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Research Paper

Chemical and radiological characterization of clay minerals used in pharmaceutics and cosmetics

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ABSTRACT

Since the early days, clays have been used for therapeutic purposes. Nowadays, they are used as active ingredients or as excipient in formulations for a variety of purposes. Despite their wide use, little information is available in literature on their content of trace elements and radionuclides. The purpose of this study was to determine the elements (As, Ba, Br, Cs, Co, Cr, Eu, Fe, Hf, Hg, La, Lu, Rb, Sb, Sc, Sm, Ta, Tb, Yb, Zn, and Zr) and the radionuclides (^{238}U, ^{232}Th, ^{226}Ra, ^{228}Ra, ^{210}Pb and ^{40}K) in Brazilian clays as well as the health and radiological implications of the use of these clays in pharmaceutical formulations.

1. Introduction

Clay minerals are used in pharmaceutical formulations as active ingredients or excipients. As an active principle, clay minerals are used in oral applications as gastrointestinal protectors, osmotic oral laxatives and antidiarrhoeaics. Topical application includes their use as dermatological protectors and in cosmetics. They are also used in spas and aesthetic medicine (Carretero, 2002; Choy et al., 2007; Viseras et al., 2007).

A material to be used in pharmaceutical formulations must have low or zero toxicity. The presence of some elements, even in trace amounts, can pose a potential threat for the patient. Due to their high specific surface area and ion exchange capability (Lópes-Galindo et al., 2007) clay minerals possess high adsorption capacity which can cause the accumulation of trace elements and radionuclides. Several articles about the use of clay minerals in health science are available (Carretero and Pozo, 2009; Gomes and Silva, 2005, 2007; Hochella, 2002; Yushkin, 2004). However, only a few offer information about the content of these elements in clay minerals used for pharmaceutical purposes. In this study eight samples of medicinal clays, acquired in pharmacies and one with no brand were analyzed for their content of As, Ba, Br, Cs, Co, Cr, Eu, Fe, Hf, Hg, La, Lu, Rb, Sb, Sc, Sm, Ta, Tb, Yb, Zn, Zr and ^{238}U, ^{232}Th, ^{226}Ra, ^{228}Ra, ^{210}Pb and ^{40}K. Physical–chemical characteristics as pH, moisture, loss on ignition and organic carbon (OC) were also determined.

2. Experimental

2.1. Sample identification

According to their organoleptic characteristics, the clays analyzed were classified as white clays (AB 1, 2, 3 4 and 5) and green clays (AV 1, 2, 3 and 4). The sample with no brand was named AB3. As described below, these clays contain kaolinite and smectites.

2.2. X-ray diffractometry

The clay minerals were identified by X-ray powder diffraction (XRD) using a Siemens automated powder diffractometer equipped with a graphite monochromator, and Cu Kα radiation at 40 kV and 40 mA. All samples were scanned in the 2θ range of 2–60° with a step size of 0.020°, using Cu Kα radiation at 40 kV and 40 mA. Three X-ray patterns were recorded: at air-dried condition, after solvation with ethyleneglycol during 24 h, and after heating at 550 °C for 3 h.

2.3. Neutron activation analysis

The elements As, Br, Co, Cr, Cs, Fe, Hf, K, Na, Rb, Sb, Sc, Se, Ta, Zn, Zr and rare earth elements (Ce, Eu, La, Lu, Nd, Sm, Tb, and Yb) were

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determined by instrumental neutron activation analysis (INAA). For multi-elemental analysis of the samples, approximately 150 mg of samples and reference materials (NIST SRM 8704 and MAG-1, USGS) were accurately weighed and sealed in pre-cleaned double polyethylene bags for irradiation. Samples and reference materials were irradiated for 16 h in a thermal neutron flux of 10^{12} cm^{-2} s^{-1} in the IEA-R1 nuclear research reactor at IPEN (*Instituto de Pesquisas Energéticas e Nucleares*). Two series of countings were made, one after one week decay, the second after 15–20 days (IAEA, 1990).

The counting time was 1.5 h for each sample and reference materials. Gamma spectrometry was performed using a coaxial Be-layer HPGe detector with 22% relative efficiency, resolution of 2.09 keV at 1.33 MeV and associated electronic devices. The spectra were acquired by a multichannel analyzer SpectrumMaster and for the analysis the WinnerGamma software was used.

2.4. Alpha spectrometry

Alpha spectrometry was used for the determination of the nuclides ^{238}U and ^{232}Th. Approximately 0.5 g of the sample was spiked with ^{232}U and ^{229}Th and dissolved in heated aqua regia mixture. The solution was neutralized with ammonia solution until iron (hydr) oxide precipitation. This precipitate was dissolved with concentrated HCl, evaporated almost to dryness and re-dissolved in 9 M HCl. The solution was passed through a pre-conditioned anion exchange resin column in 9 M HCl. The eluate was evaporated to dryness, re-dissolved with 8 M HNO_3 and passed through a pre-conditioned anion exchange resin column in 8 M HNO_3. U and Th were eluted with 0.1 M HCl. The solution was evaporated and electroplated on a steel disk during 1 h using NH_4Cl as an electrolyte (Ivanovich and Murray, 1992; Silva, 1998). The detection of alpha particles was done with a silicon barrier detector and count rates determined during 80,000 s.

2.5. Gamma spectrometry

Activity concentrations of ^{226}Ra, ^{228}Ra, ^{210}Pb and ^{40}K were measured by gamma spectrometry with a hyper-pure germanium detector, GEM-15200, from EG&G Ortec. The detector was calibrated with soil, rock and water spiked with radionuclides certified by Amersham. Samples were packed in 100 cm^3 cans and sealed for about four weeks prior to the measurement to ensure that equilibrium had been established between ^{226}Ra and its short-living decay products. The ^{226}Ra activities were determined by taking the mean activity of three separate photopeaks of its daughter nuclides: ^{214}Pb at 295 keV and 352 keV, and ^{214}Bi at 609 keV. The ^{228}Ra content of the samples was determined by measuring the intensities of the 911 keV and 968 keV gamma-ray peaks from ^{228}Ac. The concentration of ^{210}Pb was determined by measuring the activity of its low energy peak (47 keV). Self-absorption correction was applied because the attenuation for low energy gamma rays is highly dependent upon the sample composition (Custhall et al., 1983).

2.6. Hg determination by FIA CV AAS

For total mercury determination the clay samples were analyzed by FIA CV AAS technique in a Perkin Elmer Flow Injection Mercury System (FIMS 100). The samples were digested in a mixture of conc. HNO_3, conc. H_2SO_4 and 30% H_2O_2 in Teflon vials. The vials were closed and left at room temperature overnight. Then, the vials were put into an aluminium block at 90 °C and left there for 3 h. The precision and accuracy of the analytical methodology were tested with certified reference materials: Buffalo River Sediment (NIST SRM 8704), Estuarine Sediment (NIST SRM 1646^a) and Lake Sediment (BCR CRM 280).

3. Results and discussion

Clay minerals contain considerable amounts of Al, Mg, K, Ca, Na and Fe and, occasionally, less common elements such as Ti, Mn, or Li and trace elements in varying amounts.

The qualitative identification of mineral species was based on the shape, position and intensity of specific reflections. The 7 Å reflection in dry samples, which was completely lost after heating to 550 °C, was attributed to kaolinite. The 10 Å reflection which was not affected by chemical treatment or heating indicated the presence of illite. The presence of smectites was evidenced by the reflection at $d = 18.3$–18.9 Å after EG solvation.

The X-ray patterns for white and green clays are presented in Fig. 1. White clays were kaolins mainly composed of well-crystallized kaolinite, with varying amounts of quartz and illite. Green clays were bentonites containing smectites of rather low crystallinity, minor amounts of kaolinite, illite, and traces of quartz.

The mass loss at 60, 400, and 800 °C due to the desorption of moisture, hydration water, and dehydroxylation is shown in Fig. 2.

The element contents determined by INAA and Hg are listed in Table 1. Barium was the only element of higher concentration in the kaolins. The rare earth elements, Br, Na, Ta and Zr are in the same order of magnitude in both and all other elements were found in higher concentrations in green clays (bentonites). According to the mineralogical composition, kaolinites have very little substitution in the lattice and, therefore, it has a minimal layer charge and a low base exchange capacity. Smectites, on the other hand, possess a high layer charge, very fine particle size, high cation exchange capacity and a high specific surface area (Carretero et al., 2010; López et al., 2005; Marzougui and Ben Mammou, 2006; Murray, 2000). In both types of clays large-ion lithophile elements of low mobility were found in the same order of magnitude. As commonly assumed to be immobile, these elements may be present due to isomorphous substitution.

Measurable concentrations of Hg were found only in the bentonites. Comparing the concentrations obtained in these samples with the mean values in the upper continental crust (Turekian and Wedepohl, 1961), Ce, Co, Cs, Nd, Rb, Sc, Sm and Zn were enriched in the green clays. Only Ba, Sm and Ta were enriched in the kaolins. As, Sb, Hg and Ba are toxic and Rb, Cr, Zr and rare earth elements can be considered dangerous (Lópes-Galindo et al., 2007) however there is no regulation for all these elements in clay minerals for pharmaceutical and cosmetic use. According to the European Pharmacopoeia (2002) E. P. 4th and US Pharmacopoeia (USP 29 - NF 24, 2006), the level of iron should be <0,25%; of As <40 μg g^{-1} (according to FDA, the threshold limit for ingestion of As in water is 10 μg L^{-1}); of heavy metals <50 μg g^{-1}. According to the European norm (no. 391r85; no. 179r86; and no. 199r86) As, Se, Cd, Hg, Pb, Sb and Tl are not permitted in cosmetic products.

For comparison purposes, the typical concentration of Hg found in the upper continental crust is 80 ng g^{-1}, and according to the FDA, threshold limit for mercury ingestion is 1 μg g^{-1}. Pathways for Hg contamination can be inhalation, oral ingestion and through the skin. Hg concentrations in different kinds of foods range from 0 to 100 ng g^{-1}. In Brazil, the threshold limit for external exposition (Azevedo and Chasin, 2003) is 0.04 mg m^{-3}. For Cr, occupational limits are established for hexavalent chromium, as 0.04 mg m^{-3}, according to Brazilian law. The National Research Council (NRC) recommends a safe ingestion of 50–200 μg/day of Cr. Zinc is an essential element with an ingestion limit recommended of 9 and 16 mg/day for adult women and men, respectively.

Table 2 shows the activity concentration of radionuclides (^{238}U, ^{232}Th, ^{226}Ra, ^{228}Ra, ^{210}Pb and ^{40}K), pH and organic carbon content. The green clays possessed an almost constant pH near the neutral value while the kaolins showed larger pH variations. The content of OC was also higher in the bentonites. This fact may also contribute to the higher metal content due to the formation of organic complexes.

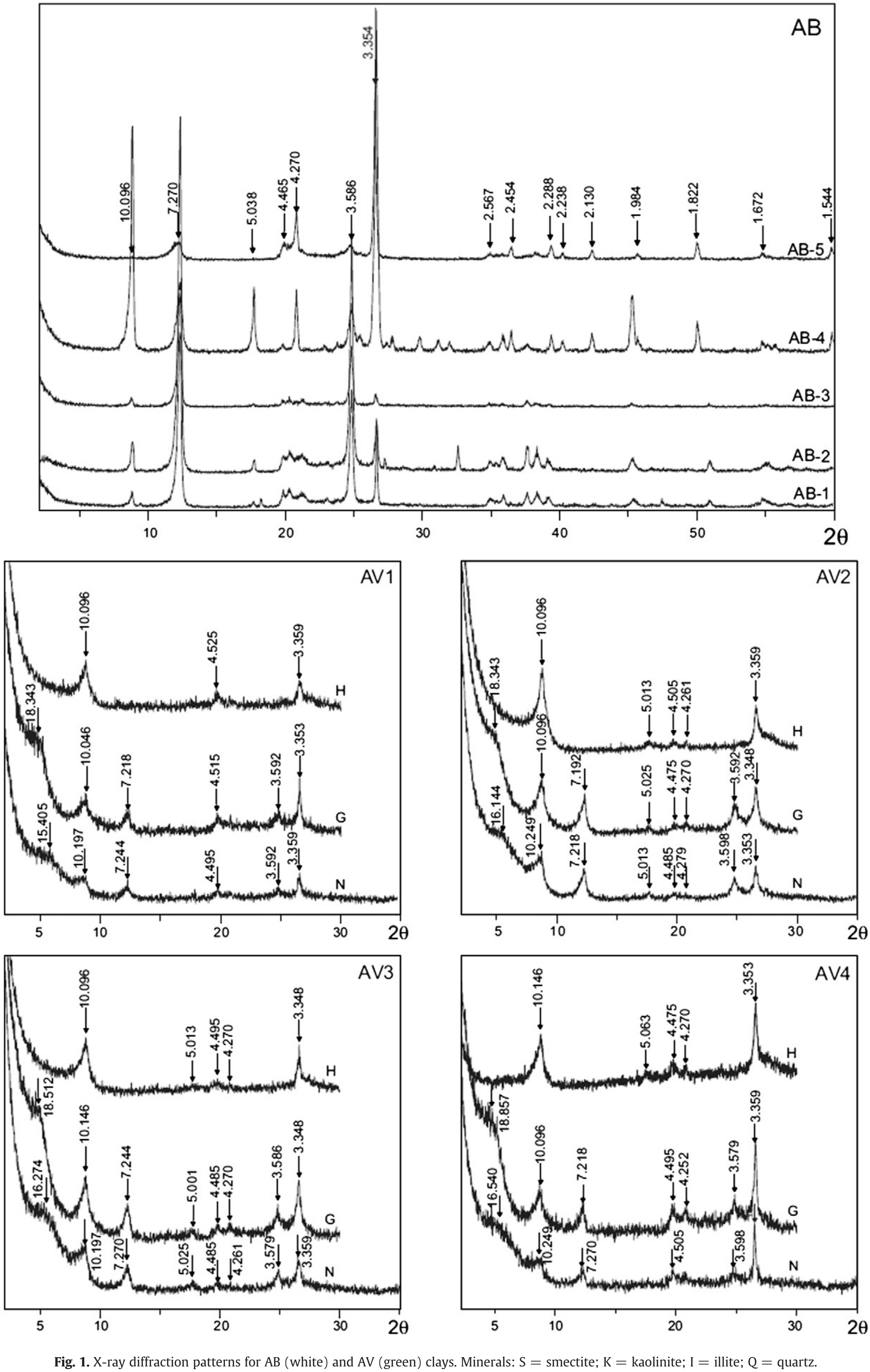

Fig. 1. X-ray diffraction patterns for AB (white) and AV (green) clays. Minerals: S = smectite; K = kaolinite; I = illite; Q = quartz.

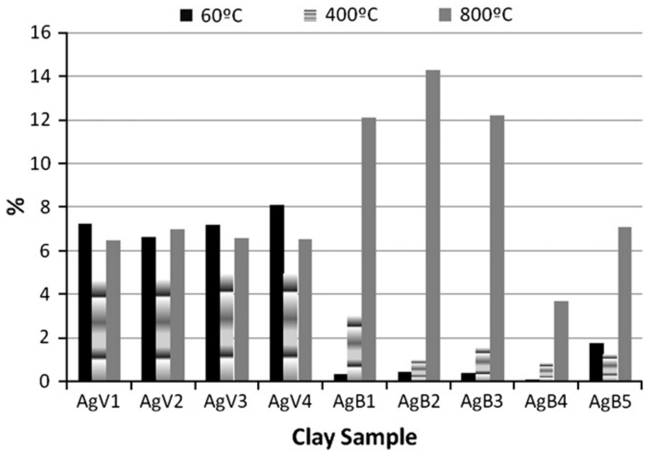

Fig. 2. Mass loss after heating at different temperatures.

Table 2
Activity concentrations of ^{238}U, ^{232}Th, ^{226}Ra, ^{228}Ra, ^{210}Pb and ^{40}K (Bq kg^{-1}), pH and organic carbon (OC in %).

	U-238	Th-232	Ra-226	Ra-228	Pb-210	K-40	pH	OC
	(Bq kg^{-1})							(%)
AV1	134 ± 19	81 ± 4	51 ± 4	72 ± 6	252 ± 20	1146 ± 92	6.98	0.71
AV2	168 ± 23	92 ± 4	42 ± 3	77 ± 6	198 ± 16	1126 ± 90	6.12	0.57
AV3	188 ± 24	77 ± 4	42 ± 3	76 ± 6	167 ± 13	1114 ± 89	6.97	0.86
AV4	136 ± 18	72 ± 3	40 ± 3	80 ± 6	189 ± 15	1088 ± 87	6.95	0.69
AB1	123 ± 15	46 ± 2	38 ± 3	64 ± 5	218 ± 17	952 ± 76	7.74	0.1
AB2	68 ± 10	45 ± 2	32 ± 3	70 ± 6	188 ± 15	828 ± 66	8.10	0.05
AB3	117 ± 14	40 ± 2	54 ± 4	82 ± 7	252 ± 20	1069 ± 86	5.68	0.12
AB4	61 ± 10	74 ± 4	27 ± 2	64 ± 5	144 ± 11	76 ± 6	6.04	0.02
AB5	58 ± 10	111 ± 5	32 ± 3	92 ± 7	162 ± 13	758 ± 61	4.57	0.12

The green clays were characterized by a higher content of radionuclides, presenting a narrower variation and an activity ratio ^{232}Th/^{238}U varying from 0.41 to 0.60. The kaolins showed a wide variation of the U, Th and K contents and the activity ratio ^{232}Th/^{238}U varied from 0.34 to 1.91, indicating that the smectites of the green clays were more homogeneous in the composition than the kaolinites of the white clays. This fact was also confirmed by the La/Th ratio that varied from 0.70 to 0.73 in the smectite samples and from 0.50 to 1.56 in the kaolinite samples.

The white clays were more enriched with ^{228}Ra over ^{226}Ra than the green clays. The ^{228}Ra also showed a pronounced enrichment over its parent nuclide, ^{232}Th. AB4 and AB5 showed enrichment of Th over U compared to the other samples. In all samples, the ^{210}Pb activity

Table 1
Concentrations of the elements in white clays (AB) and green clays (AV).

A	As (μg g^{-1})	Ba (μg g^{-1})	Br (μg g^{-1})	Ce (μg g^{-1})	Co (μg g^{-1})	Cr (μg g^{-1})	Cs (μg g^{-1})
AV1	8.0 ± 0.7	434 ± 64	0.5 ± 0.1	119 ± 6	21.2 ± 0.6	79 ± 4	14.8 ± 1.0
AV2	8.9 ± 0.8	481 ± 70	1.0 ± 0.2	147 ± 8	19.0 ± 0.6	80 ± 4	13.6 ± 0.9
AV3	7.9 ± 0.7	475 ± 36	3.3 ± 0.6	164 ± 10	22.7 ± 0.6	86 ± 4	14.4 ± 0.7
AV4	4.1 ± 0.6	433 ± 33	0.5 ± 0.2	149 ± 10	21.1 ± 0.6	79 ± 3	13.5 ± 0.6
AB1	1.8 ± 0.3	2050 ± 149	1.5 ± 0.1	82 ± 4	2.15 ± 0.06	22 ± 1	3.5 ± 0.2
AB2	2.5 ± 0.3	3018 ± 219	3.0 ± 0.1	150 ± 8	0.83 ± 0.03	30 ± 1	7.0 ± 0.3
AB3	0.6 ± 0.2	362 ± 27	1.7 ± 0.1	58 ± 3	0.70 ± 0.02	22 ± 1	1.86 ± 0.09
AB4	4.1 ± 0.5	546 ± 42	1.5 ± 0.2	97 ± 5	1.48 ± 0.05	118 ± 5	10.8 ± 0.5
AB5	0.9 ± 0.4	99 ± 11	1.6 ± 0.2	196 ± 10	1.19 ± 0.04	15 ± 1	0.93 ± 0.06

A	Eu (μg g^{-1})	Fe(%)	Hf (μg g^{-1})	K(%)	La (μg g^{-1})	Lu (μg g^{-1})	Na (%)
AV1	1.9 ± 0.1	6.5 ± 0.4	3.1 ± 0.2	3.6 ± 0.7	57 ± 3	0.5 ± 0.1	0.097 ± 0.004
AV2	2.3 ± 0.1	6.0 ± 0.4	3.0 ± 0.2	2.9 ± 0.6	68 ± 4	0.6 ± 0.2	0.073 ± 0.003
AV3	1.92 ± 0.07	6.9 ± 0.5	3.6 ± 0.2	3.3 ± 0.6	56 ± 3	0.6 ± 0.2	0.086 ± 0.003
AV4	1.75 ± 0.06	6.6 ± 0.4	3.1 ± 0.1	2.4 ± 0.5	51 ± 3	0.4 ± 0.1	0.071 ± 0.003
AB1	2.38 ± 0.09	0.31 ± 0.02	1.7 ± 0.1	0.6 ± 0.1	47 ± 2	0.5 ± 0.1	0.047 ± 0.002
AB2	1.58 ± 0.06	0.27 ± 0.02	2.9 ± 0.1	0.7 ± 0.1	70 ± 2	0.4 ± 0.1	0.059 ± 0.002
AB3	1.39 ± 0.05	0.28 ± 0.02	1.6 ± 0.1	0.6 ± 0.1	24 ± 1	0.3 ± 0.1	0.021 ± 0.001
AB4	1.13 ± 0.04	1.15 ± 0.08	7.0 ± 0.4	3.8 ± 0.4	37 ± 1	0.6 ± 0.2	0.141 ± 0.004
AB5	1.03 ± 0.04	0.34 ± 0.02	13.2 ± 0.7	ND	84 ± 3	0.8 ± 0.2	0.028 ± 0.003

A	Nd (μg g^{-1})	Rb (μg g^{-1})	Sb (μg g^{-1})	Sc (μg g^{-1})	Sm (μg g^{-1})	Ta (μg g^{-1})	Tb (μg g^{-1})
AV1	44 ± 7	199 ± 10	1.06 ± 0.08	18.5 ± 0.6	9.2 ± 0.4	1.5 ± 0.4	2.1 ± 0.6
AV2	59 ± 9	205 ± 10	1.00 ± 0.08	19.6 ± 0.6	11.3 ± 0.5	1.7 ± 0.5	2.4 ± 0.7
AV3	46 ± 8	245 ± 9	0.83 ± 0.08	19.6 ± 0.6	9.4 ± 0.4	2.2 ± 0.3	1.1 ± 0.1
AV4	43 ± 7	219 ± 8	0.48 ± 0.06	18.3 ± 0.5	8.6 ± 0.4	1.8 ± 0.2	1.1 ± 0.1
AB1	20 ± 5	57 ± 2	0.32 ± 0.04	4.7 ± 0.1	10.5 ± 0.4	2.7 ± 0.2	0.9 ± 0.1
AB2	22 ± 5	102 ± 4	0.45 ± 0.05	3.5 ± 0.1	9.0 ± 0.4	4.9 ± 0.4	1.2 ± 0.2
AB3	6 ± 2	37 ± 1	ND	1.8 ± 0.1	5.2 ± 0.2	0.8 ± 0.1	0.9 ± 0.06
AB4	4 ± 2	190 ± 7	1.91 ± 0.14	19.3 ± 0.6	6.1 ± 0.3	1.2 ± 0.1	1.1 ± 0.1
AB5	21 ± 5	19 ± 1	ND	6.3 ± 0.2	11.1 ± 0.4	1.3 ± 0.1	1.0 ± 0.1

A	Yb (μg g^{-1})	Zn (μg g^{-1})	Zr (μg g^{-1})	Hg (ng g^{-1})
AV1	2.9 ± 0.2	326 ± 15	183 ± 49	43 ± 2
AV2	3.0 ± 0.2	304 ± 14	ND	48 ± 1
AV3	3.1 ± 0.2	231 ± 6	109 ± 23	44 ± 2
AV4	3.2 ± 0,2	135 ± 4	181 ± 24	31 ± 2
AB1	3.2 ± 0,2	269 ± 8	99 ± 12	<LD
AB2	2.6 ± 0.1	29 ± 1	130 ± 13	<LD
AB3	2.0 ± 0.1	13 ± 1	98 ± 10	<LD
AB4	3.5 ± 0.2	98 ± 3	186 ± 22	<LD
AB5	4.6 ± 0.2	31 ± 1	332 ± 32	<LD

ND = not determined and LD limit of detection.

concentration was higher than ^{226}Ra, probably due to the high solubility of the latter.

As a comparison, the concentrations, in Bq kg^{-1}, for ^{238}U, ^{232}Th, ^{226}Ra and ^{40}K in soils are in the range of 16–60; 11–64; 17–60 and 140–850 (UNSCEAR, 2000). The radionuclides in the white and green clays contained higher concentrations than generally found in soils worldwide. No reference values for radionuclides were found for the application of clay minerals in pharmaceuticals. The equivalent dose calculated for the ingestion of these clay mineral samples, considering an intake of 1 g per day, is in the range of 0.06 to 0.1 mSv y^{-1} and ^{210}Pb accounts for 52 to 67% of the total dose.

Compared with mud used in spas, the concentration of ^{226}Ra in the present samples was lower. The concentrations of ^{232}Th, ^{228}Ra and ^{40}K were of the same order of concentrations in the so-called “radioactive mud” (Manic et al., 2006).

4. Conclusions

For the use of clay and clay minerals for pharmacological purposes, pharmacopoeias recommend different tests. The most significant tests are related to the identification of the clay minerals, the acidity or alkalinity, microbial limit, water content, quantity of acid soluble substances, presence of impurities (mineral salts, trace elements and radionuclides included), some chemical limitations and technical properties. Based on the values obtained for green clays, the ingestion of the clays in medicinal form may not present a threat but occupational risk must be considered. The radionuclide content determined in smectite samples (green clays) is also higher than in the kaolins (white clays). The analytical results revealed that the content of radionuclides in the white and green clays is not insignificant. Given that the increment in the annual dose is limited to 1 mSv (UNSCEAR, 2000) only the ingestion of 1 g per day of the white or green clays discussed in this paper may represent from 6 to 10% of this limit.

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