A Review on Synthetic Shampoo Ingredients and Their Adverse Health Effects

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Abstract

Shampooing is a universal daily hair care routine in this modern era. In todays' market, shampoo products have been advertised and commercialized for different purposes and grades like medicated. professional, baby, or regular shampoo for everyday use. These shampoos typically contain a range of core ingredients, such as, surfactants, foaming agents, conditioners, pearlescent agents, sequestrants, pH adjuster, antidandruff agents, colorants, perfumes, and preservatives. Most of these ingredients present in shampoos are synthetically made. For example, diethylamine, triethylamine, cocamide diethanolamine and some other by-products like 1,4-dioxane. Although regulatory agency has controlled the application of these synthetic ingredients in cosmetics, they are still capable of being dermally absorbed and elicit allergic reactions, skin irritation, contact dermatitis below restricted concentrations. Prolonged exposure to these synthetic ingredients is also carcinogenicity associated with and mutagenicity. This review mainly focuses on elucidating the common synthetic ingredients used in the shampoo formulation, their functions and their potential health risks following long term exposure.

Keywords: Synthetic Ingredients, Shampoo, Carcinogenicity, Dermal absorption, Contact Dermatitis

Introduction

Hair is a filamentous fibre that grows from the hair follicles located at the dermis layer of the skin. The hair fibre is made up of three concentric layers: (a) the cuticle layer (the outermost layer filled with flat, thin, and overlapping dead cells) which functions as the protective barrier against the external environment; (b) the cortex layer (packed, rodlike shaped cortical cells arranged with keratin filaments in an adjacent manner) which gives rise to the texture and shape of hair; and (c) the medulla layer (the innermost, opened, loosely packed and unstructured region) [1, 2] (Fig. 1).

Hair is universally seen as a sign of beauty in almost every culture. Ladies with long hair have been portrayed as a symbol of beauty. This general impression had led to the massive growth of demands in cosmetic hair and scalp care products. There are numerous products available in the market which are mainly to cater to different needs of the consumers for hair beauty purposes. For instance, hair shampoo, hair conditioner, hair oil, hair mask, hair serum, hair styling gel, dry shampoo and hair colorant.

Among all the hair products available in the market, shampoo is the most common and fundamental product which used primarily to cleanse the hair and scalp. Our hair naturally creates oils which is known as sebum. As our



Figure 1: Cross section of the hair shaft.

hair is exposed to the external environment, various impurities and contaminant particles will also build up on the hair. Dirty, clogged hair follicles can slow down hair growth and results in problems like dandruff and itching. Therefore, consistent hair washing is vital as it helps to remove excessive sebum and dirt, allowing the hair to breathe. This helps to ensure a conducive environment for hair growth, reducing scalp-associated issues and maintaning overall hair health.

A shampoo normally consists of 10 to 30 ingredients in the formulation [3]. Such as, primary and secondary surfactants, seauesterina agents, foaming agents. conditioning agents, thickening agents, antidandruff agents, pearlescent agents, pH adjusters, colourants, fragrances, and preservatives [4]. Each of these ingredients plays a crucial role in the shampoo formulation ensure its quality, to effectiveness, safety and aesthetic aspect.

Most commercial shampoos in the market are synthetically formulated. Even those shampoos labeled as "natural" or "organic" still contain some synthetic raw ingredients. Numerous scientific studies have indicated the potential adverse health effects of the synthetic ingredients. They are often considered harsh and can lead to allergic contact dermatitis, especially in individuals with sensitive skin and impaired skin barrier. By-products generated during the synthetis of synthetic components can also cause alarming health consequences. Several

animal studies have shown that some synthetic ingredients and their by-products can be significantly absorbed through the skin and into the bloodstream, posing potential carcinogenic and mutagenic risks after long term exposure. Owing to the potential hazardous health risks, regulatory agencies have established guidelines to restrict the usage levels of the synthetic ingredients. However, controlling the by-products produced during the synthesis of raw ingredients and ensuring manufacturing compliance with the established limits can be challenging to achieve. Therefore, it is vital to identify and exclude the frequently used hazardous synthetic components in the shampoo formulation.

This review highlights the common ingredients used in shampoo, their functions, and the potential adverse health risks resulting from the synthetic ingredients.

Basic Shampoo Ingredients and Their Functions

Surfactants

Among all the listed ingredients in a shampoo formulation, a surfactant plays the most eminent role in a formulation. Primary and secondary surfactants are included in a formulation for a specific purpose. Both primary and secondary surfactants are made up of amphiphilic detergent molecules. The lipophilic sites bind to oily dirt and sebum of hair, while the hydrophilic ends bind to the water. This amphiphilic character of surfactants would facilitate the removal of sebum from hair when it is rinsed with water [5]. Primary surfactant is the main ingredient of shampoo which provides detergency and lathering effects, whereas secondary surfactant is to improve detergency, foam, and hair condition. Secondary surfactant is added as an adjunct to primary surfactant [4].

Sequestering agent

Magnesium and calcium ions in hard water could react with anion surfactant in shampoo to form soap scum. Soap scum would leave a coating film on the hair, causing

the hair to appear dull [6]. Soap scum on hair and scalp could also intensify itching and seborrheic dermatitis [5]. Therefore, sequestrant will be included in the formulation as a metal ion chelating agent [5, 6].

Foaming agent

Foaming agents or foam boosters in shampoos could create a rich lather while shampooing. They are also included in the formulation to satisfy customer preference over bubbling products.

Conditioning agent

A hair conditioning agent is added in the shampoo formulation to improve manageability, softness, gloss, and anti-static properties to hair.

Thickening agent

Thickener is a viscosity enhancer usually added to enhance the physical properties of shampoo preparations. Thickening agents are added for consumer satisfaction, as consumers usually feel thicker shampoos are that thicker or more viscous shampoo works better and is more effective [7].

Antidandruff agent

High concentration of anti-dandruff agents is incorporated into the medicated shampoo formulation to manage seborrheic dermatitis and control the dandruff condition. It could slow down the scalp flaking, inhibit the growth of bacterial and fungus on the hair scalp.

Pearlescent agent

To upgrade the luxurious look and market value of a shampoo product, a pearlescent agent or opacifier is included. It will give a less transparent and rich appearance to the shampoo solution.

pH adjuster

The pH of a shampoo product must be adjusted and balanced. A pH-balanced shampoo could tighten up the hair cuticles. This could prevent moisture loss, tame hair fizziness, and reduce hair static. It also prevents the scalp from producing excessive sebum after washing. To balance the pH, a pH adjuster is used in the product formulation. A good shampoo should have the pH balanced at pH 5.5, which is similar to the scalp pH [5]. Products with a pH higher than pH 5.5 would lead to alkalization of the hair shaft and result in swelling [5]. The swelling would henceforth loosen the protective cuticle of hair fibre and the hair shaft will be more prone to external damage and breakage [6].

Fragrance

Fragrances and colourants are additives intended to make the shampoo aesthetically appeal to consumers. They do not play an important functional role in the product, but it is more for consumer perception. Fragrances could change the perception of the functional product and social attributes [8]. Fragrance could also mask the undesirable odour of other ingredients in the formulation.

Colorant

The purpose of colourants is to add colour to make the shampoo visually appealing. It does not serve cleansing purpose in shampoo, but it plays a vital role in aesthetic and marketing purpose.

Preservative

All shampoo products consist of water in the formulation. Water could support the growth of microbial in the products. Unpreserved or poorly preserved shampoo products would present a serious public health concern for consumers. The addition of preservatives in shampoo formulation could inhibit microbial growth, minimise contamination and decomposition of shampoo caused by bacteria and fungus, predominantly [6].

The examples and purposes of the common ingredients present in the commercial shampoos are summarised in (Table 1).

Health Risks Associated with Synthetic Ingredients in Hair Shampoos

Shampoo is predominantly made up of synthetic and chemical ingredients. Shampoo

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Ingredients	Purposes	Examples	References
Surfactants	To cleanse and remove the sebum and oily dirt from the hair and scalp.	Sodium lauryl sulphate, triethanolamine lauryl sulphate, sodium laureth sulphate, ammonium laureth sulphate, sodium cocoyl isethionate, sodium lauroyl sarcosinate, sodium	[5, 9-12]
Foaming agents	To create foamy lather while shampooing.	lauroamphoacetate, disodium cocoamphodiacetate, disodium laureth sulfosuccinate, Cocamidopropyl betaine, cocamide MEA, cocamide DEA, palm kernelamide DEA, TEA-dodecylbenzenesulfonate, lauryl betaine, lauryl glucoside.	
Conditioners	To improve manageability, softness, gloss, and anti-static properties to hair.	Dimethicone, simethicone, amodimethicone, cyclomethicone, dimethiconol, cyclotetrasiloxane, polyquaternium-2/6/7/10/11, glyceryl stearate, dicetyldimonium chloride, behentrimonium chloride, stearalkonium chloride, cetrimonium chloride, isopropyl myristate, isopropyl palmitate, polyethylene glycol, propylene glycol, butylene glycol, capryl glycol, panthenol, hyaluronic acid, argan oil, glycerine, hydrolysed protein, hydrolysed collagen, glutamic acid, glyceryl oleate, histidine, isoleucine,, phenylalanine, threonine, tryptophan, and valine.	[5, 10]
Pearlescent agents	To impart a pearl- like appearance to the shampoo product by reducing its clear or transparent look.	Glycol monostearate, glycol distearate.	[11]
Thickening agents	To give thick consistency to the shampoo preparation for a richness-looking appearance.	Sodium chloride, guar gum, xanthan gum, acacia gum, hydroxyethyl cellulose (HEC), hydroxypropyl methylcellulose (HPMC), beeswax, sodium xylenesulfonate, trihydroxystearin, PEG-150 distearate, carbomer, acrylates/C10-30 alkyl acrylate crosspolymer, styrene/acrylates copolymer.	[5, 10, 11, 13 14]
Sequestrants	To chelate undesirable metal ions (i.e., magnesium and calcium) which present in hard water from forming insoluble soaps, also known as "scum".	EDTA, disodium EDTA, tetrasodium EDTA, sodium phytate.	[5, 11]

Identification of New Dual PDE4/5 Inhibitors

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pH adjuster	To balance the pH of shampoo formulation for a healthy scalp skin.	Citric acid, lactic acid, sodium citrate, sodium lactate, sodium gluconate.	[5]
Antidandruff agents	To treat dandruff condition.	Selenium sulphide, ketoconazole, salicylic acid, sulfur, zinc pyrithione, tar, ciclopirox, clobetasol, pirolactone olamine.	[11, 15]
Colourants and perfumes	To impart colour and aroma to the shampoo product for aesthetic and marketing purposes.	Colourant: Titanium dioxide, iron oxides, zinc oxide, aluminium lakes, mica, silica, Food Drug and Cosmetic dyes (FD&C), Cosmetic-grade dyes (D&C).	[9, 16]
		FD&C is a colouring agent which is authorized by Food and Drug Administration (FDA) for food (F), drugs (D), or cosmetics (C), which is used externally only.	
		D&C is a colouring agent which is authorized by Food and Drug Administration (FDA) for drugs (D) or cosmetics (C), which is used externally only.	
		Fragrance: Benzyl salicylate, citronellol, coumarin, citral, eugenol, farnesol, geraniol, hexyl cinnamal, limonene, linalool.	
Preservatives	To maintain the product's freshness from microbial contamination.	Methylchloroisothiazolinone, methylisothiazolinone, methylparaben, ethylparaben, sodium benzoate, potassium sorbate, DMDM Hydantoin, quaternium-15, imidiazolidinyl urea, diazolidinyl urea, phenoxyethanol, ethylhexylglycerin, triclosan, chlorhexidine digluconate.	[5, 9, 11]

ingredients like surfactant, foaming agent, conditioner, sequestrants, thickening agent, preservatives, fragrance, and colorant are mostly synthesized from laboratories through chemical reactions. Incorporation of these synthetic ingredients are often favoured in the shampoo preparations due to their costeffectiveness and consistent availability. From a production standpoint, the manufacturing of synthetic ingredient is direct and simplified through precise chemical synthesis. Unlike natural ingredients, which often require complex cultivation, harvesting and extraction techniques, synthetic ingredients considerably reduce both costs and time [17-19]. The standardized chemical synthesis of synthetic components allows for their mass production and achieves economical scale. As a result. this guarantees the stable supply chain and makes them less expensive than their natural counterparts. The high availability of synthetic components supplies further enhance the affordability and meet the demands for efficient shampoo production.

However, concerns have arisen regarding the potential adverse effects on human health due to repeated contact with the synthetic ingredients used in cosmetics. For instance, skin irritation, contact dermatitis, allergic reaction [20]. Besides synthetic ingredients, the by-products resulting from the synthesis of the chemical ingredients have been documented to have the potential for absorption into systemic circulation. This can induce carcinogenicity and mutagenicity, as

Chemicals/ Ingredients	Functions	Restricted concentration in shampoo formulations	Side effects	References
1,4-dioxane: by-product of polyethylene glycol (PEG), polypropylene glycol (PPG), polyoxyethylene derivatives and sodium laureth sulphate (SLES)	PEG: emollient, moisturizer, thickeners, solvents PPG: humectant, moisturizer	0.001% (equivalent to 10 ppm) [23]	Dermal absorption Potential carcinogenicity: Tumours development in nasal cavity, subcutis, peritoneum and liver	[24] [28]
	Polyoxyethylene derivatives: emulsifier SLES: surfactants		Potential stillbirths and abortions Potential mutagenicity: High genes proliferating cell nuclear antigen (PCNA) and O-6- methylguanine–DNA methyltransferase (MGMT)	[20]
Diethanolamines (DEA)	pH adjuster, emulsifier	Banned for use in cosmetic products [32]	Dermal absorption and systemic absorption Potential Carcinogenicity: Increased in liver neoplasms and renal tubule neoplasms	
Triethanolamines (TEA)	pH adjuster, emulsifier, and thickening agent	2.5% [33]	Skin irritation Allergic reaction Contact dermatitis	[34] [34] [35]
Cocamide diethanolamine (CDEA)	Foam booster, foam stabilizer, and viscosity enhancer	0.5% [33]	Allergic contact dermatitis	[36,38]

evidenced in several literatures [9, 21, 22]. Table 2 outlines the overview of the adverse effects associated with the synthetic ingredients used in shampoo and the byproducts.

1,4-dioxane

1,4-dioxane is a residual by-product formed during the synthesis of ethanolamines, polyethylene glycol (PEG), polypropylene glycol (PPG), polyoxyethylene derivatives, and sodium laureth sulphate (SLES). These ingredients are commonly used as solubilising agents, emulsifiers, foaming agents, and detergents in shampoo preparations.

The maximum concentration of 1,4dioxane allowed in a finished cosmetic product should be 10 ppm or less, as per the Scientific Committee on Consumer Safety (SCCS)

guidelines [23]. It has been discovered that even shampoo with concentrations that comply with the guidelines can still lead to significant dermal absorption through daily exposure [24]. Many studies showed that 1,4-dioxane as a potential carcinogens and mutagens [25-27]. Development of tumours were found in the nasal cavity, subcutis, peritoneum, and liver of the rats and mice who were exposed to 1,4dioxane frequently [28]. As a result, daily application of shampoo containing 1,4-dioxane may pose a potential cause of carcinogenicity due to its capacity for significant absorption through the skin. Wilbur S et al. [25] also reported spontaneous abortion and stillbirths due to exposure to 1,4-dioxane. In vivo study by M Gi et al. [29] revealed that high genes proliferating cell nuclear antigen (PCNA) and O-6-methylguanine-DNA methyltransferase (MGMT) in rats, after 16 weeks of administration with 1.4-dioxane. Such mutagenic effects which caused alterations in DNA sequence can disrupt the normal cellular function and lead to uncontrolled growth of thereby contributing to cells, cancer development.

In short, exposure to shampoo such as ethanolamines, ingredients, polyethylene glycol (PEG), polypropylene glycol (PPG), polyoxyethylene derivatives and sodium laureth sulphate (SLES) may pose risks to human health. Despite strict control over the concentration of these ingredients in cosmetic products manufacturing, 1,4 dioxane can still be potentially absorbed through the skin, potentially leading to mutagenic and carcinogenic effects. As a precautionary measure, it is advisable to choose shampoo products that do not contain these ingredients.

Alkanolamines

Triethanolamine (TEA), diethanolamine (DEA) and cocamide diethanolamine (CDEA) are alkanolamines that are commonly present in hair shampoo formulas. They are primarily used as surfactants, emulsifying agents, and pH adjusters.

Diethanolamine (DEA)

M Kraeling et al. [30] discovered that shampoo with 0.1% DEA could penetrate receptor fluid, stratum corneum, epidermis, and dermis layer of in vitro human skin model, upon short term exposure around 5 and 30 minutes. 62-68% of DEA in hair shampoo formulations were found absorbed into the stratum corneum layer. Systemic diffusion of DEA into receptor fluids was also evidenced from the study [30]. Systemic absorption is a significant concern because it can cause the distribution of DEA throughout the body. DEA from shampoo could potentially diffuse into tissues and organs, thereby initiating the growth of cancerous cells.

The carcinogenicity effect associated with continuous exposure of DEA was documented, even at low doses [20]. An *in-vivo* toxicity study demonstrated a significant increase in liver neoplasms of both females and male mice after they were dermally exposed to DEA for 2 years [31]. Increased renal tubule neoplasms were also detected in the male mice. The clinical development of liver and kidney tumours in mice showed the possible carcinogenic effect in humans after long term-exposure to DEA.

According to the European Union's Cosmetic Directive, all dialkanolamines and their derivatives are forbidden from being used in cosmetics, due to their toxicity [32]. However, there is still a chance that they could show up in cosmetic products as by-products from the usage of other raw materials used in cosmetics the products. such as monoethanolamine. triethanolamine and cocamide monoethanolamine and cocamide strongly diethanolamine. Hence. it is recommended to exclude the use of alkanolamines-related raw ingredients in cosmetics preparations.

Triethanolamine (TEA)

TEA is a very common ingredient that is present in shampoo products. It can serve as a pH adjuster, emulsifier, and thickening agent. According to European Union guidelines, the maximum concentration of trialkylamines and their salts allowed for use in cosmetic products

is 2.5% [33]. Nevertheless, due to its alkaline nature, TEA can still result in skin irritation, contact dermatitis and allergic reaction at [34]. concentration permitted Contact dermatitis and hypersensitivity reactions are prevalent among hairdressers, especially with their hands being affected [34]. This is attributed to their frequent exposure to chemical shampoos containing TEA while providing hair services, such as washing hair. Apart from causing skin irritation, an animal study showed that TEA is a potential result carcinogen that could in hepatocarcinoma and adenoma [35].

To sum up, individuals who are frequently in contact with TEA, even at the permitted concentration in cosmetics, could still experience contact dermatitis and skin irritation. Despite limited studies on its carcinogenicity, in-vitro research has established its toxicity. Therefore, it is crucial to acknowledge the possible risks of TEA in cosmetic products and to prioritize the safety precautions to protect those who are routinely exposed to it.

Cocamide diethanolamine (CDEA)

CDEA is a non-ionic surfactant frequently utilized as a foam booster, foam stabilizer, and viscosity enhancer in hair shampoos [36]. The maximum allowable concentration of CDEA in cosmetic preparations is 0.5%, as per European Union rules [33]. CDEA is synthesized from the concomitant reaction of diethanolamine with coconut oil [37]. Despite its derivation from natural coconut oil, it is important to note that some individuals may still be allergic to this natural oil derivative. S Mertens et al. [36] reported an increased risk of allergic contact dermatitis associated with occupational exposure to cocamide DEA. Hairdressers, who are often exposed to CDEA-containing shampoo, are dominated as the primary group at risk of CDEA sensitization. Individuals with atopic dermatitis and compromised skin barriers are particularly susceptible to allergic reaction towards CDEA. However, it is noteworthy that even those without atopic diseases and not involved in hair-related occupations can experience sensitization. This is proven in a study where a healthy, non-atopic individual developed an allergic reaction towards CDEA. Contact dermatitis at genital part was reported after frequent use of the intimate hygienic gel wash with CDEA [38].

In summary, individuals with impaired skin barriers and those with atopic dermatitis are especially susceptible to sensitization towards CDEA. Although the fact that shampoo is designed to be rinse-off nature and has a short contact time on body, healthy individuals without a history of skin disease may still experience contact dermatitis if regularly in contact with the shampoo containing CDEA. Therefore, it is advisable to avoid the exposure to potential sensitizers like CDEA to maintain a healthy skin barrier.

Conclusion

To sum up, shampoos are mostly made up of synthetic and chemical-based ingredients. The production of many ingredients which are claimed as "naturally derived" often still entails chemical processes and they are not purely "natural origin". For example, the extraction of compounds from plants with the use of organic solvent like ethanol.

Synthetic ingredients and their byproducts hold the potential to permeate the skin barrier and enter the systemic bloodstream, thereby increasing risks of carcinogenic effect. The development of tumours has been well-established in animal studies, postulating the possible carcinogenicity and mutagenicity effects in human following long term exposure. People with a history of skin problems and those employed in hair-related occupations are more prone to developing skin irritation and allergic contact dermatitis towards synthetic-made shampoos. Therefore, it is recommended to opt for natural and herbal shampoos for regular usage as they can contribute to maintaining overall skin health.

For future research prospects, it is imperative to conduct extended-term human studies involving individuals who use synthetic shampoos over prolonged periods and to compare the resultant health outcomes with those using natural shampoos. Additionally, comprehensive а safety assessment of the synthetic ingredients should encompass evaluation of their potential for skin absorption, systemic distribution, as well as the implementation of patch test to identify potential allergens.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Gubitosa, J., Rizzi, V., Fini, P., & Cosma, P. (2019). Hair care cosmetics: from traditional shampoo to solid clay and herbal shampoo, a review. Cosmetics, 6(1): 13.

2. Feughelman, M. (1997). Mechanical properties and structure of alpha-keratin fibres: wool, human hair and related fibres: UNSW press.

3. Lazzarini, R., Costa, L. L., Suzuki, N. M., & Hafner, M. d. F. S. (2020). Allergic contact dermatitis by shampoo components: a descriptive analysis of 20 cases ☆,☆☆. Anais brasileiros de dermatologia, 95: 658-660.

4. Jaya Preethi, P., Padmini, K., Srikanth, J., Lohita, M., Swetha, K., & Vengal Rao, P. (2013). A review on herbal shampoo and its evaluation. Asian J. Pharm. Ana, 3(4): 153-156.

5. D'Souza, P., & Rathi, S. K. (2015). Shampoo and Conditioners: What a Dermatologist Should Know? Indian J Dermatol, 60(3): 248-254. doi: 10.4103/0019-5154.156355.

6. Draelos, Z. D. (2013). Shampoos, conditioners, and camouflage techniques. Dermatologic clinics, 31(1): 173-178.

7. Draelos, Z. D. (2010). Essentials of hair care often neglected: Hair cleansing. International journal of trichology, 2(1): 24.

8. Churchill, A., Meyners, M., Griffiths, L., & Bailey, P. (2009). The cross-modal effect of fragrance in shampoo: Modifying the perceived feel of both product and hair during and after washing. Food Quality and Preference, 20(4): 320-328.

9. Manayi, A., & Saeidnia, S. (2014). Cosmetics and Personal Care Products. 1043-1049. doi: https://doi.org/10.1016/B978-0-12-386454-3.00979-9.

10. Yang, J. (2017). Hair care cosmetics. Cosmetic Science and Technology: Theoretical Principles and Applications, 36: 601-615.

11. Klein, K., & Palefsky, I. (2007). Shampoo formulation. Handbook for Cleaning/Decontamination of Surfaces, 1: 277-304.

12. Rhein, L. (2007). Surfactant action on skin and hair: Cleansing and skin reactivity mechanisms Handbook for Cleaning/Decontamination of Surfaces (pp. 305-369): Elsevier.

13. Karsheva, M., Georgieva, S., & Handjieva, S. (2007). The choice of the thickener-a way to improve the cosmetics sensory properties. Journal of the University of Chemical Technology and Metallurgy, 42(2): 187-194.

14. Gandolfi, L., & Galleguillos, R. (2015). Rheology Modifiers and Consumer Perception. Harry's Cosmeticology, 9th ed.; Rosen, MR, Ed, 768-806.

15. Ranganathan, S., & Mukhopadhyay, T. (2010). Dandruff: The most commercially exploited skin disease. Indian J Dermatol, 55(2): 130.

16. Valet, B., Mayor, M., Fitoussi, F., Capellier, R., Dormoy, M., & Ginestar, J. (2007). Colouring Agents in Decorative and other Cosmetics. Analytical Methods. Analysis of Cosmetic Products, 141.

17. Shivathaya, N., Surve, R., Sawant, R., Khot, S., Biradar, K., Verma, R., & Gorav, A. (2022). Formulation and In-vitro Evaluation of Ethanolic Extract of Polyherbal Face Cream. Int J Curr Pharm Res, 14(2): 41-47.

18. Bom, S., Fitas, M., Martins, A. M., Pinto, P., Ribeiro, H. M., & Marto, J. (2020). Replacing synthetic ingredients by sustainable natural alternatives: a case study using topical O/W emulsions. Molecules, 25(21): 4887.

19. Dauber, C., Parente, E., Zucca, M., Gámbaro, A., & Vieitez, I. (2023). Olea europea and By-Products: Extraction Methods and Cosmetic Applications. Cosmetics 2023, 10: 112.

20. Arora, P., Nanda, A., & Karan, M. (2011). Shampoos based on synthetic ingredients vis-à-vis shampoos based on herbal ingredients: A review. Int J Pharm Sci Rev Res, 7(1): 42-46.

21. Russ, K. (2009). A Review of the Evidence: Health Effects of Personal Care Products. Nursing for Women's Health, 13(5), 392-401.

22. Goossens, A. (2011). Contact-allergic reactions to cosmetics. Journal of allergy, 2011.

23. (EC), E. C. (2015). Scientific Opinion on the Report of the ICCR Working Group: Considerations on Acceptable Trace Level of 1,4-Dioxane in Cosmetic Products.

24. Huang, G., Bu, H., Sun, S., Chen, A., & Zhou, Y. (2012). Study on Exposure Assessment Model of Dioxane in Shampoo. Procedia Engineering, 43: 407-412.

25. Wilbur, S., Jones, D., Risher, J. F., Crawford, J., Tencza, B., Llados, F., Lockwood, L. O. (2012). Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles Toxicological Profile for 1,4-Dioxane. Atlanta (GA): Agency for Toxic Substances and Disease Registry (US).

26. FDA), U. S. F. D. A. (2019). 1,4-Dioxane in Cosmetics: A Manufacturing Byproduct. Retrieved 30 May 2021, 2021, from https://www.fda.gov/cosmetics/ potential-contaminants-cosmetics/14-dioxanecosmetics-manufacturing-byproduct. 27. Beyer, K., Bergfeld, W., Berndt, W., Boutwell, R., Carlton, W., Hoffmann, D., & Schroeter, A. (1983). Final report on the safety assessment of triethanolamine, diethanolamine and monoethanolamine. J. Am. Coll. Toxicol, 2: 183-235.

28. Kano, H., Umeda, Y., Kasai, T., Sasaki, T., Matsumoto, M., Yamazaki, K., Fukushima, S. (2009). Carcinogenicity studies of 1, 4dioxane administered in drinking-water to rats and mice for 2 years. Food and Chemical Toxicology, 47(11): 2776-2784.

29. Gi, M., Fujioka, M., Kakehashi, A., Okuno, T., Masumura, K., Nohmi, T., Fukushima, S. (2018). In vivo positive mutagenicity of 1, 4-dioxane and quantitative analysis of its mutagenicity and carcinogenicity in rats. Archives of toxicology, 92(10): 3207-3221.

30. Kraeling, M., Yourick, J., & Bronaugh, R. (2004). In vitro human skin penetration of diethanolamine. Food and Chemical Toxicology, 42(10), 1553-1561.

31. Leung, H.-W., Kamendulis, L. M., & Stott, W. T. (2005). Review of the carcinogenic activity of diethanolamine and evidence of choline deficiency as a plausible mode of action. Regulatory Toxicology and Pharmacology, 43(3): 260-271.

32. 2016/1198, E. N. (2016). COMMISSION REGULATION (EU) 2016/1198 of 22 July 2016 amending Annex V to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products Official Journal of European Union Retrieved from https://eur-lex.europa.eu/legal-content/ EN/TXT/PDF/?uri=CELEX:32016R1198&rid=1.

33. Commission, E. (2009). Regulation (EC) No 1223/2009 of the European Parliament and of the Council.

34. Silva, E. A., Bosco, M. R. M., & Mozer, É. (2012). Study of the frequency of allergens in cosmetics components in patients with suspected allergic contact dermatitis. Anais brasileiros de dermatologia, 87(2): 263-268.

35. Lim, D. S., Roh, T. H., Kim, M. K., Kwon, Y. C., Choi, S. M., Kwack, S. J., Lee, B.-M. (2018). Risk assessment of Nnitrosodiethylamine (NDEA) and Nnitrosodiethanolamine (NDELA) in cosmetics. Journal of Toxicology and Environmental Health, Part A, 81(12): 465-480.

36. Mertens, S., Gilissen, L., & Goossens, A. (2016). Allergic contact dermatitis caused by cocamide diethanolamine. Contact Dermatitis, 75(1), 20-24.

Mayithat, Simanjuntak, 37. Ζ., L., & Yudhika, S. R. (2019). Simultaneously Trans-Esterification Amidification and Coconut into Cocamide-Dea of Oil Heterogeneous ARPN using Catalyst. Journal of Engineering and Applied Sciences, 14(11).

38. Navarro - Triviño, F. J., & Ruiz - Villaverde, R. (2021). Genital allergic contact dermatitis caused by cocamide DEA. Contact Dermatitis, 85(6): 701-703.