Supplementary Information (SI) for Journal of Materials Chemistry B.

Encapsulation of Telmisartan inside insulinoma cell-derived extracellular vesicle outperformed biomimetic nanovesicles in modulating pancreatic inflammatory microenvironment

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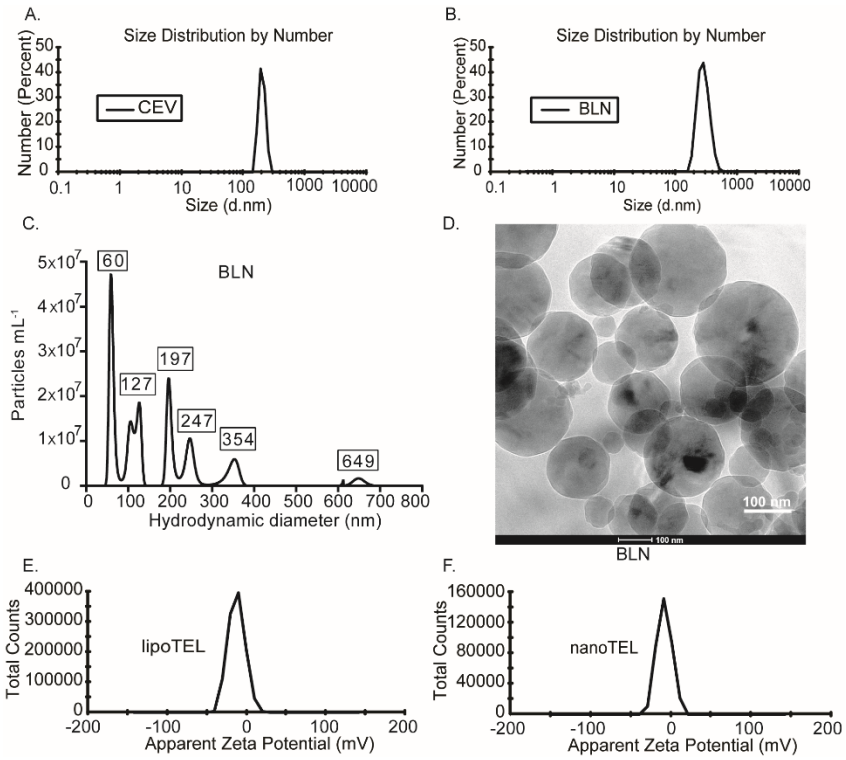
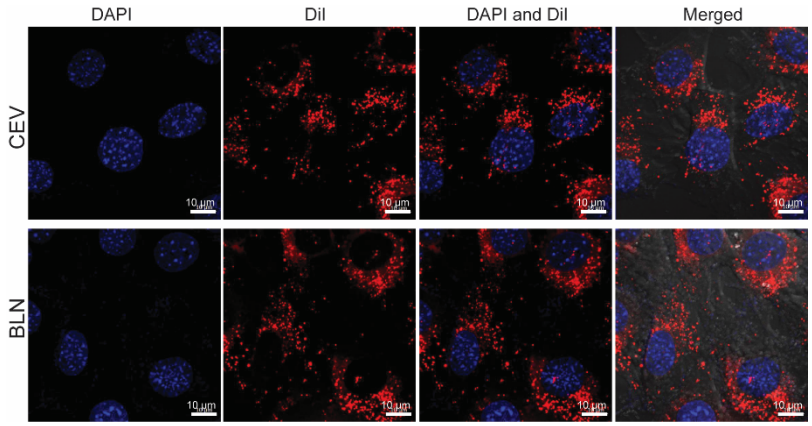
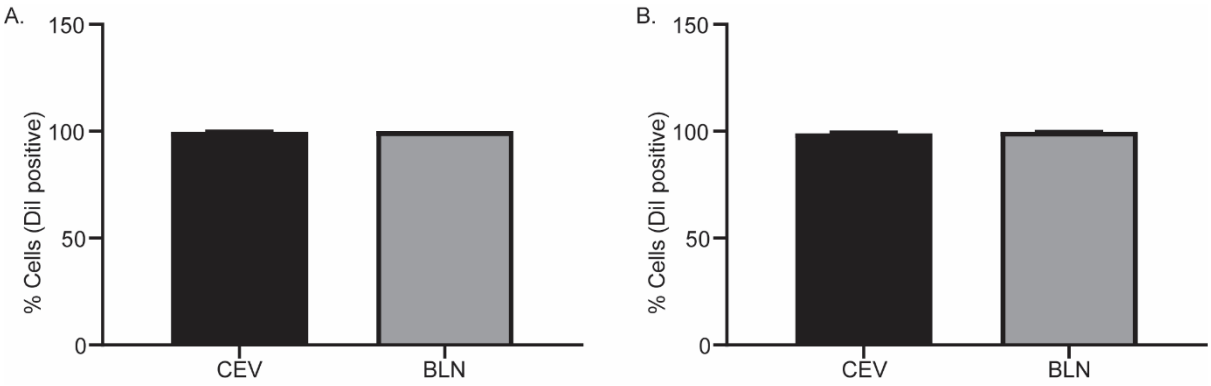


Supplementary Figure S1. Characterization of CEV, BLN, nanoTEL, and lipoTEL.

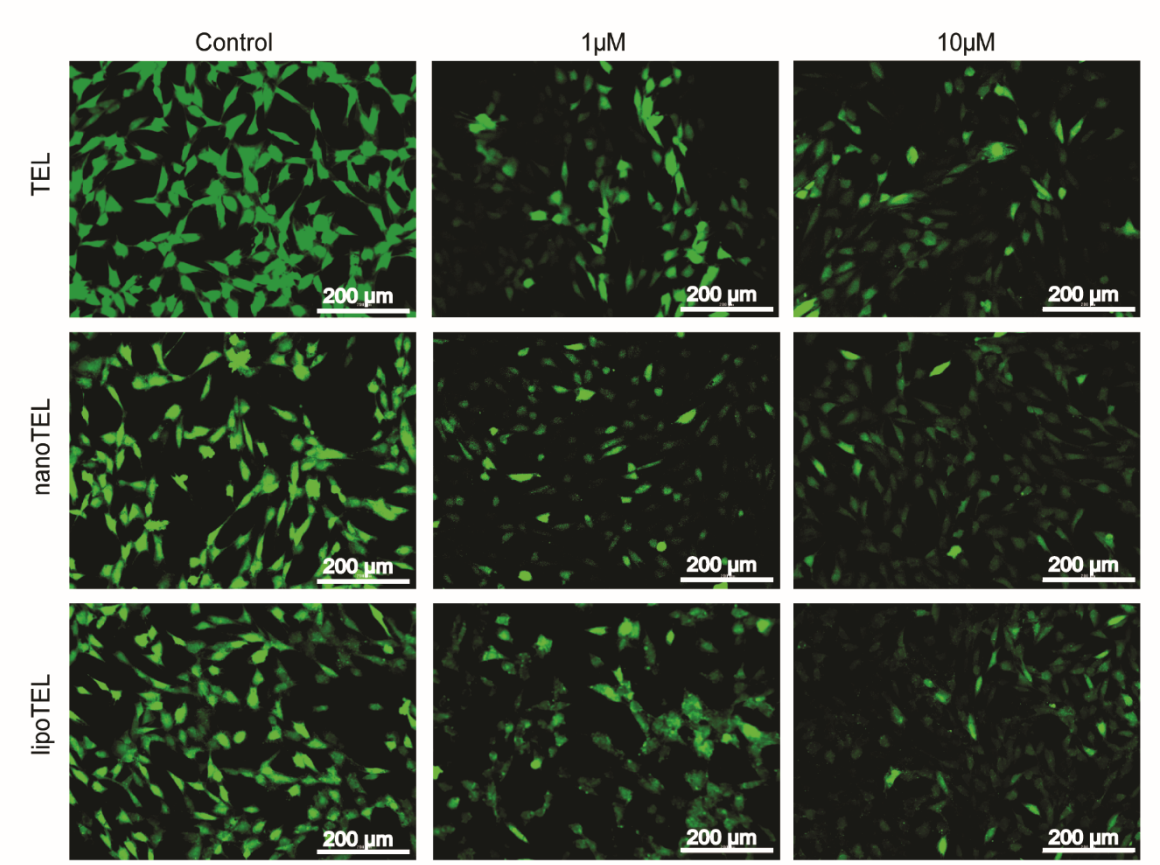
(A-B) DLS of CEV **(A)** and BLN **(B)**. **(C-D)** NTA **(C)** and cryoHRTEM images **(D)** of BLN. **(E-F)** Zeta potential of nanoTEL **(E)** and lipoTEL **(F)**.



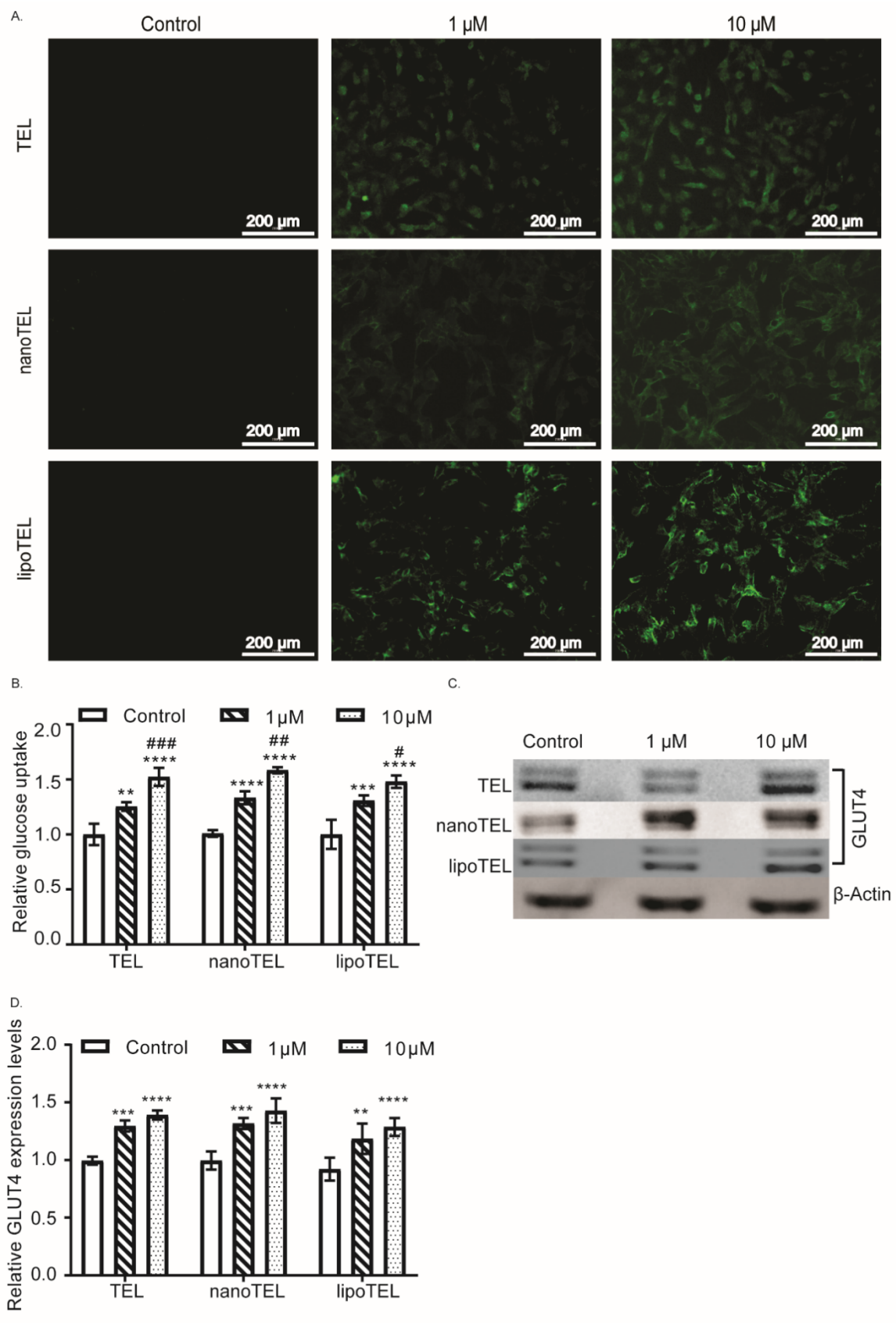
Supplementary Figure S2. *In vitro* cellular uptake. (A) Confocal microscopy images of C2C12 myotubes treated with DiI-labelled CEV and BLN at 60X magnification. DiI (red) and nucleus (blue).



Supplementary Figure S3. Quantification of cellular uptake. **A-B)** MIN6 **(A)** and C2C12 myotubes **(B)** were treated with DiI-labelled CEV and BLN followed by the determination of percentage fluorescence positive cells using flow cytometry. Results were represented as mean ± S.D, n= 3.

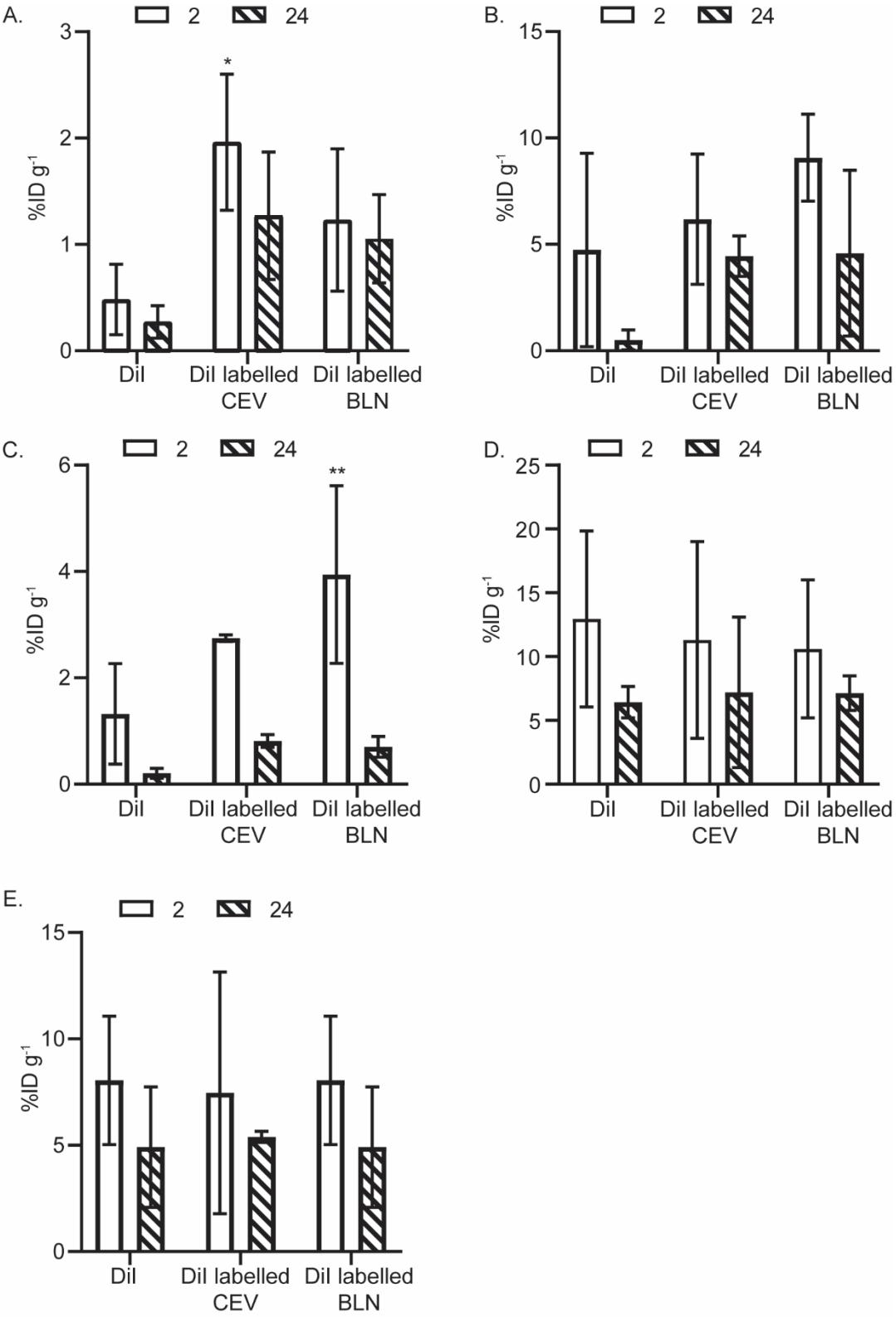


Supplementary Figure S4. **C2C12 myotubes were treated with free TEL, lipoTEL, and nanoTEL followed by carboxy DCF-DA.** Fluorescence microscopic images of cells showing the ROS levels.

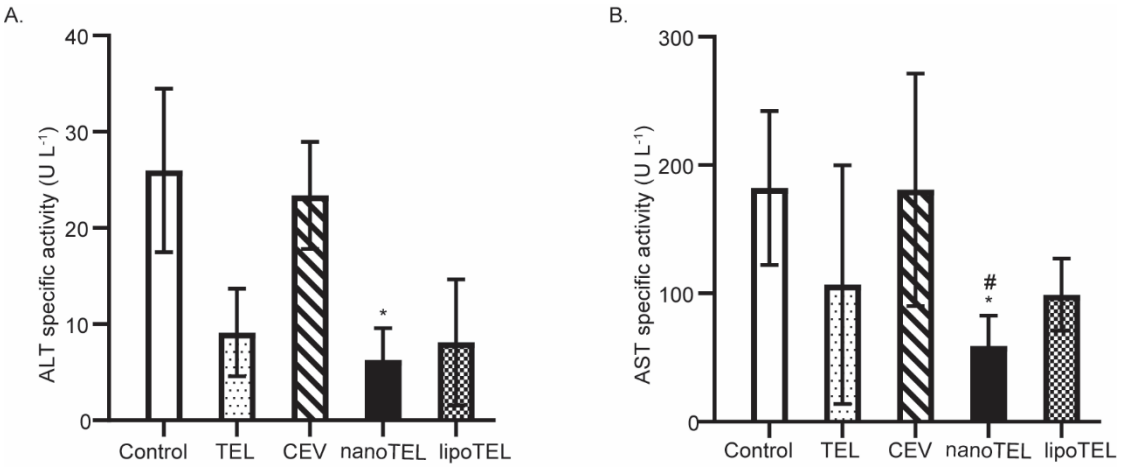


Supplementary Figure S5. Glucose uptake assay and determination of GLUT4 expression in C2C12 myotubes.

(A-B) Glucose uptake assay. Fluorecent microscopic images **(A)** and quantitative estimation **(B)** indicating relative glucose uptake. **(C-D)** Determination of GLUT4 expression. Western blot depicting GLUT4 expression **(C)** and its densitometry analysis **(D)**. Results were plotted as mean ± SD and two-way ANOVA was performed for statistical analysis. #P < 0.0216; **, ##P < 0.0022; ***, ###P < 0.0006; ****P < 0.0001 where * represents w.r.t. control and # represents w.r.t. 1 μM TEL concentration, n = 3.



Supplementary Figure S6. Biodistribution study. (A-E) For the biodistribution study, mice were intraperitoneally administered with DiI labelled nanovesicles. At 2 and 24 hrs post-injection, mice were sacrificed and different organs were excised out. DiI % ID g-1 of tissue in pancreas **(A)**, heart **(B)**, lungs **(C)**, liver **(D)**, and kidneys **(E)**. Data was represented as mean ± S.D and statistical significance was determined using by Two-way ANOVA. *P < 0.00217; **P < 0.0094 where * represents w.r.t. DiI , n= 3.



Supplementary Figure S7. Hepatotoxicity assay. At day 12, all the mice were sacrificed and blood samples were collected. Serum level of ALT **(A)** and AST **(B)**. Results were plotted as mean ± SD and two-way ANOVA was performed for statistical analysis. *,#P < 0.0497; where * represents w.r.t. control and # represents w.r.t. CEV, n = 3.