Drug Residues in Ambient Water: Initial Surveillance in New Mexico, USA

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Abstract

Pharmaceutical residues, originating in sewage effluent, have been detected in surface and ground water in other states and countries. Detected drugs include painkillers, lipid (cholesterol) regulators, antiseptics, chemotherapy agents, antibiotics, and hormones. Approximately 30-60% of prescribed medicines are excreted into sewage. Conventional sewage-treatment technologies vary greatly in their ability to eliminate drug residues. Some drug residues have caused ecological impacts such as the widespread sexual disruption of male fish exposed to estrogenic hormones, and the development of antibiotic-resistant pathogenic bacteria in rivers and birds, including Salmonella in the Rio Grande.

The State of New Mexico is testing water where drug residues would most likely occur. Grab samples of treated sewage effluent, surface water receiving treated sewage, and ground water contaminated by sewage (both septic-tank and treatment-plant plumes) are being collected. We are able to detect some analgesic, anti-convulsant, anti-depressant, anti-inflammatory, and hormonal drugs in water at the ng/L level. Samples are extracted with dichloromethane, concentrated, and analyzed by GCMS. HPLC-MS analytical capability is being developed for antibiotic, cholesterol-regulating and cardiovascular drugs. A contract laboratory has recently been used to test for tetracycline and macrolide antibiotics in treated sewage effluent.

Drug Residue Testing Results for Water in New Mexico.

Sample Media	# of Samples	Results (ng/L)
Treated Sewage Effluent	15	amitriptyline "Elavil" (30), caffeine (1000), oxytetracycline (1890-4600), phenytoin "Dilantin" (250-300), propoxyphene "Darvon" (231-820), tetracycline (660)
Surface Water	23	amitriptyline (30), caffeine (1500), estrone (140), ethynyl estradiol (10), antibiotics (not yet tested for)
Ground Water Contaminated by Sewage	8	residues not detected, antibiotics (not yet tested for)
Public Drinking Water	2	residues not detected, antibiotics (not yet tested for)

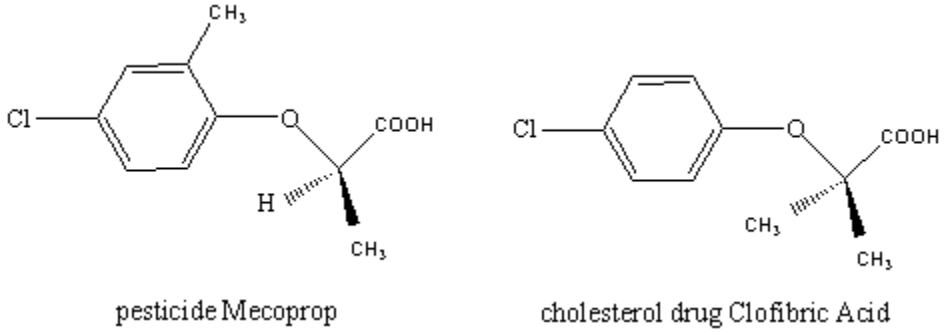
Drug residue residues were detected in 11 of 15 sewage effluent samples, and in 4 of 23 surface water samples. Estrogenic hormones, frequently detected in studies outside of New Mexico, were not detected in any sewage effluents and were detected in only 2 of 23 surface water samples. Drugs were not detected in any ground-water samples, or in any public drinking-water samples. There is no evidence that the drugs tested for thus far widely occur in ambient water in New Mexico. We have not yet developed the analytical capability, however, to test for many drugs of major clinical volume and public-health importance. Contractual analyses have detected antibiotics in all six sewage effluents that were sampled.

Laboratory studies have shown that sunlight can rapidly degrade drug residues in water. It is hypothesized that the intense sunlight in New Mexico, and generally wide and shallow river morphologies, cause rapid photolytic degradation of many drug residues discharged into surface water. The extent to which ultraviolet wastewater disinfection may destroy drug residues needs to be assessed.

Introduction

Swiss scientists studying pesticides in water serendipitously discovered Clofibric Acid (CA), the excretory metabolite of a cholesterol-lowering medication, in ambient surface water (Buser, et al., 1998a). The discovery was made because of the structural similarity between CA and the pesticide Mecoprop (Figure 1). Other studies have found that pharmaceutical residues, originating in treated sewage effluent, occur widely in European surface, ground and drinking water (Belfroid, et al., 1999, Heberer, et al., 1998, Heberer and Stan, 1996, Heberer and Stan, 1997, Hirsch, et al., 1999, Richardson and Bowron, 1985, Stumpf, et al., 1996, Stumpf, et al., 1999, Ternes, 1998, Ternes, et al., 1998, Ternes et al., 1999a, b). Drug residues were detected in all 64 drinking-water samples collected in a Berlin, Germany study (Stan, et al., 1994), and it is estimated that 48 to 96 tons of CA are dissolved in the North Sea (Buser, et al., 1998a). Studies in the United States and Brazil have also detected drug residues in ambient water (Kolpin, et al., 2002, Sieler, et al., 1999, Stumpf, et al., 1999). The U.S. Geological Survey is using five newly developed analytical to test for pharmaceuticals in water resources (Kolpin, et al., 2002). Drugs detected in Europe and/or the Americas include painkillers, lipid (cholesterol) regulators, antiseptics, chemotherapy agents, antibiotics, and hormones. The presence of caffeine and pharmaceuticals, in ground water containing elevated nitrate, has been used as an indicator of septic-tank contamination (Sieler, et al., 1999).

Figure 1. Molecular Structures of Mecoprop and Clofibric Acid. The two compounds are isomers, differing only by the location of a methyl group, CH_3.



Conventional sewage-treatment technologies vary greatly in their ability to eliminate drug residues and, in certain instances, have even been shown to increase the bioactivity of the pharmaceutical residues passing through them (Ternes et al., 1999a). Some polar drug residues readily leach through the vadose zone into ground water (Heberer and Stan, 1997, Heberer, et al., 1998). Activated carbon filtration has been shown to remove drug residues from drinking water (Hirsch, et al., 1996).

Documented ecological impacts of drug residues in ambient water include the development of antibiotic resistant bacteria in rivers and birds, and sexual disruption of fish exposed to estrogenic hormones. Antibiotic-resistant pathogenic bacteria have been detected in United States rivers, including Salmonella species in the Rio Grande and in Canadian geese near Chicago (Raloff, 1999). Male fish in rivers receiving sewage effluent produce the female egg-yolk protein, vitellogenin, resulting from exposure to estrogenic compounds (both natural and synthetic) in the low nanogram per liter (ng/L, parts-per-trillion) range. The presence of vitellogenin, a yolk sac protein normally found only in females, in male fish has been related to the widespread occurrence of intersexuality, the appearance of female characteristics and the progressive disappearance of male characteristics, in United Kingdom fish. Intersexuality can be a serious threat to the survival of affected species. Similar sexual disruption caused sterility and the extinction of certain mollusk species that were exposed to tributyltin (TBT). (Jobling, et al., 1998) Estrogenic hormones and TBT are among a complex variety of environmental contaminants, including pesticides, surfactants, and heavy metals, that have been identified as endocrine disrupting chemicals (EDCs). EDCs can bind with a hormone receptor and either mimic a hormone, triggering an identical response, or block a hormone from triggering the normal response. EDCs also can interfere with hormonal activity without bonding to the receptor.

In response to the growing body of evidence in the research literature of the ubiquitous nature of this emerging issue, the New Mexico Environment Department (NMED) and the Scientific Laboratory Division (SLD) of the New Mexico Department of Health are currently conducting initial surveillance to determine what drug residues are present in ambient water in the state, and at what concentrations. Some drugs can be detected with analytical methods used to detect other classes of organic compounds, such as pesticides. Analytical technology has pushed aqueous-phase drug detection limits into low ng/L, the range where many drugs have been detected. The most commonly prescribed drugs in the United States are listed in Table 1. SLD is currently able to detect 28 of these drugs at the ng/L level in water, including a number of anti-depressants, and hormones. SLD analyses for antibiotics, and lipid-regulating and cardiovascular pharmaceuticals will begin after SLD becomes proficient with a High-Performance Liquid Chromatograph, Mass Spectrometer (HPLC-MS), which it recently acquired with funding provided by the Centers for Disease Control. In the interim, the University of Nebraska, Water Sciences Laboratory, has been hired to perform analyses for tetracycline and macrolide antibiotics.

Table 1. Most Commonly Prescribed Drugs in the United States. (The Top 200 Prescriptions, http://www.rxlist.com).

Drug Class	Specific Drugs
Analgesics	acetaminophen, hydrocodone, ibuprofen, propoxyphene (Darvon),
Antibiotics	amoxicillin, azithromycin, cephalexin, ciprofloxacin, clarithromycin, penicillin VK
Anti-Convulsants	diazepam, phenytoin (Dilantin)
Anti-Depressants	amitriptyline (Elavil), fluoxetine (Prozac), paroxetine (Paxil), setraline,
Cardiovascular	amlodipine, digoxin, diltiazem, enalapril, diltiazem lisinopril, furosemide
Hormones	estrogen hormones, thyroxine
Lipid Lowering Agents	atorvastatin, lovastatin, simvastatin

Methods

Surveillance Strategy

Initial surveillance is focusing on the pharmaceuticals that are heavily prescribed in the United States, and are within SLD's analytical capability, along with other commonly prescribed pharmaceuticals including tricyclic antidepressants. Drugs included in the SLD analyses are listed in Table 2. Antibiotics included in the University of Nebraska, Water Sciences Laboratory, analyses are listed in Table 3.

Table 2. Drugs and drug metabolites included in the SLD analyses.

Drug Class	Specific Drugs
Analgesics	propoxyphene (Darvon)
Anti-Convulsants	phenytoin (Dilantin)
Anti-Depressants	amitriptyline (Elavil), desipramine, doxepin, fluoxetine (Prozac), imipramine, nordoxepin, nortriptyline, paroxetine (Paxil), protriptyline, sertraline, trimipramine maleate,
Anti-Inflammatory	methyprednisolone, prednisone
Hormones	equilin, estradiol, estrone, ethynyl estradiol, medroxyprogesterone, megestrol acetate, mestranol, norethindrone, norethynodrel, norgestrel, progestrorone
Other	caffeine, tamoxifen

Table 3. Antibiotics included in the University of Nebraska analyses.

Antibiotic Class	Specific Drugs
Macrolide	erythromycin A, oleandomycin, lincomycin, tiamulin, tilmicosin, tylosin
Tetracycline	chlortetracycline, minocycline, oxytetracycline, tetracycline

Samples are being collected at locations where drug residues would most likely occur. NMED staff are sampling treated sewage effluent outfalls, surface water receiving sewage, ground water contaminated by sewage (nitrate and anoxic; municipal, military, and septic tank sites), and public drinking-water systems served by surface water or by groundwater that may contain treated sewage. Locations that have been sampled to date are listed in Table 4, and identified on Figure 2.

Sewage effluents from Espanola and Las Cruces are discharged to the Rio Grande. Farmington's effluent is discharged to the San Juan River. Santa Fe's effluent is discharged to the Santa Fe River.

Ground water at Carnuel and Western Terrace was sampled from private domestic wells containing high nitrate attributed to household septic-tank discharges. The Kirtland and White Sands samples were collected from monitoring wells containing high nitrate attributed to military base sewage discharges. Ground-water samples at La Cieneguilla were collected from private domestic wells containing elevated nitrate attributed to discharges from a municipal sewage treatment plant. To date, samples of anoxic ground water contaminated by septic tank discharges have not been collected.

Farmington's public drinking-water system is supplied by an intake on the Animas River. The Walking Sands Rest Area public water system is supplied by a well containing high nitrate.

Sampling Protocol

An eight L sample, consisting of two 4 L bottles, was collected at each site. Samples were stored immediately in an ice bath, and delivered to SLD for extraction within 24 hours of collection. Two trip blanks were carried into the field and analyzed during the first sampling run, and this process was discontinued after no residues were detected in the trip blanks. Blind duplicates were submitted periodically.

SLD Analytical Methods

Two liters of each sample were extracted with 60 mL of HPLC-grade dichloromethane (DCM) within 24 hours of collection. The 2 L separatory funnels, with teflon stopcocks and either teflon or ground-glass stoppers, were shaken for two minutes. The water and DCM were allowed to separate for about 5-10 minutes, and the DCM was drained into a 250 mL flask. Another 60 mL of DCM was added to the separatory funnel, and the liquid-liquid extraction process was repeated twice, draining the DCM into the flask after each shake. Sodium Sulfate (Na_2SO_4) was baked at 400^0 C and kept in the drying oven until needed to remove water from the DCM. Approximately 10 grams of the cooled Na_2SO_4 were added to each flask, swirling the solvent while adding, and the flasks were allowed to stand for at least 30 minutes. The DCM extracts were then evaporated to 0.5 mL using a Zymark Turbo-Vap II at 38^0 to 40^0 C. The concentrates were analyzed using Electron Ionization, then Selected Ion Storage, and also Tandem MS (MS/MS) for some of the compounds. The instrument used was a Saturn 2000 Ion Trap Mass Spectrometer (Varian, Walnut Creek, CA) with a 3800 Gas Chromatograph (Varian, Walnut Creek, CA) with a 1079 Temperature Programmable injector (Varian, Walnut Creek, CA). Every sample batch was analyzed with a lab reagent blank, two lab fortified blanks, and a lab fortified matrix that were extracted and concentrated just like the samples. All positive results were quantitated using freshly-prepared standards. Chemical standards were obtained from the following manufactures: Sigma (St.louis .MO), Aldrich (Milwaukee,WI) and Alltech (Deerfield,IL). The solvents used were purchased from Burdick and Jackson.

Results

Samples were collected in 2000-2002. Analytical results for the samples collected to date are listed in Table 4. Sampling locations are identified on Figure 2 by their location codes. No drug residues were detected in the trip blanks.

Sewage Effluents

Most sewage effluents contained at least one drug residue, but did not contain a complex variety of them. Six effluents, all that have been tested for antibiotics thus far, contained oxytetracycline. Propoxyphene (Darvon) was found in four samples. Additionally, phenytoin (Dilantin) was detected in Espanola, caffeine was detected in Farmington, and amitriptyline (Elavil, Endep) was detected in Santa Fe. Estrogenic hormones were not detected in any sewage sample.

San Juan Watershed

The San Juan River at Bloomfield was the only sample that contained a detectable drug residue, ethynyl estradiol, a synthetic estrogen hormone used in birth-control pills. Neither ethynyl estradiol nor the two drugs detected in Farmington sewage effluent, caffeine and propoxyphene, were detected in the two downstream river samples (Hogback and Shiprock).

Gallinas Watershed

Drug residues were not detected either above or below the Las Vegas waste water treatment plant or at San Augustine.

Rio Grande Watershed

Drug residues were not detected in the Rio Grande at Pilar, Cochiti Lake, Bernalillo, Paseo del Norte bridge, Belen, Bernardo, San Antonio, or at Elephant Butte Lake. Amitriptyline was detected at Buckman Crossing. Caffiene and estrone were detected in the Albuquerque South Valley, about 3 Km downstream from the municipal sewage effluent outfall. Caffeine was detected at Sunland Park, immediately downstream from the sewage effluent outfall.

Ground Water Contaminated by Sewage

Drug residues were not detected in any of the eight sewage-contaminated ground-water samples.

Public Drinking Water

Drug residues were not detected in either of the two public drinking-water samples, one supplied by surface water, the other supplied by nitrate-laden ground water.

Figure 2. Drug Residue Sampling Locations.
Sample-location codes are identified in Table 4.

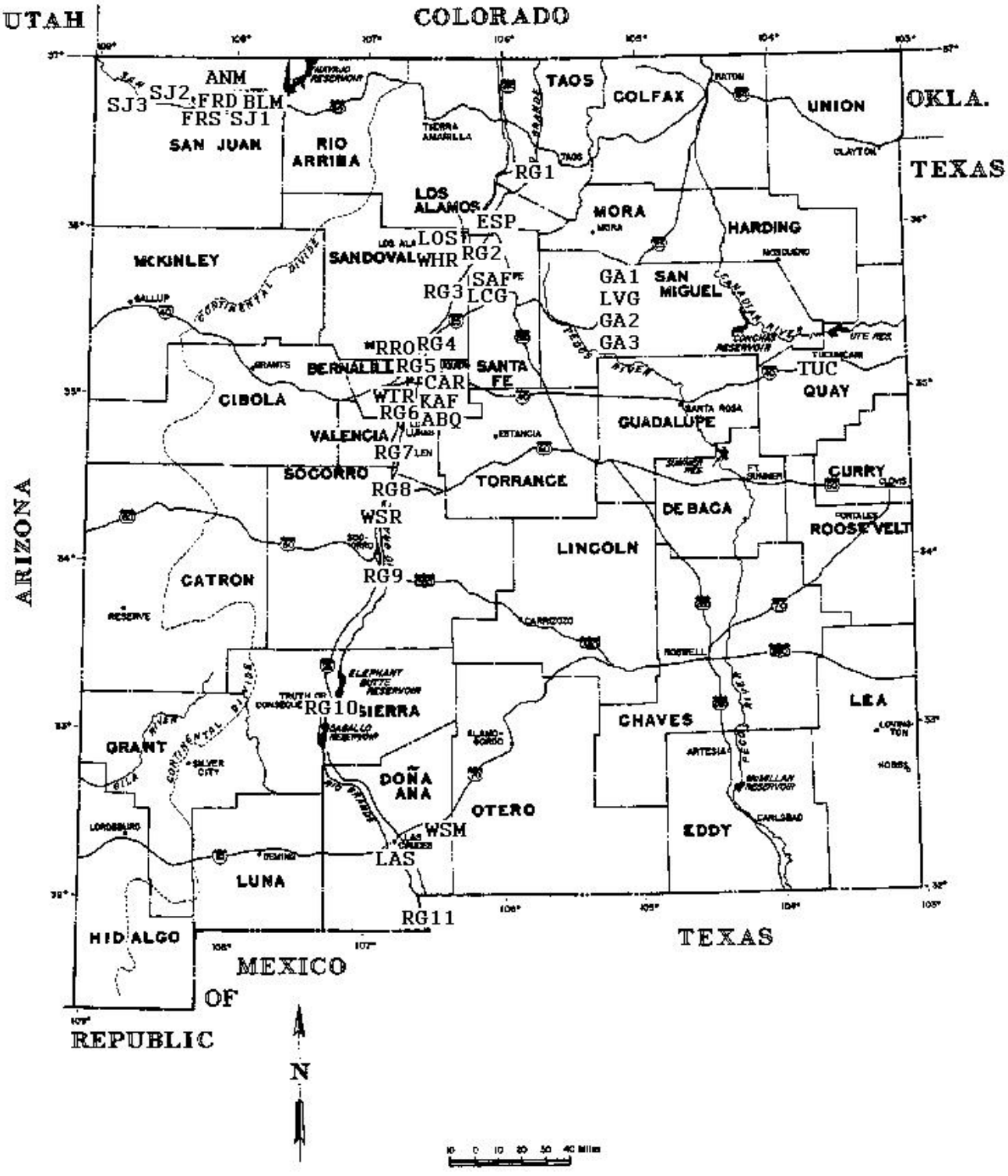


Table 4. Sample Locations and Analytical Results for Drug Residues in Water.
Sampling locations are mapped by their location codes in Figure 2. Detection limits are about 10 ng/L.

Sample Medium	Analytical Results (ng/L)
Treated Sewage	
Albuquerque effluent outfall (2 samples) (ABQ)	oxytetracycline (4600)
Bloomfield effluent outfall (BLM)	oxytetracycline (1290)
Espanola effluent outfall (ESP)	propoxyphene (500), phenytoin (300)
Espanola effluent ditch (ESP)	propoxyphene (400), phenytoin (250)
Farmington effluent outfall, 2000, 2002 (FRS)	caffeine (1000), oxytetracycline (1350), propoxyphene (820)
Las Cruces effluent outfall (LAS)	propoxyphene (231)
Las Vegas effluent outfall (LVG)	residues not detected
Los Alamos effluent outfall (LOS)	residues not detected
Rio Rancho effluent outfall (RRO)	oxytetracycline (3790)
Santa Fe river below WWTP (SAF)	amitriptyline (30)
Santa Fe effluent outfall (SAF)	oxytetracycline (2290)
Tucumcari effluent outfall (TUC)	oxytetracycline (1890), tetracycline (660)
Whiterock effluent outfall (WHR)	residues not detected
Surface Water	
Animas at Aztec (ANM)	residues not detected
Animas, Farmington water supply (FRD)	residues not detected
Gallinas above Las Vegas WWTP (GA1)	residues not detected
Gallinas below Las Vegas WWTP (GA2)	residues not detected
Gallinas at San Augustine (GA3)	residues not detected
Rio Grande at Pilar (RG1)	residues not detected
Rio Grande at Buckman Crossing (RG2)	amitriptyline (30)
Rio Grande below Cochiti Lake (RG3)	residues not detected
Rio Grande at Bernalillo, 2000, 2001 (RG4)	residues not detected
Rio Grande at Paseo del Norte Bridge, 2001, 2002 (RG5)	residues not detected
Rio Grande in Albuquerque South Valley (RG6)	caffeine (1500), estrone (140)
Rio Grande at Belen, 2001, 2002 (RG7)	residues not detected
Rio Grande at Bernardo, 2001, 2002 (RG8)	residues not detected
Rio Grande at San Antonio (RG9)	residues not detected
Rio Grande below Elephant Butte Lake (RG10)	residues not detected
Rio Grande at Sunland Park (RG11)	caffeine (200)
San Juan at Bloomfield (SJ1)	ethynyl estradiol (10)
San Juan at the Hogback (SJ2)	residues not detected
San Juan at the Hogback, blind dup.	residues not detected
San Juan at Shiprock (SJ3)	residues not detected
Ground Water Contaminated by Sewage	
Carnuel private well (CAR)	residues not detected
Kirtland Air Force Base (KAF)	residues not detected
La Cieneguilla private well #1 (LCG)	residues not detected
La Cieneguilla private well #2 (LCG)	residues not detected
La Cieneguilla private well #3 (LCG)	residues not detected
Walking Sands Rest Area (WSR)	residues not detected
Western Terrace private well (WTR)	residues not detected
White Sands Missile Range (WSM)	residues not detected
White Sands Missile Range, duplicate	residues not detected
Public Drinking Water	
Farmington drinking water; Animas River source (FRD)	residues not detected
Walking Sands Rest Area; ground water source (WSR)	residues not detected

Discussion and Conclusions

This study was designed to test for drug residues at locations where they would most likely occur (ie. treated sewage effluent outfalls, rivers that receive effluent, and ground water contaminated by sewage. Test results thus far provide no evidence that the drug residues for which significant testing was conducted (Table 2) widely occur in ambient water in New Mexico. It should be noted, however, that many of the drugs of major clinical volume and public-health importance were not included in this study (eg. lipid-regulating and cardiovascular drugs), and testing for antibiotics has just begun.

Estrogenic hormones, frequently detected in studies outside of New Mexico, were not detected in any sewage-effluent samples, and were detected in only two surface-water samples. The hormone concentrations detected, however, are of potential concern because they are within the range to which Jobling, et al. (1998) have attributed sexual disruption of wild fish. The San Juan-Bloomfield site is a trout fishery. The Rio Grande-South Valley site is within the area of concern over the Silvery Minnow, an endangered species that has caused much local controversy.

All six sewage effluents tested for antibiotics thus far contained oxytetracycline at levels exceeding 1000 ng/L. Given the presence of antibiotic-resistant pathogenic bacteria in the Rio Grande (Raloff, 1999), future testing of surface water for antibiotic residues is a high priority.

No drug residues, whatsoever, were detected in any of the eight ground-water samples. The presence of caffeine and pharmaceutical residues in ground water, therefore, was not an indicator of nitrate contamination by septic tanks at the two sites that were sampled (Carnuel and Western Terrace).

The decrease in drug concentrations between the Espanola sewage outfall and the effluent ditch located approximately 100 meters downstream from the outfall could be the result of photolysis, the destruction of drug compounds by sunlight. The samples were collected around 12:00 pm on a hot August day.

Drug residues were not detected in any of the three private domestic wells in La Cieneguilla. These wells all have elevated nitrate attributed to historical discharges of treated sewage effluent, containing approximately 30 mg/L of total nitrogen, from the Santa Fe waste-water treatment plant. Treated sewage is discharged to the Santa Fe River, a losing stream in this area, and infiltrates into the aquifer tapped by La Cieneguilla wells. Total nitrogen in the effluent was greatly reduced around 1985 after improvements were made to the treatment plant, and nitrate levels in wells closest to the plant have since decreased to less than detectable. The three wells that were sampled are located in a different area of the nitrate plume that has not yet been displaced by post-1985 sewage effluent. It is postulated that any drug residues were either destroyed by photolysis prior to infiltration, or were naturally attenuated in the subsurface. Future sampling will include wells closest to the plant that are pumping ground water containing post-1985 sewage effluent.

Buser, et al., (1998b) demonstrated that sunlight can rapidly degrade pharmaceutical residues in water. New Mexico has an arid, often sunny, climate, a high elevation, and sparse populations relative to many areas in Europe, for example. Additionally, our rivers are relatively wide and shallow, enhancing the exposure of river water to sunlight. It is hypothesized that the intense sunlight in New Mexico causes rapid photolytic degradation of drug residues discharged into surface water. The decreasing concentrations in Espanola, the absence of drug residues in the Rio Grande downstream of Albuquerque (Belen, Bernardo, San Antonio, and Elephant Butte), and the absence of drug residues in the San Juan downstream of Farmington (Hogback and Shiprock) provide strong evidence that this is the case. The extent to which ultraviolet wastewater disinfection may destroy drug residues needs to be assessed.

Acknowledgments

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