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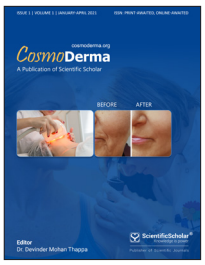

Focus

Exploring tazarotene's role in dermatology

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Received: 26 October 2024
Accepted: 03 December 2024
Published: 30 January 2025

DOI
10.25259/CSDM_179_2024

Quick Response Code:

INTRODUCTION

Topical forms of Vitamin A have been widely used since 1971. Topical retinoids are either natural or synthetic. Adapalene, tazarotene, and bexarotene are synthetic retinoids and have different chemical structures, making it more challenging for the metabolic pathway.[1] Tazarotene is an acetylenic synthetic retinoid introduced in 1997 and has a different chemical structure than other retinoids. It does not occur naturally and is approved by the United States of Food and Drug Administration (US FDA) for acne vulgaris, psoriasis, and photodamaged.[1]

STRUCTURE

Tazarotene is a synthetic retinoid and has a different structure when compared to other retinoids. It has a rigid ring-locked structure that gives limited conformational flexibility [Figure 1a].

MECHANISM OF ACTION

Tazarotene is a prodrug that is rapidly hydrolyzed in tissue to an active metabolite termed *tazarotenic acid*. Tazarotenic acid is retinoic acid receptor-specific (RAR-α, β, γ). It has a high selectivity for RAR-γ receptor, RAR-β. The predominant type of RAR expressed in the human epidermis, indicating that it may be an important mediator of retinoid action in the skin. But does not have any affinity for retinoid X receptors (RXRs).[2]

By binding to different RAR, tazarotenic acid modulates the expression of retinoid-responsive genes including:

1. Regulation of cell proliferation, cell differentiation, and inflammation
2. It downregulates the abnormal expression of keratinocyte transglutaminase 1 (Tgase 1), epidermal growth factor receptor, involucrin, skin-derived antileukoproteinase (SKALP), small praline-rich protein 2 expression, and hyperproliferative keratins K6 and K16
3. Tazarotene also induces the tazarotene-inducible gene-1,2,3 (TIG), which reduces keratinocyte proliferation and atypical keratinocytes[3]
4. Suppression of activation of the activator protein 1, which results in reduced expression of several matrix metalloproteinases from keratinocytes, which are increased in acne vulgaris
5. Decreased expression of toll-like receptor (TLR) 2 and decrease in ligand binding with *Propionibacterium acnes*, which results in inhibition of the TLR-2-induced innate response that triggers inflammation in acne[4] [Figure 1b].

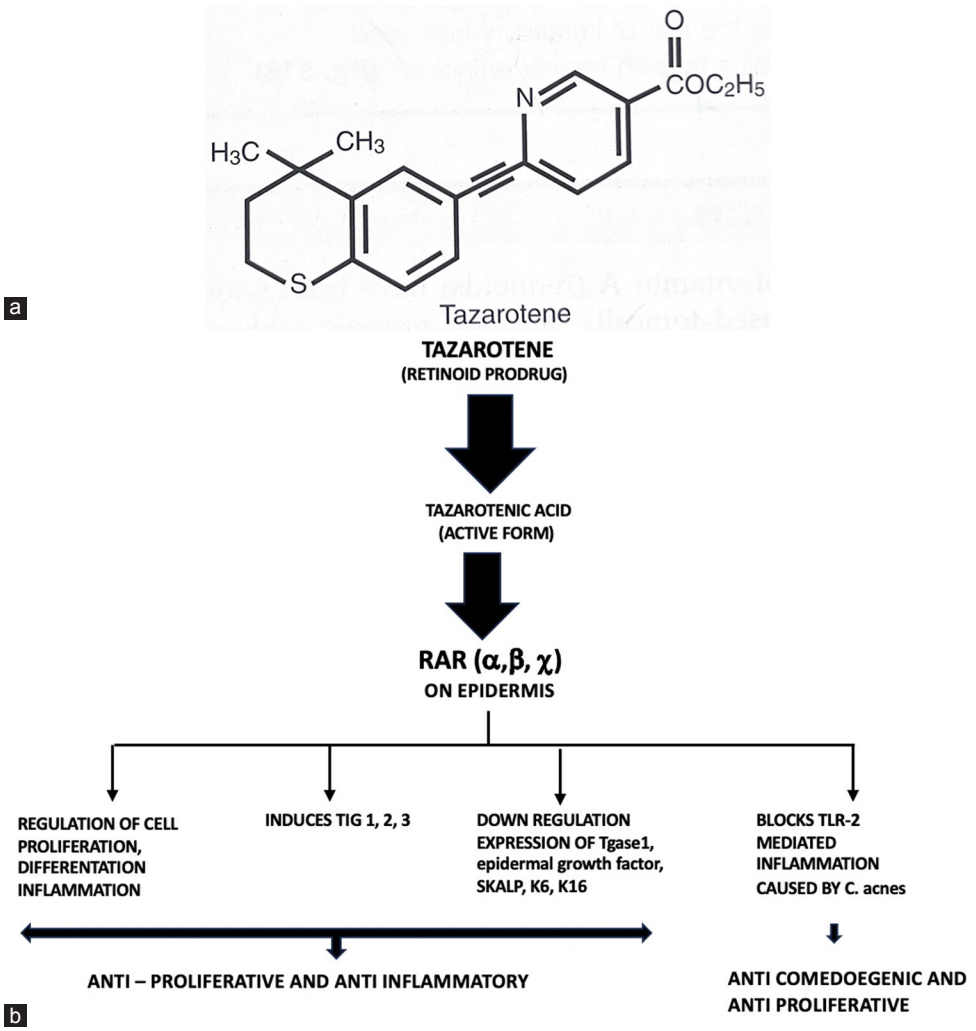

Figure 1: (a) Structure of tazarotene, (b) Mechanism of action of tazarotene. RAR: Retinoid acid receptor, TIG: Tazarotene inducible genes, TLR: Toll like receptor, Tgase1: Transglutaminase 1, SKALP: Skin derived antileukoproteinase, K6, K16: Hyperproliferative keratins keratin 6, keratin 16.

PHARMACOKINETICS

1. Half-life is <20 min
2. Maximum concentration of Tazarotenic acid is by 9 h
3. The terminal half-life of tazarotenic acid is approximately 18 h
4. Total systemic absorption is 5% in normal skin and 15% in psoriatic skin
5. Degradation by oxidation to inactive sulfoxide and sulfone derivatives that are excreted in the urine, feces, and skin desquamation.[1]

INDICATIONS

FDA approved

1. Chronic plaque psoriasis
2. Acne vulgaris
3. Photodamaged skin.[5]

Off-label indications

1. Seborrheic keratosis (SKs)
2. Atrophic scar
3. Mycosis fungoides
4. Hyperpigmentation
5. Genodermatosis (Lamellar Ichthyosis, Erythrokeratoderma variabilis)
6. Keratosis pilaris.

Contraindications

1. Pregnancy
2. Hypersensitivity to tazarotene or the vehicle

3. Eczematous skin
4. Sunburn
5. Exposure to extreme weather

Composition

It is available in
1. 0.05% cream and gel[6,7]
2. 0.1% gel, cream, and foam[1,4]
3. 0.045 % lotion and foam[4]

EFFICACY OF TAZAROTENE IN DERMATOLOGY

Role of tazarotene in psoriasis

1. The study by Weinstein *et al*. found that tazarotene creams (0.05% and 0.1%), when applied once daily, were significantly more effective than a placebo in reducing the severity of plaque psoriasis. The 0.1% concentration showed the greatest clinical improvement. Both formulations demonstrated sustained therapeutic effects for up to 12 weeks after treatment. The creams were well-tolerated and generally safe, with minimal side effects, supporting their use in psoriasis treatment.[6]
2. Lebwohl *et al*. explored the effects of combining tazarotene 0.1% gel with topical corticosteroids for treating psoriasis which resulted in significantly greater reductions in scaling, redness, and overall lesion severity compared to tazarotene with placebo. Additionally, the combination therapy led to fewer local side effects like irritation. Overall, the study concluded that combining tazarotene with corticosteroids enhances effectiveness while reducing adverse reactions.[8]
3. Combining narrow band ultraviolet B therapy (NB-UVB) therapy with topical tazarotene 0.05% gel significantly improves psoriasis treatment by accelerating clearance, reducing the number of treatment sessions, and lowering the overall cumulative NB-UVB dose. This combination therapy is well-tolerated and effective, particularly for patients with treatment-resistant plaque psoriasis.[9]

Role of tazarotene in acne

1. Only the 0.1% strength is approved by the US FDA for the treatment of acne. Cream 0.1% is indicated for acne vulgaris, and gel 0.1% is indicated for mild-to-moderate acne vulgaris
2. A study done by Swaroop showed that tazarotene 0.1% gel is a better anti-comedogenic agent with a rapid rate of clinical improvement when compared to adapalene 0.1% gel. The efficacy of both topical agents is similar for inflammatory lesions (papules and pustules).[7]
3. Tanghetti *et al*. concluded in their study that a once-daily application of 0.045% tazarotene helped in the reduction of moderate-to-severe acne and decreased patient-perceived oiliness.[10]

In photodamaged skin

Chronic sun exposure can lead to photodamage, which can present as fine and coarse wrinkles, sallowness, laxity, dyspigmentation, and tactile roughness.[11]

This study assessed the effects of tazarotene 0.1% cream on photodamaged skin. Over 24 weeks, tazarotene resulted in significant improvements compared to the vehicle, including reduced cell abnormalities in the epidermis and melanocytes, increased skin thickness and polarity, and a trend toward stratum corneum compaction. In addition, it caused widened intercellular spaces (epidermal edema). Overall, tazarotene effectively improved the structure of photodamaged skin and reduced cellular irregularities.[12]

Tazarotene in SKs

SKs are benign epidermal neoplasms presenting as waxy, brown-to-black papules and plaques. Patients often seek removal for cosmetic reasons or irritation. Twice daily application of 0.1% tazarotene cream caused remarkable clinical and histopathological correlation.[13]

Tazarotene in mycosis fungoides

Mycosis fungoides is an uncommon skin lymphoma with tumor node metastasis, early-stage shown to have a better prognosis. Topical treatments are first-line treatments in patch/plaque disease (Stage IA, IB, II A).[14]

This open-label study by Besner *et al*., evaluated topical tazarotene as monotherapy for early-stage cutaneous T-cell lymphoma, specifically stages IA to IIA, in 10 patients. After 6 months of treatment, 60% of patients achieved a complete response (CR), with a mean time to CR of 3.8 months. Reductions in erythema, scaling, and lesion size were observed, and 83% of responders maintained CR for at least 6 months. The treatment was well-tolerated, with no disease progression in non-responders.[15]

Tazarotene in hyperpigmentation

Tazarotene also led to improvements in hyperpigmentation, an inflammation-associated sequela of acne. Tazarotene 0.045% lotion was safe and well tolerated, with no application-site irritation or dermatitis after 12 weeks of once-daily treatment.[16]

Effects of tazarotene in genodermatoses

1. Type I lamellar ichthyosis improved by tazarotene 0.1% gel in a 30-year-old woman with type I lamellar ichthyosis is reported. The drug was applied to 15% of the total body surface area as follows: once daily for 2 weeks, 3 times a week for a further 2 weeks, followed by a once-weekly maintenance application. During the 1st week of treatment, a reduction of scaling on treated areas was observed. After 4 months of maintenance application, there was a marked overall improvement in the treated areas.[17]
2. Application of tazarotene 0.1% cream for a short contact period in case of linear Dariers disease showed improvement with minimal side effects within 4 weeks.[18]
3. Erythrokeratoderma variabilis, also known as Mendes da Costa syndrome, is a genodermatosis characterized by well demarcated, variable, transient, figurate patches of erythema, and localized or generalized hyperkeratotic plaques. In a case report, a child with erythrokeratoderma variabilis with no family history of this entity was successfully treated with topical tazarotene after no improvement with conventional treatment.[19]

USES OF TAZAROTENE IN OTHER CONDITIONS

1. Confluent and reticulated papillomatosis of Gougerot and Carteaud is an uncommon dermatosis of unclear cause that can be recalcitrant to therapy. A case report of an 11-year-old girl with an eruption that was completely cleared using tazarotene gel which was well tolerated.[20]
2. Keratoderma blennorrhagicum, a manifestation of Reiter's disease which responded well to tazarotene 0.1% gel after being obstinate to other treatments.[21]
3. A randomized, placebo-controlled study showed that tazarotene 0.05% cream significantly improved pruritus, erythema, and roughness in keratosis pilaris on the posterior arms, proving it effective and well tolerated.[22]

ADVERSE EFFECTS

1. Mild-to-moderate local irritation
2. Erythema as seen with the "retinization period"
3. Peeling.[23]

SAFETY PROFILE

1. First, percutaneous penetration is limited, with <6% of the applied drug being absorbed into the bloodstream
2. Second, tazarotene and its metabolites are not lipophilic, hence, minimal systemic absorption. Hence, it has more of cutaneous effects
3. They are rapidly eliminated from the blood in the urine and feces
4. The risk of teratogenic effects is minimal
5. Overall, tazarotene has a good safety profile and is not associated with contact sensitization, phototoxicity, photoallergic reactions, mutagenicity, or carcinogenicity.[24]

CONCLUSION

Tazarotene topical is a type of retinoid derived from vitamin A that is available as a cream, gel, lotion, or foam. It is used in the treatment of inflammatory dermatoses or to improve the appearance and texture of skin. Combining it with other therapies could boost effectiveness and reduce side effects. Advances in delivery systems could reduce irritation, and its potential in anti-aging, systemic inflammatory diseases, and even cancer therapies warrant further exploration. Overall, while tazarotene may not be the first-line option for every dermatological condition, it can be a valuable treatment option in certain cases, particularly when other treatments have been ineffective or when used off-label for specific indications.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent is not required, as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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How to cite this article: Bhagyashree M, Bukke P, Matety AR. Exploring tazarotene's role in dermatology. CosmoDerma. 2025;5:19. doi: 10.25259/CSDM_179_2024