Electronic Supplementary Material (ESI) for RSC Advances.

Synergistic Investigation of Azo-Thiazole Derivatives Incorporating Thiazole Moieties: Comprehensive Exploration of Synthesis, Characterization, Computational Insights, Solvatochromism, and Multimodal Biological Activity Assessment

Abstract

In the present study, a novel series of azo-thiazole derivatives (**3a-c**) containing thiazole moiety unit was successfully synthesized. The structure of these derivatives was examined by spectroscopic techniques such as ^{1}H NMR, ^{13}C NMR, FT-IR, and HRMS. Further, the novel synthesized compounds were evaluated for their in-vitro biological activities such as antibacterial and anti-inflammatory as well as for *in silico* study. The antibacterial results demonstrated that compounds **3a** and **3c** (MIC=10 µg/mL) have notable potency against *Staphylococcus aureus* compared with azithromycin (MIC=40 µg/mL); Compound **3b** displayed a fourfold higher potency (24 recovery days, 1.83 mg/day) than HAMAZINE (28 recovery days, 4.14 mg/day) in promoting burn wound healing, and it also exhibited comparable inhibitory activity against screened bacterial pathogens when compared to reference drug. Docking on 1KZN, considering the excellent impact of the compounds on the Crystal Structure of E. coli 24kDa Domain in Complex with Clorobiocin, indicated a close binding of compounds 3a-c with the active site of protein 1KZN, in line with their observed biological activity. Additionally, we conducted molecular dynamics simulations on the docked complexes of compounds 3a-c with PDB: 1KZN to assess their stability and molecular interactions. Furthermore, we assessed the compounds' electrochemical characteristics via DFT calculations. Leveraging PASS and pkCSM platforms, we gained insights into controlling bioactivity and physicochemical features, highlighting these compounds as promising candidates for new active agents

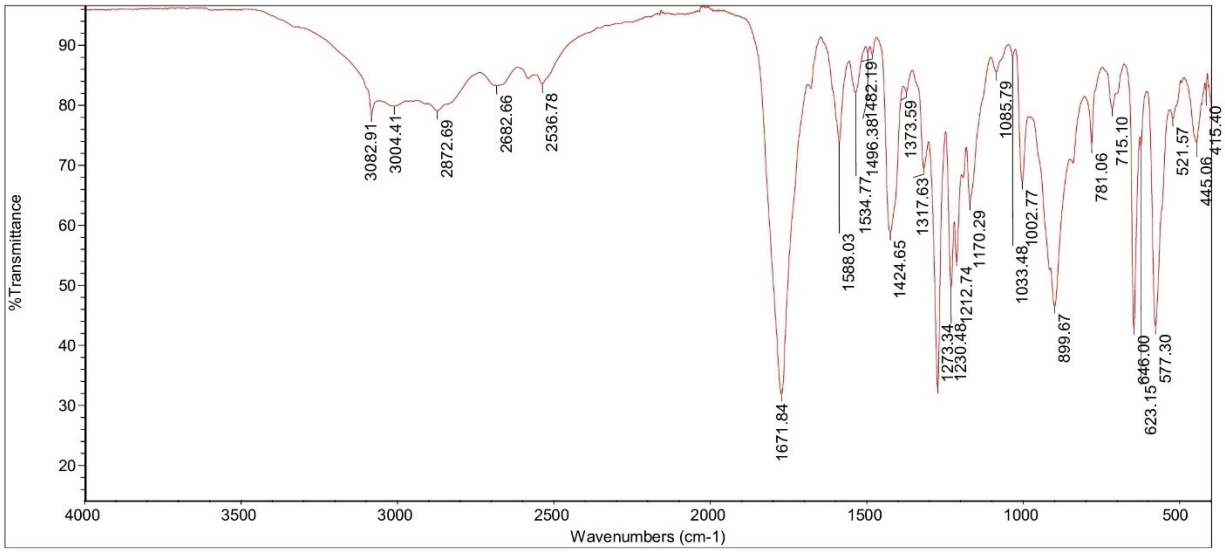

Fig .S1. Ftir spectrum of compound 3

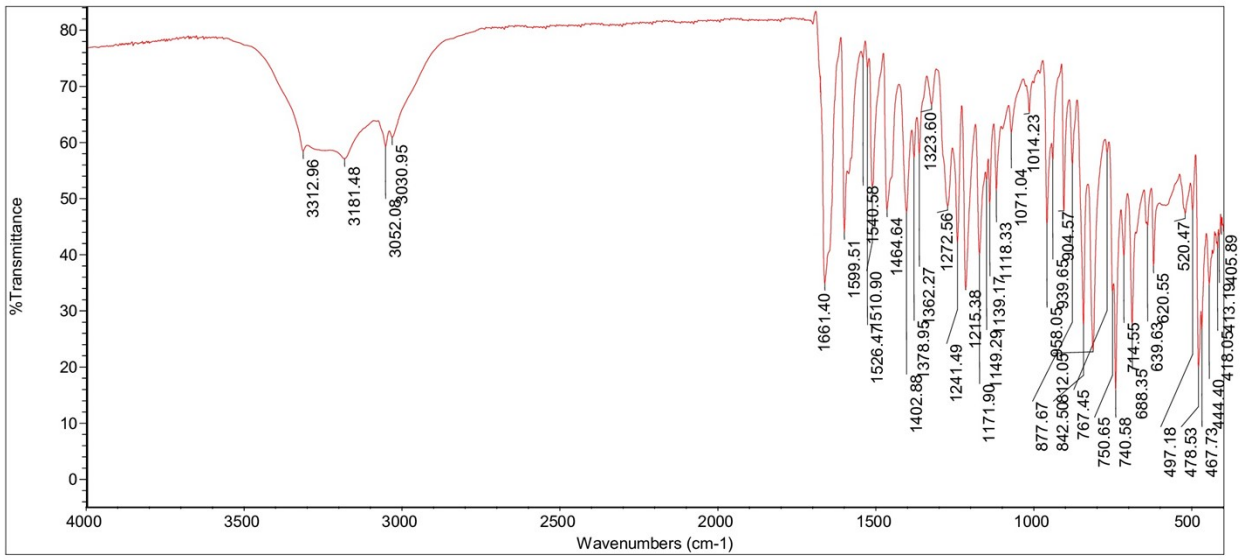

Fig .S2. Ftir spectrum of compound 3a

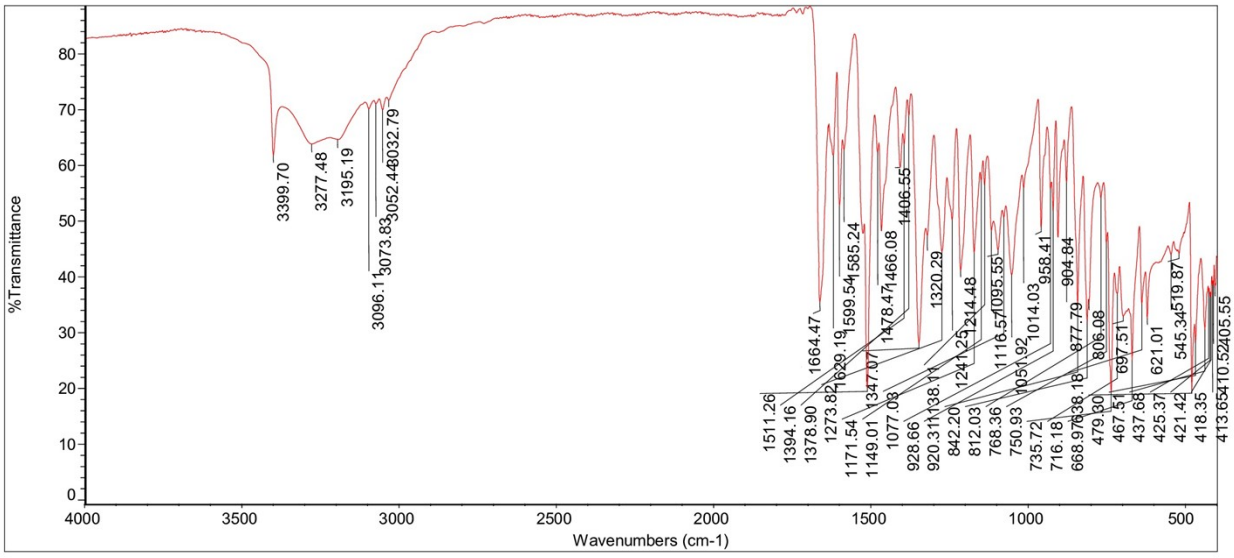

Fig .S3. Ftir spectrum of compound 3b

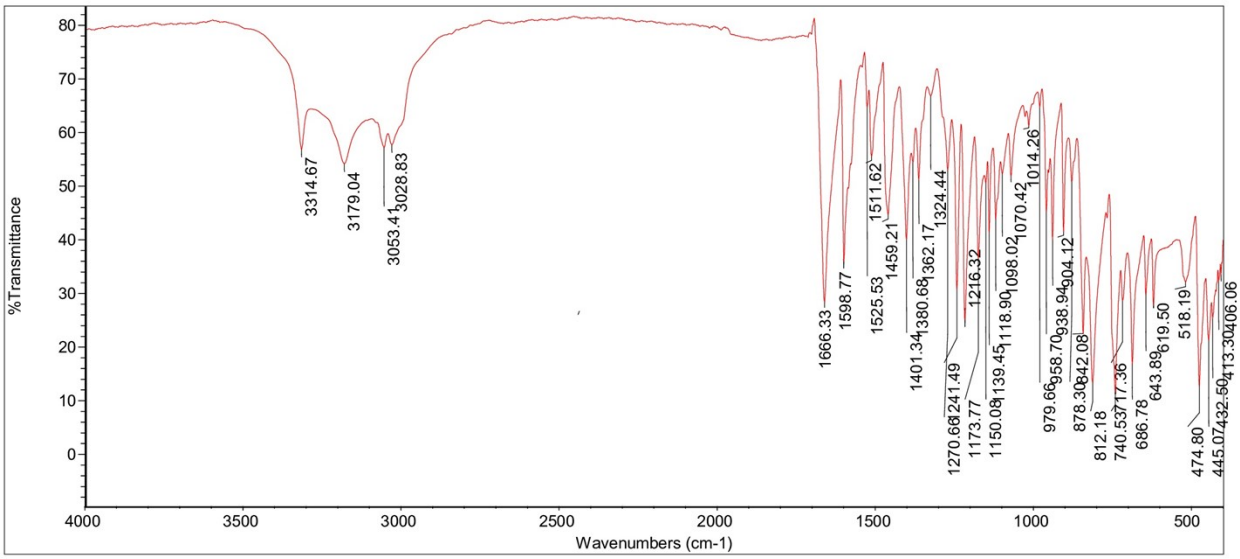

Fig .S4. Ftir spectrum of compound 3c

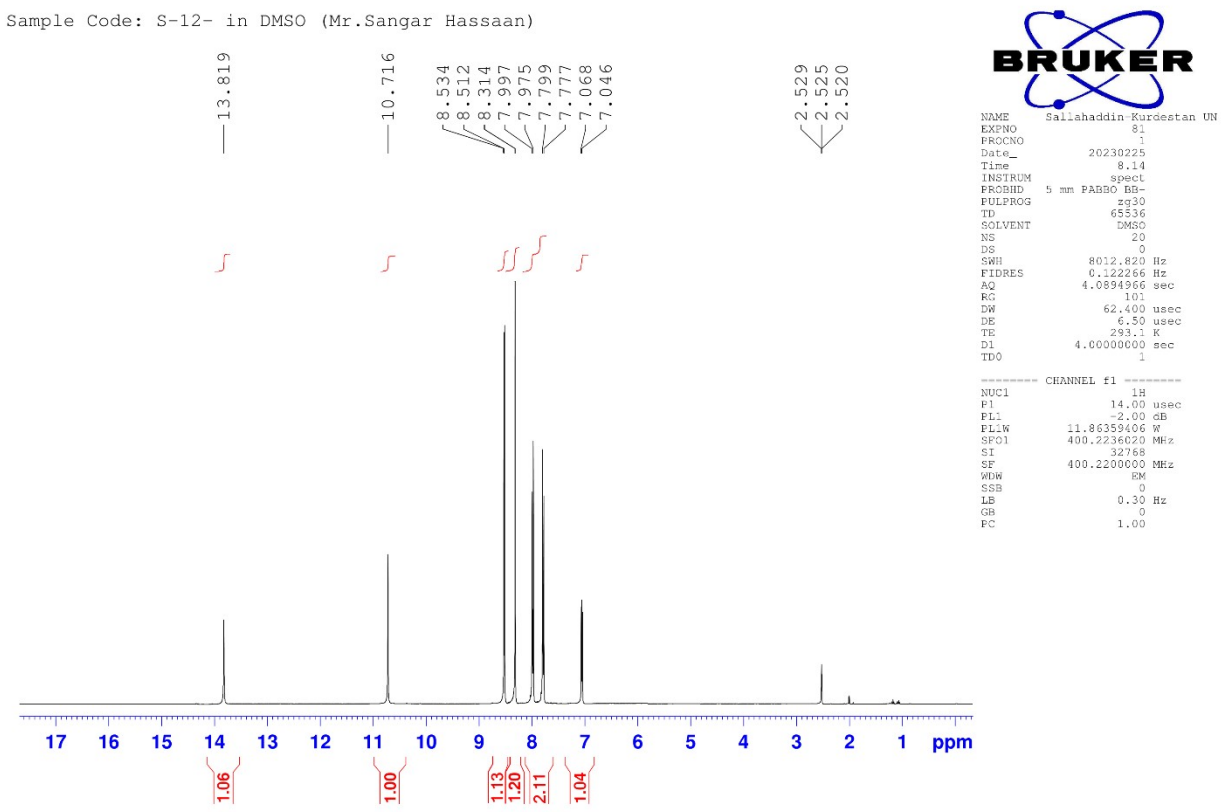

Fig.S5.hnmr spectrum of 3

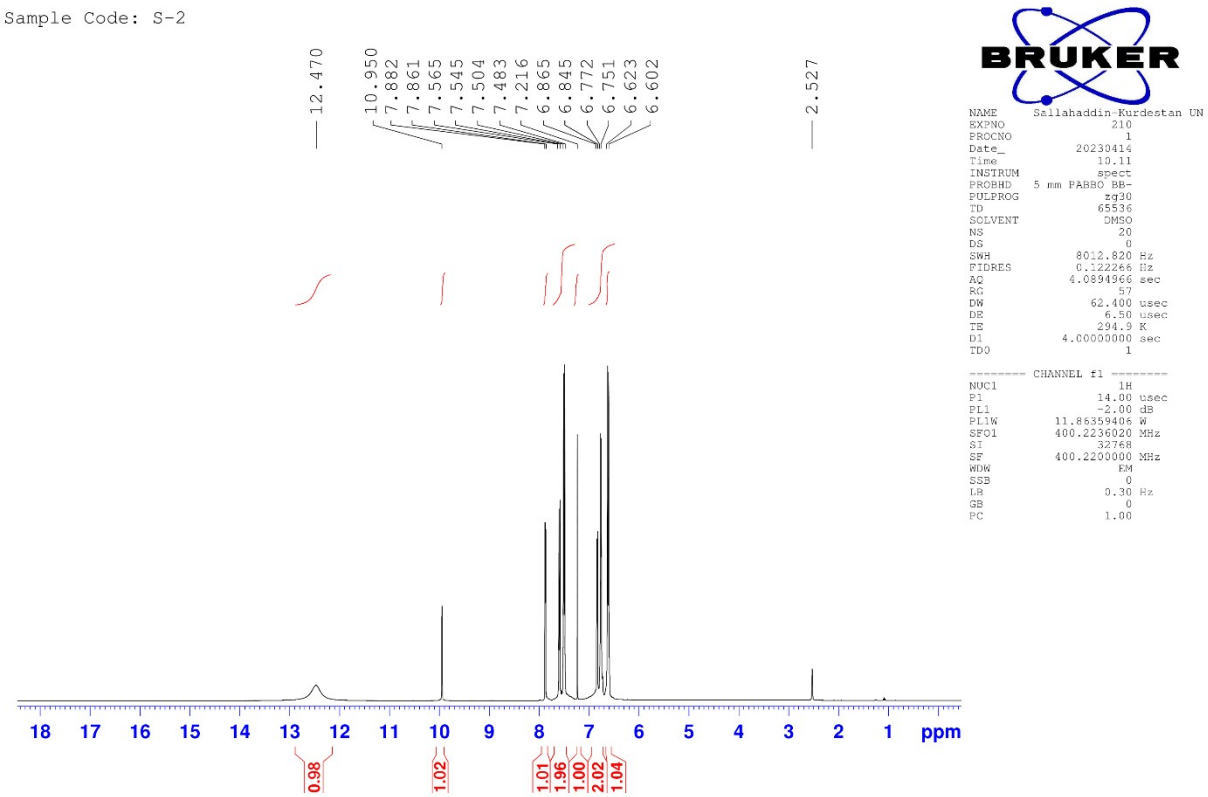

Fig.s6.1hnmr spectrum of 3a

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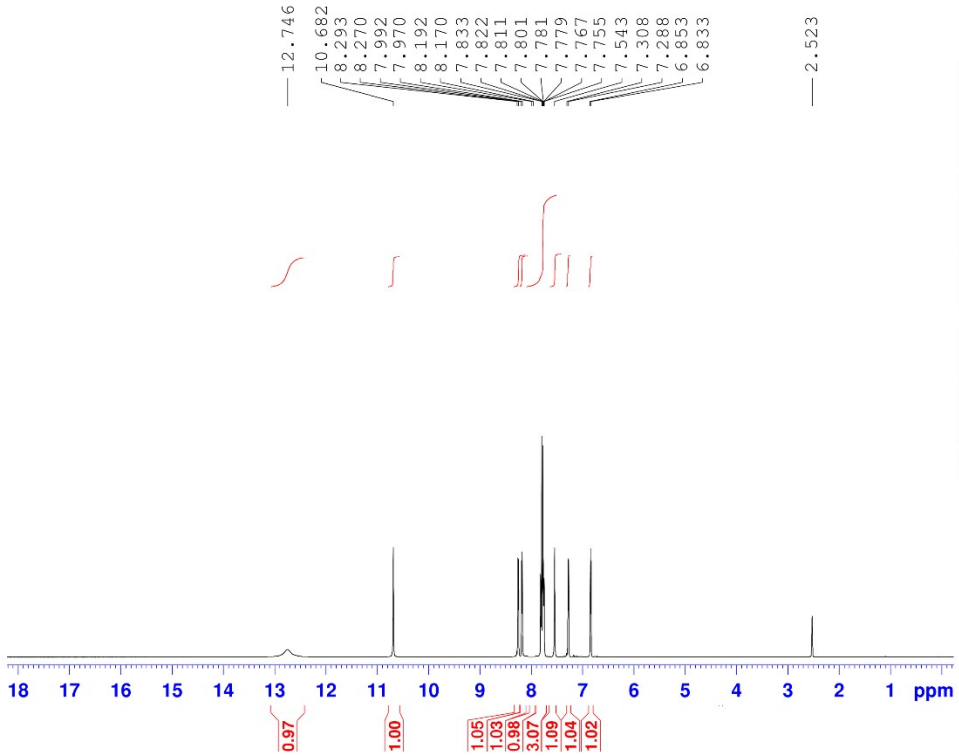


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TD                  65536
SOLVENT              DMSO
NS                     20
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SWH               8012.820 Hz
FIDRES            0.122266 Hz
AQ                4.0894966 sec
RG                     90.5
DW                   62.400 usec
DE                    6.50 usec
TE                  294.8 K
D1                4.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  14.00 usec
PL1                 -2.00 dB
PL1W          11.86359406 W
SFO1          400.2236020 MHz
SI                  32768
SF            400.2200000 MHz
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LB                   0.30 Hz
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Fig.S7.1hnmr 3b

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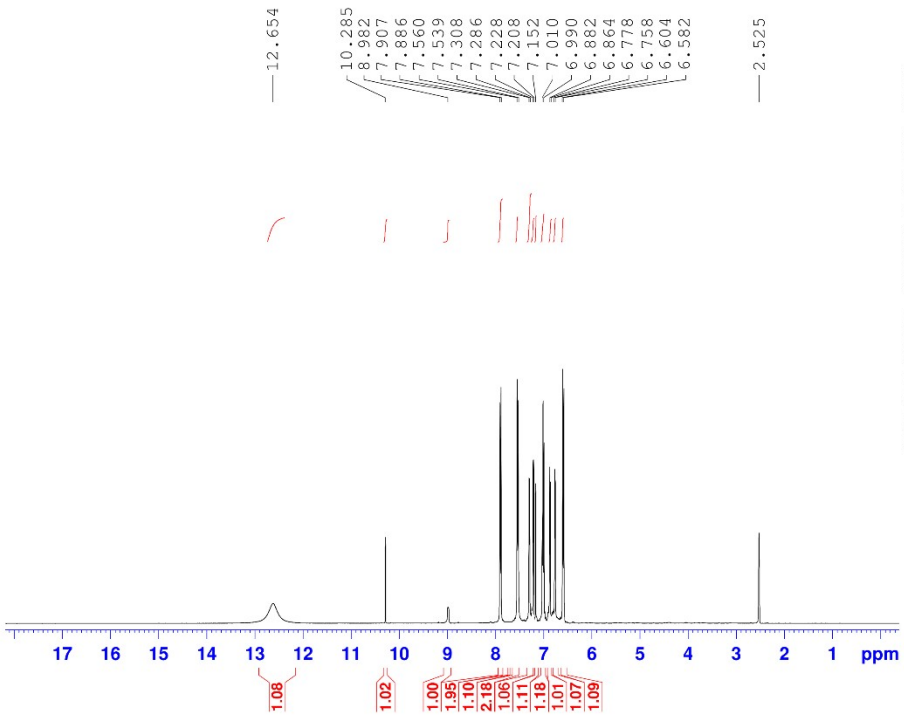


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AQ                4.0894966 sec
RG                     80.6
DW                   62.400 usec
DE                    6.50 usec
TE                  294.9 K
D1                4.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
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PL1                 -2.00 dB
PL1W          11.86359406 W
SFO1          400.2236020 MHz
SI                  32768
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Fig.S8.1hnmr spectrum of 3c

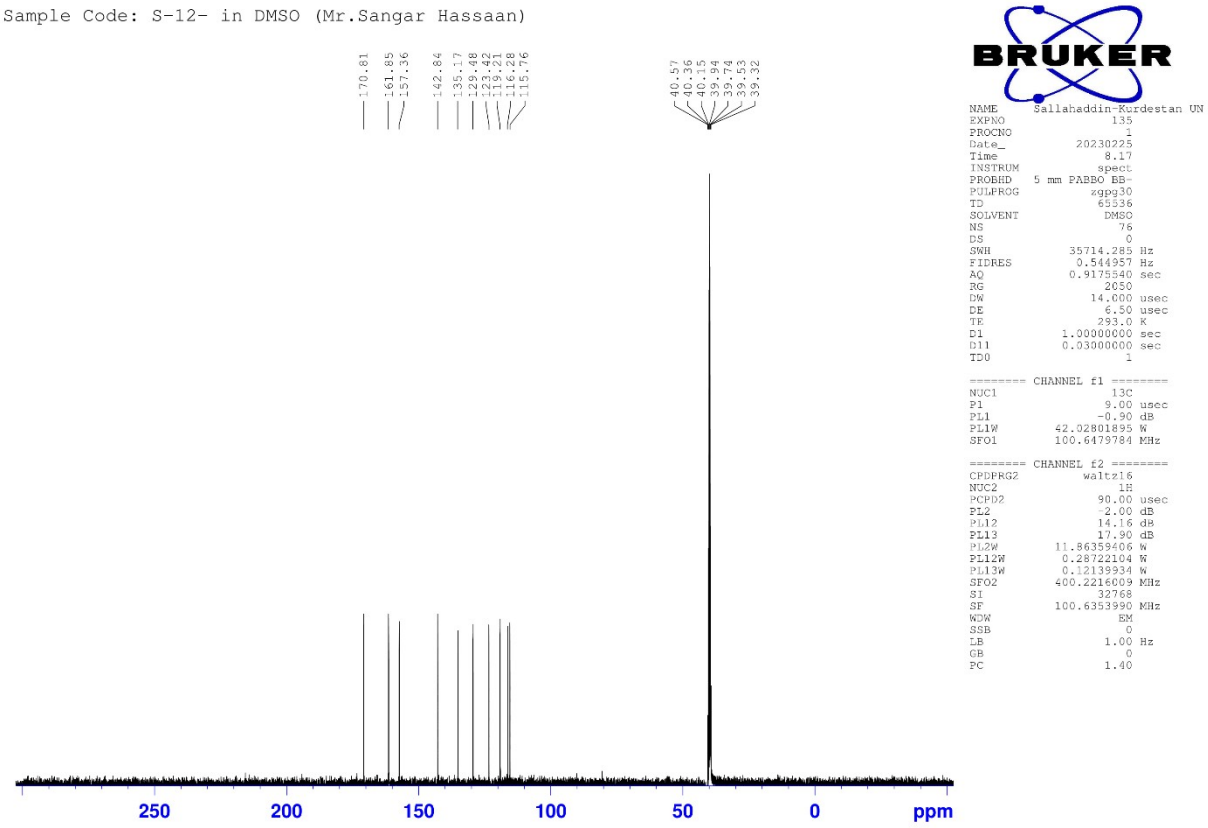


Fig.S9. 13CNMR spectrum of 3

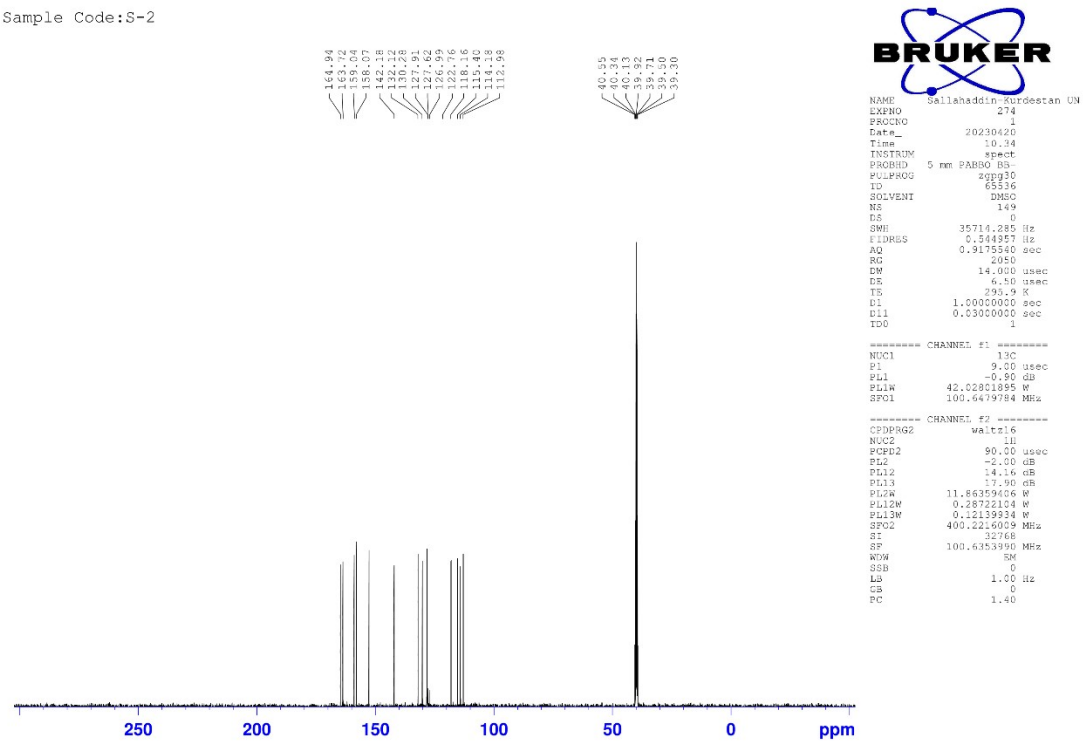


Fig.S10. 13CNMR spectrum of 3a

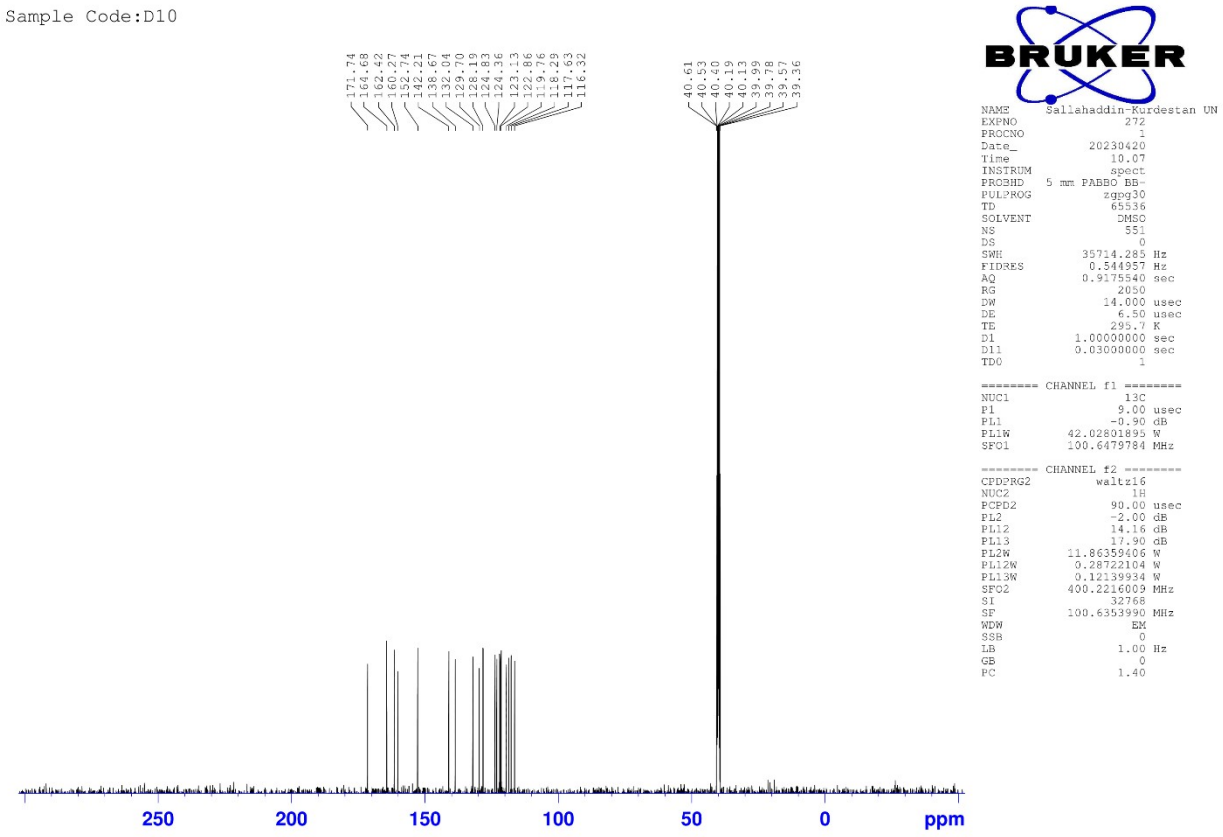


Fig.S11. 13CNMR spectrum of 3b

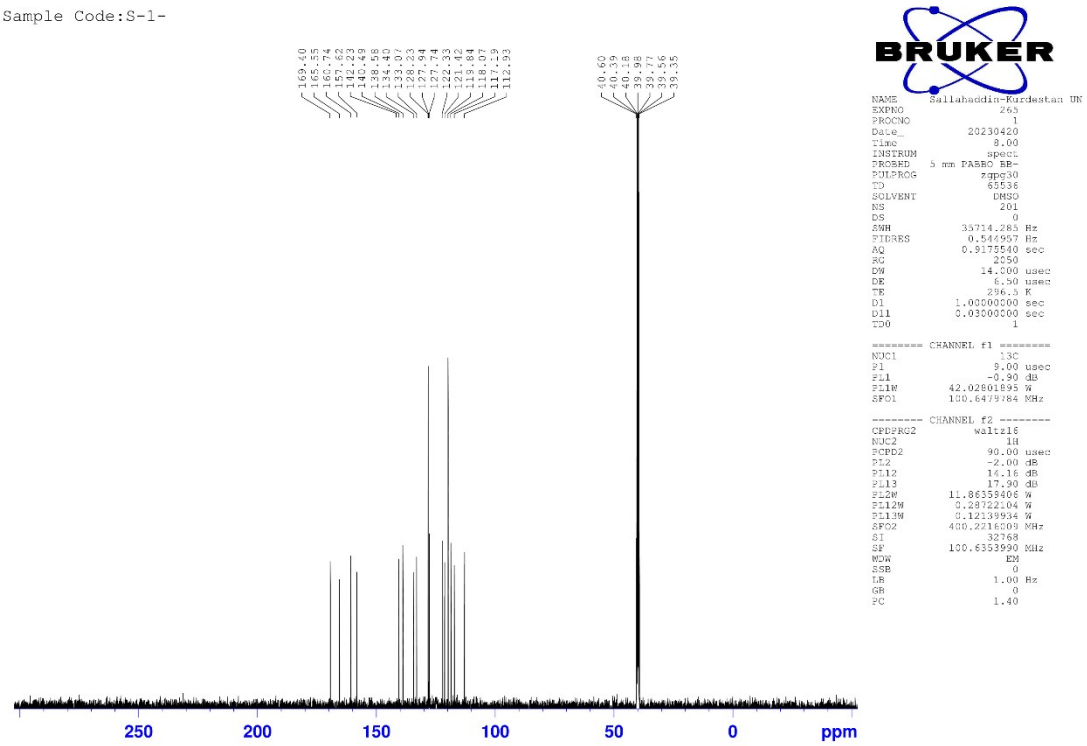


Fig.S12. 13CNMR spectrum of 3c

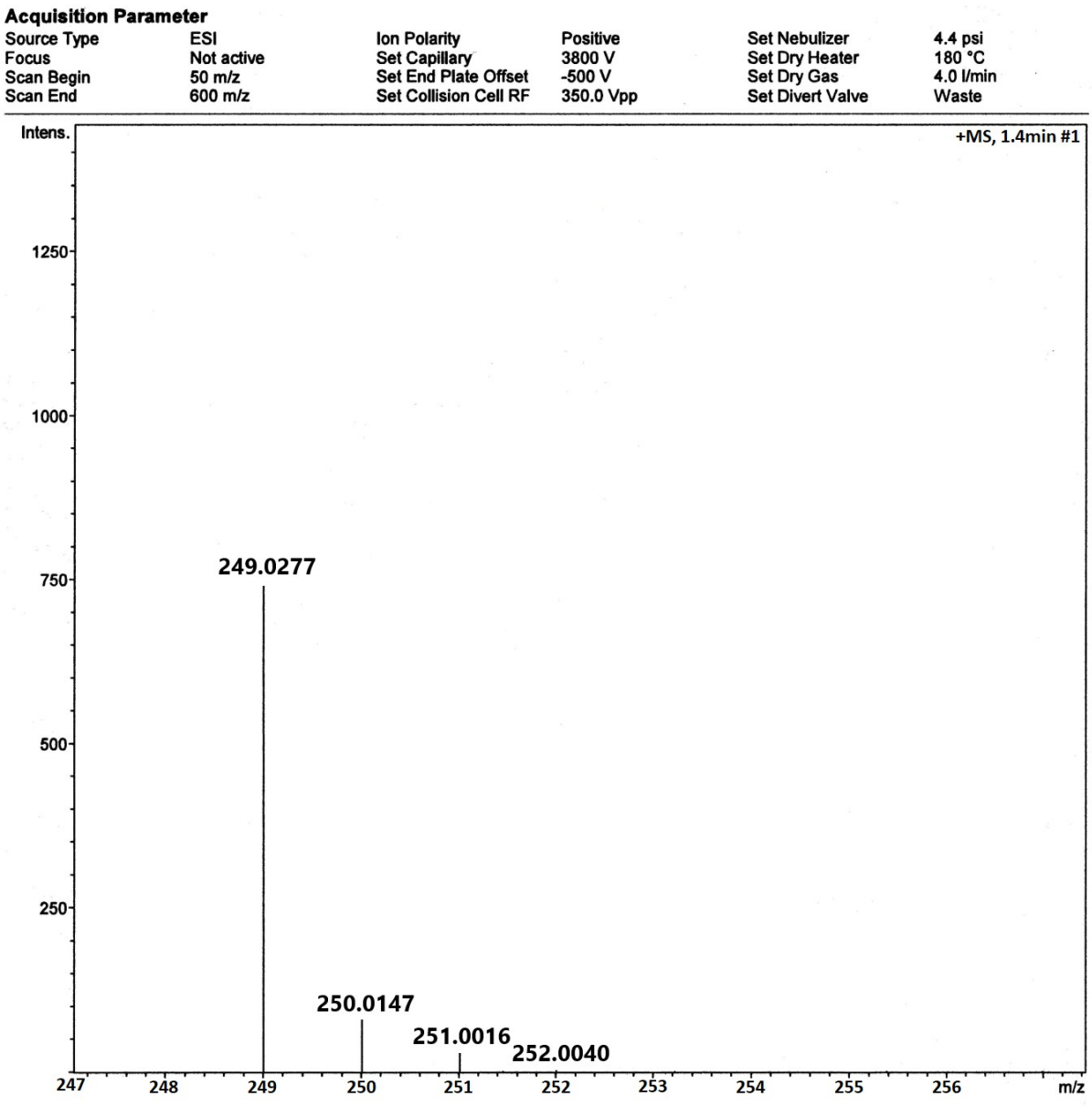


Fig.S13. HRMS spectrum of 3

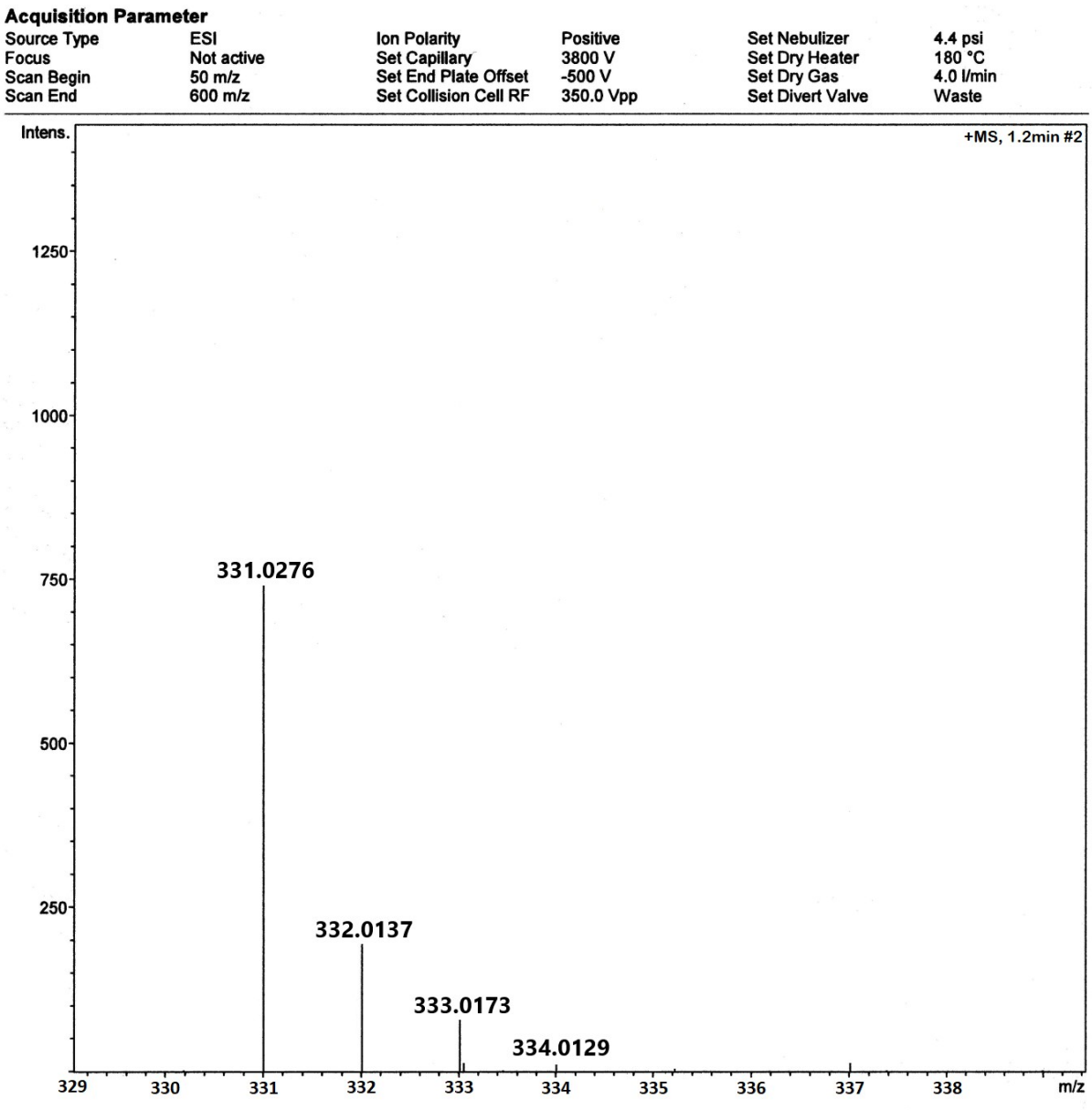


Fig.S14. HRMS spectrum of 3a

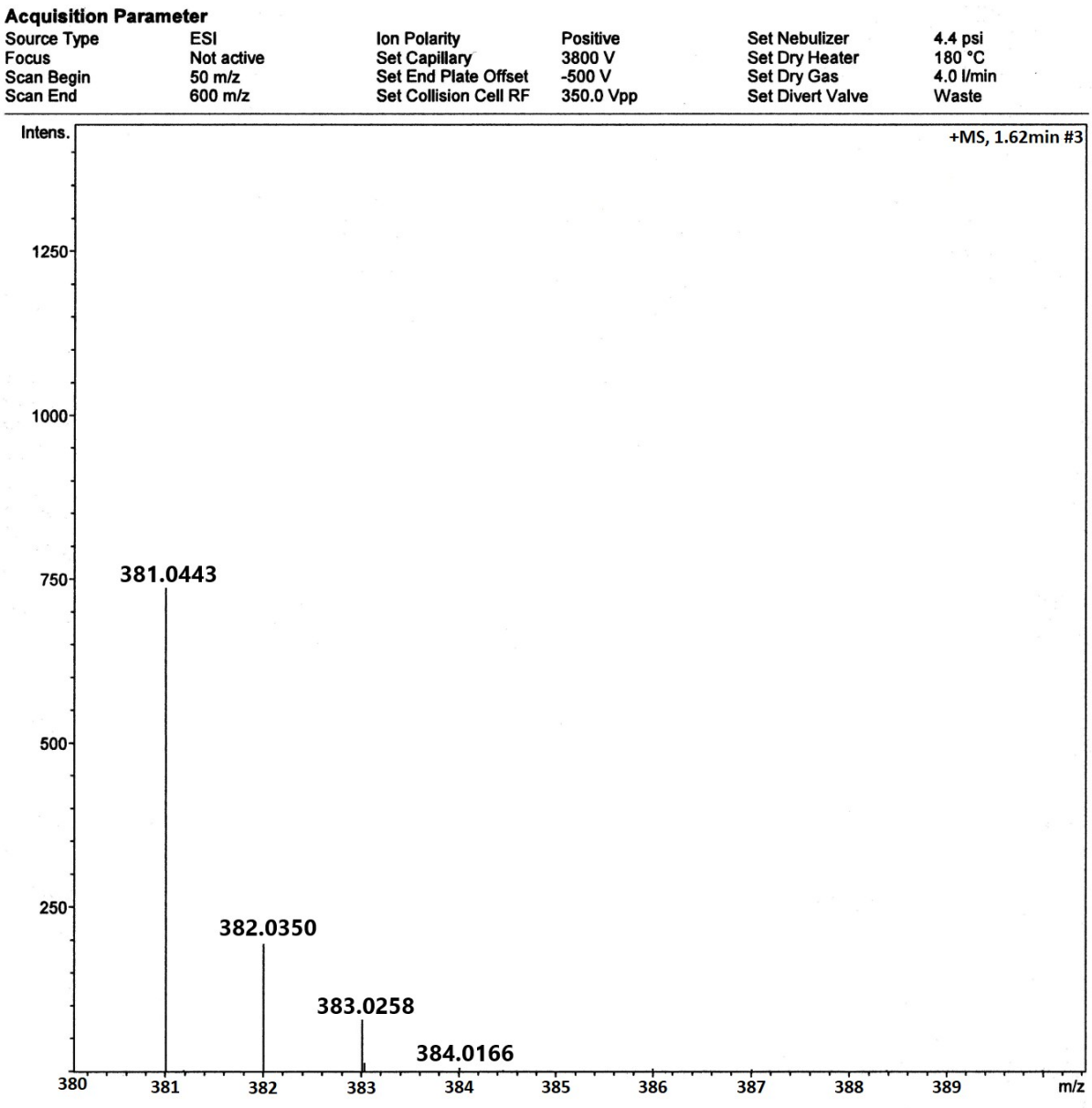


Fig.S15. HRMS spectrum of 3b

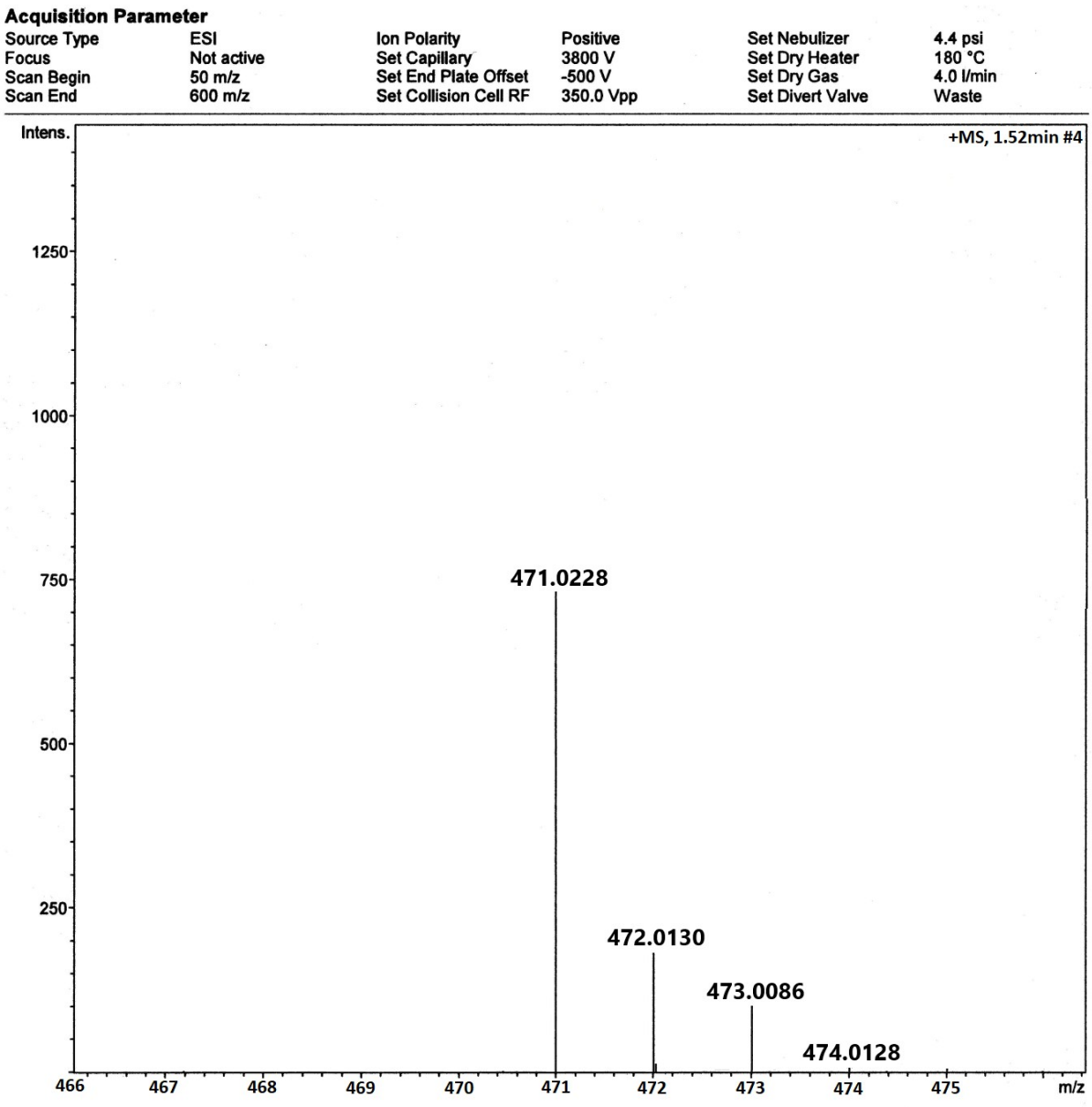


Fig.S16. HRMS spectrum of 3c

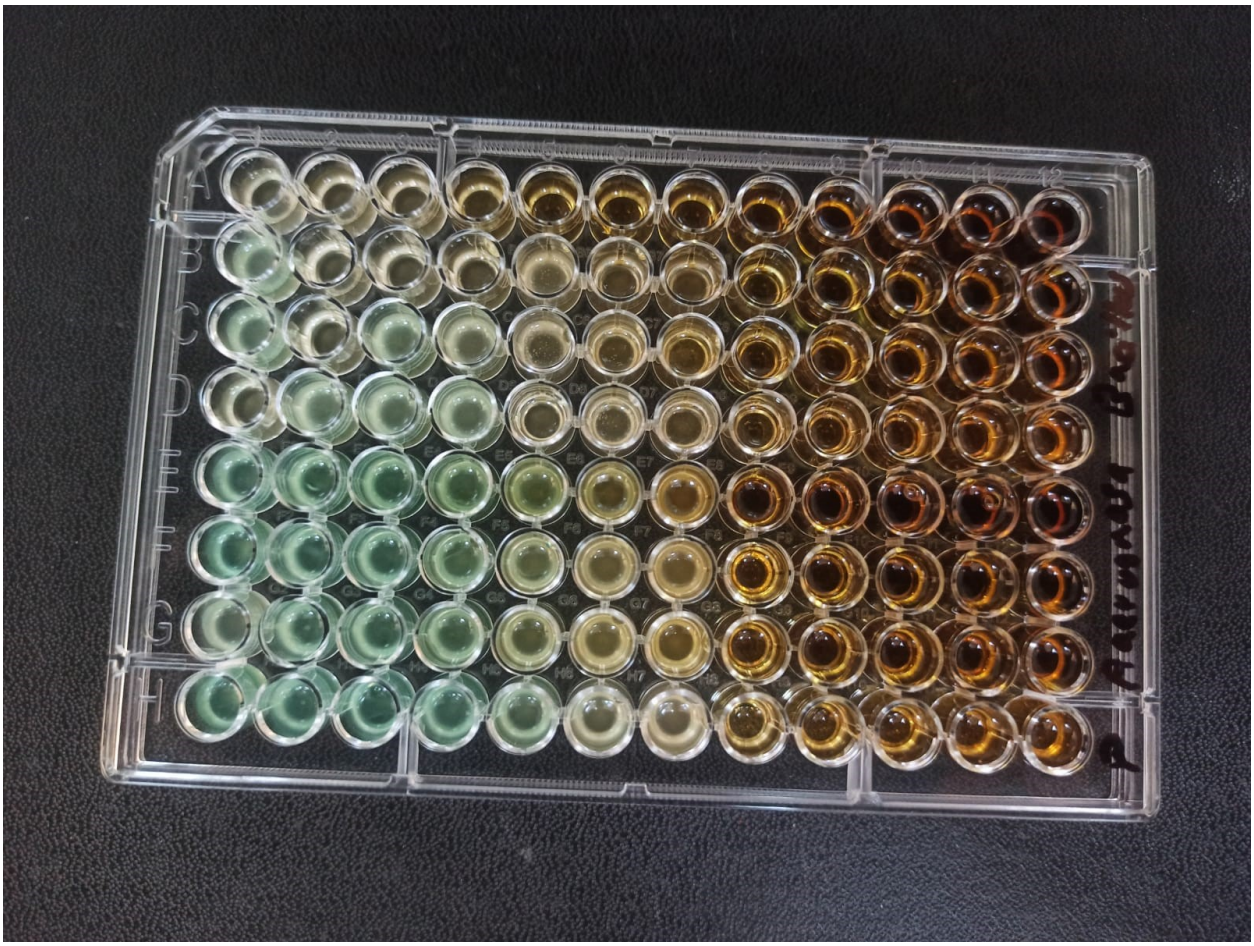


Fig.S17.MIC OF 3 and 3a-c against *Pseudomonas aeruginosa and Bacillus cereus*

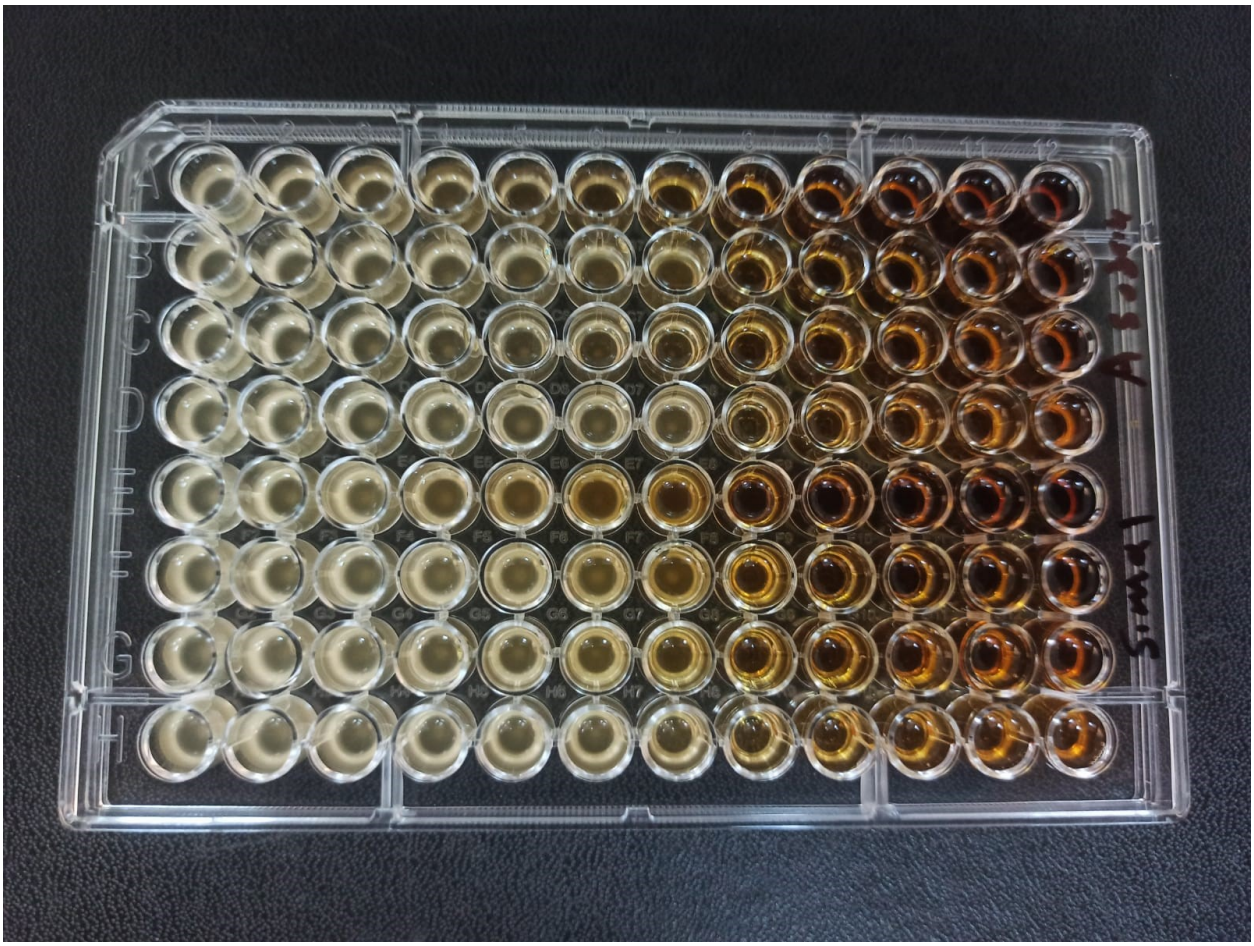


Fig.S18.MIC OF 3 and 3a-c against *Stenotrophomonas maltophilia and Aeromonas sobria*

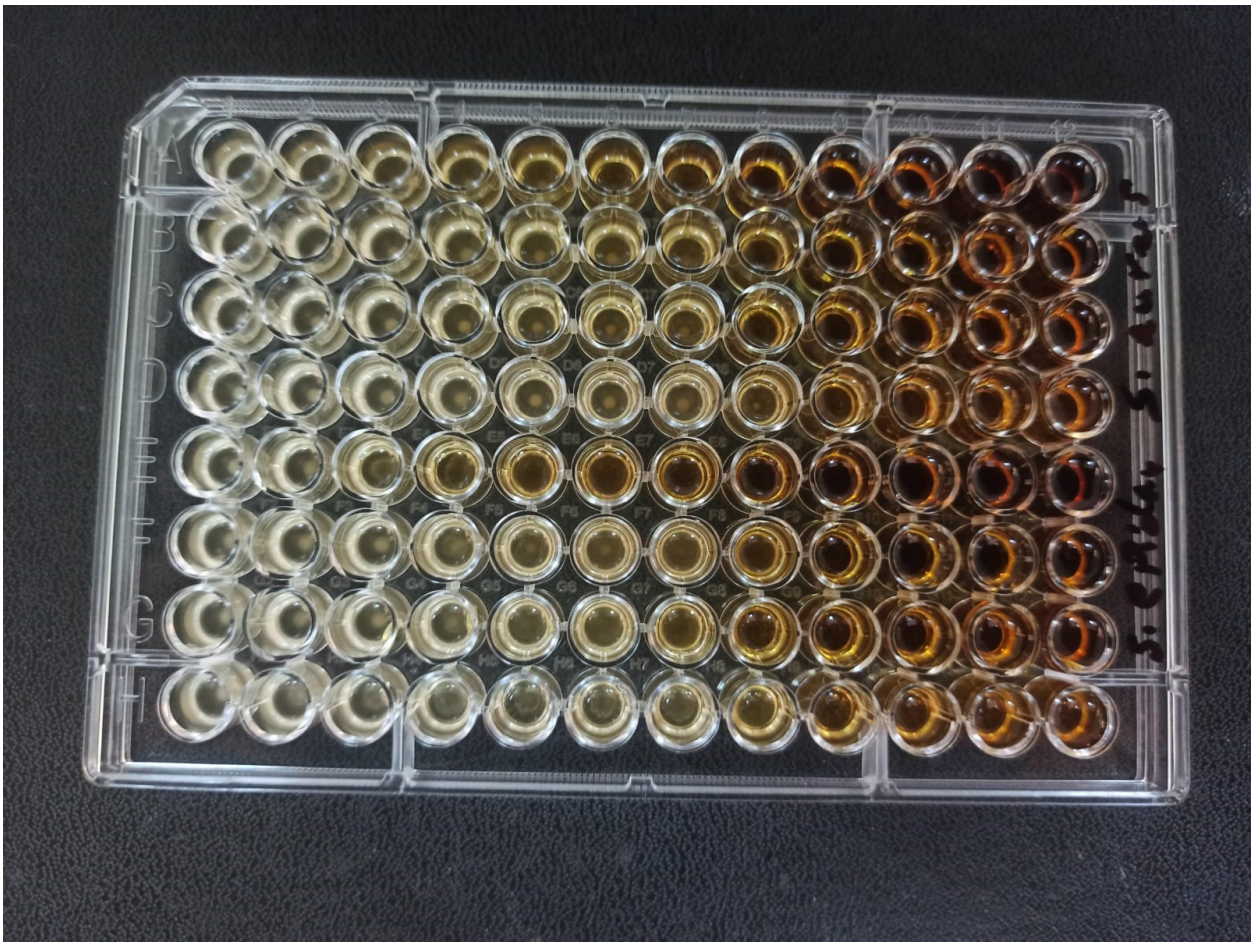


Fig.S19.MIC OF 3 and 3a-c against Staphylococcus aureus and Staphylococcus epidermidis

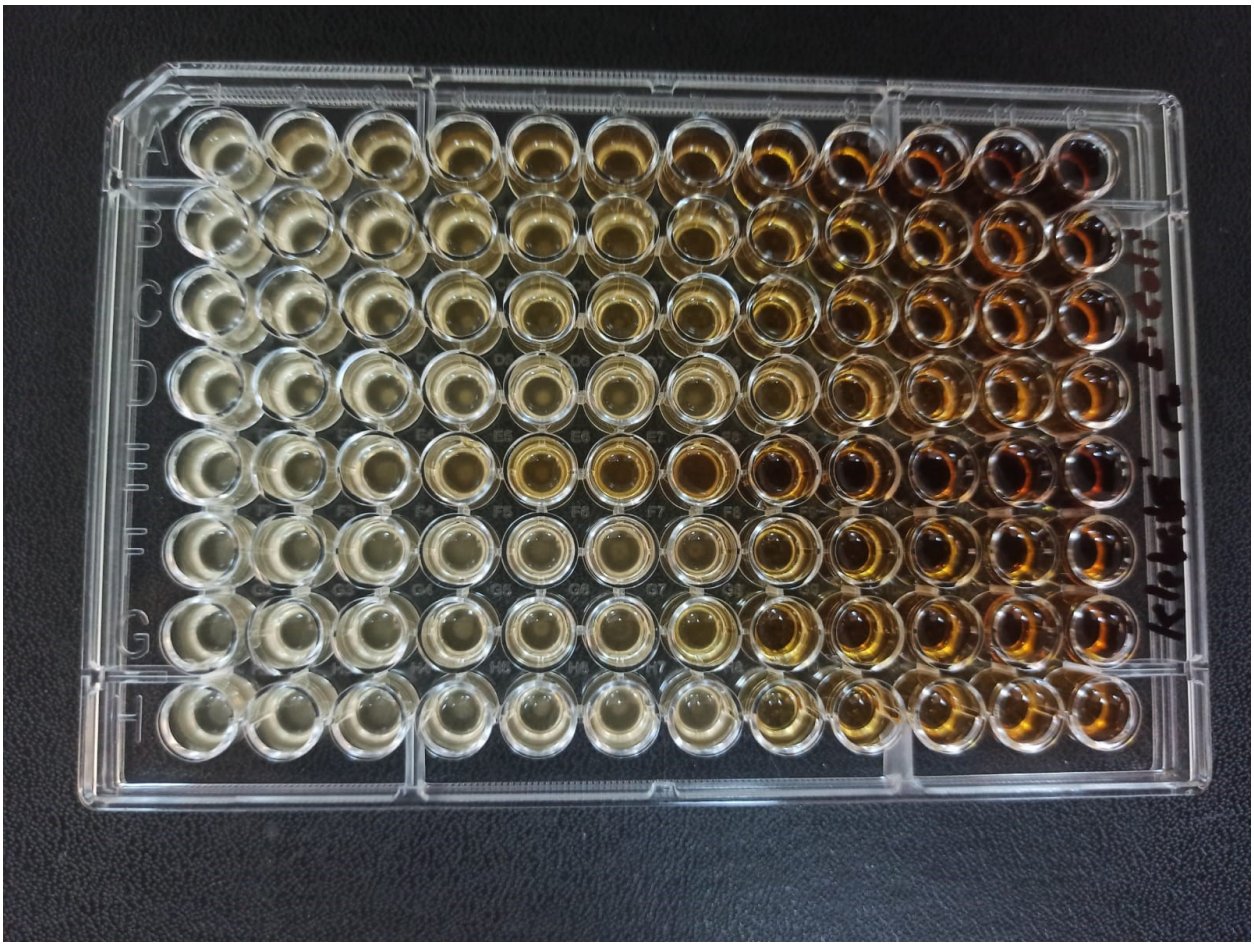
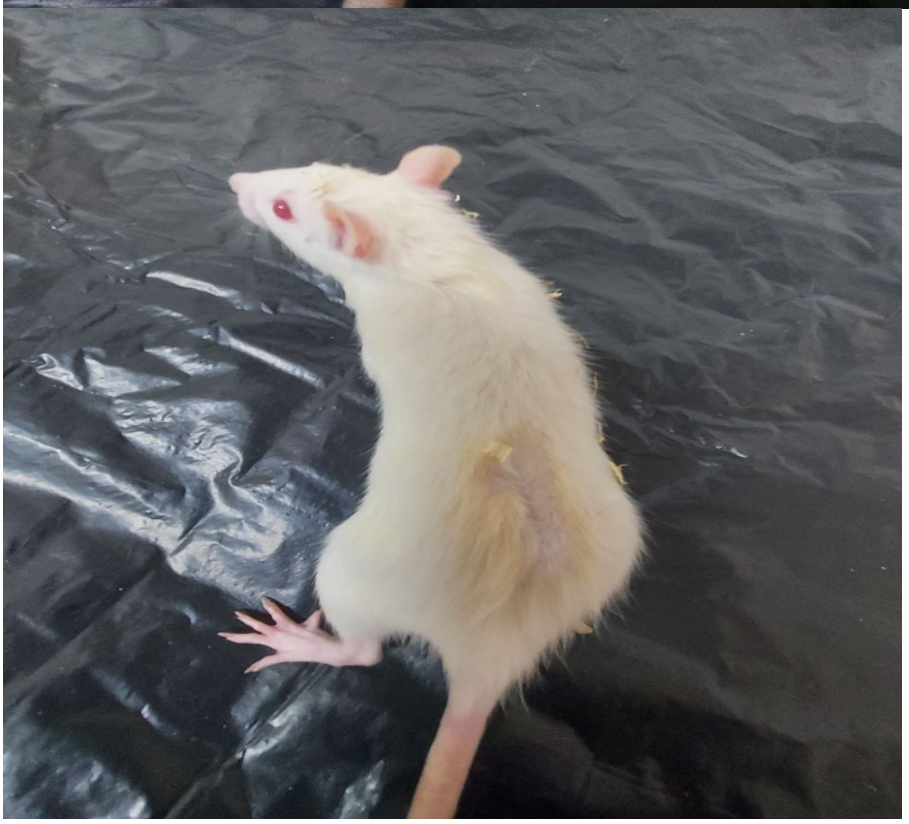
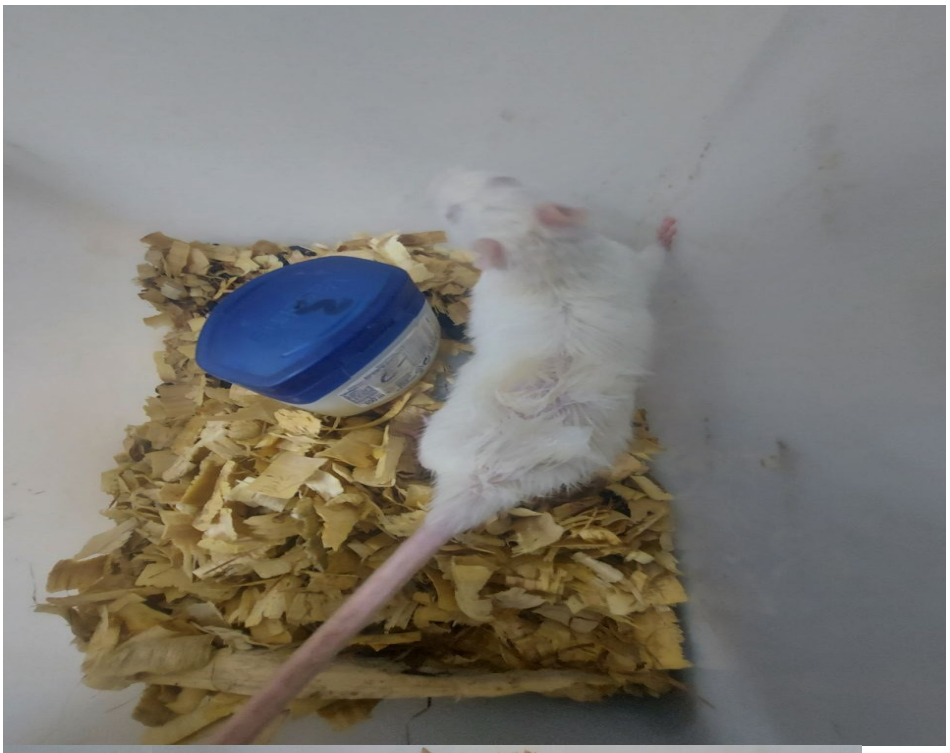
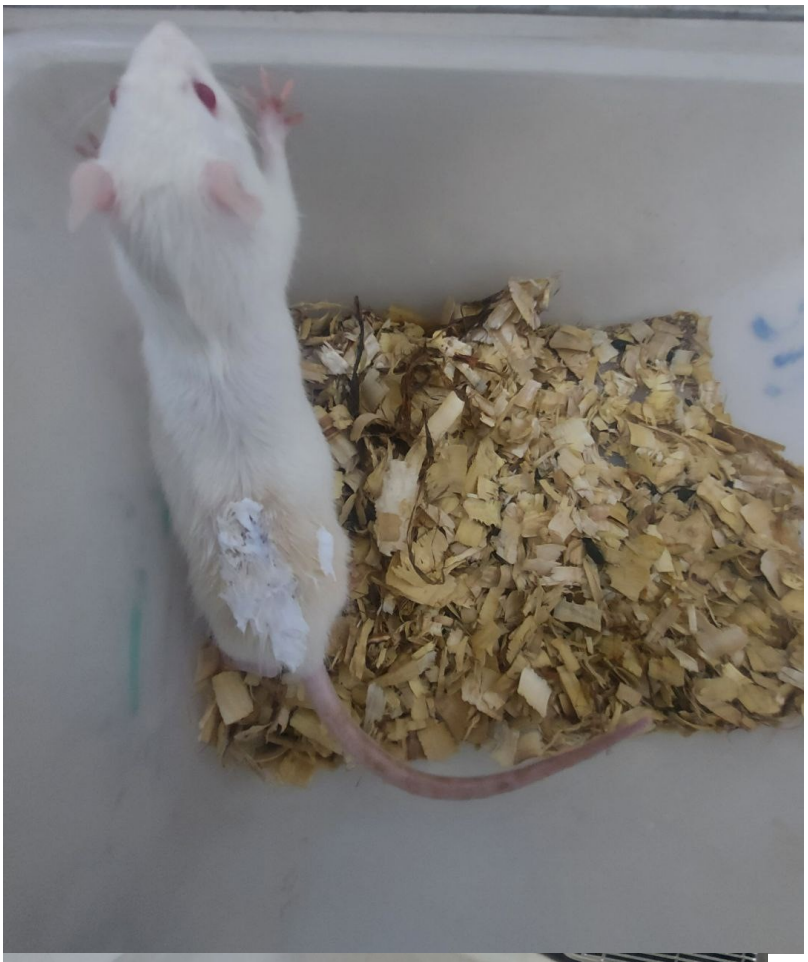


Fig.S20.MIC OF 3 and 3a-c against klebsiella pneumoniae. and Escherichia coli







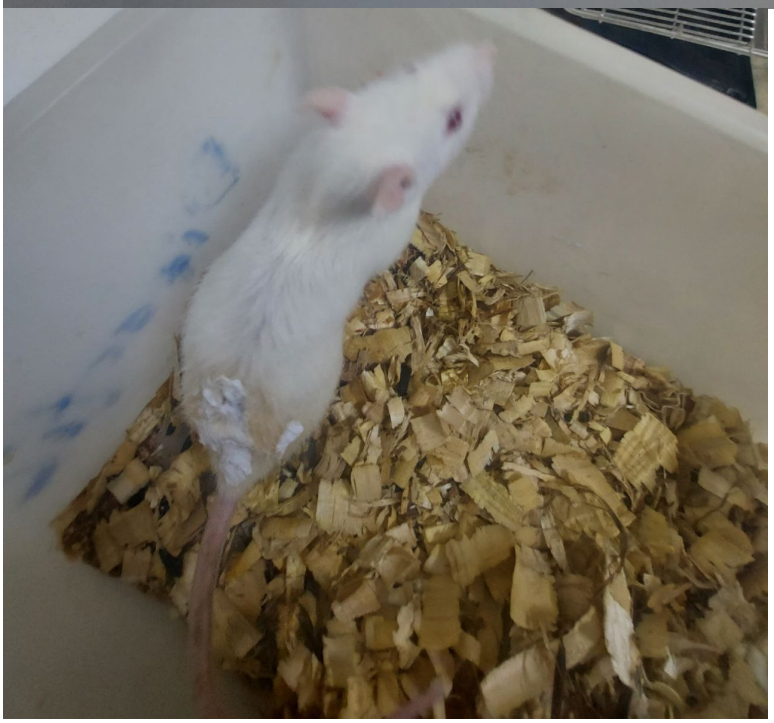
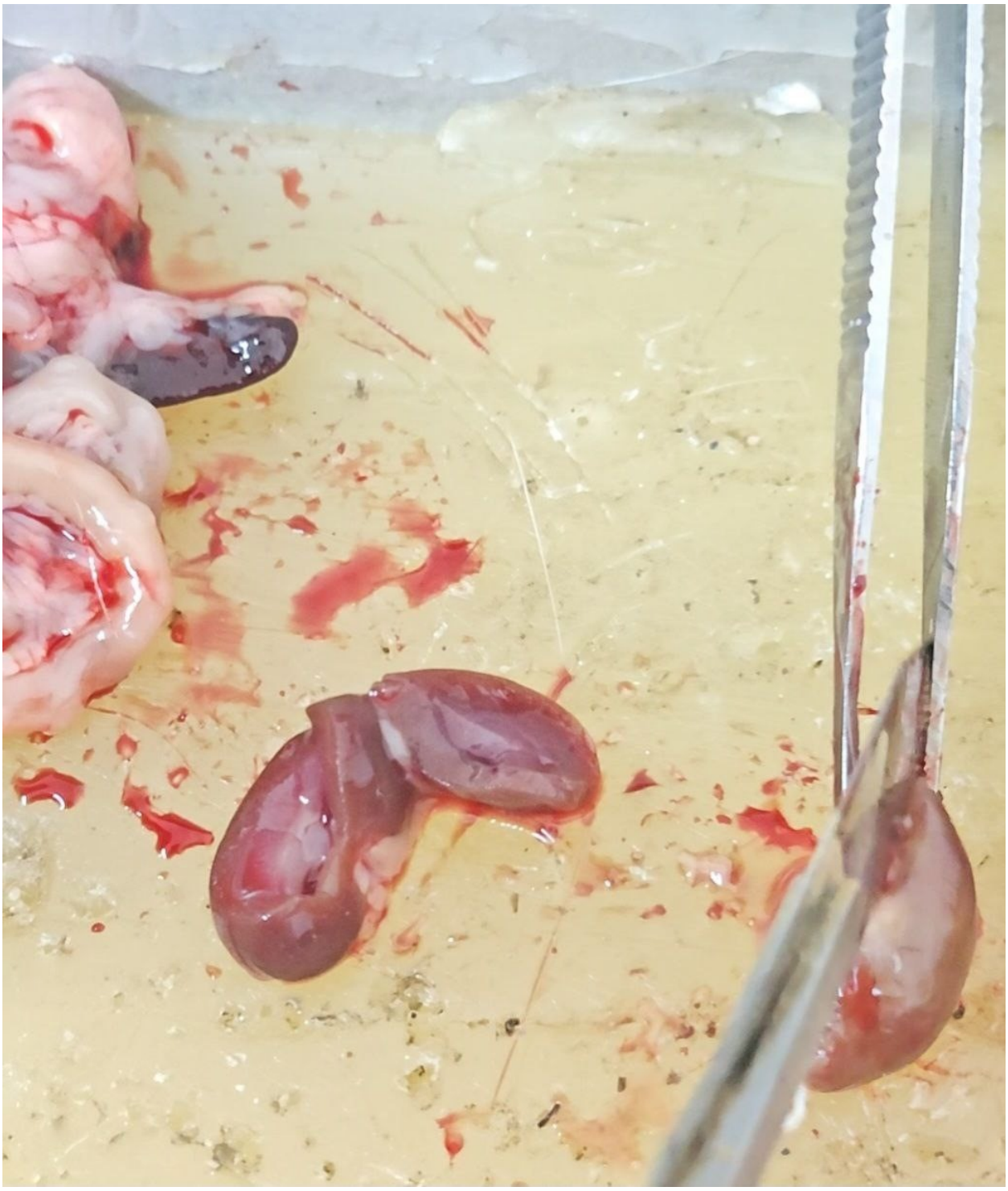
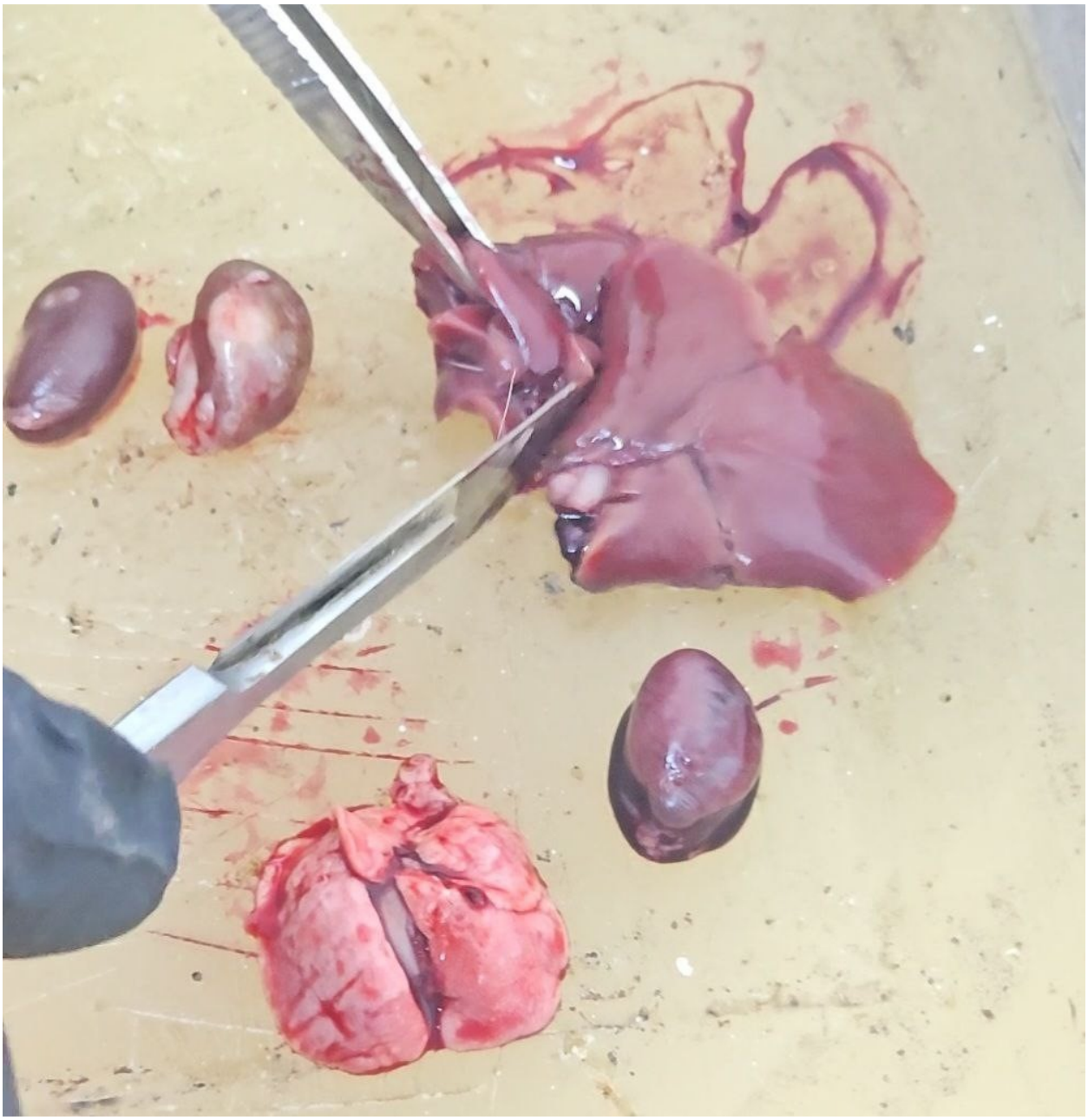
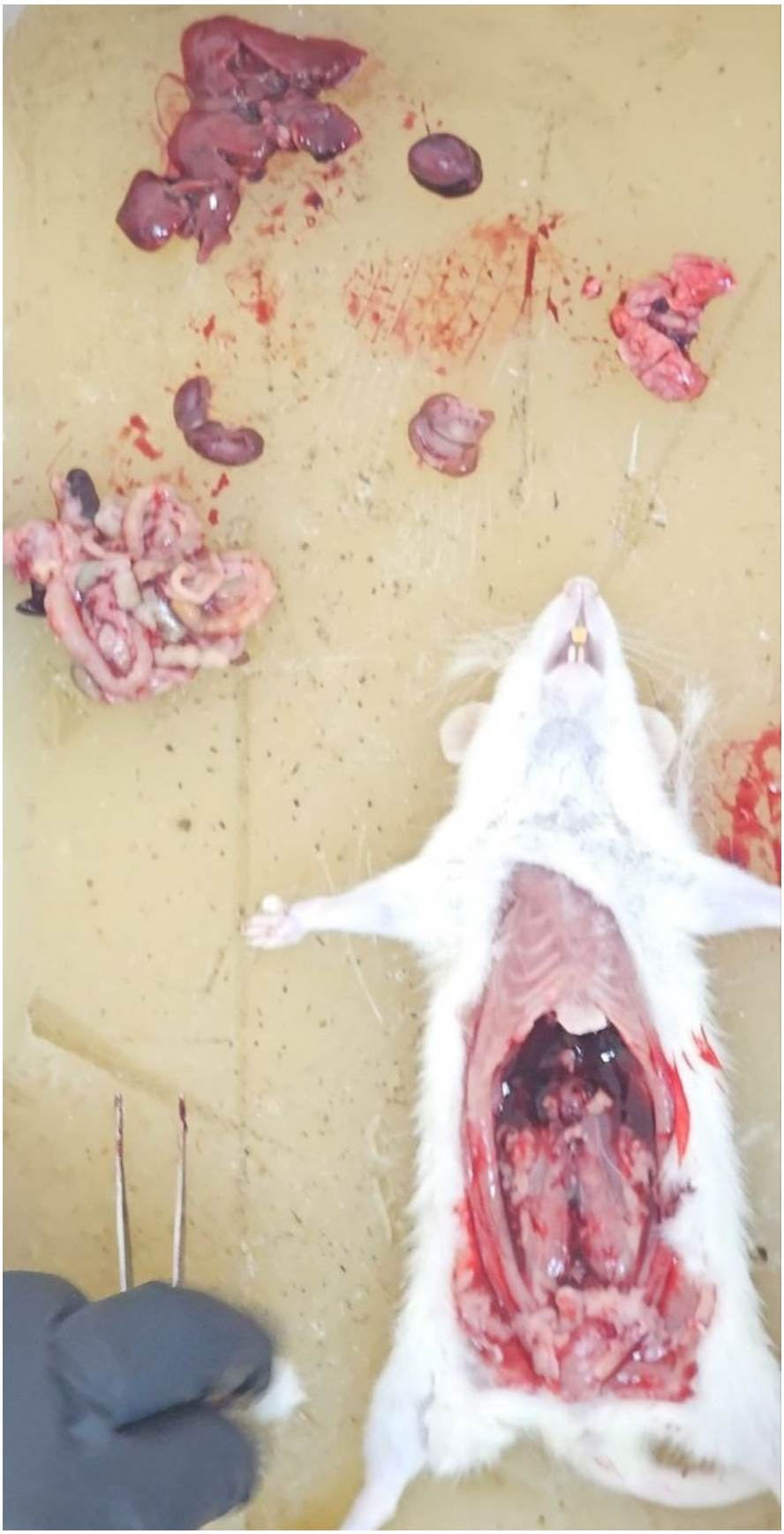
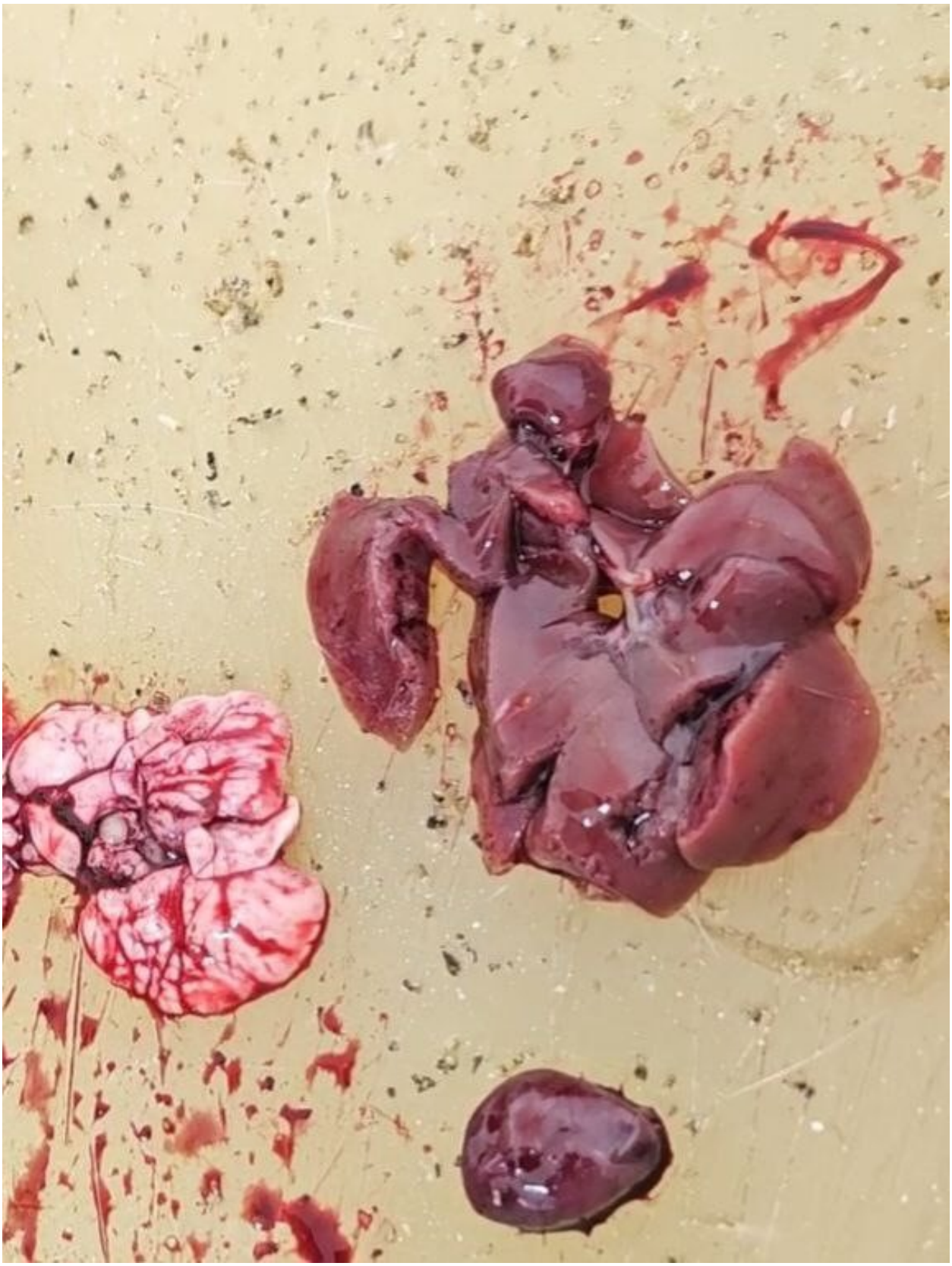


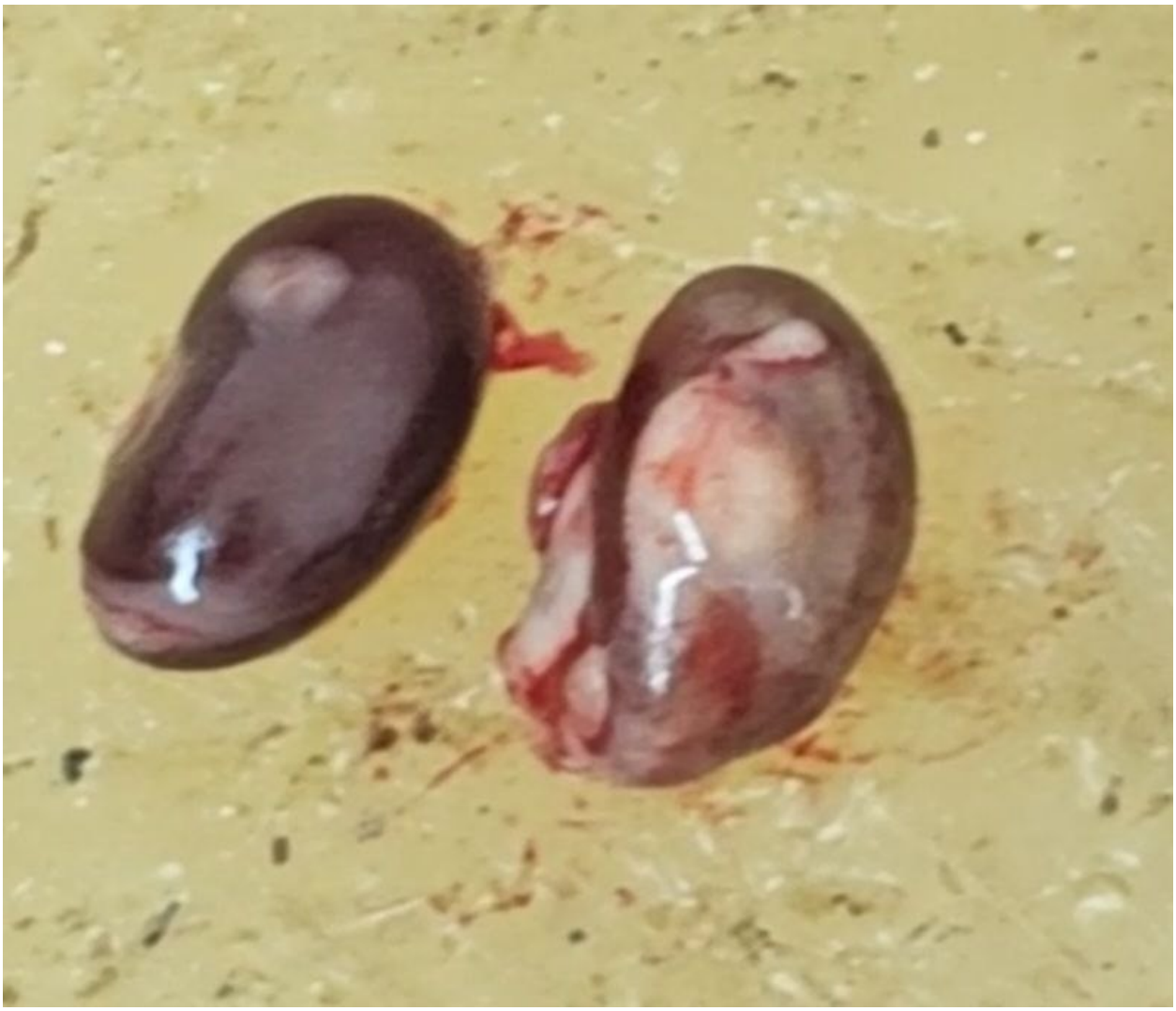
Fig.S21-S26: Standard drug and -ve control

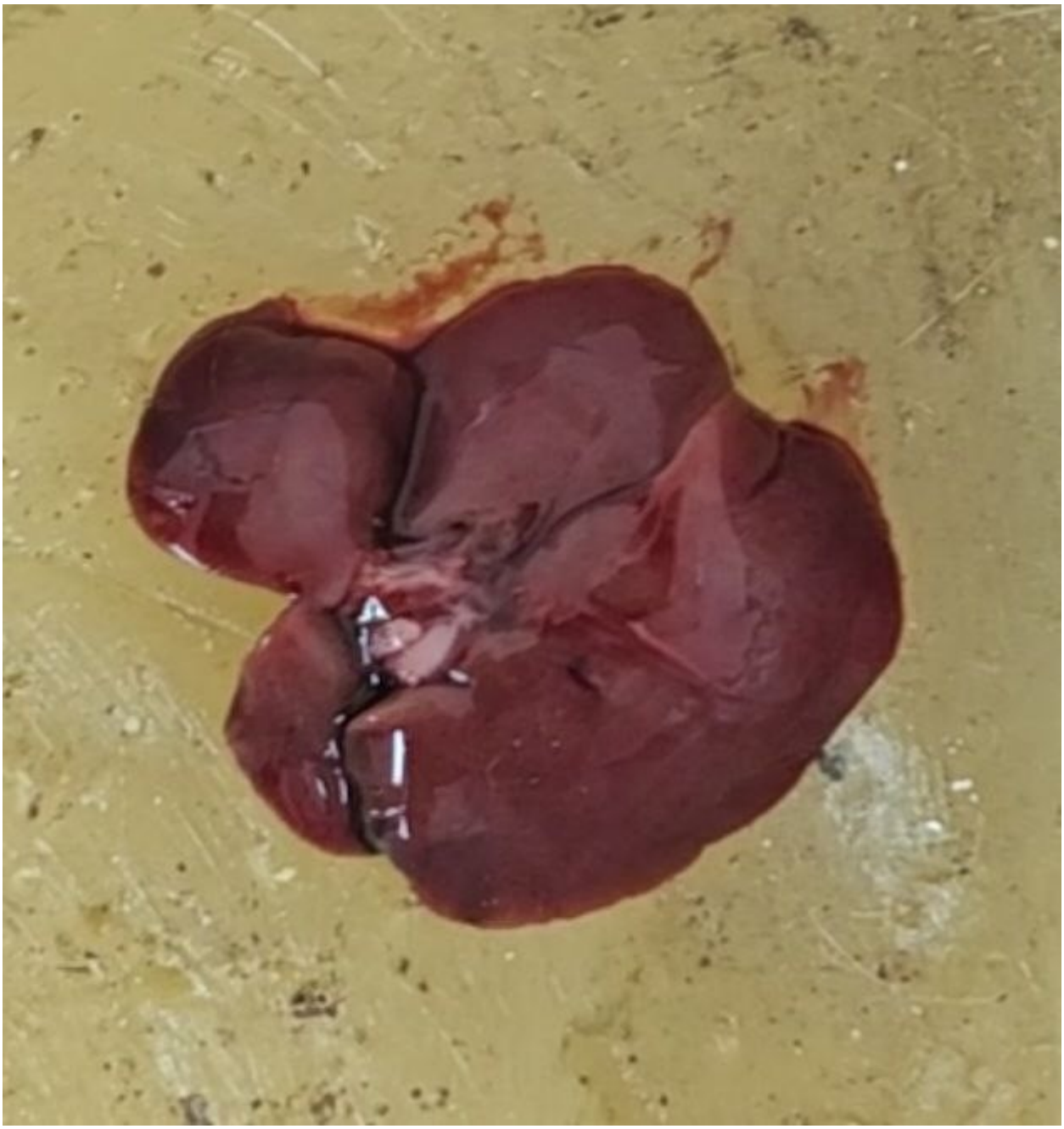












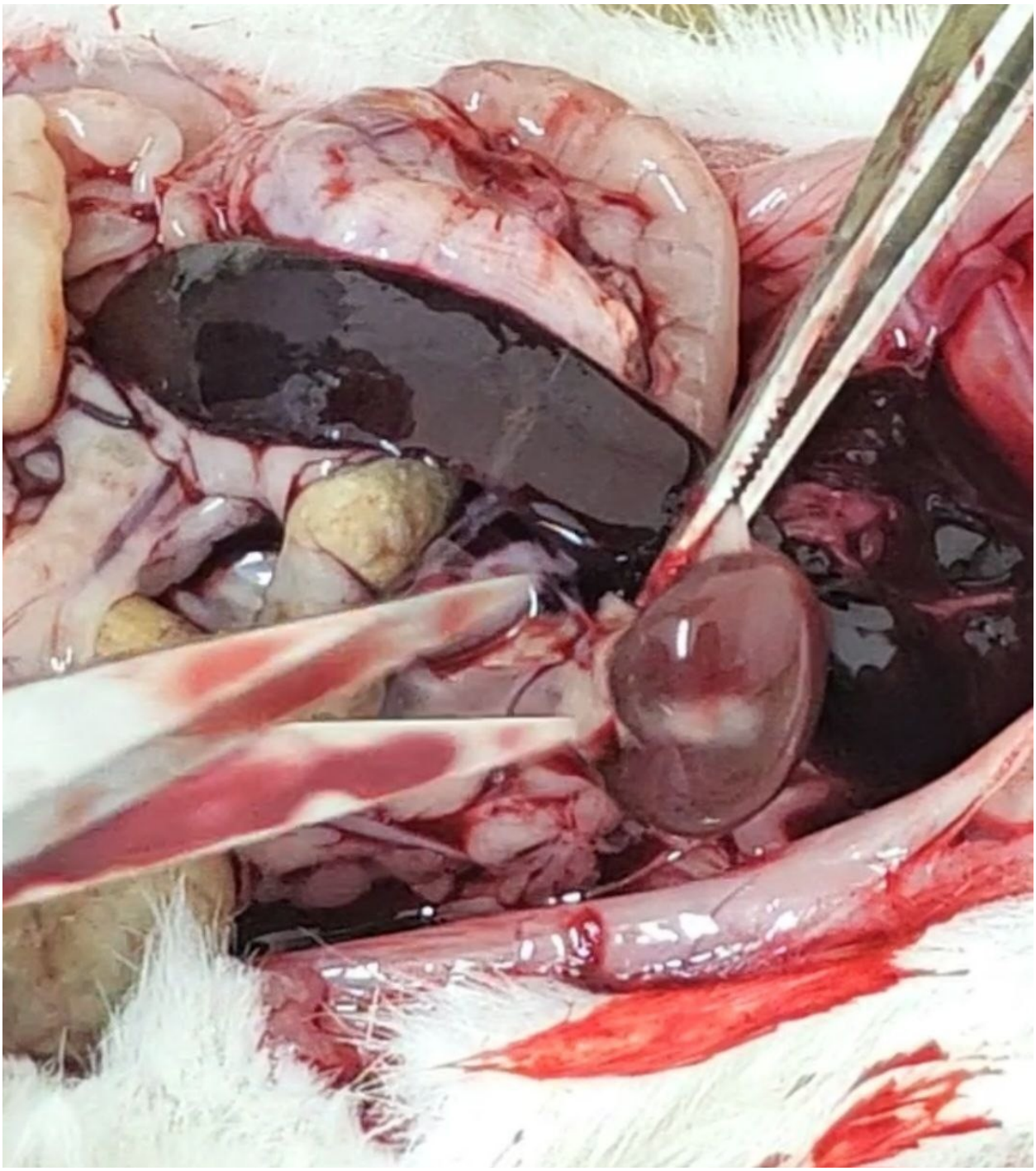


Fig.S27-S35: Standard drug and -ve control acute toxicity measurement

*Table S1. Prediction in silico of **Metabolism** of 3a-c derivatives*

Entry	Metabolism						
	CYP2D6 substrate	CYP3A4 substrate	CYP1A2 inhibitior	CYP2C19 inhibitior	CYP2C9 inhibitior	CYP2D6 inhibitior	CYP3A4 inhibitior
3a	NO	NO	YES	YES	YES	NO	NO
3b	NO	YES	YES	YES	YES	NO	YES
3c	NO	YES	YES	YES	YES	NO	YES

Table S2. Prediction in silico of **Toxicity** of 3a-c derivatives.

Entry	Toxicity									
	AMES toxicity	**Max. tolerated dose (human)**	**hERG I inhibitor**	**hERG II inhibitor**	**Oral Rat Acute Toxicity (LD50)**	**Oral Rat Chronic Toxicity (LOAEL)**	**Hepatotoxicity**	**Skin Sensitisation**	***T.Pyriformis* toxicity**	***Minnow toxicity***
3a	NO	**0.042**	NO	YES	**2.546**	**0.806**	YES	NO	**0.532**	**1.933**
3b	NO	**0.243**	NO	YES	**2.324**	**0.788**	YES	NO	**0.371**	**0.05**
3c	NO	**0.562**	NO	**YES**	**2.346**	0.417	YES	NO	**0.289**	**-0.154**