Cosmetic creams potency and storage time: the literature survey discovering the correlation of storage time to degradation of cosmetic formulations

Abstract: The quickly growing market of cosmetic products demands new formulations with new active ingredients while maintaining a prompt and effective product development life cycle. While products chemical and clinical tests may take significant time, cosmetic companies use simplified approaches for product development in order to guarantee the stability of physical appearance and safety. But at the same time data related to the chemical stability and potency of cosmetic products remains very scarce. This review summarizes information available related to degradation processes in cosmetic creams and discusses the risks of long storage before usage (mainly cosmetic emulsions). Specific attention is put on active ingredients such as vitamins and essential oils.

Conclusion: Cosmetic creams lose their potency with time even when properly stored in tightly closed containers. This provides the evidence that brands need to decrease their products shelf life, search for stable formulations or find other ways to minimize product degradation and maintain its potency.

Keywords: Cosmetics, cream, degradation, cosmeceuticals, vitamins

Introduction

The quickly growing market of cosmetic products demands new formulations with new active ingredients while maintaining a prompt and effective product development life cycle. While products chemical and clinical tests may take significant time, cosmetic companies use simplified approaches in order to guarantee physical appearance stability and safety. But how does this affect the end consumer product and its potency?

Nowadays, customers are well aware of many different ingredients that are used in cosmetic formulations, and understand their effects and function. Cosmetic products that contain chemicals products with bioactive ingredients purported to have medical benefits are categorized as "Cosmeceuticals".

The term cosmeceutical was created more than 25 years ago to define products with active substances that can neither be categorized as cosmetics nor drugs. This term has no meaning under US law. These products are found in many forms, including vitamins, peptides, growth factors, and botanical extracts. Cosmeceuticals that contain topically applied vitamins have an increasing role in skin care. There are still many controversial points regarding the ingredients used in cosmeceutical products; among them, mechanisms of action, optimal concentration, biologically active form, formulation stability, penetration, and retention within the skin. Although tests are available to answer some of these questions, it can be speculated that at times there is little interest in such data, given that cosmeceutical products are not regulated and are usually well-accepted by consumers. The question remains whether it is possible to deliver adequate doses to the skin in vivo and to produce clinical or histologic effects. It is important to evaluate these new products with a critical and careful methodology, giving consideration to intended product use and the design of available studies supporting product use. Then, one can decide if the product is useful as a main or adjuvant treatment for aging skin [1].

Cosmetic products need to be safe for consumers during their entire shelf life which is established by the producer. While the composition of cosmetics is regulated, there are no explicit legal requirements to perform stability testing. Most cosmetic formulations are tested with emphasis on microbiological stability, whereas their chemical stability is only marginally investigated. Alteration of cosmetics can occur by migration of package components, the decomposition of ingredients or the formation of compounds involving reactive contaminants. Without an investigation of the

chemical stability, the producer cannot be sure that his product is safe for the estimated shelf life [2].

To ensure that the various functions of cosmetics are realized, the first stage is to observe whether or not there are any changes in their physical and chemical properties. Chemical changes include color change, color fading, fragrance change, staining, crystallization, etc. Physical changes include separation, sedimentation, aggregation, blooming, sweating, gelling, unevenness, evaporation, solidification, softening, cracking, etc. These phenomena not only have a great effect on usability, but also make cosmetics unattractive and damage their image. Generally, product quality must be guaranteed until it is completely used by the consumer, and manufacturers should focus on this base assumption while conducting their research on improving their product level. Guaranteeing increased product life greatly helps in achieving the aforementioned base assumption.

Some pharmaceutical agents are easily degraded by atmospheric oxygen, and they are often considered to be chemically unstable compounds. For example, vitamins A, B1, B2, B6, C, etc. are all unstable. Moreover, in a cosmetic system, these compounds may be incompatible with other compounds they are mixed with. Some may also be affected by changes in pH.

To ensure the stability of pharmaceutical agents used in a product, it is also very important to understand the effects of other ingredients used, and also the effects of pH, temperature, and incompatible or reactive compounds, etc. [3].

Cosmetic products are generally formulated and tested for a shelf life of 1 - 3 years under normal storage conditions, depending on a product's composition, packaging, preservation, and other factors. Consumers should be aware that shelf life (expiration dates) are simply "rules of thumb," and that a product's safety may expire long before the expiration date especially if not stored properly [4].

To ensure the maximum durability of cosmetic products, they should be stored in a cool, dry place, away from direct sunlight and with the lids firmly closed. On the other hand, nature and physicochemical properties of active ingredients and excipients also influence product stability. Manufacturing procedure, closure, container, and the nature of packing material play an important role in maintaining the stability of preparations [5].

Degradation processes and factors influencing stability

Typical cosmetic cream is not a simple formulation. It is an emulsion in the form of oil phase in water (o/w emulsion) or water in oil (w/o emulsion).

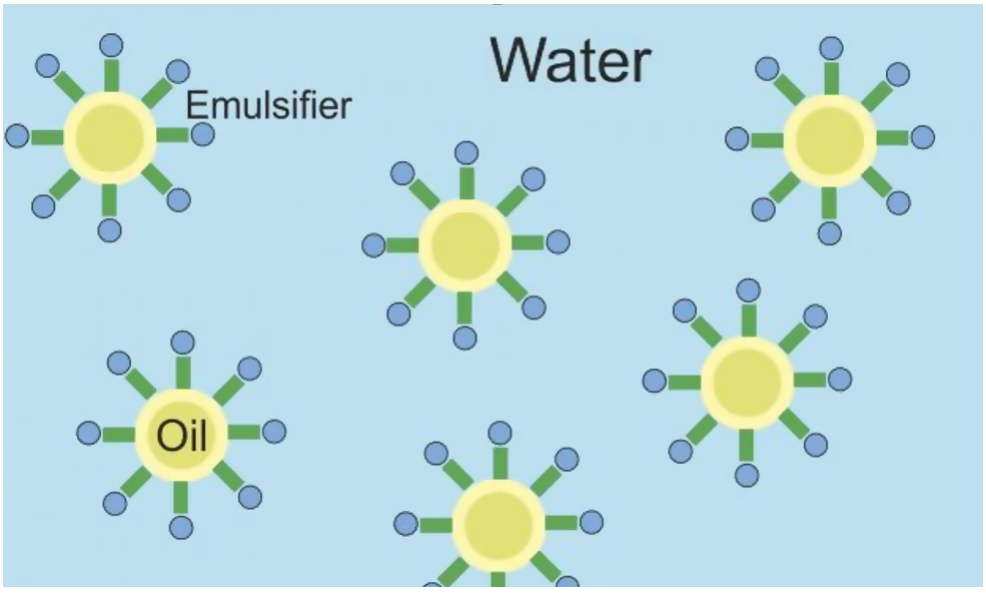

Figure 1 – Picture of a simple o/w emulsion

On one hand the two-phase system provides increased physical stability and properties, allowing for dissolution of both water and oil-soluble ingredients. On the other hand this complex mixture presents risks for ingredients. The major risks are exposure to factors such as moisture, pH, light, microbial contamination and others. These factors may lead to degradation of ingredients thus leading to decrease in their potency and the overall cosmetic product efficacy.

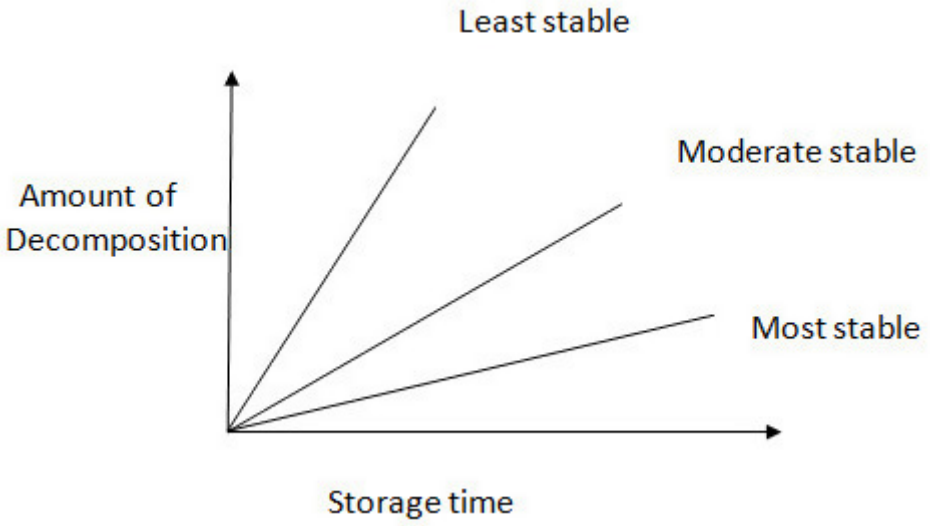

Figure 2– Simple visualization of decomposition time for several groups of ingredients [4]

Factors known to induce chemical degradation in creams:

- Hydrolysis
- Photodegradation (exposure to light)
- Temperature
- pH variations
- Remaining oxygen
- Microbial contamination
- Ingredients incompatibility

Beside human health preoccupation (modification of the natural skin flora, allergies or dangerous risks of infection to the consumer), microbiological contamination may lead to chemical changes that alter the product and limit its shelf life. Maintaining an optimal microbiological product state from production through usage is a real challenge for manufacturers. While one commonly used approach is the use of preservatives, additional risks arise:

1) Companies struggle to find the optimal amount of preservatives for increased shelf life and tend to over use them which leads to unnecessary customer exposure to extra chemicals (such as benzalkonium chloride) or to risks of preservatives degradation and formation of toxic substances (such as formaldehyde).
2) Products are insufficiently preserved. In this case active ingredients and base emulsions are a nutritional source for bacteria. This leads to a decomposition of the active ingredients and accumulation of toxic microbial products.

Manufacturers attempt to increase products shelf life directly impacts their chemical stability. Cosmetic products are not regularly tested as pharmaceutical products, and products are regularly recalled from the market due to microbiological or chemical degradation [6, 7]. Screening done by independent labs also showed microbial contamination, such as in recent research from Poland in which 6 cosmetic products were tested and 8 microbial strains were isolated from 3 products [8].

Other side effects related to microbial contamination are due to different storage conditions. Recent studies in countries with hot and humid climate have shown that products are more susceptible to

microbial contamination even while stored in sealed containers, see examples from Libya [9], Bangladesh [10], or Pakistan [11]. In Pakistan about 16.7% of the tested samples were heavily contaminated (more than 1000 CFU/g).

Though microbial contamination and degradation are considered to be manageable, they directly affect ingredients potency.

Degradation of ingredients

Vitamins

Vitamins are considered to be the most unstable ingredients used in cosmetic formulations. Though their stability isn't thoroughly evaluated, several well-designed studies showed that Vitamin C and Vitamin A shelf life when used in cosmetic creams to be several months. Which means that by the time the consumer uses the product, such vitamins might be decomposed.

More research is available on vitamins A, C, and E due to their popularity in the treatment of aging skin and the protection of against UV-induced damage. However, esterified vitamin derivatives (e.g., retinyl palmitate, ascorbyl tetraisopalmitate, and tocopheryl acetate) with improved stability have been preferentially used in topical formulations. But even in their ester forms, these vitamins can have low shelf life, as shown by Guaratini et al. [12] The authors evaluated a gel-cream formulation containing vitamin A palmitate and vitamin E acetate and observed a shelf life of 77 days, characterized by a first-order degradation reaction of the vitamin A derivative.

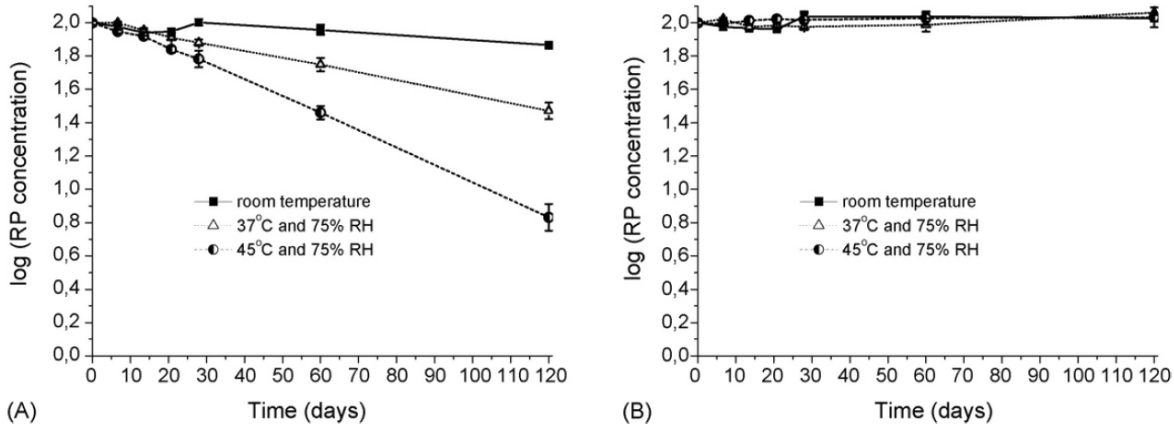

Figure 3 - Quantification of (A) retynil palmitate and (B) tocopheryl acetate expressed as logs of concentration values over time maintained at various conditions [12].

Vitamin A

Ester bonds hydrolysis is one of the often-observed degradation reactions. Cleavage of ester bonds may not be an issue if the produced chemicals are safe. Having said that, it still affects the ingredients potency which is decreased over time. One of the articles studied the chemical stability aspects of Vitamin A and E esters found that actual shelf-life (determined when 15% of active ingredients were degraded) wasn't sufficient. They found that only 85% of Vitamin A remained in the formulation after 77 days of storage at 25 °C, 21 days at 37 °C, and 14 days at 45 °C. Thus, as proposed in this study, to get the most of the Vitamin A it is advised to use the cream within 1-2 months after mixing [12].

Vitamin C

Vitamin C (ascorbic acid) is a potent antioxidant with several applications in the cosmetic and pharmaceutical fields. However, the biggest challenge is to maintain its stability and improve its delivery to the active site.

Ascorbic acid is a naturally occurring antioxidant, effective in treatment and prevention of photo aged skin and helpful in skin depigmentation and collagen synthesis. Chemical and photochemical oxidation are considered to be major cause of degradation in creams containing ascorbic acid, it also shows sensitivity towards air and light. L-dehydroascorbate (DHA), 2,3-L-diketogulonate (2,3-DKG), L-erythrulose (ERU), and oxalate are the primary degradation products of ascorbic acid [5].

Two derivatives of ascorbic acid, i.e., ascorbyl palmitate and sodium ascorbyl phosphate, which differ in stability and hydro-lipophilic properties were studied by P. Spiclin, M. Gasperlin, V. Kmetec in 2001. Ascorbyl palmitate in higher dosage was more stable to time, but light and dissolved oxygen induced oxidation. On the contrary, sodium ascorbyl phosphate was stable in both microemulsions type. Sodium ascorbyl phosphate was revealed to be convenient as an active ingredient in topical dosage form. In the case of ascorbyl palmitate, long-term stability in selected microemulsions was not adequate [13].

The physicochemical stability of ascorbic acid in different water-in-oil (w/o) creams during storage was assessed. The study examined the effect of medium pH and viscosity and use of different excipients on its physicochemical stability.

Several water in-oil (w/o) cream formulations with ascorbic acid (AA)were prepared at pH 4-6 using different humectants and emollients. Creams were placed in the dark at 30°C for a period of three months while preforming stability studies for ascorbic acid to check loss and change in physical features. Results revealed that the cream's pH influenced the stability of AA as its degradation rate rose with rise in pH by first-order kinetics. The stability of AA was improved as the viscosity of the medium increased. Creams that showed the highest rates of degradation (i.e., at pH 6) were compared to creams with the same pH but by adding citric acid as a stabilizing agent. Citric acid was found to decrease degradation rates of AA in all formulations [14].

It was observed that even though cream formulations were kept in the dark; AA underwent aerobic oxidation and ultimately photolytic reactions. Spectrophotometric results showed that the rate of oxidative degradation in the presence of light is about seventy times faster than that observed in the dark. Pharmaceutical creams show complex behavior such as formation of degradation products that may be toxic or nontoxic in nature, breakdown of cream bases, and physical and chemical instability making preparations inappropriate for use [5].

Other authors observed that the water-soluble vitamin C derivative, magnesium ascorbyl phosphate, was more stable than ascorbyl palmitate (lipid soluble derivative), which was considered very unstable, due to the lipophilic ester in position 6 that does not protect this vitamin from degradation. Another study showed that magnesium ascorbyl phosphate had a medium shelf life (7 months), which confirmed the capability of the phosphate group to protect the enediol system from hydrolysis, even when it is included in cosmetic formulations. In addition, Segall and Moyano showed that ascorbyl esters, sodium ascorbyl phosphate, and magnesium ascorbyl phosphate are more stable than ascorbyl palmitate, since after 6 months, they found a remaining concentration of 20% of ascorbyl palmitate in comparison to 70–80% of the other derivatives [15].

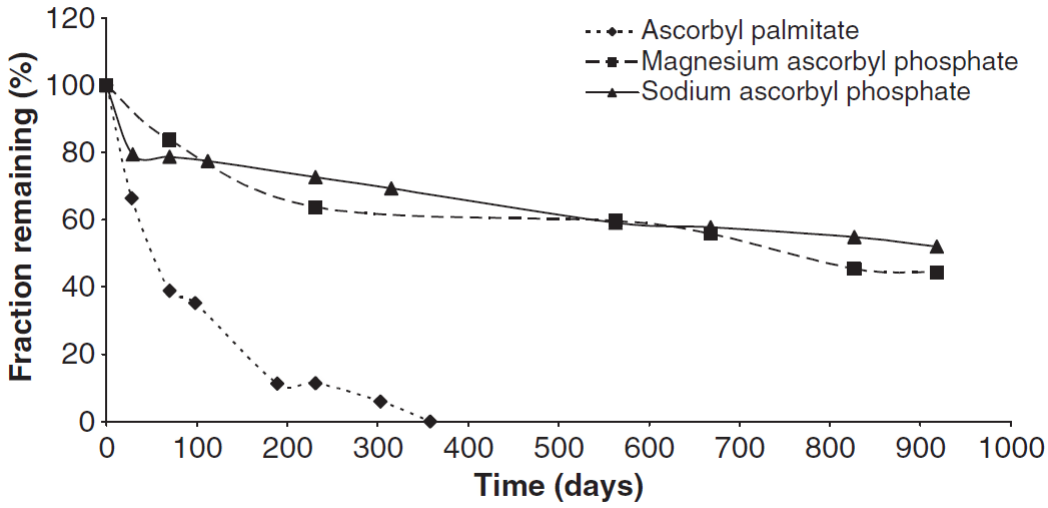

Figure 4 - Stability of various Vitamin C forms in cosmetic formulations [15]

The amount of AA was found to decrease over time in all formulations due to the oxidation of the vitamin. The % loss of AA was found to be different in each formulation which indicates the role of pH and various formulation factors on the degradation of AA. All creams stored for 3 months were found to retain AA in the range of around 9–44% with the highest values of r (~44%) observed in formulation at pH 4 whereas the maximum loss (~90%) has been observed in formulation at pH 6 (Fig. below). These values show better stability than those previously reported for w/o emulsions of AA containing soybean and moringa oil where the r values of 50% and 30% were observed after 30 days of storage at 4°C and 25°C, respectively [16, 17]

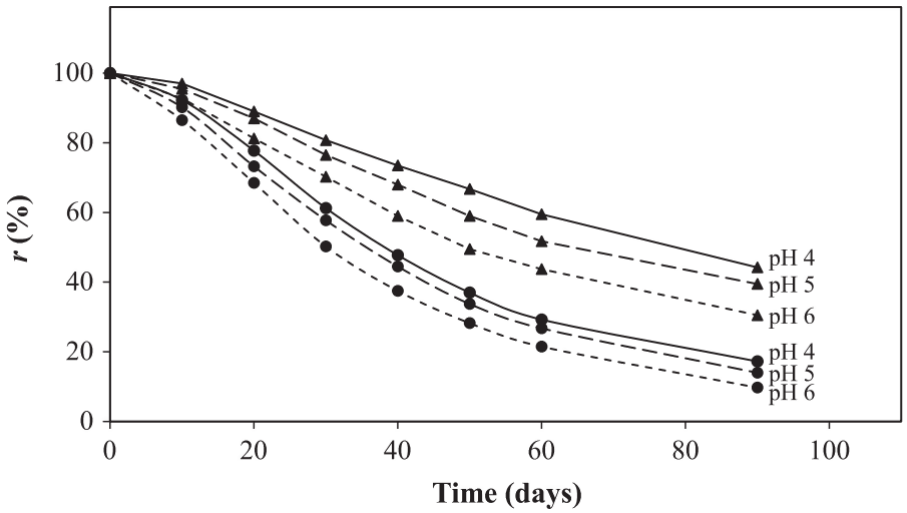

Figure 5 - Change in retention rate (r) of AA with time in two w/o cream formulations (●) and (▲) at pH 4–6 [14]

Improved stability for Vitamins in combination

Another research group found that combining different vitamins is about 2-fold more stable than Vitamin A by itself [18]. Vitamin A lost 15% of its content after 60 days and gained an additional 60 days totaling 120 days when combined with other vitamins.

Formulations containing vitamins, by themselves or in combination with other vitamins, presented different degradation kinetics for vitamins A, C and E. When these vitamins were combined in one formulation, their degradation rate was slightly lower than when they were individually used. The

shelf life of vitamins contained in combination was 120, 318 and 1,116 days for vitamin A, C and E, respectively. For single vitamins the values were 61, 173 and 757 for vitamin A, C and E, respectively. The same results were obtained experimentally in formulations maintained at room temperature, which validates the accelerated method employed for chemical stability determinations. [18]

Vitamin derivatives	**Shelf-life (days)**	
	Alone	In combination
Retinyl palmitate	61	120
Ascorbyl tetraisopalmitate	173	318
Tocopheryl acetate	757	1116

One of the studies provides evidence that shelf life of gel cream formulations with silicones containing combinations of vitamin A palmitate and vitamin E acetate were very low and that the addition of the antioxidant DL-alpha-tocopherol enhanced the period to 77 days. Other authors observed that the addition of antioxidants such as BHT, Ronoxan A®, alpha-tocopherol and glutathione increased the shelf life of formulations containing vitamin A palmitate [19].

In addition to the synergism in efficacy studies reported in the literature, the studies suggest positive interaction between the liposoluble vitamins A, C and E. As observed in the rheological study, combined vitamin derivatives did not alter the physical characteristics of the vehicle but rather enhanced the stability of the formulation by increasing the shelf life of each component. These results are consistent with the ones that observed a better stability of vitamins in combination [18].

Essential oils

Essential oils are often used in cosmetic formulations because of the wide spectrum of their biological activity, including anti-inflammatory, antibacterial and other skin effects. However, with a number of beneficial properties they also possess a number of risks for cosmetic formulations. The issue with essential oils is that they are often added in the form of a crude mixture which includes a wide range of single chemicals with different properties. Due to their structural relationship within the same chemical group, essential oil components are known to easily convert by oxidation, isomerization, cyclization, or dehydrogenation reactions, triggered either enzymatically or chemically. [20]

For instance, the main components of lavender oil are linalool and linalyl acetate, which are easily oxidized when exposed to oxygen. This happens when the oil is applied to the skin. The oxidized fragrance increases the irritancy on the skin. While freshly prepared cosmetic mixture contains unchanged components, long time storage will lead to degradation of delicate essential oil ingredients even when not exposed to oxygen.

Temperature, light, and oxygen availability are known to have a critical impact on essential oils integrity.

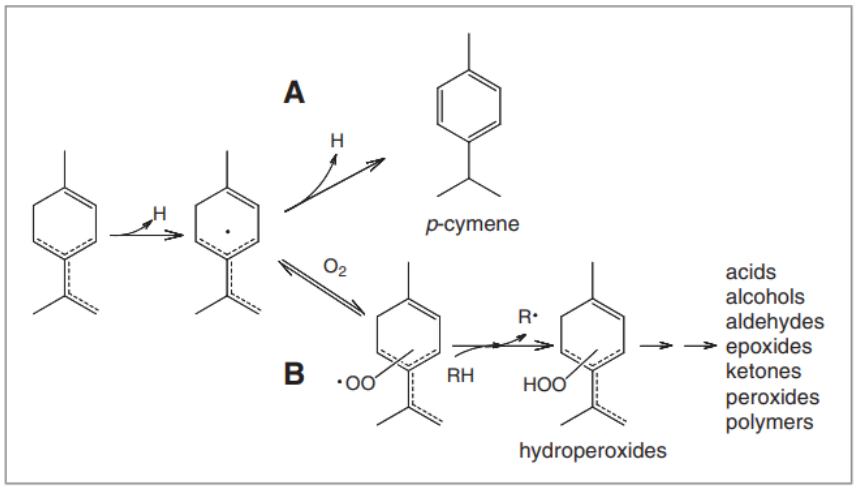

Figure 6 - Proposed oxidation scheme of terpenoids. (A) Dehydrogenation and possible hydrogen rearrangements. (B) Autoxidation pathway leading to hydroperoxides and subsequent degradation into secondary oxidation product [20]

Initiation	RH	→	R• + H•
	ROOH + RH	→	R• + H_2O + RO•
Propagation and branching	R• + $^3O_2$	→	ROO•
	ROO• + RH	→	ROOH + R•
	ROO• + R	→	ROOR•
	ROOR•	→	R>O + RO•
	RO• + RH	→	ROH + R•
	RO• + $^3O_2$	→	R'=O + HO_2•
	ROOH + ROO•	→	R'=O + HO• + ROOH
Termination	R• + R•	→	RR
	ROO• + R•	→	ROOR
	ROO• + ROO•	→	ROH + R'=O + $^3O_2$

Figure 7 - Main mechanism of autoxidation and some possible branching reactions [20]

Light. Ultraviolet (UV) light and visible (Vis) light are considered to accelerate autoxidation processes by triggering the hydrogen abstraction that results in the formation of alkyl radicals. However, compositional changes proceeded considerably faster when illumination was involved. Specifically, monoterpenes who have been shown to rapidly degrade under the effect of light. [20]

Very recently, Turek and Stintzing showed that essential oils were modified by the effect of light, however, varying by their source, the essential oils responded differently: While essential oil from thyme did not alter much, rosemary oil turned out to be very susceptible to imitated daylight which led to a change in its chemical composition [20].

Tea tree oil composition changed when exposed to oxygen, high temperature, light and humidity. The antioxidant compounds α-terpinene, ɣ-terpinene and terpinolene were converted to p-cymene. As it is sensitive to oxidation, the European Cosmetics Association recommended that the presence of tea tree oil in cosmetic products should not exceed 1% and that the product should be packed to minimize exposure to light [21].

Generally, standalone essential oils that are properly stored (low temperature, dark place) have a shelf life of about 2-3 years. When an essential oil is added to a cream formulation it is exposed to factors such as moisture, remaining oxygen and improper pH. Over time, these conditions degrade the essential oil and reduce its potency and could further cause irritation or an allergic reaction due to its effect on the formulation.

Peptides and proteins

It is well recognized that proteins and peptides in cosmetics provide a range of beneficial effects specifically in topical formulations. Collagen is the main fibrous protein of connective tissue in animals and is the most abundant protein in mammals. Collagen is used in a variety of products including skin and hair products. Most of the peptides used as ingredients in health-promoting foods, dietary supplements, pharmaceutical, and cosmeceutical preparations are obtained by chemical synthesis or by partial digestion of animal proteins. This makes them unattractive to consumers due to risks associated with solvent contamination or the use of animal derived substances. Plant and microalgae derived peptides are known to be selective, effective, safe, and well tolerated once consumed, thus they have a great potential for use in functional foods, drugs, and cosmetic products [22].

While there are a number of issues related to the use of animal, plant or synthetic peptides (animal origin, potential allergens, varying composition) they are thought to be relatively stable with no major chemical risks [23]. Peptide hydrolysis is thought to be one of the major degradation risks for peptides and proteins, but in cosmetic formulations this isn't thought to be a significant factor [24].

Hyaluronic acid

Hyaluronic acid is commonly used in cosmetic products. Hyaluronic acid (hyaluronan, HA) is a linear polysaccharide formed from disaccharide units containing N-acetyl-d-glucosamine and glucuronic acid. Its molecular mass can vary between 2 x 10^5 and 10 x 10^6 Da and its physiological properties are strongly influenced by its polymeric and polyelectrolyte character, as well as by the viscous nature of its solutions [25, 26, 27].

Degradation of hyaluronic acid as a single ingredient is well studied. Its decomposition is known to be induced by metal ions (more specifically copper), enzymatic hydrolysis, oxidation and elevated temperatures. Unfortunately, there is no sufficient evidence that shows how hyaluronic acid is degraded in cosmetic formulations [28].

Scientists have shown that Hyaluronic acid physically changes over time. Several formulations with different compositions, viscosity and other parameters were analyzed for their physical stability by Polish scientists using optical methods. They observed the migration phenomenon of particles in sample C (soft ointment with HA), and flocculation phenomenon in sample D (ointment based on lanolin). The samples lost their stability over time. Backscattering properties change with time was observed (see figure below) with major changes of physical properties at day 20. The authors concluded that manufacturers need to develop more stable mixtures or declare shorter shelf life. Apart from a 25°C temperature, it is not clear what conditions were used while storing the samples and it was not concluded how the potency changed over time [26].

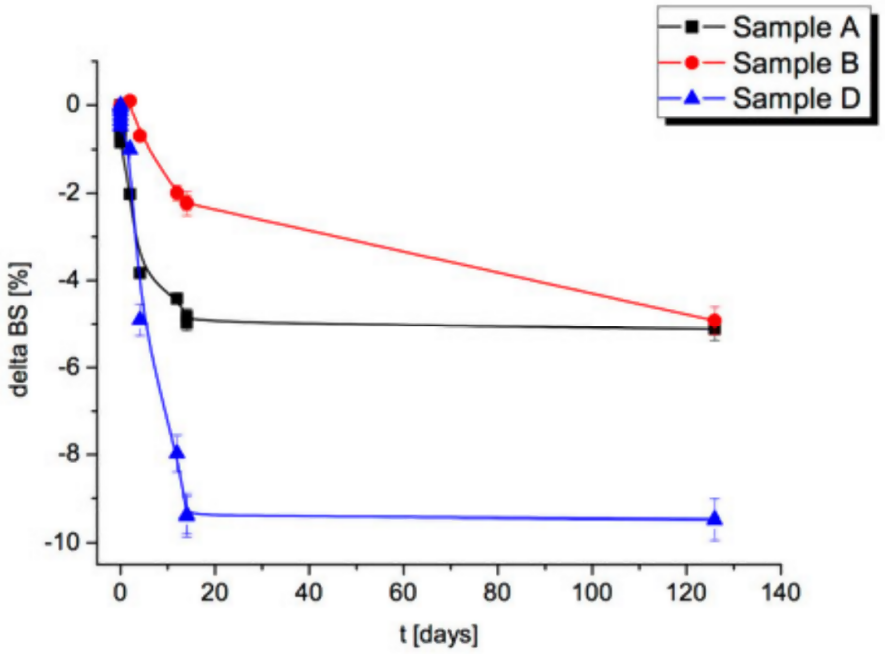

Figure 8 - Kinetics of flocculation for samples A, B and D [26]

Generally speaking, hyaluronic acid can be described as a relatively stable ingredient in cosmetic formulations but oxidation processes induced by other ingredients can lead to its decomposition.

Chemical incompatibility between ingredients

Chemical incompatibility between ingredients can lead to a decrease in product potency. The chemical incompatibility leads to changes in chemical nature, solubility, absorption and therapeutic response . Therefore, during the formulation of new products or the reformulation of existing ones, the interaction between active markers of various plant extracts and commonly used excipients should be carried out thoroughly. However, no universally accepted protocol is available for evaluating the compatibility of products with different excipients. Assessment of possible compatibility between an active component and different excipients along with the evaluation of thermal stability are crucial parts of a normal study prior to the final formulation.

The increasing interest in the use of plant-based formulations is leading to a fast-growing market for Ayurvedic, nutraceutical and polyherbal formulations. Unfortunately, the quality of a majority of them remains uncontrolled**.** Despite the advances in cosmetic chemistry which have allowed scientists to avoid many such issues, incompatibility can still occur for new and poorly studied ingredients such as kalmegh (*Andrographis paniculata*) and kutki (*Picrorhiza kurroa*) extracts in India. The study suggested that the active markers of kutki (kutkoside and picroside-I) were found to be degraded in the presence of the kalmegh extract [29].

Aloe Vera

Italian researchers studied the stability of Aloe Vera components responsible for biological activity. Namely, they examined the stability of beta-polysaccharides and aloin in common homemade preparations (grape brandy and honey) or commercial preparations with or without antioxidant (ascorbate, 0.05% or 0.005%) or antimicrobial agent (sodium azide or sodium benzoate). Samples were stored for 65 days in sealed glass tubes in the dark. Samples with added ascorbate were stored at +4 °C or +22 °C. The samples were analyzed at various time points using LC-MS/MS to measure anthraquinones and acemannan content (two components of aloin). Polysaccharides were measured by UV/Vis spectroscopy after binding with Congo Red dye. The times to decrease from 100% to 50% (DT_{50}) and to 10% (DT_{90}) were calculated. At room temperature, the aloin DT50 in whole leaf homogenate was 11-20 days, while at +4 °C the DT_{50} was 14-26 days. In the commercial preparation stored at +4 °C, the DT_{50} was 108 days and DT_{90} was 360 days. The beta-

polysaccharides were more unstable. In leaf gel at room temperature the DT_{50} was 2-3 days and DT_{90} was 7-10 days. In the commercial preparation the DT_{50} was 44 days at +4 °C and 12 days at 22 °C, and the DT_{90} was 148 days and 41 days, respectively. Thus, antimicrobial agents or antioxidants did not significantly affect the stability of the aloin or polysaccharides; however, temperature had a major effect. The commercial preparation was more stable, but still degraded even at +4 °C. [30]

Discussion and conclusions

According to the data collected above it is suggested that despite all advances in cosmetics chemistry, designing an effective, stable and attractive cosmetic product is still a challenge for manufacturers.

The most notable issue is related to the lack of chemical stability of active ingredients in cosmeceuticals. For example, Vitamin A, Vitamin C and essential oils are all easily degraded over time even when properly stored in tightly closed containers. A number of studies suggest that over time, active ingredients decompose by 50% or even more. The available scientific data provides evidence that product shelf life in a mixed form should be as minimal as possible otherwise ingredients potency is lost due to their decomposition.

Chemical degradation is a complex process and often induces a chain of unpredictable chemical reactions. With time, it is almost impossible to determine all of the produced chemicals. To date, no research describing how all ingredients react to time alongside their degradation rates has been conducted. The ingredients' behavior depends on many different factors. Scientific studies show that even minor factors such as viscosity and particle size in emulsion influence degradation processes.

Hydrolysis seems to be the main cause for the destruction of the active ingredients. This is due to the bi-phasic nature of the cream. O/w or w/o emulsions both contain water which harms ester bonds of vitamin derivatives.

Unfortunately, it is very difficult to completely remove oxygen from the emulsion as the reactive molecule is easily dissolved in water and oily phases. Therefore, though at a lower rate, oxidation can occur in containers that were never opened.

To increase product shelf life, manufacturers developed forms of vitamin A and E that are more stable to hydrolysis. However, despite the increased stability, such forms have lower bioavailability thus reducing their potency.

Environmental factors further influence the product before it reaches the consumer. Storage and transportation at elevated temperatures and humidity and/or exposure to light is harmful for cosmetic products as all accelerate chemical reaction rates. For some essential oils the reactions were accelerated by 70-fold when exposed to temperatures of 40-50 degrees Celsius. Furthermore, no oxygen is required to initiate autooxidation reactions in essential oils. Also, their exposure to light produces very reactive molecules that degrade other ingredients.

Another significant concern is the number of cosmetic product recalls. As summarized from regulatory bodies and independent laboratories, a large number of products was found to be contaminated by microbial bodies (or their products) or by excessive amounts of preservatives and their degradation products. Minor contaminations induce free radical reactions.

Some antioxidants that are meant as active ingredients for treatment can act as stabilizers for other ingredients due to inhibition of chemical oxidation that occurs in the formula.

It becomes apparent that by the time consumers receive their product, it is almost impossible to predict its chemical state and the amount of active ingredients present.

Ingredients incompatibility is not very common, but can occur when herbal ingredients are used. They tend to have a rich chemical composition. A common incompatibility factor is related to optimal pH levels between ingredients. The pH of the skin cream is important for its efficacy, and is often close to neutral value. The lower acidic pH allows for a better product conservation. Lower pH is also better for the stability of Vitamin A. pH changes over time and becomes another factor that induces decomposition. Long storage time can also lead to the release of NIAS (non-intentionally added substances) which introduces additional changes to product formulation and may increase the risk of toxicity.

It is also suggested that long storage time of hyaluronic acid or its exposure to hydrolysis or oxidation may significantly affect the product structure and viscosity which in turn can reduce its potency as well.

So, to summarize the conclusions:

- Cosmetic products include a number of very unstable ingredients. The potency of a cosmetic cream is significantly decreased due to degradation of its active ingredients over time. The less time the cream is in a mixed form prior to usage the more potent and less toxic it is. Vitamins A, C and essential oils are the least stable ingredients and will degrade first.
- Chemical degradation is a complex process producing a number of chemicals. Some of them may not only decrease product potency but also be toxic or allergenic. Over time, preservatives in a cosmetic emulsion can lead to significant microbial contamination.
- Manufacturers should find ways to improve their products, refraining from increased amounts of preservatives. Long storage in a mixed form results in a longer interaction period between all ingredients thus influencing its chemical stability. Product expiration should be from the day it was mixed (production date) rather than the day it is opened.
- Regulators are protecting consumers from unsafe products; however, they do not address products that lose quality over time. Consumers should be aware of the chemical instability and unpredictability of creams while in a mixed form and how time affects them.
- The most optimal scenario is to use a cosmetic product within 2 months after being mixed. If proper storage conditions are applied, product degradation, decrease in potency, and increase in toxins will be minimized.

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