Essential and toxic elements in clays for pharmaceutical and cosmetic use

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Abstract

Essential and toxic elements (Al, Si, P, S, K, Ca, Ti, Mn, Fe, Ni, Cu, Zn, As, Br, Rb, Sr, Ba, Cd, Ce, Nd, Pb, U, Th and La) were determined by Energy Dispersive Polarised X-Rays Fluorescence Spectrometry (EDPXRF) in 15 samples of clay materials for pharmaceutical and cosmetic use. The investigated samples were grouped according to their mineralogical composition determined by X-ray powder diffraction (XRPD). Samples made up of smectites showed the lowest content of K, Zn, La, Ce, Nd, Pb, Ti and Th and the highest content of Sr, Br and U. The sample containing smectite and kaolinite displayed the lowest content of Ca, Fe, Mn, Cu, Ni, Sr and the highest amount of Al, Si, Ba, Zn, As, La, Ce, Pb and Th. Samples composed of illite demonstrated minimal amounts of Br and the maximal content of K, Rb, Ti and Fe. In all samples analyzed, Cd and Hg were below 2.0 mgkg^{-1}.

Keywords: Clays, essential and toxic elements, EDPXRF, XRPD, cosmetic and pharmaceutical formulations

Introduction

The use of clay material for cosmetic and medical purposes has recently increased, due to the growing success of natural remedies (Carrettero, 2002). For cosmetic purposes, clays are used for external applications such facial, hair and skin treatment and dental creams in spas and in aesthetic medicine; clay minerals used in cosmetic formulations are kaolinite, smectites and palygorskite whereas other plyllosilicates such as talc are recommended only in liquid preparations (Mascolo et al., 1999). For medical purpose, clay minerals are used as active principles or excipients; as active principles clays may be orally administered (gastrointestinal protectors, osmotic oral laxatives, and antidiarrhoeaics) or applied topically (dermatological protectors); as excipients, clays are used as lubrificants, delivery systems, inert bases, emulsifiers. The use of clay minerals in pharmaceutical formulations was described previously (Carrettero, 2002; Carrettero et al., 2006; Lopez-Galindo et al., 2007;Todorovic et al-, 2002) and collected in Pharmacopeias. Clay minerals used in pharmaceutical formulations consist of smectites, palygorskite and kaolinite. A fundamental property that needs to be considered and maintained for use of a material in pharmaceutical formulations is low or null toxicity. The presence of some elements, even if in trace quantities, may pose a potential threat for the patient. It is well known that clay minerals, due to their high specific area and ion exchange capability, possess a high adsorptive capacity that results in accumulation of trace elements such as metals (Silva et al., 2005). Trace element may be located in the structure of clay minerals or their accompanying accessory phases, or adsorbed onto clay particles. In the latter case, mobilisation and transference to leaching solutions is considerably easier (Lopez-Galindo et al., 2007).

Trace element contents in these clay minerals is variable. This is the case for both those elements traditionally considered as toxic (As, Sb, Cd, Co, Cu, Pb, Ni, Zn, Hg, Ba etc.) and other less toxic elements (Li, Rb, Cr, Mo, V, REE etc.). Contamination of the ecosystem with elements such as As, Cd, Hg, Pb, Sb, which are ranked among hazardous substances of high priority by the Agency for Toxic Substances and Desease Ragistry (ATSDR, 2005), is a serious problem, threatening the habitat and the health of wild life and humans. These elements are natural components of the Earth's crust and the biological systems, and their concentrations have increased in the ecosystem during the last decades due to industrial and other anthropic activities. The activities attributed to these elements arise from exposure to aerosol particles and contaminated dust containing “heavy metals” that enter the atmosphere, are transported over large distances and result in soil and vegetation contamination of industrialised as well as non-industrialised areas (Wolkers et al., 1994).

Although Cr (III) is an essential element that helps the body requires for carbohydrate, protein and fat metabolism, Cr VI species is carcinogenic for organisms (Shi et al., 1999; Demirezen and Uruc, 2006).

Some elements such as As, Cd, Pb, Sn, Sb and Hg produce toxicity and need to be considered as a high risk factor for public health in general. Cd exerts an adverse effect on immune system, kidney, liver, lungs,reproductive organs, and bones(Ginsberg, 2012; Huang et al., 2009). Pb intoxication produces damage to the nervous and immune systems and may also result in dysfunction of the renal tubules, liver, and the cardiovascular system (Tsuchiva, 1986; Garcia-Leston et al., 2012; Counter et al., 2009). Children are particularly at risk from Pb ingestion, both before and after birth (Buchanan et al., 2011; Counter at al., 2009). Hg is a neurotoxic poison that produces neurobehavioral effects, neuroendocrine and renal damage and immuno toxicity (Chen et al.,2011; Ni et al., 2012; Sweet and Zelikoff, 2011). Arsenic is a problematic element for humans producing carcinogenesis of liver, kidney, bladder and skin (Tsai et al., 1998; Bernstam and Nriagu, 2000). It is well known that the speciation of As plays an important role in determining As-induced toxicity to humans (Zavala et al., 2008). Sb and many compounds containing this element are toxic. The effects of antimony poisoning resemble intoxication; however, toxicity of Sb is far less severe than for As which may be related to significant differences in uptake, metabolism and excretion. Since clays are used for ttreatment of various diseases, it is necessary to avoid possible intoxications via ingestion and skin absorption of elements present in the clays. Thus it is necessary to determine the concentration of toxic or potential dangerous elements in such matrixes and to understand their mobility.The potential toxic elements may be readily exchangeable during the development of therapy or they may be strongly bound to the mineral structures (Summa and Tateo, 1999).

At present, few data are available on the chemical composition of clays, especially with respect to trace elements. In this study, elemental composition of 15 clays used in health sciences was carried out by Energy Dispersive Polarised X-Rays Fluorescence Spectrometry (EDPXRF) following mineralogical characterization by X-ray powder diffraction (XRPD). EDPXRF is a simultaneous, reliable, sensitive, quantitative multi elemental and non-destructive technique, suitable for routine analysis due to minimal sample preparation. This technique was previously used successfully for characterization of different complex matrices (Desideri et al., 2011, 2012).

Materials and methods

Sample pre-treatment

Analysis were carried out on 15 clay samples for pharmaceutical and cosmetic use purchased in local stores. Most of the clays were contained in 0.5 kg sacs. Approximately 0.5 kg of sample was weighed individually, dried in an oven at 105 °C for 24 hours and dried samples were weighed and homogenized.

X-ray diffraction

Clay minerals were identified by X-ray powder diffraction (XRPD) analyses using a Philips X'Change PW 1830 diffractometer (Cu Ka radiation). Randomly oriented powders were prepared by hand crushing bulk samples and side loaded into an aluminium holder for analysis of unoriented powder (bulk composition). They were analyzed a 0.02° step, with a counting time of 1 s/step from 2° to 60° 2θ. The analytical conditions were a 35 kV accelerating potential and 30 mA filament current. Eleven peaks were indexed in the refinement, and quartz served as an internal standard. Successively, the 2 µm clay fraction was extracted by crushing, dispersion, and two-stage centrifuge. Oriented clay mounts were prepared and analyzed under conditions of air drying, presence of ethylene glycole, and heated to 335°C, then to 550°C for two hours. These were analyzed a 0.02° step, with a counting time of 1 s/step from 2° to 30° 2θ, and examined in composite diffractograms.

Energy Dispersive Polarised X-Rays Fluorescence Spectrometry (EDPXRF)

Each sample was prepared by mixing it with Wachs-C 80004005 Mikropulver, a paraffin wax that helps to reduce the sample to tablet though pressure.

The determinations were conducted with a Spectro-X-LAB2000 (SN DK 949196), Energy Dispersive Polarised X-Rays Fluorescence Spectrometry (EDPXRF).

The quality of data was assured by calibrating the instrument with the following certified reference materials (CRM): MURST-ISS-A1 Marine sediment, GBW07310 Stream sediment, GBW08303 Farmland Soil, LGC6138 Soil, SRM 12-3-12 Sludge, STD 12-1-12 Fly ash, BCR CRM 144R Sludge, CCRM LKSD1 Lake sediment, CCRM PACS-2 Marine sediment, NIST SRM 2709 Agricultural soil, NIST SRM 2711 Montana soil, NIST SRM 1633b Fly ash. The analytical precision, measured as relative standard deviation, for Pb, Cd, As, Zn, Cu, Ni, and Mn, was routinely between 4 and 6%, but about 10% for Cr. The averaged analytical standard errors observed with respect to the reported certified materials were below 10% for Cr, As and Cd, and below 7% for Mn, Ni, Cu, Zn and Pb.

Statistical analyses

For each element, the concentrations for all clays, with the minimum and maximum value, arithmetical mean, median and standard deviation are reported.

Data were also grouped according to mineralogical composition, and for each group the element concentration, expressed as arithmetical mean, and relevant standard deviation is reported. Statistical analysis using Student's *t*-test was carried out. The criterion for significance was set at $P < 0.05$

Results and discussion

Mineralogical composition

According to the procedures proposed by various investigators (Brinley and Brown, 1980; Velde, 1995; Moore and Reynolds, 1997; Setti et al., 2004), the qualitative identification of mineral species was based on the shape, position and intensity of specific reflections. The results of mineralogical analyses on bulk composition and on the clay fraction of the studied samples, as well as colour and pH, are presented in Table 1.

Concerning bulk composition, the non-clay fraction was always abundant and predominantly represented by calcite, dolomite, quartz, feldspars and gypsum. Siliciclastic and carbonate minerals such as quartz, feldspars and dolomite are common phases and present in almost all samples, whereas gypsum was rare and detected in only two samples (1 and 2).

The clay fraction (<2μm) of the studied samples exhibited strong first-order reflexions, often with asymmetrical shapes and a few associations of weak and broad diffraction bands or shoulders. The behaviour of minerals reflections under natural conditions (air-dried, ethylene glycolation and heating to 335°C and 550°C) identified a highly diverse set of clay minerals represented by illite, smectites, kaolinite and chlorites. Based on type (and association) of clay minerals, samples may be divided into five groups. Group 1 is the most represented (53% of the total samples) and has a clay fraction formed by smectites+illite+chlorites. Group 2 samples (20%) are composed by illite, whereas group 3 samples (16%) consist of smectites. Groups 4 and 5 correspond to isolated samples which have a clay fraction composed of illite+chlorites+kaolinite and smectites+kaolinite, respectively.

Chemical composition

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

The elements taken into account in this study were: Al, Si, P, S, K, Ca, Ti, Mn, Fe, Ni, Cu, Zn, As, Br, Rb, Sr, Ba, Cd, Ce, Nd, Pb, U, Th and La. The concentration, as arithmetical mean, standard deviation, median, and minimum and maximum concentration in clay minerals is shown in Tables 2 and 3. To calculate the arithmetical mean, for the concentrations below the limit of detection (LOD) (6 samples for S, 3 for Br, 1 for Nd), the relevant median detection level (MDL) was considered. All results were affected by an error of 10-25%.

The average values obtained in this study are in agreement with those reported for crustal clay by Turekian and Wedephol (Turekian and Wedephol, 1961) although some samples showed some elements to be higher than found in crustal clay (tables 2 and 3), which may due to possible contamination during manufacturing and commercialization processes.

In tables 4 and 5 data were also grouped according to mineralogical composition (Groups 1 to 5), and for every group the arithmetical mean and relevant standard deviation were reported. In the case of K content, a significant difference was noted between the samples containing illite (higher content) and those containing smectites (lower content). The Fe content was higher in samples 4,12 and 15 (illite-bearing Group 2), and lower in sample 9 (smectite + kaolinite-bearing Group 5). Ca content was maximal in Group 1(smectite + illite + chlorite-bearing) whereas it was minimal in Group 5 sample, and may be related to the amount of calcite (significant in Group 1 but absent in Group 5); S content was maximal in sample 1 (Group 1) and this is probably due to the presence of gypsum (table 1).

Samples 1 and 7 (smectites-bearing Group 3) displayed the lowest content of Zn, La, Ce, Nd, Pb and Th and the highest quantity of Sr and Br. Sample 9 (smectite + kaolinite, Group 5) presented the lowest content of Cu, Ni, Sr and the highest content of Ba, La, Ce, Pb and Th. Samples 4, 12 and 15 (illite-bearing Group 2) showed minimal content of Br and maximam levels of Rb. For the Ni, Pb and U content, a significant difference was observed between samples containing illite (higher content of Ni and Pb, lower content of U) and those containing smectites (higher content of U, lower content of Ni and Pb).

Table 6 shows the chemical limitations reported in the European Pharmacopeia of 2011 and US Pharmacopeia of 2009 (USP 32- NF27, 2009). Attention needs to be drawn to the amount of heavy metals, Pb and As present.

According to the European Norm 1223/2009 (EC, 2009) As, Se, Cd Hg, Pb, Sb and Tl are not permitted in cosmetic products.

Conclusions

For use of clays and clay minerals for pharmacological purposes, pharmaco the clay minerals, pH, microbial limit, water content, quantity of acid soluble substances, presence of impurities as trace elements. The presence of some elements, even in trace quantities, may pose a potential threat for the patient. EDPXRF technique used in this investigation for analysis of mineral samples proved to be a reliable tool to provide elemental composition. This multielemental technique, in fact, provides a rapid way to determine quantitatively nearly all elements from K to U. For some elements such as Cd, Hg, that have high LOD, preconcentration techniques might be applied to reach a lower LOD. In any case, high contamination levels, if present, would have been detected also with these measurements presented in this study.

Future research will address the study of mobility of non essential and essential elements from healing clays into humans by analyzing separate fractions obtained by sequential leaching. The effects of clay elements on human health need to take into account bio-availability of the chemical elements rather than concentration.

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Table 1

Mineralogical composition (semiquantitative estimation, + = <30%, ++ = 30-60%,+++ = > 60%), color and pH (ND= Not Detectable)

Sample (N)	Color	pH	Quartz	Calcite	Dolomite	Gypsum	Feldspars	Clays	
1	Brown	ND	X	X	X	X	X	+++	smectites
2	Green	7.74	X	X	X	(X)	X	++	Smectites+illite+chlorites
3	Brown	8.16	X	X	X		X	++	illite+chlorites+kaolinite
4	Green	8.27	X	X				+++	illite
5	Green	7.85	X	X	X		X	++	Smectites+illite+chlorites
6	Green	8.30	X	X	X		X	++	Smectites+illite+chlorites
7	white	ND	X	X	(X)			+++	smectites
8	Green	7.84	X	X	X		X	++	Smectites+illite+chlorites
9	White	ND	X		X		X	+++	Smectites+kaolinite
10	Green	8.11	X	X	X		X	++	Smectites+illite+chlorites
11	Green	8.36	X	X	X		X	++	Smectites+illite+chlorites
12	Green	7.80	X	X				+	illite
13	Green	8.50	X	X	(X)		X	++	Smectites+illite+chlorites
14	Green	8.50	X	X	(X)		X	++	Smectites+illite+chlorites
15	Green	7.70	X	X				+	illite

Table 2
Concentration (% with the relevant error) of the major elements in clays and comparison with the values reported by Turekian and Wedephol (1961) for crustal clay

SAMPLE	Al	Si	P	S	K	Ca	Ti	Mn	Fe
01	1.68	19.5	0.093	1.47	0.515	3.96	0.125	0.007	0.95
02	6.05	17.5	0.090	0.173	1.71	12.2	0.287	0.044	2.94
03	8.07	20.1	0.097	< 0.003	1.85	4.86	0.367	0.123	3.83
04	10.2	22.1	0.120	< 0.003	4.18	2.60	0.458	0.046	5.06
05	6.25	18.2	0.083	0.097	1.74	11.9	0.294	0.051	3.45
06	5.86	16.3	0.065	0.076	1.68	11.9	0.281	0.053	3.31
07	8.83	23.7	0.089	0.275	0.449	2.23	0.464	0.029	3.42
08	6.46	17.7	0.085	< 0.003	1.72	11.7	0.304	0.057	3.23
09	12.3	26.2	0.109	0.060	0.825	0.48	0.372	0.016	0.95
10	6.64	19.5	0.075	< 0.003	1.81	9.91	0.317	0.075	3.45
11	6.50	18.8	0.074	0.052	1.79	10.8	0.308	0.061	3.37
12	8.78	24.4	0.094	0.301	2.83	5.71	0.510	0.041	3.97
13	6.44	18.8	0.067	< 0.003	1.79	9.54	0.314	0.086	3.55
14	6.38	18.9	0.066	< 0.003	1.78	9.56	0.317	0.091	3.61
15	7.43	22.6	0.088	0.327	2.57	5.34	0.475	0.036	3.62
Error %	**10**	**10**	**25**	**25**	**10**	**10**	**15**	**15**	**10**
min	1.68	16.3	0.065	<0.003	0.449	0.48	0.125	0.007	0.95
max	12.3	26.2	0.120	1.47	4.18	12.2	0.510	0.123	5.06
mean	7.19	20.3	0.086	0.190	1.82	7.50	0.346	0.054	3.25
std dev	2.36	2.86	0.016	0.371	0.918	4.06	0.099	0.030	1.04
median	6.50	19.5	0.088	0.060	1.78	9.54	0.317	0.051	3.45
Crustal clay	8.0	7.3	0.07	0.24	1.1	3.9	0.46	0.08	4.7

Table 3

Trace-element content (mgkg^{-1}, with the relevant error) in clays and comparison with the values reported by Turekian and Wedephol (1961)for crustal clay

SAMPLE	Ni	Cu	Zn	As	Br	Rb	Sr	Ba	La	Ce	Nd	Pb	U	Th
01	10.3	12.8	30.7	2.4	13.9	36.7	3031	214.7	4.60	23.3	<20.0	10.8	7.41	1.90
02	75.6	29.6	75.8	3.1	6.10	108	453.2	356.2	20.0	49.2	27.9	19.9	3.25	9.70
03	50.5	44.4	84.7	13.1	2.80	101	115.4	331.3	33.5	71.4	35.4	23.8	1.22	7.20
04	35.8	27.0	140.9	29.6	<1.0	494	139.9	366.9	16.2	45.2	23.5	36.0	2.84	9.12
05	88.4	28.1	79.1	3.9	5.30	110	458.7	379.3	17.2	48.2	26.0	19.1	2.92	6.94
06	89.5	30.0	78.6	3.4	5.50	109	464.8	382.4	19.3	46.6	28.4	18.8	3.75	6.97
07	13.1	24.3	63.6	11.5	1.10	39.8	116.1	872.0	30.2	58.0	30.6	11.4	6.19	8.83
08	86.3	33.2	78.8	4.5	3.70	107	450.7	400.1	24.0	56.0	28.4	18.7	5.34	8.29
09	10.3	8.0	224.2	36.8	2.10	66.7	86.20	1589	48.9	78.6	33.0	65.4	3.37	13.4
10	128	37.6	83.6	3.2	2.80	114	453.3	481.0	21.2	53.4	37.9	20.0	2.55	8.17
11	105	31.1	79.6	3.9	4.40	112	453.8	436.2	18.9	52.4	27.3	19.4	2.98	7.32
12	38.9	25.7	86.2	10.0	<1.0	139	291.3	451.4	33.1	76.1	30.3	23.5	4.73	9.71
13	155	32.8	82.1	5.8	1.90	111	452.2	497.7	23.8	56.2	32.7	18.5	2.31	8.02
14	170	35.9	83.8	5.3	1.90	112	457.5	539.8	26.6	57.3	33.4	19.0	2.49	8.37
15	31.4	22.5	75.8	9.4	<1.0	128	250.0	461.8	34.7	76.5	36.9	20.8	3.78	7.68
Error %	**15**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**15**	**15**	**15**	**10**	**15**	**15**
min	10.3	8.0	30.7	2.4	<1.0	36.7	86.20	214.7	4.60	23.3	<20.0	10.8	1.22	1.90
max	170	44.4	224.2	36.8	13.9	494	3031	1589	48.9	78.6	37.9	65.4	7.41	13.4
mean	72.5	28.2	89.8	9.7	3.63	126	511.6	517.3	24.8	56.6	30.1	23.0	3.68	8.11
st dev	51.4	9.1	43.0	10.2	3.33	106	713.2	329.1	10.3	14.6	4.95	13.0	1.62	2.36
median	75.6	29.6	79.6	5.3	2.80	110	452.2	436.2	23.8	56.0	30.3	19.4	3.25	8.17
Crustal clay	68	45	95	13	4.0	140	300	580	92	59	5.6	-	3.7	12

Table 4
Mean concentration (%) and the relevant standard deviation of the major elements in clays for every group

Group (sample number)	Al	Si	P	S	K	Ca	Ti	Mn	Fe
Group 1 Smectite +Illite +Clorite (2,5,6,8,10,11,13,14)	6.32±0.26	18.22±1.00	0.08±0.01	0.051±0.06	1.75±0.05	10.93±1.12	0.30±0.01	0.06±0.02	3.36±0.21
Group 2 Illite (4,12,15)	8.80±1.39	23.02±1.20	0.10±0.02	0.21±0.18	3.19±0.86	4.55±1.70	0.48±0.03	0.041±0.005	4.22±0.75
Group 3 Smectite (1,7)	5.26±5.05	21.60±3.03	0.09±0.003	0.870±0.84	0.48±0.047	3.09±1.22	0.29±0.24	0.018±0.016	2.18±1.74
Group 4 Illite+Clorite+kaolinite (3)	8.07	20.1	0.097	<0.003	1.85	4.86	0.367	0.123	3.83
Group 5 Smectite + kaolinite (9)	12.30	26.21	0.109	0.060	0.83	0.48	0.372	0.016	0.95

Table 5
Mean concentration (mgkg^{-1}) and the relevant standard deviation of trace elements in clays for every group

Group, (sample number)	Ni	Cu	Zn	As	Br	Rb	Sr	Ba	La	Ce	Nd	Pb	U	Th
Group 1 Smectite +Illite +Clorite (2,5,6,8,10,11,13,14)	112.1	32.29	80.18	4.14	3.95	110.3	455.53	434.09	21.38	52.41	30.25	19.18	3.20	7.97
±Standard deviation	34.94	3.25	2.77	0.99	1.64	2.39	4.59	65.82	3.16	4.03	4.03	0.55	0.98	0.91
Group 2 Illite (4,12,15)	35.37	25.067	100.97	16.33	<1	253.7	227.07	426.70	28.00	65.93	30.23	26.77	3.78	8.83
±Standard deviation	3.77	2.316	34.97	11.49		208.2	78.26	52.05	10.25	17.96	6.70	8.11	0.95	1.04
Group 3 Smectite (1,7)	11.70	18.55	47.15	6.92	7.50	38.25	1573.5	543.35	17.40	40.65	25.30	11.10	6.80	5.37
±Standard deviation	1.98	8.13	23.26	6.47	9.05	2.19	2061.1	464.78	18.10	24.54	7.49	0.424	0.36	4.90
Group 4 Illite+Clorite+caolinite (3)	50.5	44.4	84.7	13.1	2.80	101	115.4	331.3	33.5	71.4	35.4	23.8	1.22	7.20
Group 5 Smectite + caolinite (9)	10.3	8.0	224.2	36.8	2.10	66.7	86.2	1589.0	48.9	78.6	33.0	65.4	3.37	13.42

Table 6

Chemical limitations (%) as indicated in European Pharmacopeia (2011) and US Pharmacopeia (USP 32- NF27, 2009)

Chemical limitations	Kaolinite		Talc		Bentonite		Sepiolite		Palygorskite
	EP7th	USP32	EP7th	USP32	EP7th	USP32	EP7th	USP32	USP32
Al (%)			≤2	≤2					
Ca (%)	≤0.025		≤0.9	≤0.9					
Fe (%)			≤0.25	≤0.25					
Mg (%)			17-19.5	17-19.5					
As (ppm)						≤5	≤4	≤8	≤2
Pb (ppm)		≤10	≤10	≤10		≤40			≤10
Heavy metals (ppm)	≤50				≤50		≤40	≤30	
Chloride(%)	≤0.025						≤0.050	≤0.055	
Sulfate (%)	≤0.1						≤0.5	≤0.5	
pH			7-9			9.5-10.5			7-9.5