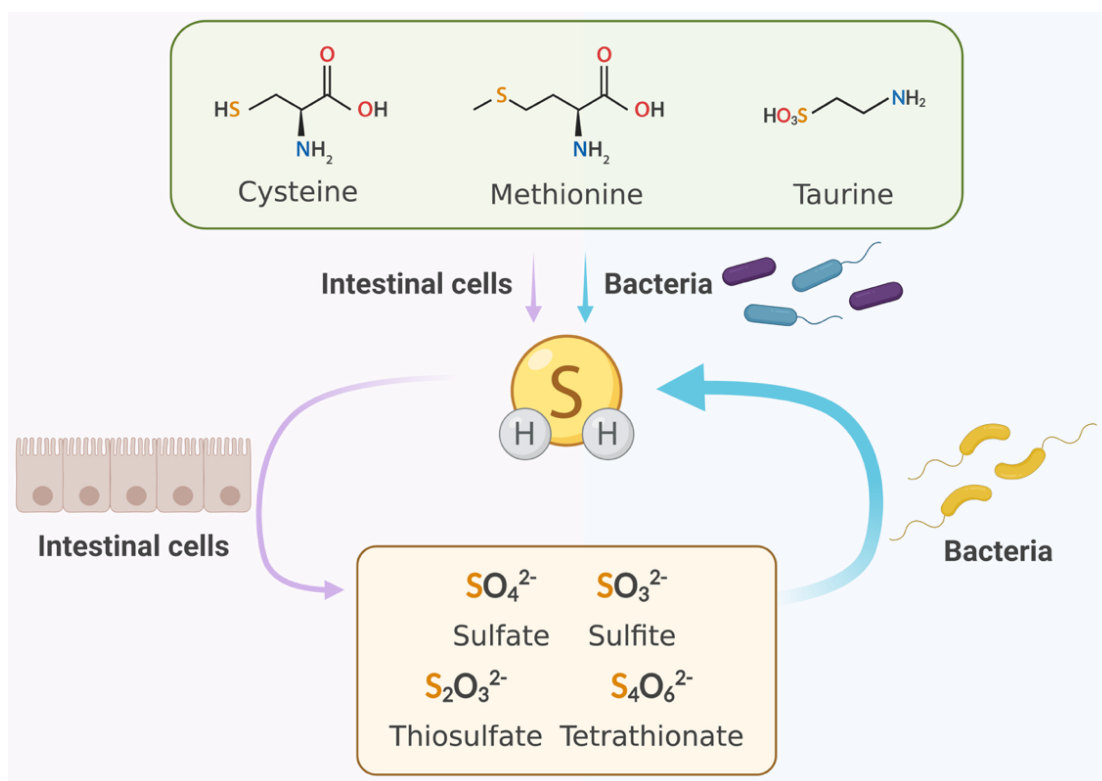


MicroBiomeRogue: Bilo

(R. M. Bernardino, A.I. Pimenta, I. A. C. Pereira)



Sulfur cycle in the human gut. Organic and inorganic sulfur compounds are biologically converted by both bacteria and intestinal cells.

Claim to infamy: causing H_2S -induced gut inflammation

Sulfur

Sulfur is an essential element for life, required for production of amino acids, hormones, vitamins, and other compounds involved in biological functions. In humans, sulfur is acquired from the diet and absorbed in the gut.

Sulfur metabolism by the gut microbiota

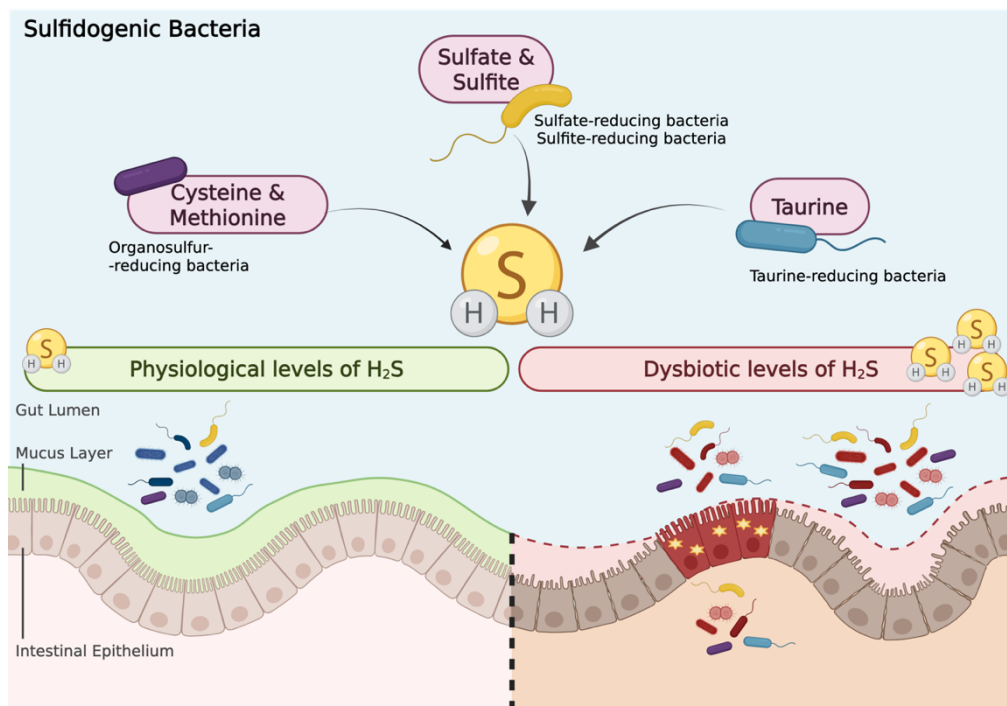
The metabolism of sulfur in the gut involves all the biological cycling transformations of sulfur-containing compounds and is mediated both by human cells and gut microbes. However, the gut microbiota is the main contributor to the metabolism of sulfur in the human body. These microorganisms, predominantly bacteria (99%), establish a symbiotic relationship with the host and have a significant influence on human physiology during both health and disease, offering numerous benefits to the host. However, to achieve these benefits, it is essential to maintain the equilibrium among the different microbial populations. Disorders in the structure and function of the microbiota can lead to a condition known as dysbiosis. Dysbiosis occurs primarily due to changes in environmental conditions such as diet, exposure to antibiotics, smoking or stress, and can contribute to the development of various diseases.

Diet and dysbiosis

Several studies have shown that dietary habits and microbiota composition are tightly linked to disease. The Western diet is characterized by high consumption of protein, sugar, animal fat, and highly processed foods. Conversely, it is low in fiber, vitamins, minerals, and other plant-derived molecules. This dietary pattern can alter the metabolic activity of the resident microbiota, disrupting the stability of the microbial community and causing a dysbiotic state that is associated with growing health risks. A diet rich in fat has been specifically associated with an increase in sulfide-producing bacteria (sulfidogenic bacteria), raising hydrogen sulfide levels in the gut, which leads to the development of inflammatory and chronic diseases that can extend beyond the GI tract.

The key role of hydrogen sulfide (H₂S) in dysbiosis

Hydrogen sulfide is a central molecule in sulfur metabolism, since it acts as a key intermediate for various biochemical processes occurring in our body. Although H₂S can be produced by human cells via the degradation of sulfur-containing amino acids (e.g. cysteine and methionine), it is the microbial production of H₂S in the human gut that contributes the most to sulfur homeostasis – the stable equilibrium of sulfur compounds in the body. Microbes can use both organic and inorganic sulfur compounds to produce H₂S. While the metabolism of inorganic compounds involves mainly the reduction of sulfate and sulfite to H₂S, organic metabolism involves the degradation and conversion of cysteine, methionine, taurine and other organosulfonates. All these transformations result in the production of H₂S and can have a big impact on our health.



Hydrogen sulfide as a key player in the gut sulfur cycle.

Overproduction of H₂S causes bowel inflammation

H₂S can have both positive and negative effects in the human body depending on its concentration. In small amounts, H₂S is beneficial as it acts as a signalling molecule – a molecule similar to hormones that influences metabolic processes – that is associated with regulation of many important cellular functions and may help prevent harmful bacteria from settling in the gut. However, in high concentrations H₂S can weaken the intestinal barrier – the gut epithelial “skin” that keeps unwanted molecules out of our body – and cause inflammation, which has been linked to conditions like inflammatory bowel diseases (IBD) and colorectal cancer. This dual role of H₂S highlights the delicate balance that is required to maintain healthy sulfur homeostasis. In the gut, H₂S bridges inorganic and organic sulfur transformations, sustaining microbial activity and regulating physiological functions.

Diet and sulfur homeostasis

Thus, sulfur metabolism in the human gut involves a complex interplay between dietary intake, microbial metabolism, and host physiology. While sulfur compounds play essential roles in maintaining gut homeostasis, imbalances in sulfur metabolism can contribute to gut dysbiosis and disease. Therefore, understanding these processes is crucial to developing strategies to modulate sulfur metabolism and promote gut health.

How do diet and microbes cause sulfur-induced intestinal problems? The key role of Bilo

Taurine, a highly abundant amino acid in our body, is one of the sulfur compounds that contributes the most to bacterially-mediated H₂S production in the gut. Consumption of high-fat foods stimulates the production of taurine-conjugated bile acids by the liver, which are required for the digestion of fats. These bile acids are subsequently metabolised in the gut, leading to accumulation of taurine. Increased levels of taurine in the gut induce the proliferation of taurine-metabolizing sulfidogenic bacteria, such as Bilo (*Bilophila wadsworthia*).

Bilo is a type of bacterium that lives in our gut, mostly in the lower part. It was discovered in the 1980s in people with severe appendicitis and got its name because it thrives in bile, a fluid produced by the liver that helps us to digest fats. This bacterium is a Gram-negative, rod-shaped organism that only survives in the absence of oxygen (anaerobe) and is motile, allowing it to move around the gut environment. Bilo is the only cultured species described in the *Bilophila* genus, which is closely related to *Desulfovibrio* spp.

Bilo is a normal member of the gut microbiota in 50% to 60% of people. Additionally, it stands as one of the most frequently encountered anaerobic microorganisms recovered from clinical infections, suggesting a strong pathogenic potential.

How can we keep Bilo in check?

In healthy individuals, Bilo plays a role in breaking down dietary fibre and producing short-chain fatty acids, which are beneficial for gut health. However, due to its ability to produce high levels of H₂S, Bilo has been associated with inflammatory bowel disease and colorectal cancer.

How to persuade Bilo to behave? Several studies suggest that changing our dietary habits to include more fibre and reduce fat consumption can help control the overgrowth of Bilo. This,

in turn, reduces H₂S production and its negative effects, thereby reducing the risk of developing inflammatory diseases and colorectal cancer.

Bilo is an important member of the gut microbiota of many people and carries out important tasks for us. But it is also a “pathobiont” – a normal member of the microbiota that can sometimes go “rogue”, by producing too much H₂S, and causing intestinal problems. Bilo is a Jekyll and Hyde character we need to keep more Jekyll than Hyde by means of a sensible diet.