# Supporting Information

# Exploring the Antimicrobial Potential of Isoniazid Loaded Cu-based Metal-Organic Framework as a Novel Strategy for Effective Killing of *Mycobacterium tuberculosis*

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[§] Pawan Kumar (Design and synthesis of Cu-MOF, characterization and drug delivery) and Ananyaashree Behera (Involved in Biological studies) contributed equally to this work

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# Contents



**Schemes and Figures**

## 1. Characterization:

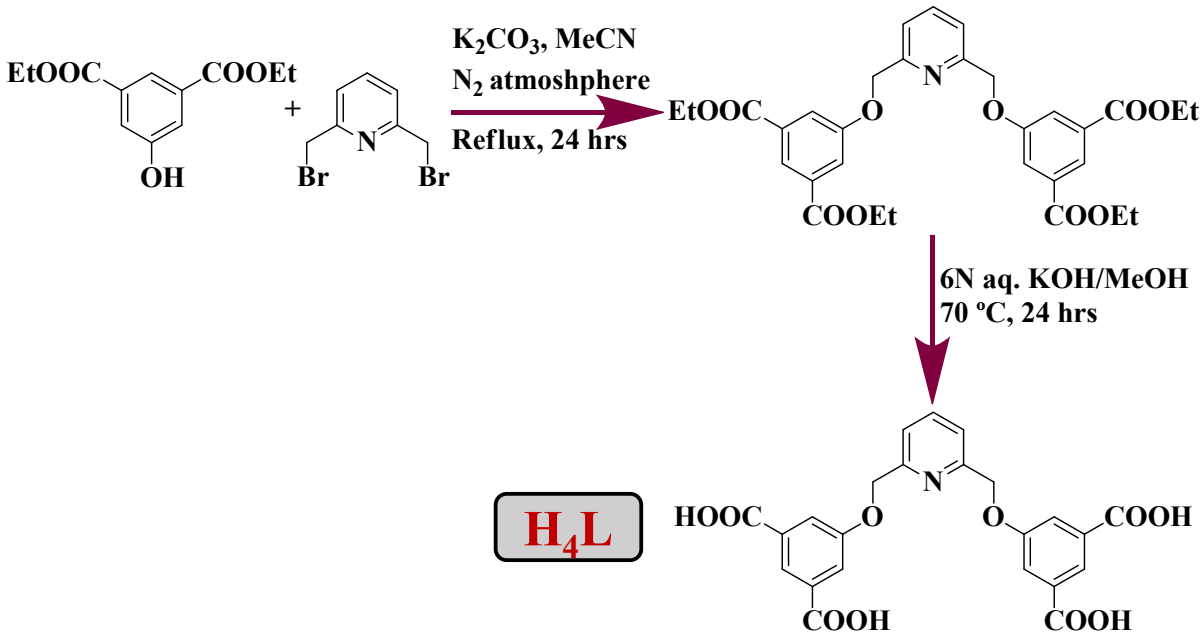
ESI-TOF-MS was used to perform high-resolution mass spectral studies (HRMS). On 500 MHz spectrometers, the $^{1}H$ and $^{13}C$ NMR spectra were captured. For $^{1}H$ NMR, data are presented as a chemical shift (ppm), multiplicity (singlet, doublet, triplet, quartet, multiplet), coupling constant J (Hz), integration, and assignment; for $^{13}C$, data are presented as a chemical shift. NMR apparatus using $Me_4Si$ as the internal standard in DMSO-$d_6$ and $CDCl_3$. Monochromatic Cu−Kα radiation (1.54 Å) was used to record the powder X-ray diffraction (PXRD) data on a Rigaku Smart-Lab X-ray diffractometer, and the tube voltage and current were 40 kV and 40 mA, respectively. FE-SEM images were recorded by JOEL-7610 F plus. The Perkin Elmer-Spectrum Two in ATR mode was used to conduct the FT-IR (Fourier Transform Infrared Spectroscopy) experiment. Thermogravimetric analysis (TGA) was performed using a Mettler Toledo (TGA/DSC 1) analyzer with STARe software and heated to 800 °C at a rate of 10 °C/min while being supplied with a continuous flow of liquid nitrogen. On an Autosorb iQ, Brunauer-Emmett-Teller (BET) surface area and Barrett-Joyner-Halenda (BJH) distribution calculations were made (Quanta chrome Instruments, version 1.11). UV-VIS data was recorded by Shimadzu's UV-1900 UV-VIS Spectrophotometer. DLS-Zeta have been recorded by The Malvern Zetasizer Nano ZSP (ZEN 5600).

## 2. Synthesis of $H_4L$:

### 2.1 Synthesis of tetraethyl 5,5'-((pyridine-2,6-diylbis (methylene)) bis(oxy))diisophthala te:

5-hydroxyisophthalic acid diethyl ester (10.4 mmol, 2.478 g) was placed in a round-bottom flask (RB) and agitated at 80 °C for 30 minutes while under an $N_2$ atmosphere. Dry acetonitrile (200 mL) and dry $K_2CO_3$ (26.4 mmol, 3.6 g) were added. 2,6-

**Scheme 1:** The systematic synthesis procedure of **$H_4L$.**




bis(bromomethyl)pyridine (4.528 mmol, 1.2 g) was then added to the mixture, and the resultant solution was refluxed for 24 hours. The entire combination was then allowed to cool to ambient temperature, solvent was evorated by rotavapour and work-up three times with EtOAc:water, before passing through the anhydrous $Na_2SO_4$. In the final step, EtOAc was evorated, a white solid was obtained. A 2.492 g product yield was obtained (4.302 mmol, 95%) (Scheme 1). HRMS (ESI-TOF) m/z $[M + Na]^+$ calculated for $C_{31}H_{33}NO_{10}Na^+$ 602.1997 and found to be 602.1990 (**Figure S1**). $^1H$ NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 2H), 7.88 (d, J = 1.2 Hz, 4H), 7.80 (t, J = 7.8 Hz, 1H), 7.51 (d, J = 7.8 Hz, 2H), 5.29 (s, 4H), 4.40 (q, J = 7.1 Hz, 8H), 1.41 (t, J = 7.1 Hz, 12H) (**Figure S2**). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 165.1, 157.9, 155.5, 137.4, 131.8, 123, 120, 119.5, 70.4, 61, 13.8. (**Figure S3**)

**2.2 Synthesis of 5,5'-((pyridine-2,6-diylbis(methylene))bis(oxy))diisophthalic acid ($H_4L$):**

Using 20 mL of 6(N) KOH solution, the chemical produced as above (4.302 mmol, 2.492 g) was refluxed in MeOH for 24 hours. The resultant solution was acidified with 6(N) HCl solution after cooling to 5 °C to produce a white precipitate. Then the white precipitate was filtered out and carefully cleaned before being dried in the air. A yield of 1.6 g of product was

discovered (3.424 mmol, 79 %). HRMS (ESI-TOF) m/z $[M - H]^-$ calculated for $C_{23}H_{16}NO_{10}^-$ 466.0769 and found to be 466.0768 (**Figure S4**). $^1H$ NMR (500 MHz, DMSO) δ 8.11 (s, 2H), 7.89 (t, J = 7.8 Hz, 1H), 7.72 (s, 4H), 7.50 (d, J = 7.7 Hz, 2H), 5.29 (s, 5H) (**Figure S5**). $^{13}C$ NMR (126 MHz, DMSO) δ 167.4, 158.2, 156.2, 138.4, 134.6, 123.1, 121.1, 119, 70.6 (**Figure S6**).

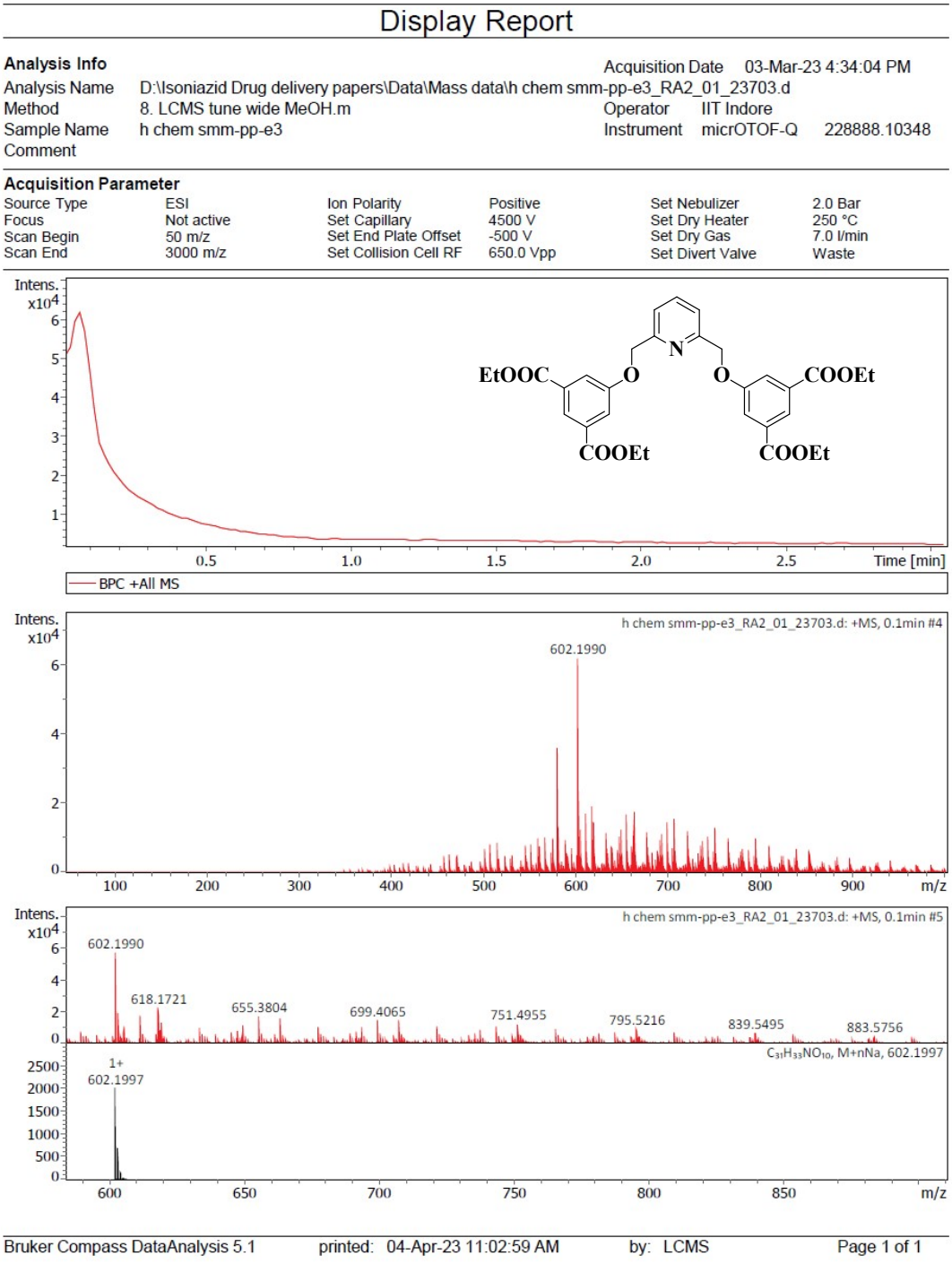



**Figure S1:** HRMS Spectrum of tetraethyl 5,5'-((pyridine-2,6-diylbis(methylene)) bis(oxy))diisophthalate.

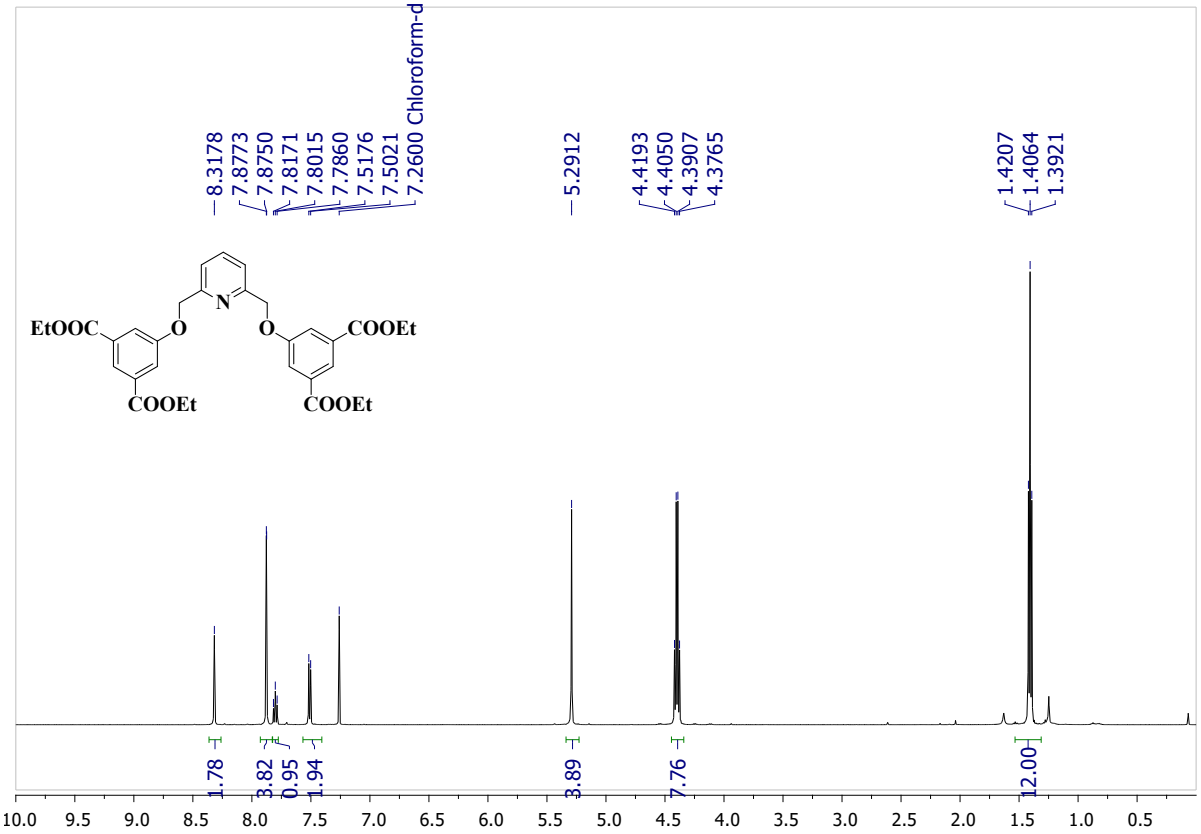



**Figure S2:** $^{1}$H NMR of 5,5'-((pyridine-2,6-diylbis(methylene))bis(oxy))diisophthalate.

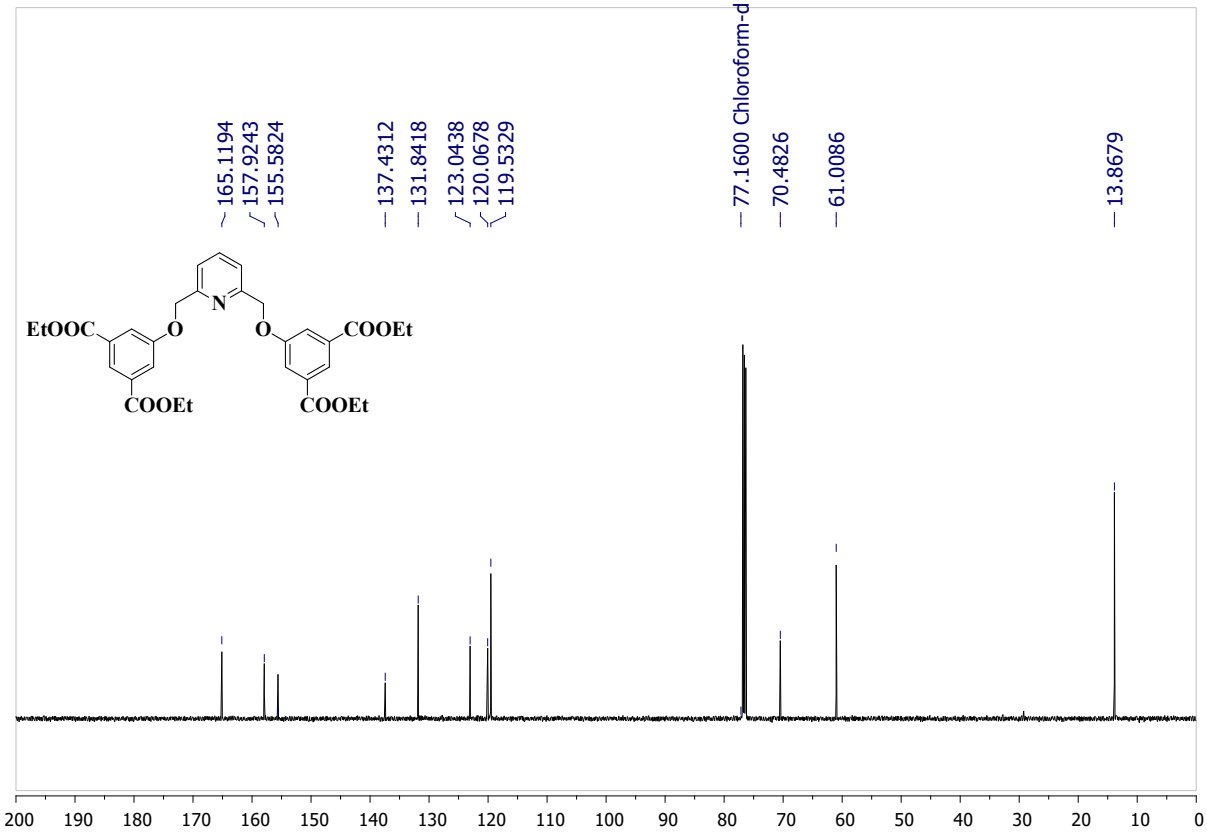



**Figure S3:** $^{13}$C NMR of 5,5'-((pyridine-2,6-diylbis(methylene))bis(oxy))diisophthalate.

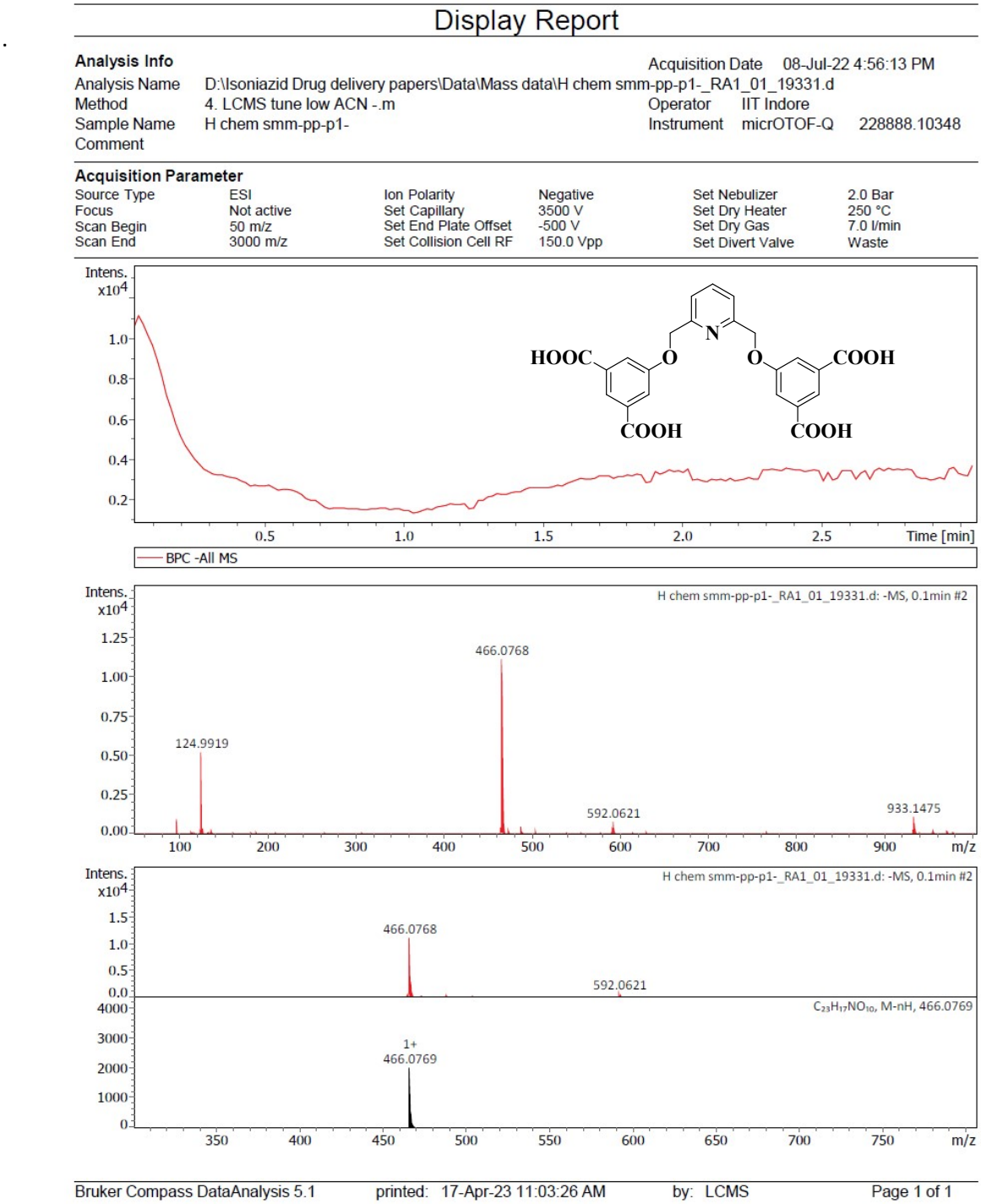



**Figure S4:** 5,5'-((pyridine-2,6-diylbis(methylene))bis(oxy))diisophthalic acid ($\mathbf{H_4L}$).

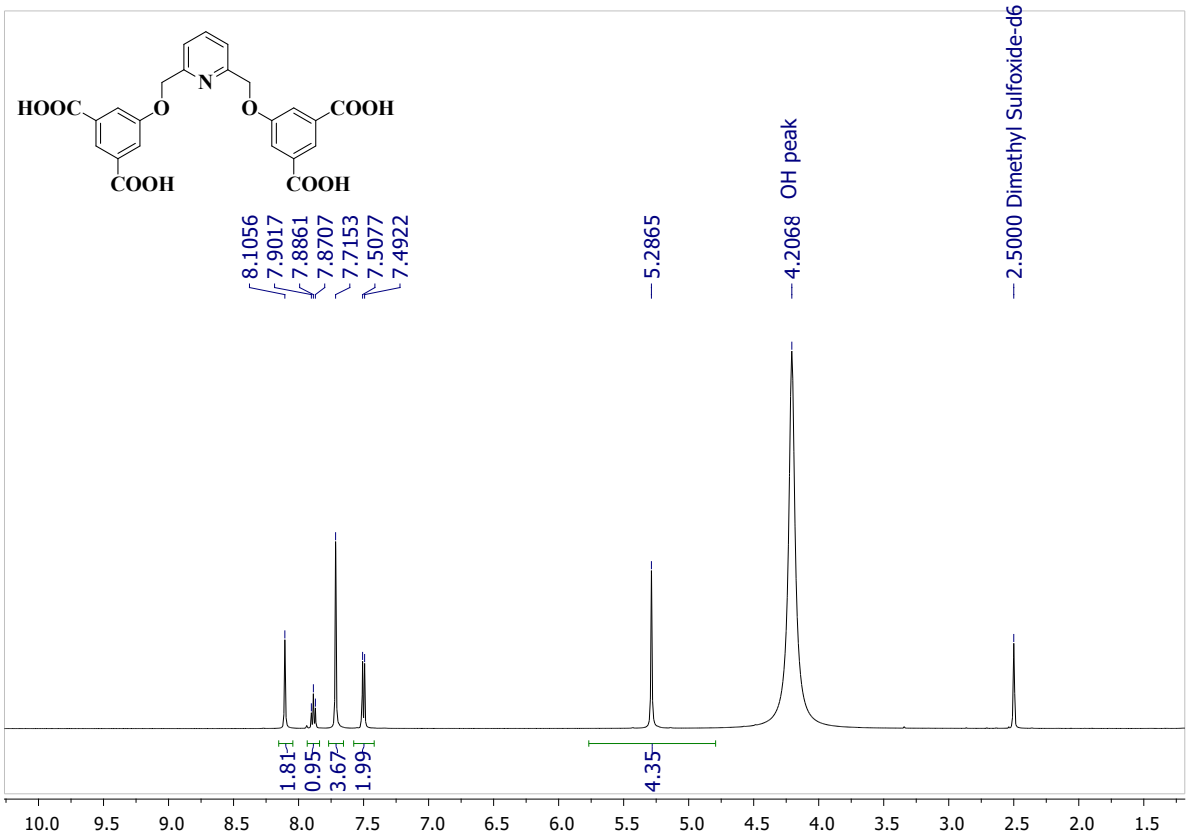



**Figure S5:** $^{1}$H NMR of 5,5'-((pyridine-2,6-diylbis(methylene))bis(oxy))diisophthalic acid.

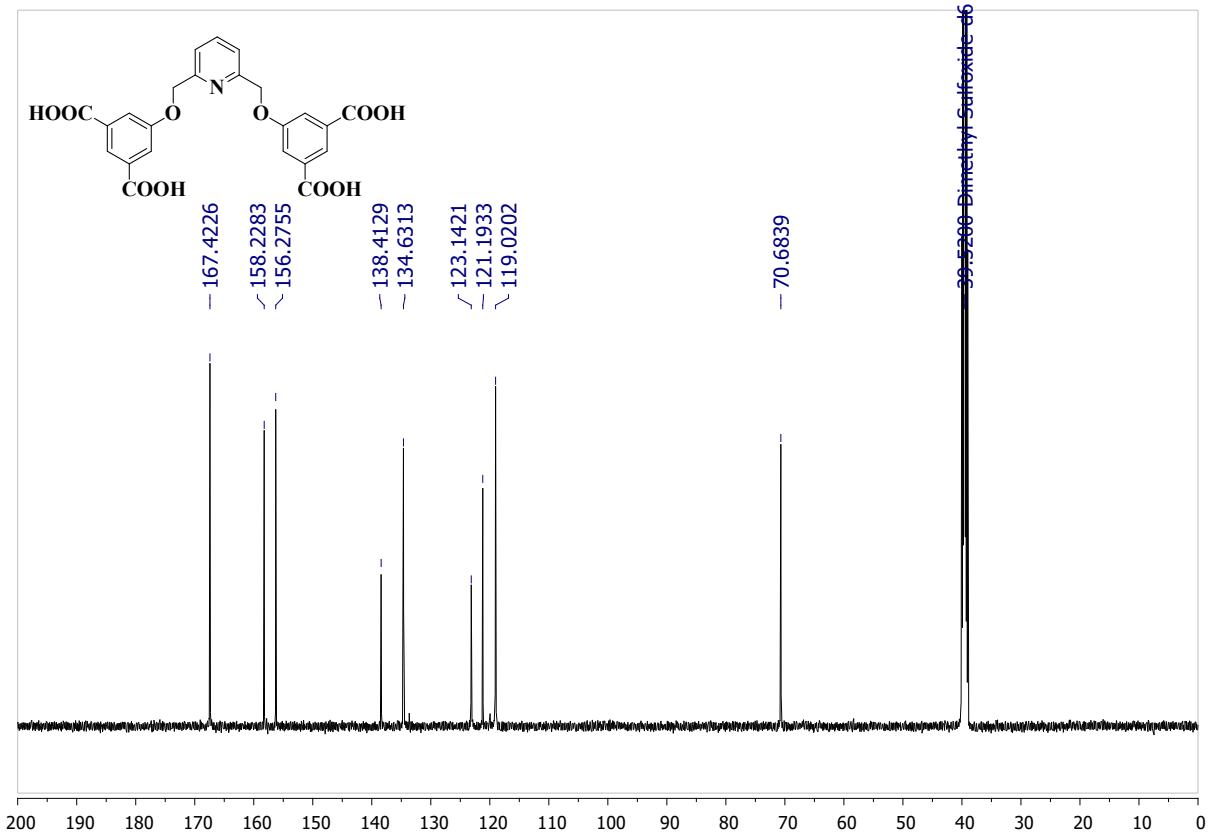



**Figure S6:** $^{13}$C NMR of 5,5'-((pyridine-2,6-diylbis(methylene))bis(oxy))diisophthalic acid.

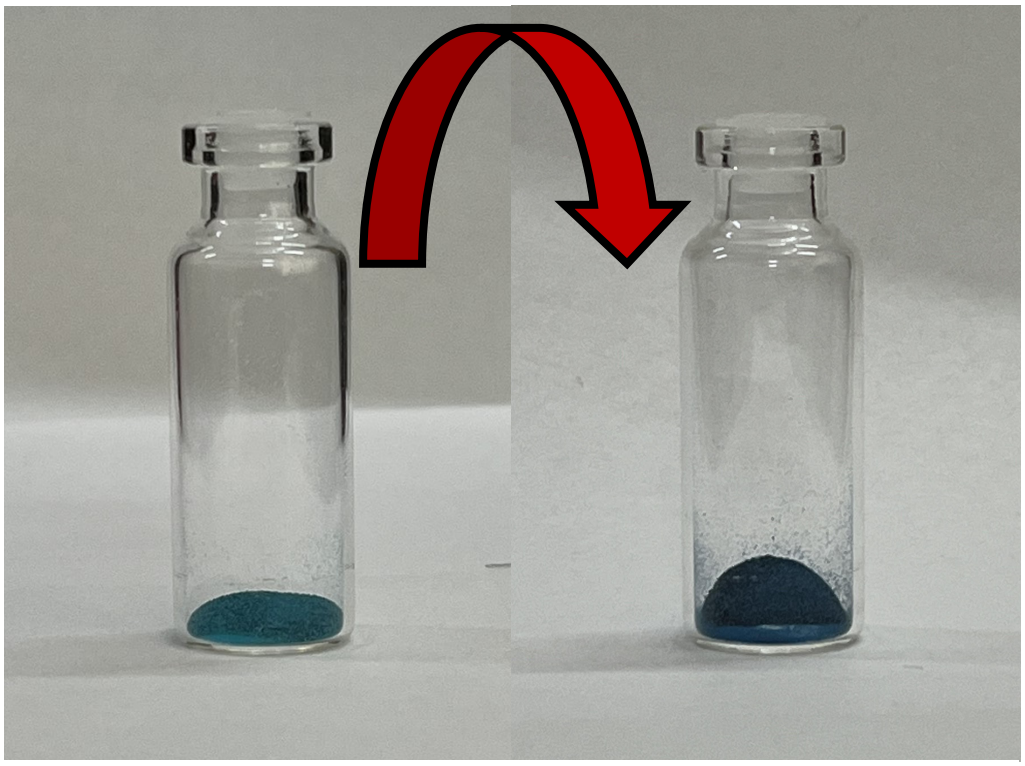


**Figure S7:** Activation of **IITI-3**.

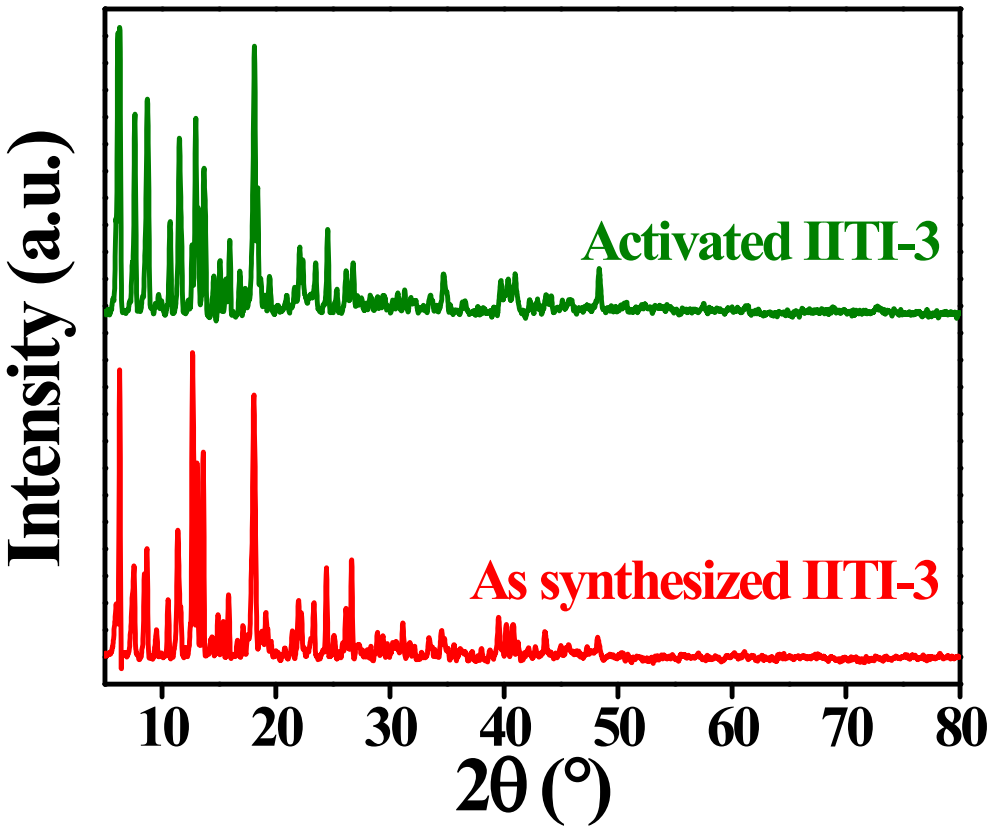



**Figure S8:** PXRD of As synthesized and Activated **IITI-3** respectively.

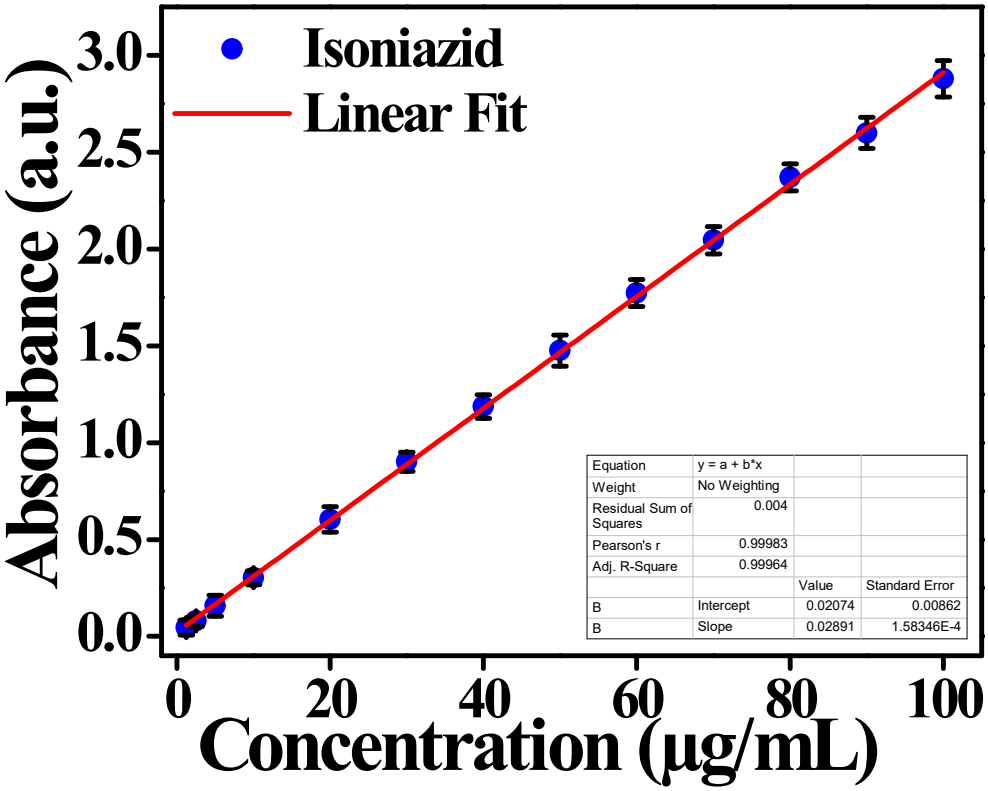



**Figure S9:** Relation between **INH** and absorbance.

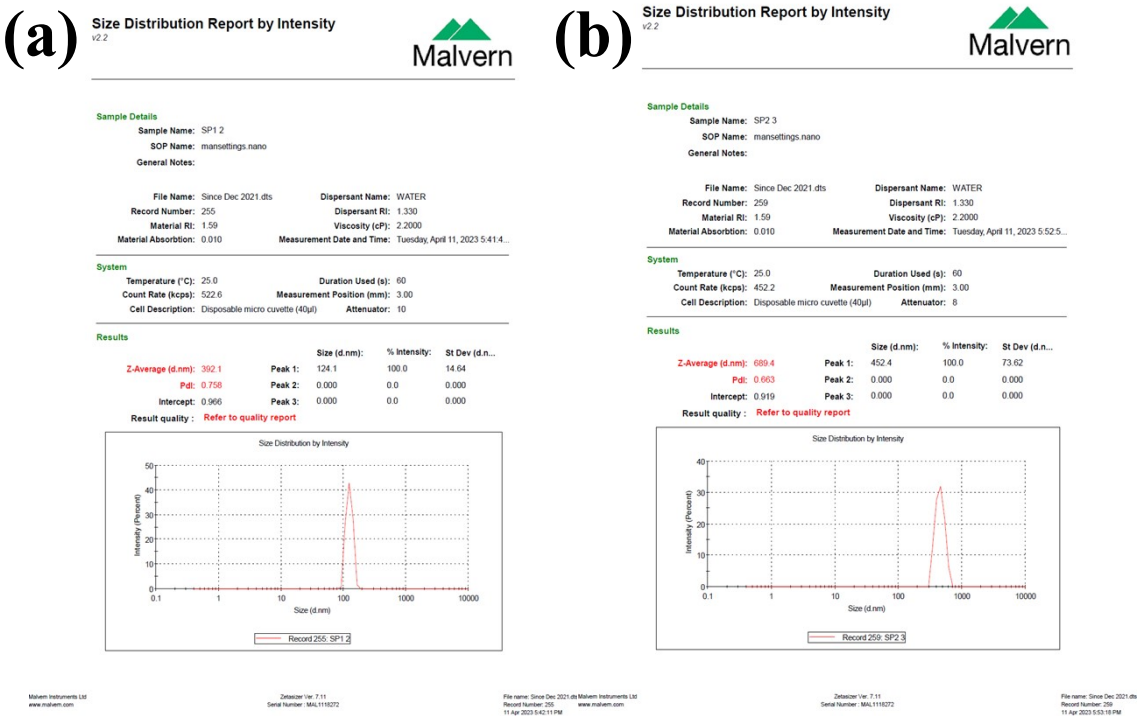



**Figure S10:** DLS: Average particle sized of **IITI-3** and **INH@IITI-3**.

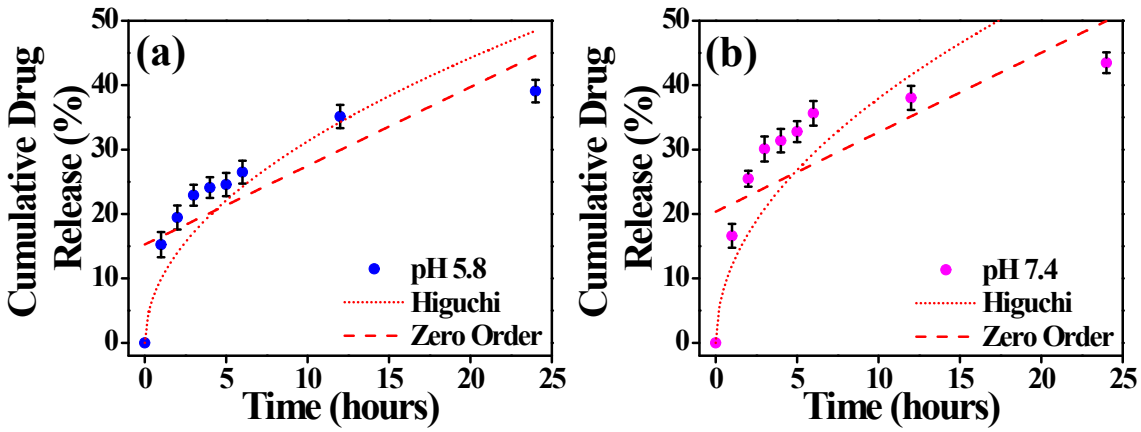



**Figure S11:** Cumulative drug release from **INH@IITI-3** at pH 5.8 and 7.4 with Higuchi and zero order kinetics respectively.

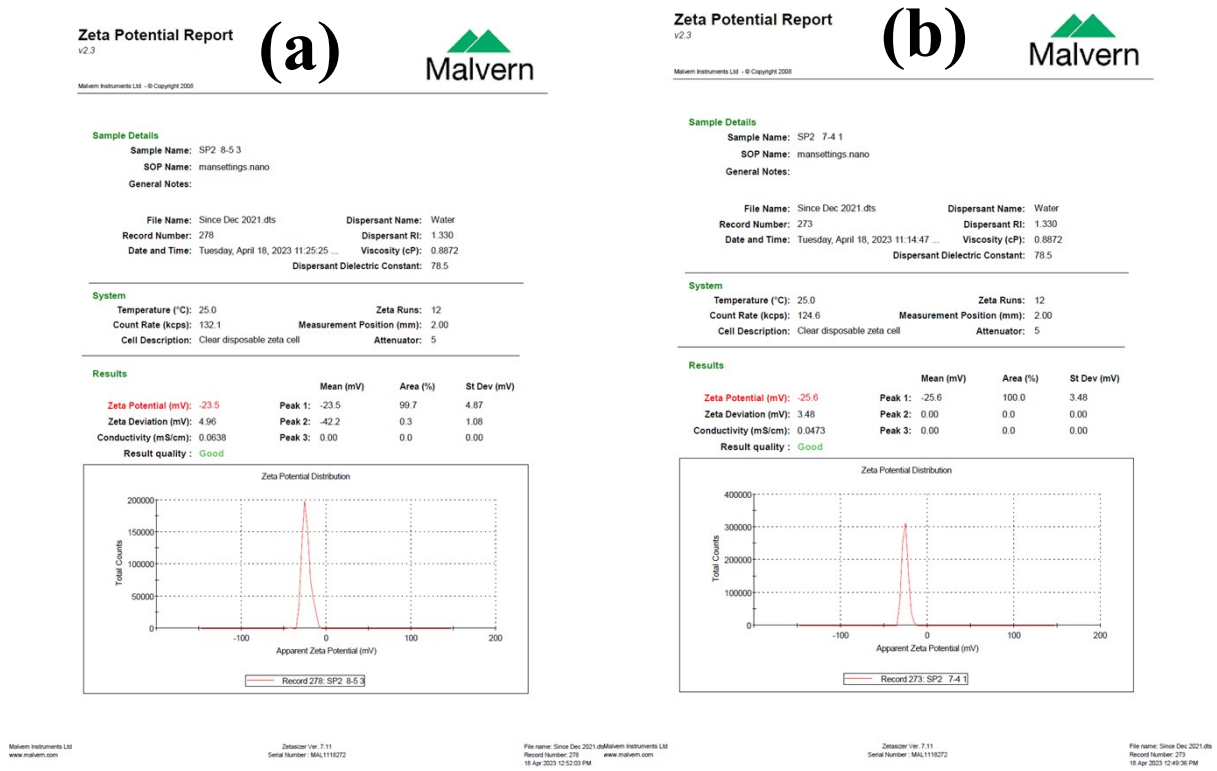



**Figure S12:** zeta potential of **INH@IITI-3** at pH 5.8 and 7.4 repectively.