

Supplementary data tables

Table 1: Solubility studies of MOP in various analytical medium (n=3)

| S. No. | Medium | Solubility (mg mL ⁻¹) |
|--------|----------------------------|-----------------------------------|
| 1 | TDW/EtOH (90:10) | 0.120 ± 0.017 |
| 2 | TDW/EtOH (80:20) | 0.204 ± 0.012 |
| 3 | TDW/EtOH (70:30) | 0.279 ± 0.011 |
| 4 | TDW/EtOH (60:40) | 0.668 ± 0.017 |
| 5 | TDW/EtOH (50:50) | 1.726 ± 0.014 |
| 6 | EtOH | 3.61 ± 0.067 |
| 7 | PBS (pH 6.4) | 0.09 ± 0.009 |
| 8 | PBS (pH 7.4) | 0.11 ± 0.05 |
| 9 | PBS (pH 7.4)/EtOH(10:90) | 0.146 ± 0.021 |
| 10 | PBS (pH 7.4)/ EtOH (20:80) | 0.169 ± 0.018 |
| 11 | PBS (pH 7.4)/ EtOH (30:70) | 0.258 ± 0.014 |
| 12 | PBS (pH 7.4)/ EtOH (40:60) | 0.301 ± 0.011 |
| 13 | PBS (pH 7.4)/ EtOH (1:1) | 1.266 ± 0.041 |

TDW: Triple distill water; EtOH: Ethanol; PBS: Phosphate buffer saline

Table 2: Coefficients of polynomial equations along with their statistical parameters for the studied response variables

| Coefficient code | Polynomial coefficients for response variables | | | | |
|------------------|--|---------------------|---------------------|---------------------|----------------------|
| | PDE | Size | PDL | J | Sd |
| β_0 | 68.02 | 263.21 | 2.34 | 6.33 | 29.54 |
| β_1 | 5.95 (p<0.005) | 72.00 (p<0.0005) | -0.32 (p<0.0001) | -2.03 (p<0.0001) | 2.90 (p<0.0001) |
| β_2 | 8.30 (p<0.0001) | -43.00 (p<0.001) | 1.07 (p<0.0001) | 0.92 (p<0.0001) | -2.85 (p<0.0001) |
| β_3 | -10.97 (p<0.0001) | -25.72 (p<0.01) | 0.22 (p<0.0001) | -0.47 (p<0.0001) | -10.32 (p<0.0001) |
| β_4 | -- | -6.72 (p<0.005) | 0.81 (p<0.0001) | -0.073 (p<0.01) | -4.29 (p<0.0001) |
| β_5 | 1.38 (p<0.1) | -- | 0.02 (p<0.001) | -0.030 (p<0.1) | 0.29 (p<0.05) |
| β_6 | -2.53 (p<0.1) | -- | -0.05 (p<0.001) | -0.49 (p<0.0001) | 1.82 (p<0.0005) |
| β_7 | -0.88 (p<0.5) | -- | 0.02 (p<0.1) | 0.12 (p<0.001) | -0.44 (p<0.05) |
| r^2 | 0.9853 | 0.9863 | 1.00 | 0.9998 | 0.9996 |
| Adj r^2 | 0.9648 | 0.9671 | 0.9999 | 0.9995 | 0.9990 |
| Pred r^2 | -0.7042 | -0.5936 | 0.9948 | 0.9751 | 0.9535 |
| Model | P<0.0005 | P<0.0005 | p<0.0001 | p<0.0001 | p<0.0001 |

$$\mathbf{PDE} = 68.02 + 5.95 X_1 + 8.30 X_2 - 10.97 X_1^2 + 1.38 X_1 X_2 - 2.53 X_1^2 X_2 - 0.88 X_1 X_2^2$$

$$\mathbf{Size} = 263.21 + 72.0 X_1 - 43.0 X_2 - 25.727 X_1^2 - 6.72 X_2^2$$

$$\mathbf{PDL} = 2.34 - 0.32 X_1 + 1.07 X_2 + 0.22 X_1^2 + 0.81 X_2^2 + 0.02 X_1 X_2 - 0.05 X_1^2 X_2 + 0.02 X_1 X_2^2$$

$$\mathbf{J} = 6.33 - 2.03 X_1 + 0.927 X_2 - 0.47 X_1^2 - 0.073 X_2^2 - 0.030 X_1 X_2 - 0.49 X_1^2 X_2 + 0.12 X_1 X_2^2$$

$$\mathbf{Sd} = 29.54 + 2.90 X_1 - 2.85 X_2 - 10.32 X_1^2 - 4.29 X_2^2 + 0.29 X_1 X_2 + 1.82 X_1^2 X_2 - 0.44 X_1 X_2^2$$

Supplementary data figures

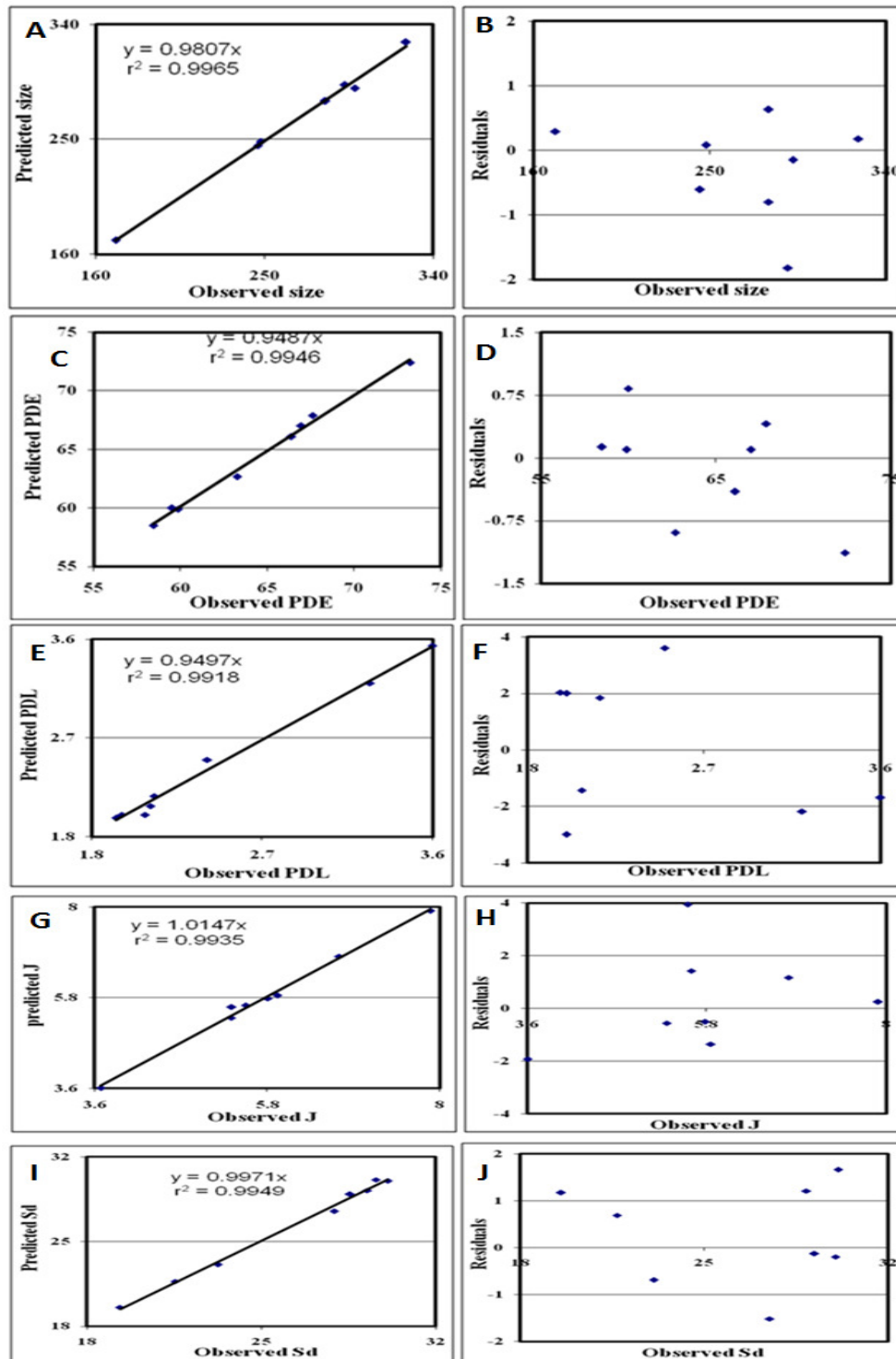


Figure 1: Linear correlation plot and residual plot between the observed and predicted values of PDE (A&B), vesicle size (C&D), PDL (E&F), flux (J) (G&H), Sd (I&J)

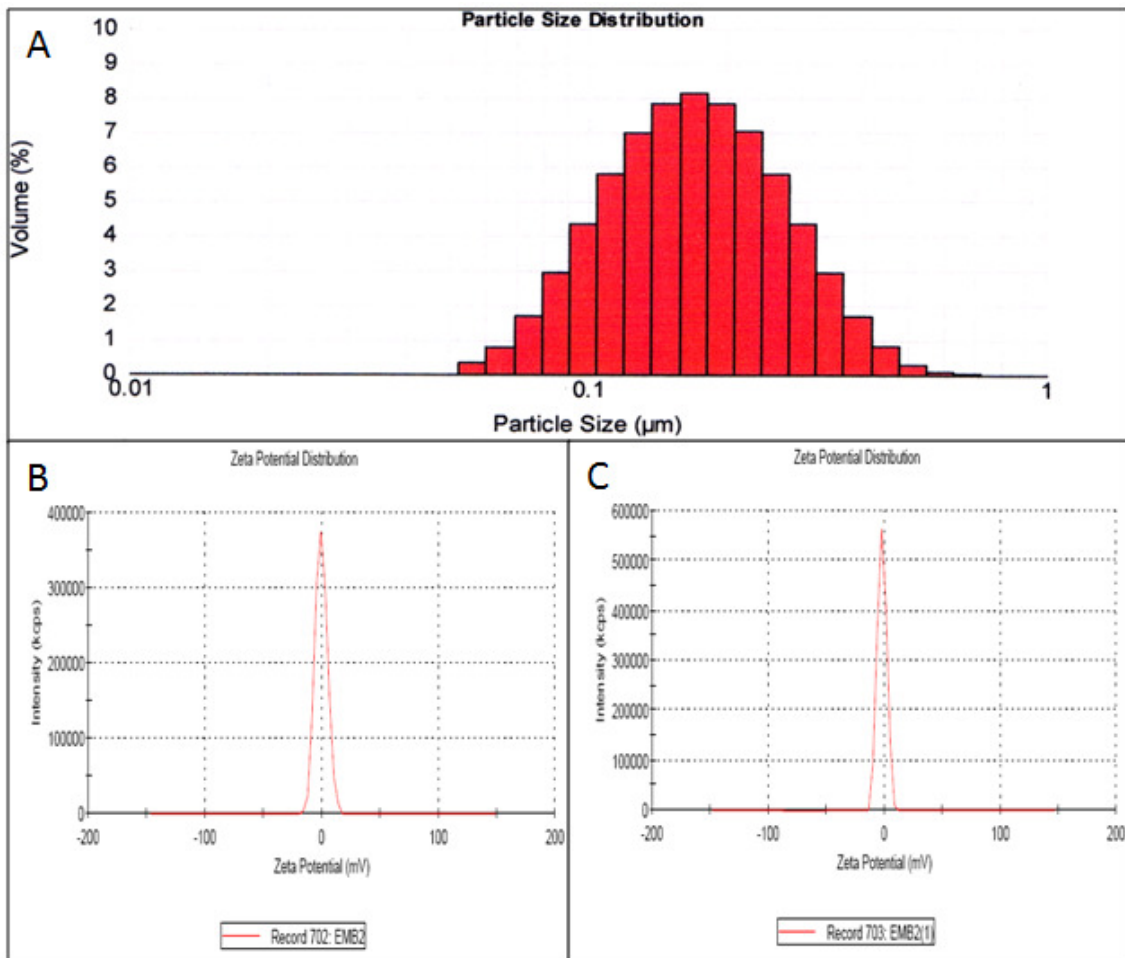


Figure 2: (A) Particle size distribution profile of ethosomal vesicles, (B) Zeta potential distribution of ethosomal vesicles, (C) Zeta potential distribution of ethosomal hydrogel