

A glucose-responsive alginate-based hydrogel laden with modified-GLP-1 and telmisartan ameliorates type 2 diabetes and reduces toxicities in liver and kidney

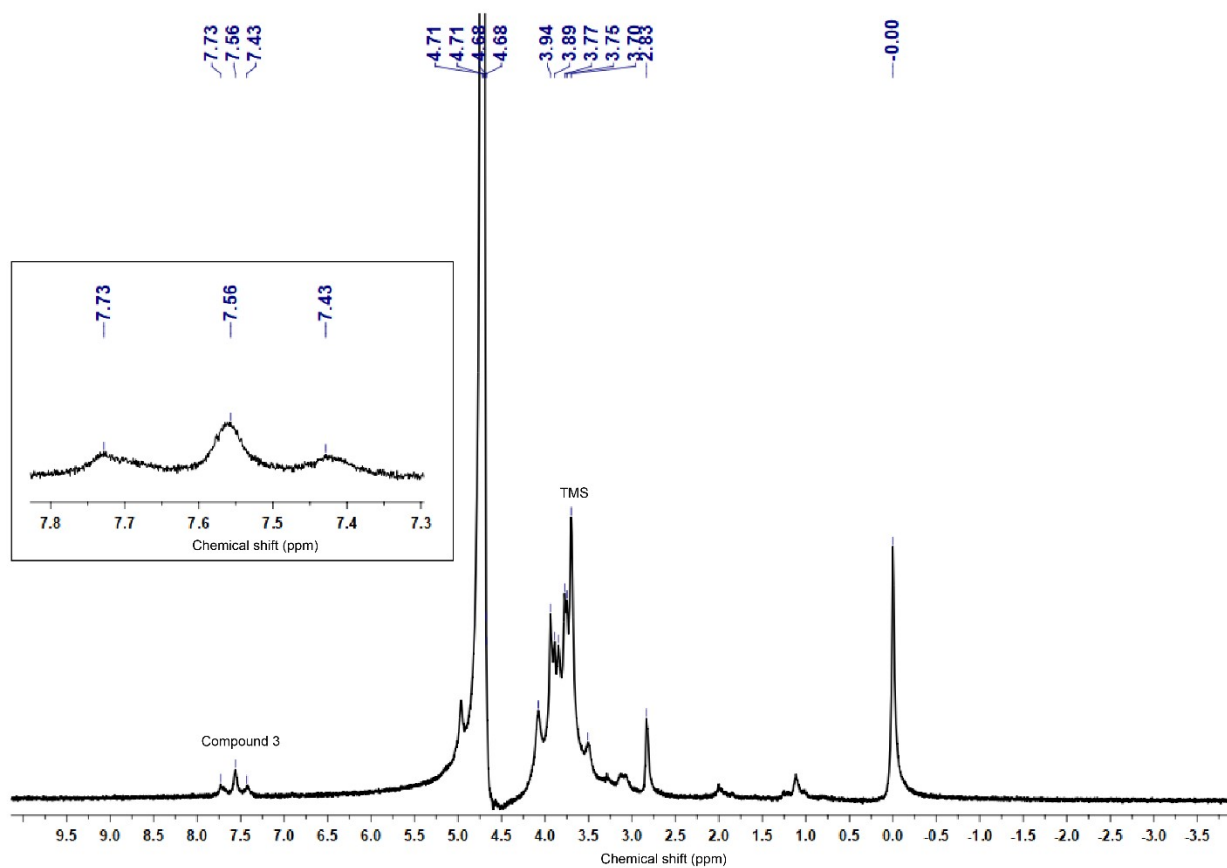
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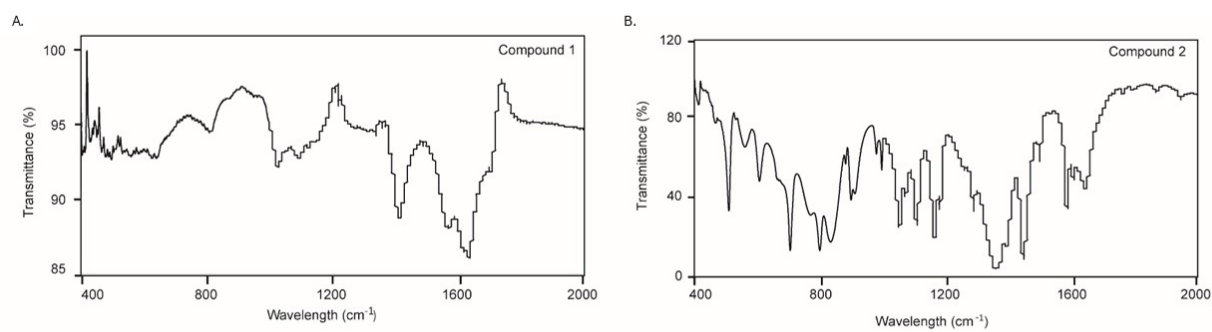
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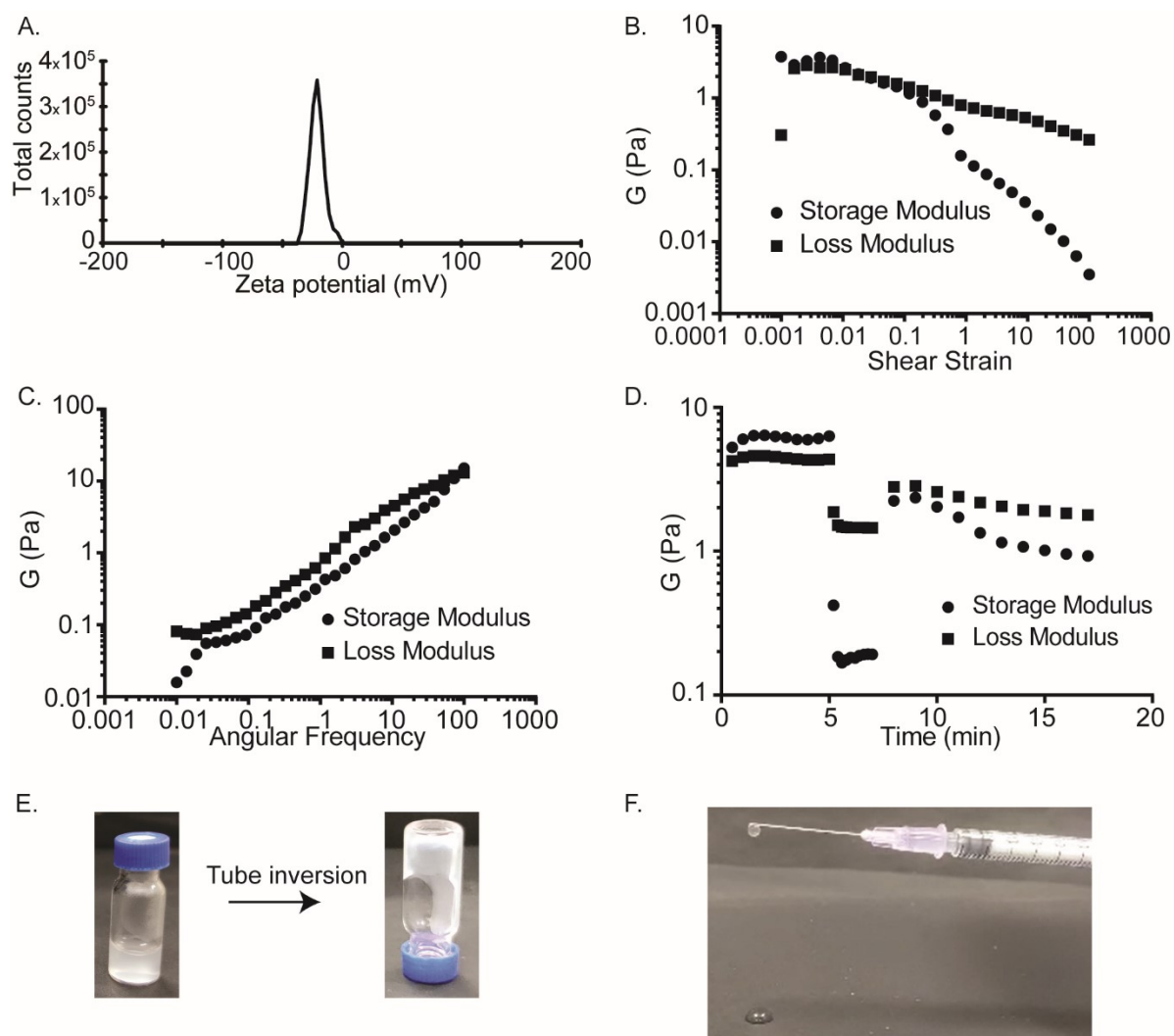
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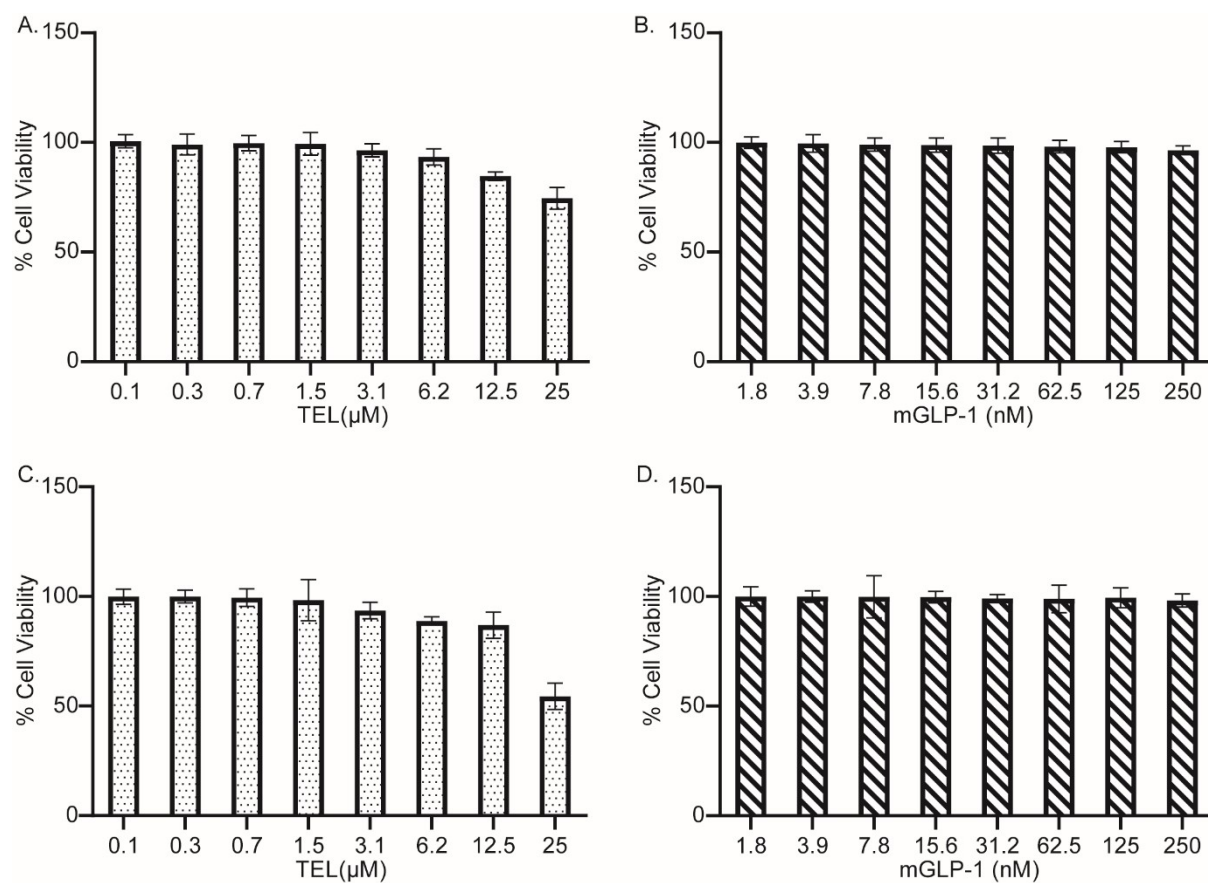
Supplementary figure S1. ^1H NMR analysis of compound 3.



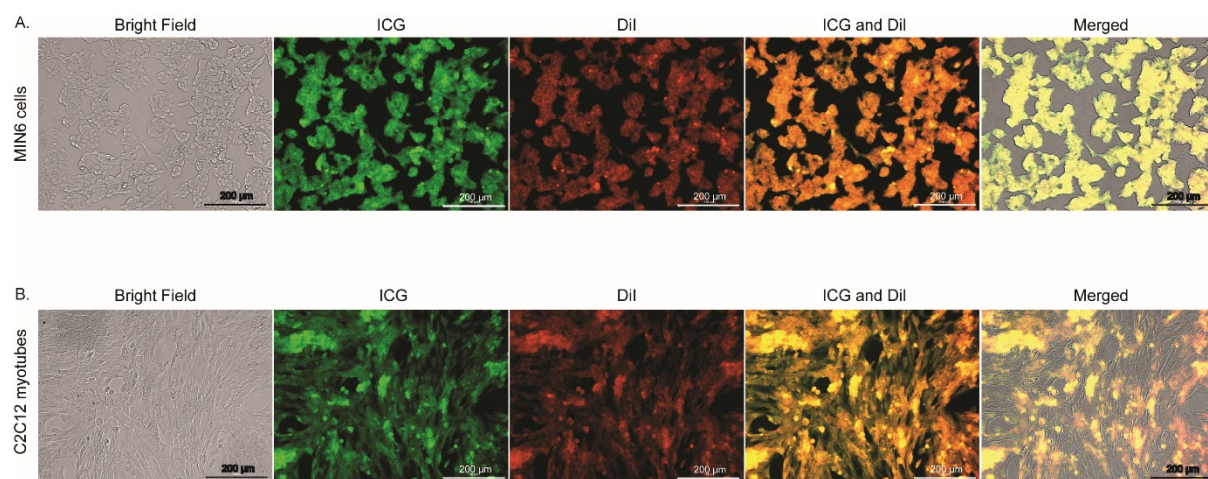
Supplementary figure S2. FTIR analysis of compound 1 (A) and 2 (B).



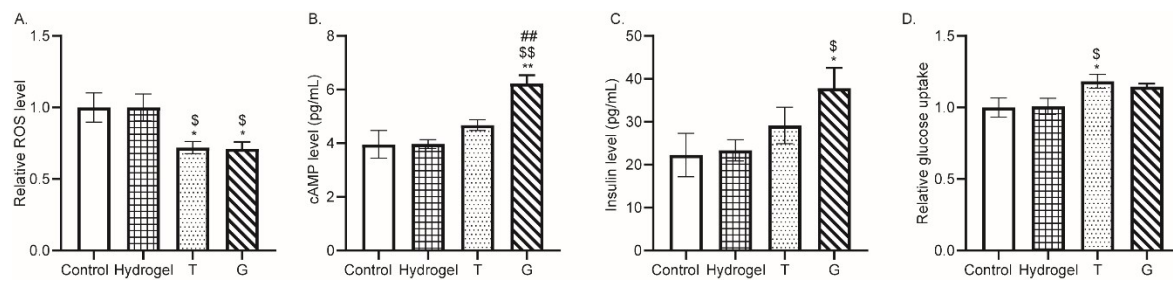
Supplementary Figure S3. Physicochemical characterization. **A)** Zeta potential of Ev. **B-C)** Strain (**B**), frequency (**C**), and time sweep analysis of Diabogel. **E-F)** Inversion tube (**E**) and syringibility (**F**) test of Diabogel.



Supplementary Figure S4. *In vitro* cell viability assay. **A-D**) *In vitro* MIN6 cell viability after the treatment of different concentration of free TEL (**A**), and mGLP-1 (**B**), **C-D**) *In vitro* C2C12 myotube cell viability after treatment of different concentration of free TEL (**C**), and mGLP-1 (**D**).

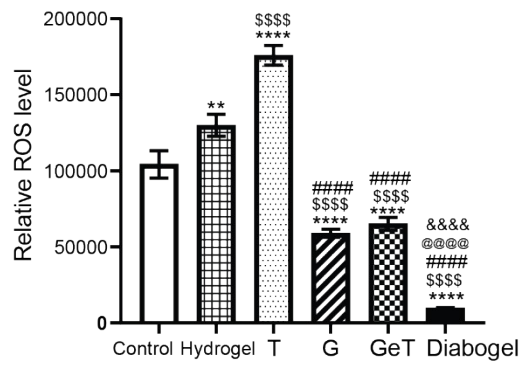


Supplementary Figure S5. *In vitro* uptake assay. **A-B**) The uptake of DiI-stained Ev-conjugated compound 3-loaded with ICG in MIN6 (**A**) and C2C12 myotubes (**B**).

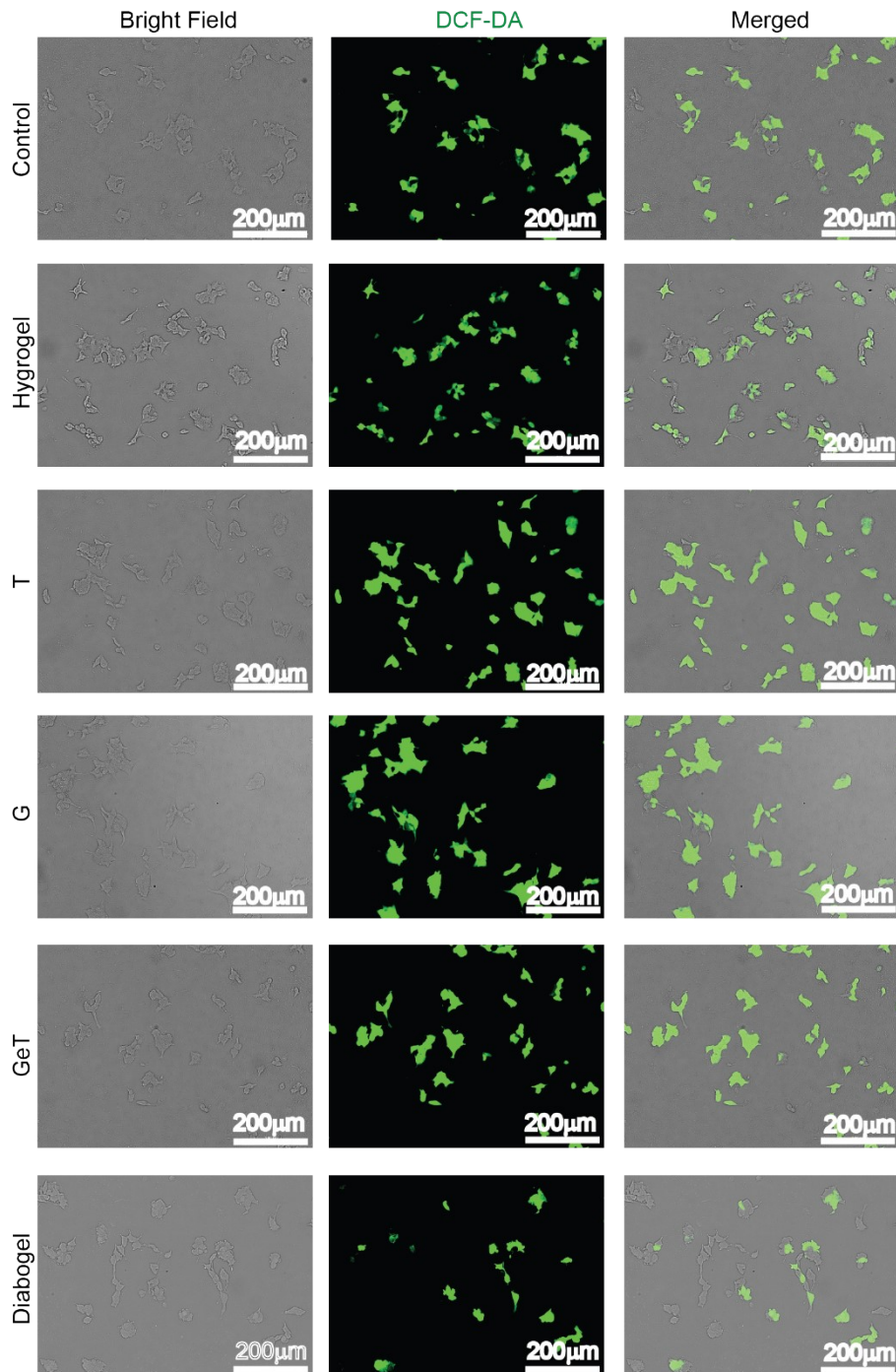


Supplementary Figure S6. *In vitro* efficacy analysis. **A-C)** Relative ROS (**A**), cAMP (**B**), and insulin (**C**) level in MIN6 cells. **D)** Relative glucose uptake by C2C12 myotubes. * and § represents w.r.t. control and hydrogel respectively; where *, § < 0.0405; **, §§ < 0.0084.

A.



B.



Supplementary Figure S7. *In vitro* efficacy analysis. **A)** Illustrative fluorescence images of MIN6 cells indicating relative intracellular ROS levels. **B)** Relative intracellular ROS levels of MIN6 cells determined by flow cytometry. *, #, @, &, and \$ represents w. r. t. control, T, G, GeT, and hydrogel respectively; where ** < 0.0016; ***, ####, @@@@, &&&&, and \$\$\$\$ < 0.0001.

	Carbon	Nitrogen	Hydrogen
Compound 1	33.57	0.28	5.23
Compound 2	49.92	9.6	6.46
Compound 3	35.95	1.63	5.6

Supplementary Table S1. Elemental analysis of compound 1, 2, and 3 indicating the percentage of carbon, nitrogen, and hydrogen.