SULFAMETHOXAZOLE: A WATER QUALITY CONCERN FOR DES MOINES WATER WORKS?

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BACKGROUND

Some public health officials fear that if pharmaceutical pollution is transferred to drinking water, the resulting involuntary low-dose medication of large population groups may compromise public health. In addition, environmentalists fear aquatic life may be adversely affected by these low dose medications. (1)

The presence of pharmaceutical antibiotics in aquatic environments is of particular concern because of fears that they may stimulate antibacterial resistance among native bacterial populations. Resistance is usually quantified as the minimum concentration required to prohibit growth of a population of cells. Whenever there is a change in susceptibility that renders an antibiotic ineffective against a certain organism, the antibiotic is referred to as resistant. Antibacterial-resistant bacteria have been detected in municipal waste water effluents, sewage-affected surface waters and even drinking water (2). The detection in aquatic environments of resistant bacteria clearly merits concern regarding the fate of pharmaceuticals in the water treatment process. A report presented by the UK House of Lords, substantiated this concern: ‘Resistance to antibiotics and other anti-infective agents constitutes a major threat to public health and ought to be recognized as such more widely than it is at present.’ (3) Since little is known as to the health consequences of these trace antibiotics in our nation’s waters, we must continue to pursue the identification of these antibiotics and investigate the adverse effects they may potentially have on human and ecological health.

Human and livestock consumption of pharmaceuticals has increased worldwide. According to a report from the institute of medicine, greater than 25 million tons of antibiotics are produced in the U.S. annually. Continued human population growth contributes to the need for pharmaceuticals, and per capita consumption increases as conditions improve in under-developed countries. The increasing number of livestock confinements also contributes to the demand and consumption of antibiotics. The rationale behind feeding livestock antibiotics is twofold. The first is to maintain healthy animals in overcrowded confinements. The second is to promote growth, enabling the livestock to quickly reach market weight. A study from the Union of Concerned Scientists reported that 70% of all the antibiotics produced annually in the U.S. are fed to livestock for non-therapeutic purposes.

Since the majority of consumed pharmaceuticals are released via the urine as its bioactive chemical or metabolite, chances are that some amount of these compounds will end up either in waste water treatment plants, confinement lagoons, or on the land. These excreted antibiotics have the potential to pollute surface, ground and treated tap water. Such pollution has been observed in studies in Europe (5) and North America (6). Antibiotic runoff from livestock manure spread on fields also has the potential to pollute surface waters. In addition, unused pharmaceuticals may be discarded in toilets, increasing the pharmaceutical pollution of source waters. Pharmaceutical concentrations in tap water have been reported in the nanogram/liter or low microgram/liter range, implying that acute pharmacological effects in exposed populations of both human and livestock should be nil. However, the possible public health effect of life-long exposure to subliminal concentrations of pharmaceuticals is not fully-understood, and cannot, consequently, be considered harmless. In addition, since pharmaceuticals are one of the few chemical classes intended to be bioactive, they are potentially harmful to aquatic flora and fauna (1).

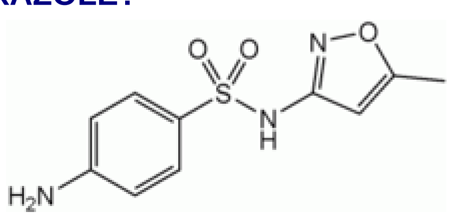
In March 2002 the United States Geological Survey (USGS) released the results of the first-ever national investigative study to determine the occurrence of pharmaceuticals, antibiotics, hormones and other organic wastewater contaminants in the United States surface waters. USGS sampled for 95 chemicals in 139 streams and rivers in 30 states and detected the presence, in trace amounts, of at least one of the contaminants at 80 percent of the sites; 82 of the 95 chemicals were detected at least once. Sulfamethoxazole (SMX) was listed as one of the top six most frequently detected compounds. The top six most frequently detected compounds were: acetaminophen, caffeine, codeine, cotinine, 17b-estradiol and sulfamehtoxazole (6).

In 2006 the Des Moines Water Works (DMWW) conducted a similar study in the Raccoon River (RR) watershed and the Fleur and Maffitt treatment plants. In the DMWW study, trace amounts of SMX were detected in river and alluvial waters at both treatment plants. SMX was also detected in the finished water at the Maffitt treatment plant following the spring runoff. Continued detection of SMX at both treatment plants was observed in the source and alluvial waters in the summer and fall. There was no detection of SMX in the finished waters at either plant in the summer or fall. In addition, the DMWW detected trace amounts of acetaminophen, caffeine, codeine, cotinine, 17b-estradiol and carbamazepine in source and finished waters after runoff events.

SMX has been frequently detected in municipal wastewaters at concentrations of 200 – 2000 ng/L; in surface waters at concentrations of 70 -150 ng/L; and in alluvial and treated drinking waters (5). Concentrations of 0-20 ng/L were detected in the alluvial source waters of both DMWW treatment plants in 2006. Concentrations of 0-17 ng/L were also detected in the finished water at the DMWW Maffitt treatment plant in 2006 after the spring runoff.

David Sedlak and Karen Pinkston of the University of California estimated that the predicted concentration of SMX in waste water could reach 3,800 ng/L. This prediction supports the hypothesis that if not removed during wastewater treatment, SMX could potentially reach water treatment plants. Therefore, drinking water treatment plants should have an action plan in place, as a safety net, that would remove SMX.

WHAT IS SULFAMETHOXAZOLE?



4-amino-*N*-(5-methylisoxazol-3-yl)-benzenesulfonamide

SMX is 4-amino-*N*-(5-methyl-3-isoxazolyl) benzenesulfon-amide. It is a white, almost odorless and tasteless compound with a molecular weight of 253.28, and its molecular formula is $C_{10}H_{11}N_3O_3S$ (7).

SMX is an anti-bacterial sulfonamide which is used to treat diseases such as bronchitis, middle ear infection, urinary tract infection, conjunctivitis, malaria, toxoplasmosis, and traveler's diarrhea. It is also a widely-prescribed veterinary antibiotic used to treat diseases and infections and is included in feed additives to promote growth and weight gain of food animals (8). Sulfonamides inhibit normal bacteria utilization of PABA for the synthesis of folic acid, an important metabolite in DNA synthesis. Bacteria resistance to SMX occurs by mutations in the folic acid enzyme that prevents the drug from binding and blocking folic acid synthesis. SMX is often combined with the antibiotic trimethoprim. This combination is commonly referred to as Bactrim, Septrin or Septra, and is used primarily to treat urinary tract infections and as an alternative to amoxicillin-based antibiotics to treat sinusitis (7).

DMWW shares the public's concern for the potential impact of pharmaceutical antibiotics in our nation's source and drinking waters. Therefore, the detection of SMX in the finished water at the DMWW Maffitt plant has prompted DMWW to take a closer look at the remediation of SMX with various powdered activate carbons (PAC). Treatment with PAC for the removal of SMX was chosen because SMX was not detected in the finished water at the DMWW Fleur treatment plant. A PAC dose of 10mg/L is routinely fed in the treatment process at the Fleur treatment plant, whereas carbon is not fed during the treatment process at the Maffitt treatment plant.

MATERIALS AND METHODS

Jar Test

Jar tests were set up to determine the amount and source of powdered activated carbon that would effectively remove a final concentration of 0.6 ppb SMX in 1 liter of alluvial water. The amount of SMX remained constant throughout the study. The amount and type of carbon were the only variables. Three independent carbon sources were each evaluated at five concentrations: 0 (control), 5, 10, 20 and 30 mg/L. Each jar contained 1 liter of alluvial water from the infiltration gallery at the Fleur plant. SMX was spiked into each jar to achieve a final concentration of 0.6 ppb. After a 1-minute mix of the SMX at 80 rpm, the various carbons were added at the pre-determined concentrations. Each jar was then mixed for 1 minute at 150 rpm. The amount and rate of mixing was based on the DMWW study: *"DMWW Laboratory Carbon Wetting Study, 8-3-04".* All variables, carbon dose and carbon type were studied in duplicate. After mixing, samples were collected from each jar and analyzed for SMX by enzyme linked immunosorbent assay (ELISA).

Sulfamethoxazole

SMX was spiked into each jar to reach a final concentration of 0.6 ppb. A 10 µg/mL stock solution was purchased from Abraxis. 60 uL of this stock was injected into each 1 liter jar.

Carbons Analyzed

Due to the tariff imposed on carbon imports from China, there were only three predominant manufacturers of PAC that were approved for drinking water at the time of this study. They were Calgon, Nordit, and Mead – Westvaco. A 1-pound PAC sample was procured from each of these manufacturers and was evaluated for SMX removal efficiency. A 10,000 mg/L stock solution was prepared from each manufacturer's carbon. Varying amounts of this stock solution were injected into each jar to achieve the five experimental carbon concentrations.

Control

Because of the potential for adsorption of the SMX onto colloidal material in the alluvial water, the jar tests were duplicated in distilled water. A SMX-spiked jar without carbon was also included with each set of jar tests in order to verify SMX removal by the various carbons.

Sulfamethoxazole ELISA Test

The SMX ELISA is a competitive enzyme immunoassay for the screening of water (groundwater, surface water, well water) samples for the presence of this antimicrobial. The assay range is between 0.025 ppb and 1.0 ppb. The antibiody binds SMX and does not cross-react with unrelated antibiotics. The kit uses a 96-well microtiter plate format. The total time for measurement is 90 minutes. The kit was purchased from Abraxis LLC. The cost of the kit was $500 at a cost per sample of approximately $10.

Results and Discussion

As seen in the tables below, overall examination of the removal data indicated SMX was effectively removed by all carbon products at a dosage of 10 mg/L or greater. Further examination of the data indicated that at a lower dosage, 5 mg/L of Calgon carbon may be more effective than Nordit and / or Mead in removing SMX. Why the Calgon carbon is more effective at the low dose is not known. One hypothesis is that the Calgon carbon particles have more active sites and/or surface area, allowing for additional adsorption of SMX. Another hypothesis might be that each site on the Calgon product may have more affinity to SMX than Nordit or Mead. A third hypothesis is that the adsorption time was quickest for Calgon carbon at the time of this study.

RELATIVE % SMX REMOVAL IN DISTILLED WATER

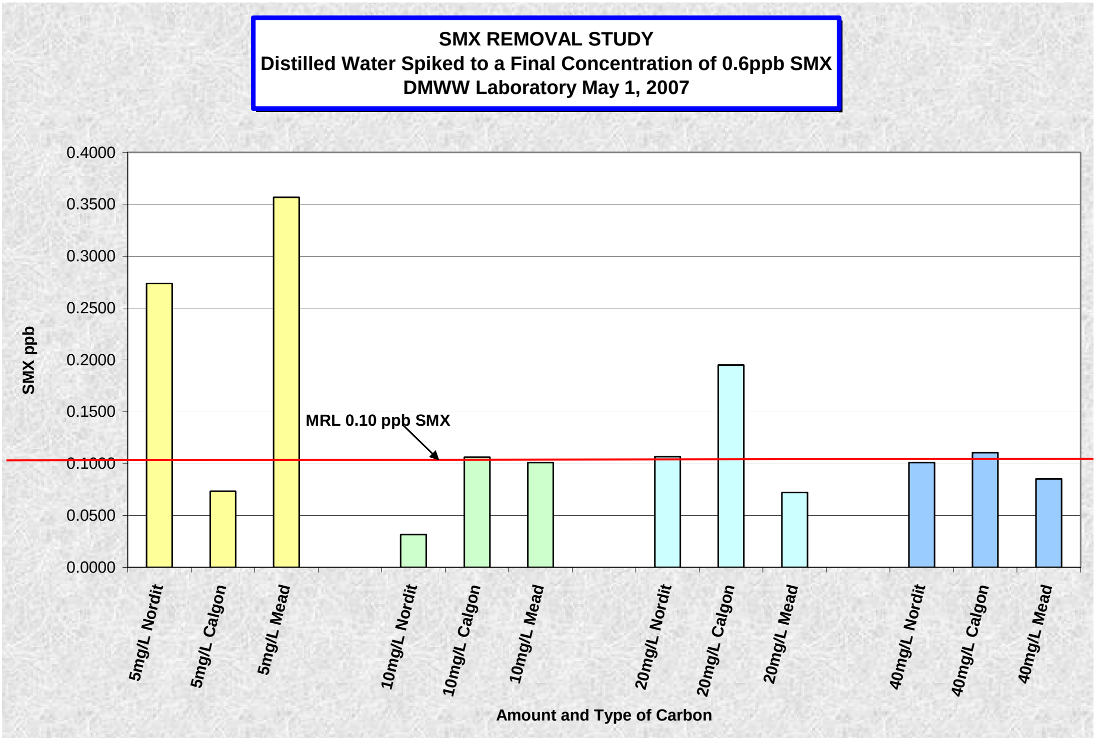
5mg/L Nordit	62.22
5mg/L Calgon	89.87
5mg/L Mead	51.94
10mg/L Nordit	95.74
10mg/L Calgon	85.69
10mg/L Mead	86.40
20mg/L Nordit	86.52
20mg/L Calgon	75.34
20mg/L Mead	90.87
40mg/L Nordit	88.26
40mg/L Calgon	87.15
40mg/L Mead	90.09

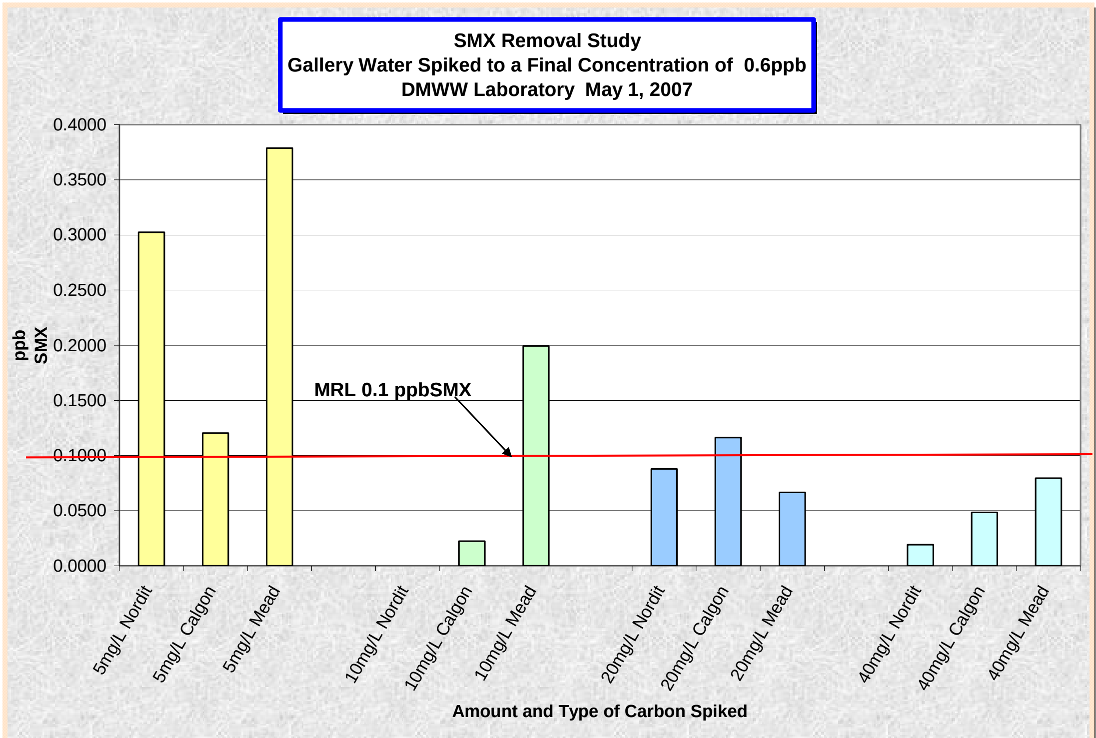
RELATIVE % SMX REMOVAL IN GALLERY WATER

5mg/L Nordit	52.45
5mg/L Calgon	81.08
5mg/L Mead	40.46
10mg/L Nordit	100.00
10mg/L Calgon	96.51
10mg/L Mead	68.65
20mg/L Nordit	87.72
20mg/L Calgon	83.76
20mg/L Mead	90.71
40mg/L Nordit	97.49
40mg/L Calgon	93.66
40mg/L Mead	89.61

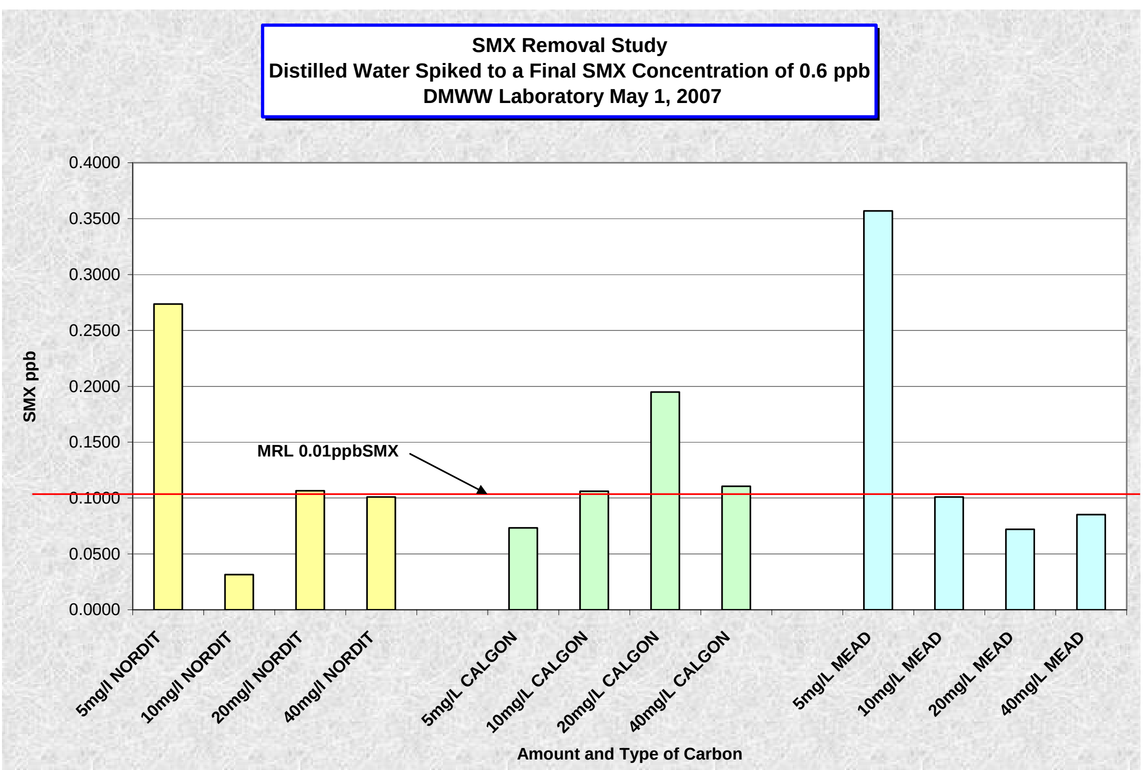
The data also indicates that from a product cost and removal standpoint, feeding 10mg/L of any of the three carbons studied would be considered an adequate dose for near-complete removal. Increased carbon dosages didn't substantially increase removal and would not be cost effective.

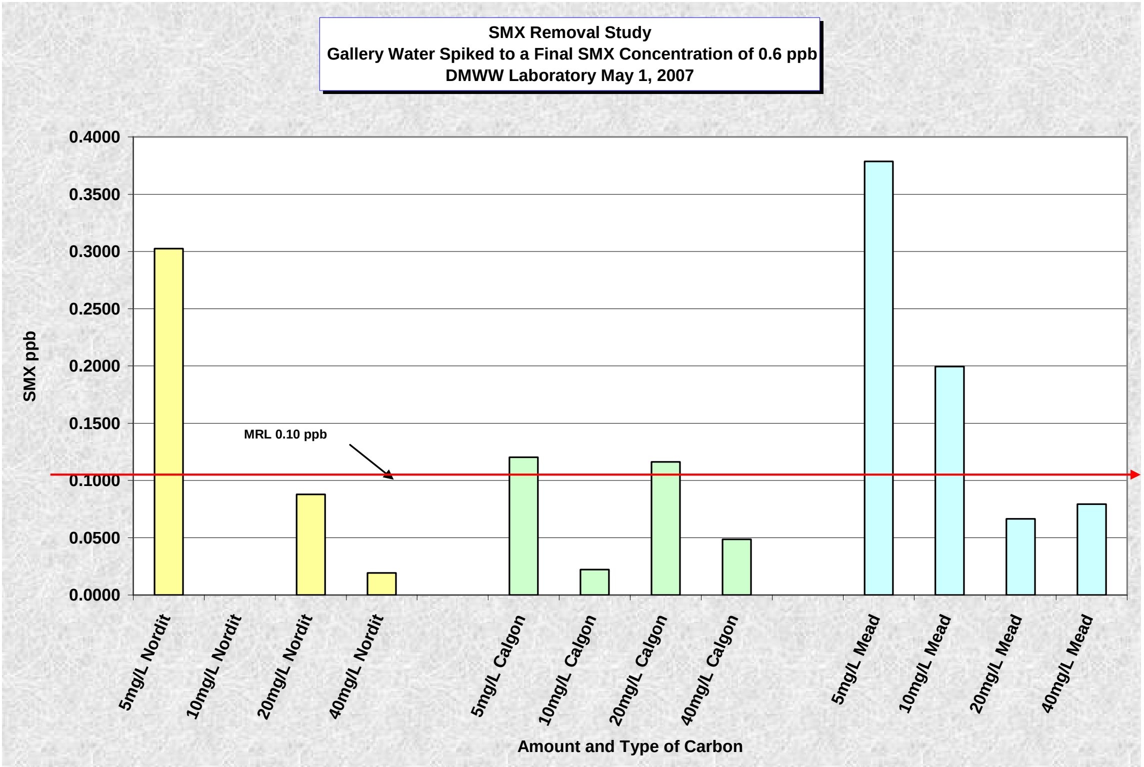
The first two graphs below depict SMX removal efficiency versus carbon dose. Analysis conducted by the DMWW laboratory indicated the minimum reporting limit for the ELISA kits utilized during this study to be 0.1ppb. Therefore any result below 0.1 ppb will be viewed as not detectable or as complete removal of SMX in this study.





The next set of graphs depicts SMX removal efficiency by product type.





The graphs indicate that the most efficient amount of carbon to feed for the removal of SMX, independent of manufacturer, would be 10mg/L, with the exception of Mead carbon used in gallery water, where the most effective dose was 20 mg/L. Calgon carbon seems to be more effective than either Nordit or Mead carbon at the lowest dose evaluated (5 mg/L).

Conclusion

Dana Koplin of USGS recently documented that SMX appears to be persistent and mobile in water. Therefore, if there was an upstream source discharging SMX into a drinking water plant's source water, the potential for detectable levels of this compound in tap water will exist. DMWW detected trace amounts of SMX in drinking water leaving its Maffitt plant in 2006. Therefore, feeding 10mg/L carbon at both Fleur and Maffitt treatment plants should be encouraged for removal of trace amounts of SMX.

Whether the detected trace concentrations of SMX are a risk to human health is a question that cannot be answered at this time.

References:

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