Development and validation of an HPLC-UV method for analysis of methylphenidate hydrochloride and loxapine succinate in an activated carbon disposal system

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ABSTRACT

Unauthorized persons run the risk of abusing unused pharmaceuticals, which may lead to significant injury. In order to keep people safe and keep the environment free of any dangers, the Food and Drug Administration (FDA) recommends that people properly dispose of any unwanted prescription medicine. Unfortunately, safety is an issue that is overlooked by many of the present disposal methods. Granular activated carbon, when added to a drug disposal pouch, provides a novel, easy, and safe way to dispose of unused or expired medicine. We examined the disposal system's deactivation effectiveness and developed a robust and verified technique for methylphenidate hydrochloride and loxapine succinate using high-performance liquid chromatography (HPLC). A C18 analytical column with the following dimensions: 250 mm × 4.60 mm and 100Å, was used to evaluate methylphenidate hydrochloride. The mobile phase consisted of acetonitrile-water with 0.05% (v/v) trifluoroacetic acid, and the flow rate was

1.5 mL/min, with a 15-minute run and a 7.8-minute retention period. Using a flow rate of 1.0 mL/min, loxapine succinate was isolated on a C8 100Å column (250 mm × 4.6 mm, 5 mm) that was kept at 25 °C. The medication had a retention duration of around 4.6 minutes, and the run time was 10 minutes. At a pH of 3.0, the mobile phase consisted of 40:60 (v/v) acetonitrile and water with 0.3% triethylamine. Both medications were dissolved in mobile phases to create reference standard solutions with a concentration of 100 mg/mL. Over the concentration range of 5-100 mg/mL for methylphenidate hydrochloride and 0.1-100 mg/mL for loxapine succinate, these techniques exhibit acceptable linearity (R2 ¼ 0.999). Research on the inactivation of these medications made good use of the test methodologies. Xi'an Jiaotong University, 2018. This website is created and hosted by Elsevier B.V. An open access paper published in accordance with the

1. Introduction

A major issue now is how to properly dispose of leftover prescription drugs. Accidental exposure, purposeful use or misuse, or both might result from storing undesired or outdated pharmaceuticals. There are social and economic ramifications to the public health problem of the possibility of abuse and addiction to prescription pharmaceuticals, even those used to treat pain. Heroin addiction affected 591,000 people in 2015, and over 33,000 people died from opioid overdoses or drug misuse disorders associated with prescription opioid painkillers [1,2]. Medication is a lifesaver when it comes to alleviating acute and severe chronic pain, but it may have disastrous consequences when prescribed excessively or without proper safety measures. The National Survey on Drug usage and Health found that after five years of non-medical prescription painkiller usage, less than 4% of individuals began using heroin [1]. Therefore, it is important to dispose of prescription medicine correctly. The disposal of two psychoactive drugs, loxapine succinate and methylphenidate hydrochloride (MPH), was the primary focus of the current investigation.By activating the neurological system, the popular prescription medicine MPH influences the brain's dopamine balance, making it an effective treatment for attention-deficit hyperactivity disorder (ADHD) [3]. When administered intranasally, MPH has a pharmacological effect comparable to cocaine, resulting in a fast release of dopamine [4]. Like morphine, it has the potential to create serious physiological dependency and is hence classified as a Schedule II, federally-controlled narcotic, due to its significant abuse potential. Because of its very satisfying euphoric effects, MPH is highly addictive [5]. Lozapine succinate is another medicine with abuse potential. For schizophrenia, doctors prescribe this medicine, which is a tricyclic antipsychotic. To control the thoughts, feelings, and behaviors often associated with schizophrenia, loxapine succinate is administered by inhibiting the activity of dopamine. The misuse of loxapine succinate is possible. since it is used for the management of schizophrenia and only gives short relief [6]. There is a higher risk of misuse for these medicines because of how often they are given.

Given the considerable misuse potential of MPH and loxapine succinate, we aimed to explore their deactivation profile via the drug disposal system. Also investigated was the analytical accuracy of the developed technique for both medications. There aren't many analytical procedures for loxapine succinate [9] and MPH [7,8] published in the literature. All of the current procedures are laborious and costly, and they rely on high-performance liquid chromatography (HPLC) or liquid chromatography-mass spectrometry (LC-MS) with various solvents used as mobile phases. Consequently, a rapid, accurate, cost-effective, and easy way to measure MPH and loxapine succinate in capsules and tablets is required. To estimate MPH and loxapine succinate in dosage forms, we created an easy-to-reproduce reverse-phase HPLC (RP-HPLC) system that follows the validation guidelines set out by the International Council for Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use [10]. Using this approach, we were able to examine how activated carbon deactivated MPH and loxapine succinate and how stable the medication was under various storage settings.

One of the methods via which unnecessary

One method to reduce medication waste is the "medicine take back program." The majority of unused prescription medications may be safely disposed of using this procedure [11]. The most convenient approach to dispose of prescriptions in home garbage is to combine them with anything unpleasant, such dirt, cat litter, or coffee grounds, if there are no medicine takeback programs or collectors recognized by the Drug Enforcement Administration (DEA) accessible. It is safe to flush potentially harmful medications down the toilet. The Food and Drug Administration (FDA) has issued several recommendations for the correct disposal of pharmaceuticals in an effort to reduce the likelihood of their inadvertent exposure or abuse [12]. A single dosage of certain medications may be lethal, especially if taken by someone other than the intended patient; this is particularly true with fentanyl patches [13]. Because combining these pharmaceuticals with things like coffee grinds or cat litter won't render them inactive, and because doing so might contaminate water systems, none of the aforementioned methods are environmentally safe [14].

When it comes to recycling, activated carbon is a great option.

medicine, since it binds chemical substances via the adsorption mechanism [15]. The active pharmaceutical ingredient (API) clings to the surface area with ease because of the material's porosity [16]. More study on appropriate disposal strategies for highly addictive prescription drugs is urgently needed, although this technology has not yet been investigated to address the drug disposal issue.

Deterras is an activated carbon-based drug disposal device, and the purpose of this research was to assess its deactivation effectiveness. The active pharmaceutical ingredient (API) is rendered inactive by a physical adsorption process, which is the foundation of MAT12's Molecular Adsorption Technology [17]. In this context, "deactivates" means that the physical adsorption process between the active ingredient and the activated carbon is permanent. We looked at the drug disposal of two hypothetical, potentially addictive, psychoactive prescription drugs: MPH and loxapine succinate.

The suggested drug deactivation system provides an innovative, safe, and efficient way to dispose of leftover, unused, or expired medicine by using granular activated carbon in a pouch. The purpose of this research is to examine the effect profile of MPH and loxapine succinate utilizing an activated

solution for the disposal of carbon. To accurately verify the system's efficiency, a technique was developed and loxapine succinate and MPH were va-lidated.

2. Experimental

2.1. *Chemicals and reagents*

MPH and loxapine succinate were purchased from Sigma-Al- drich (St. Louis, MO, USA). Dosage forms: generic MPH (20 mg, CorePharma) tablets and loxapine succinate (20 mg, Lannett) capsules were provided by Verde Environmental Technologies Inc. (Minnetonka, MN, USA). The Deterra^{s} drug deactivation system (the pouch containing 15 g of granular activated carbon within a water soluble film reservoir) was also provided by Verde En- vironmental Technologies Inc. Acetonitrile (ACN), methanol and trifluoroacetic acid (TFA), of HPLC grade, were obtained from Fisher Scientific (Pittsburgh, PA, USA). Nylon filters (0.22 mm) used for sample filtration were purchased from Medsupply Partners
(Atlanta, GA, USA). Deionized water (DI) (MQ res: 18.2 MΩ·cm,
permC: 7.4 mS/cm) was generated with a Milli-Q Direct 8 (Milli- pore, Bedford, MA, USA). All
other reagents used were of HPLC or ACS grade.

2.2. *Instrumentation*

The analysis was carried out using a Waters Alliance HPLC system (e2695 separating module) (Waters Co., Milford, MA, USA) with photodiode array detector (Waters 2996) with an autosampler and column heater. Data were collected and pro- cessed using Empower™ software (Version 2) from Waters. RP-HPLC methods were used for the quantification of all samples.

2.3. *Chromatographic conditions*

The assay method for MPH and loxapine succinate was devel- oped, validated and applied to study the drug deactivation profile of both drugs. This method was also used to predict the storage stability of MPH and loxapine succinate in water. The mobile phase was filtered through a 0.2 mm filter (GNWP 0.2 mm; Millipore, Bedford, MA, USA) and degassed using sonication.

MPH was analyzed using a C_{18} Phenomenex Kinetex, biphenyl (250 mm × 4.6 mm, 100 Å) column set at 25 °C with methanol (0.1% formic acid (FA)) and water (0.1% FA, pH 6.8 adjusted using ammonium hydroxide) (50:50 v/v) as the mobile phase. A flow rate of 1 mL/min with an injection volume of 25 mL and an ab- sorption wavelength of 258 nm were used. The run time was 15 min and the retention time of the drug was around 7.8 min.

For the analysis of loxapine succinate, the compound was se- parated on a C_8 Phenomenex Luna (250 mm × 4.6 mm, 5 mm) at an ambient temperature with acetonitrile (ACN) and water (0.3% (v/v), trimethylamine, pH 3) (40:60 v/v) as the mobile phase. A sample volume of 10 mL was injected at a flow rate of 1 mL/min and analyzed at an absorption wavelength of 211 nm. The run time was 12 min and the retention time of the drug was around 4.6 min.

2.4. *Preparation of stock and working standards solutions*

All standard solutions for MPH and loxapine succinate were prepared using deionized water to give a working standard in the range of 5–100 mg/mL and 0.1–100 mg/mL, respectively. Stock standard solutions of MPH and loxapine succinate were prepared at a concentration of 1 mg/mL in deionized water and stored at 4 °C. Working standard solutions of MPH and loxapine succinate were prepared by diluting the standard stock solution with deio- nized water to yield concentrations of 0.1, 0.25, 0.5, 1, 2.5, 5, 10, 25, 50 and 100 mg/mL. Quality control (QC) concentrations were then prepared at 50, 75 and 100 mg/mL for MPH and 25, 50 and 100 mg/mL for loxapine succinate control samples.

2.5. *Method validation*

HPLC methods were validated to ensure consistent, reliable, and accurate results to determine the levels of two psychoactive medications in all samples. The HPLC methods were validated in terms of sensitivity, linearity, accuracy, precision, specificity and robustness. Method validations for both drugs were performed over a 3-day period.

2.5.1. *Determination of the limit of detection (LOD) and limit of quantification (LOQ)*

The LOD was determined by injecting lower concentrations of MPH and loxapine succinate sequentially until a signal (peak)-to-noise ratio was obtained. The LOQ , which is the lowest quantifiable concentra- tion, was also determined from the range of concentrations analyzed for the LOD determination.

2.5.2. *Evaluation of linearity*

Standard solutions were evaluated for the linearity within a concentration range of 5–100 mg/mL for MPH and 0.1–100 mg/mL for loxapine succinate. The peak area was plotted against drug concentration and the linearity was thus calculated by the linear regression equation $y = mx + c$, where y represents the peak area and x represents either the MPH or loxapine succinate con- centration in mg/mL. A correlation coefficient of approximately 0.999 or more was considered as desirable for all calibration curves.

2.5.3. *Determination of accuracy and precision*

The inter-day validation was conducted with three sets of three QC samples of different concentrations for MPH (50, 75 and 100 mg/mL) and loxapine succinate (25, 50 and 100 mg/mL). These samples were evaluated for three days by generating a calibration curve for each day. As for the intra-day validation, six sets of three different drug samples were assayed and evaluated with reference to one calibration curve on the same run. The accuracy and pre- cision values were calculated using a standard formula, as per the ICH guidelines. The accuracy and precision of the methods were determined for both intra-day and inter-day variations using multiple analyses of different concentrations of samples on three different days.

2.5.4. *Specificity*

The specificity of each assay was determined by comparing the chromatograms of the blank solution (water) with that of the drug standard solution (drug in water) of varying concentrations. Furthermore, the specificity of the improved HPLC method was determined by analyzing the MPH and loxapine succinate dosage forms in activated carbon. Observations were made for any interfering peaks generated during the analysis.

2.5.5. *Robustness*

Robustness is a measure of method's capacity to remain unaffected by small deliberate changes. The chromatogram resolution and retention behavior were evaluated for any changes in flow rate (70.05 mL/min), organic solvent ratio (75% methanol), and pH (70.5).

2.6. *Stability*

The short-term stability of MPH and loxapine succinate under storage conditions was evaluated using three standard concentrations (10, 25 and 50 mg/mL) (*n* = 3) stored for one week at varying temperatures of 4 °C, 25 °C, and — 20 °C. All stored standard solutions were analyzed using freshly prepared calibration standards. The stability of MPH and loxapine succinate was assessed by comparing the concentration of both drugs in each solution before and after the storage period.

2.7. *Deactivation of pharmaceutical dosage forms using an activated carbon disposal system*

The assay method was applied to support the deactivation profile of MPH and loxapine succinate in the presence of an activated carbon drug disposal system. The system consisted of a pouch containing 15 g of granular activated carbon packaged within a water soluble inner film reservoir. The deactivation of tablets and capsules as dosage forms were examined over 28 days using the model psychoactive medications. Ten MPH and loxapine succinate tablets (20 mg each) were placed into individual pouches separately followed by addition of 50 mL of warm tap water at a temperature of about 43 °C. To mix the activated carbon and warm water properly, pouches were shaken for 10 s at a rate of one shake per second. This was followed by a waiting period of 30 s to release the air bubbles from the charcoal. After ensuring that all of the medications settled to the bottom of the pouch, the pouches were sealed, stored upright, and left undisturbed at room temperature. Separate pouches were set up for each time point at 8 h, 1, 2, 4, 7, 14, 21 and 28 days and samples were collected from pouches to examine deactivation of drug during the study. Before taking samples, pouches were mildly shaken from side to side to ensure the medications were mixed homogenously in the pouch. Samples were then filtered with a 0.22 mm nylon filter and analyzed by the validated HPLC methods. The deactivation rate was calculated as follows:

% Deactivated = [(Initial amount of drug in pouch − Final amount of drug in pouch)/ Initial amount of drug in pouch] × 100.

2.8. *Desorption study*

At the end of the adsorption study (28 days), the pouch contents were transferred to 500 mL bottles, and 200 mL of tap water was added to each bottle. The samples were shaken for 1 h at 150 rpm, stored upright for 23 h at room temperature, then filtered and analyzed by HPLC. The water was then completely replaced with 250 mL of 30% ethanol, shaken for an additional hour, and stored for 23 h at room temperature. After that, samples were taken from the container, filtered and analyzed by HPLC.

3. Results

3.1. *Method development and optimization*

The most suitable isocratic condition to resolve MPH with a C_{18} column, after the chromatographic conditions were optimized for specificity, resolution and retention time, was a mobile phase consisting of methanol (0.1% FA) and water (0.1% FA, pH 6.8) (50:50, v/v). For loxapine succinate, analyte was separated on a C_8 column and the mobile phase consisted of ACN and water (0.3% (v/v) triethylamine, pH 3) (40:60, v/v). When the pH of the mobile phase was increased or when a higher percentage of organic solvent was used, the resultant chromatogram had an increase either in background noise or peaks indicating the tailing effect. Thus,

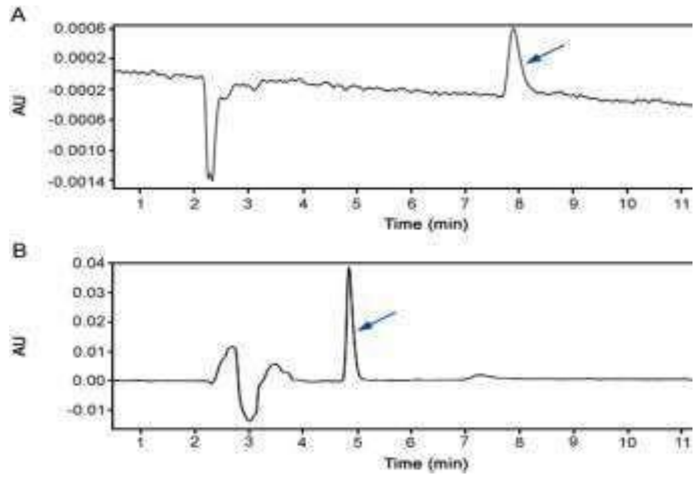

Fig. 1. Representative chromatograms of (A) methylphenidate hydrochloride standard (25

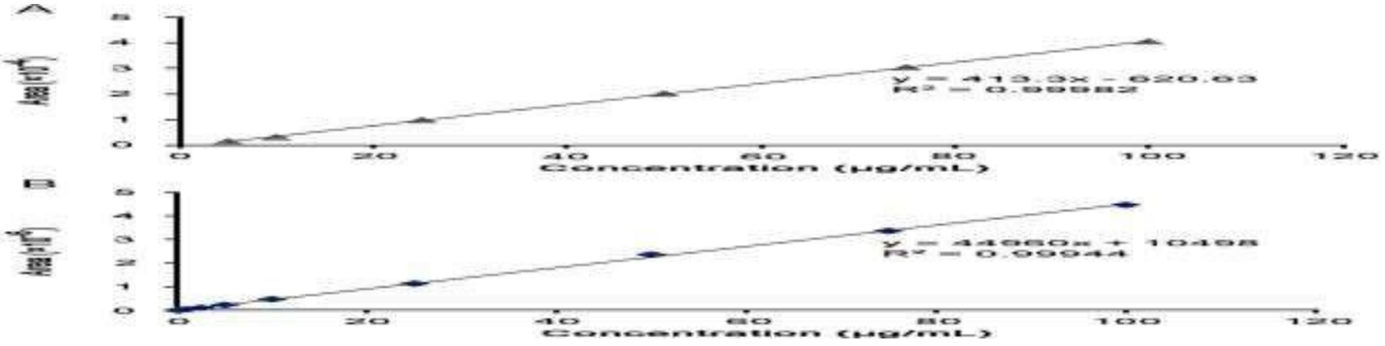

Fig. 2. Linearity of the HPLC method for analysis of (A) methylphenidate hydrochloride and (B) loxapine succinate.

3.2. *Method validation*

The method was validated according to the validation of ana- lytical procedures provided in the ICH guidelines and draft gui- dance for the industry: analytical procedures and methods validation.

3.2.1. *Linearity and range*

A linear relationship was obtained between the peak area for both drugs and corresponding concentrations. The mean standard calibration curves are presented in Fig. 2. The calibration curves exhibit linearity over the concentration range of 5–100 mg/mL for MPH and 0.1–100 mg/mL for loxapine succinate with regression coefficient values greater than 0.999. The methods ($R^2 = 0.999$) provided a good correlation between the peak area and drug concentration.

3.2.2. *Sensitivity*

The LOD was evaluated by determining the minimum levels of concentration for MPH and loxapine succinate that could be de- tected using this analytical method. The LOQ was studied by estimating the minimum concentration that could be quantified with acceptable accuracy and precision. The LOD values for MPH and loxapine succinate were determined to be 1.38 mg/mL and 0.07 mg/mL, and the LOQ values were 4.17 mg/mL and 0.20 mg/mL, respectively.

3.2.3. *Accuracy and precision*

The intra-day and inter-day accuracy and precision of the assay method were studied by analyzing replicates at 3 different concentration levels: 50, 75 and 100 mg/mL (MPH) and 25, 50 and 75 mg/mL (loxapine succinate) (Table 2). The intra-day and inter- day variation was found to be within 0.8%–6%. The intra-day and inter-day accuracy was found to be within 90%–110%.

Under the stated experimental conditions, the precision (RSD) values were a maximum of 6% and the accuracy values were within a range of 94%–99% for MPH and the precision (RSD) values were at a maximum of 4.31% and the accuracy values were within a range of 98%–105% for loxapine succinate.

3.2.4. *Robustness*

The robustness of the method was determined by deliberately changing the experimental conditions. The resolution of MPH and loxapine succinate was evaluated and the effects of changes in flow rate 70.05 mL/min, mobile phase composition 75% (for methanol), and pH 70.5 were evaluated. Both the analytes, MPH and loxapine succinate, were adequately resolved under varied chromatographic conditions. Tables 3 and 4 demonstrate all the varied chromatographic conditions performed in the methods, and the % recovery for the MPH and loxapine succinate standard

Table 1
HPLC isocratic method for methylphenidate hydrochloride and loxapine succinate.

Parameter	Methylphenidate hydrochloride	Loxapine succinate
Column	Kinetex Biphenyl C_{18} 100Å (5 mm, 250 mm × 4.6 mm)	Phenomenex Luna C_8 100Å (5 mm, 250 mm × 4.6 mm)
Mobile phase	Methanol (0.1% formic acid) and water (0.1% formic acid) at pH 6.8 and a composition of 50:50 (v/v)	Acetonitrile and water (0.3% triethylamine) at pH 3.0 and a com- position of 40:60 (v/v)
Flow rate (mL/min)	1.0	1.0
Injection volume (mL)	25	10
Wavelength (nm)	258	211
Retention time (min)	7.8	4.6

Table 2
Intra-day and inter-day accuracy and precision of HPLC assay for methylphenidate hydrochloride and loxapine succinate.

Medications	Reference value (μg/mL)	Intra-day (*n* = 6)			Inter-day (*n* = 3)		
		Mean 7 SD (μg/mL)	Precision (%)	Accuracy 7 SD (%)	Mean 7 SD (μg/mL)	Precision (%)	Accuracy 7 SD (%)
Methylphenidate hydrochloride	50	48.59 7 2.09	4.31	97.19 7 3.52	49.33 7 1.76	3.57	98.66 7 4.19
	75	73.05 7 2.92	4.00	97.40 7 3.57	74.11 7 2.68	3.61	98.81 7 3.90
	100	94.56 7 5.70	6.03	94.56 7 4.76	97.10 7 4.76	4.90	97.10 7 5.70
Loxapine succinate	25	24.90 7 0.20	0.81	99.59 7 0.80	24.98 7 0.27	1.07	99.94 7 1.06
	50	52.29 7 0.49	0.94	104.57 7 0.98	50.37 7 2.04	4.05	100.74 7 4.08
	75	74.25 7 0.86	1.16	99.90 7 1.15	73.90 7 0.74	1.00	98.53 7 0.99

Table 3
Robustness of the method for methylphenidate hydrochloride.

Parameter	Changes	Retention time (min)	Area	Concentration (µg/mL)
Flow rate (mL/min)	0.95	8.2	11,852	27.47
	1.00	7.8	11,958	27.70
	1.05	7.4	10,985	25.59
% of methanol in MP	45	10.7	11,608	26.94
	50	7.8	11,958	27.70
	55	6.0	11,430	26.56
pH	6.3	7.8	12,03	27.86
	6.8	7.8	11,958	27.70
	7.3	7.8	12,953	29.85

Table 4
Robustness of the method for loxapine succinate.

Parameter	Changes	Retention time (min)	Area	Concentration (µg/mL)
Flow rate (mL/min)	0.95	4.6	2,686,615	29.37
	1.00	4.4	2,584,496	27.97
	1.05	4.2	2,445,796	26.73
% of methanol in ACN	35	6.0	2,448,612	26.76
	40	4.4	2,458,234	26.87
	45	3.7	2,588,303	28.29
pH	2.5	4.8	2,505,610	27.39
	3.0	4.4	2,458,234	26.87
	3.5	5.0	2,478,983	27.09

concentration, 25 µg/mL, was found to be within an acceptable range of 80%–120%.

3.2.5. *Specificity*

Specificity was used to test the ability of the assay method to eliminate the effects of all interfering substances on MPH and loxapine succinate peak results, specifically by comparing the chromatograms to the blank samples. The validated method showed that the drug contents eluted with no interfering peaks generated by the excipients in the marketed products.

3.3. *Stability*

Three concentrations (10, 25 and 100 mg/mL) of MPH and loxapine succinate in water ($n = 3$) were analyzed to assess the stability. The stability was assessed after storage for one week at different storage temperatures. Stability assessments indicated that both drugs were stable in water for 1 week at room temperature (25 °C), 4 °C and — 20 °C. The % accuracies for the MPH and loxapine succinate standard concentrations were found to be within acceptable ranges of 92%–107% and 95%–105%, respectively (Fig. 3).

3.4. *Deactivation study*

The deactivation of MPH and loxapine succinate with a drug disposal system was observed over 28 days. After the addition of the dosage forms and water into the pouches, adsorption started immediately. As shown in Fig. 4, 96.9% of loxapine succinate and 99.9% of MPH were adsorbed and deactivated by the drug disposal system at the end of 8 h. Both drugs continued to be adsorbed over time, and at the end of 28 days, 100% drug deactivation was achieved. The deactivation profiles for both drugs are presented in Fig. 4.

3.5. *Desorption study*

A desorption or washout study was performed following the deactivation study in order to determine the potential for leaching of the active ingredients from activated carbon in the presence of water and alcohol. To test the robustness of the system, desorption was examined in the presence of a larger volume of water (250 mL) followed by 30% ethanol (250 mL). The results show that after 28 days, no drug leached out after one day of desorption in the presence of water, and only 1% of the drug was leached out from the activated carbon in the presence of the organic solvent ethanol (Table 5).

4. Discussion

Lack of awareness of the need for proper disposal of prescription medication leads to abuse and environmental contamination, and this problem has been increasing steadily [18]. Thus, the potential for abuse of prescription medications should be addressed in the medical community and by primary care practitioners.

MPH and loxapine succinate are examples of two commonly abused drugs, and we investigated their deactivation efficiency by using an activated carbon disposal system. MPH and loxapine succinate were successfully detected with RP-HPLC, utilizing buffered water and organic solvents (Fig. 1).

In the present study, as MPH (logP: 2.2) and loxapine (logP: 3.6) are lipophilic compounds, C_{18} reverse-phase column was used for MPH analysis and C_8 for loxapine. MPH and loxapine succinate are weak bases with pKa values of 8.8 and 7.1, respectively. MPH was separated using methanol and water as the mobile phase, and the pH was adjusted to 6.8. Similarly, loxapine was separated using ACN and water as the mobile phase with the pH adjusted to 3. More than 99% ionization was achieved for both drugs at their respective pH values, with corresponding log D value of 0. The concentrations of methanol and acetonitrile were optimized to give a symmetric peak with a reasonable run time. A detailed layout of the HPLC parameters used in the developed method is discussed in Table 1. The reliability and sensitivity of the validated methods were ensured with good linearity, accuracy, and precision within the ICH and FDA limits for the method validation of analytical samples.

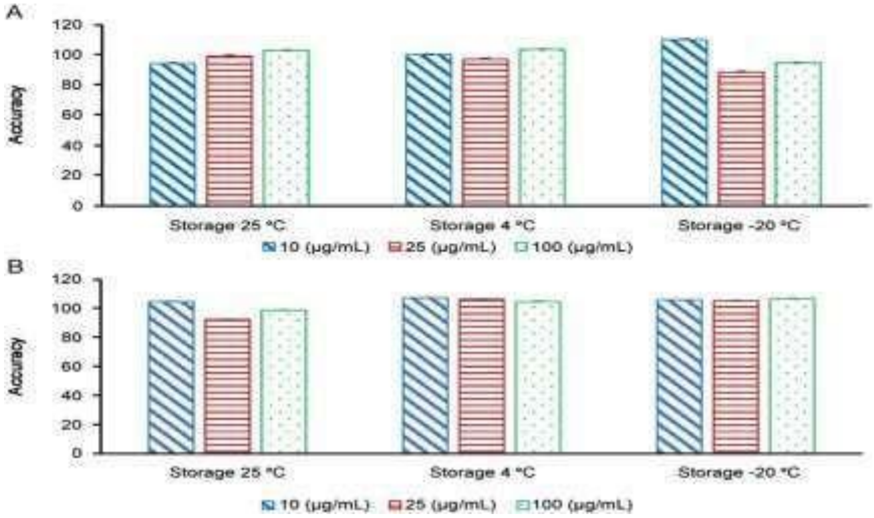

Fig. 3. Stability of (A) methylphenidate hydrochloride standards (10, 25 and 100 µg/mL) and (B) loxapine succinate standards (10, 25 and 100 µg/mL) at different temperatures, 25 °C, 4 °C and — 20 °C for one week.

In addition, analysis of the marketed preparation of MPH and loxapine succinate with the validated assay methods showed that the drug contents eluted with no interfering peaks generated by the excipients in the marketed products. Results for robustness are summarized in Tables 3 and 4, and the methods were found to remain unaffected by changing the method parameters. The study also presented that both MPH and loxapine succinate were stable in water at different temperatures, 25 °C, 4 °C and — 20 °C, for the storage over the period of one week. Both validated methods were applied to examine the ability of the disposal system to deactivate two commonly abused prescription drugs, MPH and loxapine succinate.

According to the FDA guidelines, all medications being deposed of in household trash should be mixed with unpalatable substances such as cat litter or coffee grounds, or should be flushed down the toilet [11]. However, these procedures do not deactivate the drug, and the drug is still available in the active form; this can lead to

Table 5
Amount of the drug leached from activated carbon during desorption study.

Medication	% leached in water	% leached in ethanol
Methylphenidate hydrochloride	0.0	1.0
Loxapine succinate	0.0	0.0
Average	0	0.5

contamination of the environment and the water system. Our studies were consistent with the studies performed by Har- wadkar et al. [15], in which various deactivating agents were tes- ted, and activated carbon was found to be the most efficacious deactivation agent, causing complete deactivation for various

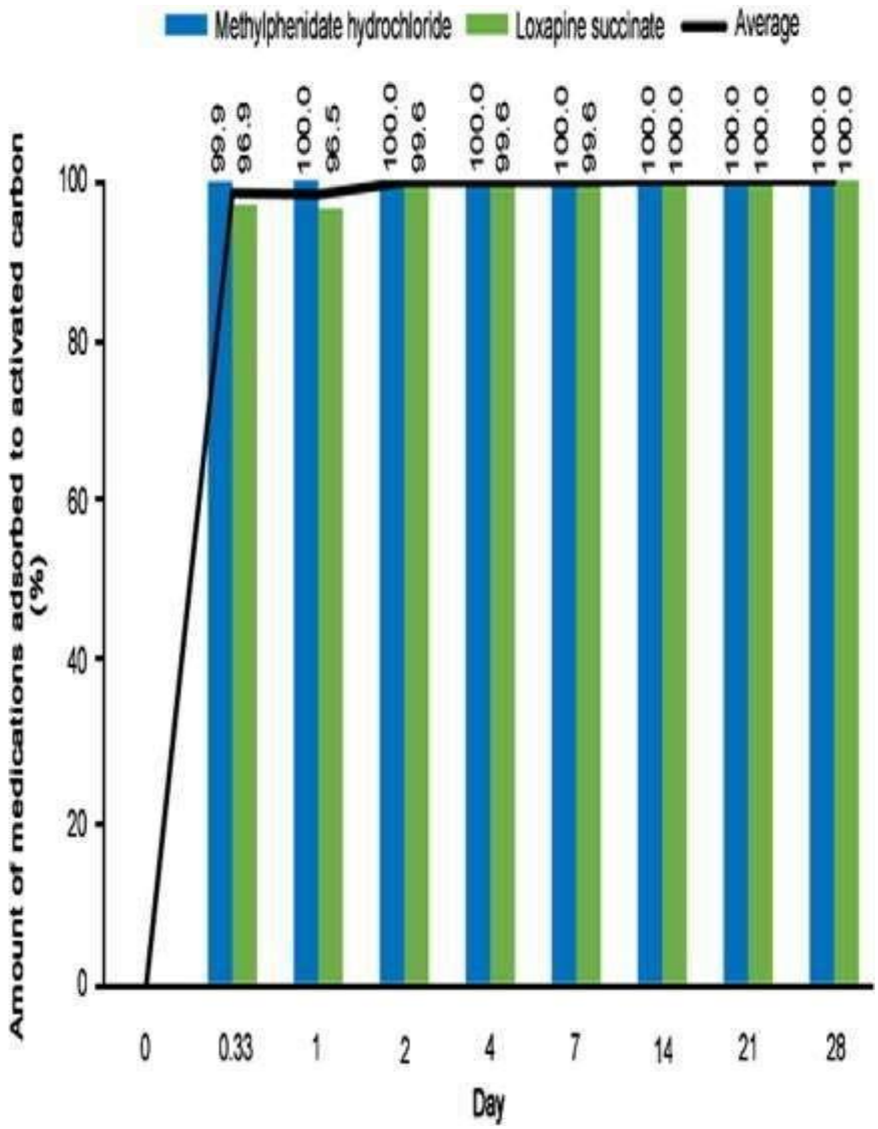

Fig. 4. Deactivation profile of methylphenidate hydrochloride and loxapine succinate dosage forms.

dosage forms of medications such as dexamethasone tablets and amoxicillin capsules.

Using activated carbon is an effective technique to remove contaminants or pollutants from the water or air, but various factors can influence the adsorption capacity. Generally, factors such as the pH of the solution, pKa, hydrophobicity and molecular weight of the compound, and type of the activated carbon used may influence the adsorption of molecules to the activated carbon, and thus affect the deactivation capability of the system. The activated carbon present in our disposal system pouch is specific for the molecular size, as it is based on MAT$_{12}$ Molecular Adsorption Technology [19]. This renders the drug irretrievable by binding to it through a physical adsorption process [20].

The pH of the drug disposal system, comprising of activated carbon in water, was close to neutral (pH 6.8), and was found to remain unaffected by the addition of drugs (MPH and loxapine succinate). It has been reported that the optimal pH for maximum adsorption capacity is near 7 [21]. The results obtained in our study are in accordance with this, as more than 95% deactivation of the drugs was achieved within 8 h.

The hydrophobicity of the compound is another factor that determines the adsorption efficiency of the activated carbon, and thus affects the hydrophobic interaction between the activated carbon and the adsorbent [22,23]. Westerhoff et al. [24] observed that the removal efficiency of the contaminants was dependent on the logK$_{ow}$ values, which are indicators of the hydrophobicity of the molecules. In addition, another study found that the hydrophobic character of the compound also influences the uptake rate of the compound [25]. The study determined that the adsorbent (polar compounds) and adsorbate (activated carbon) displayed van der Waals force of interaction toward each other, thus leading to a better adsorption capacity. Thus, hydrophobicity not only determines the adsorption capacity, but also influences the rate of adsorption to the activated carbon. In our study, MPH (logP: 2.2) [26] and loxapine (logP: 3.6) [27] were both moderately lipophilic compounds, and hence showed more than 99% deactivation after 24 h of interaction with the activated carbon (Fig. 4). Our results were consistent with the previous studies presented in the literature [28].

The MPH used were in tablet form; this could have led to faster adsorption to activated carbon compared to that of capsules. Solid dosage forms like capsules may require more dissolution time in water before adsorption can occur; this could cause a slight delay in the rate of adsorption of loxapine succinate capsules compared to that of MPH tablets. Previous research has noted the influence of molecular weight and hydrophobicity of the adsorbate on the adsorption capacity of activated carbon. In our study, we did not observe any significant differences in the adsorption capacity of the disposal system between these two model drugs.

The efficiency of the deactivation system to retain the adsorbed drug was further tested by examining the desorption. This study was aimed to simulate landfill situations which provide exposure to large volumes of water and some organic solvents. Our results showed that the activated carbon used in our study was efficient in adsorbing the drug, and did not release on exposure to these stress conditions. In the desorption study, we observed that no drug was leached out in the presence of water and, on an average, less than 1% of the drug was leached out in the presence of ethanol (Table 5).

The findings of the research indicated that the adsorption efficiency of the activated carbon was good, and it would not release the drug back into the environment when the contents of the pouch were present in the landfill, thereby providing a safer disposal method compared to other traditional alternative methods suggested by the FDA for drug disposal. This drug disposal pouch would therefore eliminate the risk of abuse of unused prescriptions, and also solve the problem of environmental and water pollution. Hence, the Deterra activated carbon disposal system provides a simple and convenient way to dispose of these medications in normal trash, without causing any environmental or safety risks.

5. Conclusions

An isocratic RP-HPLC method for the determination of MPH and loxapine succinate was developed, and is precise and reliable. The regression line equation is capable of reliably predicting the drug concentration in the range of 5–100 mg/mL and 0.1–100 mg/mL for MPH and loxapine succinate, respectively, from the peak area obtained. The stability assessments revealed that both drugs were stable in water at 25 °C, 4 °C and — 20 °C for one week. The method was successfully validated and allowed the reliable, sensitive, robust, and specific detection of MPH and loxapine succinate in a common marketed preparation.

This method was then used to test the efficiency of an activated carbon-based drug disposal system for adsorption of MPH and loxapine succinate from dosage forms to activated carbon. The system was very efficient, with more than 99% drug deactivation achieved after 24 h, and less than 0.5% of the drug was released from activated carbon by an extraction protocol that mimicked a landfill situation.

Thus, this drug disposal system offers a simple and safe method to be used by patients. These results are encouraging, and provide the basis of an environmentally friendly method of drug disposal.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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