DEVELOPMENT OF NANOEMULSION CONTAINING PUMPKIN SEED OIL AND MINOXIDIL

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Introduction

Androgenetic alopecia is characterized by progressive hair loss due to a genetic predisposition and an excessive response to androgens. This condition affects a large portion of the population, causing dissatisfaction with appearance, self-esteem, psychological discomfort, and even depression [1]. The need for effective treatments with fewer adverse effects demands the development of formulations that act directly on the mechanisms that cause alopecia, in a targeted manner on the scalp and with good skin penetration capacity.

Previous studies point to pumpkin seed oil as an interesting option, due to its antioxidant capacity and inhibitory activity of the 5α-reductase enzyme, making it a possible agent for the treatment of androgenetic alopecia [3].

Nanoemulsions are systems composed of small oil droplets dispersed in water, with dimensions on the nanometric scale between 20 and 200 nm. The small size of the droplets provides for prolonged release and rapid absorption of hydrophobic bioactive agents. In addition, nanoemulsions are kinetically stable systems, which makes them more resistant to coalescence and phase separation.[2].

In this context, this project aims to develop a nanoemulsion using pumpkin seed oil as the oil phase and carrying minoxidil sulfate.

Material and Methods

Oil-in-water (O/W) nanoemulsions were prepared based on the phase inversion temperature method. The oily phase containing pumpkin seed oil - PSO (Gran oils, obtained by cold pressing Cucurbita Pepo L seed oil) and binary mixtures of hydrophilic and lipophilic surfactants was homogenized in a vortex (Phoenix AP56) at a speed of 3.800 rpm for 2 minutes and heated to 60^0 C.

The aqueous phase was previously heated to 60^0 C and maintained at this temperature and then was slowly mixed in aliquots (5%), and between the inclusions of each aliquot, the mixture was vortexed at a speed of 3,800 rpm for 2 min. Each, until 80% of the aqueous phase is completed. Another part of cold water (4 °C) was then added and the system was quickly cooled to 4 °C in an ice bath under constant stirring to obtain a translucent O/W nanoemulsion.

Different mixtures of surfactants were tested to obtain the HLB value (hydrophilic-lipophilic balance) required by the oil. In this way, emulsions containing 5% oil and 5% surfactants were prepared. The surfactants were composed of a binary mixture of PEG 40 (Kolliphor® RH 40) and Span 80 (Span® 80) in proportions of 9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7, 2:8 and 1:9. The emulsions were observed for 15 days for visual aspects: homogeneity (non-phase separation, absence of cremation, absence of precipitates), translucent, transparent or milky appearance and viscosity and the emulsion that presented homogeneity was chosen to continue the experiment.

New formulations were prepared by varying the concentration of the PSO from 1 to 10% of the formulation. Again, the emulsions were observed for 15 days for visual aspects.

In addition to the visual aspects, measurements of the size of the nanoemulsion droplets (hydrodynamic diameter) were carried out and the polydispersity index (PDI) was measured by dynamic light scattering (DLS) with Zetasizer Pro-Blue, (Malvern Instruments, England, UK).

With the defined proportion of surfactants and PSO in the nanoemulsion, new batches were prepared by solubilizing 5% of minoxidil sulfate - MXS (Sonia Organics/India) in the oil phase before adding water. These formulations were comparatively evaluated for changes in visual aspects, nanoemulsion droplet size, and (PDI) measured by DLS.

Results and Discussion

Initially, formulations were prepared with PSO containing the isolated surfactants, Tween 80 (sorbitan monooleate), Tween 20, PEG 40, and Span 80 in proportions 1:1, PSO: surfactant. All formulations had a whitish appearance and at the end of 15 days, samples with Span 80 and PEG-40 still showed homogeneity characteristics.

From the choice of PEG-40, new mixtures in different proportions of PEG-40 and SPAN 80 were prepared, and after 15 days of preparation, it was observed by visual evaluation that the PEG/SPAN 5:5 emulsion (HLB = 8,7) was the one that showed homogeneity.

To determine the oil incorporation capacity, the proportions 8:2, 7:3, 6:4, and 5:5 (surfactants: OSA) were tested. It was verified that the formulation in the ratio 8:2 (surfactants: PSO), after 15 days, presented better quality in terms of homogeneity and translucent appearance with a bluish reflection, in addition, the DLS analysis showed a droplet size of 30.97 nm and PDI of 0.08686.

Minoxidil sulfate was incorporated into the formulation composed of 4% PEG-40, 4% Span 80, 2% PSO, and 90% water. The active ingredient was incorporated at a concentration of 5% (concentration used in commercial formulas) and homogenized in a vortex in the oily phase and the following steps were the same as those carried out in the formulations without MXS. It was verified, on day 15, that the formulation was homogeneous, with a translucent appearance and the DLS analysis showed a droplet size of 34.37 nm and PDI of 0.1238.

Conclusion

Minoxidil was successfully incorporated into a nanoemulsion with satisfactory properties. The droplet size of the manufactured nanoemulsion reached a value of 34.37 nm with adequate homogeneity. Thus, this study clarifies that an MXS-PSO nanoemulsion could be an effective nanoplatform, providing good solubility, and good release of MXS, and would also have the beneficial effects of PSO in synergy with pharmacological action of minoxidil in the treatment of androgenetic alopecia.

Acknowledgments

The authors would like to express appreciation for the support of the sponsors FAPERJ (E-26/210.915/2021) and CAPES (Finance Code 001).

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