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Review Article

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Dapsone in Dermatology: Mechanisms of Action, Clinical Indications, and Safety Monitoring - A Contemporary Review

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Abstract

Dapsone is a synthetic sulfone first developed in the early twentieth century and later recognized for its antimicrobial and anti-inflammatory properties. Although licensed primarily for the treatment of leprosy and dermatitis herpetiformis, its immunomodulatory effects have led to widespread off-label use in dermatology, particularly in neutrophilic and eosinophilic dermatoses. This review summarizes the pharmacologic mechanisms of dapsone, outlines its current dermatologic indications, discusses dosing strategies, and provides an updated overview of adverse effects and monitoring recommendations. Understanding its therapeutic potential and safety profile is essential for optimized patient selection and risk mitigation.

Keywords: Dapsone, Neutrophilic and Eosinophilic Dermatoses

1. Introduction

Dapsone (diaminodiphenyl sulfone) was first synthesized in 1908 during the development of sulfonamide derivatives for industrial use [1]. Its antibacterial properties were identified in the 1930s, leading to its introduction into clinical practice, particularly for the treatment of leprosy [2]. Over time, its role expanded significantly in dermatology due to its potent anti-inflammatory and immunomodulatory effects [3].

While the United States Food and Drug Administration (FDA) formally approves dapsone for leprosy and dermatitis herpetiformis, its off-label applications now encompass a broad spectrum of inflammatory and autoimmune dermatologic disorders. Its clinical utility is particularly notable in diseases characterized by neutrophilic or eosinophilic infiltration [4].

This review provides a comprehensive overview of dapsone's pharmacologic mechanisms, dermatologic indications, dosing considerations, adverse effect profile, and recommended monitoring strategies.

2. Pharmacologic Mechanisms of Action

Dapsone exerts both antimicrobial and anti-inflammatory effects, making it unique among dermatologic agents.

2.1. Antimicrobial Activity

Dapsone functions similarly to sulfonamides by competitively inhibiting dihydropteroate synthase, thereby disrupting dihydrofolic acid synthesis. This impairs nucleic acid production and inhibits microbial proliferation. This mechanism underlies its historical use in leprosy and other infectious dermatoses [5].

2.2. Anti-inflammatory and Immunomodulatory Effects

The anti-inflammatory properties of dapsone are central to its dermatologic applications.

i. Neutrophil Modulation

Dapsone:

- Inhibits neutrophil chemotaxis
- Suppresses myeloperoxidase-mediated oxidative burst [6,7]
- Reduces generation of reactive oxygen species [8]
- Inhibits beta-2 integrin (CD11b/CD18)-mediated neutrophil adhesion [9]

By suppressing the neutrophil respiratory burst, dapsone reduces tissue damage in neutrophil-mediated dermatoses.

ii. Cytokine Suppression

Dapsone downregulates pro-inflammatory cytokines including:

- Interleukin-8 (IL-8) [10]
- Tumor necrosis factor-alpha (TNF-α) [11]

IL-8 plays a central role in neutrophil recruitment and activation, making its inhibition particularly relevant in pustular and vasculitic disorders.

iii. Eosinophil and Monocyte Effects

Because myeloperoxidase is present in eosinophils and monocytes, dapsone demonstrates efficacy in eosinophilic dermatoses such as:

- Eosinophilic cellulitis
- Eosinophilic annular erythema

iv. Complement Pathway Inhibition

In vitro studies suggest inhibition of the alternative complement pathway, further contributing to its anti-inflammatory effects [7].

The principal antimicrobial and immunomodulatory mechanisms of dapsone are summarized in Figure 1.

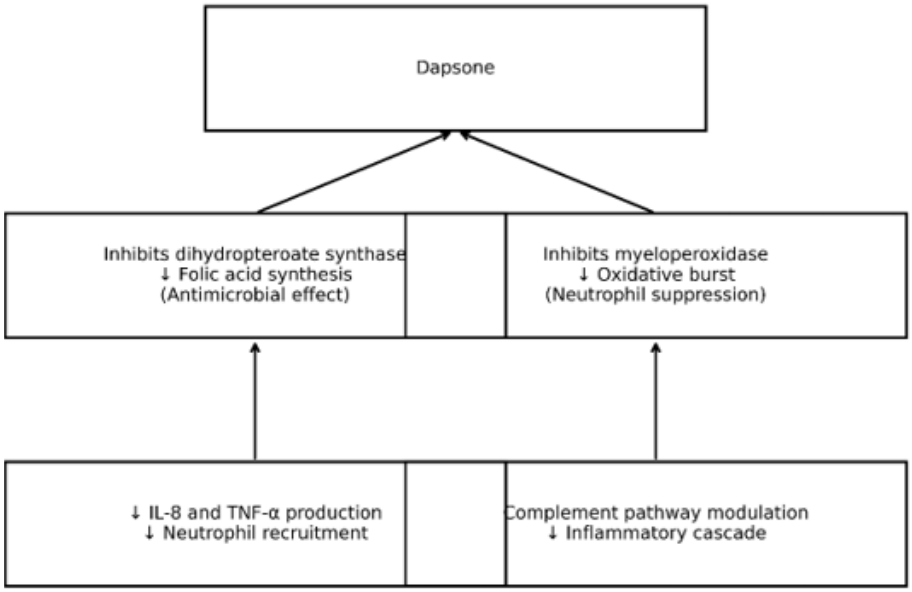

Figure 1: Mechanisms of Action of Dapsone in Dermatologic Disease

Dapsone exerts antimicrobial effects through inhibition of dihydropteroate synthase and suppresses inflammation by inhibiting myeloperoxidase-mediated oxidative burst, reducing IL-8 and TNF-α production, and modulating the complement pathway.

3. Clinical Indications in Dermatology

Dapsone is primarily used in conditions characterized by neutrophilic or eosinophilic inflammation [3,6,12].

3.1. First-Line Indications

Condition	Role of Dapsone
Dermatitis herpetiformis	First-line therapy
Leprosy	Core component of multidrug therapy
Linear IgA dermatosis	First-line
IgA pemphigus	First-line
Subcorneal pustular dermatosis	First-line
Erythema elevatum et diutinum	First-line
Cicatricial pemphigoid	First-line or steroid-sparing

Table 1: Dermatologic Indications for Dapsone

3.2. Adjunctive or Off-Label Indications

Condition	Role
Bullous pemphigoid	Adjunctive
Pemphigus vulgaris	Steroid-sparing
Cutaneous lupus erythematosus	Adjunctive
Sweet syndrome	Adjunctive
Pyoderma gangrenosum	Adjunctive
Neutrophilic urticarial dermatosis	Adjunctive
Hidradenitis suppurativa	Adjunctive
Granuloma annulare	Select cases

Table 2: Adjunctive and Off-Label Dermatologic Indications for Dapsone

Its benefit is most evident in diseases with neutrophilic dermal infiltration.

A practical clinical framework for identifying appropriate candidates for dapsone therapy is outlined in Figure 2.

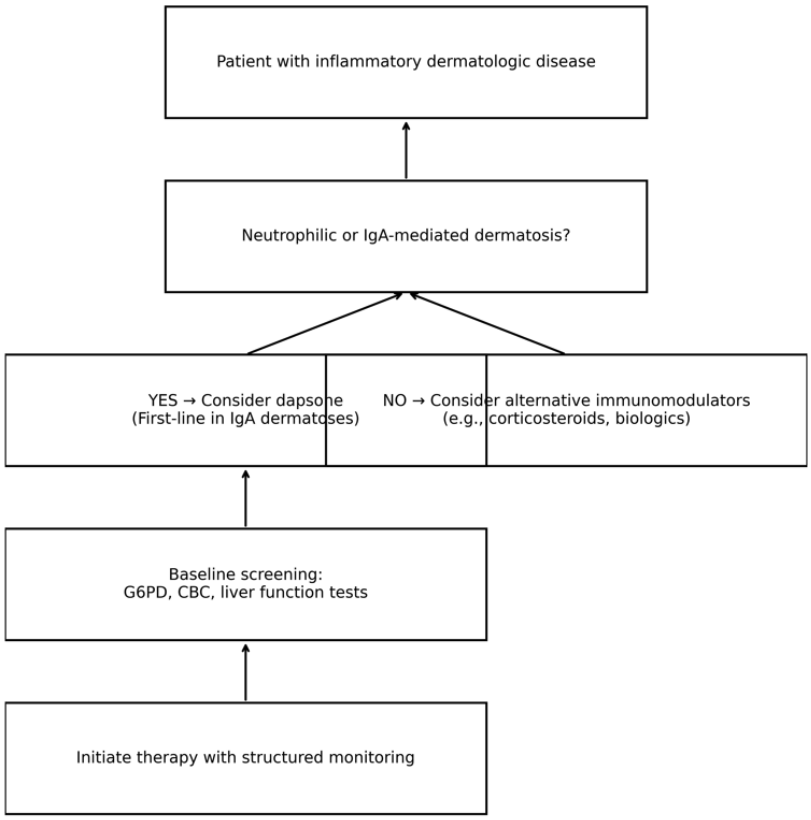

Figure 2: Clinical Decision Framework for Considering Dapsone Therapy in Dermatologic Disease

Dapsone should be considered primarily in neutrophilic and IgA-mediated dermatoses. Appropriate baseline screening, including glucose-6-phosphate dehydrogenase testing and laboratory monitoring, is essential prior to initiation.

4. Dosing and Administration

Dosing must be individualized and titrated according to clinical response and tolerability.

4.1. Adults

- Initial dose: 50–100 mg daily
- Dose escalation: May increase to 150–300 mg daily
- Reassessment: After 4–6 weeks
- Maintenance: Lowest effective dose

Higher doses require careful laboratory monitoring [6,12].

4.2. Treatment Duration

Duration depends on disease type and response. Some conditions require prolonged maintenance therapy.

5. Adverse Effects

Dapsone's adverse effects are dose-dependent and may be predictable (hematologic) or idiosyncratic.

5.1. Hematologic Effects

- Hemolytic anemia (dose-related)
- Methemoglobinemia
- Agranulocytosis (rare but potentially fatal)
- Aplastic anemia

Hemolysis is more pronounced in individuals with G6PD deficiency [5,13].

5.2. Dapsone Hypersensitivity Syndrome (DHS)

A rare but severe reaction characterized by:

- Fever
- Rash
- Lymphadenopathy
- Hepatitis

Onset typically occurs within 4–6 weeks of initiation.

5.3. Neurologic Effects

- Peripheral neuropathy (rare, usually high-dose)

5.4. Hepatic Effects

- Elevated transaminases
- Hepatitis (rare)

Absolute contraindications include prior dapsone hypersensitivity or severe hematologic reactions.

6. Monitoring Recommendations

Baseline and ongoing laboratory monitoring are essential [7].

6.1. Baseline Investigations

- G6PD level
- Complete blood count (CBC)
- Liver function tests
- Renal function tests
- Urinalysis

6.2. Follow-Up Monitoring

Investigation	Frequency
CBC with differential	Weekly for 4 weeks, then biweekly until week 12, then every 3–4 months
Reticulocyte count	As clinically indicated
Liver and renal function	Every 3–4 months
Methemoglobin level	If symptomatic

Table 3: Monitoring Protocol for Patients Receiving Dapsone

Close monitoring is particularly critical during the first three months of therapy [14].

7. Discussion

Dapsone remains a unique therapeutic agent within dermatology due to its dual antimicrobial and anti-inflammatory properties. While originally developed for infectious disease, its enduring relevance stems largely from its targeted suppression of neutrophil-mediated inflammation. Neutrophils play a central role in the pathogenesis of several dermatologic disorders, including dermatitis herpetiformis, linear IgA dermatosis, subcorneal pustular dermatosis, and Sweet syndrome. By inhibiting neutrophil chemotaxis, suppressing myeloperoxidase-mediated oxidative burst, and interfering with integrin-mediated adhesion, dapsone directly mitigates tissue damage driven by inflammatory cell infiltration [6,7,9].

The inhibitory effect on cytokine production, particularly IL-8 and TNF-α, further strengthens its role in neutrophilic dermatoses [10,11]. IL-8 is a potent neutrophil chemoattractant and activator, and its suppression may explain the rapid clinical response often observed in pustular and urticarial conditions. Moreover, inhibition of the alternative complement pathway, demonstrated in experimental models, may contribute to its benefit in immune complex–mediated dermatoses [7]. This multifaceted mechanism distinguishes dapsone from many contemporary immunomodulators that act through a single cytokine or receptor pathway.

In recent years, the therapeutic landscape of dermatology has evolved with the introduction of biologics and targeted small molecules. However, dapsone continues to offer advantages in selected patients. It is orally administered, relatively inexpensive, and widely accessible compared with biologic agents. In resource-limited settings or in patients unsuitable for systemic immunosuppressants, dapsone may serve as an effective steroid-sparing agent. Furthermore, long-standing clinical experience and decades of pharmacovigilance data provide a well-characterized safety profile when appropriate monitoring protocols are followed [6,11].

Despite its benefits, clinicians must remain vigilant regarding hematologic toxicity. Dose-dependent hemolysis and methemoglobinemia are predictable effects related to oxidative stress induced in erythrocytes [5]. While hemolysis occurs to some

degree in most patients, it is typically mild in those with normal glucose-6-phosphate dehydrogenase (G6PD) activity. However, agranulocytosis and dapsone hypersensitivity syndrome, although rare, represent potentially life-threatening complications [7]. Early recognition and routine laboratory monitoring remain essential components of safe prescribing practice.

Another important consideration is patient selection. The strongest evidence supports dapsone use in neutrophilic dermatoses and IgA-mediated blistering diseases, where rapid symptom control is frequently observed [3,5]. In contrast, its benefit in certain autoimmune blistering diseases or chronic inflammatory conditions may be more modest and often requires adjunctive therapy. Therefore, understanding the underlying inflammatory pathway of each condition is crucial in predicting therapeutic response.

Future research may further clarify biomarkers predictive of response to dapsone, particularly in diseases with mixed inflammatory patterns. Additionally, given its complement-modulating and cytokine-suppressive properties, exploration of dapsone in combination regimens with targeted biologics may provide synergistic therapeutic strategies. Although older than many current agents, dapsone continues to demonstrate relevance in modern dermatologic practice when used judiciously.

8. Conclusion

Dapsone is a versatile and effective agent in dermatology with both antimicrobial and anti-inflammatory properties. Its greatest utility lies in neutrophilic and eosinophilic dermatoses. Although associated with potentially serious adverse effects, these risks can be mitigated through appropriate patient selection and structured monitoring. When used judiciously, dapsone remains an indispensable tool in the dermatologic therapeutic armamentarium [15].

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