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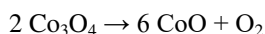
pH METRIC STUDIES OF Co (II) WITH N-ACETYL BENZENESULPHONAMIDE AND N-ACETYL-p-TOLUENESULPHONAMIDE

Dr. Shilpi Deep Mathur

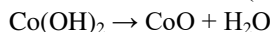
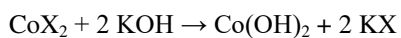
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ABSTRACT: Cobalt(II) oxide is an inorganic compound that has been described as an olive-green^[3] or gray^[4] solid. It is used extensively in the ceramics industry as an additive to create blue-colored glazes and enamels, as well as in the chemical industry for producing cobalt(II) salts. A related material is cobalt(II,III) oxide, a black solid with the formula Co₃O₄. Cobalt(II) oxide is prepared by oxidation of cobalt powder with air or by thermal decomposition of cobalt(II) nitrate or the carbonate.^{[3][4]}

Cobalt(II,III) oxide decomposes to cobalt(II) oxide at 950 °C:^[7]



It may also be prepared by precipitating the hydroxide, followed by thermal dehydration:



Cobalt(II) oxide has for centuries been used as a coloring agent on kiln fired pottery. The additive provides a deep shade of blue named cobalt blue. The band gap (CoO) is around 2.4 eV. In organic chemistry, the sulfonamide functional group (also spelled sulphonamide) is an organosulfur group with the structure R-S(=O)₂-NR₂. It consists of a sulfonyl group (O=S=O) connected to an amine group (-NH₂). Relatively speaking this group is unreactive. Because of the rigidity of the functional group, sulfonamides are typically crystalline; for this reason, the formation of a sulfonamide is a classic method to convert an amine into a crystalline derivative which can be identified by its melting point. Many important drugs contain the sulfonamide group.^[1]

A sulfonamide (compound) is a chemical compound that contains this group. The general formula is R-SO₂NR'R'' or R-S(=O)₂-NR'R'', where each R is some organic group; for example, "methanesulfonamide" (where R = methane, R' = R'' = hydrogen) is CH₃SO₂NH₂. Any sulfonamide can be considered as derived from a sulfonic acid by replacing a hydroxyl group (-OH) with an amine group.²

In medicine, the term "sulfonamide" is sometimes used as a synonym for sulfa drug, a derivative or variation of sulfanilamide. The first sulfonamide was discovered in Germany in 1932.^[2]

KEYWORDS: pH metric, n-acetyl-benzene sulphonamide, n-acetyl-p-toluenesulphonamide, sulfa, organosulphur

I. INTRODUCTION

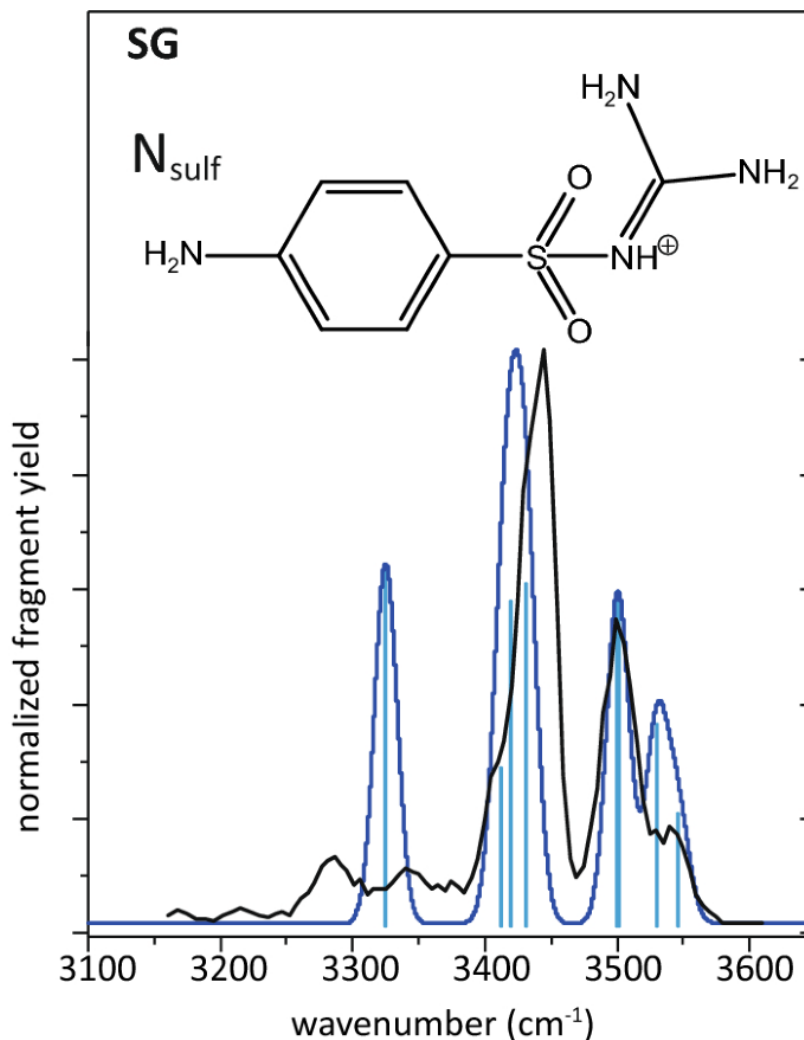
Bis(trifluoromethanesulfonyl)aniline is a source of the triflyl (CF₃SO₂)₂ group.⁸

The disulfonimides are of the type R-S(=O)₂-N(H)-S(=O)₂-R' with two sulfonyl groups flanking an amine.^[10] As with sulfonamides, this class of compounds is used as catalysts in enantioselective synthesis.^{[10][11][12]}

Sulfonamide is a functional group (a part of a molecule) that is the basis of several groups of drugs, which are called sulphonamides, sulfa drugs or sulpha drugs⁹. The original antibacterial sulfonamides are synthetic (nonantibiotic) antimicrobial agents that contain the sulfonamide group. Some sulfonamides are also devoid of antibacterial

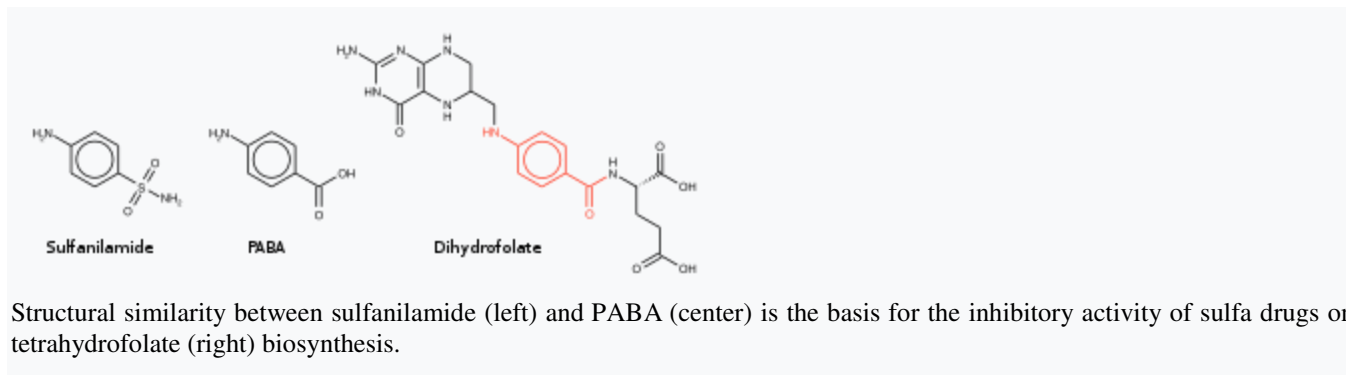
activity, e.g., the anticonvulsant sultiame. The sulfonyleureas and thiazide diuretics are newer drug groups based upon the antibacterial sulfonamides.^{[1][2]}

Allergies to sulfonamides are common.⁹



The overall incidence of adverse drug reactions to sulfa antibiotics is approximately 3%, close to penicillin,^[3] hence medications containing sulfonamides are prescribed carefully.¹⁰

Sulfonamide drugs were the first broadly effective antibacterials to be used systemically, and paved the way for the antibiotic revolution in medicine. In bacteria, antibacterial sulfonamides act as competitive inhibitors of the enzyme dihydropteroate synthase (DHPS), an enzyme involved in folate synthesis.¹⁰ Sulfonamides are therefore bacteriostatic and inhibit growth and multiplication of bacteria, but do not kill them. Humans, in contrast to bacteria, acquire folate (vitamin B₉) through the diet.^[4]



Structural similarity between sulfanilamide (left) and PABA (center) is the basis for the inhibitory activity of sulfa drugs on tetrahydrofolate (right) biosynthesis.

Sulfonamides are used to treat allergies and coughs, as well as having antifungal and antimalarial functions. The moiety is also present in other medications that are not antimicrobials, including thiazide diuretics (including hydrochlorothiazide, metolazone, and indapamide, among others), loop diuretics (including furosemide, bumetanide,¹¹ and torsemide), acetazolamide, sulfonyleureas (including glipizide, glyburide, among others), and some COX-2 inhibitors (e.g., celecoxib).

Sulfasalazine, in addition to its use as an antibiotic, is also used in the treatment of inflammatory bowel disease.^[5]

Prontosil, as Bayer named the new drug, was the first medicine ever discovered that could effectively treat a range of bacterial infections inside the body. It had a strong protective action against infections caused by streptococci, including blood infections, childbed fever, and erysipelas, and a lesser effect on infections caused by other cocci.¹² However, it had no effect at all in the test tube, exerting its antibacterial action only in live animals. Later, it was discovered by Daniel Bovet,^[8] Federico Nitti, and Jacques and Thérèse Tréfouël, a French research team led by Ernest Fourneau at the Pasteur Institute, that the drug was metabolized into two parts inside the body, releasing from the inactive dye portion a smaller, colorless, active compound called sulfanilamide.^[9] The discovery helped establish the concept of "bioactivation" and dashed the German corporation's dreams of enormous profit; the active molecule sulfanilamide (or sulfa) had first been synthesized in 1906 and was widely used in the dye-making industry; its patent had since expired and the drug was available to anyone.^[10]

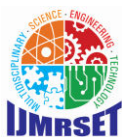
The result was a sulfa craze.^[11] For several years in the late 1930s, hundreds of manufacturers produced myriad forms of sulfa. This and the lack of testing requirements led to the elixir sulfanilamide disaster in the fall of 1937, during which at least 100 people were poisoned with diethylene glycol. This led to the passage of the Federal Food, Drug, and Cosmetic Act in 1938 in the United States. As the first and only effective broad-spectrum antibiotic available in the years before penicillin, heavy use of sulfa drugs continued into the early years of World War II.^[12] They are credited with saving the lives of tens of thousands of patients, including Franklin Delano Roosevelt Jr. (son of US President Franklin Delano Roosevelt) and Winston Churchill.^{[13][14]} Sulfa had a central role in preventing wound infections during the war. American soldiers were issued a first-aid kit containing sulfa pills and powder and were told to sprinkle it on any open wound.^[15]

The sulfanilamide compound is more active in the protonated form. The drug has very low solubility and sometimes can crystallize in the kidneys, due to its first pK_a of around 10. This is a very painful experience, so patients are told to take the medication with copious amounts of water. Newer analogous compounds prevent this complication because they have a lower pK_a , around 5–6, making them more likely to remain in a soluble form.¹³

Many thousands of molecules containing the sulfanilamide structure have been created since its discovery (by one account, over 5,400 permutations by 1945), yielding improved formulations with greater effectiveness and less toxicity. Sulfa drugs are still widely used for conditions such as acne and urinary tract infections, and are receiving renewed interest for the treatment of infections caused by bacteria resistant to other antibiotics.¹⁴

DISCUSSION

Sulfonamides have the potential to cause a variety of adverse effects, including urinary tract disorders, haemopoietic disorders, porphyria and hypersensitivity reactions. When used in large doses, they may cause a strong allergic reaction.¹⁵ The most serious of these are classified as severe cutaneous adverse reactions (i.e. SCARs) and



include the Stevens–Johnson syndrome, toxic epidermal necrolysis (also known as Lyell syndrome), the DRESS syndrome, and a not quite as serious SCARs reaction, acute generalized exanthematous pustulosis. Any one of these SCARs may be triggered by certain sulfonamides.^[3]

Approximately 3% of the general population have adverse reactions when treated with sulfonamide antimicrobials. Of note is the observation that patients with HIV have a much higher prevalence, at about 60%.^[17]

Hypersensitivity reactions are less common in nonantibiotic sulfonamides, and, though controversial, the available evidence suggests those with hypersensitivity to sulfonamide antibiotics do not have an increased risk of hypersensitivity reaction to the nonantibiotic agents.^[18] A key component to the allergic response to sulfonamide antibiotics is the arylamine group at N4, found in sulfamethoxazole, sulfasalazine,¹⁶ sulfadiazine, and the anti-retrovirals amprenavir and fosamprenavir. Other sulfonamide drugs do not contain this arylamine group; available evidence suggests that patients who are allergic to arylamine sulfonamides do not cross-react to sulfonamides that lack the arylamine group, and may therefore safely take non-arylamine sulfonamides.^[19] It has therefore been argued that the terms "sulfonamide allergy" or "sulfa allergy" are misleading and should be replaced by a reference to a specific drug (e.g., "cotrimoxazole allergy").^[20]

Two regions of the sulfonamide antibiotic chemical structure are implicated in the hypersensitivity reactions associated with the class.

- The first is the N1 heterocyclic ring, which causes a type I hypersensitivity reaction.
- The second is the N4 amino nitrogen that, in a stereospecific process, forms reactive metabolites that cause either direct cytotoxicity or immunologic response.¹⁷

The nonantibiotic sulfonamides lack both of these structures.^[21]

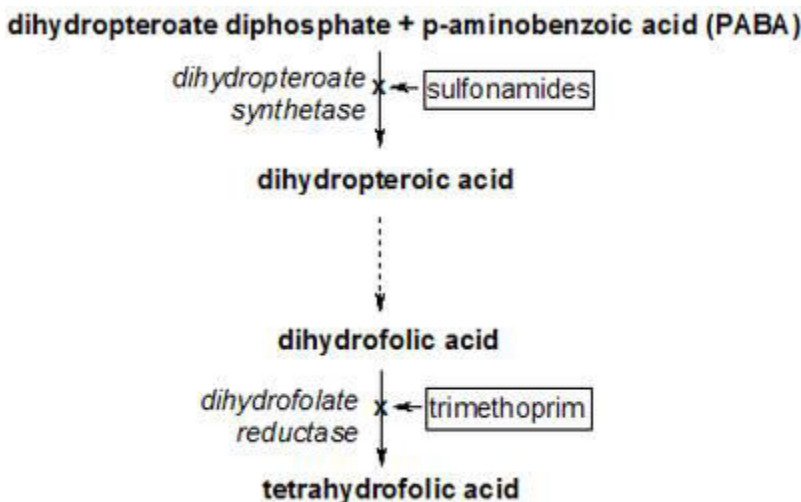
The most common manifestations of a hypersensitivity reaction to sulfa drugs are rash and hives. However, there are several life-threatening manifestations of hypersensitivity to sulfa drugs, including Stevens–Johnson syndrome, toxic epidermal necrolysis, agranulocytosis, hemolytic anemia, thrombocytopenia, fulminant hepatic necrosis, and acute pancreatitis, among others.^[22]

III.RESULTS

4-Aminobenzoic acid (also known as para-aminobenzoic acid or PABA because the two functional groups are attached to the benzene ring across from one another in the para position) is an organic compound with the formula $H_2NC_6H_4CO_2H$. PABA is a white solid, although commercial samples can appear gray. It is slightly soluble in water. It consists of a benzene ring substituted with amino and carboxyl groups.¹⁸ The compound occurs extensively in the natural world. PABA is an intermediate in the synthesis of folate by bacteria, plants, and fungi.^[5] Many bacteria, including those found in the human intestinal tract such as *E. coli*, generate PABA from chorismate by the combined action of the enzymes 4-amino-4-deoxychorismate synthase and 4-amino-4-deoxychorismate lyase.^[6] Plants produce PABA in their chloroplasts, and store it as a glucose ester (pABA-Glc) in their tissues. Humans lack the enzymes to convert PABA to folate and so require folate from dietary sources, such as green leafy vegetables. In humans, PABA is considered nonessential and, although it has been referred to historically as "vitamin B_x", is no longer recognized as a vitamin^[5] because the typical human gut microbiome generates PABA on its own.¹⁹

Sulfonamide drugs are structurally similar to PABA, and their antibacterial activity is due to their ability to interfere with the conversion of PABA to folate by the enzyme dihydropteroate synthetase. Thus, bacterial growth is limited through folate deficiency.^[7]

PABA finds use in the biomedical sector. Its derivatives are found as a structural component in 1.5% of a database of 12111 commercial drugs.^[10] Other uses include its conversion to specialty azo dyes and crosslinking agents. PABA is also used as a biodegradable pesticide, though its use is now limited due to evolution of new variants of bio-pesticides.²⁰



In the past, PABA was widely used in sunscreens as a UV filter. It is a UVB absorber, meaning it can absorb wavelengths between 290 and 320 nm.^[11] while still allowing UVA wavelengths between 320-400 nm to pass through, producing a tan.^[12] Patented in 1943, PABA was one of the first active ingredients to be used in sunscreen.^[13] The first in vivo studies on mice showed that PABA reduced UV damage. In addition, it was shown to protect against skin tumors in rodents.^[14] Animal and in vitro studies in the early 1980s suggested PABA might increase the risk of cellular UV damage.^[15] On the basis of these studies²¹, as well as problems with allergies and clothing discoloration, PABA fell out of favor as a sunscreen. However, water-insoluble PABA derivatives such as padimate O are currently used in some cosmetic products including mascara, concealer, and matte lipsticks.^[16]

As of 2008, the advancement of new sunscreen is focused on developing a broad spectrum of active ingredients that provide consistent protection across all wavelengths, including UVA. Researchers are considering the PABA-TiO₂ Hybrid Nanostructures that result from the method of aqueous in situ synthesis with PABA and TiO₂.^[17]

IV. CONCLUSIONS

Sulfonamides are prepared by the reaction of a sulfonyl chloride with ammonia or an amine. Certain sulfonamides (sulfadiazine or sulfamethoxazole) are sometimes mixed with the drug trimethoprim, which acts against dihydrofolate reductase. As of 2013, the Republic of Ireland is the largest exporter worldwide of sulfonamides, accounting for approximately 32% of total exports²²

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