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TEM1-targeting PEGylated PLGA shikonin nanoformulation for immunomodulation and eradication of ovarian cancer

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Table S1. Drug loading characteristics before and after modifications

Parameters' equations	**Plain NPs**	**PEGylated NPs**	**Fc-armed NPs**
$DC\% = (\frac{D_t\ mass - D_f\ mass}{NP\ mass}) \times 100$	10.7	9.1	8.9
$DE\% = (\frac{D_t\ mass - D_f\ mass}{D_t\ mass}) \times 100$	91.5	76.1	78.3
$DL\% = (\frac{D_t\ mass - D_f\ mass}{P_t\ mass}) \times 100$	10.8	9.0	9.2
$YE\% = (\frac{NP\ mass}{D_t\ mass + P_t}) \times 100$	96.5	88.4	92.5

(DC%, DE%, and *DL%,:* Drug content, entrapment and loading efficiencies *respectively, YE%:* process yielding efficiency.

Table S2. The kinetics models used to fit the release data

Kinetic model	Equation	The coefficient of determination (R^2)			
		pH 4.4	pH 5.4	pH 6.4	pH 7.4
Zero-order	$F = k_0 t$	0.846	0.837	0.854	0.760
First-order	$Ln(1-F) = -k_f t$	0.952	0.892	0.928	0.932
Higuchi	$F = k_H \sqrt{t}$	0.846	0.837	0.854	0.760
Power law (Korsmeyer-Peppas)	$LnF = Lnk_p + pLnt$	0.924	0.924	0.788	0.886
Square root of mass	$1 - \sqrt{1-F} = k_{\frac{1}{2}} t$	0.888	0.879	0.888	0.837
Hixson-Crowell	$1 - \sqrt[3]{1-F} = k_{\frac{1}{3}} t$	0.933	0.882	0.915	0.900
Three seconds root of mass	$1 - \sqrt[3]{(1-F)^2} = k_{\frac{2}{3}} t$	0.906	0.904	0.805	0.864
Weibull	$Ln[-Ln(1-F)] = -\beta Ln\, t_d + \beta Lnt$	0.885	0.880	0.740	0.836
Linear probability	$Z = Z_0 + qt$	0.638	0.749	0.637	0.563
Wagner Log – probability	$Z = Z'_0 + q' Lnt$	0.991	0.991	0.982	0.994
Hopfenberg	$\frac{F}{F'} = 1 - [1 - \frac{k_0 t}{F_L a}]^n$	0.846	0.837	0.854	0.760
Baker Lonsdale	$\frac{3}{2}\left[1 - \left(1 - \frac{F}{100}\right)^{\frac{2}{3}}\right] - \left(\frac{F}{100}\right) = kt$	0.790	0.840	0.820	0.780
Gompertz	$F = F' e^{[-ae^{\beta log t}]}$	0.811	0.797	0.771	0.756
Quadratic	$F = 100(kt^2 + kt)$	0.807	0.797	0.815	0.715
Logistic	$F = \frac{F'}{[1+ae^{\beta log t}]}$	0.961	0.811	0.804	0.915

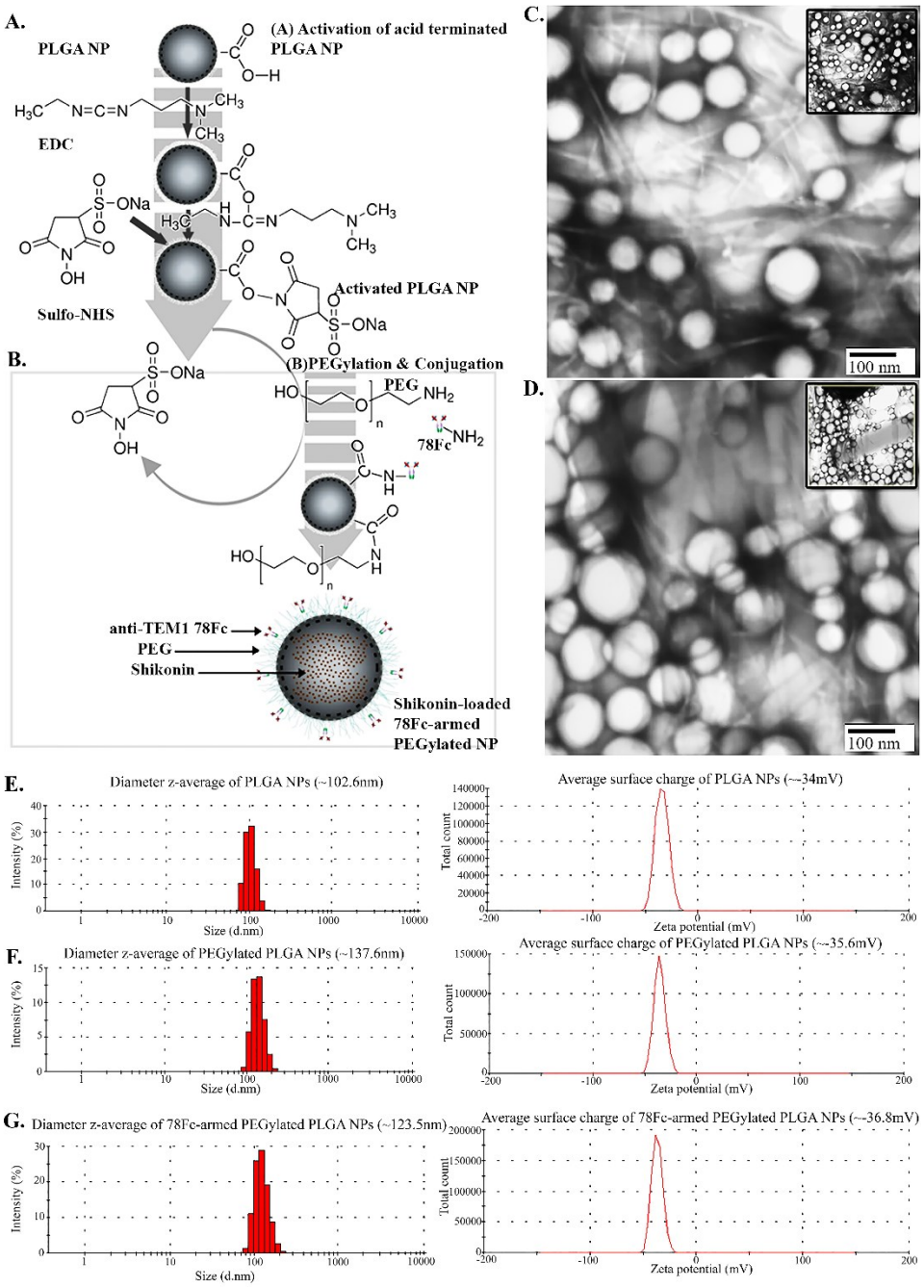

Fig. S1. Antibody-armed PEGylated shikonin (SHK)-loaded SHK-loaded poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs). A) Schematic illustration of PEGylation and antibody conjugation. Activation of poly (D,L-lactide-co-glycolide) (PLGA) nanoparticles (NPs) by N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (EDC), N-hydroxysulfosuccinimide (NHS). B) One-step PEGylation and antibody conjugation. C) Transmission electron microscopy (TEM) micrographs of PLGA PEGylated NPs (inset: size distribution). D) TEM image of PLGA PEGylated anti-TEM1 78Fc conjugated NPs (inset: size distribution). E) The size distribution and zeta potential of unmodified SHK-loaded PLGA NPs. F) The size distribution and zeta potential of SHK-loaded PEGylated PLGA NPs. G) The size distribution and zeta potential of SHK-loaded PEGylated anti-TEM1 Fc conjugated PLGA NPs.