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ORIGINAL PAPER

Cuttlefish bone powder as an efficient solid-phase extraction sorbent of anti-SARS-CoV-2 drugs in environmental water

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Abstract

Many antiviral drugs were developed to counteract coronavirus disease, 2019 (COVID-19) with severe acute respiratory syndrome. Therefore, the scientific community's efforts have focused on the detection and quantification of antiviral compounds currently being tested for COVID-19 treatment. Cuttlefish bone powder (CFBP) has been used for the first time as solid-phase extraction (SPE) sorbent for the extraction of SARS CoV-2 antiviral drugs (chloroquine, ritonavir and indomethacin) from water samples. An effective and sensitive method was developed by combining SPE and liquid chromatography- UV detection (LC-UV). An experimental design was applied for the optimization of extraction process. Experimental variables were optimized using Doehlert matrix. The developed method included 50 mg of CFBP sorbent, 20 mL of water sample at pH = 9 and 5 mL of ACN/KH_2PO_4 buffer solution (80:20, v/v) in the elution step. For validation of the method, selectivity, linearity precision, and sensitivity were evaluated. Extraction recovery percentage of all Sars cov-2 antivirals were above 98.2%. The detection and quantification limits were between 0.1 and 0.5 µg L^{-1} and 0.6 and 2 µg L^{-1}, respectively. The current study suggested that CFBP has the application potential for the enhanced SPE of SARS CoV-2 antiviral drugs from water samples.

Keywords Green materials · Cuttlefish bone powder · SARS CoV-2 antiviral drugs · Solid-phase extraction · HPLC–UV and chemometrics

Introduction

Since December 2019, an infectious disease, the 2019 coronavirus disease (COVID-19), has spread to more than 200 countries worldwide, and a global pandemic has been announced by the World Health Organization (WHO) (Columbus et al. 2020; Whitworth 2020; Brüssow 2020). Considering the novelty of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the lack of data on clinical treatments, many medications are suggested. Anti-HIV, anthelmintics, immunoglobulins, neutralizing antibodies, antimalarials, interferons, anti-influenza, antihepaciviruses, antineoplastics, and antiprotozoals have been used to treat patients affected by the virus (Waffo Tchounga et al. 2021; Yang et al. 2021).

However, the massive use of these antivirals causes the contamination of various environmental matrices (Tlili et al. 2016; Ben Sghaier et al. 2017; Gupta et al. 2021) and impacts the functioning of the ecosystem which leads to risks for human and animal health (Yang et al. 2017; Rigueto et al. 2021). An overview of management practices and effective treatment processes for removing emerging contaminants from hospital wastewater was reported (Khan et al. 2021). Therefore, the development of analytical methods of separation of antivirals and processes of elimination of these organic micropollutants has become a necessity.

The direct analysis of antivirals in water is impossible since they are present at trace levels with numerous interferents. Therefore, a preconcentration or pretreatment step is necessary before analysis. Previous studies, including chitosan (Karimi-Maleh et al. 2021), algae (Arias et al. 2017; Chen et al. 2021), and clay materials (Thiebault 2020; Aljeboree et al. 2020), for the removal of the pharmaceutical residues from environmental matrices with solid-phase extraction (SPE) were reported. Various biosorbents have been

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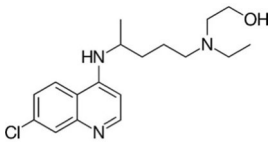
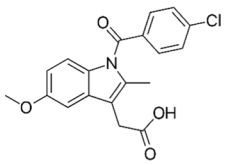
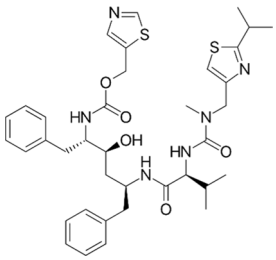
used in SPE in the last decades because of their low toxicity, easy applicability, and biodegradability. They become desirable sorbent allowing the use of renewable sources. Considerable attention has been paid to biochar sludge sewage. Ihsanullah et al. reported the applications of sludge-based biochar for the adsorption of pharmaceuticals from water (Ihsanullah et al. 2022).

Cuttlefish bone powder (CFBP) is a new ecological sorbent. Few studies were reported in the literature dealing with removing drugs and pharmaceuticals from aqueous solutions. The adsorption of two common pharmaceuticals clarithromycin and atenolol on CFBP has been investigated (Khazri et al. 2018). To the best of our knowledge, the use of CFBP as biosorbent in SPE procedure for the pretreatment of surface water has not been explored so far.

This work discussed an efficient extraction using cuttlefish bone powder as an adsorbent for SPE of antivirals SARS-CoV-2 in combination with liquid chromatography–UV detection. Simultaneous separation of chloroquine, ritonavir, and indomethacin drugs is investigated. In addition, the adsorption process of chloroquine was investigated. The solid-phase extraction parameters such as pH, sample volume, and percentage of ACN in the elution solvent were optimized according to experimental design. Responses of the three factors are presented in the entire studies field.

Table 1 Molecular structure and main physicochemical properties of the studied antivirals

Drug	Molecular structure	Brut formula	pKa
Chloroquine		$C_{18}H_{26}ClN_3$	10.1
Indometacin		$C_{19}H_{16}ClNO_4$	4.50
Ritonavir		$C_{37}H_{48}N_6O_5S_2$	2.84 13.68

Materials and methods

Reagents chemicals and standard solutions

HPLC grade methanol, acetonitrile and water, orthophosphoric acid (H_3PO_4), and monopotassium phosphate (KH_2PO_4) were purchased from Sigma-Aldrich (Saint-Louis, USA). In addition, chloroquine (CHLO), ritonavir (RIT), and indomethacin (IND) drugs were also purchased from Sigma-Aldrich (Saint-Louis, USA) with a purity ≥ 98%. Standard stock solutions of 1000 mg L^{-1} were prepared in methanol or HPLC grade water, depending on the compound's solubility. These solutions were stored at 4 °C. Then freshly prepared working solutions were obtained by diluting the prepared stock solutions. The chemical structures of all studied compounds are shown in Table 1.

Instrumentations

The separations were carried out on an HPLC system (SYKAM S 1125 with S3245 UV–VIS detector, Germany). The analytical column was an Inertsil ODS C18 (125 mm × 4 mm i.d., dp = 4 µm). Advanced chromatography software (Clarity, DataApex Czech Republic) was used for data management and setting up the analyses. The characterization of the cuttlefish bone powder (CFBP) was performed using a Fourier transform infrared (FT-IR), spectrophotometer (model 100 series, PerkinElmer), and an X-ray powder diffractometer (X'Pert PRO MPD, Malvern Panalytical Ltd, UK). A Tecnai ultra Twin G2- Philips (Netherlands) connected with an energy-dispersive X-ray spectroscopy (TEM/EDX) were used to investigate the morphology and the elemental composition of CFBP. The adsorption studies were carried out with a UV–VIS spectrophotometer (model Scinco-3000 Plus, China).

Chromatographic conditions

The chromatographic method was developed using a C18 column with an isocratic elution of acidified water (pH = 3.5) and acetonitrile at a proportion of 40:60 (v/v). The pH was adjusted using H_3PO_4 (0.05 M), and the mobile phase was pumped at the rate of 1 mL min^{-1}. The injection volume was 20 µL, and the ultraviolet (UV) detection was done at 205 nm.

Preparation of CFBP

Cuttlefish bones were acquired from the local market without any cost. It was rinsed with deionized water, boiled for 10 min, and dried at 103–105 ˚C for 24 h to desorb any impurities. Bones were crushed, sieved into 150 µm particles, and stored in a glass bottle.

Batch adsorption experiments

CHLO was selected to evaluate the adsorption of the newly prepared cuttlefish potential. In this study, 50 mg of CFBP was added to 25 mL of a doped solution. The mixture was magnetically stirred (250 rpm) in various experimental conditions. Contact time (1–240 min), initial CHLO concentrations (50–250 mg L^{-1}), pH (3–11), and temperature (298–330 K) were investigated. The concentration of CHLO in the supernatant solution was measured at 205 nm using a UV–vis spectrophotometer after centrifugation. Table 2 summarizes the mathematical models employed in this study.

Optimization of parameters in CFBP-SPE

50 mg of CFBP was filled up in polypropylene cartridges (3 mL). The CFBP cartridges were conditioned with 3 mL of methanol followed by 3 mL of water. The water samples were doped with the three compounds solution (10 mg L^{-1}), and the pH was regulated with HCl 1 M. The retained analytes were desorbed and concentrated to 1 mL under a gentle stream of nitrogen. In order to enhance the solid-phase extraction process and examine the effects of the interaction among other factors, increased attention has been given to experimental design methodology. In this research, the Doehlert matrix was chosen to generate mathematical models. The factors governing the extraction of the various antivirals (AVS) are sample volume (U_1), % elution of ACN (U_2), and pH sample (U_3). Table 3 shows the maximum and minimum values for each component. The choice of the limits of the investigated region was determined using data from the literature (Colombo et al. 2016; Attimarad et al. 2020; Babas et al. 2021). A total of 15 tests were required to optimize AVS extraction efficiency. Analysis of results was performed with NEMROD software.

Table 3 Fit of parameter values of the kinetic and isotherm models for biosorption of Chloroquine by CFBP (298 K and pH = 9)

Models	Parameters	Value
Pseudo-first order	Qe (mg g^{-1})	11.64
	k_1 (min^{-1})	0.016
	R^2	0.879
Pseudo-second order	Q_e (mg g^{-1})	0.369
	k_2 (g mg^{-1} min^{-1})	0.024
	R^2	0.998
Langmuir	Q_m (mg g^{-1})	50.01
	K_L	0.613
	R^2	0.992
Freundlich	K_F (mg g^{-1}) (mg L^{-1}) $^{-1/n}$	4.340
	n	0.770
	R^2	0.995

Results and discussion

Characterization of CFBP

FT-IR study in the range of 4000–400 cm^{-1} at a distance of 2 cm was achieved to check the presence of the functional groups on the CFBP. The bands with wave numbers 854 and 706 cm^{-1} were ascribed to CH2 = C– and –CH = CH, respectively, as shown in Fig. 1. A wideband at 1475 cm^{-1} was assigned to C–O. The absorption peaks of aragonite were found at 1080 cm^{-1} and 852 cm^{-1} of CO_3^{2-} in CFBP. The findings are consistent with those reported (Yazid et al. 2021). Examination of the textural structure of cuttlefish bone can be perceived through the TEM images in Fig. 2.

The cuttlefish bone shows a very porous structure with a non-homogeneous and non-smooth surface. As shown

Table 2 Kinetic and equilibrium models equations (Rigueto et al. 2021)

	Equations	Parameters
	Q (mg g^{-1}) = $(C_0 - C_e)\frac{V}{W}$ (1)	C_e (mg L^{-1}) equilibrium concentration, C_0 (mg L^{-1}) initial concentration (mg L^{-1}), V(mL) volume and W (mg) mass
	% Adsorption = $\frac{C_0 - C_e}{C_0} \times 100$ (2)	C_0 (mg L^{-1}) initial concentration, C_e (mg L^{-1}) equilibrium concentration
Kinetic models		
Pseudo-first order	ln (Q_e – Q_t) = ln Q_e – [$k_1 \times t$] (3)	k_1 (min^{-1}) constant rate of pseudo-first order; Q_e (mg. g^{-1}) theoretical value of the adsorption capacity
Pseudo-second order	$\frac{t}{Qt} = \frac{1}{[k_2 \times Q_e^2]} + \frac{t}{Q_e}$ (4)	k_2 (g mg^{-1} min^{-1}) constant rate of pseudo-second order; Q_e (mg g^{-1}) theoretical value of the adsorption capacity
Isotherm models		
Langmuir	$Q_e = \frac{Q_m K_L C_e}{1 + K_L C_e}$ (5)	Q_m (mg g^{-1}) maximum adsorption capacity; K_L (L mg^{-1}) Langmuir constant; C_e (mg L^{-1}) equilibrium concentration
Freundlich	$Qe = K_F C_e^{1/n}$ (6)	K_F (mg g^{-1}) (mg L^{-1}) $^{-1/n}$;1/n Freundlich constant; C_e (mg L^{-1}) equilibrium concentration

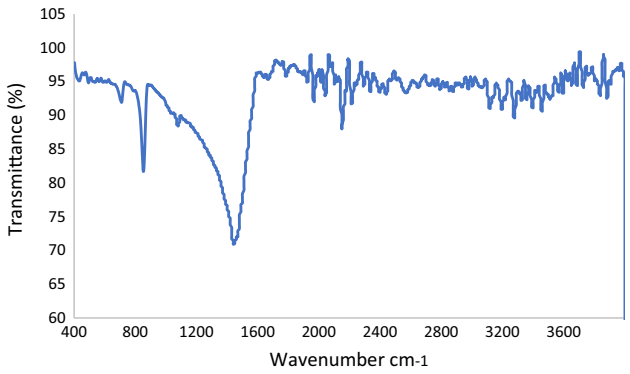


Fig. 1 FTIR spectra of CFBP

in Fig. 3, the cuttlefish bone has a high proportion of pure calcium carbonate $CaCO_3$ with trace amounts of Mg, P, and other elements. The X-ray diffraction pattern, recorded in the range of 2θ values from 5° to 90°with a step size of 0.02°, was used for the investigation on the crystalline carbon contents in CFBP. The results demonstrate that the CFBP has a well-crystallized shape with a calcium carbonate's characteristic line (2teta = 26.189) crystallizing under the aragonite variety (Fig. 4). Furthermore, several $CaCO_3$ peaks on the right side of the spectrum are reasonably dominating, indicating the presence of a $CaCO_3$ source.

Adsorption kinetics and isotherm

Effect of contact time

The influence of extraction time on elimination efficiency was investigated in this study throughout a time range of 1–240 min. Figure 5 depicts that the adsorption of CHLO represents three distinct phases: a quick initial phase during which the rate of CHLO removal is high-speed, taking less

Fig. 2 SEM of CFBP

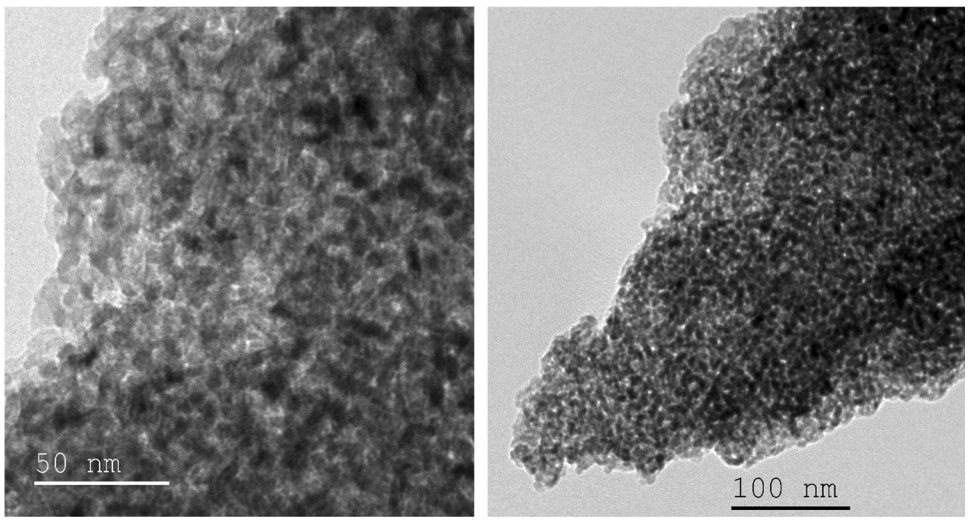
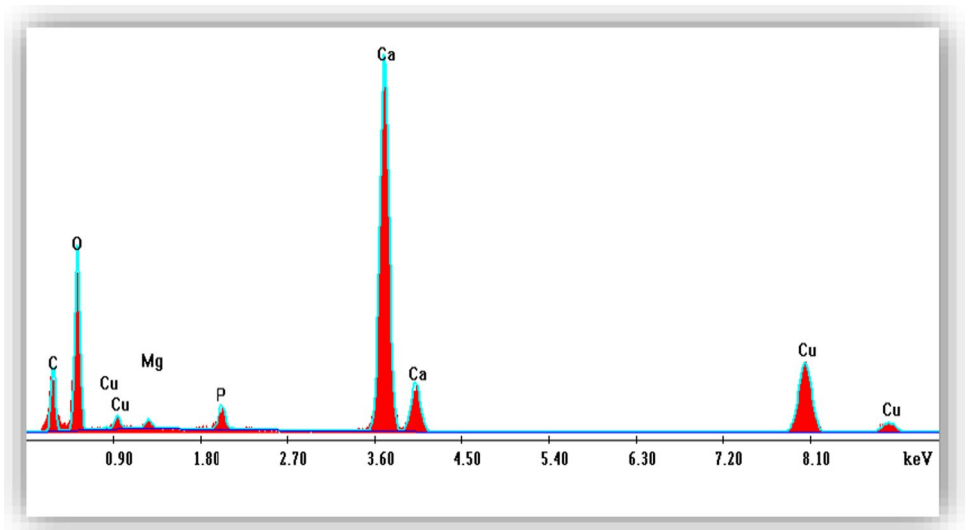


Fig. 3 Elemental analysis of CFBP (EDX)



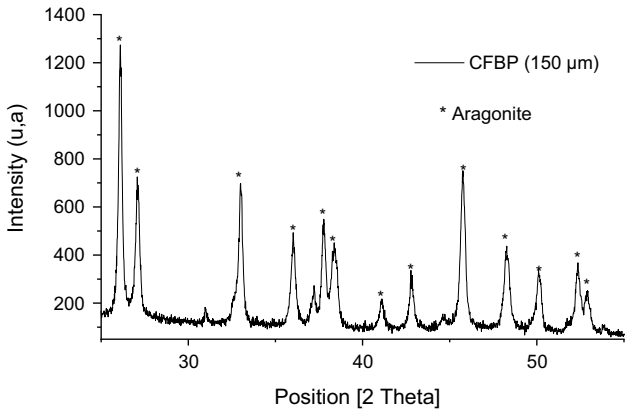


Fig. 4 XRD pattern of CFBP

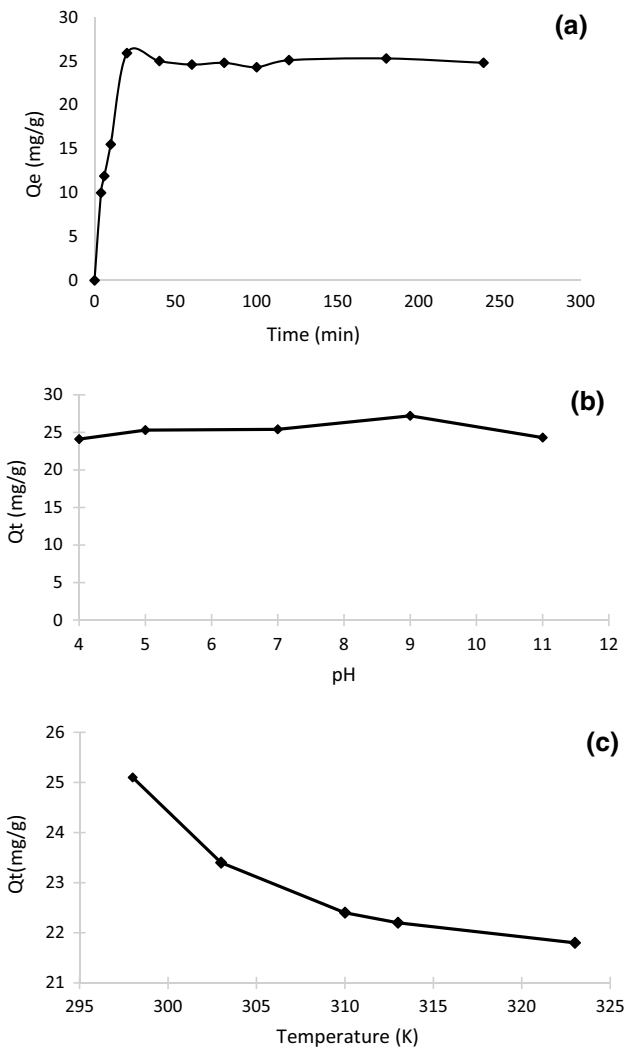


Fig. 5 (**a**) The effect of contact time, (**b**) pH and (**c**) the temperature on the adsorption rate of chloroquine on CFBP

than 20 min. The high adsorption rate can be explained by the presence of many accessible pores initially on the adsorbent material's surface (Poompradub et al. 2008; Khedri et al. 2016; Ghaneian et al. 2012). In the second phase and after 20 min, the adsorption efficiency decreased gradually. This may be due to the beginning of the saturation of the pores (Wan et al. 2021). Finally, after 60 min, the removal rate of CHLO has been stabilized significantly, indicating the achievement of equilibrium and the non-availability of sorption sites.

Influence of pH

The pH of aqueous solutions is an essential parameter in the adsorption process, affecting both the degree of ionization of the antiviral and the surface properties of the biosorbent. To study the pH, chloroquine solutions were prepared with an initial concentration of 25 mg L^{-1} at pH equal to 4, 5, 7, 9, and 11. According to the results shown in Fig. 6, increasing the initial pH from 4 to 11 had no significant influence on adsorption efficiency.

Effect of temperature

The impact of temperature on CHLO sorption by CFBP has been evaluated at the temperature range of 298–333 K. Figure 6 depicts the adsorption isotherms of chloroquine at different temperatures. The results clearly stipulate that the sorption process decreased with temperature increase. Besides, as the temperature rises, the adsorption capacity decreases. The rise of temperature can lead to the destabilization of the physical forces involved (Doğan et al. 2006). So, we chose to work at 298 K in order to promote the adsorption of chloroquine.

Kinetic and equilibrium essays

Pseudo-first-order (PFO) and pseudo-second-order (PSO) kinetic models were examined. Table 3 displays the linearized plot and the fit of parameter values of the PFO and PSO models, respectively, for the adsorption of CHLO on CFBP. The highest correlation values coefficients R^2 were observed in the PSO model. The PSO model proposes that the rate-limiting step is the adsorbent surface that involves the physicochemical interactions between the two phases to promote CHLO removal from a solution.

The linear plots of Langmuir and Freundlich isotherm models are showed in Table 3. The correlation coefficient R^2 obtained was equal to 0.992 and 0.995 for Langmuir and Freundlich models, respectively. Therefore, both models were able to describe the adsorption process.

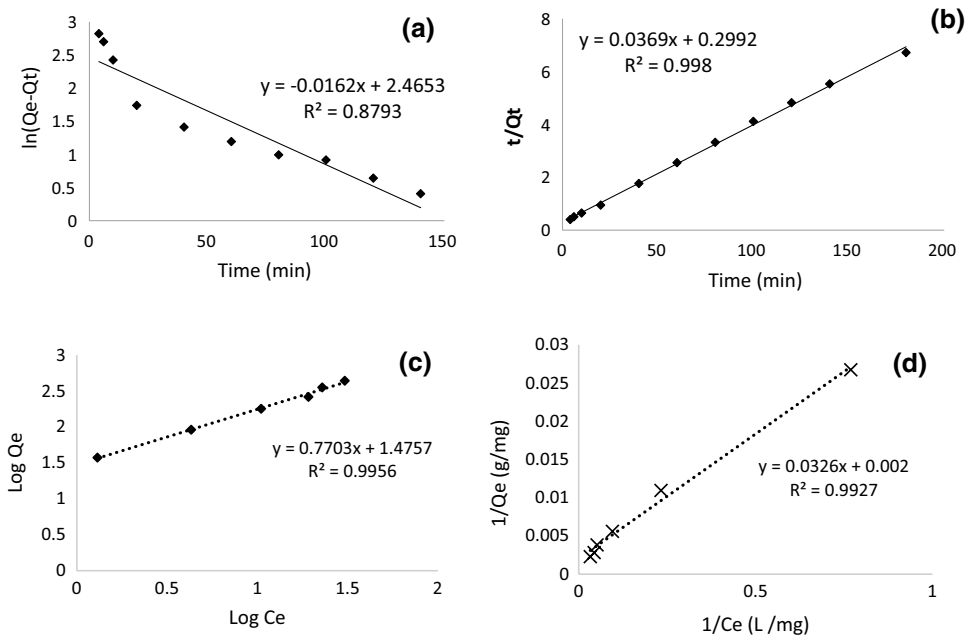


Fig. 6 (**a**) Pseudo-first order, (**b**) pseudo-second order, (**c**) Freundlich model and (**d**) Langmuir model

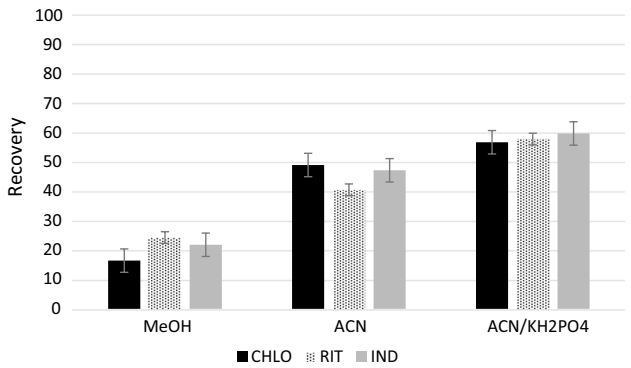


Fig. 7 Influence of the solvent type on the extraction recovery of studied antivirals

Determination of optimal conditions of SPE-CFBP of AVS

Three solvents were used to study the effect of the nature of the elution solvent on the extraction recovery of AVS: methanol (MeOH), acetonitrile (ACN), and ACN/KH_2PO_4 buffer solution (50:50, v/v). First, 30 mL of water sample spiked with 1 mL of AVS standard solution was charged into the CFBP cartridges. Then the analytes were eluted with 3 mL of chosen solvent. Figure 7 exhibits the recoveries of the three AVS obtained from the three types of solvents. The results demonstrated that simultaneous extraction of these drugs with ACN/KH_2PO_4 buffer solution (50:50, v/v) as elution solvent yielded higher recovery.

In order to optimize the rest of variables, multivariate techniques have been used. These methods are able to generate mathematical models that permit to estimate the relevance of factors (Fig. 8). Three variables were regarded as factors that might potentially affect the extraction efficiency. The maximum and the minimum values of each factor are listed in Table 4. A second-order model describes the response (Y) for predicting the response in all experimental regions from the following equation:

$$Y = b_0 + b_1X_1 + b_2X_2 + b_3X_3 + b_{11}X_1^2 + b_{22}X_2^2 + b_{33}X_3^2 + b_{12}X_1X_2 + b_{13}X_1X_3 + b_{23}X_2X_3$$

where Y is the experimental response, Xi is the coded variable, bi is the estimation of the principal effect of factor i for the response Y, and bij is the estimation of the interaction effect between factors i and j for the response Y (Latrous El Atrache et al. 2013).

According to the obtained results from NEMROD software, the coefficients of the polynomial model were calculated by the following equation:

$$Y = 40.047 - 31.290\,X_1 - 1.164\,X_2 - 4.839\,X_3 + 9.685\,X_1 - 4.846\,X_2 - 22.677\,X_3$$

Fifteen experiments (including three center replicates) were conducted in random order under the experiment design (Table 5). Response surface profiles were drawn in terms pH, sample volume, and percentage of ACN in the elution solvent (%ACN) and the three-dimensional representation of the same plots using the NEMROD software. Figure 9 indicates the resulting graphs for three of the selected responses. One of three factors was kept constant at its center value in each representation. The first isoresponse

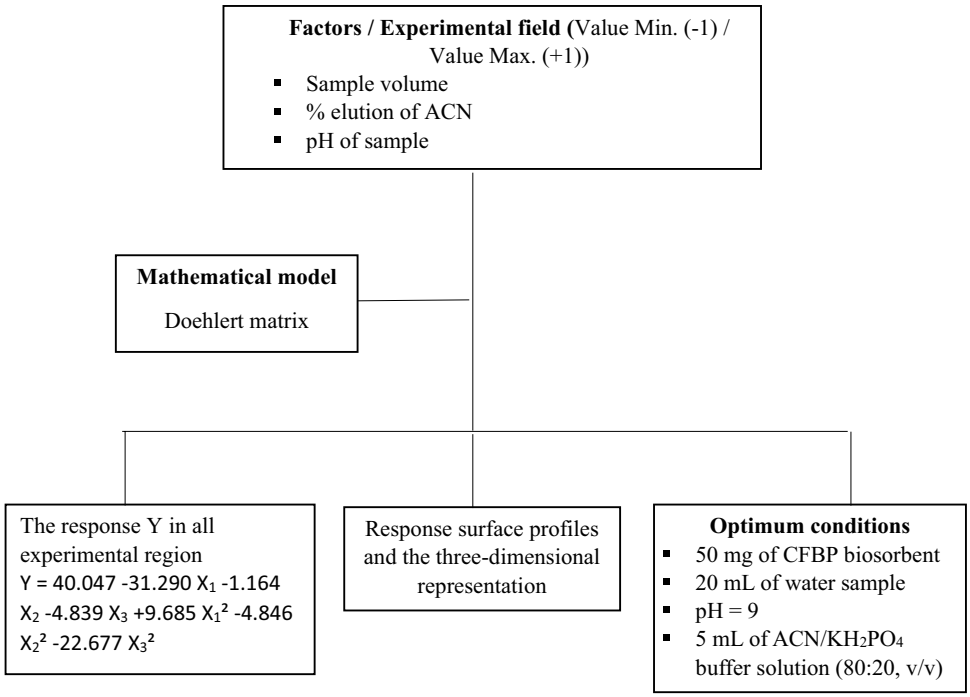


Fig. 8 Schematic of experimental design

Table 4 Investigated variables and their levels studied in the 2^3 factorial design

Coded variables (X_i)	Factors (U_i)	Experimental field value min. (−1)	Coded variables (X_i) value max. (+1)
X_1	U_1: sample volume (mL)	10	30
X_2	U_2: % elution of ACN (%)	20	80
X_3	U_3: pH of sample	3	11

Table 5 Doehlert matrix experiments

N° exp	Rand	pH	V_{ACN} mL	Volume sample mL
1	4	11	2.50	20.00
2	10	3	2.50	20.00
3	6	9	3.80	20.00
4	14	5	1.20	20.00
5	11	9	1.20	20.00
6	15	5	3.80	20.00
7	13	9	2.93	28.16
8	1	5	2.07	11.84
9	2	9	2.07	11.84
10	8	7	3.37	11.84
11	3	5	2.93	28.16
12	12	7	1.63	28.16
13	7	7	2.50	20.00
14	9	7	2.50	20.00
15	5	7	2.50	20.00

curve of pH versus % of ACN elution exhibits a better yield at pH between 7 and 11 and a % of ACN between 50 and 100. The second is the response curve of pH versus sample volume which shows a better yield at pH ranges from 7 to 11 and a sample volume between 10 and 20 mL. The last curve validates the areas obtained in the two previous curves already analyzed. Analyzing the isoresponse curves at the chosen experimental field delimited by a circle reveals that the maximum extraction recovery is obtained when 20 mL of water sample at pH = 9 pass through CFBP cartridge, then eluted with 5 mL ACN/KH_2PO_4 buffer solution (80:20, v/v).

Validation of the proposed method

The optimized SPE-CFBP-HPLC/UV method has been validated. Method validation was carried out under the requirements of ICH and EMA (Fical et al. 2021). Selectivity has been confirmed since no interfering peaks were found in the blank extract at the retention time of the investigated

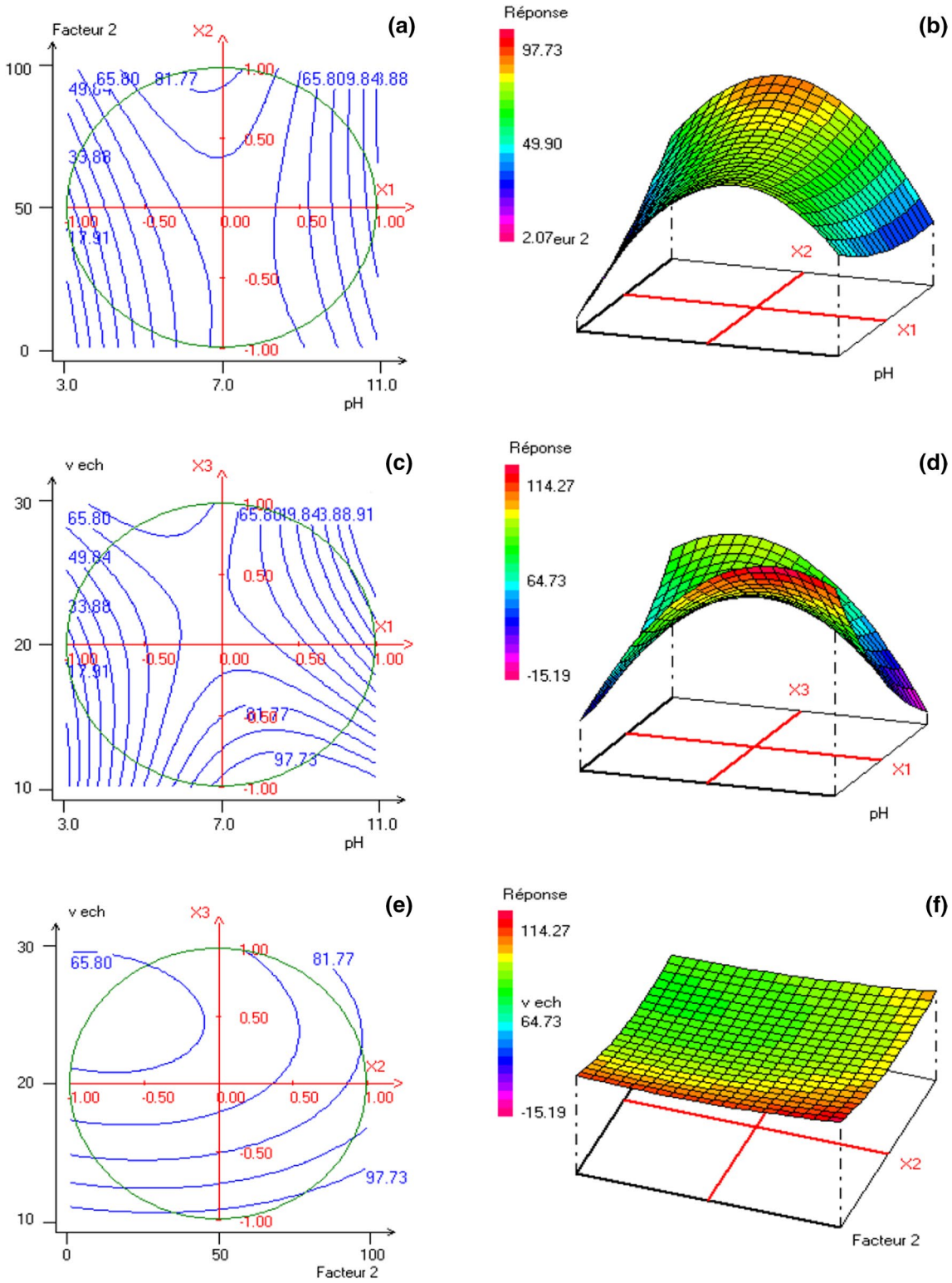


Fig. 9 (**a**) Contour plots of extraction recovery versus pH and percent ACN elution (%); (**b**) corresponding three-dimensional plot; (**c**) contour plots of extraction recovery versus pH and sample volume(mL); (**d**) corresponding three-dimensional plot; (**e**) contour plots of extraction recovery versus percent ACN elution (%) and sample volume (mL); (**f**) corresponding three-dimensional plot

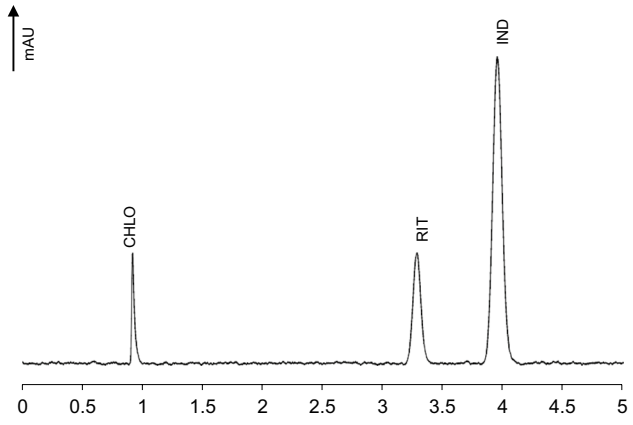


Fig. 10 Chromatogram obtained from the analysis of three AVS in water sample by the optimized CFBP-SPE-HPLC/UV method

analytes (Tahrani et al. 2017). Extract chromatograms reported in Fig. 10 presented the satisfactory chromatographic resolution. The calibration curves ($n=6$) for CHLO, RIT and IND were linear across an extensive concentration range of 0.1–10 mg L^{-1} with R^2 equal to 0.999, 0.999 and 0.998 respectively.

The method's precision was determined in water samples spiked with three standards (10 mg L^{-1}) and submitted to the method, using three repetitions, the estimation coefficient of variation (CV) was evaluated. The extraction recovery percentage (% R) and the CV obtained are presented in Table 6. The sensitivity of the optimized method was evaluated by the determination of the LOD and LOQ. The detection limit of the proposed method was determined as being equal to at least 3 times the base line signal (noise) obtained for water samples free of antiviral drugs (blank), fortified with antivirals between 0.1 and 10 mg L^{-1}, submitted to the SPE technique and analyzed by LC-UV. The quantification limit was determined as being the signal at least 10 times greater than the noise signal. The LOD for CHLO, RIT, and IND were 0.2, 0.5, and 0.1 µg L^{-1}, respectively, and LOQ were 0.8, 2, and 0.6 µg L^{-1}, respectively. The low value of LOQ attained for the three analytes confirms the pertinence of the proposed SPE-CFBP-HPLC/UV method for quantifying trace concentrations of CHLO, RIT, and IND in water.

In Table 7, the developed SPE is compared with some relevant solid-phase procedures reported in the literature to analyze micropollutants in water samples using liquid chromatography. The obtained results show that the proposed method is suitable to analyze antivirals in water samples.

The use of CFBP as biosorbent decreases the process cost and makes it ecofriendly since it is prepared from waste/abundant material. Nowadays, a huge market exists for cheap and efficient biosorbents. The future prospects look

Table 6 Correlation coefficients, coefficients of variation, Recovery percentage, LOD and LOQ obtained from the application of SPE–CFBP-HPLC/UV method with three repetitions, in water samples fortified with AVS (10 mg L^{-1})

	Linearity	Precision	Recovery	Sensitivity	
AVS	R^2	CV	R %	LOD (µg L^{-1})	LOQ (µg L^{-1})
Chloroquine	0.999	0.60	95.6	0.2	0.8
Ritonavir	0.998	0.93	92.7	0.5	2
Indometacin	0.999	0.41	98.2	0.1	0.6

Table 7 Reported solid-phase extraction methods for determination of micropollutants in water samples

Sorbent	Analytical method	Micropollutants	Recovery (%)	LOD	Refs.
Pine bark	HPLC–UV	Phenylbutazone, sulfamethazine, carbendazim, and linuron	–	0.11—0.4 µg L^{-1}	Khazri et al. (2022)
Moringa oleifera seed	HPLC–UV	Ttriazole fungicides	70–112	30–50 µg L^{-1}	(Kachangoon et al. (2022)
Chitosan/lawsone composite	HPLC–UV	Dimethyl phthalate, di-butyl phthalate and benzyl butyl phthalate	67–106	0.03–0.15 ng g^{-1}	Samadi and Es'haghi (2022)
Fe_3O_4-MWCNTs	HPLC–MS/MS	Naproxen, Ketoprofen, Piroxicam, Diflunisal, Celecoxib	78–93	0.05–3.6 ng mL^{-1}	Hsen and Latrous (2022)
CFBP	HPLC–UV	Chloroquine, ritonavir, and indometacin	98.2	0.1–0.5 µg L^{-1}	The present work

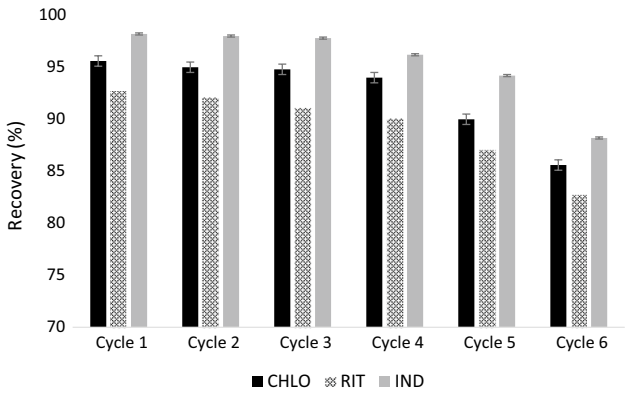


Fig. 11 AVS removal efficiencies in six successive recycle runs

promising with selecting selective biosorbents and assessments of the cost's developments (Gupta et al. 2015).

Reusability of CFBP

The CFBP was subjected to SPE experiments numerous times, up to six times, to investigate its reusability. The utilized material was cleaned numerous times with methanol and water. It was then repeatedly employed in the SPE procedure. The extraction efficiency of CFBP for antiviral drugs was slightly declined with the regeneration of the adsorbent, as shown in Fig. 11. After the sixth cycle, the extraction recovery decreased to 90% showing that the prepared CFBP exhibited acceptable reusability during the SPE technique.

Conclusion

A novel method SPE-HPLC/UV for simultaneous quantification of Sars-CoV-2 antivirals chloroquine, ritonavir, and indometacin has been developed. Cuttlefish bone powder, a natural and inexpensive adsorbent, was used to remove Sars-CoV-2 antiviral contaminations. The CFBP was characterized with X-ray powder diffractometer, transmission electron microscopy coupled with energy-dispersive X-ray spectroscopy (TEM/EDX), and Fourier transformed infrared (FTIR) spectroscopy indicating the presence of $CaCO_3$ source.

Then chloroquine was chosen to investigate the sorption of Sars-CoV-2 antivirals on CFBP. The equilibrium adsorption is reached within 20 min with maximum percentage adsorption capacity of 96% at pH 3.0 and 25 °C. Moreover, optimal conditions of the CFBP-SPE procedure were optimized by the experimental design methodology. The developed SPE method included 50 mg of CFBP biosorbent, 20 mL of water sample at pH = 9 and 5 mL of ACN/KH_2PO_4 buffer solution (80:20, v/v). Extraction recovery percentage of all antivirals were above 98.2% and the detection limits ranged from 0.1 to 0.5 µg L^{-1}. The results demonstrate the potential use of CFBP as a new biosorbent in solid-phase extraction devices to remove Sars-CoV-2 antivirals in surface water.

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Declarations

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

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