# Supporting Information.

## Inclusion of a Phytomedicinal Flavonoid in Biocompatible Surface-Modified Chylomicron Mimic Nanovesicles with Improved Oral Bioavailability and Virucidal Activity: Molecular Modeling and Pharmacodynamic Studies

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**Table S1**: The effect of storage on the physical characteristics of optimized F9 preparation.

| Parameter | Fresh F9 | F9 post-3M at 4˚C | F9 post-3M at 25˚C |
|---|---|---|---|
| **EE%** | 89.6±2.9 | 87.8±1.2 | 86.1±1.8 |
| **PS** | 227.4±13.5 | 229.1±10.2 | 231.5±5.4 |
| **Q8h** | 78.9±6.7 | 80.1±8.5 | 82. 3 ±5.7 |

*Note:* All values exploited as mean±SD (n=3), @ non-significant difference at (P>0.05) compared to that of fresh F9]. *Abbreviations:* EE%, entrapment efficiency percentage; PS, particle size; Q8h, % of MH released after 8 h.

**Table S2: Computer-aided ADMET parameters of morin hydrate.**

| | | | |
|---|---|---|---|
| **BBB_Lev**[a] | 4 | **CYP2D6 Prob**[e] | 0.4 |
| **Absorption Lev**[b] | 2 | **CYP2D6** [f] | 0 |
| **AQ SOL Lev**[c] | 2 | **Alog P98**[g] | 1.63 |
| **Hepatotox**[d] | 1 | **ADMET PSA Lev**[h] | 140.30 |

*Notes.*

*a*: Blood brain barrier level: 4= undefined, 2= medium penetration, 1= high penetration.

*b*: Absorption level: 3= very low absorption, 2= low absorption, 1= moderate, 0= good absorption.

*c*: Aqueous solubility level: 4= optimal, 3= good, 2= low solubility, 1= very low but soluble, 0= extremely low.

*d:* Hepatotoxicity level: 1= toxic, 0= nontoxic.

*e:* CYP2D6 inhibition probability.

*f:* CYP2D6 inhibition: 1= likely to inhibit, 0= non inhibitor.

*g:* Alog P98: compounds must have log p value not greater than 5.0 to attain reasonable probability of being well absorbed.

*h:* PSA Lev (polar surface area level): compounds with PSA > 140 have poor bioavailability

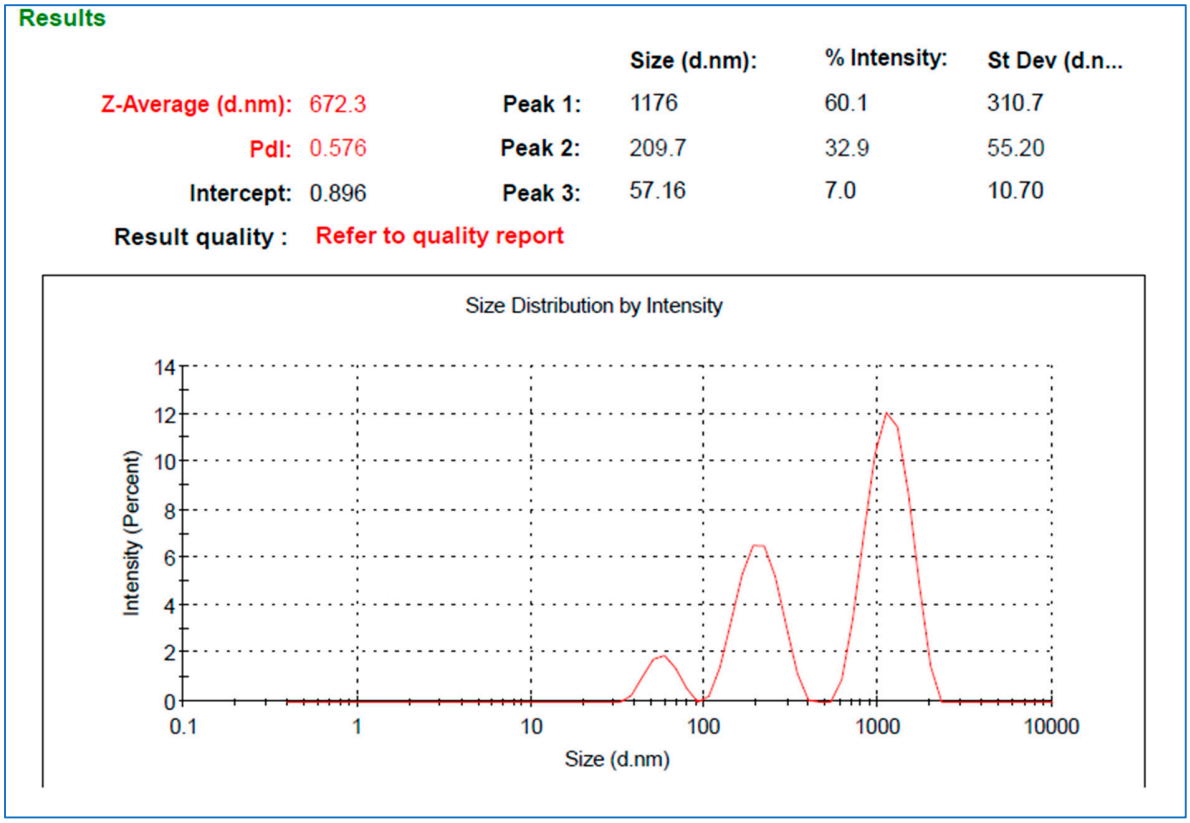



**Figure S1**. Particle size distribution determination of the MH dispersion.

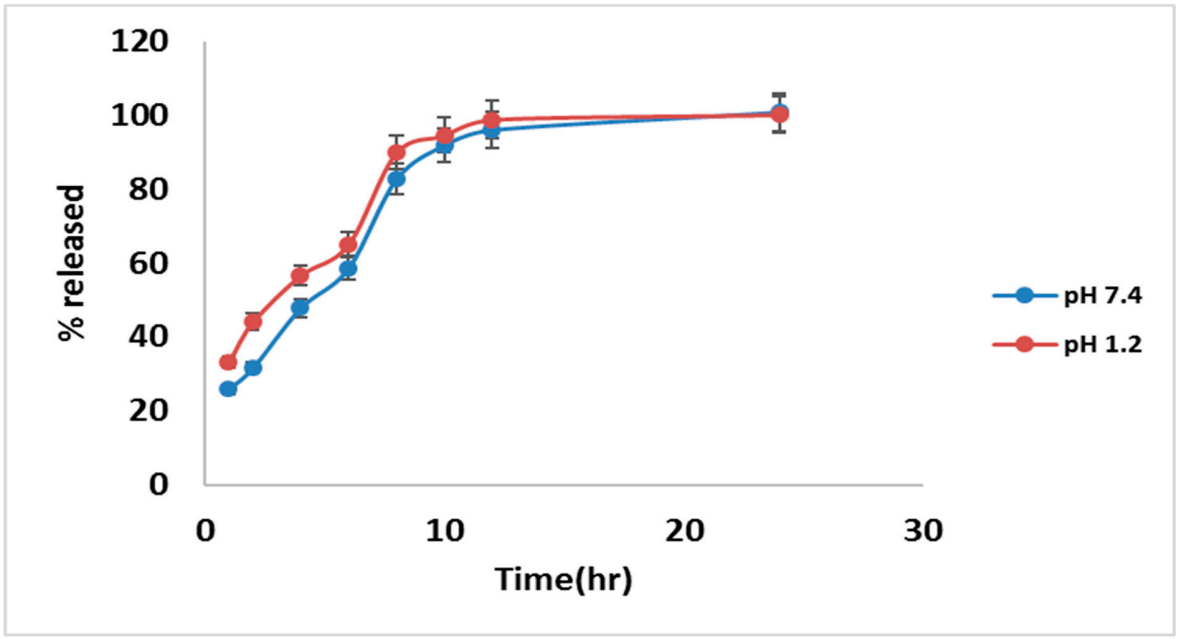
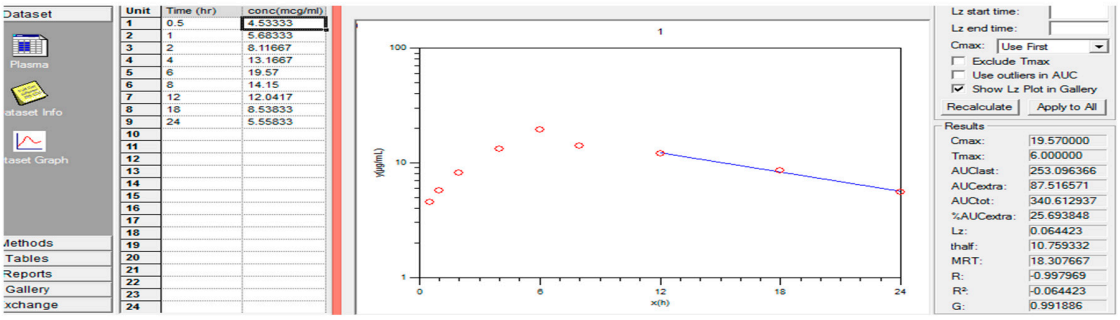
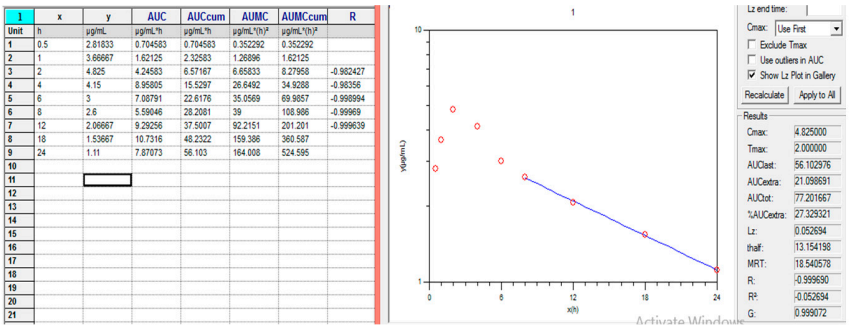



**Figure S2**. In-vitro drug release study of the optimal MH-Loaded PCM Formulation F9 in pH 1.2 acidic media and at pH 7.4 . The pH utilized in the release study was 7.4 to simulate that of the physiological fluid. At pH 1.2 there is initially greater stability.

**For F9:**

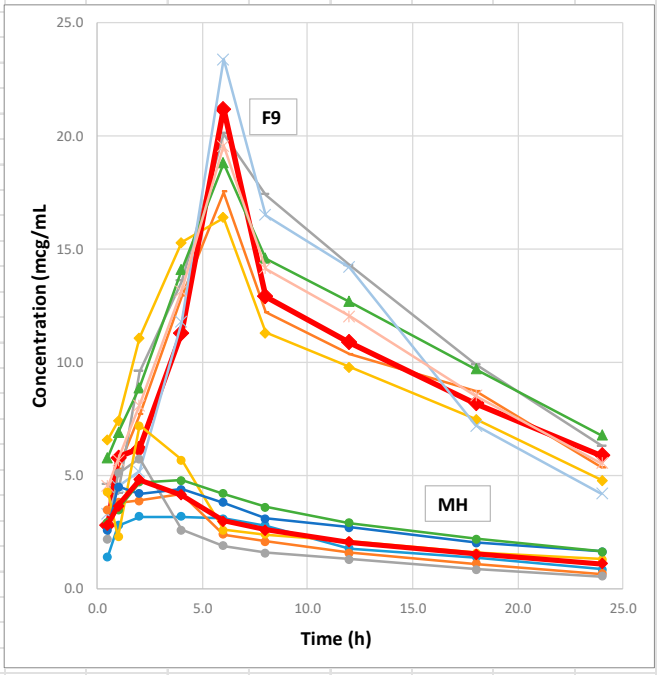



**MH-dispersion:**




| Time | Formula | | | | | | Average | SD |
|---|---|---|---|---|---|---|---|---|
| 0.5 | 4.1 | 4.6 | 6.6 | 2.8 | 5.8 | 3.3 | **4.5** | 1.5 |
| 1.0 | 5.3 | 4.2 | 7.4 | 5.8 | 6.9 | 4.5 | **5.7** | 1.3 |
| 2.0 | 7.7 | 9.6 | 11.1 | 6.2 | 8.9 | 5.2 | **8.1** | 2.2 |
| 4.0 | 12.9 | 13.6 | 15.3 | 11.3 | 14.1 | 11.8 | **13.2** | 1.5 |
| 6.0 | 17.5 | 20.1 | 16.4 | 21.2 | 18.8 | 23.4 | **19.6** | 2.5 |
| 8.0 | 12.2 | 17.4 | 11.3 | 12.9 | 14.6 | 16.5 | **14.2** | 2.4 |
| 12.0 | 10.4 | 14.3 | 9.8 | 10.9 | 12.7 | 14.2 | **12.0** | 2.0 |
| 18.0 | 8.7 | 9.9 | 7.5 | 8.2 | 9.7 | 7.2 | **8.5** | 1.1 |
| 24.0 | 5.4 | 6.3 | 4.8 | 5.9 | 6.8 | 4.2 | **5.6** | 1.0 |

| Time | MH | | | | | | Average | SD |
|---|---|---|---|---|---|---|---|---|
| 0.5 | 1.41 | 3.50 | 2.20 | 4.30 | 2.60 | 2.90 | **2.8** | 1.0 |
| 1.0 | 2.80 | 3.80 | 5.10 | 2.30 | 4.50 | 3.50 | **3.7** | 1.0 |
| 2.0 | 3.20 | 3.90 | 5.75 | 7.20 | 4.20 | 4.70 | **4.8** | 1.4 |
| 4.0 | 3.20 | 4.20 | 2.60 | 5.70 | 4.40 | 4.80 | **4.2** | 1.1 |
| 6.0 | 3.10 | 2.40 | 1.90 | 2.60 | 3.80 | 4.20 | **3.0** | 0.9 |
| 8.0 | 2.80 | 2.10 | 1.60 | 2.40 | 3.10 | 3.60 | **2.6** | 0.7 |
| 12.0 | 1.80 | 1.60 | 1.30 | 2.10 | 2.70 | 2.90 | **2.1** | 0.6 |
| 18.0 | 1.40 | 1.10 | 0.87 | 1.60 | 2.05 | 2.20 | **1.5** | 0.5 |
| 24.0 | 0.85 | 0.67 | 0.54 | 1.30 | 1.65 | 1.65 | **1.1** | 0.5 |




**The heavy red lines are the Average Values**

**Figure S3.** Experimental data for the concentration profiles of morin hydrate *vs* time after oral administration of optimized F9 PCM formula *Left:* F9 (*top*) and MH dispersion (*bottom*) to each of six animals with each reagent. The thick red lines are the profiles of the average concentration values at each data point. *Right:* . MERS-CoV plaque assays ± S.D.