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Development of minoxidil nanocrystals for follicular delivery

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Drugs formulated as nanocrystals exhibit special features such as increased saturation solubility and dissolution velocity, resulting in increased bioavailability. For dermal application, yet another feature can be exploited: the fact that particles with a size bellow 700 nm have the potential of follicular targeting [1-3]. In the case of topical application of minoxidil, a nanocrystal formulation would not only allow targeting to the follicle but also create an alternative to the currently marketed formulations containing a high concentratrion of ethanol and/or propilene glycol. Therefore, in this study, the development of minoxidil nanocrystals for topical application was investigated.

Minoxidil powder (donation from Flamma S.p.A., Italy) was dispersed in various 1% stabilizer solutions, e.g. TPGS, Plantacare 2000 UP, Poloxamer 407 and Plantacare 810 UP, and processed by high pressure homogenization (HPH) using an LAB 40 (APV Deutschland GmbH, Germany). Additionally, selected formulations were processed by bead milling using a PML-2 (Bühler AG, Switzerland). Zeta potential and particle size were assessed by laser Doppler anemometry and photon correlation spectroscopy (PCS) using a Zetasizer Nano ZS (Malvern Instruments, UK) and light microscopy (LM).

Minoxidil is being used topically to treat hair loss. Because it is poorly soluble in water, the formulations on the market are ethanolic solutions, which can be irritative to the scalp. Besides, after evaporation of ethanol, minoxidil might re-crystallize, limiting its dermal penetration. For the production of a minoxidil aqueous nanosuspension, two production methods were investigated: high pressure homogenization (HPH) and wet bead milling. The particle sizes achieved by HPH were all around 1,400 nm. The best result was obtained for the stabilizer Plantacare 2000 UP after 15 HPH cycles (1,428 nm). But this size is still not sufficiently small. When this same formulation was processed by bead milling, after only 5 minutes milling, the particle size was already 330 nm and polydispersity index was 0.18. Longer processing did not further reduce the particle size, on the contrary, the nanosuspension destabilized and aggregated. These results were all confirmed by light microscopy.

The industrially feasible wet bead milling proved to be the best production method. Sufficiently small minoxidil nananocrystals in aqueous medium for follicular targeting could be successfully produced. By adapting the milling time, different sizes between 1000 nm and 330 nm can be produced, allowing optimization of nanocrystal size for follicular targeting.

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