

Electronic Supplementary Information (ESI)

The preparation of oxidized methylcellulose crosslinked by adipic acid dihydrazide loaded with vitamin C for traumatic brain injury

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Table S1. Abbreviation and definition of specimen.

Abbreviation	Definition
MC	Methylcellulose
oxi-MC	Oxidized methylcellulose
oxi-MC-ADH	Oxidized methylcellulose cross-linked with adipic acid dihydrazide
oxi-MC-ADH-VC	For <i>in-vitro</i> study: Oxidized methylcellulose cross-linked with adipic acid dihydrazide contented 2.5 mg/mL vitamin C For <i>in-vivo</i> study: Oxidized methylcellulose cross-linked with adipic acid dihydrazide contented 0.2 g/mL vitamin C

Table S2. Modified neurological severity scores (mNSS) (S. F. Chen, Hsu, Huang, & Wang, 2008).

Test	Point
Motor tests	
Raising rat by the tail	
Flexion of forelimb	1
Flexion of hindlimb	1
Head moved 10° to vertical axis within 30 s	1
Placing rat on the floor	
Normal walk	0
Inability to walk straight	1
Circling toward the paretic side	1
Fall down to the paretic side	1
Sensory tests	
Placing test (visual and tactile test)	1
Proprioceptive test (deep sensation)	1
Beam balance tests	
Balances with steady posture	0
Grasps side of beam	1
Hugs the beam and one limb falls down from the beam	2
Hugs the beam and two limbs fall down from the beam, or spins on beam (> 60 s)	3
Attempts to balance on the beam but falls off (> 40 s)	4
Attempts to balance on the beam but falls off (> 20 s)	5
Falls off: No attempt to balance or hang on to the beam (< 20 s)	6
Reflexes absent and abnormal movements	
Pinna reflex (head shake when touching the auditory meatus)	1
Corneal reflex (eye blink when lightly touching the cornea with cotton)	1
Startle reflex (motor response to a brief noise from snapping a clipboard paper)	1
Seizures, myoclonus, myodystony	1
Maximum points	18

One point is awarded for the inability to perform the tasks or for the lack of a tested reflex; severity indicates severe injury (13-18), moderate injury (7-12); mild injury (1-6).

Table S3. Biochemical and hematological tests.

	Control	Hydrogel-treated TBI-rats
GOT (U/L)	69.00 ± 10.00	72.33 ± 13.80
GPT (U/L)	27.67 ± 5.03	23.67 ± 3.21
ALP (U/L)	812.67 ± 105.26	863.00 ± 91.04
BUN (mg/dL)	16.27 ± 5.12	14.70 ± 0.33
CRE (mg/dL)	0.30 ± 0.17	0.23 ± 0.06
RBC (10 ⁶ /μL)	8.49 ± 0.11	8.25 ± 0.71
WBC (10 ³ /μL)	11.89 ± 1.32	10.82 ± 1.20
NE (10 ³ /μL)	2.57 ± 0.26	2.58 ± 0.69
MO (10 ³ /μL)	0.78 ± 0.07	0.57 ± 0.12
EO (10 ³ /μL)	0.06 ± 0.04	0.06 ± 0.04
BA (10 ³ /μL)	0.04 ± 0.03	0.04 ± 0.04
LY (10 ³ /μL)	70.63 ± 5.32	70.21 ± 5.05
PLT (10 ³ /μL)	840.00 ± 114.69	680.75 ± 211.00

GOT - Aspartate aminotransferase; GPT - Alanine aminotransferase; ALP - Alkaline phosphatase; BUN - Blood urea nitrogen; CRE- Creatinine; RBC- Red blood cell; WBC- White blood cell; NE- Neutrophil; MO- Monocyte; EO- Eosinophil; BA- Basophil; LY- Lymphocyte; PLT- Platelet.

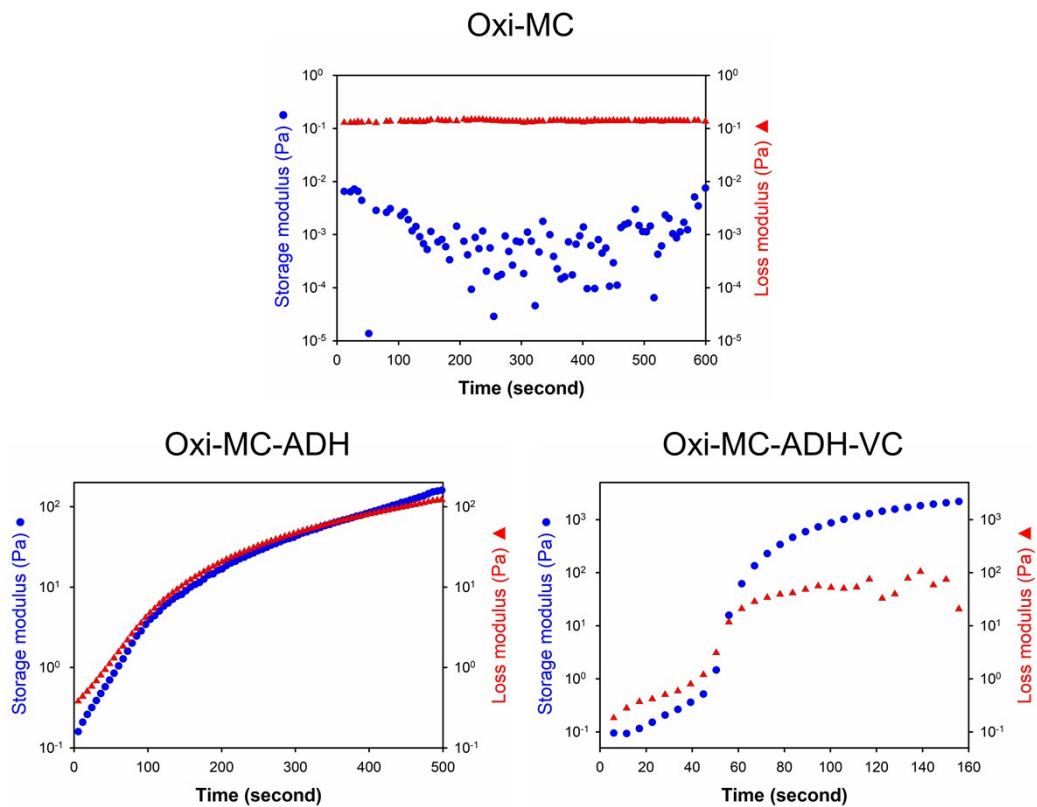


Fig. S1 The rheological data of oxi-MC, oxi-MC-ADH, and oxi-MC-ADH-VC.

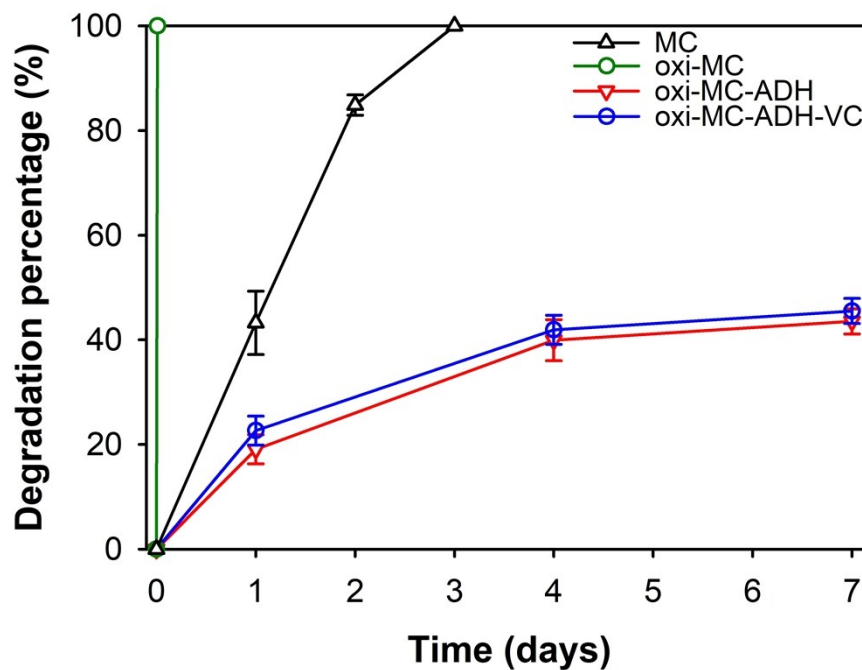


Fig. S2 Degradation percentage of MC, oxi-MC, oxi-MC-ADH, and oxi-MC-ADH-VC.

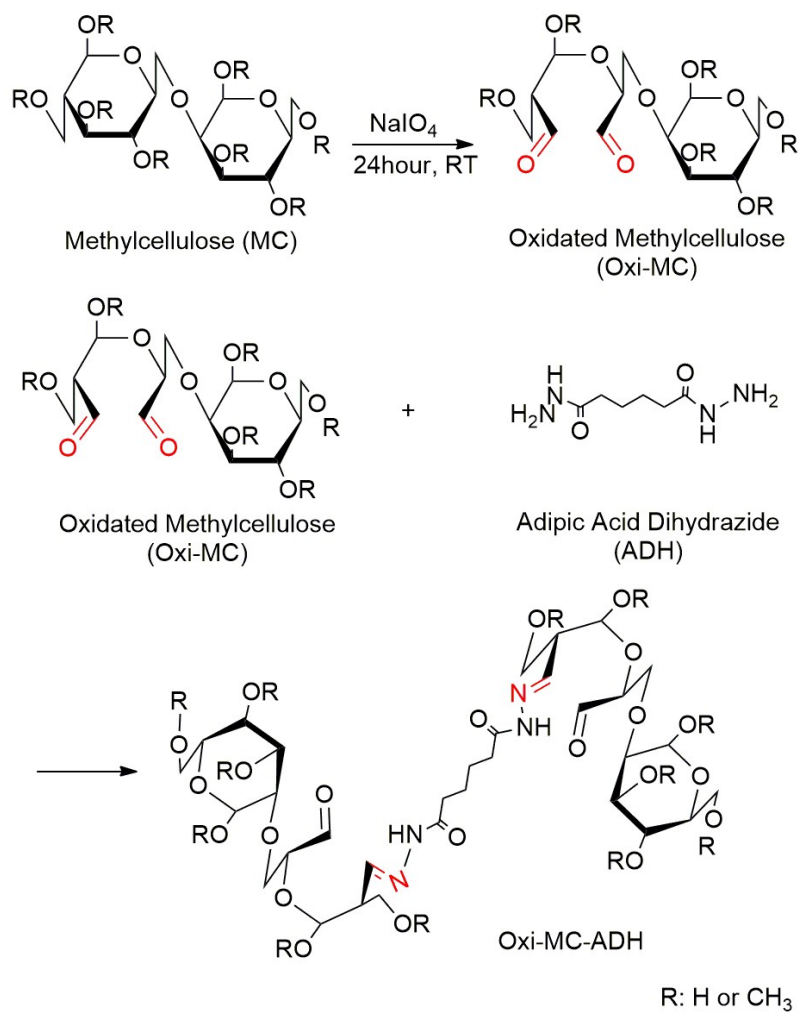


Fig. S3 Chemical schematic of methylcellulose oxidation by sodium *meta*-periodate, and chemical crosslinking mechanism of oxi-MC-ADH hydrogel.

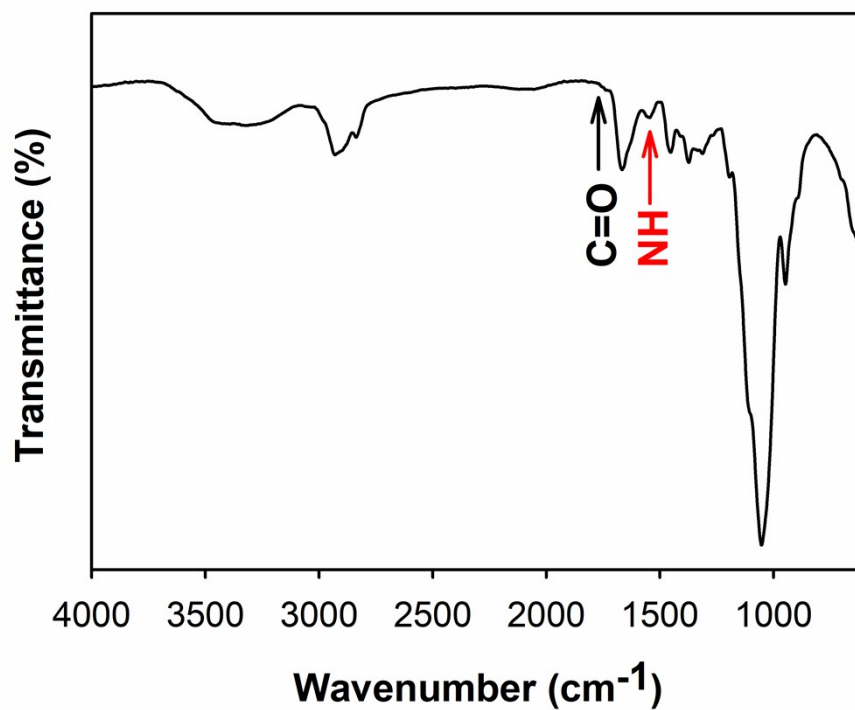
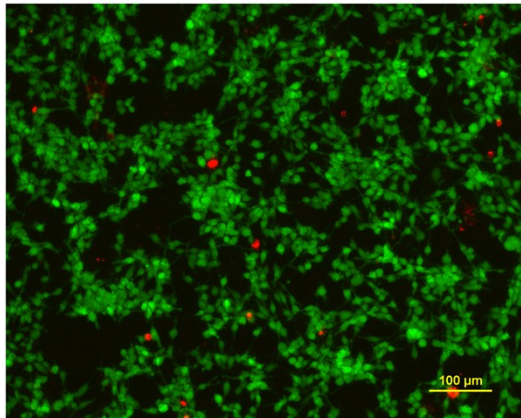
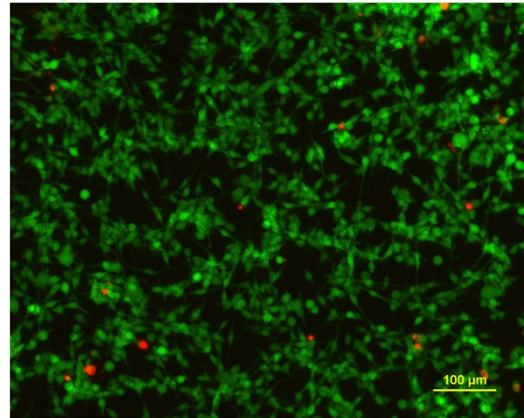


Fig. S4 The FT-IR spectrum of oxi-MC-ADH.

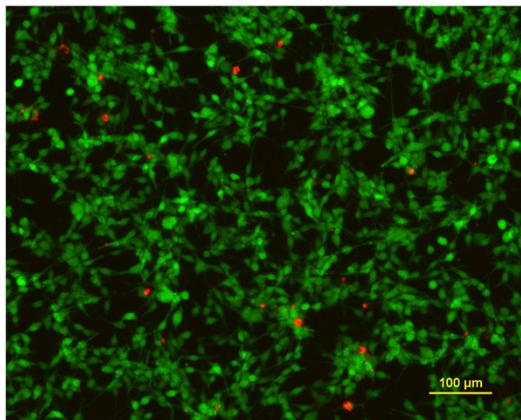
Control



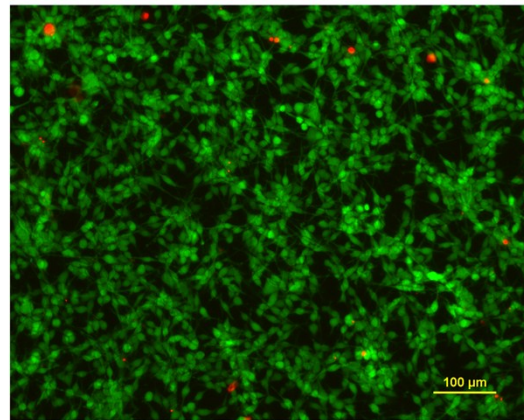
50 μg/ml vitamin C



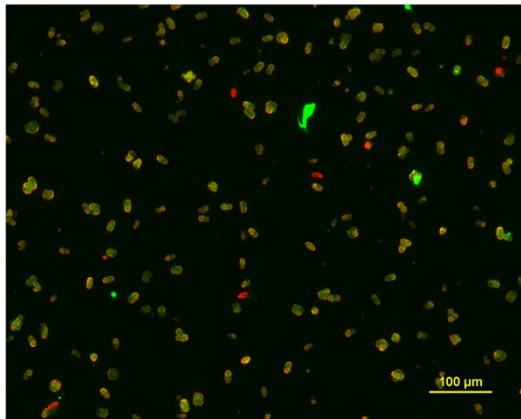
100 μg/ml vitamin C



250 μg/ml vitamin C



500 μg/ml vitamin C



1000 μg/ml vitamin C

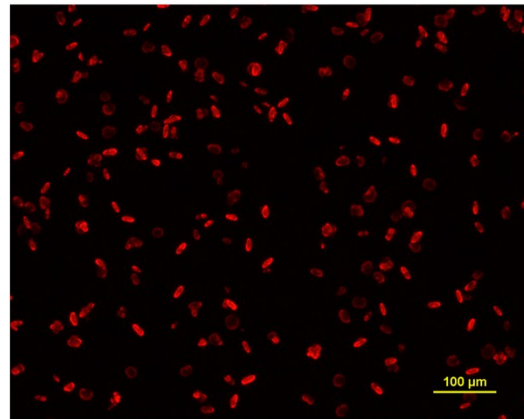


Fig. S5 Concentrations of vitamin C were selected by Live/dead staining for various concentration cultured with B35 cells. Cells were stained with fluorescent probes to reveal live cells (green) and dead cells (red) (scale bar: 100 μm).

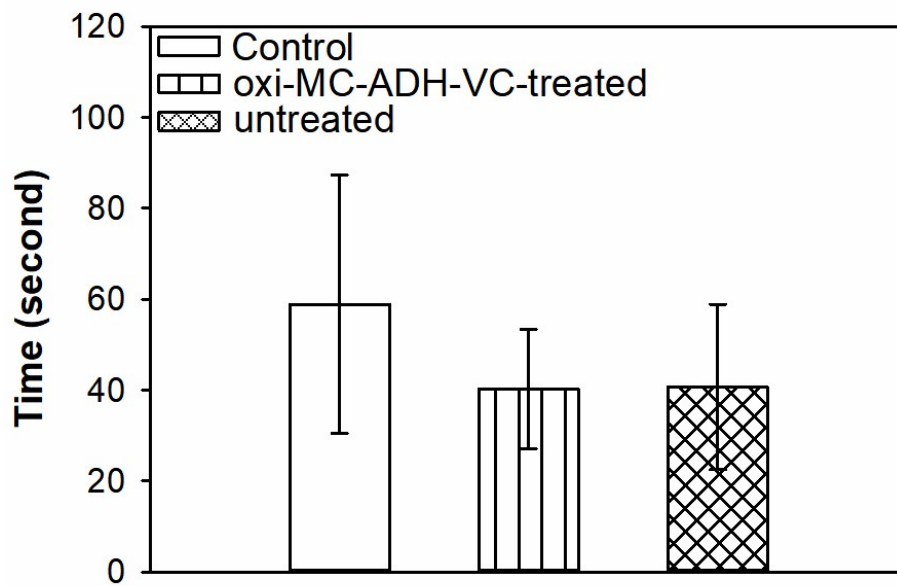


Fig. S6 The mean (\pm standard deviation) of rotarod performance.

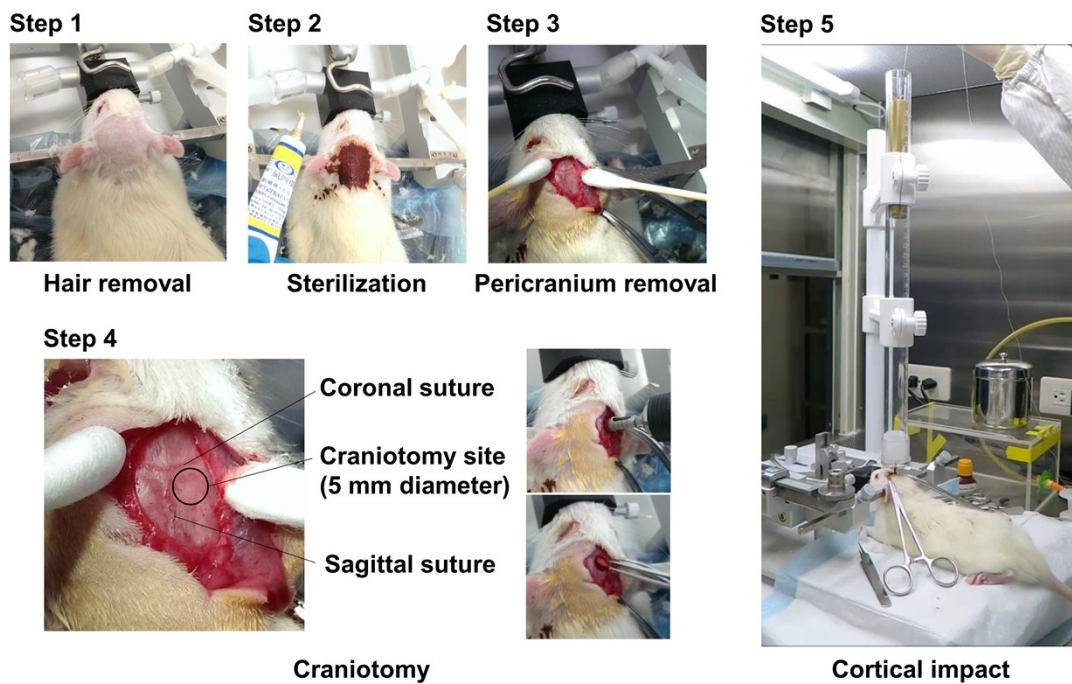


Fig. S7. Procedure of TBI animal model by cortical impact