Dapsone – Should It Be Considered as a Treatment Option for Acne, Rosacea and Hidradenitis Suppurativa?

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ABSTRACT

Dapsone – Should It Be Considered as a Treatment Option for Acne, Rosacea and Hidradenitis Suppurativa?

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Dapsone is a chemical compound belonging to the sulfone group, primarily used as a first-line treatment for leprosy. Beyond this indication, it possesses a broad spectrum of antibacterial, antiparasitic, immunosuppressive/immunomodulatory, and anti-inflammatory properties, playing a key role in the management of numerous dermatological conditions. It is considered the first-line therapy for dermatitis herpetiformis and erythema elevatum diutinum. Additionally, it is employed in the treatment of other skin disorders such as bullous pemphigoid, mucous membrane pemphigoid, cutaneous lupus erythematosus, among others.
This article discusses the therapeutic potential of dapsone in the treatment of acne vulgaris, rosacea, and hidradenitis suppurativa. Furthermore, an overview of dosing regimens used in other dermatological diseases is provided.

Keywords: *acne vulgaris, dapsone, hidradenitis suppurativa, rosacea.*

STRESZCZENIE

Dapson – czy zasadne jest stosowanie dapsonu jako opcji terapeutycznej w leczeniu trądziku zwykłego, trądziku różowatego oraz trądziku odwróconego?

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Dapson to związek chemiczny z grupy sulfonów, który jest stosowany jako lek pierwszego rzutu w leczeniu trądu. Poza tym wskazaniem wykazuje szerokie spektrum działania przeciwbakteryjnego, przeciwpasożytniczego, immunosupresyjnego/immunomodulującego oraz przeciwzapalnego i odgrywa istotną rolę w terapii wielu chorób dermatologicznych. Dapson jest lekiem pierwszego wyboru w terapii opryszczkowatego zapalenia skóry oraz w rumieniu wyniosłym i długotrwałym. Ponadto bywa wykorzystywany w leczeniu innych schorzeń, takich jak pemfigoid pęcherzowy, pemfigoid błon śluzowych, skórna postać tocznia rumieniowatego i innych. W niniejszym artykule przedstawiono potencjał terapeutyczny dapsonu w leczeniu trądziku pospolitego, trądziku różowatego oraz trądziku odwróconego. Dodatkowo omówiono schematy dawkowania stosowane w innych chorobach dermatologicznych.

Słowa kluczowe: *dapson, trądzik odwrócony, trądzik pospolity, trądzik różowaty.*

Mechanism of action: Why Dapsone is effective in neutrophilic disorders

Dapsone demonstrates significant efficacy in neutrophilic dermatoses, primarily through modulation of inflammatory pathways. A central aspect of its mechanism involves the inhibition of neutrophil chemotaxis, largely mediated by the suppression of neutrophil activity, which plays a pivotal role in the pathogenesis of neutrophil-dominant inflammation [1,2]. By reducing interleukin-8 (IL-8) production by keratinocytes, dapsone limits neutrophil infiltration and the resulting tissue damage [1]. Furthermore, it impairs neutrophil adhesion to IgA- and IgG-bound basement membrane antigens and downregulates the activity of lysosomal enzymes and myeloperoxidase, thereby attenuating oxidative injury. Although its effects are primarily observed in neutrophilic conditions, dapsone may also modulate eosinophilic responses by inhibiting eosinophil peroxidase-induced mast cell activation and subsequent histamine release [1]. Additionally, it exhibits antimicrobial activity by inhibiting dihydrofolic acid synthesis through competitive inhibition of dihydropteroate synthase [3].

Table 1. Mechanism of action of dapsone and its effects on neutrophilic disorders

Mechanism of action	Result
Inhibition of neutrophil chemotaxis	Limits migration of neutrophils to inflammatory sites
Reduction of adhesion to IgA and IgG bound to basement membrane	Decreases neutrophilic infiltration and tissue damage
Suppression of IL-8 production by keratinocytes	Reduces neutrophil recruitment and local inflammation
Inhibition of lysosomal enzymes and myeloperoxidase	Lowers oxidative stress and tissue injury
Inhibition of 5-lipoxygenase (5-LO)	Reduced production of leukotriene B4 (LTB4)
Reduced production of leukotriene B4 (LTB4)	Decreased neutrophil chemotaxis and activation
Reduction of eosinophil peroxidase-induced mast cell activation	Decreases histamine release and eosinophilic inflammatory response
Binding to dihydropteroate synthase	Inhibits dihydrofolic acid synthesis, contributing to antimicrobial effect

The use of dapsone in dermatological disorders

Leprosy: Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*. Initially, sulfone antibiotics – particularly dapsone – were highly effective in treating this condition due to their antibacterial mechanism. Dapsone inhibits the synthesis of dihydrofolic acid by competing with para-aminobenzoic acid (PABA) for the active site of dihydropteroate synthase, thereby disrupting bacterial DNA synthesis. However, the emergence of resistance necessitated the introduction of combination therapy with other antibiotics. Currently, the World Health Organization recommends multidrug therapy (MDT) comprising dapsone, rifampicin, and clofazimine [4].

Given its mechanism of action, dapsone is used in various forms across a range of neutrophil-mediated and other inflammatory diseases. The table below presents dosing regimens reported in the available literature.

Acne vulgaris: Dapsone may be effective in the treatment of acne vulgaris due to its mechanism of action, which includes inhibiting neutrophil chemotaxis, reducing reactive oxygen species, and lowering IL-8 levels [1,5]. *In vitro* studies have also demonstrated its antibacterial activity against *Cutibacterium acnes* [10]. Dapsone therapy may be considered for acne vulgaris in cases where medications such as isotretinoin are contraindicated. Oral dapsone has been reported to be both effective and safe for patients with acne fulminans or nodulocystic acne who are unable to take isotretinoin [10]. The usual dosage ranges from 50 to 100 mg per day; however, if results are insufficient, the dose can be increased to 150–300 mg per day.

Dapsone gel leads to lower systemic exposure to the drug and its metabolites compared to oral formulations. Applying 5% dapsone gel twice daily significantly reduces acne lesions – particularly inflammatory ones – with a 58.2% decrease observed after 12 weeks [10]. The 7.5% dapsone gel improves patient adherence due to once-daily application and has a favorable safety profile. Studies show it provides greater improvement in acne for women and adults compared to men and adolescents [10]. Dapsone appears particularly effective in treating acne in adult women compared to adolescent females [5].

Studies have found that topical formulations result in lower systemic absorption, a reduced risk of hemolytic anemia in G6PD-deficient patients, and improved safety and efficacy. Additionally, the lower incidence of side effects may be a key reason for choosing the gel over the oral form [11]. The study by Angela Yen Moore et al. identified the 7.5% gel formulation as safe and well-tolerated in treating acne in children aged 9–11 years. They also observed an improvement in comedonal lesion count [11]. The observed reduction in comedonal lesions during topical dapsone therapy may be attributed to its anti-inflammatory effects, normalization of follicular keratinization, and antimicrobial activity, which together help modulate early acne pathogenesis.

A study comparing the combination of dapsone with tretinoin and clindamycin with tretinoin found that the dapsone combination may be more beneficial for acne involving non-inflammatory lesions [12]. On the other hand, a comparison between 5% topical spironolactone and 5% dapsone revealed that spironolactone led to more significant improvement in mild to moderate acne [13]. In a study involving 58 acne patients, combining isotretinoin with 5% dapsone gel resulted in a greater reduction in lesion count compared to isotretinoin combined with placebo [13].

Table 2. Dosage of dapsone in the treatment of selected dermatological diseases

Disease	Comments	Dosage
Leprosy	*First-line treatment. FDA-approved*	*Multibacillary Leprosy:* *Oral:* Adults: 100 mg/day for 12 months. Children >10 years old: 50 mg/day for 12 months. Children <10 years old: 2 mg/kg. For *paucibacillary leprosy*, the same dosage for 6 months. Combined therapy with rifampicin and clofazimine for 6–12 months [4,5].
Dermatitis herpetiformis	*First-line treatment. FDA-approved*	*Oral:* 50 mg/day initially to minimize potential side effects, gradually increased to 200 mg/day until disease control is achieved. Maintenance therapy: 0.5–1 mg/kg/day [5].
Erythema elevatum et diutinum (EED)	*Moderate response to treatment [6]*	*Oral:* 50–100 mg/day.
Pemphigus vulgaris	*Further alternative. Conflicting reports on efficacy from uncontrolled trials [6]*	*Oral:* Up to 1.5 mg/kg/day [1].
Pemphigus foliaceus	*Subsequent therapeutic approach*	*Oral:* 25–300 mg/day, combined with systemic corticosteroids at 1 mg/kg/day, associated with excellent response [5]. For neutrophilic pustules, dapsone is the preferred adjunct treatment to reduce visible neutrophilic infiltration [5].
Granuloma annulare	*Second-line option [6]*	*Topical*: 5% twice daily for 3 weeks. Consider oral 100–200 mg/day if steroids and calcineurin inhibitors are ineffective [5].
Granuloma faciale	*Used when topical treatment is ineffective [6]*	*Oral:* 50–100 mg/day.
Lupus miliaris disseminatus faciei (LMDF)	*Subsequent therapeutic approach*	*Oral:* 100 mg/day of dapsone during the early inflammatory stage [5].
Bullous systemic lupus erythematosus (BSLE)	*Indications approved [6]*	*Oral:* 50–200 mg/day (even low doses of 25–50 mg may elicit a response [7]).
Sweet's syndrome	*Empirical indication [6]*	*Oral:* 50–150 mg/day [8].
Pyoderma gangrenosum (PG)	*Empirical indication [6]*	*Topical*: 5%–7.5% gel [9]. *Oral:* Adults: 50–100 mg/day; up to 200–300 mg/day if needed. Children: 2 mg/kg/day (>9 years old) [9].
Well's syndrome	*Subsequent therapeutic approach*	*Oral:* 100 mg daily until lesion remission, typically after 2 weeks. Then, the dose is reduced to 50 mg daily for 6 weeks, followed by 50 mg three times a week [5].
Erosive pustular dermatosis (EPD)	*Subsequent therapeutic approach*	*Oral:* 50–100 mg/day [5].
Allergic vasculitis	*Good and rapid response*	*Oral*: 50–200 mg/day.

One drawback of dapsone is its poor water solubility and limited skin permeability. Researchers are investigating ways to enhance its absorption and effectiveness. One study demonstrated that dapsone-loaded micelles incorporated into a gel improved drug release and skin penetration, suggesting this approach could enhance therapeutic performance [13]. The study also noted that using dapsone in combination with corticosteroids may help reduce the required corticosteroid dose, potentially minimizing associated side effects.

It is not recommended to combine topical dapsone with topical benzoyl peroxide, as this combination may lead to undesirable yellow discoloration of the skin and facial hair [5,10]. According to the authors, dapsone in combination with topical retinoids is recommended for treating comedonal acne [10]. There are documented cases demonstrating the effectiveness of oral dapsone in treating fulminant acne, particularly where isotretinoin therapy has failed. Dosages typically start at 50 mg per day and should be adjusted according to body weight [14].

Hidradenitis suppurativa: The increasing resistance to commonly used antibiotics is one of the key factors driving the search for new treatment options for hidradenitis suppurativa (HS). Due to its immunomodulatory properties – such as inhibition of IL-8 and TNF-α – dapsone may be used in the treatment of HS [5]. Dapsone is currently recommended as a third-line antibiotic for patients with mild to moderate HS.

Table 3. Oral and local treatment of various forms of acne, hidradenitis suppurativa and rosacea

Disease	Oral	Topical
Acne vulgaris	50–100 mg/day [10]	5% twice a day or 7.5% once a day [11]; apply a thin layer to lesions. *FDA-approved.*
Acne fulminans	50–75 mg/day, rarely 100–200 mg/day (used in combination with prednisolone or isotretinoin, as per literature)	
Hidradenitis suppurativa	25–200 mg/day [3]	
Rosacea		5% or 7.5% for 12 weeks [5,15].
Rosacea fulminans	100 mg/day with a 50 mg/day maintenance dose [18]	

It is typically administered in daily doses ranging from 25 to 200 mg, depending on individual tolerance. However, the overall quality of evidence supporting its effectiveness remains low [3]

Rosacea: The use of 5% dapsone gel in the treatment of rosacea with telangiectasia has shown a reduction in redness and burning sensations [15]. The 7.5% topical dapsone formulation demonstrates effectiveness in managing papulopustular rosacea during both the first and second months of treatment, regardless of patient age [16].

Granulomatous rosacea: In the case described [17], treatment with metronidazole and doxycycline was ineffective. The patient declined the use of corticosteroids and isotretinoin, so treatment with dapsone at 100 mg daily was initiated [17]. After three months of therapy and long-term observation, the desired effect was achieved. This case confirmed the potential of dapsone as a therapeutic option [17].

Rosacea fulminans: In the treatment of rosacea fulminans – where conventional therapies for standard rosacea are often ineffective – dapsone at a dose of 100 mg per day led to remission after just five weeks of treatment [18].

Side effects of Dapsone

Dapsone undergoes hepatic metabolism, resulting in the formation of its active metabolite, dapsone hydroxylamine (DDS-NOH). This compound exerts anti-inflammatory effects by inhibiting neutrophil chemotaxis. However, due to its strong oxidative properties, DDS-NOH is associated with adverse effects such as methemoglobinemia, hemolytic anemia, and agranulocytosis. Symptoms typically occur at plasma concentrations above 5 mg/L, which correspond to doses exceeding 200 mg per day [6]. Dapsone syndrome is characterized by fever, rash, eosinophilia, and hepatosplenomegaly [6]. Some studies suggest that these effects may occur in all patients to varying degrees of clinical significance [1]. Cimetidine may reduce the risk of adverse effects by inhibiting hydroxylation via the CYP450 enzyme system [6].

To reduce the risk of complications, patients should be screened for glucose-6-phosphate dehydrogenase (G6PD) deficiency, which can help prevent hemolysis and guide closer monitoring [6]. Before initiating treatment, baseline evaluations should include a complete blood count, reticulocyte count, liver and kidney function tests, urinalysis, and methemoglobin levels [9]. The most accurate indicator of dapsone-related toxicity is the methemoglobin concentration, which should ideally be measured approximately two weeks after therapy begins [9]. Ongoing monitoring should include weekly laboratory testing during the first month, followed by monthly assessments for the next three months, and then every three months during maintenance therapy [9].

Conclusions

Although current data on the use of dapsone in various forms of acne are limited and often of uncertain reliability, there are case reports in the literature describing successful outcomes. When considering dapsone as a treatment option, it is essential to carefully weigh the potential benefits against the risks, particularly with regard to adverse effects. Dapsone should certainly be considered a therapeutic option in neutrophil-mediated conditions, including acne vulgaris, hidradenitis suppurativa, and rosacea – especially in cases where standard therapies are contraindicated, poorly tolerated, or declined by the patient.

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Paulina Petrosyan-Chrościcka declares no conflict of interests.
Bartłomiej Kwiek reported serving as a clinical study investigator for AbbVie, Amgen Inc., Arcutis Biotherapeuthics, Almirall, Aslan, Bristol-Myers Squibb, Celdex Therapeutics, Celltrion, Dermira, Galderma, Glenmark, Incyte, Janssen Pharmaceuticals, LEO Pharma, Novartis, Pfizer, Regeneron, Samsung.

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