Skin sensitisers in cosmetic products: what is the clinical problem?

Carola Lidén
Professor, MD
Institute of Environmental Medicine
Karolinska Institutet

- **Research**
  - Contact allergy and contact dermatitis
  - Hazardous skin exposure and skin exposure assessment
  - Workers and consumers

- **Risk assessment etc.**
  - Skin sensitisation (EC, OECD)
  - Classification and restrictions (CLP, REACH)
  - CEN
  - SCCP, SCCS (2004-2012)
Contact allergy

- Contact allergy
  \(\rightarrow\) activation of allergen-specific T-cells

- Most frequent sensitisers
  \(\rightarrow\) metals (Ni, Cr, Co), fragrances, preservatives, hair dyes, rubber chemicals, epoxy resin etc.

- 15-20% of adults are allergic to at least one substance

Diagnostic procedure

- Diagnostic patch test
  \(\rightarrow\) baseline series (30 test preparations, 50 substances)
  \(\rightarrow\) special series
  \(\rightarrow\) serial dilutions
  \(\rightarrow\) products, ingredients, extracts

- Repeated open application test (ROAT)
Sensitisation vs. elicitation

1. Sensitisation may be induced by
   - single exposures to potent allergens
   - repeated exposure, sometimes for decades
   - lifelong allergy

2. Elicitation of allergic contact dermatitis
   - requires significantly less exposure than induction

Preservatives

- Isothiazolinones
  - Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI)
  - Methylisothiazolinone (MI)
  - Benzisothiazolinone (BIT)
- Methyl dibromo glutaronitrile (MDBGN)
- Formaldehyde releasers
  - Diazolidinyl urea
  - DMDM hydantoin
  - Imidazolidinyl urea
  - Quaternium-15
- Iodopropynyl butylcarbamate (IPBC)
- Parabens
Contact allergy to preservatives

Ban: leave-on
Ban: Rinse-off

Methylisothiazolinone (MI)

- In chemical products since 2000
  - Use concentrations unknown, not classified
- Allowed in cosmetic products 2005
  - 100 ppm
- Rapid allergy increase noted since 2010
- Current alarming epidemic
- SCCS opinion 2013
  - Leave-on: no safe concentration demonstrated
  - Rinse-off: 15 ppm considered safe for induction; no information for elicitation
Alarming increase in allergy to MI

- Recent publications (examples):
  - Johnston GA et al. *The rise in prevalence of contact allergy to methylisothiazolinone in the British Isles*. Contact Dermatitis 2014
  - Lundov MD et al. *Methylisothiazolinone contact allergy - growing epidemic*. Contact Dermatitis 2013
  - Geier J et al. *Recent increase in allergic reactions to methylchloroisothiazolinone/methylisothiazolinone: is methylisothiazolinone the culprit?* Contact Dermatitis 2012
  - Hosteing S et al. *Outbreak of contact sensitization to methylisothiazolinone: an analysis of French data from the REVIDAL-GERDA network*. Contact Dermatitis 2014

- SCCS opinion on MI, December 2013:

Ingredients in 4991 cosmetic products in Germany 2006-2009
Fragrances

Second most common group of contact allergens
- 16% of patch tested patients
  → Fragrance mix I and II
- 1-3% of the adult general population

Substances of special concern (SCCS opinion 2012)

- Cinnamal
- Cinnamyl alcohol*
- Citral
- Coumarin
- Eugenol*
- Farnesol*
- Geraniol*
- Hydroxycitronellal
- Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC)
- Isoeugenol*
- Limonene (oxidised)
- Linalool* (oxidised)

*including their respective esters
SCCS opinion on fragrance allergens (2012)

- EC proposal for amendment of Cosmetics Regulation, 2014
  - additional substances for labelling in the list of ingredients
  - HICC, atranol and chloroatranol prohibited in cosmetic products
- RAC: classification of HICC as H317 (skin sens sub-cat 1A)

Uter et al., 2013; Karlberg et al., 2013

Coupled exposure to fragrances in cosmetic products
Linalool and limonene most frequent, often in combination

Uter et al., Contact Dermatitis 2013
Hair dye substances

- Hair dyeing is increasingly popular. Hairdressers and consumers develop allergy and dermatitis
- Dermatologists have focused on p-phenylenediamine
- Risk assessment has focused on possible cancer risks
- SCCP/SCCS compiled animal data on the sensitising potency of 114 hair dye substances:
  - 50% are skin sensitisers, 31% are potent (strong or extreme)
Underestimation of hair dye allergy

- Only one substance (p-phenylenediamine) in routine diagnostic patch testing
- The most frequently used dyes are not tested
- Exposure to several substances
- Some cross reactivity
- Additive or synergistic effect?
Cosmetics Regulation:
“Cosmetic products should be safe under normal or reasonably foreseeable conditions of use”

- Cosmetic products contain many skin sensitisers
- Use concentrations are often not safe
- Consumers and occupationally exposed suffer from contact allergy to cosmetics
Thank you

Carola Lidén

Unit of Occupational and Environmental Dermatology
Institute of Environmental Medicine
Karolinska Institutet