In addition, we are puzzled by the remark "I assume that authors of the article know flowers only as research objects and have never tried them". We want to stress that it is *not* a qualification in toxicology to have tried the test material yourself.

We thank the editor for offering us the opportunity to reply to the comment to our article.

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