

PHARMACEUTICAL WASTE MANAGEMENT: A CHALLENGE TO MAKE ENVIRONMENT ECOFRIENDLY

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ABSTRACT

The pharmaceutical industry has made progress over the past several years to minimizing use of reagents that are hazardous to the environment and by designing alternate synthesis pathways. It is anticipated that they will extend these principles to product design, through such measures as increasing therapeutic efficacy by enhancing delivery to the target site, thus minimizing dosage required. The industry should be encouraged to investigate expiration dates to establish a maximum shelf life for a drug product, to minimize wastage.

Pharmaceutical pollution, all sectors involved in health care pharmaceutical developers and manufacturers, hospitals, individual physicians and all those involved in the health care system, law enforcement agencies, pharmacies, waste management agencies, consumers, environmental protection organizations, and governmental agency to participate in preventing pharmaceutical pollution. This powerful approach provides a comprehensive solution to an issue that has the potential to affect much of life on earth to make the environment eco friendly.

KEYWORDS: pollution, pharmaceutical industry, health care

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INTRODUCTION

Pharmacy plays an integral part of health care systems to make the environment healthy and pollution free. It is necessary to manage the hazardous waste comes out from health care industries. Pharmaceutical waste is potentially generated through a wide variety of activities in a health care facility, including but not limited to intravenous (IV) preparation, general compounding, spills/breakage, partially used vials, syringes, and IVs, discontinued, unused preparations, unused unit dose repacks, patients' personal medications and outdated pharmaceuticals. Waste may also be generated in other areas such as patient's rooms, operating rooms, nursing stations and emergency rooms. Pharmacies may generate wastes via compounding or preparation, outdated pharmaceuticals, damaged packages, or consumer returns.

Health care industries can generate hazardous waste from many sources, including disposal of pharmaceuticals. Pharmaceutical waste may also include expired Drugs, Patients' Personal Medications, Waste Materials Containing Excess, drugs (syringes, IV bags, tubing, vials, etc.), Open Drugs that cannot be used and Containers that held drugs, Drugs that are intended to be discarded, contaminated garments, absorbents and spill cleanup material, except for materials with only trace contamination.

Characteristic Hazardous Waste

A characteristic hazardous waste is defined as a waste that has been identified to exhibit one or more of the following attributes (D-list wastes):

1. Ignitable:

A. Flash point is less than 140 degrees Fahrenheit. (Example: solutions containing more than 24% alcohol).

B. An oxidizer defined by DOT.

C. An ignitable compressed gas as defined by the U.S. Department of Transportation. (Example: some aerosol propellants).

2. Corrosive:

A. The pH is less than or equal to 2.0 or greater than or equal to 12.5.

B. It is a liquid and corrodes steel at a rate greater than six and thirty-five-hundredths millimeters per year.

(Example: compounding chemicals, including strong acids, such as glacial acetic acid, and strong bases, such as sodium hydroxide).

3. Reactive:

A. Reacts violently with water

B. It is normally unstable and readily undergoes violent change without detonating.

C. It forms potentially explosive mixtures with water.

D. When mixed with water, it generates toxic gases, vapors or fumes in a quantity sufficient to present a danger to human health.

4. Toxic: Fails the Toxicity Characteristic Leaching Procedure (TCLP). (Example: contains arsenic, barium, cadmium, chloroform, chromium, lindane, m-cresol, mercury, selenium or silver at a concentration equal to or greater than the regulatory level).

Listed Hazardous Waste

A listed hazardous waste is defined as a waste that appears on one of four lists of known hazardous wastes (F, P, K or U lists). Most pharmaceutical wastes will be listed under the P- and U-lists.

Hazardous waste, if managed improperly, may harm human health and the environment. According to Crane et al., 2006 the widespread detection of waste pharmaceuticals in environmental samples the risks associated with their introduction into wildlife habitats is becoming an important issue for both regulators and the pharmaceutical industry. Although a wide range of different classes of pharmaceuticals are used in human and veterinary medicine, only a few are considered of environmental importance, because of their consumption volumes, toxicity, and persistence in the environment. These are beta-blockers, cyostatics and cancer therapies, analgesics and anti inflammatory, steroid hormones, neuroactive compounds, antiparasitic drugs, blood lipid lowering agents, and antibiotics (Fent et al., 2006). Many pharmaceuticals may pose a risk to aquatic wildlife health a review on the research work done in past was

entitled in table no.1. However, analysis of occurrence and toxicity of all waste pharmaceuticals is impractical (Kostich and Lazorchak, 2008).

SOME OTHER PHARMACEUTICAL WASTE

Pharmaceutical drugs include all the medicines used for the diagnosis, treatment, and prevention of disease; illicit or recreational drugs; veterinarian medicines (including those for agricultural livestock); over-the-counter medications; and nutritional supplements or nutraceuticals. Personal care products (PCPs,) include fragrances, lotions and creams, cosmetics, sunscreen, and other consumer chemicals (including “inert” ingredients). The use of PPCPs continues to grow worldwide on par with many agrochemicals. Unlike agrochemicals, which are disposed of or discharged into the environment on a continual basis via domestic/industrial sewage and wet-weather runoff, PPCPs are in part subjected to the metabolism of the user; then, excreted metabolites plus some unaltered parent compounds are released. These pharmaceuticals and personal care products (PPCPs) enter our environment and act as a trigger on organisms regularly exposed to them (ecotoxicology).

There are three main human activities that cause changes in ecosystems:

Habitat fragmentation, alteration of community structure, and chemical pollution. (**Table 1**)

Various Regulatory Bodies that Oversee Pharmaceutical Waste Management

- Environmental Protection Agency (EPA)
- Department of Transportation (DOT)
- Drug Enforcement Administration (DEA)
- Occupational Safety and Health Administration (OSHA)
- State Environmental Agencies,
- State Pharmacy Boards, and
- Local Publicly Owned Treatment Works (POTW)

Wastes that are not listed and do not exhibit a characteristic are considered solid waste. Solid wastes should be discarded according to state and/or local regulations including regulated medical waste requirements. There are situations where a solid waste should be handled as a hazardous waste applying best management practices.

Role of Pharmacist

Pharmacists, as a part of the health care systems and contribute to increased health and wealth. That health system is more than health care and includes disease prevention, health promotion and efforts to influence other health professionals to address health concerns.

That pharmacists' unique role in primary and secondary care must be dedicated to improving people's health and wealth.

Pharmacist can help to ensure that unused medications are returned to the pharmacy and dispose them appropriately through hazardous waste companies. By educating patients on proper disposal, pharmacists contribute significantly to preventing medications from entering the water supply. By discouraging inappropriate use and overuse of prescription, nonprescription and alternative medications, pharmacists can help decrease the amount of medication that is purchased and eventually discarded, or unnecessarily ingested and excreted into our environment. With new prescription, it makes sense to limit initial prescription size and determine patient tolerability, thereby minimizing drug wastage.

PROMOTE ENVIRONMENT FRIENDLY PRODUCTS

The pharmaceutical industry has made progress over the past several years in practicing “green chemistry”, for example, by minimizing use of reagents that are hazardous to the environment and by designing alternate synthesis pathways. It is anticipated that they will extend these principles to product design, through such measures as increasing therapeutic efficacy by enhancing delivery to the target site, thus minimizing dosage required. The industry should be encouraged to investigate expiration dates to establish a maximum shelf life for a drug product, to minimize wastage.

REFERENCES

1. www.pharmainfo.net (Assessed on 18th march 2009).
2. <http://www.hcp.com/news/newsdetails.php/id/81151>(Assessed on 19th march 2009).
3. http://www.teleosis.org/pdf/symbiosis/Preventing_Pollution_Sustainable_Medicine.pdf (Assessed on 20th march 2009)
4. Neil J Morley. A Review Environmental risk and toxicology of human and veterinary waste pharmaceutical exposure to wild aquatic host–parasite relationships: *Environmental Toxicology and Pharmacology*. 2009;27: 161–175.
5. <http://www.ndhealth.gov/wm/Publications/NorthDakotaPharmaceuticalWasteGuidance.pdf> (Assessed on 18th march 2009)
6. El-Aggan HA, El-Gebaly WM, Khedr MM, Gastro-vascular and microvascular changes in chronic murine Schistosomiasis mansoni response to propranolol. *J. Egypt : Soc. Parasitol* 1992;22: 415–423.
7. Davila DF, Angel F, Arata de Bellabarba, G Donis JH, Effects of metoprolol in chagasic patients with severe heart failure: *Int. J. Cardiol*. 2002;83: 55–260.
8. Glazier AP, Kokwaro GO, Ismail S, Edwards G, Effect of experimental malaria infection on the metabolism of phenacetin in the rat isolated perfused liver. *Xenobiotic* 1994; 785–793.
9. Young LE, Young RE, Bundy DAP, Photoreceptor evoked potentials and phototactic behaviour in *Cercaria caribbea* LXXI *Cable*. 1987; 88: 619–624.
10. Warbrick EV, Ward SA, The effect of catecholamines and catecholamine antagonists on the third larval moult of *Dirofilaria immitis* in vitro. *J. Helminthol*. 1992;66: 273–278.
11. Ohnishi ST, Sadanaga KK, Katsuoka M, Weidanz WP, Effects of membrane acting- drugs on *Plasmodium* species and sickle cell erythrocytes. *Mol. Cell. Biochem*. 1989;91: 159–165.
12. Coppi A, Merali S, Eichinger D, The enteric parasite *Entamoeba* uses an autocrine catecholamine system during differentiation into the infectious cysts stage. *J. Biol. Chem*. 2002; 277: 8083–8090.
13. Huggett DB, Brooks BW, Peterson B, Foran CM, Schlenk D, Toxicity of select Beta Adrenergic receptor-blocking pharmaceuticals (B-blockers) on aquatic organisms. *Arch. Environ. Contam. Toxicol*. 2002; 43: 229–235.
14. Kuris AM, Trophic interactions—similarity of parasitic castrators to parasitoids. *Rev. Biol* 1974;49:129 148.
15. Hurd H, Physiological and behavioural interactions between parasites and invertebrate hosts. *Adv. Parasitol*. 1990;29: 271–318.
16. Williams H, Jones A, *Parasitic Worms of Fish*. Taylor and Francis; London. 1994; 593.
17. Jones-Brando L, Torrey EF, Yolkem R, Drugs used in the treatment of schizophrenia and bipolar disorder inhibit the replication of *Toxoplasma gondii*. *Schizophr. Res.*; 2003: 62: 237–244.
18. Ritterson AL, Effect of immunosuppressive drugs (6-mercaptopurine and methotrexate) on resistance of Chinese hamsters to the tissue phase of *Trichinella spiralis*. 1968;118: 365–369.
19. Mitchell GF, Goding JW, Rickard MD, Studies on immune responses to larval cestodes in Mice; Increased susceptibility of certain mouse strains and hypothymic mice to *Taenia taeniaeformis* and analysis of passive transfer of resistance with serum. 1977; 55: 165–186.
20. Herman R, Shiroishi T, *Plasmodium gallinaceum*: selective immunosuppression by cyclophosphamide in preerythrocytic malaria. 1973;34: 295–305.
21. Sheehy TW, Dempsey H, Methotrexate therapy for *Plasmodium vivax* malaria. *JAMA*; 1970;214: 109–114.
22. Miguel DC, Yokoyama-Yasunaka JKU, Andreoli WK, Mortara RA, Uliana SRB, Tamoxifen is effective against *Leishmania* and induces a rapid alkalinization of parasitophorous vacuoles harbouring *Leishmania (Leishmania) amazonensis* amastigotes. *J. Antimicrob. Chemother*. 2007;60: 526–534.
23. Makled MKI, Abbas MMS, El-Seoud SFA, Ismail AK, Effect of immunosuppression of the virulence of *Giardia lamblia* cysts. *J. Egypt. Soc. Parasitol*. 1994;24: 205–210.
24. Harris C, Salgo MP, Tanowitz HB, Wittner M, In vitro assessment of antimicrobial agents against *Toxoplasma gondii*. *J. Infect. Dis*. 1988;157: 14–22.

25. Ellenberger TE, Wright JE, Rosowsky A, Beverley SM, Wild-type and drugresistant *Leishmania* major hydrolyze methotrexate to N-10-methyl-4-deoxy-4-aminopteroate without accumulation of methotrexate polyglutamates. *J. Biol. Chem.* 1989;264: 15960–15966.
26. Scott DA, Coombs GH, Sanderson BE, Effects of methotrexate and other antifolates on The growth and dihydrofolate reductase activity of *Leishmania* promastigotes. *Biochem. Pharmacol.* 1987;36: 2043–2045.
27. Menard DB, Gisselbrecht C, Marty M, Reyes F, Dhumeaux D, Antineoplastic agents and the liver. *Gastroenterology*; 1980;78: 142–164.
28. Martin S, The adverse health effects of occupational exposure to hazardous drugs. *Community Oncol.* 2005; 2: 397–400.
29. Quan N, Mhlanga JDM, Whiteside MB, Kristensson K, Herkenham M, Chronic sodium salicylate treatment exacerbates brain neurodegeneration in rats infected with *Trypanosoma brucei*. *Neuroscience* 2000; 96:181–194.
30. Farag MM, Salama MA, Abou-Basha L, Experimental murine schistosomiasis: reduced hepatic morbidity after pre- and/or post-infection treatment with ibuprofen or diclofenac sodium. *Ann. Trop. Med. Parasitol*; 1995;89: 497–504.
31. Mahmoud MR, Zoheiry MMK, Nosseir MMF, Effect of combined chemotherapy and anti-inflammatory drugs on murine schistosomiasis. *Arzneimittel Forschung/Drug Res* 2002;52: 294–301.
32. Srivastava DK, Shukla OP, Encystment of *Acanthamoeba culbertsoni* by organic effectors. *Indian J. Exp. Biol.* 1983;21: 444–447.
33. Whaun JM, The effects of aspirin-containing serum in the continuous culture of *Plasmodium falciparum*. *J. Protozool.* 1984;31: 381–384.
34. Douch PGC, Blair SSB, Themetabolism of foreigncompounds in the cestode, *Moniezia expansa*, and the nematode, *Ascaris lumbricoides* var *suum*. *Xenobiotica*; 1975;5: 279–292.
35. Jobling S, Tyler CR, Endocrine disruption, parasites and pollutants in freshwater fish. *Parasitology*; 2003;126: S103–S108.
36. Wang R, Belosevic M, Estradiol increases susceptibility of goldfish to *Trypanosoma danilewskyi*. *Dev. Comp. Immunol.* 1994;18: 377–387.
37. Harris C, Salgo MP, Tanowitz HB, Wittner M, In vitro assessment of antimicrobial agents against *Toxoplasma gondii*. *J. Infect. Dis.* 1988; 157: 14–22.

Table 1: List of some Research envisaged on Pharmaceutical waste drugs categories

Category	Researches	Work Entitled
Beta blockers	El-Aggan et al., 1992; El-Tourabi et al., 1994).	At therapeutic concentrations beta blockers are known to have a number of effects on parasitic infections in mammals. Propranolol can reduce mortality caused by secondary portal hypertension and gastro-vascular pathology induced by the trematode <i>Schistosoma mansoni</i> .
	Davila et al., 2002	Whilst metoprolol improves the clinical status and left ventricular function of individuals with severe congestive heart failure caused by an infection of the protozoan <i>Trypanosoma cruzi</i> .
	Glazier et al., 1994	In contrast infections of rodents with malaria, <i>Plasmodium berghei</i> , were found not to interfere with cytochrome P450-mediated drug metabolism of metoprolol.
	Young et al., 1987, 1988	Beta blockers may also effect parasite functional biology. The free living aquatic stages (cercariae) of trematodes have been found to be susceptible to aqueous exposure to propranolol with swimming behaviour, survival, and phototaxis being negatively affected.
	Ohnishi et al., 1989, Coppi et al., 2002, Huggett et al., 2002; Cleuvers, 2005	Propranolol may also significantly reduce the number of <i>Dirofilaria immitis</i> nematode larvae capable of completing 3rd-stage moul in vitro inhibit the growth of the malaria parasite <i>Plasmodium falciparum</i>
	Kuris, 1974; Hurd, 1990;	whilst encystment of the protozoan <i>Entamoeba</i>

	Williams and Jones, 1994; Morley, 2006	<p>invadens was inhibited in the presence of metoprolol.</p> <p>Studies on beta blocker toxicity to aquatic invertebrates and fish would appear to indicate a limited toxic effect to invertebrates, although there appeared to be a significant risk to fish reproduction.</p> <p>In parasitized animals this risk may be further elevated due to the pathological effects caused by parasites which alone may effect host reproductive potential</p>
Chemotherapeutic Agents	Ritterson, 1968; Mitchell et al., 1977; Wells et al., 1977; Boroskova et al., 2001, Horna et al., 1997 Herman and Shiroishi, 1973; Herman and Shiroishi, 1973; Joyner and Norton, 1974; Johnson et al., 1974; Johnson et al., 1974; Raote et al., 1991, 1992.	<p>Methotrexate and cyclophosphamide are both potent immunosuppressants and have been extensively reported to cause an increase in disease prevalence and intensity in host-parasite systems often leading to a longer retention of infection in exposed hosts.</p> <p>A similar increase in parasite abundance can also occur in birds. which resulted in a number of effects on the avian host including suppressed weight gain and changes to cholesterol, globulin, albumin, and plasma protein levels compared to birds not immunosuppressed by drug exposure.</p>
	Sheehy and Dempsey, 1970; Mukherjee et al., 2004; Miguel et al., 2007.	<p>Direct effects on parasite functional biology have also been recorded for this class of drugs. Doxorubicin, tamoxifen, and methotrexate have all been reported as effective parasiticide agents against many protozoan species</p> <p>In contrast cyclophosphamide appears to have little effect</p>
	Herman and Shiroishi, 1973; Makled et al., 1994. Harris et al., 1988), Babesia bovis (Nott and Bagnara, 1993), (Sanchez et al., 1994), (Ellenberger et al., 1989), Scott et al. 1987.	<p>Whilst methotrexate has also been shown to have no or little effect on certain protozoans including Toxoplasma gondii and Leishmania tropica, possibly because they have different mechanisms of drug metabolism.</p> <p>Indeed, susceptibility may not be the same across related species as found that promastigote growth of the protozoan Leishmania major was inhibited by methotrexate but the related species Leishmania mexicana mexicana and Leishmania donovani were insensitive, possibly due to poor drug transport</p>
	Menard et al., 1980; Martin 2005; Williams and Jones, 1994; Morley, 2006; Morley et al., 2006; Mayer and Fried, 2007	<p>methotrexate have been reported to induce greater liver cirrhosis and fibrosis with frequent small doses than intermittent large doses.</p> <p>These compounds, who are exposed to low concentrations over long periods of time, indicate there is an increase in liver damage, a decline in female reproductive health including infertility, spontaneous abortions, foetal and menstrual-cycle abnormalities, and an increased occurrence of cancers, particularly leukemia.</p> <p>If these kinds of low concentration symptoms were replicated in the aquatic environment there could be serious repercussions, as parasites are known to significantly effect host reproductive efficiency, liver function, and the progress of cancers.</p>
Analgesics and antiinflammatory drugs	Quan et al., 2000; Schaub et al., 1983	Analgesics and NSAID have also been reported. Both increased and decreased pathological symptoms after aspirin administration have been reported including exacerbated brain neurodegeneration caused by the protozoan Trypanosom brucei. and reduced blood vessel damage caused by the heartworm D. immitis
	Farag et al., 1995, Mahmoud et al., 2002	Ibuprofen, naproxen and diclofenac can significantly reduce the size of liver granulomas surrounding S. mansoni eggs formed by the host
	Srivastava and Shukla, 1983; Whaun, 1984)	Parasite functional biology can also be affected by NSAID, particularly aspirin. The growth, development, and encystment of protozoans are inhibited in the presence of aspirin
	Douch and Blair, 1975; Dauschies, 1995;	Effects on helminths appear more restricted as they are known to possess the enzymes necessary to metabolize this drug Nevertheless larval

	Joachim et al., 2005	exsheathment rates and development of the nematode <i>Oesophagastumdentatum</i> were inhibited after exposure.
Steroid hormones	Jobling and Tyler, 2003	Of particular relevance is the widespread use of human steroid contraceptives and their occurrence in the aquatic environment
	Wang and Belosevic, 1994	They have a high potency at low concentrations and have been associated with many endocrine disruptive conditions in fish.
	Harris et al., 2000	The effects of steroid hormones to aquatic host-parasite dynamics have formed the basis of a number of studies. An increased disease susceptibility caused by hormonal modulators has been reported in fish. Oestradiol increased the susceptibility of cyprinids to haemoflagellates by the suppression of lymphocyte proliferation. The steroid hydrocortisone is the synthetic form of cortisol, a corticosteroid hormone involved in the response to stress increasing blood pressure and sugar levels and acting as an immunosuppressive. It is widely used as an antiinflammatory and as an antagonist in the treatment of allergies, and has a number of effects on aquatic parasites. At relatively high concentrations hydrocortisone administration can cause an increase in the intensity of ectoparasitic infections on fish including host species considered to have a low susceptibility to infection.

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