



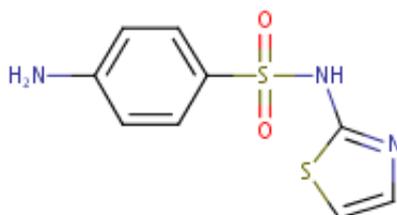
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SULFATHIAZOLE

CASRN: 72-14-0



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Human Health Effects:

Human Toxicity Excerpts:

/SIGNS AND SYMPTOMS/ The physician should be alert to the signs, including high fever, severe headache, stomatitis, conjunctivitis, rhinitis, urethritis, and balanitis, which may precede the onset of the cutaneous lesions of the Stevens-Johnson syndrome. If a rash develops during therapy, the sulfonamide should be discontinued at once. In rare instances, a skin rash may precede a more serious reaction such as Stevens-Johnson syndrome, toxic epidermal necrolysis, hepatic necrosis, and/or serious blood disorders. **/Sulfonamides/**
 [American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] ****PEER REVIEWED****

/EPIDEMIOLOGY STUDIES/ In the Collaborative Perinatal Project, the frequency of congenital anomalies was no greater than expected among children of 100 women who were treated with sulfathiazole during the first four lunar months of pregnancy or among the children of 124 women treated with this drug anytime in pregnancy.
 [Heinonen O et al; Birth Defects and Drugs In Pregnancy p.434-435 (1977)] ****PEER REVIEWED****

Drug Warnings:

The number of conditions for which the sulfonamides are therapeutically useful and constitute drugs of first choice has been reduced sharply by the development of more effective antimicrobial agents and by the gradual increase in the resistance of a number of bacterial species to this class of drugs. **/Sulfonamides/**
 [Hardman, J.G., L.E. Limbird, P.B. Molinoff, R.W. Ruddon, A.G. Goodman (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 9th ed. New York, NY: McGraw-Hill, 1996., p. 1062] ****PEER REVIEWED****

Many of the adverse effects that have been attributed to the sulfonamides appear to be hypersensitivity reactions. The incidence of hypersensitivity reactions appears to increase with increased sulfonamide dosage. Although cross-sensitization has been reported to occur between the various anti-infective sulfonamides, some diuretics such as acetazolamide and the thiazides, some goitrogens, and sulfonylurea antidiabetic agents, the association between hypersensitivity to sulfonamide anti-infectives and subsequent sensitivity reactions to non-anti-infective sulfonamides (e.g., thiazides, sulfonylurea antidiabetic agents, furosemide, dapson, probenecid) appears to result from a predisposition to allergic reactions in general rather than to cross-sensitivity to the sulfa moiety per se. **/Sulfonamides/**
 [American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] ****PEER REVIEWED****

Various dermatologic reactions, including rash, pruritus, urticaria, erythema nodosum, erythema multiforme (Stevens-Johnson syndrome), Lyell's syndrome (may be associated with corneal damage), Behcet's syndrome, toxic epidermal necrolysis, and exfoliative dermatitis, have been reported in patients receiving sulfonamides.

Because photosensitivity may also occur, patients should be cautioned against exposure to UV light or prolonged exposure to sunlight. A relatively high proportion of fatalities has occurred as a result of the Stevens-Johnson syndrome, especially in children. Although long-acting sulfonamides (which are no longer commercially available) have been associated most often with the Stevens-Johnson syndrome, other sulfonamides also have been reported to cause this reaction. The physician should be alert to the signs, including high fever, severe headache, stomatitis, conjunctivitis, rhinitis, urethritis, and balanitis, which may precede the onset of the cutaneous lesions of the Stevens-Johnson syndrome. If a rash develops during therapy, the sulfonamide should be discontinued at once. In rare instances, a skin rash may precede a more serious reaction such as Stevens-Johnson syndrome, toxic epidermal necrolysis, hepatic necrosis, and/or serious blood disorders. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Fever, which may develop 7-10 days after the initial sulfonamide dose, is a common adverse effect of sulfonamide therapy. Serum sickness syndrome or serum sickness-like reactions (e.g., fever, chills, rigors, flushing, joint pain, urticarial eruptions, conjunctivitis, bronchospasm, leukopenia), have been reported; rarely, anaphylactoid reactions and anaphylaxis may occur. Lupus erythematosus-like syndrome, disseminated lupus erythematosus, angioedema, vasculitis, vascular lesions including periarteritis nodosa and arteritis, cough, shortness of breath, chills, pulmonary infiltrates, pneumonitis (which may be associated with eosinophilia), fibrosing alveolitis, pleuritis, pericarditis with or without tamponade, allergic myocarditis, hepatitis, hepatic necrosis with or without immune complexes, parapsoriasis varioliformis acuta, alopecia, conjunctival and scleral injection, periorbital edema, and arthralgia have also been reported. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

If a hypersensitivity reaction occurs during sulfonamide therapy, the drugs should be discontinued immediately. Desensitization to sulfasalazine has been used when reinstitution of therapy with the drug was considered necessary in patients with inflammatory bowel disease who had hypersensitivity reactions to the drug. Desensitization to sulfadiazine has also been used in several patients with acquired immunodeficiency syndrome (AIDS) when use of sulfadiazine for the treatment of toxoplasmosis was considered necessary in patients who had hypersensitivity reactions to the drug. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Adverse hematologic effects, including methemoglobinemia, sulfhemoglobinemia, granulocytopenia, leukopenia, congenital neutropenia, eosinophilia, hemolytic anemia, agranulocytosis, aplastic anemia, purpura, clotting disorder, thrombocytopenia, myelodysplastic syndrome, hypofibrinogenemia, and hypoprothrombinemia, rarely resulting in death, have been associated with sulfonamide therapy. Acute hemolytic anemia may occur during the first week of therapy as a result of sensitization or glucose-6-phosphate dehydrogenase (G-6-PD) deficiency. This reaction may also occur in the fetus or premature infant in whom G-6-PD is normally deficient. Mild, chronic hemolytic anemia may occur during prolonged sulfonamide therapy. Agranulocytosis may rarely occur 10-14 days after initiation of therapy. Complete blood cell counts should be performed regularly in patients receiving sulfonamides for longer than 2 weeks. If signs of adverse hematologic effects such as sore throat, fever, pallor, purpura, jaundice, or weakness occur, sulfonamide therapy should be discontinued until the possibility of a blood disorder is eliminated. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Functional and morphologic hepatic changes, possibly causing jaundice, may appear within 3-5 days after initiation of sulfonamide therapy. Focal or diffuse necrosis of the liver has been reported rarely. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Renal damage, manifested by renal colic, nephritis, urolithiasis, toxic nephrosis with anuria and oliguria, hematuria, proteinuria, kidney stone formation, and elevation of BUN and creatinine concentrations, is usually a result of crystalluria caused by precipitation of the sulfonamide and/or its N4-acetyl derivative in the urinary tract. The occurrence of crystalluria is related to the urinary concentration and the solubility characteristics of the sulfonamide and its metabolites. The risk of crystalluria may be decreased by maintaining an adequate urinary output and by increasing urinary pH. Unless the urine is highly acidic and/or the drug is relatively insoluble, alkalinization of the urine is usually not necessary if the urinary output is maintained at a minimum of 1500 mL daily. Urinary alkalinization may be achieved by administering ... sodium bicarbonate orally... . Urinalysis and kidney function tests should be performed weekly to detect any renal complications. If persistent, heavy crystalluria, hematuria, or oliguria occurs, sulfonamide therapy should be discontinued and alkali therapy maintained. Nephritis and hemolytic-uremic syndrome also have been reported. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Nausea and vomiting occur frequently in patients receiving sulfonamides. Abdominal pain, anorexia, glossitis, stomatitis, pancreatitis, gastroenteritis, diarrhea, neutropenic enterocolitis, GI hemorrhage, melena, flatulence, and salivary gland enlargement also have been reported. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Clostridium difficile-associated diarrhea and colitis (also known as antibiotic-associated pseudomembranous colitis) caused by toxin-producing clostridia has been reported following sulfonamide therapy. If C. difficile-associated diarrhea and colitis occurs, mild cases may respond to discontinuance of sulfonamide therapy alone, but diagnosis and management of moderate to severe cases should include sigmoidoscopy (or other appropriate endoscopic examination), appropriate bacteriologic studies, and treatment with fluid, electrolyte, and protein supplementation as indicated. If colitis is moderate to severe or is not relieved by discontinuance of sulfonamide therapy alone, appropriate anti-infective therapy effective against C. difficile (e.g., oral metronidazole or vancomycin) should be administered. Isolation of the patient may be advisable. Other causes of colitis also should be considered.

/Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Headache occurs frequently in patients receiving sulfonamides. Dizziness, vertigo, peripheral neuritis, ataxia, mental depression, hallucinations, disorientation, confusion, seizures, intracranial hypertension, tinnitus, hearing loss, anxiety, apathy, and acute psychosis, occur less frequently. Peripheral neuropathy, paresthesia, weakness, fatigue, drowsiness, lassitude, restlessness, insomnia, meningitis, cauda equina syndrome, and Guillain-Barre syndrome also have been reported. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Other reported adverse effects of sulfonamides include goiter production, hypothyroidism, hypoglycemia, diuresis, pharyngitis, arthralgia, acidosis, and cyanosis. The nonabsorbable sulfonamides reportedly decrease bacterial synthesis of vitamin K1, which may result in hypoprothrombinemia and hemorrhage; these sulfonamides may also reduce fecal output of thiamine. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Sulfonamides should be used with caution and in reduced dosage in patients with impaired hepatic function, impaired renal function, or urinary obstruction, since excessive accumulation of the drugs may occur in these patients. The drugs should also be administered with caution in patients with blood dyscrasia, severe allergies or asthma, or G-6-PD deficiency. The development of sore throat, fever, rash, pallor, arthralgia, cough, shortness of breath, purpura, or jaundice during sulfonamide therapy may be an early sign of a serious adverse reaction. Renal function tests and complete blood cell counts should be performed frequently during sulfonamide therapy, especially during prolonged therapy with the drugs. Microscopic urinalyses should be done weekly when patients are treated with a sulfonamide for longer than 2 weeks. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Because pseudomembranous colitis has been reported with the use of nearly all anti-infective agents, including sulfonamides, and may range in severity from mild to life threatening, it should be considered in the differential diagnosis of patients who develop diarrhea during the administration of sulfonamides. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

The frequency of resistant organisms limits the usefulness of sulfonamides as sole therapy in the treatment of urinary tract infections. Since sulfonamides are bacteriostatic and not bactericidal, a complete course of therapy is needed to prevent immediate regrowth and the development of resistant urinary pathogens. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Sulfonamides are contraindicated in patients with a history of hypersensitivity to sulfonamides or other chemically related drugs (e.g., sulfonyleureas, thiazides). The drugs are also contraindicated in patients with marked renal or hepatic impairment. Sulfonamides are contraindicated in patients with porphyria, since the drugs may precipitate an acute attack. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Kernicterus, caused by displacement of bilirubin from protein binding sites, has occurred in neonates treated with sulfonamides. Unless indicated for the treatment of congenital toxoplasmosis, sulfonamides are generally contraindicated in children younger than 2 months of age. Pending further accumulation of data on use of the drugs in pediatric patients, sulfacytine should not be used in children younger than 14 years of age.

/Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Because sulfonamides are distributed into milk, and because of the potential for serious adverse reactions from the drugs in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the woman. Because of the risk of kernicterus in infants younger than 2 months of age, use of sulfonamides is contraindicated in lactating women who are nursing such infants.

/Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Sulfonamide resistance in *Neisseria meningitidis* is mediated by altered forms of the chromosomal gene for the drug target enzyme dihydropteroate synthase. Sulfonamides have been used for decades both for prophylaxis and the treatment of meningococcal disease, and resistance is common. Two types of resistance determinants have been identified, and regions important for drug insusceptibility to the corresponding enzyme have been defined by site-directed mutagenesis. Both types of resistance traits have spread among strains of *N. meningitidis* of different serogroups and serotypes, and the large differences at the nucleotide level in a comparison of the resistance genes with the dhps genes of susceptible meningococci indicate the origin of one or maybe both types in other *Neisseria* species. One sulfonamide-sensitive strain of *N. meningitidis* was found to have a mosaic dhps gene with a central part identical to the corresponding part of a gonococcal strain. This observation supports the idea of an interspecies transfer of genetic material in *Neisseria* species as a mechanism for the development of chromosomally mediated resistance.

[Fermer C et al; J Bacteriol 177 (16): 4669-75 (1995)] **PEER REVIEWED** [PubMed Abstract](#) Full text: [PMC177231](#)

The sulfonamides readily cross the placenta to the fetus during all stages of gestation. Equilibrium with maternal blood is usually established after 2-3 hr., with fetal levels averaging 70-90% of maternal. Significant levels may persist in the newborn for several days after birth when given near term. The primary danger of sulfonamide administration during pregnancy is manifested when these agents are given close to delivery. Toxicities that may be observed in the newborn include jaundice, hemolytic anemia and, theoretically, kernicterus. /Sulfonamides/ [Briggs, G.G, R.K. Freeman, S.J. Yaffe. A Reference Guide to Fetal and Neonatal Risk. Drugs in Pregnancy and Lactation. 4th ed. Baltimore, MD: Williams & Wilkins 1994., p. 795] **PEER REVIEWED**

Sensitization may occur from topical application of sulfonamides. /Sulfonamides/

[American Medical Association, AMA Department of Drugs. AMA Drug Evaluations. 4th ed. Chicago: American Medical Association, 1980., p. 1316] **PEER REVIEWED**

...Orally administered sulfathiazole and sulfadiazine frequently impaired depth perception, causing tendency to exophoria at near and decrease of adduction power.

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 860] **PEER REVIEWED**

Reportedly in 4% of patients receiving sulfathiazole, conjunctivitis has appeared between 5th and 9th day, sometimes involving only the conjunctiva, but in other cases associated with skin eruptions & fever. Majority of cases...have cleared within few days after discontinuing drug. ...serious cases...have produced symblepharon.

[Grant, W. M. Toxicology of the Eye. 2nd ed. Springfield, Illinois: Charles C. Thomas, 1974., p. 951] **PEER REVIEWED**

Populations at Special Risk:

Acute hemolytic anemia may occur during the first week of therapy as a result of sensitization or glucose-6-phosphate dehydrogenase (G-6-PD) deficiency. This reaction may also occur in the fetus or premature infant in whom G-6-PD is normally deficient. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Sulfonamides are absorbed from the vaginal mucosa and are distributed into breast milk. Use is not recommended in nursing mothers since sulfonamides may cause hyperbilirubinemia in the infant. In addition, sulfonamides may cause hemolytic anemia in glucose-6-phosphate dehydrogenase (G6PD)-deficient neonates. /Sulfonamides/

[USP. Convention. USPDI - Drug Information for the Health Care Professional. 20th ed. Volume I. Micromedex, Inc. Englewood, CO., 2000. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2857] **PEER REVIEWED**

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 3,171 workers (1,476 of these were female) were potentially exposed to sulfathiazole in the US(1). Occupational exposure to sulfathiazole may occur through inhalation and dermal contact with this compound at workplaces where sulfathiazole is produced or used. Use data indicate that the general population may be exposed to sulfathiazole via dermal contact and administration of pharmaceutical products containing sulfathiazole(SRC).

[(1) NIOSH; NOES. National Occupational Exposure Survey conducted from 1981-1983. Estimated numbers of employees potentially exposed to specific agents by 2-digit standard industrial classification (SIC). Available at <http://www.cdc.gov/noes/> as of Apr 14, 2008.] **PEER REVIEWED**

Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, ***** SULFONAMIDES *****, is relevant for this HSDB record chemical.

Life Support:

- o This overview assumes that basic life support measures have been instituted.

Clinical Effects:

0.2.1 SUMMARY OF EXPOSURE

A) WITH THERAPEUTIC USE

- 1) Adverse reactions to sulfonamides can involve nearly every organ system; many effects appear to be hypersensitivity reactions, and are dose related. Although there is a difference as to the frequency of toxic effects between the short-acting and long-acting, there is also considerable overlap. **DERMATOLOGIC:** Various dermatological reactions, including rash, pruritus, erythema nodosum, and quite severe and often fatal erythema multiforme of the Stevens-Johnson type have been reported. Lyell's Syndromes are usually associated with the use of a long-acting sulfonamides. **GASTROINTESTINAL:** Nausea and vomiting are common. **HYPERSENSITIVITY REACTION:** Transient myopia, conjunctivitis, hepatic injury, and keratitis may occur in association with a hypersensitivity reaction. **NEUROLOGIC:** Headache, depression, and hallucinations have been reported with therapy.

B) WITH POISONING/EXPOSURE

- 1) Data limited. Effects may be an extension of adverse events reported with sulfonamides. Methemoglobinemia has been reported after overdose.
- 2) Refer to "SULFASALAZINE" management for further information.
- 3) Refer to "TRIMETHOPRIM-SULFAMETHOXAZOLE" management for further information.

0.2.4 HEENT

- A) Transient myopia, conjunctivitis, and keratitis may occur in association with hypersensitivity reaction.

0.2.7 NEUROLOGIC

- A) Headache, depression, and hallucinations have been reported with therapeutic use of sulfonamides. Tremor occurred in one patient following a fixed-dose combination of trimethoprim/sulfamethoxazole.
- 0.2.8 GASTROINTESTINAL
- A) Nausea and vomiting are likely to occur.
- 0.2.9 HEPATIC
- A) Hypersensitivity reactions to sulfonamide antibiotics may produce hepatic injury.
- 0.2.10 GENITOURINARY
- A) Adverse effects increase in renal failure without dose reduction.
- 0.2.12 FLUID-ELECTROLYTE
- A) Hyperkalemia has been reported following therapeutic use of trimethoprim/sulfamethoxazole.
- 0.2.13 HEMATOLOGIC
- A) Hematologic effects are uncommon, but several have been reported. These include acute hemolytic anemia, agranulocytosis, thrombocytopenia, aplastic anemia, and methemoglobinemia.
- 0.2.14 DERMATOLOGIC
- A) Various dermatological reactions, including rash, pruritus, erythema nodosum, and quite severe and often fatal erythema multiforme of the Stevens-Johnson type have been reported.
- 1) The Stevens-Johnson and Lyell's Syndromes are usually associated with the use of a long-acting sulfonamide, although other sulfonamides have been reported to cause these reactions.
- 2) This serious reaction has been reported even with the use of ophthalmic preparations. Rashes and fever appear ten days after initiation of therapy and reoccur immediately upon additional courses of the therapy.
- 0.2.17 METABOLISM
- A) Administration to premature infants leads to kernicterus. Longer acting sulfonamides may displace other drugs and metabolites from their protein binding sites. Hypoglycemia may occur in patients with chronic renal failure.
- 0.2.20 REPRODUCTIVE
- A) Mafenide acetate, sulfADIAZINE, and sodium sulfacetamide are classified as FDA pregnancy category C. Silver sulfADIAZINE is classified as FDA pregnancy category B. At the time of this review, there are no adequate and well-controlled studies of mafenide acetate, sodium sulfacetamide, sulfADIAZINE, or silver sulfADIAZINE use in pregnant women. In animal studies, there was evidence of increased cleft palate and bony abnormalities with high oral doses of sulfonamides. Sulfonamides compete with bilirubin for binding to plasma albumin, which may result in kernicterus in the newborn.
- B) It is not known whether mafenide acetate, sodium sulfacetamide, or silver sulfADIAZINE are excreted in breast milk. However, other sulfonamides, including sulfADIAZINE, are excreted in breast milk. SulfADIAZINE is contraindicated as it may increase the risk of kernicterus.
- C) NOTE: For information on other sulfonamides, please refer to individual documents.

Laboratory:

- A) The hepatotoxicity and nephrotoxicity of these pharmaceuticals may alter lab tests of liver function and kidney function. These systems as well as the hematopoietic should be monitored.

Treatment Overview:

0.4.2 ORAL/PARENTERAL EXPOSURE

- A) Treatment is symptomatic and supportive. There is no specific antidote for sulfonamide intoxication.
- B) **ACTIVATED CHARCOAL:** Administer charcoal as a slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.
- C) **HYPERSENSITIVITY REACTION**
- 1) The drug should be immediately discontinued and the patient observed for the possibility of anaphylactic shock. In this situation the normal treatment for anaphylaxis is carried out with the establishment of an open airway, epinephrine, and diphenhydramine.
- D) **HYPOTENSION:** Infuse 10 to 20 mL/kg isotonic fluid. If hypotension persists, administer dopamine (5 to 20 mcg/kg/min) or norepinephrine (ADULT: begin infusion at 0.5 to 1 mcg/min; CHILD: begin infusion at 0.1 mcg/kg/min); titrate to desired response.
- E) **DIURESIS:** If kidney function is normal, consider administration of D5/0.45 NaCl with a diuretic such as furosemide 1 mg/kg to a maximum of 40 mg/dose to obtain a urine flow of 3 to 6 mL/kg/hr.
- F) For anuria or agranulocytosis, dialysis and/or isolation should be considered. Obtain a baseline CBC, hepatic and renal function test.
- G) **CHRONIC THERAPY:** Discontinue the use of the drug; provide symptomatic and supportive care.
- H) **SEIZURES:** Administer a benzodiazepine; DIAZEPAM (ADULT: 5 to 10 mg IV initially; repeat every 5 to 20 minutes as needed. CHILD: 0.1 to 0.5 mg/kg IV over 2 to 5 minutes; up to a maximum of 10 mg/dose. May repeat dose every 5 to 10 minutes as needed) or LORAZEPAM (ADULT: 2 to 4 mg IV initially; repeat every 5 to 10 minutes as needed, if seizures persist. CHILD: 0.05 to 0.1 mg/kg IV over 2 to 5 minutes, up to a maximum of 4 mg/dose; may repeat in 5 to 15 minutes as needed, if seizures continue).
- 1) Consider phenobarbital or propofol if seizures recur after diazepam 30 mg (adults) or 10 mg (children greater than 5 years).
 - 2) Monitor for hypotension, dysrhythmias, respiratory depression, and need for endotracheal intubation. Evaluate for hypoglycemia, electrolyte disturbances, and hypoxia.
- I) **METHEMOGLOBINEMIA:** Determine the methemoglobin concentration and evaluate the patient for clinical effects of methemoglobinemia (ie, dyspnea, headache, fatigue, CNS depression, tachycardia, metabolic acidosis). Treat patients with symptomatic methemoglobinemia with methylene blue (this usually occurs at methemoglobin concentrations above 20% to 30%, but may occur at lower methemoglobin concentrations in patients with anemia, or underlying pulmonary or cardiovascular disorders). Administer oxygen while preparing for methylene blue therapy.
- J) **METHYLENE BLUE:** INITIAL DOSE/ADULT OR CHILD: 1 mg/kg IV

over 5 to 30 minutes; a repeat dose of up to 1 mg/kg may be given 1 hour after the first dose if methemoglobin levels remain greater than 30% or if signs and symptoms persist. NOTE: Methylene blue is available as follows: 50 mg/10 mL (5 mg/mL or 0.5% solution) single-dose ampules and 10 mg/1 mL (1% solution) vials. Additional doses may sometimes be required. Improvement is usually noted shortly after administration if diagnosis is correct. Consider other diagnoses or treatment options if no improvement has been observed after several doses. If intravenous access cannot be established, methylene blue may also be given by intraosseous infusion. Methylene blue should not be given by subcutaneous or intrathecal injection. NEONATES: DOSE: 0.3 to 1 mg/kg.

- K) Concomitant use of methylene blue with serotonergic drugs, including serotonin reuptake inhibitors (SRIs), selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), norepinephrine-dopamine reuptake inhibitors (NDRIs), triptans, and ergot alkaloids may increase the risk of potentially fatal serotonin syndrome.

Range of Toxicity:

- A) Since many of the adverse effects appear to be hypersensitivity reactions, there is no specific toxic dose. The incidence of the adverse effects appears to increase with increased sulfonamide dosage.

[Rumack BH POISINDEX(R) Information System Micromedex, Inc., Englewood, CO, 2017; CCIS Volume 172, edition expires May, 2017. Hall AH & Rumack BH (Eds): TOMES(R) Information System Micromedex, Inc., Englewood, CO, 2017; CCIS Volume 172, edition expires May, 2017.] **PEER REVIEWED**

Antidote and Emergency Treatment:

Maintain an open airway and assist ventilation if necessary. Treat coma, seizures, hypotension, anaphylaxis, and hemolysis if they occur. Replace fluid losses resulting from gastroenteritis with intravenous crystalloids. Maintain steady urine flow with fluids to alleviate crystalluria ... Administer activated charcoal orally if conditions are appropriate. Gastric lavage is not necessary after small to moderate ingestions if activated charcoal can be given promptly. Most antibiotics are excreted unchanged in the urine, so maintenance of adequate urine flow is important. The role of forced diuresis is unclear. Hemodialysis is not usually indicated, except perhaps in patients with renal dysfunction and a high level of a toxic agent. /Antibacterial agents/

[Olson, K.R. (Ed.); Poisoning & Drug Overdose. 5th ed. Lange Medical Books/McGraw-Hill. New York, N.Y. 2007., p. 82] **PEER REVIEWED**

Animal Toxicity Studies:

Non-Human Toxicity Excerpts:

/LABORATORY ANIMALS: Acute Exposure/ The guinea pig maximization test is one of the preferred test methods for the identification of skin sensitizers. The OECD/EC test guidelines allow for the conduct of a rechallenge in case doubtful reactions are obtained after challenge. The relevance of rechallenging was investigated by performing multiple challenges (up to four) in the maximization test with four well-known sensitizers of varying strength: nickel sulfate, sulfathiazole, benzocaine, and 1-chloro-2,4-dinitrobenzene. In addition, the effect of sodium lauryl sulfate (SLS)-pretreatment during topical induction with weak sensitizers on rechallenging was investigated. In contrast to what has frequently been hypothesized, rechallenge did not result in an increase of skin reaction as compared with the reactions observed after the first treatment. sodium lauryl sulfate pretreatment was very effective in increasing the initial challenge response to weak sensitizers. Subsequent rechallenging in these cases however again showed a decrease in sensitivity of the animals.

[Prinsen MK et al; Food Chem Toxicol 35 (9): 923-6 (1997)] **PEER REVIEWED** [PubMed Abstract](#)

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Sodium sulfathiazole was administered once daily, seven days a week, for thirteen weeks by oral intubation to three groups of 15 male and 25 female Charles River, Sprague-Dawley, CD rats (approximately 7-8 weeks of age) at dosage levels of 2, 6, and 18 mg/kg bw/day. Two additional groups of 15 male and 15 female rats served as controls and each received the vehicle only (distilled water) on a similar regimen. Treatment with sulfathiazole failed to elicit systemic toxicity at any dose. Appearance, behavior, growth rate, food consumption, and survival data for the test animals were comparable with that of the controls. No compound-related findings were observed with respect to clinical laboratory studies, ophthalmoscopic examinations, organ weights, organ/body weight ratios, or gross or microscopic pathology.

[WHO/FAO; Joint Expert Committee on Food Additives; Food Additive Series 25: Sulfathiazole (72-14-0) (1990). Available from, as of July 21, 2008: <http://www.inchem.org/pages/jecfa.html> **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Sodium sulfathiazole was administered orally in gelatin capsules once daily, seven days a week, for 13 weeks to three groups of four male and four female purebred beagle dogs at dosage levels of 2, 6 and 18 mg/kg bw/day. Two additional groups of four male and four female dogs each served as two separate control groups and received empty gelatin capsules on a similar regimen. The authors concluded that there was no sign of drug-induced systemic toxicity at any dose throughout the 13 week treatment period. Although not mentioned by the authors, there were slight increases, which were not statistically significant, in the thyroid weight and thyroid to body weight ratio in female dogs receiving the 18 mg/kg bw/day dose. /Sodium sulfathiazole/

[WHO/FAO; Joint Expert Committee on Food Additives; Food Additive Series 25: Sulfathiazole (72-14-0) (1990). Available from, as of July 21, 2008: <http://www.inchem.org/pages/jecfa.html> **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Sulfathiazole 2% in diet to mice for 14 days increased cholesterol formation in parotid, submandibular, & sublingual glands but decreased formation in liver. Fecal excretion was decreased.

[SUMIDA J, NAKAMURA H; SHIKA KISO IGAKKI ZASSHI 19 (4): 561 (1977)] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ Injected into fertilized eggs sulfathiazole exhibited growth depressing & lethal effects on the embryos, also exerted teratogenic effects hydrops & bill abnormalities.

[CHOY I; SHOWA IGAKKAI ZASSHI 35 (3): 187 (1975)] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ ... ICR female mice were placed on a diet containing no folic acid (FA) and including 1% succinyl sulfathiazole (SS) for 4 weeks before mating. Control mice were fed diets with either: 1) FA and 1% SS [+SS only diet]; 2) FA [normal diet]; or 3) a breeding diet. Dams and fetuses were examined during various days of gestation. Blood analysis showed that by gestational day 18, plasma folate concentrations in the -FA+SS fed dams decreased to 1.13 ng/mL, a concentration approximately 3% of that in breeding diet fed dams (33.24 ng/mL) and 8% of that in +SS only/normal fed dams (13.59 ng/mL). RBC folate levels showed a similar decrease, whereas homocysteine concentrations increased. Reproductive outcome in the -FA+SS fed dams was poor with increased fetal deaths, decreased fetal weight, and delays in palate and heart development. /Succinyl sulfathiazole/

[Burgoon J et al; Teratology 65 (5): 219-27 (2002)] **PEER REVIEWED** [PubMed Abstract](#)

/GENOTOXICITY/ Sulfathiazole was tested for mutagenicity in the Salmonella/microsome preincubation assay using the standard protocol approved by the National Toxicology Program. Sulfathiazole was tested at doses of 1.0, 3.0, 10, 16, and 33 ug/plate in as many as 5 Salmonella typhimurium strains (TA1535, TA1537, TA97, TA98, and TA100) in the presence and absence of rat or hamster liver S-9. Sulfathiazole was negative in these tests and the highest ineffective dose tested in any S. typhimurium strain was 33 ug/plate. The solvent used was DMSO and both a solvent and a positive control group were included in this experiment.

[Mortelmans K et al; Environ Mutagen 8:1-119 (1986)] **PEER REVIEWED**

Ecotoxicity Excerpts:

/AQUATIC SPECIES/ The photocatalytic degradation of sulfacetamide, sulfathiazole, sulfamethoxazole and sulfadiazine in water solutions during their illumination of UV radiation (gamma max 366 nm) with TiO2 catalyst was examined. The growth-inhibition effect of sulfonamides and intermediate products their photodegradation was investigated in aqueous solution with the green alga Chlorella vulgaris. The biodegradability of the investigated compounds was determined in the illuminated solutions and is expressed as Biochemical Oxygen Demand. It was found that all of the investigated sulfonamides in the initial solutions were resistant to biodegradation and were toxic relative to C. vulgaris. The toxicity (EC50 values) relative to C. vulgaris increased in the following order sulfacetamide, sulfathiazole, sulfamethoxazole, sulfadiazine. All of the investigated sulfonamides undergo photocatalytic degradation. The toxicity of intermediate products of the sulfonamides degradation was significantly lower than the toxicity of sulfonamides in the initial solutions and was dependent on

illumination time and degradation rate. The intermediate products of photocatalysis in contrast to the initial sulfonamides, might be mineralized using biological methods.

[Baran W; Chemosphere 65 (8): 1295-9 (2006)] **PEER REVIEWED** [PubMed Abstract](#)

Non-Human Toxicity Values:

LD50 Mouse oral 4500 mg/kg

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 3154] **PEER REVIEWED**

Ongoing Test Status:

The following link will take the user to the National Toxicology Program (NTP) Test Agent Search Results page, which tabulates all of the "Standard Toxicology & Carcinogenesis Studies", "Developmental Studies", and "Genetic Toxicity Studies" performed with this chemical. Clicking on the "Testing Status" link will take the user to the status (i.e., in review, in progress, in preparation, on test, completed, etc.) and results of all the studies that the NTP has done on this chemical. [http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=72-14-0]

[Available from: http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=72-14-0]

Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

Although the liver is the major site of metabolism, sulfonamides may also be metabolized in other body tissues. Most sulfonamides are metabolized mainly by N4-acetylation. The degree of acetylation, which is a function of time, varies from less than 5% for sulfamethizole to up to 40% for sulfadiazine. The N4-acetyl metabolites, which do not possess antibacterial activity, have greater affinity for plasma albumin than does the nonacetylated drug and are usually less soluble than the parent sulfonamide, particularly in acidic urine. Like acetyl derivatives, glucuronide derivatives do not possess antibacterial activity; however, glucuronide derivatives are water soluble, appear to resemble the nonacetylated sulfonamide in plasma binding capacity, and have not been associated with adverse effects. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 425] **PEER REVIEWED**

Metabolism of sulfonamide drugs in animals includes conjugation at the N4-position (acetyl, sulfate, glucuronic acid, and glucose), conjugation at the N1-position (sulfate and glucuronic acid), removal of the p-amino group (formation of the desamino metabolite), ring hydroxylation, and conjugation of the ring hydroxylation products. Dietary nitrite enhances the production of the desamino metabolite of sulfathiazole.

[WHO/FAO; Joint Expert Committee on Food Additives; Food Additive Series 25: Sulfathiazole (72-14-0) (1990). Available from, as of July 21, 2008: <http://www.inchem.org/pages/jecfa.html>] **PEER REVIEWED**

Sulfathiazole...is one of the short-acting sulfonamides & in man is excreted in urine as unchanged sulfathiazole (63% of dose), N4-acetylsulfathiazole (29%), sulfathiazole-N4-glucuronide (0.8%), sulfathiazole-N4-sulfate (0.5%) & sulfathiazole-N1-glucuronide (3.8%).

[Parke, D. V. The Biochemistry of Foreign Compounds. Oxford: Pergamon Press, 1968., p. 180] **PEER REVIEWED**

Deposition kinetics, metabolism and urinary excretion of sulfathiazole were investigated in German black head sheep following single oral administration (100 mg/kg). Kinetic evaluation of plasma levels was performed using a two-compartment best fit model. Sulfathiazole is significantly metabolized to N4-acetyl metabolite in the rumen fluid. The drug is very poorly absorbed since the minimum effective concentration in plasma was not attained at any time following oral administration. The prolonged elimination half-life in sheep may be due to a low rate of drug absorption from the rumen and gastro-intestinal tract. Sulfathiazole was mainly excreted in the urine as free drug and N4-acetyl metabolite.

[Jain S, Hapke H; Dtsch Tierarztl Wochenschr 102 (10): 394-5 (1995)] **PEER REVIEWED** [PubMed Abstract](#)

The antimicrobial agents may undergo a change in the complex stomach particularly in the rumen as a result of microbial fermentation in ruminants. Present investigation deals with the influence of ruminal fluid probably the role of ruminal microorganisms on the degradation of sulfathiazole in vitro and its metabolism and disposition following its single intraruminal administration (100 mg/kg) in adult German black head sheep. Sulfathiazole is metabolized to N4-acetyl sulfathiazole in the rumen fluid after its in vitro incubation at different concentrations (10-60 micrograms/mL) for varying time intervals (1-6 hr) at a temperature of 38 +/- 0.5 degrees C. Likewise in vivo it is significantly metabolized to its N-acetyl metabolite in the rumen after an intraruminal administration. The

levels of sulfathiazole are maintained above minimum effective therapeutic concentration (40 micrograms/mL) for more than 24 hr in rumen fluid. The drug is poorly absorbed into the circulation after intraruminal administration since the levels in plasma could not reach up to minimum effective therapeutic concentration at any time. The biological half-life of sulfathiazole was found to be 16.7 hr following single intraruminal administration. Results of this investigation suggest that oral or intraruminal application of sulfathiazole has only local effects in the rumen fluid. A systemic treatment is not possible after this path of application.

[Jain S et al; Dtsch Tierarztl Wochenschr 102 (5): 193-5 (1995)] **PEER REVIEWED** [PubMed Abstract](#)

(14)C-Sulfamethazine (4-amino-N-(4,6-dimethyl-2-pyrimidinyl)benzene-(U-14(C)-sulfonamide, 220 mg/kg of body weight) was given orally or iv to lactating dairy cows. Milk collected from 0-48 hr after dosing accounted for 2.0% (oral dose) and 1.1% (iv dose) of the total (14)C-activity administered. Sulfamethazine accounted for 70-79% (oral dose) and 54-75% (iv dose) of the total (14)C in milk samples collected from 0-48 hr after dosing. N4-acetylsulfamethazine accounted for 1-2% (oral dose) and 1-4% (iv dose) of the (14)C in milk. The major (14)C-labelled metabolite in the milk was isolated and identified as the N4-lactose conjugate of sulfamethazine, a unique type of metabolite not previously reported. This metabolite accounted for 10-14% (oral dose) and 9-20% (iv dose) of the (14)C-activity in the milk collected from 0-48 hr after dosing with (14)C-sulfamethazine. N4-lactose conjugates of sulfapyridine, sulfamerzine, sulfathiazole, sulfadimethoxine and sulfaquinoxaline were present in the milk from cows orally dosed with these five sulfonamide drugs.

[Paulson GD et al; Xenobiotica 22 (8): 925-939 (1992)] **PEER REVIEWED** [PubMed Abstract](#)

Absorption, Distribution & Excretion:

Individual sulfonamides differ markedly in their absorption, distribution, and elimination. With the exception of sulfapyrimidine and sulfasalazine, which are only slightly absorbed, sulfonamides are generally well absorbed from the GI tract. Approximately 70-90% of an oral dose of the absorbable sulfonamides is reportedly absorbed from the small intestine; small amounts may also be absorbed from the stomach. Sulfamethazole and sulfisoxazole (no longer commercially available in the US) are absorbed rapidly; peak blood concentrations are usually obtained within 2-4 hours. Sulfadiazine and sulfapyridine are absorbed at a slower rate with peak blood concentrations occurring within 3-7 hours. Administration of oral sulfonamides with food appears to delay, but not reduce, absorption of the drugs. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 425] **PEER REVIEWED**

Absorption of sulfonamides from the vagina, respiratory tract, or abraded skin is variable and unreliable; however, enough drug may be absorbed to induce sensitization or toxicity. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 425] **PEER REVIEWED**

Although only free (unmetabolized and unbound) sulfonamides are microbiologically active, blood concentrations are often determined on the basis of total sulfonamide concentration. Generally, sulfonamide plasma concentrations are approximately twice the blood concentrations. Wide variations in blood concentrations have been reported in different individuals receiving identical doses of the same sulfonamide. Blood total sulfonamide concentrations of 12-15 mg/dL have been reported to be optimal; blood concentrations greater than 20 mg/dL have been associated with an increased incidence of adverse reactions. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 425] **PEER REVIEWED**

Absorbable sulfonamides are widely distributed in the body. Although most sulfonamides appear to cross cell membranes, sulfisoxazole appears to be distributed only in extracellular fluid. Sulfonamides may appear in pleural, peritoneal, synovial, amniotic, prostatic, and seminal vesicular fluid, and aqueous humor. Concentrations of some sulfonamides in the CSF may reach 35-80% of blood concentrations. Small amounts of sulfonamides are also distributed into sweat, tears, saliva, and bile. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 425] **PEER REVIEWED**

Sulfonamides readily cross the placenta; fetal plasma concentrations may exceed 50% of maternal plasma concentrations. Sulfonamides are distributed into milk. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 425] **PEER REVIEWED**

Sulfonamides are bound in varying degrees to plasma proteins. Sulfadiazine and sulfapyridine are reportedly 32-70% bound to plasma proteins and sulfamethazole and sulfisoxazole are reportedly 85-90% bound to plasma proteins. All sulfonamides are loosely bound, mainly to albumin, but small amounts of the drugs may be bound by serum globulin. Protein-bound sulfonamides do not have antibacterial activity and there is evidence that the concentration of sulfonamide in tissues is related to the concentration of unbound sulfonamide in serum. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 425] **PEER REVIEWED**

Sulfonamides and their metabolites are excreted mainly by the kidneys via glomerular filtration, but the drugs vary widely in their rates of excretion and solubility characteristics at various urinary pH values. Although alkalization of urine increases the solubility of sulfonamides and their metabolites (except sulfamethazine and N4-acetylsulfamethazine), alkalization decreases tubular reabsorption, resulting in increases renal excretion of the drugs and decreased sulfonamide blood concentrations. The metabolites do not appear to be reabsorbed by the tubules and their concentration in urine is greater than in blood. Protein-bound sulfonamides cannot be filtered by the glomeruli. Except for the poorly absorbed sulfonamides (sulfapyridine, sulfasalazine) only small amounts of sulfonamides are excreted in feces. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 425] **PEER REVIEWED**

/Sulfathiazole/ is very poorly absorbed since the minimum effective concentration in plasma was not attained at any time following oral administration. The prolonged elimination half-life in sheep may be due to a low rate of drug absorption from the rumen and gastro-intestinal tract. Sulfathiazole was mainly excreted in the urine as free drug and N4-acetyl metabolite.

[Jain S, Hapke H; Dtsch Tierarztl Wochenschr 102 (10): 394-5 (1995)] **PEER REVIEWED** [PubMed Abstract](#)

A physiological flow model was developed for the distribution of sulfathiazole residues in various tissues in swine. The approach was compartmental, in which the compartments and equilibrium constants had physiological meaning. Differential equations were developed, and appropriate parameter values and initial conditions were substituted and solved by a fourth-order Runge-Kutta technique. Simulation values corresponded with the experimentally determined concentration values in plasma and kidney, liver, muscle, fat, and heart tissues.

[Duddy J et al; J Pharm Sci 73 (11): 1525-8 (1984)] **PEER REVIEWED** [PubMed Abstract](#)

Following single iv injection in buffaloes (100 mg/kg), sulfathiazole was rapidly eliminated, with t/2 of 198 min, volume of distribution was 452 mL/kg, & 24 hr after 10.10 ug/mL was found in plasma. High concentration of parent & acetylated derivative was found in urine.

[ATEF M ET AL; ZENTRALBL VETERINAERMED, REIHE A 28 (2): 122 (1981)] **PEER REVIEWED**

The plasma, urine, and tissue sulfathiazole concentrations were determined at various times following intravenous administration to 12 sheep. The plasma and urine data were consistent with a one-compartment pharmacokinetic model, with an elimination half-life of 1.1 hr and a volume of distribution of 0.39 liter/kg. Sulfathiazole was eliminated by excretion of unchanged drug in urine (67%) and by formation of two metabolites. The data obtained from eight tissue sites were consistent with the one-compartment pharmacokinetic model presented and confirmed that tissue residues of sulfathiazole can be calculated from serum and urine drug concentration.

[Bevill R et al; J Pharm Sci 66 (9): 1297-300 (1977)] **PEER REVIEWED** [PubMed Abstract](#)

Sulfathiazole was excreted through the ruminal wall & salivary glands in cows, being acetylated (16.2%) & rapidly excreted (2 hr).

[ATEF M ET AL; ZENTRALBL VETERINAERMED REIHE A 28 (2): 113 (1981)] **PEER REVIEWED**

When sulfathiazole was injected into the femoral vein of rats it was detected 6 hr later in the bile, the excretion was 1.3%.

[CANTELLI FORTI G, BIAGI GL; BOLL SOC ITAL BIOL SPER 48 (24): 1233 (1972)] **PEER REVIEWED**

Rate constants of acetylation and excretion for sulfathiazole was studied in inbred rats. Excretion rate after iv administration was markedly influenced by urinary pH it doubled when urinary pH was increased to 8.6.

Sulfonamides may be reabsorbed from renal tubule in the unionized form.

[YAMAZAKIM ET AL; CHEM PHARM BULL 16 (4): 721 (1968)] **PEER REVIEWED** [PubMed Abstract](#)

The plasma pharmacokinetics and tissue penetration of sulfathiazole (ST) and sulfamethazine (SM) after intravenous and intramuscular injection in pigs were studied. Following a single intravenous dose of 40 mg sulfathiazole/kg of bodyweight or 80 mg sulfamethazine/kg of bodyweight, the plasma sulfathiazole and sulfamethazine concentrations were best fitted to a two-compartment model. The areas under the curve were 447 +/- 39 and 1485 +/- 41 mg/hr/L, clearances were 0.090 +/- 0.007 and 0.054 +/- 0.001 L/kg/hr, volumes of distribution were 1.16 +/- 0.16 and 0.77 +/- 0.06 L/kg, half-lives in distribution phase were 1.18 +/- 0.57 and 0.23 +/- 0.16 hr and half-lives in eliminations phase were 9.0 +/- 1.6 and 9.8 +/- 0.6 hr. When the two compounds were administered simultaneously as a single intravenous injection, the pharmacokinetic parameters for sulfathiazole were not significantly different. The values for sulfamethazine show statistical difference for some important parameters: alpha, beta and the AUC0-> were significantly decreased and t1/2alpha, Vd and ClB were significantly increased. It can be concluded that after a single intravenous injection of 40 mg/kg, sulfathiazole has a high t1/2beta resulting in higher tissue concentrations. This half-life, which is higher than what is reported in the literature, is not influenced by the presence of sulfathiazole. Sulfathiazole and sulfamethazine were also administered simultaneously as an intramuscular injection to healthy pigs at a dosage of 40 and 80 mg/kg

bodyweight. Pharmacokinetic experiments were conducted on three pigs. From this pharmacokinetic study it can be concluded that upon a single intramuscular administration of 40 mg/kg of sulfathiazole and 80 mg/kg of sulfamethazine the absolute bioavailability in pigs is 0.92 +/- 0.04 for sulfathiazole and 1.01 +/- 0.07 for sulfamethazine. Six pigs received five intramuscular (im) injections, as a single dose of sulfathiazole and sulfamethazine, every 24 hr for five consecutive days for the residue study. The pigs were slaughtered at different times after the last dose was given, and samples were taken from various tissues and organs. Concentrations were determined by a microbiological method and a HPTLC method. No edible tissue contained more than 100 µg/kg of the individual sulfonamides after 10 days of withdrawal. It means that adult animals, which have a shorter half-life and, thus, lower tissue concentrations, will certainly meet the economic community (EC) maximum residue limits after a 10 days withdrawal period.

[Van Poucke LSG, Van Peteghem CH; Journal of Food Protection 57 (9): 796-801 (1994)] **PEER REVIEWED**

Urine levels of silver and sulfathiazole were measured in thermal injured guinea pigs who were treated with 500 mg/day silver sulfathiazole (Argosulfan) cream for 7 days. Very small amounts of silver and significant quantities of sulfathiazole were detected in the urine. The mean content of silver in 1 mL urine was 2.26 µg and the corresponding average daily excretion of silver in the urine amounted to 62.72 µg/24 hr. The mean concentration of sulfathiazole in urine was 226 µg/mL, corresponding to daily amounts averaging 5.43 mg. /Silver sulfathiazole/

[Stozowska W et al; STP Pharma Sci 5 (6): 452-455 (1995)] **PEER REVIEWED**

Biological Half-Life:

Sulfonamides are generally classified as short-acting, intermediate-acting, or long-acting depending on the rate at which they are absorbed and eliminated. Sulfamethizole, sulfasalazine, and sulfisoxazole are generally considered to be short-acting sulfonamides and reportedly have plasma half-lives of about 4-8 hours. Sulfadiazine and sulfapyridine are generally considered to be intermediate-acting sulfonamides and reportedly have plasma half-lives of about 7-17 hours. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 425] **PEER REVIEWED**

The plasma, urine, and tissue sulfathiazole concentrations were determined at various times following intravenous administration to 12 sheep. The plasma and urine data were consistent with a one-compartment pharmacokinetic model, with an elimination half-life of 1.1 hr..

[Bevill R et al; J Pharm Sci 66 (9): 1297-300 (1977)] **PEER REVIEWED** [PubMed Abstract](#)

Mechanism of Action:

Sulfonamides are usually bacteriostatic in action. Sulfonamides interfere with the utilization of p-aminobenzoic acid (PABA) in the biosynthesis of tetrahydrofolic acid (the reduced form of folic acid) cofactors in susceptible bacteria. Sulfonamides are structural analogs of PABA and appear to interfere with PABA utilization by competitively inhibiting the enzyme dihydropteroate synthase, which catalyzes the formation of dihydropteroic acid (a precursor of tetrahydrofolic acid) from PABA and pteridine; however, other mechanism(s) affecting the biosynthetic pathway also may be involved. Compounds such as pyrimethamine and trimethoprim, which block later stages in the synthesis of folic acid, act synergistically with sulfonamides. Only microorganisms that synthesize their own folic acid are inhibited by sulfonamides; animal cells and bacteria which are capable of utilizing folic acid precursors or preformed folic acid are not affected by these drugs. The antibacterial activity of the sulfonamides is reportedly decreased in the presence of blood or purulent body exudates. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

The sulfonamides are structural analogs of para-aminobenzoic acid (PABA) and competitively inhibit an enzymatic step (dihydropteroate synthetase) during which PABA is incorporated into the synthesis of dihydrofolic acid (folic acid). Because dihydrofolate synthesis is reduced, the levels of tetrahydrofolate (folinic acid) formed from dihydrofolate diminish. Tetrahydrofolate is an essential component of the coenzymes responsible for single carbon metabolism in cells. Acting as antimetabolites to PABA, sulfonamides eventually block, in a complex fashion, several enzymes. These enzymes include those needed for the biogenesis of purine bases; for the transfer of desoxyuridine to thymidine; and for the biosynthesis of methionine, glycine, and formylmethionyl-transfer-RNA. This results in suppression of protein synthesis, impairment of metabolic processes, and inhibition of growth and multiplication of those organisms that cannot use preformed folate. The effect is bacteriostatic, although a bactericidal action is evident at the high concentrations that may be found in urine.

[Kahn, C.M. (Ed.); The Merck Veterinary Manual 9th ed. Merck & Co. Whitehouse Station, NJ. 2005, p. 2076] **PEER REVIEWED**

Interactions:

Since salicylates and other nonsteroidal anti-inflammatory agents (e.g., fenoprofen, indomethacin, meclofenamate) are highly protein bound, these drugs theoretically could be displaced from binding sites by

sulfonamides, or could displace sulfonamides from binding sites. Although no clinically important drug interactions have been reported, patients receiving sulfonamides concomitantly with nonsteroidal anti-inflammatory agents should be observed for adverse effects. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Because...sulfathiazole may form insoluble precipitates with formaldehyde in the urine, their concomitant administration with methenamine compounds (eg, methenamine mandelate [mandelamine]) should be avoided.

[American Medical Association, AMA Department of Drugs. AMA Drug Evaluations. 4th ed. Chicago: American Medical Association, 1980., p. 1310] **PEER REVIEWED**

The most important interactions of the sulfonamides involve those with the oral anticoagulants, the sulfonyleurea hypoglycemic agents, and the hydantoin anticonvulsants. In each case, sulfonamides can potentiate the effects of the other drug by mechanisms that appear to involve primarily inhibition of metabolism and, possibly, displacement from albumin. Dosage adjustment may be necessary when a sulfonamide is given concurrently.

/Sulfonamides/

[Hardman, J.G., L.E. Limbird, P.B. Molinoff, R.W. Ruddon, A.G. Goodman (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 9th ed. New York, NY: McGraw-Hill, 1996., p. 1062] **PEER REVIEWED**

Antacids tend to inhibit the GI absorption of sulfonamides. /Sulfonamides/

[Kahn, C.M. (Ed.); The Merck Veterinary Manual 9th ed. Merck & Co. Whitehouse Station, NJ. 2005, p. 2079] **PEER REVIEWED**

Some sulfonamides act as microsomal enzyme inhibitors, which may lead to toxic manifestations of concurrently administered drugs such as phenytoin.

[Kahn, C.M. (Ed.); The Merck Veterinary Manual 9th ed. Merck & Co. Whitehouse Station, NJ. 2005, p. 2079] **PEER REVIEWED**

The effects of sulfathiazole on binding by albumin of tolbutamide and N-(p-toluenesulfonyl)-5-methyl-2-pyrazoline-1-carboxamide are presented. The binding was found to be decreased.

[WOJCIKOPWSKI C, SZLABOWICZ D; POL J PHARMACOL PHARM 28 (2:) 129 (1976)] **PEER REVIEWED** [PubMed Abstract](#)

Solid dispersions of sulfathiazole in povidone (polyvinylpyrrolidone) were prepared by mechanical activation and characterized in vitro. The apparent solubility and rate of solvation of sulfathiazole were greatly increased when it was previously mechanically treated with povidone. As the fraction of povidone increased, the efficiency of mechanicochemical action increased. Drug release from solid dispersions with a polymer to drug ratio of 1:3, 1:1, and 3:1 was examined, a polymer to drug ratio of 3:1 gave the highest solubility. It was concluded that the preparation of sulfathiazole-povidone solid dispersions by mechanical activation significantly enhances drug solubility.

[Boldyrev VV et al; Drug Dev Ind Pharm 20 (6): 1103-1114 (1994)] **PEER REVIEWED**

Pharmacology:

Therapeutic Uses:

Anti-Infective Agents /SRP: Antibacterial/

[National Library of Medicine's Medical Subject Headings online file (MeSH, 1999)] **PEER REVIEWED**

The US FDA announced on May 31, 1979, that its Anti-infective and Topical Drugs Advisory Committee and Fertility and Maternal health Advisory Committee, as well as other studies, had concluded there was no adequate evidence that the then-available vaginal sulfonamides formulations were effective either for the treatment of vulvovaginitis caused by *Candida albicans*, *trichomonas vaginalis*, or *Gardnerella vaginalis* (*Hemophilus vaginalis*) or for relief of the symptoms of these conditions. /Sulfonamides/

[USP. Convention. USPDI - Drug Information for the Health Care Professional. 20th ed. Volume I. Micromedex, Inc. Englewood, CO., 2000. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2857] **PEER REVIEWED**

In the opinion of USP medical experts, triple sulfa vaginal preparations are not effective for any indication, including vulvovaginitis caused by *Gardnerella vaginalis* and use as a deodorant in saprophytic infections following radiation therapy. Also, USP medical experts do not recommend the use of vaginal sulfonamides, including the reformulated single-entry preparations, for the treatment of fungal infections of the vagina. /Sulfonamides/

[USP. Convention. USPDI - Drug Information for the Health Care Professional. 20th ed. Volume I. Micromedex, Inc. Englewood, CO., 2000. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2857] **PEER REVIEWED**

MEDICATION (VET): Antibacterial

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 1529] **PEER REVIEWED**

Sodium sulfathiazole is effective against a wide range of gram positive and gram negative pathogenic

microorganisms. Common uses of sulfathiazole in cattle include: the treatment of bovine respiratory disease complex (shipping fever complex); bacterial pneumonia; calf diphtheria and necrotic pododermatitis (foot rot) and acute metritis. /Sodium sulfathiazole/

[WHO/FAO; Joint Expert Committee on Food Additives; Food Additive Series 25: Sulfathiazole (72-14-0) (1990). Available from, as of July 21, 2008: <http://www.inchem.org/pages/jecfa.html> **PEER REVIEWED**

Common uses of sulfathiazole in pigs include: treatment of bacterial pneumonia; porcine colibacillosis (bacterial scours); and, in combination with chlortetracycline and penicillin, for increased rate of weight gain and improved feed efficiency, reduction of the incidence of cervical abscesses, and treatment of bacterial swine enteritis (salmonellosis or necrotic enteritis and vibronic dysentery). /Sodium sulfathiazole/

[WHO/FAO; Joint Expert Committee on Food Additives; Food Additive Series 25: Sulfathiazole (72-14-0) (1990). Available from, as of July 21, 2008: <http://www.inchem.org/pages/jecfa.html> **PEER REVIEWED**

Sulfathiazole is commonly in wound powders to prevent invasion /of burn wounds/ by many gram-negative and gram-positive organisms.

[Kahn, C.M. (Ed.); The Merck Veterinary Manual 9th ed. Merck & Co. Whitehouse Station, NJ. 2005, p. 2076] **PEER REVIEWED**

The effects of four topical medications on the rate and character of healing of cutaneous wounds were studied in six common garter snakes (*Thamnophis sirtalis*) held at an ambient temperature of 30 deg C. Two sets of five 6-8 mm round excisional wounds, four test and one control site in each set, were created on the dorsolateral body wall of each snake. Wounds were examined daily and treated for ten days, then the snakes were killed and sections of all wounds were examined by light microscopy. Composite scores, derived by ranking each treatment group in relation to the control group (control score = 0) for each of 22 characteristics associated with wound healing, were used to compare the overall effects of each treatment. Statistical comparisons were made between groups for 20 characteristics. Wounds treated with a polyurethane film merited a score of +12 and had significantly more advanced healing than untreated control for three characteristics. Wounds treated with an ointment containing scarlet red scored +6 but healing was not significantly greater than controls. Wounds treated with an antibacterial spray powder and an antibacterial ointment healed more slowly than controls and had scores of -6 and -12 respectively.

[Smith DA et al; Can J Vet Res 52 (1): 129-33 (1988)] **PEER REVIEWED** [PubMed Abstract](#) Full text: [PMC1255411](#)

Drug Warnings:

The number of conditions for which the sulfonamides are therapeutically useful and constitute drugs of first choice has been reduced sharply by the development of more effective antimicrobial agents and by the gradual increase in the resistance of a number of bacterial species to this class of drugs. /Sulfonamides/

[Hardman, J.G., L.E. Limbird, P.B. Molinoff, R.W. Ruddon, A.G. Goodman (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 9th ed. New York, NY: McGraw-Hill, 1996., p. 1062] **PEER REVIEWED**

Many of the adverse effects that have been attributed to the sulfonamides appear to be hypersensitivity reactions. The incidence of hypersensitivity reactions appears to increase with increased sulfonamide dosage. Although cross-sensitization has been reported to occur between the various anti-infective sulfonamides, some diuretics such as acetazolamide and the thiazides, some goitrogens, and sulfonylurea antidiabetic agents, the association between hypersensitivity to sulfonamide anti-infectives and subsequent sensitivity reactions to non-anti-infective sulfonamides (e.g., thiazides, sulfonylurea antidiabetic agents, furosemide, dapson, probenecid) appears to result from a predisposition to allergic reactions in general rather than to cross-sensitivity to the sulfa moiety per se.

/Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Various dermatologic reactions, including rash, pruritus, urticaria, erythema nodosum, erythema multiforme (Stevens-Johnson syndrome), Lyell's syndrome (may be associated with corneal damage), Behcet's syndrome, toxic epidermal necrolysis, and exfoliative dermatitis, have been reported in patients receiving sulfonamides. Because photosensitivity may also occur, patients should be cautioned against exposure to UV light or prolonged exposure to sunlight. A relatively high proportion of fatalities has occurred as a result of the Stevens-Johnson syndrome, especially in children. Although long-acting sulfonamides (which are no longer commercially available) have been associated most often with the Stevens-Johnson syndrome, other sulfonamides also have been reported to cause this reaction. The physician should be alert to the signs, including high fever, severe headache, stomatitis, conjunctivitis, rhinitis, urethritis, and balanitis, which may precede the onset of the cutaneous lesions of the Stevens-Johnson syndrome. If a rash develops during therapy, the sulfonamide should be discontinued at once. In rare instances, a skin rash may precede a more serious reaction such as Stevens-Johnson syndrome, toxic epidermal necrolysis, hepatic necrosis, and/or serious blood disorders. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Fever, which may develop 7-10 days after the initial sulfonamide dose, is a common adverse effect of sulfonamide

therapy. Serum sickness syndrome or serum sickness-like reactions (e.g., fever, chills, rigors, flushing, joint pain, urticarial eruptions, conjunctivitis, bronchospasm, leukopenia), have been reported; rarely, anaphylactoid reactions and anaphylaxis may occur. Lupus erythematosus-like syndrome, disseminated lupus erythematosus, angioedema, vasculitis, vascular lesions including periarteritis nodosa and arteritis, cough, shortness of breath, chills, pulmonary infiltrates, pneumonitis (which may be associated with eosinophilia), fibrosing alveolitis, pleuritis, pericarditis with or without tamponade, allergic myocarditis, hepatitis, hepatic necrosis with or without immune complexes, parapsoriasis varioliformis acuta, alopecia, conjunctival and scleral injection, periorbital edema, and arthralgia have also been reported. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

If a hypersensitivity reaction occurs during sulfonamide therapy, the drugs should be discontinued immediately. Desensitization to sulfasalazine has been used when reinstatement of therapy with the drug was considered necessary in patients with inflammatory bowel disease who had hypersensitivity reactions to the drug. Desensitization to sulfadiazine has also been used in several patients with acquired immunodeficiency syndrome (AIDS) when use of sulfadiazine for the treatment of toxoplasmosis was considered necessary in patients who had hypersensitivity reactions to the drug. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Adverse hematologic effects, including methemoglobinemia, sulfhemoglobinemia, granulocytopenia, leukopenia, congenital neutropenia, eosinophilia, hemolytic anemia, agranulocytosis, aplastic anemia, purpura, clotting disorder, thrombocytopenia, myelodysplastic syndrome, hypofibrinogenemia, and hypoprothrombinemia, rarely resulting in death, have been associated with sulfonamide therapy. Acute hemolytic anemia may occur during the first week of therapy as a result of sensitization or glucose-6-phosphate dehydrogenase (G-6-PD) deficiency. This reaction may also occur in the fetus or premature infant in whom G-6-PD is normally deficient. Mild, chronic hemolytic anemia may occur during prolonged sulfonamide therapy. Agranulocytosis may rarely occur 10-14 days after initiation of therapy. Complete blood cell counts should be performed regularly in patients receiving sulfonamides for longer than 2 weeks. If signs of adverse hematologic effects such as sore throat, fever, pallor, purpura, jaundice, or weakness occur, sulfonamide therapy should be discontinued until the possibility of a blood disorder is eliminated. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Functional and morphologic hepatic changes, possibly causing jaundice, may appear within 3-5 days after initiation of sulfonamide therapy. Focal or diffuse necrosis of the liver has been reported rarely. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Renal damage, manifested by renal colic, nephritis, urolithiasis, toxic nephrosis with anuria and oliguria, hematuria, proteinuria, kidney stone formation, and elevation of BUN and creatinine concentrations, is usually a result of crystalluria caused by precipitation of the sulfonamide and/or its N4-acetyl derivative in the urinary tract. The occurrence of crystalluria is related to the urinary concentration and the solubility characteristics of the sulfonamide and its metabolites. The risk of crystalluria may be decreased by maintaining an adequate urinary output and by increasing urinary pH. Unless the urine is highly acidic and/or the drug is relatively insoluble, alkalization of the urine is usually not necessary if the urinary output is maintained at a minimum of 1500 mL daily. Urinary alkalization may be achieved by administering ... sodium bicarbonate orally... . Urinalysis and kidney function tests should be performed weekly to detect any renal complications. If persistent, heavy crystalluria, hematuria, or oliguria occurs, sulfonamide therapy should be discontinued and alkali therapy maintained. Nephritis and hemolytic-uremic syndrome also have been reported. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 423] **PEER REVIEWED**

Nausea and vomiting occur frequently in patients receiving sulfonamides. Abdominal pain, anorexia, glossitis, stomatitis, pancreatitis, gastroenteritis, diarrhea, neutropenic enterocolitis, GI hemorrhage, melena, flatulence, and salivary gland enlargement also have been reported. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Clostridium difficile-associated diarrhea and colitis (also known as antibiotic-associated pseudomembranous colitis) caused by toxin-producing clostridia has been reported following sulfonamide therapy. If C. difficile-associated diarrhea and colitis occurs, mild cases may respond to discontinuance of sulfonamide therapy alone, but diagnosis and management of moderate to severe cases should include sigmoidoscopy (or other appropriate endoscopic examination), appropriate bacteriologic studies, and treatment with fluid, electrolyte, and protein supplementation as indicated. If colitis is moderate to severe or is not relieved by discontinuance of sulfonamide therapy alone, appropriate anti-infective therapy effective against C. difficile (e.g., oral metronidazole or vancomycin) should be administered. Isolation of the patient may be advisable. Other causes of colitis also should be considered. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Headache occurs frequently in patients receiving sulfonamides. Dizziness, vertigo, peripheral neuritis, ataxia, mental depression, hallucinations, disorientation, confusion, seizures, intracranial hypertension, tinnitus, hearing loss, anxiety, apathy, and acute psychosis, occur less frequently. Peripheral neuropathy, paresthesia, weakness, fatigue, drowsiness, lassitude, restlessness, insomnia, meningitis, cauda equina syndrome, and Guillain-Barre syndrome also have been reported. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Other reported adverse effects of sulfonamides include goiter production, hypothyroidism, hypoglycemia, diuresis, pharyngitis, arthralgia, acidosis, and cyanosis. The nonabsorbable sulfonamides reportedly decrease bacterial synthesis of vitamin K1, which may result in hypoprothrombinemia and hemorrhage; these sulfonamides may also reduce fecal output of thiamine. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Sulfonamides should be used with caution and in reduced dosage in patients with impaired hepatic function, impaired renal function, or urinary obstruction, since excessive accumulation of the drugs may occur in these patients. The drugs should also be administered with caution in patients with blood dyscrasia, severe allergies or asthma, or G-6-PD deficiency. The development of sore throat, fever, rash, pallor, arthralgia, cough, shortness of breath, purpura, or jaundice during sulfonamide therapy may be an early sign of a serious adverse reaction. Renal function tests and complete blood cell counts should be performed frequently during sulfonamide therapy, especially during prolonged therapy with the drugs. Microscopic urinalyses should be done weekly when patients are treated with a sulfonamide for longer than 2 weeks. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Because pseudomembranous colitis has been reported with the use of nearly all anti-infective agents, including sulfonamides, and may range in severity from mild to life threatening, it should be considered in the differential diagnosis of patients who develop diarrhea during the administration of sulfonamides. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

The frequency of resistant organisms limits the usefulness of sulfonamides as sole therapy in the treatment of urinary tract infections. Since sulfonamides are bacteriostatic and not bactericidal, a complete course of therapy is needed to prevent immediate regrowth and the development of resistant urinary pathogens. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Sulfonamides are contraindicated in patients with a history of hypersensitivity to sulfonamides or other chemically related drugs (e.g., sulfonyleureas, thiazides). The drugs are also contraindicated in patients with marked renal or hepatic impairment. Sulfonamides are contraindicated in patients with porphyria, since the drugs may precipitate an acute attack. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Kernicterus, caused by displacement of bilirubin from protein binding sites, has occurred in neonates treated with sulfonamides. Unless indicated for the treatment of congenital toxoplasmosis, sulfonamides are generally contraindicated in children younger than 2 months of age. Pending further accumulation of data on use of the drugs in pediatric patients, sulfacytine should not be used in children younger than 14 years of age.

/Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Because sulfonamides are distributed into milk, and because of the potential for serious adverse reactions from the drugs in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the woman. Because of the risk of kernicterus in infants younger than 2 months of age, use of sulfonamides is contraindicated in lactating women who are nursing such infants.

/Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Sulfonamide resistance in *Neisseria meningitidis* is mediated by altered forms of the chromosomal gene for the drug target enzyme dihydropteroate synthase. Sulfonamides have been used for decades both for prophylaxis and the treatment of meningococcal disease, and resistance is common. Two types of resistance determinants have been identified, and regions important for drug insusceptibility to the corresponding enzyme have been defined by site-directed mutagenesis. Both types of resistance traits have spread among strains of *N. meningitidis* of different serogroups and serotypes, and the large differences at the nucleotide level in a comparison of the resistance genes with the dhps genes of susceptible meningococci indicate the origin of one or maybe both types in other *Neisseria* species. One sulfonamide-sensitive strain of *N. meningitidis* was found to have a mosaic dhps gene with a central part identical to the corresponding part of a gonococcal strain. This observation supports the idea of an

interspecies transfer of genetic material in *Neisseria* species as a mechanism for the development of chromosomally mediated resistance.

[Fermer C et al; *J Bacteriol* 177 (16): 4669-75 (1995)] **PEER REVIEWED** [PubMed Abstract](#) Full text: [PMC177231](#)

The sulfonamides readily cross the placenta to the fetus during all stages of gestation. Equilibrium with maternal blood is usually established after 2-3 hr., with fetal levels averaging 70-90% of maternal. Significant levels may persist in the newborn for several days after birth when given near term. The primary danger of sulfonamide administration during pregnancy is manifested when these agents are given close to delivery. Toxicities that may be observed in the newborn include jaundice, hemolytic anemia and, theoretically, kernicterus. /Sulfonamides/ [Briggs, G.G, R.K. Freeman, S.J. Yaffe. A Reference Guide to Fetal and Neonatal Risk. Drugs in Pregnancy and Lactation. 4th ed. Baltimore, MD: Williams & Wilkins 1994., p. 795] **PEER REVIEWED**

Sensitization may occur from topical application of sulfonamides. /Sulfonamides/

[American Medical Association, AMA Department of Drugs. AMA Drug Evaluations. 4th ed. Chicago: American Medical Association, 1980., p. 1316] **PEER REVIEWED**

...Orally administered sulfathiazole and sulfadiazine frequently impaired depth perception, causing tendency to exophoria at near and decrease of adduction power.

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 860] **PEER REVIEWED**

Reportedly in 4% of patients receiving sulfathiazole, conjunctivitis has appeared between 5th and 9th day, sometimes involving only the conjunctiva, but in other cases associated with skin eruptions & fever. Majority of cases...have cleared within few days after discontinuing drug. ...serious cases...have produced symblepharon.

[Grant, W. M. Toxicology of the Eye. 2nd ed. Springfield, Illinois: Charles C. Thomas, 1974., p. 951] **PEER REVIEWED**

Interactions:

Since salicylates and other nonsteroidal anti-inflammatory agents (e.g., fenoprofen, indomethacin, meclofenamate) are highly protein bound, these drugs theoretically could be displaced from binding sites by sulfonamides, or could displace sulfonamides from binding sites. Although no clinically important drug interactions have been reported, patients receiving sulfonamides concomitantly with nonsteroidal anti-inflammatory agents should be observed for adverse effects. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Because...sulfathiazole may form insoluble precipitates with formaldehyde in the urine, their concomitant administration with methenamine compounds (eg, methenamine mandelate [mandelamine]) should be avoided.

[American Medical Association, AMA Department of Drugs. AMA Drug Evaluations. 4th ed. Chicago: American Medical Association, 1980., p. 1310] **PEER REVIEWED**

The most important interactions of the sulfonamides involve those with the oral anticoagulants, the sulfonylurea hypoglycemic agents, and the hydantoin anticonvulsants. In each case, sulfonamides can potentiate the effects of the other drug by mechanisms that appear to involve primarily inhibition of metabolism and, possibly, displacement from albumin. Dosage adjustment may be necessary when a sulfonamide is given concurrently.

/Sulfonamides/

[Hardman, J.G., L.E. Limbird, P.B. Molinoff, R.W. Ruddon, A.G. Goodman (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 9th ed. New York, NY: McGraw-Hill, 1996., p. 1062] **PEER REVIEWED**

Antacids tend to inhibit the GI absorption of sulfonamides. /Sulfonamides/

[Kahn, C.M. (Ed.); The Merck Veterinary Manual 9th ed. Merck & Co. Whitehouse Station, NJ. 2005, p. 2079] **PEER REVIEWED**

Some sulfonamides act as microsomal enzyme inhibitors, which may lead to toxic manifestations of concurrently administered drugs such as phenytoin.

[Kahn, C.M. (Ed.); The Merck Veterinary Manual 9th ed. Merck & Co. Whitehouse Station, NJ. 2005, p. 2079] **PEER REVIEWED**

The effects of sulfathiazole on binding by albumin of tolbutamide and N-(p-toluenesulfonyl)-5-methyl-2-pyrazoline-1-carboxamide are presented. The binding was found to be decreased.

[WOJCIKOPWSKI C, SZLABOWICZ D; *POL J PHARMACOL PHARM* 28 (2): 129 (1976)] **PEER REVIEWED** [PubMed Abstract](#)

Solid dispersions of sulfathiazole in povidone (polyvinylpyrrolidone) were prepared by mechanical activation and characterized in vitro. The apparent solubility and rate of solvation of sulfathiazole were greatly increased when it was previously mechanically treated with povidone. As the fraction of povidone increased, the efficiency of mechanicochemical action increased. Drug release from solid dispersions with a polymer to drug ratio of 1:3, 1:1, and 3:1 was examined, a polymer to drug ratio of 3:1 gave the highest solubility. It was concluded that the preparation of sulfathiazole-povidone solid dispersions by mechanical activation significantly enhances drug solubility.

[Boldyrev VV et al; *Drug Dev Ind Pharm* 20 (6): 1103-1114 (1994)] **PEER REVIEWED**

Drug Tolerance:

Both chromosomal and R-factor-mediated resistance to sulfonamides have been attributed to altered forms of dihydropterate synthetase (for which sulfonamides have a lowered affinity). Another mechanism of resistance is the overproduction of PABA, which overcomes the metabolic block imposed by the inhibition of dihydropterate synthetase. Cross-resistance between sulfonamides is the general rule. Resistance does emerge gradually and is widespread in many animal populations; continued use of sulfonamides increases the incidence. Plasmid-mediated sulfonamide resistance in intestinal gram-negative bacteria is often linked with ampicillin and tetracycline resistance.

[Kahn, C.M. (Ed.); The Merck Veterinary Manual 9th ed. Merck & Co. Whitehouse Station, NJ. 2005, p. 2077] **PEER REVIEWED**

Environmental Fate & Exposure:**Environmental Fate/Exposure Summary:**

Sulfathiazole's production and use as both a human and veterinary antibiotic may result in its release to the environment through various waste streams. If released to air, an estimated vapor pressure of 4.2×10^{-8} mm Hg at 25 deg C indicates sulfathiazole will exist in both the vapor and particulate phases in the atmosphere. Vapor-phase sulfathiazole will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 7 hrs. Particulate-phase sulfathiazole will be removed from the atmosphere by wet or dry deposition. Sulfathiazole contains chromophores that absorb at wavelengths >290 nm and therefore may be susceptible to direct photolysis by sunlight. If released to soil, sulfathiazole is expected to have moderate to high mobility based upon a Koc values of 200 and 97. The pKa values of sulfathiazole are 2.2 and 7.2, indicating that this compound will exist partially in the anion form in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts. Volatilization from moist soil surfaces is not expected to be an important fate process for the neutral species based upon an estimated Henry's Law constant of 5.8×10^{-14} atm-cu m/mole. In general, sulfonamides are not readily biodegraded. If released into water, sulfathiazole is expected to adsorb to suspended solids and sediment based upon the Koc values. Volatilization from water surfaces is not expected to be an important fate process for the neutral species based the estimated Henry's Law constant. An estimated BCF of 3 suggests the potential for bioconcentration in aquatic organisms is low. Sulfathiazole is not expected to undergo hydrolysis in the environment since amphoteric sulfonamides behave as weak acids. Occupational exposure to sulfathiazole may occur through inhalation and dermal contact with this compound at workplaces where sulfathiazole is produced or used. Use data indicate that the general population may be exposed to sulfathiazole via dermal contact and administration of pharmaceutical products containing sulfathiazole. (SRC)

PEER REVIEWED

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 3,171 workers (1,476 of these were female) were potentially exposed to sulfathiazole in the US(1). Occupational exposure to sulfathiazole may occur through inhalation and dermal contact with this compound at workplaces where sulfathiazole is produced or used. Use data indicate that the general population may be exposed to sulfathiazole via dermal contact and administration of pharmaceutical products containing sulfathiazole(SRC).

[(1) NIOSH; NOES. National Occupational Exposure Survey conducted from 1981-1983. Estimated numbers of employees potentially exposed to specific agents by 2-digit standard industrial classification (SIC). Available at <http://www.cdc.gov/noes/> as of Apr 14, 2008.] **PEER REVIEWED**

Artificial Pollution Sources:

Sulfathiazole's production and use as both a human(1) and veterinary antibiotic(2) may result in its release to the environment through various waste streams(SRC).

[(1) O'Neil MJ, ed; The Merck Index. 14th ed. Whitehouse Station, NJ: Merck and Co., Inc. p. 1524 (2006) (2) Aiello SE et al, eds; The Merck Veterinary Manual. 8th ed. Whitehouse Station, NY: Merck & Co., p. 1765 (1998)] **PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Based on a classification scheme(1), Koc values of 200(2) and 97(3) indicate that sulfathiazole is expected to have moderate to high mobility in soil(SRC). The pKa of sulfathiazole is 7.24(4), indicating that this compound will exist partially in the anion form in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts(5). Volatilization

from moist soil surfaces is not expected to be an important fate process for the neutral species based upon an estimated Henry's Law constant of 5.8×10^{-14} atm-cu m/mole(SRC), using a fragment constant estimation method(6). Sulfathiazole is not expected to volatilize from dry soil surfaces(SRC) based upon an estimated vapor pressure of 4.2×10^{-8} mm Hg(SRC), determined from a fragment constant method(7). In general, sulfonamide antimicrobials are not readily biodegraded and persist in soils(8).

[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Tolls J; Environ Sci Technol 35: 3397-406 (2001) (3) Thiele-Bruhn S; J Plant Nutr Soil Sci 166: 145-67 (2003) (4) Boreen AL et al; Environ Sci Technol 38: 3933-40 (2004) (5) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds. Boca Raton, FL: Lewis Publ (2000) (6) Meylan WM, Howard PH; Environ Toxicol Chem 10: 1283-93 (1991) (7) Lyman WJ; p. 31 in Environmental Exposure From Chemicals Vol I, Neely WB, Blau GE, eds, Boca Raton, FL: CRC Press (1985) (8) Bialk HM et al; Environ Sci Technol 39: 4463-73 (2005)] **PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), Koc values of 200(2) and 97(3) indicate that sulfathiazole is not expected to adsorb to suspended solids and sediment(SRC). The Henry's Law constant for the neutral species of sulfathiazole is estimated as 5.8×10^{-14} atm-cu m/mole(SRC) using a fragment constant estimation method(4). This Henry's Law constant indicates that the neutral species is expected to be essentially nonvolatile from water surfaces(5). A pKa of 7.2(6) indicates sulfathiazole will exist partially in the anion form at pH values of 5 to 9 and therefore volatilization from water surfaces is not expected to be an important fate process(7). Volatilization from water surfaces is not expected to be an important fate process for the neutral species based upon an estimated Henry's Law constant of 5.8×10^{-14} atm-cu m/mole(SRC), developed using a fragment constant estimation method(8). According to a classification scheme(9), an estimated BCF of 3(SRC), from an estimated log Kow of 0.05(10) and a regression-derived equation(11), suggests the potential for bioconcentration in aquatic organisms is low(SRC). Sulfathiazole is expected to be readily photodegraded in most natural waters as the anionic form is most susceptible to direct photodegradation(6). A biodegradation rate in soil of 50 kg/wk as part of a land treatment study(12) suggests that biodegradation is not an important environmental fate process in water(SRC).

[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Tolls J; Environ Sci Technol 35: 3397-406 (2001) (3) Thiele-Bruhn S; J Plant Nutr Soil Sci 166: 145-67 (2003) (4) Meylan WM, Howard PH; Environ Toxicol Chem 10: 1283-93 (1991) (5) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (6) Boreen AL et al; Environ Sci Technol 38: 3933-40 (2004) (7) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds. Boca Raton, FL: Lewis Publ (2000) (8) Meylan WM, Howard PH; Environ Toxicol Chem 10: 1283-93 (1991) (9) Franke C et al; Chemosphere 29: 1501-14 (1994) (10) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC: Amer Chem Soc p. 55 (1995) (11) Meylan WM et al; Environ Toxicol Chem 18: 664-72 (1999) (12) Huddleston RL et al; pp. 41-61 in Water Resourc Symp., 13(Land Treat: Hazard Waste Manage Altern) (1986)] **PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), sulfathiazole, which has an estimated vapor pressure of 4.2×10^{-8} mm Hg at 25 deg C(SRC), determined from a fragment constant method(2), will exist in both the vapor and particulate phases in the ambient atmosphere. Vapor-phase sulfathiazole is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is estimated to be 7 hrs(SRC), calculated from its rate constant of 5.4×10^{-11} cu cm/molecule-sec at 25 deg C(SRC) that was derived using a structure estimation method(3). Particulate-phase sulfathiazole may be removed from the air by wet or dry deposition(SRC). Sulfathiazole contains chromophores that absorb at wavelengths >290 nm(4) and therefore may be susceptible to direct photolysis by sunlight(SRC).

[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Lyman WJ; p. 31 in Environmental Exposure From Chemicals Vol I, Neely WB, Blau GE, eds, Boca Raton, FL: CRC Press (1985) (3) Meylan WM, Howard PH; Chemosphere 26: 2293-99 (1993) (4) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 8-12 (1990)] **PEER REVIEWED**

Environmental Biodegradation:

AEROBIC: A biodegradation rate of 50 kg/wk was reported following the addition of 10,000 ppm added to soil, as part of an analysis of land treatment capacity for effective biodegradation of waste effluent(1). This rate was slow to moderate in comparison to other organo-sulfur compounds tested, the most rapid being sodium-taurocholate at 950 kg/wk and the slowest being sodium-diethyldithiocarbamate at 10 kt/wk(1). Biodegradation of organic sulfur compounds may result in lower soil pH as a result of sulfur mineralization(1). In general, sulfonamide antimicrobials are not readily biodegraded and persist in soils(2).

[(1) Huddleston RL et al; pp. 41-61 in Water Resourc Symp., 13(Land Treat: Hazard Waste Manage Altern) (1986) (2) Bialk HM et al; Environ Sci Technol 39: 4463-73 (2005)] **PEER REVIEWED**

Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of sulfathiazole with photochemically-produced hydroxyl radicals has been estimated as 5.4×10^{-11} cu cm/molecule-sec at 25 deg C(SRC) using a structure estimation method(1). This corresponds to an atmospheric half-life of about 7 hours at an atmospheric concentration of 5×10^5 hydroxyl radicals per cu cm(1). Sulfathiazole is not expected to undergo hydrolysis in the environment since amphoteric sulfonamides behave as weak acids and are much more soluble in alkaline than acidic environments(4); they form salts in strongly acid or basic solutions(3). Sulfathiazole is expected to be readily photodegraded in most natural waters as the anionic form is most susceptible to direct photodegradation. In aqueous solution, direct photolysis

rates were reported as 2.3×10^{-5} /sec (pH 2.5); 2.3×10^{-5} /sec (pH 3.9); 2.5×10^{-5} /sec (pH 4.9); 5.7×10^{-5} /sec (pH 6.3); 13×10^{-5} /sec (pH 8.4), resulting in sulfanilic acid(5). Sulfathiazole does contain chromophores that absorb at wavelengths >290 nm(2) and therefore may be susceptible to direct photolysis by sunlight(SRC).

[(1) Meylan WM, Howard PH; Chemosphere 26: 2293-99 (1993) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 8-12 (1990) (3) Thiele-Bruhn S; J Plant Nutr Soil Sci 166: 145-67 (2003) (4) Aiello SE et al, eds; The Merck Veterinary Manual. 8th ed. Whitehouse Station, NY: Merck & Co., p. 1765 (1998) (5) Boreen AL et al; Environ Sci Technol 38: 3933-40 (2004)] **PEER REVIEWED**

Environmental Bioconcentration:

An estimated BCF of 3 was calculated in fish for sulfathiazole(SRC), using a log Kow of 0.05(1) and a regression-derived equation(2). According to a classification scheme(3), this BCF suggests the potential for bioconcentration in aquatic organisms is low(SRC).

[(1) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC: Amer Chem Soc p. 55 (1995) (2) Meylan WM et al; Environ Toxicol Chem 18: 664-72 (1999) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)] **PEER REVIEWED**

Soil Adsorption/Mobility:

A Koc of 200 (Kd 4.9) has been reported for sulfathiazole using a loamy sand soil with a pH of 5.2(1). A Koc of 97 was reported using a clay loam soil (pH 6.0, organic content 3.1%)(2). According to a classification scheme(3), these Koc values suggests that sulfathiazole is expected to have moderate to high mobility in soil. The pKa values of sulfathiazole are 2.2 and 7.2(4), indicating that this compound will exist partially in the anion form in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts(5). However, aromatic amines are expected to bind strongly to humus or organic matter in soils due to the high reactivity of the aromatic amino group(6,7), suggesting that mobility may be much lower in some soils(SRC). Treated waste water effluent containing sulfathiazole was applied to soil columns over 23 days; the compound was not detected (detection limit 0.05 ug/L) in the drainage samples(8).

[(1) Tolls J; Environ Sci Technol 35: 3397-406 (2001) (2) Thiele-Bruhn S; J Plant Nutr Soil Sci 166: 145-67 (2003) (3) Swann RL et al; Res Rev 85: 17-28 (1983) (4) Boreen AL et al; Environ Sci Technol 38: 3933-40 (2004) (5) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds. Boca Raton, FL: Lewis Publ (2000) (6) Bollag JM et al; J Agric Food Chem 26: 1302-6 (1978) (7) Adrian P et al; Toxicol Environ Chem 20-21: 109-20 (1989) (8) Cordy GE et al; Ground Water Monit Remed 24: 58-69 (2004)] **PEER REVIEWED**

Volatilization from Water/Soil:

The Henry's Law constant for the neutral species of sulfathiazole is estimated as 5.8×10^{-14} atm-cu m/mole(SRC) using a fragment constant estimation method(1). This Henry's Law constant indicates that the neutral species is expected to be essentially nonvolatile from water surfaces(2). The pKa values of 2.2 and 7.2(3) indicates sulfathiazole will exist partially in the anion form at pH values of 5 to 9 and therefore volatilization from water surfaces is not expected to be an important fate process(4). Sulfathiazole is not expected to volatilize from dry soil surfaces(SRC) based upon an estimated vapor pressure of 4.2×10^{-8} mm Hg(SRC), determined from a fragment constant method(5).

[(1) Meylan WM, Howard PH; Environ Toxicol Chem 10: 1283-93 (1991) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Boreen AL et al; Environ Sci Technol 38: 3933-40 (2004) (4) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds. Boca Raton, FL: Lewis Publ (2000) (5) Lyman WJ; p. 31 in Environmental Exposure From Chemicals Vol I, Neely WB, Blau GE, eds, Boca Raton, FL: CRC Press (1985)] **PEER REVIEWED**

Environmental Water Concentrations:

SURFACE WATER: Sulfathiazole was not detected in 139 US streams sampled from 1999-2000, detection limit of 0.05 ug/L(1). It was not detected in 76 water samples collected during 2001 from upstream and downstream of select towns and cities in Iowa during high-, normal-, and low-flow conditions, detection limit 0.05 ug/L(2). Sulfathiazole was not detected in 12 stream and raw water samples collected in a heavily populated, highly urbanized US drainage basin during November and December 2001, reporting level of 0.10 ug/L(3). The compound has been found up to the low ug/L-level in surface water samples(4).

[(1) Kolpin W et al; Environ Sci Technol 36: 1202-11 (2002) (2) Kolpin DW et al; Sci Total Environ 348: 119-130 (2004) (3) Stackelberg PE et al; Sci Total Environ 329: 99-113 (2004) (4) Heberer T; Toxicol Lett 131: 5-17 (2002)] **PEER REVIEWED**

Effluent Concentrations:

Leachate samples were collected on September 6, 2000, down gradient from the Norman Municipal Landfill research site in central Oklahoma; the landfill was established in the 1920s and closed in 1985(1). Sulfathiazole was tested for but not detected, reporting limit 0.10 ug/L(1). The average concentration in daily flushwater of a US swine confined feeding operation was 971 ug/L assuming 2500 head, average weight of 180 lbs, average administration of 496 mg/day/animal(2). Sulfathiazole was not detected in final effluents of eight wastewater

treatment plants in five Canadian cities, sampled in 2002; detection limit 0.004 ug/L(3). The compound has been found up to the low ug/L-level in unspecified sewage samples(4).

[(1) Barnes KK et al; Ground Water Monit Remed 24: 119-26 (2004) (2) Huang CH et al; pp. 4532-43 in Conf Proc - Water Environ Fed Annual Conf and Exposition, 74th Atlanta, GA, Oct 13-17, 2001 (2001) (3) Miao XS et al; Environ Sci Technol 38: 3533-41 (2004) (4) Heberer T; Toxicol Lett 131: 5-17 (2002)] **PEER REVIEWED**

Food Survey Values:

Sulfathiazole residues were tested for in 2,363 farm and fish samples on the market from 1994 to 1998 in Slovenia(1). Sulfonamides were not detected in 99.37% of samples (detection limit = 0.01 mg/kg); no residues were found in poultry samples and half of the positive samples belong to pig tissues(1). Sulfathiazole was detected in one unspecified sample at a concentration between 10 and 50 ng/g wet weight(1).

[(1) Sinigoj-Gacnik K, Dognac DZ; Bull Environ Contam Toxicol 64: 235-41 (2000)] **PEER REVIEWED** [PubMed Abstract](#)

Milk Concentrations:

Because sulfonamides are distributed into milk, and because of the potential for serious adverse reactions from the drugs in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the woman. Because of the risk of kernicterus in infants younger than 2 months of age, use of sulfonamides is contraindicated in lactating women who are nursing such infants.

/Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 424] **PEER REVIEWED**

Other Environmental Concentrations:

Sulfathiazole was not detected in pig urine following prescribed administration, detection limit of 0.01 to 1.6 mg/L, depending on analytical method(1).

[(1) Ellinghaus U; pp 1166-70 in Residues of Veterinary Drugs in Food; Proc Euroresidue Conf, Noodwijkerhout, The Netherlands, May 21-23, 1990. Haagsma M et al, eds. (1990)] **PEER REVIEWED**

Environmental Standards & Regulations:

FDA Requirements:

A tolerance of 0.1 part per million is established for negligible residues of sulfathiazole in the uncooked edible tissues of swine.

[21 CFR 556.690 (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of July 30, 2008: <http://www.ecfr.gov> **PEER REVIEWED**

The Approved Drug Products with Therapeutic Equivalence Evaluations List identifies discontinued drug products. Sulfathiazole is included on this list.

[DHHS/FDA; Electronic Orange Book-Approved Drug Products with Therapeutic Equivalence Evaluations. Available from, as of August 1, 2008: <http://www.fda.gov/cder/ob/> **PEER REVIEWED**

The Generic Animal Drug and Patent Restoration act requires that each sponsor of an approved animal drug must submit to the FDA certain information regarding patents held for the animal drug or its method of use. The Act requires that this information, as well as a list of all animal drug products approved for safety and effectiveness, be made available to the public. Sulfathiazole is included on this list.

[US FDA/Center for Veterinary Medicine; The Green Book - FDA Approved Animal Drug Products. Available from, as of July 30, 2008: http://www.fda.gov/cvm/Green_Book/greenbook.html **PEER REVIEWED**

The following drug products were withdrawn or removed from the market because such drug products or components of such drug products were found to be unsafe or not effective. The following drug products may not be compounded under the exemptions provided by section 503A(a) of the Federal Food, Drug, and Cosmetic Act: All drug products containing sulfathiazole (except those formulated for vaginal use).

[21 CFR 216.24 (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of July 30, 2008: <http://www.ecfr.gov> **PEER REVIEWED**

New animal drugs for use in animal feeds. Chlortetracycline, sulfathiazole, penicillin. Type A medicated articles: (1) 20 grams of chlortetracycline hydrochloride, 4.4 percent (20 grams) sulfathiazole, and procaine penicillin equivalent to 10 grams of penicillin per pound to No. 046573 in section 510.600(c) of this chapter. (2) 40 grams of chlortetracycline hydrochloride, 8.8 percent (40 grams) sulfathiazole and procaine penicillin equivalent in activity to 20 grams of penicillin per pound to No. 046573 in section 510.600(c) of this chapter. ... Indications for use: For reduction of incidence of cervical abscesses. Treatment of bacterial enteritis (salmonellosis or necrotic enteritis

caused by Salmonella choleraesuis and vibronic dysentery). Maintenance of weight gains in the presence of atrophic rhinitis. Swine 10 pounds of body weight to 6 weeks post-weaning: Increased rate of weight gain and improved feed efficiency. Swine 6 to 16 weeks post-weaning: Increased rate of weight gain. ... Limitations: For swine raised in confinement (dry-lot) or on limited pasture. Feed as sole ration. Withdraw 7 days prior to slaughter. [21 CFR 558.155 (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of July 30, 2008: <http://www.ecfr.gov> **PEER REVIEWED**

Chemical/Physical Properties:

Molecular Formula:

C9-H9-N3-O2-S2

PEER REVIEWED

Molecular Weight:

255.32

[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1534] **PEER REVIEWED**

Color/Form:

Brown plates, rods or powder from 45% alcohol

[Lide, D.R. CRC Handbook of Chemistry and Physics 86TH Edition 2005-2006. CRC Press, Taylor & Francis, Boca Raton, FL 2005, p. 3-464] **PEER REVIEWED**

Yellowish-white prismatic rods and six sided plates and prisms

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 10th ed. Volumes 1-3 New York, NY: John Wiley & Sons Inc., 1999., p. V3: 3444] **PEER REVIEWED**

Melting Point:

175 deg C (form a); 202 deg C (form b)

[Lide, D.R. CRC Handbook of Chemistry and Physics 86TH Edition 2005-2006. CRC Press, Taylor & Francis, Boca Raton, FL 2005, p. 3-464] **PEER REVIEWED**

Dissociation Constants:

pKa1 = 2.2; pKa2= 7.24

[Boreen AL et al; Environ Sci Technol 38: 3933-40 (2004)] **PEER REVIEWED** [PubMed Abstract](#)

Octanol/Water Partition Coefficient:

log Kow = 0.05

[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995., p. 55] **PEER REVIEWED**

Solubilities:

Soly at 26 deg C (mg/100 mL): water 60 (pH 6.03); alcohol 525. Sol in acetone, dil mineral acids, KOH and NaOH solns, ammonia water. Sparingly soluble in ethanol. Practically insoluble in chloroform, ether.

[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1534] **PEER REVIEWED**

Slightly soluble in dimethyl sulfoxide.

[Lide, D.R. CRC Handbook of Chemistry and Physics 86TH Edition 2005-2006. CRC Press, Taylor & Francis, Boca Raton, FL 2005, p. 3-464] **PEER REVIEWED**

In water, 373 mg/L at 25 deg C

[Yalkowsky, S.H., He, Yan., Handbook of Aqueous Solubility Data: An Extensive Compilation of Aqueous Solubility Data for Organic Compounds Extracted from the AQUASOL DATABASE. CRC Press LLC, Boca Raton, FL. 2003., p. 563] **PEER REVIEWED**

Spectral Properties:

IR: 106 (Sadtlar Research Laboratories IR Grating Collection)

[Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V2: 1181] **PEER REVIEWED**

UV: 119 (Sadtlar Research Laboratories Spectral Collection)

[Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V2: 1181] **PEER REVIEWED**

Raman: 542 (Sadtlar Research Laboratories)

[Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V2: 1181] **PEER REVIEWED**

MASS: 65076 (NIST/EPA/MSDC Mass Spectral database, 1990 version)

[Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V2: 1181] **PEER REVIEWED**

Vapor Pressure:

4.22X10⁻⁸ mm Hg at 25 deg C (est)

[US EPA; Estimation Program Interface (EPI) Suite. Ver.3.12. Nov 30, 2004. Available from, as of Apr 14, 2008: <http://www.epa.gov/oppt/exposure/pubs/episuited1.htm> **PEER REVIEWED**

Other Chemical/Physical Properties:

Crystals or white powder or granules. Also occurs as the monohydrate and pentahydrate. One gram dissolves in approx 2.5 mL water, in approx 15 mL alc. pH of 1% aq soln 9.35; of 10% soln 10.2. /Sodium salt sesquihydrate/ [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1524] **PEER REVIEWED**

Amorphous powder. Practically insol in water /Polymer with formaldehyde/

[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1524] **PEER REVIEWED**

The microstructure of sulfathiazole crystals obtained by recrystallization at 0, 30, and 70DGC was studied using high resolution transmission electron microscopy. Low magnification electron microscopy study of the crystals showed featureless morphology, yet the resolved lattice images showed imperfections such as dislocations, lattice irregularities and regions of discontinuity.

[Luklinska ZH et al; J Pharm Pharmacol 41: 559-561 (Aug 1989)] **PEER REVIEWED**

Several interfacial and partitioning processes were incorporated into a mathematical model describing the in vitro diffusion of drug from a submicron oil-in-water emulsion across a semipermeable membrane. Drug ionization and its effects on charge dependent interfacial, partitioning and mass transport processes are considered. Release studies using sulfathiazole as a test compound were found to be consistent with the model.

[Lostritto RT et al; Bull Parenter Drug Assoc 41: 214-219 (Nov-Dec 1987)] **PEER REVIEWED**

X-ray diffraction and infrared spectrophotometric studies were carried out to determine interactions between cellulose acetate phthalate film coatings and either sulfathiazole or sulfathiazole sodium in tablets. A surface interaction was noted when the sodium salt was used.

[Joachim J et al J Pharm Belg 41: 406-416 (Nov-Dec 1986)] **PEER REVIEWED**

The stability of sulfathiazole in hydrochloric acid at elevated temperatures was investigated. Two hydrolytic decomposition products were isolated and identified using LC with UV detection.

[Klimes J and M Zahradnicek; Cesk Farm 35 : 385-387 (Sep 1986)] **PEER REVIEWED**

Crystal growth of sulfathiazole in aqueous suspension was studied using a projecting microscope. Temperature, agitation, concentration of povidone and suspension concentration effects on crystal growth were examined. Povidone concentration in excess of one percent inhibited the growth rate. Agitation, temperature increase and a decrease in suspension concentration had significant growth accelerating effects.

[Motawi AM et al; Acta Pharm Technol 28 (3): 211-215 (1982)] **PEER REVIEWED**

Henry's Law constant = 5.85X10⁻¹⁴ atm-cu m/mol at 25 deg C (est)

[US EPA; Estimation Program Interface (EPI) Suite. Ver.3.12. Nov 30, 2004. Available from, as of Apr 14, 2008: <http://www.epa.gov/oppt/exposure/pubs/episuited1.htm> **PEER REVIEWED**

Hydroxyl radical reaction rate constant = 5.63X10⁻¹¹ cu cm/molec-sec at 25 deg C (est)

[US EPA; Estimation Program Interface (EPI) Suite. Ver.3.12. Nov 30, 2004. Available from, as of Apr 14, 2008: <http://www.epa.gov/oppt/exposure/pubs/episuited1.htm> **PEER REVIEWED**

Chemical Safety & Handling:

Hazardous Reactivities & Incompatibilities:

Sulfonamide solutions are incompatible with calcium- or other polyionic-containing fluids as well as many other preparations. /Sulfonamides/

[Kahn, C.M. (Ed.); The Merck Veterinary Manual 9th ed. Merck & Co. Whitehouse Station, NJ. 2005, p. 2079] **PEER REVIEWED**

Hazardous Decomposition:

When heated to decomposition it emits very toxic fumes of /nitrogen and sulfur oxides/.

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 3154] **PEER REVIEWED**

Stability/Shelf Life:

The stability of sulfamethazine (sulfadimidine) sulfathiazole, sulfameter (sulfamethoxydiazine), and sulfacetamide during acid hydrolysis in one mol/L of hydrochloric acid under increased temperature was examined using high pressure liquid chromatography. Kinetic characteristics of the process of decomposition were calculated from the found values of the concentration of undecomposed sulfonamide in relation to time. The calculated values of activation energy for the individual sulfonamides are given. The paper stresses the illustrativeness of HPLC in the examination of decomposition products.

[Klimes J and M Zahradnicek; Folia Pharm 11 (1): 41-55 (1988)] **PEER REVIEWED**

Storage Conditions:

Solutions of the sodium salts of most sulfonamides are strongly basic and deteriorate rapidly. Most sulfonamides slowly darken on exposure to light and should be stored in tight, light-resistant containers. /Sulfonamides/

[American Society of Health System Pharmacists. AHFS Drug Information 2008. Bethesda, Maryland 2008, p. 425] **PEER REVIEWED**

Disposal Methods:

SRP: At the time of review, criteria for land treatment or burial (sanitary landfill) disposal practices are subject to significant revision. Prior to implementing land disposal of waste residue (including waste sludge), consult with environmental regulatory agencies for guidance on acceptable disposal practices.

PEER REVIEWED

Occupational Exposure Standards:**Manufacturing/Use Information:****Uses:**

THERAP CAT (VET): Antibacterial

[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1534] **PEER REVIEWED**

THERAP CAT: Antibacterial

[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1534] **PEER REVIEWED**

MEDICATION (VET) (See also: [Therapeutic Uses](#))

PEER REVIEWED

MEDICATION (See also: [Therapeutic Uses](#))

PEER REVIEWED

Intrauterine use in cows /Polymer with formaldehyde/

[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1524] **PEER REVIEWED**

Manufacturers:

Napp Technologies, Inc., 199 Main St., Lodi, NJ 07644, (201) 773-3900; Production site: Lodi, NJ 97844

[SRI. 1995 Directory of Chemical Producers-United States of America. Menlo Park, CA: SRI International, 1995, p. 741] **PEER REVIEWED**

Dominion Veterinary Laboratories Ltd., 1199 Sanford St., Winnipeg, Manitoba, Canada, R3# 3A1, (204) 589-7361 /Triple Sulfa Bolus formulator/

[North American Compendiums. Drugs.com Veterinary edition. Triple Sulfa Bolus (Canada). Available from, as of Apr 15, 2008: <http://www.drugs.com/vet/triple-sulfa-bolus-can.html> **PEER REVIEWED**

Dominion Veterinary Laboratories Ltd., 1199 Sanford St., Winnipeg, Manitoba, Canada, R3# 3A1, (204) 589-7361 /Powder 21 formulator/

[North American Compendiums. Drugs.com Veterinary edition. Powder 21 (Canada). Available from, as of Apr 15, 2008: <http://www.drugs.com/vet/powder-21-can.html> **PEER REVIEWED**

United States Pharmacopeial Convention, Inc., 12601 Twinbrook Pkwy, Rockville, MD 20852, (301) 881-0666 /Formulator/

[USP; Material Safety Data Sheet. Sulfathiazole. May 16, 2002. Available from, as of Apr 15, 2008: <http://www.usp.org/pdf/EN/referenceStandards/msds/1636504.pdf> **PEER REVIEWED**

Vetoquinol Canada, Inc., 200, Chemin Georges, Lavaltrie, Quebec, J5T 3S5, Canada, (450) 586-2252 /Sulfa-MT formulator/

[North American Compendiums. Drugs.com Veterinary edition. Sulfa-MT (Canada). Available from, as of Apr 15, 2008: <http://www.drugs.com/vet/sulfa-mt-can.html> **PEER REVIEWED**

Vetoquinol Canada, Inc., 200, Chemin Georges, Lavaltrie, Quebec, J5T 3S5, Canada, (450) 586-2252 /S-M-T formulator/

[North American Compendiums. Drugs.com Veterinary edition. S-M-T (Canada). Available from, as of Apr 15, 2008: <http://www.drugs.com/vet/s-m-t-can.html> **PEER REVIEWED**

Methods of Manufacturing:

SULFATHIAZOLE MAY BE SYNTHESIZED...BY CONDENSING HALOGENOKETONES, ALDEHYDES, OR ESTERS WITH N(4)-ACETYLSULFANILYLTHIOUREAS.

[The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 1158] **PEER REVIEWED**

General Manufacturing Information:

SHIGELLA & E COLI ISOLATED SIMULTANEOUSLY FROM DYSENTERY PATIENT SHOWED HIGH RESISTANCE TO SULFATHIAZOLE.

[MANAKHILOVA V ET AL; EPIDEMIOL MIKROBIOL INFEKTS BOLES 12 (3): 209 (1975)] **PEER REVIEWED**

FORMS A SOLUBLE SODIUM SALT /MONOSODIUM 2-SULFANILAMIDOTHIAZOLE; SOLUBLE SULFATHIAZOLE/.

[The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 1158] **PEER REVIEWED**

...among the most widely used antibacterial agents in veterinary medicine, chiefly because of low cost and relative efficacy in some common bacterial diseases /Sulfonamides/

[Aiello, S.E. (ed.). The Merck Veterinary Manual. 8th ed. Merck & Co., Inc., National Publishing Inc., Philadelphia, PA. 1998., p. 1765] **PEER REVIEWED**

Formulations/Preparations:

Formosulfathiazole, formaldehyde-sulfathiazole, Forbina, formo-Cibazol, Socatil. Contains approx 11% formaldehyde. /Polymer with formaldehyde/

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 1529] **PEER REVIEWED**

Soluble sulfathiazole /Sodium salt sesquihydrate/

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 1529] **PEER REVIEWED**

U. S. Production:

Production volumes for non-confidential chemicals reported under the Inventory Update Rule.

Year	Production Range (pounds)
1986	10 thousand - 500 thousand
1990	No Reports

1994	No Reports
1998	No Reports
2002	No Reports

[US EPA; Non-confidential Production Volume Information Submitted by Companies for Chemicals Under the 1986-2002 Inventory Update Rule (IUR). Benzenesulfonamide, 4-amino-N-2-thiazolyl- (72-14-0). Available from, as of March 6, 2008:
<http://www.epa.gov/oppt/iur/tools/data/2002-vol.html> **PEER REVIEWED**

Laboratory Methods:

Clinical Laboratory Methods:

HPLC METHOD FOR THE SEPARATION & QUANTITATIVE DETERMINATION OF SULFATHIAZOLE IN PURE SOLN AS WELL AS IN CATTLE URINE.

[SHARMA JP ET AL; J PHARM SCI 65 (NOV): 1606 (1976)] **PEER REVIEWED** [PubMed Abstract](#)

A SIMPLE HIGH-PRESSURE LIQ CHROMATOGRAPHY FOR THE DETECTION OF SULFATHIAZOLE IN PLASMA & URINE.

[SIOUFI A ET AL; J CHROMATOGR 221 (2): 419 (1980)] **PEER REVIEWED** [PubMed Abstract](#)

GAS-LIQUID CHROMATOGRAPHY AND SPECTROPHOTOMETRY WERE USED FOR THE DETERMINATION OF FIVE SULFONAMIDES. SULFATHIAZOLE WAS RECOVERED FROM LIVER, KIDNEY & MUSCLE AT LEVEL OF 0.1 PPM.

[GOODSPEED DP ET AL; J ASSOC OFF ANAL CHEM 61 (5): 1050 (1978)] **PEER REVIEWED** [PubMed Abstract](#)

Analyte: sulfathiazole; matrix: milk; procedure: capillary zone electrophoresis with ultraviolet detection at 214 and 254 nm

[Lin CE et al; J Chromatogr A 755: 261-269 (1996). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: milk; procedure: capillary zone electrophoresis with ultraviolet detection at 254 nm and atmospheric pressure ionization mass spectrometry

[Johansson IM et al; J Chromatogr 559: 515-528 (1991). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: milk; procedure: high-performance liquid chromatography with ultraviolet detection at 270 nm; limit of detection: 62.5 ng/mL

[Long AR et al; J Chromatogr 502: 87-94 (1990). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: milk; procedure: high-performance liquid chromatography with ultraviolet detection at 265 nm; limit of detection: 1.0 ppb

[Smedley MD, Weber JD; J Assoc Off Anal Chem 73: 875-879 (1990). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: milk; procedure: high-performance liquid chromatography with ultraviolet detection at 254 nm and thermospray mass spectrometry; limit of detection: 2 ng (HPLC-UV); 5-20 ng (TMS)

[Abian J et al; J Chromatogr 629: 267-276 (1993). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: milk, urine; procedure: high-performance liquid chromatography with ultraviolet detection at 254 nm

[Yang S, Khaledi MG; J Chromatogr A 692: 311-318 (1995). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: tissue; procedure: capillary zone electrophoresis with ultraviolet detection at 254 nm

[Ackermans MT et al; J Chromatogr 596: 101-109 (1992). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: tissue (kidney, muscle); procedure: high-performance liquid chromatography with ultraviolet detection at 270 nm and fluorescence detection [395 nm (excitation) and 495 nm (emission)] following post-column reaction; limit of detection: 0.5-5 ppb

[Pacciarelli B et al; Mitt geb Lebensmittelunters Hyg 82: 45-55 (1991). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: tissue (kidney, liver, muscle); procedure: high-performance liquid chromatography with ultraviolet detection at 550 nm following post-column reaction; limit of detection: 2 ppb

[Guggisberg D et al; Mitt geb Lebensmittelunters Hyg 84: 263-273 (1993). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: tissue (liver, muscle); procedure: high-performance liquid chromatography with ultraviolet detection at 265 nm and thermospray mass spectrometry

[Boison JO, Keng LJY; J AOAC Int 78: 651-658 (1995). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: tissue; procedure: high-performance liquid chromatography with fluorescence detection at 400 nm (excitation) and 495 nm (emission) following post-column reaction; limit of detection: 1 ng/g

[Gehring TA et al; J AOAC Int 80: 751-755 (1997). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: blood (serum), milk; procedure: high-performance liquid chromatography with fluorescence detection at 390 nm (excitation) and 475 nm (emission); limit of detection: 0.1 ng/mL

[Tsai CE, Kondo F; J AOAC Int 78: 674-678 (1995). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: blood (whole), urine; procedure: high-performance liquid chromatography with photodiode-array ultraviolet detection at 200.5 nm

[Gaillard Y, Pepin G; J Chromatogr A 763: 149-163 (1997). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: urine; procedure: high-performance liquid chromatography with ultraviolet detection at 490 nm; limit of detection: 200 ng/mL

[Simo-Alfonso EF et al; J Chromatogr B 670: 183-187 (1995). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analytic Laboratory Methods:

THIN-LAYER CHROMATOGRAPHY WAS USED FOR THE SEPARATION OF A SERIES OF SULFONAMIDES.

[BIAGI GL ET AL; J CHROMATOGR 106 (2): 349 (1975)] **PEER REVIEWED** [PubMed Abstract](#)

SULFATHIAZOLE WAS CONVERTED TO THE DIAZONIUM SALT, COUPLED WITH 8-HYDROXYQUINOLINE-5-SULFONIC ACID, & ASSAYED SPECTROPHOTOMETRICALLY @ 530 NM.

[BALICA G ET AL; REV CHIM (BUCHAREST) 26 (5): 424 (1975)] **PEER REVIEWED**

GAS-LIQUID CHROMATOGRAPHIC DETERMINATION OF SULFATHIAZOLE, SULFAMERAZINE, SULFAMETHAZINE, & SULFAQUINOXALINE IN FINISHED FEEDS AT LEVELS FROM 0.002-0.05%.

[DAUN RJ; J ASSOC ANAL CHEM 54 (6): 1277-1282 (1971)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: chemical identification; procedure: infrared absorption spectrophotometry with comparison to standards

[U.S. Pharmacopeia. The United States Pharmacopeia, USP 31/The National Formulary, NF 26; Rockville, MD: U.S. Pharmacopeial Convention, Inc., p.3305 (2008)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: chemical identification; procedure: dissolution in hydrochloric acid; addition of sodium nitrite solution and water; addition of 2-naphthol in sodium hydroxide solution; formation of an orange-red precipitate that darkens on standing

[U.S. Pharmacopeia. The United States Pharmacopeia, USP 31/The National Formulary, NF 26; Rockville, MD: U.S. Pharmacopeial Convention, Inc., p.3305 (2008)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: chemical purity; procedure: dissolution in hydrochloric acid and water; potentiometric titration with sodium nitrite using a suitable electrode system

[U.S. Pharmacopeia. The United States Pharmacopeia, USP 31/The National Formulary, NF 26; Rockville, MD: U.S. Pharmacopeial Convention, Inc., p.3305 (2008)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: chemical identification; procedure: infrared absorption spectrophotometry with comparison to standards

[Council of Europe, European Directorate for the Quality of Medicines. European Pharmacopoeia, 5th Ed., Volume 2; Strasbourg, France, p.2516 (2004)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: chemical identification; procedure: thin-layer chromatography with comparison to standards

[Council of Europe, European Directorate for the Quality of Medicines. European Pharmacopoeia, 5th Ed., Volume 2; Strasbourg, France, p.2516 (2004)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: chemical identification; procedure: dissolution in water and sodium hydroxide; reaction with copper sulfate; formation of a grayish-blue or purple precipitate

[Council of Europe, European Directorate for the Quality of Medicines. European Pharmacopoeia, 5th Ed., Volume 2; Strasbourg, France, p.2516 (2004)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: chemical identification; procedure: dissolution in hydrochloric acid; dilution with water; production of an intense orange or red color usually with same color precipitate

[Council of Europe, European Directorate for the Quality of Medicines. European Pharmacopoeia, 5th Ed., Volume 2; Strasbourg, France, p.2516 (2004)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: chemical purity; procedure: dissolution in hydrochloric acid; titration with sodium nitrite, determining the endpoint electrochemically

[Council of Europe, European Directorate for the Quality of Medicines. European Pharmacopoeia, 5th Ed., Volume 2; Strasbourg, France, p.2516 (2004)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: capillary zone electrophoresis with ultraviolet detection at 254 and 280 nm and micellar electrokinetic chromatography

[Wright PB, Dorsey JG; Anal Chem 68: 415-424 (1996). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: capillary electrophoresis with ultraviolet detection at 205 nm

[Hows MEP et al; J Chromatogr A 768: 97-104 (1997). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: capillary electrophoresis with ultraviolet detection at 214 nm

[Lin CE et al; J Chromatogr A 792: 37-47 (1997). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: capillary zone electrophoresis with ultraviolet detection at 254 nm

[Lin CE et al; J Chromatogr A 759: 203-209 (1997). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: capillary zone electrophoresis with ultraviolet detection at 254 nm

[Lin CE et al; J Chromatogr A 768: 105-112 (1997). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation (capsule, suspension, tablet); procedure: high-performance liquid chromatography with ultraviolet detection at 490 nm; limit of detection: 200 ng/mL

[Garcia-Alvarez-Coque MC et al; J Pharm Biomed Anal 13: 237-245 (1995). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: reversed-phase high-performance liquid chromatography with ultraviolet detection at 254 nm

[Roos RW, Lau-Cam CA; J Chromatogr 370: 403-418 (1986). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: reversed-phase and ion-exchange high-performance liquid chromatography with ultraviolet detection at 254 nm

[Slingsby RW, Rey M; J Liq Chromatogr 13: 107-134 (1990). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: high-performance liquid chromatography with ultraviolet diode array detection at 270 nm and ion-spray tandem mass spectrometry

[Pleasant S et al; J Chromatogr 558: 155-173 (1991). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: high-performance liquid chromatography with ultraviolet detection at 254 nm

[Capparella M et al; J Chromatogr A 691: 141-150 (1995). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: high-performance liquid chromatography with ultraviolet detection at 270 nm

[Ricci MC, Cross RF; J Liq Chromatogr Rel Technol 19: 365-381 (1996). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: pharmaceutical preparation; procedure: high-performance liquid chromatography with ultraviolet detection at 270 nm

[Ricci MC, Cross RF; J Liq Chromatogr Rel Technol 19: 547-564 (1996). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: wastewater; procedure: high-performance liquid chromatography with ultraviolet detection at 260 nm

[Jen JF et al; J Chromatogr A 793: 378-382 (1998). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: food (egg, honey), milk; procedure: high-performance liquid chromatography with ultraviolet detection at 260 nm; limit of detection: 70 ng/mL

[Vinas P et al; Chromatographia 40: 382-386 (1995). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: food (egg), milk, tissue; procedure: high-performance liquid chromatography with ultraviolet detection at 450 nm following post-column reaction; limit of detection: 5-10 ng/g

[Aerts MML et al; J Chromatogr 435: 97-112 (1988). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: feed; procedure: reversed-phase high-performance liquid chromatography with ultraviolet detection at 450 nm following post-column reaction

[Smallidge RL et al; J Assoc Off Anal Chem 71: 710-717 (1988). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Analyte: sulfathiazole; matrix: feed, premix; procedure: high-performance liquid chromatography with ultraviolet detection at 450 nm following post-column reaction; limit of quantitation: 1.65 ug/mL

[Stringham RW et al; J Assoc Off Anal Chem 65: 823-827 (1982). As cited in: Lunn G; HPLC and CE Methods for Pharmaceutical Analysis. CD-ROM. New York, NY: John Wiley & Sons (2000)] **PEER REVIEWED**

Special References:

Special Reports:

Anwar J et al; J Pharm Sci 78: 337-342 Apr 1989. Polymorphism of sulfathiazole.

Burger A and RD Dialer; Pharm Acta Helv 58: 72-78 Mar 1983. New investigational results of sulfathiazole polymorphism.

Alpar HD and JA Hersey; Farmaco Ed Prat 34: 532-541 Dec 1979. Effect of suspending agents on the bioavailability of suspensions of sulfathiazole.

Synonyms and Identifiers:

Synonyms:

2-(P-AMINOBENZENESULFONAMIDO)THIAZOLE

PEER REVIEWED

2-(P-AMINOBENZENESULPHONAMIDO)THIAZOLE

PEER REVIEWED

4-AMINO-N-2-THIAZOLYLBENZENESULFONAMIDE

PEER REVIEWED

AZOQUIMIOL

PEER REVIEWED

AZOSEPTALE

PEER REVIEWED

BENZENESULFONAMIDE, 4-AMINO-N-2-THIAZOLYL-

PEER REVIEWED

CERAZOL (SUSPENSION)

PEER REVIEWED

CHEMOSEPT

PEER REVIEWED

CIBA 3714

PEER REVIEWED

CIBAZOL

PEER REVIEWED

DUATOK

PEER REVIEWED

DULANA

PEER REVIEWED

ELEUDRON

PEER REVIEWED

ESTAFILOL

PEER REVIEWED

FORMOSULFATHIAZOLE

PEER REVIEWED

M+B 760

PEER REVIEWED

M&B 760

PEER REVIEWED

NEOSTREPSAN

PEER REVIEWED

NORSULFASOL

PEER REVIEWED

NORSULFAZOL

PEER REVIEWED

NORSULFAZOLE

PEER REVIEWED

PLANOMIDE

PEER REVIEWED

POLISEPTIL

PEER REVIEWED

RP 2090

PEER REVIEWED

SANOTIAZOL

PEER REVIEWED

STREPTOSILTHIAZOLE

PEER REVIEWED

SULFAMUL

PEER REVIEWED

SULFANILAMIDE, N(SUP 1)-2-THIAZOLYL-

PEER REVIEWED

SULFANILAMIDE, N(1)-2-THIAZOLYL-

PEER REVIEWED

SULFANILAMIDOTHIAZOLE

PEER REVIEWED

2-SULFANILAMIDOTHIAZOLE

PEER REVIEWED

2-(SULFANILYLAMINO)THIAZOLE

PEER REVIEWED

SULFATHIAZOL

PEER REVIEWED

SULFOCEROL

PEER REVIEWED

SULPHATHIAZOLE

PEER REVIEWED

SULZOL

PEER REVIEWED

N(SUP 1)-2-THIAZOLYLSULFANILAMIDE

PEER REVIEWED

THIACOCINE

PEER REVIEWED

THIASULFOL

PEER REVIEWED

THIAZAMIDE

PEER REVIEWED

N(1)-2-THIAZOLYLSULFANILAMIDE

PEER REVIEWED

THIOZAMIDE

PEER REVIEWED

USAF SN-9

PEER REVIEWED

WINTRAZOLE

PEER REVIEWED

Associated Chemicals:

Sulfathiazole, sodium salt;144-74-1

Formulations/Preparations:

Formosulfathiazole, formaldehyde-sulfathiazole, Forbina, formo-Cibazol, Socatil. Contains approx 11% formaldehyde. /Polymer with formaldehyde/

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 1529] **PEER REVIEWED**

Soluble sulfathiazole /Sodium salt sesquihydrate/

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 1529] **PEER REVIEWED**

Administrative Information:**Hazardous Substances Databank Number:** 4380**Last Revision Date:** 20090105

Last Review Date: Reviewed by SRP on 9/18/2008

Update History:

Complete Update on 2009-01-05, 48 fields added/edited/deleted
Field Update on 2003-06-10, 0 fields added/edited/deleted
Complete Update on 02/14/2003, 1 field added/edited/deleted.
Complete Update on 11/08/2002, 1 field added/edited/deleted.
Complete Update on 01/14/2002, 1 field added/edited/deleted.
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Complete Update on 02/02/2000, 1 field added/edited/deleted.
Complete Update on 09/21/1999, 1 field added/edited/deleted.
Complete Update on 08/27/1999, 1 field added/edited/deleted.
Complete Update on 05/12/1999, 1 field added/edited/deleted.
Complete Update on 03/19/1999, 1 field added/edited/deleted.
Complete Update on 10/15/1998, 33 fields added/edited/deleted.
Field Update on 06/02/1998, 1 field added/edited/deleted.
Complete Update on 03/17/1997, 2 fields added/edited/deleted.
Complete Update on 01/28/1996, 1 field added/edited/deleted.
Complete Update on 01/03/1995, 1 field added/edited/deleted.
Complete Update on 11/01/1993, 1 field added/edited/deleted.
Complete Update on 01/20/1993, 1 field added/edited/deleted.
Field update on 01/02/1993, 1 field added/edited/deleted.
Complete Update on 10/10/1990, 1 field added/edited/deleted.
Complete Update on 04/16/1990, 1 field added/edited/deleted.
Field update on 12/29/1989, 1 field added/edited/deleted.
Complete Update on 04/22/1988, 1 field added/edited/deleted.
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