

# About OMICS Group

- OMICS Group is an amalgamation of Open Access Publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 500 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 500 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

# OMICS International Conferences

OMICS International is a pioneer and leading science event organizer, which publishes around 500 open access journals and conducts over 500 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

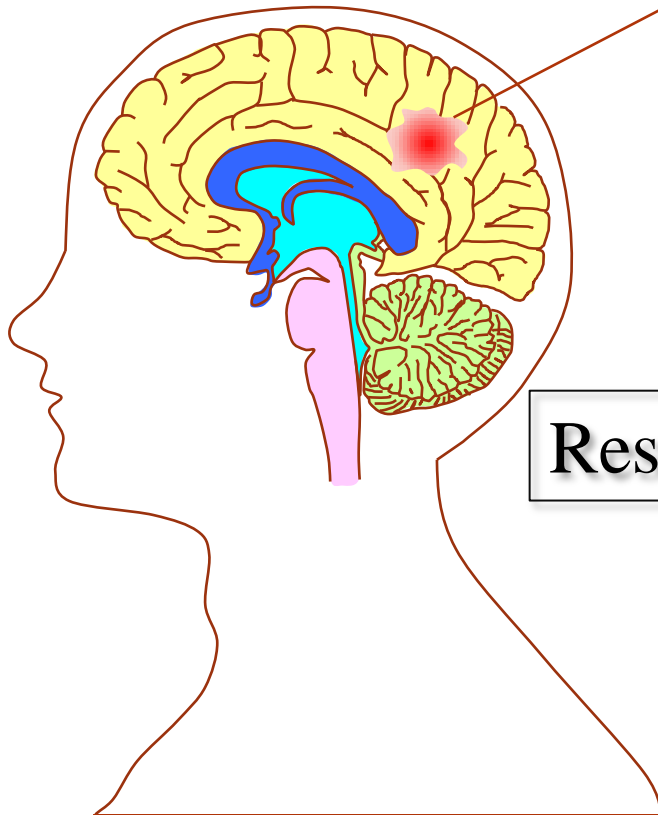
# Targeting delivery of etoposide to inhibit the growth of human glioblastoma multiforme using lactoferrin- and folic acid-grafted poly(lactide-*co*-glycolide) nanoparticles

Department of Chemical Engineering, National Chung Cheng University,  
Chia-Yi, Taiwan 62102, Republic of China



# Introduction

Glioblastoma multiforme (GBM)



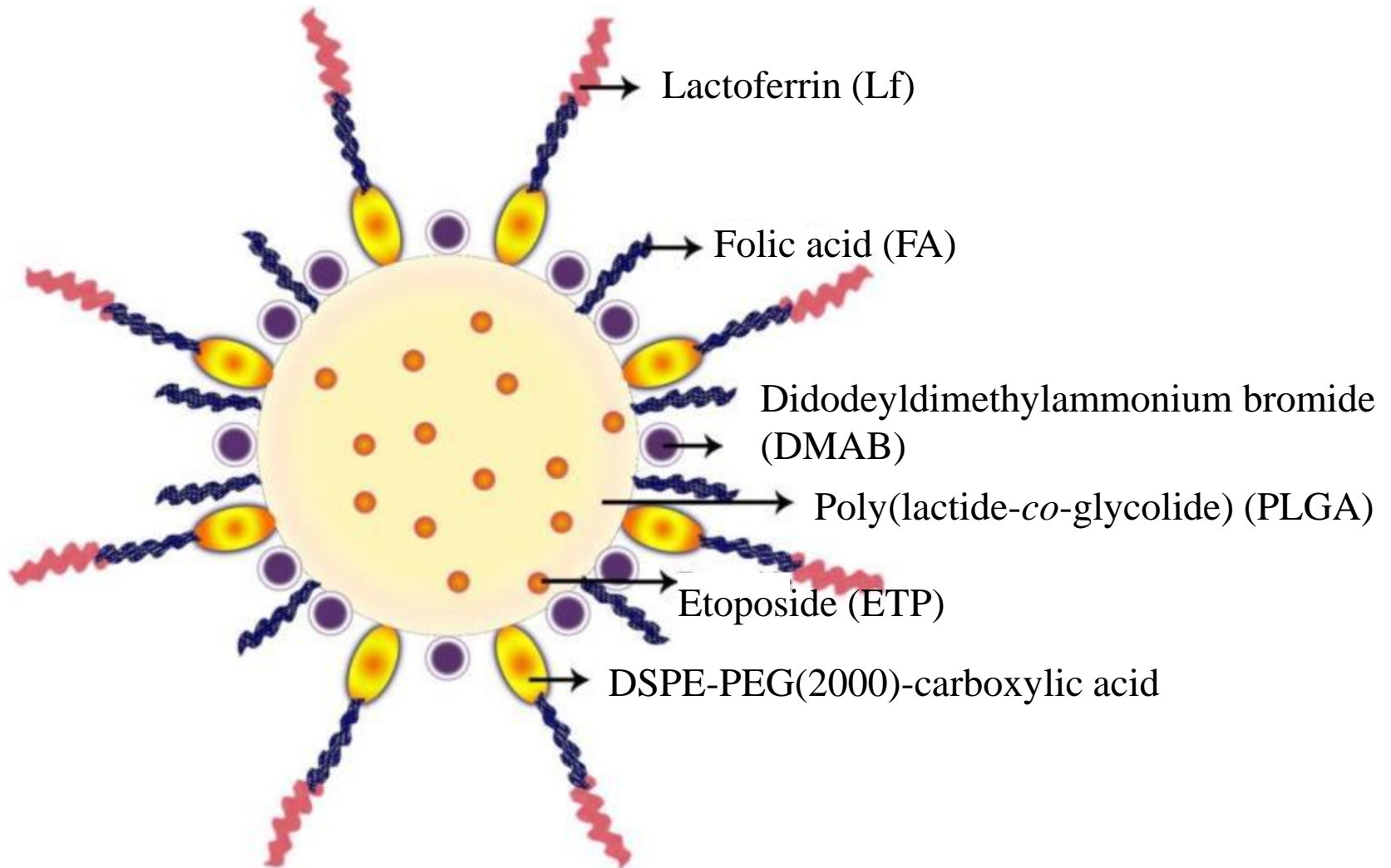
Resection

Antiangiogenic therapy

Chemotherapy

Radioative therapy

Supportive care



**Figure 1.** An schematic structure of an Lf-FA-ETP-PLGA nanoparticle (NP).

# Produce ETP encapsulated PLGA formulations with FA and Lf grafting

## Physicochemical property

Morphology

Average diameter and zeta potential

Grafting efficacy of FA and Lf

Entrapment efficacy of ETP

Dissolution of ETP

## *In-Vitro* test

TEER and permeability for BBB model

Viability of BBB cells with PLGA NPs stimulation

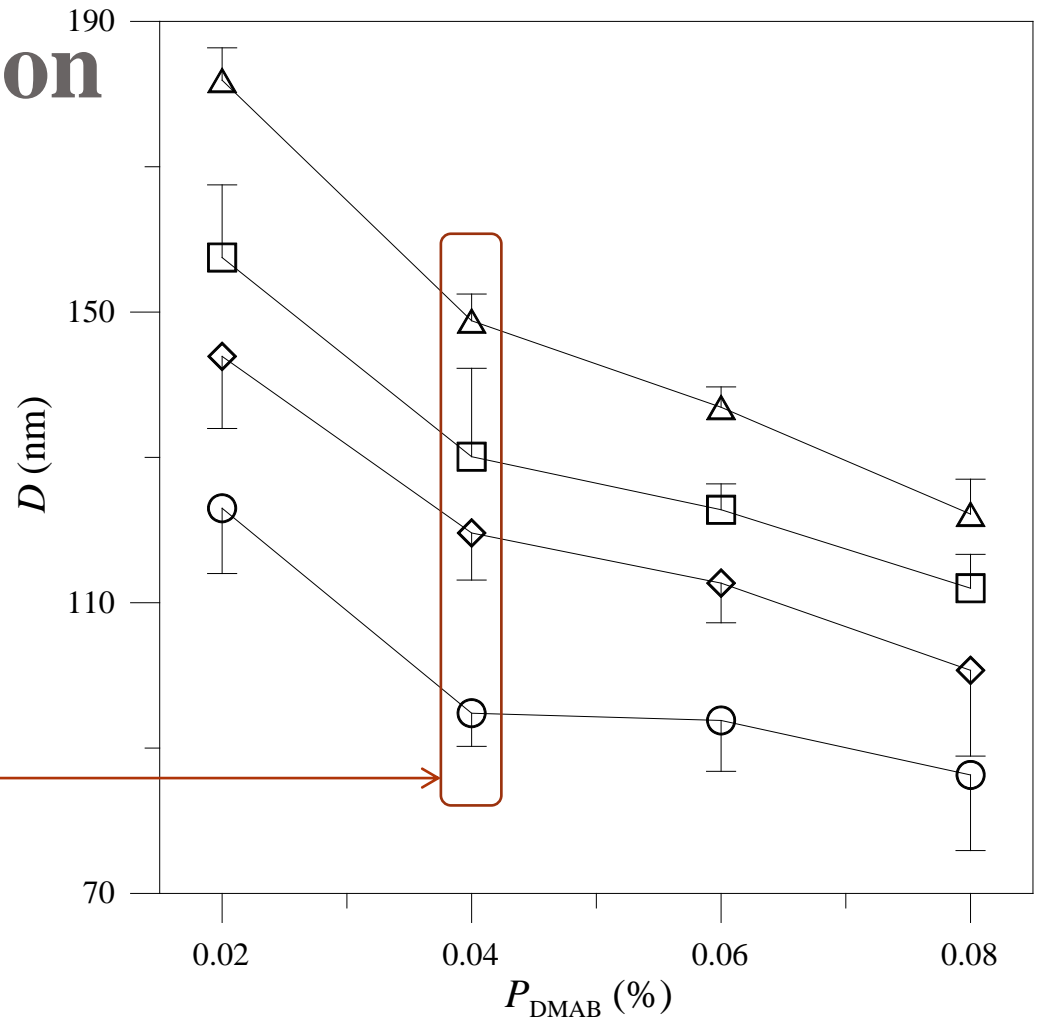
Viability of U87MG cells with PLGA NPs stimulation

Immunochemical staining of HBMECs

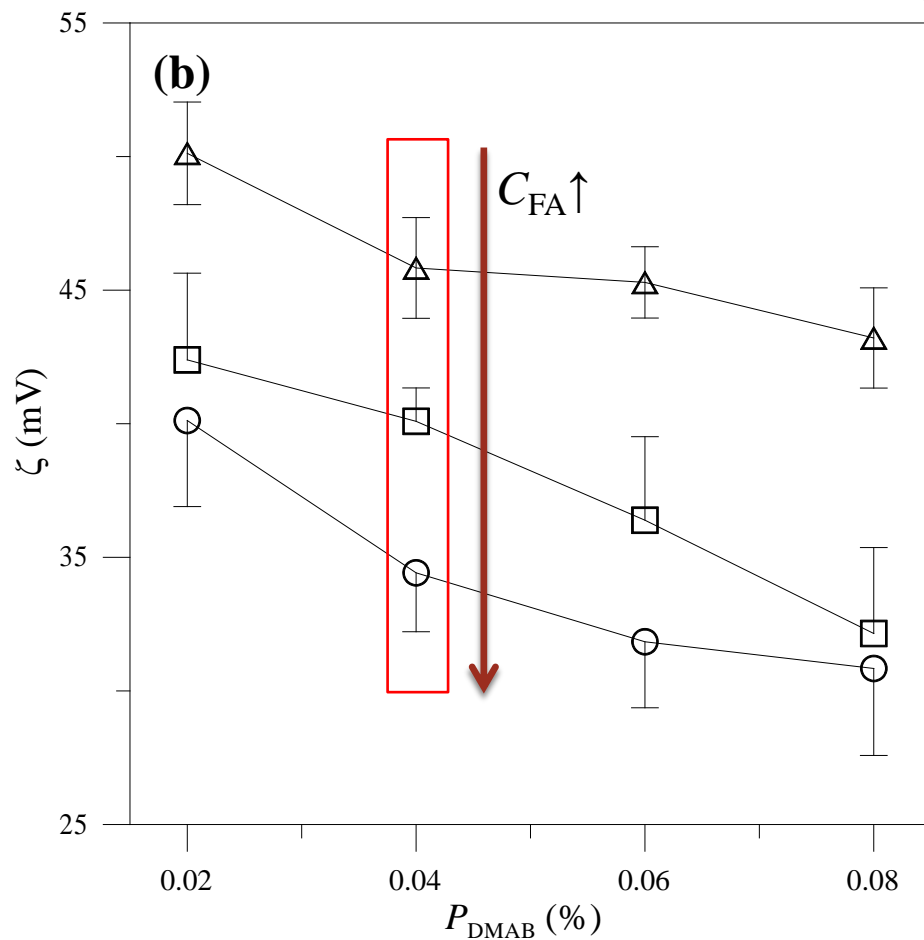
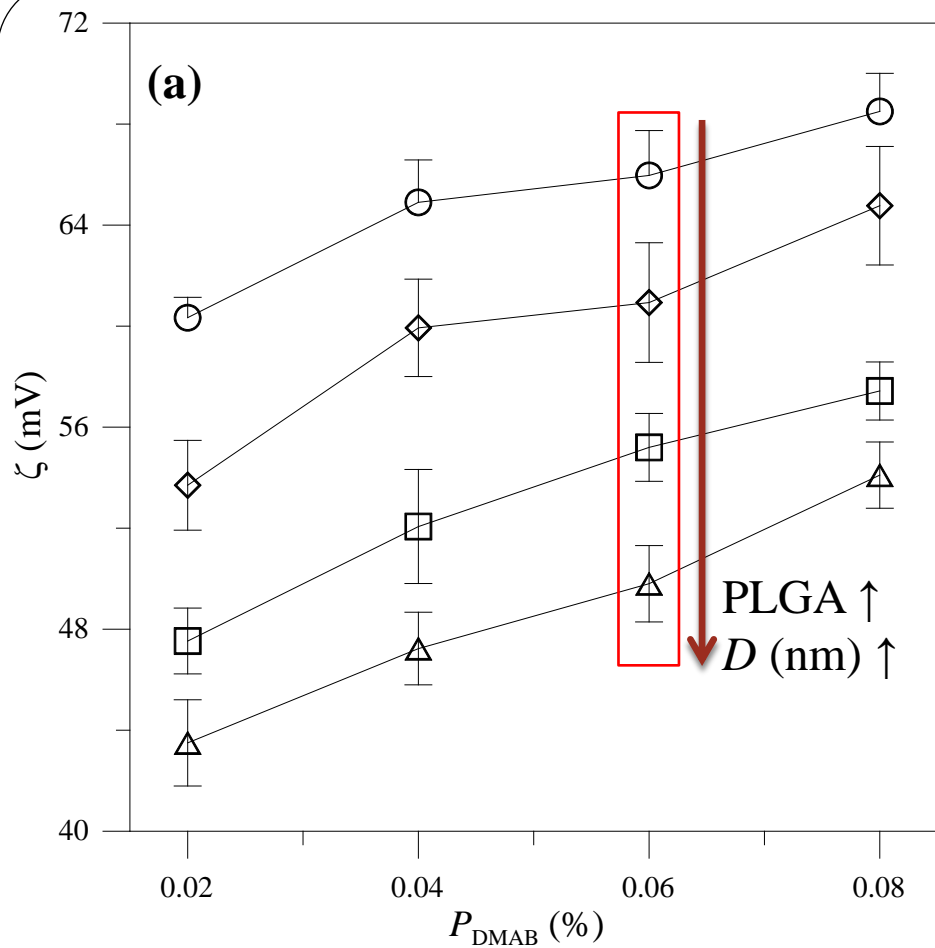
Immunochemical staining of U87MG cells

# Result and discussion

At a high level of PLGA, probability of polymeric collision increased during emulsification and the enhanced viscosity of organic phase reduced fluidic mobility.

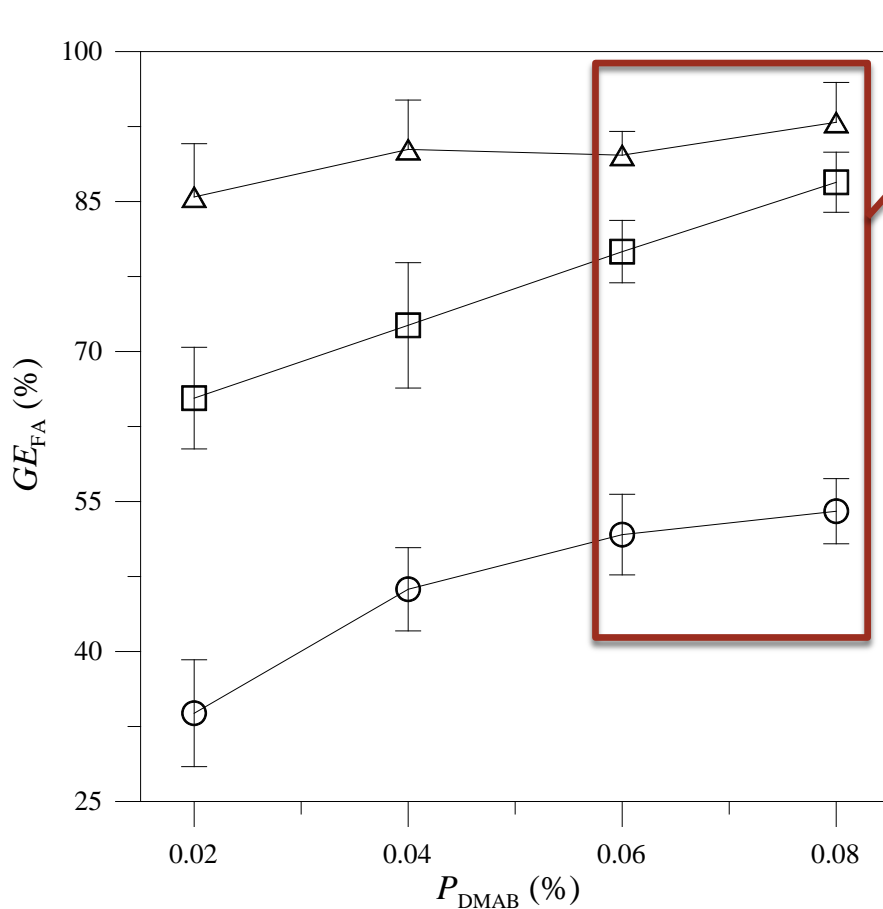


**Figure 2.** Effect of DMAB weight percentage on average diameter. (○)  $P_{PLGA} = 0.02\%$  (w/v); (◇)  $P_{PLGA} = 0.04\%$  (w/v); (□)  $P_{PLGA} = 0.06\%$  (w/v); (△)  $P_{PLGA} = 0.08\%$ .  $n = 3$ .



**Figure 3.** Effect of DMAB weight percentage on zeta potential. (a): ( $\circ$ )  $P_{\text{PLGA}} = 0.02\%$  (w/v); ( $\diamond$ )  $P_{\text{PLGA}} = 0.04\%$  (w/v); ( $\square$ )  $P_{\text{PLGA}} = 0.06\%$  (w/v); ( $\triangle$ )  $P_{\text{PLGA}} = 0.08\%$ ; (b):  $P_{\text{PLGA}} = 0.02\%$  (w/v). ( $\triangle$ )  $C_{\text{FA}} = 0.01\%$  (w/v); ( $\square$ )  $C_{\text{FA}} = 0.05\%$  (w/v); ( $\circ$ )  $C_{\text{FA}} = 0.1\%$  (w/v).  $n = 3$ .



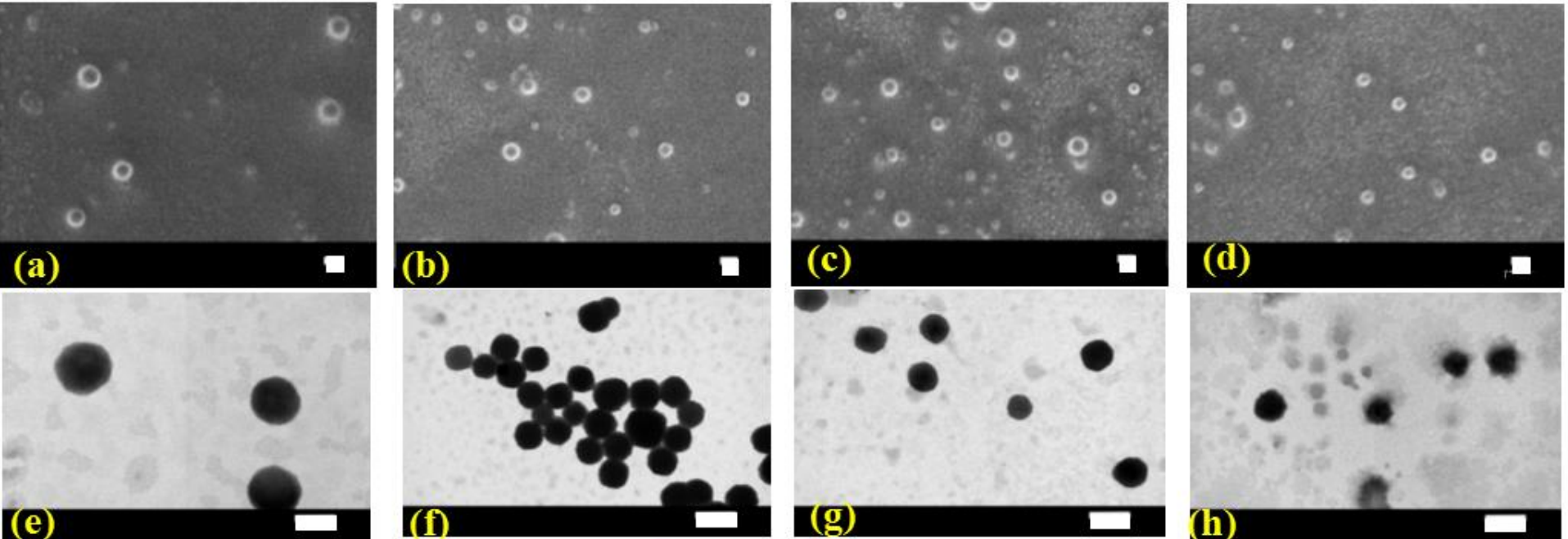


**Saturation of grafting site for free FA.**

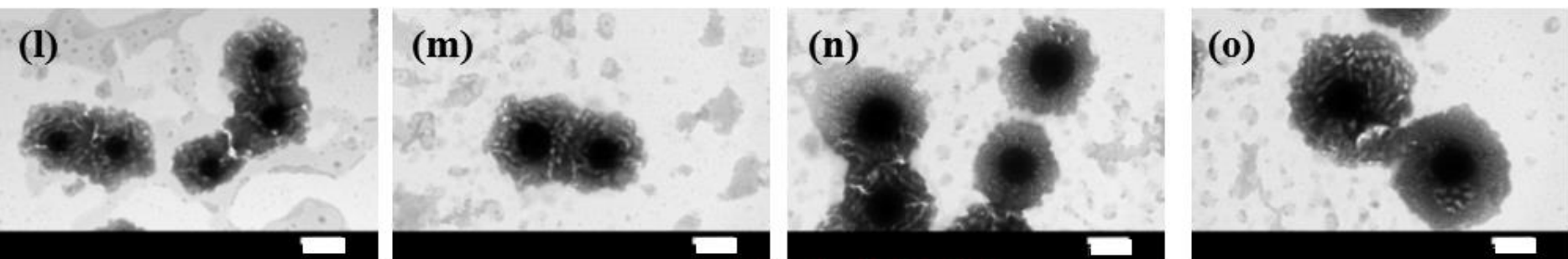
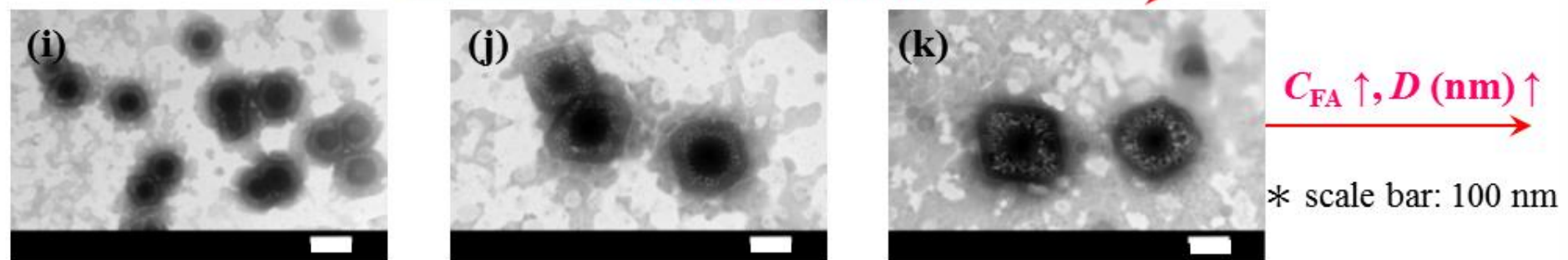
**Table 1.** The concentration of Lf versus zeta potential and grafting efficiency of Lf.

$P_{Lf}$ (%) (w/v)	$\zeta$ (mV)	$GE_{Lf}$ (%)
<b>0</b>	$30.841 \pm 3.253$	-
<b>0.02</b>	$32.147 \pm 2.035$	$94.965 \pm 2.215$
<b>0.04</b>	$34.595 \pm 4.938$	$77.278 \pm 4.548$
<b>0.06</b>	$39.192 \pm 3.193$	$56.412 \pm 2.889$
<b>0.08</b>	$40.212 \pm 2.844$	$40.070 \pm 3.416$

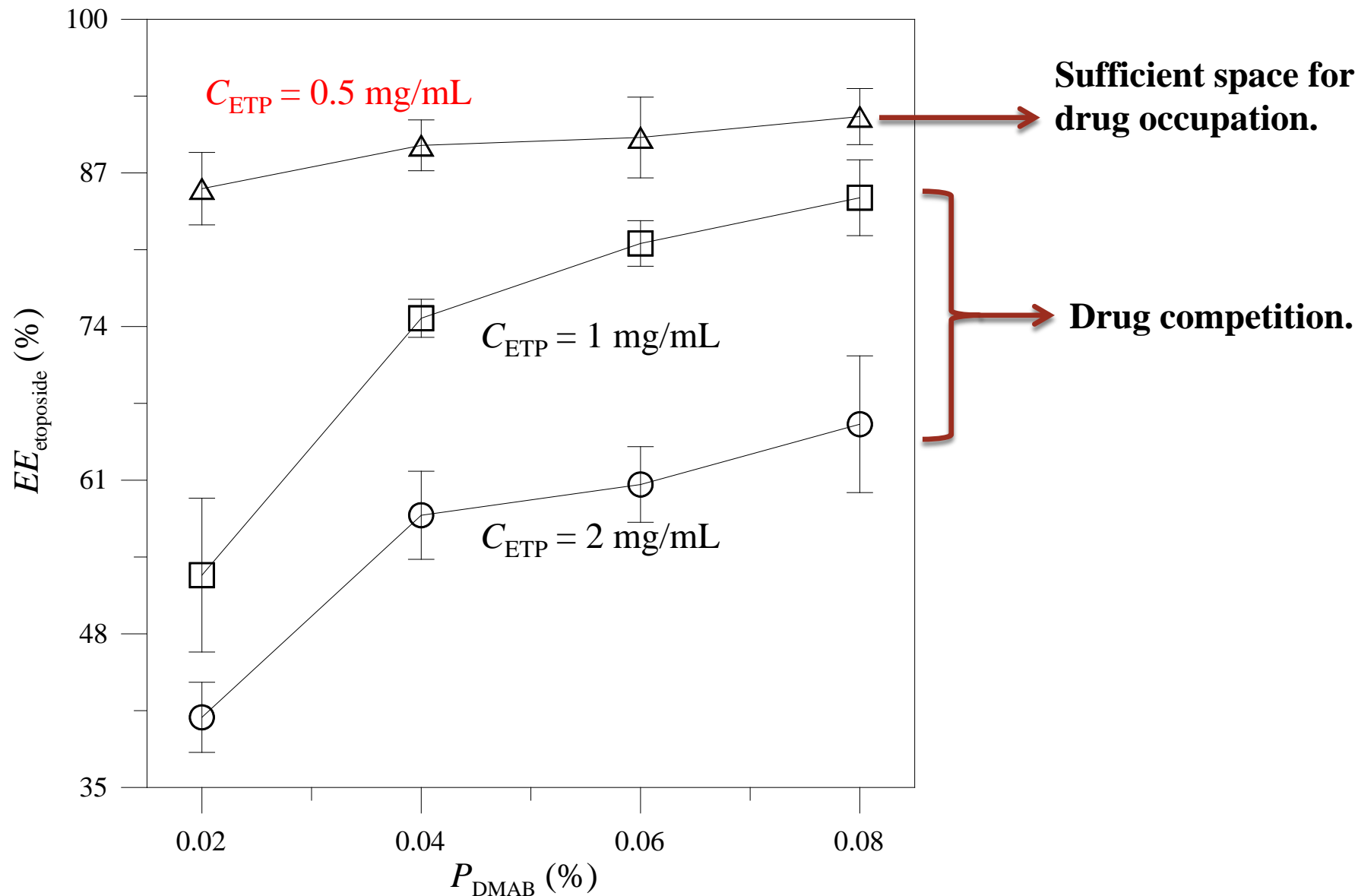
**Figure 4.** Effect of DMAB weight percentage on FA grafting efficiency.  $P_{PLGA} = 0.02\%$  (w/v). ( $\Delta$ )  $C_{FA} = 0.01\%$  (w/v); ( $\square$ )  $C_{FA} = 0.05\%$  (w/v); ( $\circ$ )  $C_{FA} = 0.1\%$  (w/v).  $n = 3$ .



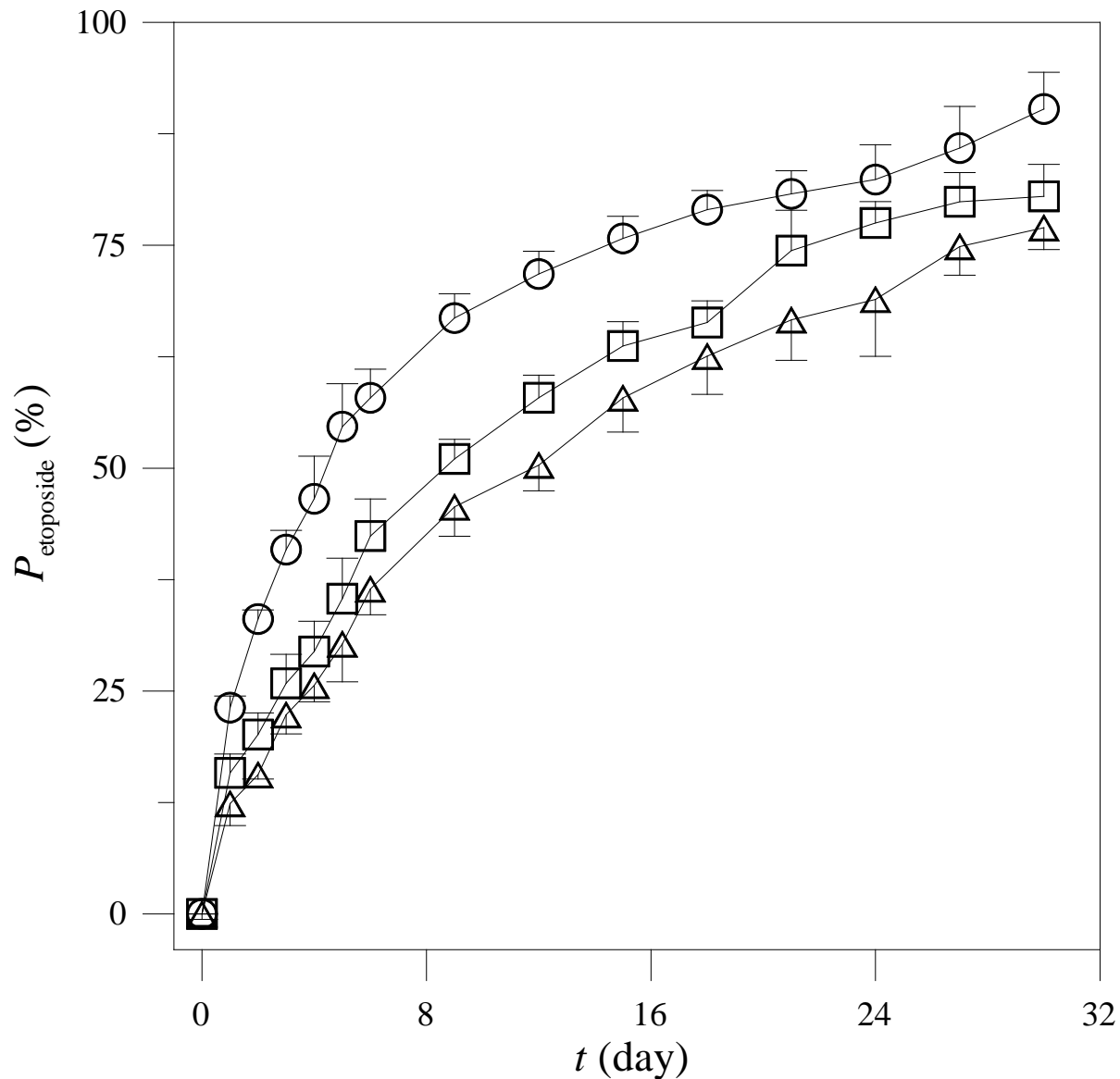
$P_{\text{DMAB}} \uparrow, D \text{ (nm)} \downarrow$



$C_{\text{Lf}} \uparrow, D \text{ (nm)} \uparrow$

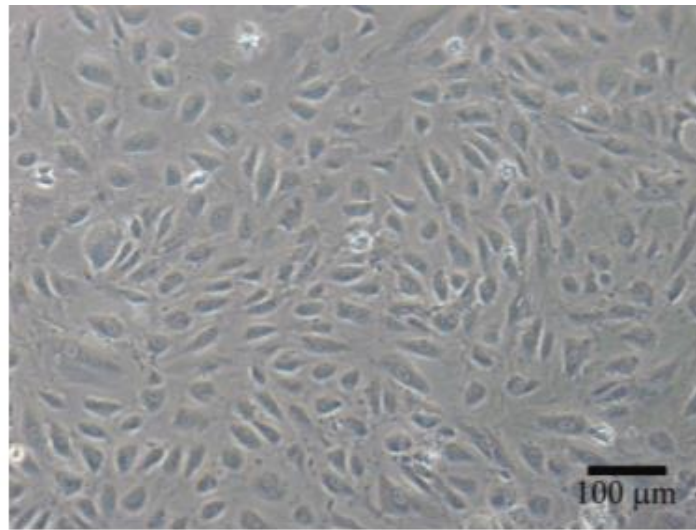


**Figure 5.** Effect of DMAB weight percentage on ETP entrapment efficiency.  $P_{\text{PLGA}} = 0.02\%$  (w/v). ( $\triangle$ )  $C_{\text{ETP}} = 0.5 \text{ mg/mL}$ ; ( $\square$ )  $C_{\text{ETP}} = 1 \text{ mg/mL}$ ; ( $\circ$ )  $C_{\text{ETP}} = 2 \text{ mg/mL}$ .  $n = 3$ .



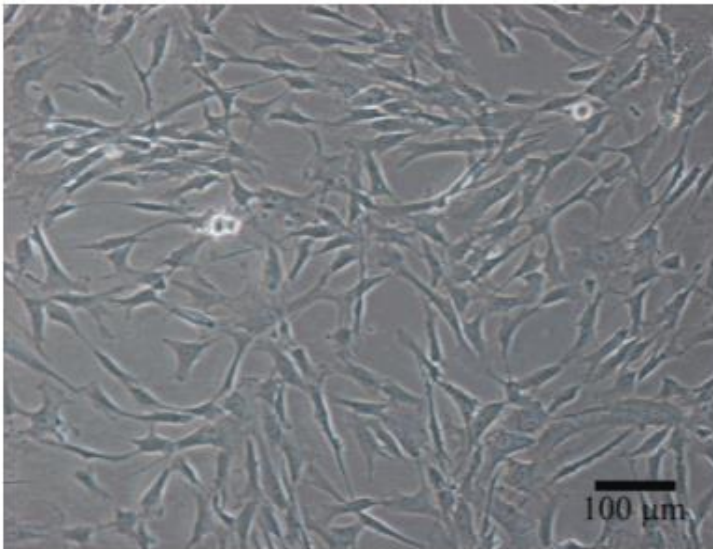
**Figure 6.** Dissolution profile for ETP from PLGA NP formulation.  $P_{\text{PLGA}} = 0.02\%$ ,  $P_{\text{DMAB}} = 0.08\%$ ,  $C_{\text{ETP}} = 2 \text{ mg/mL}$ . ( $\circ$ ) PLGA NPs; ( $\square$ ) FA-ETP-PLGA NPs,  $P_{\text{FA}} = 0.1\%$ ; ( $\triangle$ ) Lf-FA-ETP-PLGA NPs,  $P_{\text{Lf}} = 0.08\%$ ,  $P_{\text{FA}} = 0.1\%$ .  $n=3$ .

**(a)**



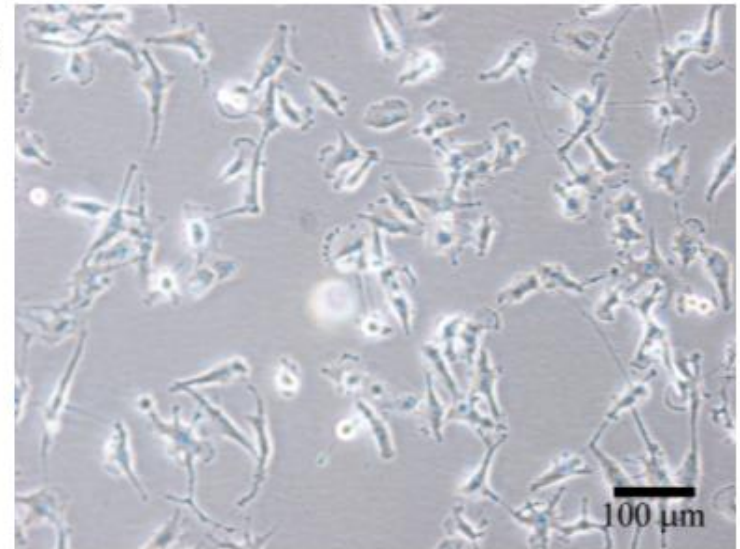
**HBMECs**

**(b)**



**HAs**

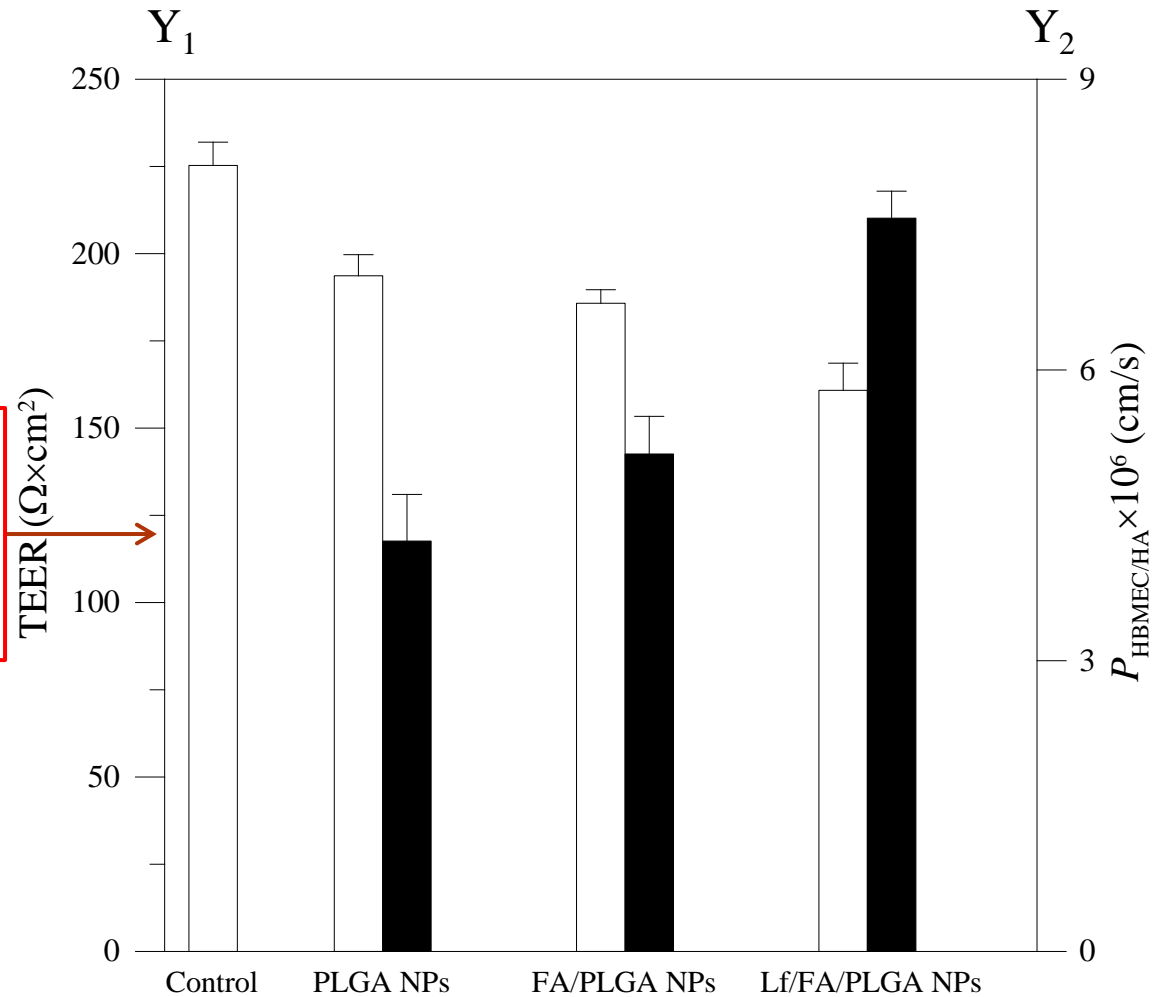
**(c)**



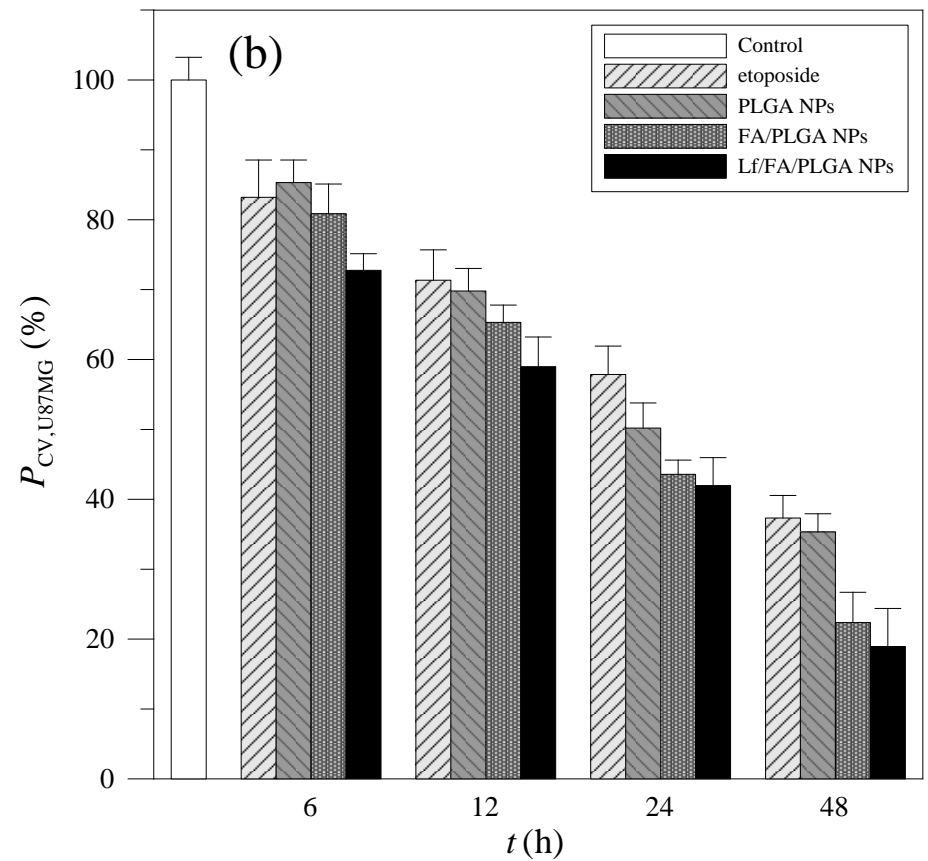
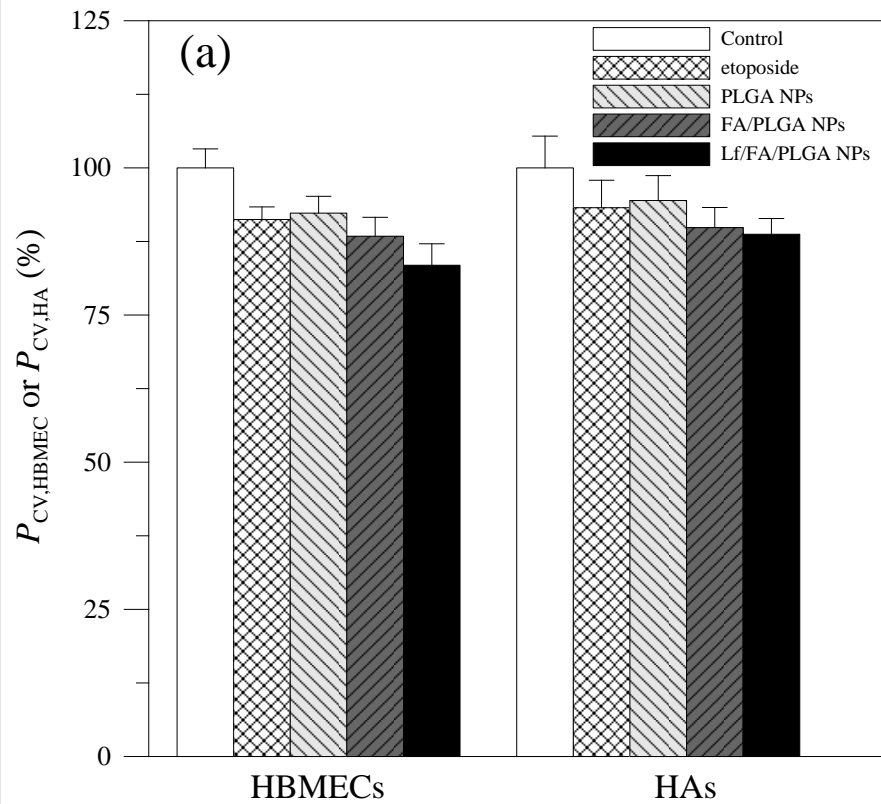
**U87MG cells**

**Figure 7.** Morphology of HBMECs, HAs and U87MG cells. (a) HBMECs cultured at day 6; (b) HAs cultured at day 6; (c) U87MG cells cultured at day 4.

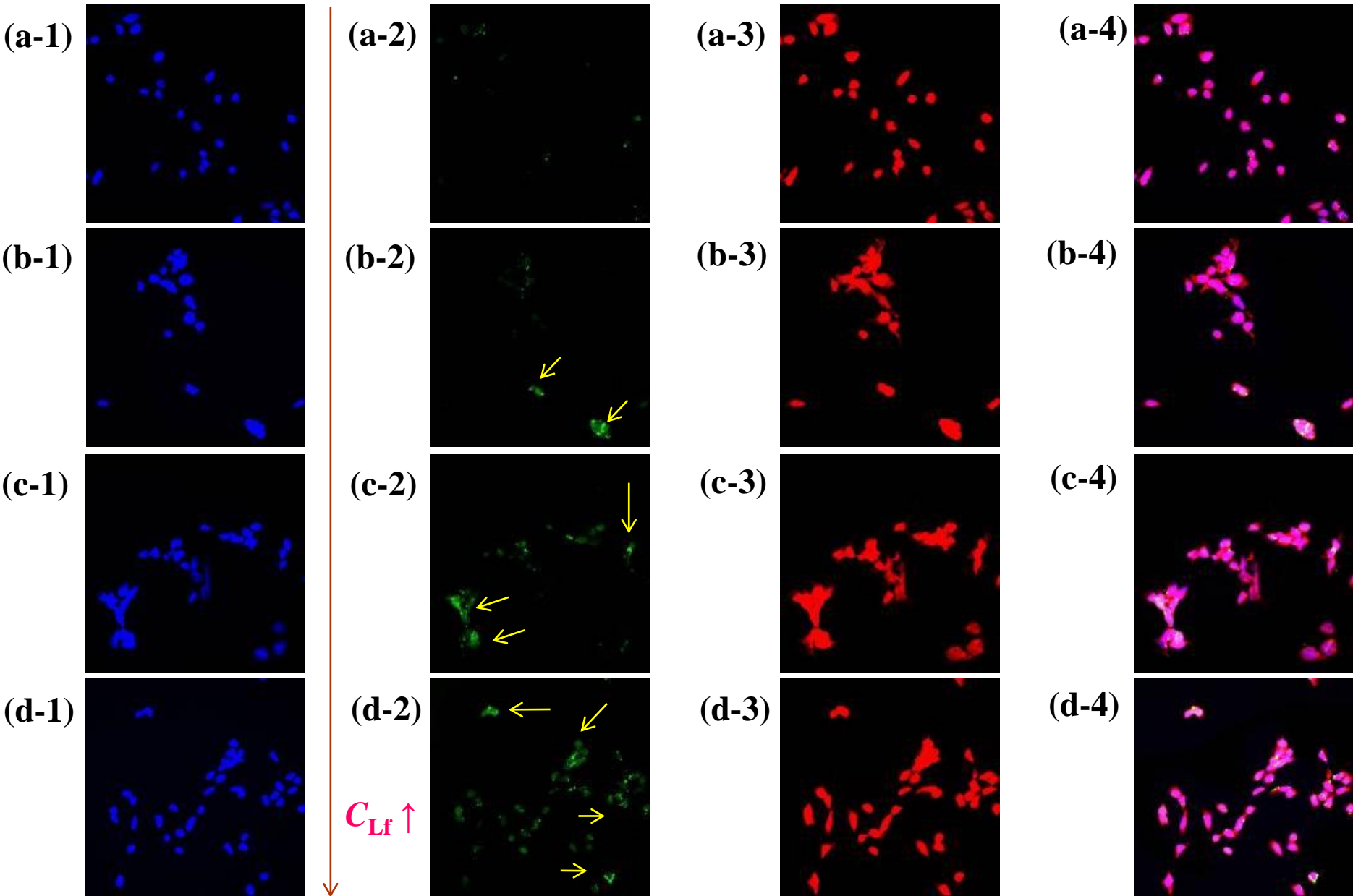
The blood-brain barrier (BBB) model was satisfactory and reasonable when TEER was over  $120 \Omega \times \text{cm}^2$ .



**Figure 8.** TEER and permeability of ETP across the monolayer of HBMECs/HAs using PLGA formulation.  $P_{\text{PLGA}} = 0.02\%$ ;  $P_{\text{DMAB}} = 0.08\%$ ;  $P_{\text{FA}} = 0.1\%$ ;  $P_{\text{Lf}} = 0.08\%$ ,  $C_{\text{ETP}} = 2 \text{ mg/mL}$ . White bar: TEER, Y<sub>1</sub>; black bar: permeability, Y<sub>2</sub>.  $n = 3$ .

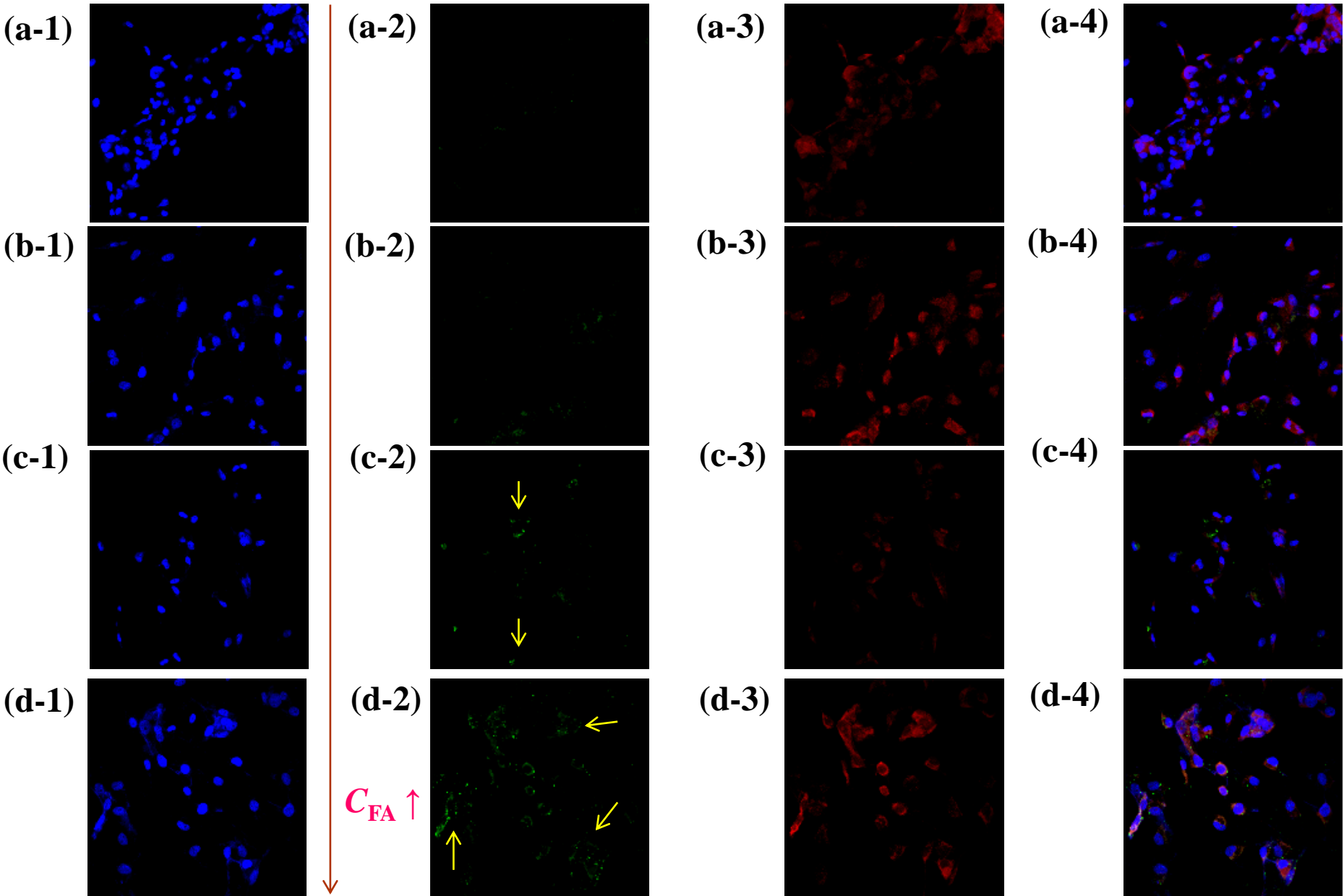


**Figure 9.** (a) Viability of HBMECs, HAs after treatment with PLGA NP formulation; (b) viability of U87MG cells by treatment with PLGA NP formulation over 48 hours.  $n = 3$ .



**Figure 10.** Immunofluorescence staining images of Lf-FA-ETP-PLGA NPs interacting with HBMECs.  $P_{\text{PLGA}} = 0.02\%$ ,  $P_{\text{DMAB}} = 0.08\%$ ,  $C_{\text{ETP}} = 2 \text{ mg/mL}$ . (a-#)  $C_{\text{Lf}} = 0.02\%$ ; (b-#)  $C_{\text{Lf}} = 0.04\%$ ; (c-#)  $C_{\text{Lf}} = 0.06\%$ ; (d-#)  $C_{\text{Lf}} = 0.08\%$ ; (\*-1): nuclei for blue; (\*-2): Lf-FA-ETP-PLGA NPs for green; (\*-3): Lf receptor for red; (\*-4): merged image. \* is 1, 2, 3, or 4; \* is a, b, c, or d.





**Figure 11.** Immunofluorescence staining images of Lf-FA-ETP-PLGA NPs interacting with U87MG cells.  $P_{PLGA} = 0.02\%$ ,  $P_{DMAB} = 0.08\%$ ,  $C_{ETP} = 2 \text{ mg/mL}$ . (a-#)  $C_{FA} = 0\%$ ; (b-#)  $C_{FA} = 0.01\%$ ; (c-#)  $C_{FA} = 0.05\%$ ; (d-#)  $C_{FA} = 0.01\%$ ; (\*-1): nuclei for blue; (\*-2): Lf-FA-ETP-PLGA NPs for green; (\*-3): folate receptor for red; (\*-4): merged image. \* is 1, 2, 3, or 4; \* is a, b, c, or d.

# Conclusions

- PLGA NPs incorporated with DMAB can increase the physical stability via enhancing zeta potential.
- The biocompatibility of PLGA formulation to the BBB cells was quite high and suitable for drug delivery system.
- PLGA NPs grafted with Lf and FA could enhance the permeability across the BBB and the internalization of PLGA NPs for inhibiting the proliferation of malignant glioblastoma cells.

- Thank you for attention!

# Let us meet again..

---

We welcome you to our future conferences of OMICS International

**2<sup>nd</sup> International Conference and Expo**

**on**

**Drug Discovery & Designing**

**On**

**October -31 November-02, 2016 at Istanbul, Turkey**

<http://drug-discovery.pharmaceuticalconferences.com/>