Environmental Toxicology and Pharmacology 52 (2017) 214–220

Contents lists available at ScienceDirect

Environmental Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/etap

The capacity and effectiveness of diosmectite and charcoal in trapping the compounds causing the most frequent intoxications in acute medicine: A comparative study

Michaela Mináriková[a], Veronika Fojtikova[a], Eliška Vyskočilová[b], Jan Sedláček[c], Milan Šikut[d], Lucie Borek-Dohalska[a], Marie Stiborová[a], Marketa Martinkova[a,*]

[a] Department of Biochemistry, Faculty of Science, Charles University, Hlavova (Albertov) 2030-8, Prague 2, Czech Republic
[b] University of Chemistry and Technology Prague, Faculty of Chemical Technology, Department of Organic Technology, Technická 1905, 166 28 Prague 6, Czech Republic
[c] Department of Physical and Macromolecular Chemistry, Faculty of Science, Charles University, Hlavova (Albertov) 2030-8, Prague 2, Czech Republic
[d] Hospital Mělník, Pražská 528, 276 01 Mělník, Czech Republic

ARTICLE INFO

Keywords:
Diosmectite
Charcoal
Adsorption
Acute intoxication

ABSTRACT

The aim of the study was to compare the adsorption ability of two adsorbent materials, namely diosmectite and activated charcoal towards selected model compounds that are most commonly involved in acute intoxication. Eleven model compounds were selected: acetylsalicylic acid, α-amanitin, amlodipine, digoxin, phenobarbital, ibuprofen, imipramine, carbamazepine, oxazepam, promethazine, and theophylline. Of the tested compounds, promethazine and imipramine were the most effectively adsorbed to diosmectite. Their adsorption to diosmectite (0.356 ± 0.029 mg promethazine/mg diosmectite and 0.354 ± 0.019 mg imipramine/mg diosmectite, respectively) was significantly higher than their adsorption to activated charcoal. The effect of temperature and pH on the adsorption efficiencies was also evaluated. In the case of experiments with mixture of both adsorbents, they mostly behaved in a solution independently or in a slightly antagonistic way. Using various methods such as N_2 adsorption and thermogravimetric analysis, the structure and texture of diosmectite and activated charcoal were attained.

1. Introduction

Activated charcoal and diosmectite are considered to be useful gastrointestinal decontamination agents that limit the absorption of ingested toxins into blood and therefore into whole human body (Albengres et al., 1985; Dupont and Vernisse, 2009; Guarino et al., 2009; Lucas and Henderson, 1933; Martirosian et al., 1998).

Diosmectite is a natural aluminomagnesium silicate (from the group of clay minerals – phylosilicates) taking the form of layers of fine sheets, from 12 to 15 Å thick. Each sheet consists of a layer of octahedral aluminum oxide surrounded by two layers of tetrahedral silicon oxide. The replacement of an aluminum atom by a cation with a lower valency (e.g. magnesium) results in an excess negative charge at the surface of the leaflet, which is neutralized by a labile cation such as Na^+ or Ca^{2+} (Albengres et al., 1985). Diosmectite avidly adsorbs certain compounds. This is explained by its multilayer organization and swelling ability, which creates a large surface for exchanges. In addition, the diffuse negative charges confer a large adsorption capacity for mineral and organic cations. The degree of adsorption of the biologically important compounds such as drugs studied previously varied widely (Castela-Papin et al., 1999).

Binding of drugs to diosmectite *in vitro* was frequently studied utilizing labelled molecules. The studies indicated that acidic drugs are not adsorbed to diosmectite, whereas the alkaline drugs are adsorbed effectively (Albengres et al., 1985). Drug interactions with diosmectite *in vitro* were also studied using an artificial stomach–duodenum model. Such model conditions differed mainly in pH values. The behavior of neutral and ionisable drugs with pKa values below 8 was monitored to determine the physicochemical characteristics of the interactions (Castela-Papin et al., 1999). The main neutral and acid drug substances were moderately fixed by the clay, in a pH-independent manner. The compounds with alkaline properties and a pKa < 7 were strongly fixed

Abbreviations: Asa, acetylsalicylic acid; Ama, α-amanitin; Aml, amlodipine besylate; BET, Brunauer-Emmett-Teller; BJH, Barrett-Joyner-Halenda; Cbz, carbamazepine; Dig, digoxin; Ibf, ibuprofen; Imi, imipramine hydrochloride; Oxa, oxazepam; Phb, phenobarbital; Pmz, promethazine hydrochloride; S_{BET}, the Brunauer-Emmett-Teller specific surface area; Thp, theophylline; V_{me}, mesopore volume; V_{mi}, micropore volume; V_{tot}, total pore volume

* Corresponding author.
E-mail address: marketa.martinkova@natur.cuni.cz (M. Martinkova).

http://dx.doi.org/10.1016/j.etap.2017.04.011
Received 10 January 2017; Received in revised form 4 April 2017; Accepted 14 April 2017
Available online 17 April 2017

in acid media, and fully released under neutral conditions. Amphoteric and alkaline compounds with a pKa ≥7 were adsorbed by more than 81% by diosmectite under conditions characteristic for gastric and duodenal compartments. In the part of the model representing the distal duodenum, only the substances that remained positively charged (amphoteric and alkaline compounds) showed a large reduction in their available free fraction. Ionization of drug substances administered per os concomitantly with diosmectite plays a crucial role in these interactions (Castela-Papin et al., 1999). Moreover, diosmectite is also involved in the treatment of enterocolitics for its ability to adsorb viruses and bacterial toxins secreted into the intestinal lumen (Brouillard and Rateau, 1989).

The second adsorbent utilized in human medicine for many years is charcoal (Lucas and Henderson, 1933). Its use is also not limited to poisoning cases alone. In the clinic, treatment of gastroenteritis and acute enteritis with charcoal results in a rapid disappearance of the symptoms. Application of charcoal is also the intervention of choice in almost all acute intoxication treatment procedures (Olson, 2004; Pelclová, 2009) in order to eliminate the poison from the gastrointestinal tract and suppress its absorption into human body.

It is important to underline that majority of the compounds causing the most frequent intoxications possesses alkaline character. Therefore, there is a high probability that they would be effectively adsorbed to diosmectite. The search for an optimal adsorbent is particularly important for the tricyclic antidepressants since they decelerate the stomach function and thereby their natural elimination process from the body is slowed down (Huang et al., 2013). The investigation and application of an optimal adsorbent is critical to minimize resorption (absorption) of tricyclic antidepressants into human body. Theophylline represents another example of drugs with special requirement on the elimination step in case of poisoning. Since theophylline takes part in the enterohepatic cycle (Okolicsanyi et al., 1986), only adsorbents with high affinity to the compound can be utilized to prevent it from the participation in the cycle and therefore from resorption (absorption) to blood. Tricyclic antidepressants and theophylline are only two representatives from the list of several chemicals causing most often acute intoxications in several European countries including the Czech Republic demonstrating that an alternative adsorbent to widely used charcoal will be very beneficial in acute medicine (Olson, 2004; Pelclová, 2009). Diosmectite can represent such an alternative, but it has still not been recommended as a therapy in acute intoxications treatment. Hence, it is very important to compare the charcoal and diosmectite properties in term of their adsorption capacity and trapping effectiveness towards the compounds causing the most often acute intoxications.

This study addresses still unsettled questions regarding the elimination step of medical treatment of acute intoxication. It will have unquestionable practical importance since it will be clear which of commercially available adsorbents (diosmectite or charcoal) is better choice for treatment of particular intoxication. In some cases there could be even possible that a mixture of both adsorbents will be recommended. Such a comparison between commercially available adsorbents has not been described yet. However, it can definitely be beneficial for patients suffering from acute intoxication in terms of better and more specific treatment in the elimination step of their therapy.

2. Materials and methods

2.1. Chemicals and materials

Acetylsalicylic acid, α-amanitin, amlodipine, digoxin, phenobarbital, ibuprofen, imipramine, carbamazepine, oxazepam, promethazine, and theophylline were obtained from Sigma-Aldrich (St. Louis, MO, USA). Diosmectite was provided by the IPSEN PHARMA S.A.S. company (Boulogne-Billancourt, France). It is the active substance contained in the “Smecta” product. Activated charcoal was obtained from Sigma-Aldrich (St. Louis, MO, USA). All other used chemicals were of the highest purity grade available from commercial sources and used without further purification.

2.2. N_2 adsorption measurements

The Brunauer – Emmett – Teller (BET) specific surface area, S_{BET}, and pore volume of diosmectite and charcoal were obtained from N_2 adsorption/desorption isotherms recorded at 77 K. Diosmectite and charcoal samples were treated (degassed) at a flow of helium (1.5 l/h) at 300 °C for 2 h before the adsorption measurements. The N_2 adsorption/desorption experiments were carried out on a commercial apparatus Pulse Chemisorb 2700 (Micromeritics) or ASAP 2020 V3. The specific surface area was ascertained from the adsorption isotherm (region of nitrogen relative pressures, p/p_0, from 0.05 to 0.25) using linearized form of BET equation (Brunauer et al., 1938). The micropore volume, V_{mi}, was estimated from the amount of N_2 adsorbed at $p/p_0 = 0.1$ ($p_0 = 101325$ Pa). The total pore volume, V_{tot}, resulted from the amount of N_2 adsorbed at $p/p_0 = 0.99$. The mesopore volume, V_{me}, was obtained as follows: $V_{me} = V_{tot} - V_{mi}$.

2.3. Thermogravimetric analysis

For the thermogravimetric analysis a thermobalance Stanton Redcroft TG 750 (temperature range 20–500 °C) was used. Analysis was performed in the range of 20–400 °C with step 5 °C per minute under air.

2.4. X-ray fluorescence

Structural elemental analysis of diosmectite sample was performed using X-ray fluorescence. An ARL 9400 XP sequential WD-XRF spectrometer (Thermo ARL, Ecublens, Switzerland) was used. The spectrometer was equipped with a Rh anode end-window and X-ray tube type 4GN fitted with a 75 μm Be window. All peak intensity data were collected by the WinXRF software. The generator settings-collimator-crystal-detector combinations were optimized for all 79 measured elements with an analysis time of 6 s per element. The obtained data were evaluated by the Uniquant 4 software tool.

2.5. X-ray diffraction

X-ray powder diffraction was used to confirm the interlayer distance of diosmectite sheets and the change of this value after intercalation of promethazine. The sample with promethazine was prepared as follows – 10 g of diosmectite was incubated with 10 mg of promethazine in water solution for an hour, then the mixture was filtered and the suspension was dried for 3 h at 90 °C. X-ray powder diffraction data were collected at room temperature with an X'Pert PRO θ-θ powder diffractometer with parafocusing Bragg-Brentano geometry using CuKα radiation (λ = 1.5418 Å, U = 40 kV, I = 30 mA). Data were scanned with an X'Celerator ultrafast detector over the angular range of 5°–64° (2θ) with a step size of 0.0167° (2θ). Data evaluation was carried out in the HighScore Plus software package.

2.6. Adsorption capacity and trapping effectiveness of diosmectite and charcoal for the model compounds

For investigation of the adsorption capability of either diosmectite or charcoal, 1 mg of the corresponding adsorbent was incubated with 1 mg of the model compound dissolved in 1 ml of the liquid phase (water, HCl(aq), buffer solution). The incubation proceeded mostly at 37 °C for 20 min at 200 rpm. The study of saturation kinetics of adsorption (37 °C) was performed using the following incubation times: 1 min, 5 min, 10 min, 20 min and 1 h. The following model compounds were tested: acetylsalicylic acid, α-amanitin, amlodipine besylate,