

# **Stimuli responsive nanocarrier for an effective delivery of multi-frontline tuberculosis drugs**

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<sup>1</sup>Polymer Research Centre, Department of Chemical Sciences, and <sup>2</sup>Department of Biological Sciences, Indian Institute of Science Education and Research Kolkata (IISER K), India.

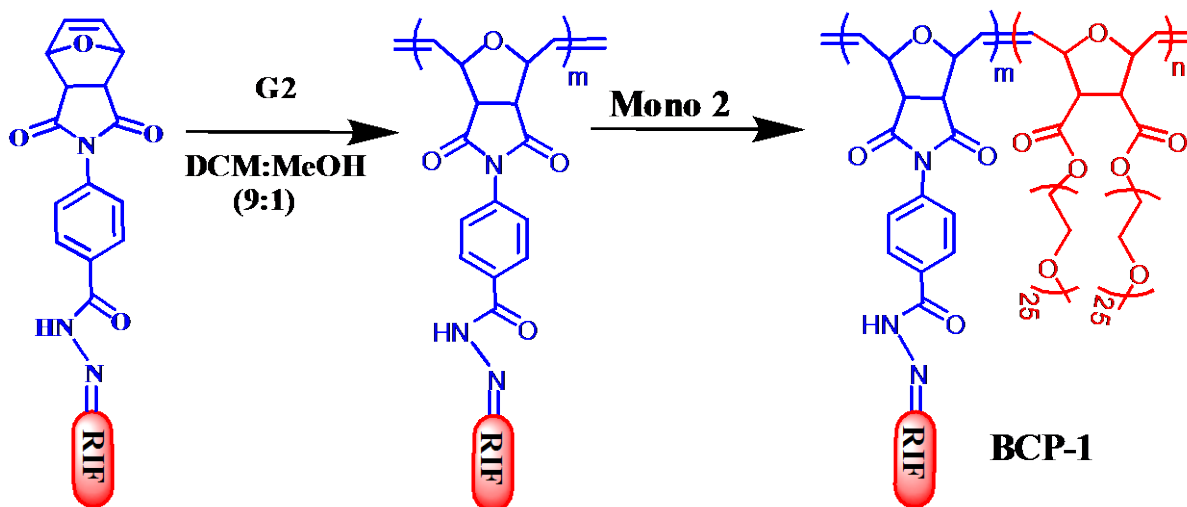
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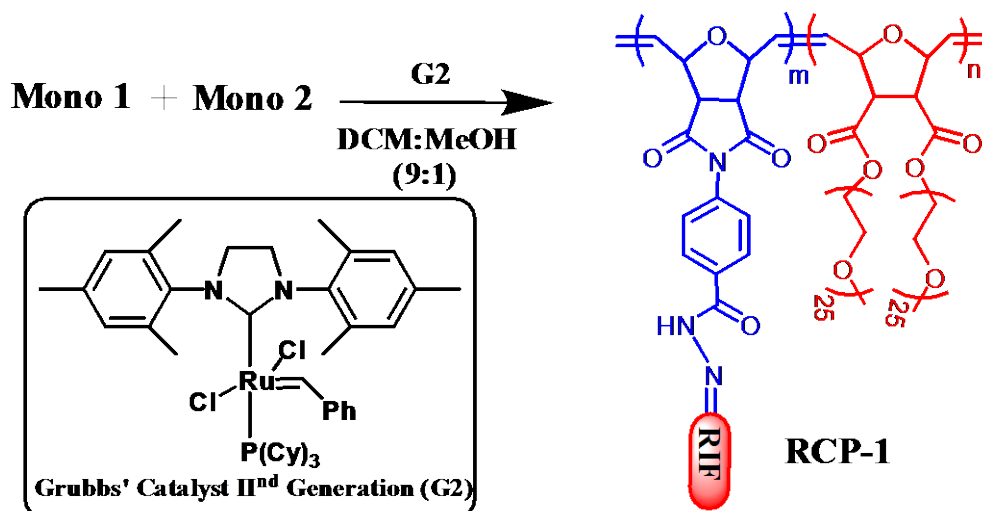
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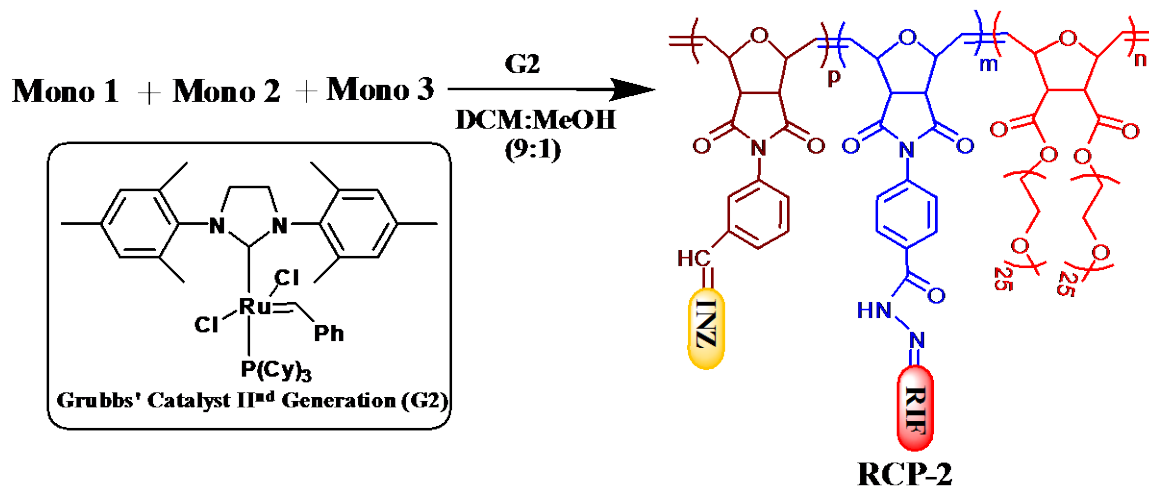
Scheme S1. Schematic representation of block copolymer, BCP-1 synthesis.



Scheme S2. Schematic representation of synthesis of random copolymer RCP-1.



Scheme S3. Schematic representation of synthesis of random copolymer RCP-2 (NOR-INZ-RIF-PEG).



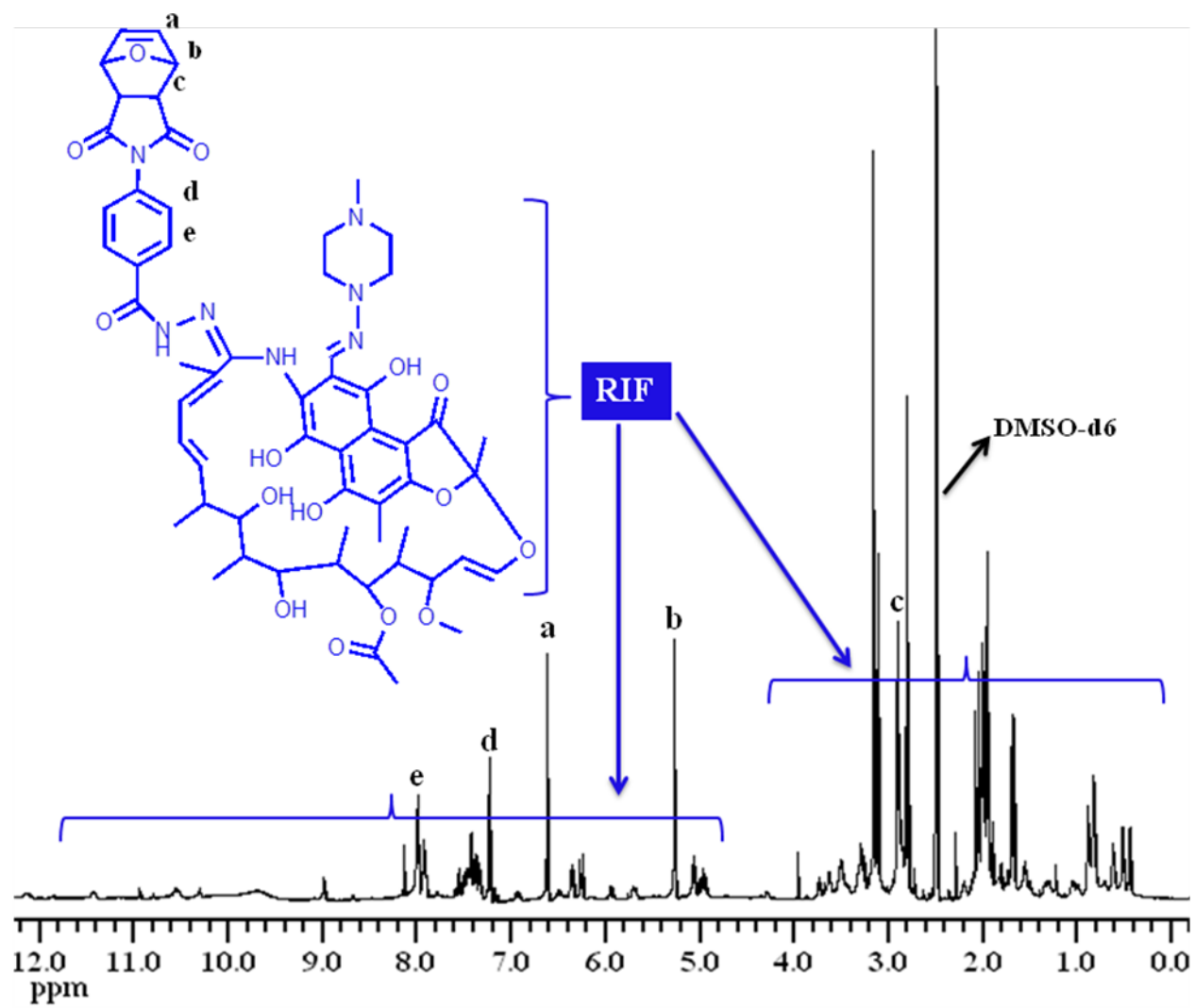


Fig. S1:  $^1\text{H}$  NMR spectrum of Mono 1 in  $\text{DMSO-d}_6$ .

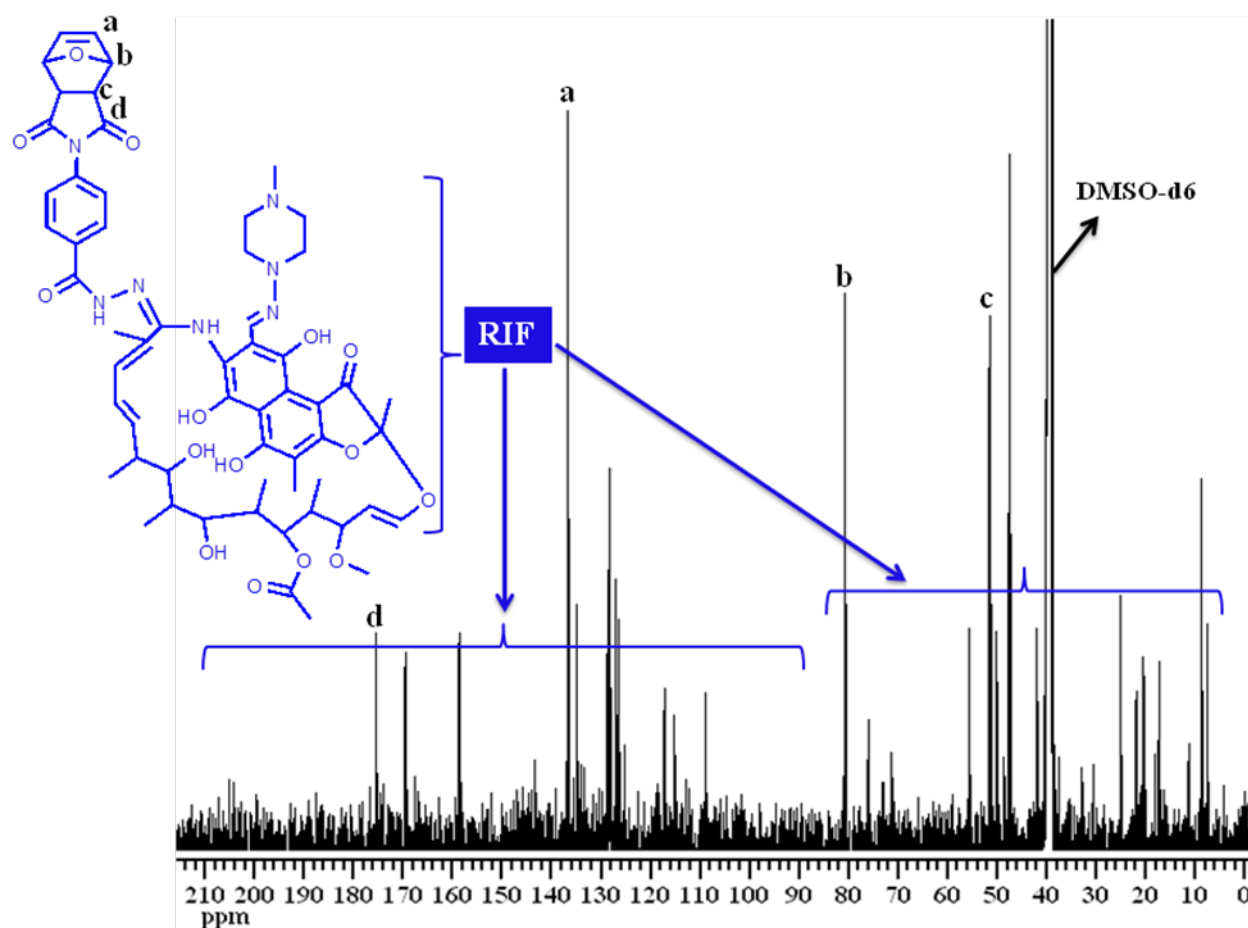


Fig. S2:  $^{13}\text{C}$  NMR spectrum of Mono 1 in  $\text{DMSO-d}_6$ .

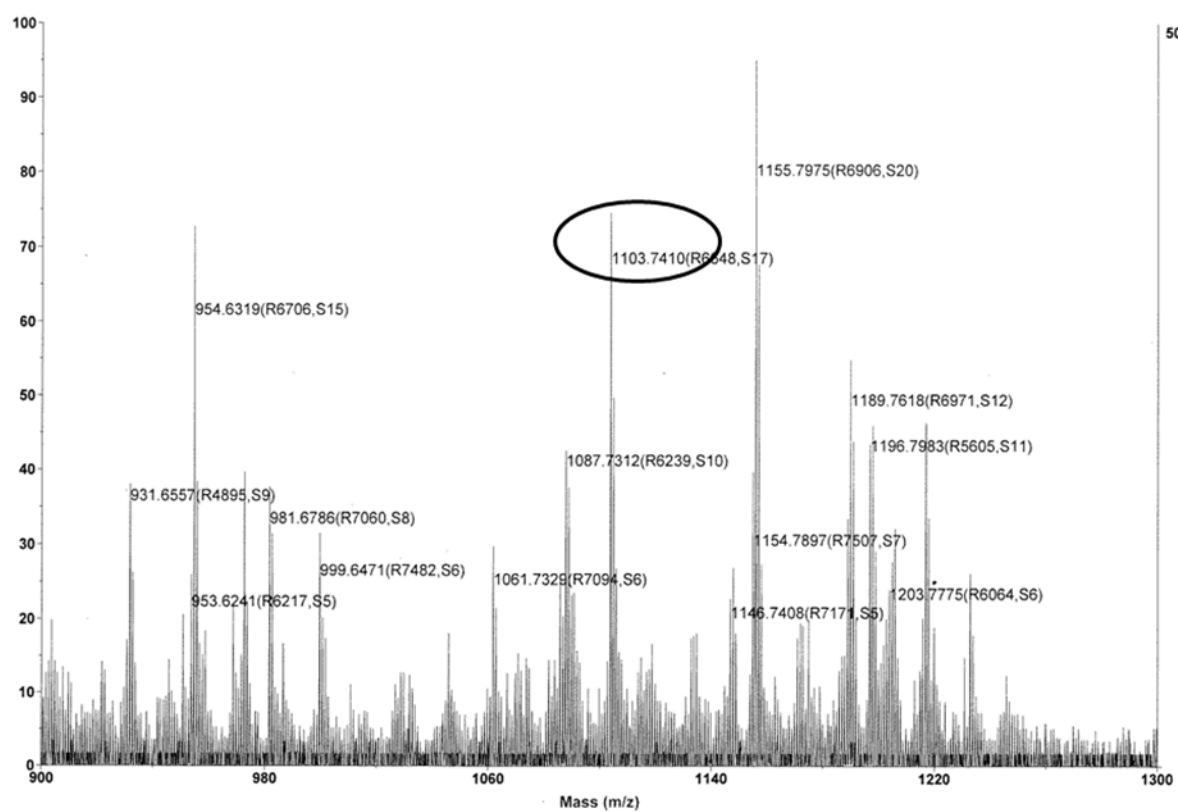
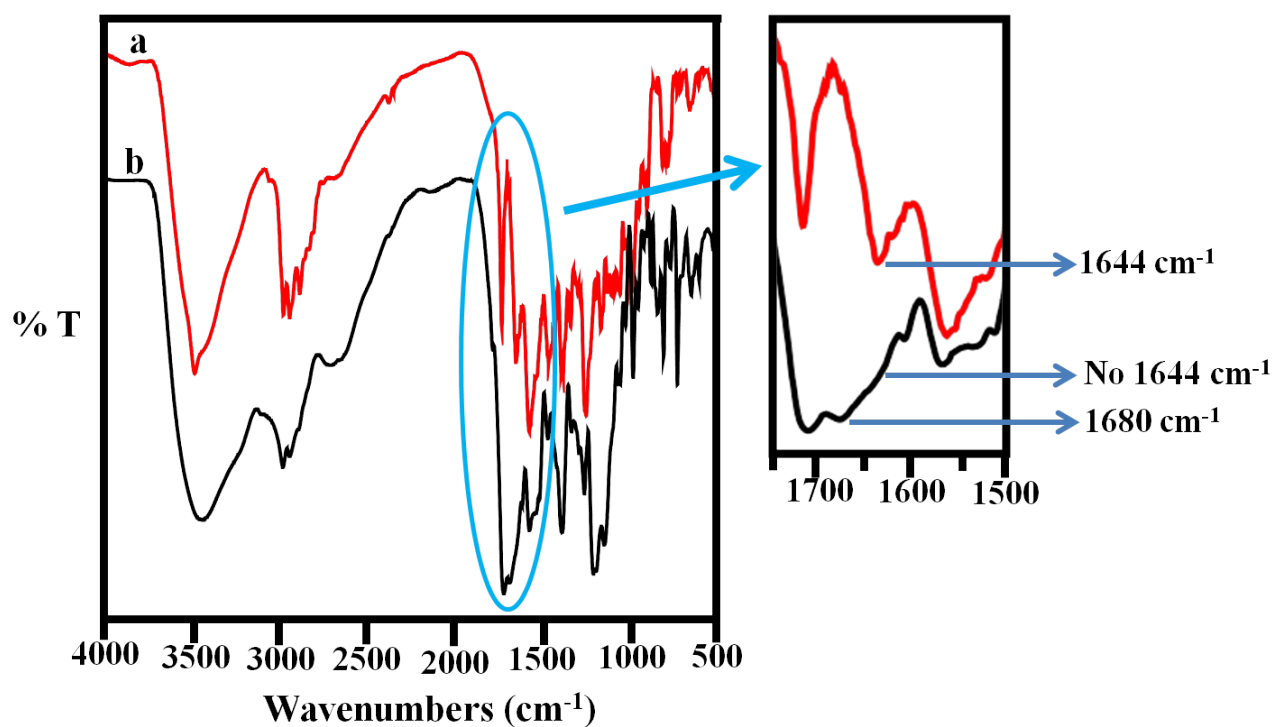
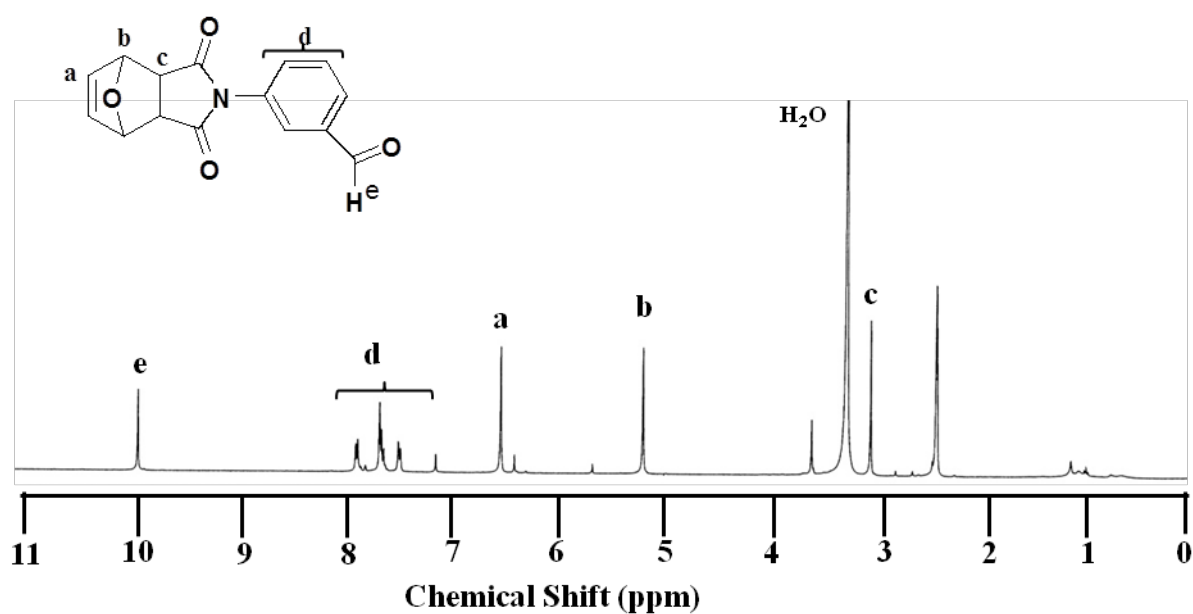


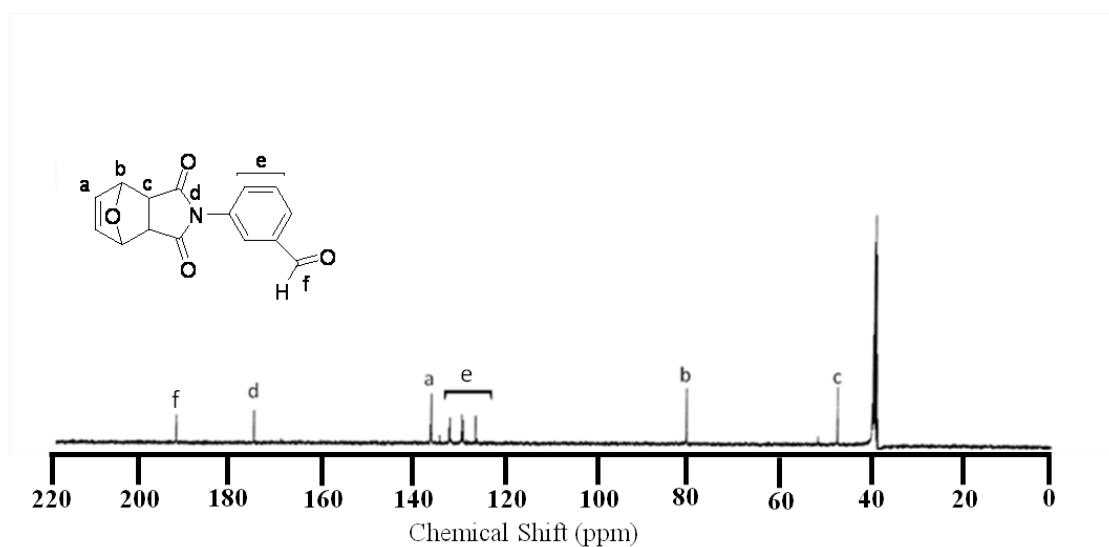
Fig. S3: MALDI-TOF spectrum of Mono 1.



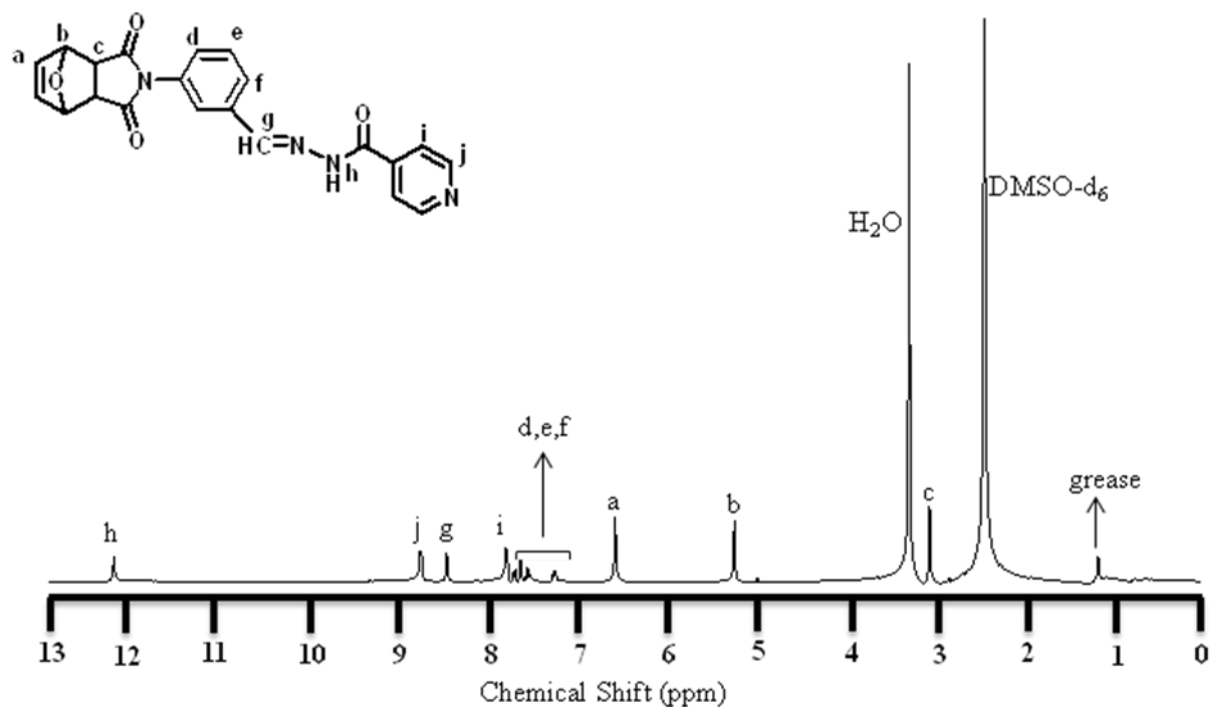
**Fig. S4:** FT-IR spectrum of (a) Rifampicin and (b) Mono 1.



**Fig. S5:**  $^1\text{H}$  NMR spectrum of compound 5 in  $\text{DMSO-d}_6$

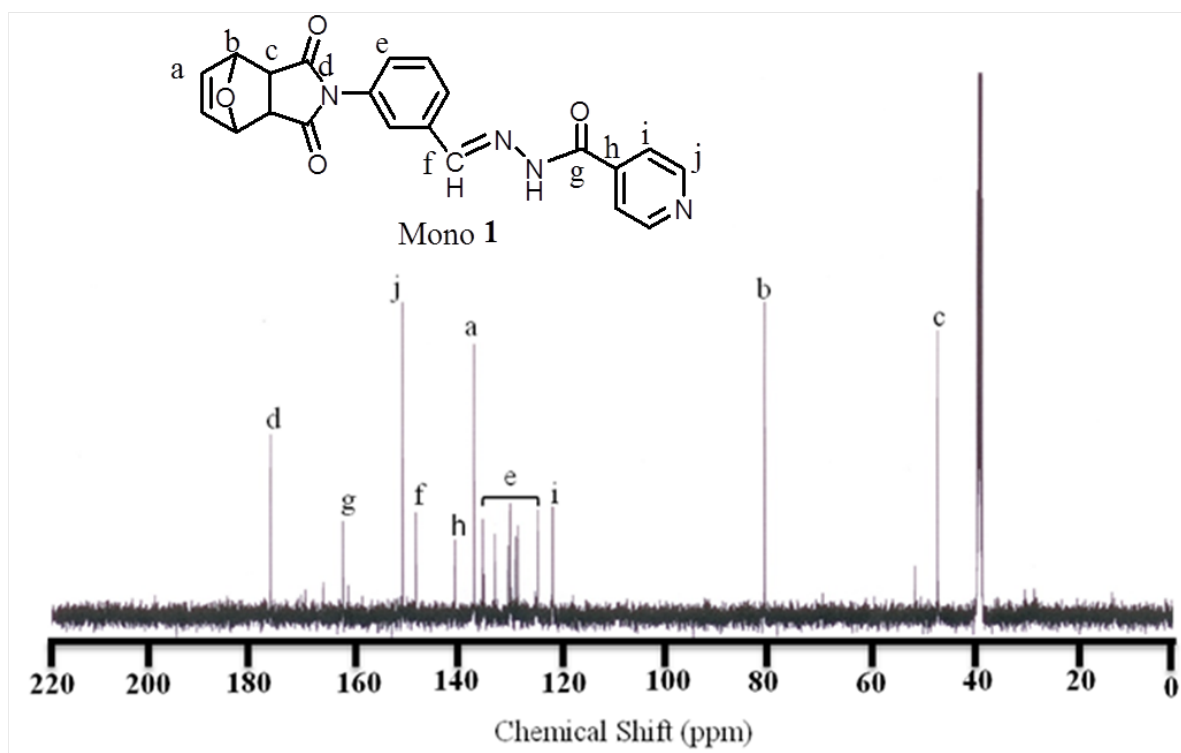


**Fig. S6:**  $^{13}\text{C}$  NMR spectrum of compound **5** in  $\text{DMSO-d}_6$ .

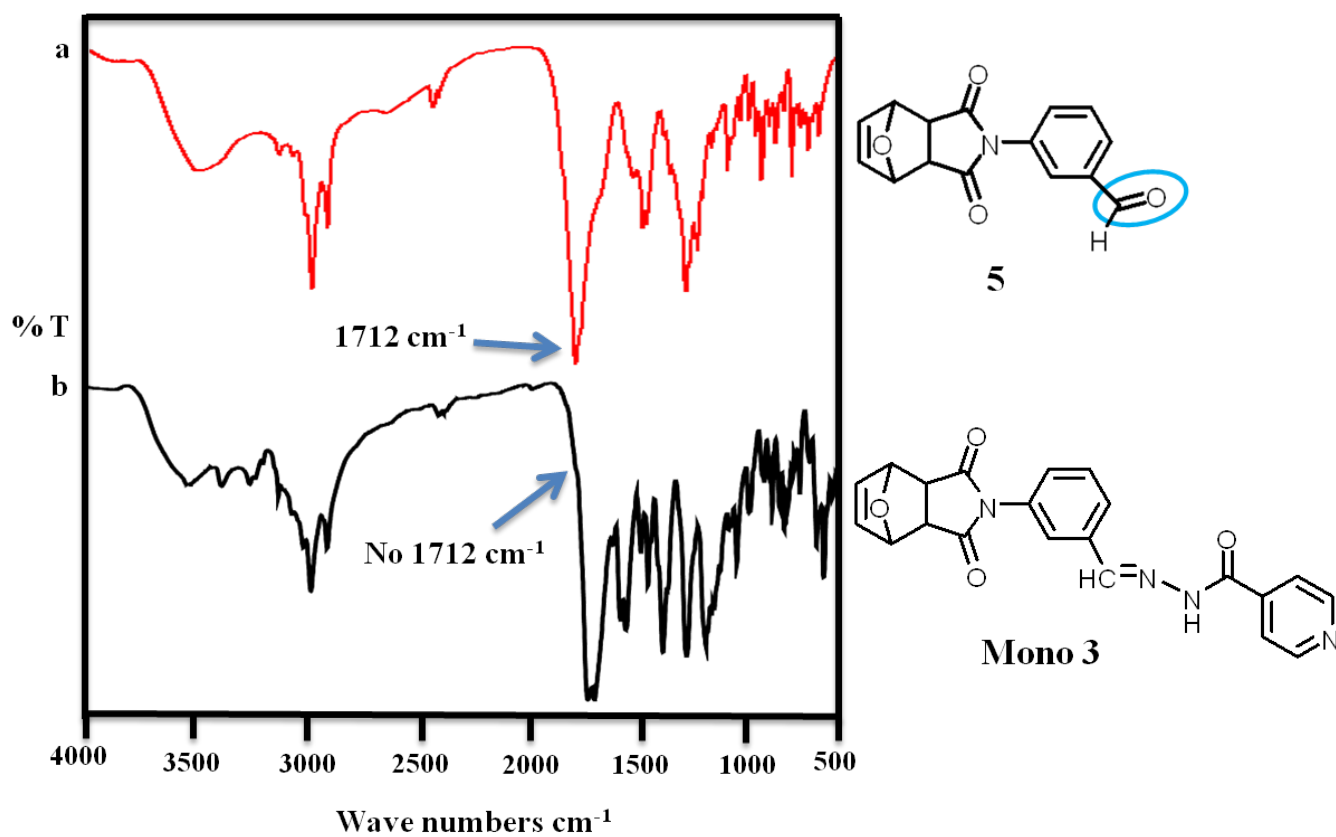


**Fig. S7:**  $^1\text{H}$  NMR spectrum of **Mono 3** in  $\text{DMSO-d}_6$ .





**Fig. S8:**  $^{13}\text{C}$  NMR spectrum of **Mono 3** in  $\text{DMSO-d}_6$ .



**Fig. S9:** FT-IR spectrum of (a) compound **5** and (b) **Mono 3**.

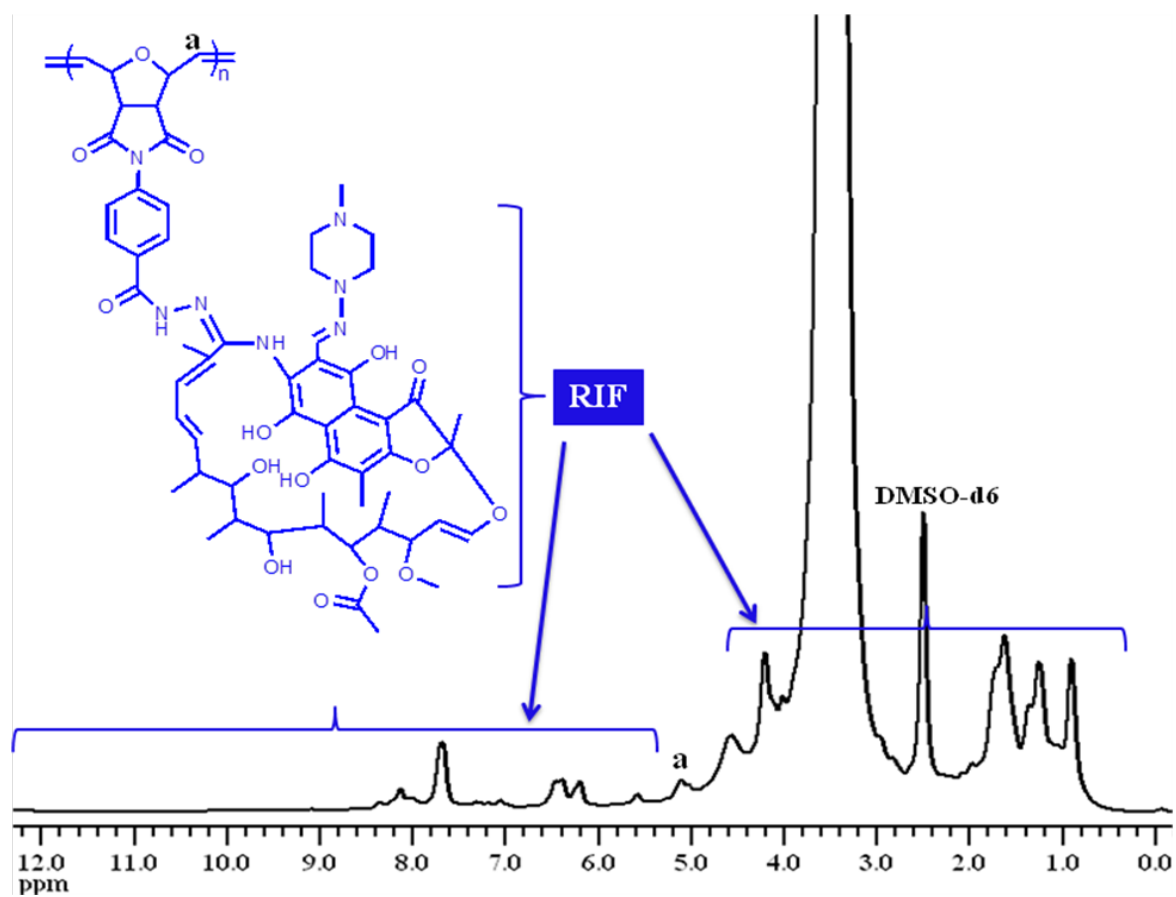


Fig. S10:  $^1\text{H}$  NMR spectrum of RIF-HP 4.

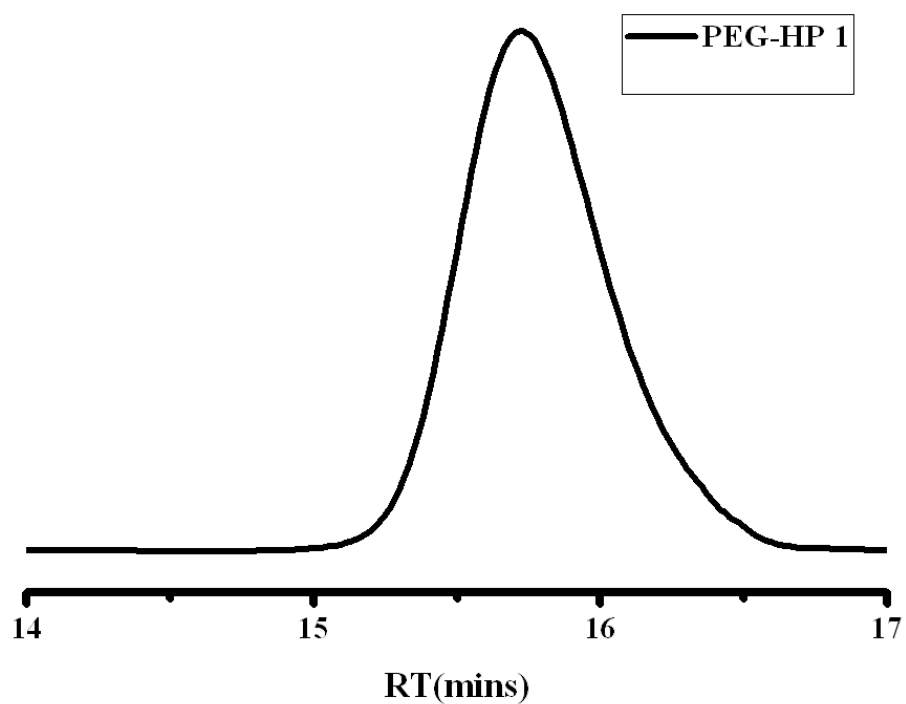
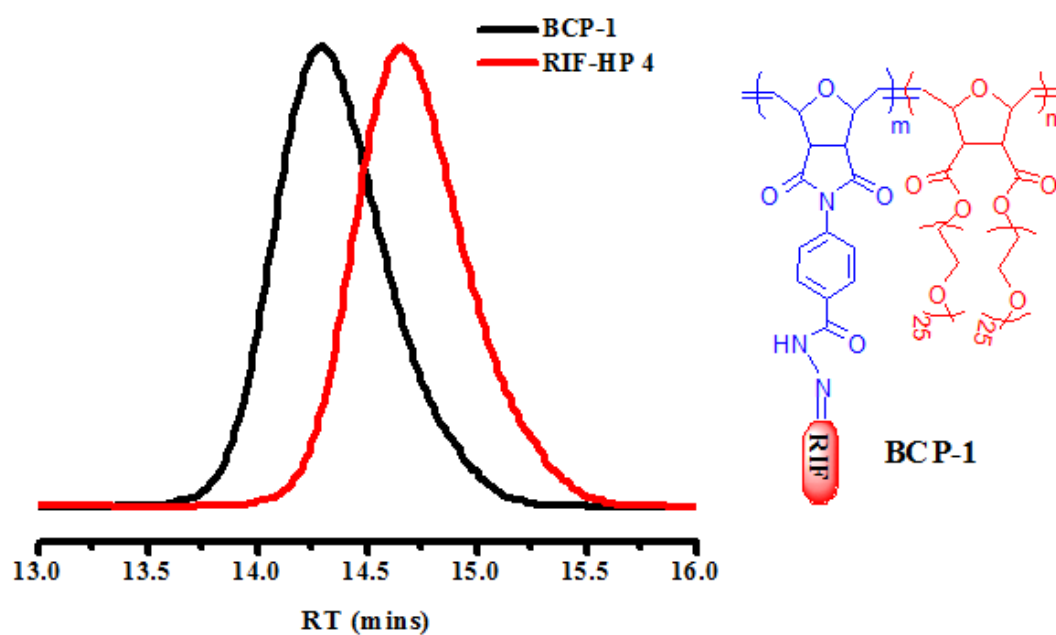
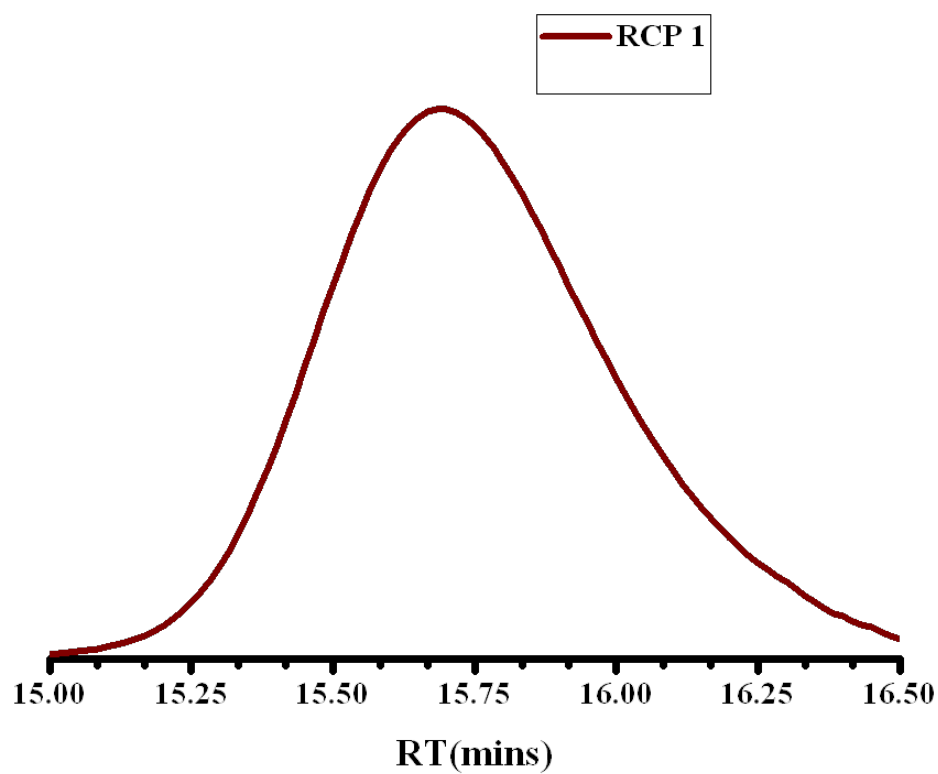


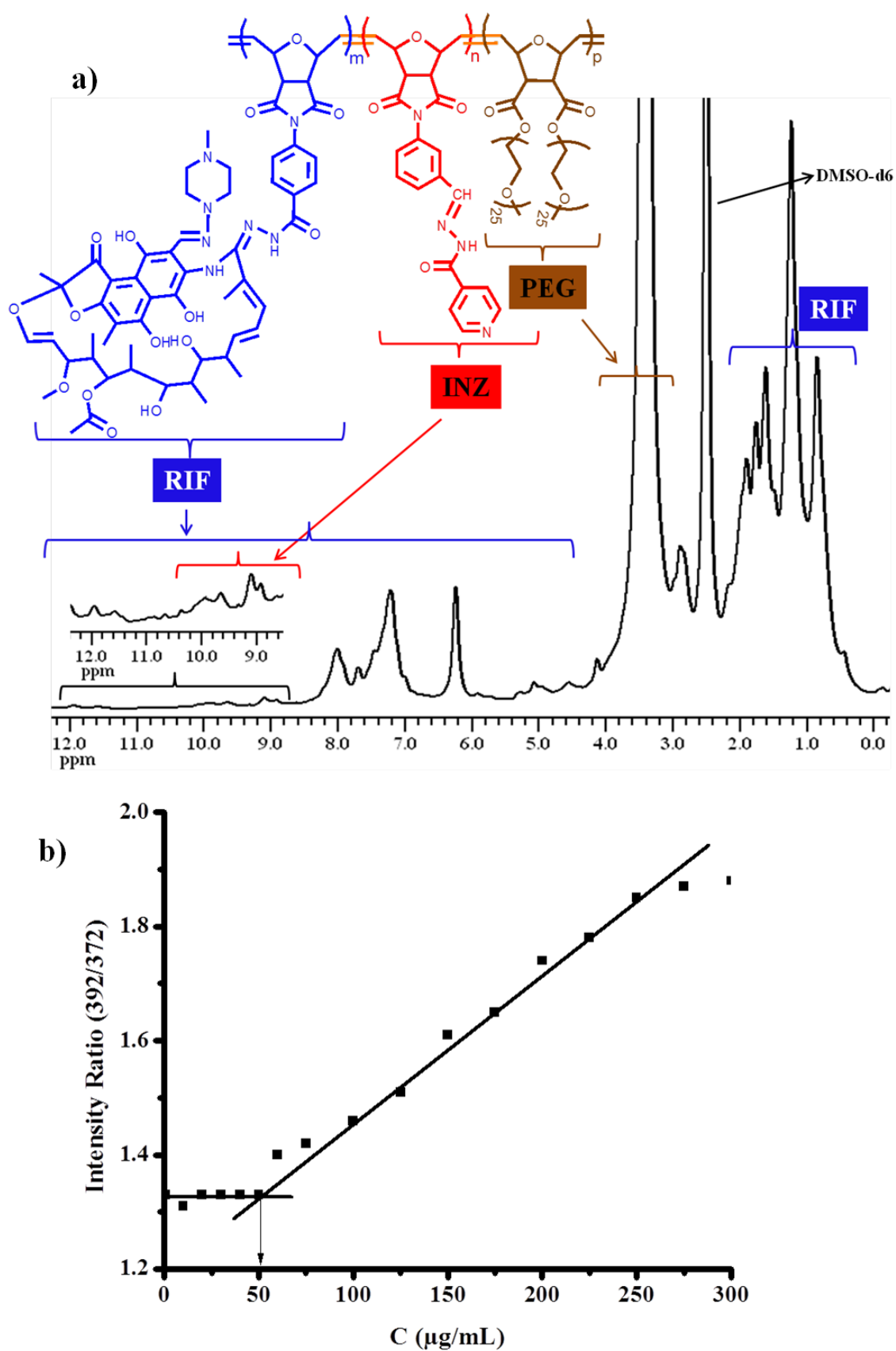
Fig. S11: GPC traces for PEG-HP 1 ( $M_n = 11400$ , PDI 1.07).



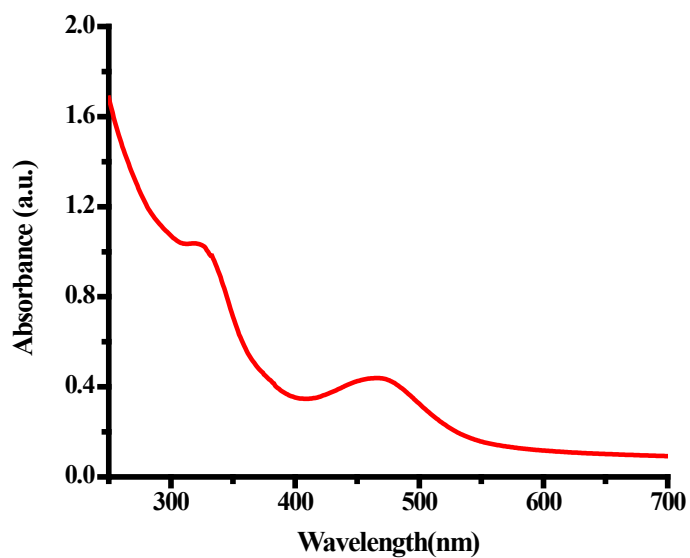
**Fig. S12:** A representative GPC traces for **BCP-1**( $M_n = 42000$ , PDI 1.10) (black) and **RIF-HP 4** ( $M_n = 32200$ , PDI 1.09) (red).



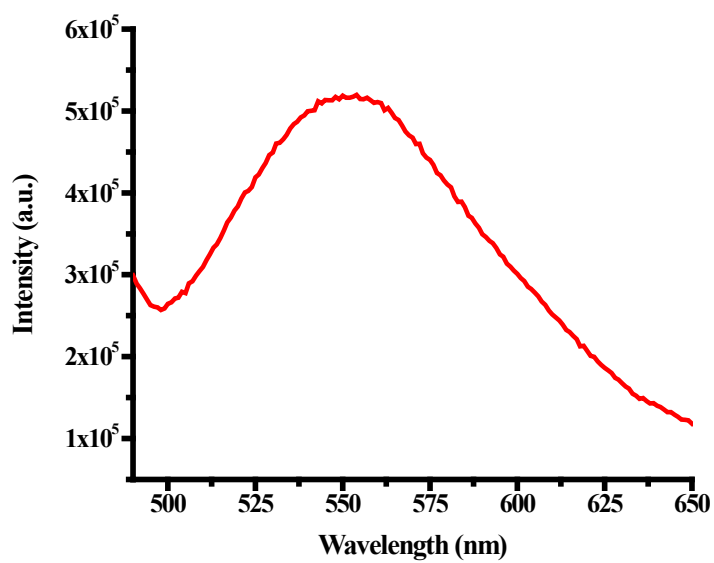
**Fig. S13:** GPC traces for **RCP- 1** ( $M_n = 11700$ , PDI 1.09).



**Fig. S14:** (a)  $^1\text{H}$  NMR spectra for **RCP-2** in  $\text{DMSO-d}_6$ . (b) CAC study of **RCP-2** in water using pyrene as the probe, the observed CAC is  $50 \mu\text{g mL}^{-1}$ ,



**Fig. S15:** UV spectra of RCP- 2.



**Fig. S16:** Fluorescence spectra of RCP -2 excited at 469 nm.

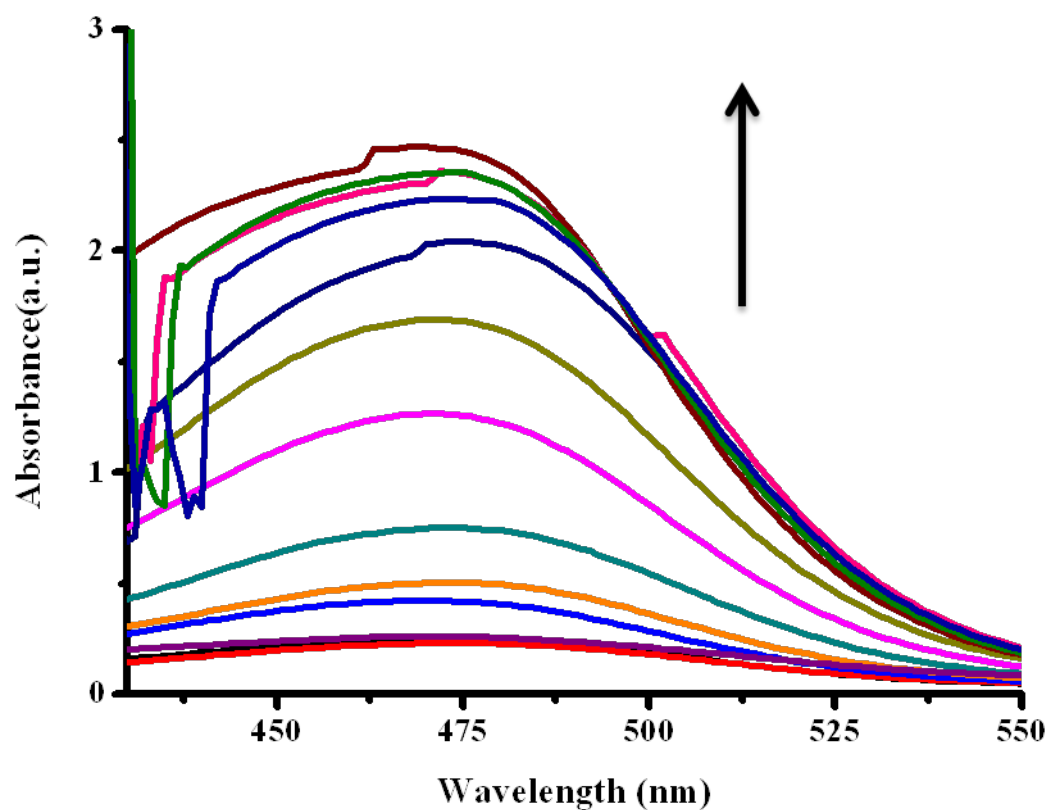


Fig. S17: UV spectra for drug release from RCP-2 at pH 5.5 by Dialysis method .

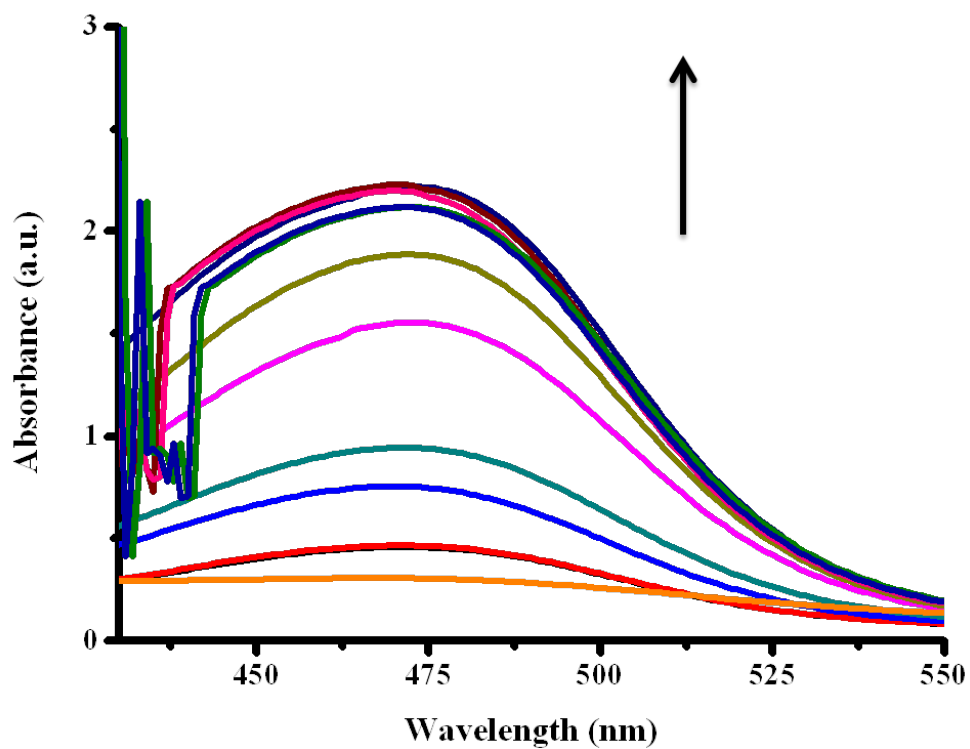
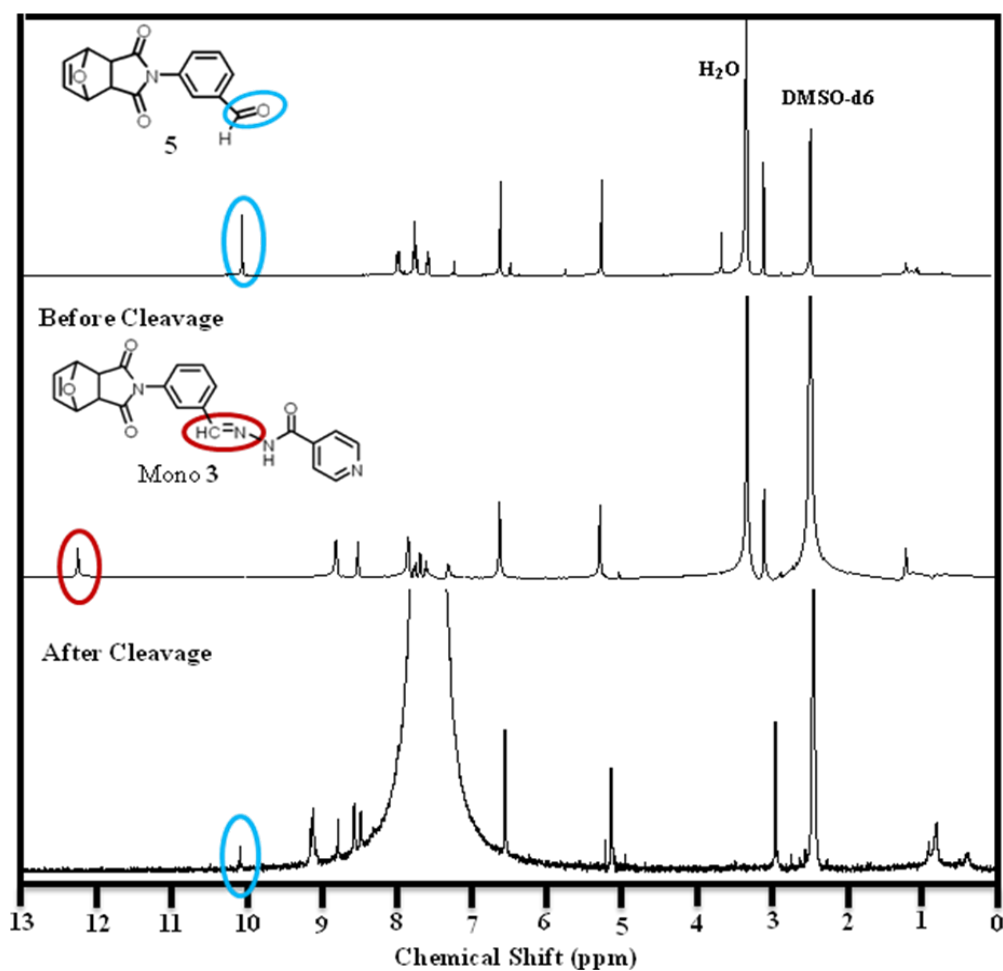


Fig. S18: UV spectra for drug release from RCP-2 at pH 6.5 by Dialysis method .



**Fig. S19:** A comparative <sup>1</sup>H NMR spectroscopy of compound **5**, **Mono 3** and **Mono 1** after exposure to the acidic condition in DMSO-d<sub>6</sub>.

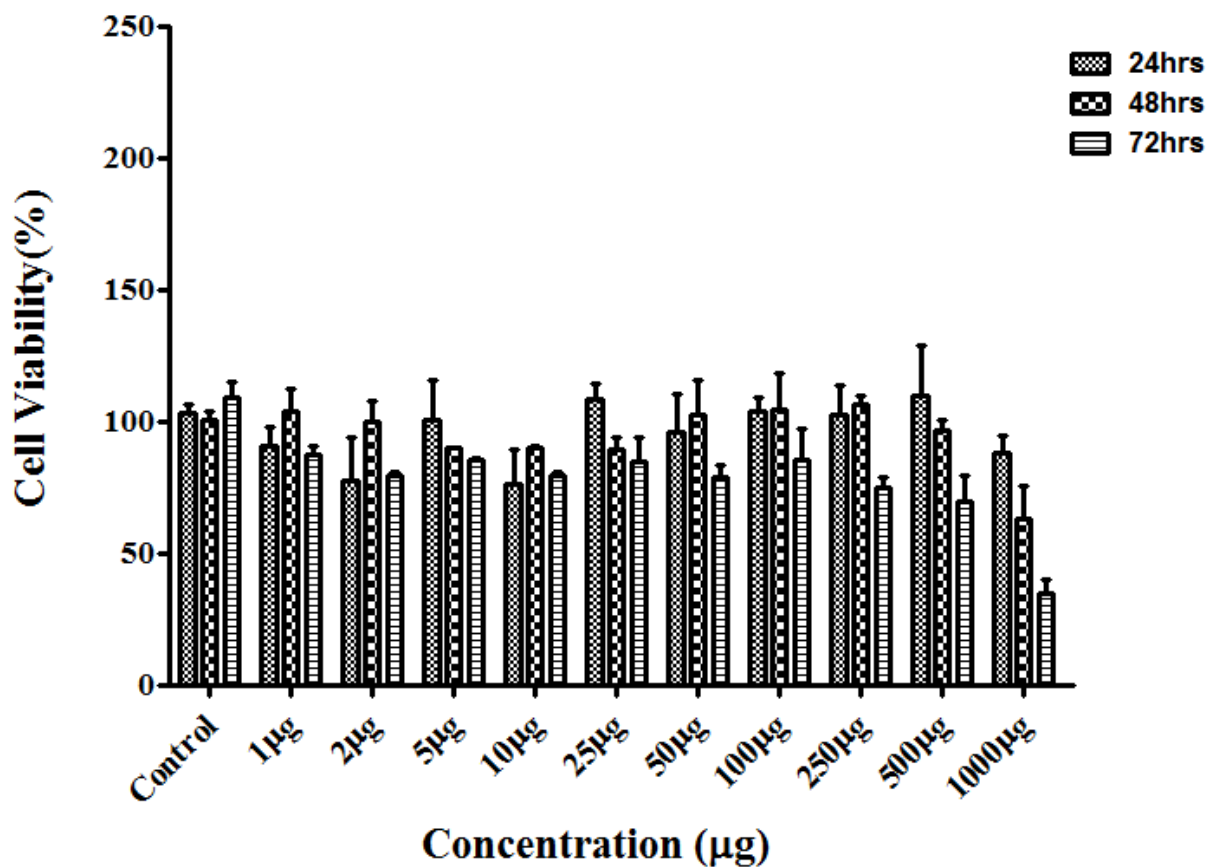


Fig. S20 : Cytotoxicity assay of Isoniazid.

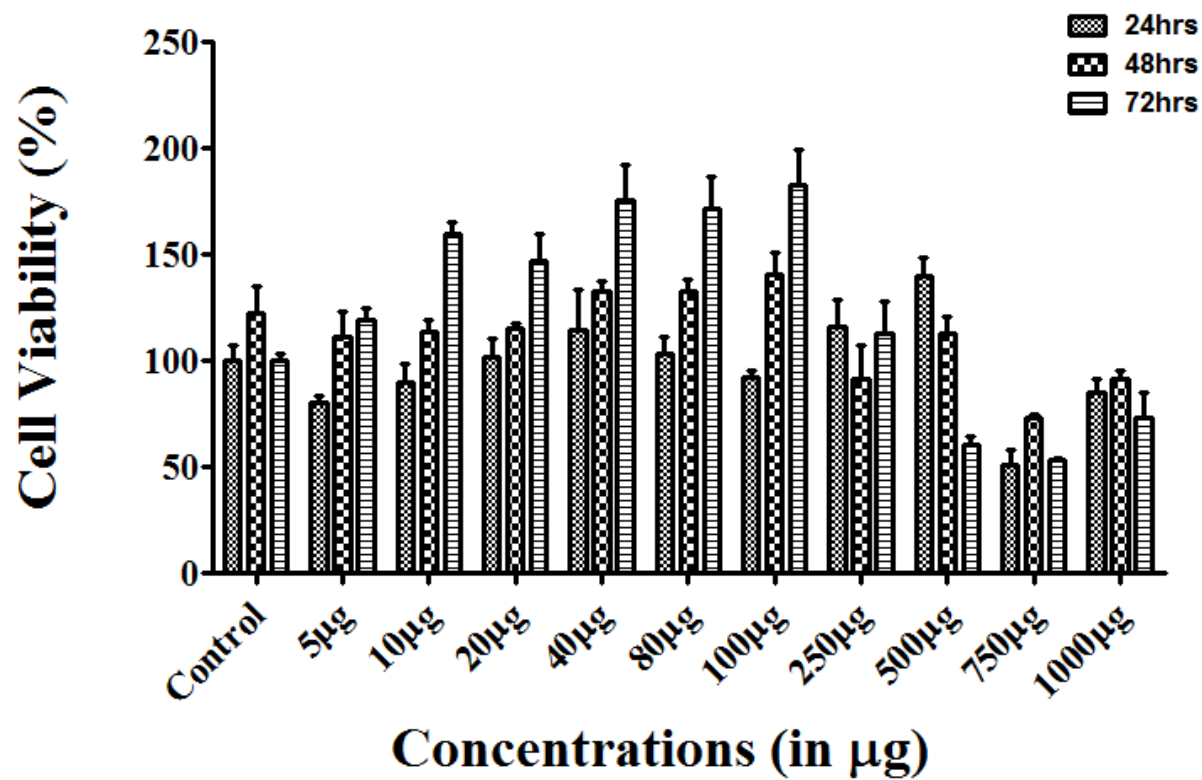


Fig. S21 : Cytotoxicity assay of Rifampicin on A549 cell line.



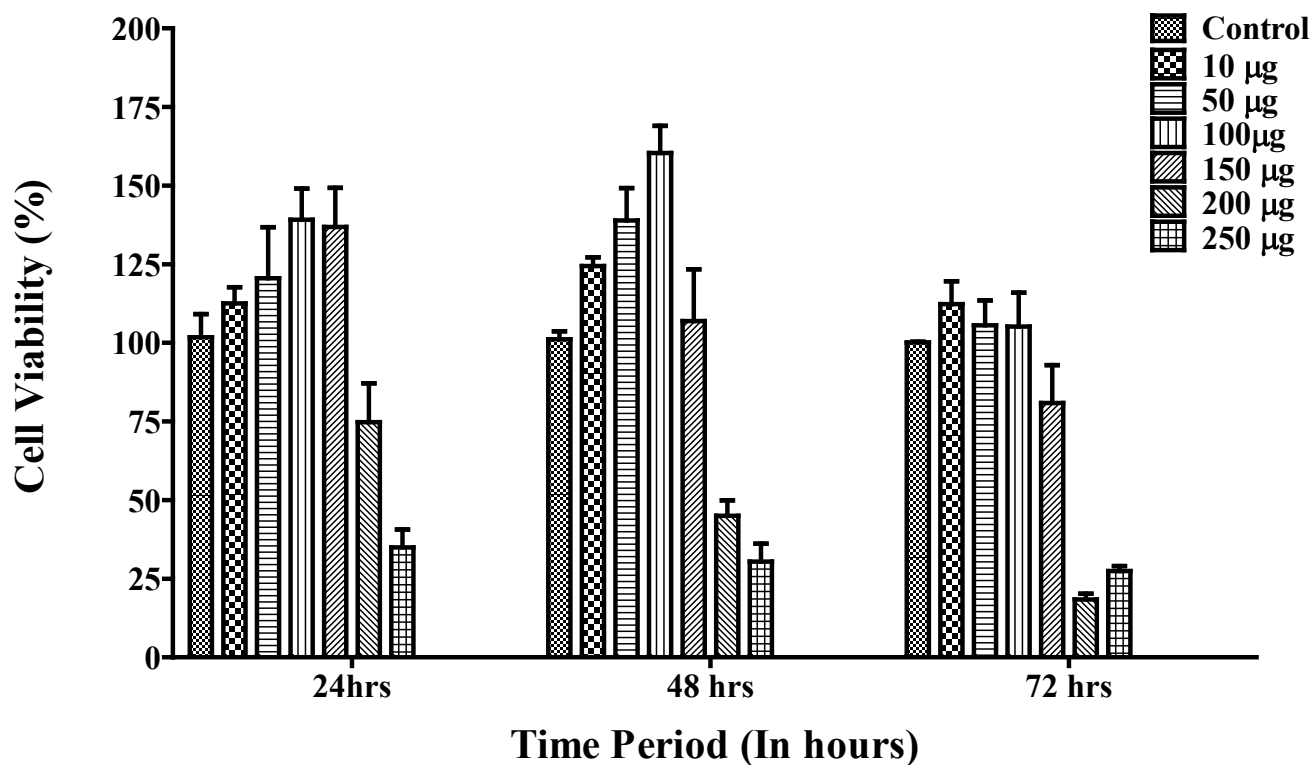


Fig. S22 : Cytotoxicity assay of Norbornene polymer alone tested in HEK 293 cell line.

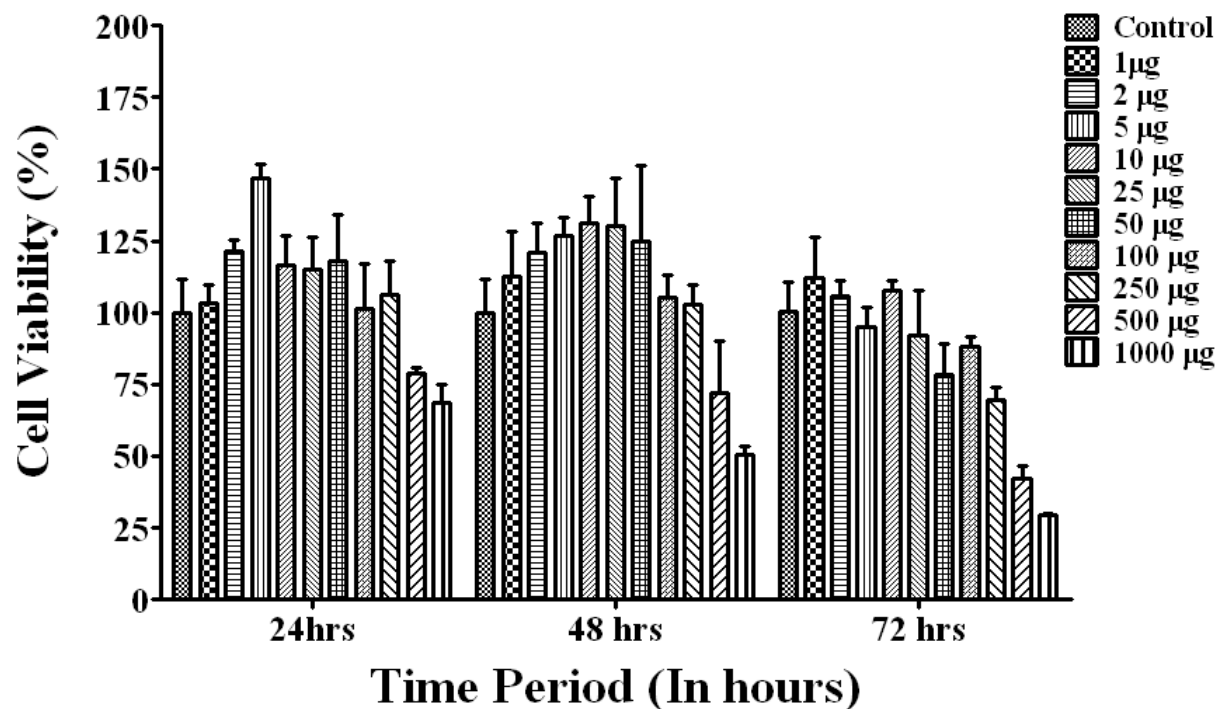


Fig. S23 : Cytotoxicity assay of the nanocarrier tested in normal healthy cells( HEK 293 cell line).

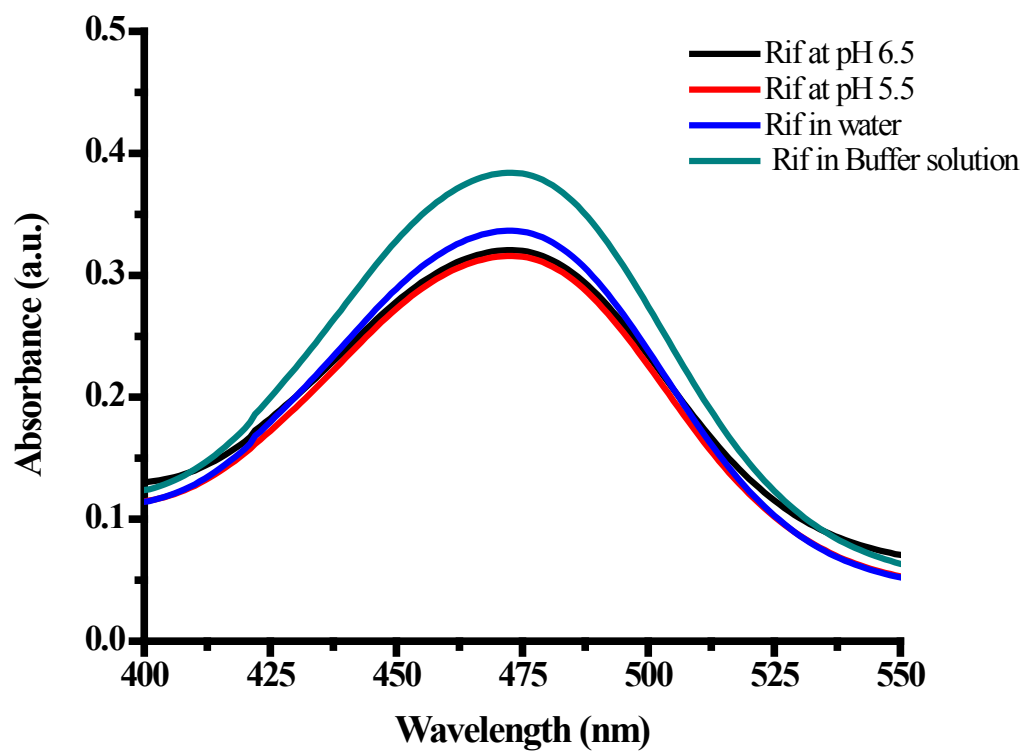
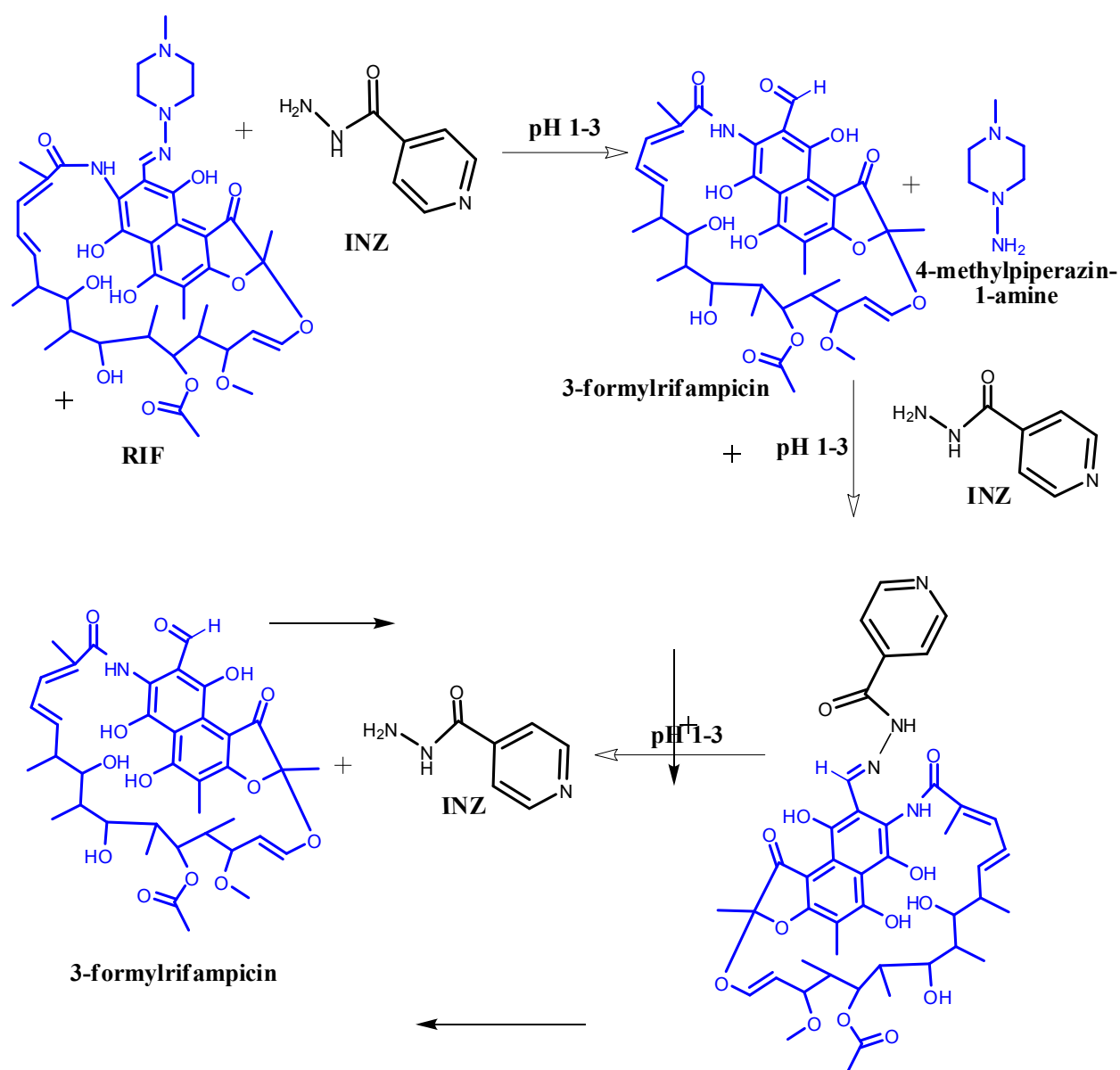


Fig. S24 : UV spectra of Rifampicin in different solutions.



**Fig. S25** : Decomposition scheme for RIF. **Ref:** Singh, S., Mariappan, T. T., Sharda, N., Kumar, S., Chakraborti, A. K. *Pharm. Pharmacol. Commun.* **2000**, *6*, 405-410.

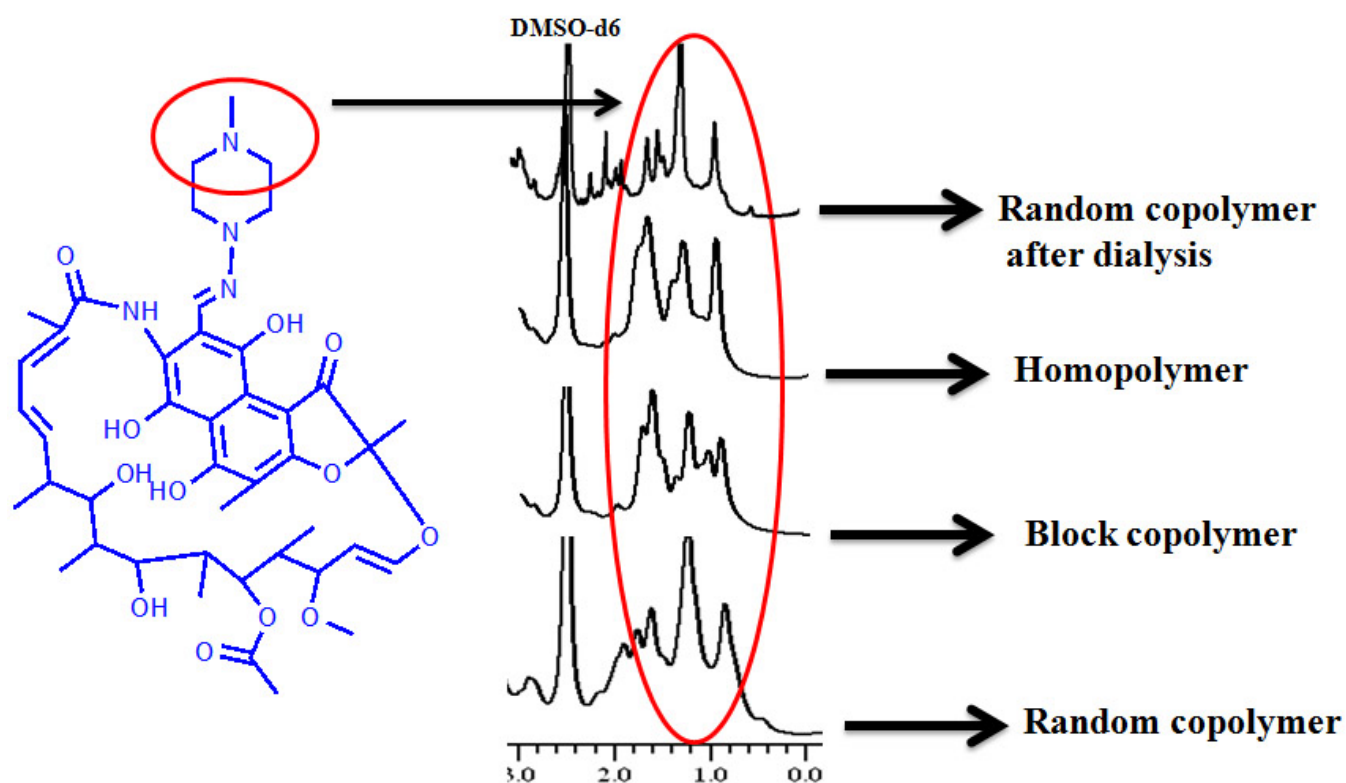


Fig. S26 : Control experiment to prove the delivery of undecomposed RIF drug.

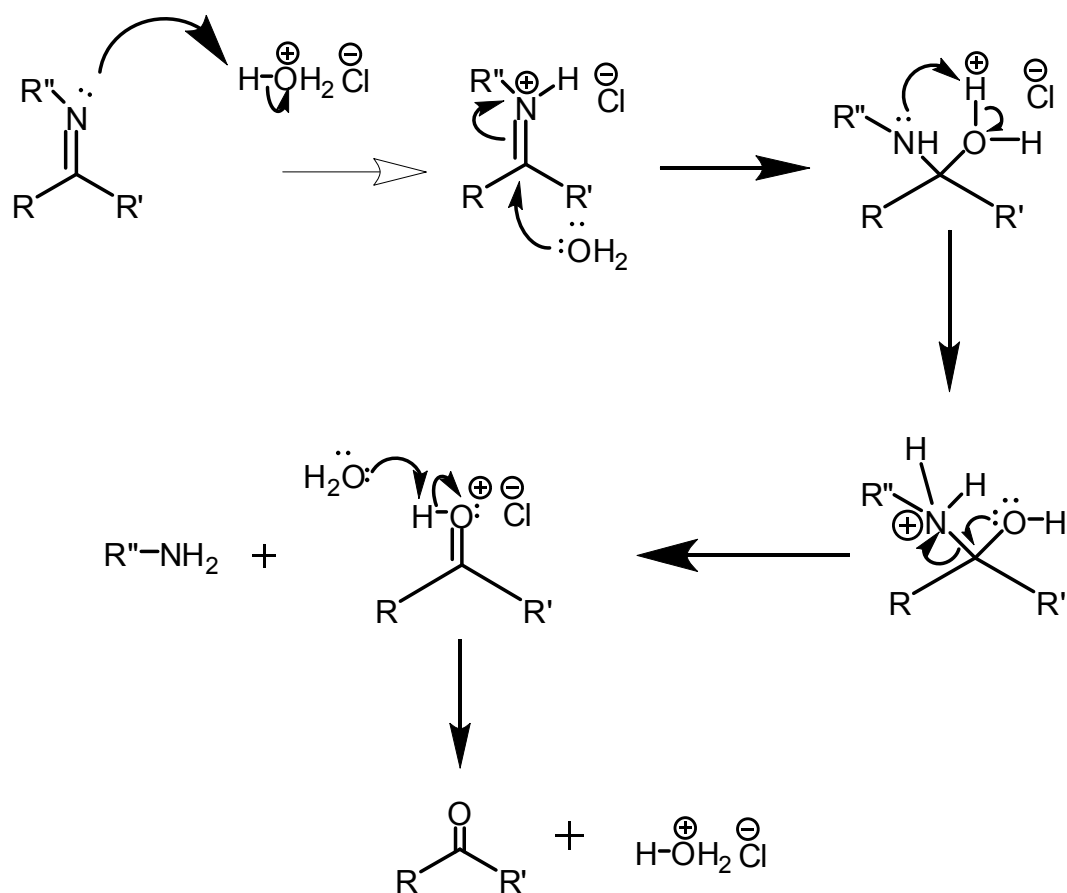


Fig. S27 : General mechanism for imine hydrolysis in acidic condition.