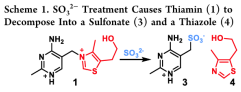
Known Sulfite Mopper Uppers

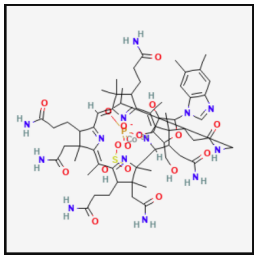
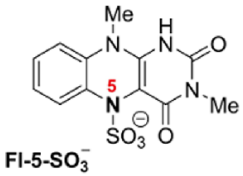
(Recommendations are general guidelines and not meant to substitute for an evaluation with a health care provider regarding your individual needs. Please consult with your provider before making changes to your diet, supplements, medications, or lifestyle.)

Substance	Effects	Supplement?
Thiamine  Scheme 1. SO_3^{2-} Treatment Causes Thiamin (1) to Decompose Into a Sulfonate (3) and a Thiazole (4) [Sulfite-Catalyzed Nucleophilic Substitution Reactions with Thiamin and Analogous Pyrimidine Donors Proceed via an SNAE Mechanism | The Journal of Organic Chemistry]	When treated with sulfite, thiamin undergoes a substitution reaction to release a thiazole leaving group and the corresponding sulfonate. Another proposed mechanism is the addition of sulfite to C6' of the 4-aminopyrimidine of thiamine.	**Yes.** **We definitely need B1 as it is actively being destroyed by sulfite.** However, if you worsen with sulfite toxicity issues after starting B1, this could be due to decreases in alpha-ketoglutarate, which is part of the natural inhibition of cysteine dioxygenase (CDO), leading to lower sulfite production from cysteine. Elliot Overtone explains the benefits of high-dose thiamine to kick start the alpha-ketoglutarate dehydrogenase enzyme (KGDH) here. It's possible that B1 can help mop up sulfite, but if the cause of your B1 deficiency is sulfite coming from increased CDO activity, you may end up worsening your sulfite issue by taking away the inhibition of alpha-ketoglutarate on CDO activity. How do you know if your sulfite issues are related to intracellular sulfite from sulfite oxidase not working well? Check S-sulfocysteine levels using OMX. If these are low, likely that your sulfite intolerance is coming from white blood cells (neutrophils) that release sulfite during an immune attack. SSC is a marker for inadequate sulfite oxidase activity. **B1 can also be problematic for individuals in alkalosis,** as in alkalosis, B1 becomes a thiol and can free NO from its storage form, bound to glutathione, GSNO. (If you are in the "I'm not okay, I'm not okay" state of sulfite toxicity causing a panic attack and hyperventilation, please continue reading this column all the way to the bottom.) **The versions that are most likely to "mop up sulfite" (or be destroyed by sulfite) are Thiamine HCl, Thiamine Mononitrate, and Thiamine Pyrophosphate**

		because they would be vulnerable to immediate nucleophilic attacks by free sulfite in cells and the blood. **Benfotiamine is not immediately affected by sulfite because it must be taken up into cells before conversion into thiamine.** Benfotiamine is an S-benzoylthiamine O-monophosphate, a thioester derivative in which the thiazole ring is protected by a benzoyl group and the molecule is phosphorylated. This modification blocks the nucleophilic attack by sulfite at the methylene bridge. Benfotiamine is activated within cells by dephosphorylation to S-benzoylthiamine by ecto-alkaline phosphatases at the cell membrane, followed by intracellular hydrolysis of the thioester bond to release free thiamine, which is then phosphorylated to thiamine diphosphate (ThDP), the active coenzyme form. Once activated, it is still vulnerable to sulfite. **Caution: Metabolism of benfotiamine yields significant amounts of BENZOATE.** Benzoate is detoxified by glycine conjugation. First CoA is added by medium-chain fatty acid CoA ligases (this step is inhibited by salicylates). Then glycine is added. The product is hippuric acid. If you have low glycine status, this can worsen glycine depletion. Glycine is one of the amino acids needed for making glutathione. https://pubmed.ncbi.nlm.nih.gov/24399744/ https://pubmed.ncbi.nlm.nih.gov/24754494/ https://pubmed.ncbi.nlm.nih.gov/1352215/ https://pubmed.ncbi.nlm.nih.gov/27907139/ **TTFD would be partially protected from the immediate attack by sulfite** because the tetrahydrofurfuryl group and the disulfide bond protect the thiazole ring and the methylene bridge from direct nucleophilic attack by sulfite. **ALKALOSIS and B1** **Those with chronically low blood pressure, high ammonia, using bicarbonate supplements, or hyperventilating theoretically could be at risk for a high “free” nitric oxide state.** During alkalosis (high CO2 in blood, high blood pH), there is a possibility that B1 can free nitric oxide (NO) from glutathione (GSNO), which can occur when the body

		is holding on to bicarbonate or bicarbonate is increased. ***This is a well-researched theory that I came up with to explain why so many individuals have reached out to me, saying they were doing great with B1, but then suddenly it went downhill quickly despite supplementing with potassium (bicarbonate) or increasing sodium bicarbonate because they were told it would help with lactate symptoms.*** **Bicarbonate supplements**. Someone using sodium bicarbonate (baking soda) or potassium bicarbonate supplements has a risk of too much bicarbonate. This can lead to alkalosis. **High or chronically high normal aldosterone**. Someone with a chronically activated aldosterone system from low blood pressure may be in alkalosis. **Anxiety.** Anyone having a panic attack, such as someone who is in a "I'm not okay" state, will have increased respiration leading to alkalosis. **In an alkalosis state, thiamine is metabolized to a thiol form.** This removes glutathione (GSH) from NO (GSNO is a storage form of nitric oxide in the body). When someone is in a high NO state, several things can happen. https://pubmed.ncbi.nlm.nih.gov/15823089 https://pubmed.ncbi.nlm.nih.gov/9454793 https://pubmed.ncbi.nlm.nih.gov/8962068 https://pubmed.ncbi.nlm.nih.gov/12060567 1. **Low Blood Pressure.** High levels of NO in the blood can cause vasodilation (widening of the blood vessels) and low blood pressure. This will lead to the release of aldosterone from the adrenal glands. Aldosterone tells the kidneys to uptake more sodium to help increase blood volume (sodium holds on to water). At the same the kidneys will release potassium into the urine. This can cause low potassium (hypokalemia). **SYMPTOMS of LOW POTASSIUM:** seizures, muscle weakness, muscle cramps, excessive urination, nighttime urination, fatigue, premature

		ventricular contractions, tachycardia, ventricular fibrillation, and torsades de points. **IF THIS CONTINUES:** Continued vasodilation and an increase (even physiological levels) of aldosterone will lead to **decrease magnesium reabsorption** from the urine. Aldosterone activates ENaC, which leads to **magnesium and potassium wasting in the urine**. Once magnesium goes low, it's harder to hold on to potassium in the kidneys. **Low magnesium status can lead to loss of phosphate in the urine.** 2. **High levels of NO release during alkalosis can alter the diaphragm function**. Excess NO can contribute to peroxynitrite formation, which alters energy metabolism in the diaphragm. The NO itself can cause injury to the muscles of the diaphragm, worsening diaphragm function. (If your alkalosis was caused by a panic attack, then the slowing of the diaphragm could lead to reversal of this state). https://pubmed.ncbi.nlm.nih.gov/10463956 https://pubmed.ncbi.nlm.nih.gov/10444640 https://pubmed.ncbi.nlm.nih.gov/9817721 https://pubmed.ncbi.nlm.nih.gov/11253781 https://pubmed.ncbi.nlm.nih.gov/8833903 https://pubmed.ncbi.nlm.nih.gov/11253787 **Solution:** Talk with your practitioner about your iNOS status and pH. Avoid bicarbonate forms of potassium and sodium, as without daily or at a minimum weekly CO2 checks, it's very hard to manage an appropriate bicarbonate level to consume. Avoid nitric oxide inducers (arginine, nitrates). Consider iNOS inhibitor (ginger, rooibos tea). Consider checking for an underlying infection causing intolerances to B1 (infections increase iNOS). **Oxalate Dump From Liver**. Additionally, be aware that when adding B1, it may mop up sulfite in the blood so well that you can experience an oxalate dump. This is due to the immediate decrease in sulfite inhibition of SAT-1. https://journals.physiology.org/doi/epdf/10.1152/ajprenal.90401.2008

Vitamin B12 	Functional B12 deficiency. Sulfite binds to the cobalt center of B12. This makes the binding of methyl groups and adenosyl groups impossible. There is some concern that this can occur in the digestive tract and could be a significant source of B12 deficiency.	**Yes.** B12 is needed for methionine salvage that helps to regenerate SAMe. SAMe is needed for making molybdenum cofactor (MoCo). Caution for individuals with sleep apnea, B12 is sequestered in the brain. Long-term intermittent hypoxia has been shown to cause cobalt toxicity of the brain. B12 can also induce the HIF-1alpha pathway, which should be good, but in the presence of SUOX/MoCo deficiency, this can lead to increased intestinal sulfite. Titrating up slowly may be needed. **Dose:** Injections- 200 mcg hydroxocobalamin or per practitioner Oral - 50 mcg drop (1 drop of pure encapsulations hydrox/cobalamin) every hour. Oral - 250 mcg sublingual every 4 hours (Avoid exposure to light, as light can degrade B12 into cobalt)
Riboflavin  Fl-5-SO_3^-	Sulfite can irreversibly bind to the ketone group of riboflavin. It has been shown to bind to flavin proteins at the N5 position on the isoalloxine ring, altering enzyme activity. It can decrease the enzyme activity of choline oxidase, glycolate oxidase, sarcosine oxidase, and d-amino oxidase.	**Yes.** Riboflavin can increase butyrate production in the intestines. The only caution is for those with elevated ethylmalonic acid (EMA), as butyrate is metabolized to ethylmalonyl CoA. Dose: Per individual tolerance. In migraines, dosing is 400 mg per day. However, spacing this dose out would be helpful to buffer sulfite better, as riboflavin is lost quickly in urine.

Betaine aldehyde	Betaine aldehyde binds sulfite. During free sulfite toxicity, the enzyme choline oxidase can be inhibited by sulfite. This leads to low betaine aldehyde levels. Sulfite can also inhibit the enzyme ALDH7A1 leading to low production of betaine.	**Not directly.** There are no betaine aldehyde supplements. **Choline intake is important** because choline oxidase can make betaine aldehyde, and overall, the choline cycle is impaired by sulfite Betaine supplementation can help restore betaine needed for the methionine salvage pathway. This makes SAMe needed to make choline in the body from ethanolamine.
Vitamin B6	Sulfite can form adducts with the aldehyde group on pyridoxal phosphate, but also sulfite inhibits ALDH7A1, involved in lysine metabolism, which leads to a buildup of P6C and binding of P6C to pyridoxal phosphate, making it inactive.	**Yes.** Avoid pyridoxine forms of vitamin B6, as these can lead to competition for cofactor sites and B6 toxicity symptoms. B6 restores CBS and CSE activity. It can lead to a sudden surge in cysteine production through CBS as well as H2S production. It may lead to sudden increases in polyamine synthesis. In theory, individuals with SUOX/MoCo deficiency grow bacteria to make H2S and polyamines to compensate for the lack of production of these in their bodies. Increasing B6 quickly may lead to sudden H2S toxicity and polyamine toxicity. **Dose**: Start with 5 mg P5P once/day with food. Increase to 5 mg P5P every 4 hours with foods.
Dihydro-biopterin (qBH_2)	Sulfite reacts with dihydropterin. This may be the cause of high urinary losses of biopterin and contribute to BH4 deficiency..	**Unsure.** There is no good supplemental form of BH4 on the market. There are drugs to treat BH4 deficiency, such as saropterin dihydrochloride. BH4 is needed for healthy nitric oxide production as well as the conversion of phenylalanine and tyrosine metabolism