

CHEMICAL AND RADIOLOGICAL CHARACTERIZATION OF CLAY MINERAL OF PHARMACEUTICAL AND COSMETIC USE

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Abstract. Since the early days, clays have been used for therapeutic purposes. Nowadays, clay minerals are used as active ingredient or as excipient in formulations for a variety of purposes such as anti-inflammatory, pharmaceuticals and cosmetic. Although the large use, few information is available in literature on their content of metals, trace elements and radionuclides. This paper aims to determine the elements (As, Ba, Br, Cs, Co, Cr, Cu, Eu, Fe, Hf, Hg, La, Lu, Rb, Sb, Sc, Sm, Ta, Tb, Yb, Zn, Zr) and the radionuclides (^{238}U , ^{232}Th , ^{226}Ra , ^{228}Ra , ^{210}Pb and ^{40}K) and to discuss the physical-chemical characteristics of Brazilian clays.

Keywords: Radionuclides, clay mineral, pharmaceutical, cosmetic.

1. Introduction

Clay minerals are used in pharmaceutical formulations as active ingredient or excipient. As 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. It is also used in spas and aesthetic medicine¹.

The properties of the clay minerals, which made them appropriate for therapeutic uses, are fundamentally: a high specific area and adsorptive capacity, rheological properties and chemical inertness.

A fundamental property that must be observed for the use of a material in pharmaceutical formulations is its low or null toxicity. The presence of some elements, even in trace quantities, can pose a potential threat for the patient. It is well known that clay mineral, due to its high specific area and ion exchange capability², possess a great adsorptive capacity which can cause the accumulation of trace elements such as metals and radionuclides. Several articles deals with the use of clay minerals in health science³⁻⁷, but few papers deals with information on the content of these elements in clay minerals used for pharmaceutical purposes. In this work eight samples of medicinal clay bought in pharmacies and one with no trade mark were analyzed for their content of As, Ba, Br, Cs, Co, Cr, Cu, Eu, Fe, Hf, Hg, La, Lu, Rb, Sb, Sc, Sm, Ta, Tb, Yb, Zn, Zr and ²³⁸U, ²³²Th, ²²⁶Ra, ²²⁸Ra, ²¹⁰Pb and ⁴⁰K. Physical-chemical characteristics as pH, moisture, loss on ignition and organic carbon were also determined. According to their organoleptic characteristics, the clays analyzed were classified as white clay (AB 1, 2, 3 4 and 5) and green clay (AV 1, 2, 3 and 4). The sample with no trade mark was named AB3.

2. Experimental

Instrumental Neutron Activation Analysis

The elements As, Br, Co, Cr, Cs, Fe, Hf, K, Na, Rb, Sb, Sc, Se, Ta, Th, U, Zn and rare earths (Ce, Eu, La, Lu, Nd, Sm, Tb, Yb) were determined by neutron activation analysis. For multielemental 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 hours in a thermal neutron flux of $10^{12} \text{ cm}^{-2} \text{ s}^{-1}$ in the IEA-R1 nuclear research reactor at IPEN (Instituto de Pesquisas Energéticas e Nucleares). Two series of counting were made: the first, after one week decay and the second after 15-20 days.

The counting time was 1.5 hours for each sample and reference material. 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 multichannel analyzer SpectrumMaster and for the analysis, WinnerGamma software was used.

Alpha spectrometry were used for the determination of the nuclides ^{238}U and ^{232}Th . Approximately 0,5g of the sample was weighed, spiked with ^{232}U and ^{229}Th and dissolved with a heated aqua regia mixture. The solution was neutralized with NH_4OH till the iron-hydroxide precipitation. Precipitate was dissolved with concentrated HCl, evaporated almost to dryness and re-dissolved in 9 mol L^{-1} HCl. The obtained solution was passed through a pre-conditioned anionic exchange resin column in $\text{HCl } 9 \text{ mol L}^{-1}$ media. The eluate was evaporated to dryness and re-dissolved with 8 mol L^{-1} HNO_3 , and passed through a pre-conditioned anionic exchange resin column in 8 mol L^{-1} HNO_3 media. Both, U and Th were eluted with 0.1 mol L^{-1} HCl, evaporated and electroplated in a steel disk during one hour using NH_4Cl as electrolyte⁸. The detection of alpha particles was done with a silicon barrier detector and count rates determined during 80,000 seconds.

Activity concentrations of Ra-226, Ra-228, Pb-210 and K-40 were measured in clay samples by gamma spectrometry with a hyper-pure germanium detector, GEM-

15200, from EG&G Ortec. The detector was calibrated using natural soil, rock and water spiked with radionuclides certified by Amersham. Samples were packed in 100 cm³ cans and sealed for about four weeks prior to the measurement in order to ensure that equilibrium has been reached between Ra-226 and its decay products of short half-life. The Ra-226 activities were determined by taking the mean activity of three separate photopeaks of its daughter nuclides: Pb-214 at 295 keV and 352 keV, and Bi-214 at 609 keV. The Ra-228 content of the samples was determined by measuring the intensities of the 911 keV and 968 keV gamma-ray peaks from Ac-228. The concentration of Pb-210 was carried out by measuring the activity of its low energy peak (47 keV). Self-absorption correction was applied since the attenuation for low energy gamma rays is highly dependent upon sample composition. The approach used was that suggested by Cutshall⁹.

For total mercury determination clay samples were analysed by FIA-CV-AAS technique in a Flow Injection Mercury System (FIMS 100) by Perkin Elmer. Samples were digested by a mixture of conc HNO₃, conc H₂SO₄ and 30% H₂O₂ in Teflon vials. The vials were closed and left at room temperature overnight. In the following day, the vials were put into an aluminium block at 90⁰C and left there for 3 hours. The efficiency curve was performed by certified reference materials analysis: Buffalo River Sediment (NIST SRM 8704), Estuarine Sediment (NIST SRM 1646^a) and Lake Sediment (BCR CRM 280).

3. Results and discussion

Clay mineral is a mineralogical term referring to part of a family (the phyllosilicates) consisting of hydrated aluminosilicates containing considerable amounts of Mg, K, Ca, Na and Fe and, occasionally, less common ions such as Ti, Mn, or Li and trace elements in different amounts. Despite its varied chemical composition, it can be classified in just a few major groups — smectites, micas, kaolin, talcum, chlorites, vermiculites, fibrous and interstratified. Apart from being efficient in the pharmacological or cosmetic function for which it is chosen, clays should also be seen to comply with a number of chemical, physical and toxicological requirements for which there are specific technical specifications for each clay and its intended use². Correct characterization of the product should therefore be accompanied by a detailed account of its trace element content.

Figure 1 shows the results for moisture, crystallization water and loss on ignition for the samples. Green clays loses 6 to 8% of moisture while white clays less than 1%. At 400°C green clays loses approximately 4% of its mass and white, less than 1%. At 800°C white clays present a higher loss on ignition (approximately 13%) compared to green clays (approximately 6%). Table 1 presents the results for pH and organic carbon. It can be seen that green clays present a more constant pH, near the neutral value while white clay show greater variations from acid to basic values. The content of OC was also higher in green clay samples. This fact can contribute to the higher values of metal observed.

Table 2 shows the obtained results for the elements determined by INAA and Hg. Barium was the only element that presented higher concentration in white clay than

green clay. Rare earth elements and Br, Na, Ta and Zr generally presented the same order of magnitude in both clays samples. All other elements presented higher amounts in green clay. In the case of Hg, only green clays presented measurable concentrations; all white clay samples presented concentrations below the detection limit ($0,01 \text{ ng g}^{-1}$). Comparing the concentrations obtained in these samples with mean values for the upper continental crust¹⁰ the elements Ce, Co, Cs, Nd, Rb, Sc, Sm and Zn are enriched in green clay and only the elements Ba, Sm and Ta, in white clay. According Lopes-Galindo¹ et al. the following elements are considered toxic (As, Sb, Co, Zn, Hg, Ba) or in some grade, dangerous (Rb, Cr, Zr and rare earth elements). There's no regulation for all these elements in clay minerals, but according to E. P¹¹. 4th and USP 29¹² the level of iron can not be higher than 0,25%; for As, not higher than $40 \text{ } \mu\text{g g}^{-1}$ (according to FDA, the threshold limit for ingestion of As in water is $10 \text{ } \mu\text{g L}^{-1}$); and for heavy metals not higher than $50 \text{ } \mu\text{g g}^{-1}$.

For comparison, typical concentration of Hg found in continental crust is 80 ng g^{-1} , and according to FDA, threshold limits for mercury ingestion is $1 \text{ } \mu\text{g g}^{-1}$. Main pathway for Hg contamination is inhalation, oral ingestion and cutaneous ingestion. Hg concentrations in different kind of food range from 0 to 100 ng g^{-1} and in Brazil, threshold limit for external exposition¹³ is $0,04 \text{ mg m}^{-3}$. For Cr, occupational limits are established for hexavalent chromium, as $0,04 \text{ mg m}^{-3}$, according to Brazilian Law. The National Research Council (NRC) recommends a safe ingestion of 50 – 200 $\mu\text{g/day}$ of Cr. Zinc is an essential element with limit of ingestion recommended of 9 and 16 mg/day for adult woman and man, respectively.

In table 3 are presented the results for radionuclides activity concentration (^{238}U , ^{232}Th , ^{226}Ra , ^{228}Ra , ^{210}Pb and ^{40}K). It can be seen that green clays are characterized by

the higher content, presenting a narrower variation. White clay presents a great variation mainly in its content of U, Th and K.

White clay is more enriched in ^{228}Ra over ^{226}Ra than green clay and ^{228}Ra presents a pronounced enrichment over its parent nuclide, Th-232. AB4 and AB5 samples show an enrichment of Th over U compared to the other samples. All samples presented ^{210}Pb activity concentration higher than ^{226}Ra probably due to the great solubility of the later.

As a comparison the concentration, in Bq kg^{-1} , of ^{238}U , ^{232}Th , ^{226}Ra and ^{40}K found in soil are in the range 16 – 60; 11 – 64; 17 – 60 and 140 – 850¹⁴, respectively. Reference values for intake of some kinds of food are presented in table 4. As no reference values for radionuclides were found for the application of clay mineral as pharmaceutical, the mean values for the analyzed elements in some foods presented in a normal diet¹⁵, were also presented. The levels of radionuclides analyzed in this study present higher concentrations than that generally found in soil worldwide and much higher than that presented in the day-to-day diet.

Compared with mud used in spas the concentration of ^{226}Ra in the present samples is lower than that found in literature, on the other hand, concentrations of ^{232}Th , ^{228}Ra and ^{40}K are of the same order of that found for the so called “radioactive mud”¹⁶.

4. Conclusions

For the use of clays minerals as pharmacological purposes, pharmacopoeias recommend different tests to be carried out before use. The most significant are those concerning the correct identification of the product, 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. Considering the obtained values for green clay the ingestion of the clay in a medicine form can do not represent a threat but occupational risk must be considered. The content of radionuclides determined Green clay also present higher concentrations than that called white clay. As clay minerals are used in pharmaceutical formulations and in cosmetics, the obtained results show that its content of radionuclides is not insignificant and deserves further investigations.

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Table 1: Values of pH and organic carbon in clay samples

	<i>pH</i>	<i>OC</i>
AB1	7.74	0.1
AB2	8.10	0.05
AB3	5.68	0.12
AB4	6.04	0.02
AB5	4.57	0.12
AV1	6.98	0.71
AV2	6.12	0.57
AV3	6.97	0.86
AV4	6.95	0.69

Table 2: Concentration of the elements measured by INAA in clay mineral samples, in $\mu\text{g g}^{-1}$, except were indicated % and Hg concentration in ng g^{-1} . ND = not determined and LD limit of detection

A	As	Ba	Br	Ce	Co	Cr	Cs
AV1	8.0 \pm 0.7	434 \pm 64	0.5 \pm 0.1	119 \pm 6	21.2 \pm 0.6	79 \pm 4	14.8 \pm 1.0
AV2	8.9 \pm 0.8	481 \pm 70	1.0 \pm 0.2	147 \pm 8	19.0 \pm 0.6	80 \pm 4	13.6 \pm 0.9
AV3	7.9 \pm 0.7	475 \pm 36	3.3 \pm 0.6	164 \pm 10	22.7 \pm 0.6	86 \pm 4	14.4 \pm 0.7
AV4	4.1 \pm 0.6	433 \pm 33	0.5 \pm 0.2	149 \pm 10	21.1 \pm 0.6	79 \pm 3	13.5 \pm 0.6
AB1	1.8 \pm 0.3	2050 \pm 149	1.5 \pm 0.1	82 \pm 4	2.15 \pm 0.06	22 \pm 1	3.5 \pm 0.2
AB2	2.5 \pm 0.3	3018 \pm 219	3.0 \pm 0.1	150 \pm 8	0.83 \pm 0.03	30 \pm 1	7.0 \pm 0.3
AB3	0.6 \pm 0.2	362 \pm 27	1.7 \pm 0.1	58 \pm 3	0.70 \pm 0.02	22 \pm 1	1.86 \pm 0.09
AB4	4.1 \pm 0.5	546 \pm 42	1.5 \pm 0.2	97 \pm 5	1.48 \pm 0.05	118 \pm 5	10.8 \pm 0.5
AB5	0.9 \pm 0.4	99 \pm 11	1.6 \pm 0.2	196 \pm 10	1.19 \pm 0.04	15 \pm 1	0.93 \pm 0.06
A	Eu	Fe(%)	Hf	K(%)	La	Lu	Na
AV1	1.9 \pm 0.1	6.5 \pm 0.4	3.1 \pm 0.2	3.6 \pm 0.7	57 \pm 3	0.5 \pm 0.1	0.097 \pm 0.004
AV2	2.3 \pm 0.1	6.0 \pm 0.4	3.0 \pm 0.2	2.9 \pm 0.6	68 \pm 4	0.6 \pm 0.2	0.073 \pm 0.003
AV3	1.92 \pm 0.07	6.9 \pm 0.5	3.6 \pm 0.2	3.3 \pm 0.6	56 \pm 3	0.6 \pm 0.2	0.086 \pm 0.003
AV4	1.75 \pm 0.06	6.6 \pm 0.4	3.1 \pm 0.1	2.4 \pm 0.5	51 \pm 3	0.4 \pm 0.1	0.071 \pm 0.003
AB1	2.38 \pm 0.09	0.31 \pm 0.02	1.7 \pm 0.1	0.6 \pm 0.1	47 \pm 2	0.5 \pm 0.1	0.047 \pm 0.002
AB2	1.58 \pm 0.06	0.27 \pm 0.02	2.9 \pm 0.1	0.7 \pm 0.1	70 \pm 2	0.4 \pm 0.1	0.059 \pm 0.002
AB3	1.39 \pm 0.05	0.28 \pm 0.02	1.6 \pm 0.1	0.6 \pm 0.1	24 \pm 1	0.3 \pm 0.1	0.021 \pm 0.001
AB4	1.13 \pm 0.04	1.15 \pm 0.08	7.0 \pm 0.4	3.8 \pm 0.4	37 \pm 1	0.6 \pm 0.2	0.141 \pm 0.004
AB5	1.03 \pm 0.04	0.34 \pm 0.02	13.2 \pm 0.7	ND	84 \pm 3	0.8 \pm 0.2	0.028 \pm 0.003
A	Nd	Rb	Sb	Sc	Sm	Ta	Tb
AV1	44 \pm 7	199 \pm 10	1.06 \pm 0.08	18.5 \pm 0.6	9.2 \pm 0.4	1.5 \pm 0.4	2.1 \pm 0.6
AV2	59 \pm 9	205 \pm 10	1.00 \pm 0.08	19.6 \pm 0.6	11.3 \pm 0.5	1.7 \pm 0.5	2.4 \pm 0.7
AV3	46 \pm 8	245 \pm 9	0.83 \pm 0.08	19.6 \pm 0.6	9.4 \pm 0.4	2.2 \pm 0.3	1.1 \pm 0.1
AV4	43 \pm 7	219 \pm 8	0.48 \pm 0.06	18.3 \pm 0.5	8.6 \pm 0.4	1.8 \pm 0.2	1.1 \pm 0.1
AB1	20 \pm 5	57 \pm 2	0.32 \pm 0.04	4.7 \pm 0.1	10.5 \pm 0.4	2.7 \pm 0.2	0.9 \pm 0.1
AB2	22 \pm 5	102 \pm 4	0.45 \pm 0.05	3.5 \pm 0.1	9.0 \pm 0.4	4.9 \pm 0.4	1.2 \pm 0.2
AB3	6 \pm 2	37 \pm 1	ND	1.8 \pm 0.1	5.2 \pm 0.2	0.8 \pm 0.1	0.9 \pm 0.06
AB4	4 \pm 2	190 \pm 7	1.91 \pm 0.14	19.3 \pm 0.6	6.1 \pm 0.3	1.2 \pm 0.1	1.1 \pm 0.1
AB5	21 \pm 5	19 \pm 1	ND	6.3 \pm 0.2	11.1 \pm 0.4	1.3 \pm 0.1	1.0 \pm 0.1
A	Yb	Zn	Zr	Hg			
AV1	2.9 \pm 0.2	326 \pm 15	183 \pm 49	43 \pm 2			
AV2	3.0 \pm 0.2	304 \pm 14	ND	48 \pm 1			
AV3	3.1 \pm 0.2	231 \pm 6	109 \pm 23	44 \pm 2			
AV4	3.2 \pm 0.2	135 \pm 4	181 \pm 24	31 \pm 2			
AB1	3.2 \pm 0.2	269 \pm 8	99 \pm 12	<LD			
AB2	2.6 \pm 0.1	29 \pm 1	130 \pm 13	<LD			
AB3	2.0 \pm 0.1	13 \pm 1	98 \pm 10	<LD			
AB4	3.5 \pm 0.2	98 \pm 3	186 \pm 22	<LD			
AB5	4.6 \pm 0.2	31 \pm 1	332 \pm 32	<LD			

TABLE 3 – Activity concentrations of ^{238}U , ^{232}T , ^{226}Ra , ^{228}Ra , ^{210}Pb and ^{40}K (Bqkg^{-1}), pH and organic carbon (CO) in the analyzed samples

	<i>U-238</i>	<i>Th-232</i>	<i>Ra-226</i>	<i>Ra-228</i>	<i>Pb-210</i>	<i>K-40</i>	<i>pH</i>	<i>OC</i>
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
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

TABLE 4 – Reference values for meat, grains and vegetables found in diary diet in mBq kg^{-1}

	^{238}U	^{226}Ra	^{210}Pb	^{232}Th	^{228}Ra
Meat	2	15	80	1	10
Grain	20	80	50	3	60
Vegetable*	3	30	30	0,5	20

* Root vegetables and fruits

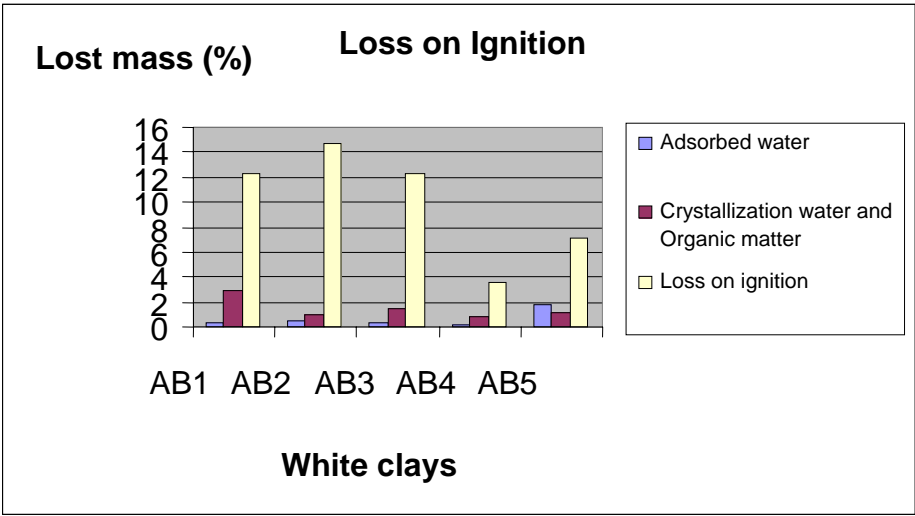
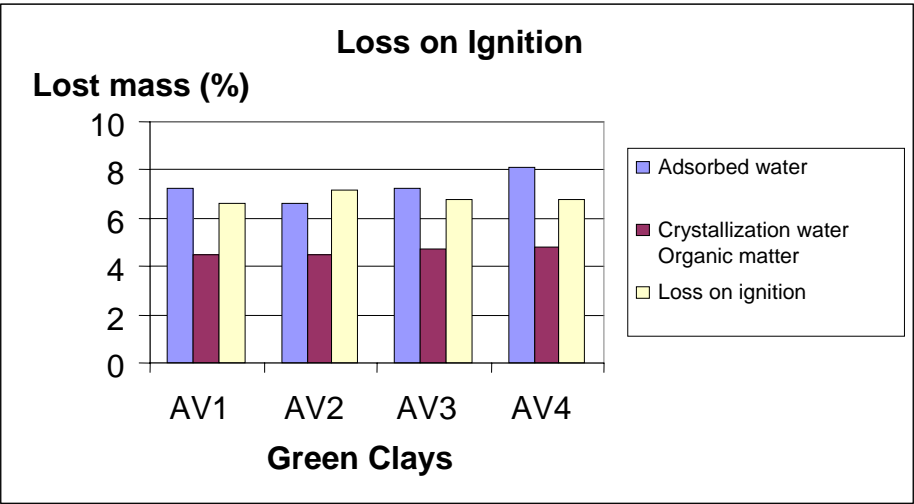


Figure 1: Percent of lost mass on ignition at different temperatures: adsorbed water at 60°C during 25 h, crystallization water and organic matter at 400°C for 2 h and loss on ignition at 800°C during 2 h.