ISSN 1984-5693
Vol.16, 2024,
http://dx.doi.org/10.22407/1984-5693.2024.v16.p.e20241612

Artigo de Revisão

APPROACHING ALOPECIA TREATMENT VIA POLYMERIC NANOPARTICLES

Perspectivas de tratamento da alopécia usando nanopartículas poliméricas

[1]Gabriela dos Santos David Ribeiro, [2]Anne Caroline da Silva Rocha, [*3]Lívia Rodrigues de Menezes

[1]Mestre em Ciências e Tecnologia de Polímeros, Universidade Federal do Rio de Janeiro, Instituto de Macromoléculas Professora Eloisa Mano, Rio de Janeiro, Brasil.

[2]Doutora em Ciências e Tecnologia de Polímeros, Universidade Federal do Rio de Janeiro, Centro de Tecnologia Mineral CETEM, Rio de Janeiro, Brasil.

[3]Doutora em Ciências e Tecnologia de Polímeros, Universidade Federal do Rio de Janeiro, Instituto de Macromoléculas Professora Eloisa Mano, Rio de Janeiro, Brasil.

Submetido em: 07.10.2024; Aceito em: 17.12.2024; Publicado em: 23.12.2024.

***Autor para correspondência:** liviarmenezes@ima.ufrj.br

Resumo: A queda capilar é uma realidade que assola muitas pessoas. Uma das causas da queda capilar mais comum atualmente é a alopécia androgênica, que se trata de uma miniaturização do folículo que ocorre de maneira progressiva. Após a pandemia da COVID-19, os casos de alopécia tiveram um aumento acentuado no número de casos registrados, indicando que a infecção causada pelo vírus SARS-CoV-2 possivelmente estimula a queda capilar decorrente do stress causado pela infecção, modificação no sistema imune e surgimento de microtrombos na região do folículo piloso. Existem no mercado alguns medicamentos de formulações bem estabelecidas com fármacos de conhecimento internacional, como, por exemplo, minoxidil, finasterida e espirinolactona, que já são utilizados para o tratamento da alopécia. Contudo, esses fármacos apresentam dificuldades para chegar até os folículos pilosos. Neste contexto, a veiculação de fármacos em nanopartículas poliméricas têm demonstrado ser uma estratégia promissora, sendo observada uma maior eficiência na vetorização desses ativos para o interior dos folículos pilosos, promovendo assim uma maior eficácia no tratamento da patologia em questão.

Palavras-chave: alopécia; nanopartículas poliméricas; perda capilar, folículos pilosos.

Abstract: Hair loss is a reality that plagues many people. One of the most common causes of hair loss today is androgenic alopecia, which is a progressive miniaturization of the follicle. After the COVID-19 pandemic, cases of alopecia had a sharp increase in the number of registered cases, indicating that an infection caused by the SARS-CoV-2 virus possibly stimulated a hair loss due to the stress caused by the infection, modification in the immune system and the emergence of microthrombi in the region of the hair follicle. There are some medicines in the market with drugs of international knowledge, such as minoxidil, finasteride and spirinolactone, which are already used for the treatment of alopecia. However, these drugs have difficulties in reaching the hair follicles, therefore, the delivery of drugs in polymeric nanoparticles has been shown to be a promising strategy, with greater efficiency in the vectorization of these assets into the interior of the hair follicles, thus promoting greater effectiveness in the treatment of the pathology in question.

Keywords: alopecia, polymeric nanoparticles, Hair loss, follicles.

INTRODUCTION

Human hair has gained a wide space in the scientific and esthetic fields and has been studied through the years due to its social and biological importance. Basically, the hair structure is made of two parts that are of extreme importance: the hair follicle and the hair fiber. The hair follicle (HF) is defined as the region of the skin where the hair fiber develops and is nourished, while the hair fiber is the hair strand itself (LLAMAS-MOLINA *et al.,* 2022).

There are many causes of hair loss and shedding (YORK *et al.,* 2020; WANG *et al.,* 2021; CHAN *et al.,* 2021; WALTER, 2022; SHIMOURA, 2023), but alopecia has gained prominence as a major cause. Alopecia can be defined as a disease that leads to the decrease or absence of hair in the human body. There are many kinds of alopecia, but three can be highlighted as more common: androgenetic alopecia, alopecia areata, and chemotherapy-induced alopecia (RAMBWAWASVIKA *et al.,* 2021).

ISSN 1984-5693
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The process of shedding and hair loss is directly linked to self-esteem, leading many people to experience self-image problems and depression (ALOMAISH *et al.*, 2022; VELASCO *et al.*, 2022). In recent years, these hair loss conditions have gained greater attention and relevance due to the significant increase in the number of cases of alopecia after the COVID-19 pandemic (FIVENSON, 2021; GENTILE, 2022; NGUYEN & TOSTI, 2022; ALAILAN *et al.*, 2023; KIM *et al.*, 2024).

There are different formulations for alopecia treatment available in the market. The formulations based on topical minoxidil and oral finasteride are the most common, due to the relatively satisfactory efficacy of these drugs. Moreover, these drugs are the only treatments for alopecia approved by the Food and Drug Administration (FDA) (OLIVEIRA *et al.*, 2020; GARCIA, 2023; AMUDIMEEGH *et al.*, 2024). Although they present good clinical prospects, one of the main obstacles regarding these treatments is the delivery of active ingredients into the hair follicle in adequate quantities for the treatment of alopecia. Thus, new studies have been developed to evaluate the use of polymeric nanoparticles to increase the effectiveness of treatments for alopecia (GLÓWKA *et al.*, 2014; ROQUE *et al.*, 2017; KIM *et al.*, 2019; JEONG *et al*., 2019; HAN *et al.*, 2022).

Hair follicle and hair fiber structure

The hair is a filament mainly constituted by dead and keratinized cells. In general, the hair structure consists of two parts: the hair follicle and the hair fiber. The hair follicle is responsible for producing the hair and also for its shape, while the hair fiber corresponds to the hair strands themselves (SCHLAKE, 2007; GRYMOWICZ *et al.*, 2020).

The hair follicle (HF) can be defined as the region of the skin in which the hair fiber develops and is nourished. Besides generating the hair fibers, the structure still works as an anchor for sensory neurons, arrector pili muscles, and blood vessels (LLAMAS-MOLINA *et al.*, 2022). The hair follicle's basic structure is composed of epithelial and mesenchymal cells (Figure 1). The epithelial cells are responsible for the growth of hair fiber. In general, these cells present a high proliferative capacity, and as they differentiate, they accumulate keratin in their cytoplasm until the entire cell is filled with this protein, leading the cells to apoptosis. The hair fiber is composed of this group of dead cells filled with keratin (BROWN; KRISHNAMURTH, 2022).

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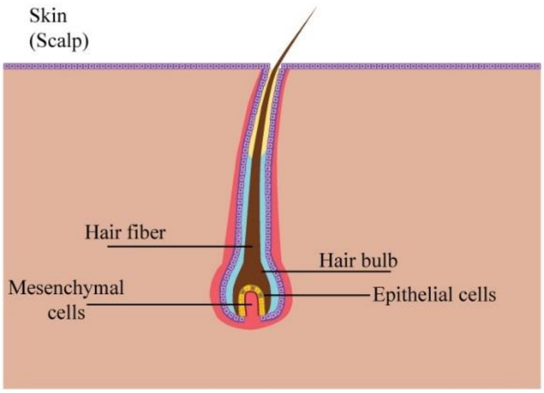

Figure 1. Schematic representation of the main structures interconnected to the capillary anatomy. Elaborado por Fernanda R. de Memezes.

Alopecia and its current treatments

Alopecia is a pathological change characterized by the decrease or loss of body hair. It is classified as an inflammatory disease that affects the hair follicle mainly in males and Caucasians, with 30% being men around 30 years old and 3% women in the same age range (VUJOVIC; DEL MARMOL, 2014). This clinical condition causes changes in parameters such as the number of hair follicles per unit area of skin, changes in hair follicle size, and the length of the hair growth cycle (RAMOS & MIOT, 2023).

Regarding the causes of alopecia, there is no well-defined information, but it involves a series of factors that describe the disease in specific types. Therefore, it can occur due to the malfunction of one or more signaling pathways, but also due to other factors, such as autoimmune diseases, genetic predisposition, and microbial infections (RISHIKAYSH *et al.*, 2014).

Recently, the incidence of alopecia has been increasingly prominent due to the important role of COVID-19 in the emergence of these hair loss conditions (FIVENSON, 2021; GENTILE, 2022; NGUYEN & TOSTI, 2022). In the last years, the world's population was devastated by the pandemic caused by the SARS-CoV-2 virus, which is characterized by a systemic infection whose repercussions include changes in the respiratory, cardiac, and nervous systems, as well as skin and ophthalmic repercussions and hair loss (GENTILE, 2022; REZAEIA *et al.*, 2022).

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Although the link between COVID-19 and alopecia has not yet been clearly established, it is confirmed that this link exists. Current literature indicates that COVID-19 infection may stimulate the onset of alopecia due to: (1) the stress resulting from infection by this virus, (2) the change of the immune system caused by the pathology, and (3) the appearance of microthrombi in the region of the hair follicle that can alter the local blood supply, leading to the weakening of the hair fiber. These factors may accelerate pre-existing alopecia cases or create new cases of the pathology, making hair loss more relevant in recent years (FLVENSON, 2021; GENTILE, 2022; NGUYEN & TOSTI, 2022).

Many treatment options were created to deal with the impacts caused by hair loss, among which the clinical applications of topical minoxidil and the use of oral finasteride stand out. These two drugs currently are the only treatments approved by the US Food and Drug Administration (FDA) due to their already proven clinical efficacy in the treatment of alopecia in its various presentations (RAMBWAWASVIKA *et al.*, 2021).

The studies demonstrated that the application of topical minoxidil increased the lifespan of keratinocytes (cells present in the epidermis), by improving the grouping of cysteine and glycine present in the hair follicle. Currently, topical minoxidil has international recognition and is accepted as the main treatment for men and women with alopecia (OLIVEIRA *et al.*, 2020; KIM *et al.*, 2022).

Finasteride, in turn, is a 5-alpha-reductase type 2 inhibitor, which prevents the conversion of testosterone into dihydrotestosterone (DHT) and, consequently, reduces the androgenic action that affects hair distribution in men. It should be noted that it does not reduce the physiological actions of testosterone, it only reduces DHT concentrations. Treatment with finasteride should be continuous without a defined end, as interruption results in the gradual progression of the issue (GARCIA, 2023; HU *et al.*, 2015). However, there is a contraindication for pregnant women, since its use can cause malformation in the fetus (KIM *et al.*, 2022).

Due to the still relatively low effectiveness of hair loss treatments, nanocarriers are currently being developed to increase the arrival of the drugs at the hair follicle, to possibilitate more efficient treatments in this sector.

ISSN 1984-5693
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Many compositions have been evaluated in the development of polymeric carriers that have been shown to be efficient in vectorizing drugs into hair follicles (GLÓWKA *et al.*, 2014; MATOS *et al.*, 2015; ROQUE *et al.*, 2017; KIM *et al.*, 2019; JEONG *et al.*, 2019; FERREIRA-NUNES *et al.*, 2021; HAN *et al.*, 2022).

Polymeric nanoparticles in the treatment of hair loss caused by alopecia

Composition and properties of nanoparticles for the treatment of alopecia

In recent years, nanoparticles (NPs) have attracted the attention of researchers and gained space in the scientific field as potential carriers of active ingredients in the treatment of hair loss (KIM *et al.*, 2019; JEONG *et al*., 2019; FERREIRA-NUNES *et al.*, 2021; HAN *et al.*, 2022).

Early on the NPs were obtained from non-biodegradable polymers such as polystyrene, polyacrylates, polyacrylamide, and poly(methyl methacrylate). However, these carriers had an undesirable effect, causing local inflammatory reactions which stimulated the development of studies of nanoparticles based on biodegradable and biocompatible matrices that became the main focus of the last decade (PEREIRA *et al.*, 2018).

The polymers highlighted in these studies are chitosan (CS), albumin, gelatin, and alginate, acquired from natural sources, and synthetically produced poly(ε-caprolactone) (PCL), copolymers of poly(lactic-co-glycolic acid) (PLGA) and poly(lactic acid) (PLA). To better understand the panorama of current research in this sector, a more extensive survey was carried out on publications in this sector over the last 10 years, using the Google Scholar repository as a search source. For this survey, the word “alopecia” combined with the terms “polymeric nanoparticles”, “polymeric nanocarrier" and, “polymeric nanocapsules” were used as keywords. This survey excluded articles that had the term review in their title or abstract, to keep only research articles on obtaining and/or applying particles in the treatment of alopecia in the survey.

The inclusion or exclusion of search terms for article mining was performed using the platform's own advanced search tools. The results of this survey (Figure 2) show the use of natural polymers stands out when compared to synthetic ones, although the latter still represents the focus of 42.3% of the research published and present in the repository researched.

ISSN 1984-5693
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Regarding polymeric matrices, chitosan stands out as the most used material in the development of nanoparticles for the treatment of alopecia. Next, we have PLGA and albumin as the second and third most evaluated materials in this sector.

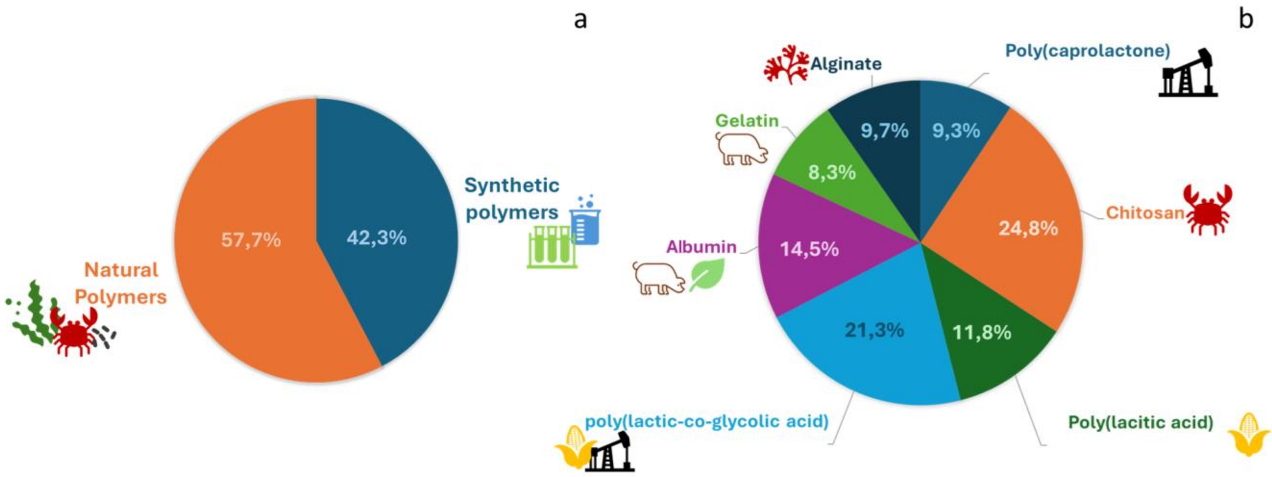

Figure 2. Results of the bibliometric survey on the (a) classes and (b) types of polymers most commonly used in the production of polymeric carriers for the treatment of alopecia. Survey carried out in the Google Academic database - Years 2014 to 2024.

The hair follicles are regions of interest in the release of active ingredients in the cutaneous region, whether in the hair region or the body hair region. The interest in this region, especially regarding the application of nanoformulations, is due to the fact that nanocarriers tend to accumulate in hair follicles, which serve as a long-term reservoir for trans or percutaneous release.

This aspect indicates that nanoformulations are promising options in the development of formulations for alopecia since these carriers tend to vectorize to the region of interest (hair follicles). It has already been demonstrated that nanocarriers can be stored in the follicular reservoir for up to 10 days (LADEMAN *et al.*, 2006; LADEMAN *et al.*, 2007).

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Many formulations have been evaluated in the literature and the results show that particles with dimensions smaller than 3 μm can permeate the region of the hair follicles, with better permeation when these carriers reach dimensions smaller than 750 nm (GÖKÇE, GÜNGÖR; 2020). However, when it comes to reaching the deeper regions of the hair follicles, nanocarriers with dimensions between 200-300 nm presented superior effectiveness and tend to accumulate effectively inside the hair follicles, reducing the percutaneous transposition of these particles (GÖKÇE; GÜNGÖR, 2020; CARDOSO *et al.*, 2021).

Studies regarding the applicability of polymeric nanoparticles in hair loss treatment

Based on the above, Glówka and collaborators (2014) evaluated the production of PCL nanoparticles, via emulsion evaporation, containing roxithromycin (ROX) at different concentrations. The drug used is an antibiotic usually applied to skin infections, which had its use expanded to hair loss after studies showed its ability to inhibit the apoptosis of hair bulb cells. The particles obtained were evaluated by dynamic light scattering (DLS), scanning electron microscopy (SEM), and zeta potential (ZP).

As a result, the authors observed the formation of monodispersed particles with negative ZP particles (from – 3 mV to – 8 mV), smooth and irregular surfaces and a spherical morphology with diameters between 270 and 390 nm. The ZP of the various formulations had no significant differences between them and were not high enough to prevent the aggregation of nanoparticles due to electrostatic repulsions. Regarding the average particle size, it was observed that the particle diameter decreased with the increase in drug concentration, although this behavior was not expected. In this study, specifically such evidence is linked to the different concentrations of polymers in the dispersed phase. In this case, according to the authors, the blank sample had a larger particle diameter resulting in an increase in viscosity and formation of larger particles in comparison to the samples that had different drug concentrations (GLÓWKA *et al.*, 2014).

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Matos and collaborators (2015) evaluated the use of chitosan (CS) nanoparticles for releasing minoxidil sulfate (MS) which is a drug largely used in hair loss treatment. As such, the authors obtained CS nanoparticles cross-linked with tripolyphosphate (TPP) using the ionic gelatinization method. Initially, the authors evaluated the impact of three drug concentrations (10%, 20%, and 30%) on the properties of size, polydispersity index (PDI), ZP, and retention efficiency (RE) of the nanoparticle. Based on the results, the authors verified the formation of particles with strongly positive ZP (from +32 to +47 mV) with particle diameters between 230 and 280 nm and a monomodal polydispersity profile. Regarding the effect of MS and its concentration on particle size, the authors reported no significant changes in the systems regarding their size and PDI. In addition, it was observed that the increase in MS concentration generated a decrease in the retention efficiency of the systems and the ZP modulus. The decrease in ZP observed is possibly due to free drug in the external phase of the particle suspension, since its structure is rich in oxygenated groups that ionize negatively in an aqueous environment. The RE decrease, in turn, reflects the saturation of the systems. Also, regarding the permeation into the hair follicles (HF), after in vitro analysis using pig ear skin, the authors confirmed the presence of nanoparticles in the HF, confirming the arrival of the carriers in the regions of interest, its maximum content being found after 6 hours of permeation.

Roque and collaborators (2017) evaluated the obtaining of PLGA charged with the drug finasteride through the emulsion-evaporation technique using Poloxamer 188 as a surfactant. The drug used in this study is traditionally used in hair loss using an oral administration route, and the authors evaluated the possibility of its topical application through its nanoencapsulation. The authors obtained PLGA particles without the drug and particles containing 10% of finasteride for comparison. After obtaining the systems, they were evaluated regarding size and particle geometry, ZP, RE, release profile, and permeation in an artificial membrane that simulates the scalp.

The results indicated the formation of spherical particles with diameters of 185.3 ± 9.3 nm for particles without the drug and 316.5 ± 14.4 nm for particles charged with finasteride; for both formulations, a ZP of -5 mV was found. The particles presented high RE (79.49%) and showed a modified release profile for up to 3 hours of release, with a faster release in the first 1.5 hours of release (release speed of 0.84%/min), followed by a slower release until completing the 3 hours of release (release speed of 0.28%/min).

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http://dx.doi.org/10.22407/1984-5693.2024.v16.p.e20241612

For the permeation test, a poly(dimethylsiloxane) membrane that simulates the scalp was used and the particles were transported in suspension, in the form of shampoo and lotion. The results of the permeation test showed the capacity of the particles to remain in the membranes for up to 24 hours and indicated that the use of shampoo delivery is what provides the highest permeate content (ROQUE *et al.*, 2017).

Kim and collaborators (2019) studied the obtaining of poly(γ-Glutamic Acid) (PGA)/Chitosan (CS) hydrogel nanoparticles with fermented herbal extract via ionic gelatinization to enhance hair growth. The drug that stayed inside the PGSA/CS matrix was a mix of fermented herbal extract (4HGF) which presents significant anti-inflammatory activity and considerable relevance for promoting hair growth. Initially, the particles were characterized by SEM and transmission electron microscopy (TEM). With the microscopy results, the authors were able to observe the formation of particles with spherical morphology and rough surface with a size of approximately 300 nm for the PGA/CS particles and 400 nm for the PGA/CS-4HGF sample. According to the authors, the increase in the diameter of the particles can be related to the volume occupied by the extract inside the particles. Additionally, the authors highlighted that the presence of the extract increased the roughness of the particle surface which may result from the presence of the extract on the surface during the drying process.

Regarding the ZP of the systems, the authors observed the formation of particles with +12.15 ± 8.91 for the PGA/PCL sample and +16.99 ± 1.23 for the PGA/CS-4HGF system, in which the positive charge comes from the NH_2 groups of the CS that ionize positively. As for the retention efficiency, the authors highlighted that the retained active was around 49%, which may reflect the cruder composition of the herbal extract, where different partition coefficients of the constituents may lead to the predominance of some of them in the aqueous phase. The formulations obtained by the authors were able to permeate the hair follicles of the pig skin, indicating that the systems are promising for the increase in hair growth (KIM *et al.*, 2019).

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Jeong and collaborators (2019) evaluated the topical administration of PLGA particles with minoxidil (MXD), using both uncoated particles and particles coated with hyaluronic acid (HA). The authors used a water/oil/water type double emulsion method for obtaining these particles. The nanoparticles were characterized via DLS, TEM, and ZP to determine the size and dispersion of the particles, their morphology, and surface potential. As for results, the authors obtained spherical particles with average sizes of 159 ± 12 nm (PDI: 0.074) for PLGA particles with MXD (PLGA/MXD NPs) and 243 ± 44 nm (PDI: 0.182) for PLGA and MXD particles coated with HA (HA-PLGA/MXD NPs). The increase in particle diameter upon particle coverage was expected and reflects the formation of the HA layer around the particles. Furthermore, according to the authors, even with an increase in the PDI of the system containing HA, systems with a low polydispersity index were obtained for both formulations, which, together with the sizes below 300 nm, indicate that were obtained systems with suitable sizes for topical administration of MXD. The authors also evaluated the ZP of the systems, and based on the results, it was observed that the PLGA/MXD NPs had a -0.4 mV zeta potential and the HA-PLGA/MXD NPs, in turn, presented a ZP of – 43.2 mV.

The HA-coated particles were also characterized regarding their cytocompatibility with the fibroblast lineage and their ability to permeate rat skin. The results obtained by the authors showed high cell viability of fibroblasts when in contact with concentrations of up to 200 μg/ml of HA-PLGA/MXD NPs, which indicated high cytocompatibility of these systems. Finally, the authors evaluated the permeation of the obtained particles and showed that the HA-PLGA/MXD particles were able to permeate the skin, tending to concentrate in the outermost region of the skin (stratum corneum) and inside the hair follicles (JEONG *et al.*, 2019).

Ferreira-Nunes and collaborators (2021) studied the properties of both poly(caprolactone) (PCL) and Eudragit® L100 nanoparticles for the alopecia treatment with the incorporation of the drug spironolactone. The nanoparticles were prepared using the nanoprecipitation technique and, after preliminary studies, the authors set the drug content at 10 mg for all formulations, varying the concentration of the PCL polymer (126 mg and 180 mg). In the formulations based on Eudragit L100 (EL), the authors used 102 mg of the polymeric matrix. For all systems, formulations with and without the drug were obtained and all experimental conditions of nanoprecipitation were fixed for all systems.

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The systems obtained were initially characterized by DLS, ZP, and UV-Vis spectroscopy to evaluate the retention efficiency. The results indicate that particles smaller than 200 nm with a low polydispersity index (between 0.07 and 0.16 PDI) and high RE (between 74 and 88%) were obtained for all formulations evaluated. The nanoparticles were also evaluated regarding their release profile, irritability to the skin tissue, and permeation capacity in the region of hair follicles. Based on the results, the authors were able to observe that the particles presented a sustained release for up to 12 hours, a period in which the NPs release only about 30 to 40% of the total drug incorporated in the systems. Regarding the composition of the systems, neither the change in the encapsulation polymeric matrix nor the change in the concentration of PCL caused big changes in the release profile. Regarding skin irritability, no system showed potential for skin irritation, which makes them promising for topical application. In addition, regarding the permeation into the hair follicle, the authors observed that the encapsulated samples led to more efficient permeations than the free active (FERREIRA-NUNES *et al.*, 2021).

Han and collaborators (2022) studied the development of PLGA nanoparticles charged with Minoxidil (MXD) through double emulsion. According to the results, the authors were able to determine the formation of spherical nanoparticles of 124.1 ± 1.3 nm for nanoparticles obtained by double emulsion without the drug (DE-NPs), and 137.8 ± 0.8 nm for particles containing minoxidil (MXD-DE-NPs), indicating a slight increase of the carrier size after the drug inclusion. Based on an animal model, a deep permeation capacity of the nanoparticles through the hair follicles of mice was proven, as well as a satisfactory hair growth effect in mice after three weeks. In comparison to traditional MXD formula systems with ethanol and propylene glycol, the particles exhibited similar hair growth capabilities without the need for ethanol, which can dry out and irritate the scalp (HAN *et al.*, 2022).

Matos and collaborators, 2023 evaluated the use of two different carriers, polymeric and lipid nanoparticles, for the simultaneous encapsulation of minoxidil and betamethasone and compared the follicular drug delivery provided by topical application of each of these formulations. The polymeric nanoparticles were obtained by nanoprecipitation using PCL as a polymeric matrix and tween 80 as the surfactant of the system. The obtained nanoparticles presented a monodispersed size distribution profile and low polydispersity indices for both the formulation containing only PCL (0.04 PDI) and the formulation containing the drugs (0.18 PDI).

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Regarding size and potential, the formation of particles with strongly negative surface potentials of -32 to -20 mV and nanometric particle diameters that ranged from about 270 nm for the drug-free formulation to about 400 nm for the drug-containing formulation was observed. The retention efficiency of both actives was highly satisfactory, specifically 99.1 ± 13.0% for minoxidil and 70.2 ± 12.8% for betamethasone which explains the large change in size suffered by these carriers.

Regarding the lipid nanoparticles, the authors used a microemulsion technique based on stearic acid and oleic acid (organic phase) and tween 80 as a surfactant. These systems presented higher polydispersity indices than the polymeric nanoparticles (0.23 PDI). As for the size of the nanoparticles, the system without the drug presented similar sizes to those of the polymeric formulation (around 270 nm). The formulation containing the drug, in turn, showed larger sizes (around 560 nm) than the polymeric system. The retention efficiency of these lipid carriers was 99.4 ± 0.1 for the minoxidil and 80.7 ± 0.1% for betamethasone, with bigger retentions of betamethasone than those observed for the polymeric particles (MATOS *et al.*, 2023).

*In vitro p*ermeation studies with porcine skin, polymeric nanoparticles provided a 2.6-fold increase in minoxidil penetration into the hair follicle region when compared to the free drug. Regarding the betamethasone penetration, no significant change was observed when compared to the free drug. In turn, the lipid carriers provided a 10-fold increase in minoxidil penetration into hair follicles and led to slightly higher betamethasone concentrations when compared to the free drug. Due to the good permeation of both carriers, the authors concluded that both polymeric and lipid nanoparticles were effective in increasing the permeation of Minoxidil into the hair follicle region but highlighted that in the context of the study carried out, the lipid particles showed superior performance (MATOS *et al.*, 2023).

Conclusions

Based on the survey carried out in the present study, it can be observed that alopecia cases lead to hair reduction or loss and represent a significant problem, mainly from the perspective of their psychological impacts on their sufferers. Recent studies aim to improve treatment effectiveness, and its demand has increased significantly due to the influence of the SARS-Cov-2 virus, which plays an important role in the activation, maintenance, and increase the severity of alopecia.

In this scenario, some drugs are showing great promise in the treatment of alopecia, but their effectiveness in treatment still faces the main obstacle of reaching the region of interest for treatment, the hair follicles. In this sense, some studies were found regarding the use of polymeric NPs for vectorization of active ingredients to hair follicles, aiming at the treatment of alopecia.

The studies present in the current literature are promising, with some of them demonstrating efficiency in this vectorization process to the hair follicle region. The evaluated articles indicate as a current trend the main use of biodegradable polymers due to their satisfactory biocompatibility properties. Finally, the authors indicate that it is necessary to use particles with sizes between 200 nm and 300 nm to guarantee the effectiveness of the drug vectorization to the interior of the hair follicles.

FUNDING INFORMATION

The authors would like to thank the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) for financial support - Financial edital E26/211.665/2021 (269591) – E_27/2021 – AUXÍLIO BÁSICO À PESQUISA (APQ1) EM ICTs SEDIADAS NO ESTADO DO RIO DE JANEIRO – 2021 and Financial edital E26/210.045/2024 (290330) – E_07/2023 – PROGRAMA DE APOIO À JOVEM CIENTISTA MULHER COM VÍNCULO EM ICTS DO ESTADO DO RJ - 2023.

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ISSN 1984-5693
Vol.16, 2024,
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