# The role of volumetry, shape and primary packaging material in retinol stability

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## Abstract

Retinoids were introduced to treat skin disorders and their use in cosmetic products has gradually increased. However, there are some difficulties such as their stability in formulations, due to its high rate of degradation against oxygen, light and heat and its fat-soluble character. In this way, the present study aims to evaluate the stability of cosmetic formulation containing retinol in different types of packaging and to observe the impact of packaging alone in retinol protection. A gel cream containing 0.2% nanoencapsulated retinol was packaged in five types of packaging: plastic pump tube packaging 40g, plastic ophthalmic tube 40g, opaque glass pump bottle dispenser 30g, amber glass jar 40g and clear glass jar 100g. The samples were stored at 5°C, 23°C and 40°C for 90 days and retinol content was measured. More stable results were observed in the plastic pump tube packaging wtih above 80% retinol recovery in all conditions until the end of the 90 days. The lowest values were found for the amber glass jar packaging, which in 30 days at 40°C condition had only 41% of retinol recovery. The results indicate the relevance of packaging in the development of products containing retinoids, demonstrating that the shape, opening and volumetry of the packaging can significantly influence the preservation of retinol in the formula. The study intends to collaborate with the decision-making process in the development of cosmetic products containing retinoids, suggesting that adequate formula and packaging can bring better results in protecting retinoids over time.

**Keywords:** cosmetic; retinol; packaging; stability.

## Introduction.

The group of retinoids is formed by retinol (vitamin A) and its natural derivatives, such as retinal, retinoic acid and retinyl esters, and synthetic derivatives, such as adapalene and tazarotene [1]. As vitamin A cannot be synthesized by the body, it must be obtained through food in the forms of retinol esters and beta-carotene. Retinoids are fundamental to the organism and are involved in many biological processes: embryogenesis, reproduction, vision, anti-inflammation, growth, differentiation, proliferation and apoptosis [2,9].

In the 1970s, the use of retinoids for the treatment of skin disorders was introduced [3] and, since then, their use in cosmetic products has been gradually increasing. Because they act significantly in the processes of cell differentiation and proliferation, stimulate collagen type I and III and reduce the flattening of the dermo-epidermal junction, they are widely used by the cosmetic industry in products for cell renewal, peeling, wrinkle reduction, acne and blemish treatment [4,2,9].

However, there are some difficulties in the development of cosmetic products containing retinoids, such as their stability in formulation [5]. Due to its high degradation rate in the presence of oxygen, light and heat and its liposolubility, there are many restrictions regarding the formula and packaging, as well as specific care during the manufacturing and filling process. In view of this complexity, CATEC Technical Opinion nº 3 of March 22 TH 2002 determines that complementary tests must be presented to prove the chemical stability of the active in the final product, aiming at protecting consumer rights and their safety [6].

In order to reduce retinoid stability problems, several solutions have been developed over time: active delivery systems with application in cosmetic formulations such as nanoemulsions, liposomes, nanocapsules; packaging with air less system; factory production in a controlled environment, with lower incidence of light and exclusive reactor; modified atmosphere packaging [7,5,10,11]. Since factory adaptations are more expensive and often do not compensate the production volume, evaluating the combination of retinoids in a delivery system associated with the most appropriate packaging can be a faster and cheaper solution to enable the manufacture of this kind of product.

There are several studies demonstrating variations in the stability of retinoids in different formulations, but there are still few studies evaluating the impact of packaging on cosmetic products containing retinoids. Most articles address the stability of vitamin A (or retinol) in food products [8]. Thus, the objective of the present study is to evaluate the stability of cosmetic formulations containing retinol in different types of packaging and to observe the impact of packaging alone in protecting retinol.

**Materials and Methods**.

In laboratory scale, a gel cream was produced containing 0.2% nanoencapsulated retinol. The same batch of formulation was packaged in five types of packaging: 1) plastic pump tube packaging 40g in green polyethylene; 2) plastic ophthalmic tube 40g in green polyethylene; 3) opaque glass pump bottle dispenser 30g using post consumption glass; 4) amber glass jar 40g using post consumption glass; 5) clear glass jar 100g.

The samples were stored at 5°C, 23°C and 40°C for 90 days. Retinol content was measured using high performance liquid chromatography at 0, 30, 60 and 90 days. The chromatographic analysis was carried out using HPLC Agilent 1260 integrated system equipped with an automated injector, pump and multiwavelength diode-array detector (Agilent, Santa Clara, CA, USA). The chromatographic separation of the compounds was achieved with a reversed phase column, ECLIPSE XDB-C18 (4.6 mm × 150 mm, 5 μm) operating at constant temperature (30°C). The chromatographic data were analyzed using Agilent OpenLab. The compounds under study were identified by their retention times and their UV spectral characteristics. Chromatographic separation was obtained using a mobile

phase composed of isopropanol, metanol and 0,4% acetic acid pH 5,2 eluted in gradient mode.

**Results**.

More stable results were observed in the plastic pump tube packaging with above 80% retinol recovery in all conditions until the end of the 90 days. The lowest values were found for the amber glass jar packaging, which in 30 days at 40°C condition had only 41% of retinol recovery, reaching 2.97% in the same condition in 90 days. The other packages obtained intermediate results, reaching values above 34% or 50% in all conditions at the end of 90 days. For all packages the lowest results in retinol content are found in the 40°C condition, while the highest results are in 5°C.

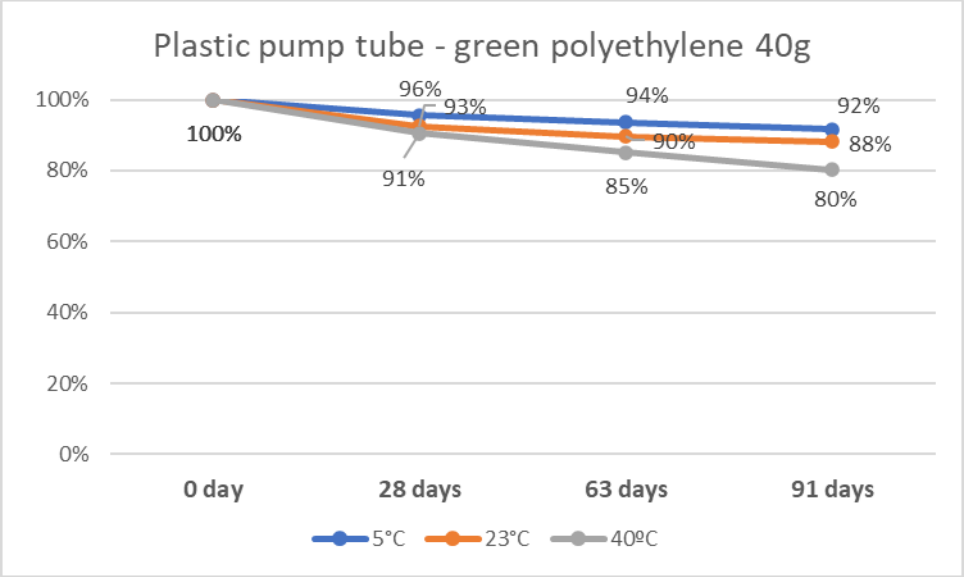


Figure 1 – Retinol recovery over 90 days under conditions of 5°C, 23°C and 40°C in plastic pump tube packaging.

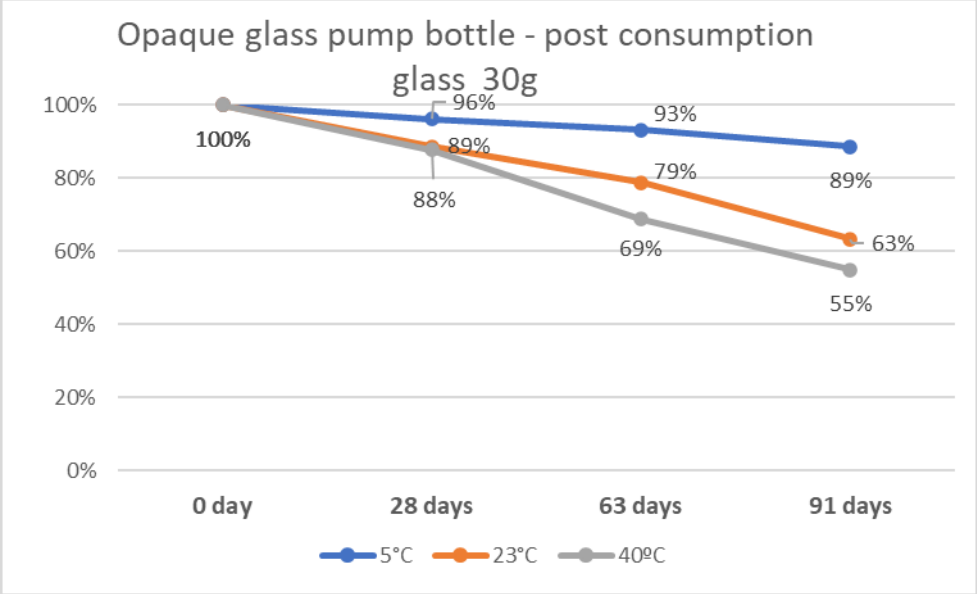


Figure 2 – Retinol recovery over 90 days under conditions of 5°C, 23°C and 40°C in opaque glass pump bottle packaging.

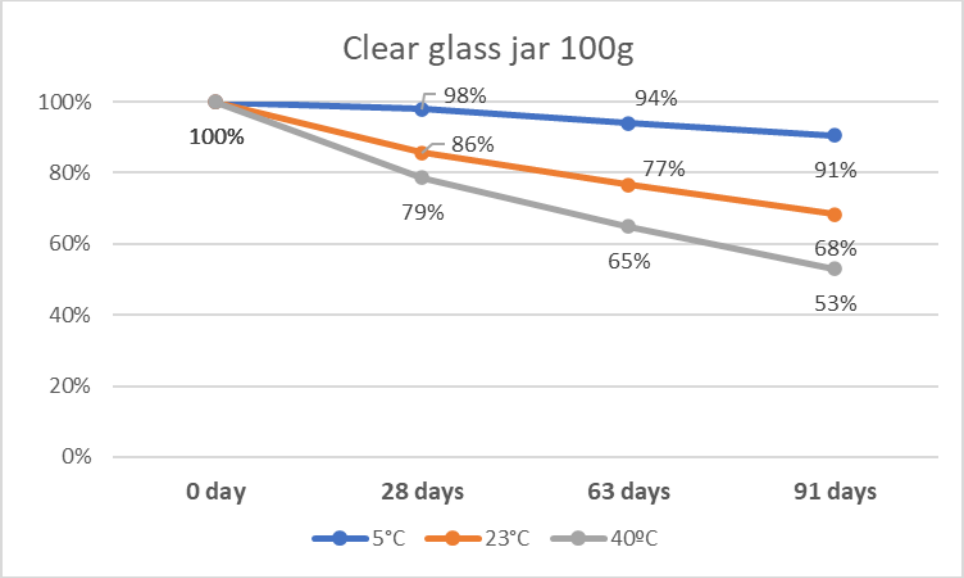


Figure 3 – Retinol recovery over 90 days under conditions of 5°C, 23°C and 40°C in clear glass jar packaging.

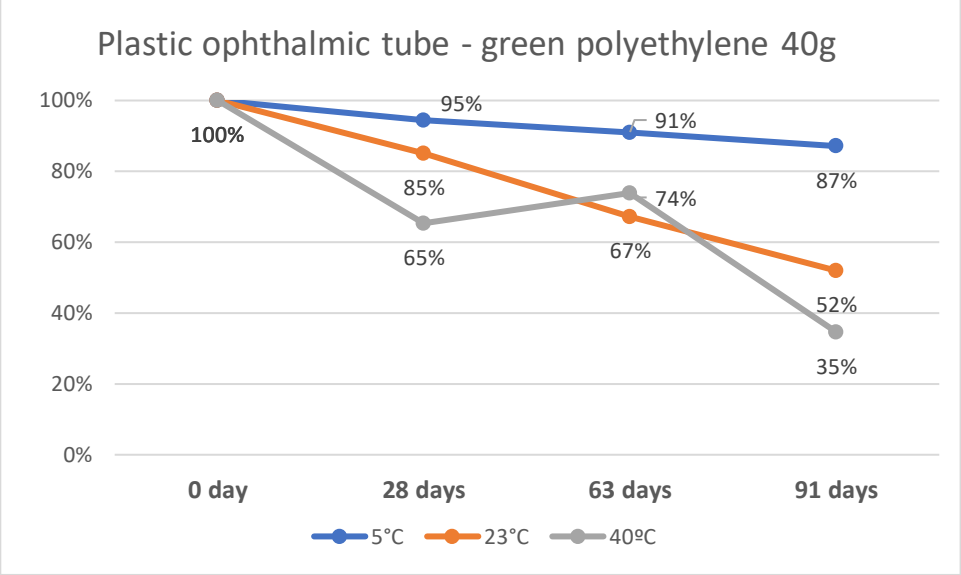


Figure 4 – Retinol recovery over 90 days under conditions of 5°C, 23°C and 40°C in plastic ophthalmic tube packaging.

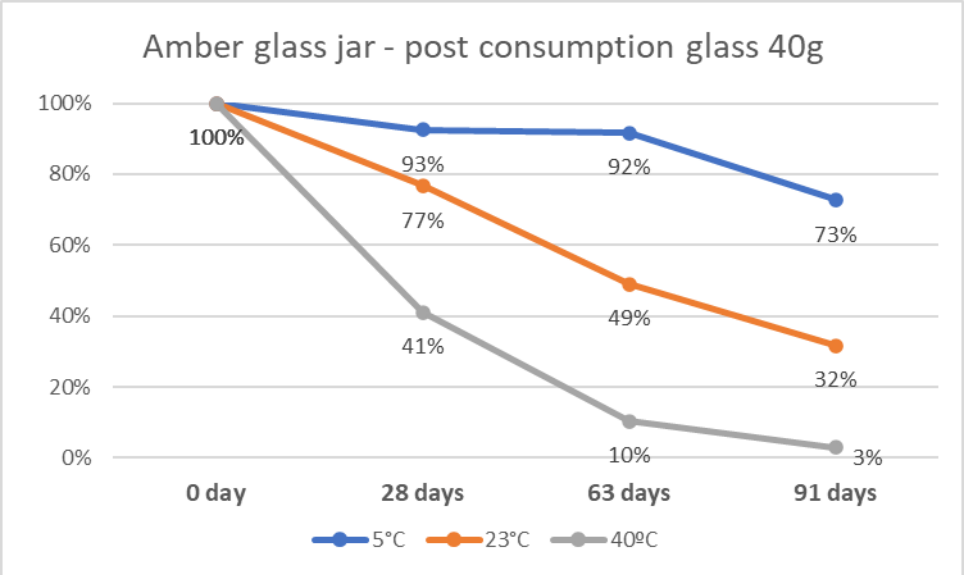


Figure 5 – Retinol recovery over 90 days under conditions of 5°C, 23°C and 40°C in amber glass jar packaging.

**Discussion.**

Based on the results, it is possible to observe the correlation of packaging with wider opening and smaller volumetry (40g jar) to lower results of retinol, while packaging with narrow opening and smaller volumes (tubes, pump bottle dispenser) had better results. This is mainly related to the greater exposure to oxygen in containers such as pot, which favors

the degradation of retinol [12,5] It is also interesting to note that despite being a clear 100g pot, the larger volume was positive for greater protection of retinol and the results obtained in this package are very close to the plastic ophthalmic tube and pump bottle. Thus, there are indications that larger amounts of bulk better preserve the retinol content over time, which may be an additional factor when choosing the product volumetry.

The formula was produced using nanoencapsulated retinol, which is recognized as a more stable version than free active [13,5,10,11,12] As retinoids in delivery systems are more used in the cosmetic industry, we use the active in this format to be closer to the market reality. A certain difference in the retinol content between the packages was expected, but the results were very far, reaching rates of 80% recovery after 90 days at 40°C in the plastic pump tube package, compared to 3% in the same period and condition in amber glass jar. The influence of the packaging on the protection of retinol is quite evident, especially in more extreme conditions.

For all packages the worst condition in retinol recovery was 40°C. Heat accelerates retinol degradation regardless of the type of packaging, although some of them (plastic pump tube) obtained much better values in this condition than others (amber glass jar).

The study also addresses the interaction of bulk with different packaging materials such as glass, polyethylene, green polyethylene. As they are more sustainable packaging and our first choice to utilize in final products, we prioritize the study with them. We expected that the glass could get better results, however the pot did not perform well in retinol measure. Despite being an inert material, the other packages also proved to be and the most relevant factors for the preservation of retinol in the product tend to be the shape, opening and volume of the package.

The results demonstrate the relevance of packaging in the development of products containing retinoids, demonstrating that the shape, opening and volumetry of the packaging can significantly influence the preservation of retinol in the formula, according to very different results obtained for each packaging.

As next steps we intend to test the bulk in other types of packaging, with different shapes and volumes, for example dropper and plastic pump bottle. In the future, the intention is to achieve favorable results of retinol content in glass or plastic jars, which are the most challenging packaging in terms of stability. In addition, we intend to test formulations with different textures and concentrations of retinol, observing their influence on the active stability. The tests aim to expand and make the retinoid products portfolio accessible, avoiding very specific manufacturing and packaging processes or very complex packaging.

## **Conclusion**.

The results presented not only demonstrate the influence of packaging on the preservation of retinol in the formula, but also draw attention to the importance of combining technologies to achieve better stability results, as an active in a delivery system associated with appropriate packaging in shape and volumetry. The study intends to collaborate with the decision-making process in the development of cosmetic products containing retinoids, suggesting that adequate formula and packaging can bring better results in protecting

retinoids over time, avoiding higher investments in specific manufacturing and packaging processes.

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**Conflict of Interest Statement**.

NONE.

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