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Review Article

Pharmaceutical Waste Management - A Study

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Abstract

In this ever-improving world of medical science, medicative waste materials, in general termed as pharmaceutical wastes are piled up in alarming levels and demands quick disposal, otherwise ignorance and negligence of their continual chemical decomposition will put the lives of the entire world at stake. Just like any other common waste management processes, the topic of pharmaceutical waste management has really turned out to be one of the most significant and emerging areas of discussion in recent times. Thanks to the active role of print media as well as the electronic and social media to raise the general awareness on this issue and pharmacists (both budding and professional) all over the world have come to the forefront, so far as taking the initiatives of aiding and educating common people about safe drug disposal is concerned. Accordingly, in this work some daily-used drugs like aspirin (an analgesic, antipyretic drug), lidocaine (a general anaesthetic drug) etc. are studied to learn about their positive impacts in living bodies as well as the negative effect on the environment i.e., when they can be regarded as "pharmaceutical waste", considering various perspectives. As an example, for smooth, painless operations lidocaine is a boon, but if not stored at temperatures below 25°C they degenerate and lose their therapeutic activity and literally become waste. So, at the end, general as well as drug-specific neutralization methodologies are discussed in detail to make this world a pharmaceutical waste-free space.

Keywords: Pharmaceutical Waste; Quick Disposal; Chemical Decomposition; Daily-used Drugs; Therapeutic Activity; Neutralization

Abbreviations

OTC: Over the Counter; API: Active Pharmaceutical Ingredient; PIB: Press Information Bureau; CAGR: Compounded Annual Growth Rate; CFC: Chloro Fluoro Carbon; NSAID: Non-Steroidal Anti-Inflammatory Drug; FDA: Food and Drug Administration; WHO: World Health Organization; ADME: Absorption Distribution Metabolism Excretion; GMP: Good Manufacturing Practices

Introduction

A pharmaceutical waste is generally regarded as a type of waste which contains medicinal drugs or OTC drugs that are either expired, unused, contaminated, damaged or discontinued [1,2] which requires proper management strategies. But pharmaceutical wastes are also generated during manufacturing of an API and formulations. Actually, any pharmaceutical product is not hazardous from the ground up as it is a combination of an API and excipients (builders, glidants, solvent system, preservatives etc.) [1]. Normally it is the API that is the most harmful and demands immediate, effective and long-term management strategies.

Thanks to the constant improvement in medical science as a whole resulting in radical increase in the life span of common people as well as producing an inflation of pharmaceutical prod-

uct usage, which causes more pharmaceutical waste generation [3]. As explained by the PIB in 2016 [4], India generates about 62 million tonnes of waste (containing both recyclable and non-recyclable waste) of which almost 10-15 million tonnes are bio-medical and pharmaceutical waste, with an expected average annual growth rate of 4% which is quite alarming. A study conducted jointly by industry body 'ASSOCHAM' and 'Velocity' [5] confirmed that India is likely to generate about 775.5 tonnes of medical waste per day by 2022 from the current level of 550.9 tonnes daily which means medical waste is expected to grow at a CAGR of about 7%.

So for reducing the hazards of disposing pharmaceutical waste, which may cause harm to the healthy environment, special techniques are being utilised which are quite different from the regular wastes eradication methods. In addition to that, new methods always keep replacing the old ones to ensure safety and lessen the hazardous factor involved in their disposal. Moreover, owing to pharmaceutical chemical's inability to be removed from the waste-water, they tend to enter the aquatic environment through the sewers. This in turn goes on to affect marine life, also adversely affecting human beings via various food chains. So, considering the above issues, the topic is chosen to be studied.

Materials and Methods

Different possible routes through which pharmaceutical wastes are generated and released into the environment are identified. It was found that household wastes are mixed with medicinal/drug remnants, unused and expired drugs as released from hospitals, medical stores and settlements get dumped into open pits causing soil pollution. The excretion of urine and faeces mix with the soil and groundwater causes water pollution. Wastes may also leach out from various defective landfills, compost pits etc. Aerosol inhalations (anaesthetic) may cause air pollution and especially the presence of greenhouse gases like carbon dioxide (CO_2), nitrous oxide (NO) and even some fluorinated hydrocarbons like Freon, CFC etc. [3] are responsible for global warming in the long run.

These threats of improper pharmaceutical-waste release are quite intense. So, it is utterly important that they should be disposed-off properly and obviously in the safest possible ways. For that purpose, a set of daily-used drugs which exists in various dosage forms are considered here as study materials [6]. The positive and negative impacts of such common drugs in the daily lives are detected along with their ideal working conditions and accordingly their specific disposal and management procedures [6,7] are identified to be followed when form wastes.

Study starts with the most common ASPIRIN which is a white, crystalline, bitter NSAID used as an analgesic in the treatment of mild or moderate pain. It is highly soluble in organic solvents but possess good solubility also in inorganic solvents and manufactured mainly as tablets and in some cases as aspirin suppositories. Ignitable at around >140°C, it releases toxic acrid fumes of carbon monoxide, carbon dioxide causing eye irritation, skin irritations including upper respiratory system problems, increased blood clotting time, nausea, vomiting, liver and kidney injury. It possesses a shelf life of 2-3 years (approx.) after packaging.

Second drug considered in the class of NSAID is DICLOFENAC which exists in odorless, colorless solid crystalline form with antipyretic actions also. It is partially soluble in both organic solvents and inorganic solvents at temperatures ranging between 25°C-30°C and applicable mainly as tablets, topical lotions, creams, gels to abolish pain and inflammation. Ignitable at >30°C it should be stored in air-tight containers protected from sunlight, moisture. Being highly toxic and even lethal, >25% (w/v) concentration especially if ingested, it may cause damage to unborn foetus, and already it destroyed vulture population over a period of 10-15 years at concentrations as low as (even 20% w/v). Depending upon use, its shelf life is approx. 1-2 years.

PANTOPRAZOLE is a solid, off-white coloured material, odourless and tasteless potent inhibitor of gastric acidity which is widely used in the therapy of gastroesophageal reflux and peptic ulcer disease. Being a weak base, it crosses the parietal cell membrane by entering the acidic parietal cells and restricting both basal and stimulated gastric acid production. Freely soluble in water at 25°C and insoluble in organic solvents, it is marketed as enteric coated tablets. Highly toxic at > 11% (w/v) concentration especially if ingested, it causes skin irritation and respiratory problems (22.22% w/v), eye irritation (33.33% w/v). It is suspected to be carcinogenic, mutagenic, causing harm to breast-fed infants, very toxic to aquatic life. Anaphylaxis has been reported with the use of IV pantoprazole which demands immediate medical intervention and drug discontinuance. Expiry date stands at maximum 3 years.

Broad-spectrum antibiotic ERYTHROMYCIN is a fluffy, white or slightly yellow-colored odorless and bitter solid medication

with either bacteriostatic or bactericidal activity. Highly soluble in inorganic solvents, fairly soluble in organic solvents at 25°C, its manufacturing is done using fermentation and growth of a strain of *Streptomyces erythreus* bacterium and marketed as tablets, suspensions, ointments (eye, ear) and parenterals. Body incompatibility is the main and common problem with erythromycin tablets where at times it may cause a muscle disease, a condition that affects heart rhythm with other symptoms like severe dizziness, fainting etc. Depending upon use and storage conditions its shelf life is approx. 8 months - 1 year with a maximum of 2 years and should not be used after crossing the expiry date.

To treat venous thrombosis in high-risk patients by preventing the polymerization of fibrin and the subsequent formation of clots thus avoiding heart failures, HEPARIN is a very common medication which is solid, white or pale-colored amorphous powder, odorless and tasteless, sulfur-rich organic mixture with anticoagulant properties. Highly water soluble at temperatures above 20°C, but insoluble in organic solvents, it is mainly marketed in parenteral dosage forms. Ignitable at > 60°C, it is stored in tight, light-resistant containers. Being highly toxic at > 15% (w/v) concentration especially, it causes eye irritation and also suspected to be carcinogenic and at the same time its overdose may result in excessive bleeding due to cuts or wounds. It has a very short shelf-life of only 48-72 hrs and generally loses potency within 3 years.

Again, to cause local anaesthesia, LIDOCAINE is used as an ideal solid in white or slightly yellow, crystalline form. It is used as a cardiac depressant or an antiarrhythmic agent as it stabilizes the neuronal membrane by binding to and inhibiting voltage-gated sodium channels, thereby initiating and conducting impulses. It is highly soluble in organic solvents with good solubility in water at temperatures of above 30°C and marketed as parenterals or even as topical ointments, lotions, creams or sprays. But it is highly toxic at > 80% (w/v) concentration, especially if ingested. Lidocaine hydrochloride injections and commercially available solutions of the drug get degenerated and lose their therapeutic activity if stored at temperatures exceeding 25°C. Its shelf life depending upon use varies between 28 days to few months.

To eradicate the effects of cough and cold, BENADRYL is very common which is an oily-colored, odorless and tasteless histamine antagonist used as an antiemetic, antitussive ingredient in common cold preparations like cough syrups, linctuses by reducing bronchoconstriction and gastro-intestinal smooth muscle spasms. It is highly soluble in inorganic solvents but insoluble in organic solvents. Organoleptic agents are added in the preparation to make it applicable for ingestion as oral capsules, solutions, tablets as well as parenterals. But it is slightly inflammable at temperatures > 100°C with high toxicity at > 70% (w/v) concentration especially if ingested or if accidentally bought into eye and skin contact. Considerable overdosage can lead to myocardial infarction, coma or even death. It has a shelf life of approximately 3 years after which it loses its efficacy and potency marginally though still remains usable.

INSULIN is a long-lasting hypoglycaemic agent used to manage blood glucose levels in patients with DIABETES MELLITUS. Generally given prior to meals with its onset of action within 1-2 hours and duration up to 24 hours, it mostly binds with the albumin protein (> 98%) and is administered only via parenteral route. Hypoglycaemia may occur with its inappropriately high doses showing symptoms including trembling, palpitations, sweating, anxiety, hunger, nausea, lethargy, drowsiness, headache, dizziness etc. Injection-site reactions may also occur redness, inflammation, bruising, swelling and itching. Shelf life stands at 30 days unrefrigerated and 3 months refrigerated.

Results and Discussion

The drugs mentioned above tend to generate pharmaceutical wastes from a very small amount to a huge one if working conditions are not maintained either individually or in mass-use causing a variety of environmental hazards along with physical ones. In order to eradicate these pharmaceutical wastes, all need to plan an effective management strategy to restrict their generation at controllable limits and come up with good and safe disposal methodologies. According to the current FDA and WHO guidelines, a good number of steps need to be adopted to dispose unwanted pharmaceuticals which are essential before practical actions to be taken. These are as follows;

- Institutions involved with pharmaceutical programs like hospitals/nursing homes, pharmacy stores, pharmaceutical manufacturing units have to decide the optimum time to initiate the disposal of accumulated and unwanted pharmaceuticals.

- Appropriate authority then must approve and sanction the disposal of these identified pharmaceuticals.

- Available disposal options are to be planned, depending upon the nature of the pharmaceuticals and available human resources with necessary expertise and equipment.
- Considering volume and composition of the stock, pharmaceuticals are sorted into different categories and accordingly, an expert team of pharmaceutical technicians will finally conduct disposal works under the supervision of a pharmacist with appropriate protective measures as per requirement.

Accordingly, the disposal methods adopted and commercialized for management of the drugs under consideration [3] when form wastes, are tabulated below (Table 1).

Name of the Medications with dosage forms	Disposal and Management Methods
Solid medications (Aspirin, Pantoprazole)	Mix with unappealing substances such as kitty litter or ground coffee, put into disposable containers, and throw in the trash or take away via community drug takeback programs or deposit in high temperature incinerators (Temp. 850°C to 1200°C)/approved site for solid waste disposal by the Pollution Control Board (PCB).
	Disposal of trace amount of such biodegradable raw solid medications, typically lesser than 0.5% of the total daily waste, can also be done by safely dumping them into a landfill and covering with treated municipal waste. Some stringent landfill management & disposal protocols and a control over unwanted scavenging by scavenger birds like vultures should make the process safe, environment friendly & less time consuming.
Liquid medicines (lidocaine, Benadryl, Heparin, Insulin)	Mix with salt, flour, charcoal, or nontoxic powdered spice, such as turmeric or mustard, to give the mixture with an unappealing smell and texture to dispose them off.
	Industrial scale muffle-furnaces may be used for complete incineration at > 500°C.
	These liquid medications with a low toxicity profile can be safely deposited into fast flowing streams, rivers or flowing sewers after undergoing adequate hydrophilic dilution of around 1:50000
Aerosol dispensing medications (lidocaine/benzocaine)	They contain volatile constituents present in pressurized actuator-fitted metal/glass containers/canisters and are generally emptied completely and then these containers are sent to incinerators or furnaces where they are incinerated at temperatures as high as (800-1000) °C and the remnants are recycled further.
	But disposable aerosol canisters must be treated separately, as if incinerated, they might explode causing injury to operators. So those should be disposed of in a landfill, dispersing among municipal solid wastes provided they do not contain poisonous substances.
Topical medications (Diclofenac & Erythromycin)	As present in plastic or metal tubes, these should be completely pumped out and tightly wrapped with duct tapes and seal-packed in opaque disposable bottles or cartons. After proper drug disposal all packaging material must be recycled properly for reusing or completely incinerated as scrap.

Table 1: Name of the Medication and used Disposal Methods.

Present methods

But in recent times, a newer concept of "Pharmaceutical Waste Immobilization" [2] has become a runaway success in this field with a drop in pharmaceutical waste formation by over 20% [1] which is quite substantial. Every type of wasted/unused medicinal formulation can be either made 'pharmaceutically inert' or 'pharmaceutically encapsulated/immobile'.

Pharmaceutical waste inertization

This process is solely used for inertizing solid unused/expired pharmaceutical waste products. At first these solid medications

are removed from their blister packaging and crushed under an industrial grinder or a road roller. This turns them into a powdery mass which are then transferred into a mixing vat where they are mixed with cement, lime and water (in the ratio of 65 :15 :15 :05 by weight) to form a homogenous consistent paste. This mass is then transported to landfills in the outskirts of cities and is filtered, decanted and converted into treated municipal/urban waste or into bituminous sludge useful for road-building purposes. But putting this into Indian perspective, it is found out that such innovations are not very popular even today barring some cities like Bengaluru, Chennai and Hyderabad. During Inertization, as there is a risk of powders being liberated when tablets or capsules are being crushed, all workers should wear boots, gloves, masks and caps.

Pharmaceutical waste encapsulation

The process of encapsulation generally involves immobilizing the raw pharmaceutical product (semi-solid or liquid product) by converting it into a solid block inside a plastic or a steel drum. Thoroughly cleaned drums are filled to nearly 75% of its capacity with the pharmaceutical waste, and the remaining space is filled up by pouring in a cement or cement/lime mixture, plastic foam or bituminous sand. Once those drums are full to the required limit, the mixture of lime, cement and water is added and the drum is fully filled. After that steel lids are then welded into the drum so that it is tightly sealed. Then it is dumped at the base of a landfill and covered with treated landfill waste. This significantly reduces the environmental load and is also inexpensive.

Use of nanotechnology

Nanotechnology in pharmaceutical drug development is the hot topic in Research and Developmental activities at present around the world. Nanoparticle containing drugs have completely different physiological and biochemical properties compared to any standard drug molecule [8]. Its unique ability to provide target-specific drug delivery and to bypass other organ systems reducing the risk of toxicity and side effects, is what sparks interest among research fellows from the pharma and medical fraternity. Recent studies have shown that technically better ADME properties of these particles improve drug efficacy and patient compliance which indirectly help in reducing the generation of pharmaceutical waste. Even though the advantages and disadvantages of nano-drug particles are still under observation, various African and European countries have already figured out a way to manage dumped pharmaceutical wastes, for example, in the form of unused expired aspirin tablet strips. These are found in streams near the countryside and by using nanosorbents and nanocomposites [9] having a ceramic, polymer, and a metal matrix, are not only absorbing the drug remnants but are also able to measure the number of residual wastes present in the water body.

Pharmaceutical waste management practices

Here it may be mentioned that most of the above-mentioned pharmaceutical waste management methods are applied in various countries in general with a constant innovative mindset of the pharmaceutical technicians and the workforce depending upon their national policies, infrastructural constraints, regulatory guidelines and action plans along with the advancement of country-specific practices using corresponding technological aids [10].

For example, identifying the pharmaceutical waste in the form of clinical waste in Australia and medical waste in Cambodia, the information regarding quantities of waste production is a crucial step in safe waste disposal considering budgeting and environmental impact assessments.

In Australia, the polluter-pays principle facilitates an effective pharmaceutical waste management system. In Cambodia, various technologies include the provision of sustainable treatment, including autoclave and shedders as well as a national incinerator to treat wastes that are potentially hazardous in nature.

In Japan, the Waste Management and Public Cleansing Law, prescribes the necessary management structure to control such wastes environmentally. Japan has no policy or any existing national action plan on Health Care Waste Management including pharmaceutical waste management, but practical guidelines for infectious waste have been developed, including guidelines for home-based pharmaceutical waste and for the manual handling of such wastes.

Similarly, New Zealand also has no specific law on such waste management strategies though several guidelines have been issued on the management and safe handling of drugs and its related wastes and the ban on onsite incineration.

So, as an enhancement, different health-care institutions are expected to incorporate an integrated waste management approach in the near future to treat pharmaceutical wastes.

Conclusion

In this study, authors have looked upon various aspects of pharmaceutical waste management strategies and possible disposal techniques. Since this field is a constantly evolving area in waste management studies, newer technologies and management ideas keep popping up but the greatest challenge that remains is their acceptability and accessibility to common people, spreading general awareness. Strict surveillance and monitoring of these activities should be carried out in a sustainable manner in the present dynamic scenario by introducing pharmaco-waste-management officer posts in the existing protocol which is still non-existent. Commercialization of acceptable technologies and a more stringent amendment of the present Pollution Control Board rules and World Health Organization guidelines can act as stepping stones to such initiatives. In this context, it is worth mentioning that now many pharmacies operate on an idea of the concept of "Return of Pharmaceuticals to the Manufacturer" falling under a Buy-Back policy. This has a huge positive impact on the environment as it will evoke manufacturers to develop their own in-house recycling facilities and also force them to meticulously follow GMP in accordance with 'Schedule M' of the Drugs and Cosmetics Act, 1945 [11]. As a whole, pharmaceutical waste management being a global issue demands united hands for tackling.

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Conflict of Interest

The authors declare that there has been no financial interest or other forms of conflict of interest reported during or before final submission of the manuscript.

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