Supporting Information

Designing coordination polymers as multi-drug-self-delivery system for tuberculosis and cancer therapy: in vitro viability and in vivo toxicity assessment

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1. TableS1: Crystallographic table

Identification code	**IZIBU**	**IZFEN**	**IZNAP**	**IZDIC**	**IZMEF**
CCDC No	2116236	2116240	2116237	2116241	2116238
Crystalizing Solvent	Water:MeOH:EtOH (1:1:1)	Water:MeOH:EtOH (1:1:1)	Water:MeOH:EtOH (1:1:1)	Water:MeOH:EtOH (1:1:1)	Water:MeOH:EtOH (1:1:1)
Empirical formula	$C_{32}H_{41}N_3O_5Zn$	$C_{18}H_{15}N_{1.5}O_{3.5}Zn_{0.5}$	$C_{34}H_{35}N_3O_8Zn$	$C_{34}H_{27}Cl_4N_5O_5Zn$	$C_{53}H_{50}N_6O_{7.5}Zn_2$
Formula weight	613.05	341.00	679.02	792.77	1021.73
Temperature/K	296.15	150	298	293	108.68
Crystal system	monoclinic	monoclinic	orthorhombic	orthorhombic	monoclinic
Space group	$P2_1/c$	C2/c	$P2_12_12_1$	$Pna2_1$	$P2_1/n$
a/Å	5.5050(2)	34.8416(12)	5.6410(10)	9.945(16)	12.3515(9)
b/Å	15.5099(5)	5.7437(2)	15.610(3)	9.340(15)	20.4246(15)
c/Å	36.8473(10)	18.0193(6)	35.093(7)	36.37(6)	19.0171(14)
α/°	90	90	90	90	90
β/°	90.06	119.322(2)	90	90	97.138(2)
γ/°	90	90	90	90	90
Volume/Å^3	3146.09(18)	3144.02(19)	3090.1(10)	3378(9)	4760.3(6)
Z	4	8	4	4	4
ρ_{calc}g/cm^3	1.294	1.441	1.460	1.559	1.426
μ/mm^{-1}	0.823	0.837	0.853	1.094	1.069
F(000)	1296.0	1412.0	1416.0	1616.0	2120.0
Crystal size/mm^3	$0.5 \times 0.3 \times 0.1$	$0.36 \times 0.2 \times 0.1$	$0.3 \times 0.15 \times 0.1$	$0.31 \times 0.31 \times 0.21$	$0.32 \times 0.3 \times 0.2$
Radiation	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)
2Θ range for data collection/°	2.848 to 52.036	4.524 to 54.706	2.856 to 50.782	4.48 to 54.568	4.536 to 57.99
Index ranges	-6 ≤ h ≤ 6, -19 ≤ k ≤ 19, -45 ≤ l ≤ 44	-44 ≤ h ≤ 44, -7 ≤ k ≤ 7, -22 ≤ l ≤ 23	-6 ≤ h ≤ 6, -18 ≤ k ≤ 18, -42 ≤ l ≤ 42	-12 ≤ h ≤ 12, -12 ≤ k ≤ 11, -46 ≤ l ≤ 46	-16 ≤ h ≤ 16, -27 ≤ k ≤ 27, -25 ≤ l ≤ 25
Reflections collected	38063	20524	38249	42885	55019
Independent reflections	5639 [R_{int} = 0.0786, R_{sigma} = 0.0956]	3359 [R_{int} = 0.1088, R_{sigma} = 0.0941]	5652 [R_{int} = 0.0947, R_{sigma} = 0.0684]	7516 [R_{int} = 0.0547, R_{sigma} = 0.0411]	12443 [R_{int} = 0.0659, R_{sigma} = 0.0627]
Data/restraints/parameters	5639/0/382	3359/0/243	5652/0/422	7516/1/450	12443/0/692
Goodness-of-fit on F^2	0.895	1.260	1.111	1.038	1.095
Final R indexes [I>=2σ (I)]	R_1 = 0.0435, wR_2 = 0.0912	R_1 = 0.0998, wR_2 = 0.1787	R_1 = 0.0535, wR_2 = 0.0857	R_1 = 0.0531, wR_2 = 0.1285	R_1 = 0.0571, wR_2 = 0.1214
Final R indexes [all data]	R_1 = 0.0929, wR_2 = 0.1019	R_1 = 0.1474, wR_2 = 0.1922	R_1 = 0.0859, wR_2 = 0.0952	R_1 = 0.0720, wR_2 = 0.1383	R_1 = 0.0781, wR_2 = 0.1291
Largest diff. peak/hole / e Å^{-3}	0.28/-0.23	0.95/-0.96	0.44/-0.64	0.50/-0.43	0.95/-0.93
Flack parameter	-	-	0.017(8)	-	-

2. IR data of the Coordination polymers (CPs).
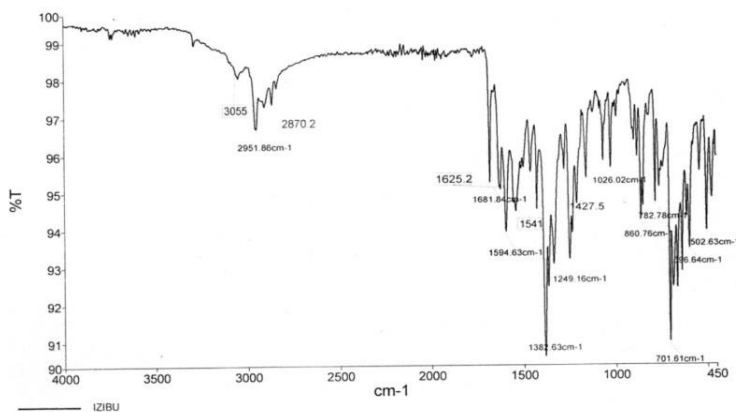
Figure S1: FT-IR spectra of **IZIBU**
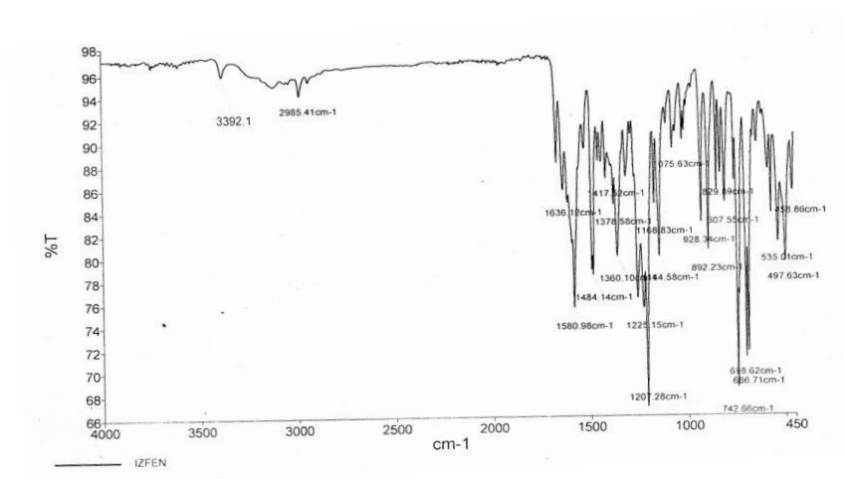
Figure S2: FT-IR spectra of **IZFEN**
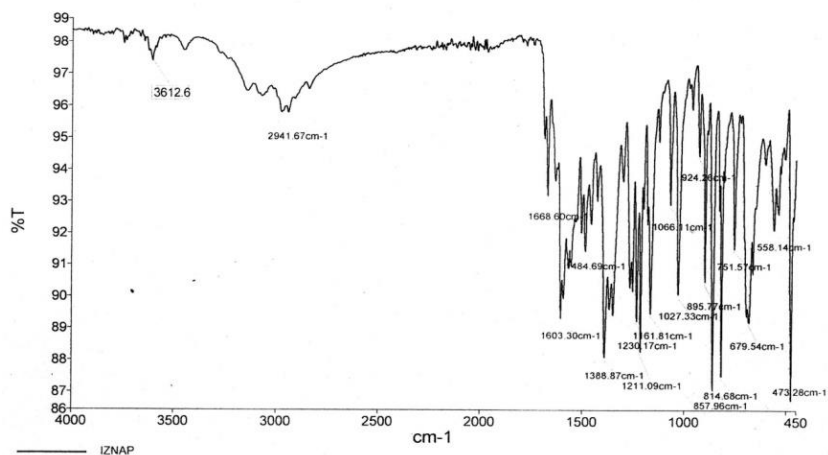
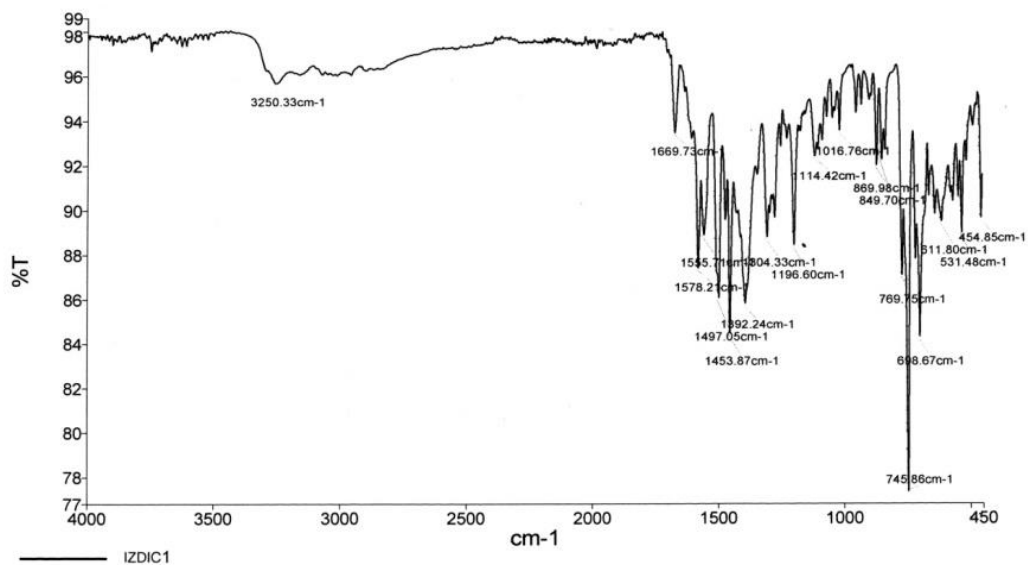**Figure S3:** FT-IR spectra of **IZNAP**

Figure S4: FT-IR spectra of **IZDIC**
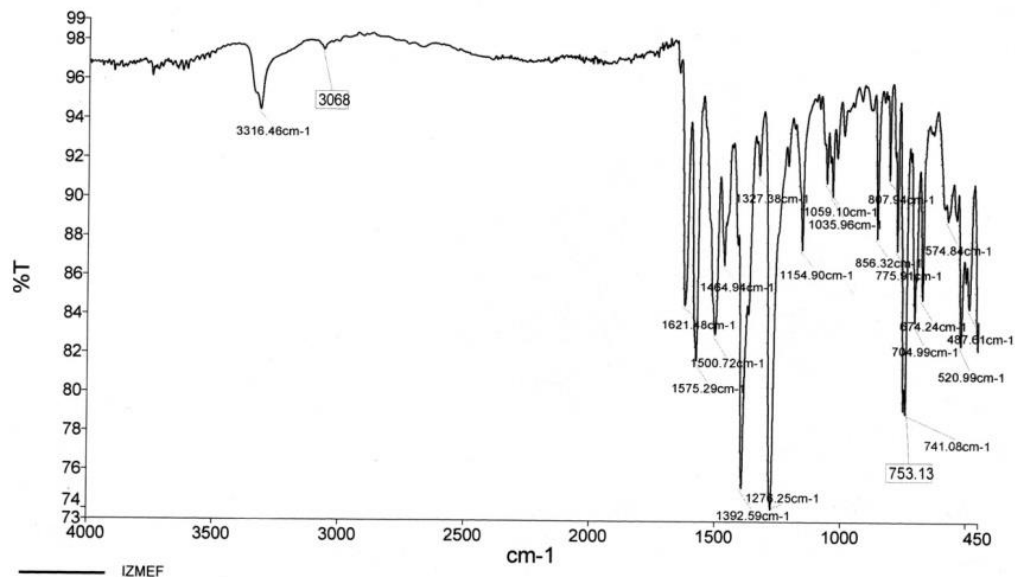
Figure S5: FT-IR spectra of **IZMEF**

3. ORTEP and H bond table of the crystals structure

Figure S6: ORTEP of **IZIBU**.
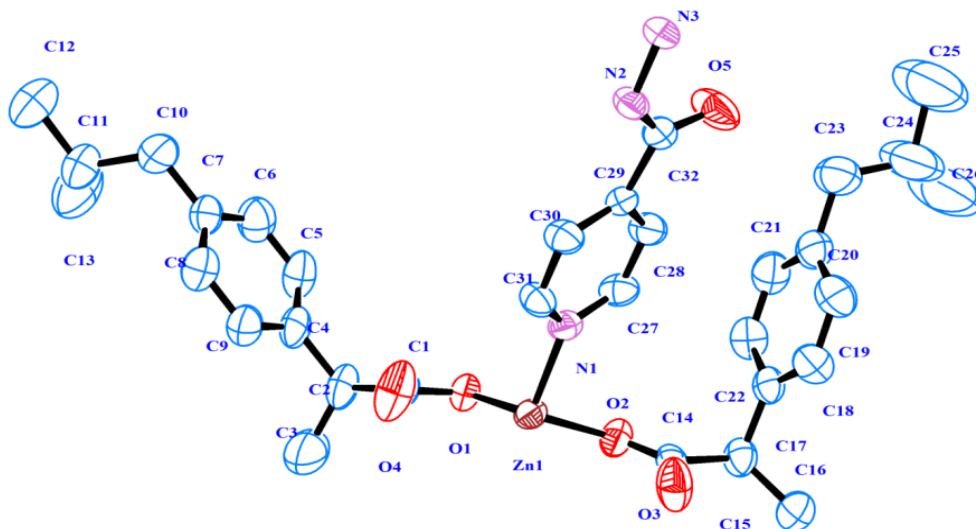
Table S2 - Hydrogen Bonds (Angstrom, Deg) for: **IZIBU**					
D-H···A	**d(D-H) (Å)**	**d(H···A) (Å)**	**∠DHA (°)**	**d(D···A) (Å)**	**Symmetry**
N2 - H2···O3	0.91(4)	1.81(4)	166(3)	2.708(4)	[2-x, 1/2 +y,1/2 –z]
N3 - H3A···O1	0.98(4)	2.01(4)	167(3)	2.964(4)	[1-x, 1/2 +y,1/2 –z]
C2 - H2A···O4	0.98	2.59	177	3.564(5)	[-1+x, y, z]
C30 - H30···O3	0.93	2.54	150	3.377(4)	[2-x, 1/2+y,1/2-z]
C31 -H31···O1	0.93	2.52	148	3.344(4)	[1+x, y, z]

Figure S7: ORTEP of **IZFEN**.
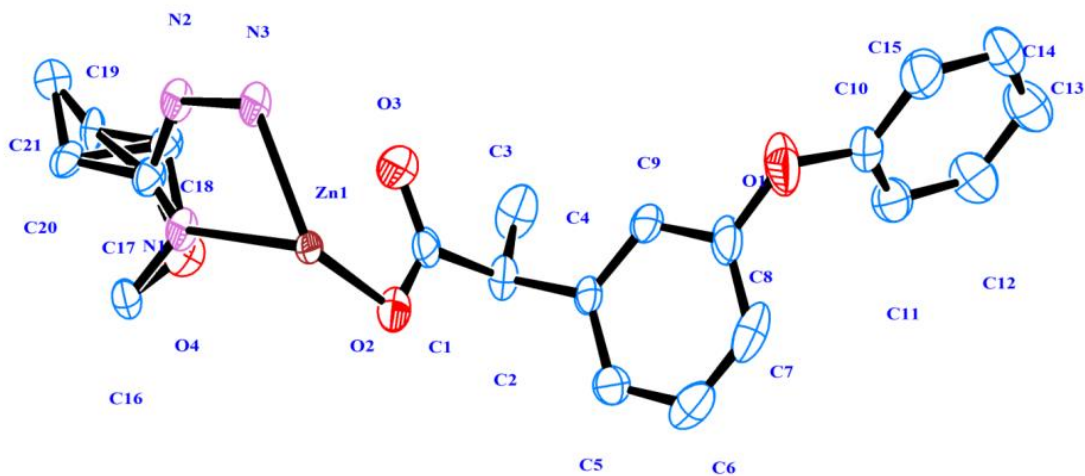
Table S3 - Hydrogen Bonds (Angstrom, Deg) for: **IZFEN**					
D-H···A	**d(D-H)** **(Å)**	**d(H···A)** **(Å)**	**∠DHA (°)**	**d(D···A)** **(Å)**	**Symmetry**
N3-H3···O3	0.94(8)	2.23(7)	124(6)	2.870(14)	[1-x, 1+y, 3/2-z]
C5-H5···31	0.93	2.43	170	3.354(9)	[1-x, +y, z]

Figure S8: ORTEP of **IZNAP.**
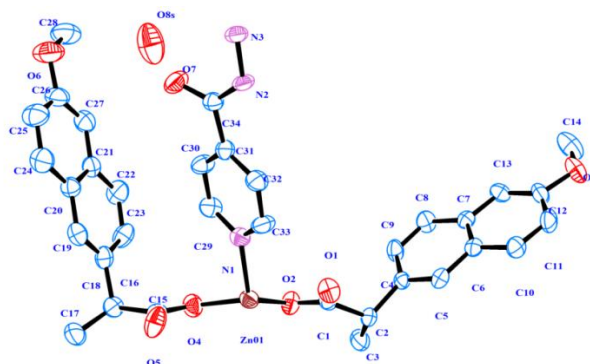
Table S4 - **Hydrogen Bonds (Angstrom, Deg) for: IZNAP**					
D-H···A	**d(D-H)** **(Å)**	**d(H···A)** **(Å)**	**∠DHA (°)**	**d(D···A)** **(Å)**	**Symmetry**
N2-H2···O5	0.86	1.903	150.57	2.686(6)	[-x+2, y+1/2, -z+3/2]
N3-H3A···O8S	0.89	2.018	163.25	2.882(8)	[x+1, y, z]
N3-H3B···O2	0.89	2.125	163.02	2.987(6)	[-x+1, y+1/2, -z+3/2]
C3-H3E···O1	0.96	2.53	3.484(7)	175	[-1+x,y,z]
C23-H23···O5	0.93	2.4900	3.381(7)	161	[-1+x,y,z]

Figure S9: ORTEP of **IZDIC.**
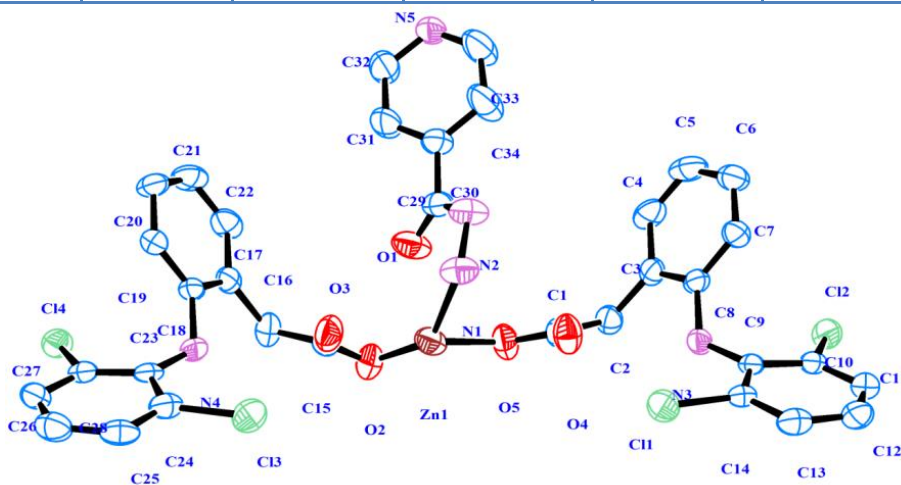
Table S5 - Hydrogen Bonds (Angstrom, Deg) for: **IZDIC**					
D-H···A	**d(D-H) (Å)**	**d(H···A) (Å)**	**∠DHA (°)**	**d(D···A) (Å)**	**Symmetry**
N1-H1A···O1	0.89	2.351	132.22	3.022(10)	[x-1/2,- y+1/2, z]
N2- H2···O5	0.56	2.002	152.9	2.796(10)	[x-1/2, -y+1/2, z]
C32-H32···O3	0.93	2.630	122.56	3.226(12)	[x, y+1, z]
C33-H33 ···O43	0.93	2.333	141.43	3.114(12)	[x,y+1,z]
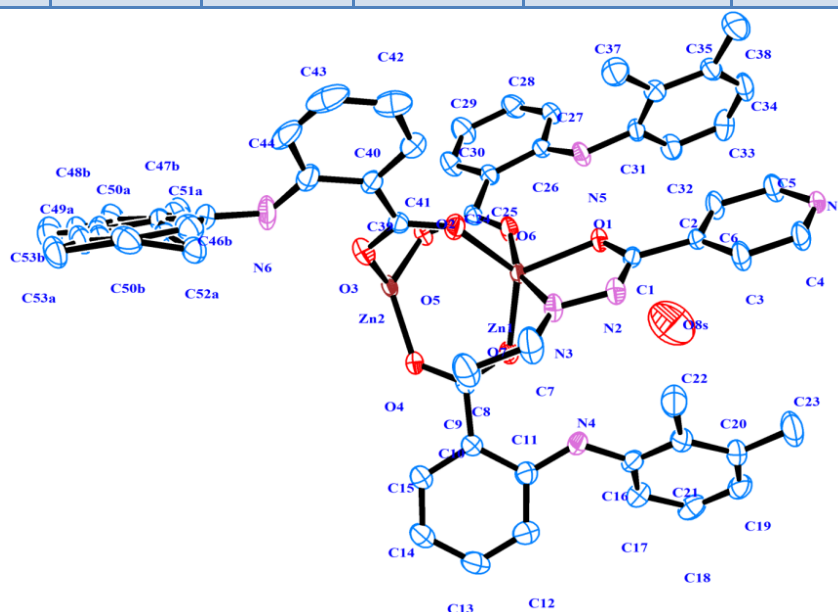
Figure S10: ORTEP of **IZMEF**.

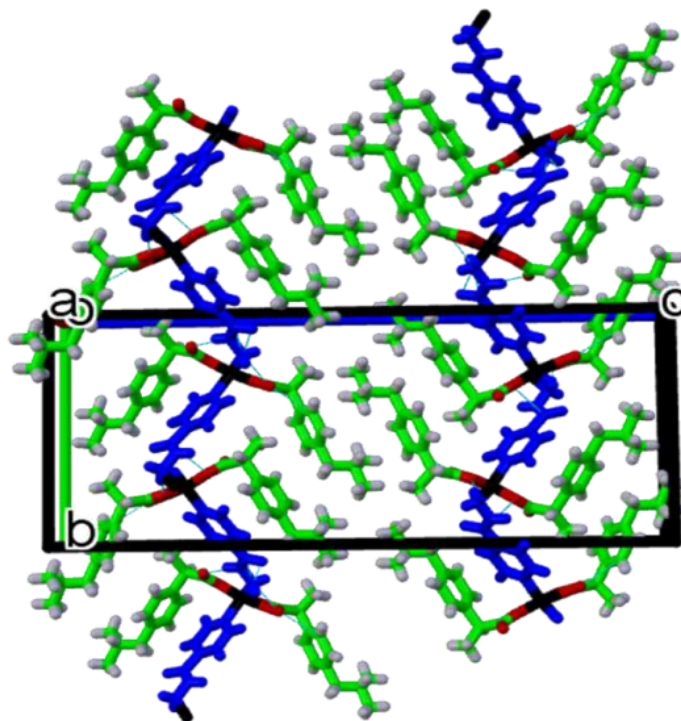| Table S6 - Hydrogen Bonds (Angstrom, Deg) for: IZMEF					
D-H···A	**d(D-H) (Å)**	**d(H···A) (Å)**	**∠DHA (°)**	**d(D···A) (Å)**	**Symmetry**
C13-H13···O8S	0.95	2.51	137	3.269(10)	1+x,y,z
C18-H18··· O5	0.95	2.49	155	3.376(4)	1/2+x,3/2-y,1/2+z
C43-H43···O1	0.95	2.43	153	3.309(6)	-1/2+x,3/2-y,-1/2+z
C53A-H53C···O5	0.98	2.52	155	3.428(9)	-1/2+x,3/2-y,-1/2+z

4. Single Crystal structure and model.

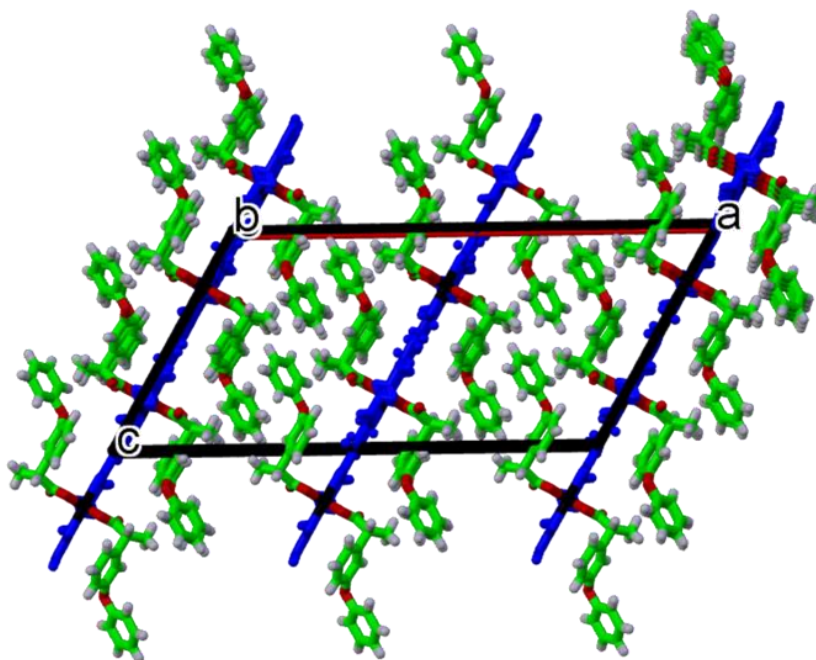**Figure S11:** Overall packing diagram of **IZIBU** in its crystal structure.

Figure S12: Overall packing diagram of **IZFEN** in its crystal structure.
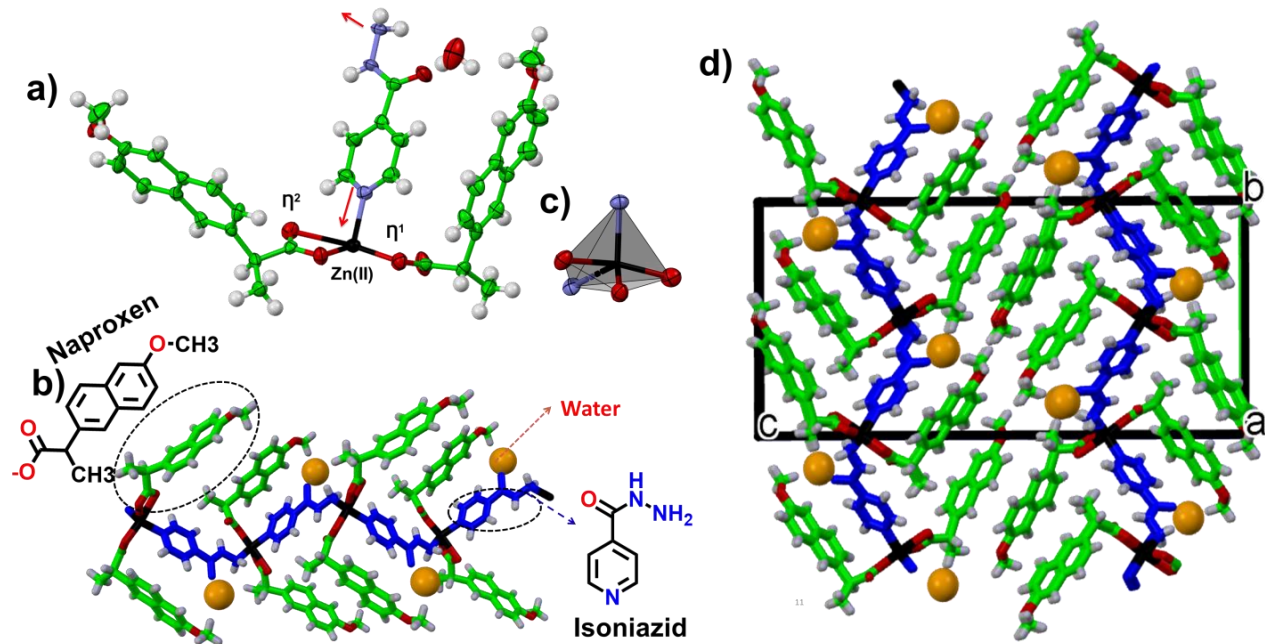
Figure S13: Crystal structure illustration of **IZNAP**; a) the asymmetric unit, b) 1D extended polymeric chain c) coordination environment of Zn(II) metal d) overall packing diagram.
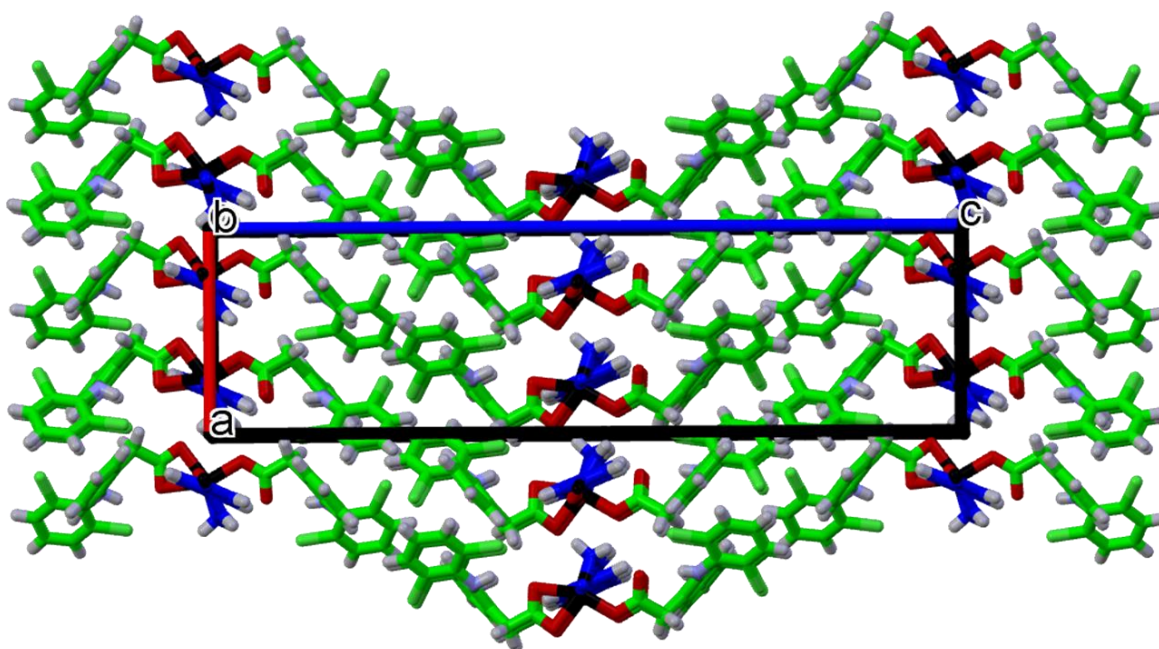

Figure S14: Overall packing diagram **of IZDIC** in its crystal structure.
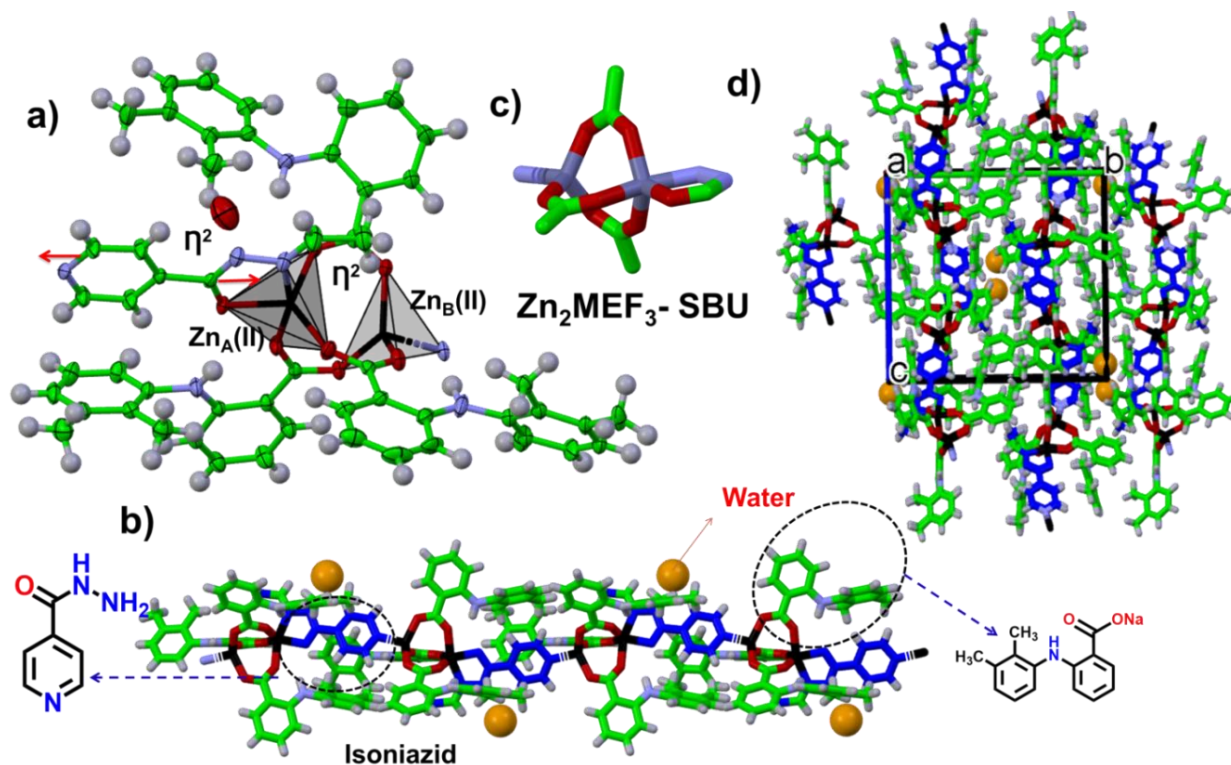
Figure S15: Crystal structure illustration of **IZMEF** (**IZ-EtMEF**); a) the asymmetric unit, b) 1D extended polymeric chain c) [Zn(II)]₂[**MEF**]₃ cluster d) overall packing diagram.

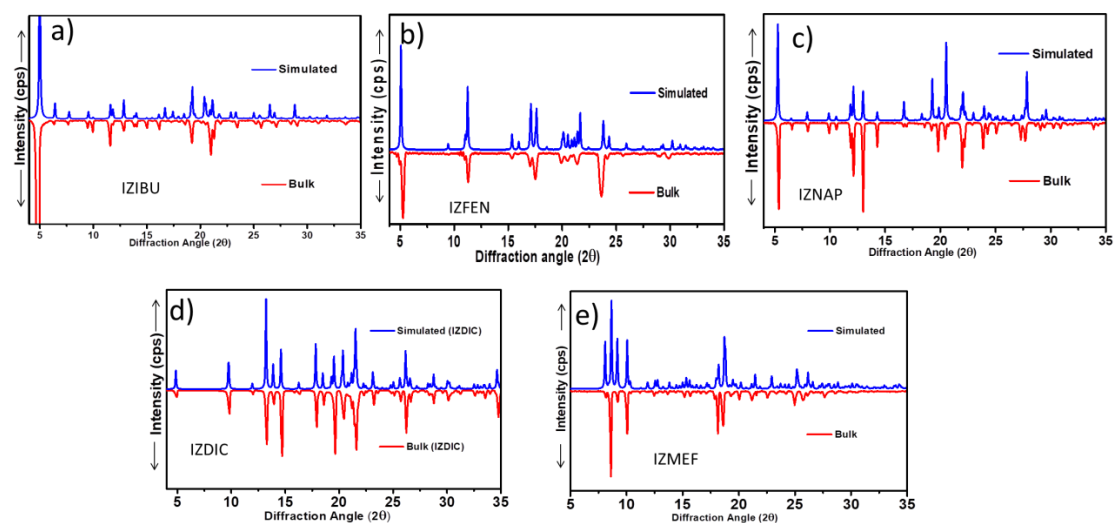## 5. Powder X-ray diffration study

Figure S16: PXRD patterns of a) **IZIBU**, b) **IZFEN**, c) **IZNAP**, d) **IZDIC**, e) **IZMEF** represented as mirror plot to assess the agreement of peak position.

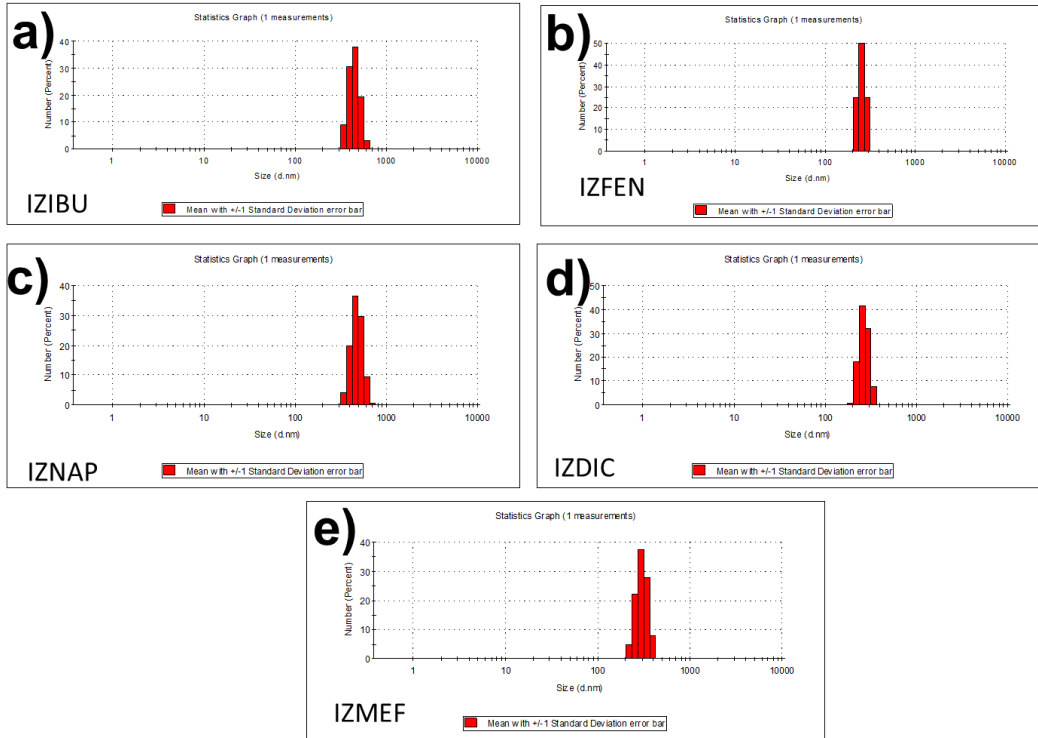## 6. Dynamic Light scattring and Zeta potential measurements

Figure S17: DLS traces of water dispersed nano CPs a) **IZIBU**, b) **IZFEN**, c) **IZNAP**, d) **IZDIC**, e) **IZMEF**
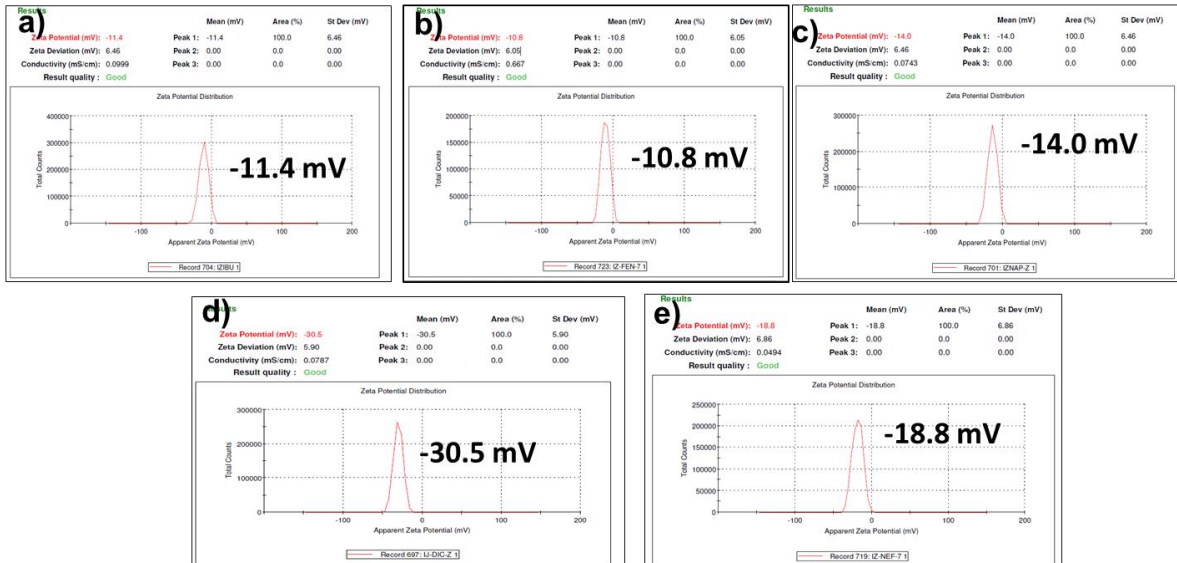

Figure S18: Zeta potential measurement of water dispersed nano CPs a) **IZIBU**, b) **IZFEN**, c) **IZNAP**, d) **IZDIC**, e) **IZMEF.**

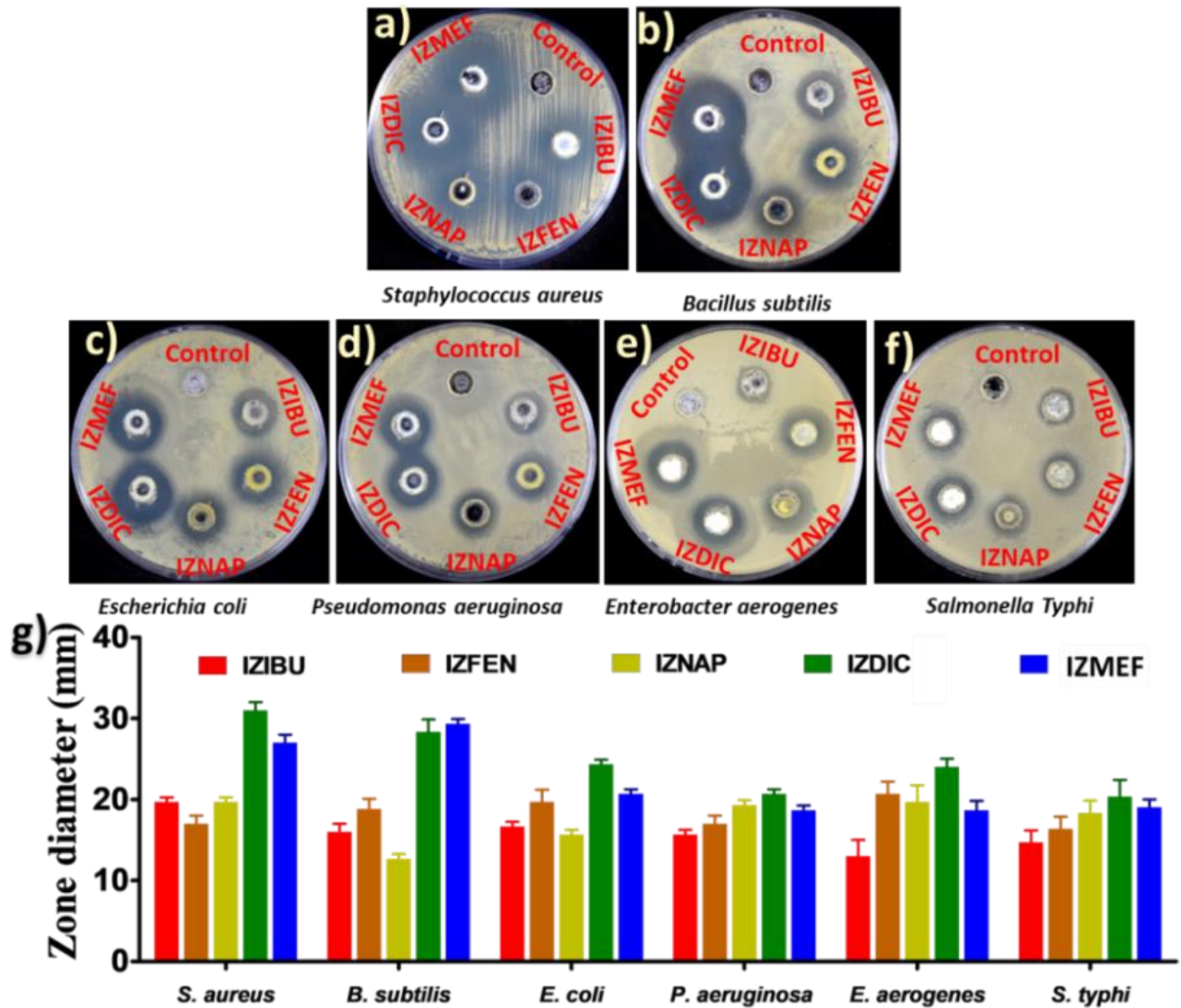## 7. Anti-bacterial zone inhibition assays:

Figure S19: Assessing anti-bacterial property of the CP by zone inhibition assay (each groove contains 1 mg CP in 20 µL DMSO; control - 20 µL DMSO); a-b) gram +ve bacteria, c-f) gram –ve bacteria g) zone diameter.
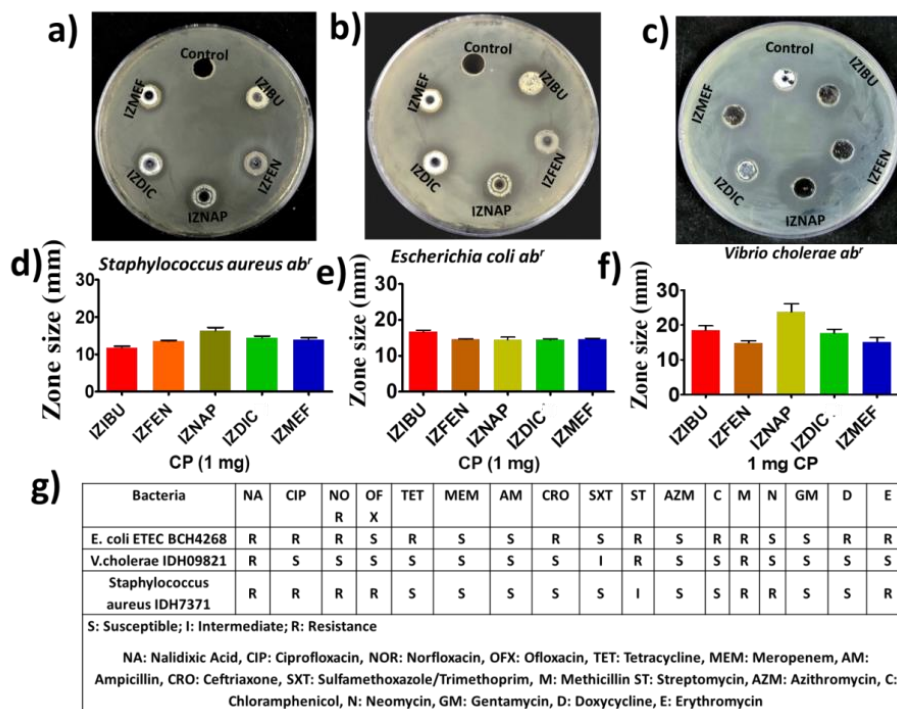
Figure S20: Assessing anti-bacterial property of the CP by zone inhibition assay (each groove contains 1 mg CP in 20 μL DMSO; control - 20 μL DMSO) against a-c) antibiotic resistant strains, d-f) zone diameter, g) antibiogram of the bacterial strains.
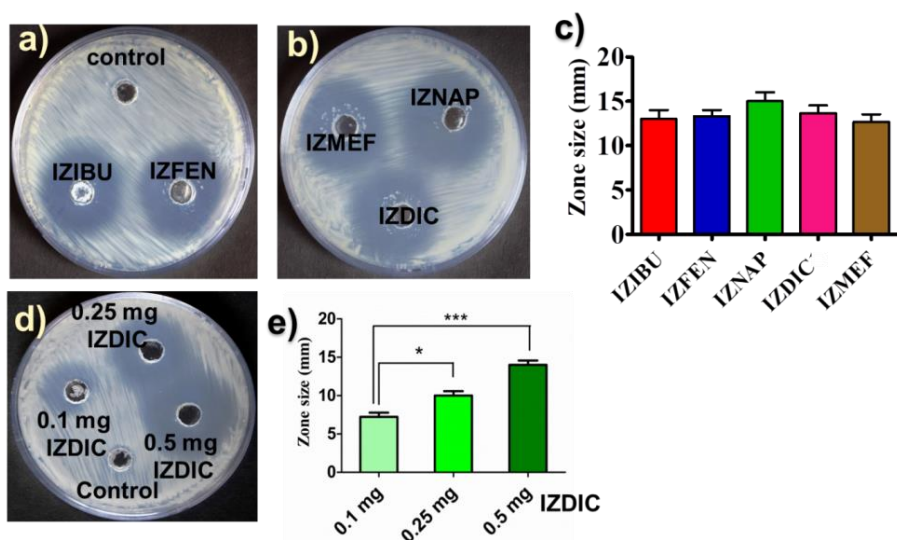

Figure S21: Assessing anti-bacterial property of the CP by zone inhibition assay (each groove contains 0.5 mg CP in 20 μL DMSO; control - 20 μL DMSO) against a-b) M.smeg, c) zone diameter, d) concentration dependent zone inhibition of M.smeg by **IZDIC** and e) the corresponding zone diameters (data represented as mean + SD, where *p<0.05, ***p<0.001 , n=3)
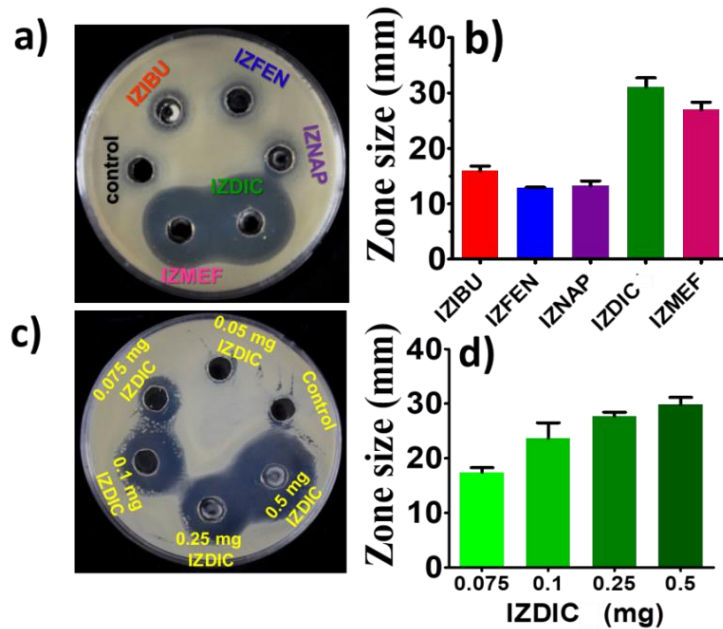
Figure S22: Assessing anti-bacterial property of the CP by zone inhibition assay (each groove contains 0.5 mg CP in 20 µL DMSO; control - 20 µL DMSO) against a-b) M.tb, c) zone diameter, d) concentration dependent zone inhibition of M.Tb by **IZDIC** and e) the corresponding zone diameters (data represented as mean + SD, where $*p<0.05$, $***p<0.001$, n=3)

8. Turbidity and Resazurin assays

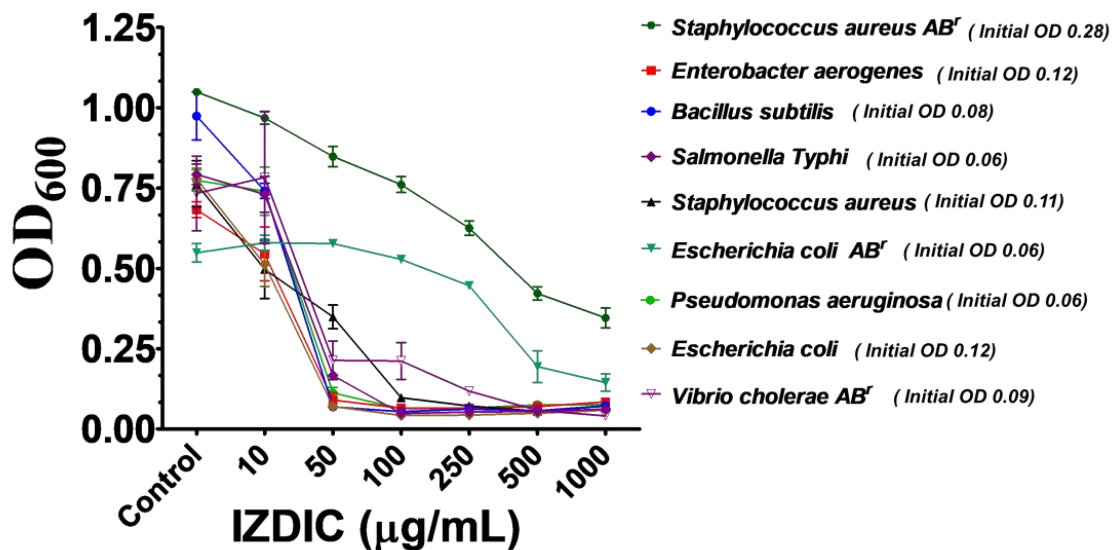**Figure 23:** Assessing MIC of **IZDIC** by turbidity assay (incubation period 24h).
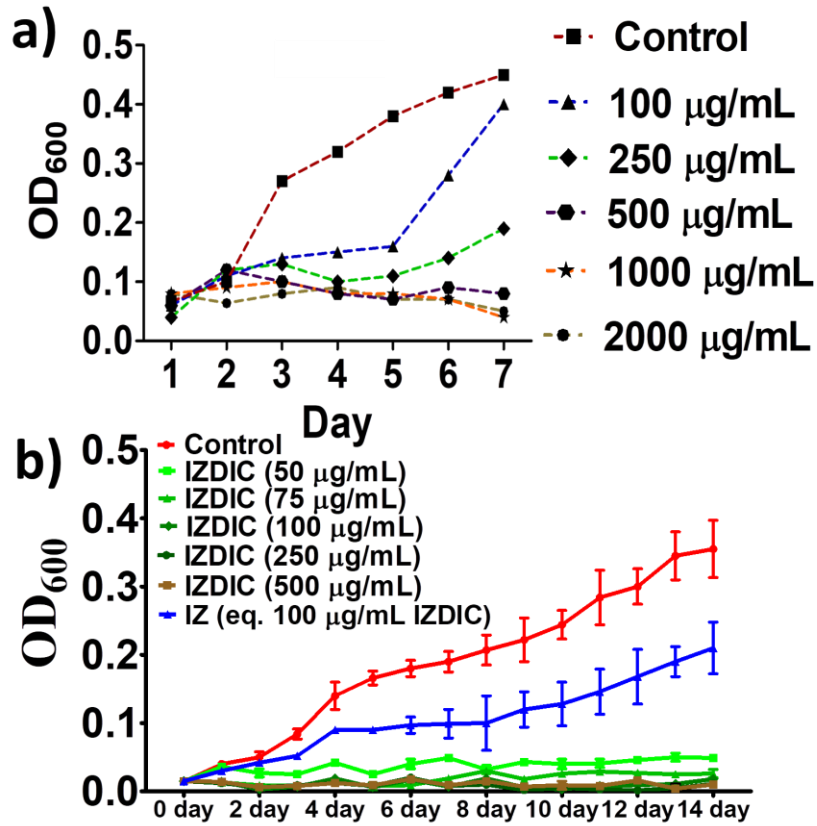
Figure S24: Assessing MIC of **IZDIC** by turbidity assay against a) M.smegmatis, b) M.tb
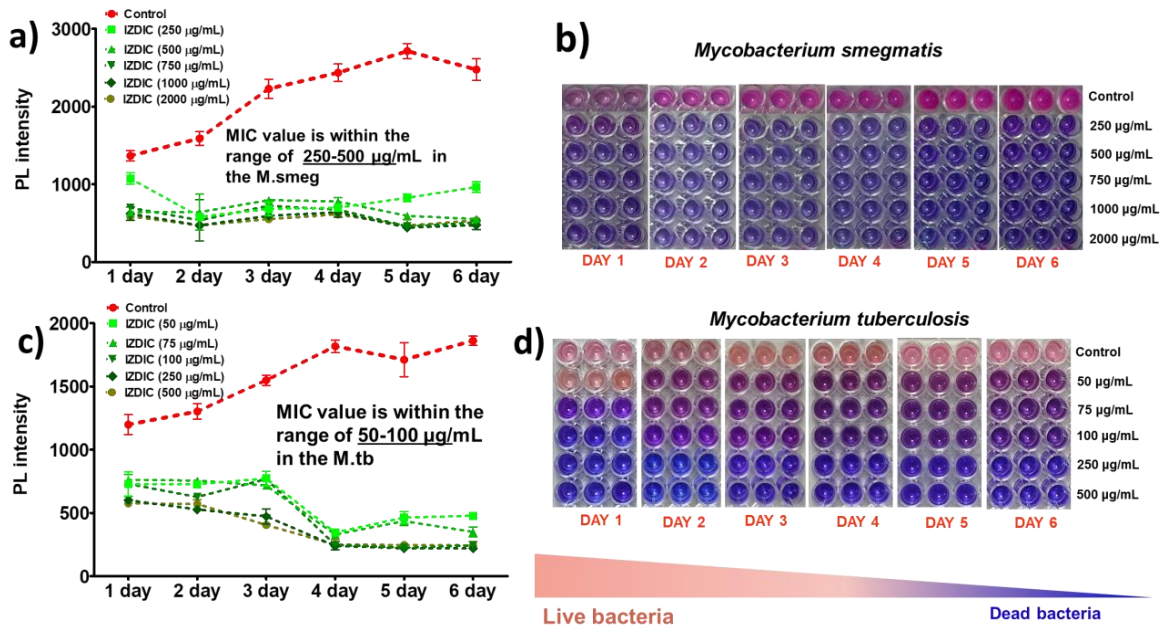

Figure S25: Assessing MIC of **IZDIC** by resazurin assay against mycobacterium sp. with fluorometric measurements and its optical colourisation; a-b) M. smegmatis, c-d) M.tb.
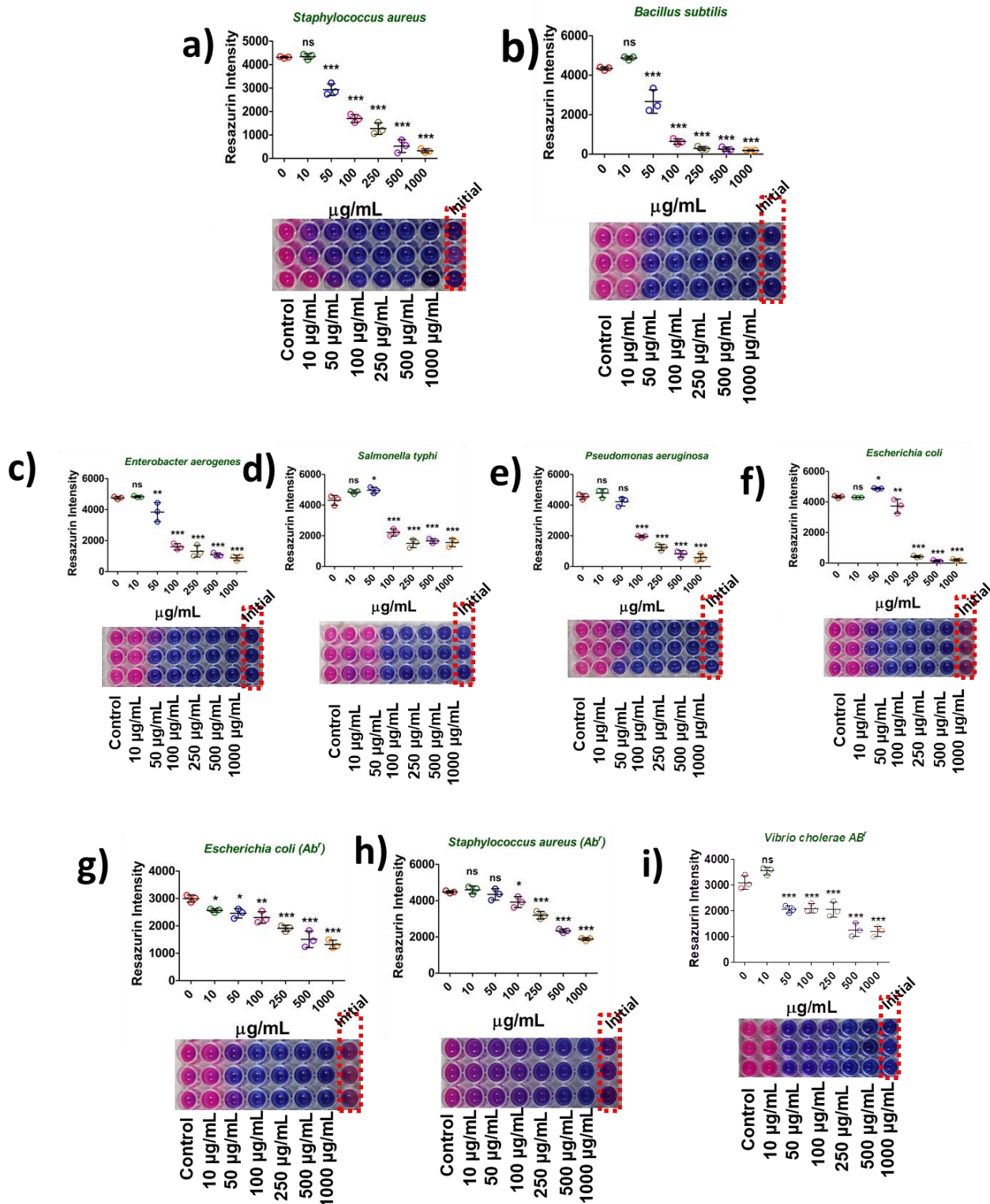
Figure S26: Assessing MIC of **IZDIC** by resazurin assay against a-b) gram positive bacteria, c-f) gram negative bacteria, g-i) various antibiotic resistant strains.(optical colourisation of each bacterial set shown below the graph)

9. Flow cytometry data of M.tb

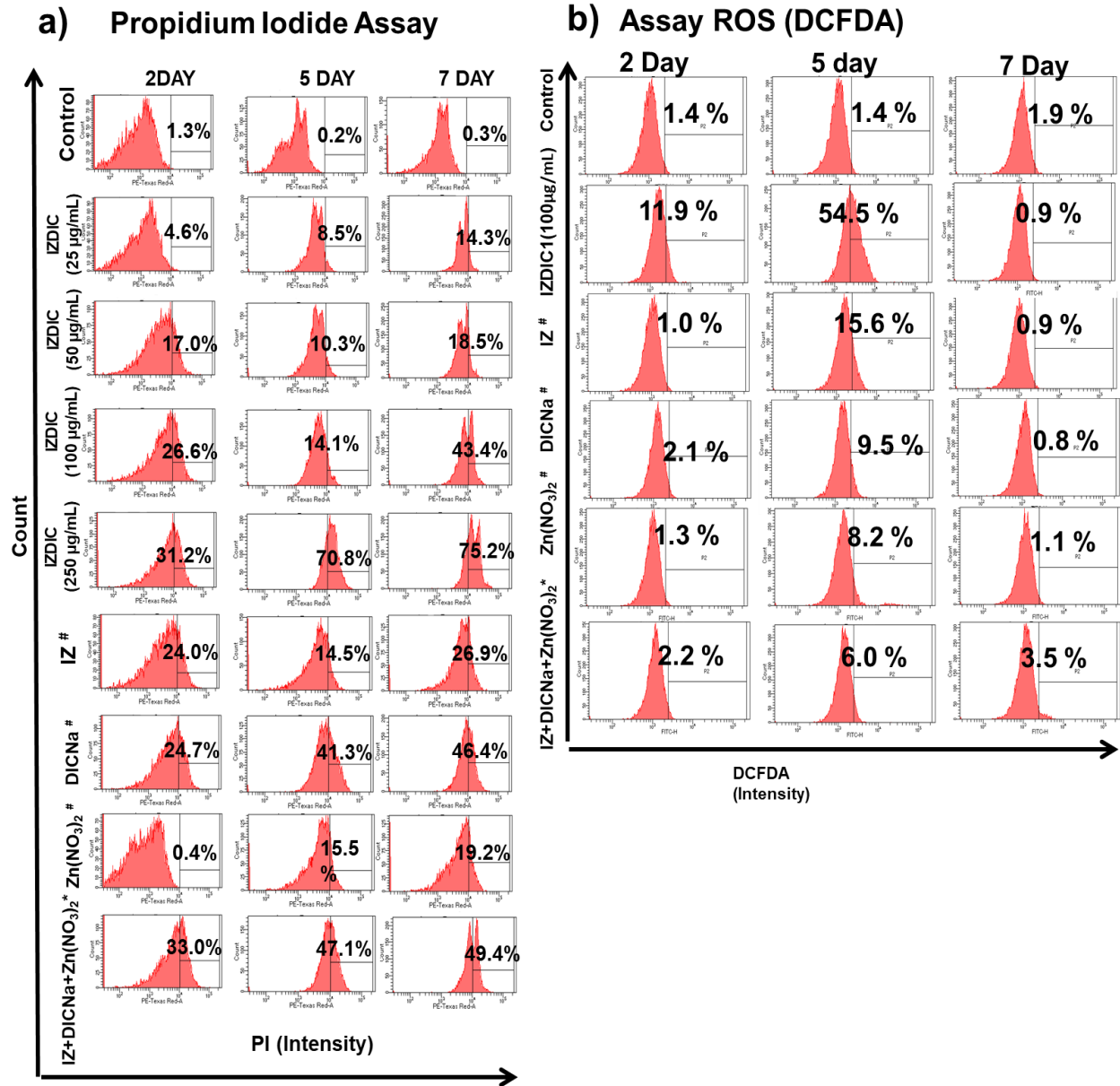**Figure S27:** Flow cytometry data of variously treated M. tb bacteria under different staining conditions; a) cell barrier permeability assay (PI staining), b) ROS assay (DCFDA staining) ([#]The components **IZ**, **DICNa** and $Zn(NO_3)_2$ of **IZDIC** were treated individually with equivalent concentration of 100 μg/mL, [*]physical mixture of the components of **IZDIC** at the same concentration of 100 μg/mL)

Figure S28: Assessing NO formation: a) flow cytometry data of variously treated M.tb bacteria stained with DAN ($^{\#}$The components **IZ**, **DICNa** and $Zn(NO_3)_2$ of CP were treated individually with equivalent concentration of 100 µg/mL, * physical mixture of components of 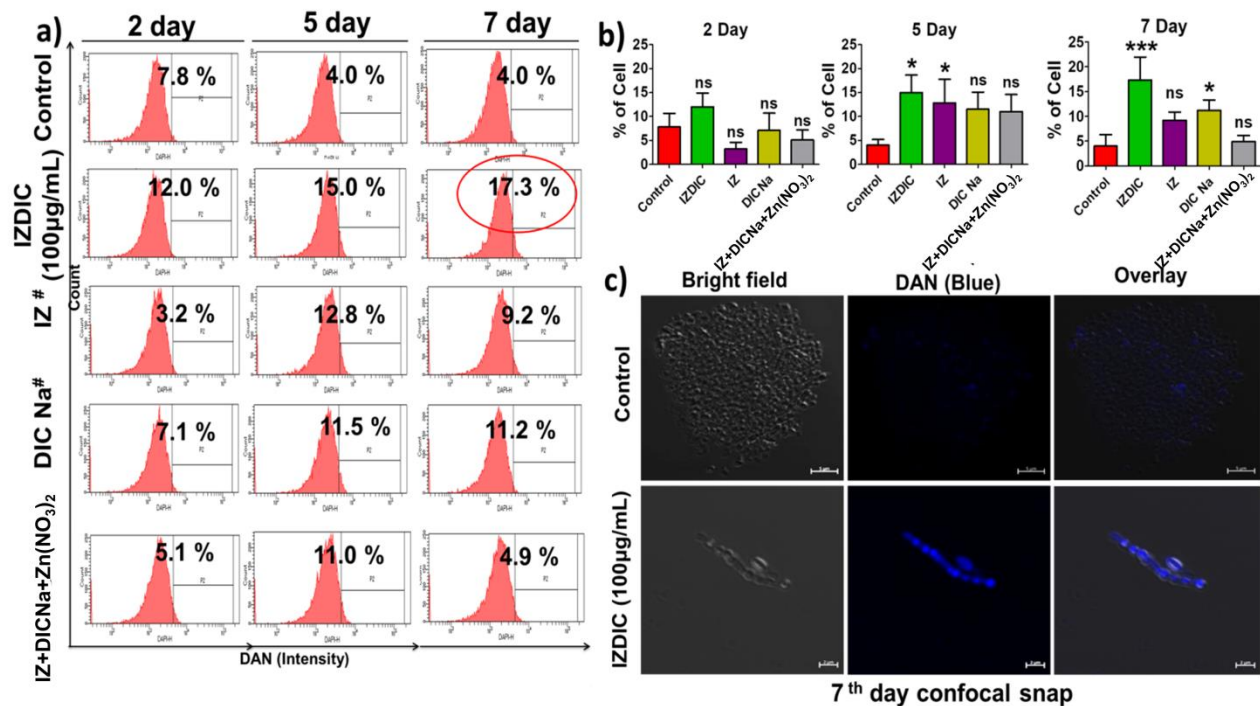**IZDIC** at the same concentration of 100 µg/mL), b) Measurements plot of flow cytometry data with statistical analysis (Data represented as mean + SD, where *p<0.05, ***p<0.001 and ns represent non-significant n=3), c) CLSM images of M.tb under various conditions.

10.   MTT-Assay data

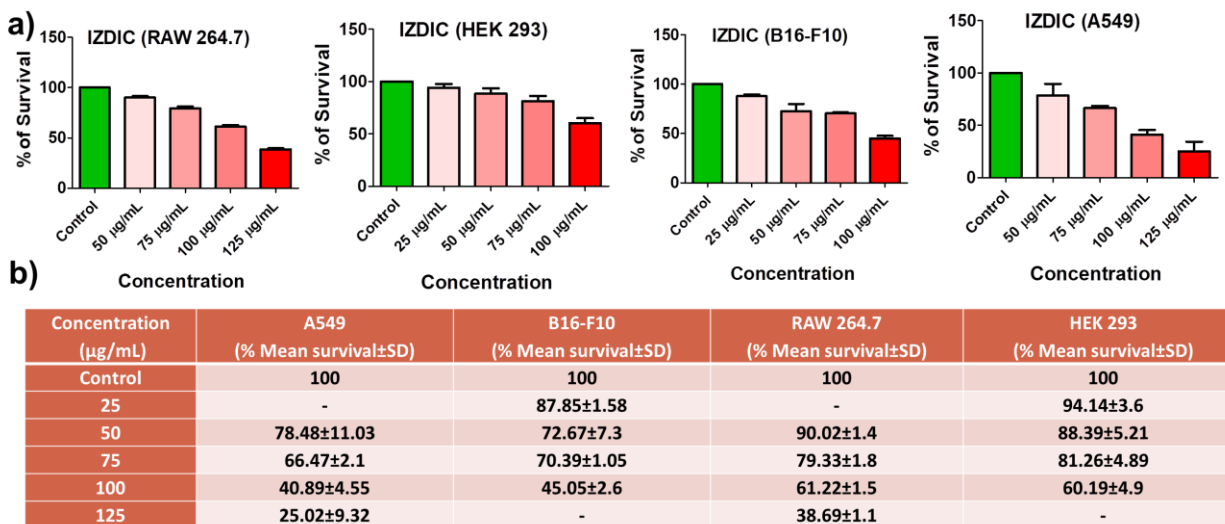| Concentration (µg/mL)	A549 (% Mean survival±SD)	B16-F10 (% Mean survival±SD)	RAW 264.7 (% Mean survival±SD)	HEK 293 (% Mean survival±SD)
Control	100	100	100	100
25	-	87.85±1.58	-	94.14±3.6
50	78.48±11.03	72.67±7.3	90.02±1.4	88.39±5.21
75	66.47±2.1	70.39±1.05	79.33±1.8	81.26±4.89
100	40.89±4.55	45.05±2.6	61.22±1.5	60.19±4.9
125	25.02±9.32	-	38.69±1.1	-

Figure S29: MTT-assay of **IZDIC** in different cell lines incubated for 72 h: a)in bar plot, b) in tabular form.
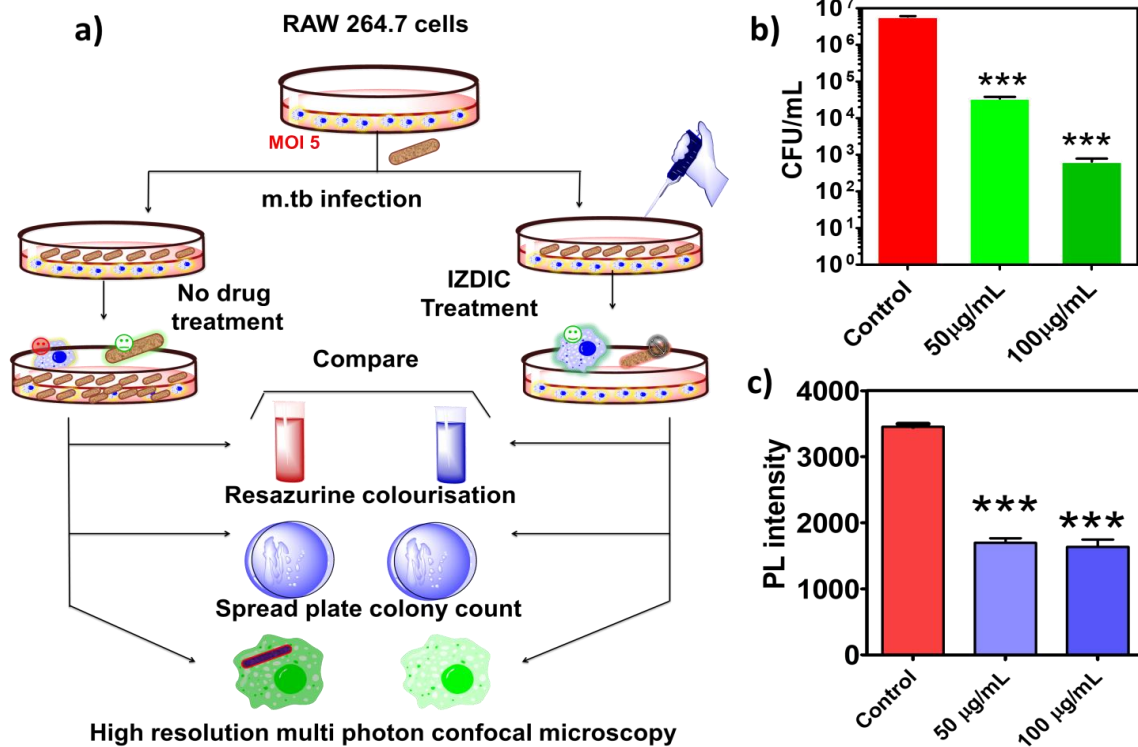
11. Infection experiment

Figure S30: Treatment of M.tb infected macrophage (RAW 264.7) with **IZDIC**: a) experimental scheme, b) CFU measurement c) resazurin assay; (data represented as mean + SD, where ***p<0.001).
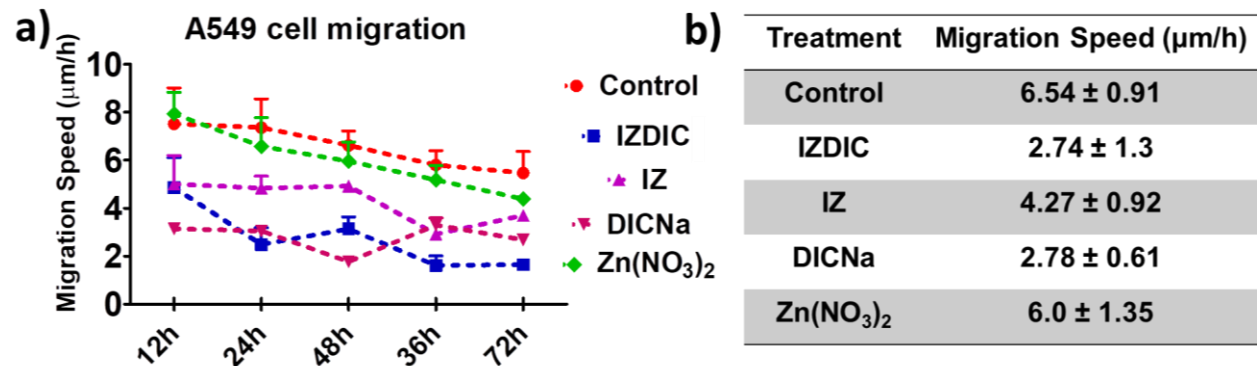
12. Cell Migration data

Treatment	Migration Speed (μm/h)
Control	6.54 ± 0.91
IZDIC	2.74 ± 1.3
IZ	4.27 ± 0.92
DICNa	2.78 ± 0.61
Zn(NO$_3$)$_2$	6.0 ± 1.35

Figure S31: a) time dependent migration speed of cancer cell A549 and b) average migration speed.
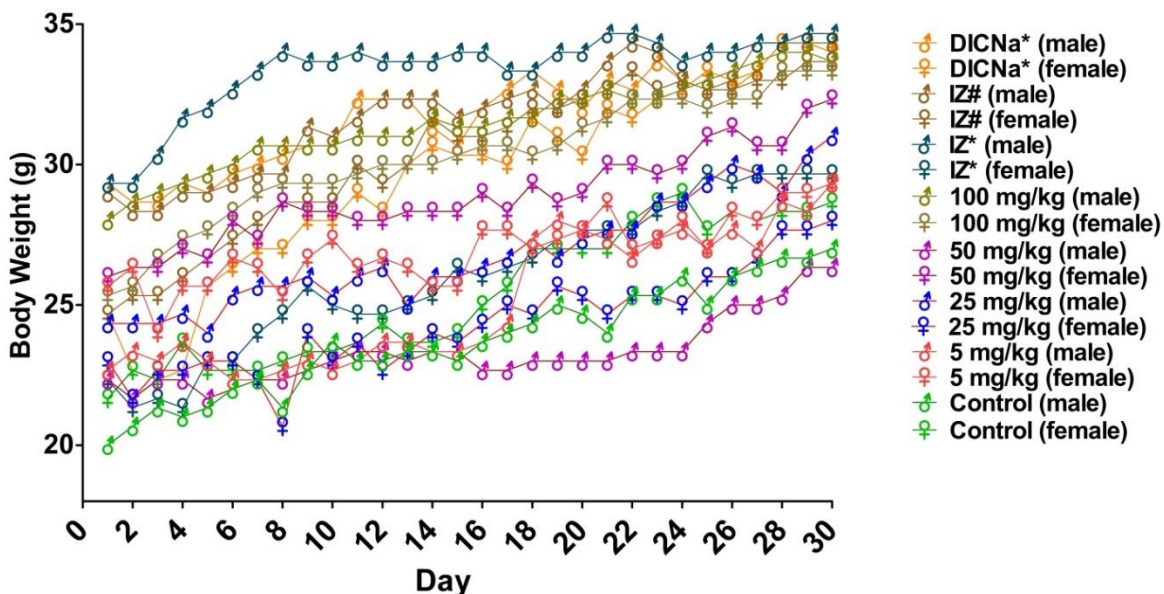
13.   Invivo experimental data

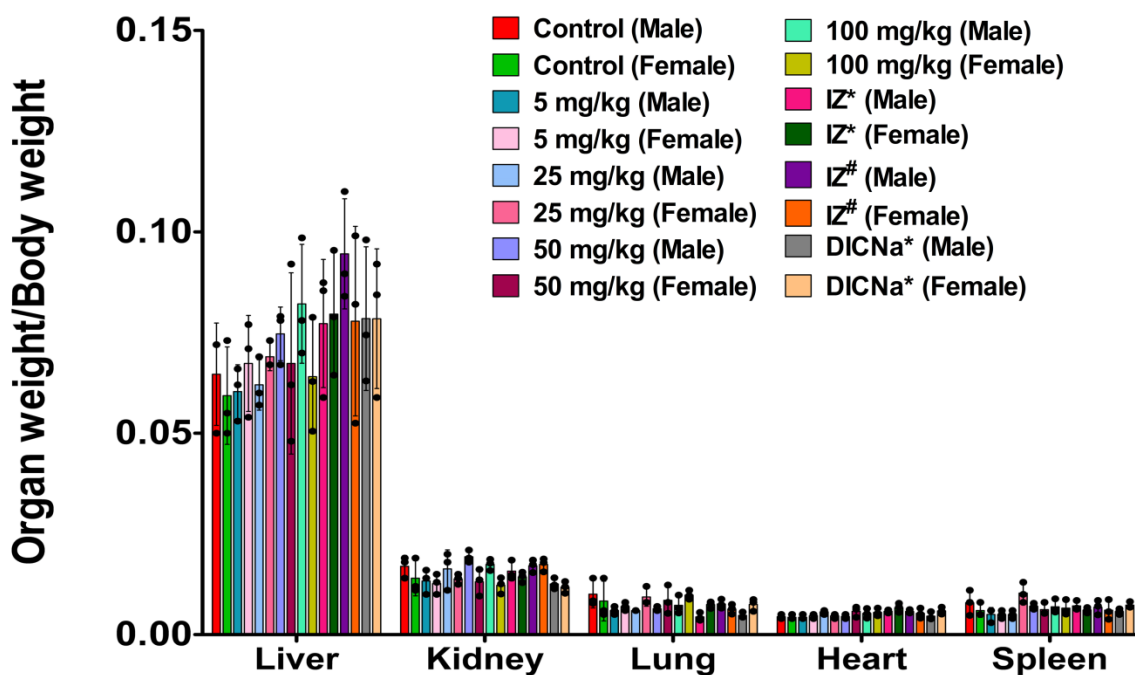**Figure S32: M**ean body weight of the mice treated with **IZDIC** and control set with time.

Figure S33: Organ to body weight ratio of mice under treatment and control condition (*IZ treatment at the concentration of equivalent amount present in 100mg/kg dosing of **IZDIC**, #only IZ treatment at the 100mg/kg), (data represented as mean ± SD, where n=6 (3 male and 3 female).
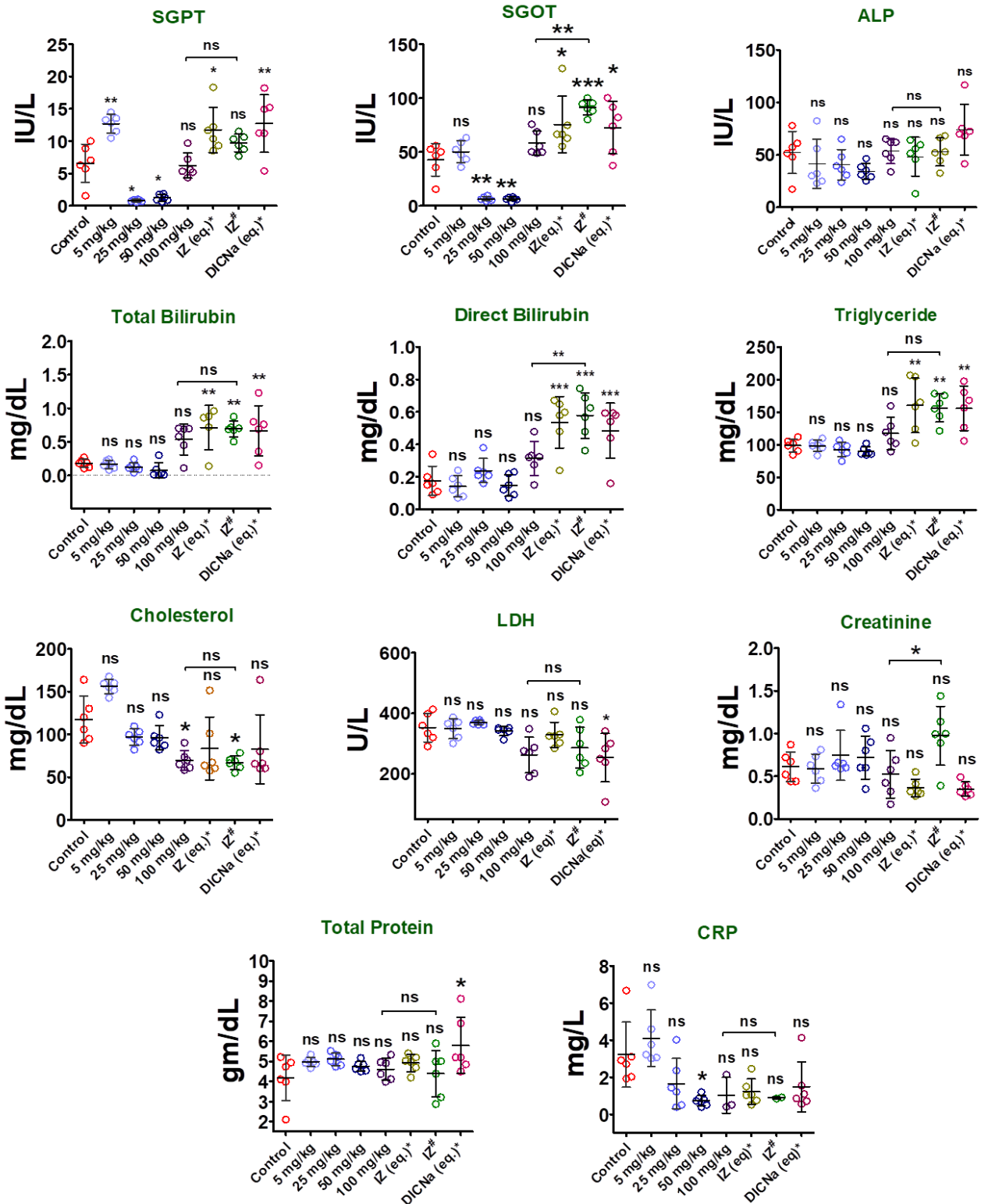
Figure S34: Serum parameter of the mice under various treatment (data represented as mean ±SD, where *p<0.05, **p<0.01 ***p<0.001 and ns represent non-significant (n=6; 3 male and 3 female).

Table S7: Serum parameter analysis in tabular form

|	Control	IZDIC (5 mg/kg)	IZDIC (25 mg/kg)	IZDIC (50 mg/kg)	IZDIC (100 mg/kg)	IZ* (eq. to100mg/kg)	IZ# (100 mg/kg)	DICNa* (eq. to 100mg/kg)
ALP (IU/L)	52.25 ±20.02	41.46±23.30	40.59±14.51	34.29 ±7.56	53.58 ±11.94	48.32 ±18.44	52.83 ±13.40	74.04 ±24.23
SGOT (IU/L)	42.74 ±15.05	50.21 ±10.05	6.58 ±1.94	6.43 ±1.73	58.14 ±11.34	75.56 ±26.23	91.48 ±7.01	72.61 ±24.32
SGPT (IU/L)	6.59 ±2.93	12.69 ±1.46	0.81 ±0.17	1.24 ±0.52	6.24 ±1.93	11.75 ±3.5	9.71 ±1.38	12.71 ±4.45
Total Bilirubin (mg/dL)	0.18 ±0.06	0.16 ±0.06	0.12 ±0.06	0.07 ±0.1	0.53 ±0.23	0.71 ±0.33	0.69 ±0.11	0.66 ±0.37
Direct Bilirubin (mg/dL)	0.17 ±0.08	0.14 ±0.06	0.23 ±0.07	0.14 ±0.06	0.31 ±0.10	0.53 ±0.15	0.57 ±0.14	0.48 ±0.16
LDH (U/L)	352.7 ±47.09	349.2 ±32.70	369.1 ±6.98	341.3 ±14.76	262.3 ±59.01	329.1 ±41.53	286.4 ±67.22	253.6 ±80.32
Creatinine (mg/dL)	0.61 ±0.17	0.59 ±0.16	0.74 ±0.29	0.71 ±0.25	0.52 ±0.27	0.36 ±0.10	0.97 ±0.34	0.34 ±0.08
Cholesterol (mg/dL)	117.5 ±27.26	156.2 ±8.46	96.94 ±9.58	96.26 ±14.33	69.87 ±11.48	83.71 ±36.80	66.91 ±7,93	82.83 ±40.33
Triglyceride (mg/dL)	98.93 ±10.11	98.57 ±8.84	92.71 ±11.02	89.91 ±6.84	117.5 ±24.85	160.4 ±41.92	156.5 ±21.44	156.0 ±34.22
CRP (mg/L)	3.228 ±1.75	4.108 ±1.52	1.660 ±1.35	0.7517 ±0.28	1.027 ±0.96	1.224 ±0.68	0.8880 ±0.04	1.489 ±1.33
Total Protein (gm/dL)	4.180 ±1.12	4.975 ±0.22	5.103 ±0.30	4.753 ±0.25	4.612 ±0.53	4.917 ±0.42	4.395 ±1.16	5.795 ±1.40
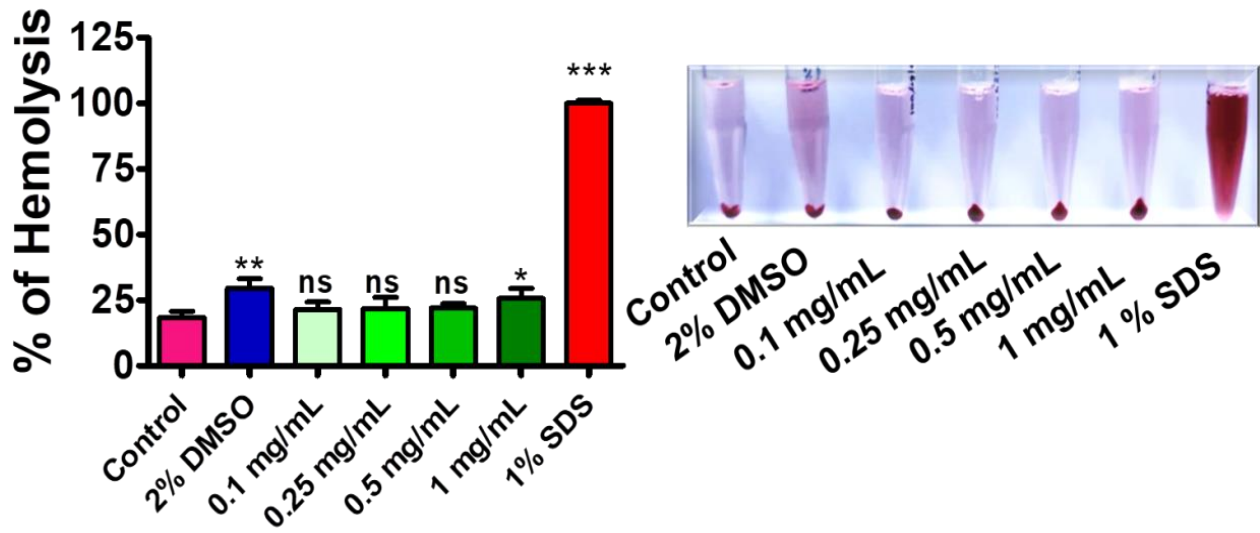
Figure S35: Hemolysis of mice blood sample treated with varying concentration of **IZDIC** (control experiment with 1% SDS considered as 100 % hemolysis, (data represented as mean ± SD, where *p<0.05, **p<0.01 ***p<0.001 and ns represent non-significant, n=3)

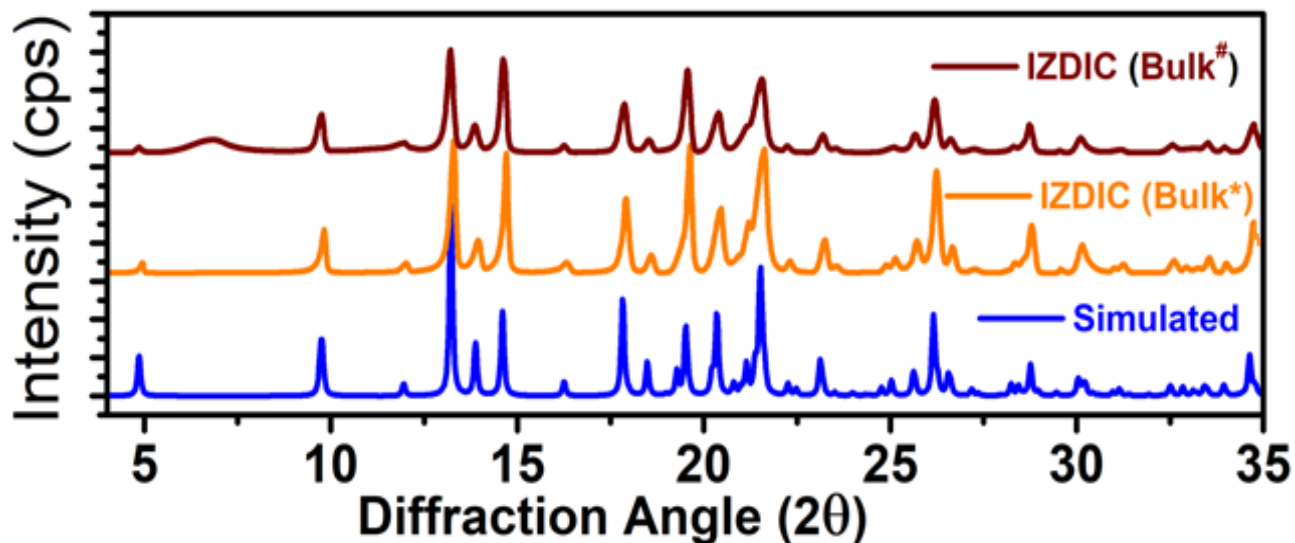## 14. Bulk PXRD, TGA and temparature varient PXRD data IZDIC

Figure S36: PXRD of **IZDIC** under various conditions; (bulk* - as synthesized in bulk scale, bulk# - crystals kept over six month under ambient condition followed by keeping it in a humid chamber for 72h).
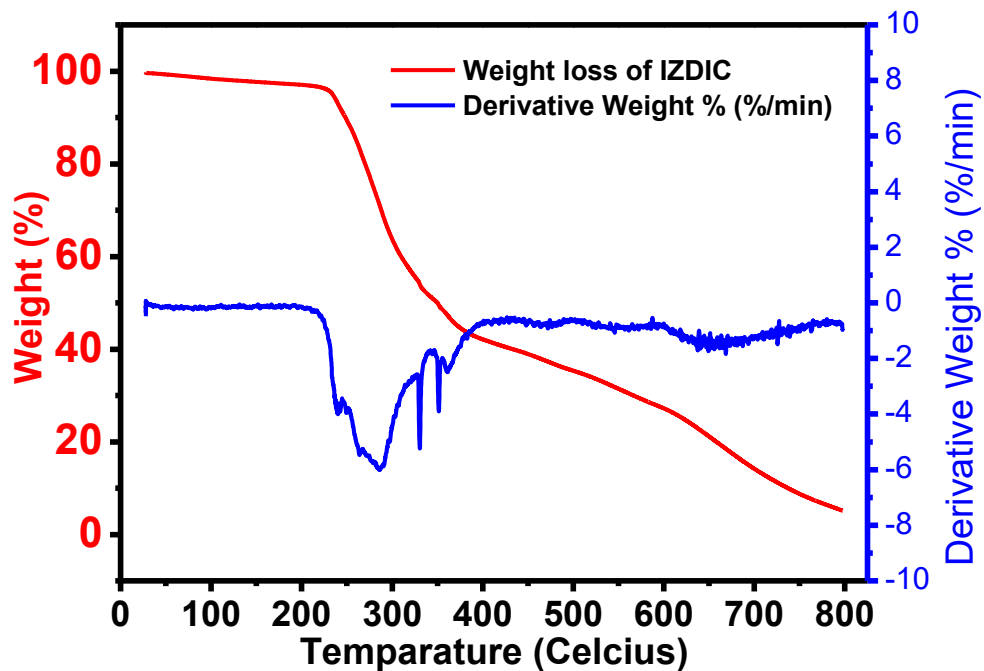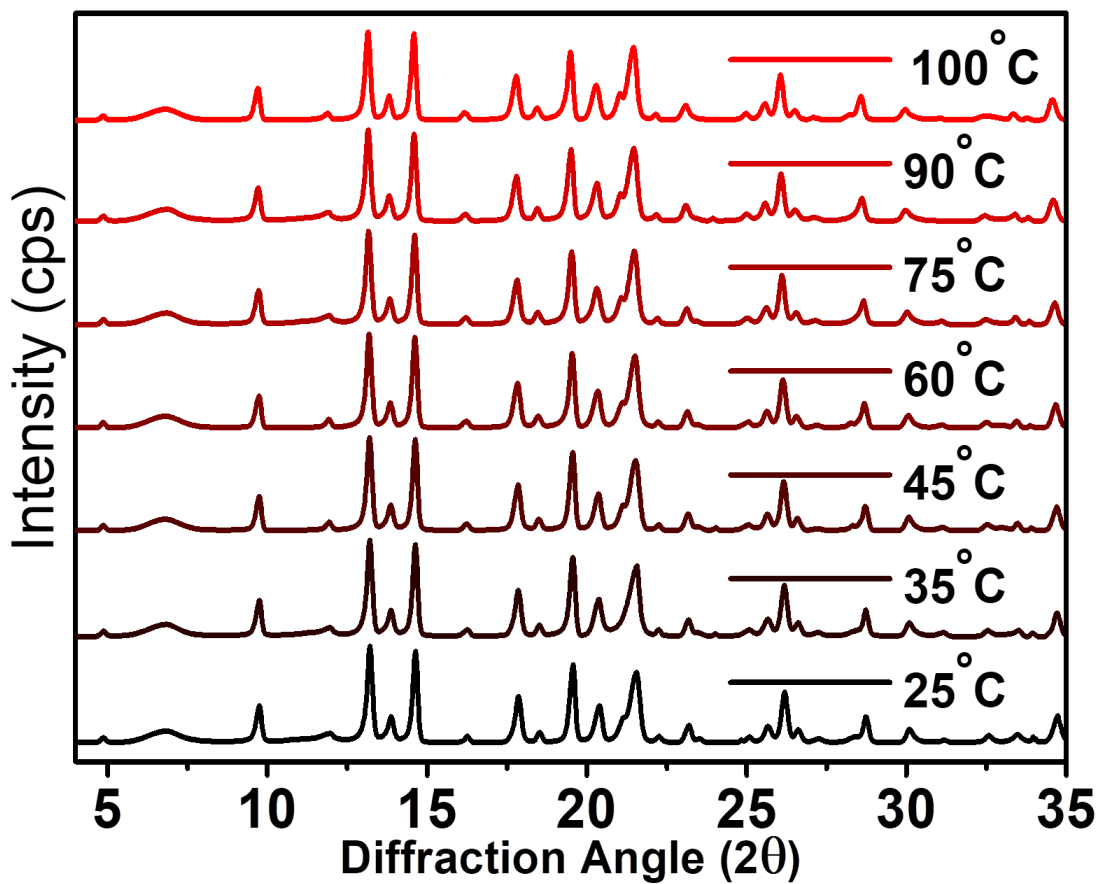

Figure S37: Thermogravimetric analysis (TGA) of **IZDIC**.

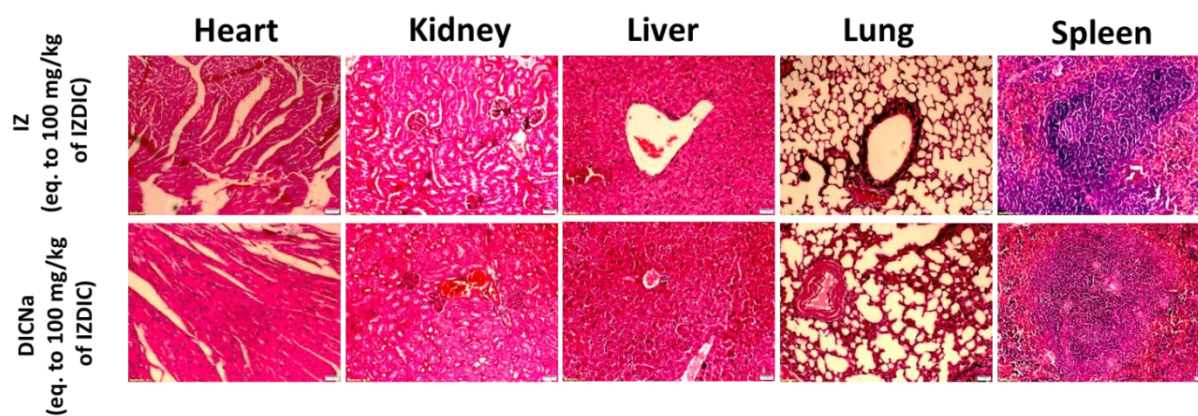**Figure S38:** Temperature dependent PXRD of **IZDIC**.

Figure S39: Histopathological images of different organs of mice treated with **IZ** and **DICNa**. (Scale bar in 50μm).