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Irritant patch test reactions to cosmetic ingredients

Reakcje z podrażnienia na składniki kosmetyków w testach płatkowych

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ABSTRACT

Introduction: The use of cosmetics and skin care products is on a steady increase, especially in developed countries. Despite increasingly strict regulations, ingredients with irritant potential are still widely used in cosmetic products. On patch tests, irritant reactions may be mistaken for allergic reactions, leading to misdiagnoses.

Aim: To compile and analyze available data on irritant reactions to cosmetic ingredients from patch test studies in humans.

Material and methods: Data on irritant reactions to cosmetic ingredients in patch tests were extracted from published patch test studies indexed in PubMed, Embase, Web of Science or Google Scholar. The available data were pooled to assess the frequency and create a ranking list of irritant cosmetic ingredients.

Results: Data on the prevalence of irritant reactions among people undergoing patch testing (routine or experimental) were available for 47 cosmetic ingredients. Among ingredients routinely tested in the European Baseline Series, the highest rates of irritant reactions were reported for Myroxylon pereirae resin (balsam of Peru, irritant reactions in 3.40% of patch test patients), followed by Fragrance mix II (2.83%), Fragrance mix I (2.34%), colophonium (1.14%), p-phenylenediamine 1% (0.99%), hydroxyisohexyl 3-cyclohexene carboxaldehyde (0.70%), Paraben mix (0.48%) and Quaternium 15 (0.29%).

Conclusions: A range of widely used cosmetic ingredients possess irritative properties, which may contribute to irritant contact dermatitis in the consumers. In routine patch testing, irritant reactions to cosmetic ingredients may emerge in as many as one in ten patients. As irritant reactions to cosmetic ingredients in patch tests may contribute to false diagnosis of allergic contact dermatitis, doctors should be aware of the risk and able to single out such reactions.

KEY WORDS

cosmetic ingredients, irritative potential, patch tests, irritant reactions.

ABSTRACT

Wprowadzenie: Konsumpcja kosmetyków i środków do pielęgnacji skóry nieprzerwanie wzrasta, szczególnie w krajach rozwiniętych. Mimo coraz bardziej restrykcyjnych regulacji, nadal w produktach kosmetycznych szeroko stosowane są składniki o działaniu drażniącym. W testach płatkowych reakcje z podrażnienia mogą być błędnie interpretowane jako alergiczne, co może skutkować błędną diagnozą.

Cel pracy: Kompilacja opublikowanych danych na temat reakcji z podrażnienia na składniki kosmetyków badane w testach płatkowych.

Materiał i metody: Wyniki badań z zastosowaniem testów płatkowych indeksowanych w bazach bibliograficznych PubMed, Embase, Web of Science lub Google Scholar przeszukano pod kątem informacji na temat częstości występowania reakcji z podrażnienia na składniki kosmetyczne. Pozyskane dane zsumowano i na podstawie sumarycznych wskaźników stworzono ranking składników kosmetycznych pod względem potencjału drażniącego.

Wyniki: Dane na temat reakcji z podrażnienia w testach płatkowych (rutynowych lub eksperymentalnych) u ludzi były dostępne w przypadku 47 składników kosmetyków. Wśród składników testowanych rutynowo w ramach Europejskiej Serii Podstawowej najwyższe odsetki reakcji z podrażnienia obserwowano w przypadku żywicy Myroxylon pereirae (balsam peruwiański, reakcje z podrażnienia u 3,40% testowanych), dalsze miejsca zajmowały Mieszanka zapachowa II (2,83%), Mieszanka zapachowa I (2,34%), kalafonia (1,14%), parafenylenodiamina (0,99%), karboksyaldehyd hydroksyizoheksylo-3-cykloheksenu (0,70%), Mieszanka parabenów (0,48%) oraz Quaternium 15 (0,29%).

Wnioski: Powszechnie stosowane składniki kosmetyków wykazują potencjał drażniący i mogą przyczynić się do rozwoju wyprysku kontaktowego z podrażnienia. W rutynowych testach płatkowych reakcje z podrażnienia na składniki kosmetyków mogą pojawiać się u co dziesiątego pacjenta. Błędnie zinterpretowane reakcje z podrażnienia na składniki kosmetyków w testach płatkowych mogą skutkować mylnym rozpoznaniem alergicznego wyprysku kontaktowego, dlatego lekarze muszą być świadomi tego ryzyka i umieć zidentyfikować takie reakcje.

SŁOWA KLUCZOWE

składniki kosmetyków, potencjał drażniący, testy płatkowe, reakcje z podrażnienia.

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INTRODUCTION

The use of cosmetics and skin care products is on a steady increase, especially in developed countries [1]. Despite increasingly strict regulations, ingredients with irritant potential are still widely used in cosmetic products. 13–60% of women and 5–40% of men have experienced adverse reactions to cosmetics, with irritant reactions thought to be more common than allergic ones [2, 3]. Willis *et al.* [4] reported that 51.4% of women and 38.2% of men believe that they have sensitive skin; side effects after using cosmetics or skin care products had been experienced by 57.0% and 31.4% of them, respectively [4]. In India, 42.9% of adverse reactions to cosmetics were diagnosed as irritant contact dermatitis [5]. In a questionnaire survey, 39.1% of students of a Polish medical university reported experiencing irritant reactions after using cosmetics [6]. Most common causes of cosmetic irritant

reactions are face creams, eye lid creams, face masks, deodorants, shampoos, mascaras, perfumes, body gels and hair dyes [6, 7].

In the course of irritant contact dermatitis (ICD), chemicals or physical factors cause non-specific damage of epidermis resulting in keratinocytes secreting proinflammatory cytokines. Detergents, solvents, acids, alkalis, emulsifiers, preservatives and other cosmetic ingredients can provoke ICD [8, 9]. ICD is a non-specific reaction, meaning that virtually every person will develop an inflammatory reaction to noxious agents after its dose exceeds the individual tolerance threshold. The acute form of ICD develops quickly – within a few minutes to several hours after exposure to strong irritant (corrosive) substances. Chronic ICD develops gradually over weeks, months or even years in a cumulative response to repeated or prolonged exposure to weak irritants [8, 9].

AIM

The aim of this study was to compile and analyze available data on irritant reactions to cosmetic ingredients from patch test studies in humans.

MATERIAL AND METHODS

The first stage of the work was to establish a list of cosmetic ingredients with known irritant potential. For this purpose, the query combining keywords “cosmetic” AND (“dermatitis” OR “eczema” OR “irritant” OR “toxic” OR “toxicity” OR “irritancy”) was carried out in bibliographic databases PubMed, Embase, Web of Science and Google Scholar. Articles indicated by bibliographic databases as related to the publications found and references in bibliographies of identified articles were also included into the analysis. Cosmetic ingredients mentioned in the papers were analyzed for their known irritant potential as reported in the literature. With regard to patch tests, a query “x AND (“patch tests” OR “ROAT”) was carried out, where “x” stands for names of cosmetic ingredients identified in the previous step. Articles presenting results of patch tests in which authors provided information on the occurrence of irritant reactions were used for the extraction of data necessary for the calculation of weighted average frequency rates of irritant reactions to particular cosmetic ingredients. Special attention was paid to cosmetic ingredients present in the European Baseline Series and Polish Baseline Series, as well as other ones used in routine testing of patients with dermatitis [10, 11].

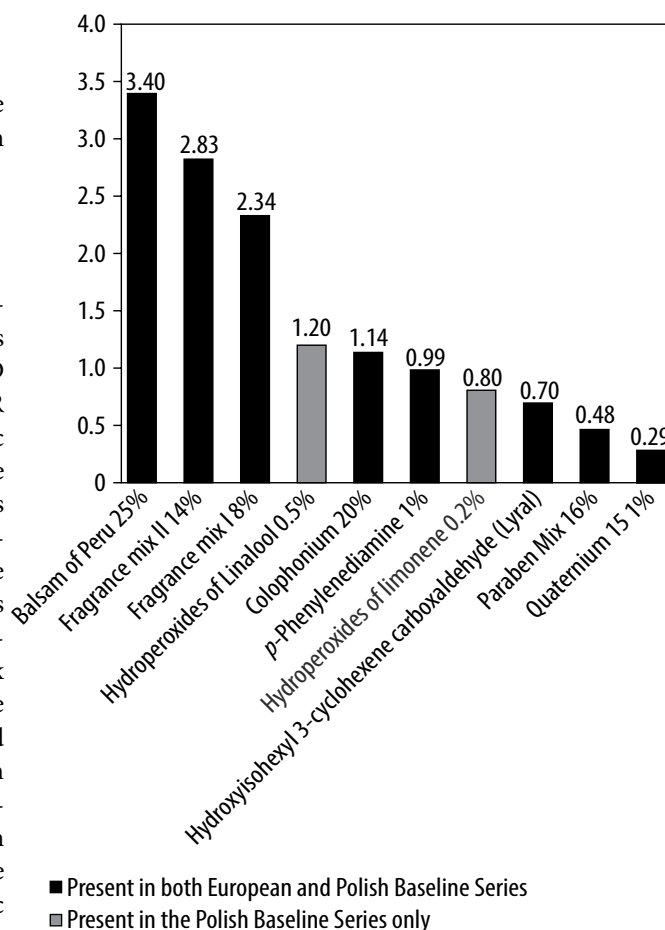


FIGURE 1. Weighted average rates of irritant reactions for substances included in the European Baseline Series and the Polish Baseline Series (vehicle: petrolatum)

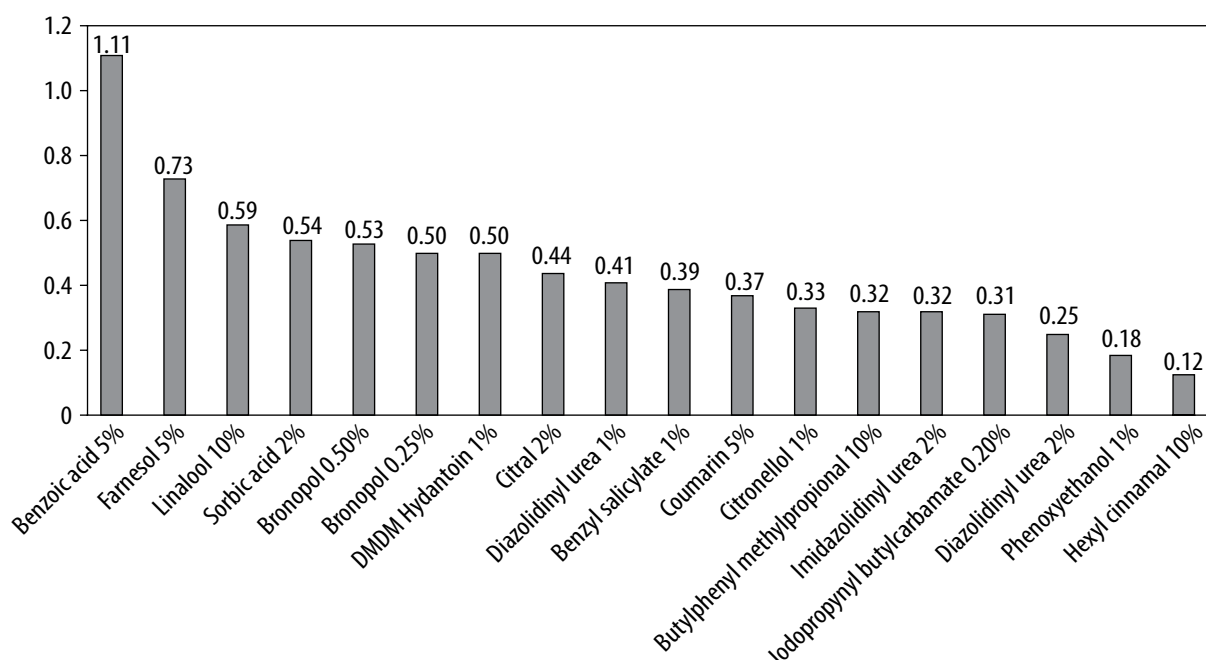


FIGURE 2. Weighted rates of irritant patch test reactions for other cosmetic ingredients used in routine patch testing (vehicle: petrolatum)

RESULTS

Altogether 16 studies were qualified for inclusion in the present analysis. Data on the prevalence of irritant reactions among people undergoing patch testing (routine or experimental) were available for 47 cosmetic ingredients with rates of irritant reactions ranging from 0.01% to 10.58% (Supplementary Material 1). Among ingredients routinely tested in both the European Baseline Series and the Polish Baseline Series, the highest rates of irritant reactions were reported for Myroxylon pereirae resin (balsam of Peru), followed by Fragrance mix II and Fragrance mix I (Figure 1). Grey bars in the figure present rates for hydroperoxides of linalool and limonene, which are included into the Polish Baseline Series, but not into the European

Baseline Series. Results for cosmetic ingredients that are not included into baseline series but are present in other series for routine patch testing are shown in Figure 2.

Experimental studies in humans of the relation between the patch test concentration of cosmetic ingredients and the rate of irritant reactions have shown an increase in irritancy with higher concentrations for 12 out of 14 ingredients studied: anise alcohol, benzyl salicylate, DMDM hydantoin, eugenol, Evernia prunastri extract, Fragrance mix II, geraniol, hydroperoxides of limonene, hydroperoxides of linalool, hydroxycitronellal, isoeugenol (increase followed by a plateau) and bronopol (increase followed by a decrease), while a steady decrease was observed only for butylphenyl methylpropional and diazolidinyl urea (Figure 3).

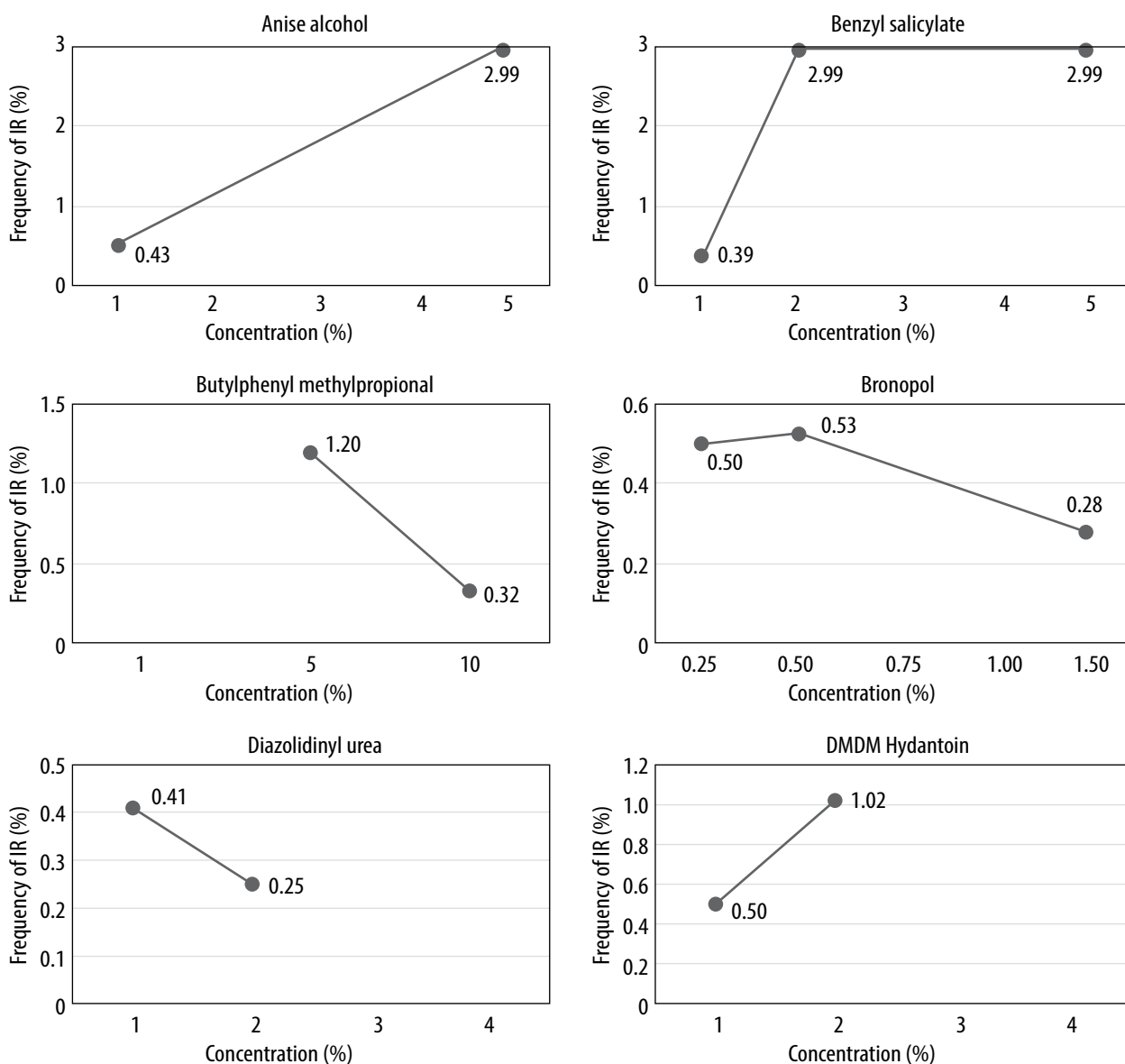


FIGURE 3. Correlation between the concentration of cosmetic ingredients and the rate of irritant reactions (raw data in Supplementary Material 2)

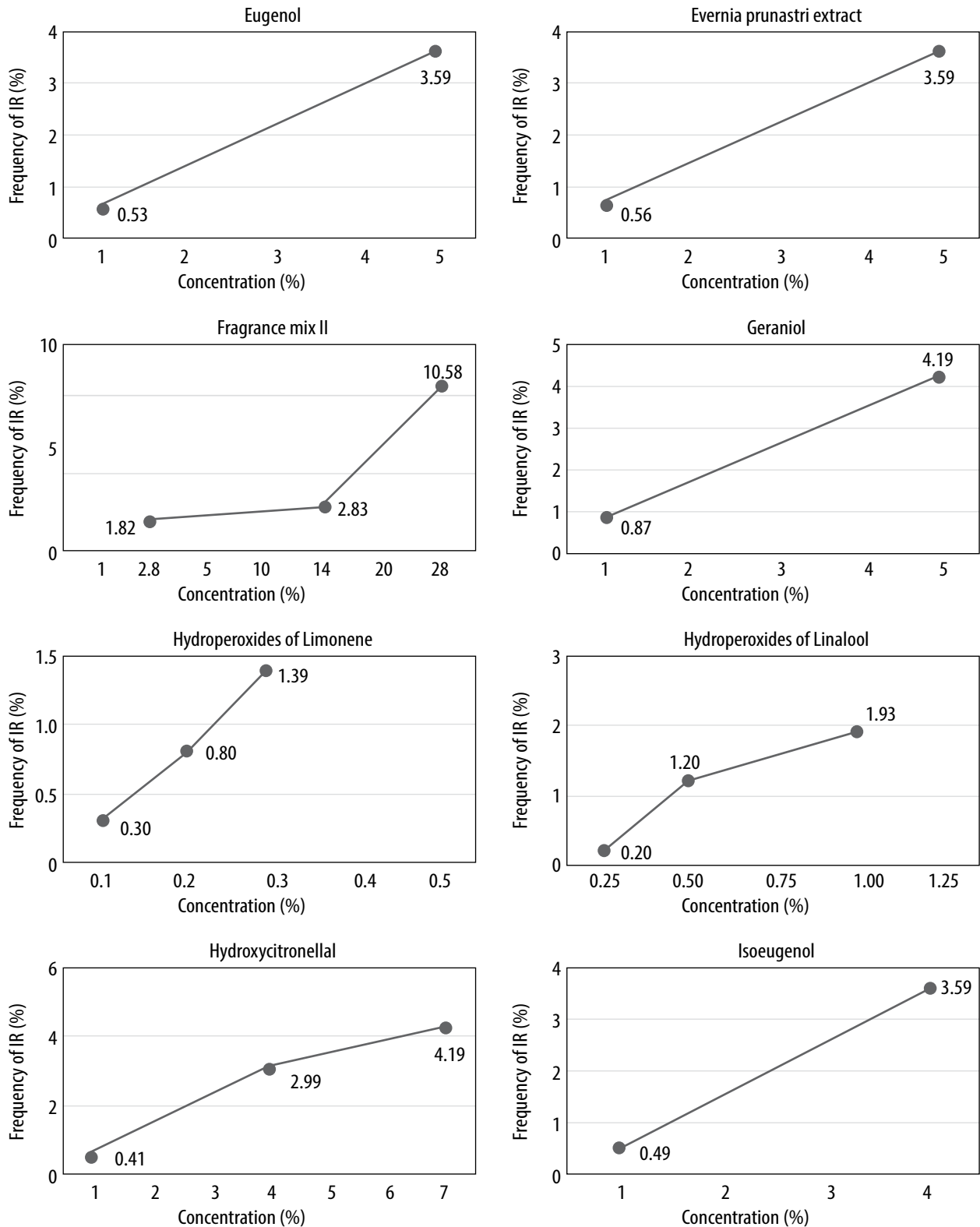


FIGURE 3. Cont.

TABLE 1. Pooled frequency of irritant reactions (IR) to cosmetic ingredients in human patch test studies (vehicle: petrolatum). Weighted average was calculated for pooled data. Patch test preparations were made in petrolatum

No.	Name of the ingredient	Concentration (%)	Frequency of IR* (%)	Number of studies
1	Balsam of Peru	25	3.40	4
2	Fragrance mix II	14	2.83	3
3	Fragrance mix I	8	2.34	5
4	Hydroperoxides of linalool	0.50	1.20	1
5	Colophonium	20	1.14	3
6	Benzoic acid	5	1.11	2
7	<i>p</i> -Phenylenediamine	1	0.99	1
8	Hydroperoxides of limonene	0.20	0.80	1
9	Farnesol	5	0.73	3
10	Hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyrall)	5	0.70	1
11	Linalool	10	0.59	2
12	Sorbic acid	2	0.54	3
13	Bronopol	0.50	0.53	3
14	Bronopol	0.25	0.50	2
15	DMDM Hydantoin	1	0.50	2
16	Paraben mix	16	0.48	2
17	Citral	2	0.44	3
18	Diazolidinyl urea	1	0.41	2
19	Benzyl salicylate	1	0.39	3
20	Coumarin	5	0.37	4
21	Citronellol	1	0.33	3
22	Butylphenyl methylpropional	10	0.32	3
23	Imidazolidinyl urea	2	0.32	5
24	Iodopropynyl butylcarbamate	0.20	0.31	2
25	Quaternium 15	1	0.29	5
26	Diazolidinyl urea	2	0.25	3
27	Phenoxyethanol	1	0.18	1
28	Hexyl cinnamal	10	0.12	2

*Weighted averages were calculated whenever data were available from multiple studies. IR – irritant reactions.

TABLE 2. Patterns of irritant reactions on patch testing [12]

Type of irritant reactions	Characteristics
Homogenous	Homogenous erythema confined to the test area, sharply defined borders, no infiltration or edema, no papules, no vesicles
Punctate	Punctate erythema, sometimes slightly papular or hemorrhagic, presenting as small dots distributed within the test area
Pustular	One or more pustules in the exposed area, typically within sharply defined erythema with no infiltration or edema

DISCUSSION

Many cosmetic ingredients possess irritative properties, which may contribute to irritant contact dermatitis in the consumers, especially in case of extensive use. As mentioned above, about one in two people have experienced irritant reactions to cosmetics at least once in a lifetime. The risk of irritant reactions depends on chemical properties and concentration of the agent. The irritant potential of cosmetic ingredients has been convincingly demonstrated in dose-response studies, where an increase in concentration resulted in higher rates of irritant reactions (Figure 3). The somewhat surprising decrease seen for the fragrance butylphenyl methylpropional and preservative diazolidinyl urea (Figure 3) might be explained by toxic effects on cells involved in inflammation as the chemicals were tested at concentrations exceeding those used in real cosmetics.

As irritant potential of haptens interferes with specificity of the patch test, a careful choice of concentrations used in patch testing is of utmost importance (Table 1). It seems logical that the probability of an irritant reaction increases with more ingredients tested in a patient. Even when taking into account only irritant reactions to “flagship cosmetic components” present in Baseline Series (Figure 1) and allowing for some overlapping, we assess that irritant reactions may emerge in as many as one in ten patch tested patients. Therefore, doctors performing patch tests should be aware of this risk in order to avoid situations when irritant reactions are confused with allergy, thus leading to a false diagnosis. This knowledge, along with proper training are necessary for reducing such risk. There are some visual clues hinting on the irritant nature of a reaction (Table 2). Rapid healing seen on subsequent readings (“decrecendo pattern”) is also typical, while true allergic patch test reactions tend to persist or even intensify (“crescendo pattern”) in days following the removal of patch test units. Children below 8 y.o. also are more prone to irritant reactions [12]. Needless to say, a pivotal factor in avoiding misinterpretations and misdiagnoses is a strict adherence to the rules of good clinical practice of patch testing [13].

CONCLUSIONS

A range of widely used cosmetic ingredients possess irritative properties, which may contribute to irritant contact dermatitis in the consumers. In routine patch testing, irritant reactions to cosmetic ingredients may emerge in as many as one in ten patients. As irritant reactions to cosmetic ingredients in patch tests may contribute to false diagnosis of allergic contact dermatitis, doctors should be aware of the risk and able to single out such false positive reactions.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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