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Topic: Hair and nail disorders

Clascoterone and androgenic alopecia: mechanistic rationale and therapeutic potential

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Introduction
Androgenetic alopecia (AGA), the most common form of non-scarring hair loss in both men and women, is characterized by progressive miniaturization of terminal hair follicles into vellus follicles. AGA is determined by genetic predisposition and increased follicle sensitivity to androgens, especially dihydrotestosterone (DHT). Despite being non-life-threatening condition, it can profoundly impact self-esteem and quality of life. Current treatment - minoxidil and 5α-reductase inhibitors - have limited efficacy. Clascoterone, a topical androgen receptor (AR) antagonist approved for the treatment of acne, may offer a novel therapeutic option for AGA based on its mechanism of action. This review evaluates the biological and mechanistic rationale for clascoterone as a potential AGA treatment, based on its pharmacology and current understanding of AGA pathophysiology.

Materials and Methods
A narrative review was performed, including previously published review articles on clascoterone and its potential application in AGA. Literature searches were conducted in PubMed, Embase, and Cochrane Library using relevant keywords related to clascoterone and AGA. A total of 8 articles met the inclusion criteria and were analyzed in this review. Two reviewers independently conducted the eligibility assessment and data extraction

Results
Clascoterone is a selective, locally active AR antagonist that competitively binds to cytoplasmic ARs in sebocytes and hair follicles, thereby reducing DHT-induced signaling. In vitro studies have shown that clascoterone competes with DHT for AR binding in sebocytes and exhibits a higher affinity for these receptors than DHT, leading to effective inhibition of androgen-regulated gene transcription. This results in decreased sebum production, lower levels of proinflammatory cytokines, and reduced dermal inflammation. This mechanism is biologically relevant to AGA, in which excessive AR activation contributes to progressive hair follicle miniaturization. Clascoterone is rapidly metabolized to an inactive form, limiting systemic exposure, and clinical data from acne studies indicate minimal systemic effects.

Conclusions
Based on its mechanism of action as a selective, locally active AR antagonist, clascoterone represents a new therapeutic approach for AGA. Its ability to competitively inhibit DHT-mediated AR signaling in hair follicles, combined with rapid local metabolism and minimal systemic exposure observed in acne studies, supports its potential suitability for a topical use in AGA. Although clinical trials on clascoterone for AGA have been conducted, results are not yet publicly available, preventing definitive conclusions on efficacy and safety. Nevertheless, there is a need for further studies to confirm its effectiveness and long-term safety in patients with AGA.