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Solid-Phase Adsorption of Curcumin from Turmeric Extracts by Lamellar Solids and Magnesium Oxide and Hydroxide

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Abstract

Solid-phase extraction and solid-phase adsorption are currently convenient experimental techniques employed to the concentration and purification of secondary metabolites of plant, microbial, and fungal origin. The aim of this research article was the screening of the capacity by 16 solid sorbents including layered structures (hydrotalcites and zirconium phosphates), magnesium oxide and hydroxide, and the phyllosilicates talc and bentonite to selectively concentrate curcumin from raw extract solutions of turmeric, *Curcuma longa*l. (Fam. Zingiberaceae). HPLC analysis, coupled to PDA detection, showed that, among the sorbents employed, magnesium oxide was the most effective one reaching a percentage of adsorption of 96.6%. Other solids able to concentrate curcumin on their surface in percentages varying from48.9 to 68.7% included the hydrotalcites magnesium aluminum hydroxy acetate, magnesium aluminum acetate, magnesium aluminum hydroxy chloride, and magnesium aluminum nitrate, and finally magnesium hydroxide (47.0%). We have finally shown that these sorbents can be readily recovered an recycled without significant losses of adsorption capacities. Although a similar procedure has been recently described using anthraquinones from laxative plants as substrates, the application of these supports for the extraction in the solid phase of curcumin as a representative compound of the diarylheptanoid family is reported herein for the first time in the literature.

Keywords Curcumin · Hydrotalcites · Lamellar solids · Magnesium oxide · Solid-phase extraction · Turmeric

Introduction

Solid-phase extraction (SPE) and solid-phase adsorption (SPA) are well-validated techniques for the pre-concentration, extraction, and purification of several analytes deriving from different matrices. These experimental procedures have some advantages over the other ones employed for the same purposes like high recoveries and enrichment factors, low cost, rapid phase separations, easiness of synthesis and handling, extensive recyclability and reuse, and finally the possibility to combine the extraction step with numerous detection techniques. The selection of the sorbent has a deep influence on key analytical parameters such as selectivity, affinity, and capacity of adsorption. Activated carbon, silica, alumina, molecularlyimprinted polymers, resins, and nanosized materials are commonly used as solid phases in SPE and SPA. However, the search for novel, more efficient, more selective, and more adaptable materials to accomplish SPE and SPA is a field of current and growing interest with a great potential for pilot plant and industrial applications in the pharmaceutical, cosmetic, agricultural, and nutraceutical fields.

Layered double hydroxides (LDHs), known also as "hydrotalcites" or "mineral clays", are functional materials nowadays used for multiple purposes. These can be synthesized in a very easy and cheap way providing a wide panel of different two-dimensional and three-dimensional structures. Conventionally, LDHs comprise positively charged layers of metal hydroxides with charge-balancing anions and have the capacity to host water molecules in the interlayer spaces. LDHs are compounds of general formula $[M(II)_{1-x}M(III)_x(OH)_2]^{x+}[A^{n-}{}_{x/n}]^{x-}$ x n H_2O in which *M(II)* is a divalent metal cation (in most cases Mg or Zn), *M(III)* is a trivalent one, (mostly Al), A^{n-} is an exchangeable inorganic or organic anion which compensates for the positive charge of the layer, and *n* are the moles of water hosted (Mishra et al. 2018). LDHs are biocompatible and have in general low toxicity

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(Saifullah and Hussein 2015). For these reasons, they have been extensively used as pharmaceutical ingredients with improved properties: explicative examples to this concern are the antiacid TALCID®, the non-steroidal anti-inflammatory drugs and methotrexate controlled release, and colon-targeted drug delivery (Choy et al. 2004; Gordijo et al. 2005; Oh et al. 2006).Few examples have been cited in the literature about the applications of the title solids for plant extraction and similar activities. These are represented by the removal of organic pollutants from wastewaters deriving from plant processing (*Anirudhan and Suchitra* 2007*;* Grünewald et al. 2008), the depolimerazion of lignin (Kruger et al. 2016), and the encapsulation of root extracts of *Angelica gigas* Nakai (Fam. Apiaceae) (Kim et al. 2016) and lutein (Li et al. 2020). Very recently, we reported that, among a panel of 16 mineral clays and phyllosilicates, the hydrotalcite zinc aluminum oleate and magnesium oxide exhibited the best capacity in adsorbing the anthraquinone emodin from an ethanolic solution of raw extracts of the Japanese medicinal plant *Polygonum cuspidatum* (sin. *Reynoutriajaponica* Houtt., Fam. Polygonaceae) (Genovese et al. 2020).

As a continuation of our studies devoted to investigate the interaction of plant extracts and solid sorbents, in this short communication, we wish to outline the performance of hydrotalcites, derivatized lamellar zirconium phosphates, phyllosilicates, magnesium oxide, and hydroxide for the selective concentration of the diarylheptanoid curcumin(Fig. 1) from raw solid extracts of turmeric, *Curcuma longa* L. (Zingiberaceae).

Curcumin was selected as it represents one of the most fashioned natural product claimed to exert a plethora of beneficial activities for human welfare (Zielińska et al. 2020; Ahmad et al. 2020; Hewlings and Kalman 2017). The great interest of the scientific community towards curcumin is also witnessed by hundreds of manuscripts per year published in the literature during the last decade. Furthermore, the use of turmeric as a plant food is historically well-documented.

Roots and rhizome of this plant have been used as a food supplement since the 6th BC by Assyrians and later by numerous populations of South and East Asia, from which its use has spread throughout the Western world up to our times.

Thus, turmeric is one of the key ingredients in several Asian dishes, providing a mustard-like, earthy aroma, and pungent, slightly bitter flavor to foods. It is also used in many food preparations like canned beverages, baked products, dairy products, ice cream, yogurt, yellow cakes, orange juices, biscuits, popcorn color, cereals, sauces, and gelatin. Although commonly consumed in its dried powdered form, turmeric is also used fresh, like ginger, and as such has numerous uses in East Asian recipes, such as a pickle that contains large chunks of fresh soft turmeric. It is also consumed as a beverage in combination with coconut milk. Finally, turmeric is the main ingredient in curry powder (*Priyadarsini* 2014).

While numerous reports about the incorporation of pure curcumin into hydrotalcites using conventional hydrotalcites synthetic methodologies (e.g. co-precipitation at a variable orconstant pH, under low or high supersaturation, hydrothermal, and mechanochemical synthesis) "merely" for controlled release and/or chemical stability preservation and enhancement of the biological activity purposes have been cited in the literature (Gonçalves et al. 2017; Gayani et al. 2019; Pavel et al. 2020), the direct interaction of LDHs and structurally similar solid supports with curcumin as part of a phytocomplex is unprecedented in the literature to the best of our knowledge.

Materials and Methods

Chemistry and Plant Material

Curcumin (purity≥ 97.5%) was purchased from Extrasynthese (Genay Cedex France). Solvents (all UHPLC grade) were purchased from Dasit-Carlo Erba Reagents (Milan, Italy). Water HPLC grade was produced in the same way already reported (Genovese et al. 2017). All solid supports have been provided by Prolabin &Tefarm Srl (Perugia, Italy). A stock solution of curcumin (1.0 mg/mL) was obtained by its

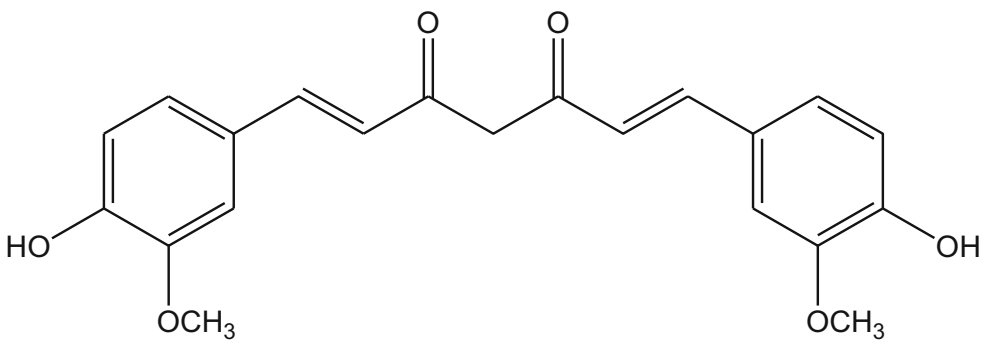

Fig. 1 Structure of curcumin

dissolution in EtOH. The dried extract sample from *C. longa* was purchased from a local market. A voucher specimen (CL-DE-2020-1) has been stored in the repository of the Laboratory of Chemistry of Natural Compounds at the Department of Pharmacy of the University "G. D'Annunzio" of Chieti-Pescara.

Solid-Phase Adsorption Procedure

The screening of the efficiency of sorbents was accomplished by adding 50 mg of each into a solution obtained dissolving 10 mg of the turmeric extract in 20 mL of EtOH. The resulting suspension was vigorously shaked under magnetic stirring at room temperature for 1 h. The solid was filtered, the filtrate centrifuged (13,000 rpm, 5 min., room temperature), and the solution directly used for HPLC analysis after an 1:50 dilution with EtOH. The stock solution of the original extract was prepared dissolving 10 mg of the powder in 20 mL of EtOH. For HPLC analysis to quantify the content in curcumin of the untreated extract, 1 mL of the solution was diluted to 50 mL with EtOH.

HPLC Experimental Conditions and Method Validation

Analysis was carried out adopting an experimental procedure similar to that already reported recently in the literature (Genovese et al. 2020). The only differences were the flow rate (1.2 mL/min.) and the detection wavelength (425 nm).The method validation followed the recommendations provided by ICH guidelines (Bhavyasr et al. 2019) and was assessed as already reported in the literature (Genovese et al. 2020). Linearity was calculated in the range 0.30–100 μg/mL. Precision was recorded at three concentration levels ($QC_{Low} = 0.45$ μg/mL, $QC_{Medium} = 30.0$ μg/mL, and $QC_{High} = 90$ μg/mL determined following the criteria already reported for our previous studies) in three replicates. The accuracy of the method was assayed spiking turmeric extract samples with the standard solutions at QC_L, QC_M, and QC_H concentrations. All samples were spiked in triplicates, and three consecutive chromatographic HPLC runs were recorded. Selectivity was determined by the comparison of the calibration curve of standard curcumin with calibration curves obtained from *C. longa* extracts containing the lowest concentration of this analyte. The carry-over effect was recorded after injection of two aliquots of turmeric extract followed by two samples spiked with pure curcumin at the LOQ concentration. The matrix effect determination was accomplished according to the method already reported (Zhou et al. 2017).

Results and Discussions

The chemico-physical parameters of the sorbents we used to accomplish the SPA of curcumin from the raw dried solid extract of *C. longa* are equal to those already reported in the literature (Genovese et al. 2020). First, we measured the content of curcumin of the turmeric parent extract. The retention time of curcumin was 4.24 (± 0.05) min. A representative chromatogram of the standard analytes is shown in Fig. 2.

The overall adsorption capacities of solid materials employed in the present study was then recorded. To this aim, a suspension of the sorbent and the extract in EtOH was kept under magnetic stirring at room temperature for 1 h. After filtration under vacuum, the filtrates were analyzed for their contents in curcumin and the corresponding values compared to its concentrations in the parent turmeric extract. The amounts adsorbed on the sorbents were finally calculated as concentration expressed in mg/g of extract and percentage differences in their quantities in the original plant extracts and those present in the filtrate after HPLC analysis. Results of these quantifications are reported in Table 1.

Three independent chromatographic runs and analysis to reach the final recorded concentrations were carried out. In all cases experimental *t* test values [95% confidence level ($\nu = 2$)] are lower than the theoretical ones (data not shown).

Data in Table 1 show that several sorbents were capable to effectively adsorb curcumin in good to excellent yields. The most efficient one to this purpose was magnesium oxide that virtually concentrated the whole quantity of curcumin present in the parent extract with a percentage of 96.6%. In this, it closely resembles what we have recently observed for extracts from *P. cuspidatum* and selective adsorption of the anthraquinone emodin (Genovese et al. 2020).

Good percentages of adsorption have been recorded also for the hydrotalcites magnesium aluminum nitrate (entry 4, 48.9%), magnesium aluminum hydroxide chloride (entry 6, 49.7%), magnesium aluminum hydroxide acetate (entry 7, 68.7%) and magnesium aluminum acetate (entry 9, 53.0%), and finally for magnesium hydroxide (entry 13, 47.0%).

However, contrary to the study on emodin, the presence of medium- to long-chain carboxylic acids like azelate (entry 5) and oleate (entry 1) in the interlayer spaces of LDHs do not seem to favor adsorption of diarylheptanoids.

Phyllosilicates were not shown to be effective: the highest but very poor percentage recorded in this group was that of bentonite (10.0%). This finding in part confirms the low trend exhibited by such clays to adsorb curcumin from its raw solid extracts in the absence of other auxiliary sorbent materials, like polyvinylpyrrolidone already observed in the recent literature (Pan-on et al. 2018).

As for the previous and very recent study with *P. cuspidatum* (Genovese et al. 2020), also in this case, the optimal and standardized experimental conditions were a 5:1

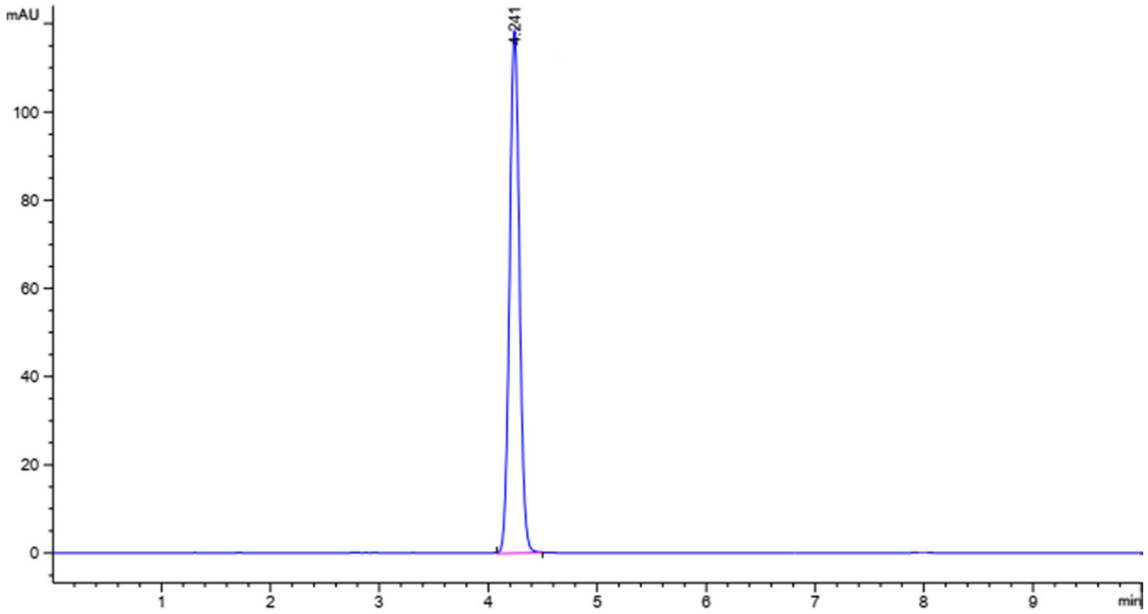

Fig. 2 Sample HPLC chromatogram of standard curcumin

w/w ratio between the extract and the solid support and a robust magnetically stirring of suspensions for 1 h at room temperature. Increases or decreases of such parameters failed to improve adsorption yields. In particular, temperatures > 60 °C resulted in a rapid darkening of turmeric extract solution to deep brown with precipitation of amorphous solids. This may indicate a chemical degradation of curcumin due to high temperatures as already reported in the literature (Suresh et al. 2009).

For what concerns the HPLC method, it is noteworthy to highlight that a complete baseline separation of the standard analyte with no interferences from other peaks of the matrices was achieved. A 13-point calibration curve, recorded at 425 nm as the detection wavelength, was plotted using weighted ($1/x^2$) linear least-squares regression analysis and was linear over all the concentration range tested (0.30–100 μg/mL, $r^2 \geq 0.9985$). The repeatability and trueness of the HPLC method were determined as already described in the literature (Genovese et al. 2020). Data about all relevant parameters are outlined in Table 2.

RSD values of the intra- and interday precisions were not higher than 3.2%, while the BIAS% ones referred to the intra- and interday accuracies were in the range − 1.1 to 2.7%. These data suggest that in the frame of ICH guidelines, the method

Table 1 Effectiveness of solid inorganic and inorganic/organicmaterials for the SPA of curcumin from raw solid extracts of *C. longa*

Entry	Concentration*	% Adsorption
Parent extract	598.90 ± 0.88	–
1	1.56 ± 0.09	0.2
2	215.07 ± 0.66	35.9
3	133.63 ± 0.71	22.3
4	292.96 ± 0.54	48.9
5	150.86 ± 0.61	25.1
6	298.01 ± 0.31	49.7
7	411.28 ± 0.45	68.7
8	2.11 ± 0.02	0.3
9	317.78 ± 0.32	53.0
10	28.69 ± 0.09	0.9
11	2.34 ± 0.04	0.4
12	1.98 ± 0.02	0.3
13	281.73 ± 0.38	47.0
14	578.48 ± 0.51	96.6
15	60.10 ± 0.19	10.0
16	2.11 ± 0.04	0.3

*Values expressed as mg of curcumin/g of dry extract

Table 2 Calibration curve, precision, and accuracy data

Slope	119,812
Intercept	1562
r^2	0.9985
LOD (μg/mL)	0.45
LOQ (μg/mL)	0.35
Precision	
Intra-day (n=6)	2.1–4.4
Inter-day (n=6)	2.3–4.2
Accuracy	
Intra-day (n=6)	1.9–4.2
Inter-day (n=6)	0.9–2.1

set-up herein is featured by more than acceptable accuracy, precision, and reproducibility. The carry-over effect (< 0.18%) was not observed. In all cases for HPLC runs of samples coming from the adsorption steps, the retention time of curcumin fully matched that recorded for the pure standard. Recovery of the analyte was > 98.4% with a good precision (RSD < 2.4%).

To ascertain and generalize the recyclability and reusability of the most effective sorbents (entries 7 and 14), after the first experiment, curcumin was desorbed from each solid support by repeated washing of the solid with acetone followed by filtration until no analyte could be recorded by HPLC analysis.

The support was then dried in oven at 60 °C for 12 h and reused to accomplish 4 further experiments using the same experimental protocol as described above. Percentages of curcumin adsorbed on magnesium oxide (entry 14) and magnesium aluminum hydroxide acetate (entry 7) were 96.2%, 95.4%, 96.0%, 95.2%, and 68.1%, 68.1%, 67.4%, 68.4% respectively. Thus, it can be concluded that no appreciable loss of adsorption capacities by both solid supports occurred upon their recycling after each experiment.

Data reported in Table 1 allow to draw some hypothesis to account for the very different pattern of adsorption recorded among the 16 inorganic and mixed inorganic/organic solids assayed in the present investigation. With the only exception of magnesium aluminum hydroxide carbonate (entry 8), only magnesium-containing sorbents without intercalated organic anions are effectively able to adsorb curcumin in good to excellent yields, and the efficiency is largely higher than zinc-containing hydrotalcites (entries 1–3). This can be explained mainly in terms of an effective intercalation of curcumin into the interlayer spaces of magnesium-based LDH (entries 4, 6, 7, and 9), and the extent of such an intercalation could be enforced by the planar structure of curcumin and is more favorable in interlayer spaces deprived of sterically bulky anions like oleate (entry 1) and azelate (entry 5). Furthermore, a strong complexation interaction between the β-dicarbonyl portion of curcumin and Mg^{+2} ions could be evoked to explain such a preference with a mechanism similar to that previously hypothesized for the interaction of emodin in the magnesium oxide crystal lattice. This may account also for the largely greater percentage of adsorption of this solid with respect to other magnesium-containing ones (Genovese et al. 2020). The strong tendency of curcumin to form stable coordination complexes with Mg^{+2} ions has already been well-outlined in the literature (Zebib et al. 2010; Guo et al. 2020).

Finally, it is noteworthy to highlight how data reported herein may represent valid basis to extend the current uses of some of the sorbents mentioned in this manuscript beyond laboratory-scale applications. This is because we have clearly outlined how solids are extremely easy to handle using very mild experimental conditions and are completely recyclable and reusable coupled to a well-validated HPLC protocols for quality control purposes. Magnesium oxide is already used at an industrial level in soil and groundwater remediation, wastewater, drinking water, and air emissions treatments (Hua et al. 2012). Also numerous hydrotalcites find similar industrial applications (Nalawade et al., 2009). The large adsorption capacity for curcumin exhibited by some solid sorbents suggests their potential usage also in the current practice of herbal and phytotherapy companies.

Finally, the findings described herein can contribute to enforce the beneficial role of curcumin as an individual phytochemicals and as a part of turmeric extract from at least two points of view: first treatment of turmeric extract alcoholic solutions with LDHs and magnesium oxide and hydroxide is an efficient mean to provide curcumin-enriched phytopreparations. These latter have been recently seen to be more powerful in terms of healthy effects with respect to parent turmeric extracts, and new ways to obtain curcuminoid-enriched materials are on their ways to be effectively developed (Brent Friesen et al., 2019). As a consequence, such novel phytopreparations from turmeric can be seen nowadays as novel food supplements able to provide ameliorated beneficial effects to human and animal welfare (Boyanapalli and Tony Kong 2015).

Conclusions

The present investigation represents part of our ongoing studies having as the main scope to test the efficiency of solid inorganic and mixed inorganic/organic solids to adsorb selected classes of natural compounds. Such a research topic has a sure potential for the next future for pharmaceutical, cosmetic, and nutraceutical applications. Results reported herein enforce the concept of LDH and magnesium oxide as effective agents for adsorption and concentration naturally occurring biologically active products. In this case, we added diarylheptanoids to the categories screened in addition to anthraquinones. For this reason, data outlined in the present investigation are in our opinion greatly encouraging for the continuation of studies in the same research field and of general interest to the overall scientific community operating in this research field, for the evaluation of a wider panel of lamellar solids with different structures, in particular those having a “hybrid” structure (inorganic + organic). Likewise, the interaction of solid sorbents with other categories of natural products (polyphenols and phenylpropanoid in general, glycosides, terpenes, alkaloids, phytochemicals of mixed biosynthetic origin) could be also investigated. In our opinion, we have described a valid alternative to the already described materials used for the same scopes until now.

Availability of Data Material Not applicable.

Authors' Contribution **Serena Fiorito:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing-original draft, Writing-review and editing.

Francesco Epifano: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing-original draft, Writing-review and editing.

Francesca Preziuso: Investigation, Methodology, Software, Validation, Visualization.

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Fabio Cardellini: Investigation, Methodology, Software, Supervision, Validation, Visualization.

Roberto Spogli: Conceptualization, Formal analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization.

Salvatore Genovese: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing-original draft, Writing-review and editing.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Code Availability Not applicable.

Informed Consent Not applicable.

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