SUPPORTING INFORMATION

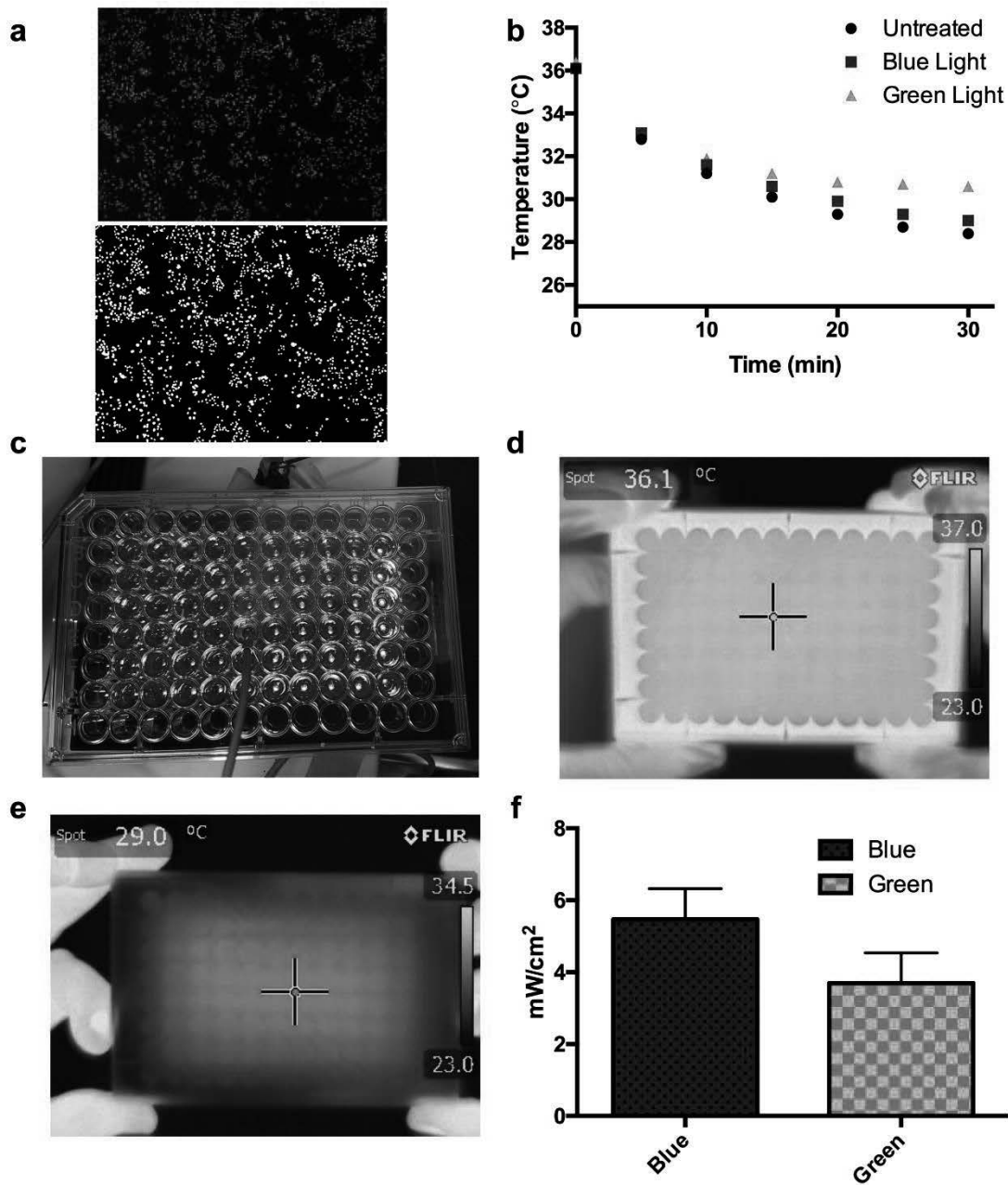**Development of Photoactive Sweet-C$_{60}$ for Pancreatic Cancer Stellate Cell Therapy**

1.0 PHOTODYNAMIC THERAPY LED SYSTEM

a) Validation of accurate automated segmentation algorthim used to count dead cell nuclei using DRAQ7 fluorescent stain, top panel raw image and bottom binary image of segmented dead cell nuclei). b) Temperature in wells during PDT treatment with blue and green light obtained via optical thermal probe. c) Plate and PDT LED set-up displaying the position of a thermal probe to measure intra-well temperatures during treatment d) IR image of bottom of cell plate at start and (e) end of PDT treatment. (f) Mean light intensity (mW/cm^2) across all 60 wells in a 96 well plate during blue and green light exposure.
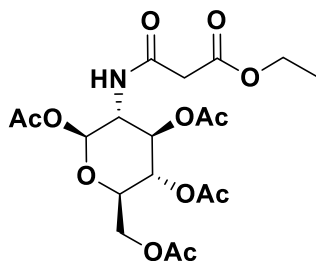
2.0 CHARACTERIZATION OF SUBSTRATES AND PRODUCTS

1 (white solid)

^{1}H-NMR (*D_2O,400MHz, ppm*): 5.12(d, *J*= 3.5 Hz, 1H, *α-H1*); 4.11(q, *J*= 7.2 Hz, 2H, <u>*CH*$_2$</u>*CH$_3$*); 3.81 (dd, *J$_1$*= 3.5 Hz, *J$_2$*=10.7 Hz, 1H, C<u>H</u> 6-H); 3.76 (m, 1H, H-5); 3.73 (m, 1H, H-4); 3.69 (t, *J*= 5.2 Hz, 1H, H-3); 3.65 (dd, *J$_1$*= 3.6 Hz, *J$_2$*=10.4 Hz, 1H, C<u>H</u> H-6); 3.37 (d, *J*=5.4 Hz, 2H, *CO-<u>CH$_2$</u>-CO*); 3.35 (m, 1H, H-2); 1.16 (t, *J*= 7.2 Hz, 3H, *CH$_2$<u>CH$_3$</u>).

^{13}C-NMR (*D_2O,100MHz, ppm*):169.8 (C=O); 168.8 (C=O); 90.7 ($C_α$-1); 71.5 ($C_α$-5); 70.6 ($C_α$-3); 70.0 ($C_α$-4); 62.6 ($C_α$-6); 60.6 (-<u>C</u>H$_2$-CH$_3$); 54.2 ($C_α$-2); 42.3 (O=C-<u>C</u>H$_2$-C=O); 13.2 (-CH$_3$)

HRMS (ESI): 316.0991 [M+Na]$^+$ (calc. for $C_{11}H_{19}NO_8Na$: 316.1003)

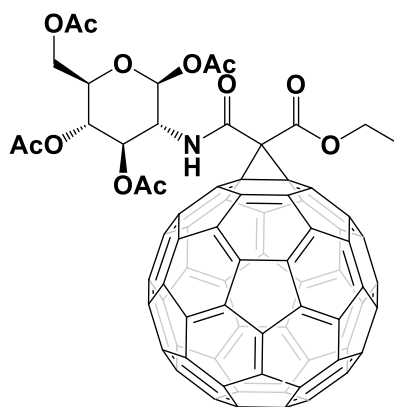**Purity:** 96.3 %, **R$_t$=** 2.34 min

2 (yellow syrup)

^{1}H-NMR (*CDCl$_3$,400MHz, ppm*): 7.35 (d, *J*= 8 Hz, 1H, H-1); 6.21 (d, *J*= 3.7 Hz, 1H, H-3); 5.34 (dd, *J$_1$*= 10.8 Hz; *J$_2$*= 9.5 Hz, 1H, H-2); 5.21 (t, *J*= 9.8 Hz, H-4); 4.54 (ddd, *J$_1$*= 10.8 Hz, *J$_2$*= 9.2 Hz, *J$_3$*= 3.8 Hz, 1H, H-5); 4.28 (dd, *J$_1$*= 12.4 Hz; *J$_2$*= 4 Hz, 1H, H-6); 4.19 (q, *J*= 7.2 Hz, 2H, CH$_2$CH$_3$); 4.09 (dd, *J$_1$*= 13,2 Hz; *J$_2$*=3.4 Hz, 1H, H-6); 3.27 (s, 2H, *CO-<u>CH$_2$</u>-CO*); 2.23 (s,3H, CH$_3$-C=O); 2.11 (s, 3H, CH$_3$-C=O); 2.06 (s,3H, CH$_3$-C=O); 1.29 (t, *J*= 7.2 Hz, 3H, -CH$_3$).

^{13}C-NMR (*CDCl$_3$,100MHz, ppm*): 171.2 (CH$_3$-<u>C</u>=O); 170.7 (CH$_3$-<u>C</u>=O); 169.2 (<u>C</u>=O); 169.1 (CH$_3$-<u>C</u>=O); 168.9 (CH$_3$-<u>C</u>=O); 165.4 (HN-<u>C</u>=O); 90.4 ($C_α$-1); 70.5 ($C_α$-5); 69.8 ($C_α$-4); 67.6 ($C_α$-

3); 61.8 (C_α-6) ; 61.5 (-$\underline{C}H_2$-CH_3) ; 50.8 (C_α-2); 40.7 (O=C-$\underline{C}H_2$-C=O); 20.8 (CH_3-C=O); 20.7 (CH_3-C=O); 20.6 (CH_3-C=O); 20.5 (CH_3-C=O); 14.0 (-CH_3)

HRMS (ESI): 484.1439 [M+Na]$^+$ (calc. for $C_{19}H_{27}NO_{12}Na$: 484.1425).

Purity: 98.6 %**, R$_t$=** 3.23 min

3

^{1}H-NMR (*CDCl$_3$,400MHz, ppm*): 7.19 (d, *J*= 8.8 Hz, 1H, H-1); 6.43 (d, *J*= 3.7 Hz, 1H, H-3); 5.49 (dd, *J$_1$*= 11.6 Hz, *J$_2$*= 9.6 Hz, 1H, H-2); 4.72 (ddd, *J$_1$*= 11.1 Hz; *J$_2$*= 8.8 Hz; *J$_3$*= 3.7 Hz, 1H, H-5); 4.54 (m, 2H, CH$_2$CH$_3$); 4.33 (dd, *J$_1$*= 12.8 Hz, *J$_2$*= 4.0 Hz, H-4)); 4.13 (m, 2H, H-6); 2.23 (s,3H, CH$_3$-C=O); 2.12 (s,3H, CH$_3$-C=O); 2.08 (s,3H, CH$_3$-C=O); 1.99 (s,3H, CH$_3$-C=O); 1.47 (t, *J*= 7.1 Hz)

^{13}C-NMR (*CDCl$_3$,100MHz, ppm*): 171.56, 170.71, 169.21, 168.66, 164.61, 161.37, 145.86, 145.54, 145.35, 145.30, 145.28, 145.27, 145.27, 145.24, 145.20, 145.14, 145.12, 144.96, 144.94, 144.89, 144.83, 144.76, 144.73, 144.71, 144.68, 144.60, 144.58, 144.57, 143.88, 143.83, 143.78, 143.75, 143.14, 143.09, 143.06, 143.05, 143.04, 143.00, 142.99, 142.98, 142.20, 142.17, 142.15, 142.02, 142.00, 141.94, 141.04, 141.02, 141.00, 140.93, 138.46, 138.32, 137.88, 89.83, 77.38, 72.54, 71.97, 69.97, 69.90, 67.59, 64.14, 61.48, 55.21, 53.48, 52.22, 50.90, 23.87, 20.90, 20.73, 20.65, 20.61, 14.26.

Purity: 99.1 %**, R$_t$=** 4.12 min

MALDI TOF (negative): 1177.9 Da [M-H]$^-$

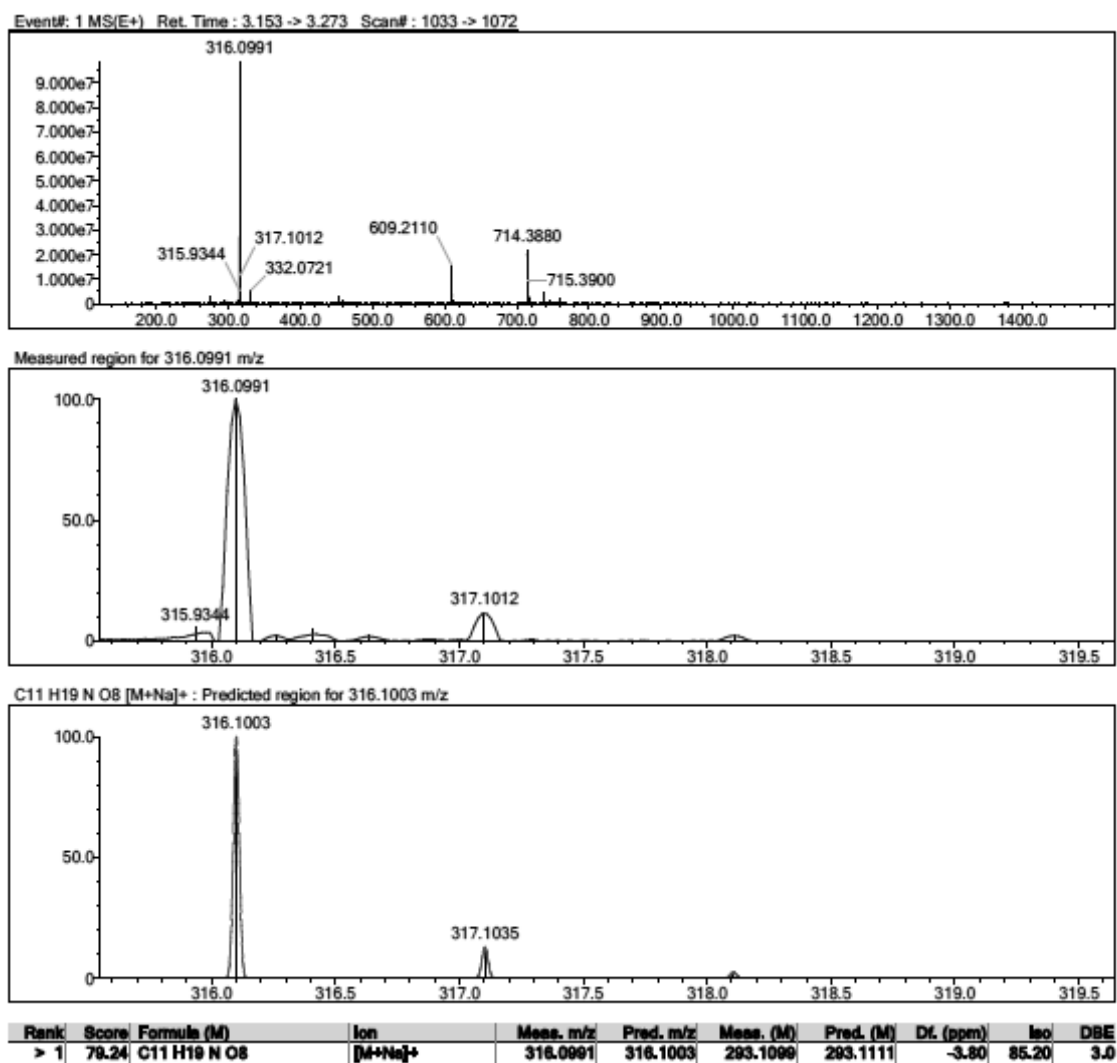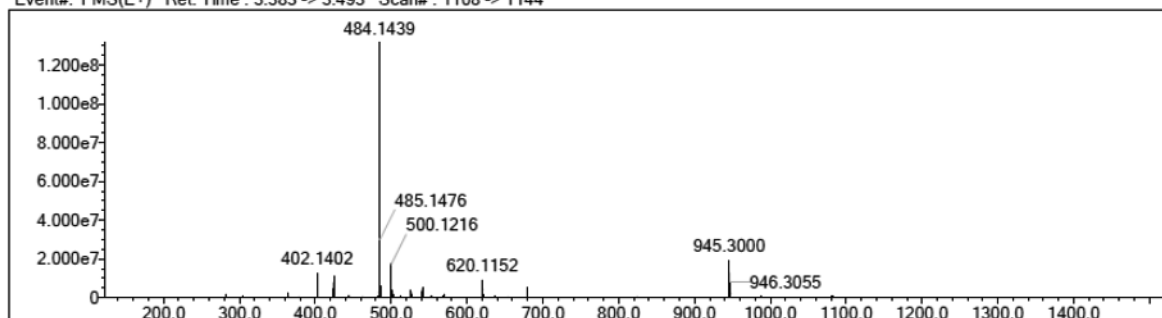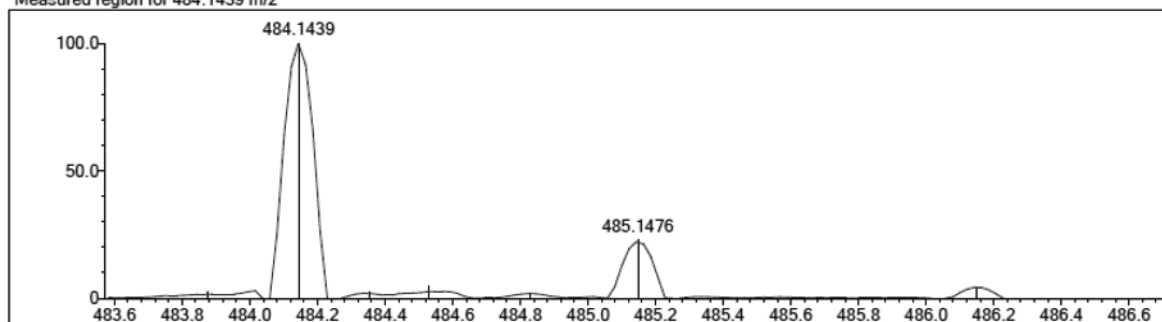## 3.0 MASS SPECTROMETRY OF SELECTED PRODUCTS

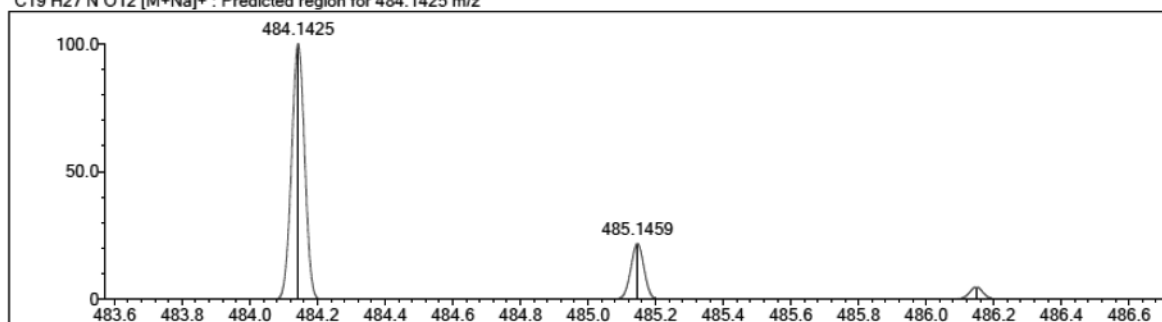**Figure S1:** HRMS(ESI) of **1**

Event#: 1 MS(E+)   Ret. Time : 3.383 -> 3.493   Scan# : 1108 -> 1144

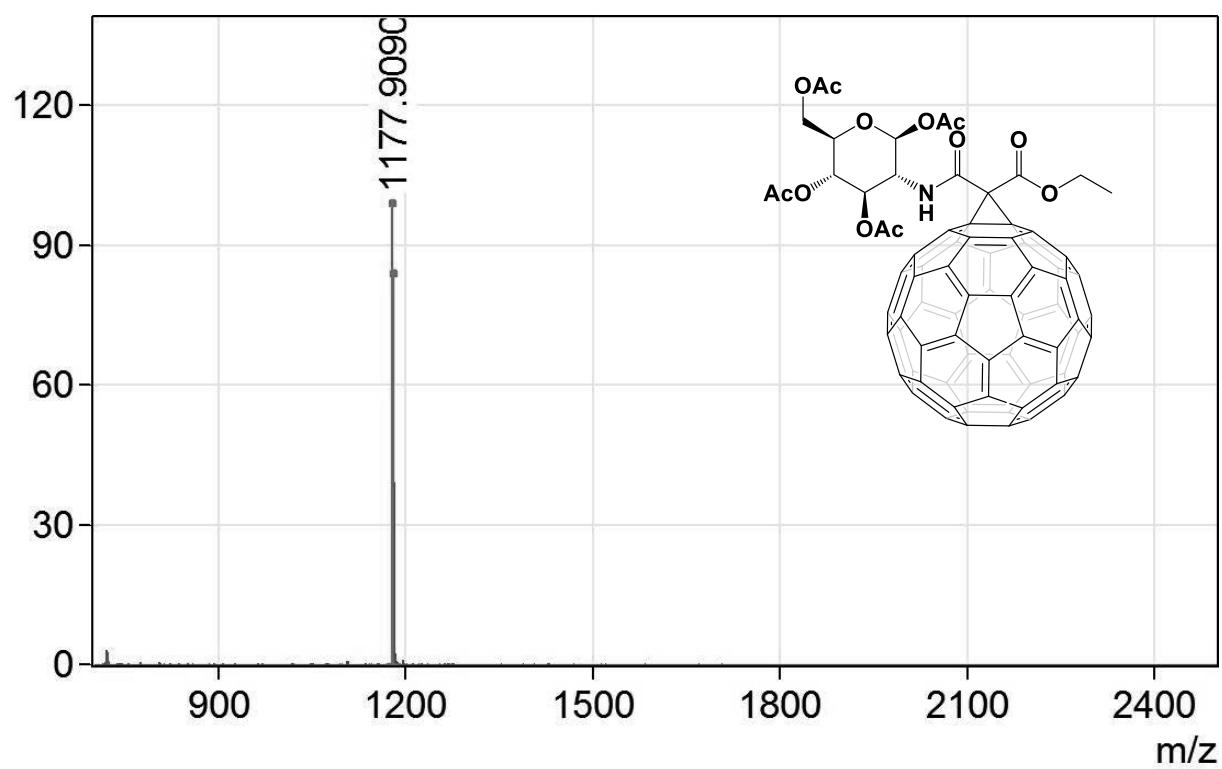Measured region for 484.1439 m/z

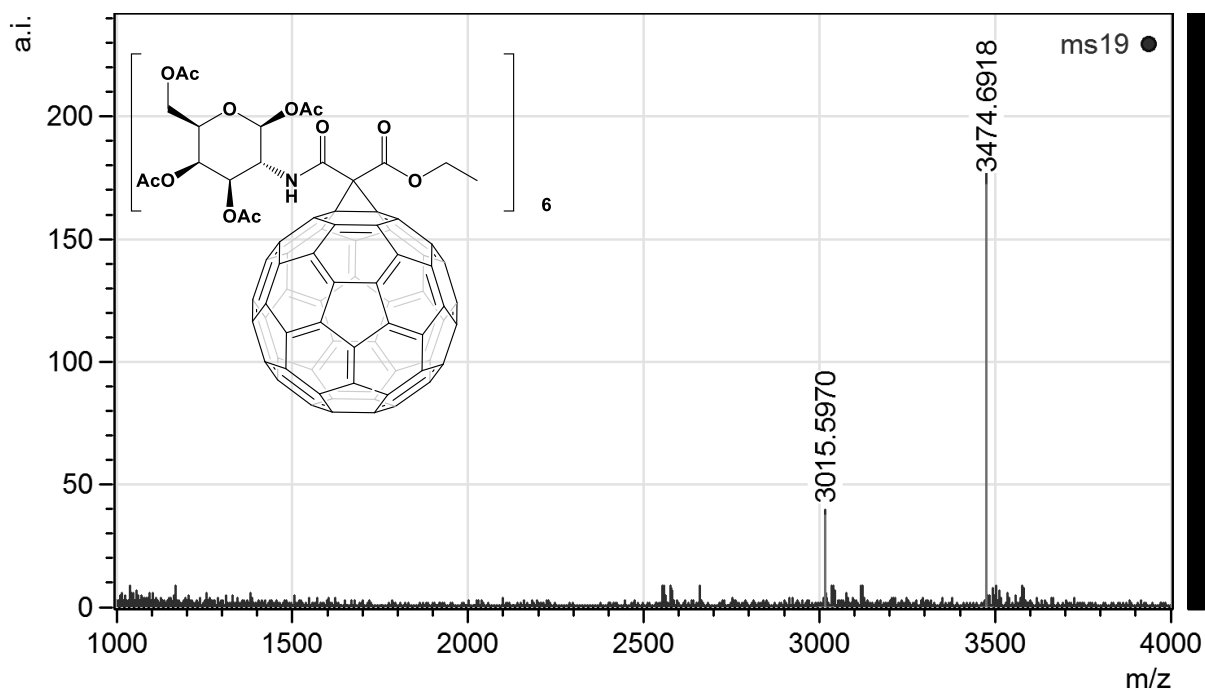C19 H27 N O12 [M+Na]+ : Predicted region for 484.1425 m/z

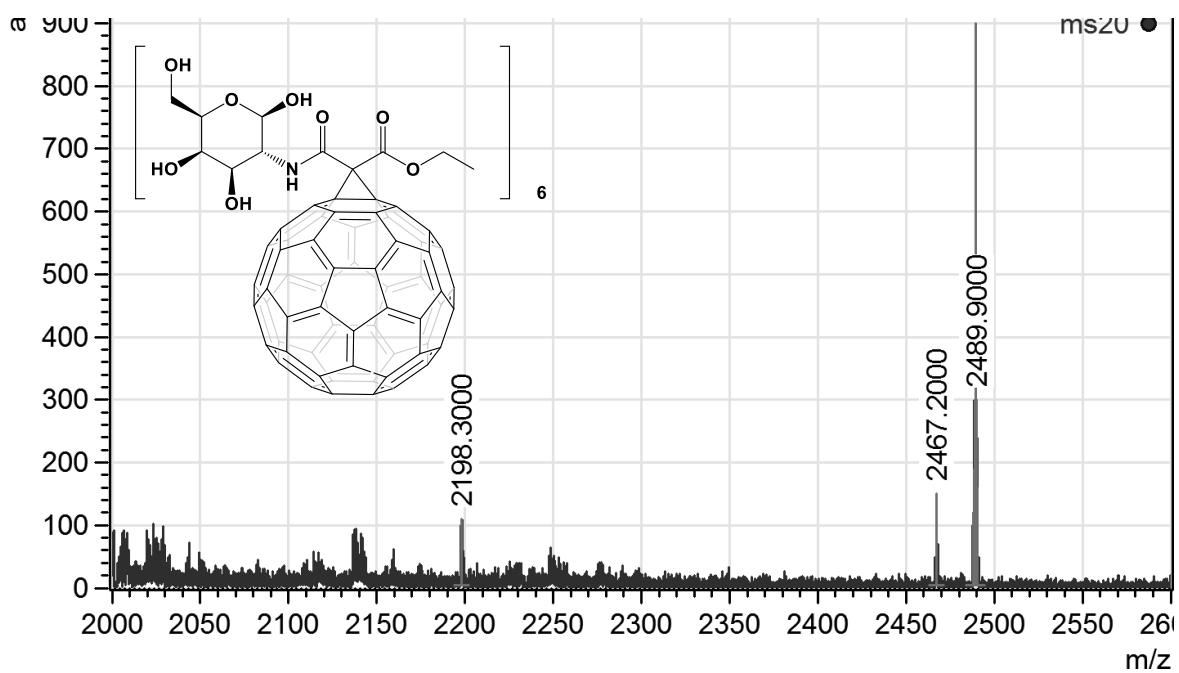| Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Meas. (M)	Pred. (M)	Df. (ppm)	Iso	DBE
1	99.62	C20 H23 N5 O8	[M+Na]+	484.1439	484.1439	461.1547	461.1547	0.00	99.62	12.0
> 2	94.24	C19 H27 N O12	[M+Na]+	484.1439	484.1425	461.1547	461.1533	2.89	98.92	7.0

Figure S2: HRMS (ESI) of **2**
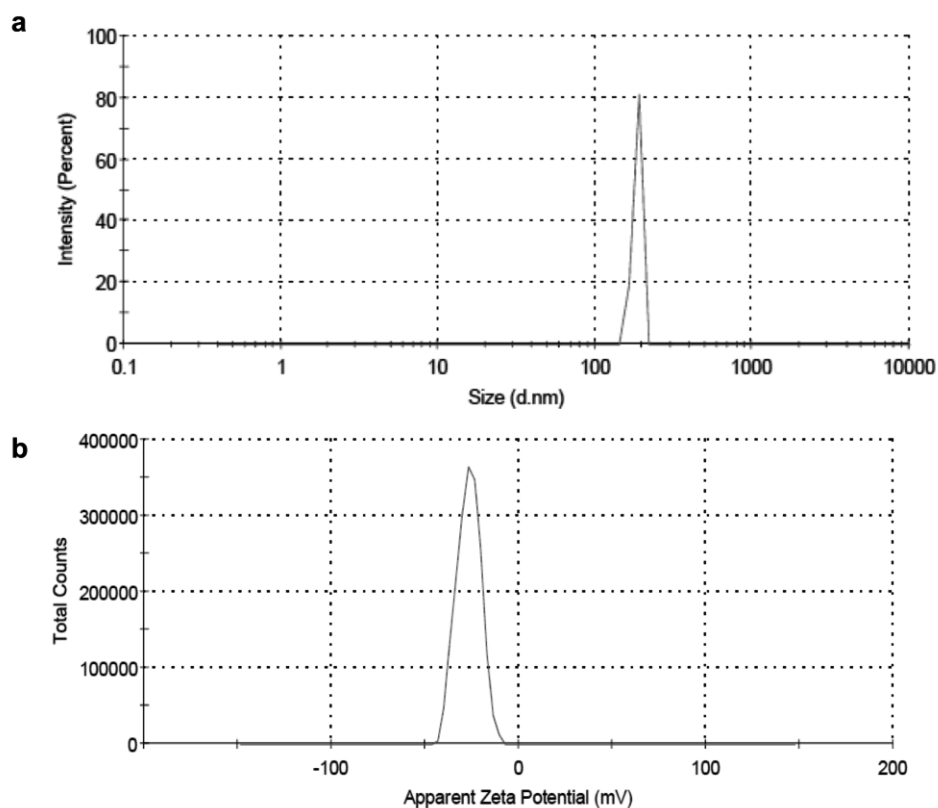
Figure S3: MALDI TOF (NEGATIVE) of **3**

Figure S4: MALDI TOF (POSITIVE) of protected (acetylated) **4.**

Figure S5: ESI-MIRCOTOF (POSITIVE) of deprotected **4** (a.k.a. Sweet-C$_{60}$).
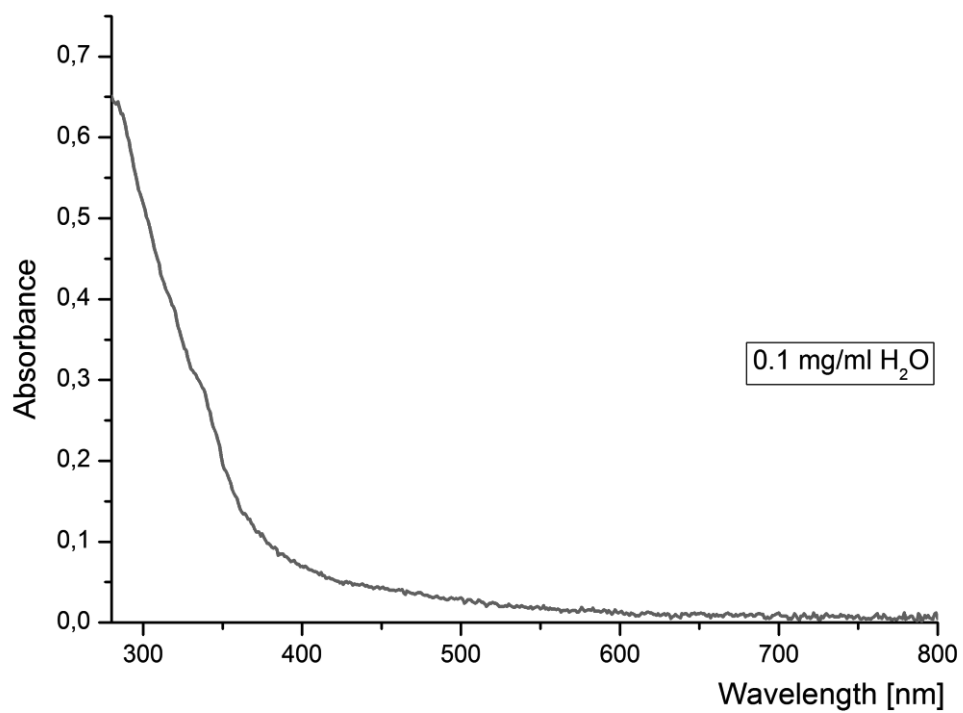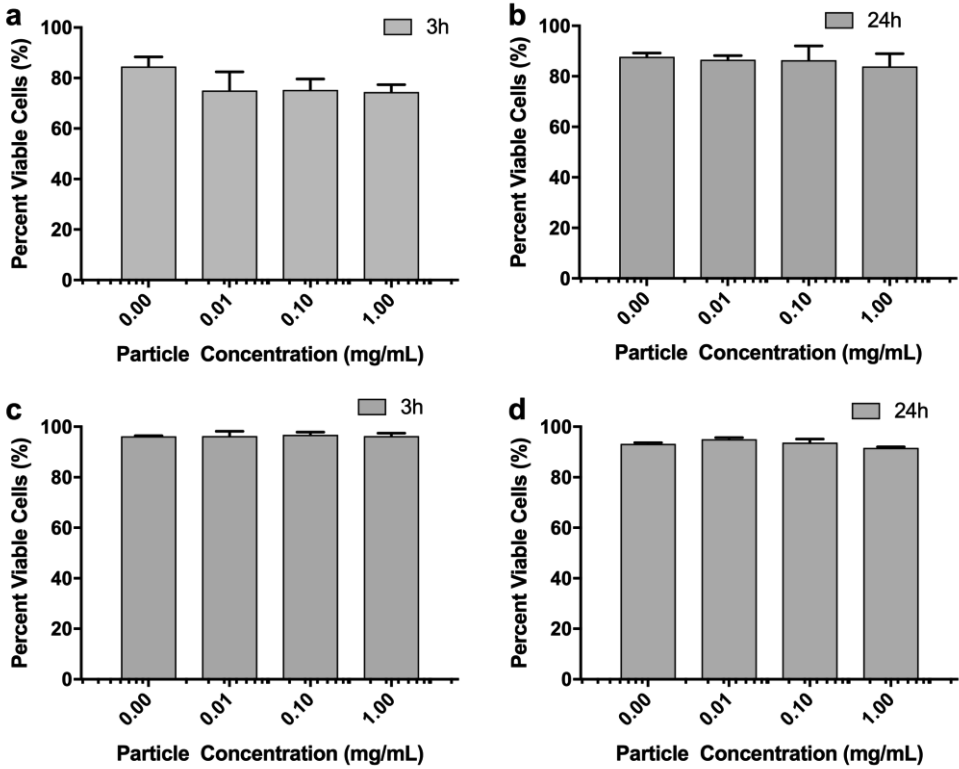
4.0 DYNAMIC LIGHT SCATTERING OF SWEET-C$_{60}$

Figure S6: Size and surface charge of Sweet-C$_{60}$. Dynamic light scattering (**A**) and zeta potential measurements (**B**) of Sweet-C$_{60}$, showing an average size distribution at 185 nm and zeta potential at -27 mV.

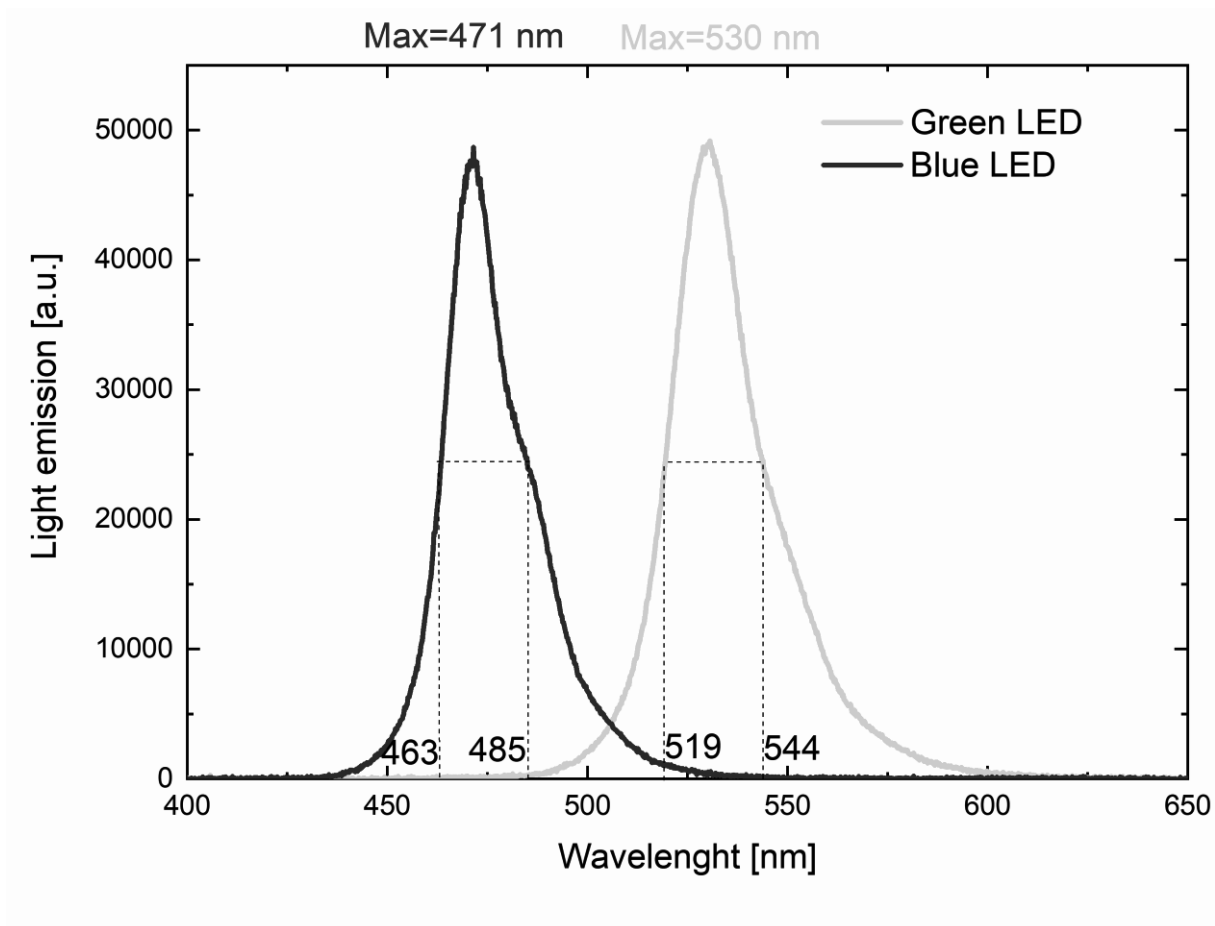## 5.0 UV-VIS SPECTRUM OF SWEET-C$_{60}$

Figure S7: UV-VIS spectrum of Sweet-C$_{60}$ in water (c= 0.1 mg/ml)

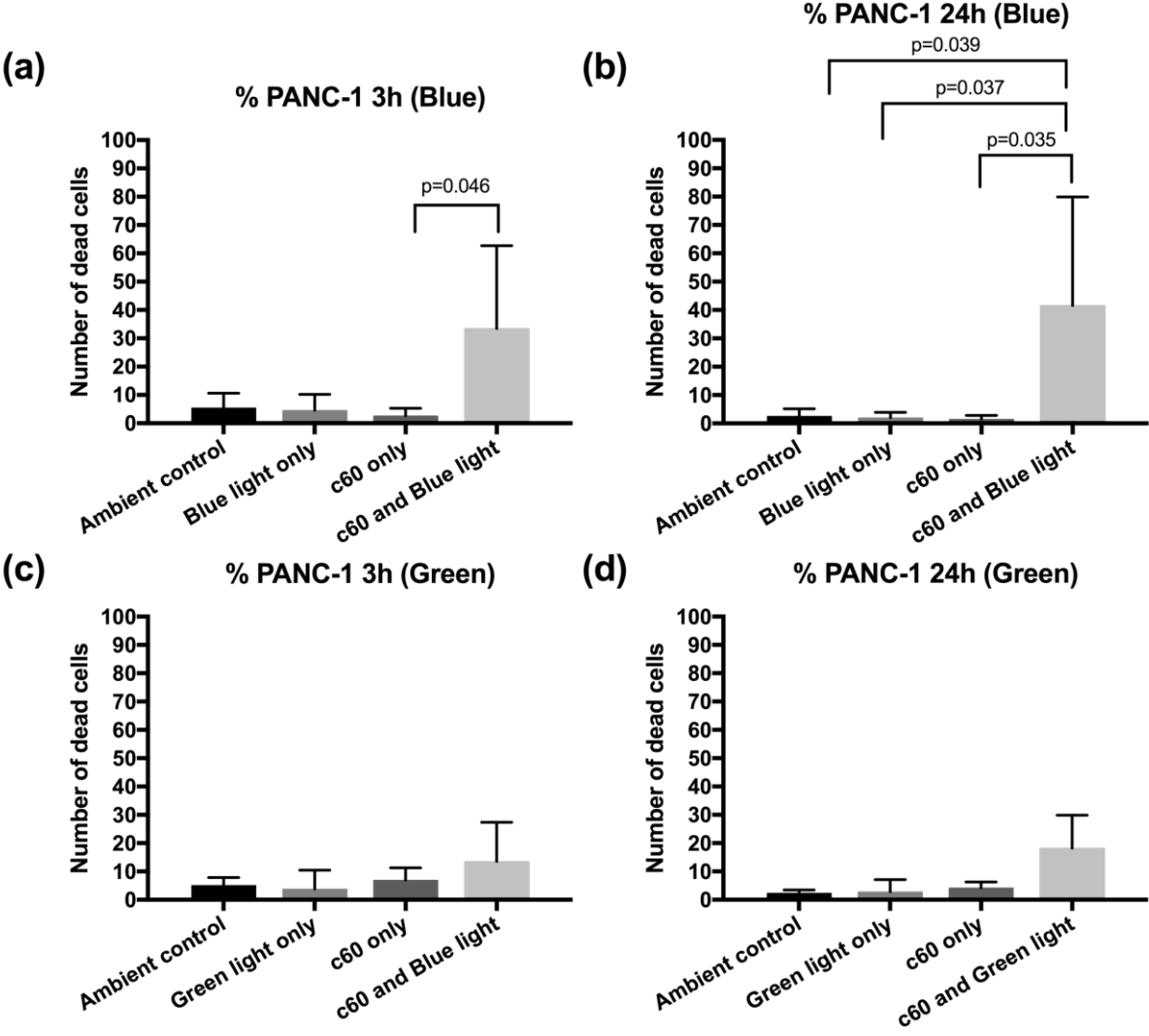## 6.0 CELL BASED VIABILITY ASSAYS AND LED SPECTRUM

Figure S8: Cell flow cytometry data showing concentration- and time-dependent Sweet-C60 cytotoxicity profile in PANC-1 cells (top row) and PSC cells (bottom row).

Figure S9: LED Emission spectrum.

Figure S10: Phototoxicity effects of Sweet-C_{60} (0.1 mg/ml) on PANC-1 cells. a) Number of dead PANC-1 cells at 3h and (b) 24hr time point, after blue and light exposure. c) Number of dead PANC-1 cells at 3h and (d) 24hr time point, after green light exposure. Data are represented as mean with error bars representing standard deviation.

7.0 REFERENCES

1. Hwang, R. F.; Moore, T.; Arumugam, T.; Ramachandran, V.; Amos, K. D.; Rivera, A.; Ji, B.; Evans, D. B.; Logsdon, C. D. *Cancer research* **2008,** 68, (3), 918-926.
2. Bachem, M. G.; Schunemann, M.; Ramadani, M.; Siech, M.; Beger, H.; Buck, A.; Zhou, S.; Schmid-Kotsas, A.; Adler, G. *Gastroenterology* **2005,** 128, (4), 907-21.
3. Erkan, M.; Kleeff, J.; Reiser, C.; Hinz, U.; Esposito, I.; Friess, H.; Buchler, M. W. *Digestion* **2007,** 75, (2-3), 165-71.
4. Miao, Y.; Xu, J.; Shen, Y.; Chen, L.; Bian, Y.; Hu, Y.; Zhou, W.; Zheng, F.; Man, N.; Shen, Y.; Zhang, Y.; Wang, M.; Wen, L. *ACS Nano* **2014,** 8, (6), 6131-6144.