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The Review on Dapsone

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ABSTRACT

Dapsone (4,4'-diaminodiphenylsulfone) is the only remaining sulfone used in anthropoid therapeutics and is commercially available as an oral formulation, an inhaled preparation, and a 5% or 7.5% cream.Dapsone is widely used in the treatment of leprosy and several chronic inflammatory dermatological conditions.The natural history of IgA vasculitis is generally self-limiting; however, one-third of patients experience symptom recurrence and a refractory course.Dapsone in dermatology and beyond.antiinflammatory mechanisms that initially were elucidated by inflammatory animal models. Thus, dapsone clearly has dual functions of both:Pharmacology and mechanisms of action are determining factors for clinical use of dapsone chiefly in neutrophilic and/or eosinophilicdermatoses and in chronic disorders outside the field of dermatology.The study consisted of 80 patients (54 leprosy and 26 non-leprosy patients), prescribed with dapsone 100 mg oral once daily.The prescribing patterns of dapsone in leprosy and other dermatological conditions (non-leprosy) were analyzed and the safety, efficacy and appropriateness of the doses prescribed were reviewed.

Keywords: leprosy; drug resistance; genes mutations; dapsone; rifampicin; ofloxacin.

Introduction:

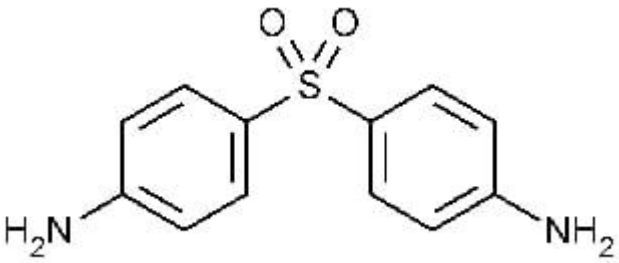
Dapsone is the principal drug in a multidrug regimen recommended by the World Health Organization for the treatment of leprosy.Dapsone was first studied as an antibiotic in 1937.Its use for leprosy began in 1945.It is on the World Health Organization's List of Essential Medicines.The form, which is taken by mouth, is available as a generic drug and not very expensive.

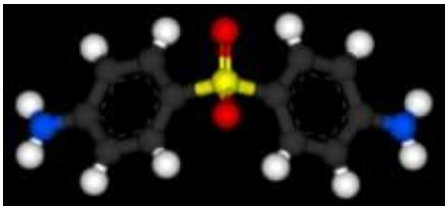
History :

Who discovered dapsone?

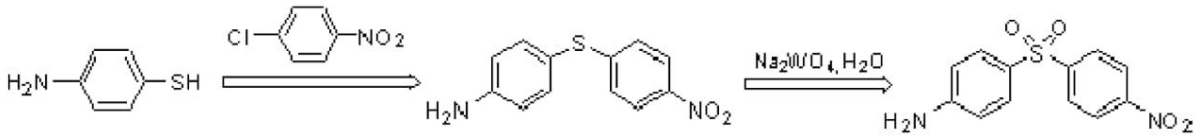
Historical perspective. Dapsone was synthesized in 1908 by Fromm and Wittmann. From 1936 until 1996, the drug dapsone treated a diverse array of diseases, including tuberculosis, leprosy, malaria, and AIDS-related pneumonia. This article explores how dapsone transformed from a cure for one disease into a treatment for a totally different malady.dapsone developed Dapsone was first synthesized in 1908

Structure of Dapsone





Synthesis of Dapsone :



Synthesis of dapsone : from 4-nitrochlorobenzene by E. Fromm and J. Wittmann , 1908

In the early 20th century, the German chemist Paul Ehrlich was developing theories of selective toxicity based largely on the ability of certain dyes to kill microbes. Gerhard Domagk, who would later win a Nobel Prize for his efforts, made a major breakthrough in 1932 with the discovery of the antibacterial prontosil red (sulfonamidochrysoidine). Further investigation into the involved chemicals opened the way to sulfa drug and sulfone therapy, first with the discovery of sulfanilamide, the active agent of prontosil, by Daniel Bovet and his team at Pasteur Institute (1935), then with that of dapsone independently by Ernest Fourneau in France and Gladwin Buttle in the United Kingdom.

Clinical data :
Trade Name :Aczone, Others
Route of Administration : By mouth,topical

Legal status :
Legalstatus:USRxonly
Ingeneral
(Rx prescription only**)**

PharmacokineticData:
Bioavailability : 70 to 80%
Protein binding : 70 to 90%
Metabolism :Liver
Elimination Half Life : 20 to30 hours
Excretion : kidney

Identifies:
IUPAC name : 4-[(4-aminobenzene)sulfonyl]aniline

Chemical and physicaldata:
Formula : C12H12N2O2S
Molar Mass : 248.30 g·mol−1
Melting Point : 175 to 176 °C (347 to 349 °F)

Mechanism of action:

As an antibacterial, dapsone inhibits bacterial synthesis of dihydrofolic acid, via competition with para-aminobenzoateforthe active site of dihydropteroate synthase, thereby inhibiting nucleic acid synthesis.Though structurally distinct fromdapsone, the sulfonamide group of antibacterial drugs also work in this way.As an anti-inflammatory, dapsone inhibits the myeloperoxidase-H2O2-halide-mediated cytotoxic system in polymorphonucleocytes.As part of the respiratory burst that neutrophils use to kill bacteria, myeloperoxidase converts hydrogen peroxide (H2O2) into hypochlorous acid(HOCl). HOCl is the most potent oxidant generated by neutrophils, and can cause significant tissue damage during inflammation. Dapsone arrests myeloperoxidase in an inactive intermediate form, reversibly inhibiting the enzyme. This prevents accumulationof hypochlorous acid, and reduces tissue damage during inflammation Myeloperoxidase inhibition has also been suggested as a neuron-sparing mechanism for reducing inflammationin neurodegenerative diseases such as Alzheimer's disease and stroke.Dapsoneacts against bacteria and protozoa in the same wayas sulphonamides, that is by inhibiting the synthesis ofdihydrofolic acid throughcompetition with para-amino-benzoate for the active site of dihydropteroatesynthetase. The anti-inflammatory action of the drug is unrelated to its antibacterial action and is still not fully understood.

How to use Dapsone :

Take this medication by mouth with or without food, usually once daily or as directed by your doctor.
Medications for heartburn/reducing stomachacid (such aslarge amounts of antacids, ranitidine, famotidine), or didanosine may prevent full absorption of dapsone into your bloodstream, possibly reducing its effectiveness. Separate your dose of dapsone from your doses of any of these products by at least 2 hours. Ask your doctor or pharmacist for more details.
If you are taking dapsone for a skin disorder, your doctor may start youon a low dose ofdapsone and gradually adjust your dose to control your disease. If you are taking this medication to treat Hansen's disease or to prevent infections due to HIV, the drug is usually taken for years or for life.
Dosage is based on your medical condition and response to treatment. In children, the dosage is also based on ageand weight.
Medical uses:
Uses : This medication is used to treat a certain type of skin disorder (dermatitis herpetiformis). It is also used with other drugs to treat Hansen's disease. Dapsone belongs to a class of drugs known as sulfones. It works by decreasing swelling (inflammation) and stopping the growth of bacteria.This medication will not work for viral infections (such as common cold, flu). Unnecessary use or misuse of any antibiotic can lead to its decreased effectiveness.

Proposed use in antimalarialdrugs :
The spread of drug-resistant malaria in Africa has encouraged the development of new, low-cost antimalarial drugs. Plasmodium falciparum, one of the Plasmodium species that causes malaria, has developed resistance both to chloroquine and sulfadoxine/pyrimethamine, two of the most common treatments for malaria.
Dapsonegel :
Dapsone had been reported in a few cases to effectively treat acne, but the risk of hemolytic anemia kept it from being widely used for this purpose. For many years scientists attempted to develop a topical formulation of dapsone that would be as effective against acne as oral dapsone, but without the hemolysis side effect. This was difficult to accomplish because dapsone is highly insoluble in aqueous solvents. In the early 2000s QLT USA developed Aczone, a 5% dapsone gel that was shown to be effective against acne without causing clinically significant declines in hemoglobin levels, even in subjects with G6PD deficiency. In February 2016, the FDA approved a 7.5% dapsone gel. This higher strength has the advantage of a once-daily application, versus twice-daily application of the 5% formulation.
Adverse effects :
Hypersensitivity reactions occur in 1.4% of persons treated with dapsone, and can be fatal in medical settings with low resources. It is a form of severe cutaneous adverse reactions (SCARs) in which a SCARs disorder, primarily the DRESS syndrome or a DRESS syndrome-like reaction occurs.
blood :- Hemolysis is the most prominent side-effect, occurring in about 20 % of patients treated with dapsone, although it is dose-related. It may lead to hemolytic anemia and methemoglobinemia. The side-effect is more common and severe in those with glucose-6-phosphate dehydrogenase deficiency, leading to the dapsone-containing antimalarial combination Lapdap being withdrawn from clinical use. A case of hemolysis in a neonate from dapsone in breast milk has been reported.Agranulocytosis occurs rarely when dapsone is used alone but more frequently in combination regimens for malaria prophylaxis.Abnormalities in white blood cell formation, including aplastic anemia, are rare, yet are the cause of the majority of deaths attributable to dapsonetherapy.Methemoglobinemia occurs in about 15 % of patients treated with long-term dapsone at standard doses (100 mg/day). Only special multi-wawelengthoximeters (CO-oximeters) can detect methemoglobinemia directly. When there is a "saturation gap" between a low ordinary pulse oximeter reading and a high arterial blood gas analysis result, methemoglobinemia may be suspected.
Liver :- Toxic hepatitis and cholestatic jaundice have been reported by the manufacturer. These toxic reactions may also occur as part of the dapsone hypersensitivity syndrome (a form of SCARs-see above) or dapsone syndrome (see below). Dapsone is metabolized by the Cytochrome P450 system, specifically isozymes CYP2D6, CYP2B6, CYP3A4, and CYP2C19.Dapsone metabolites produced by the cytochrome P450 2C19 isozyme are associated with the methemoglobinemia side effect of the drug.
Skin :- When used topically, dapsone can cause mild skin irritation, redness, dry skin, burning, and itching. When used together with benzoyl peroxide products, temporary yellow or orange skin discolorations can occur.
Other adverse effects :
Other adverse effects include nausea, headache, and rash (which are common), and insomnia, psychosis, and peripheral neuropathy. Effects on the lung occur rarely and may be serious, though are generally reversible.

Dapsone hypersensitivity syndrome :
Hypersensitivity reactions occur in some patients. This reaction may be more frequent in patients receiving multiple-drug therapy.
The reaction always involves a rash, may also include fever, jaundice, and eosinophilia, and is likely to be one manifestation of the SCARs reaction viz., the DRESS syndrome (see above).In general, these symptoms will occurwithin the first sixweeks of therapy or not at all, and may be ameliorated by corticosteroid therapy.
Before Using dapsone (tablet) :
In deciding to use a medicine, the risks of taking the medicine must be weighed against the good it will do. This is a decision you and your doctor will make. For this medicine, the following should be considered:
•Allergies:-
Tell your doctor if you have ever had any unusual or allergic reaction to this medicine or any other medicines. Also tell your health care professional if you have any other types of allergies, such as to foods, dyes, preservatives, or animals. For non-prescription products, read the label or package ingredients carefully.
•Pediatric:-Although there is no specific information comparing use of dapsone in children with use in other age groups, this medicine is not expected to cause different side effects or problems in children than it does in adults.
•Geriatric

Many medicines have not been studied specifically in older people. Therefore, it may not be known whether they work exactly the same way they do in younger adults or if they cause different side effects or problems in older people.

•Breastfeeding :-
There are no adequate studies in women for determining infant risk when using this medication during breastfeeding. Weigh the potential benefits against the potential risks before taking this medication while breastfeeding.

Side Effects :
Nausea, vomiting, loss of appetite, dizziness, or blurred vision may occur. If any of these effects last or get worse, tell your doctor or pharmacist promptly.

Overdose :
If someone has overdosed and has serious symptoms such as passing out or trouble breathing, call 911. Otherwise, call a poison control center right away. US residents can call their local poison control center at 1-800-222-1222. Canada residents can call a provincial poison control center. Symptoms of overdose may include: seizures, bluish skin (cyanosis), sudden vision changes, sudden loss of vision.

Precaution :
Before taking dapsone, tell your doctor or pharmacist if you are allergic to it; or to similar drugs such as sulfoxone; or if you have any other allergies. This product may contain inactive ingredients, which can cause allergic reactions or other problems.

Interactions :
Drug interactions may change how your medications work or increase your risk for serious side effects. This document does not contain all possible drug interactions. Keep a list of all the products you use (including prescription/nonprescription drugs and herbal products) and share it with your doctor and pharmacist. Do not start, stop, or change the dosage of any medicines without your doctor's approval.

Drug Interactions :

Although certain medicines should not be used together at all, in other cases two different medicines may be used together even if an interaction might occur. In these cases, your doctor may want to change the dose, or other precautions may be necessary. Using this medicine with any of the following medicines is usually not recommended, but may be required in some cases. If both medicines are prescribed together, your doctor may change the dose or how often you use one or both of the medicines.
•Warfarin
•Zidovudine
Using this medicine with any of the following medicines may cause an increased risk of certain side effects, but using both drugs may be the best treatment for you. If both medicines are prescribed together, your doctor may change the dose or how often you use one or both of the
•medicines.
•Amprenavir
•Atazanavir
•Fosamprenavir
•Rifabutin
•Rifapentine

Other Interactions:
Certain medicines should not be used at or around the time of eating food or eating certain types of food since interactions may occur. Using alcohol or tobacco with certain medicines may also cause interactions to occur. Discuss with your healthcare professional the use of your medicine with food, alcohol, or tobacco.

Other Medical Problems :
The presence of other medical problems may affect the use of this medicine. Make sure you tell your doctor if you have any other medical problems, especially:
Anemia (severe) or
Glucose-6-phosphate dehydrogenase (G6PD) deficiency or
Methemoglobinreductase deficiency—There is an increased risk of severe blood disorders and a decrease in red blood cell survival
Liver disease—Dapsone may on rare occasion cause liver damage.

Storage :
Store the medicine in a closed container at room temperature, away from heat, moisture, and direct light. Keep from freezing.
Keep out of the reach of children Do not keep outdated medicine or medicine no longer needed.

Conclusion :
Dapsone is effective in the prevention of PCP and in combination with TMP is effective in the treatment of this pneumonitis. It is not the drug of first choice for either prophylaxis or treatment of patient who can take TMP-SMZ. The data currently available are adeqate to consider its drug second choice for patient who have experience adverse effects from TMP-SMZ.Dapsone has been studied by far most frequently in vitro—under strictly defined experimental settings. Overall, results of these experiments paint a picture of possible mechanisms of action of dapsone. In addition, many data from human in vivo studies are available including experience in dapsone-sensitive diseases.

References :

1) Weber E, Reynaud Q, Fort R, Durupt S, Cathébras P, Durieu I, Lega JC (September 2017). "Immunomodulatory treatments for persistent and chronic immune thrombocytopenic purpura: A PRISMA-compliant systematic review and meta-analysis of

28 studies". Medicine (Baltimore). 96 (37): e7534. doi:10.1097/MD.0000000000007534. PMC 5604622. PMID 28906353.

2) Antia C, Baquerizo K, Korman A, Alikhan A, Bernstein JA (October 2018). "Urticaria: A comprehensive review: Treatment of chronic urticaria, special populations, and disease outcomes". J. Am. Acad. Dermatol. 79 (4): 617–633. doi:10.1016/j.jaad.2018.01.023. PMID 30241624. S2CID 52312492.
3) Liang SE, Hoffmann R, Peterson E, Soter NA (2019). "Use of Dapsone in the Treatment of Chronic Idiopathic and Autoimmune Urticaria". JAMA Dermatol. 155 (1): 90–95. doi:10.1001/jamadermatol.2018.3715. PMC 6439569. PMID 30476976.
4) Rapini RP, Warner NB (2006). "Relapsing polychondritis". Clin. Dermatol. 24 (6): 482–5. doi:10.1016/j.clindermatol.2006.07.018. PMID 17113965.
5) 6)Forks, TP (2000). "Brown recluse spider bites". J Am Board FamPract. 13 (6): 415–23. doi:10.3122/15572625-13-6-415. PMID 11117338.
6) Momen, S.E.; Jorizzo, J.; Al-Niaimi, F. (December 2014). "Erythema elevatumdiutinum: a review of presentation and treatment". Journal of the European Academy of Dermatology and Venereology. John Wiley & Sons. 28 (12): 1594–1602. doi:10.1111/jdv.12566. PMID 25288365. S2CID 30029976.
7) Lukács, J.; Schliemann, S.; Elsner, P. (August 2015). "Treatment of generalized granuloma annulare – a systematic review". Journal of the European Academy of Dermatology and Venereology. John Wiley & Sons. 29 (8): 1467–1480. doi:10.1111/jdv.12976. PMID 25651003. S2CID 20884856.
8) Zhang FR, Liu H, Irwanto A, et al. (October 2013). "HLA-B*13:01 and the dapsone hypersensitivity syndrome". N Engl J Med. 369 (17): 1620–8.
9) Bocquet H, Bagot M, Roujeau JC (December 1996). "Drug-induced pseudolymphoma and drug hypersensitivity syndrome (Drug Rash with Eosinophilia and Systemic Symptoms: DRESS)". SeminCutan Med Surg. 15 (4): 250–7. doi:10.1016/S1085-5629(96)80038-1. PMID 9069593.
10) Tempark T, Satapornpong P, Rerknimitr P, Nakkam N, Saksit N, Wattanakrai P, Jantararoungtong T, Koomdee N, Mahakkanukrauh A, Tassaneeyakul W, Suttisai S, Pratoomwun J, Klaewsongkram J, Rerkpattanapipat T, Sukasem C (December 2017). "Dapsone-induced severe cutaneous adverse drug reactions are strongly linked with HLA-B*13: 01 allele in the Thai population". Pharmacogenetics and Genomics. 27 (12): 429–437. doi:10.1097/FPC.0000000000000306. PMID 28885988. S2CID 4283457.
11) Greenwood, David (2008). Antimicrobial Drugs: Chronicle of a Twentieth Century Medical Triumph. Oxford University Press. p. 197. ISBN 9780199534845. Archived from the original on 2016-03-04.
12) Thomas L. Lemke (2008). Foye's Principles of Medicinal Chemistry. Lippincott Williams & Wilkins. p. 1142. ISBN 9780781768795. Archived from the original on 2016-03-04.
13) Rapini RP, Warner NB (2006). "Relapsing polychondritis". Clin. Dermatol. 24 (6): 482–5. doi:10.1016/j.clindermatol.2006.07.018. PMID 17113965.
14) Stotland, Mira; Shalita, Alan R.; Kissling, Robert F. (June 2009). "Dapsone 5% Gel: A Review of its Efficacy and Safety in the Treatment of Acne Vulgaris". American Journal of Clinical Dermatology. 10 (4): 221–227. doi:10.2165/00128071-200910040-00002. PMID 19489655. S2CID 19485887.
15) Stotland, Mira; Shalita, Alan R.; Kissling, Robert F. (June 2009). "Dapsone 5% Gel: A Review of its Efficacy and Safety in the Treatment of Acne Vulgaris". American Journal of Clinical Dermatology. 10 (4): 221–227. doi:10.2165/00128071-200910040-00002. PMID 19489655. S2CID 19485887.
16) Schoustra, Sybren K.; Dijksman, Joshua A.; Zuilhof, Han; Smulders, Maarten M. J. (2021). "Molecular control over vitrimer-like mechanics – tuneable dynamic motifs based on the Hammett equation in polyimine materials". Chemical Science. 17)293–302. doi:10.1039/d0sc05458e. ISSN 2041-6520. PMC 8178953. PMID 34163597.
17) Puavilai S, Chutha S, Polnikorn N, et al. (July 1984). "Incidence of anemia in leprosy patients treated with dapsone". J Med Assoc Thai. 67 (7): 404–7. PMID 6512448.
18) Sanders SW, Zone JJ, Foltz RL, Tolman KG, Rollins DE (April 1982). "Hemolytic anemia induced by dapsone transmitted through breast milk". Ann Intern Med. 96 (4): 465–6. doi:10.7326/0003-4819-96-4-465. PMID 7065565.
19) Firkin FC, Mariani AF (1977). "Agranulocytosis due to dapsone". Med. J. Aust. 2 (8): 247–51. doi:10.5694/j.1326-5377.1977.tb117649.x. PMID 909500. S2CID 34641425.
20) World Health Organization (2019). World Health Organization model list of essential medicines: 21st list 2019. Geneva: World Health Organization. hdl:10665/325771. WHO/MVP/EMP/IAU/2019.06. License: CC BY-NC-SA 3.0 IGO.
21) "Dapsone and Acne Vulgaris". ScienceOfAcne.com. 2012-10-10. Archived from the original on 2012-07-29. Retrieved 2012-08-17.
22) Thomas L. Lemke (2008). Foye's Principles of Medicinal Chemistry. Lippincott Williams & Wilkins. p. 1142. ISBN 9780781768795. Archived from the original on 2016-03-04.
23) "Dapsone (Systemic) Monograph for Professionals". The American Society of Health-System Pharmacists. Archived from the original on 2015-01-12. Retrieved January 12, 2015.
24) Liang SE, Hoffmann R, Peterson E, Soter NA. Use of Dapsone in the Treatment of Chronic Idiopathic and Autoimmune Urticaria. JAMA Dermatol. 2019 Jan 01;155(1):90-95. [PMC free article] [PubMed]
25) Ramos FS, Ferreira FR, Rabay FMO, Lira MLA. Neutrophilicdermatosis of the dorsal hands: response to dapsonemonotherapy. An Bras Dermatol. 2018 Sep-Oct;93(5):730-732. [PMC freearticle] [PubMed]
26) Kumar B. Re: Antimicrobial resistance in leprosy: results of the first prospective open survey conducted by a WHO surveillance network for the period 2009-2015. ClinMicrobiol Infect. 2019 May;25(5):644-645. [PubMed]
27) Din RS, Tsiaras WG, Li DG, Mostaghimi A. Efficacy of Systemic Dapsone Treatment for PyodermaGangrenosum: A Retrospective Review. J Drugs Dermatol. 2018 Oct 01;17(10):1058-1060.[PubMed]
28) Ferreira PM, Rato IR, Rigor J, Mota M. Hansen's disease - a forgotten disease? JRSM Open. 2021 Aug;12(8):20542704211035995. [PMC free article] [PubMed]31) Wang Y, Yang B, Zhou G, Zhang F. Two Cases of

Dermatitis Herpetiformis Successfully Treated with Tetracycline and Niacinamide. ActaDermatovenerol Croat. 2018 Oct;26(3):273-275. [PubMed]32)Ghaoui N, Hanna E, Abbas O, Kibbi AG, Kurban M. Update on the use of dapsone in dermatology. Int J Dermatol. 2020 Jul;59(7):787-795. [PubMed

29) Lewis JS, Jacobs ZG. Subtle case of dapsone-induced methaemoglobinaemia. BMJ Case Rep. 2020 Aug 24;13(8) [PMC free article] [PubMed]

30) Ahmad RA, Rogers HJ. Pharmacokinetics and protein binding interactions of dapsone and pyrimethamine. Br J ClinPharmacol. 1980;10:519–524. [PMC free article] [PubMed] [Google Scholar]

31) Altagracia M, Monroy-Noyola A, Osorio-Rico L, Kravzov J, Varado-Calvillo R, Manjarrez-Marmolejo J, Rios C. Dapsone attenuates kainic acid-induced seizures in rats. NeurosciLett. 1994;176:52–54. [PubMed] [Google Scholar]