

## Supporting Information

### New Roxadustat Amino Acid Drug Conjugation Derivatives: Molecular Docking, Molecular Dynamics Simulation and in vitro assay

#### Authors

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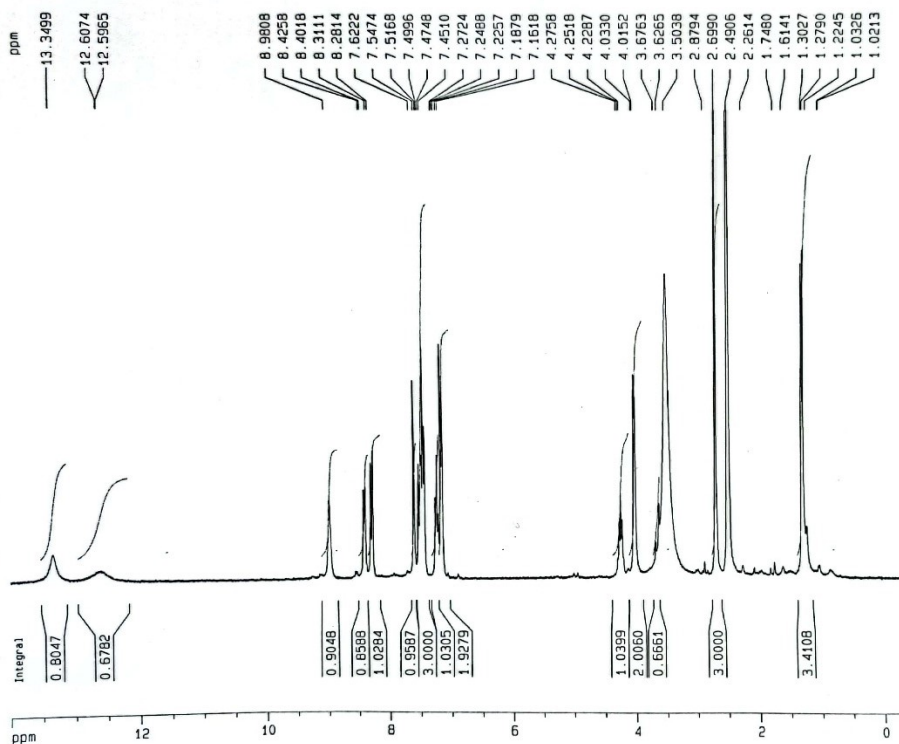
## Synthesis procedure

### Representative Procedure for the synthesis of (Roxadusta+AA):

1 gram of 2-CTC resin was poured into an appropriate glass vessel. 10 mL of DCM was added, and the mixture was shaken for 10 minutes, then the solution was filtered and washed with DCM. Next, 1 equivalent of Fmoc-Ala-OH, 1 equivalent of DIEA, and 10 mL of DMF were added. The mixture was shaken for 2 hours, then filtered and washed. To remove the Fmoc group, 16 mL of 25% piperidine in DMF was added, shaken for 20 minutes, and then the resin was washed with DMF and DCM. A Kaiser test was performed to ensure complete removal of the Fmoc group. Roxadustat was then loaded with the activation reagent HATU, and the mixture was shaken for 2 hours, then filtered. Finally, the product was cleaved from the resin using TFA, the filtrate was evaporated to concentrate it, and DEE was added to precipitate the obtained product.

**<sup>1</sup>H NMR spectra for compounds in manuscript:**

Rox-Ala



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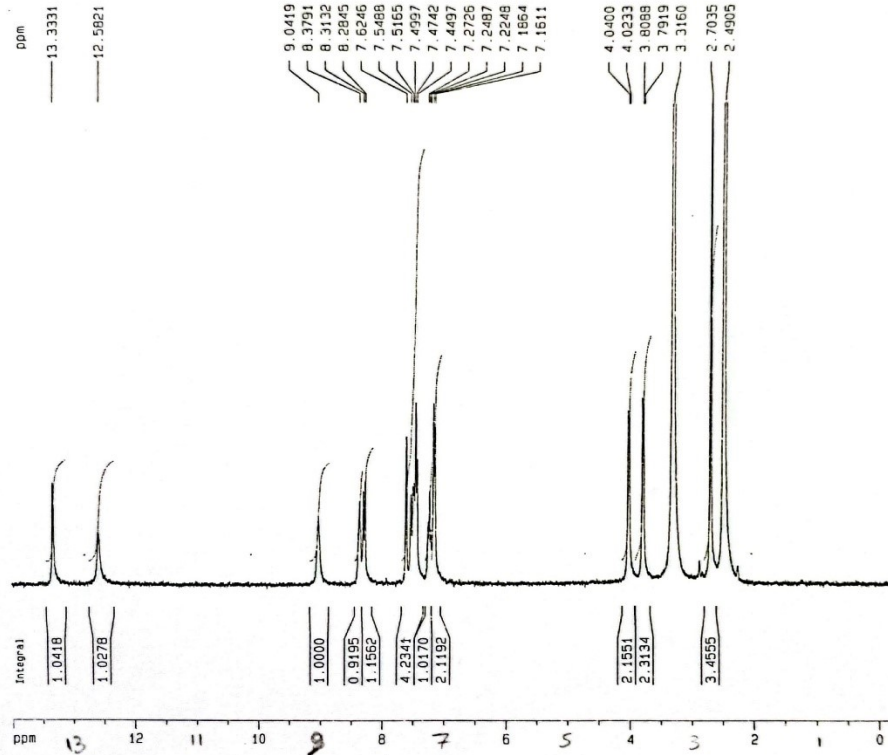
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 F1 4201.82 Hz  
 F2P -90.300 ppm  
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FOX-GLY



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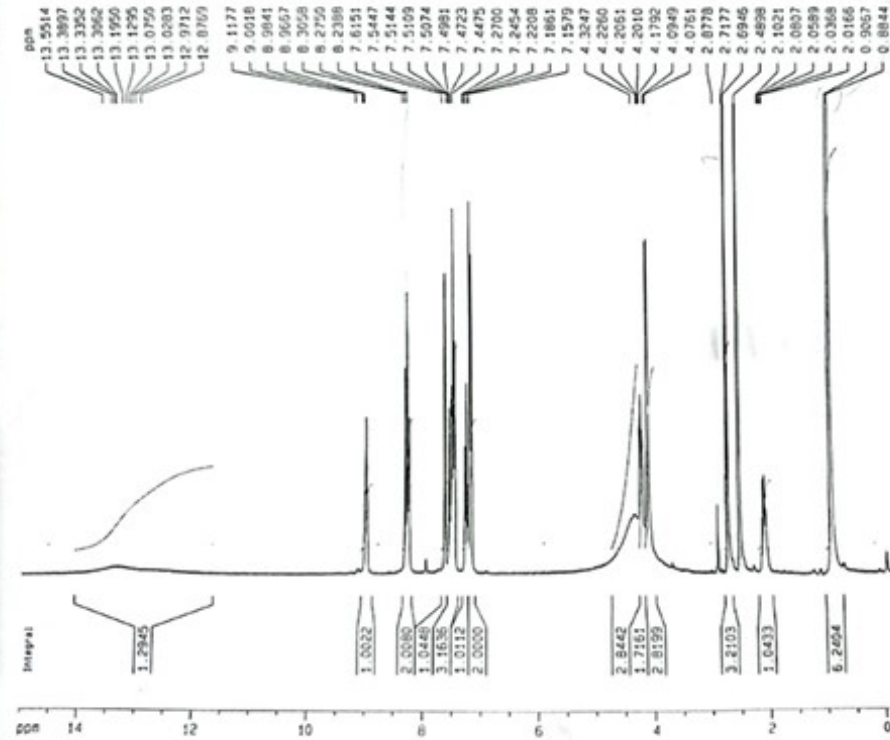
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Rox-Va1



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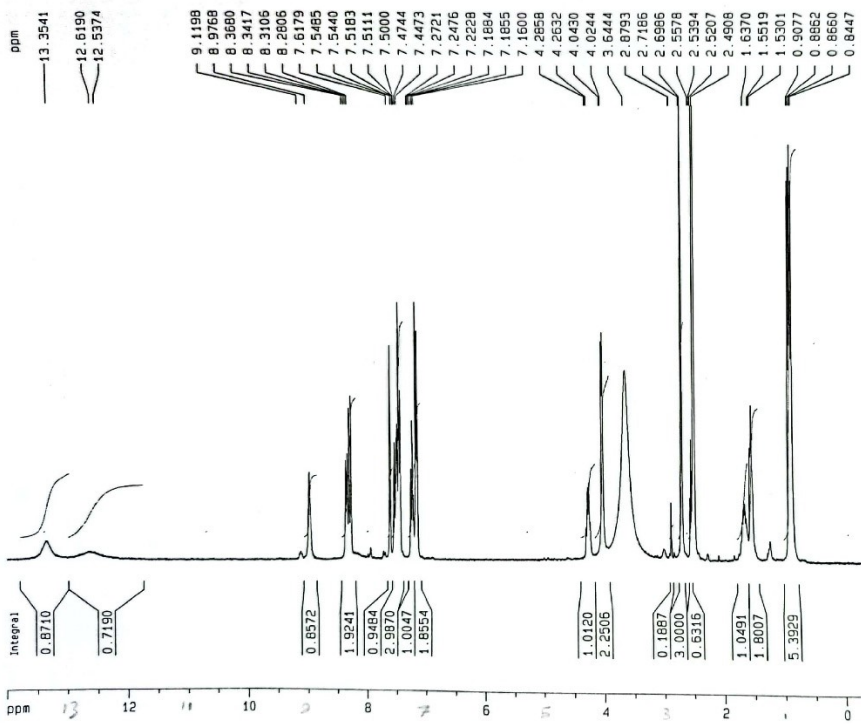
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 CY: 25.00 cm  
 FXP: 15.000 ppm  
 FI: 4581.95 Hz  
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 NZCM: 229.59944 Hz/cm

Rox-1eu



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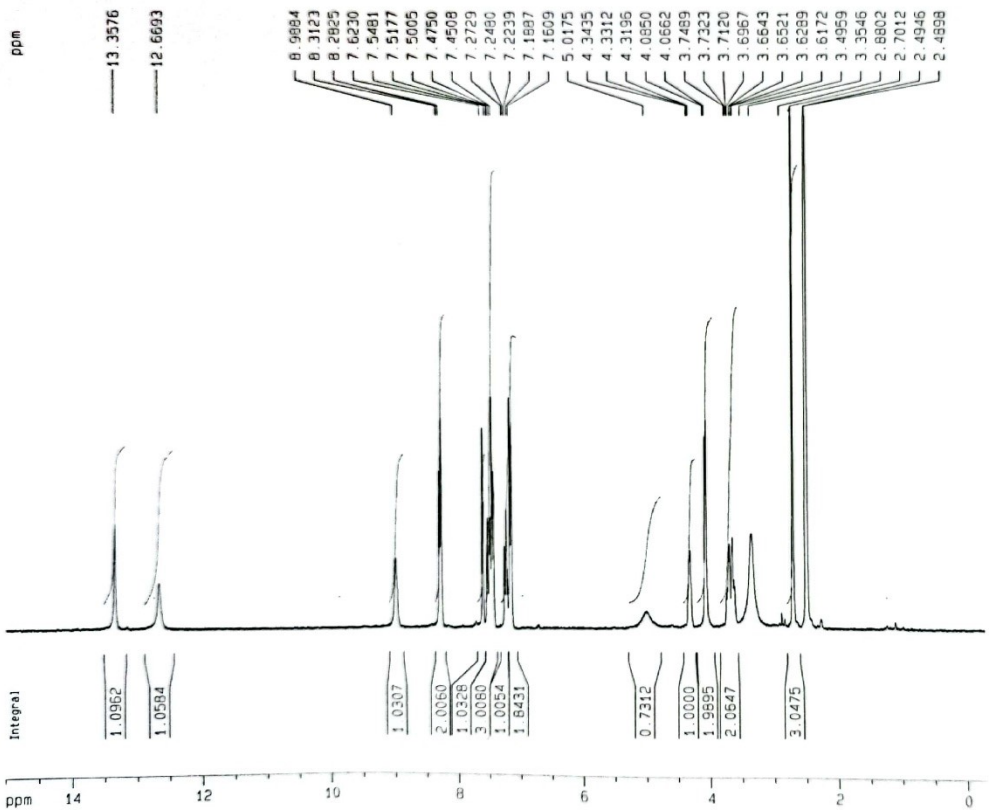
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ID NMR plot parameters  
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 CY 25.00 cm  
 F1P 14.000 ppm  
 F1 4201.82 Hz  
 F2P -0.300 ppm  
 F2 -90.04 Hz  
 PPRCM 0.71500 ppm/cm  
 HZCM 214.59296 Hz/cm

Rox-Ser



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EXPNO 9  
PROCNO 1

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AQ 1.3271540 sec  
RG 912.3  
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DE 6.00 usec  
TE 300.0 K  
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\*\*\*\*\* CHANNEL f1 \*\*\*\*\*

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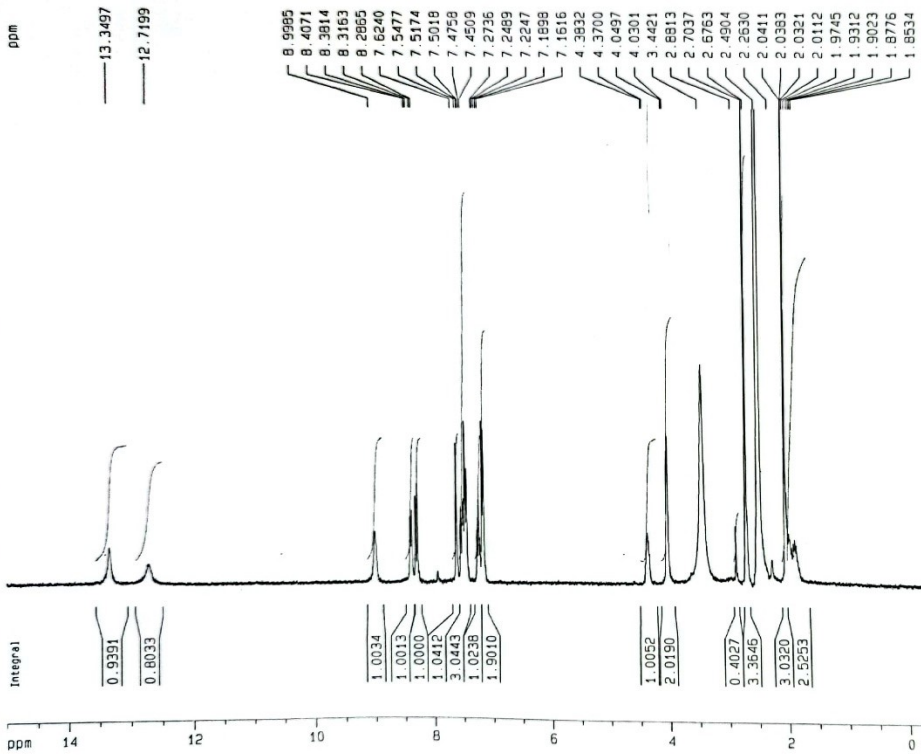
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CY 25.00 cm  
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F1 4501.95 Hz  
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HZCM 229.59944 Hz/cm

Rox-Met



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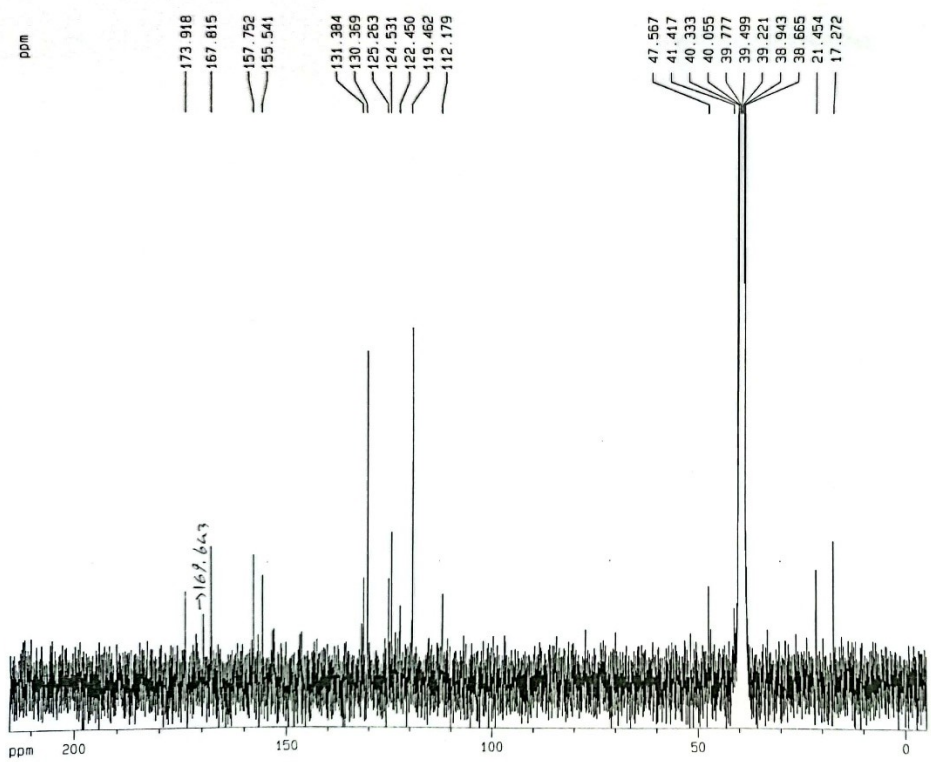
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1D NMR plot parameters  
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 F1 4501.95 Hz  
 F2P -0.300 ppm  
 F2 -90.04 Hz  
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 HZCM 229.59944 Hz/cm

<sup>13</sup>C NMR spectra for compounds in manuscript:

Rox-Ala



```

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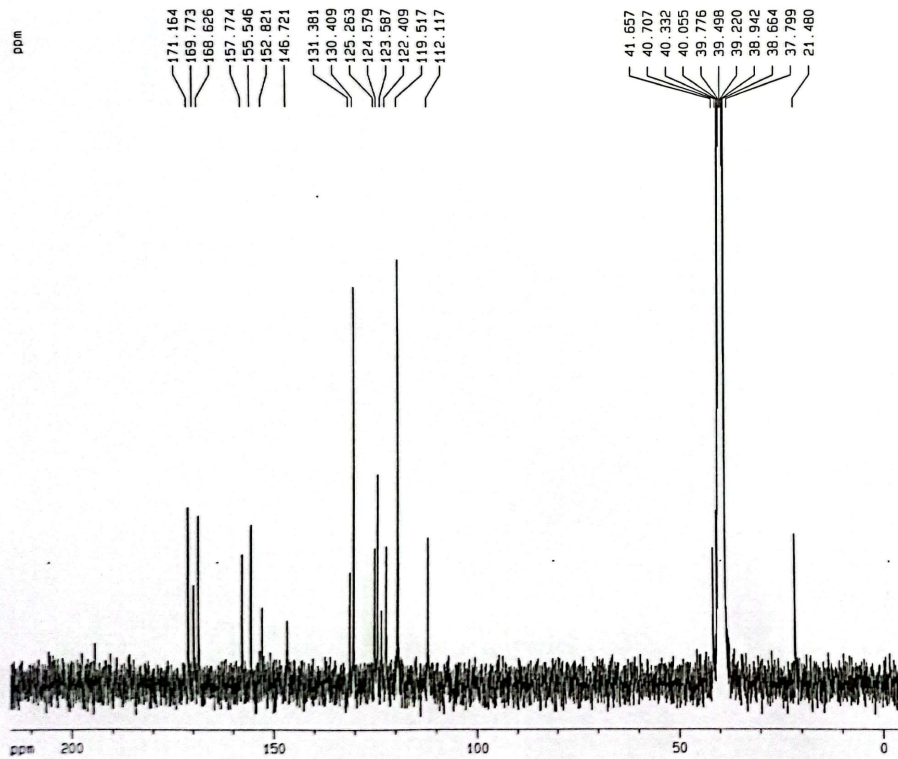
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ID NMR plot parameters
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F2P           -5.000 ppm
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ROX-GLY repeat



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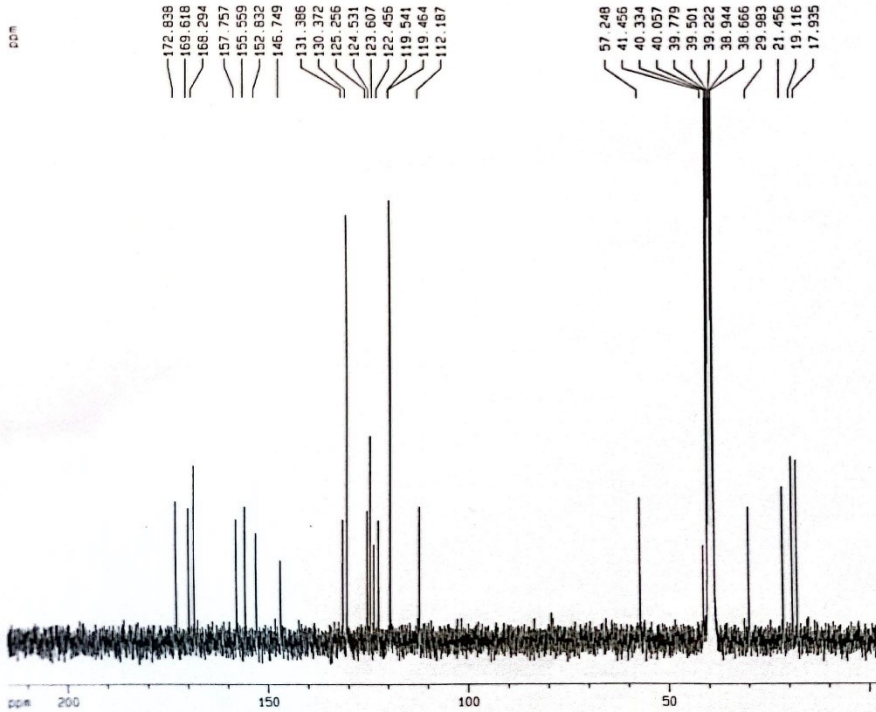
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1D NMR plot parameters
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Rox-Va1



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FIDRES 0.548877 Hz  
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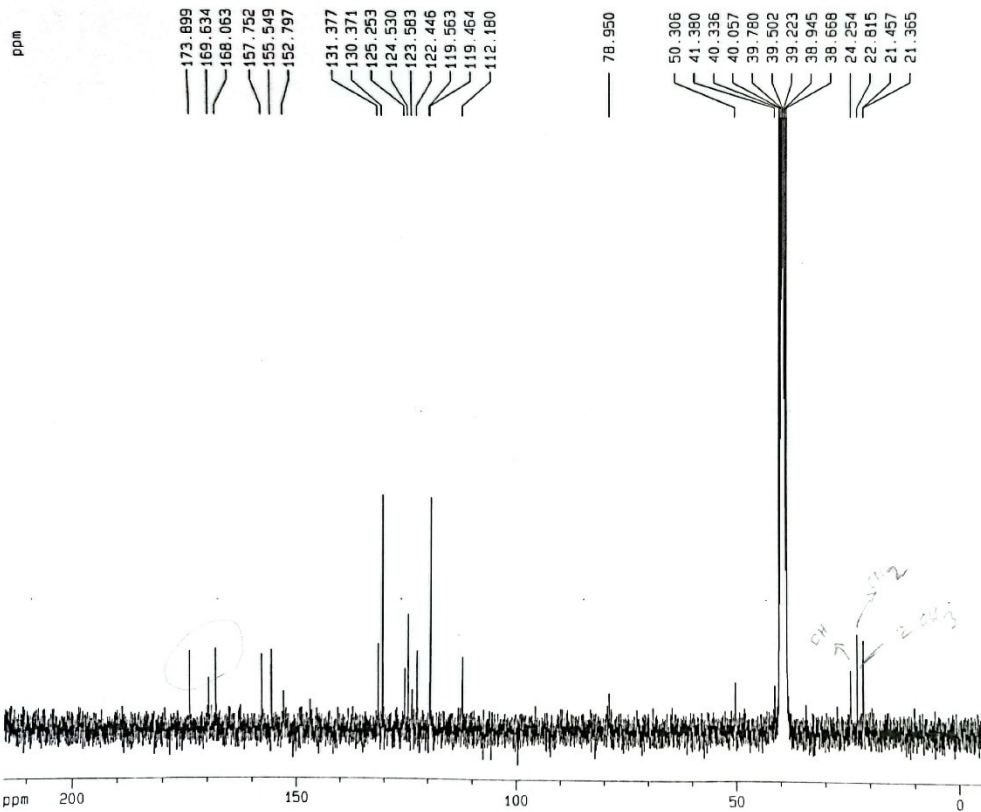
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Rox-Leu



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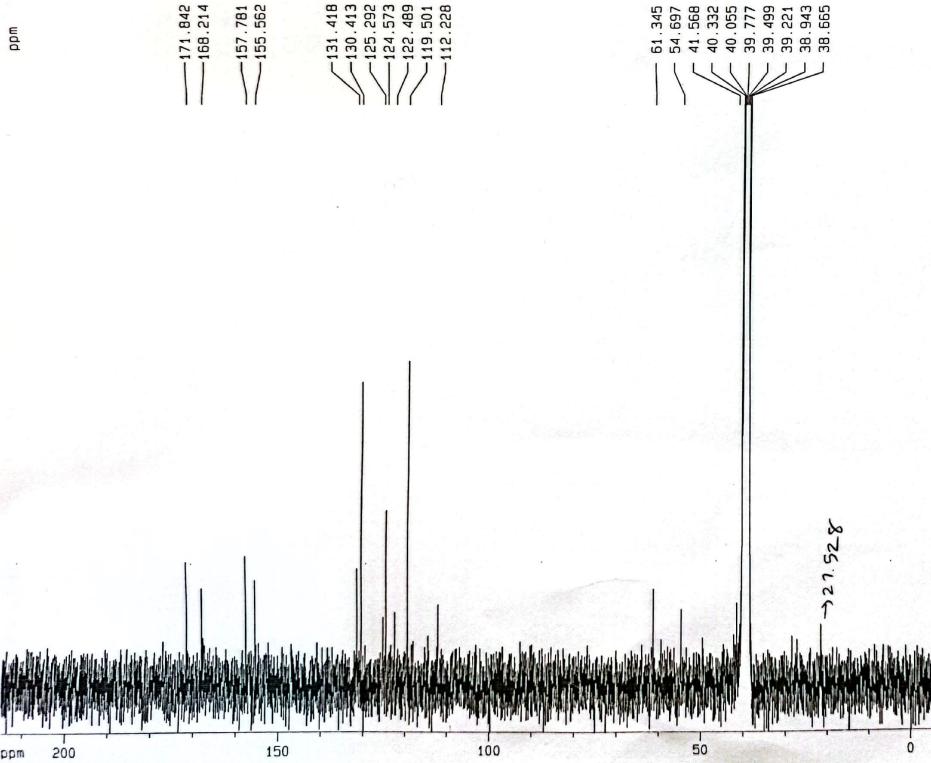
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1D NMR plot parameters  
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F2P -5.000 ppm  
F2 -377.34 Hz  
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Rox-ser



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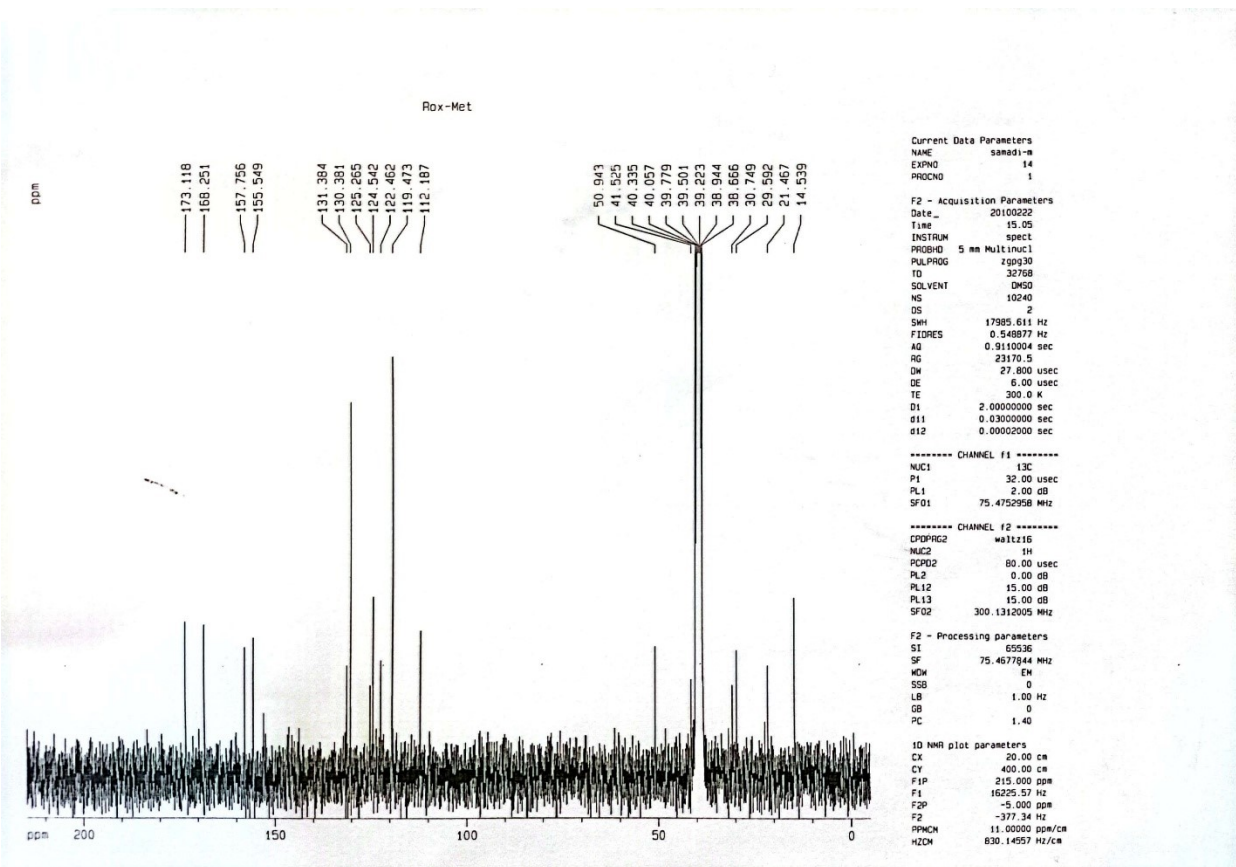
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1D NMR plot parameters  
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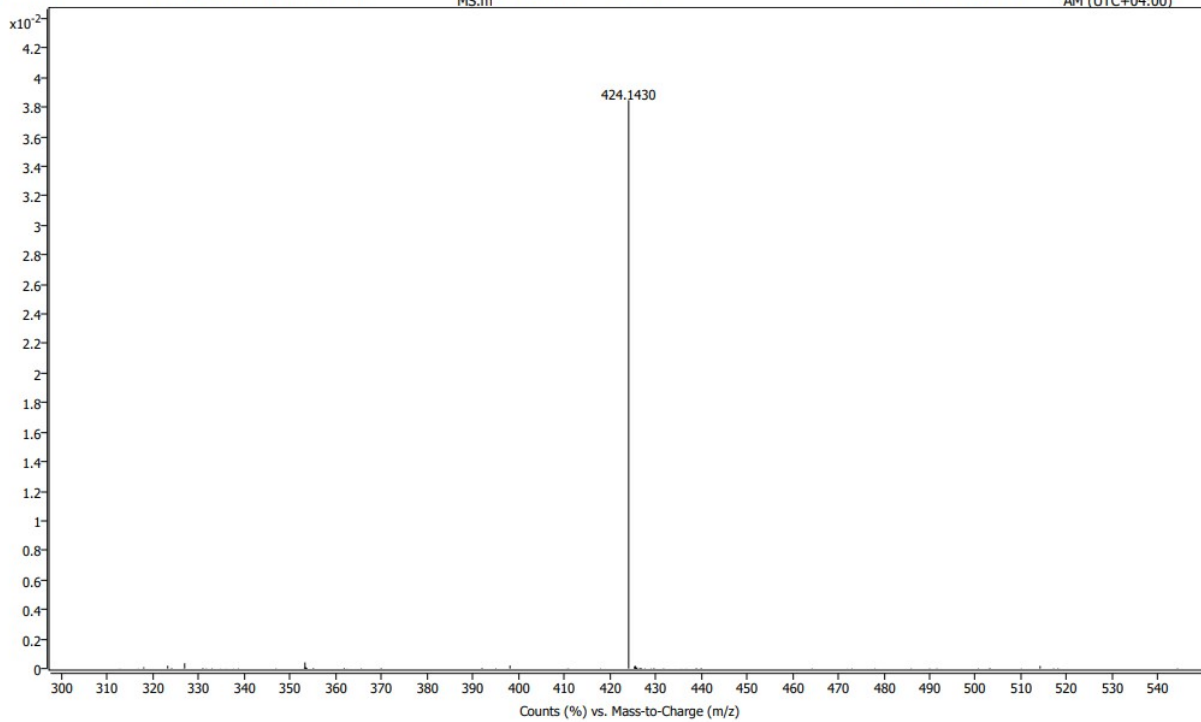


# HRMS spectra for compounds in manuscript:

## Spectrum Plot Report



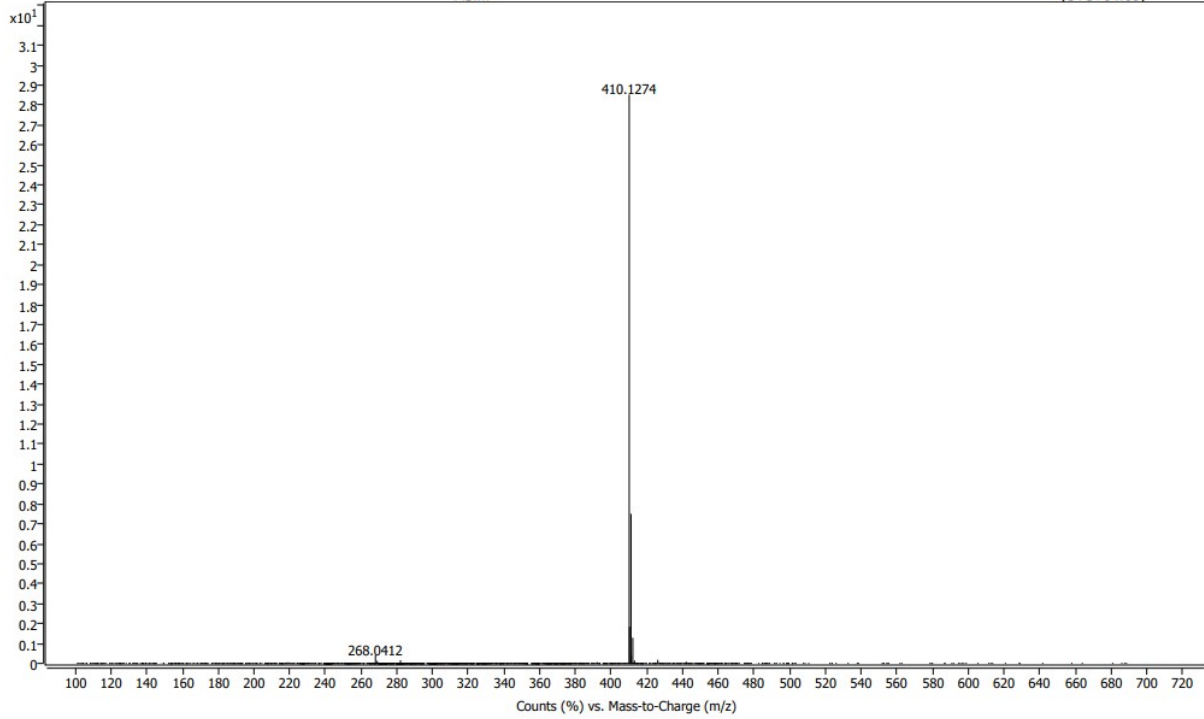
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# Spectrum Plot Report



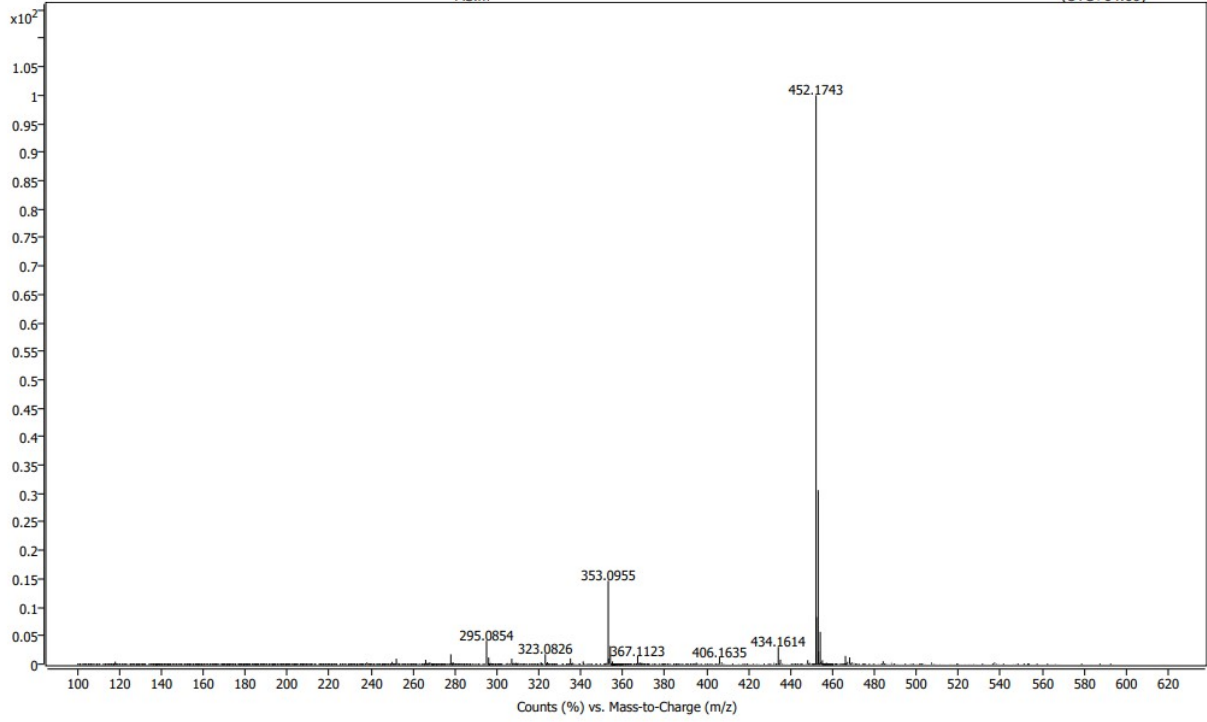
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# Spectrum Plot Report



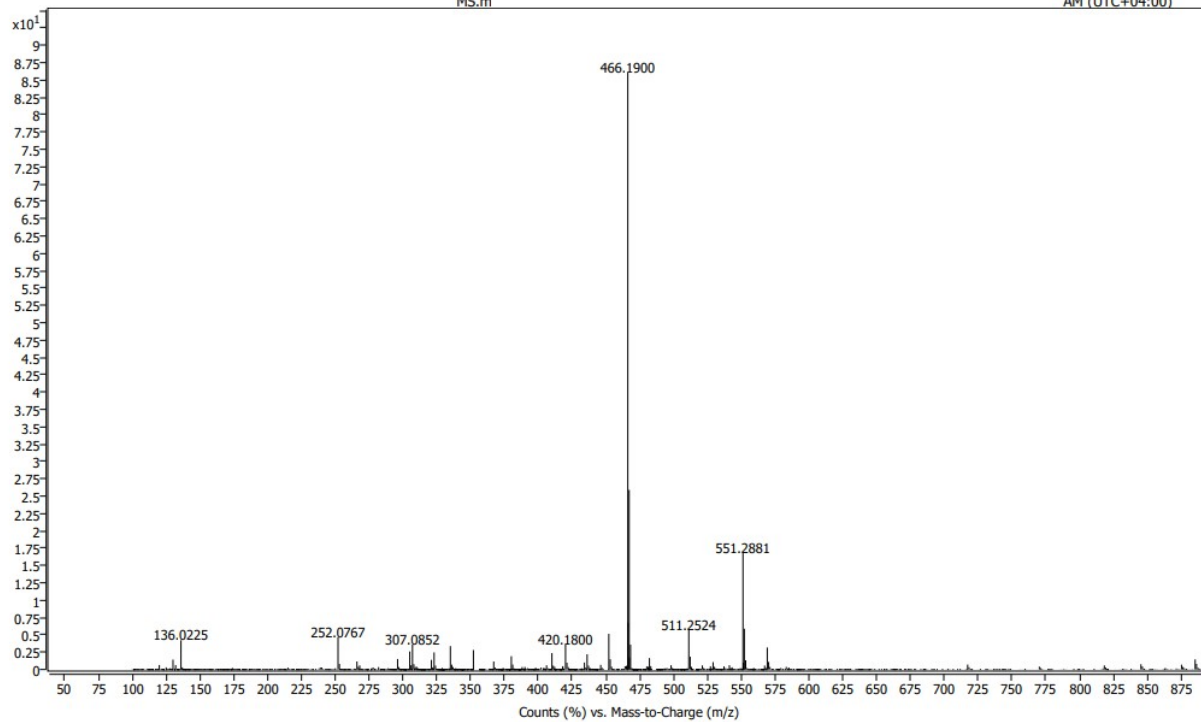
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# Spectrum Plot Report



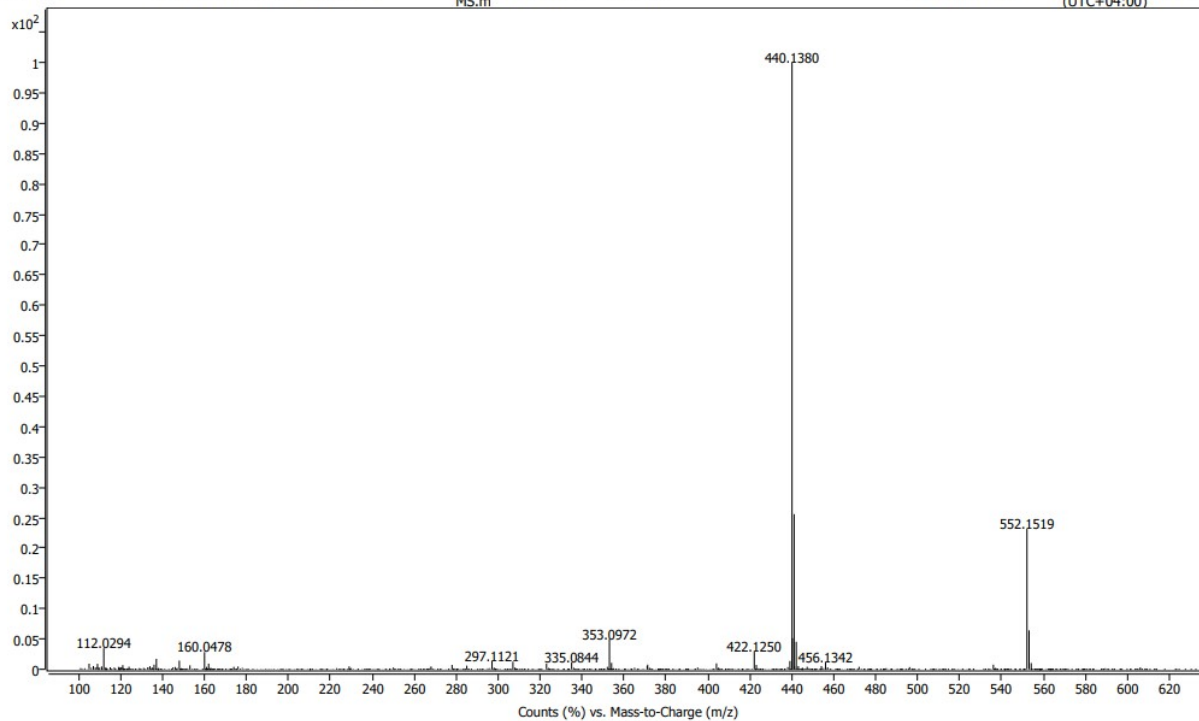
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# Spectrum Plot Report



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# Spectrum Plot Report



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