Methanogenesis is the anaerobic respiratory pathway of methanogenic archaea which methane the final carbon product. Methanogenesis is known to be inhibited by both nitrate and sulfate, both indirectly as a result of competition for electron donating substrates and directly by the formation of toxic metabolic intermediates. In this study, we investigated the co-inhibition of methanogenesis by nitrate and sulfate in the sediments of a freshwater urban wetland with in vitro factorial experiments. While both amendments inhibited methanogenesis individually, their combined effects were additive, likely because they are both electron acceptors for anaerobic methane oxidation. Nitrate amendment caused sulfate to accumulate and similarly, sulfate amendment caused nitrate (as well as nitrite) to accumulate, likely because the two electron acceptors competed for the same pool of electron donors to respiration. However, nitrate, but not sulfate inhibited carbon dioxide production, suggesting that in addition to the competitive interactions, nitrate and the metabolic intermediates of denitrification had a toxic effect on sulfate reduction.