MI Q&A

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Prepared by: Elizabeth Anderson
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IS A 'SULFUR' ALLERGY POSSIBLE?

Background

The terms sulfur, sulphur or sulfa allergy are misleading, inaccurate and should NOT be used.

Sulfur is a ubiquitous element in our world, and a constituent of every cell. Although patients may state they have a sulfur/sulphur allergy, such an allergy is **not** possible.

Confusion can arise when the imprecise term of 'sulfa drugs' is used as although it is most commonly applied to antibacterial sulfonamides, it has been used for other drugs as well. The term 'sulfa' relates to a sulfonamide moiety (see below) and this structure can be present in various drugs which do not have allergic cross-reactivity (*see Table 1*).

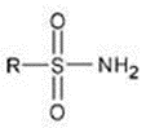
Other drugs contain sulfur groups, but they are **not** structurally related to sulfonamides. These include sulfhydryl drugs, sulfate salts and sulfites (*see Table 1*).

It is crucial to take a careful and thorough allergy history. The nature of the drug reaction, the temporal relationship between starting the drug and the onset of symptoms, and other drugs being used at the time should be carefully considered

Sulfamethoxazole/trimethoprim
Patients who have had a prior allergic reaction to the combination of sulfamethoxazole and trimethoprim (Bactrim®, Septrin®, Resprim®) have a potential allergy to trimethoprim and/or sulfamethoxazole and should avoid both until proven otherwise.

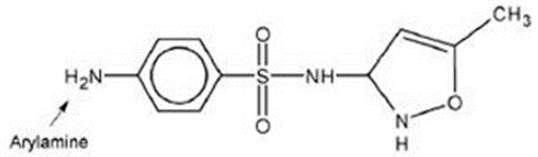
What is a sulfonamide?

A sulfonamide is an analogue of para-aminobenzoic acid. The basic sulfonamide structure consists of a sulfonamide moiety or sulfonyl group.



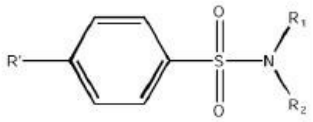
Sulfonamides can be divided into three groups (*see Table 1 for examples*):

1. A **sulfonylarylamine** is a sulfonamide moiety directly connected to a benzene ring with an unsubstituted amine (-NH2) moiety at the N4 position. All sulfonamide antibiotics are sulfonylarylamines, and they are the second most common cause of drug allergy.



Chemical structure for sulfamethoxazole

2. A **non-sulfonylarylamine** is a sulfonamide moiety connected to a benzene ring or other cyclic structure without the amine moiety at the N4 position.



3. Drugs that contain a **sulfonamide moiety group**

What to do

Record all allergic adverse reactions to medications in the patient's medical notes and medication chart:

i) Use the specific name of the drug(s). For example, co-trimoxazole or sulfamethoxazole/trimethoprim. **Do not write or accept 'sulfur', 'sulphur' or 'sulfa' allergy**.

ii) Record the nature of the adverse reaction

Cross-reactivity

When a true sulfonamide allergy is present, cross-reactivity with structurally related agents may occur. Patients allergic to sulfamethoxazole are most likely to cross-react with other sulfonylarylamines; therefore,

these drugs should be avoided if there has been prior hypersensitivity.

From current evidence, cross-reactivity does not occur for sulfonylarylamine allergic patients to non-sulfonyl arylamine drugs, due to structural differences. This conflicts with the product information for many non-sulfonylarylamines. Sulfhydryl or sulfate drugs have no cross-reactivity to sulfonamides at all as they do not contain the structural groups required to form the same immunogenic metabolites. Sulfites also have no cross-reactivity to sulfonamides. However, some patients specifically have sulfite allergy (e.g. sodium metabisulfite) which may be used in pharmaceuticals as an antioxidant.

Management of drug allergy

The mainstay of management in patients with a true allergy to sulfonamides is avoidance. Patients allergic to sulfonylarylamines should avoid all sulfonylarylamine compounds. In patients with serious sulfonylarylamine allergies and/or multiple medication allergies, use of non-sulfonylarylamine medications must be assessed on an individual basis. Where appropriate, drug challenges or desensitisation may be carried out under the supervision of the Clinical Immunology & Allergy team. Ensure as much information as possible is documented about the drug and allergy history.

Table 1 Examples of drug groups and possibility of cross-reactivity

Drug groups	Cross-reactivity
Sulfonylarylamines (*antibacterial* sulfonamides)	
sulfacetamide sulfadiazine sulfamethoxazole sulfasalazine (contains sulfapyridine)	**Allergic cross-reactivity** within this group is possible. Avoid same structure compounds in allergic patients.
Sulfonylarylamines (*antiretroviral* sulfonamides)	
darunavir fosamprenavir	Allergic cross-reactivity with antibacterial sulfonylarylamines is possible on structural grounds but has not been established.
Non-sulfonylarylamines (non-antibacterial sulfonamides)	
Acetazolamide, brinzolamide, bumetanide, celecoxib, diazoxide dorzolamide, furosemide (frusemide), gliclazide, glimepiride, hydrochlorothiazide, indapamide	Current evidence suggests that allergy to antibacterial sulfonylarylamines is **not** associated with increased risk of allergy to these drugs.
Sulfonamide moiety containing drugs	
Probenecid, sotalol, topiramate, triptans (e.g. sumatriptan)	Current evidence suggests that allergy to antibacterial sulfonylarylamines is **not** associated with increased risk of allergy to these drugs.
Sulfhydryl drugs	
Acetylcysteine, captopril, penicillin, piroxicam	No relationship to sulfonamide allergy, i.e. no cross reactivity.
Sulfate drugs	
Ferrous sulfate, glucosamine sulfate, heparin sulfate, hydroxychloroquine sulfate, magnesium sulfate, morphine sulfate, salbutamol sulfate	No relationship to sulfonamide allergy, i.e. no cross reactivity.
Sulfone derivative	
Dapsone	Contains an N4 arylamine. Approximately 20% cross-reactivity with sulfonylarylamines.
Sulfites	
Food code numbers 220 to 228 (sulfur dioxide, sodium sulfite, sodium bisulfite, sodium metabisulfite, potassium metabisulfite, calcium sulfite, calcium bisulfite, potassium bisulfite)	No relationship to sulfonamide allergy, i.e. no cross reactivity.

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MI Q&A aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications. The topics presented are based on frequently encountered medicines information requests made to Medicines Information centres and/or matters of current clinical importance. Note that any treatment decisions should be made with careful consideration of the individual clinical circumstances of each patient. Comments, contributions or suggestions are welcome. Please join the SHPA Medicines Information stream at:
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