Supporting Information

for

Biodegradable, biocompatible transdermal device derived from carboxymethyl cellulose and multi-walled carbon nanotube for sustained release of diclofenac sodium

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Characterization

FTIR spectral analysis was performed using a JASCO FTIR spectrophotometer in the scan range of 400 - 4000 cm-1. Thermogravimetric analysis was carried out using TGA analyser (STA449F3, Netzsch, Germany) with inert atmosphere of N2. Heating rate was 5 °C/min. The surface morphology was studied using field emission scanning electron microscopy (FESEM Supra 55, Zeiss, Germany). Topographic analyses were executed with an AFM Scanner (Bruker Dimension Icon Nanoscope V, Germany) in the scan range of 10μm in x-y. The process was executed by using scan assist mode AFM in air. Further the sectional analysis as well as roughness was measured over the entire scan size of 10 μm × 10 μm. The transmission electron microscopy (TEM) observation was accomplished on a JOEL 3010 microscope. For this analysis, the sample was prepared by dropping the suspended nanocomposite (in water) on carbon coated copper grids.

Swelling study and its kinetics

The stimuli-responsive behavior of CMC and CMC-MWCNT nanocomposites were performed by measuring the equilibrium swelling at phosphate buffer (pH: 7.4) at 32 °C. The detailed methodology has been explained in Supporting Information. Briefly, 0.5 g of dried CMC and composites were kept into tea-bag. Then the bags were immersed in buffers and then left to swell for 10 h. The swollen samples were withdrawn after every 1 h and the surface water was blotted off carefully using tissue paper. Afterwards, it was reweighted. The % ESR was assessed using the equ^{n}. (1)

$$ESR\ (\%) = \frac{W_{eqm} - W_d}{W_d} \text{---------} \quad (1)$$

Where W_{eqm} and W_d correspond to the equilibrium weight and dry weight of the sample under study.

Biodegradation study:

A pre-weighted amount of CMC-MWCNT 3 composite film (2×2×0.1 mm3) was immersed in lysozyme solution (1.5μg/mL) in pH 7.4 at 37 °C. The media was altered regularly to constant the enzyme activity. After 3, 7 and 14 days the material were filtered from the lysozyme solution, washed thrice with double distilled water, and dried in a vacuum oven for 72 h. Then it was reweighted. The degree of in-vitro degradation has been expressed as percent weight loss of the dried films vs. time.

Cytotoxicity test and morphological assessment:

Cytotoxicity of the CMC-MWCNT 3 nanocomposite dissolved in DMEM high glucose medium containing 10% fetal calf serum, 100 U/mL penicillin and 100 μg/mL streptomycin (all purchased from Gibco, USA) was tested by cultivation of primary rat fibroblasts (RFBs). The media containing 1mg/mL of nanocomposite was filtered with 0.22 μm Syringe Filters (Merck Millipore) before treating to the cells.

Briefly, 104 nos. of RFBs were seeded in 24-well tissue culture plates and cultivated for 1, 3 or 7 days, respectively, either with nanocomposite containing medium or normal medium. On completing the respective cultivation period, samples were washed thrice in PBS and the number of viable cells was calculated using Vybrant® MTT Cell Proliferation Assay Kit (Invitrogen, USA) according to the manufactures instruction. Graphs show mean ± standard deviation (n = 3).

For morphological assessment, RFBs were cultured in 12 well plates with lysine coated coverslips either with nanocomposite dissolved medium (1 mg/mL) or normal medium. The coverslips were removed at desired time and permeabilized using Triton-X-100 followed by blocking the non-specific sites using bovine serum albumin (Sigma) and stained with rhodamine–phalloidin (catalog no. R415, Invitrogen, USA) and DAPI (4, 6-diamidino-2-

phenylindole, catalog no. D1306, Invitrogen, USA). The cells were then imaged using fluorescence microscope (Zeiss Axio Observer Z1, Carl Zeiss, Germany).

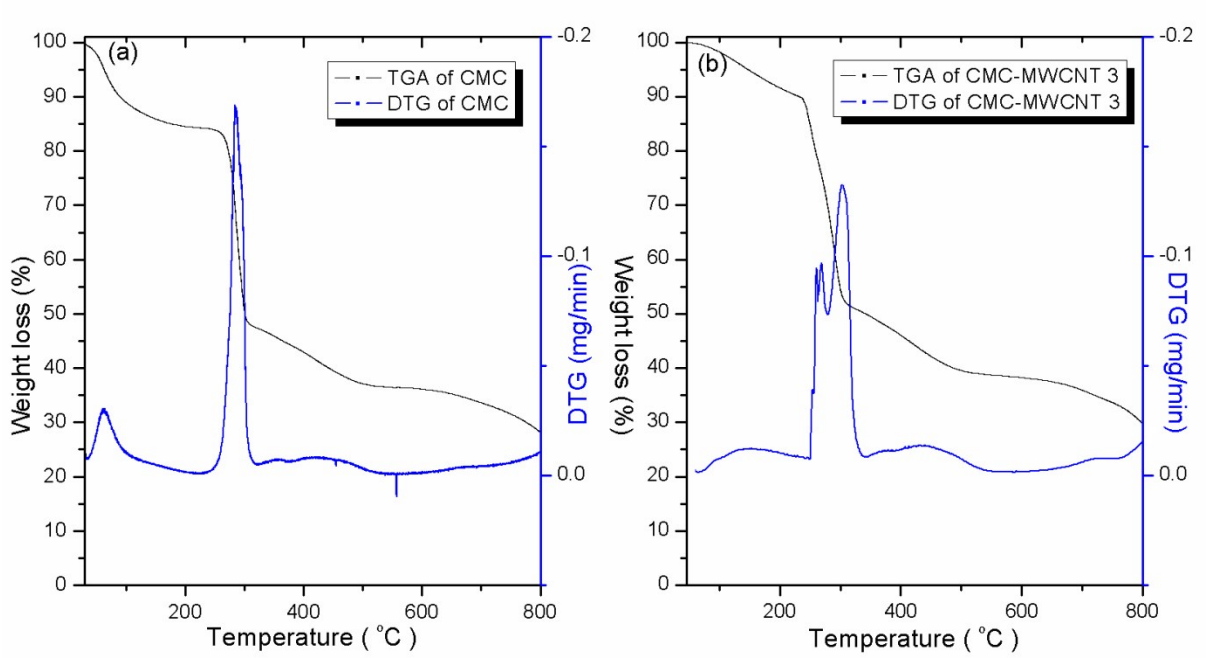

Fig. S1: TGA and DTG analyses of (a) CMC and (b) CMC-MWCNT 3 composite

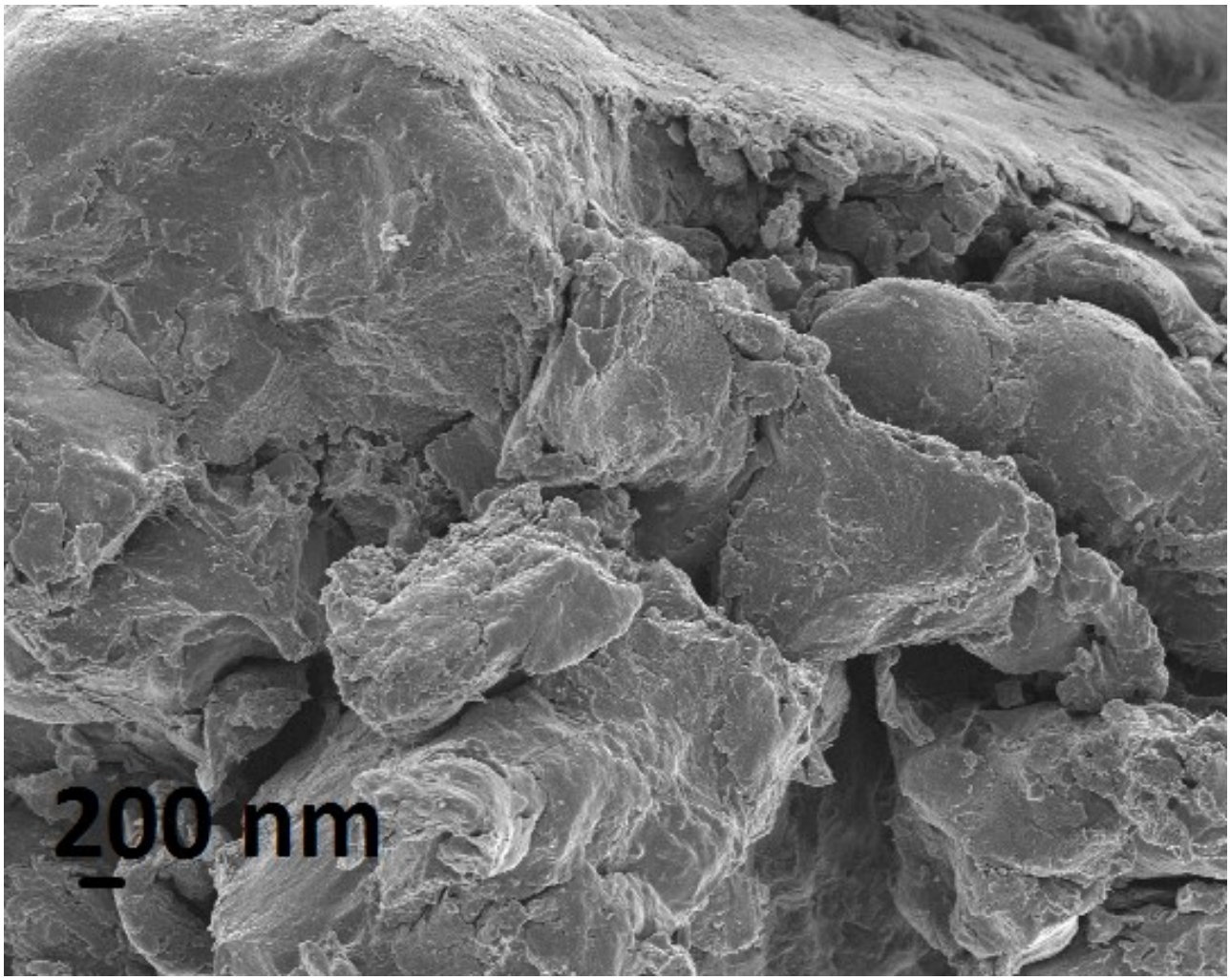

Fig. S2: FESEM image of CMC.

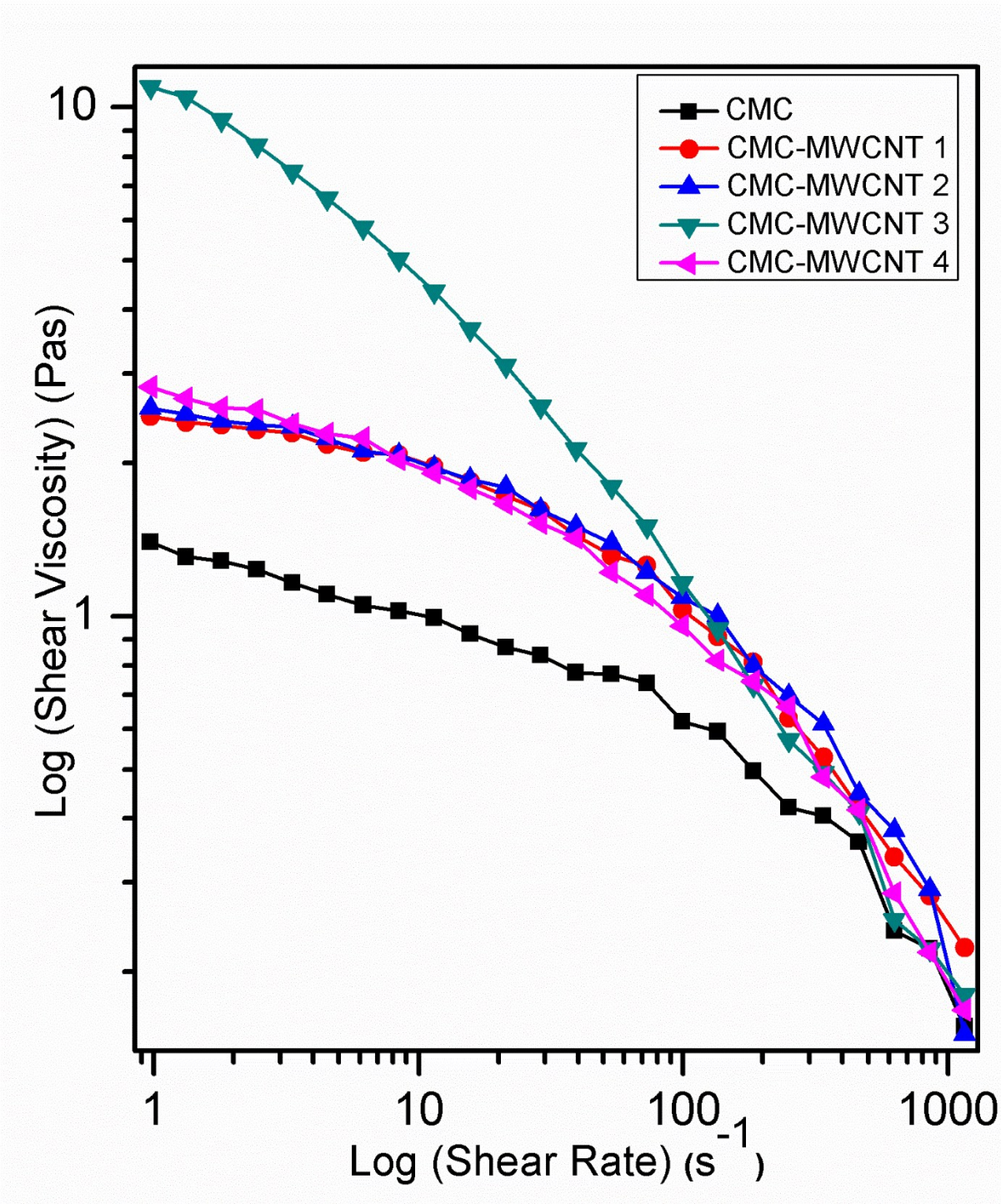

Fig. S3: Shear viscosity vs. shear stress curve of CMC and various nanocomposites.

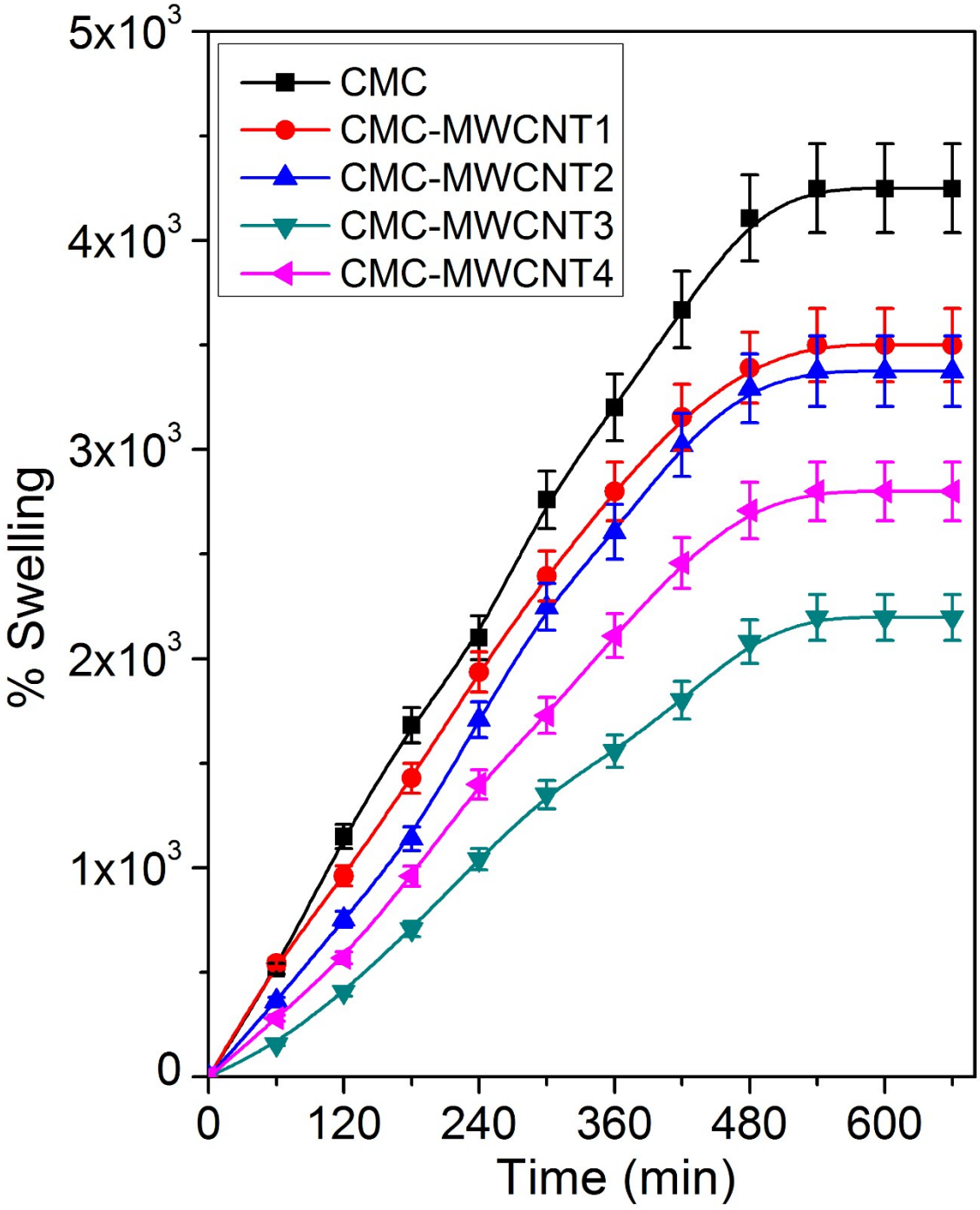

Fig. S4: Swelling characteristics of CMC and various nanocomposites using phosphate buffer (pH: 7.4) at 37 °C.

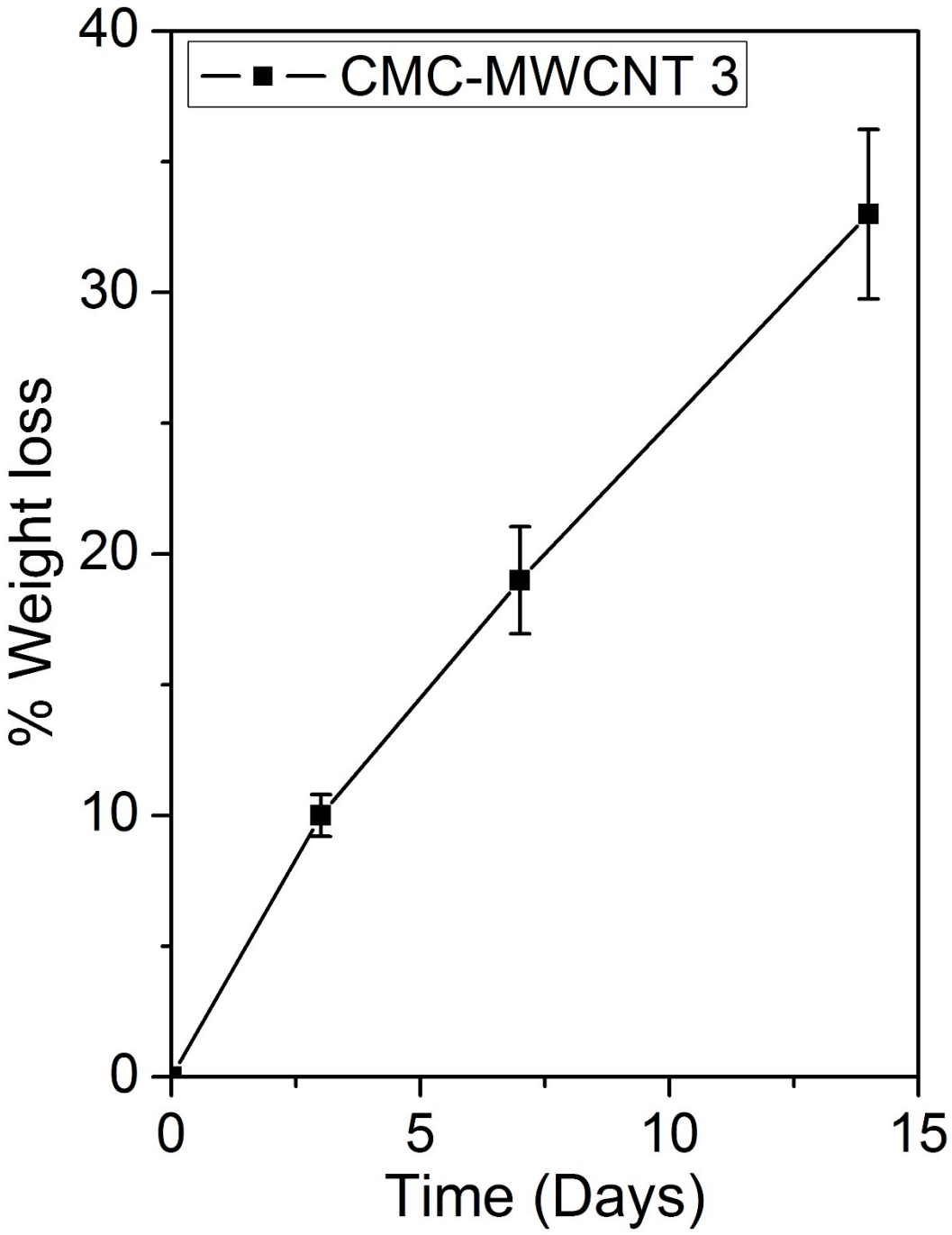

Fig. S5: Biodegradation result of CMC-MWCNT 3 composite.

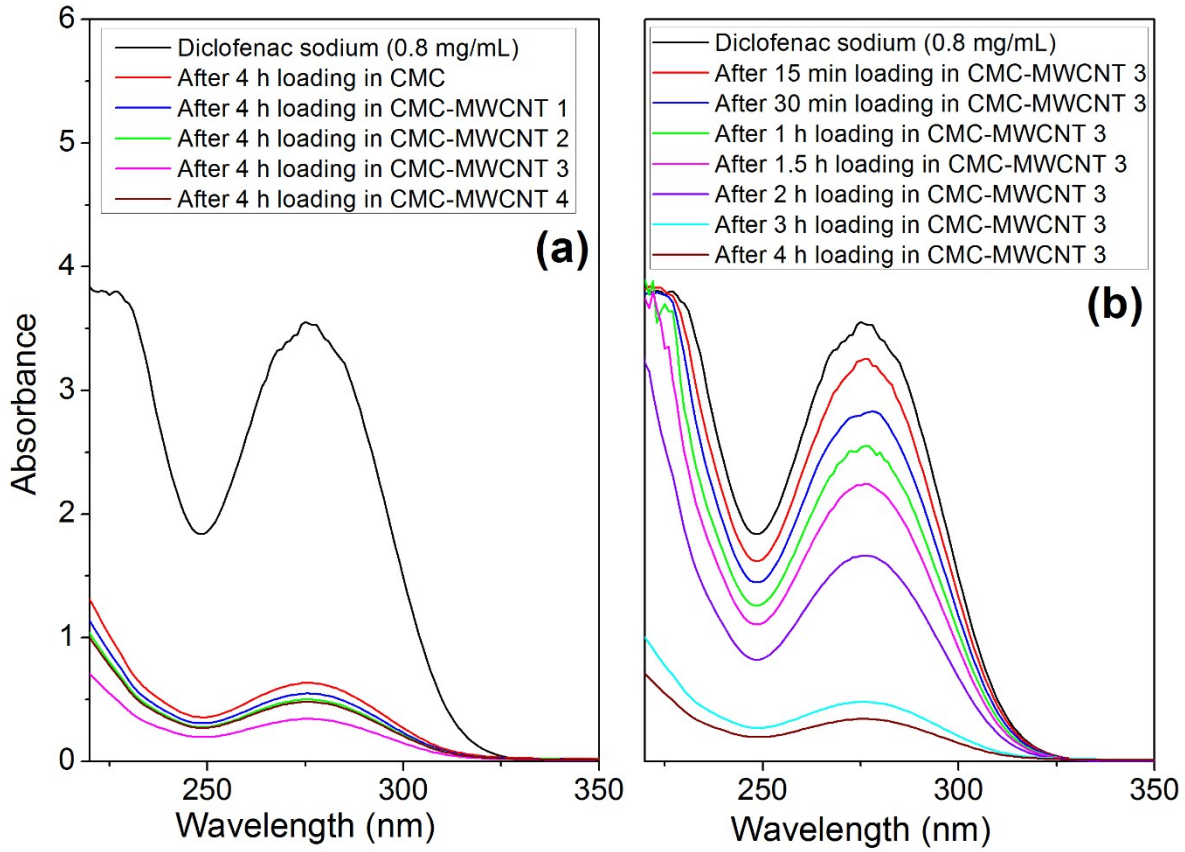

Fig. S6: (a) Diclofenac sodium loading on CMC and various nanocomposites, (b) Diclofenac sodium loading on CMC-MWCNT 3 at various time intervals.

Table S1: Loading efficiency and encapsulation efficiency of diclofenac sodium in CMC and various CMC-MWCNT nanocomposites after different time of intervals.

Polymers	% loading after 4 h	% entrapment efficiency after 4 h	Composite	Time (min)	% loading	% entrapment efficiency
			CMC-MWCNT 3	15	1.32	7.96
				30	3.40	20.39
CMC	13.68	82.08		60	4.67	28.04
CMC-MWCNT 1	14.08	84.49		90	6.10	36.63
CMC-MWCNT 2	14.31	85.87		120	8.82	52.96
CMC-MWCNT 3	15.05	90.31		180	14.40	86.41
CMC-MWCNT 4	14.40	86.41		240	15.05	90.31

Table S2: Stability study result. Each value represent mean ± SD (n=3)

Sl. No	Parameters	In CMC		In CMC-CNT 3 nanocomposites	
		Initial	3 Month	Initial	3 Month
1	Description	Complies	Complies	Complies	Complies
2	Average weight (mg)	150.56 ± 4.01	151.23 ± 2.67	150.25 ± 3.52	150.36 ± 3.27
3	Content assay (%)	99.85 ± 1.25	89.87 ± 2.58	99.36 ± 3.28	97.42 ± 3.69
4	Drug release at 12 h in pH 5.6	89.70 ±3.42	94.89 ±4.74	33.10±1.63	35.77±1.78