

Moisturizers: A Comparison Based on Allergens and Economic Value

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Background: The economic burden of cosmetics, such as moisturizers, has been increasing. Despite the high price of some market moisturizers, there have been no studies evaluating the allergenicity of these products.

Objective: The aim of this study was to evaluate the potential allergens within moisturizers based on economic value, by analyzing the substances found in moisturizers available online at the largest drugstore chain—CVS Health (CVS Health, Woonsocket, RI).

Methods: In this cross-sectional study, ingredients found in 50 expensive and 50 inexpensive moisturizers were matched with sensitizers within the Core Allergen Series published by the American Contact Dermatitis Society and the North American Contact Dermatitis Group. Student *t* test was used to compare the mean number of allergens present in each group. A χ^2 test or Fisher exact test, where necessary, was used to compare the rates of specific allergen groups between the expensive and inexpensive products.

Results: Twenty-six allergenic substances were present overall in the 100 total products surveyed. The expensive moisturizers averaged significantly more allergens per product (8.28 vs 5.60, $P = 0.003$) than the inexpensive products.

Conclusions: The sensitizing potential of expensive moisturizers may be higher than that of inexpensive moisturizers. Physicians may counsel cosmetic-induced allergic contact dermatitis (ACD) patients that monetary value is not a suitable proxy for evaluating the risk of ACD.

The relationship between cosmetic exposure and onset of allergic contact dermatitis (ACD) has been well documented for more than 50 years, with 3.7% of the population estimated to be sensitized to a cosmetic ingredient and 10% of the population experiencing general adverse effects from cosmetics.^{1–4}

In 2006, the market value of the cosmetics industry was estimated to be approximately \$48 billion in the United States, with a per capita spending of \$161 in the European Union.⁵ With 21% of the market value in the United States specific to skin care, the economic value of skin care products, such as moisturizers, as well as its significance in individual spending, is undeniable.⁵ Although there are studies examining the frequency of allergenic ingredients in consumer products,^{6–8} none has examined the allergenicity of products in terms of economic value. Therefore, we evaluated the potentially allergenic components of moisturizers that are ubiquitous to the public based on price, by presenting a comprehensive analysis of the ingredients present in moisturizers available online at the largest retail drugstore corporation in the United States—CVS Health

(CVS Health, Woonsocket, RI). These data may provide clinicians with the information to determine possible allergen exposure in patients due to their moisturizers, suggest affordable yet less allergenic alternatives, and educate patients on the use of costly moisturizers that may be as allergenic, if not more, than inexpensive options.

METHODS

We examined 100 total moisturizers present and available online from CVS Health as of June 2017 because of their status as the largest retail pharmacy in the United States by number of stores.⁹ A detailed list of moisturizers was found on the CVS online catalog (Home > Shop > Beauty > Skin Care > Face). We selected “Creams and Serums,” “Moisturizing,” “Moisturizer,” “Cream,” “Face Cream,” and “Night Cream” in the Product Type criteria, resulting in 607 products. Using the Sort By: Price High-Low and Price Low-High options, the 50 most expensive (from here on referred to as “expensive”) and least expensive (from here on referred to as “inexpensive”) moisturizers and their ingredients were queried. Exclusion criteria included any product categorized as eye creams, neck creams, serums, or emulsions; products containing SPF; tinted products; and medicated products.

Potential allergens present in the American Contact Dermatitis Society (ACDS) Core Allergen Series of 80 allergens¹⁰ and the North American Contact Dermatitis Group screening allergen series of 70 allergens¹¹ that were likewise found in moisturizers were noted and tallied using Microsoft Excel. Nascent potential allergens not

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included in either series were also obtained based on the expert opinion of author T.L.S., as well as previously published studies.⁶ Institutional review board approval was not obtained because human subjects were not involved in this study.

Statistical analyses were performed using R 3.4.3 (www.R-project.org) and packages available through CRAN (cran.r-project.org). After determining normality, Student *t* test was used to compare the mean number of allergens present between the inexpensive and expensive groups. Allergens were then grouped as has been described previously (acrylates, botanicals, emulsifiers, fragrances, preservatives, tocopherols, and other) and then sorted by whether the allergen was present to generate categorical data.^{6–8} A χ^2 test or Fisher exact test, where necessary, was used to compare the frequencies of each allergen group between the inexpensive and expensive products. $P < 0.05$ was considered statistically significant.

RESULTS

The price per ounce of the inexpensive moisturizers ranged from \$0.99 to \$8.50, whereas the price per ounce of the expensive moisturizers ranged from \$39.99 to \$579.99. Across the 26 distinct allergenic substances, expensive moisturizers contained a total of 414 individual allergens, whereas the inexpensive group contained a total of 280 individual allergens in the 50 products (Table 1). The expensive group averaged significantly more allergens per product (8.28 vs 5.60, $P = 0.003$) than the inexpensive products (Table 1). A full record of the allergens by name can be found in Table 1, along with the raw number of each allergen found in the expensive and inexpensive groups. The proportions of the same allergens found in each product group are recorded in Table 2. The 26 allergenic substances were then subcategorized into 7 groups—acrylates, botanicals, emulsifiers, fragrances, preservatives, tocopherols, and other—for analysis (Table 3).

The most to least common potential allergens in the expensive moisturizers were fragrances (88%), preservatives (80%), tocopherols (58%), botanicals (40%), emulsifiers (38%), acrylates (14%), and other (8%) (Table 3). Most to least common for the inexpensive moisturizers were preservatives (88%), fragrances (62%), tocopherols (60%), botanicals (56%), emulsifiers (36%), acrylates (6%), and other (2%) (Table 3).

The expensive products had significantly higher rates (88% vs 62%, $P = 0.006$) of fragrances than the inexpensive products (Table 3). There were no significant differences in rates of products with acrylates (14% vs 6%, $P = 0.23$), botanicals (40% vs 56%, $P = 0.16$), emulsifiers (38% vs 36%, $P = 1$), preservatives (80% vs 88%, $P = 0.41$), and tocopherols (58% vs 60%, $P = 1$) between the expensive and inexpensive products (Table 3).

DISCUSSION

ACD to Moisturizer Ingredients

With 8% to 15% of contact dermatitis cases connected to cosmetic use and the expansion of the cosmetics industry, the impact of

cosmetic-induced contact dermatitis on consumer quality of life is substantial in a multifactorial way.^{4,12} Furthermore, consumers desire products that yield the most benefit in comparison to its economic value.¹³ The present data, however, suggest that expensive moisturizers contain more allergens on average than the inexpensive moisturizers (8.28 vs 5.60, $P = 0.003$) (Table 1), with the difference being driven mainly by the rates of fragrances present within the products (88% vs 62%, $P = 0.006$) (Table 3).

Fragrances

The fragrances present in the study include amylcinnamaldehyde, hydroxycitronellal, geraniol, eugenol, citral, farnesol, citronellol, hexyl cinnamic aldehyde, coumarin, limonene, linalool, linal, benzyl salicylate, and sesquiterpene lactones/ α -bisabolol. Many products also contained unspecified “fragrances” that were counted within the study, as US regulations allow for unnamed labeling in order to protect company “trade secrets,” despite unspecified fragrances being the major cause of most ACD fragrance reactions.^{14,15} Whereas fragrance allergens have low individual positive patch test (PPT) rates, fragrances account for 16% of all patients patch tested for suspected ACD.^{11,16} This incongruous outcome has been attributed to enhanced sensitization and response elicitation caused by mixing allergenic substances generating an increased memory T-cell response during the primary response.¹⁷ Because various synthetic and natural fragrances are frequently combined to create more complex aromas,¹⁴ fragrances have a unique coexposure factor that may enhance their collective sensitization beyond their individual allergenic capabilities. Therefore, in an effort to create a multifaceted scent, the expensive moisturizers not only had a significantly higher rate of fragrances than the inexpensive products (88% vs 62%, $P = 0.006$) but also may have fragrance blends that result in synergistic sensitizations.^{17,18}

Preservatives

Preservatives are often used in skin care products in order to prevent microbial growth and have been identified as the most common cosmetic contact allergen.^{19,20} The preservatives present within the hundred products surveyed in our study include benzalkonium chloride (BAK), benzyl alcohol and benzoic acid, diazolidinyl urea, disodium sulfite/sodium metabisulfite, dimethyloldimethyl (DMDM) hydantoin, ethylhexylglycerin, imidazolidinyl urea, iodopropynyl butylcarbamate, methylisothiazolinone (MI), parabens, phenoxyethanol, sodium benzoate, and sorbic acid (and its associated substances, such as polysorbate 20 and potassium sorbate). It should be noted that benzyl alcohol may also be used for fragrance purposes, although it has been designated as a preservative in this study.²¹

The ACDS identified 2 preservatives, formaldehyde and MI, as Contact Allergens of the Year in 2015 and 2013, respectively. After this announcement, these 2 preservatives have been largely avoided in skin care products. However, this has led to the increasing use of both new and old preservatives that may cause ACD, some of which include preservatives found within this study.⁶ Formaldehyde has been largely replaced by formaldehyde-releasing preservatives, such

TABLE 1. Total Amount of Potential Allergens in Expensive and Inexpensive Moisturizers

	Expensive Moisturizers (n = 50)	Inexpensive Moisturizers (n = 50)
α -Bisabolol	2	3
α -Tocopherol	43	32
Acrylates	7	3
BAK	Not observed	1
Benzoic acid	16	7
Benzyl alcohol	6	10
Benzyl salicylate	5	2
BHT	3	Not observed
Botanicals	24	46
Chlorhexidine digluconate	1	Not observed
Diazolidinyl urea	Not observed	3
DMDM hydantoin	Not observed	3
Ethylhexylglycerin	5	7
Fragrances	173	54
Hydroquinone	Not observed	1
Imidazolidinyl urea	Not observed	1
Iodopropynyl butylcarbamate	Not observed	3
Lanolin	1	0
MI	2	2
Parabens	50	26
Phenoxyethanol	29	24
PG	11	4
Sodium benzoate	5	9
Sodium metabisulfite	1	Not observed
Sorbic acid	15	19
SSO	15	20
Total	414	280
Average allergens	8.28	5.60

P = 0.003

as diazolidinyl urea, DMDM hydantoin, and imidazolidinyl urea, in order to reduce sensitization and decrease the amount of formaldehyde used.²² However, formaldehyde releasers are able to cause allergic reactions as well because of the free formaldehyde present in these substances, as seen in the relationship between the PPT reactions to formaldehyde releasers and formaldehyde.^{6,23} Forty percent to 60% of reactions to releasers are due to sensitization to the formaldehyde within; therefore, many of those sensitized to formaldehyde may also be sensitive to the releasers.²³ Likewise, following the increasing prevalence of contact dermatitis to MI and its naming as the Contact Allergen of the Year by the ACDS, it has been banned for use in leave-on products by the European Commission.²⁴ However, it remains increasingly prevalent in the United States, with PPT rates rising accordingly from 2.5% to 6.8% from 2012 to 2014.^{24,25} Other preservatives, such as ethylhexylglycerin, sodium benzoate, and sodium metabisulfite, have also been described as progressively significant allergens.^{26–30} The use of parabens, odorless and inexpensive antimicrobials, rather than formaldehyde releasers, reduces the allergenicity of products as they are one of the least sensitizing preservatives.³¹ Unfortunately, they have been associated with hormonal dysregulation and breast cancer in the lay press because of studies in laboratory animals involving exceptionally high concentrations of parabens.^{32–34}

The ubiquity of preservatives found within this study in both the expensive and inexpensive moisturizers (80% vs 88%, *P* = 0.41) further emphasizes their status as the most common contact allergen, and as new preservatives emerge and are combined with existing high-PPT-rate substances such as BAK, preservatives become a higher sensitizing risk for consumers.³⁵

Acrylates

The acrylate sensitizers found in this study include 2-hydroxyethyl methacrylate, ethyl acrylate, and methyl methacrylate. In a recent study, 10.9% of patch-tested patients tested positive to at least 1 iteration of an acrylate monomer, whereas another reported 2-hydroxyethyl methacrylate and methyl methacrylate as the most allergenic substances.^{36,37} However, it should be noted that acrylates do not exist as monomers in moisturizers and are therefore not allergens in these products. Furthermore, their frequency was low in this study, and the difference between the expensive and inexpensive groups was insignificant (14% and 6%, *P* = 0.23).

Botanical Extracts

Botanical allergens present within the products include *Aloe vera*, *Anthemis nobilis*, *Apis mellifera*, *Arnica montana*, *Chamomilla*

TABLE 2. Proportion of Expensive Versus Inexpensive Products That Have Allergens Present

	Expensive Moisturizers (n = 50)	Inexpensive Moisturizers (n = 50)
α -Bisabolol	2 (4)	3 (6)
α -Tocopherol	29 (58)	30 (60)
Acrylates	6 (12)	3 (6)
BAK	Not observed	1 (2)
Benzoic acid	14 (28)	7 (14)
Benzyl alcohol	6 (12)	10 (20)
Benzyl salicylate	5 (10)	2 (4)
BHT	3 (6)	Not observed
Botanicals	20 (40)	27 (54)
Chlorhexidine digluconate	1 (2)	Not observed
Diazolidinyl urea	Not observed	3 (6)
DMDM hydantoin	Not observed	3 (6)
Ethylhexylglycerin	5 (10)	7 (14)
Fragrances	42 (84)	28 (56)
Hydroquinone	Not observed	1 (2)
Imidazolidinyl urea	Not observed	1 (2)
Iodopropenyl butylcarbamate	Not observed	3 (6)
Lanolin	1 (2)	Not observed
MI	2 (4)	2 (4)
Parabens	19 (38)	10 (20)
Phenoxyethanol	29 (58)	24 (48)
PG	11 (22)	4 (8)
Sodium benzoate	5 (10)	9 (18)
Sodium metabisulfite	1 (2)	Not observed
Sorbic acid	15 (30)	17 (34)
SSO	12 (24)	15 (30)
Total	50 (100)	48 (96)

P = 0.49

officinalis, *Echinacea angustifolia*, *Echinacea purpurea*, *Lavandula angustifolia*, *Matricaria chamomilla*, and ylang-ylang oil derived from *Cananga odorata*. It should be noted that botanicals may also be used to perfume moisturizing products; however, the substances listed in this section were not doubly included as fragrances.

Rates of sensitization to these botanicals range from as low as 1.13% for *A. montana* to 13.9% for lavender.^{38–40} However, in contrast to the relatively low frequency of acrylates within the surveyed products, botanical ingredients were major possible allergens found in 40% of the expensive and 56% of the inexpensive moisturizers. The high frequency of botanicals may lead to a greater absolute number of ACD patients, despite the lower PPT rate to some of the less sensitizing botanicals, such as *A. vera*, *A. montana*, beeswax, chamomile, *E. angustifolia*, *E. purpurea*, and ylang-ylang oil.^{11,38–53}

Emulsifiers and Emollients

The emulsifier allergens present in our study include lanolin, propylene glycol (PG), and sorbitan sesquioleate (SSO), along with SSO-related substances that may cause cross-reactions, such as polysorbate, sorbitan monooleate, sorbitan monostearate, and sorbitol.⁵⁴ Positive patch test rates to these emulsifiers range from 3.5% for PG to 8.9% for SSO and its derivatives. Although PG is considered to be a weak allergen with a low PPT rate, both PG

and SSO are considered emerging allergens as their PPT rates have been increasing over the past 20 years.^{6,54–59} Considering that 38% and 36% of all surveyed products within this study contained some form of emulsifiers and that emulsifier-associated sensitization rates are thought to be on the rise, emulsifiers may pose a significant risk to consumers in the future.

Tocopherol Derivatives

α -Tocopherol and tocopheryl acetate, or vitamin E, have antioxidant, moisturizing, and antiaging properties. Allergic contact dermatitis to tocopherol is infrequent (0.66%), and the PPT rate does

TABLE 3. Comparison of Grouped Allergens Between Expensive and Inexpensive Products

	Expensive Products (n = 50)	Inexpensive Products (n = 50)	<i>P</i>
Acrylates	7 (14)	3 (6)	0.23
Botanicals	20 (40)	28 (56)	0.16
Emulsifier	19 (38)	18 (36)	1
Fragrances	44 (88)	31 (62)	0.006
Preservatives	40 (80)	44 (88)	0.41
Tocopherols	29 (58)	30 (60)	1
Other	4 (8)	1 (2)	0.36

not seem to have increased considerably over the past 20 years.⁶⁰ However, as described with the botanical allergens, the high rates of tocopherols within both the expensive and inexpensive products (58% vs 60%, $P = 1$) may lead to a greater absolute number of ACD patients, despite the lower PPT rate.

Other

Other miscellaneous ingredients found in this study at miniscule quantities and frequencies include butylated hydroxytoluene (BHT), chlorhexidine digluconate, and hydroquinone. Butylated hydroxytoluene is an antioxidant and preservative used in food products, cosmetics, and petroleum-based commodities. It has been a rare and weak inducer of ACD in those who use BHT-containing products.^{61,62} Chlorhexidine digluconate, an antiseptic and preservative, is used in health care settings and in cosmetics. A 2013 study performed in Australia reported a positive reaction rate of 3%, indicating its existence as an emerging allergen in those commonly exposed, such as health care workers.⁶³ Hydroquinone is a skin-depigmenting agent that has been shown to cause ACD, albeit a rare cause.⁶⁴

LIMITATIONS

Our study had several limitations. We only partially surveyed 1 drug store's online catalog in the United States during the month of June, despite many other moisturizers being available to the public. Potential allergens, as well as their concentrations, may also change frequently in each product because of changes in formulation. Furthermore, uncommon, unidentified, or relatively unstudied potential allergens may be missing from our study. However, the selection of allergens from the ACDS and North American Contact Dermatitis Group panels, expert opinion, and previous studies was an attempt to mitigate this concern. Finally, our sample size is only a small fraction of the available commercial products, and the statistical realities of small sample sizes likely lead to an underestimation of the number of significant differences between the expensive and inexpensive products.

CONCLUSIONS

Patients would understandably expect a strong, positive relationship between price and product quality.⁶⁵ However, the results of the present study suggest that the overall allergenic potential of expensive moisturizers may be higher than that of inexpensive moisturizers. Upon a more detailed analysis, fragrance sensitizers result in the greatest difference between the 2 product groups, accounting for almost half of the total quantity of allergens found in the expensive CVS moisturizers. This information may be helpful to clinicians, after patch testing to determine exact allergens, in advising patients about the allergenic risk of their leave-on products. Specifically, the counseling may suggest that monetary value may not be a suitable proxy for assessing the risk of ACD. We hope to facilitate a discussion about affordable and less sensitizing substitutions and to benefit patients by educating them on the use of expensive moisturizers that may be more allergenic than their inexpensive counterparts.

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