Barcoding drug information to recycle unwanted household pharmaceuticals: a review

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Received: 31 January 2022 / Accepted: 15 February 2022 / Published online: 27 April 2022
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Abstract
Huge quantities of unwanted pharmaceuticals are left in households, notably as a consequence of the rising drug demand caused by improved healthcare and the aging population. Unwanted pharmaceuticals may thus easily end up polluting ecosystems upon disposal. This pharmaceutical waste issue has been aggravated during the coronavirus disease pandemic (COVID-19) by excess prescription and panic buying. Unwanted household pharmaceuticals are normally collected by owners and volunteers, then incinerated in centralized facilities, yet with low efficiency during the COVID-19 lockdowns. Most pharmaceuticals could be recycled because they are rather stable, however there is actually no sustainable strategy to manage unwanted pharmaceuticals in a pandemic. Here I review the management of unwanted pharmaceuticals in households during the pandemic, with emphasis on drug take-back programs, waste minimization and recycling efforts. Reducing pharmaceutical waste could be done by informing people on what to do with unwanted pharmaceutical products; using machine-readable codes for automatic sorting; and applying existing techniques for recovery of active pharmaceutical ingredients for reuse. I propose a new strategy where owners sort their unwanted pharmaceuticals and submit information online. This will generate coded mailing labels that allow the owner to separate pharmaceuticals into categories such as opened, unused, expired, and non-expired. Once collected by recycling facilities and manufacturers, active ingredients will be extracted to create new pharmaceuticals which will be recycled to other patients.

Keywords Medicine · Drug · Recycle · Recovery · Pandemic · Coronavirus

Introduction
An aging global population and rising health-seeking awareness have resulted in the long-term growth of pharmaceutical use over the past few decades (Caban and Stepnowski 2021; Pandey 2019; Singh et al. 2021). Every year, there is an enormous quantity of pharmaceuticals left unused or expired after being dispensed to patients due to patient noncompliance, over-prescription, improvements on medical conditions and, in some cases, the decease of patients (Insani et al. 2020). In the United States alone, patients waste more than $1 billion worth of prescription drugs every year by disposing them as general household wastes or pilling them up in medical cabinets at home (Opar 2006). In the United Kingdom, the equivalent figure is about £300 m a year (Trueman et al. 2010). Since 2020, the outbreak of the coronavirus disease 2019 (COVID-19) pandemic has increased the global demand for pharmaceuticals, with large quantities of expired, unused, and unwanted medications pile up in households. The COVID-19 pandemic caused an anticipated surge of use and purchases of medications around the world, driving demand to an unprecedented level (Gwenzi et al. 2021). In China, people rushed to local pharmacies and hoarded Lianhua Qingwen (Lotus Plague Clearing) capsules, a traditional Chinese medicine, after hearing reports that the medicine showed effects in treating COVID-19 symptoms (NATCM 2020; Zeng et al. 2020). Yiling Pharmaceuticals, a manufacturer of Chinese traditional medicines, reported that sales of Lianhua Qingwen capsules increased by nearly 150% in 2020 compared with the previous year, driven by the surging demand (SYP 2020). In 2020, sales of pharmaceuticals in the U.S. totaled over 530 billion, representing an overall growth of 8% compared with the equivalent figure in 2019 (Statista 2022a). In the meantime, some manufacturing
plants were shut down to prevent the spread of COVID-19, resulting in a persisting shortage of some pharmaceuticals (US Pharmacist 2021).

Expired or unused medicines are potent bioactive substances that should be carefully managed to avoid potential toxicological effects in the environment (Michael et al. 2019). Referred to as ‘agents of subtle change’, pharmaceutical residues have high bioactivity and can cause various adverse effects in aquatic biota at low part-per-billion levels and pose health risks to human through drinking water or trophic transfer (Mechelke et al. 2020; Glassmeyer et al. 2009; Zarei et al. 2020). Since the early 2000s, a significant amount of research efforts has been expended on understanding the occurrence and fate of pharmaceuticals in the environment, as well as their effects on aquatic biota and human. Many pharmaceutical compounds show persistence to the biological treatment processes in municipal wastewater treatment plants, and surveys showed the ubiquitous occurrence of pharmaceutical compounds and their metabolites in the natural environment (Khasawneh and Palaniandy 2021). Residues of prescription and over-the-counter drugs were found in leachates of municipal solid waste landfills, while antibiotics that can alter natural bacterial species, anti-depressants, diabetes and hormone drugs were found in groundwater and surface water (Kümmerer 2009; Świacka et al. 2022). A potential source of xenobiotic pollutants in the environment, those unused, non-expiring drugs also represent a vast resource to alleviate persisting shortages for some drugs and help other patients in need. Active pharmaceuticals ingredients have been reported to be extremely well preserved long after their labeled expiring dates. They present some of the most high-value chemicals and, in the meantime, potent bioactive environment toxins once released to the natural environment. The surging demand, stalled collection programs, and a prolonging COVID-19 pandemic catalyzed the pressing need for a new imperative in managing expired, unused, and other unwanted pharmaceuticals in households on a global scale. This article reviews the guidelines, current practices, major challenges, as well as the infrastructures and technologies available for addressing this longstanding gap.

**Choices for disposal of unwanted household pharmaceuticals**

The U.S. Environment Protection Agency (EPA) encourages the public to take advantage of the drug take-back programs that accept both prescription and over-the-counter drugs, as these offer a safe, convenient, and environmentally-conscious way to dispose of unwanted medicines. Owners could drop off their expired, unused, opened, or other unwanted drugs at a designated drug take-back site (FDA 2020a), such as a local pharmacy, healthcare provider, or law enforcement agency e.g., police station (EPA 2022). The U.S. Drug Enforcement Administration (DEA) sponsors the National Prescription Drug Take Back Day, offering about 11,000 collection sites in communities nationwide. As of May 2021, DEA collected 14,524,391 pounds, or nearly 6600 metric tons, of unused, expired, and unwanted medications along with its law enforcement partners since the inception of the National Prescription Drug Take Back Initiative in 2010 (DEA 2021). Drug take-back programs have also been established in European countries and other industrialized nations since the early 2000s. The Article 127b of the European Union Directive 2004/27/EC (2004) of the European Parliament and of the Council requires that member States shall have appropriate collection systems in place for unused or expired medicinal products. A survey conducted by the European Federation of Pharmaceutical Industry Association reported that, 3 years later, 20 of the 28 nations surveyed established a pharmaceutical waste collection scheme, most of which were pharmacy-based collection systems (Glassmeyer et al. 2009). In the United Kingdom, pharmacies are obliged to accept unwanted medicines from households and individuals (PSNC 2022), where waste contractors would collect those at regular intervals (NHS 2004). In Australia, the Return Unwanted Medicines (RUM) project is a national government-financed scheme for collecting expired and unwanted medicines from the general public via community pharmacies. Since the launch of the RUM project in December 2002, a total of 11,380 tons of medicines have been collected (NRDUM 2022). In Canada, natural health products—along with unused or expired prescription and over-the-counter drugs—can also be brought to local pharmacies, as a further effort to reduce the entry of consumer healthcare products in the environment (Government of Canada 2014). The Health Products Stewardship Association offer return programs for unwanted medications to reduce their likelihood of being thrown in the garbage, poured down the sinks, flushed or misused. Since its inception, the programs have collected nearly 3800 tons of medications (HPSA 2022).

These collection programs, however, were deterred under the impact of COVID-19, potentially due to the reduced trips and the perceived risk of viral transmission in public settings (Chen et al. 2021a; He and Han 2021; Wang et al. 2021). The National Prescription Drug Take Back Day scheduled on 25 April 2020 was canceled due to COVID-19 (DEA 2022). It collected 447 metric tons of medications across the country in 2020, which was about half of the quantity collected in 2019, i.e., 826 tons (DEA 2022). Owners are faced with two options if a drug take-back program is not available. If the unwanted medication is on the ‘Flush List’, an example list of pharmaceutical products published by U.S. Food and Drug Administration (FDA) containing ten...
opioids and three non-opioid active pharmaceutical ingredients (Table 1), owners are advised to flush it down the toilet. By listing medicines that are potentially sought for misuse or abuse or medicines that can result in death from one single dose if inappropriately taken, the ‘Flush List’ is created for human safety—rather than environmental sustainability—in mind. If the medication is not on the flush list, however, owners would throw them in trash following the steps for household disposal of medicines (Fig. 1), a practice again focusing on human safety not environmental impact (FDA 2020a). In an effort to address the concern of environmental risk, FDA published a paper that evaluated the environmental and human health risks associated with the flushing of 15 active ingredients in medicines (Khan et al. 2017). The public health agency concluded that there were negligible risks with the flushing of those active ingredients, but acknowledged that additional data would be helpful for confirming the findings for some of the medicines (FDA 2020b). The FDA study, however, did not address the risks associated with the practice of disposing of unwanted pharmaceuticals in household trash. In reality, the latter scenario encompasses a far wider range of active pharmaceutical ingredients and presents a much more common practice for household disposal of unwanted pharmaceuticals. Prior to the COVID-19 pandemic, a cross-sectional study (n = 306) in Southern California, United States showed that ‘throwing medications in the trash’ was the most common method for the disposal of medications among households (63%), and half of the surveyed households (50%) would throw those in trash during drug take-back events, followed by flushing down the toilet (26%) (Law et al. 2015). No significant relationship was found between age, ethnicity, education, income, insurance and the number of unused medications among the households. A recent study conducted by Health Products Stewardship Association showed that one in three Canadians do not know about proper disposal for unwanted medications, despite the fact that 90 percent of pharmacies offer take back programs within the participating provinces.

Table 1 Examples of products on the ‘Flush List’ for certain medicines recommended by the U.S. Food and Drug Administration, adapted from FDA (2020b)

| Drug name | Examples of products on the flush list |
|-----------|---------------------------------------|
| Drugs that contain opioids | Belbuca, Buavai, Butrans, Suboxone, Subutex, Zubsolv |
| Any drug that contains the word “buprenorphine” | Abstral, Actiq, Duragesic, Fentora, Onsolis |
| Any drug that contains the word “fentanyl” | Exalgo |
| Any drug that contains the word “hydromorphone” | Demerol |
| Any drug that contains the word “meperidine” | Arymo Er, Avinza, Embeda, Kadian, Morphabond Er, Ms Contin, Oramorph Sr |
| Any drug that contains the word “morphine” | Xyrem, Xywav |
| Drugs that do not contain opioids | Daytrana |
| Any drug that contains the term “sodium oxybate” or “sodium oxybates” | |

Owners are referred to specific disposal instructions in each medicine’s labeling. The most current drug labeling can be found at [http://www.fda.gov/drugsatfda](http://www.fda.gov/drugsatfda) or [https://ntcr-crs.fda.gov/fdalabel/ui/search](https://ntcr-crs.fda.gov/fdalabel/ui/search). A peer-reviewed study was published by the U.S. Food and Drug Administration in 2017, addressing the environmental and human health risks of 15 active ingredients found in the ‘Flush List’ medicines (Khan et al. 2017)
(HPSA 2021). Surveys in the Organisation for Economic Co-operation and Development (OECD) countries showed an average per capita spending of 564 USD per year on retail pharmaceuticals in 34 countries, and that ‘throwing in waste bin’ and ‘flushing down the toilet or sink’ represent the most common methods of disposal in households in 10 of 13 countries surveyed between 2009 and 2018 (Fig. 2). No survey data, however, have been published to date on the methods of disposal of expired or unwanted pharmaceuticals by the public under the impact of the COVID-19 pandemic.

As the world’s most populous nation, China has established the second largest market for pharmaceutical products, with a global share of about 8% in sales in 2020 (Statista 2022b). In the “Expired Drugs Recycling in Chinese Families (2004–2014)”, a white paper published in 2014 by a leading Chinese pharmaceutical manufacturer, it was reported that more than three quarters of households in China (78.6%) had medical cabinets in which 30–40% of medications in storage had expired over 3 years ago. Meanwhile, more than 80% of the households did not regularly clean up expired medications in their medical cabinets, which resulted in about 15,000 metric tons of expired drugs accumulated in households. An earlier survey conducted by the Shanghai Food and Drug Administration in 18 nationally representative regions across the country revealed that the principal method of disposal of unwanted pharmaceuticals in Chinese households was to throw them into the household trash, which accounted for 80.3% of the responses (SFDA 2009). In 2021, the Ministry of Ecology and Environment of China published the “National Inventory of Hazardous Wastes (2021)” with a “List of Exempted Hazardous Wastes” (MEEPRC 2021). As per the ministerial guidelines, unwanted pharmaceuticals and packaging materials in households are categorized as non-hazardous wastes, and only those collected as ‘hazardous trash’ under the new trash separation rules would be categorized as hazardous wastes (SCPRC 2021). Although China introduced mandates on household trash separation in 2019, the new regulations are only applicable to municipalities and prefectural-level cities, where household pharmaceuticals and packaging materials are required to be disposed of as hazardous trash. Counties, towns, and rural areas are, however, exempted from these rules (GPRC 2021). To date, there is no national drug take-back program to collect expired or unwanted household pharmaceuticals in China. Overall, current practices of disposal of expired and unwanted household pharmaceuticals are unsustainable and pose looming threats for the environmental and public health. Under the impact

### Table 2

| Product nameb | Active ingredient | Mode of action | Final disposal instructions | List priceb |
|---------------|-------------------|----------------|-----------------------------|--------------|
| Deterra (MedsAway) | Activated carbon | Adsorption of chemicals to carbon | Garbage/solid waste system | $4.99: single pouch/15 pills |
| | | | | $6.99: large pouch/90 pills |
| | | | | $34.99: 1.8 L bottle/450pills |
| DiposeRx | Cross-linking polymer | Unknown (ingredients not identified) | Garbage/solid waste system | Not stated |
| Drug Buster | Activated carbon | Adsorption of chemicals to carbon | Garbage/solid waste system per local regulations | $9.95: 4 oz/50 pills |
| | | | | $15.99: 16 oz/300 pills |
| | | | | $34.99: 64 oz/1500 pills |
| Element MDS (Medication Disposal System) | Organic plant-based powder | Unknown (ingredients not identified) | Garbage/solid waste system | $6.99: 17 oz/500 pills not sold individually. $349.50 for 50 kits |
| Pill Catcher | Bentonite clay | Adsorption of chemicals to clay | Garbage/solid waste system | $4.95: pint/120 pills |
| | | | | $6.96: quart/300 pills |
| | | | | $22.60: gallon/1500 pills |
| Pill Terminator | Calcium hypochlorite, Fuller's earth, absorbent polymer | Oxidation and adsorption | Garbage/solid waste system | $9.95: 300 mL/300 pills |
| | | | | $24.95: gallon size/capacity not stated |
| Rx Destroyer | activated carbon and proprietary agents | Adsorption of chemicals to carbon | Garbage/solid waste system. Check federal, state, local regulations | $4.16: 4 oz/50 pills |
| | | | | $8.75: 16 oz/300 pills |
| | | | | $48.75: 1.0 gallon/3000 pills |

*Deterra, i.e., when used by healthcare facilities, Drug Buster, and Rx Destroyer are for use with non-hazardous pharmaceuticals only, as specified by manufacturers

*List prices were of March 2017, in US dollars. Further information on these products is compiled by Community Environmental Health Strategies in their report for San Francisco Department of the Environment (CEHS 2017)
of COVID-19, inappropriate disposal of medications may gain favor in households around the globe.

Disposal of pharmaceutical products collected from various take-back programs

To date, the disposal of pharmaceuticals collected from consumer take-back programs has predominantly relied on incineration. The U.S. Environment Protection Agency (EPA) released a memorandum in September 2012 which recommended incineration as the preferred method of disposal for household pharmaceuticals collected through take-back programs (EPA 2012). The DEA or other law enforcement agencies collecting controlled substances in these events are also obliged to dispose of these substances. Most controlled substances collected from take-back programs are incinerated. Within the European Union, the final disposal of unused and expired medication is generally done by high-temperature incineration (> 1000 °C) equipped with adequate exhaust gas cleaning or alternatively, incineration at lower temperatures (850 °C or higher) in countries where municipal solid waste incineration is prevalent and owners are instructed to dispose of their unwanted medications in mixed household waste (OECD 2021). In Australia, returned medicines from the RUM project are disposed of by high-temperature incineration, in accordance with regulatory and EPA requirements (NRC 2006). Since the inception of...
the RUM project, more than 10,000 tons of unwanted or expired medicines collected from community pharmacies and wholesalers were incinerated in EPA-approved incinera-
tors (RUM 2019).

In the lack of a ‘pandemic-scenario protocol’ for safe disposal of unwanted pharmaceuticals from individuals and households, the guidelines by the World Health Organization offer the most appropriate point of reference for governments and authorities (Table 3). The World Health Organization published these guidelines in 1999 to advise on the safe disposal of unusable pharmaceuticals from drug donations in emergencies and in countries where official assistance and advice are unavailable or insufficient. While incineration is universally effective in eliminating pharmaceutical wastes, it is among the most expensive and unsustainable methods of waste disposal and also requires access to specialized waste combustors to minimize the emission of toxic fumes from the incineration process (WHO 1999). Other methods of disposal, such as landfilling and waste encaps-
ulation, do not have an impact on the activity of drugs. The active pharmaceutical ingredients retained in wastes would eventually leach out, promoting the growth of drug-resistant microbes in municipal solid waste landfills or polluting soils and groundwater through landfill leachates and leakages. Further, as these guidelines focus on the end disposal of donated pharmaceuticals, they did not address how unwanted pharmaceuticals could be collected, in a practical manner, from individual owners and households nationwide in a prolonged pandemic scenario. In particular, the information gathering, logistics, and sorting present unprecedented challenges for environmental authorities to manage these pharmaceuticals ever since they became a recognized issue to environmental and public health agencies. To conclude, the bulk quantities of unwanted pharmaceuticals collected

| Table 3  | Guidelines on disposal of unwanted pharmaceuticals from drug donations in and after emergencies by the World Health Organization, adapted from WHO (1999) |
|----------------|---------------------------------------------------------------------------------------------------------------------------------|
| **Disposal methods** | **Types of pharmaceutical** | **Comments** |
| Return to donor or manufacturer, transfrontier transfer for disposal | All bulk waste pharmaceuticals, particularly antineoplastics | Usually not practical—transfrontier procedures may be time consuming |
| High temperature incineration with temperatures greatly in excess of 1200 °C | Solids, semisolids, powders, antineoplastics, controlled substances | Expensive |
| Medium temperature incineration with two-chamber incinerator with minimum temperature of 850 °C. Cement kiln incineration | In the absence of high temperature incinera-
tors, solids, semi-solids, powders. Control-
ted substances | Antineoplastics best incinerated at high tem-
perature |
| Immobilization | Waste encapsulation | Solids, semi-solids, powders, liquids, antineo-
plastics, controlled substances |
| Inertization | Solids, semi-solids, powders, antineoplastics, controlled substances | |
| Landfill | Highly engineered sanitary landfill | Limited quantities of untreated solids, semi-
solids and powders. Disposal of waste phar-
maceuticals after immobilization preferable. Polyvinyl chloride (PVC) plastics |
| Engineered landfill | Waste solids, semi-solids and powders, preferably after immobilization. Polyvinyl chloride (PVC) plastics | |
| Open uncontrolled non-engineered dump | As last resort untreated solids, semisolids, powders—must be covered immediately with municipal waste. Immobilization of solids, semi-solids, powders is preferable | Not for untreated controlled substances |
| Sewer | Diluted liquids, syrups, intravenous fluids, small quantities of diluted disinfectants (supervised) | Antineoplastics, and undiluted disinfectants and antiseptics not recommended |
| Fast-flowing watercourse | Diluted liquids, syrups, intravenous fluids; small quantities of diluted disinfectants (supervised) | Antineoplastics, and undiluted disinfectants and antiseptics not recommended |
| Burning in open containers | As last resort, packaging, paper, cardboard | Not acceptable for polyvinyl chloride (PVC) plastics or pharmaceuticals |
| Chemical decomposition | Not recommended unless special chemical expertise and materials available | Not practical for quantities over 50 kg |
from households through various take-back programs are predominately incinerated under the current waste management schemes, which is expensive and requires access to specialized waste combustors. There is also a lack of protocols or guidelines for the collection or disposal of expired and unwanted household pharmaceuticals in a pandemic scenario. More effective and sustainable mechanisms are needed to minimize the generation of waste pharmaceuticals at the household level and further to recycle the pharmaceuticals collected in the current pandemic and beyond.

Waste minimization and recycling efforts

Minimization and recycling generally offer the most sustainable strategies for waste management, and pharmaceuticals are no exception. France and Japan offer valuable lessons on tackling the issue of unwanted pharmaceuticals in households. As one of the early countries tackling this issue, France founded the National Pharmaceutical Recycling Association in 1993 which, apart from the recycling of pharmaceutical packaging, recycles all unwanted medicines, including those within or beyond their expiration date. Recycling bins were placed at retail pharmacies where unwanted drugs were collected voluntarily and free of charge. Nearly 90 percent of pharmacies in France participated in this initiative. Nearly 11,000 tons of unused medicines were recovered across the country in 2016. In 2018, 80% of the French population reported returning their unused medicines to their pharmacists, and 60% did so on a routine basis. Once collected, the unwanted medicines were roughly separated into the ‘Reusable’ and ‘To-be-destroyed’ batches. Pharmaceutical manufacturers or wholesalers would pick up these collected medicines from pharmacies and complete the fine-sorting. After quality checking, unopened and non-expiring medicines would be donated to domestic or international humanitarian organizations collaborating with the Association, which would then distribute these to individuals or countries in need of the medicines. Expired drugs containing usable ingredients would be sent to institutions or laboratories for extraction and reuse. Expired drugs and packaging that are deemed completely useless would be transported as medical wastes to specialized facilities for incineration. In Japan, there is a more innovative model of co-managing household pharmaceuticals where households are responsible for regularly cleaning out their expired drugs while pharmaceutical companies, which leave their medical cabinets in customers’ homes for free, charge their customers only for the quantities of drugs they take and periodically take away the expired medicines and replenish the cabinets with new ones. The ‘pay-as-you-go’ model, which is common in Japanese households and similar to soda drinks kept in refrigerators in hotel rooms, minimizes the amounts of wastes of pharmaceuticals generated in households in the first place, which offers a valuable example for other countries.

In China, a pharmaceutical manufacturer initiated the “Expired Medicine Collection & Change-for-Free” program for households in 2004 (GPHL 2018a). Since its launch, over 1500 tons of expired medications have been collected from individuals and households between 2004 and 2018. In 2018, a group of major pharmaceutical companies and logistics firms joined forces and set up the “National Coalition for Expired Medicine Recycle” (GPHL 2018b). The non-government-led initiative became the first and the only nationwide scheme for collecting expired medications from households. Since then, logistics and information technology have played an increasingly important role in such efforts. Under this new scheme, owners would scan a 20-digit barcode on the product package with their mobile apps, and then fill in their contact information to arrange pick-ups for their expired medications. The whole process can be done with a smart phone at home and is free of charge. The collected expired medications would then be shipped to centralized facilities and incinerated at 1200 °C. This service, however, is only offered for a limited time every year between March 13 and 31, which is only available in seventeen metropolitan areas with high population densities and modernized logistics services in place.

In the United States, the redistribution of unused, non-expiring drugs has long been advocated as a means of better serving patient’s needs. The 2013 National Health Interview Survey, conducted by the National Center for Health Statistics of the U.S. Centers for Disease Control and Prevention (CDC) administering face-to-face interviews in a nationally representative sample of households, found that about 8% of adults in the U.S. do not take medicines as prescribed because they could not afford the costs (LeWine 2015). As of November 2021, drug donating is allowed in 38 states, and there are regulations in place to oversee the donation and re-distribution process. More than half of the states where laws have been passed have established operating programs for drug re-distribution. For instance, states like Colorado and Florida accept unused drugs prescribed for cancer treatments, while Georgia and Iowa accept all prescription and over-the-counter drugs as long as they are in sealed packaging (Recovery Village 2021). Beyond the government-led drug donation programs, individuals could also contact authorized organizations including, most notably, World Medical Relief, GoodPill.org, Volunteers in Medicine, and Memorial Sloan Kettering Cancer Center. Most organizations only accept unused drugs in original packages with unbroken seals. In 2020, the World Medical Relief received 803,178 pounds (364 tons) of donated medications from donors around the globe, with an estimated value of $2.3 million. Overall, there are existing models that
are innovative and effective on minimizing the expired and unwanted pharmaceuticals in households, and various organizations accept donations of unused pharmaceutical products for humanitarian purposes. Meanwhile, the advancement of information technology and logistics brings new opportunities to address this longstanding issue.

**Recovery of active pharmaceutical ingredients**

Waste pharmaceuticals have been largely overlooked as a vast source of valuable chemical compounds. A recent study reported that most of the active ingredients in commonly discarded medicines continue to be stable for many years after their expiration dates printed on product labels (Marić et al. 2021). Most pharmaceutical ingredients have very high purities, are costly to make, and belong to a group of high-value chemicals if recovered. Adding to these incentives, the formulations of most chemical drugs are not complex, with common additives present in the product. Compared with natural products, they represent much ‘cleaner’ matrices for extraction and selective recovery of target compounds. Overall, recovering active ingredients is economically attractive than synthesizing those ingredients from scratch owing to the simplicity of drug ingredients in many products and the inexpensive separation and purification technologies available (Pratama et al. 2020).

The most studied techniques for recovering active ingredients from pharmaceuticals matrices involve solvent extraction. Table 4 presents the advantages and drawbacks of solvent-based extraction methods (Sharma et al. 2019). However, these operations have the common drawbacks associated with the use of volatile and toxic organic solvents. New separation technologies based on aqueous biphasic systems were also investigated in recent research and employed to separate active ingredients from pharmaceutical solids and further to fractionate recovered compounds (Marić et al. 2021). Recently, Pratama et al. (2020) demonstrated the proof of concept of drug recycling by recovering active ingredients from unused tablets and capsules. The recovery process comprised three stages, namely, solid–liquid extraction, filtration, and crystallization, with yields of 58.7 wt%, 73.1 wt%, and 67.6 wt% for acetaminophen, tetracycline HCl, and ibuprofen, respectively (Fig. 3). Liquid chromatography analyses showed that the recovered ingredients were of high purity when compared with the standards. Other methods such as membrane separation or chromatographic separation often require high energy inputs and time-consuming steps (Basiahaqari and Gardas 2021).

Absorptive polymers, many of which are of a generic nature and available as industrial-grade bulk materials, display remarkable binding affinity and specificity for pharmaceutical compounds, showing high capacities, uptake rates, and compound selectivity that are superior to conventional porous adsorbents for extractive recovery of compounds (Figs. 4, 5) (Han et al. 2010, 2012a, 2013a). Driven by a hybrid mechanism of adsorption and solid-phase partitioning, the materials function as ‘solid-phase extractants’ for compounds dissolved in aqueous phase (Fig. 6). The process takes place spontaneously, requiring no energy input or specialized equipment, and are safer than liquid–liquid

| Brief description | Ultrasound-assisted extraction | Microwave-assisted extraction | Supercritical fluid extraction | Accelerated solvent extraction |
|-------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Extraction time   | 10–60 min                     | 3–30 min                      | 10–60 min                     | 10–20 min                    |
| Sample size       | 1–30 g                        | 1–10 g                        | 1–5 g                         | 1–30 g                       |
| Solvent use       | 50–200 mL                     | 10–40 mL                      | 2–5 mL for solid trap; 30–60 mL for liquid trap | 15–60 mL                    |
| Investment        | Low                           | Moderate                      | High                          | High                         |
| Advantages        | Easy to use                   | Rapid                         | Rapid                         | No filtration necessary      |
|                    |                               | Easy to handle                | Low solvent consumption       | Low solvent consumption      |
|                    |                               | Moderate solvent consumption  | Concentration of the extract  | Possible high selectivity    |
|                    |                               |                               | No filtration necessary       |                              |
|                    |                               |                               | Possible high selectivity     |                              |
|                    |                               |                               | Many parameters to optimize   | Possible degradation of ther- |
|                    |                               |                               |                              | molable analytes             |
|                    |                               |                               |                              |                              |
| Drawbacks          | Large amount of solvent       | Extraction solvent must       |                               |                              |
|                    | consumption                   | absorb microwave energy       |                               |                              |
|                    | Filtration step required      | Filtration step required      |                               |                              |

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 extraction processes using volatile and flammable organic solvents. In general, there are various techniques and processes for extracting active pharmaceutical compounds in solvent and aqueous phases, which may have been under-investigated in the past as means of recovering valuable compounds from expired and unwanted pharmaceuticals that are collected in bulk quantities.

The imperative of managing unwanted pharmaceuticals during and after COVID-19

With global weekly new infections exceeding 20 million and reaching new peaks, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its variants are still circulating in our communities, making the eradication of COVID-19 a distant goal in the near future (He et al. 2021; Wang and Han 2022; WHO 2022). In this context, new policies, mandates, and advice are needed to respond to the changing circumstances and urgent needs to protect the environmental and public health both under the impact of the current pandemic and beyond (Chen et al. 2021b; Han et al. 2021; Han and He 2021a, b; Han and Zhang 2020; Wang et al. 2020). In particular, the global outbreak and continuation of the COVID-19 pandemic have brought the need for collection, sorting, and reuse of unwanted pharmaceuticals to an unprecedented level. Here, we propose a new integrative policy and technology framework for the collection and recycling of expired, unused, and unwanted medicines from individuals and households (Fig. 7). In this framework, owners need to first separate their unwanted medications into opened and unopened products. Opened pharmaceutical products need to be deposited at or mailed to collection points, then sent to centralized plants for incineration. For the unopened medications, users could utilize the existing Internet and logistics infrastructure by filling in the drug information including its commercial name, expiring date, quantity, and manufacturer and submitting this information via the Internet. Using the present day’s technology, the easiest way to do this is to scan the barcode on the product package to automatically fill in the information and then to ask for the owners’ confirmation before submission. The system auto-generates free, coded mailing labels, which can be printed individually and attached on each product for shipment by leaving those in the curbside mailbox for collection. In-person pick-ups or other human contact should be avoided during the COVID-19 pandemic to reduce the risks of viral transmission (Dai et al. 2020; Sun et al. 2021). Once arrived at sorting facilities, packages are further categorized by automatic sorting facilities after reading the printed codes and retrieving the information from an internet-based database. Based on the information submitted by owners, products are categorized by their active ingredients, expiration dates, and forms, i.e., pills, capsules, powders, or gels. Unopened,
non-expiring pharmaceuticals that are in shortages of supply are preserved for further quality check and potential redistribution to patients in need. Other pharmaceuticals are sorted and prepared before being sent to specialized processing plants for subsequent extraction, recovery, and purification of their active ingredients into various products such as chemical reagents, veterinary drugs, or agrochemicals. Products with proprietary formulations are sent back to their manufacturers in bulk quantities for deformulation and reuse. After processing, quality checks

Fig. 4 (Top) a schematic diagram of the rapid column uptake apparatus for continuous capture of ethinylestradiol (EE2, CAS No. 57-63-6), a common active ingredient in birth control pills, from aqueous solutions. The column has a fixed end with an adjustable end made of Teflon to minimize solute adsorption. Filtrate was collected in a 500-mL measuring cylinder for real-time reading of filtrate volume. A pressure gauge was installed at the pump discharge to monitor the system pressure to detect blockage and leakage. When operating, the system pressure fluctuated at 10–15 psi (69–103 kPa). A regenerated cellulose (RC) filter was installed at the outlet to filter out particles in the solution after column sorption. (Bottom) rapid column retention of EE2 by polyamide 612 particles. Feed concentrations (EE2): 30–3000 µg L⁻¹ (ca. 0.1–10 µM); column loading: 1.0 g; bed volume (BV): 2.25 cm³; bed height: 2.9 cm; flow rate: 1.0–1.25 mL/min; at 25 °C. Column breakthrough was determined by liquid chromatography of samples collected at regular intervals. Adapted from Han et al. (2012b)
are implemented to ensure the purity and safety of products for their prospective use. Such an integrated policy and technology framework will not only reduce the entry of bioactive pharmaceutical compounds into the environment, but alleviate the shortage and costs of pharmaceuticals and raw ingredients by tapping into the vast amounts of expired and unwanted pharmaceuticals that are left from the current pandemic and beyond.

Conclusion

The increasing demand and use of pharmaceuticals have resulted in the accumulation of expired and unwanted pharmaceuticals in households, which may have reached unprecedented quantities in the COVID-19 pandemic. Inappropriate disposal of pharmaceuticals, an inevitable compromise due to lockdowns and resource shortage under the impact of the pandemic, poses a significant threat to the ecological system and public health. We reviewed the gaps in the current policies for the collection and disposal of household pharmaceuticals, and proposed a simple policy and technology framework for effective and sustainable management of unwanted pharmaceuticals in households in an epidemic or pandemic context. The integrated framework involves efforts from government agencies, drug manufacturers and other participating parties from the private sector, and more importantly, drug owners. Building on existing internet and logistics infrastructure, it enables owners to complete drug sorting and information gathering at the point of use, and generates labels with machine-readable codes to streamline the fine-sorting of unopened pharmaceuticals for subsequent processing or re-distribution. These will reduce the ongoing discharge of pharmaceutical compounds into the environment while recycle intact pharmaceutical products or raw chemical ingredients, thus closing the gap in current policies and practices of managing household pharmaceuticals. By circumventing the long-recognized difficulties in collecting and sorting household pharmaceuticals, this strategy may offer a feasible and timely solution to address the pressing issue of mounting unwanted pharmaceuticals while tap into the vast resource left in households around the globe.
Fig. 7  A proposed integrated policy and technology framework for managing expired, unused, and unwanted pharmaceuticals in households, an unintended and environmentally-threatening legacy of the novel coronavirus disease (COVID-19) pandemic and beyond.
Acknowledgements This work was funded by the Young Talent Support Plan of Xi’an Jiaotong University and the Natural Science Basis Research Plan in Shaanxi Province of China (2021JM-008).

Funding This work was funded by the Young Talent Support Plan of Xi’an Jiaotong University and the Natural Science Basis Research Plan in Shaanxi Province of China [Grant No. 2021JM-008].

Declarations

Conflict of interest The author declares no conflict of interest in this work.

References

Basaiaghari A, Gardas RL (2021) Ionic liquid–based aqueous biphasic systems as sustainable extraction and separation techniques. Curr Opin Green Sustain Chem 27:100423. https://doi.org/10.1016/j. cocsc.2020.100423

Caban M, Stepnowski P (2021) How to decrease pharmaceuticals in the environment? A review. Environ Chem Lett 19:3115–3138. https://doi.org/10.1007/s10311-021-01194-y

Chen B, Jia P, Han J (2021a) Role of indoor aerosols for COVID-19 viral transmission: a review. Environ Chem Lett 19:1953–1970. https://doi.org/10.1007/s10311-020-01174-8

Chen B, Han J, Dai H et al (2021b) Biocide-tolerance and antibiotic-resistance in community environments and risk of direct transfers to humans: unintended consequences of community-wide surface disinfecting during COVID-19? Environ Pollut 283:117074. https://doi.org/10.1016/j.envpol.2021.117074

Community Environmental Health Strategies (CEHS) (21 April 2017) Overview of eight medicine disposal products: report for San Francisco Department of the Environment. https://ssfenvironment.org/sites/default/files/filters/files/overviewmedicinedisposalproducts_21april2017.pdf. Accessed 10 Feb 2022

Dai H, Han J, Lichtfouse E (2020) Who is running faster, the virus or the vaccine? Environ Chem Lett 18:1761–1766. https://doi.org/10.1007/s10311-020-01110-w

Deterra (2022) Deterra drug deactivation and disposal pouches. https://deterrasystem.com/products/pouches/. Accessed 10 Feb 2022

Drug Enforcement Administration (DEA) (2021) DEA and partners announce results of 20th national prescription drug take back day. https://www.dea.gov/press-releases/2021/05/03/dea-and-partners-announce-results-20th-national-prescription-drug-take. Accessed 10 Feb 2022

Drug Enforcement Administration (DEA) (2022) Results. https://www.dea.gov/takebackday/results. Accessed 10 Feb 2022

Environmental Protection Agency (EPA) (2012) Recommendation on the disposal of household pharmaceuticals collected by take-back events, mail-back, and other collection programs. https://rcrares.com/files/14833.pdf. Accessed 10 Feb 2022

Environmental Protection Agency (EPA) (2022) Collecting and disposing of unwanted medicines. https://www.epa.gov/hwgenerators/collecting-and-disposing-unwanted-medicines. Accessed 10 Feb 2022

Food & Drug Administration (FDA) (2018) Drug disposal: dispose “Non-Flush List” medicine in trash. https://www.fda.gov/drugs/disposal-unused-medicines-what-you-should-know/drug-disposal-non-flush-list-medicine-trash. Accessed 10 Feb 2022

Food and Drug Administration (FDA) (2020b) Drug disposal: FDA’s flush list for certain medicines. https://www.fda.gov/drugs/disposal-sal-unused-medicines-what-you-should-know/drug-disposal-fdas-flush-list-certain-medicines#. Accessed 10 Feb 2022

Gao X, Bakshi P, Sunkara S et al (2018) Evaluation of an activated carbon-based deactivation system for the disposal of highly abused opioid medications. Drug Dev Ind Pharm 44:125–134. https://doi.org/10.1080/03639045.2017.1386199

Glassmeyer ST, Hinchey EK, Boehme SE et al (2009) Disposal practices for unwanted residential medications. https://www.fda.gov/files/14833.pdf. Accessed 10 Feb 2022

Government of Canada (2014) Safe disposal of prescription drugs. https://www.canada.ca/en/health-canada/services/safe-disposal-prescription-drugs.html. Accessed 10 Feb 2022

Government of the People’s Republic of China GPRC (2021) Notice on commencing household trash separations in cities at prefectural-level or above. http://www.gov.cn/xinwen/2019-06/11/content_5399088.htm. Accessed 25 Jan 2022

Guangzhou Phar Holdings (GPHL) (2018a) Family expired medicine collection mechanism. http://en.gpc.com.cn/article/199.html. Accessed 10 Feb 2022

Guangzhou Phar Holdings (GPHL) (2018b) AliHealth co-founded ‘National Coalition for Expired Medicine Recycle’. http://en.gpc.com.cn/article/175.html. Accessed 10 Feb 2022

Gwenzi W, Selvasembian R, Offiong N-AO et al (2021) Covid-19 drugs in aquatic systems: a review. Environ Chem Lett. https://doi.org/10.1007/s10311-021-01356-y

Han J, He S (2021a) Need for assessing the inhalation of micro(nano) plastic debris shed from masks, respirators, and home-made face coverings during the COVID-19 pandemic. Environ Politi 268:115728. https://doi.org/10.1016/j.envpol.2020.115728

Han J, He S (2021b) Urban flooding events pose risks of virus spread during the novel coronavirus (COVID-19) pandemic. Sci Total Environ 755:142491. https://doi.org/10.1016/j.scitotenv.2020.142491

Han J, Zhang Y (2020) Microfiber pillow as a potential harbor and environmental medium transmitting respiratory pathogens during the COVID-19 pandemic. Ecotox Environ Saf 205:111177. https://doi.org/10.1016/j.ecoenv.2020.111177

Han J, Qiu W, Gao W (2010) Adsorption of estrogen in microfiltration membrane filters. Chem Eng J 165(3):819–826. https://doi.org/10.1016/j.cej.2010.10.024

Han J, Qiu W, Hu J et al (2012a) Chemisorption of estrogen in nylon microfiltration membranes: adsorption mechanism and potential use for estrogen removal from water. Water Res 46(3):837–881. https://doi.org/10.1016/j.watres.2011.11.066

Han J, Qiu W, Meng S et al (2012b) Removal of ethinylestradiol (EE2) from water via adsorption on aliphatic polyamides. Water Res 46(17):5715–5724. https://doi.org/10.1016/j.watres.2012.08.001

Han J, Meng S, Dong Y et al (2013a) Capturing hormones and bisphenol A from water via sustained hydrogen bond driven sorption in polyamide microfiltration membranes. Water Res 47(1):197–208. https://doi.org/10.1016/j.watres.2012.09.055

Han J, Qiu W, Cao Z et al (2013b) Adsorption of ethinylestradiol (EE2) on polyamide 612: molecular modeling and effects of water chemistry. Water Res 47(7):2273–2284. https://doi.org/10.1016/j.watres.2013.01.046

Han J, Cao Z, Qiu W et al (2017) Probing the specificity of polyurethane foam as a ‘solid-phase extractant’: extractability-governing molecular attributes of lipophilic phenolic compounds. Talanta 172:186–198. https://doi.org/10.1016/j.talanta.2017.05.020

Han J, Zhang X, He S et al (2021) Can the coronavirus disease be transmitted from food? A review of evidence, risks, policies and
knowledge gaps. Environ Chem Lett 19:5–16. https://doi.org/10.1007/s10311-020-01101-x
He S, Han J (2021) Electrostatic fine particles emitted from laser printers as potential vectors for airborne transmission of COVID-19. Environ Chem Lett 19:17–24. https://doi.org/10.1007/s10311-020-01100-9
He S, Han J, Lighthouse E (2021) Backward transmission of COVID-19 from humans to animals may propagate reinfections and induce vaccine failure. Environ Chem Lett 19:763–768. https://doi.org/10.1007/s10311-020-01140-4
Health Products Stewardship Association (HPSA) (2021) One in three Canadians lack proper knowledge on where to safely dispose of unused or unwanted medications and sharps. https://www.globewire.com/en/news-release/2021/07/14/2262863/0/en-One-in-three-Canadians-lack-proper-knowledge-on-where-to-safely-dispose-of-unused-or-unwanted-medications-and-sharps.html. Accessed 10 Feb 2022
Health Products Stewardship Association (HPSA) (2022) https://healthsteward.ca/. Accessed 10 Feb 2022
Herwadkar A, Singh N, Anderson C et al (2016) Development of disposal systems for deactivation of unused/residual/expired medications. Pharm Res 33(1):110–124. https://doi.org/10.1007/s11095-015-1768-1
Insani WN, Qonita NA, Jannah SS et al (2020) Improper disposal practices of unused or unwanted medications and sharps. https://www.meeprc.gov.cn/xinxiservice/meiti/baodao/2020-03-18/14048.html. Accessed 10 Feb 2022
National Health Service (NHS) (2004) Community pharmacy contractual framework essential service—disposal of unwanted medicines. https://psnc.org.uk/wp-content/uploads/2013/07/Service-Spec-ES3-Waste-Disposal.pdf. Accessed 10 Feb 2022
National Return & Disposal of Unwanted Medicines (NRDUM) (2022) Return unwanted medicines. https://returnmed.com.au/. Accessed 10 Feb 2022
Northeast Recycling Council (NRC) (2006) Disposal of unwanted medicines: a resource for action in your community. https://web.extension.illinois.edu/unusedmeds/disposal/Unwanted_Meds_Toolkit_April_2011.pdf. Accessed 10 Feb 2022
Opar A (2006) Rising drug costs prompt new uses for old pills. Nat Med 12(12):1333. https://doi.org/10.1038/nm1206-1333
Organisation for Economic Co-operation and Development (OECD) (2021) Working party on resource productivity and waste: management of pharmaceutical household waste guidance for efficient management of unused or expired medicine. https://healthsteward.ca/wp-content/uploads/2021/08/ENV-EPOC-WPRPW2020_Management-of-Pharmaceutical-Household-Waste.pdf. Accessed 10 Feb 2022
Pratama DE, Hsieh W, Elmaamoun A et al (2020) Recovery of active pharmaceutical ingredients from unused solid dosage-form drugs. ACS Omega 5:29147–29157. https://doi.org/10.1021/acs.omega.0c03878
Recovery Village (TRV) (2021) Can unused prescription drugs be donated? https://www.therecoveryvillage.com/prescription-drug-addiction/can-unused-drugs-be-donated/. Accessed 10 Feb 2022
State Council of the People’s Republic of China (SCPRC) (2021) Answers of State Food and Drug Administration to netizen’s questions about “how to deal with expired drugs” http://www.gov.cn/hudong/2021-02/01/content_5584353.htm. Accessed 25 Jan 2022
Statista (2022a) Global pharmaceutical sales from 2017 to 2020, by region. https://www.statista.com/statistics/272181/world-pharmaceutical-sales-by-region/. Accessed 10 Feb 2022
Statista (2022b) Market share of top 10 national pharmaceutical markets worldwide in 2020. https://www.statista.com/statistics/245473/market-share-of-the-leading-10-global-pharmaceutical-markets/. Accessed 10 Feb 2022b

Sun S, Li J, Han J (2021) How human thermal plume influences near-human transport of respiratory droplets and airborne particles: a review. Environ Chem Lett 19:1971–1982. https://doi.org/10.1007/s10311-020-01178-4

Świącka K, Maculewicz J, Kowalska D et al (2022) Presence of pharmaceuticals and their metabolites in wild-living aquatic organisms—current state of knowledge. J Hazard Mater 424(Part A):127350. https://doi.org/10.1016/j.jhazmat.2021.127350

Trueman P, Lowson K, Bligh A et al (York Health Economics consortium, University of York) & Taylor D, Newbold J, Bury M et al (the School of Pharmacy, University of London) (2010) Evaluation of the scale, causes and costs of waste medicines, https://discovery.ucl.ac.uk/id/eprint/1350234/1/Evaluation_of_NHS_Medicines_Waste__web_publication_version.pdf. Accessed 10 Feb 2022

US Pharmacist (2021) Drug shortages amid the COVID-19 pandemic. https://www.uspharmacist.com/article/drug-shortages-amid-the-COVID-19-pandemic. Accessed 10 Feb 2022

Wang CQ, Han J (2022) Will the COVID-19 pandemic end with the Delta and Omicron variants? Environ Chem Lett. https://doi.org/10.1007/s10311-021-01369-7

Wang X, Han J, Lichtfouse E (2020) Unprotected mothers and infants breastfeeding in public amenities during the COVID-19 pandemic.