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**Dates:** Received: 17 March, 2017; Accepted: 25  
March, 2017; Published: 27 March, 2017

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## Case Report

# Periocular Erythema and Eczema after Local Application of Calendula Officinalis in Pediatric Age

## Abstract

*Calendula officinalis* is a plant belonging to the Asteraceae family. Herbal preparations from Calendula have been used topically as a natural anti-inflammatory medicine and for the healing of wounds and leg ulcers. Although data on dermal irritation and sensitization are available, the risk of subchronic systemic toxicity following dermal application of *Calendula officinalis* preparations has not been evaluated. The threshold of toxicological concern is only based on a pragmatic risk assessment approach that gained regulatory acceptance for food. Here we describe a case of a 12 year old girl forced to the hospital for an acute periocular erythema and eczema after use for two days of Calendula Officinalis compresses on the eyes.

The use of Calendula extracts is very common in traditional medicine, as these products are highly available because sold in many countries as food supplements or medical devices. Even though it is not considered toxic, adequate safety data of use in children are not existing. On the light of the case here reported, we think that pediatric use of these extracts should be very careful, especially in subjects allergic to Asteraceae.

All Authors make substantial contributions to acquisition and interpretation of data, research of literature data and about writing of the manuscript.

Each author have singularly participated sufficiently in the work as follows:

Patella V. and Gangemi S. participated in writing and design of the study and provided a contribution from the allergologic point of view, Calapai G., Cafeo V. and Calapai F. participated in writing and design of the study and purchased their contribution from the pharmacological point of view. All authors read and approved the final manuscript.

## Introduction

*Calendula officinalis* is a plant of the Asteraceae family. Extract from this plant have been used for traditional medicinal uses and suggested for many therapeutic uses such as: anti-inflammatory, anti-tumor-promoting, and cytotoxic activities [1]. Chemical constituents of Calendula include sugars, carotenoids, phenolic acids, sterols, saponins, flavonoids, resins, sterins, quinones, mucilages, vitamins, polyprenylquinones, and essential oils [2]. Assessment of therapeutic indications performed by the European Medicines Agency (EMA) recognized the traditional medicinal use of *Calendula officinalis* products for the following two indications: symptomatic treatment of minor inflammations of the skin (such as sunburn) and as an aid in healing of minor wounds; symptomatic treatment of minor inflammations in the mouth or the throat [3]. Preclinical experiments conducted on

rodents indicate that the extract possesses an acceptable toxic profile. The dried flowers have been also used as a spice and is considered to be generally recognized to be safe [4], however minimal ocular irritation was seen with one formulation in the laboratory animal [5]. *Calendula Officinalis* extract is reported to be used in almost 200 cosmetic formulations, over a wide range of product categories [6]. Although data on dermal irritation and sensitization of CF and CFE's are available, the risk of subchronic systemic toxicity following dermal application has not been evaluated. The threshold of toxicological concern (TTC) is a pragmatic, risk assessment based approach that has gained regulatory acceptance for food and has been recently adapted to address cosmetic ingredient safety [7].

## Case Description

We describe a case of a 12 year old girl forced to the hospital

for an acute bilateral periocular erythema and eczema after use for two days of *Calendula Officinalis* compresses on the eyes for the treatment of an episode of conjunctivitis. The compresses were made with a cotton wool soaked in one tablespoon of a macerated oil (a preparation with *Calendula* Flowers wherein the solvent is oil-based) and three tablespoons of water. A familiar history of allergies or previous allergic diseases were denied. Then the patient underwent allergological investigation. Routine blood chemical tests were normal but total seric IgE were elevated. Skin Prick test to Asteraceae was positive (+++). Patch test 20% aqueous dilution of the product was applied on the surface of her left upper arm and reading was made after 48h and 72 hours with positive result (+ and +++ respectively). Treatment with the product has been withdrawn and it is not reused. Intensity of itching and severity of dermatitis were reduced in two-three days after topical therapy with steroids and systemic oral therapy with antihistaminic drugs, symptoms were completely resolved after two weeks. Assessment of causality relationship, according to the Naranjo algorithm (score 6) showed it as probable [8].

## Discussion

Even though allergenic sesquiterpene lactones are amongst the chemicals contained in *Calendula officinalis*, until now *Calendula* extracts have been considered weakly sensitizing due to the scarcity of case reports until recently. This contradictory issue has been justified with the remark that sesquiterpene lactones are lacking in the flowers, the part of plant commonly used to obtain medicinal herbal preparations from *calendula* [9]. Scientific literature comprises only one case reporting of an anaphylactic shock caused by gargling with *Calendula* tincture [10], a different herbal preparation of the plant with respect to that used in the case here reported. *While, it is possible, an IgE-mediated reaction for acute hypersensitivity and a cellular-mediate reaction for the delayed hypersensitivity. Likely, as it happens with a common allergen, House Dust Mite (Dermatophagoides), that are implicated at same time in various diseases like atopic dermatitis, asthma, rhinitis and perennial, with prick- and patch- test positives. It has also been proven that patch testing with Dermatophagoides pteronyssinus (DP) is important for detection of contact sensitization in chronic dermatitis.*

## Conclusion

This is the first reporting of an adverse reaction linked to the use of *Calendula officinalis* in pediatric age. The use of *Calendula* extracts is very common in traditional medicine, as these products are highly available because sold in many

countries as food supplements or medical devices. Moreover, different herbal preparations derived from *Calendula* are cosmetic ingredients currently used also in pediatric age, including the adolescents. Because it is not considered toxic even if adequate safety data of use in children and adolescents are lacking, we think that pediatric subjects and in particular in who is allergic to Asteraceae should be very careful to use *Calendula* derived products.

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