Supplementary information

A Ca-Based Nano Bio-Coordination Polymer Providing Reversible Structural Conversion with Ability to Enhancing Cytotoxicity of Curcumin and Inducing Apoptosis in Human Gastric Cancer AGS Cells

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Preparation of single crystals of bio-CP 1, $\{[Ca(NA)_2.2H_2O].3H_2O\}_n$

$Ca(NO_3)_2.4H_2O$ (0.9 mmol, 0.21 g) and vitamin B3 (1.8 mmol, 0.22 g) were dissolved in 15 mL twice distilled water on the heater stirrer, and the final pH was adjusted to about 7 with NaOH (1 M) solution. The clear solution was filtrated with filter paper. The final solution was placed in a beaker and placed at room temperature. Colorless crystals were obtained after about three weeks (yield: 60 %, based on the final products).

Fig. S1. Set up for preparation of COCl-terminated bio-CP **2**.

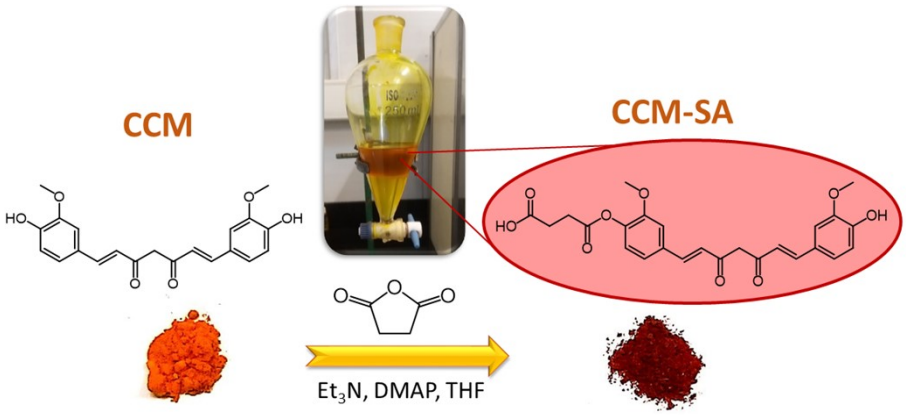

Fig. S2. Synthesis procedure of CCM-SA.

Table S1. Selected bond lengths (Å) and angles (deg) for $\{[Ca(NA)_2.2H_2O].3H_2O\}_n$ (bio-CP **1**).

Ca(1)-O(1)	2.3515(5)	O(3)-Ca(1)-C(6)	163.34(2)
Ca(1)-O(1)	2.7242(6)	O(2)-Ca(1)-C(6)	25.157(19)
Ca(1)-O(2)	2.4266(6)	O(2)-Ca(1)-C(6)	82.43(2)
Ca(1)-O(3)	2.4043(6)	O(1)-Ca(1)-C(6)	82.309(19)
Ca(1)-Ca(1)	4.00328(14)	O(1)-Ca(1)-C(6)	25.429(17)
Ca(1)-Ca(1)	4.00328(14)	O(1)-Ca(1)-C(6)	101.22(2)
Ca(1)-H3A	2.766(16)	O(1)-Ca(1)-C(6)	105.42(2)
O(1)-Ca(1)-O(1)	145.20(3)	O(3)-Ca(1)-C(6)	163.33(2)
O(1)-Ca(1)-O(3)	85.96(2)	O(3)-Ca(1)-C(6)	84.27(2)
O(1)-Ca(1)-O(3)	74.76(2)	O(2)-Ca(1)-C(6)	82.43(2)
O(1)-Ca(1)-O(3)	74.76(2)	O(2)-Ca(1)-C(6)	25.157(19)
O(1)-Ca(1)-O(3)	85.96(2)	O(1)-Ca(1)-C(6)	25.429(17)
O(3)-Ca(1)-O(3)	112.25(3)	O(1)-Ca(1)-C(6)	82.309(19)
O(1)-Ca(1)-O(2)	80.32(2)	C(6)-Ca(1)-C(6)	79.34(3)
O(1)-Ca(1)-O(2)	124.82(2)	O(1)-Ca(1)-Ca(1)	41.346(15)
O(3)-Ca(1)-O(2)	84.01(2)	O(1)-Ca(1)-Ca(1)	156.899(15)
O(3)-Ca(1)-O(2)	148.781(19)	O(3)-Ca(1)-Ca(1)	124.684(14)
O(1)-Ca(1)-O(2)	124.82(2)	O(3)-Ca(1)-Ca(1)	75.293(14)
O(1)-Ca(1)-O(2)	80.32(2)	O(2)-Ca(1)-Ca(1)	73.587(14)
O(3)-Ca(1)-O(2)	148.78(2)	O(2)-Ca(1)-Ca(1)	84.358(14)
O(3)-Ca(1)-O(2)	84.01(2)	O(1)-Ca(1)-Ca(1)	34.766(12)
O(2)-Ca(1)-O(2)	95.31(3)	O(1)-Ca(1)-Ca(1)	116.142(14)
O(1)-Ca(1)-O(1)	76.11(2)	C(6)-Ca(1)-Ca(1)	93.732(15)
O(1)-Ca(1)-O(1)	130.00(2)	C(6)-Ca(1)-Ca(1)	59.978(14)
O(3)-Ca(1)-O(1)	153.781(18)	O(1)-Ca(1)-Ca(1)	156.899(15)
O(3)-Ca(1)-O(1)	81.593(19)	O(1)-Ca(1)-Ca(1)	41.345(15)
O(2)-Ca(1)-O(1)	74.33(2)	O(3)-Ca(1)-Ca(1)	75.293(14)
O(2)-Ca(1)-O(1)	50.403(18)	O(3)-Ca(1)-Ca(1)	124.684(14)
O(1)-Ca(1)-O(1)	130.00(2)	O(2)-Ca(1)-Ca(1)	84.358(14)
O(1)-Ca(1)-O(1)	76.11(2)	O(2)-Ca(1)-Ca(1)	73.587(14)
O(3)-Ca(1)-O(1)	81.593(19)	O(1)-Ca(1)-Ca(1)	116.143(14)
O(3)-Ca(1)-O(1)	153.781(18)	O(1)-Ca(1)-Ca(1)	34.766(12)
O(2)-Ca(1)-O(1)	50.403(18)	C(6)-Ca(1)-Ca(1)	59.978(14)
O(2)-Ca(1)-O(1)	74.33(2)	C(6)-Ca(1)-Ca(1)	93.732(15)
O(1)-Ca(1)-O(1)	95.31(3)	Ca(1)-Ca(1)-Ca(1)	147.154(10)
O(1)-Ca(1)-C(6)	105.42(2)		
O(1)-Ca(1)-C(6)	101.21(2)		
O(3)-Ca(1)-C(6)	84.27(2)		

Table S2. Selected bond lengths (Å) and angles (deg) for $[Ca(NA)_2]_n$ (bio-CP **2**).

Ca(1)-N(1)	2.5186(12)	O(4)-Ca(1)-O(2)	91.39(4)
Ca(1)-N(2)	2.5300(16)	O(1)-Ca(1)-N(1)	176.28(4)
Ca(1)-O(1)	2.2604(10)	O(3)-Ca(1)-N(1)	85.13(4)
Ca(1)-O(2)	2.3176(10)	O(4)-Ca(1)-N(1)	81.83(4)
Ca(1)-O(3)	2.2802(10)	O(2)-Ca(1)-N(1)	84.39(4)
Ca(1)-O(4)	2.2832(14)	O(1)-Ca(1)-N(2)	83.65(4)
O(1)-Ca(1)-O(3)	93.20(4)	O(3)-Ca(1)-N(2)	85.46(4)
O(1)-Ca(1)-O(4)	95.08(4)	O(4)-Ca(1)-N(2)	177.58(3)
O(3)-Ca(1)-O(4)	96.68(4)	O(2)-Ca(1)-N(2)	86.75(4)
O(1)-Ca(1)-O(2)	97.80(3)	N(1)-Ca(1)-N(2)	99.51(5)
O(3)-Ca(1)-O(2)	165.73(4)		

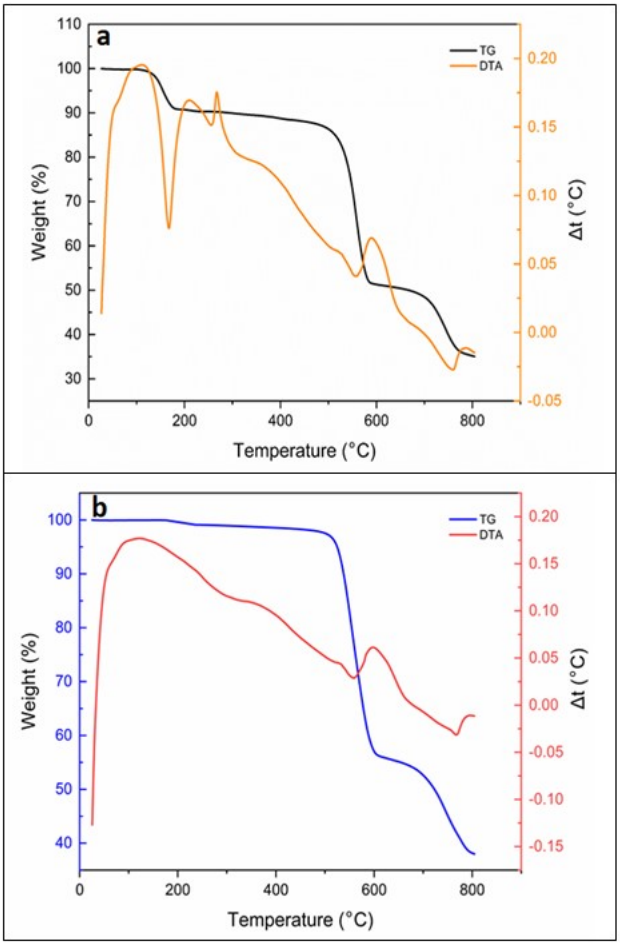

Fig. S3. Thermal behavior of a) bio-CP **1** and b) bio-CP **2**.

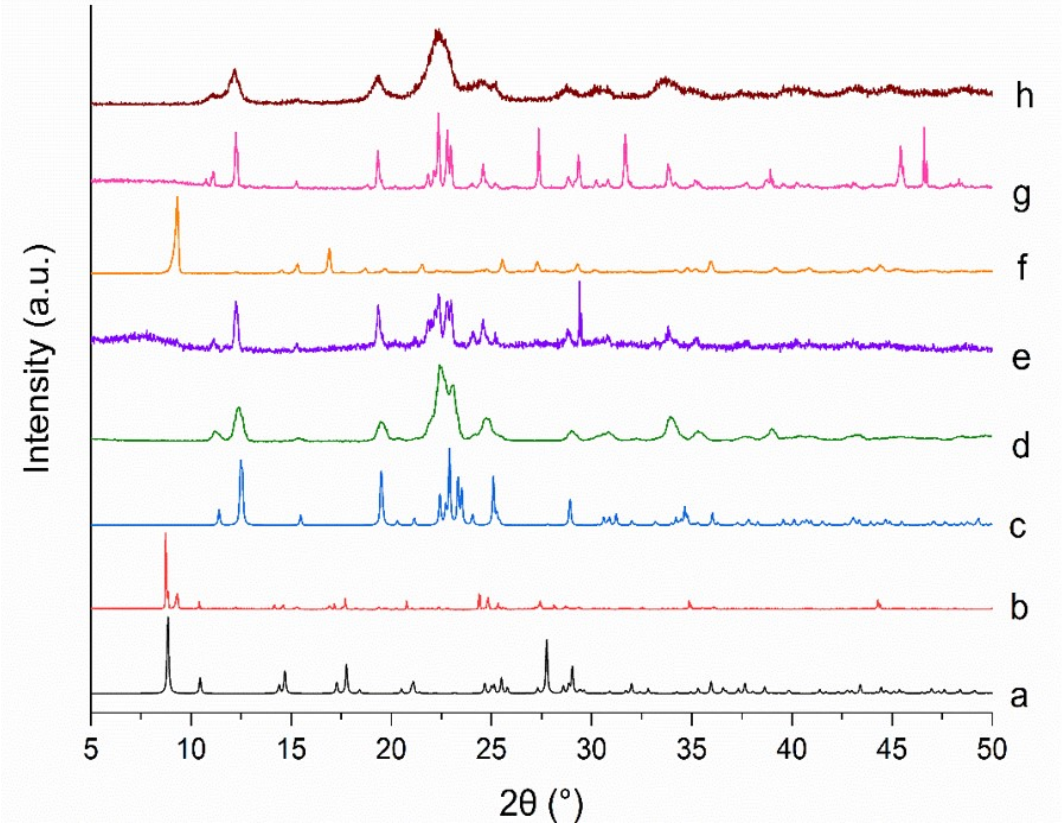

Fig. S4. PXRD pattern of bio-CPs. a) The simulated pattern of bio-CP **1**. b) Pattern of a bulk sample of bio-CP **1**. c) Simulated pattern of bio-CP **2**. d) Pattern of a bulk sample of bio-CP **2**. e) Thermal treatment of bio-CP **1**. f) Water treatment of bio-CP **2**. g) Sonic synthesis of bio-CP **2**. h) PXRD pattern of bio-CP **1** in Ethanol for a week.

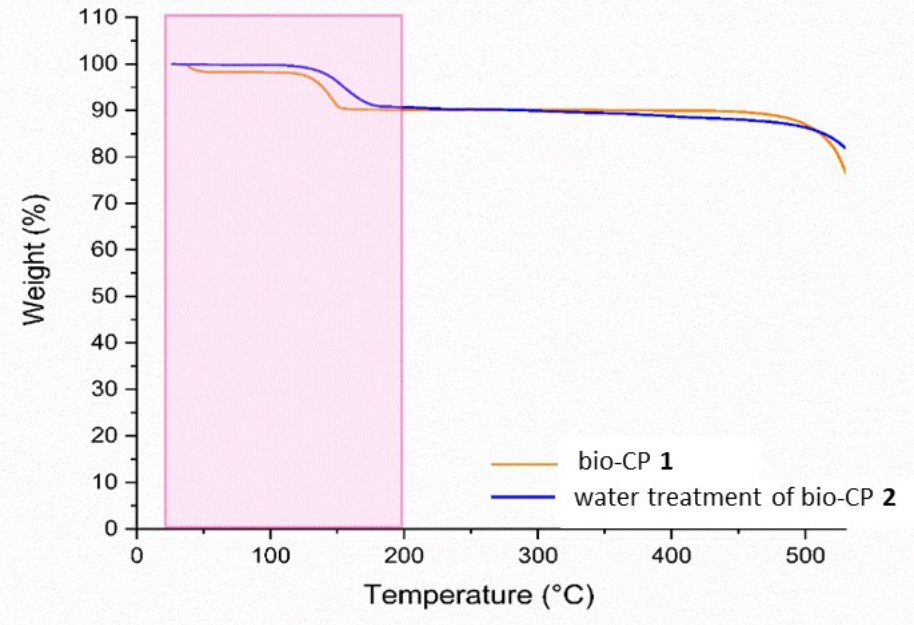

Fig. S5. Comparison between TG of bio-CP **2** after water treatment and bio-CP **1.**

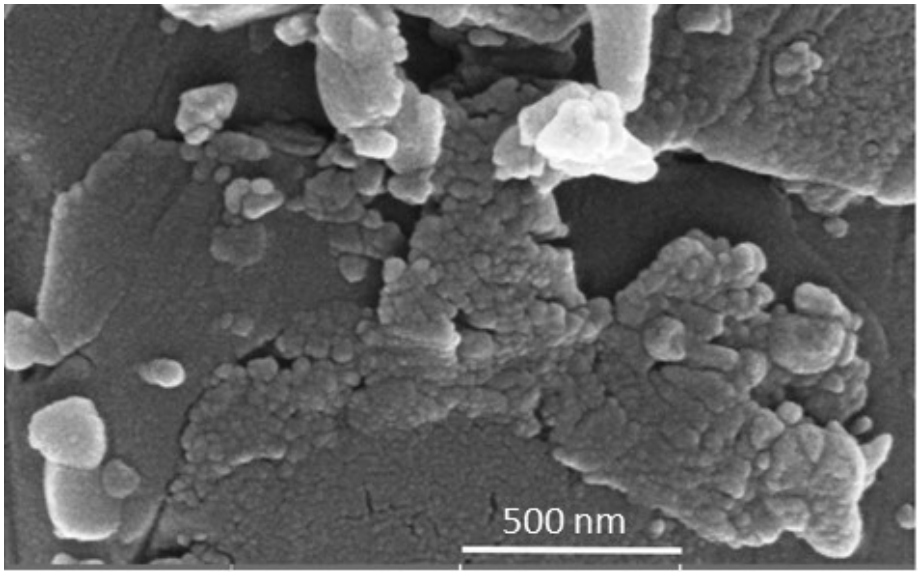

Fig. S6. The SEM image of nano-sized bio-CP **2**.

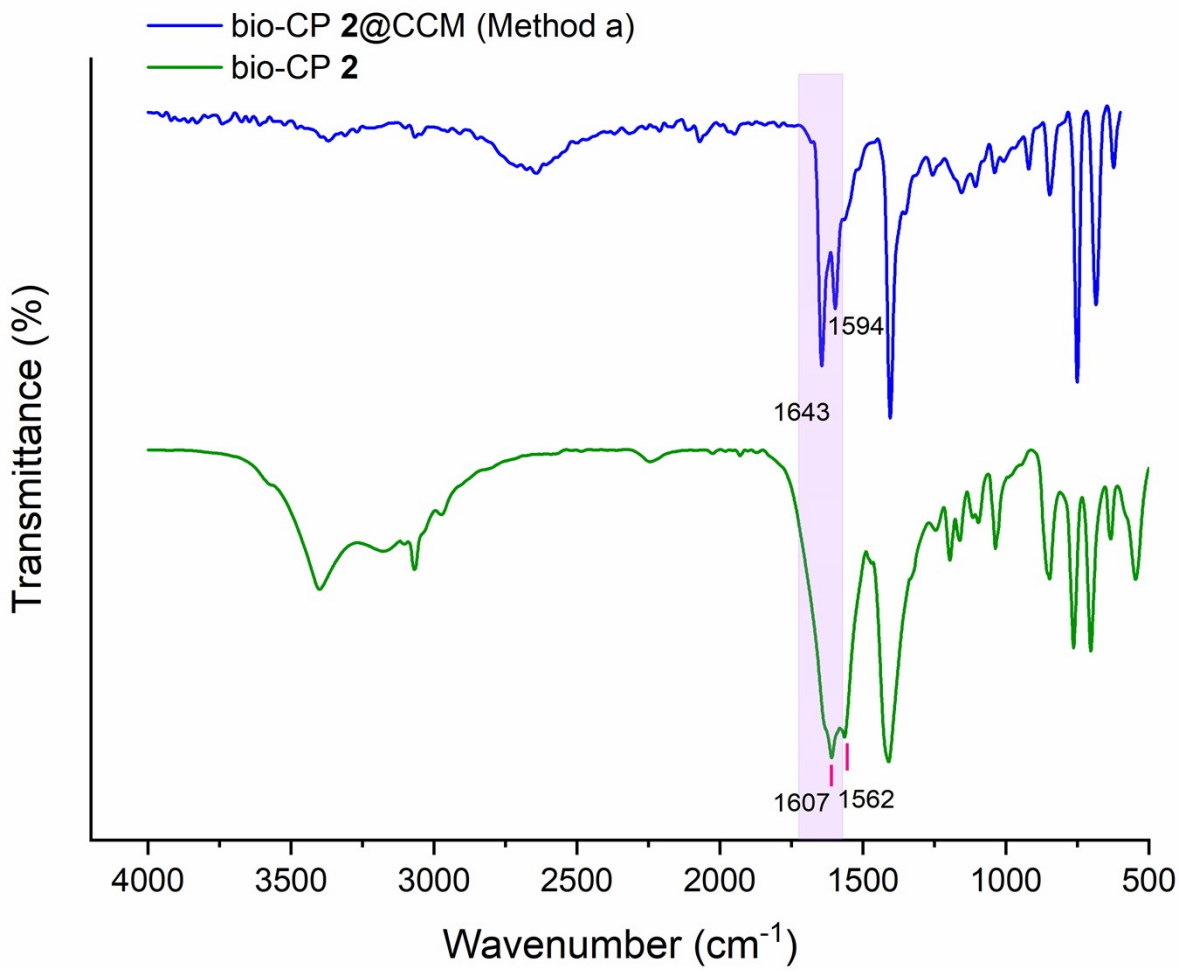

Fig. S7. FT-IR spectra of bio-CP **2** before and after the drug loading process.

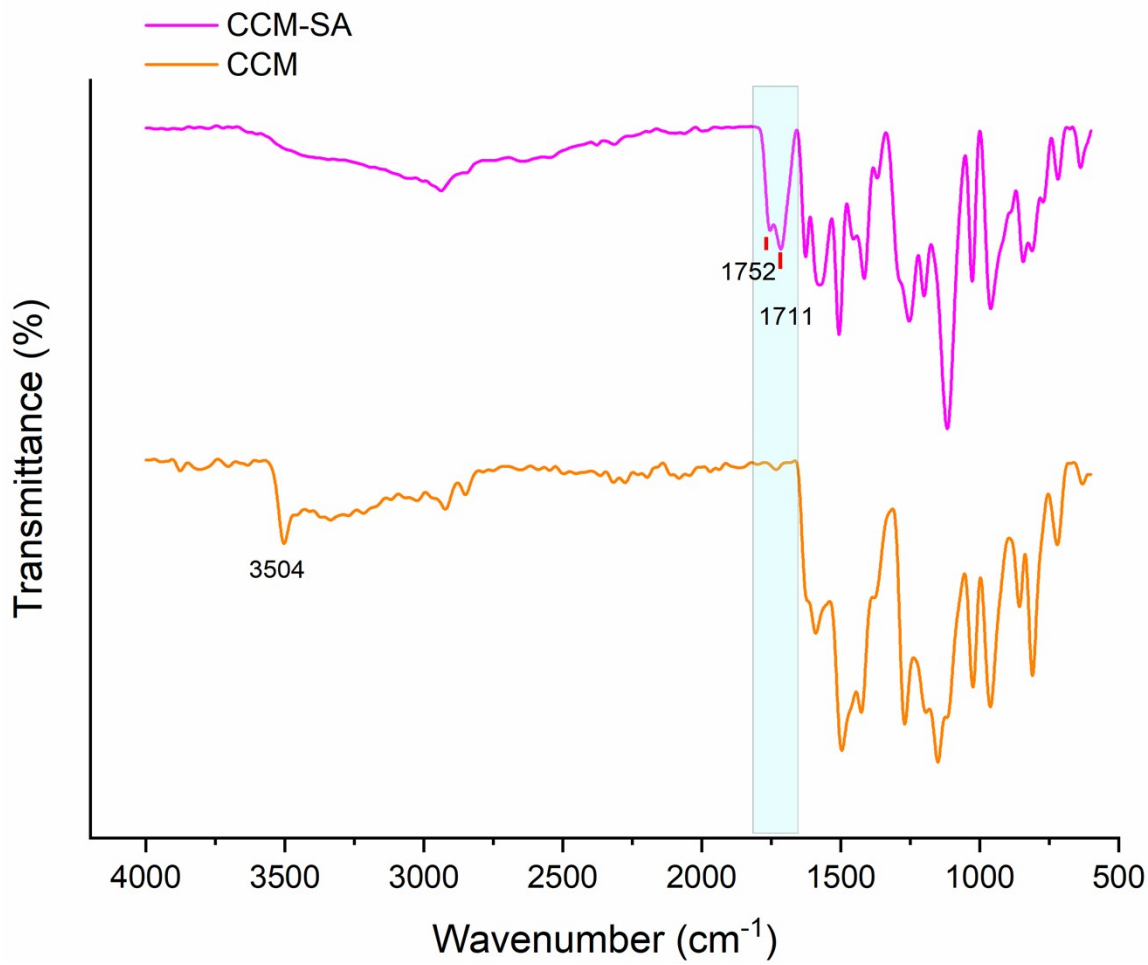

Fig. S8. FT-IR spectra of CCM and CCM-SA.

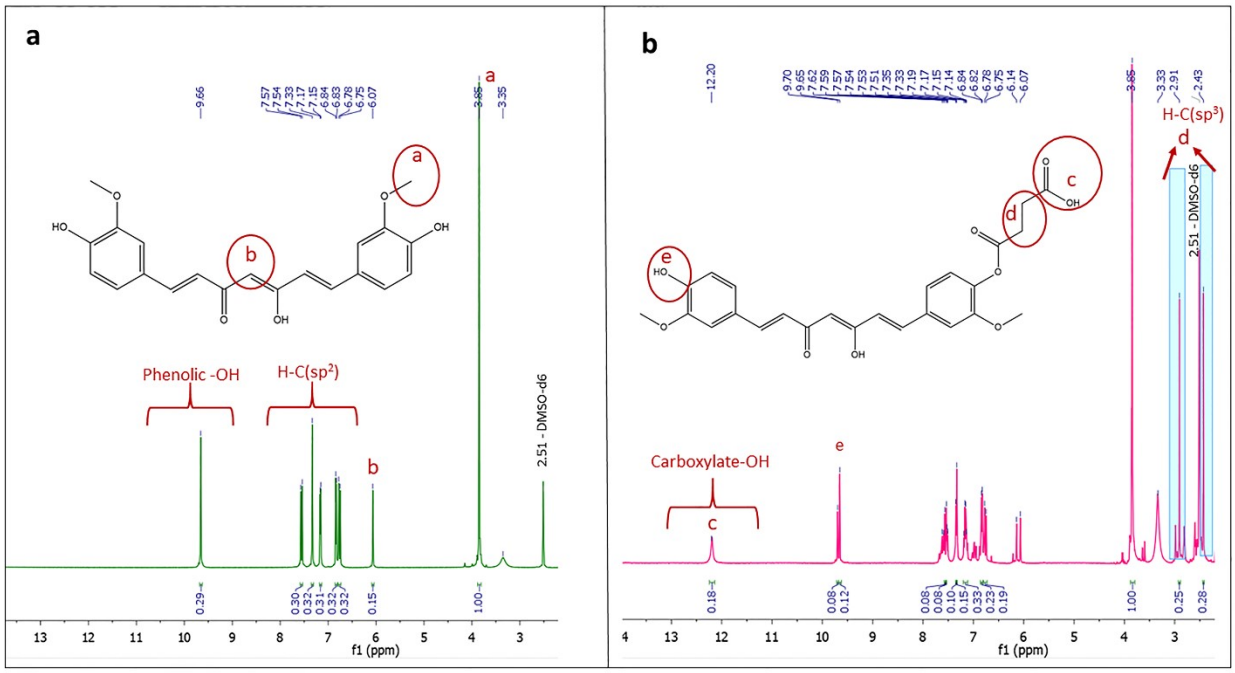

Fig. S9. [1]H-NMR spectra of a) CCM and b) CCM-SA.

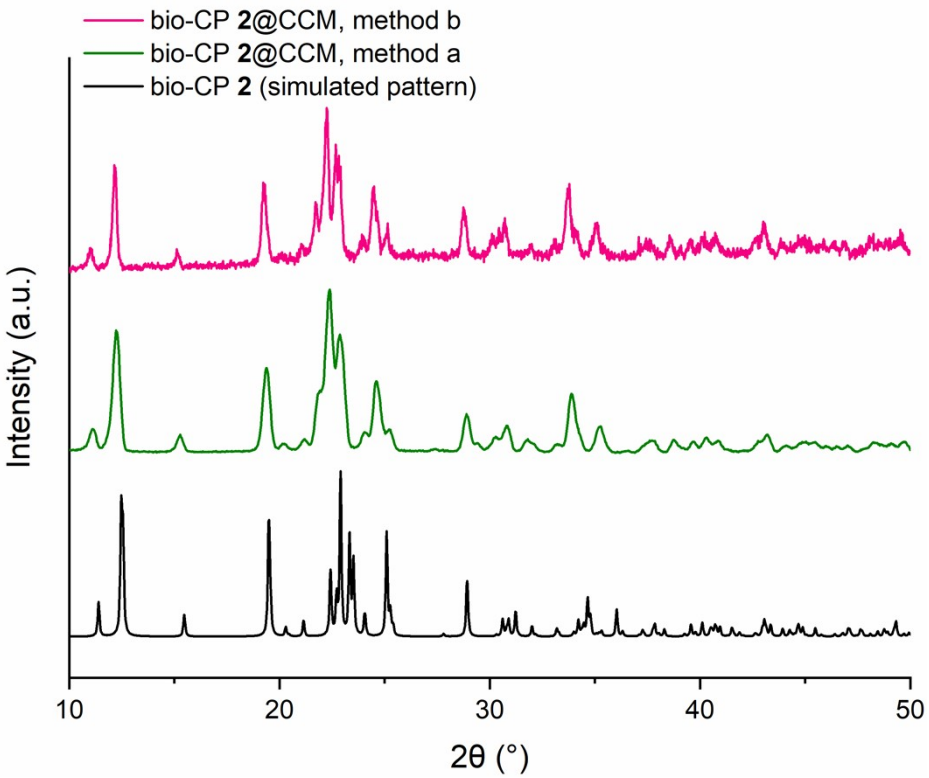

Fig. S10. PXRD pattern of bio-CP **2** before and after drug loading with methods a and b.

Drug loading on bio-CP 2 by impregnation method

0.2 g of CCM was dissolved in 62.5 mL ethanol. Then 0.2 g nano bio-CP **2** was added to this solution and stirred in a dark condition for 3 days (at room temperature). After this time, the solution was filtrated and dried in a vacuum oven at room temperature. The obtained product was digested in HCl (1M) and ethanol with 1:3 ratios. The amount of drug loading was obtained based on the calibration curve of CCM in similar conditions (in HCl (1M) and ethanol with 1:3 ratios). In this study, the following equations have been used for the calculation of drug loading with all methods:

$$\% \text{ Drug loading} = \frac{amount\ of\ loaded\ CCM}{amount\ of\ MOF@CCM} \times 10_0$$

The amount of drug loading was calculated based on the obtained equation (A= 121.03 C) from the calibration curve of CCM in a solution of HCl (1M) and ethanol (with 1:3 ratios).

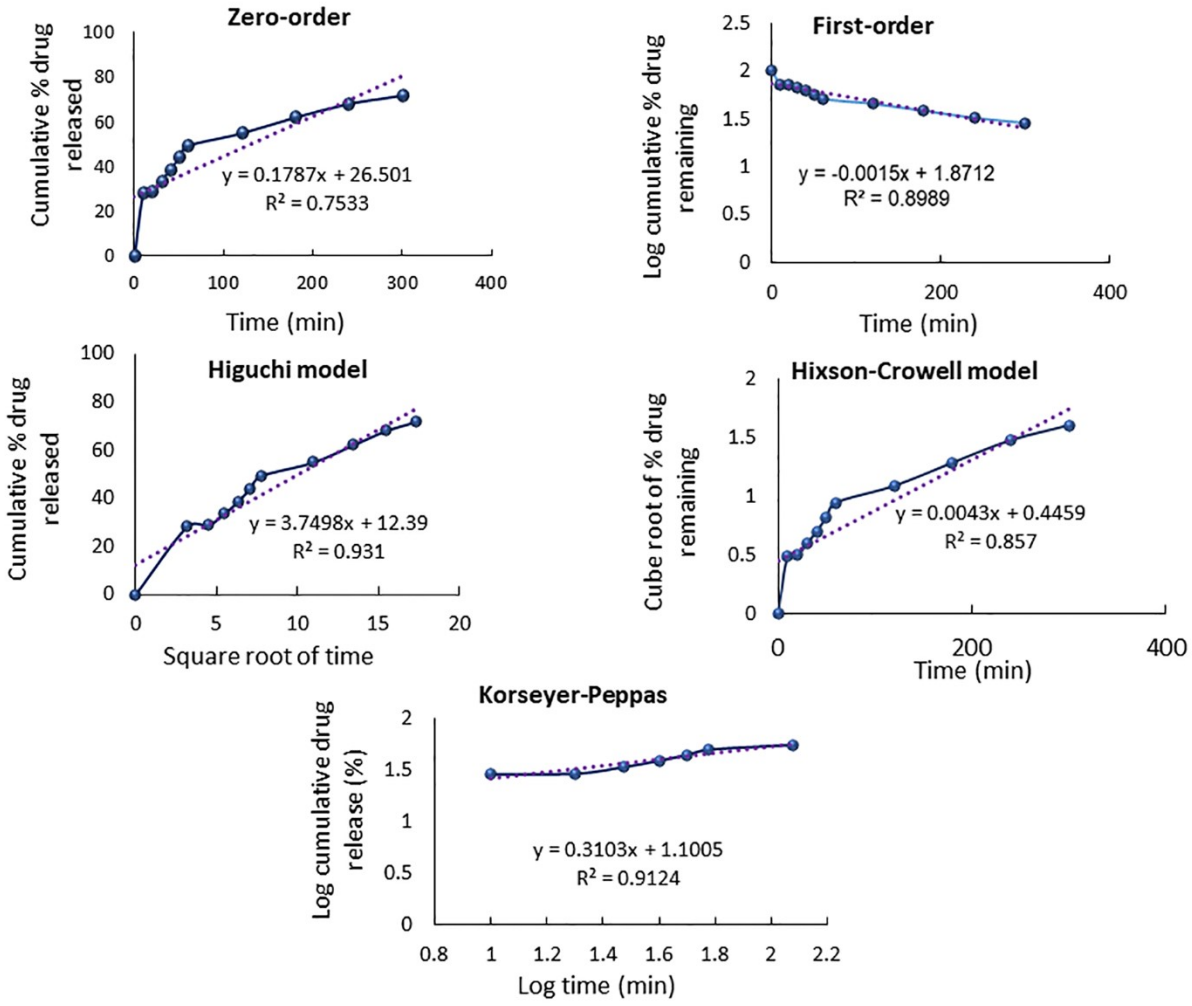

Fig. S11. Fitting of drug release data on some mathematical models.

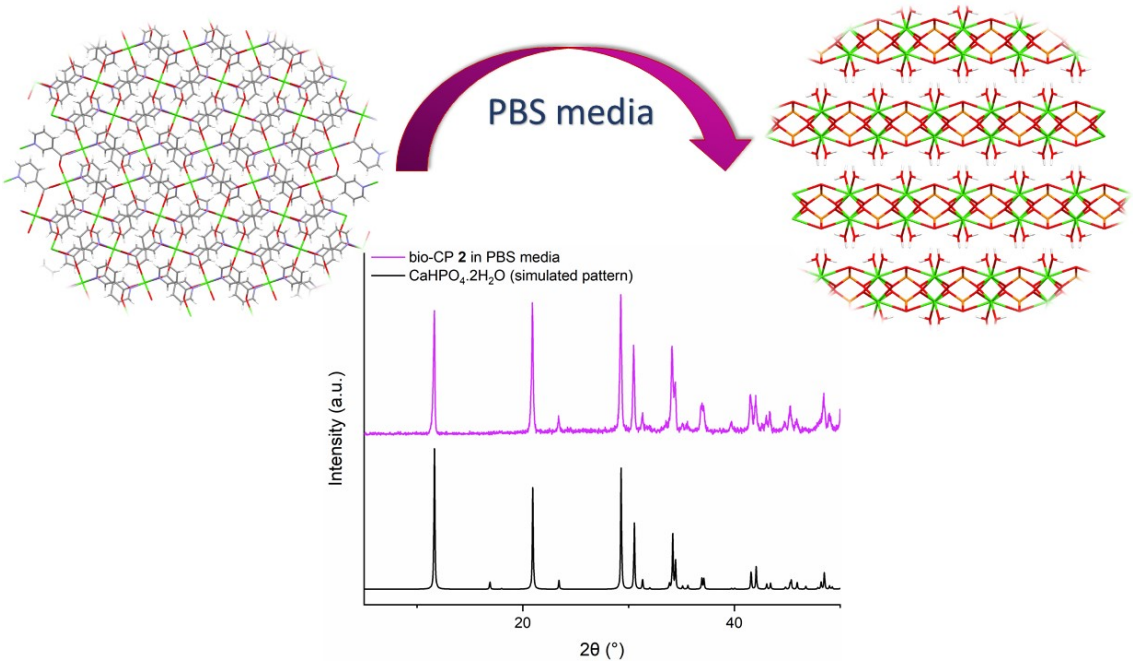

Fig. S12. Comparison between PXRD pattern of bio-CP **2** in PBS media and simulated pattern of $CaHPO_4.2H_2O$. The Ca, O, and P atoms are represented by green, red, and orange colors.

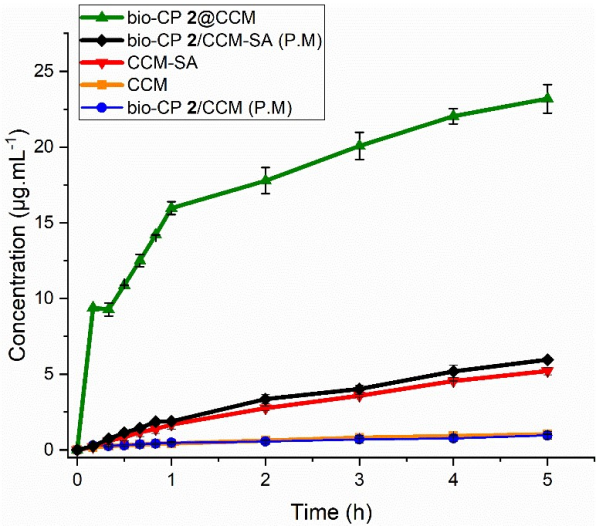

Fig. S13. The release profile of CCM in SG media from bio-CP **2**@CCM and its comparison with the solubility of free CCM, free CCM-SA, and their physical mixture (P.M) with nano bio-CP **2**.