Nanomilling of poorly soluble drugs for encapsulation in sebum-like microparticles – a new approach for follicle targeting

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With a prevalence of 80% among Western European adolescents, acne vulgaris is one of the most common skin deseases involving the sebaceous gland and hair follicle. Benzoyl peroxide (BPO) as an OTC monotherapeutic or prescription combination product with retinoids or antibiotics plays a key role in topical acne therapy despite its undesirable side effects such as itching, dehydration to the point of scaling and erythema of the skin, and discoloration of clothing on treated skin areas. Formulation concepts to minimize undesirable effects that often lead to premature discontinuation of treatment take into account the combination of BPO with refatting substances and 'moisturizers', encapsulation of BPO with delayed release of active ingredient and/or specific 'targeting' of the sebaceous gland and hair follicle. Targeting of the sebaceous gland and upper infundibulum of the hair follicle is successful with particles in the micrometer range of 3 to 10 µm while nanoparticulate structures can reach the lower part of the hair follicle. In addition to polymer-based microstructures for encapsulation of BPO, lipid-based microparticles of the size range mentioned above, in which BPO is dipersed in nanoparticulate form, are also suitable, while adapalene as a lipid affinity retinoid is present solubilized in the lipid-based microparticle without risk of oxidation by BPO. Nanomilling of BPO and/or other poorly soluble drugs such as griseofulvin is only successful as wet milling in a liposomal dispersion to avoid the risk of explosion in the case of highly reactive BPO and to efficiently stabilize the wet-milled nanoparticles of griseofulvin with a phospholipid coating against particle growth. For incorporation of wet-milled nanoparticles into a lipid matrix, prior freeze-drying of the nanosuspension is required. Upon contact of the loaded microparticles with sebum, the microparticles erode and release the active ingredients, whereas upon contact with lipids of the stratum corneum lipids, no such interaction occurs and the microparticles remain intact. Thus undesirable side effects of topical BPO treatment are successfully minimized.

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