Supporting Information

A new efficient domino approach for the synthesis of coumarin-pyrazolines as antimicrobial agents targeting bacterial D-alanine-D-alanine ligase

Asha V. Chate,[a]* Ankita A. Redlawar,[a] Girabala M. Bondle,[a] Aniket P. Sarkate,[b] Shailee V. Tiwari,[c] Deepak K. Lokwani[d]

[a]Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad-431 004, MS., India.

[b]Department of Chemical Technology, Dr Babasaheb Ambedkar Marathwada University, Aurangabad-431004, MS, India.

[c]Department of Pharmaceutical Chemistry, Durgamata Institute of Pharmacy, Dharmapuri, Parbhani-431401, MS, India.

[d]R. C. Patel Institute of Pharmaceutical Education & Research, Shirpur-425405, MS, India.

*Corresponding author-*chateav@gmail.com*

Table of Contents

Experimental

Materials and methods

All the chemicals used were of laboratory grade. Melting points of all the synthesized compounds were determined in open capillary tube and are uncorrected. The Progress of the reaction was monitored by thin layer chromatography on Merck's silica plates and visualization was accomplished by iodine/ultraviolet light. IR spectra were obtained on a Bruker ALPHA (Eco-ATR) spectrometer. ^{1}H NMR spectra of were recorded with a Bruker AvIII HD-400 MHz spectrometer operating at 400 MHz using DMSO solvent and tetramethylsilane (TMS) as the internal standard and chemical shift in δH ppm. Mass spectra were recorded on a Waters UPLC-TQD (ESI-MS and APCI-MS) instrument and elemental analysis was recorded on CHNS autoanalyzer (Thermofischer EA1112 SERIES).

General procedure for the synthesis of 3-(5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one and 3-(1,5-diphenyl-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one derivatives 5 (a-w): The mixture of salicylaldehyde (0.5 gm, 1 mol), ethyl acetoacetate (0.67 gm, 1 mol), and hydrazine hydride (2.0 gm, 1 mol) and benzaldehyde (0.42 gm, 1 mol) were added in β-cyclodextrin (15 mol %) solution containing water. The resulting mixture was heated at 80-100 ˚C. After completion of the reaction (monitored by TLC), the reaction mixture was cooled. The solid obtained was filtered and washed by hot water and dried. The resulting crude product was purified by crystallized from ethanol to afford the desired product **5a**. The filtrate was then cooled to 0 ˚C to recover β-CD reappeared as white solid. Thus the obtained solid mass then filtered and washed with water to recover β-CD. The recovered β-CD was reused for 2-3 consecutive runs in this reaction without any significant loss in yield and catalytic activity. All the newly synthesized compounds have been characterized by elemental analysis and various spectroscopic methods, the results obtained are summarized in **(Table 2)**. The rest of product **5 (b-w)** were prepared by a procedure similar to that for 5a. The known compounds showed satisfactory spectroscopic data in agreement with those reported in the literature.

Spectra Data of 3-(5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (5a): IR (ATR) ν_{max}/cm^{-1} 3323 (Ar-NH), 1591 (C=N), 1472 (Ar C=C); ^1H NMR (400 MHz, DMSO) δH = 2.50 (d, 1H, 4-H_{cis} of pyrazoline), 4. 81 (d, 1H, 5-H of pyrazoline), 3.32 (d, 1H, 4-H_{trans} of pyrazoline), 6.95-7.70 (m, 9H, Ar-H), 7.90 (s, 1H, pyrazoline), 9.06 (s, 1H, coumarin); MS, m/z (%): 291.12 (M+1); Elemental Analysis Calcd. For $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65; Found: C: 74.40; H: 4.90; N: 9.60.

3-(5-(3,4-dimethoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (5b): IR (ATR) ν_{max}/cm^{-1} 3223 (Ar N-H), 1641 (C=N), 1470 (Ar C=C), 1170 (–OCH_3); ^1H NMR (400 MHz, DMSO) δH = 3.31 (s, 1H, -OCH_3), 3.44 (s, 1H, -OCH_3), 3.52 (d, 1H, 4-H_{trans} of pyrazoline), 3.60 (d, 1H, 4-H_{cis} of pyrazoline), 4.85 (d, 1H, 5-H of pyrazoline), 6.98-7.71 (m, 7H, Ar-H), 7.89 (s, 1H, pyrazoline), 7.92 (s, 1H, coumarin); MS, m/z (%): 251.16 (M+1); Elemental Analysis Calcd. For $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00; Found: C: 68.50; H: 5.24; N: 8.05.

3-(5-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (5c): IR (ATR) ν_{max}/cm^{-1} 3263 (Ar N-H), 1648 (C=N), 1479 (Ar C=C), 1090 (Ar-Cl); ^1H NMR (400 MHz, DMSO) δH = 2.91 (d, 1H, 4-H_{trans} of pyrazoline), 3.41 (d, 1H, 4-H_{cis} of pyrazoline), 3.45 (d, 1H, 5-H of pyrazoline), 6.84-6.84 (dd, 2H, Ar-H), 7.58-7.60 (dd, 2H, Ar-H), 7.76-7.80 (m, 4H, Ar-H), 7.80 (s, 1H, pyrazoline), 7.90 (s, 1H, coumarin); MS, m/z (%): 325.20 (M+1); Elemental Analysis Calcd. For $C_{18}H_{13}ClN_2O_2$: C, 66.57; H, 4.03; N, 8.63; Found: C: 66.48; H: 4.06; N: 8.58.

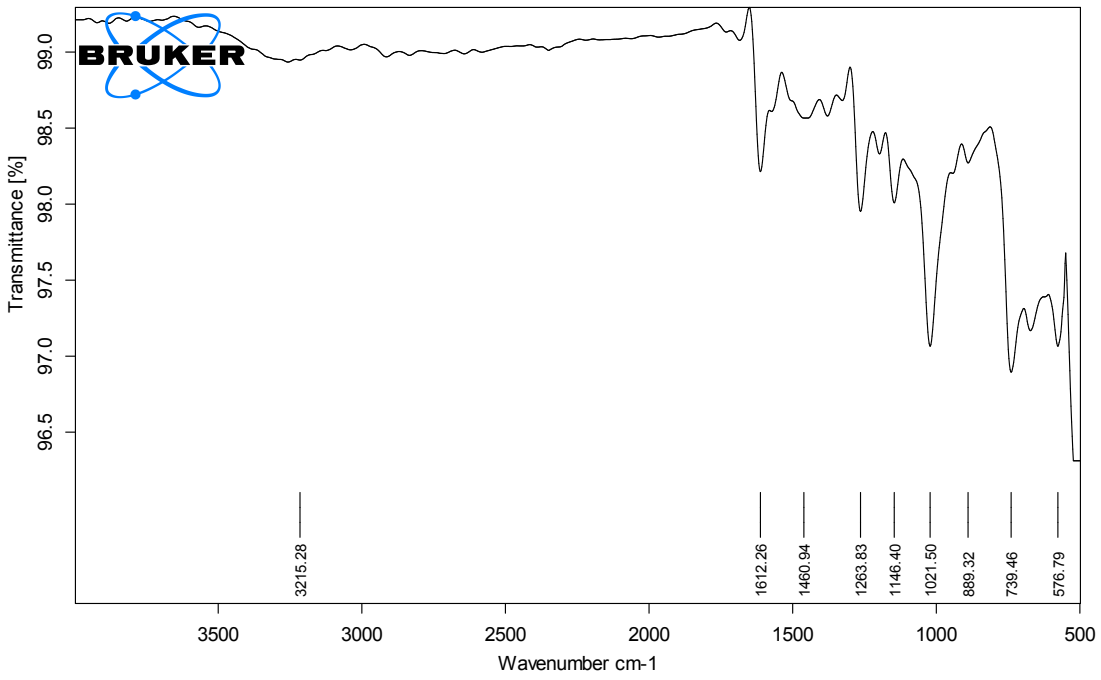
3-(5-(2,6-dichlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (5i): IR (ATR) ν_{max}/cm^{-1} 3266 (Ar N-H), 1658 (C=N), 1470 (Ar C=C), 1091 (Ar-Cl); ^1H NMR (400 MHz, DMSO) δH = 3.40 (d, 1H, 4-H_{trans} of pyrazoline), 3.53 (d, 1H, 4-H_{cis} of pyrazoline), 4.80 (d, 1H, 5-H of pyrazoline), 7.09-7.11 (m, 3H, Ar-H), 7.15-7.19 (m, 4H, Ar-H), 7.25 (s, 1H, pyrazoline), 7.28 (s, 1H, coumarin); MS, m/z (%): 358.10 (M+); Elemental Analysis Calcd. For $C_{18}H_{12}Cl_2N_2O_2$: C, 60.19; H, 3.37; N, 7.80; Found: C: 60.12; H: 3.41; N: 7.74.

3-(1,5-diphenyl-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (5m): IR (ATR) ν_{max}/cm^{-1} 1736 (lactone of coumarin), 1658 (C=N), 1470 (Ar C=C), 1091 (Ar-Cl); ^1H NMR (400 MHz, DMSO) δH = 3.51 (d, 1H, 4-H_{trans} of pyrazoline), 4.85 (d, 1H, 4-H_{cis} of pyrazoline), 5.76 (dd, 1H of pyrazoline), 6.99-7.28 (m, 4H, Ar-H), 7.30-7.48 (m, 5H, Ar-H), 7.54-7.85 (m, 4H, Ar-H),

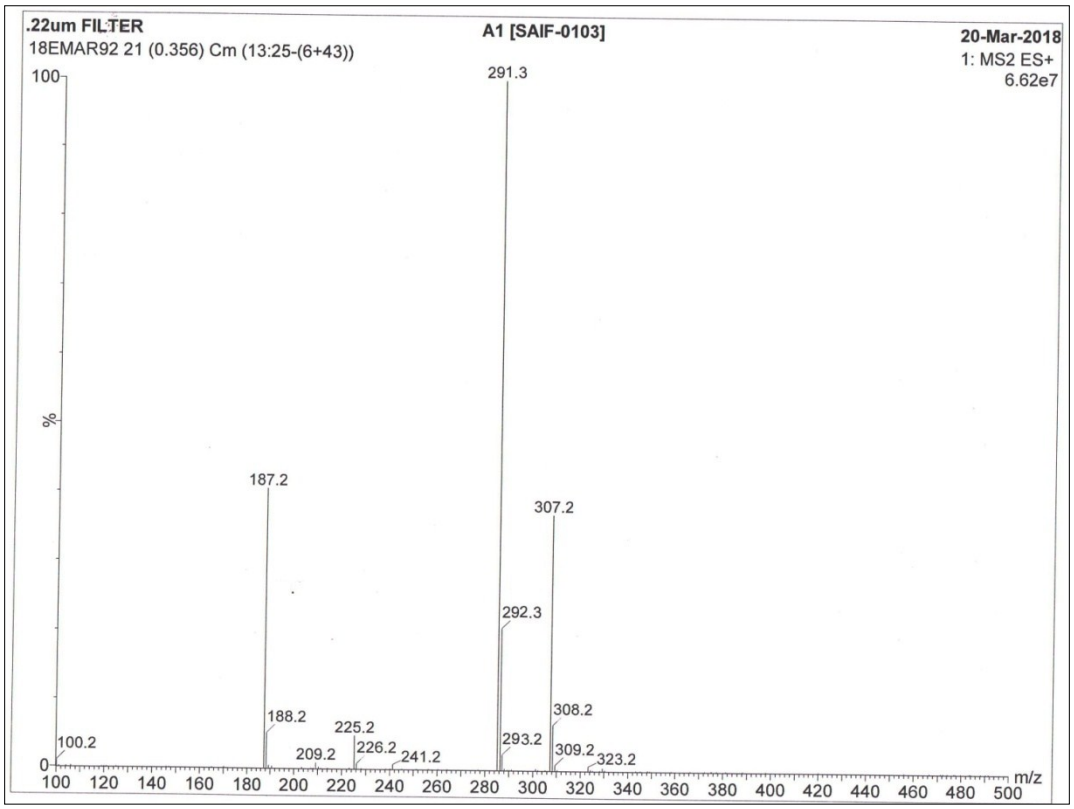
9.01 (s, 1H, coumarin); MS, m/z (%): 366.10 (M+); Elemental Analysis Calcd. For $C_{24}H_{18}N_2O_2$: C, 78.67; H, 4.95; N, 7.65; Found: C: 78.61; H: 4.99; N: 7.60.

3-(1-phenyl-5-(p-tolyl)-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (5n): IR (ATR) ν_{max}/cm^{-1} 3266 (Ar N-H), 1658 (C=N), 1470 (Ar C=C); ^1H NMR (400 MHz, DMSO) δH = 3.30 (d, 1H, 4-H_{trans} of pyrazoline), 3.50 (d, 1H, 4-H_{cis} of pyrazoline), 4.43 (dd, 1H of pyrazoline), 7.08-7.66 (m, 14H, Ar-H), 7.92 (s, 1H, pyrazoline), 7.98 (s, 1H, coumarin); MS, m/z (%): 381.10 (M+); Elemental Analysis Calcd. For $C_{24}H_{18}N_2O_2$: C, 78.67; H, 4.95; N, 7.65; Found: C: 78.61; H: 5.01; N: 7.58.

IR of Comp. (5a)



Mass of Comp. (5a)



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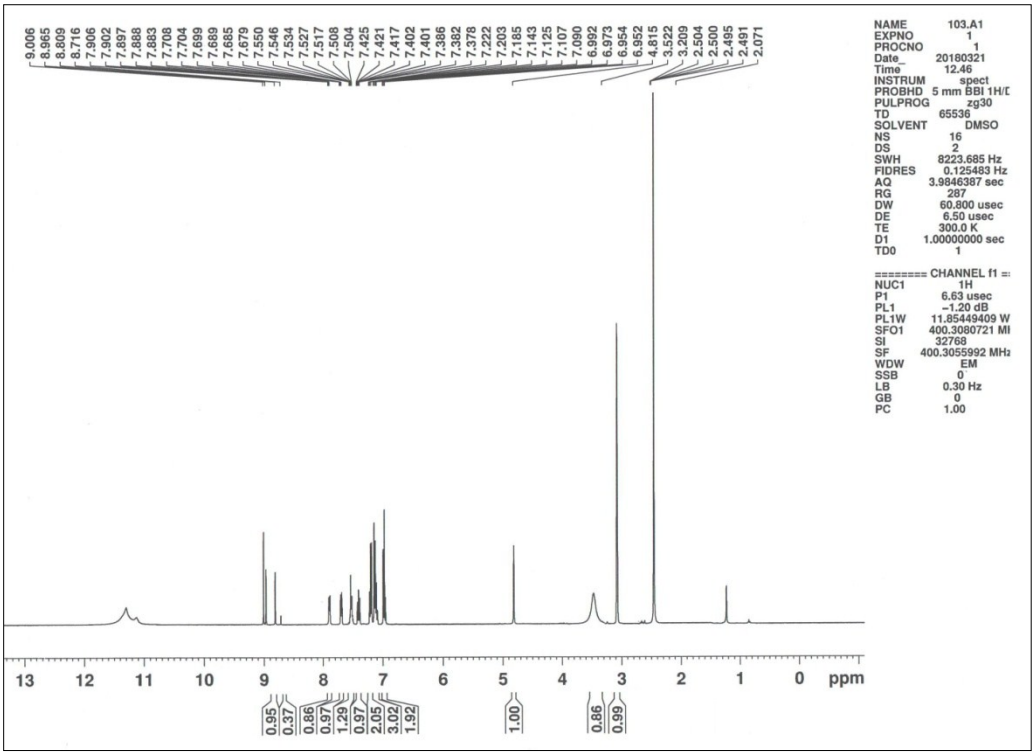

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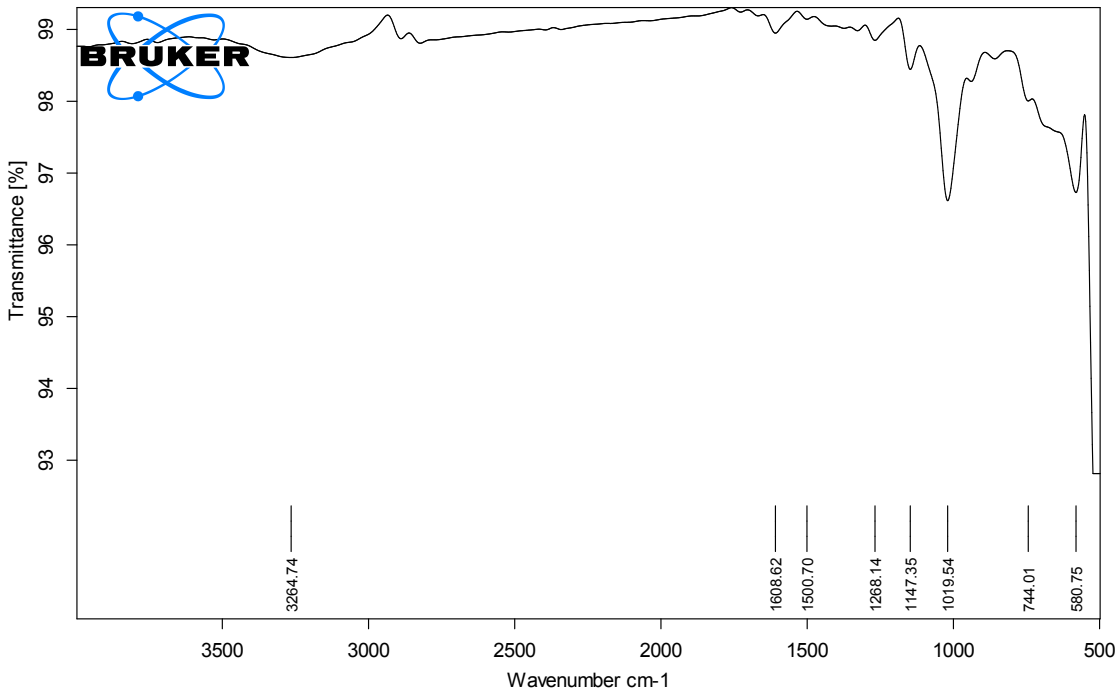

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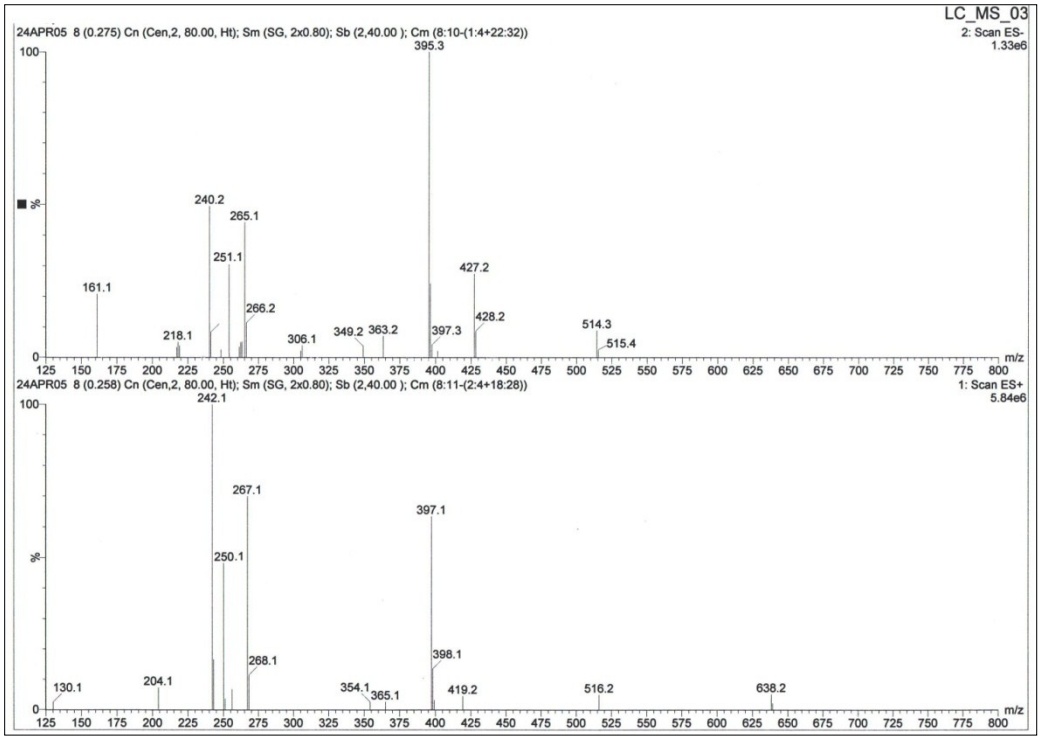

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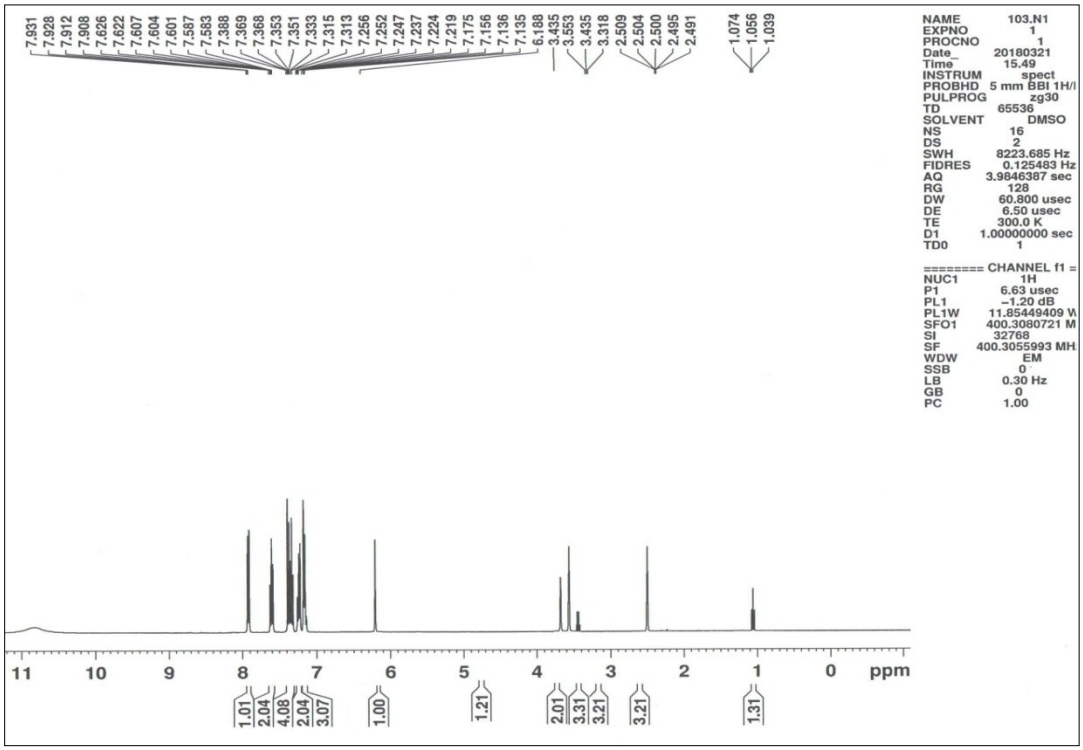

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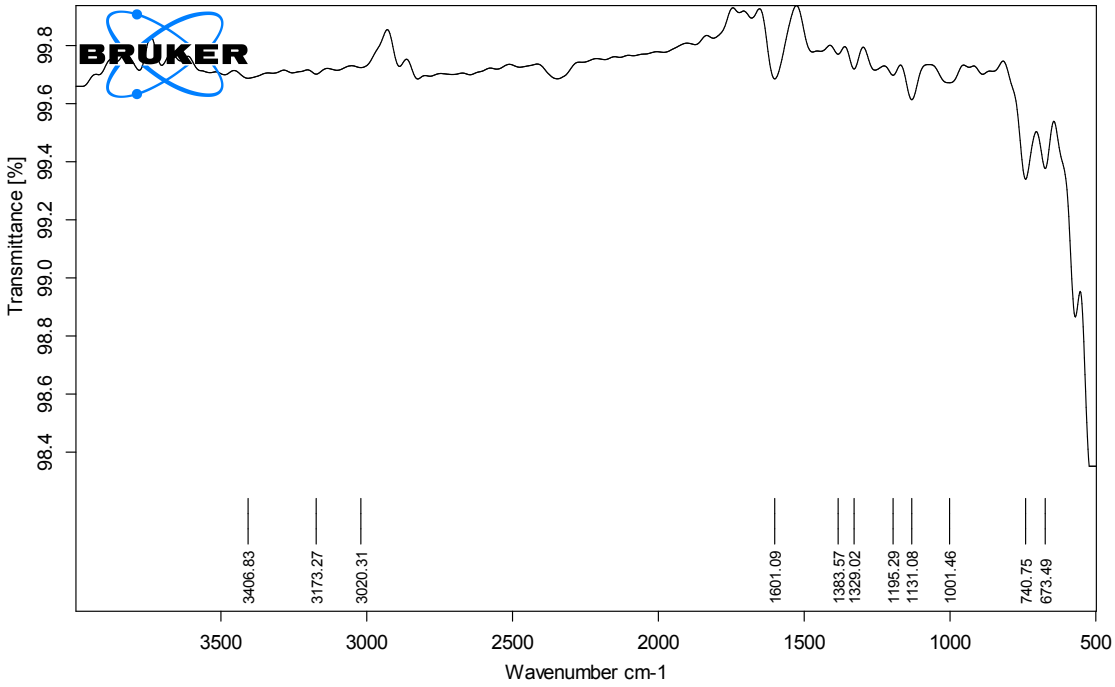

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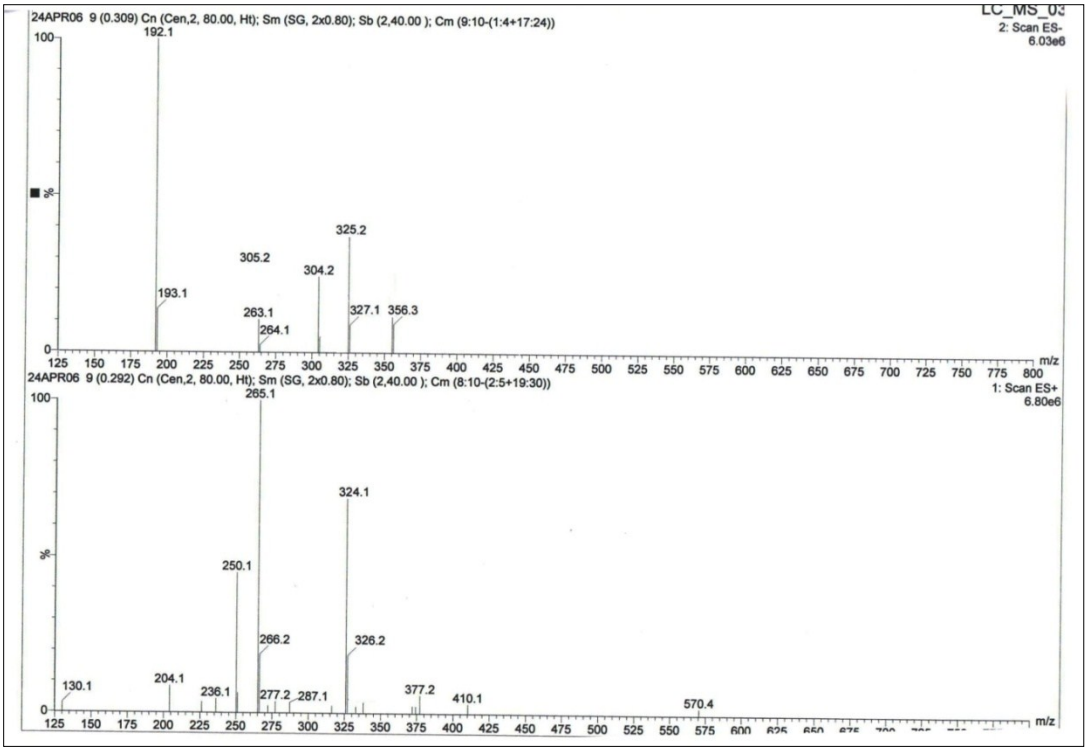

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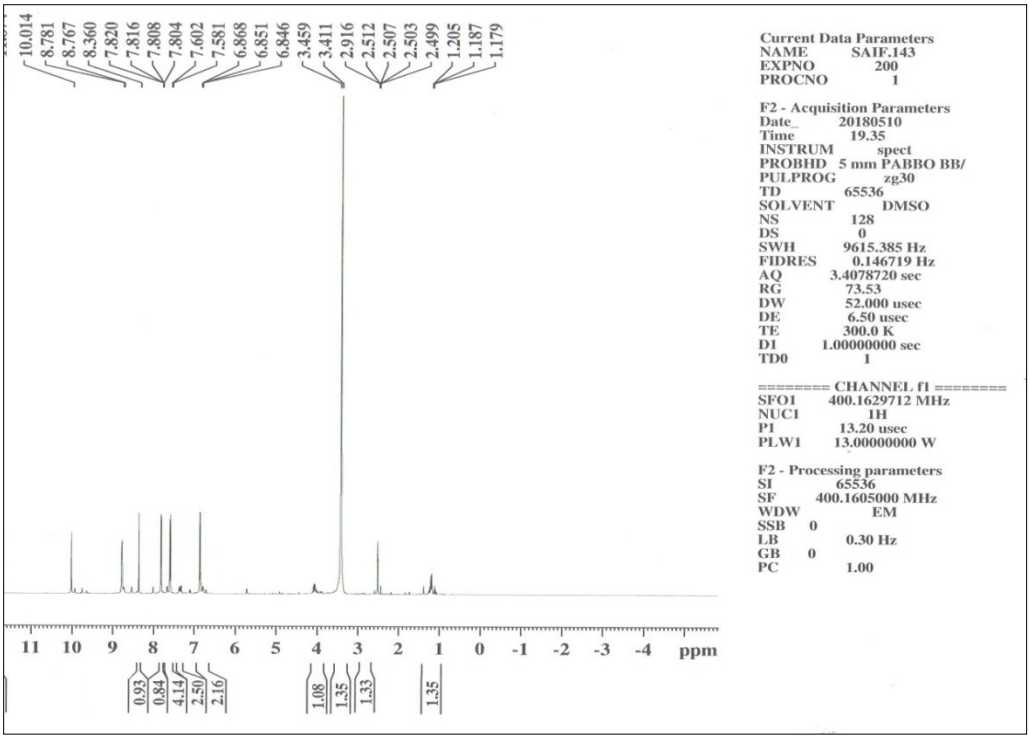

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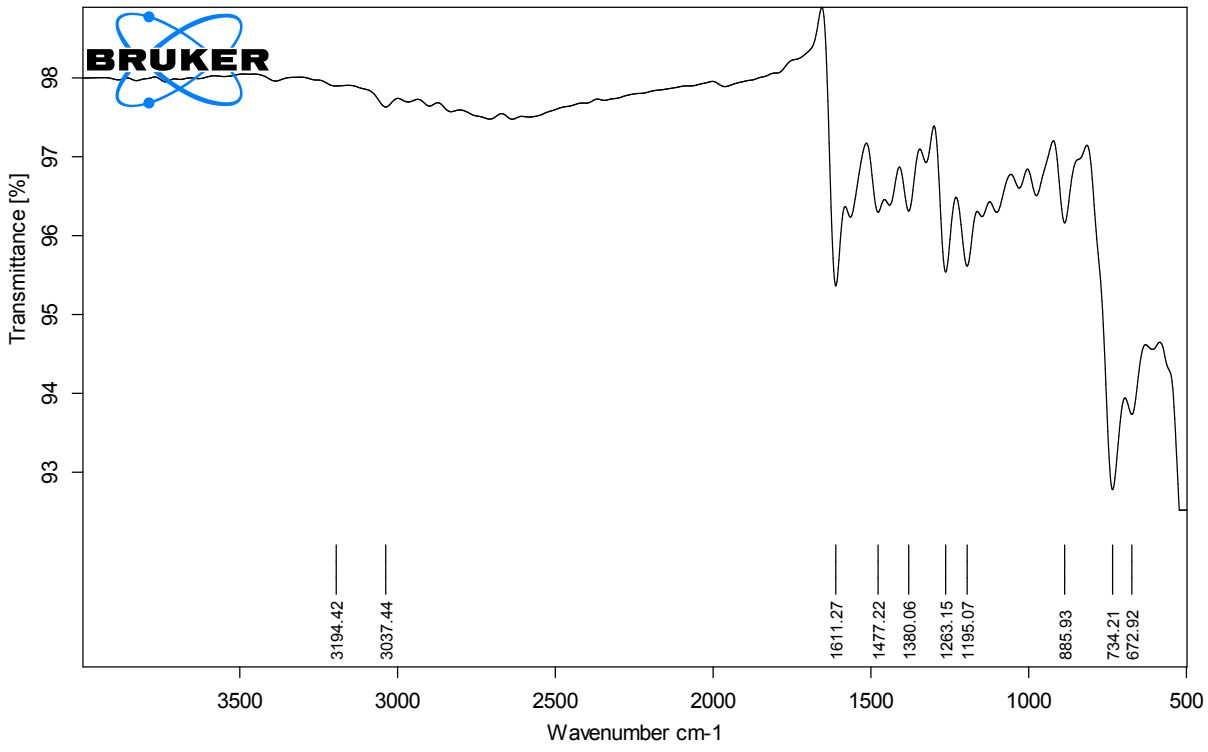

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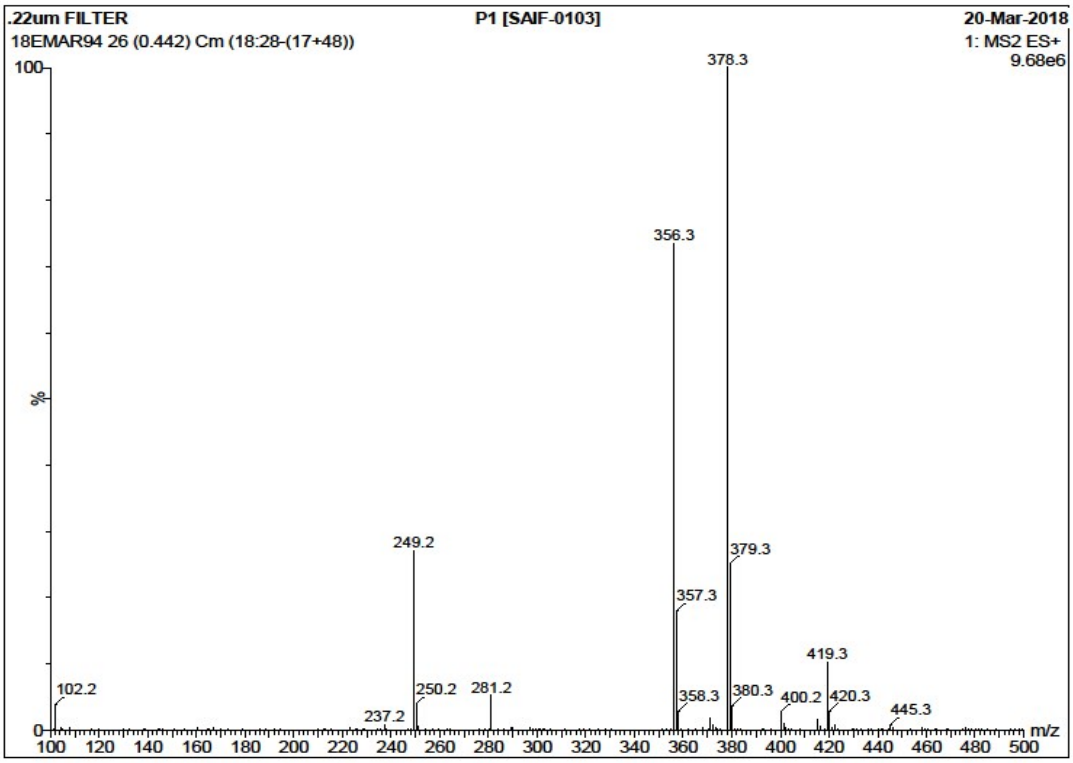

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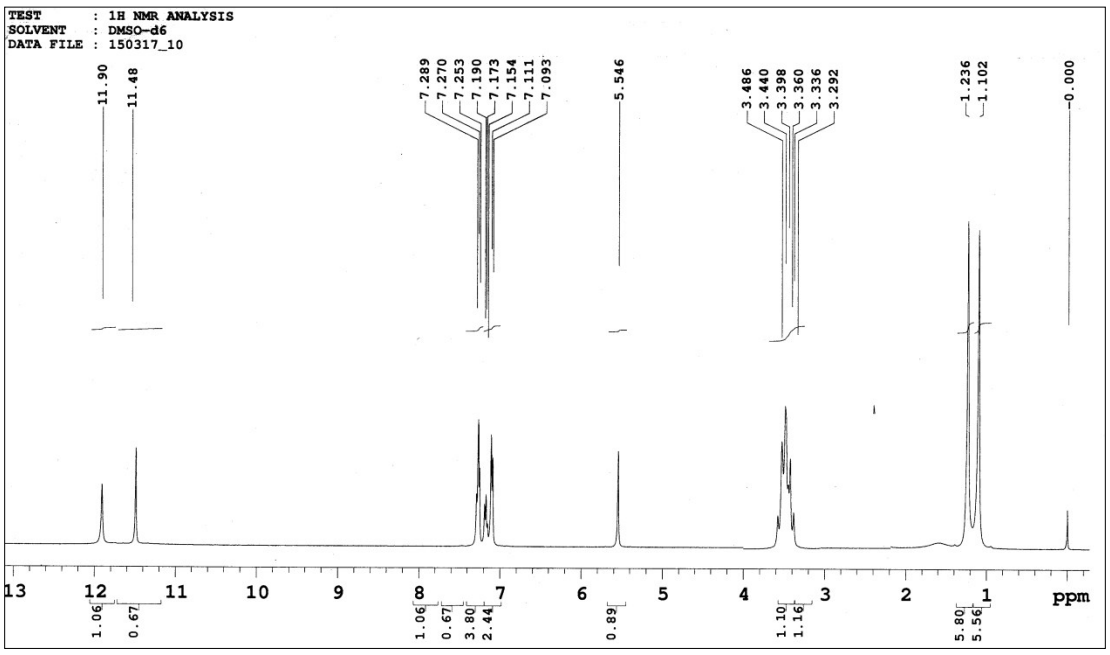

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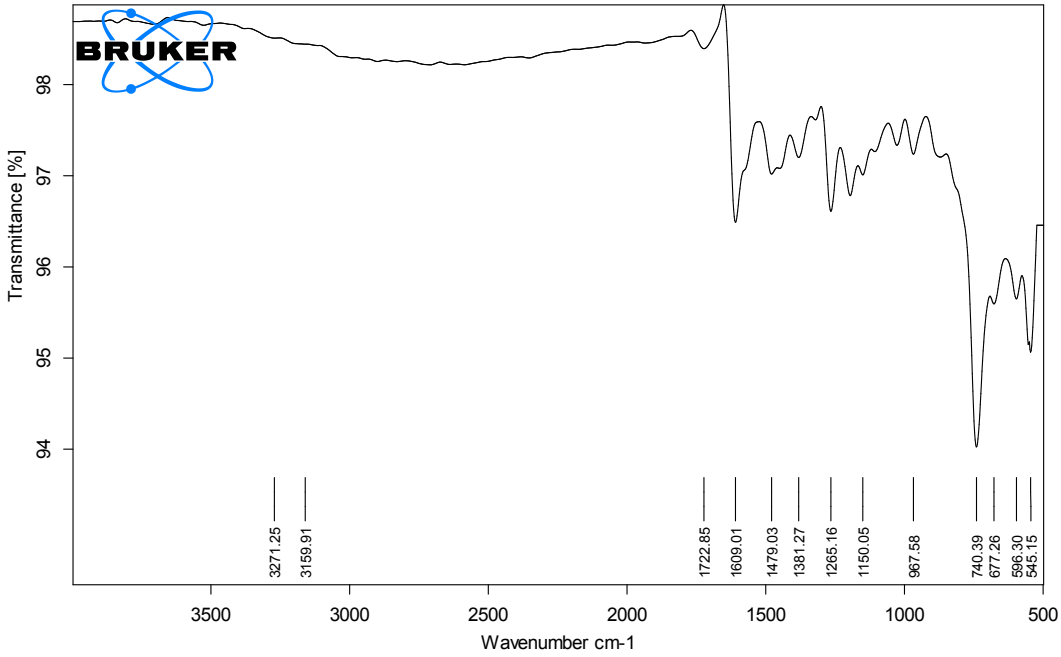

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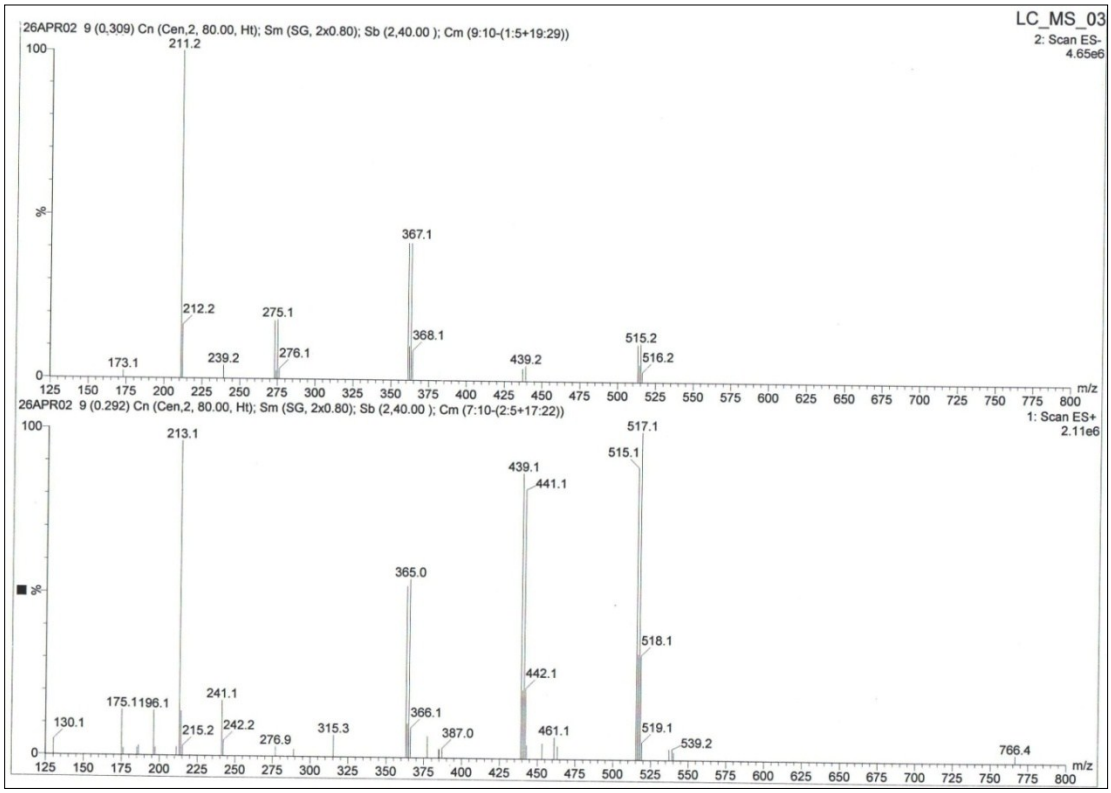

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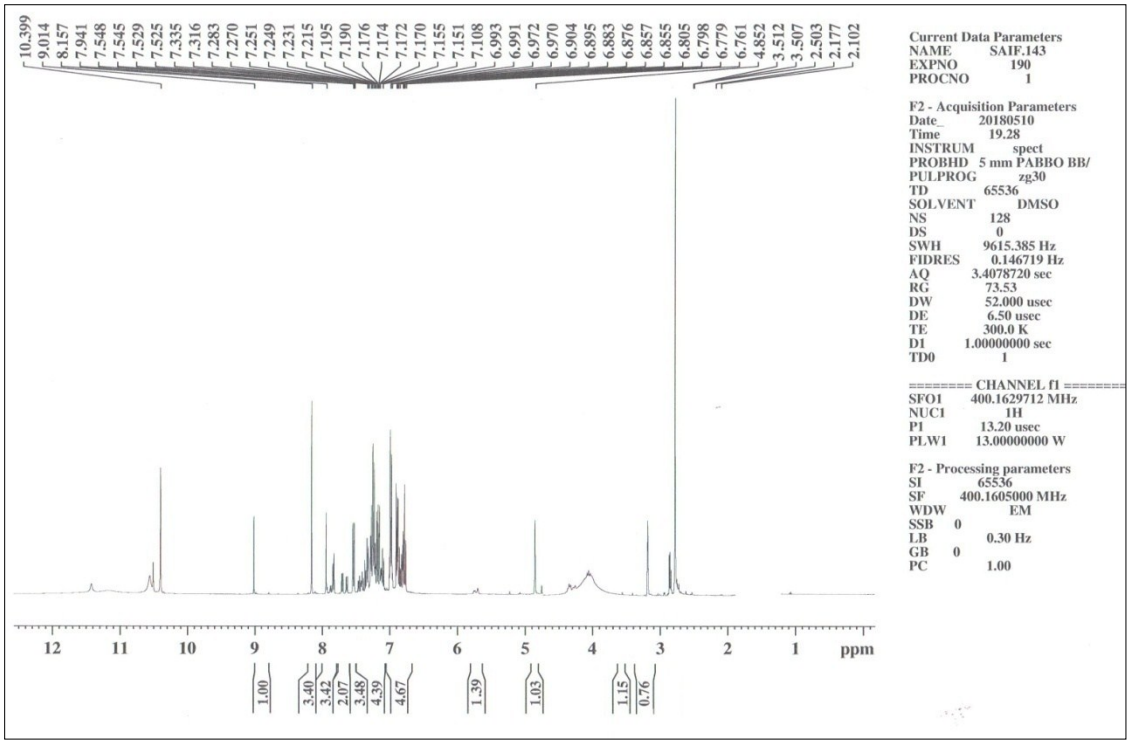

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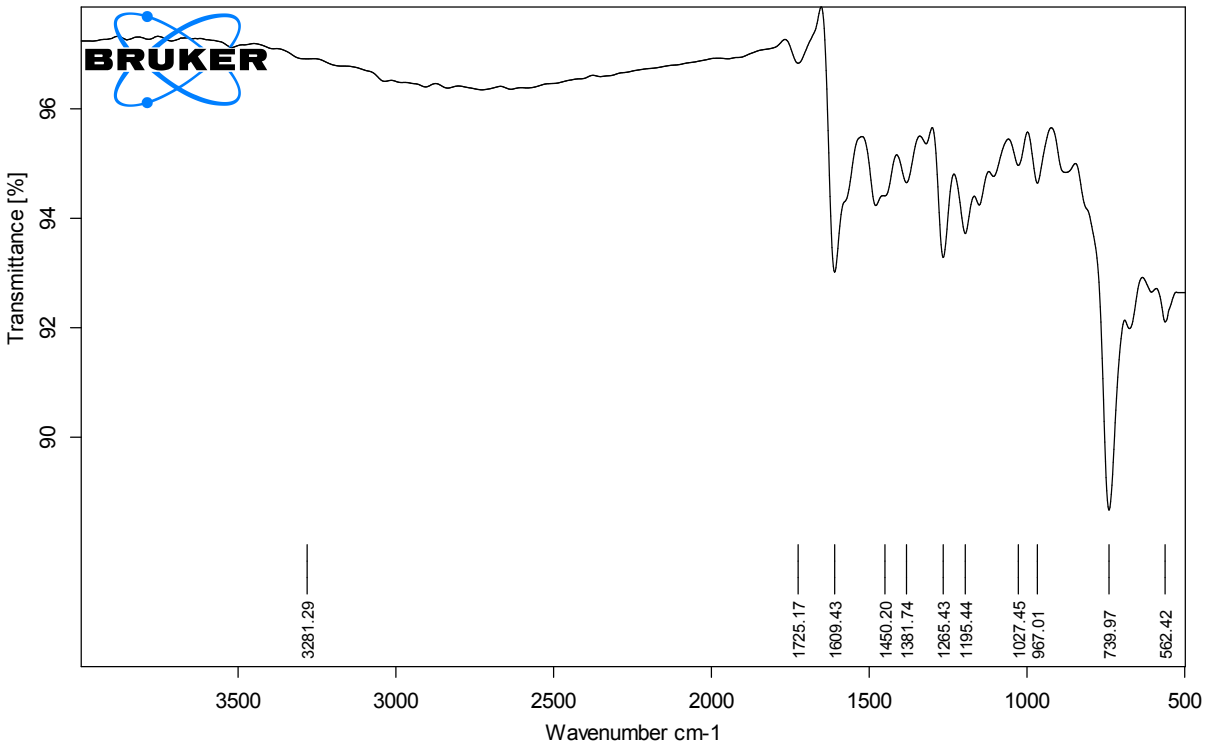

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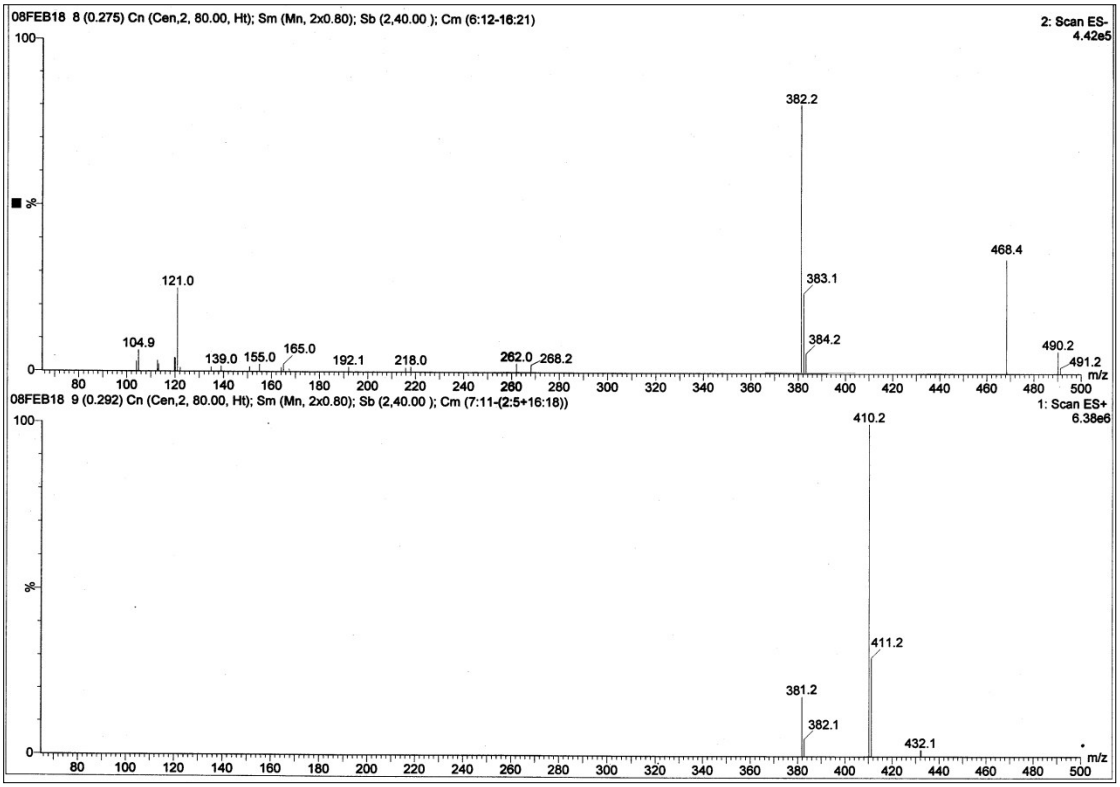

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