***Supplementary information***

**Reactivity of Fe(III)-containing pyrophosphate salts with phenolics: complexation, oxidation, and surface interaction**

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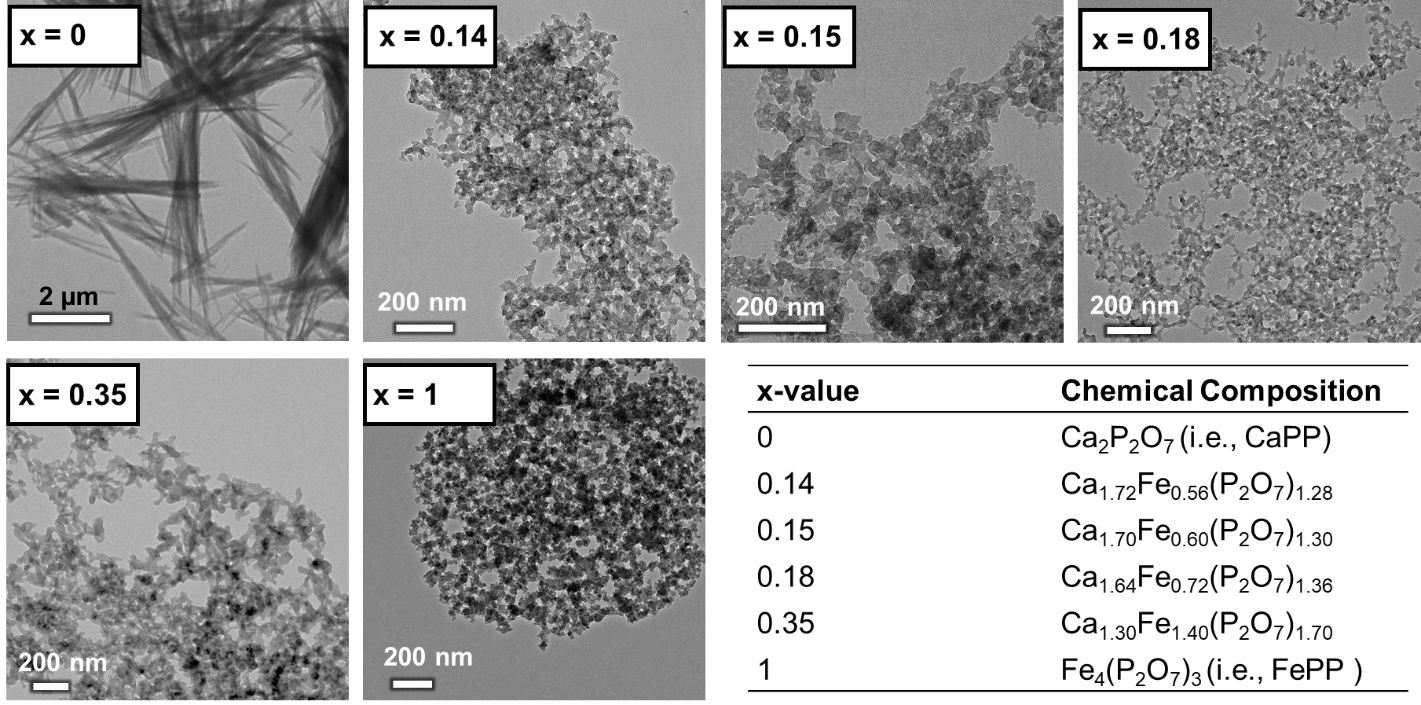
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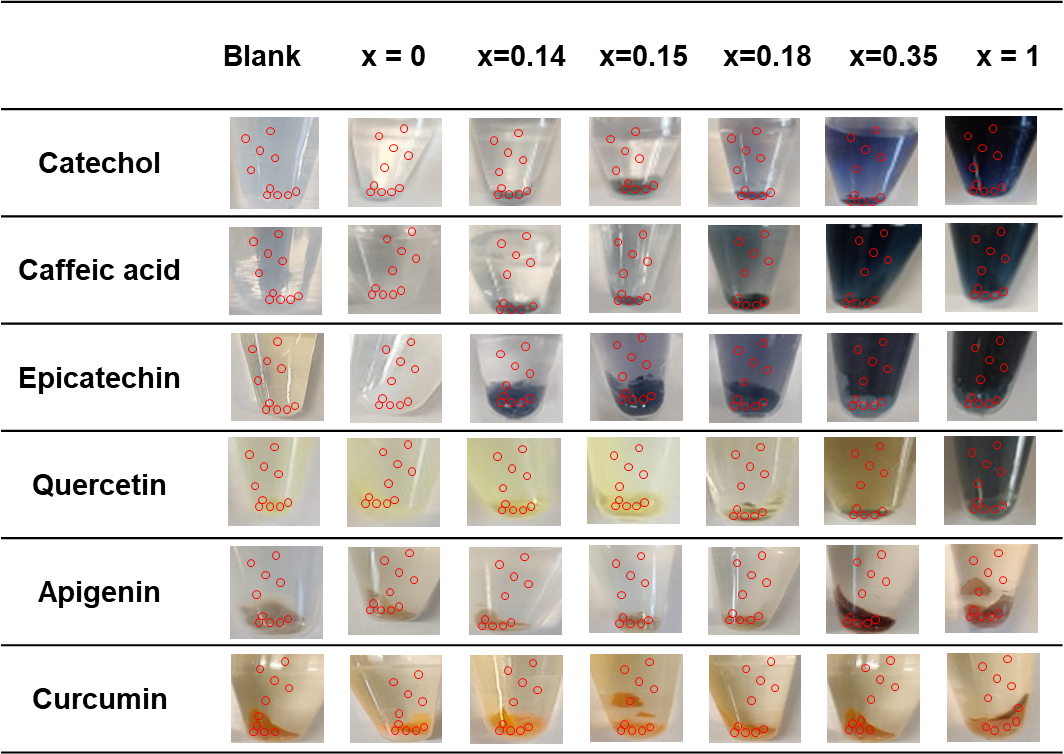
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**Fig. S1.** TEM images of the CaPP (x = 0), FePP (x = 1), and mixed Ca-Fe(III) pyrophosphate salts with x = 0.14, 0.15, 0.18, and 0.35 prepared by coprecipitation. The x*-*values and chemical formula of the pure and mixed salts were obtained from the elemental composition determined by EDX.

**Method S1: Dissolution of CaPP, FePP, and mixed Ca-Fe(III) pyrophosphate salts in the presence of phenolics by inductively coupled plasma – atomic emission spectroscopy (ICP-AES)**

Inductively coupled plasma–atomic emission spectroscopy (ICP-AES) was used for independent verification of the iron quantification by the ferrozine assay. For ICP-AES measurements, CaPP, FePP, and the mixed Ca-Fe(III) pyrophosphate salts were redispersed in water by stirring (~250 rpm) with a magnetic stir bar (final amount of salt 10 mg/ml) followed by the addition of aqueous solutions (i.e., catechol, caffeic acid, and epicatechin) or dispersions (i.e., quercetin, apigenin, and curcumin) of the phenolics at a final concentration of 5 mM. pH was set to reach a target pH 3, 6, or 8 after 2 h of incubation at 23 °C while mixing at 1000 rpm. Samples were five times diluted in 0.14 M HNO3, before injection in the ICP-AES system (Agilent 5110 VDV; Agilent Technologies, Tokyo, Japan). Independent duplicate samples were taken from the salt at each pH point by independent titrations. The concentration of iron, calcium, and phosphorus was determined using scandium as an internal standard. The limit of detection values of iron, calcium, and phosphorus were respectively 0.05, 0.05, and 0.20 mg/l, the limit of quantification values were 0.15, 0.15, and 0.61 mg/l respectively.

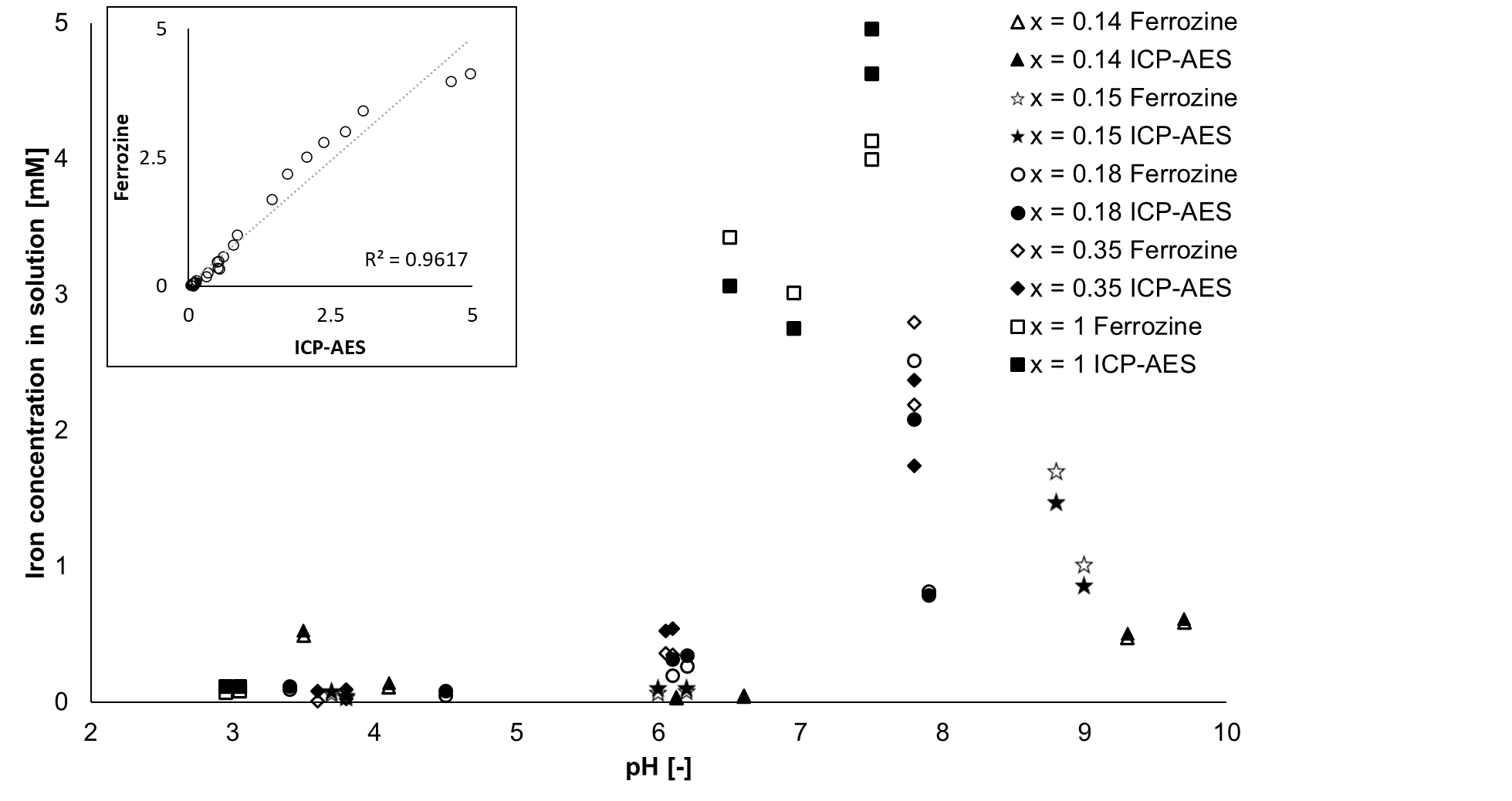
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**Fig. S2.** Images of Eppendorfs containing phenolics in combination with CaPP (x = 0), FePP (x = 1), and mixed Ca-Fe(III) pyrophosphate salts with x = 0.14, 0.15, 0.18, and 0.35 at pH 6. The red spots indicate the positions where the *L\*a\*b\** values were extracted using a standard image analysis software (Photoshop CC2021, Adobe)

**Method S2: Elution profiles reversed-phase chromatography**

The following elution profile was used to measure the solubility of the phenolics at pH 3, 6, and 8: 0.00 – 1.09 min, isocratic on 1 vol.%B; 1.09 – 20.72 min, linear gradient from 1 – 55 vol.%B; 20.72 – 21.81 min linear gradient from 55 – 100vol.% B; 21.81 – 27.26 min isocratic on 100vol.% B; 27.26 – 28.35 min linear gradient from 100 – 1 vol.% B; 28.35 – 33.81 min isocratic on 1 vol.% B.

The following elution profile was used to monitor the oxidation of epicatechin and quercetin: 0.00 – 1.09 min, isocratic on 1 vol.%B; 1.09 – 13.45 min, linear gradient from 1 – 35 vol.%B; 13.45 – 14.54 min linear gradient from 35 – 100 vol.% B; 14.54 – 19.99 min isocratic on 100 vol.% B; 19.99 – 21.08 min linear gradient from 100 – 1 vol.% B; 21.08 – 26.54 min isocratic on 1 vol.% B.

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**Fig. S3.** Soluble iron concentration from FePP (x = 1) and mixed Ca-Fe(III) pyrophosphate salts with x = 0.14, 0.15, 0.18, and 0.35 in the presence of epicatechin as a function of pH determined by ICP-AES (filled markers) and by the ferrozine (open markers) methods. The inset depicts the correlation between the iron concentration measured using both methods. The iron concentrations in solution measured by the two different methods were found to be in good agreement (R2 = 0.96).

**Table S1.** Iron content (%), theoretical maximum concentration (mM), and measured iron concentration (mM) from FePP (x =1) and mixed Ca-Fe(III) pyrophosphate salts with x = 0.14, 0.15, 0.18, and 0.35, based on the iron content of the salt and the amount of salt in the starting dispersion (10 mg/ml for all salts).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **x-value** | **Iron content**  **(Mole %)** | **Theoretical maximum iron concentration (mM)** | **Measured iron concentration (mM)** | | |
| **pH 3** | **pH 6** | **pH 8** |
| 0.14 | 4.06 | 17.35 | 0.232±0.000a | 0.006±0.000 | 0.059±0.001 |
| 0.15 | 4.29 | 17.75 | 0.365±0.017 | 0.032±0.003 | 0.307±0.014 |
| 0.18 | 4.93 | 21.03 | 0.265±0.005 | 0.147±0.002 | 0.608±0.009 |
| 0.35 | 7.78 | 32.87 | 0.080±0.004 | 1.422±0.037 | 3.148±0.037 |
| 1 | 12.90 | 53.69 | 0.028±0.001 | 0.810±0.029 | 3.198±0.016 |

a standard deviation of independent duplicates

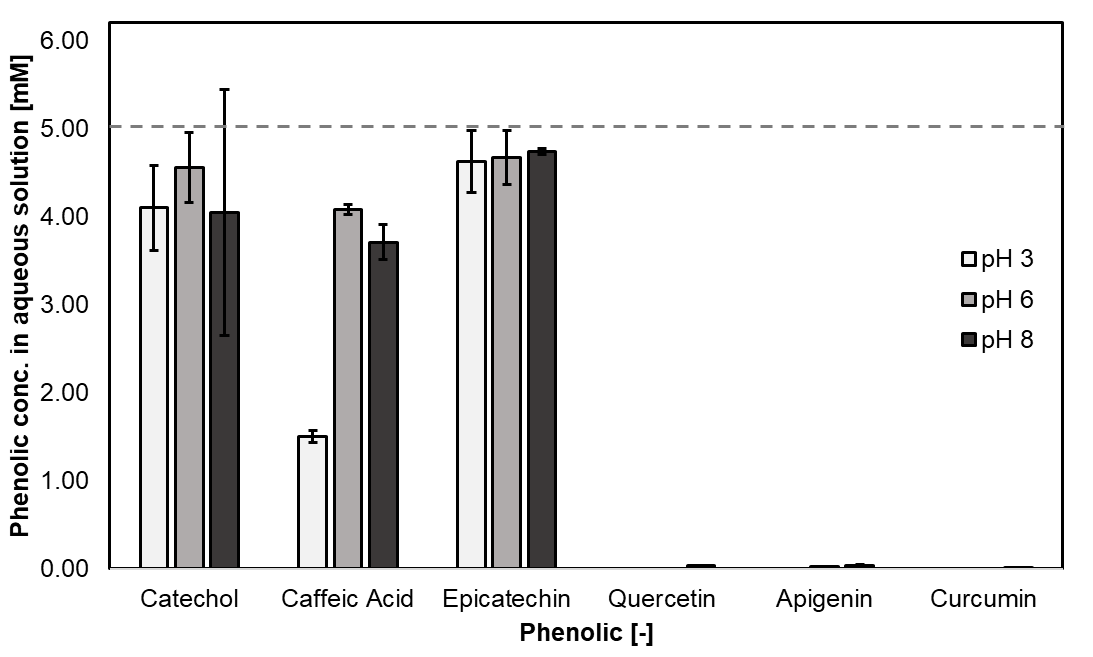


Fig. S4. Water solubility of the phenolics in absence of any iron- or calcium-containing salts at pH 3, 6, and 8 as quantified by RP-UHPLC-PDA-MS. The dashed line indicates the prepared concentration of the phenolic solution.

**Table S2.** Reported stability constants of Fe(III) with the phenolic compounds tested in this study.

|  |  |  |
| --- | --- | --- |
| Phenolic | Logβ | Reference |
| Catechol | 43.8 | (Avdeef, Sofen, Bregante, & Raymond, 1978) |
| Caffeic acid | 18.9 | (Hynes & O'Coinceanainn, 2004) |
| Catechin | 47.4 | IUPAC. (1979). IUPAC stability constants of metal–ion complexes, part B, organic ligands. Oxford, UK: Pergamon Press. (Perron & Brumaghim, 2009) |
| Quercetin | 44.2 | (Escandar & Sala, 1991) |
| Apigenin | Not reported |  |
| Curcumin | 22.1 | (Borsari, Ferrari, Grandi, & Saladini, 2002) |

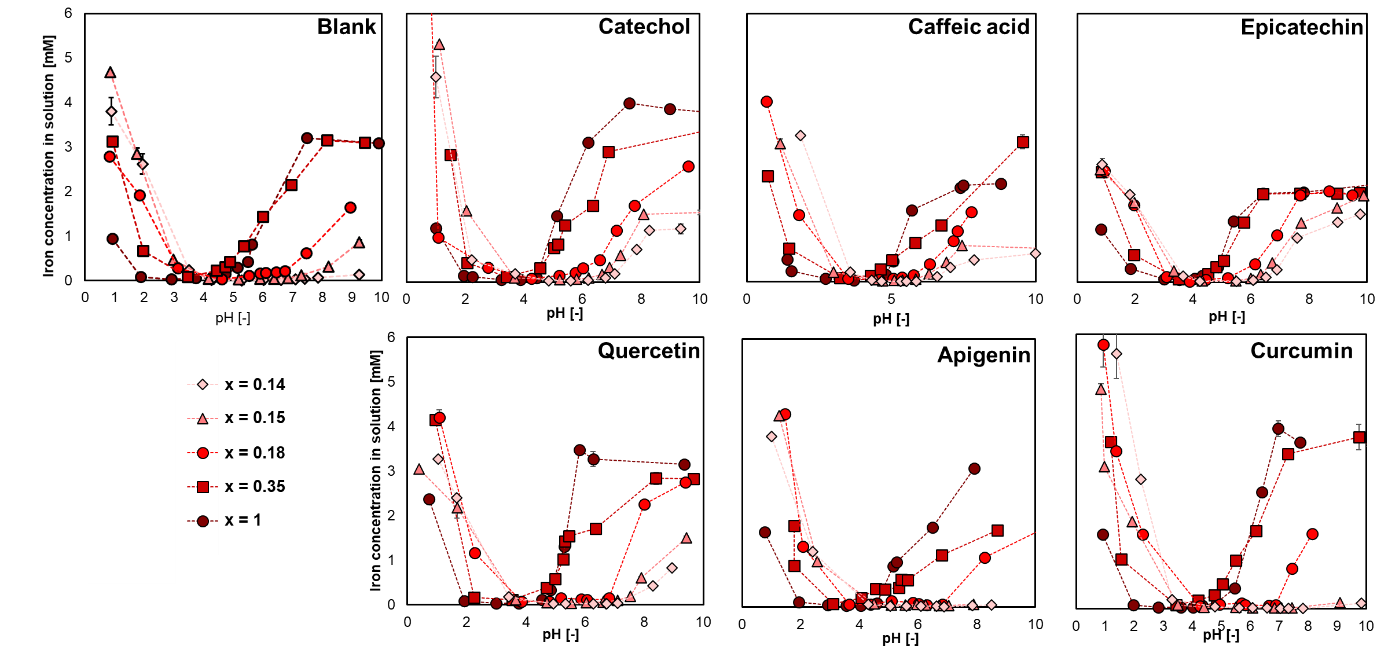


Fig. S5. Dissolution behavior of iron from FePP (x = 1) and the mixed Ca-Fe(III) pyrophosphate salts with x = 0.14, x = 0.15, x = 0.18, and x = 0.35 at pH 1-10; in the absence of phenolics (blank), and in presence of catechol, caffeic acid, epicatechin, quercetin, apigenin, and curcumin at 23 °C.

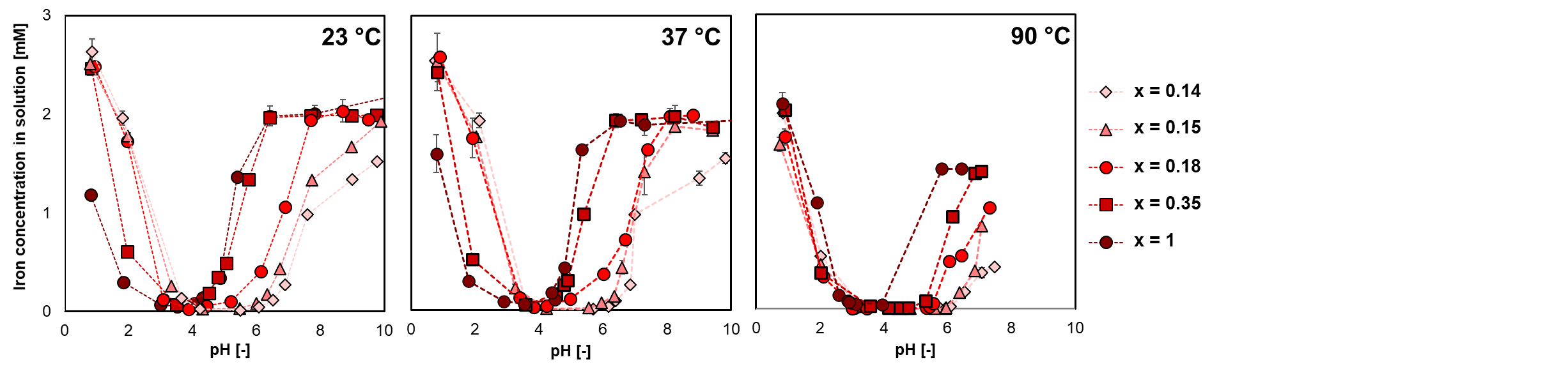
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Fig. S6. Dissolution behavior of iron from FePP (x = 1) and the mixed Ca-Fe(III) pyrophosphate salts with x = 0.14, x = 0.15, x = 0.18, and x = 0.35 at pH 1-10 in the presence of epicatechin at 23, 37, and 90 °C.

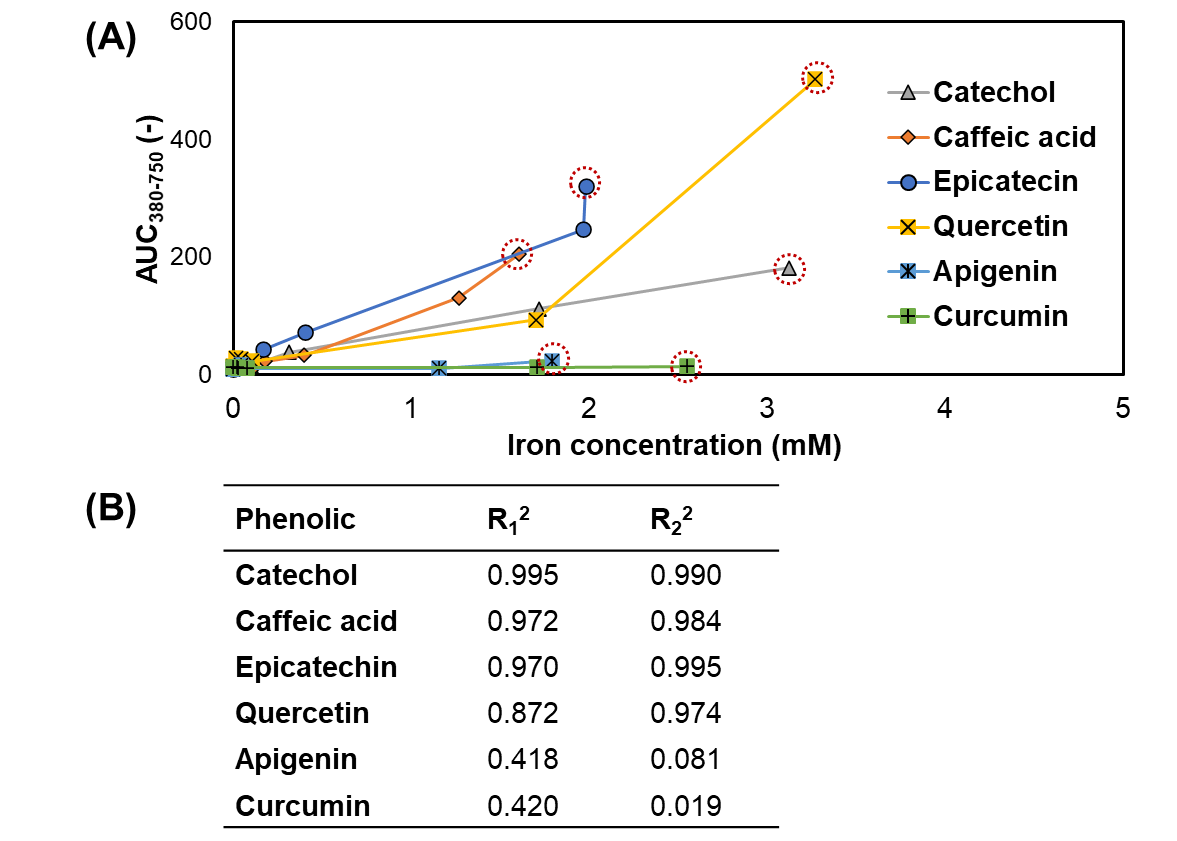


Fig. S7. (A) Relationship between the area under the curve in the visible light spectra (AUC380-750) versus the iron concentration in solution and (B) R12 the regression value from the mixed salts and FePP (including the red dashed point from A), and R22 the regression value of the mixed salts only (excluding the red dashed point from A).

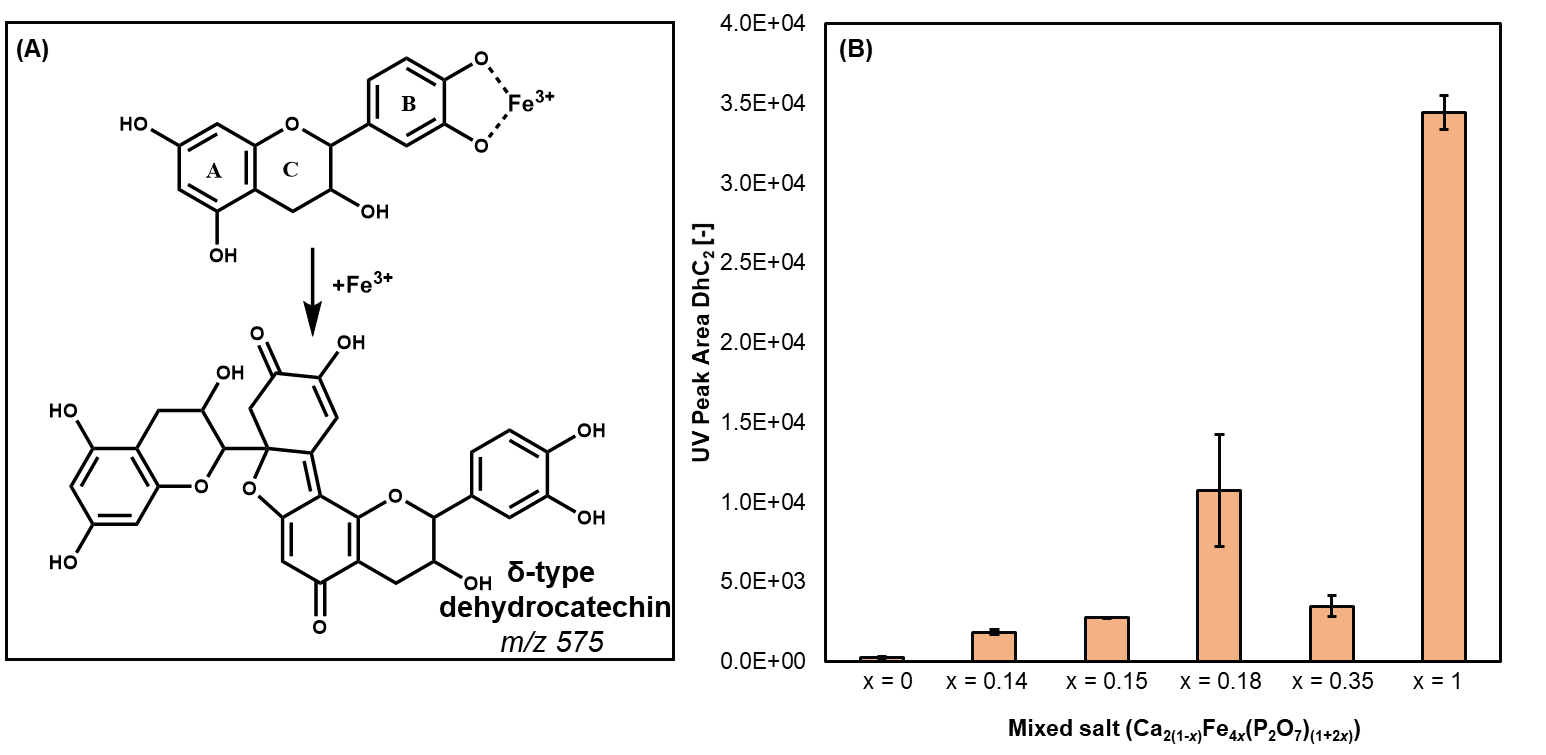


Fig. S8. (A) Proposed main oxidation compound (δ-type dehydrocatechin; δ-type DhC2) of Fe(III)-mediated oxidation of epicatechin (Bijlsma, de Bruijn, Velikov, & Vincken, 2022; Tan, de Bruijn, van Zadelhoff, Lin, & Vincken, 2020). (B) Bar graph indicating the peak area of δ-type DhC2 after incubation of CaPP (x =0), FePP (x = 1), and mixed Ca-Fe(III) pyrophosphate salts with epicatechin at pH 6.

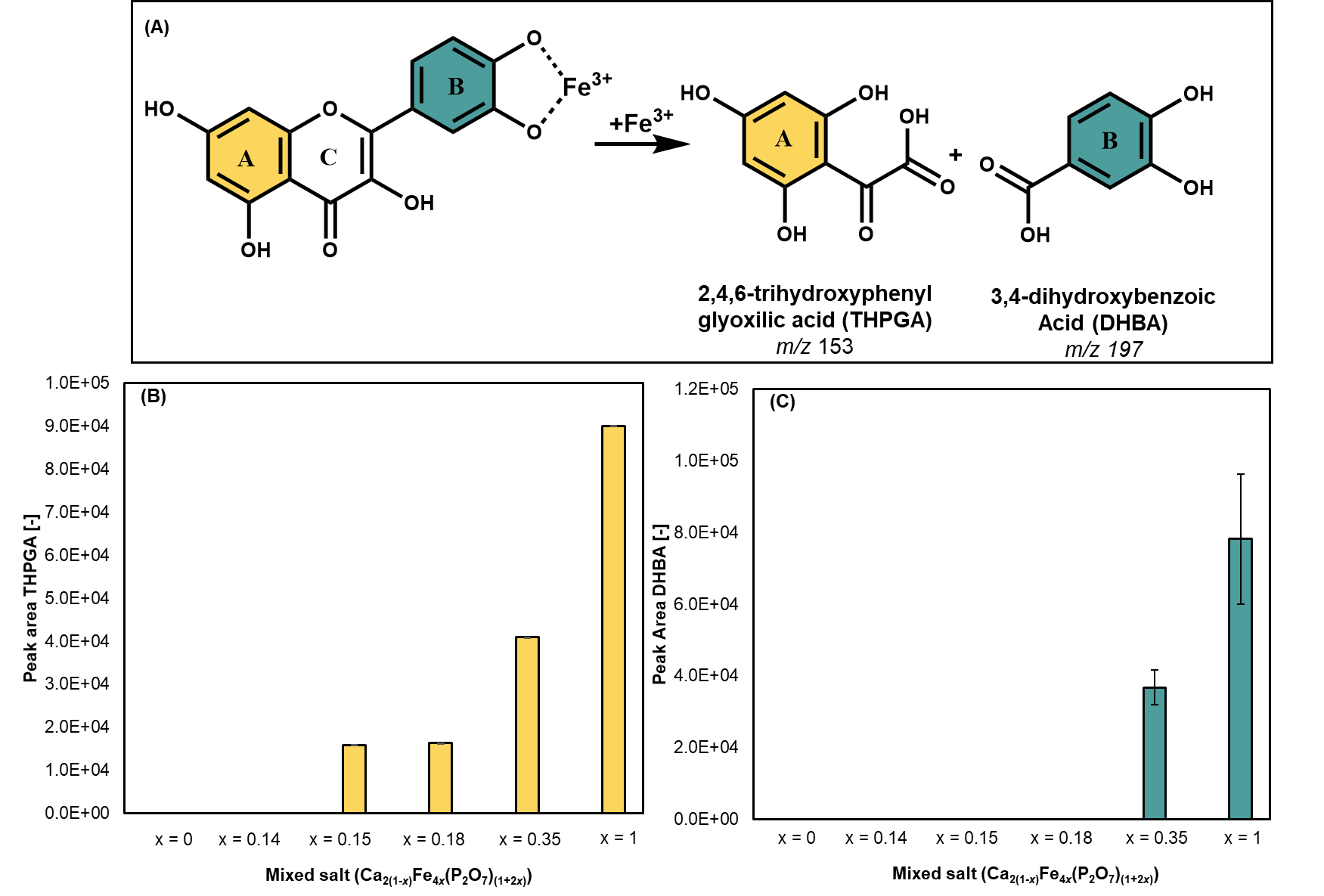


Fig. S9. (A) Main oxidation compounds of Fe(III)-mediated oxidation of quercetin (Bijlsma et al., 2022). (B) Bar graph indicating the peak area of THPGA and (C) of DHBAafter incubation of CaPP (x = 0), FePP (x = 1), and mixed Ca-Fe(III) pyrophosphate salts with x = 0.14, 0.15, 0.18, and 0.35, with quercetin at pH 6.

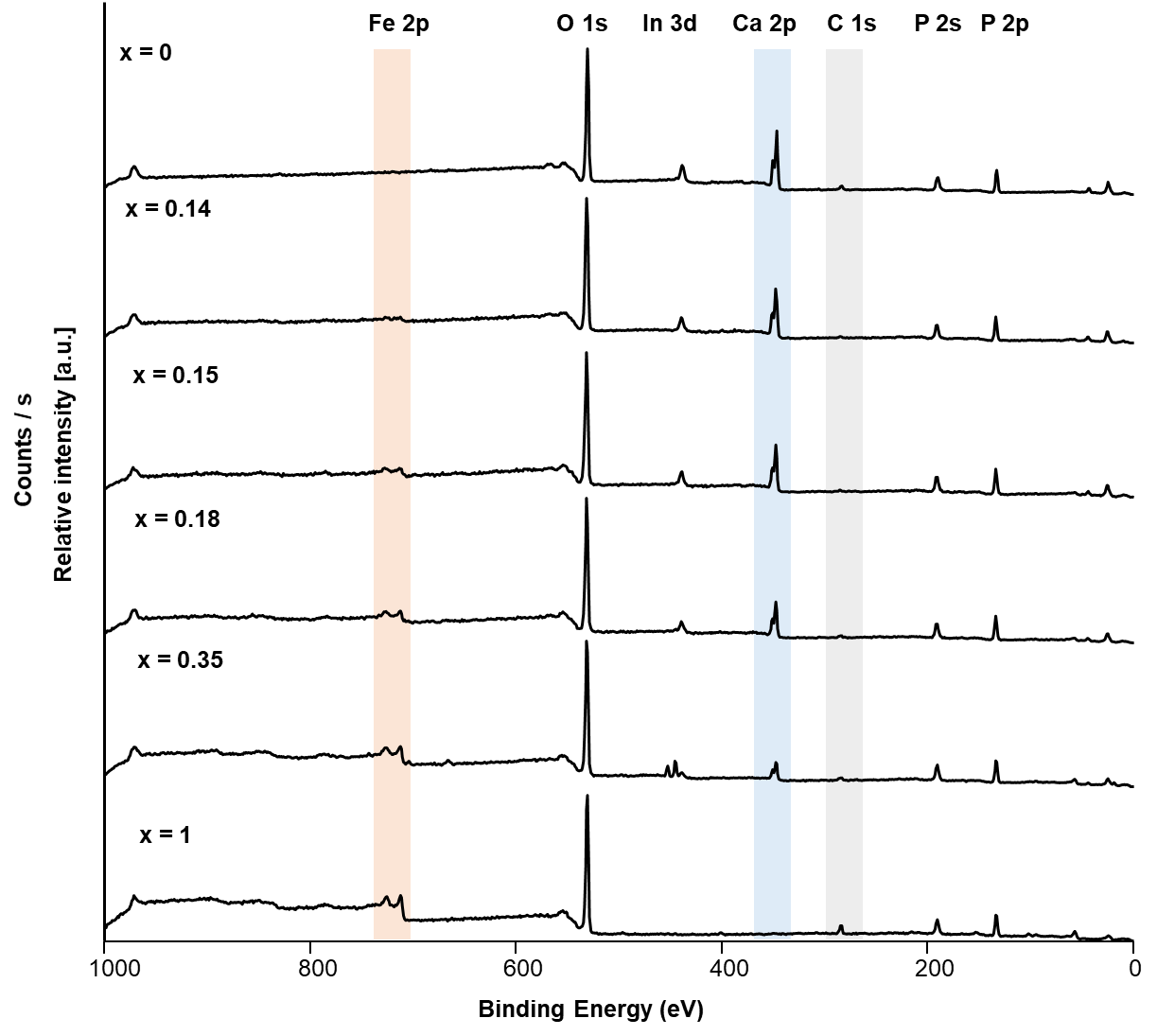


Fig. S10. XPS Wide scan spectrum of CaPP (x = 0), FePP (x =1), and mixed Ca-Fe(III) pyrophosphate salts with x = 0.14, 0.15, 0.18, and 0.35. The salts were measured on a indium (In) surface.

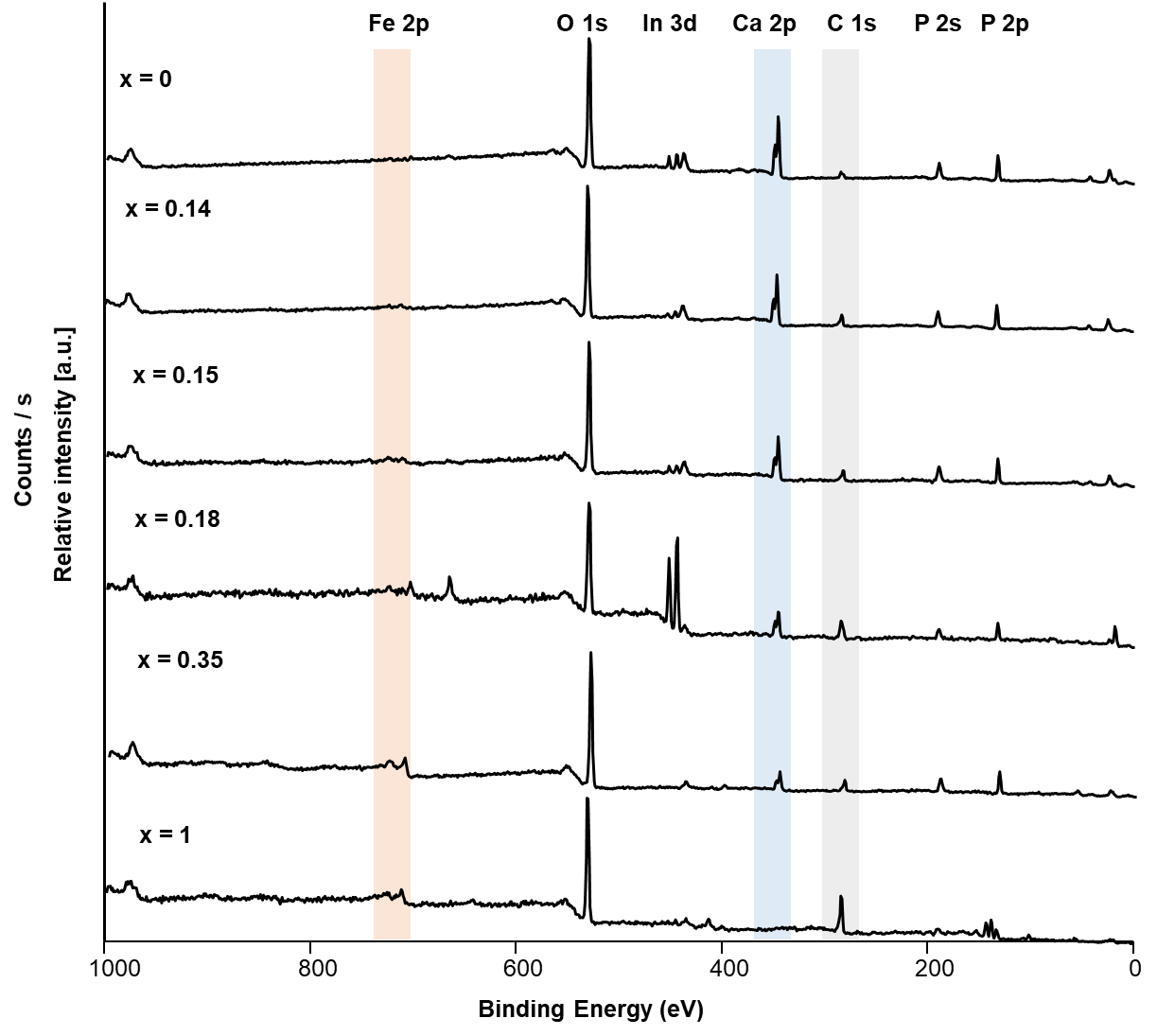
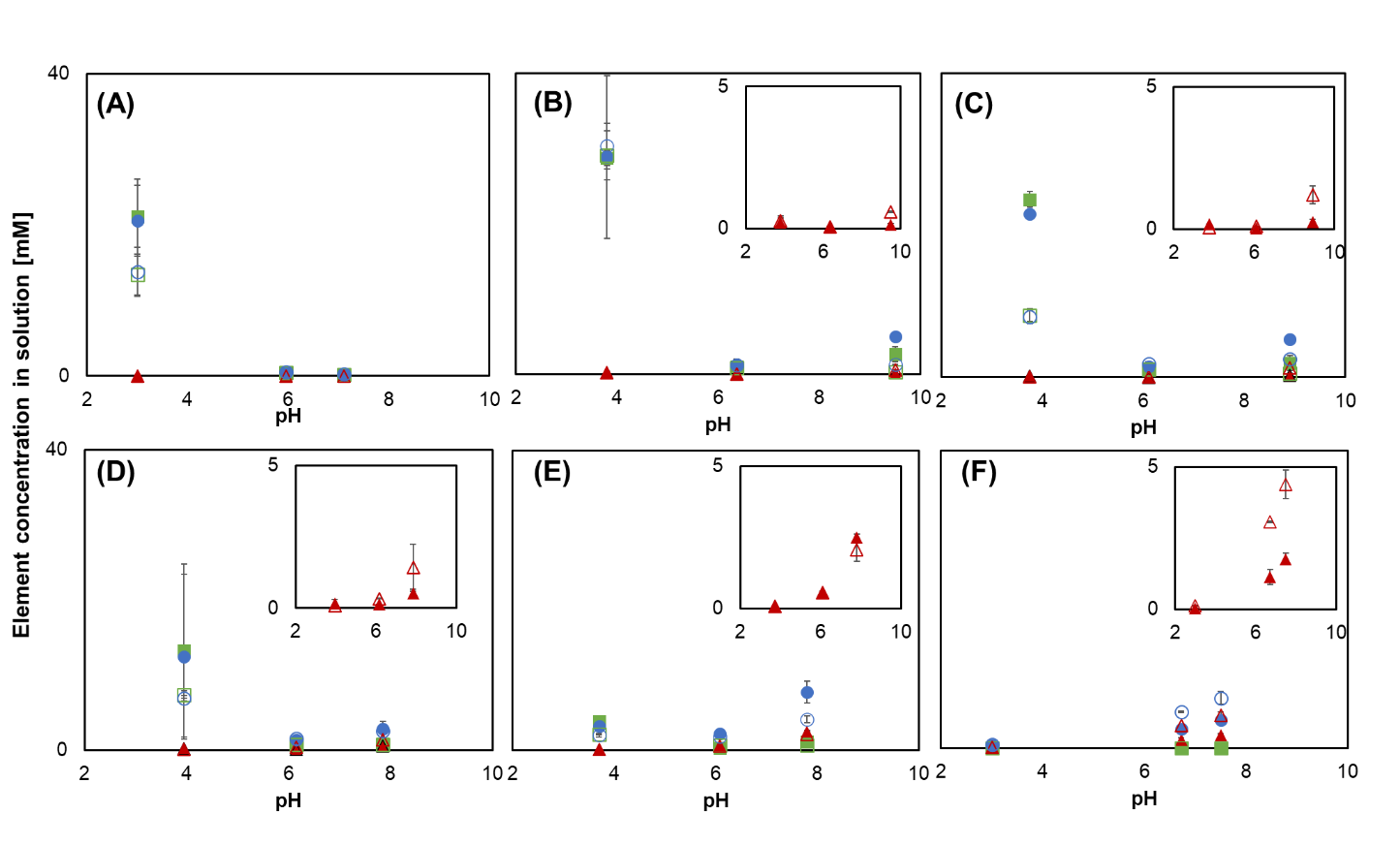


Fig. S11. XPS Wide scan spectrum of CaPP (x = 0), FePP (x =1), and mixed Ca-Fe(III) pyrophosphate salts with x = 0.14, 0.15, 0.18, and 0.35 after incubation with epicatechin (pH 6). The salts were measured on a indium (In) surface.



**Fig. S12** Concentration of iron (red triangle), calcium (green square), and phosphorus (blue circle) quantified by ICP-AES in aqueous supernatant for (A) CaPP (x = 0) and the mixed Ca-Fe(III) pyrophosphate salts with (B) x = 0.14; (C) x = 0.15; (D) x = 0.18; (E) x = 0.35; and (F) FePP (x = 1) in the absence (filled markers) and presence (open markers) of epicatechin. The insets show the corresponding iron concentration in solution.

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