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In vitro Assessment of the Adsorption Efficacy of Activated Charcoal versus Kaolin on some used Medications of Narrow Index of Safety

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Abstract

This work aims to study the in vitro adsorption capacity of three types of adsorbents, namely, activated charcoal, light kaolin, and heavy kaolin, at a concentration of 0.2% (w/v) on high dosages of specified medicines possessing a small margin of safety (diazepam, metoclopramide, theophylline, digoxin, and diltiazem HCl). This test was executed by dissolving the drugs in the company of adsorbents using simulated gastric fluid as a medium. Evaluation of the efficiency of such adsorbents as antidotes in the treatment of oral overdoses of these medicines was necessary to designate the success of the process. It was found that activated charcoal had the capability of virtually completely adsorbing all of the drugs. Both the light and heavy versions of kaolin were only able to produce a restricted quantity of the abovementioned drugs.

Keywords: Adsorption, Charcoal, Digoxin, Heavy kaolin, Light kaolin

Introduction

Dissolved, liquid and gaseous ions, atoms and solid molecules combine on solid surfaces through the adsorption process, a property that includes the adhesion of adsorbate molecules to the surface of the adsorbent. Adsorption is different from absorption, which is a physical or chemical phenomenon that involves the involvement of the solvent within the liquid or solid phase of the solvent. There are many applications of adsorption in pharmaceutical sciences, including the formulation of drugs, especially the use of surface tension reduction materials to obtain stable-spreading drug mixtures, as well as increasing the solubility of poorly water-soluble drugs, as well as useful in drug delivery systems and masking the unwanted taste of some drugs by adhering to the excipients [(1)].

Activated charcoal (AC) is a black powder that is odorless, tasteless, has superior porosity power, and is non-toxic. The phenomenon of adsorption encloses a multi-faceted application significance, as it is the adsorption of small molecules, ions or atoms on the surfaces of adsorbents that have an extended surface area. [(2)]. AC is considered as an effective adsorbent particularly for medication of low molecular weight. Drug poisoning is common worldwide and occurs when drugs are swallowed or inhaled, as well as through injection and skin contact, and may lead to severe damage to the body and even death. Poisoning could occur with the many medications particularly those of narrow margin of safety. The employing of some adsorbents such as AC is beneficial in the inhibition of excessive absorption of drugs [(3,4)]. Hassen HJ et *el* investigated the power of AC to adsorb fexofenadine and the impact of the multiple dosing on quantity adsorbed. The results revealed that the percentage of adsorbed drug was decreased by increasing the pH and increased with time of contact [(4)]. AC is employed in for treatment of poisonings and overdoses as it binds to the poison and hinders its absorption in biological systems [(5,6)].

Activated carbon also has the ability to purify air and filter waste water [(7,8)]. Kaolin is a crystalline material also called Kaolinite. Kaolin and other clays have been employed for medicinal pursuits; their therapeutic activity is attributed to their adsorption capability. There are considerable investigations on the adsorption of amino acids as well as other biomolecules and biopolymers on clays like kaolin [(9)]. Diazepam (DZ) is marketed as 2 mg, 5 mg, or 10 mg tablets. Overdose of DZ may diminish breathing

or even arrest it ultimately [10-12]. Metoclopramide (MC) is an antiemetic drug; its overdose results in extrapyramidal side effects [13]. Theophylline (TH) possesses bronchodilatation characteristics that relax muscles in the lungs and chest, reduce allergic reactions, has narrow therapeutic window, high level of TH can cause fatal adverse effects [14]. Diltiazem HCl (DT) is categorized as a calcium channel blocker, that possesses antihypertension ability through the heart and blood vessels muscles relaxing, and its overdose may be lethal [15]. Digoxin (DG) is a cardiac glycoside utilized for heart failure, and arrhythmias treatment. Overdose of DG may lead to death [16,17]. The objective of this research was to investigate the effect of AC, LK, and HK at 0.2% w/v on the in vitro dissolution of high doses (10 tablets) of some medications (DZ, MC, TH, DT, and DG). Release studies were carried out in simulated gastric fluid to determine the activity of these adsorbents as antidotes to be used for the treatment of oral overdoses of narrow safety index medications.

Materials and Methods

Chemicals and drugs

Activated charcoal (AC) (Calgon Carbon Corporation, India). Heavy kaolin (HK) (Kaylene division, Australia). Light kaolin (LK) (Gerhard K.G, Germany). Diazepam tablets (DZ) 10 mg tablets, Metclopramide tablets (MC) 5mg tablets, and Theophylline (TH) 120 mg tablets (Samara-Iraq). Digoxin (DG) 0.25mg tablets (Activs, UK). Diltiazem (DT) 60mg tablets (Menarini International, Italy). Acetonitrile, HPLC grade; E. (Merck, Darmstadt, Germany). Purified water was obtained from Milli-Q purifying.

Methodology

dissolution and release profile of the tested medications tablets

Ten tablets of each of the 5 tested medications were placed in each dissolution jar (apparatus II) [Veego, India] containing one liter of 0.1 M HCl pH (1.2) for 1 h and 100 rpm. Samples of 5 ml were withdrawn at appropriate time intervals, and the volumes of samples were replaced with the same dissolution media solution after each withdrawal to keep a constant sink condition. Samples were filtered, diluted, and the absorbance was measured for each drug against a blank using a UV spectrophotometer at λ_{max} of 242, 240, 263 and 236 nm for DZ, MC, TH, and DT, respectively, except in the case of digoxin, which was assessed by HPLC [18] and the results were reported. The experiments were done for all of the tested medications separately [19,20].

Effect of adsorbents on the release percentage of drugs

Karaman R et al (2018) method was employed to assess the effect of AC, LK, and HK on the used medications [19]. The release studies mentioned above were repeated using 10 tablets of each drug with the addition of 2 g of powdered AC, and the experiment continued for the same period. The same experiment mentioned above was repeated by using 2g of LK and HK (in separate experiments), and the same parameters were determined regarding the release process of the tested medications, the magnitude of adsorption by the adsorbents, and the amount released with and without the presence of adsorbents after 30 minutes was compared.

Results and Discussion

The release profiles of DZ in 0.1 N HCl and in the presence of AC, LK, and HK are shown in Figure 1, where only 7% of DZ was released after 30 min in the presence of AC, while its release in the presence of HK and LK was about 86.5% and 80.5%, respectively, but its release without any adsorbents was > 90%. Figure 2 revealed that the release of MC was about 91.3%, while in presence of HK, LK, and AC was 79.9%, 86.5% and 1.5%, respectively. The release of TH revealed in Figure 3 was about 67.1%, while in the presence of HK, LK, and AC, it was 60.1%, 58.2%, and 4.6%, respectively. The release of DT tablets in the medium (0.1 N HCL) was 57.2%, while in existence of HK, LK, and AC, it was 49.2, 50.3%, and 2%, respectively, as represented in Figure 4. The release of DG tablets was 61%, while in the existence of HK, LK, and AC, it was 56.2%, 58.1% and 0%, respectively, as represented in Figure 5.

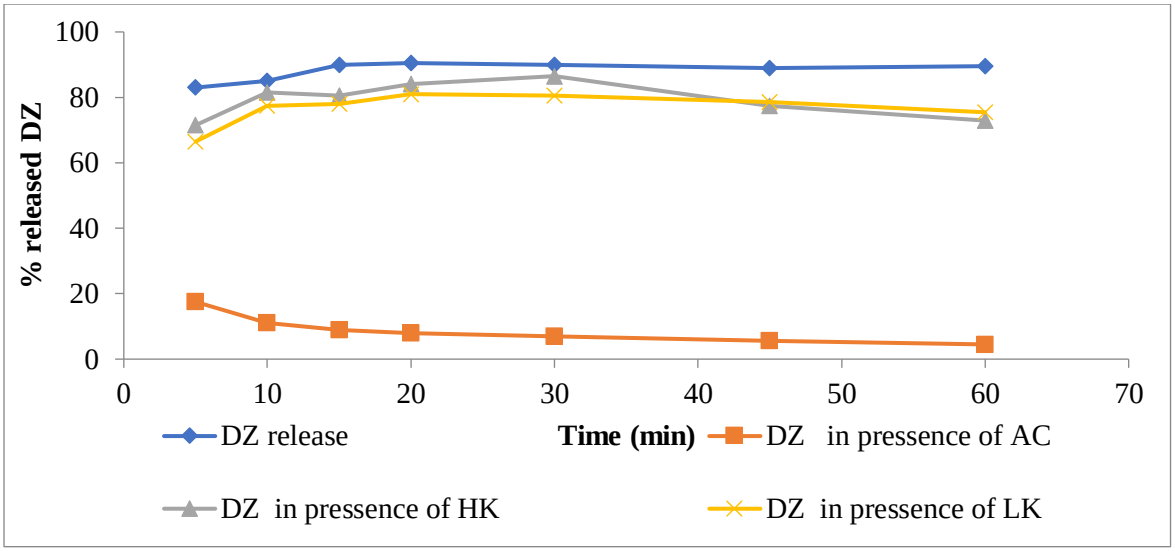

Figure 1. Release profile of DZ in 0.1 N HCl and in the presence of AC, LK and HK

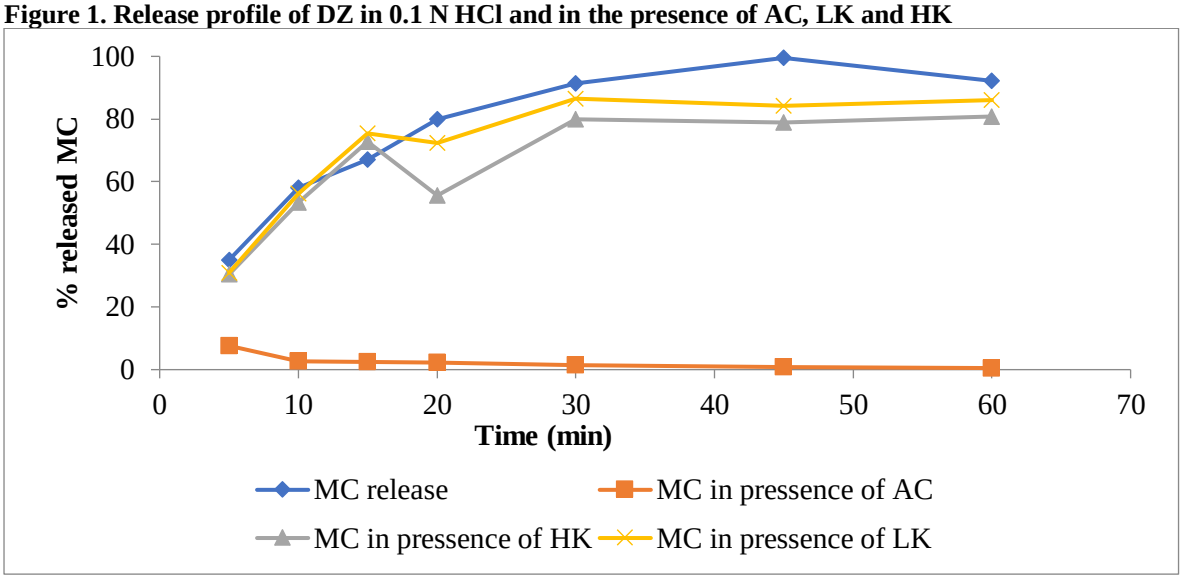

Figure 2. Release profile of MC in 0.1 N HCl and in the presence of AC, LK, and HK

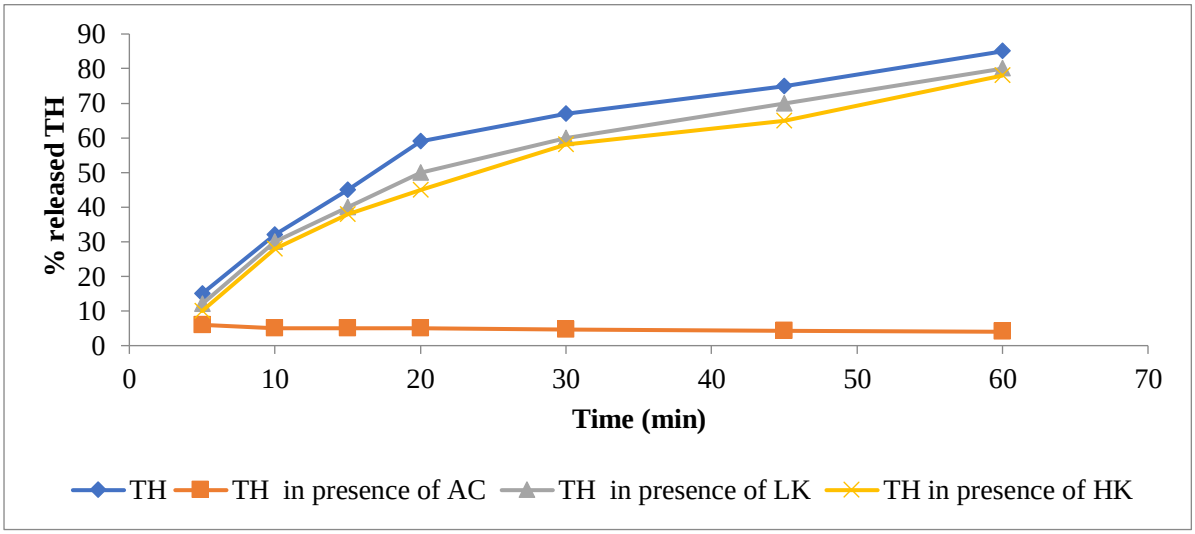

Figure 3. Release profile of TH in 0.1 N HCl and in the presence of AC, LK, and HK

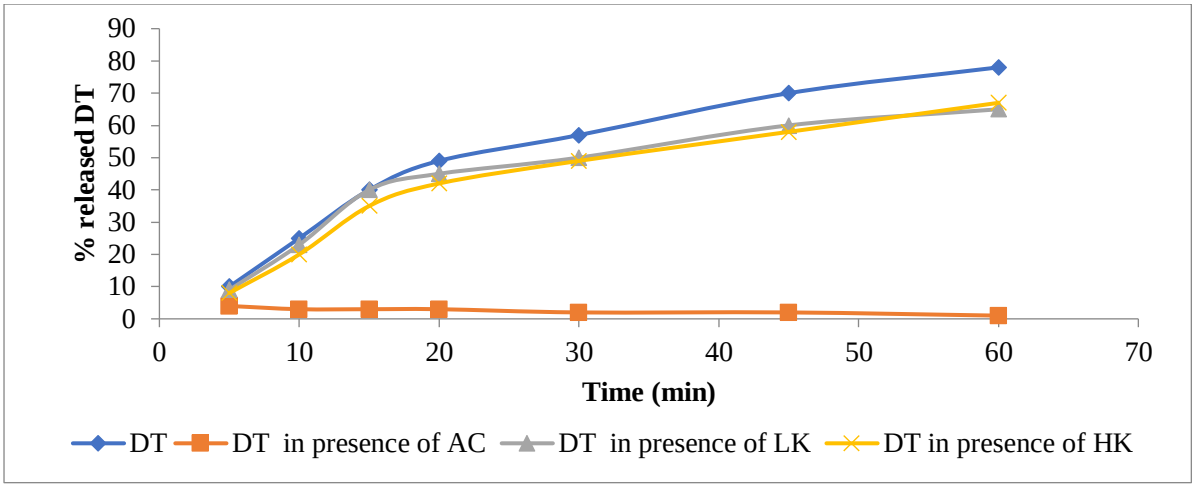

Figure 4. Release profile of DT in 0.1 N HCl and in the presence of AC, LK and HK

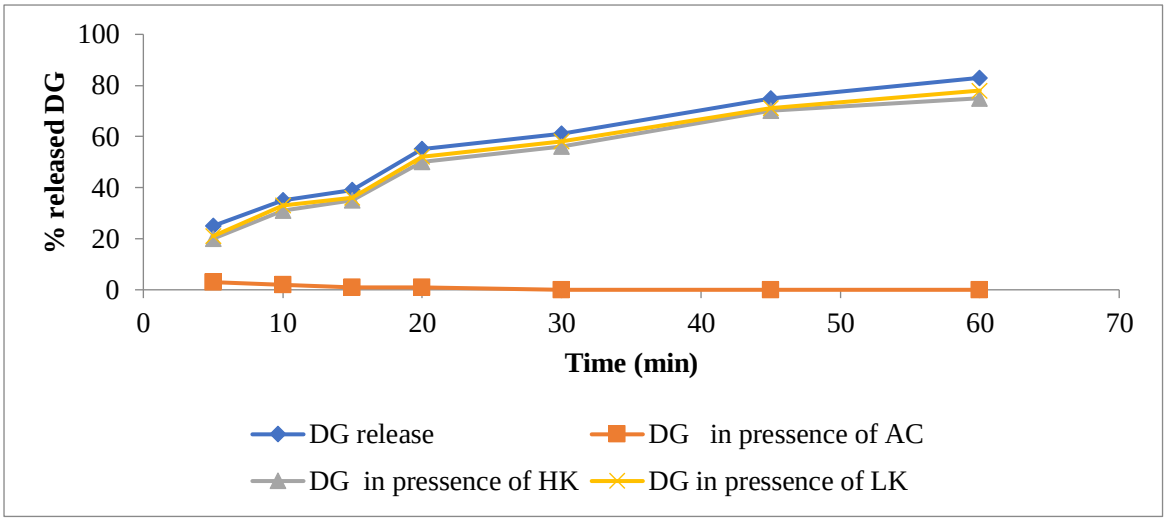

Figure 5. Release profile of DG in 0.1 N HCL and in the presence of AC, LK and HK

Table 1 demonstrates the % release from each drug and in the presence of each adsorbent. The outcomes indicated the highest performance of AC to adsorb drugs as compared to other adsorbents. AC captures 83.3%, 89.8%, 62.5%, 55.2% and 61%, respectively while LK captures 9.8 %, 4.8%, 7%, 6.9%, and 2.9% respectively and HK captures 3.8%, 11.4%, 8.9%, 8%, and 4.8%, respectively, for DZ, MC, TH, DT and DG.

Table 1. The mean percent released of the drug with and without presence of adsorbents

Drug	Release after 30 min			
	Without adsorbents	**In presence of AC**	**In presence of LK**	**In presence of HK**
DZ	90.3%	7%	80.5%	86.5%
MC	91.3%	1.5%	86.5%	79.9%
TH	67.1%	4.6%	60.1%	58.2%
DT	57.2%	2%	50.3%	49.2%
DG	61%	0%	58.1%	56.2%

Depending on the results above, the dissolution of most medications is rapid in simulated gastric pH at higher doses. The tested medications DZ, MC, DT, TH, and DG were adsorbed nearly entirely on AC and to a lesser extent on LK and HK. Therefore, our results prove the superior efficacy of AC as an effective adsorbent on the used medications because AC has a higher porosity and an extended surface area [21, 22]. Therefore, the capture and disposal of many pharmaceutical compounds is necessary to enable the medical staff in emergency health facilities to dispose of excess quantities of these medicines in cases of toxicity. Our research results were in great agreement with

many published scientific studies. For instance, Isoardi ZK et *al.* carried out a retrospective study on the management of aspirin overdose for nineteen years and found that sooner administration of activated charcoal greatly reduced further absorption [23]. Furthermore, Hatanaka K et *al*, investigated certain cases of lamotrigine poisoning where multiple administrations of AC accelerated the adsorption of the drug [24].

Conclusion

AC could adsorb all medications used (diazepam, metoclopramide, theophylline, and diltiazem HCL and digoxin) and was more efficient than that of light and heavy kaolin.

Conflicts of Interest

None

Funding

We fund ourselves.

Ethics Statements

The study does not need ethical approval

Author Contribution

Firas Aziz Rahi and Asmaa Abdelaziz Mohamed designed the study. Amna F. Alberqdar and Teeba A. Aziz performed the data collection. All authors performed data analysis and interpretation of the results. Asmaa Abdelaziz Mohamed wrote the initial draft of the manuscript. Firas Aziz Rahi and Asmaa Abdelaziz Mohamed wrote and revised the full paper. All authors have read and approved to the final manuscript version.

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تقييم مختبرى لفعالية امتزاز الفحم النشط مقابل الكاولين لبعض الأدوية ذات معامل الأمان الضيق

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الخلاصة

تهدف الدراسة الى تقييم قدرة الامتزاز في المختبر لثلاثة أنواع من الممتزات وهي: الفحم المنشط ، الكاولين الخفيف ، والكاولين الثقيل بتركيز ٠,٢٪ (وزن / حجم) على جرعات عالية من مجموعة من الأدوية التي لها مؤشر أمان ضيق (ديازيبام ، ميتوكلوبراميد ، ثيوفيلين ، ديجوكسين ، وديلتيازيم هيدروكلورايد) و تم إجراء الاختبار عن طريق إذابة الأدوية في وجود الممتزات باستخدام سائل معدي محاكى لتقييم فعالية هذه الممتزات كمضادات لعلاج الجرعات الزائدة من هذه الأدوية و اختبار مدى نجاح الامتزاز و قد وجد أن الفحم النشط لديه القدرة على امتصاص جميع الأدوية. اما كلا النوعين الخفيف والثقيل من الكاولين كانا قادرين فقط على امتصاص كمية محدودة من الأدوية المذكورة.

الكلمات المفتاحية: الامتزاز ، الفحم المنشط، ديجوكسين، كاولين خفيف، كاولين ثقيل