ES Energy & Environment

Removal of Fluticasone Propionate and Clobetasol Propionate by Calcium Peroxide: Synergistic Effects of Oxidation, Adsorption, and Base Catalysis

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Performance of calcium peroxide (CaO_2) in fluticasone propionate (FP) and clobetasol propionate (CP) removal was investigated. The removal mechanisms in CaO_2 treatment were explored. Specifically, degradation intermediates of FP and CP in CaO_2 treatment were firstly identified. CaO_2 treatment can be a practical and effective technology for FP and CP removal because of its synergistic effects in oxidation, adsorption, and base catalysis. Over 99.4% and 84.4% of FP and CP could be removed in 0.5 min at CaO_2 dosage of 0.1 - 4 g L^{-1} at initial pH of 7, respectively. HO• was the dominant radicals responsible for FP and CP degradation in CaO_2 oxidation while $•O_2^-$ also accelerated the removal. The suitable increase of solution pH (< 9) by $Ca(OH)_2$ released from CaO_2 and the adsorption effects of CaO_2 particles also contribute to FP and CP removal. CaO_2 treatment remained effective in complex water matrix with the presence of humic acid (HA) and common anions except for HCO_3^-. Moreover, nine intermediates were revealed for the first time during CaO_2 treatment indicating the decrease of glucocorticoid toxicity by CaO_2 treatment.

1. Introduction

The existence of endocrine disrupting compounds (EDCs) in water has caused a widespread of concerns for the past 20 years, due to their potential ecological hazards.[1] EDCs are chemicals that have negative effects on the endocrine systems of humans and wildlife. EDCs include natural estrogens, natural androgens, artificial synthetic estrogens, phytoestrogens, and other industrial compounds.[2] Research on environmental EDCs mainly focuses on the chemicals that disrupt the sex hormone signaling pathways, especially estrogenic and androgenic compounds.[3] In the recent years, the disruption of corticosteroid signaling pathways in wildlife and humans from environmental chemicals, such as glucocorticoids (GCs), has attracted increasing attention.[4] Gcs are a kind of steroid hormones which have anti-inflammatory effects.[5] They are widely used as medicals for humans and animals.[6] The presence of toxicity of GCs in surface water and wastewater was first detected in the Netherlands.[7] Then they were discovered frenquently in other countries, such as the United States,[8] the Czech Republic,[9] Switzerland,[9] Australia,[10] and Japan.[1] Increasing amount of GCs is

detected in aquatic environment in different areas as summarized in Table S1. In a study conducted in France, the GC concentration reported reached up to 23 μg L^{-1} in a sample of an industrial sewage treatment plant (STP).[11] Exposure to GCs even at low concentration levels could cause adverse effects on fish reproduction, growth, and development.[12] Therefore, occurrence and fate of GCs in the environment have been increasingly concerned.[13]

Although the occurrence and environmental toxicity of GCs have been confirmed, the research on GC removal is still in its infancy. Moreover, most researches on GCs selected cortisone, prednisolone, cortisol, prednisone, or dexamethasone (Dex) as target compounds because of their high concentrations in environment,[1] whereas the other GCs have not been sufficiently investigated. However, Jia *et al*.[5] reported that four synthetic GCs (clobetasol propionate (CP), triamcinolone acetonide (TA), fluocinolone acetonide (FA), and fluticasone propionate (FP)), instead of Dex, prednisolone, prednisone, cortisol, and cortisone, are the major GC activity contributors in environmental samples. Among the four synthetic GCs, FP and CP have much higher bioactivity (70 times and 38 times as high as the activity of dexamethasone, respectively) and large consumption and release (among the top 100 most prescribed drugs in the United States).[5] Their molecular structures and atoms label are shown in Fig. 1. These two synthetic glucocorticoids (FP and CP) should be prioritized in future study on GC removal.

Information about the removal of FP and CP is rarely available, most of which only focus on the removal in STPs.[13-15] Unfortunately, these researches have shown that traditional treatment processes

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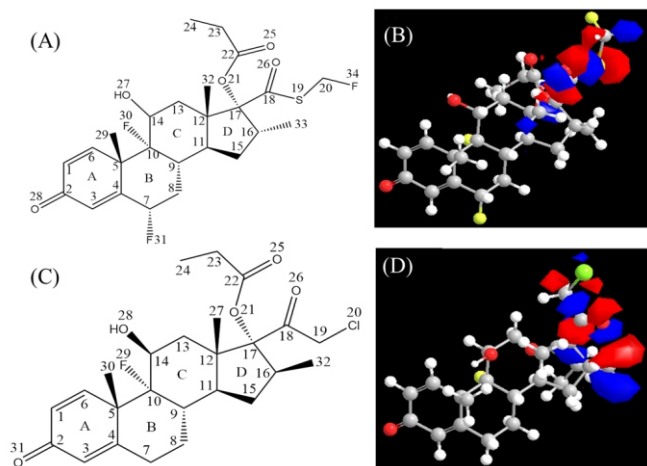
Fig. 1 Molecular structure and atoms' label for FP (A) and CP (C); Calculated frontier electron densities of FP (B) and CP (D) (red for positive and blue for negative).

involved in STPs are not fully effective in eliminating FP and CP.[10] In contrast, the concentrations of some GCs in the final effluent of STPs are even larger than those in influent since their conjugates are hydrolyzed during STP treatment.[16] The incomplete removal and even increase of GCs in STPs will worsen their pollution to surface water, soil, and groundwater through effluents, irrigation, landfills, and leachate inevitably[17] as shown in Fig. S1. Therefore, other advanced or more efficient technologies were required urgently to remove FP and CP pollution.

As an environmentally friendly chemical being able to release oxygen (O_2) and hydrogen peroxide (H_2O_2) at controllable rate, calcium peroxide (CaO_2) has been widely applied in environmental remediation as summarized in Table S2.[18] Compared with other peroxides which can produce H_2O_2 (such as magnesium peroxide), CaO_2 is more economical, efficient, and safe.[19,20] The annual US market for CaO_2 is a few hundred metric tons and the price is about $ 2.8/kg.[21] The commercially available material is commonly used in pharmaceuticals and dough conditioning formulations to provide better handling dough.[21] Moreover, CaO_2 could release H_2O_2 for a long time and decrease H_2O_2 disproportionation,[18] leading to higher micro-pollutant removal efficiencies than using liquid H_2O_2.[22] In addition, CaO_2 particles could provide active surface sites for oxidation or low steady-state levels of H_2O_2 to reaction with "built-in" activators and offer an alkaline environment conducive to certain oxidation pathways.[23] However, little information is available on the application of CaO_2 to remove GCs. Particularly, the removal efficiencies and degradation mechanisms of FP and CP during oxidation have not been elucidated clearly.

Therefore, it is of great interest to examine if the CaO_2 treatment could remove FP and CP pollution effectively. There is also a major data gap regarding the removal mechanisms of FP and CP during CaO_2 treatment. So this study targets on (1) the feasibility of CaO_2 treatment for FP and CP, (2) the removal mechanisms of CaO_2 for remove FP and CP, (3) the influence of coexisting inorganic ions and HA in matrix on FP and CP removal, (4) the degradation intermediates of FP and CP during CaO_2 oxidation. This is the first study on the removal of FP and CP by CaO_2. The synergistic effects of oxidation, adsorption, and base catalysis of CaO_2 in pollutant removal are also raised for the first time.

2. Materials and methods

2.1 Materials

The FP and CP standards were obtained from Sigma-Aldrich (St. Louis, MO, USA). Stock FP and CP solutions were prepared in acetonitrile at 4 °C in brown bottles. Analytical grade CaO_2 (75% CaO_2, 25% $Ca(OH)_2$) and HA (fulvic acid > 90%) were purchased from Aladdin Reagent Co. Ltd. (Shanghai, China). Methanol, acetonitrile, water and acetic acid (high-performance liquid chromatography (HPLC) grade) were purchased from Sigma-Aldrich, USA. Tert-butyl alcohol (($CH_3)_3OH$, TBA, 99.0%), trichloromethane ($CHCl_3$, 99.0%), and various inorganic salts were obtained from Shanghai Lingfeng Chemical Reagent Co. Ltd. (Shanghai, China).

2.2 Experimental procedures

2.2.1 CaO₂ performance on FP and CP removal

The ability of CaO_2 in removing FP and CP at different dosages was determined. Experiments were conducted in a 1 L, magnetically stirred, brown flasks at 25 °C. Desired stock FP or CP solution was diluted with water to the desired concentration. Specific amount of CaO_2 was added to start the reaction. At desired time intervals, samples were withdrawn, and excess $Na_2S_2O_3$ was immediately added to the samples to quench the reaction. Effects of CaO_2 dosage (0.05 - 4 g L^{-1}) was investigated at the initial pH value of 7 and 0.02 mM FP or CP . Controlled experiment without CaO_2 was carried out simultaneously. As there were little hydrolytic stability data for FP and CP, hydrolysis behavior was examined in this study at different pH values (2, 4, 6, 8, 10, and 12) at 25 °C at initial FP or CP concentration of 0.02 mM, just as with the procedures described above without the addition of CaO_2.

2.2.2 ROS identification and their effects

TBA (scavenge HO•) and $CHCl_3$ (scavenge •O_2^-)[20] had been applied to observe the changes of FP and CP removal efficiencies during CaO_2 treatment at unadjusted pH, CaO_2 dosage of 0.1 g L^{-1}, and FP or CP at 0.02 mM. ROS scavenger concentrations were set at 35, 173, and 347 mM. The metal elements in CaO_2 reagent were identified using an inductive coupled plasma emission spectrometer (ICP, Agilent 720ES) as described in Supporting Information (SI).

2.2.3 Effects of solution pH and CaO₂ adsorption on FP and CP removal

Effects of initial pH values from 1.8 to 11.6 adjusted by 1 M of H_2SO_4 or NaOH were investigated at 0.1 g L^{-1}, CaO_2 and 0.02 mM FP or CP. Samples were withdrawn to test solution pH and concentrations of FP and CP as described in section 2.2.1.

The adsorption experiments were carried out as described in section 2.2.1 at CaO_2 of 0.1 g L^{-1}, FP or CP at 0.2 mM, and unadjusted pH . After stirring for 0 and 18 min, the solutions were filtered through 0.22 μm glass fiber filters and the residuals on the filters were freeze-dried and investigated by scanning electron microscopy (SEM) equipped with energy dispersive spectroscopy (EDS; FEI Quanta 200).

2.2.4 Effects of solution matrix on FP and CP removal

The effects of inorganic ions (Cl^-, HCO_3^-, SO_4^{2-}, NO_3^-, PO_4^{3-}) on FP and CP removal were investigated at ion concentrations of 1 to 100 mM. Effects of precipitation of Ca^{2+} and CO_3^{2-} or SO_4^{2-} on CP removal by adsorption were also evaluated at various Ca^{2+} concentrations. Effects of HA in matrix on FP and CP removal by CaO_2 were tested at HA of 0, 0.1, 0.5, 1, and 2 g L^{-1} as described in section 2.2.1 at unadjusted pH, CaO_2 of 0.1 g L^{-1}, and FP or CP at

0.02 mM. The adsorption effects of HA at 0.1, 0.5, 1, and 2 g L^{-1} were also evaluated.

2.2.5 Identification of byproducts

For identification of byproduct, the initial FP or CP concentration was set at 0.1 mM. After oxidized by 0.1 g L^{-1} CaO$_2$ for 0, 0.5, 2, 4, 8, 10, and 15 min, 2 mL water sample was withdrawn, respectively. The samples were filtered and detected immediately.

2.3 Analytical methods

For analysis of FP and CP, 100 mL of water sample was enriched by solid phase extraction (SPE) according to the method described by Jia *et al.*[5] An Agilent 1100 HPLC (USA) was used to analyze the GC concentrations in samples. The column in HPLC was a reversed-phase C-18 column (4.6 mm × 250 mm, 5 μm, Agilent, USA). Detailed information such as mobile phase and the procedure are described in SI.

For identification of intermediates of FP and CP, an Agilent 1290 ultra-high-performance liquid chromatography (UHPLC) was employed for separation. Samples were loaded on an Agilent Zorbax

Extend - C18 analytical column (2.1 mm × 100 mm, 1.8 μm). A high-resolution Agilent 6540 Quadrupole Time-of-Flight mass spectrometer (QTOF-MS) system was used in negative mode. Detailed sample preparation, instrument analysis, and method performance are provided in detail in SI.

3. Results and Discussion

3.1 Effectiveness of CaO$_2$ in removing FP and CP

The effects of CaO$_2$ dosage on FP and CP removal efficiencies were shown in Figs. 2a&b. As shown in Fig. 2a, FP was removed very fast during CaO$_2$ treatment. Over 99.4 % of FP was removed in 0.5 min at CaO$_2$ dosage of 0.05 - 4 g L^{-1}. For CP, over 91.3 % could be removed in 18 min at CaO$_2$ of 0.05 - 4 g L^{-1} (Fig. 2b). So CaO$_2$ treatment is effective on FP and CP removal.

Particularly, the blank tests for FP and CP removal without CaO$_2$ addition showed minor loss (< 10 %). Notable hydrolysis of FP and CP were observed at all investigated pH values as presented in Figs. 2c&d. After 20 h of hydrolysis at 25 °C, 22.5, 18.3, 20.8, 16.5, 14.9, and 18.5% of FP and 26.1, 25.9, 20.9, 78.4, 62.0, and 92.8% of
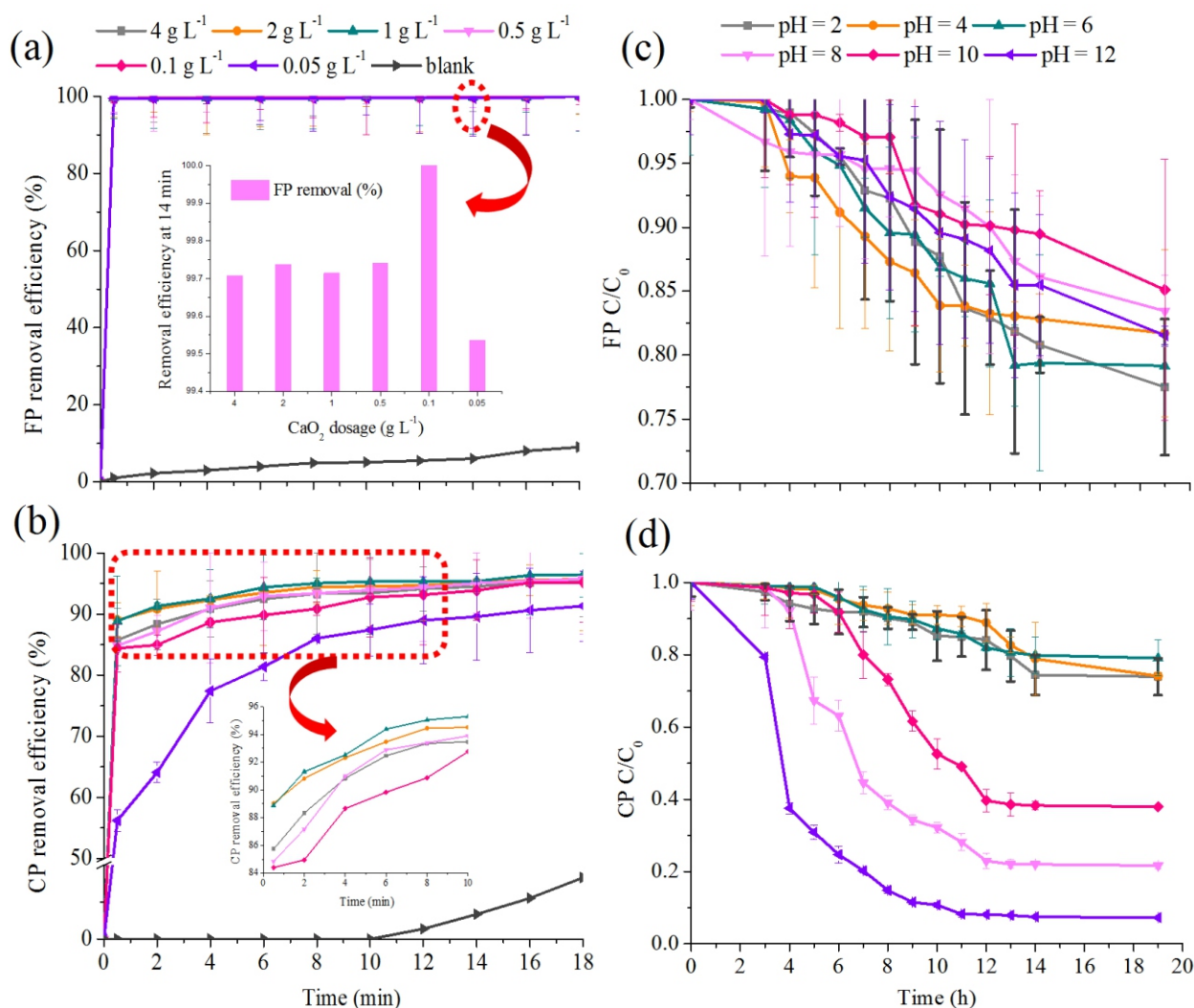

Fig. 2 Removal efficiencies of FP (a) and CP (b) at different CaO$_2$ dosages (unadjusted pH , initial FP and CP concentration = 0.02 mM) and C/Co (concentration ratio of residual GC to initial GC) of FP (c) and CP (d) during hydrolysis process at different initial pH (initial FP and CP concentration = 0.02 mM).

CP were hydrolyzed at pH 2, 4, 6, 8, 10, and 12, respectively (Figs. 2c&d). The results confirmed that FP hydrolysis was unreliable on pH while CP hydrolysis was closely dependent on pH values. An alkaline pH solution was found to be favourable for CP hydrolysis (Fig. 2d). As the hydrolysis products may convert back to the parent compounds at certain circumstances, it is still necessary to remove them by other methods.[24] As the studied reaction time for CaO_2 treatment was only 18 min (0.3 h), the FP and CP removal efficiency by hydrolysis (< 10% in 18 min) could be neglected during CaO_2 treatment. The results in Figs. 2c&d explained the phenomenon of the blank tests in Figs. 2a&b. Their hydrolysis products and mechanisms would be identified and evaluated in our future study.

With raising CaO_2 dosages, the removal efficiencies of FP and CP increased at low CaO_2 dosages and decreased at high CaO_2 dosages (shown in Fig. 2a). At CaO_2 of 0.05 to 0.1 g L^{-1}, the FP removal efficiency at 14 min is proportional to CaO_2 dosage (Fig. 2a). However, at CaO_2 dosage exceeding 0.1 g L^{-1}, the FP removal efficiency at 14 min decreased (Fig. 2a). For CP, the removal efficiencies promoted significantly from 64.1 to 91.3 % in 2 min with increasing CaO_2 from 0.05 to 1 g L^{-1}. However, increasing CaO_2 over 1 g L^{-1} decreased CP removal efficiency from 91.3 to 88.3 % (Fig. 2b). The reason may be explained by HO• generation. With raising CaO_2 dosage, the amount of H_2O_2 increased as shown in Eq. (1) and more HO• were generated to degrade FP and CP:

$$CaO_2 + 2H_2O \rightarrow Ca(OH)_2 + H_2O_2 \quad (1)$$
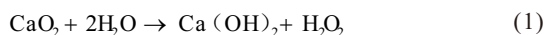
However, excessive CaO_2 generates an excessive H_2O_2 which could inversely scavenge the reactive oxygen species (ROS) as shown in Eqs. (2) and (3):[25]

$$H_2O_2 + HO\bullet \rightarrow H_2O + O_2^- \bullet \quad (2)$$

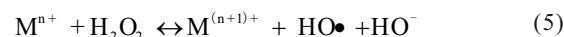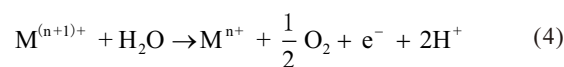$$HO\bullet + HO\bullet \rightarrow H_2O_2 \quad (3)$$
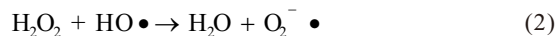
These chain reactions involved in CaO_2 treatment were explored and verified as the following section.

3.2 Effect of ROS on FP and CP removal during CaO_2 oxidation

In order to verify the function of ROS for FP and CP removal during CaO_2 treatment, TBA and chloroform were added in CaO_2 system to scavenge HO• and •O_2^-, respectively. As shown in Fig. 3a, the FP and CP removal were inhibited significantly by TBA. Increasing TBA concentration from 0 to 347 mM, the FP and CP removal efficiencies decreased for 3% (from 99.6% to 96.5%) and 37% (from 84.9% to 48.0%) in 2 min, respectively. Northup and Cassidy[26] also obtained the similar conclusion during the removal of 2-propanol in CaO_2 system. During •O_2^- scavenging tests, the FP and CP removal efficiencies decreased 2% (from 99.6% to 97.5%) and 29% (from 84.9% to 56.0%) in 2 min with the increase of chloroform from 0 to 347 mM, respectively (shown in Fig. 3b). This result showed that both HO• and •O_2^- contributed to FP and CP removal. As TBA has more obvious inhibition effects than chloroform (Fig. 3b), most of the FP and CP were removed by the oxidation of HO• as shown in Fig. 3c.

The raw materials for producing of commercial CaO_2 (purity less than 80%) usually contain marbles. Since various mineral impurities originally are present in the marble, they may inevitably exist in

CaO_2 reagent, catalyzing ROS generation in CaO_2 treatment. Various metal ions were detected in CaO_2 reagent as shown in Fig. 3c. Among these ions, Mg, Fe, and Al ions were commonly detected at relatively high concentrations (Fig. 3c). Our previous study[25] demonstrated that the Mg, Al, Co, Fe, and Mn ions could accelerate the EDC removal during advanced oxidation processes. These metals in CaO_2 reagent may participate in Fenton-type reactions and leading to producing of •OH radicals as shown in Eqs. (4) and (5),[27]

$$M^{(n+1)+} + H_2O \rightarrow M^{n+} + \frac{1}{2}O_2 + e^- + 2H^+ \quad (4)$$

$$M^{n+} + H_2O_2 \leftrightarrow M^{(n+1)+} + HO\bullet + HO^- \quad (5)$$

where M represents the metal ions. Based on the above results, the reacting system of CaO_2 treatment applicable in this study is summarized in Fig. 3c.

For comparison, performance of H_2O_2 and Fenton oxidation on CP removal were studied as shown in Fig. S2. Compared with individual H_2O_2 treatment, Fenton oxidation achieved higher CP removal efficiencies. At H_2O_2 dosage of 0.47, 0.94, and 1.88 g L^{-1} during Fenton oxidation, CP removal efficiencies were 7.6, 24.8, and 34.8% at 18 min, respectively. Notably, CaO_2 treatment achieved much higher CP removal efficiencies (96.3, 95.7, and 95.5% CP removal at CaO_2 dosage of 1, 2, and 4 g L^{-1}, at 18 min, respectively (Fig. 2b) than Fenton oxidation at equivalent H_2O_2 concentrations calculated by Eq. (1), indicating the efficiency of CaO_2 treatment and the existing of other mechanisms besides oxidation during CaO_2 treatment.
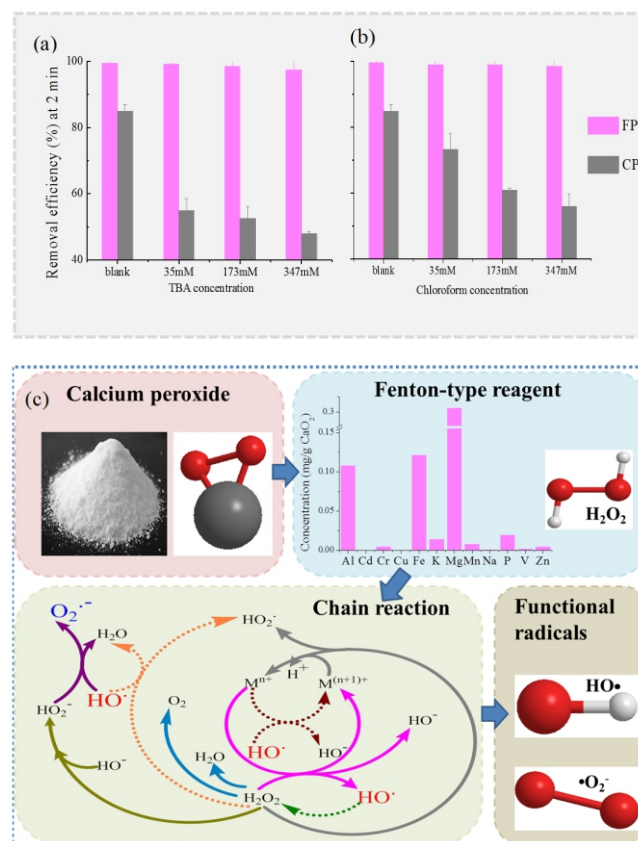
Fig. 3 Effects of TBA (a) and chloroform (b) at various concentrations on FP and CP removal during CaO_2 oxidation at 2 min and proposed reaction system of CaO_2 oxidation (c).

## 3.3 Effects of solution pH and CaO$_2$ adsorption on FP and CP removal

As shown in section 3.2, TBA and chloroform could not thoroughly inhibit FP and CP removal in CaO$_2$ treatment. So other mechnisms may also be involved in FP and CP removal during CaO$_2$ treatment. CaO$_2$ could generate Ca(OH)$_2$ in water (Eq. (6)), increasing the pH solution of the adsorbed FP and CP as a solid form:

$$2CaO_2 + 2H_2O \rightarrow 2Ca(OH)_2 + O_2 \uparrow \qquad (6)$$
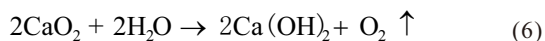
So the effects of solution pH and CaO$_2$ adsorption on FP and CP removal were evaluated in our study.

As shown in Figs. 4a&b, the FP and CP removal efficiencies altered significantly at different solution pH values. Adding CaO$_2$ for 1 g L^{-1} increased the solution pH from 1.8, 3.7, 6.8, 8.1, 9.7, 11.6 to 1.9, 3.8, 7.9, 9.5, 10.8, and 11.9, respectively. It was clear that the highest removal efficiencies of FP and CP were both obtained at solution pH of 7.9 (Figs. 4a&b). The removal efficiencies of FP and CP were lowest at acidic pH conditions of 1.9 and 3.8 (corresponding to initial pH of 1.8 and 3.7, respectively) (Figs. 4a &b). The solution pH could affect the generation of H$_2$O$_2$ in CaO$_2$ treatment as shown in Eq. (1).[20] Arienzo[21] found that adding phosphoric acid to CaO$_2$ slurry sharply increased the H$_2$O$_2$ release. At pH values of 1.9 - 3.8, large amount of H$_2$O$_2$ may release rapidly from CaO$_2$, causing excessive disproportionation as presented in Eq. (7)[25] and lead to low FP and CP removal efficiencies:

$$2H_2O_2 \rightarrow O_2 + 2H_2O \qquad (7)$$
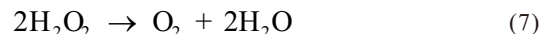
However, a high solution pH over 9 is also unfavorable for CaO$_2$ treatment (Figs. 4a&b). At solution pH over 9, CaO$_2$ was difficult to dissolve to generate H$_2$O$_2$,[21] and the main reaction during CaO$_2$ treatment was generating O$_2$ instead of H$_2$O$_2$ (shown in Eq. 6),[18] causing a decrease in FP and CP removal efficiencies. In comparison, at solution pH of 7.9, CaO$_2$ could persistently release H$_2$O$_2$ for a long time and the disproportionation of H$_2$O$_2$ could be reduced sharply.[21] So the optimum CaO$_2$ dosage should be decided considering the improved solution pH by released Ca(OH)$_2$ and the initial pH values in practical situation. The CaO$_2$ treatment could be the most effective at near-neutral initial pH values. The suitable increase of solution pH (< 9) by Ca(OH)$_2$ is favorable for FP and CP removal during CaO$_2$ treatment.

With the SEM-mapping of CaO$_2$ particles before and after treatment, the adsorption effect of CaO$_2$ particles was investigated as shown in Figs. 4(c–h). C and O elements detected on CaO$_2$ particles
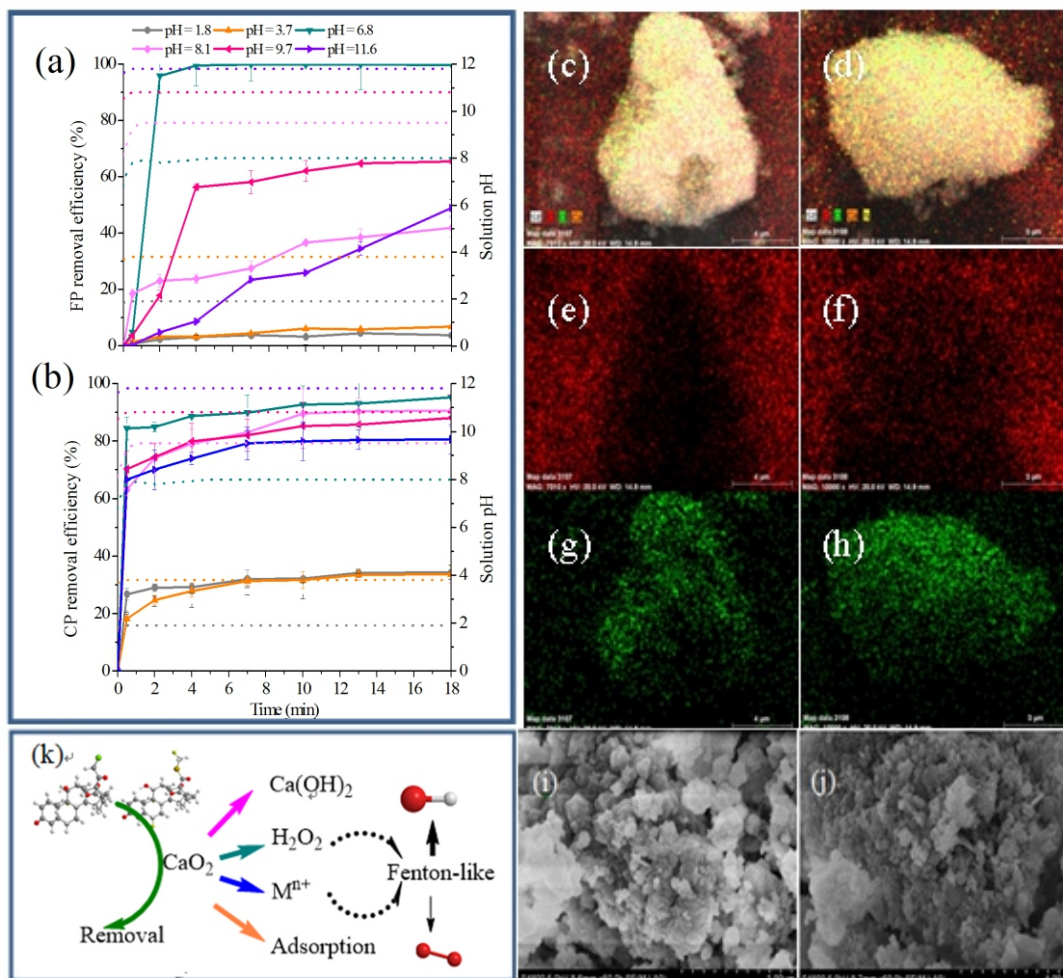

Fig. 4 Effects of initial pH on FP (a) and CP (b) removal efficiencies and changes of solution pH (CaO$_2$ at 0.1 g L^{-1}); EDS distribution maps for CaO$_2$ particles (c and d), C (e and f), and O (g and h) before (c, e, and g) and after (d, f, and h) treatment; SEM images of CaO$_2$ before (i) and after (j) treatment; Proposed roles of CaO$_2$ during FP and CP removal (k) .

after treatment (Figs. 4f&h) were much more than those before treatment (Figs. 4e&g). The surface morphology of CaO_2 particles during FP treatment at 0 min and 18 min were also characterized using SEM (Figs. 4i&j). As shown in Fig. 4i, the SEM images indicate porous and semi spherical – flaky shape CaO_2 particles at 0 min, indicating the existence of surface area for adsorption. However, the CaO_2 particles are agglomerated after reaction for 18 min as shown in Fig. 4j, which may decrease the surface area for adsorption. Zhang *et al.*[28] have detected the pore volume and the Brunauer-Emmett-Teller (BET) specific surface area of CaO_2 particles during oxidation and found that the CaO_2 particles could adsorb organic pollutants and its adsorption effects decreased during the oxidation. So increasing surface area of CaO_2 particles and improving their dispersion capacity would be beneficial for pollutant removal by adsorption during CaO_2 treatment. Based on the above results, the efficient FP and CP removal could be attributed to the synergistic effects of oxidation, adsorption, and base catalysis as summarized in Fig. 4k.

3.4 Effect of matrix on FP and CP removal during CaO_2 treatment

3.4.1 HA effect

As FP and CP could be adsorbed by CaO_2, natural organic matter in water matrix may also affect FP and CP removal by adsorption during CaO_2 treatment. HA can effectively absorb FP and CP as shown in Fig. 5a. With the increase of HA concentration in the absence of CaO_2, FP and CP removal efficiencies by HA adsorption increased (Fig. 5a). However, with the addition of CaO_2, the removal efficiencies of FP and CP increased with the increase of HA concentrations and then decreased (Figs. 5b&c). The presence of HA promoted CP removal at low HA concentrations (≤ 0.5 g L^{-1}) and inhibited FP and CP removal at high HA concentrations (> 0.5 g L^{-1}) during CaO_2 treatment (Figs. 5b&c). Basically, HA could interact with target compounds by adsorption, catalytic reactions, and competition.[29] The adsorption and competition are two opposite effects to FP and CP removal. HA can improve FP and CP removal efficiencies by adsorption. On the other hand, HA could react with HO• easily with high rate constants[30] and compete with FP and CP for the ROS during CaO_2 oxidation, causing the decrease in removal efficiencies (Fig. 5d). Thus, the overall role of HA in CaO_2 treatment depends on the balance between the two opposite effects as shown in Fig. 5d. According to the results (Fig. 5), CaO_2 is favorable for FP and CP removal from waters containing low HA concentrations (≤ 0.5 g L^{-1}).
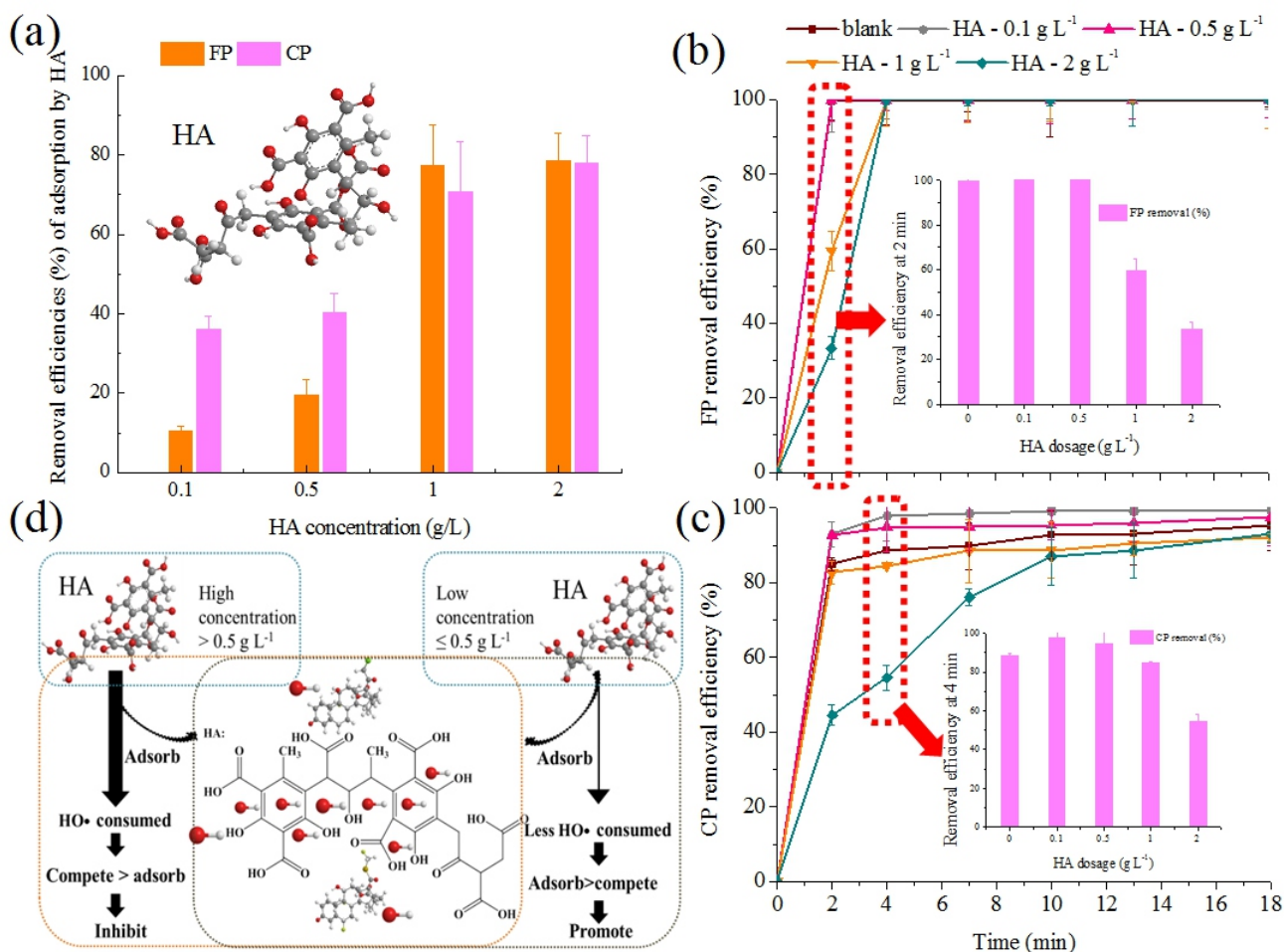
Fig. 5 Role of HA during CaO_2 oxidation (a: GC adsorption by HA at various HA concentrations without CaO_2 addition; b and c: Effects of HA on FP (b) and CP (c) removal at various HA concentrations; d: Coupling induction of HA adsorption and competing effects in CaO_2 system for GC removal.).

3.4.2 Anion effect

Effects of 5 common inorganic ions in matrix on FP and CP removal were evaluated and shown in Fig. 6. For FP, the presence of the 5 anions from 1 to 100 mM does not show any effects on its removal except for the HCO_3^- (Figs. 6a - e). Increasing HCO_3^- concentration to 100 mM resulted in the decrease of FP removal efficiency to 42.6 % within 18 min during CaO_2 oxidation (Fig. 6b). For CP, the presence of the Cl^-, HCO_3^-, and SO_4^{2-} from 1 to 100 mM significantly inhibits its removal while NO_3^- has no obvious effect and PO_4^{3-} has promotion effect from 1 to 100 mM (Figs. 6f-j). The CP removal by $CaCO_3$ and $CaSO_4$ adsorption could be neglected (< 15 %) as shown in Fig. S3. The possible mechanisms for the effects of these anions on pollutant removal during HO• or CaO_2 oxidation were summarized in Figs. 6k - o. Briefly, Cl^-, HCO_3^-, and SO_4^{2-} could consume HO• and formed other radicals much less reactive than HO• radicals (as shown in Figs. 6k, 6l, and 6n), causing the decrease in FP and CP removal efficiencies. It is worth noted that

PO_4^{3-} addition could accelerate CP removal during CaO_2 treatment (increased by 15 % at 100 mM for 2 min). Yang et al. [31] found that the existence of PO_4^{3-} in CaO_2 system could lead to the generation of ROS (HPO_5^{2-}), thus promoting pollutant removal. Moreover, PO_4^{3-} could stabilize H_2O_2[31] as shown in Fig. 6o. So CaO_2 is suitable for FP and CP removal from waters containing NO_3^- and PO_4^{3-}.

3.5 Degradation intermediates of FP and CP by CaO_2 oxidation

Analyses of treated solutions at different reaction times by UHPLC-QTOF and extraction of chemical features by Agilent Mass Profinder and Mass Profiler Professional (MPP) software based on high-resolution TOF scan data revealed 5 distinct FP decomposition products and 4 distinct CP decomposition products as listed in Table 1 which have never been reported before. Their Extracted-ion mass
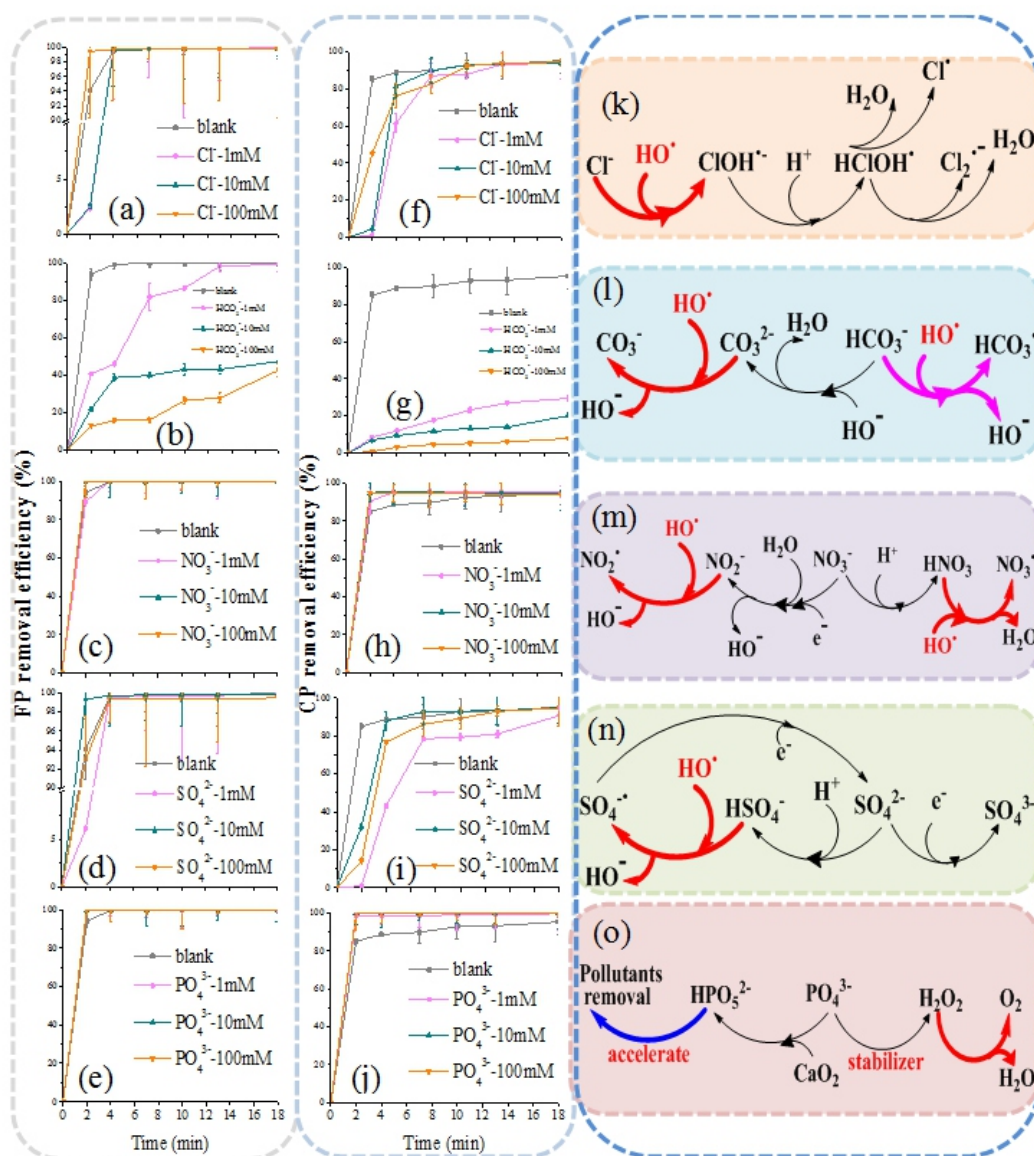
Fig. 6 Effects of inorganic ions (a and f: Cl^-; b and g: HCO_3^-; c and h: NO_3^-; d and i: SO_4^{2-}; e and j: PO_4^{3-}) on FP (a - e) and CP (f - j) removal at various concentrations and their roles (k: Cl^-; l: HCO_3^-; m: NO_3^-; n: SO_4^{2-}; o: PO_4^{3-}) in HO• or CaO_2 oxidation systems.

chromatographs and the mass spectrometry fragments of the LC-QTOF results can be found in Figs. 7a - 7e, 8a-8d and S4.

According to the frontier orbital theory by Fukui,[32] the frontier electron densities of C, O, S, F, and Cl atoms in FP and CP are listed in Table S3 and shown more visually in Figs. 1b and 1d. Seen from Table S3 and Figs. 1b and 1d, S19, O21, F34, F30, and C17 atoms in FP and Cl20, O26, O25, F29, and C17 atoms in CP have the largest frontier electron densities, indicating that these atoms are easy to be attacked by HO• radicals.

Combining the molecular formulas (Table 1) with the mass spectrometry fragments of the LC-QTOF results (Fig. S4), the possible byproducts of FP and CP during CaO_2 treatment were proposed and shown in Figs. 7f - 7j and 8e - 8h. The changes of their concentrations are also exhibited in Figs. 7k - o and 8i - 8l. As shown in Figs. 7c, 8a - 8d, concentrations of $C_{21}H_{31}F_3O_3S$, $C_{17}H_{26}O_3$,

$C_{23}H_{30}O_3$, $C_{23}H_{32}O_2$, and $C_{25}H_{43}FO_3$ increased with time at first and then decreased, meaning that they can be degraded further. On the contrary, $C_{23}H_{33}F_3O_4S$, $C_{21}H_{27}FO_5$, $C_{22}H_{33}F_3O_3S$, and $C_{19}H_{28}F_2O_5$ (shown in Figs. 7a, 7b, 7d, and 7e) are stable byproducts.

Sandra et al.[33] reported that decreased glucocorticoid activity could be achieved by elimination of the double bond at C1 and C6 and substitution at the C17 position. They also reported that the lipophilicity of the steroid and the metabolic resistance of GCs could be greatly increased by halogenation (fluorination/chlorination) of the B ring at the C10 and/or C7 and by adding acetal or ester groups at C17 and C16. For FP and CP, the addition and epoxidation of the unsaturated bond of C1 and C6 (Figs. 7b - 7e, 8b, and 8d), changes by oxidizing ester group at C17 (Figs. 7a, 7c - 7e, 8a - d), and the dehalogenation (defluorination) at C10 (Figs. 7b and 8a - 8c) represents the decrease of GC activity during CaO_2 treatment.
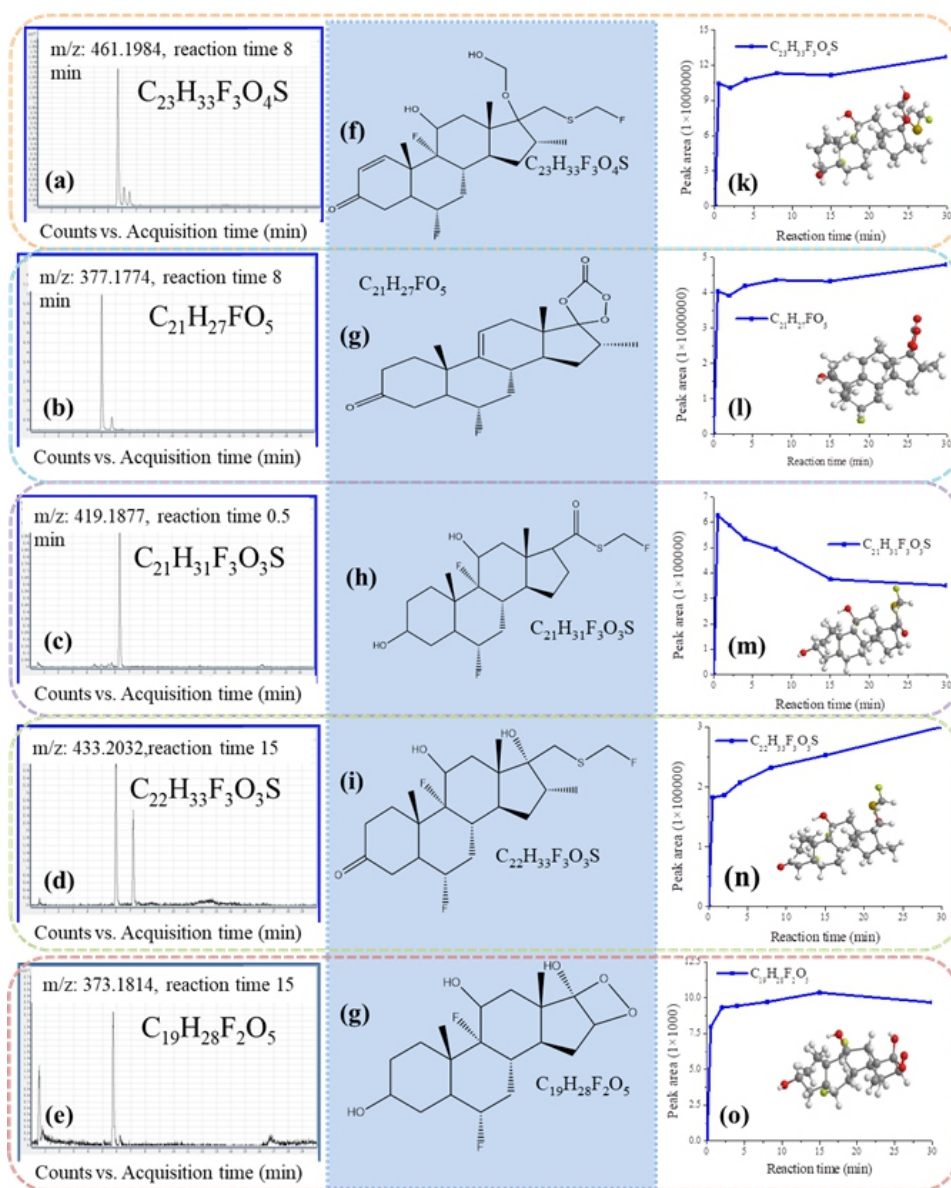
Fig. 7 The extracted-ion mass chromatographs for the intermediates of FP (a - e) during CaO_2 oxidation. All figures presented the relatively higher intensity of each product at the corresponding reaction time. Chemical structures of byproducts of FP (f – g). The change of peak area of each byproducts of FP (k – o).

**Table 1** General information on identified byproducts of FP and CP in CaO$_2$ treatment.

Product	Specie	m/z	Chemical formula	Measured M	Diff (ppm)	Score
FP-P1	(M-H)$^-$	461.1985	C$_{23}$H$_{33}$F$_3$O$_4$S	462.2052	-2.03	91.46
FP-P2	(M-H)$^-$	377.1774	C$_{21}$H$_{27}$FO$_5$	378.1843	-0.91	99.19
FP-P3	(M-H)$^-$	419.1877	C$_{21}$H$_{31}$F$_3$O$_3$S	420.1946	-1.33	93.29
FP-P4	(M-H)$^-$	433.2032	C$_{22}$H$_{33}$F$_3$O$_3$S	434.2103	-1.02	92.80
FP-P5	(M-H)$^-$	373.1822	C$_{19}$H$_{28}$F$_2$O$_5$	374.1905	2.44	96.45
CP-P1	(M-H)$^-$	277.1810	C$_{17}$H$_{26}$O$_3$	278.1882	-0.30	99.26
CP-P2	(M-H)$^-$	353.2121	C$_{23}$H$_{30}$O$_3$	354.2195	0.71	98.97
CP-P3	(M-H)$^-$	339.2328	C$_{23}$H$_{32}$O$_2$	340.2402	0.27	98.62
CP-P4	(M-H)$^-$	409.3112	C$_{25}$H$_{43}$FO$_3$	410.3196	3.01	85.75

4. Conclusions

This study researched the feasibility of CaO$_2$ in removing FP and CP. Efficient FP and CP removal were achieved due to the coupled effects of oxidation, adsorption, and alkaline condition in CaO$_2$ treatment. HO• radicals played the most important role for FP and CP removal by CaO$_2$ while •O$_2^-$ also contributes. The suitable increase of solution pH (< 9) resulting from Ca(OH)$_2$ releasing and the adsorption effects of CaO$_2$ particles also contribute to FP and CP removal.

CaO$_2$ treatment remained effective in complex water matrix with the presence of humic acid (HA) and common anions except for HCO$_3^-$. The presence of HA could promote FP and CP removal at low HA concentrations (≤ 0.5 g L^{-1}) while PO$_4^{3-}$ could also accelerate FP and CP removal.

Nine degradation intermediates of FP and CP were identified for the first time, indicating the decrease of GC toxicity. The results show that CaO$_2$ treatment could be efficient for FP and CP removal.
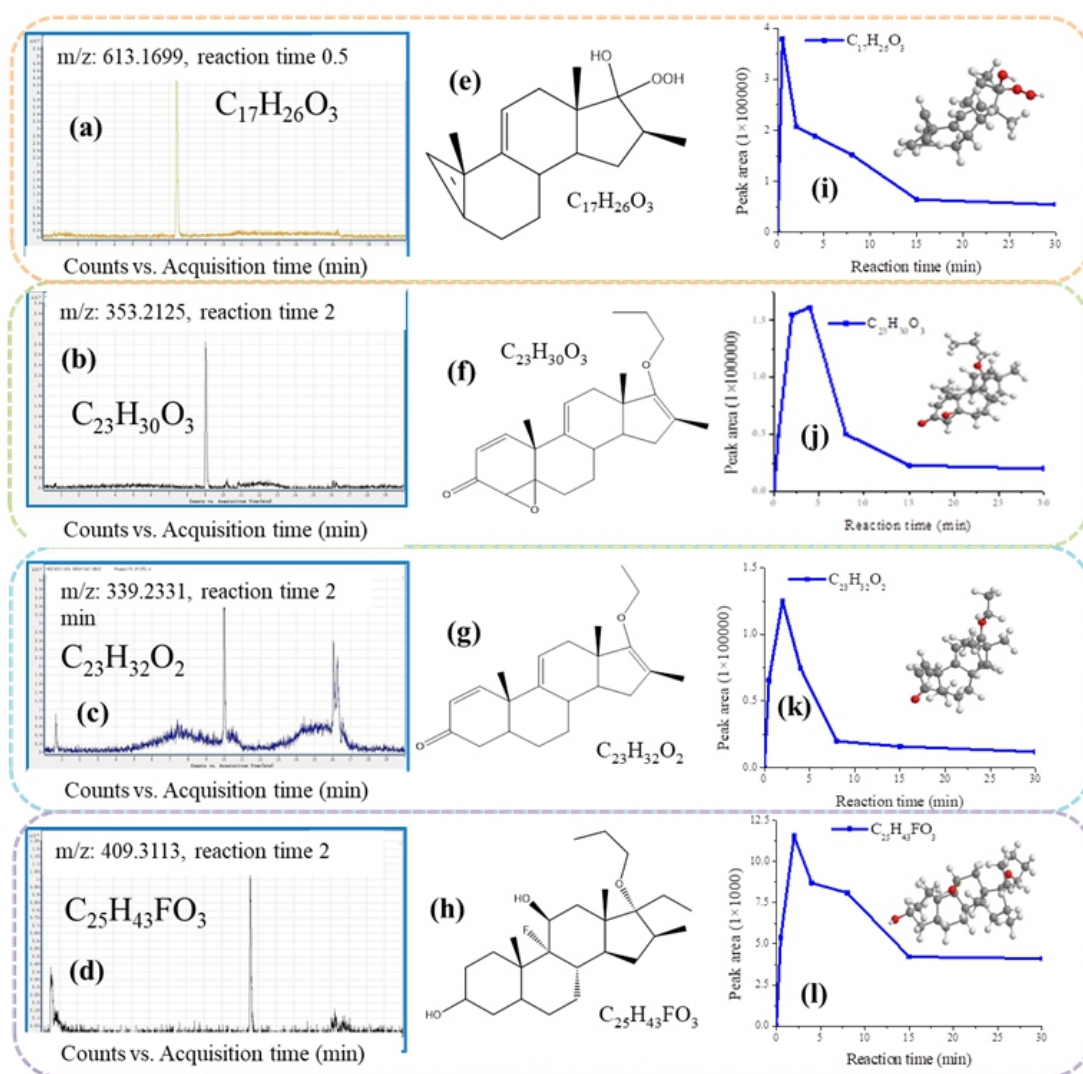
Fig. 8 The extracted-ion mass chromatographs for the intermediates of CP (a – d) during CaO$_2$ oxidation. All figures presented the relatively higher intensity of each product at the corresponding reaction time. Chemical structures of byproducts of CP (e – h). The change of peak area of each byproducts of CP (i – l)

Conflict of interest

The authors declare no competing financial interest and human conflicts.

Acknowledgments

Appendix A. Supplementary data

Supplementary data to this article can be found in the supporting information.

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