Supporting information

Folate decorated delivery of self assembled betulinic acid nano fibers: A biocompatible anti-leukemic therapy

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Running title: Cancer targeted delivery of self assembled betulinic acid through folate receptor

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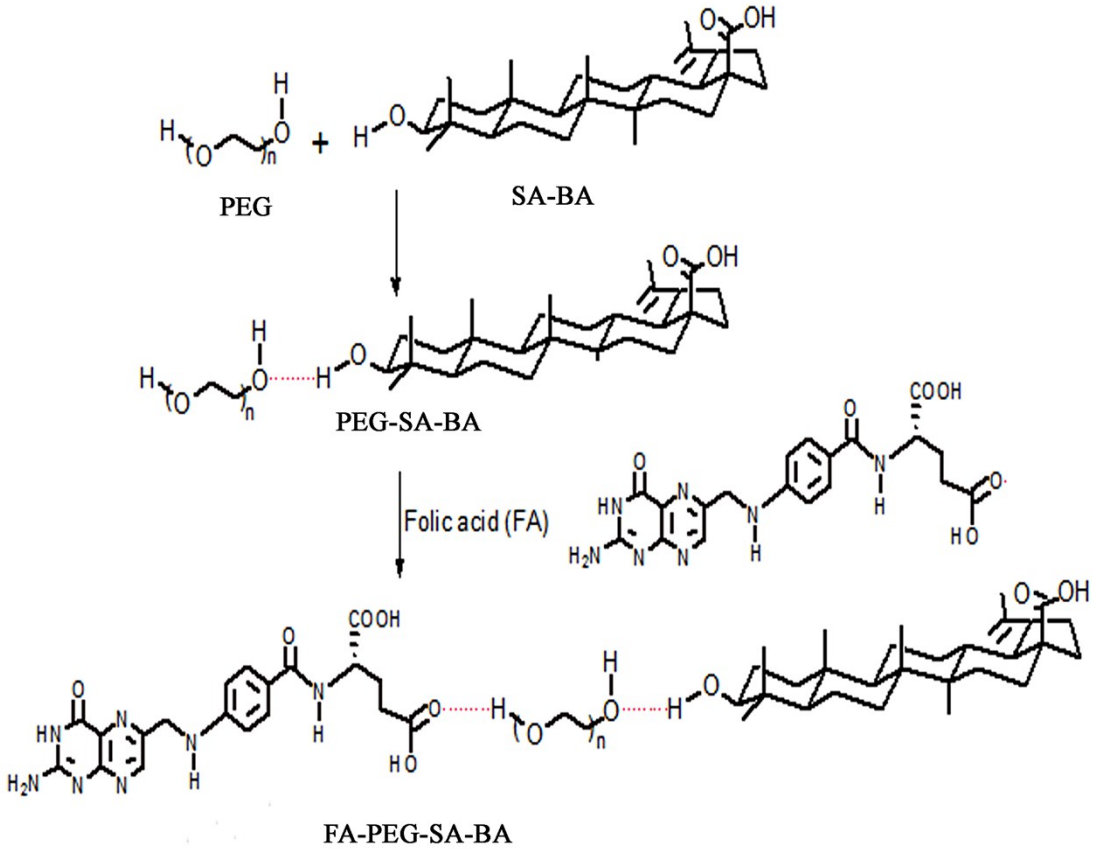
SL. No	Composition	Dry weight of conjugates (mg)	Encapsulation efficiency (EF %)	Loading capacity (LC %)
1.	PEG+SA-BA	10+2	86.47±1.068	74.31±1.629
2.	FA+PEG-SA-BA	1.5+5	61.77±2.058	59.438±2.047
3.	FA+PEG-SA-BA	2.5+5	96.22±1.73	83.661±2.840

Table S1: Encapsulation efficiency (EE) and loading capacity (LC) of PEG with SA-BA and FA with PEG-SA-BA.



Scheme S1: Schematic representation of synthesis of BA-PEG and FA-PEG-BA conjugates.

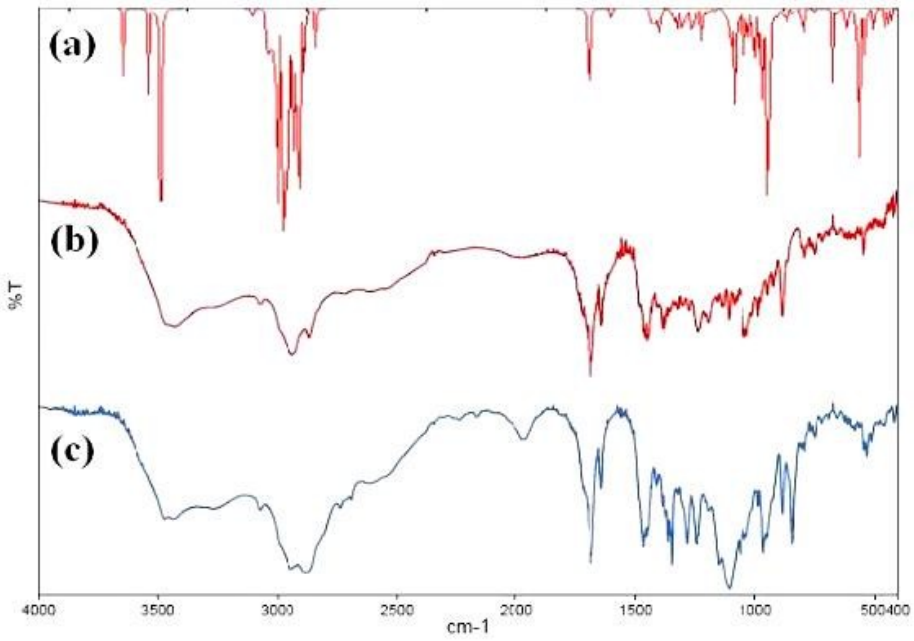


Figure S1: FTIR spectrum: (**a**) Theoretical IR of the mixture of SA-BA and PEG (PEG-SA-BA), (**b**) only SA-BA, and (**c**) experimental FTIR of the mixture of SA-BA and PEG (PEG-SA-BA).

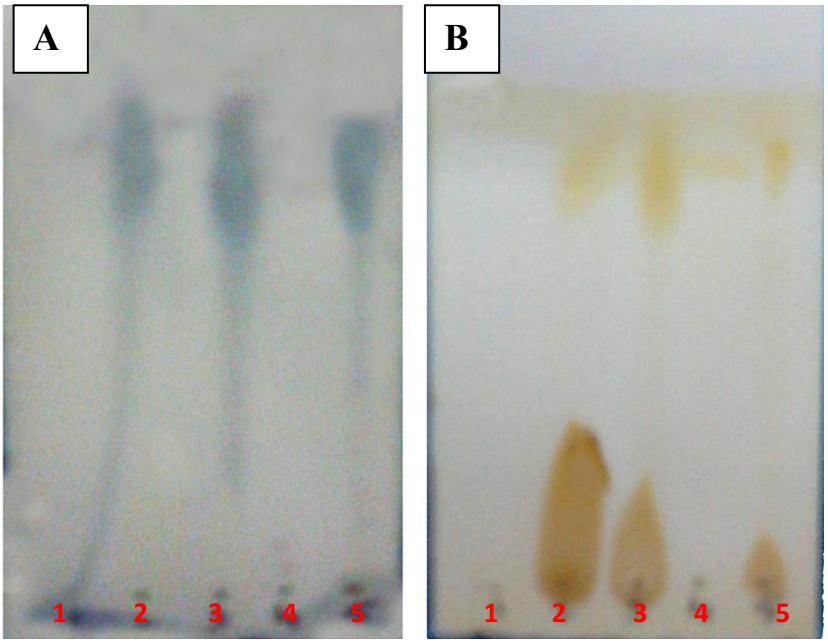
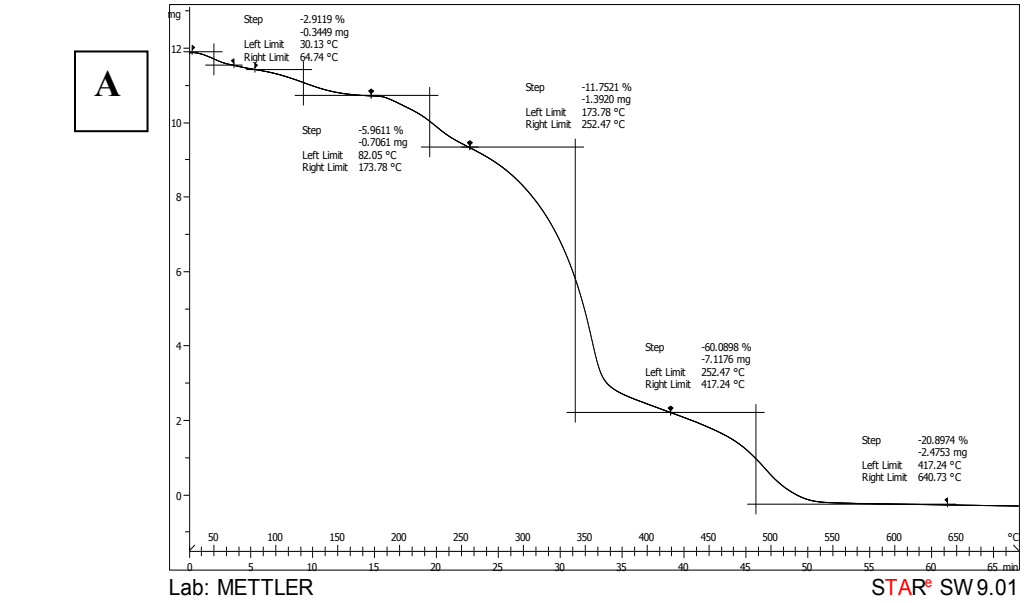


Figure S2: Thin layer chromatography identification of successful synthesized FA-PEG-SA-BA. **A**: The chromatographic paper stained with PMA solution and **B**: The chromatographic paper stained with Iodine vapor. Here, 1= SA-BA; 2=PEG; 3=PEG-SA-BA; 4=FA; 5=FA-PEG-SA-BA



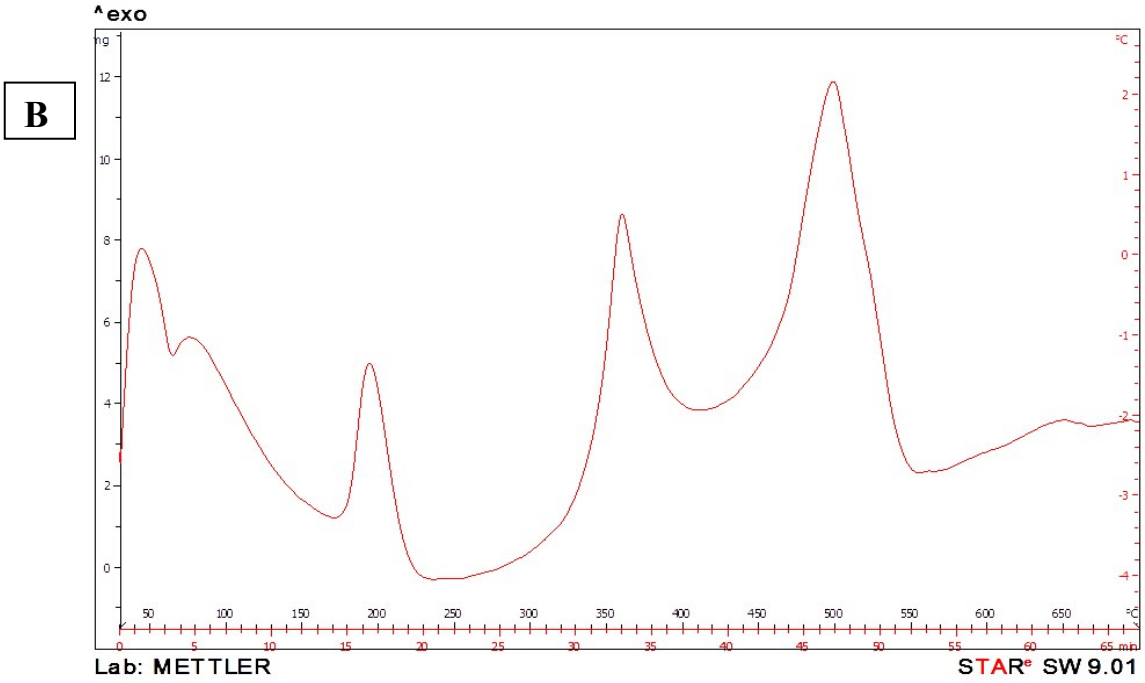


Figure S3: Thermogravimetry analysis of FA-PEG-SA-BA composite. Here: (**A**): Graphical representation of TGA data of FA-PEG-SA-BA and (**B**): Graphical representation of SDTA data of FA-PEG-SA-BA.

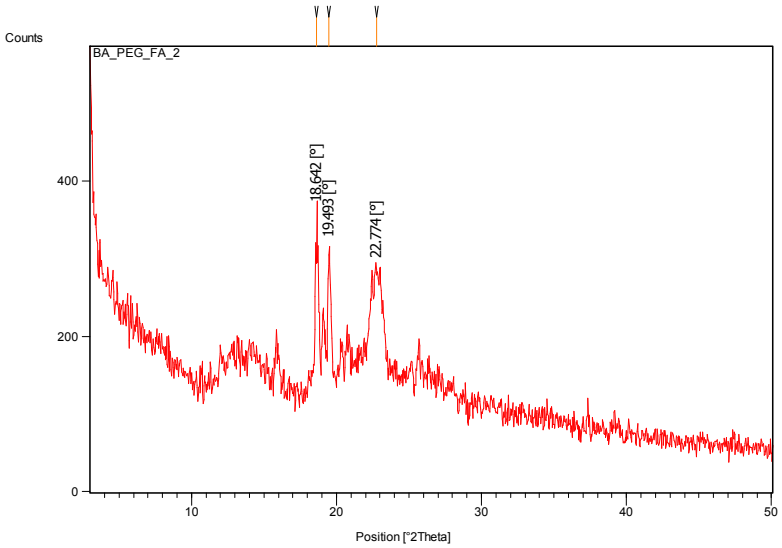


Figure S4: X-Ray diffraction analysis of FA-PEG-SA-BA.

PEG-SA-BA: 1H-NMR (300 MHz, $CDCl_3$) δ: 3.65 (O-CH_2, s), 4.66 (1H, s), 4.53 (1H, s), 1.68 (6H, s), 0.96(3H, s), 0.93 (3H, s), 0.82 (3H, s), 0.75 (3H, s).

The appearance of peaks for polyethylene glycol and betulinic acid indicated the formation of PEG-SA-BA conjugate.

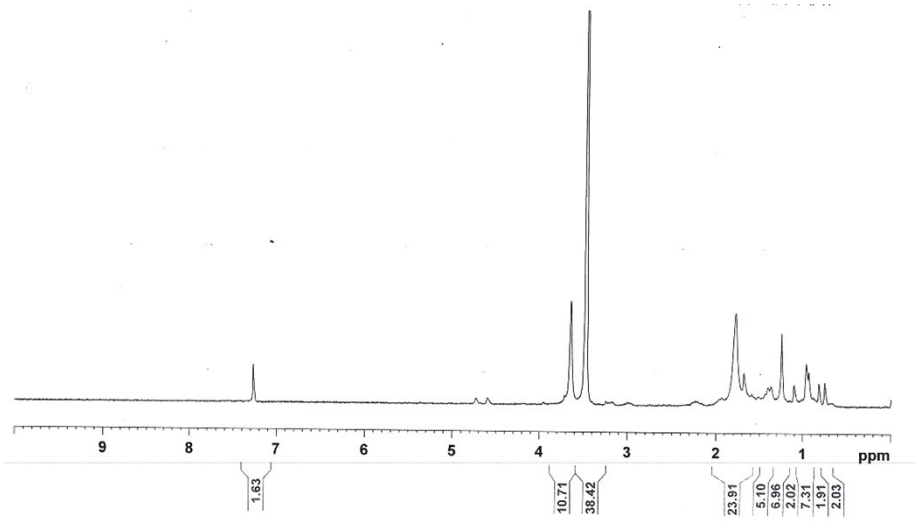


Figure S5: [1]H NMR of PEG conjugated SA-BA (PEG-SA-BA)

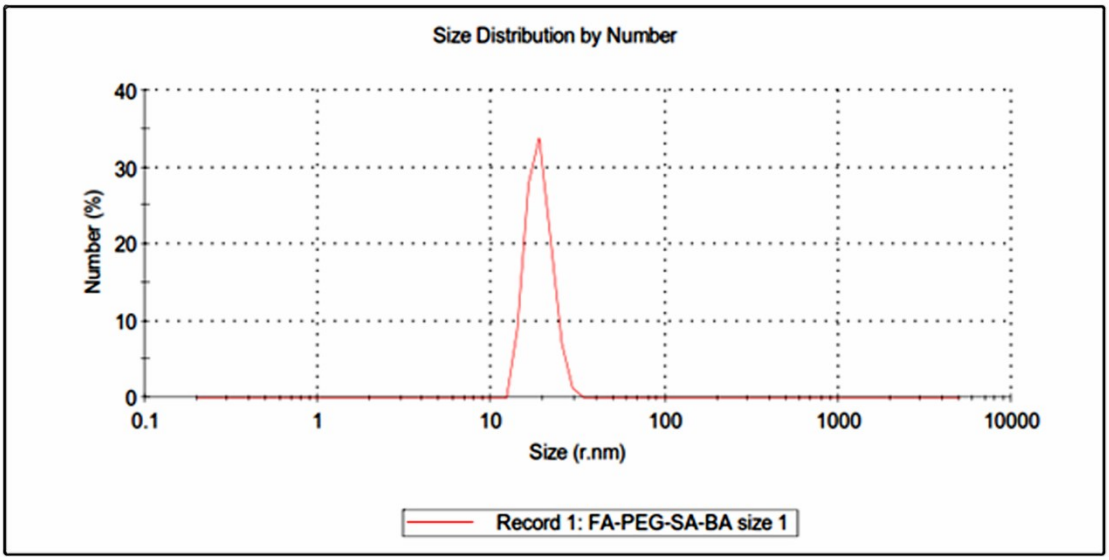


Figure S6: DLS of FA-PEG-SA-BA conjugates in aqueous medium.

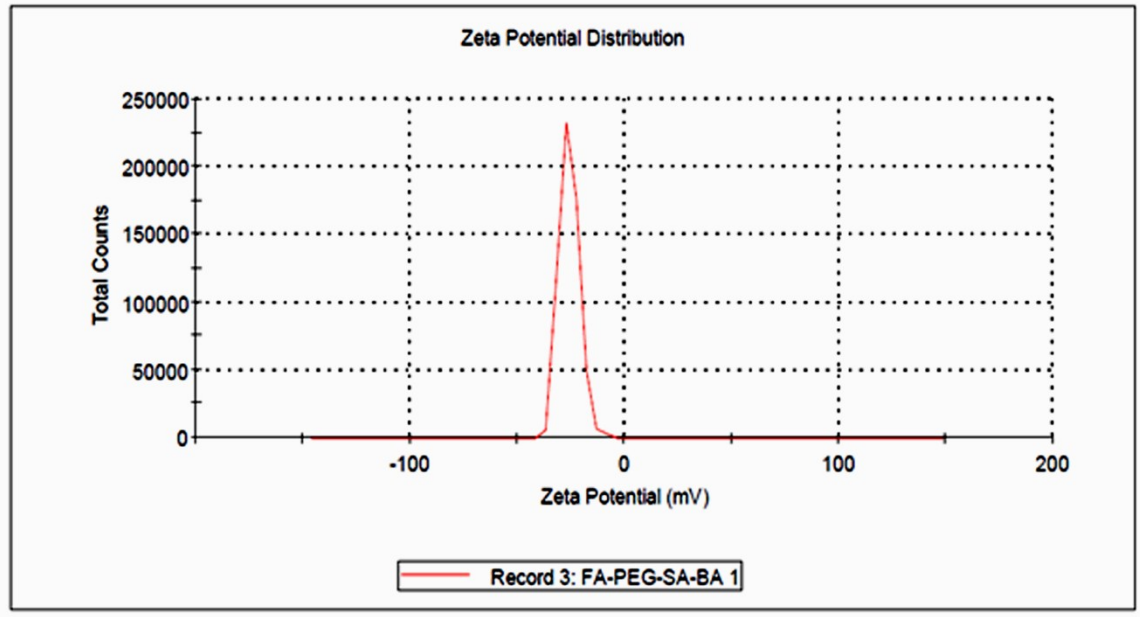


Figure S7: Zeta potential of FA-PEG-SA-BA conjugates in aqueous medium.

Betulinic Acid (BA): 1H-NMR (300 MHz, DMSO-d_6) δ: 4.66 (1H, s), 4.53 (1H, s), 2.97-2.95 (2H, m), 2.26-0.90 (m, terpenoids protons, 20H), 1.62 (6H, s), 0.91(3H, s), 0.85 (3H, s), 0.75 (3H, s), 0.65 (3H, s).

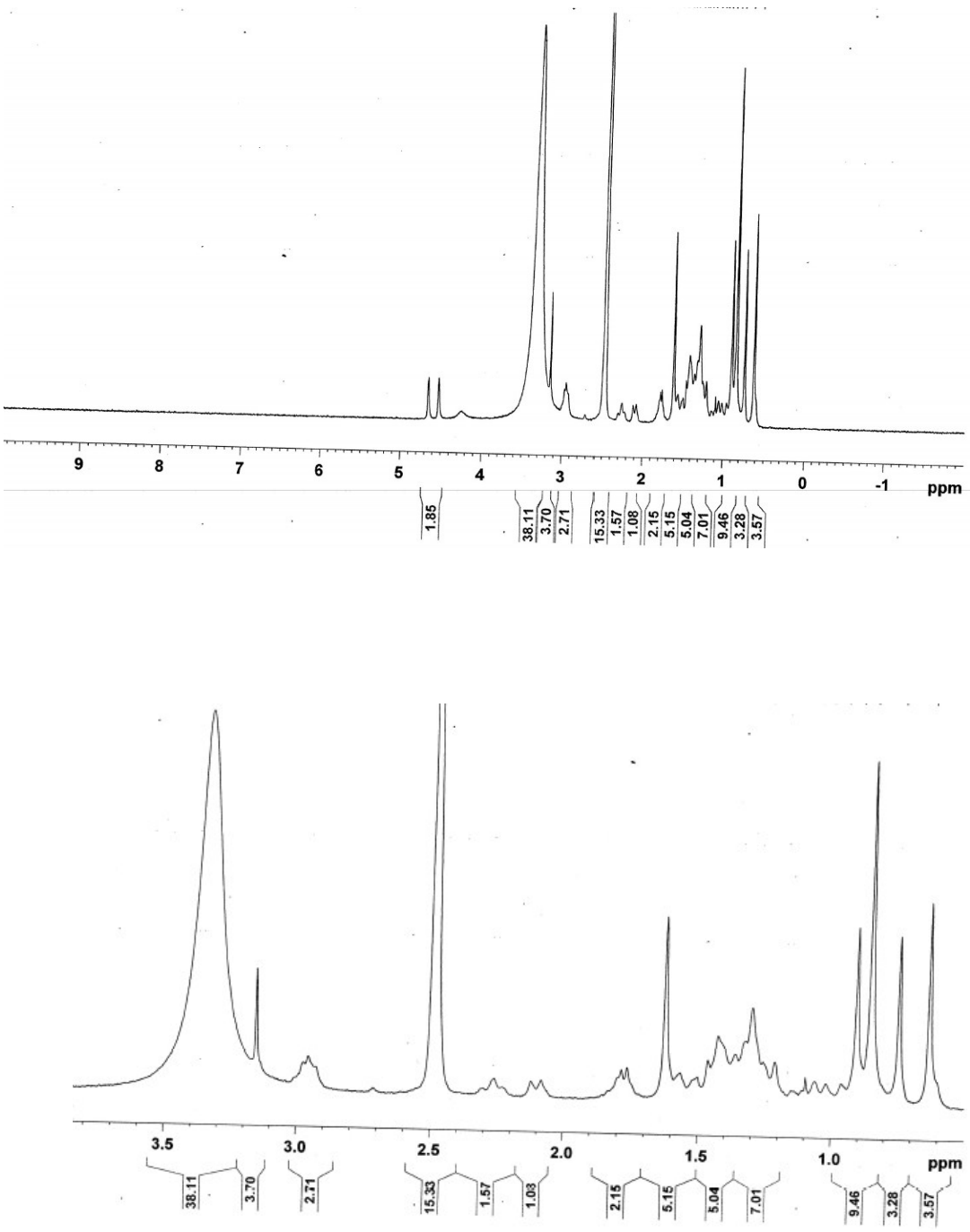


Figure S8: ^{1}H NMR of Betulinic acid.

Polyethylene glycol (PEG): 1H-NMR (300 MHz, $CDCl_3$) δ: 3.62 (O-CH_2, s), 2.66 (2H, s).

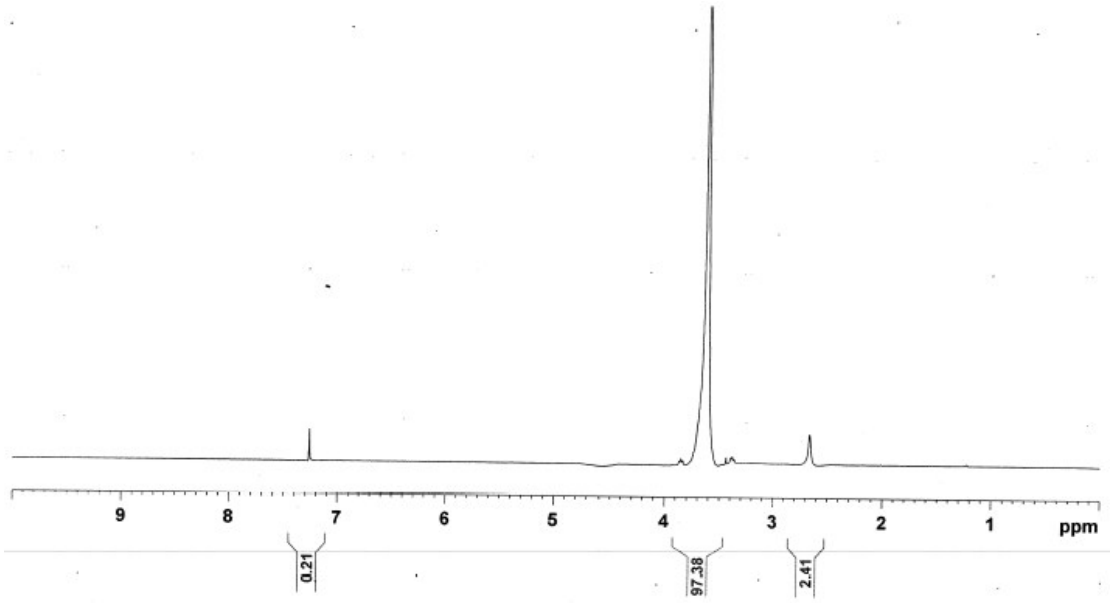
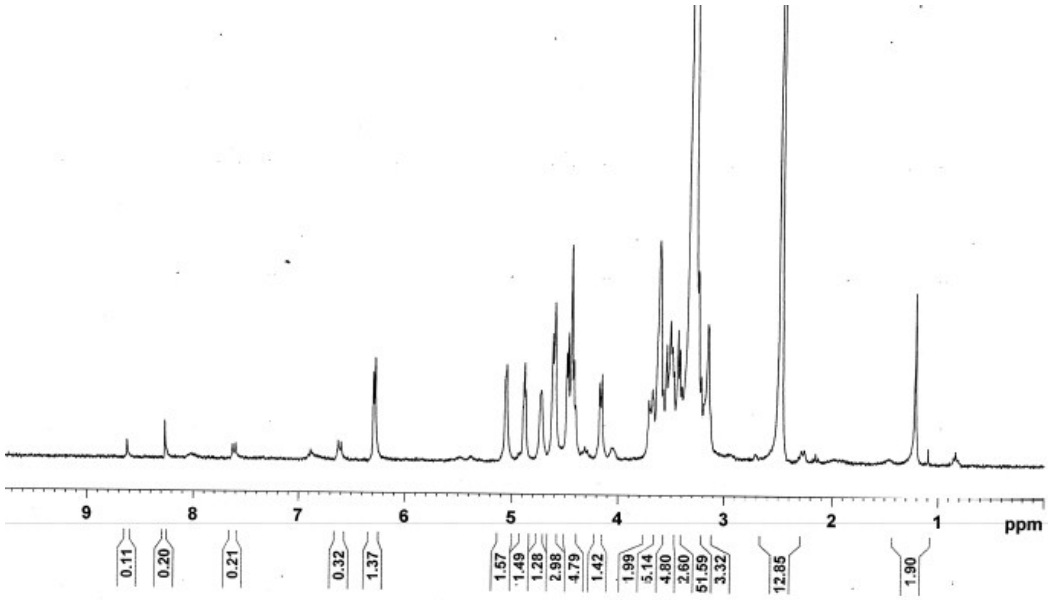


Figure S9: ^{1}H NMR of PEG.

Folic Acid (FA): 1H-NMR (300 MHz, DMSO-d_6) δ: 8.63 (1H, s), 8.27 (1H, s), 7.64-7.61(2H, d), 6.63-6.60 (1H, d), 6.30-6.28 (1H, d), 4.48-4.42 (2H, m), 4.17 (1H, m), 2.29-2.66 (2H, m), 1.22 (2H, s).



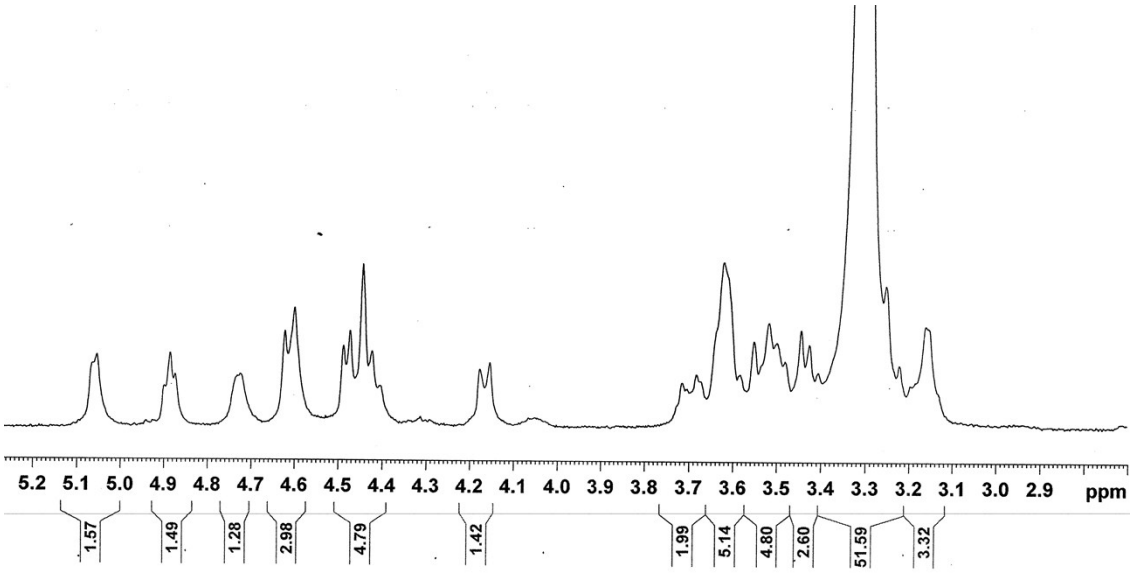
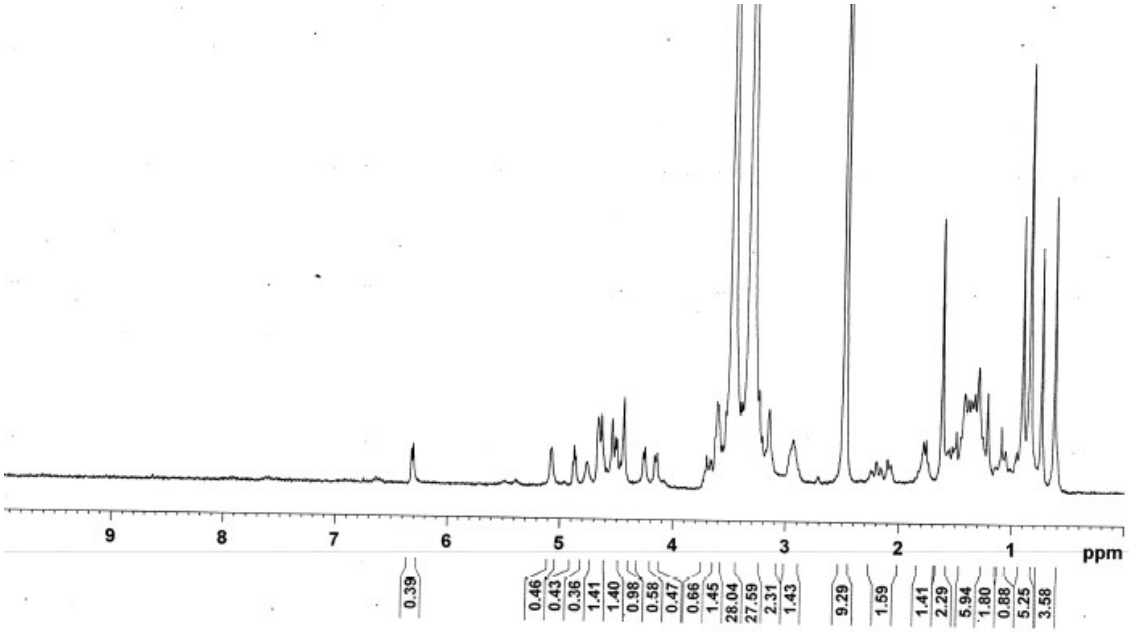


Figure S10: ^{1}H NMR of FA.

FA-PEG-SA-BA: 1H-NMR (300 MHz, DMSO-d_6) δ: 6.32-6.31(1H, d), 4.66 (1H, s), 4.63 (1H, s), 4.54-4.44 (2H, m), 4.17-4.15 (1H, m), 3.61 (O-CH_2, s), 1.63 (3H, s), 0.96 (3H, s), 0.91(3H, s), 0.85 (3H, s), 0.74 (3H, s), 0.63 (3H, s), 2.02-0.96 (m, terpenoids protons, 20H).

In the 1H-NMR spectrum of FA-PEG-SA-BA, the appearance of characteristic peaks for folic acid, polyethylene glycol and betulinic acid clearly indicated the formation of FA-PEG-SA-BA conjugate.



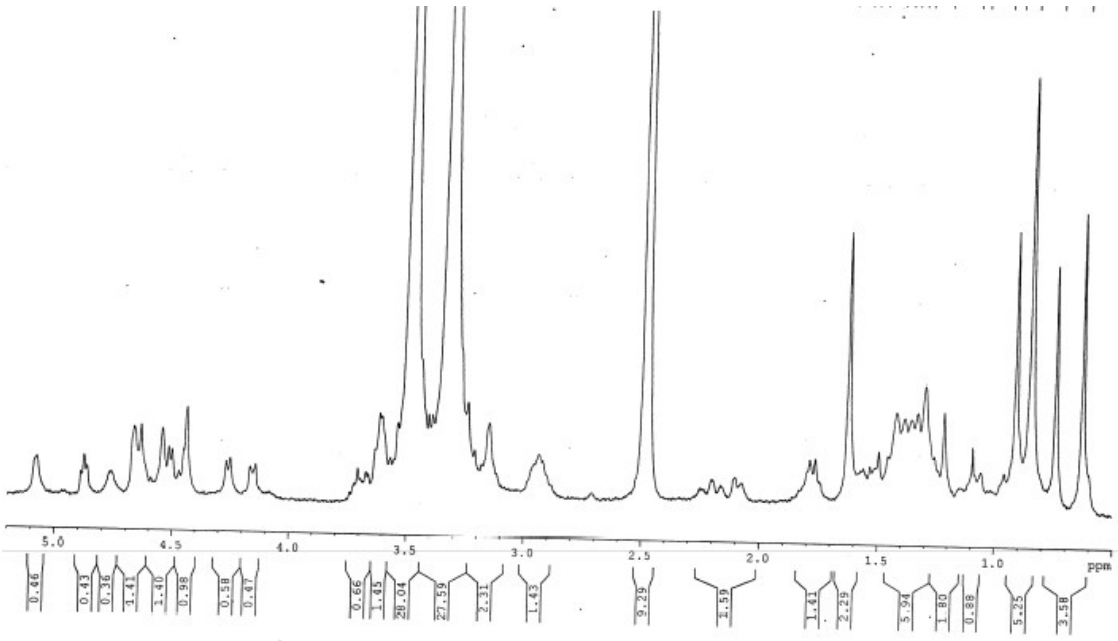


Figure S11: ^{1}H NMR of FA-PEG-SA-BA conjugate.