

# Creating Diverse Target-Binding Surfaces on FKBP12: Synthesis and Evaluation of a Rapamycin Analogue Library

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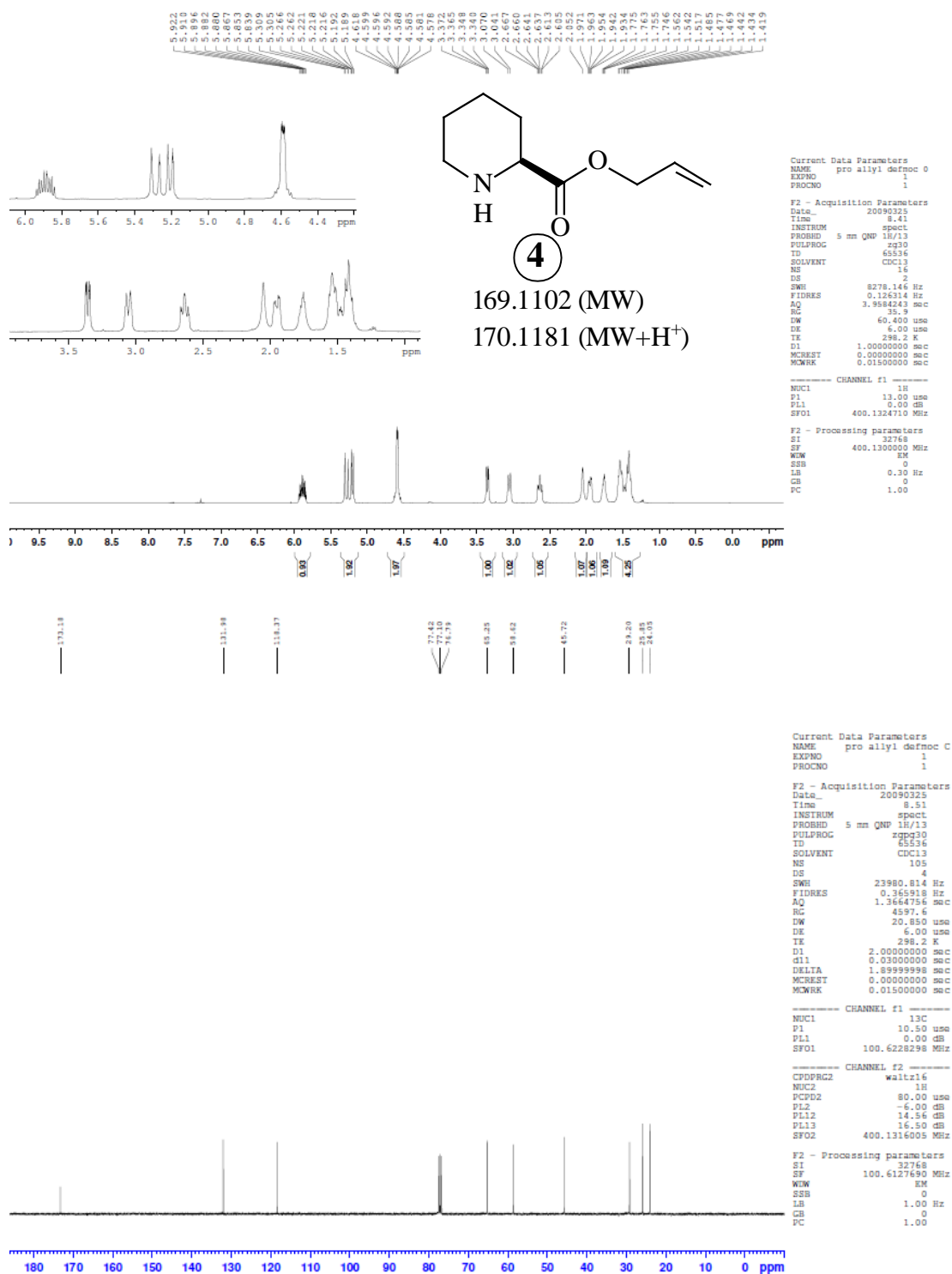
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**Figure S1.**  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, and High-Resolution MS of Compounds **4**, **5**, and **3a-c**

**Compound 4**



# Display Report

## Analysis Info

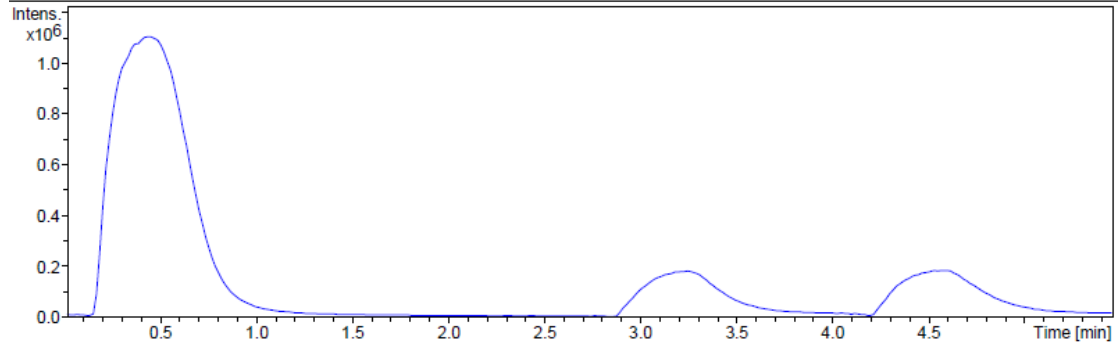
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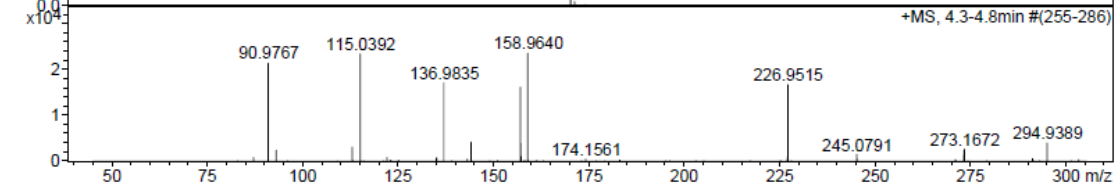
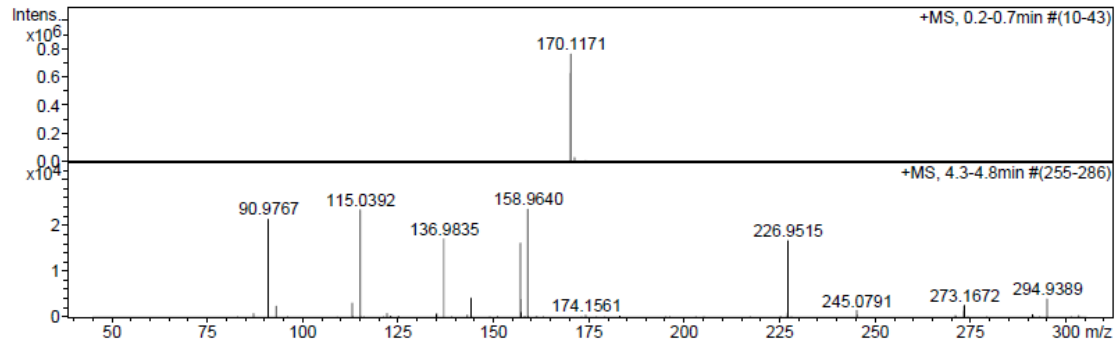
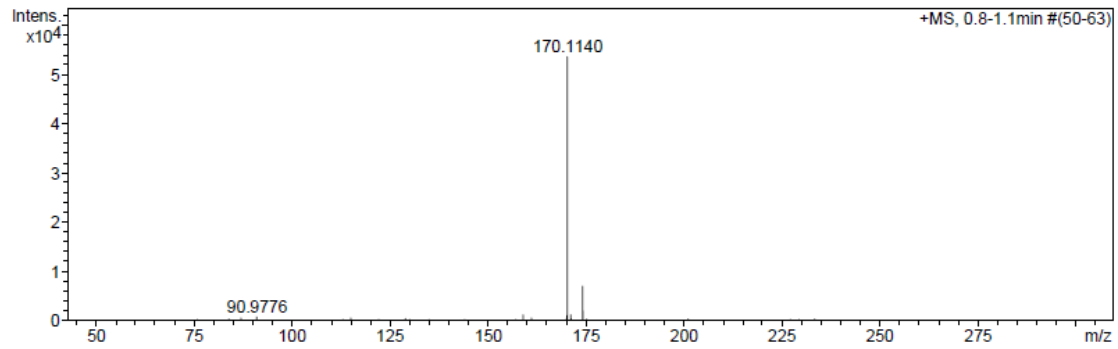
Operator xwu  
Instrument / Ser# micrOTOF 194

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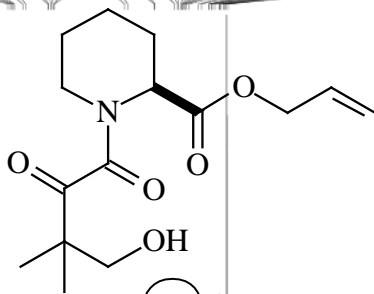
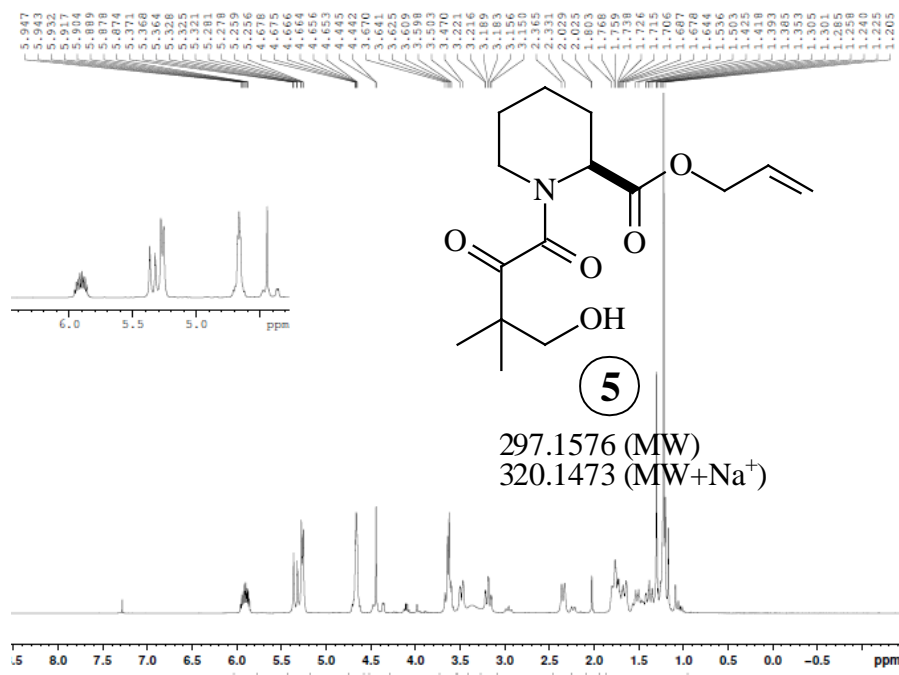
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Scan End	300 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



TIC +All MS



# Compound 5



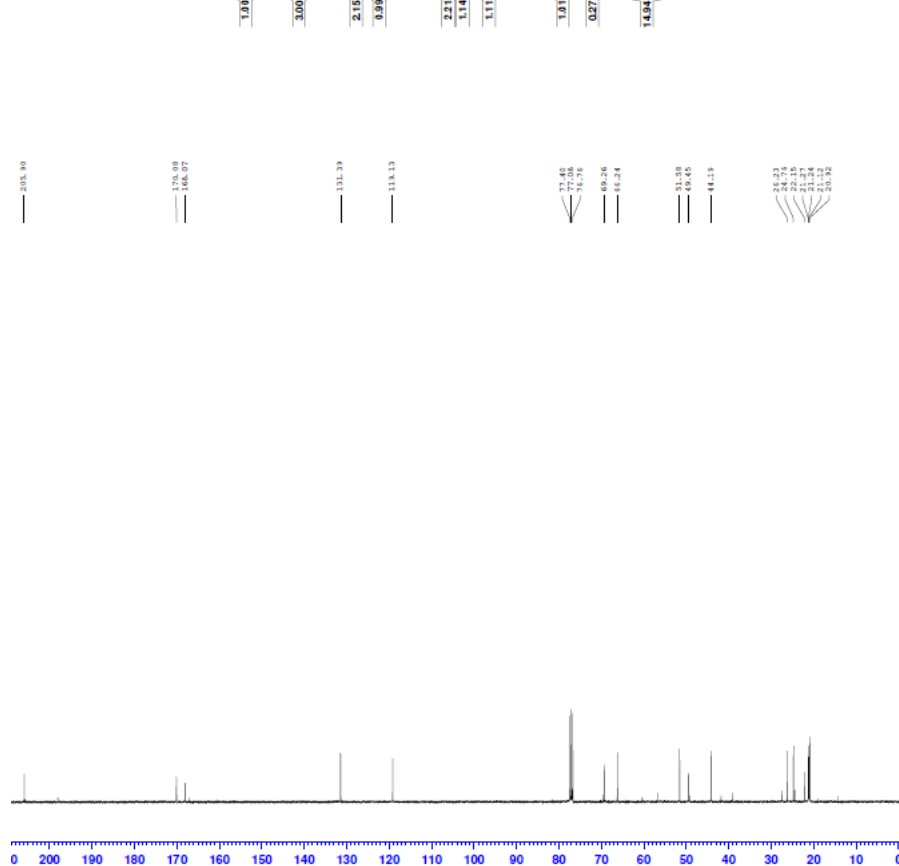
**5**  
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PROCNO 1

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FIDRES 0.126314 Hz
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DW 60.400 usec
DE 6.00 usec
TE 298.2 K
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MCWRR 0.01500000 sec

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# Display Report

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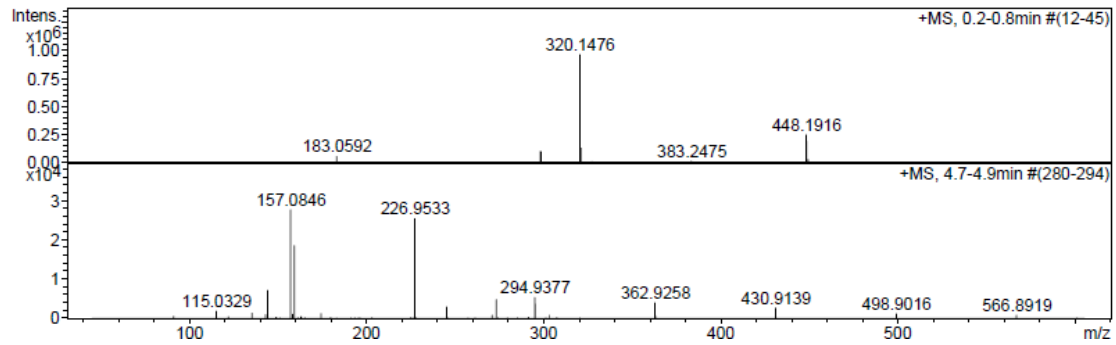
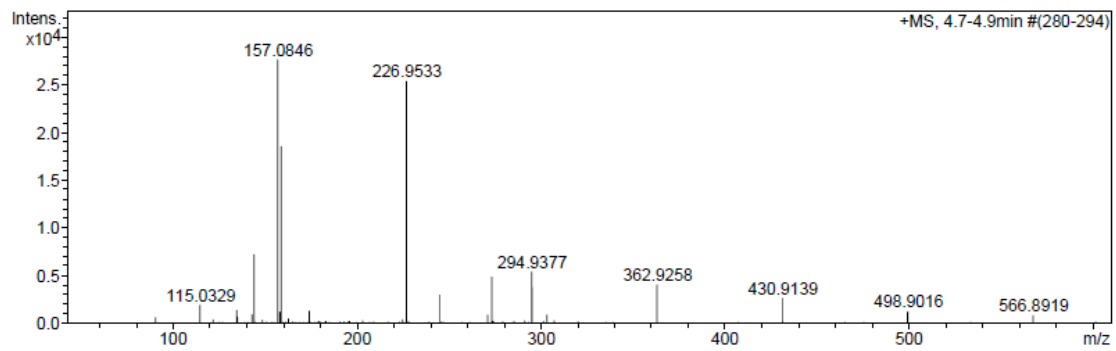
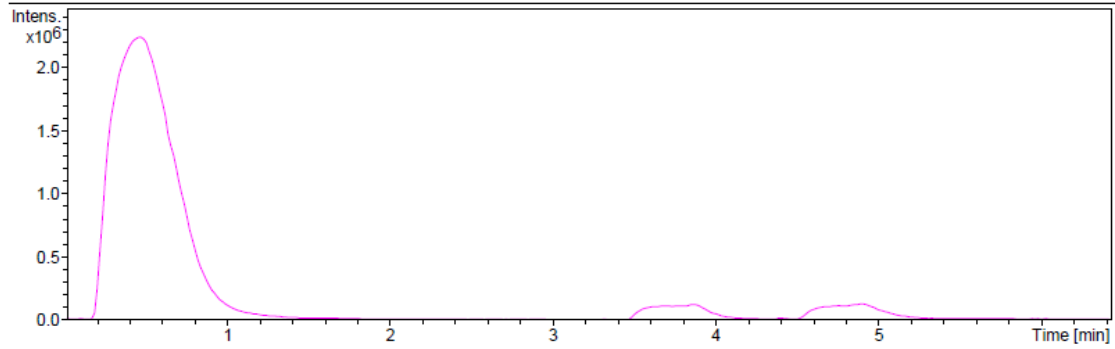
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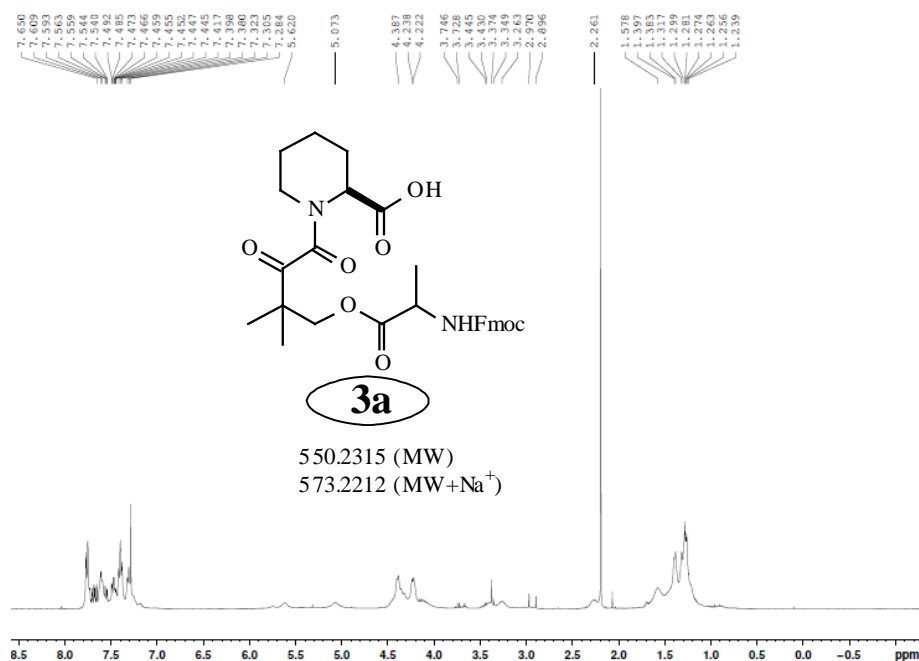
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Instrument / Ser# micrOTOF 194

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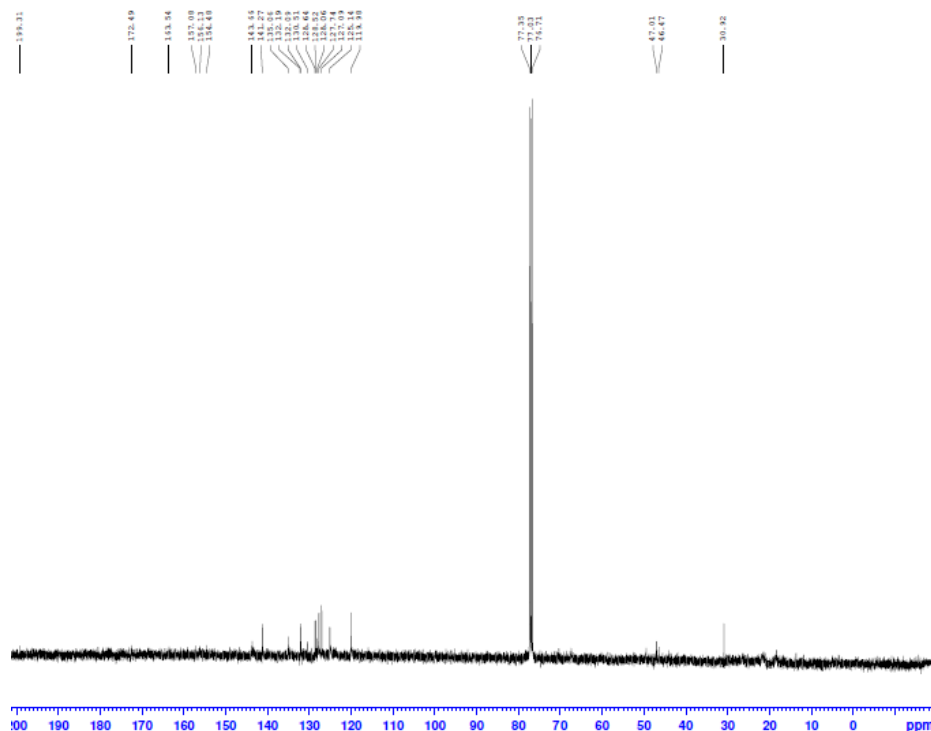
The Ohio State University  
Department of Chemistry  
NMR Facility  
400MHz - 0083

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DE 6.00 usec  
TE 300.2 K  
D1 1.00000000 sec  
TDO 1

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PL1 0.00 dB  
SFO1 400.1324710 MHz

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LB 0.30 Hz  
GB 0  
PC 1.00



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PROCNO 1

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Time 15:10  
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SOLVENT CDCl3  
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FIDRES 0.365918 Hz  
AQ 1.3664756 sec  
RG 5160.6  
SW 20.850 usec  
DE 6.00 usec  
TE 300.2 K  
D1 2.00000000 sec  
d11 0.03000000 sec  
DELTA 1.89999998 sec  
TDO 1

CHANNEL f1  
NUC1 13C  
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PL1 0.00 dB  
SFO1 100.6228298 MHz

CHANNEL f2  
CPDPRG2 waltz16  
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PL12 14.56 dB  
PL13 16.50 dB  
SFO2 400.1316005 MHz

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PC 1.00

# Display Report

## Analysis Info

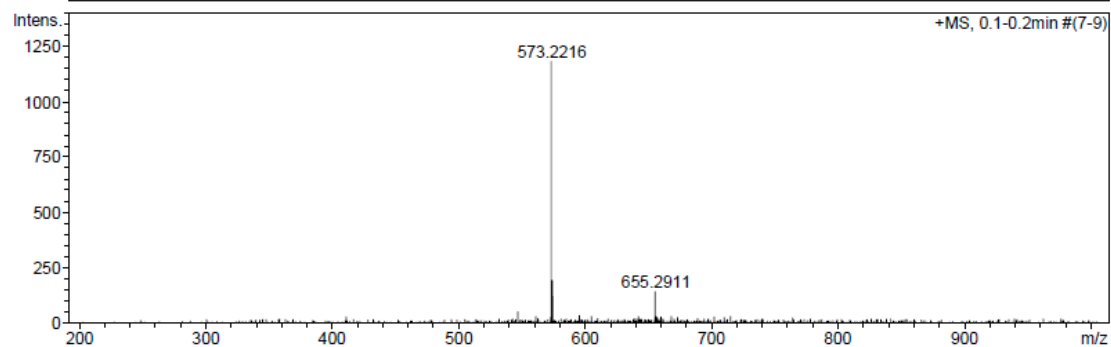
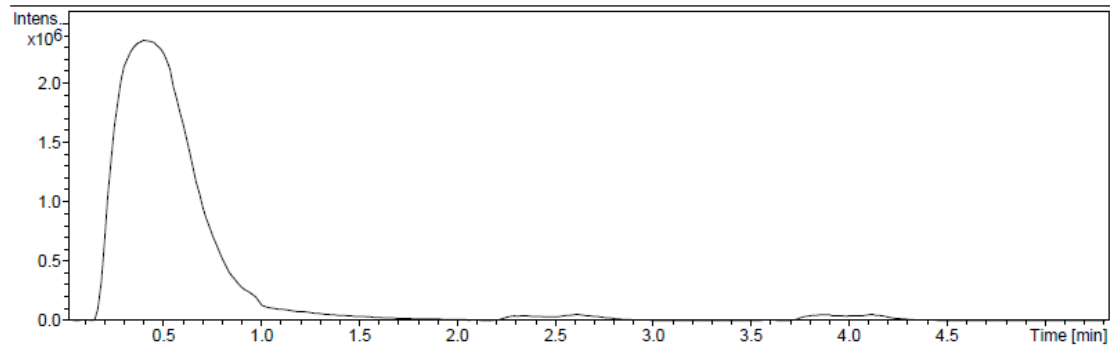
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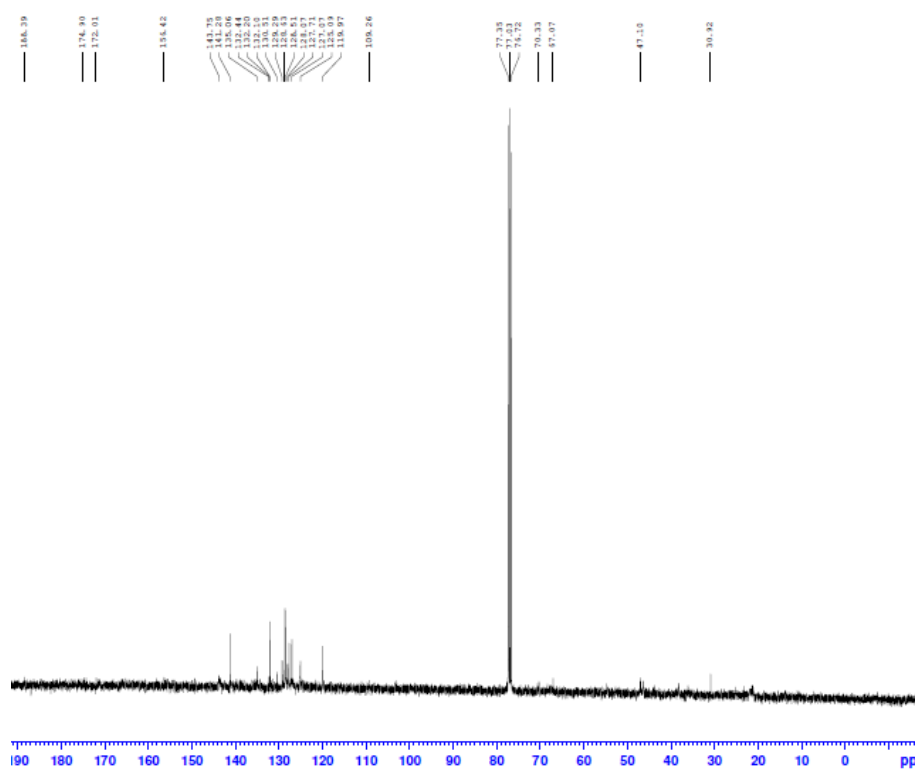
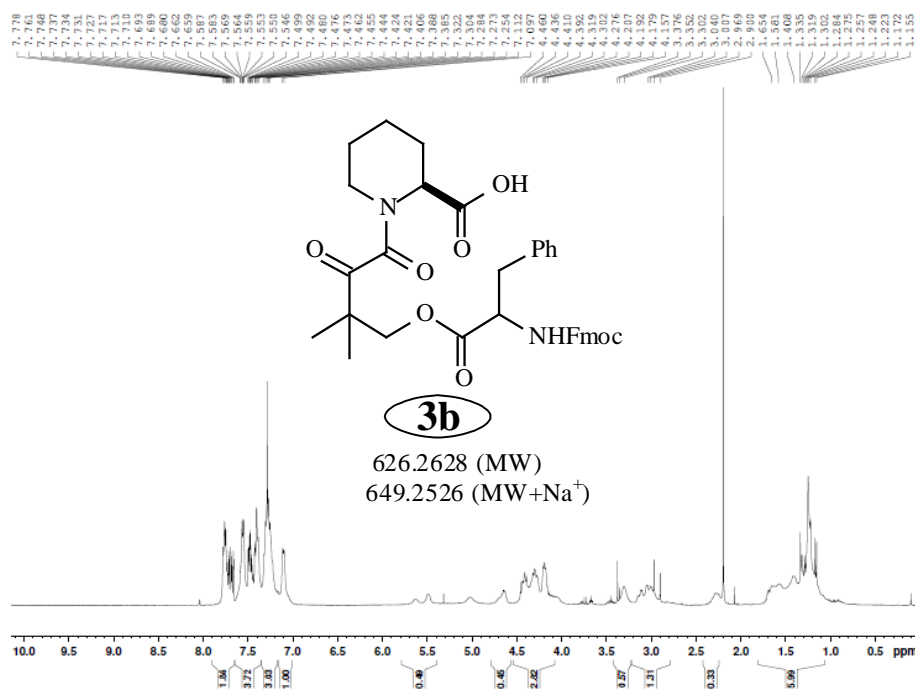
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## Acquisition Parameter

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# Compound 3b





# Display Report

## Analysis Info

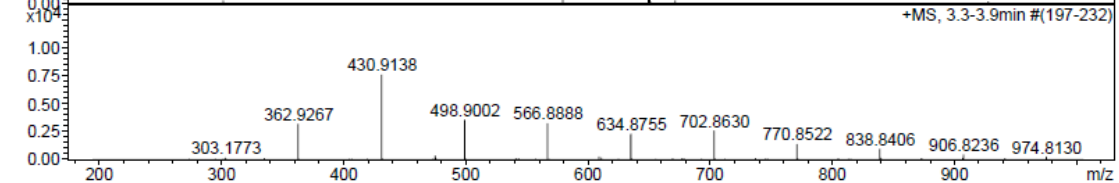
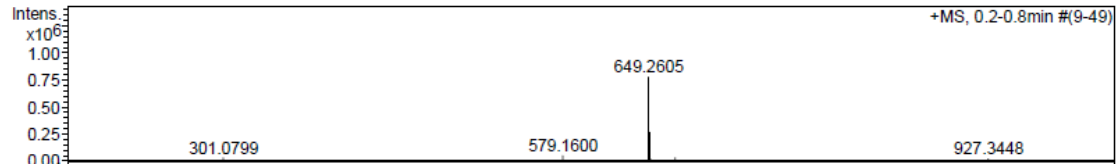
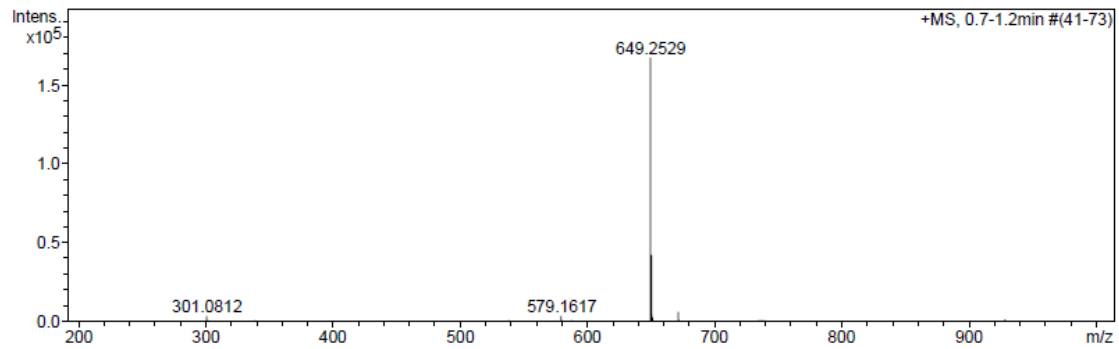
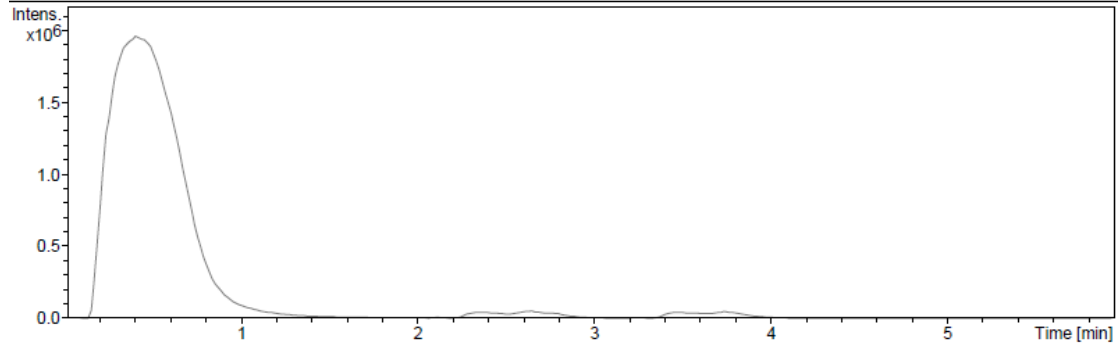
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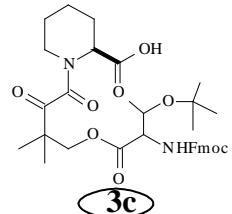
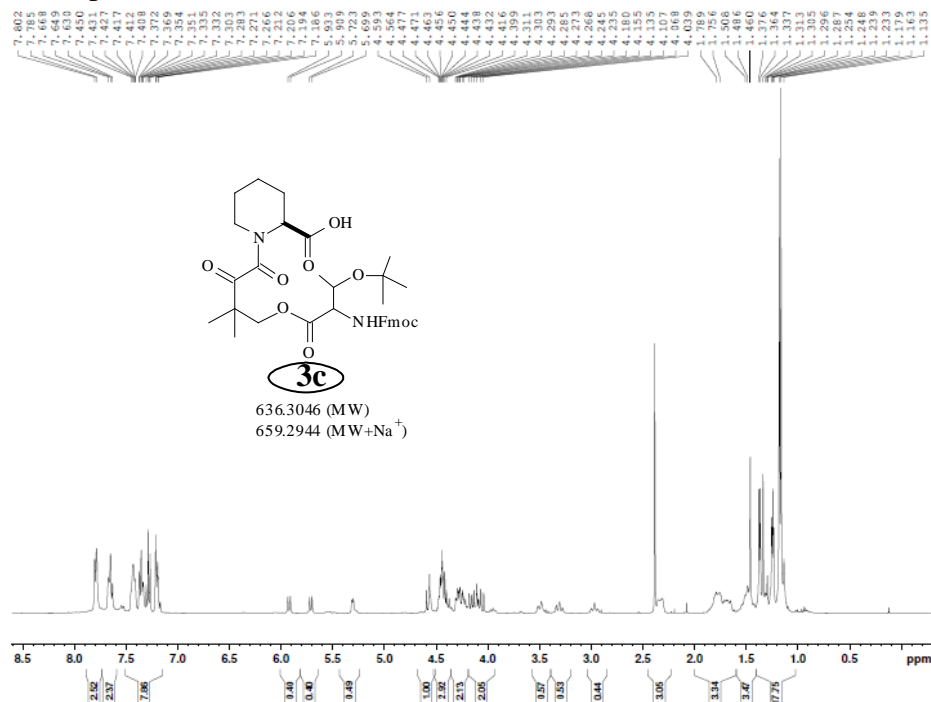
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Instrument / Ser# micrOTOF 194

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Scan End	1000 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



# Compound 3c



636.3046 (MW)  
659.2944 (MW+Na<sup>+</sup>)

The Ohio State University  
Department of Chemistry  
NMR Facility  
400MHz - 0953

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RG 35.9  
DW 60.400 usec  
DE 6.00 usec  
TE 300.2 K  
D1 1.00000000 sec  
TD 1

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PL1 0.00 dB  
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# Display Report

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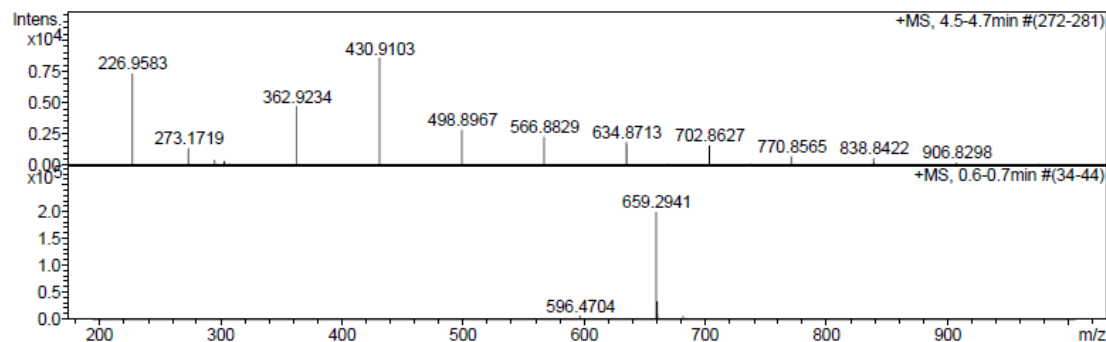
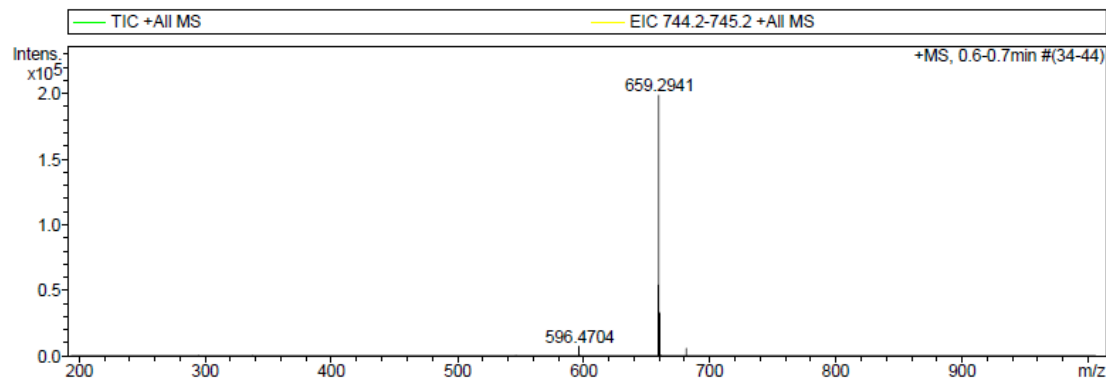
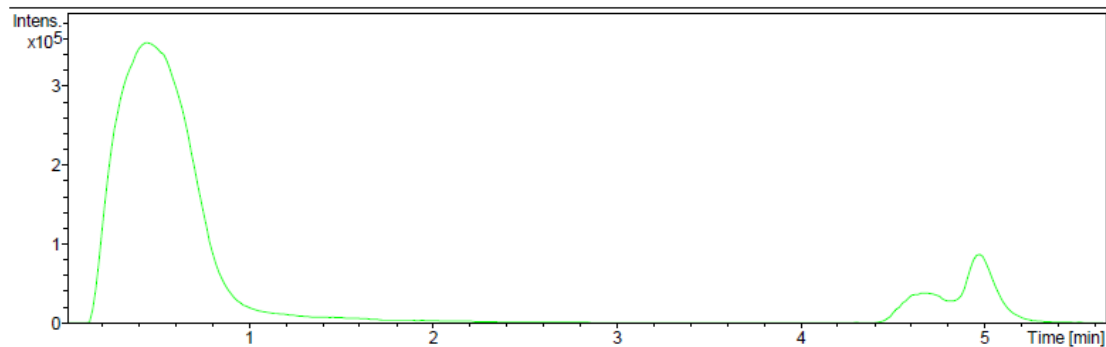
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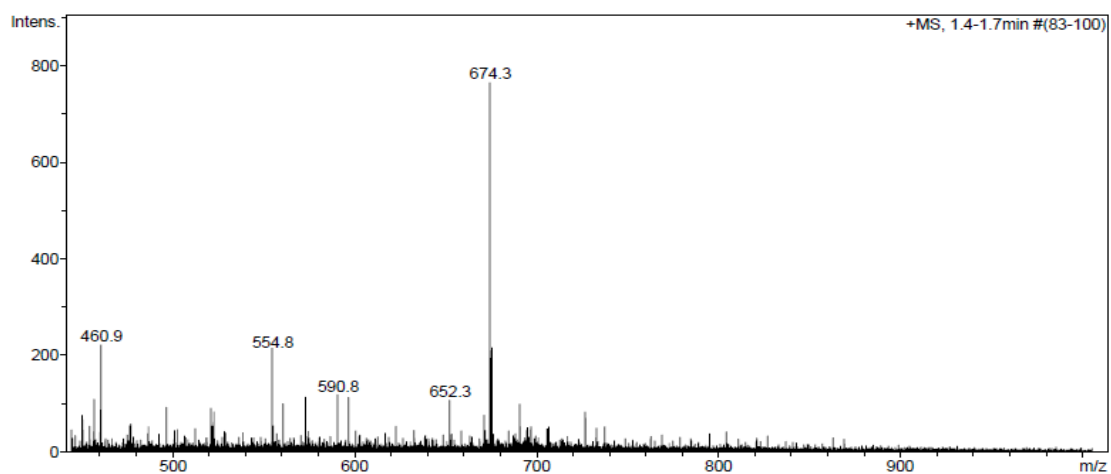
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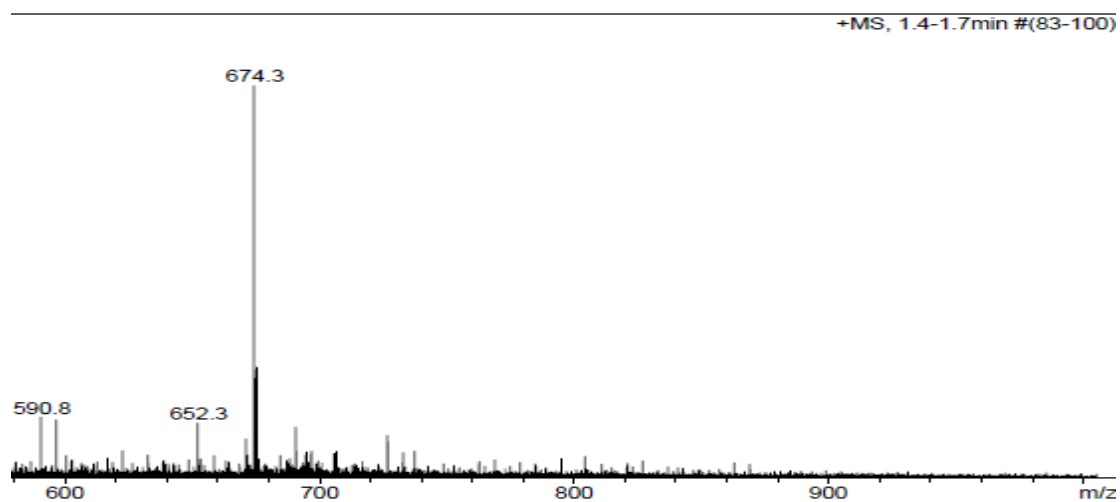


**Figure S2.** ESI MS of Rapalogs **2a-y** in Table 1

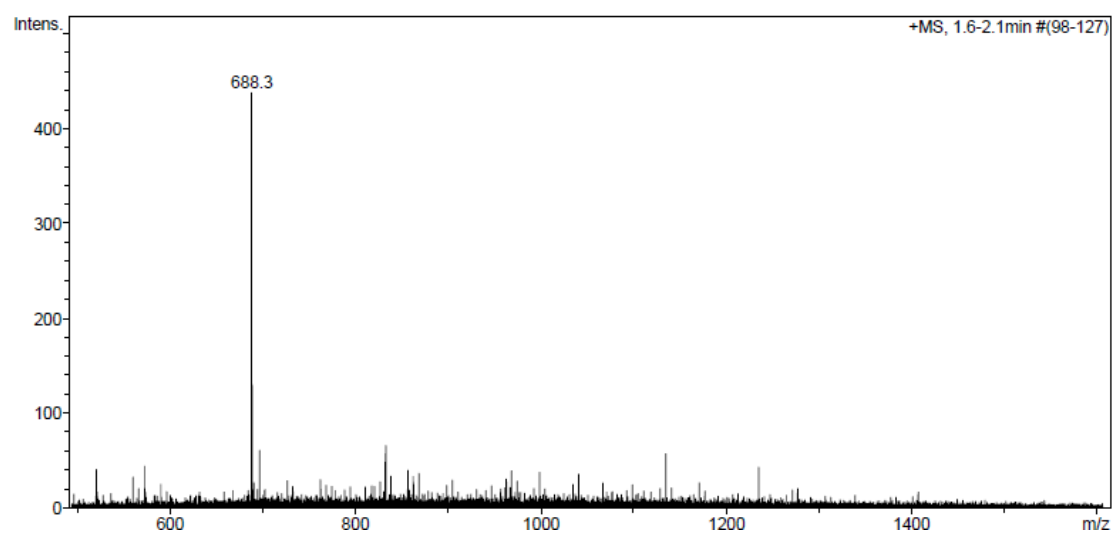
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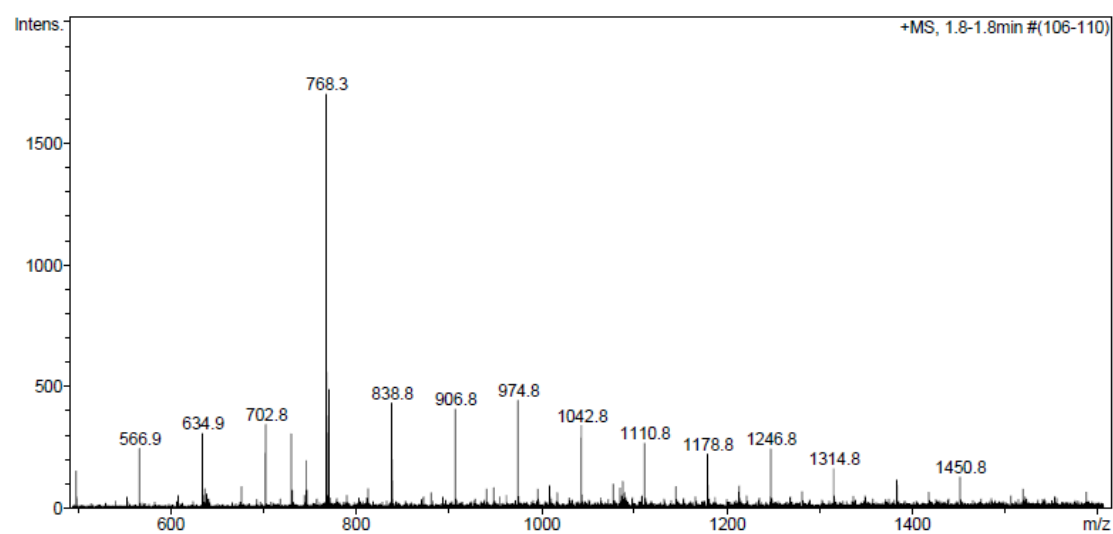
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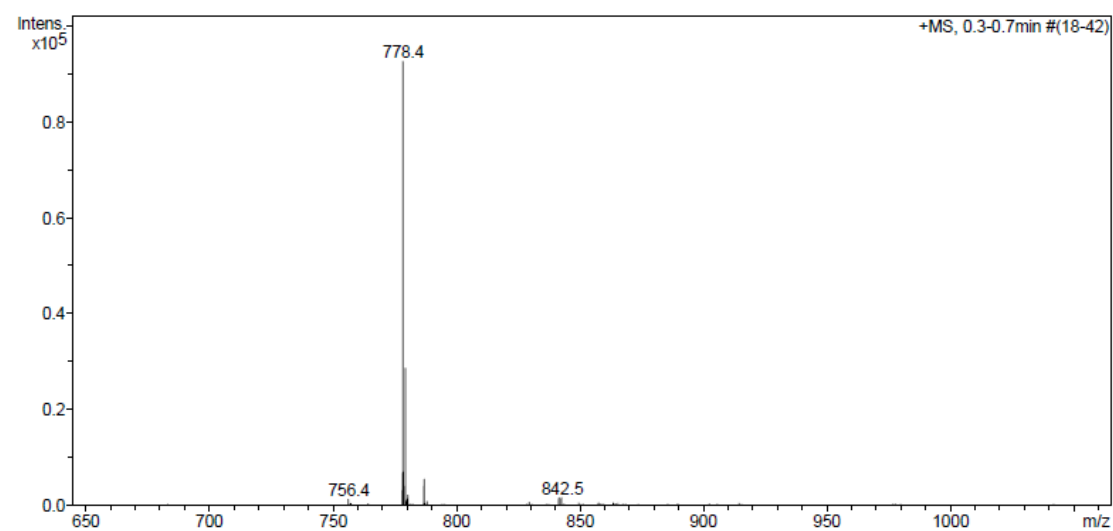
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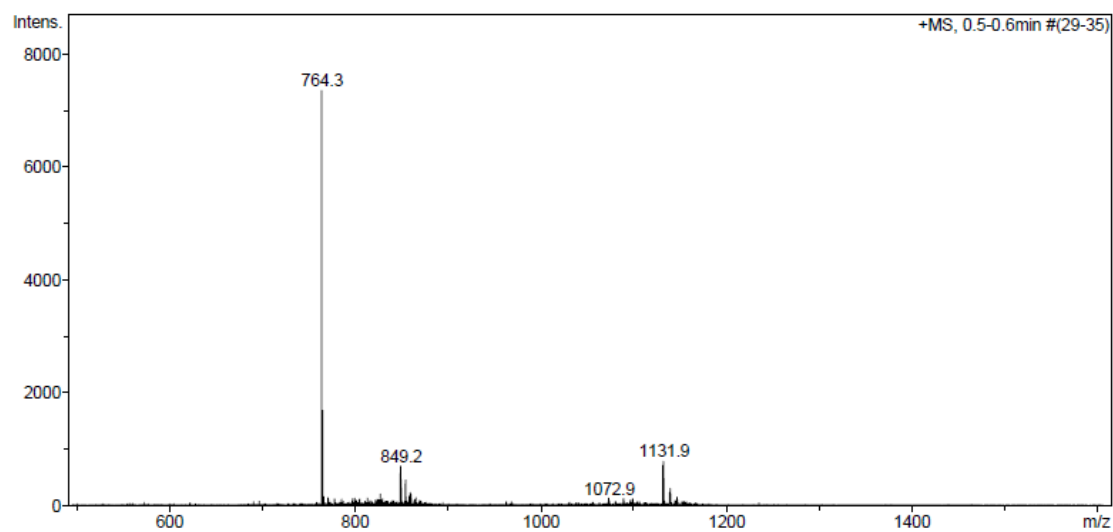
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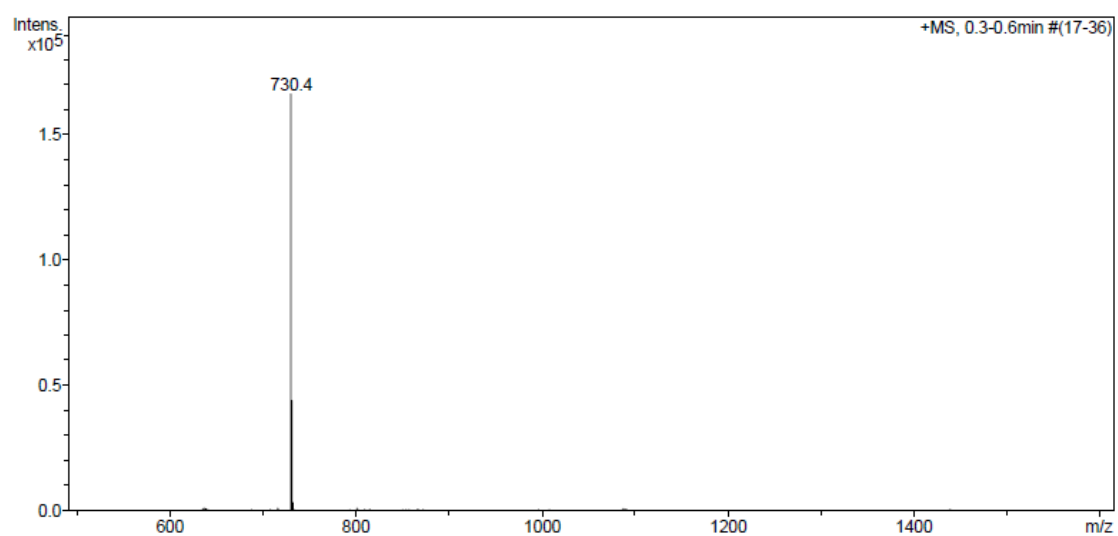
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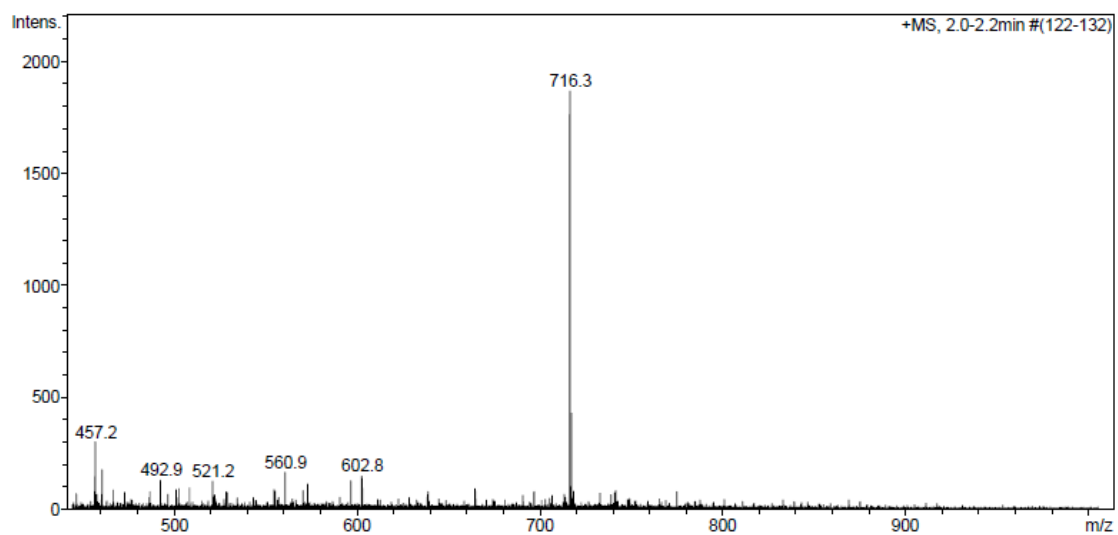
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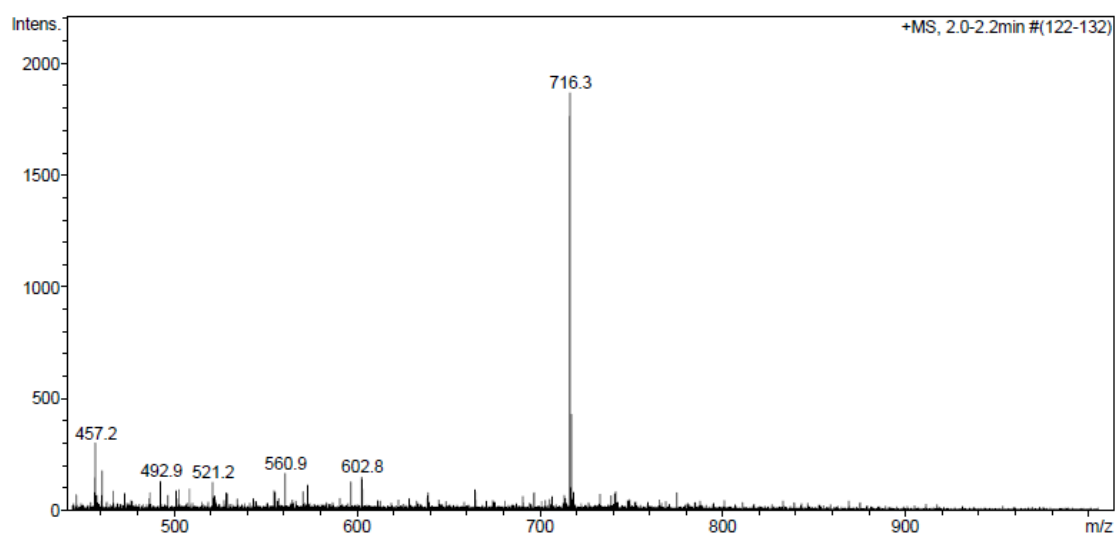
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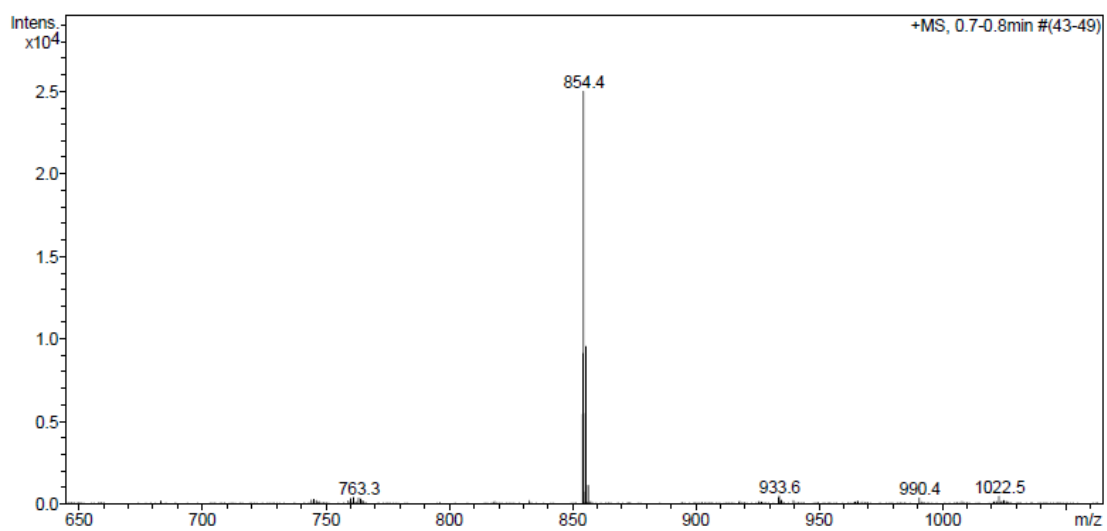
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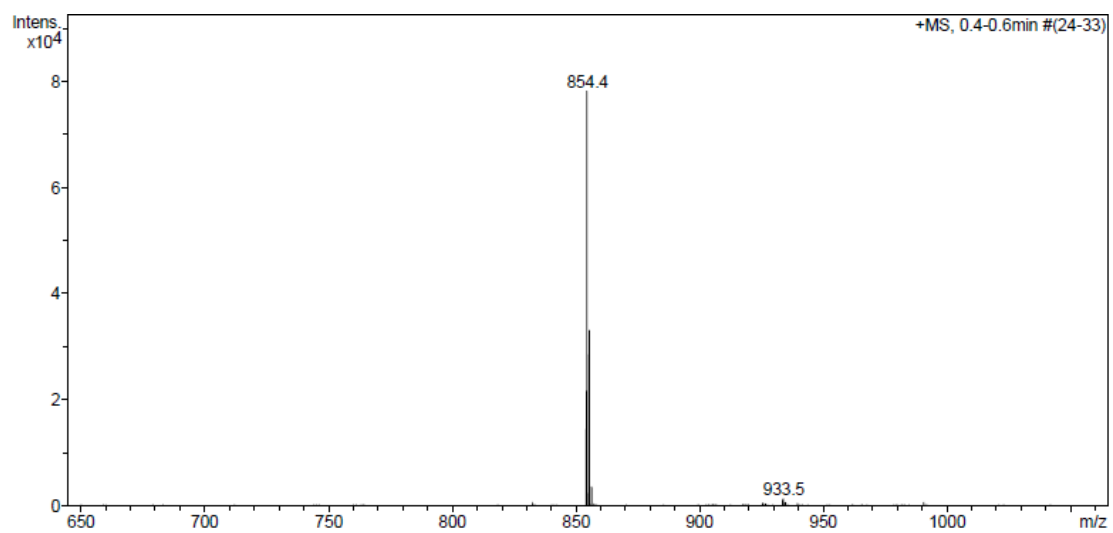
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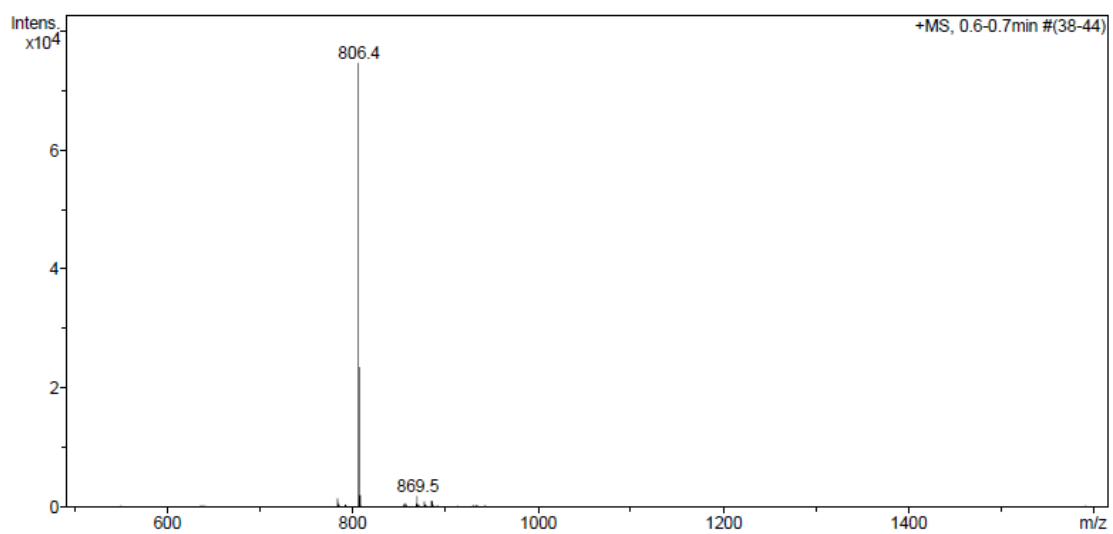
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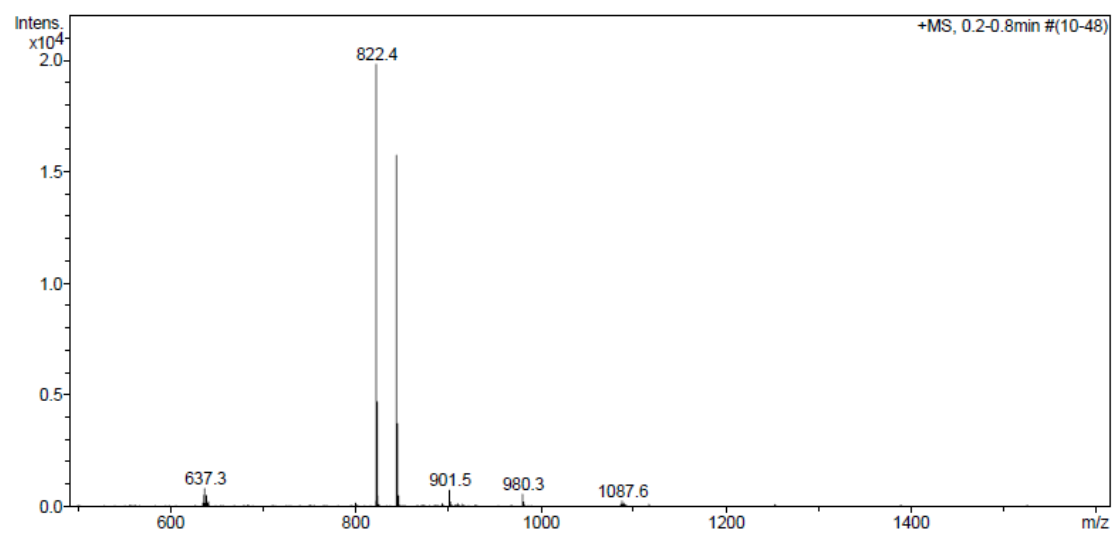
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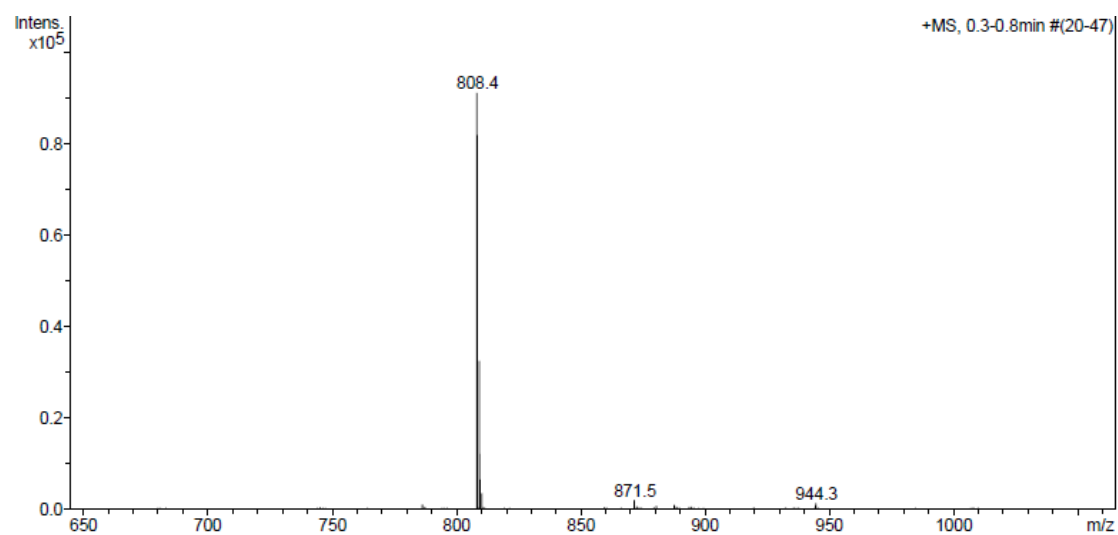
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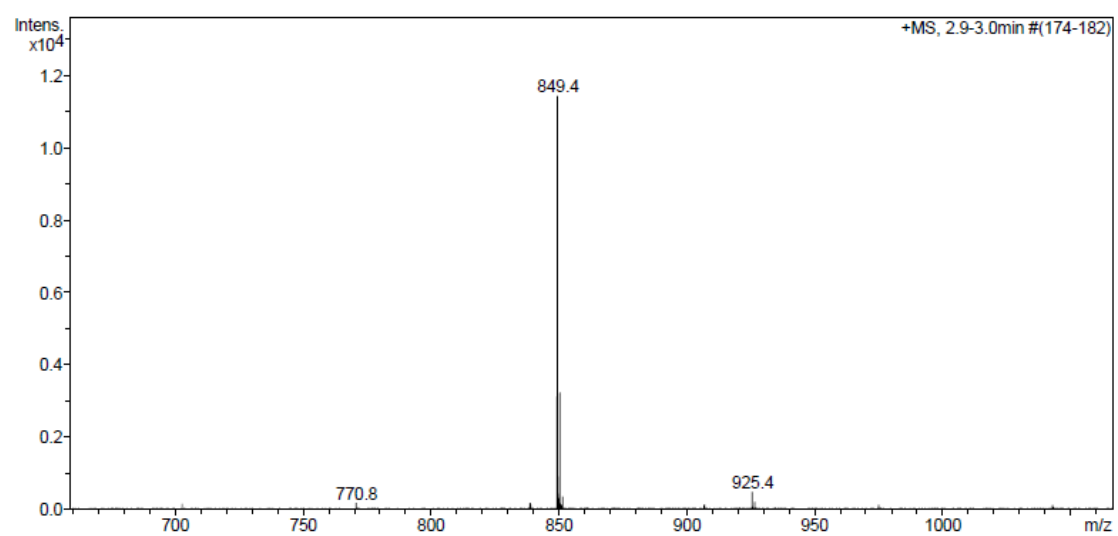
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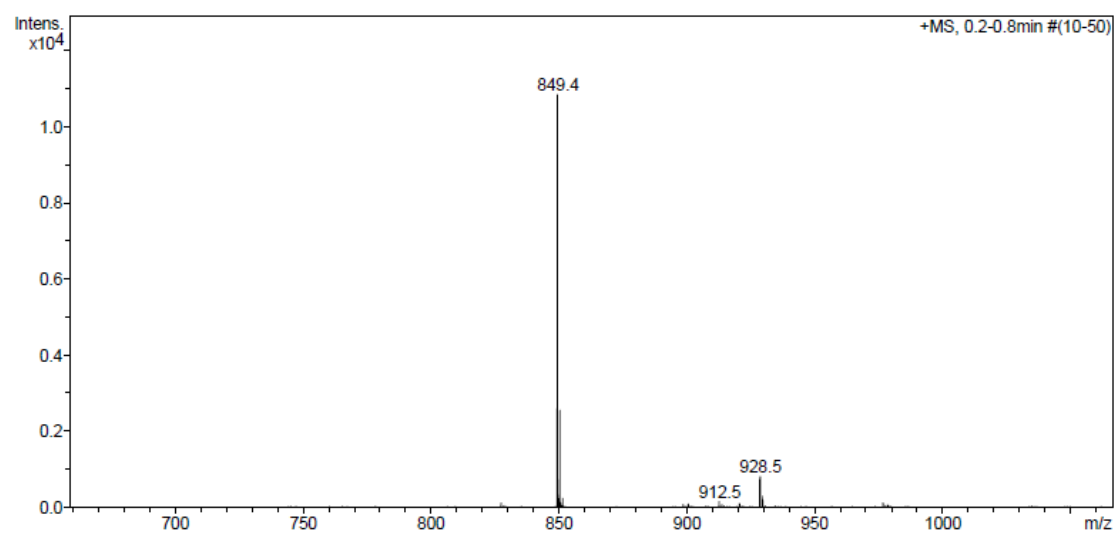


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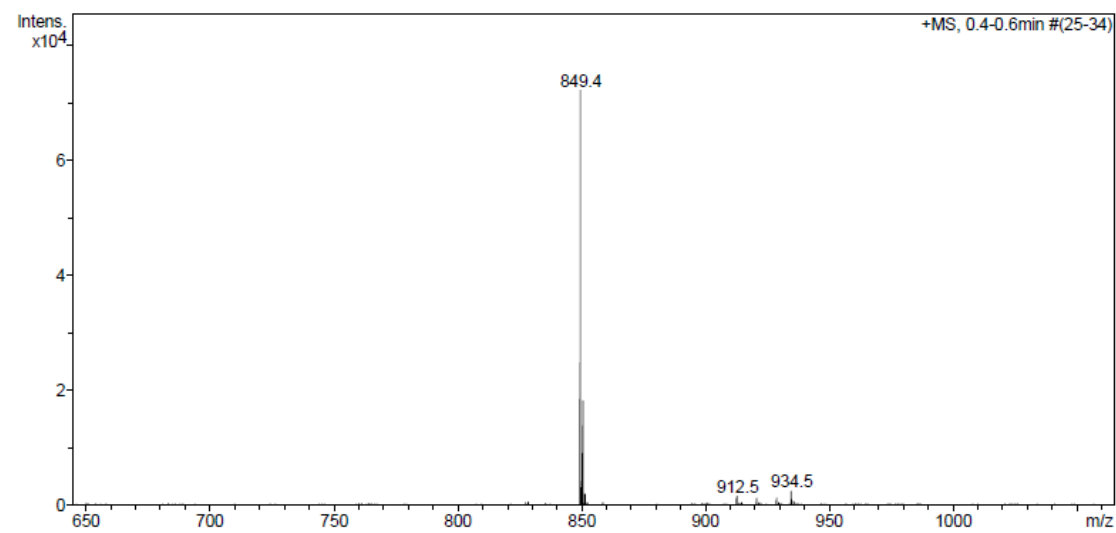




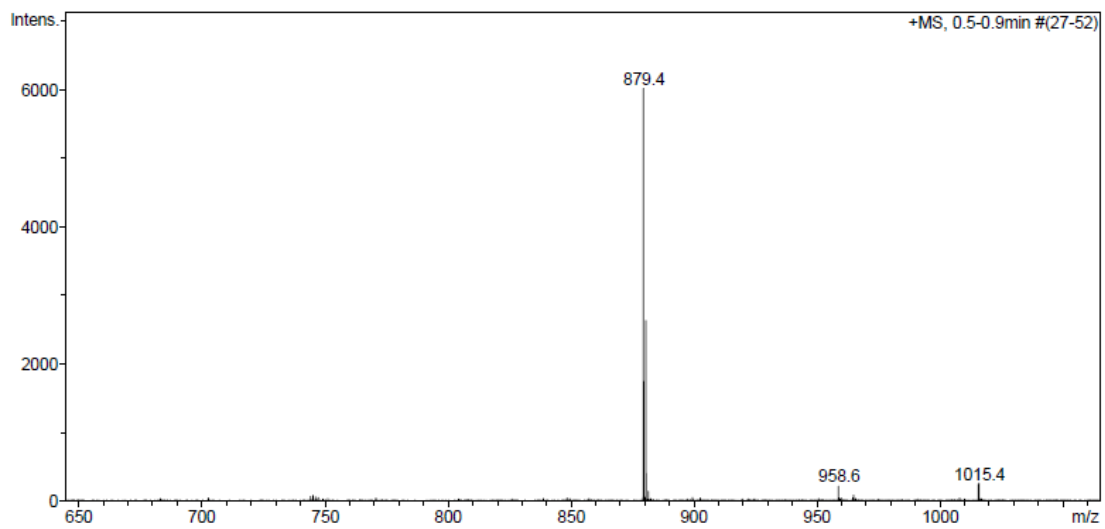
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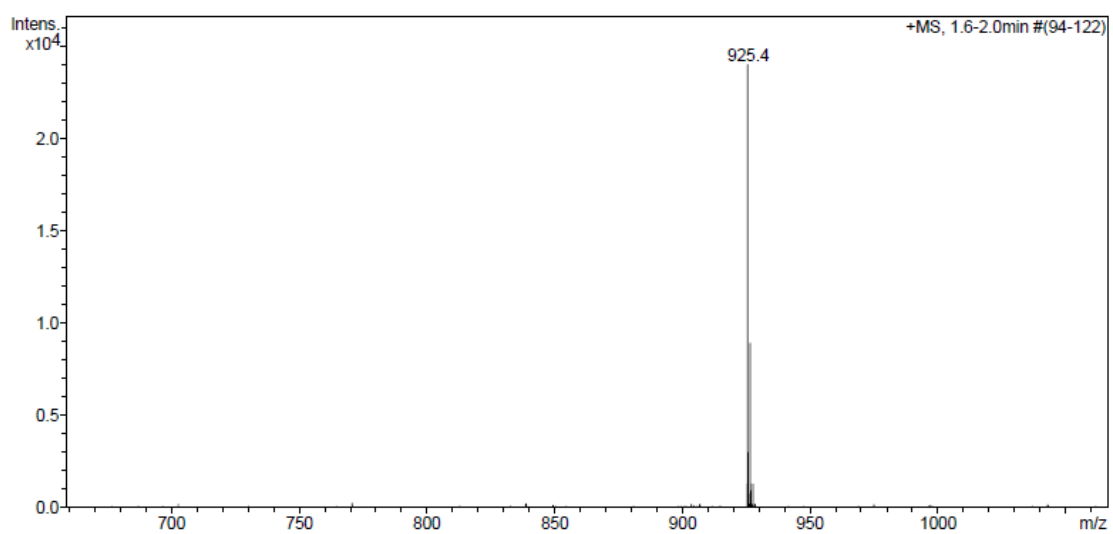
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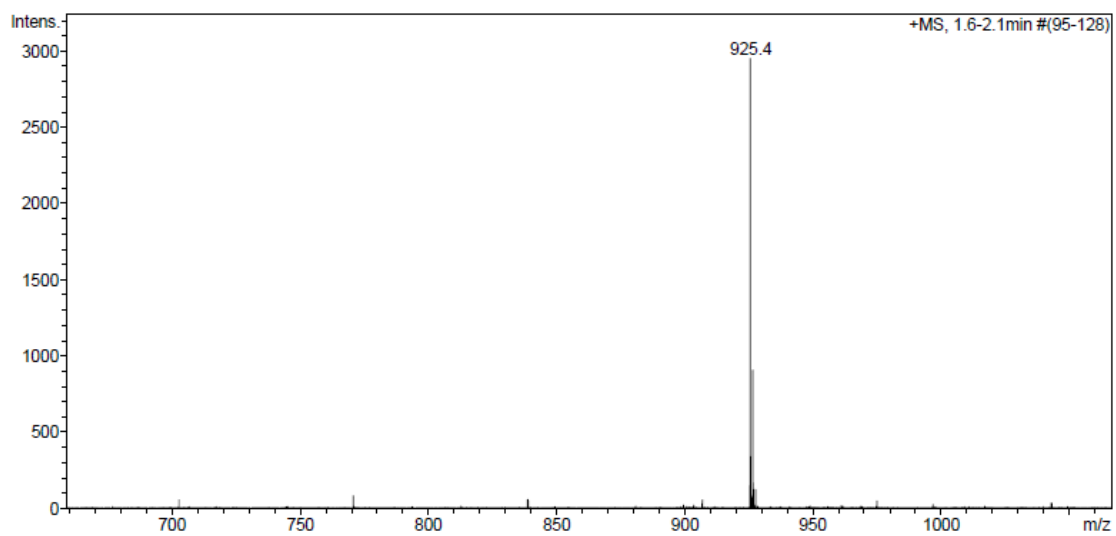
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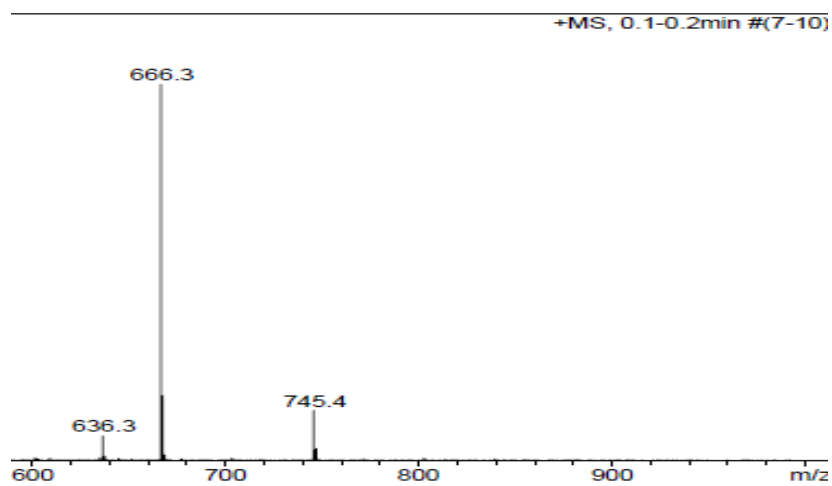
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2t

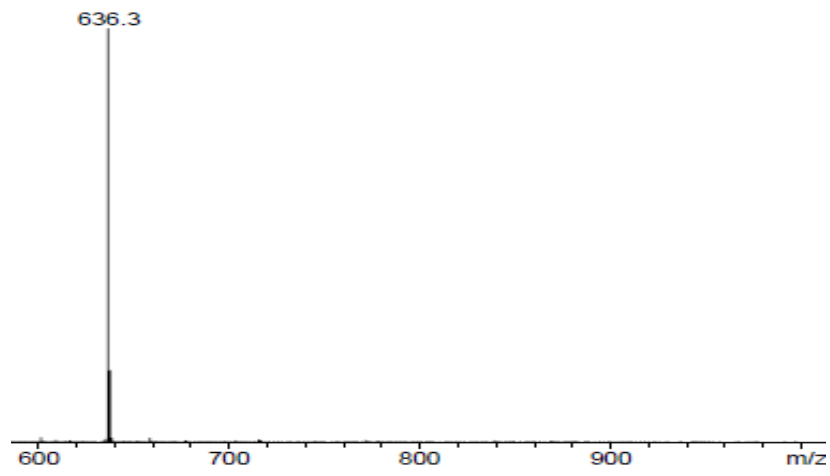


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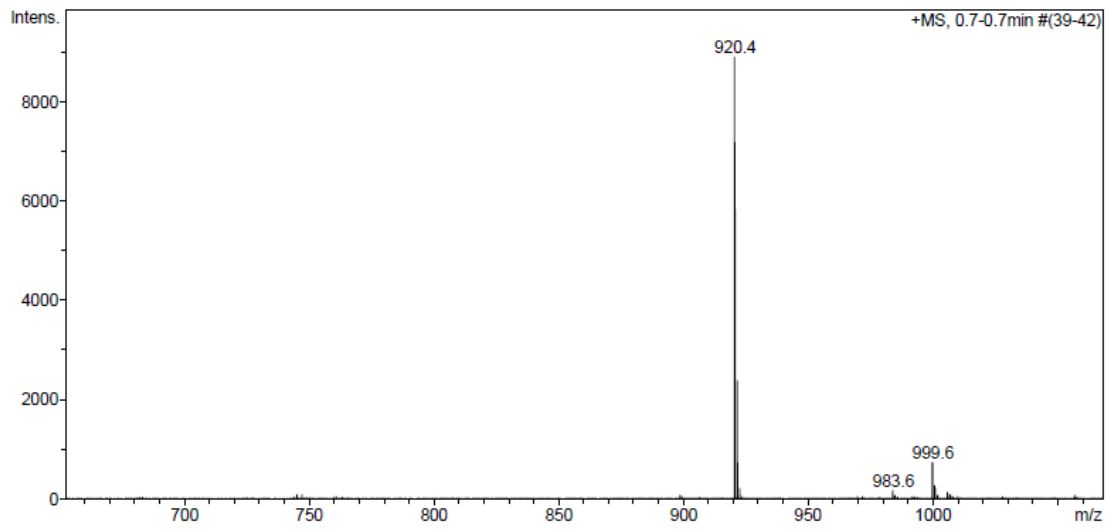
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+MS, 0.2min #(9)



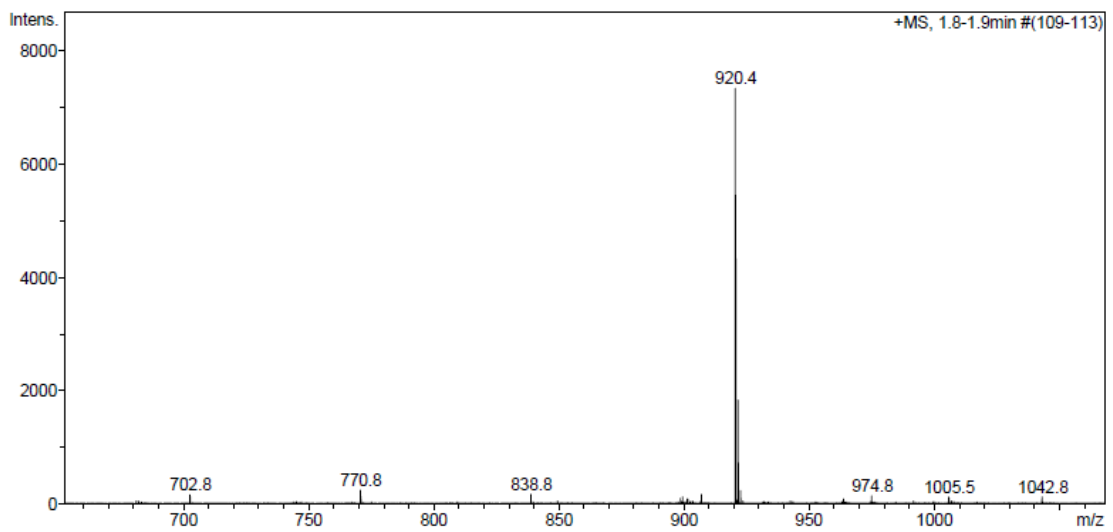
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+MS, 0.7-0.7min #(39-42)

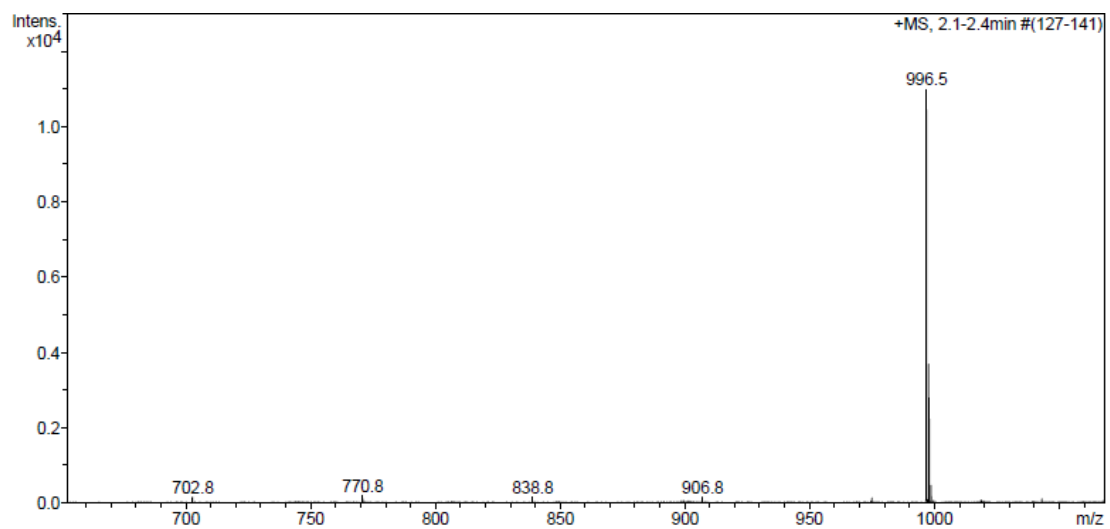


2x

+MS, 1.8-1.9min #(109-113)

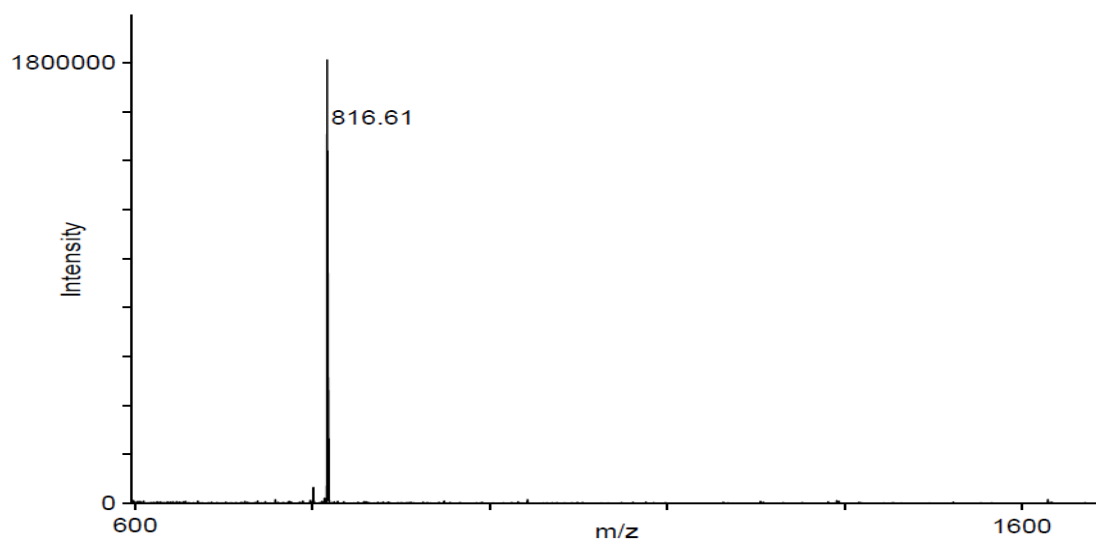


2y

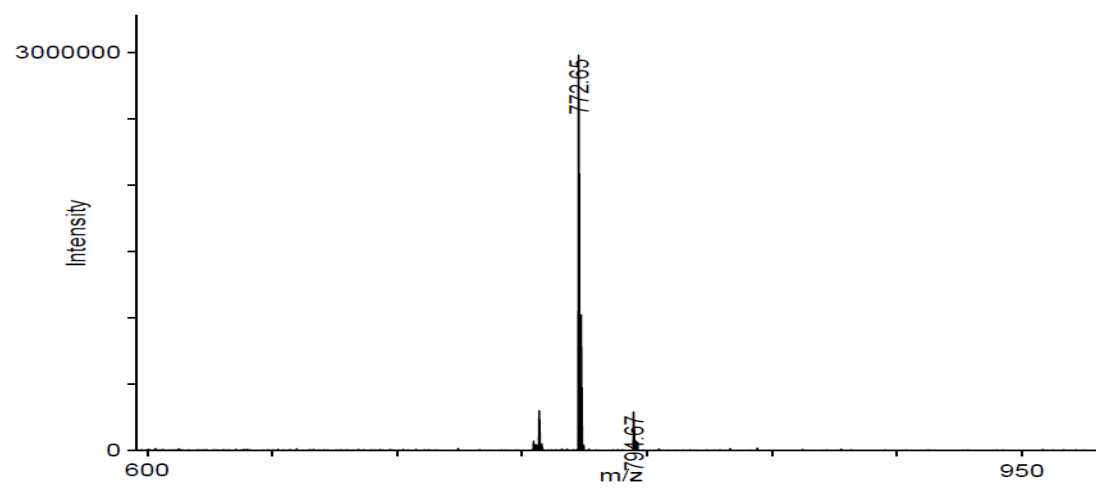


**Figure S3.** MALDI-TOF MS of Rapalogs **11** in Table 2

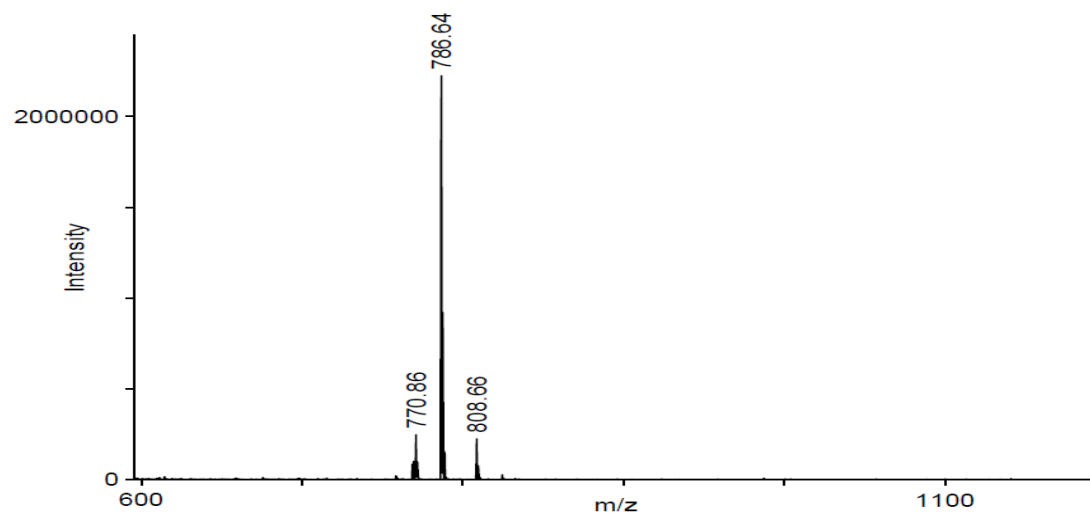
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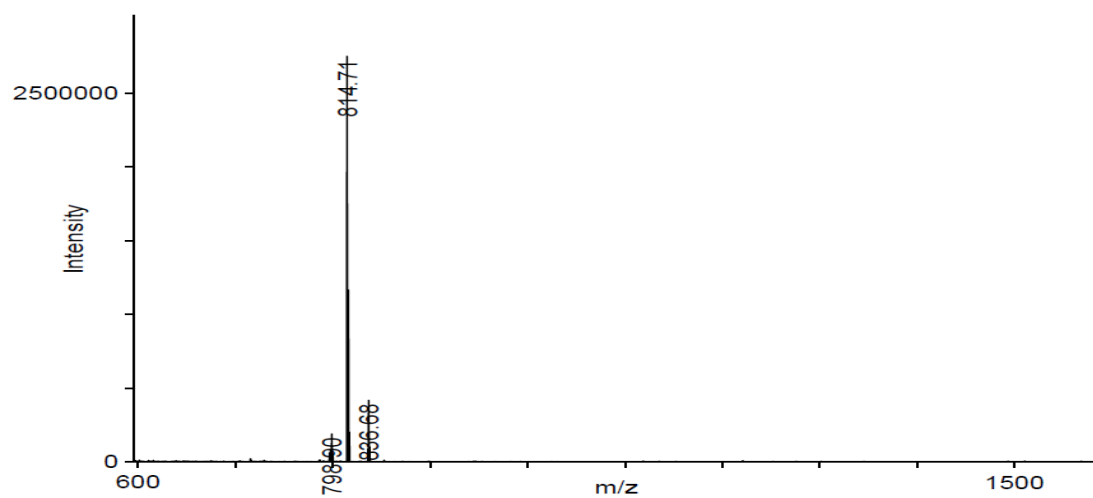
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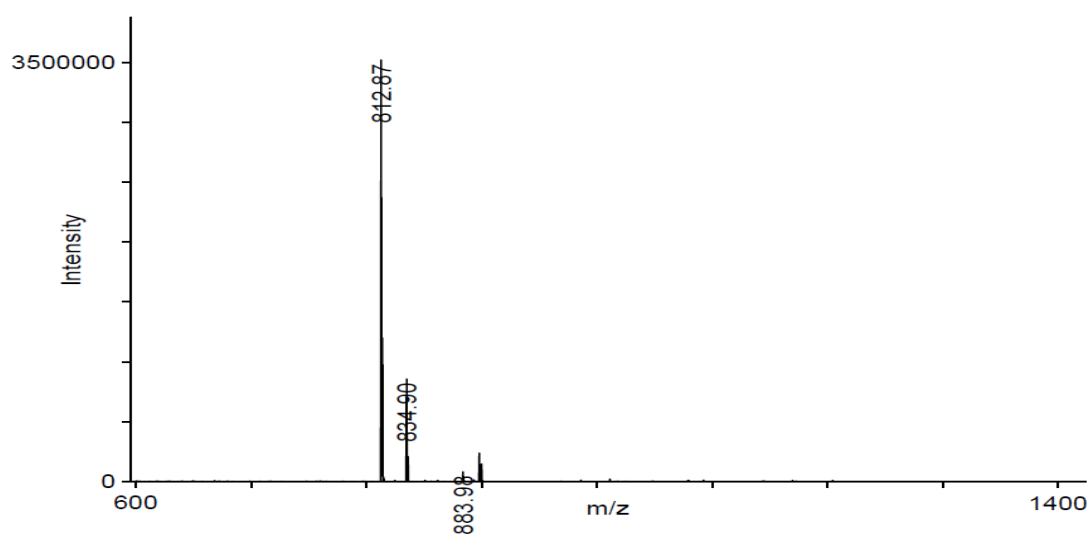
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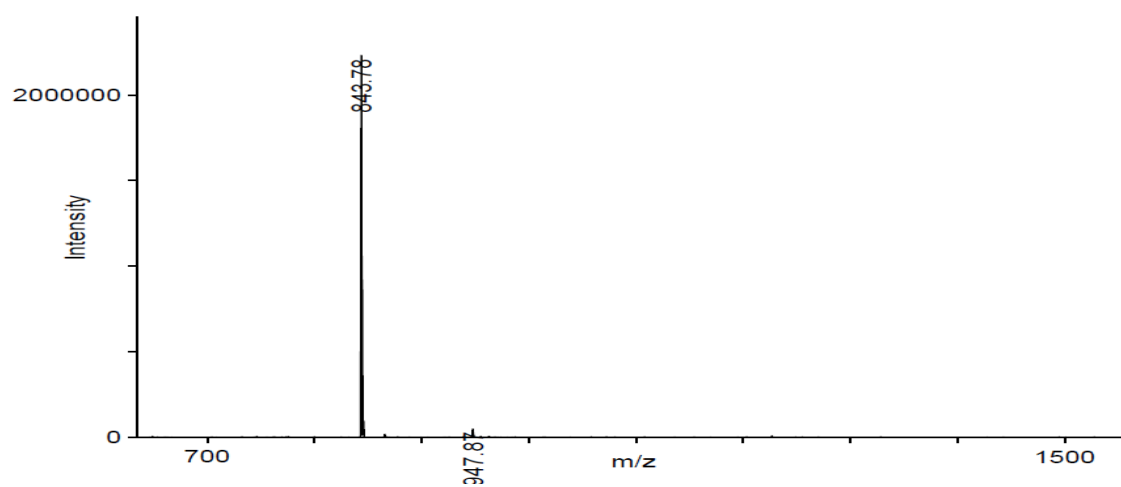
### 11 D-Thr-D-Val



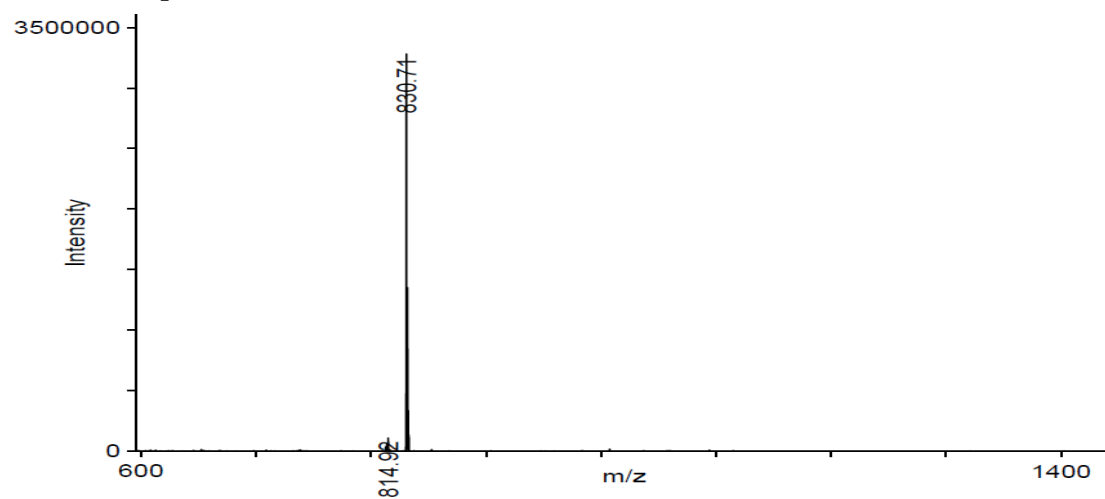
### 11 D-Thr-Pro



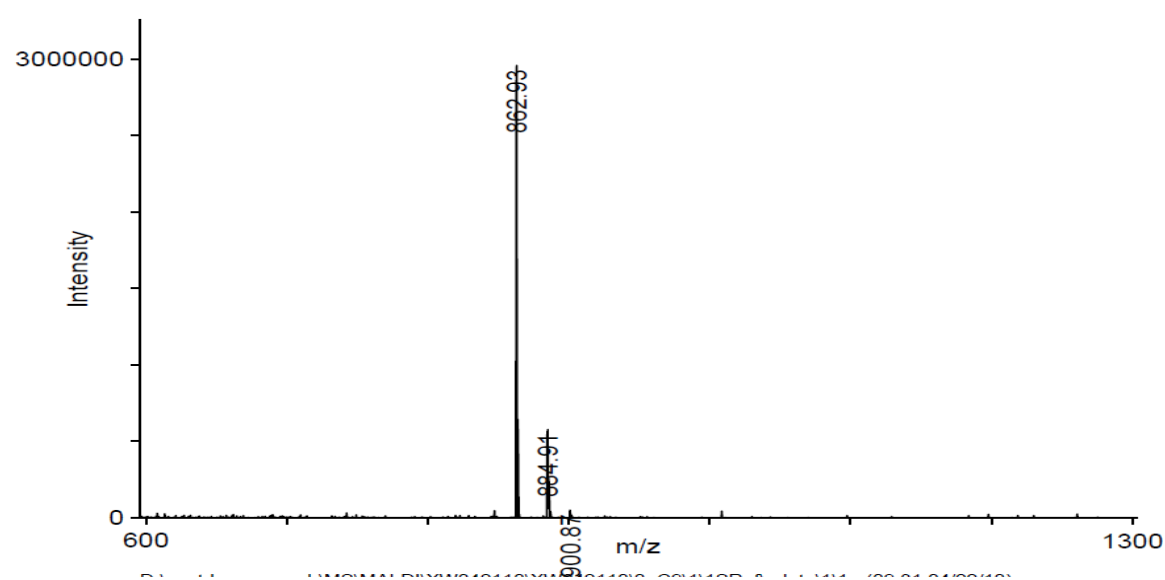
### 11 D-Thr-Lys



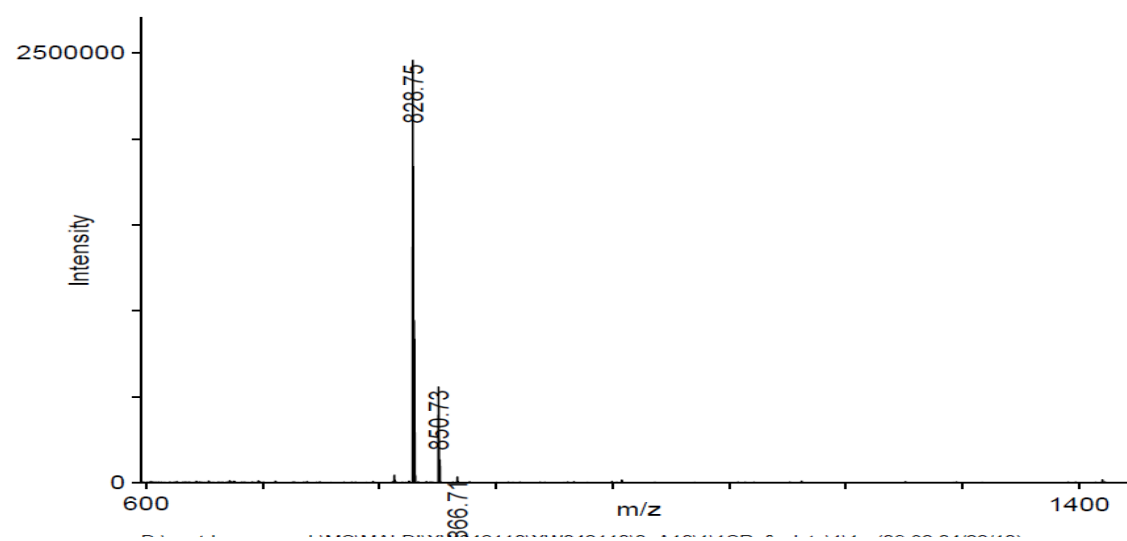
### 11 D-Thr-Asp



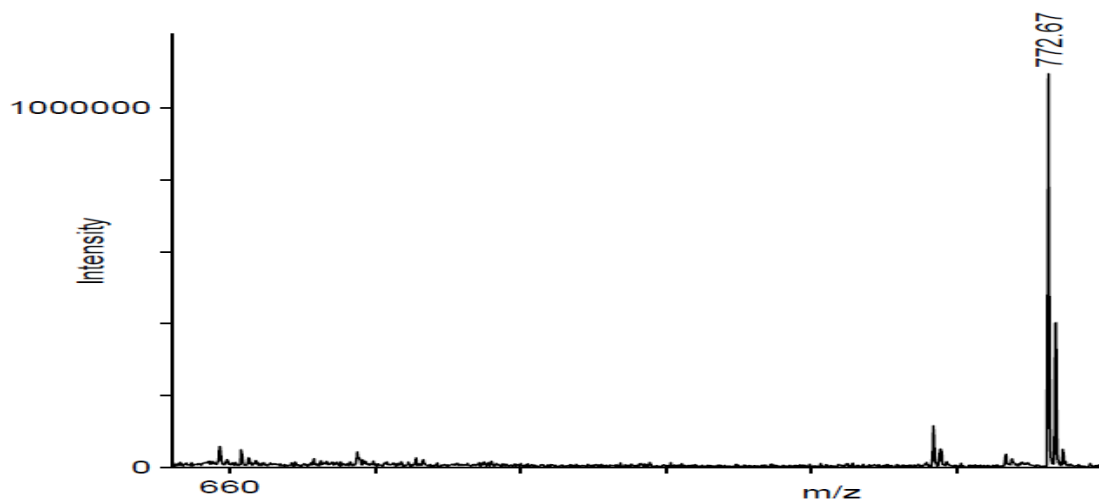
### 11 D-Thr-D-Phe



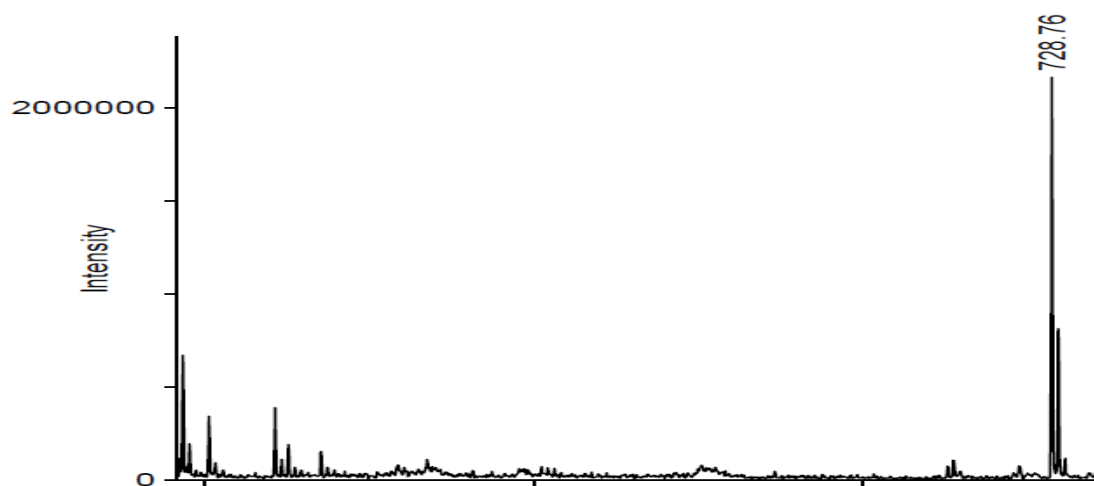
### 11 D-Thr-Nle



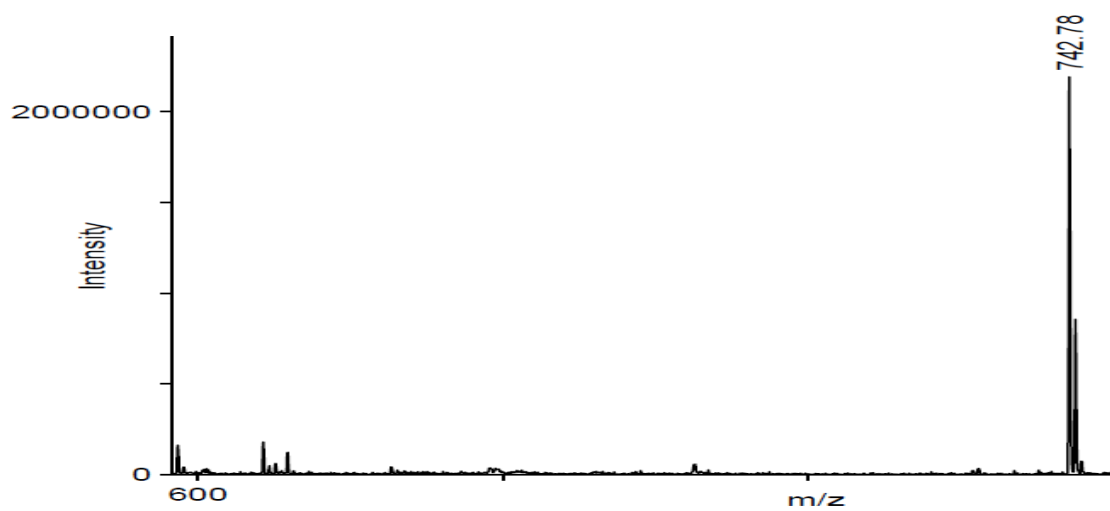
11 Gly-D-Thr



11 Gly-Gly

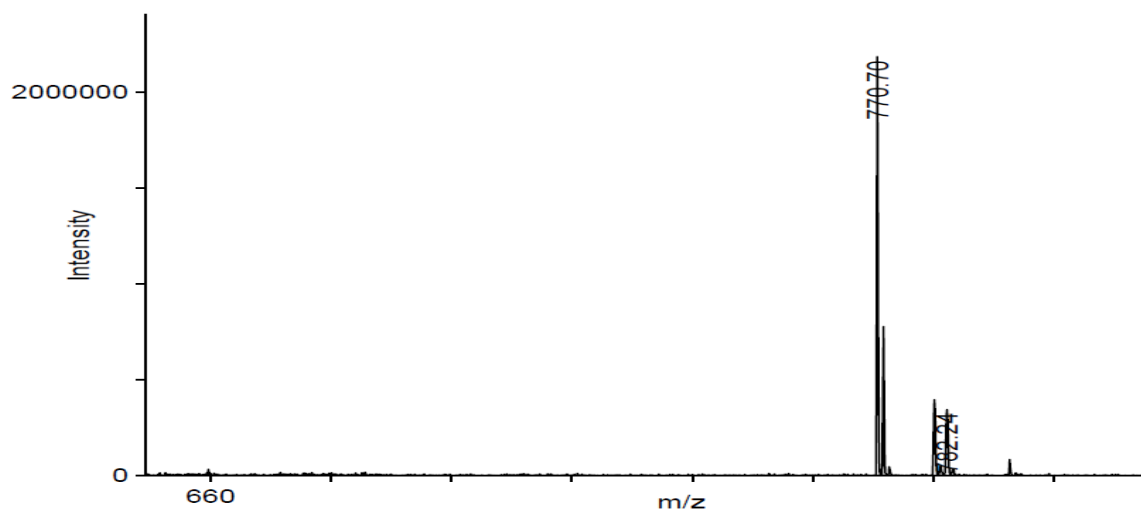


11 Gly-Ala

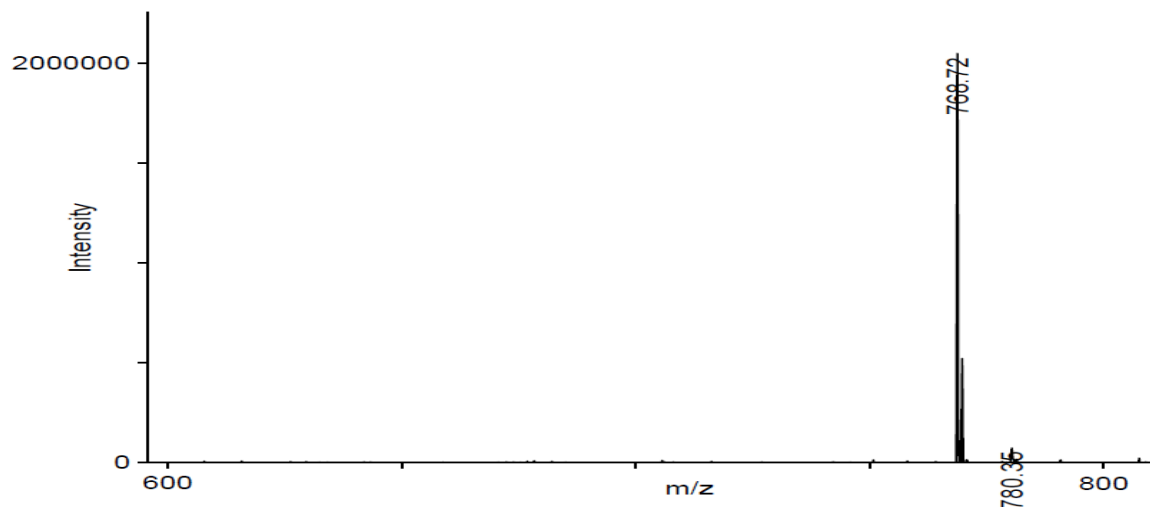




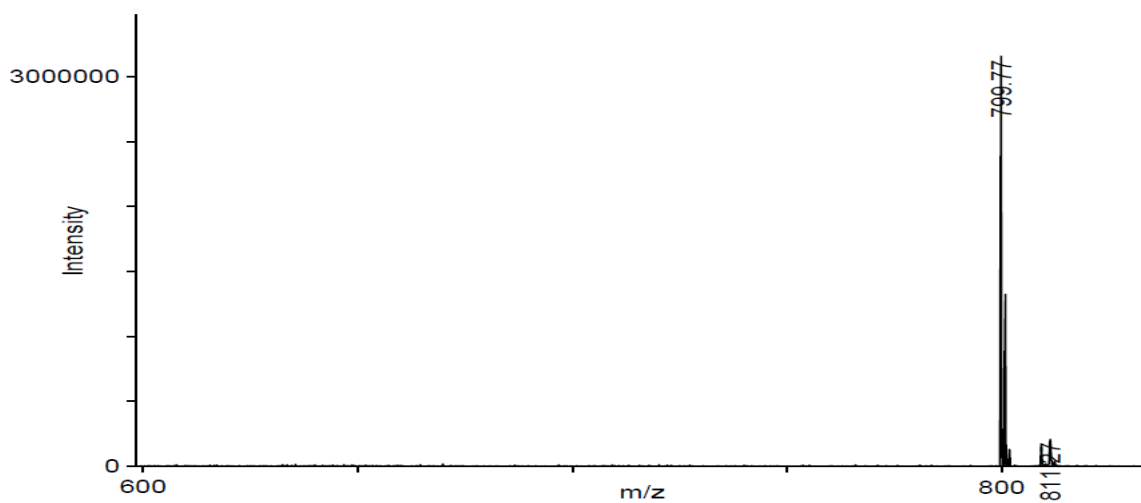
### 11 Gly-D-Val



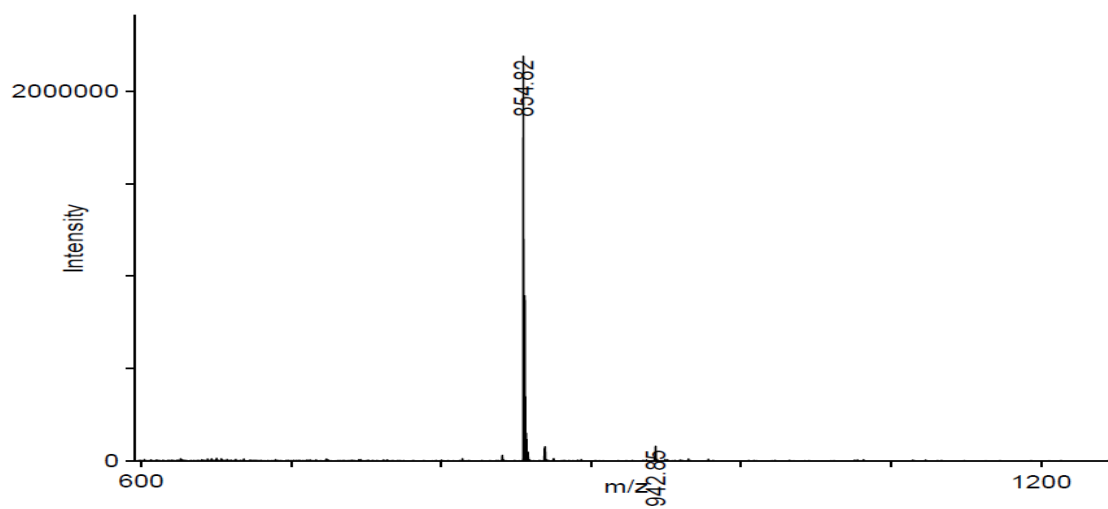
### 11 Gly-Pro



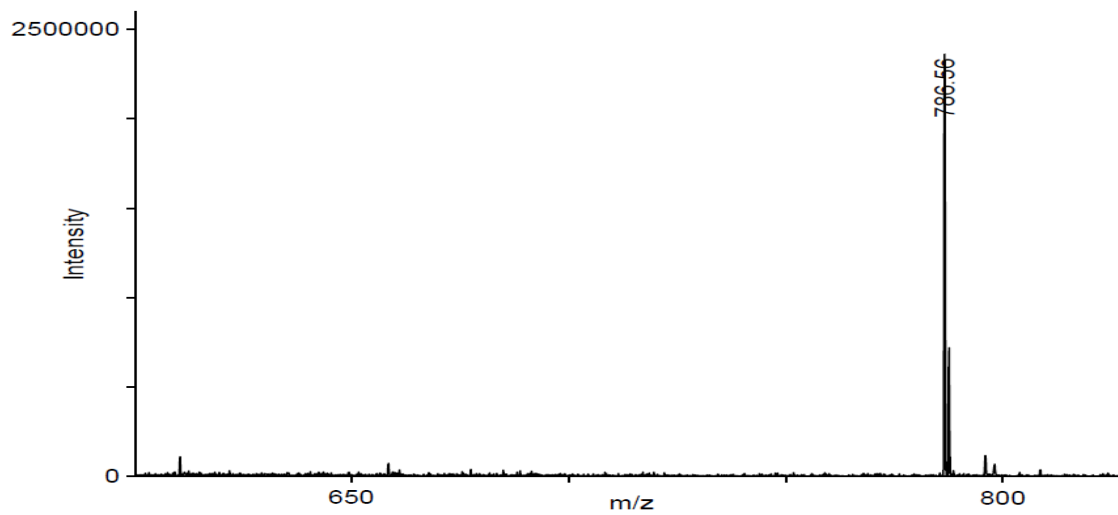
### 11 Gly-Lys



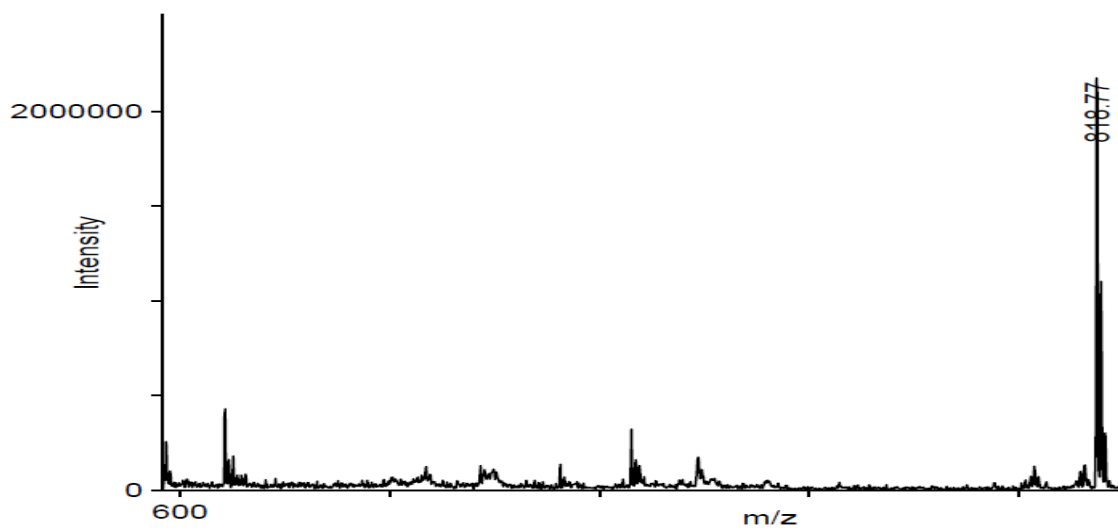
### 11 Gly-Trp



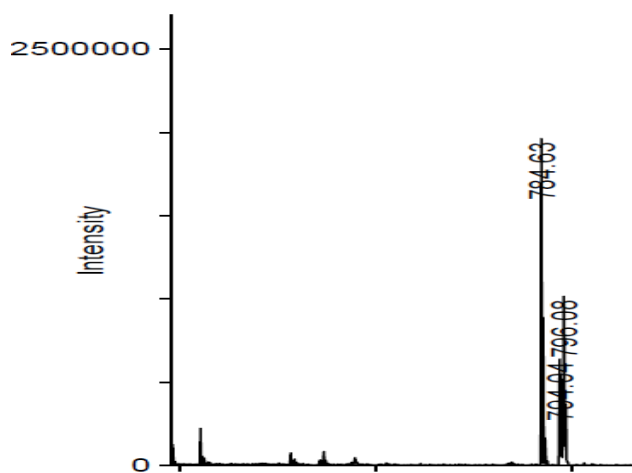
### 11 Gly-Asp



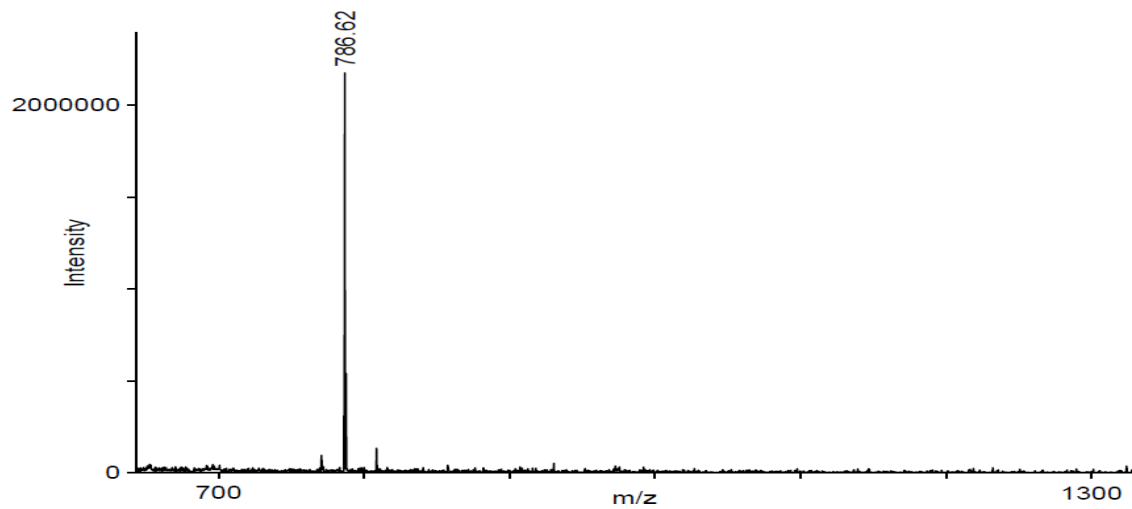
### 11 Gly-D-Phe



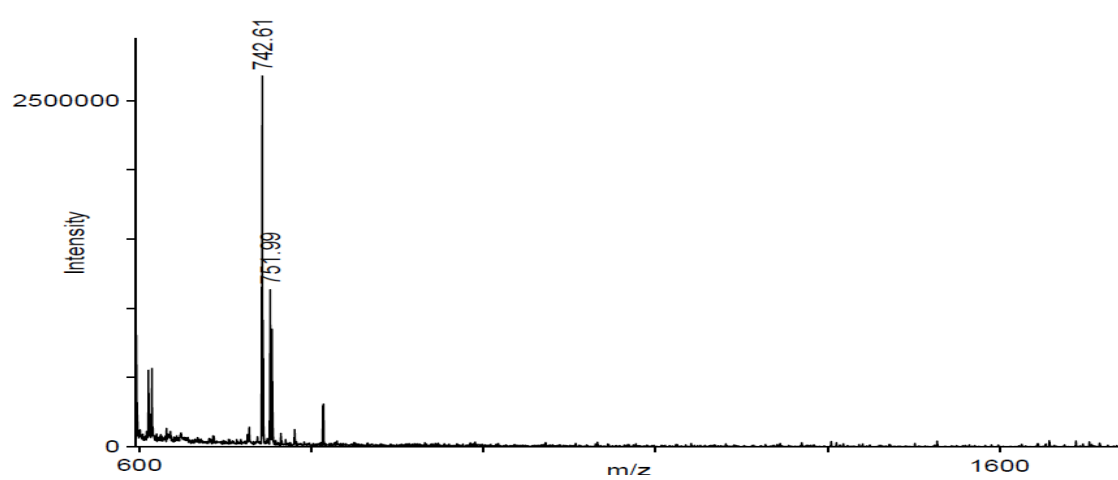
### 11 Gly-Nle



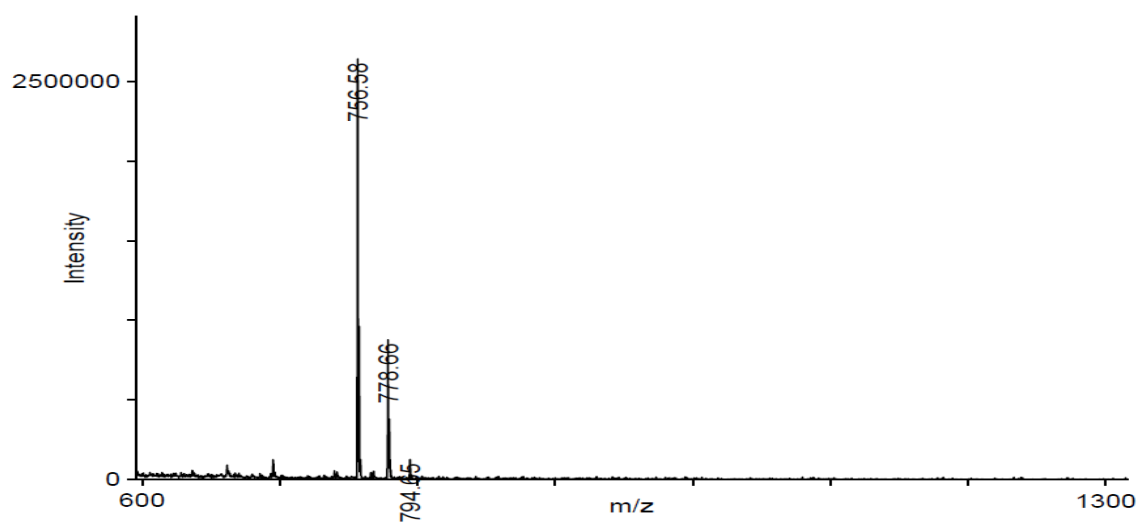
### 11 Ala-D-Thr



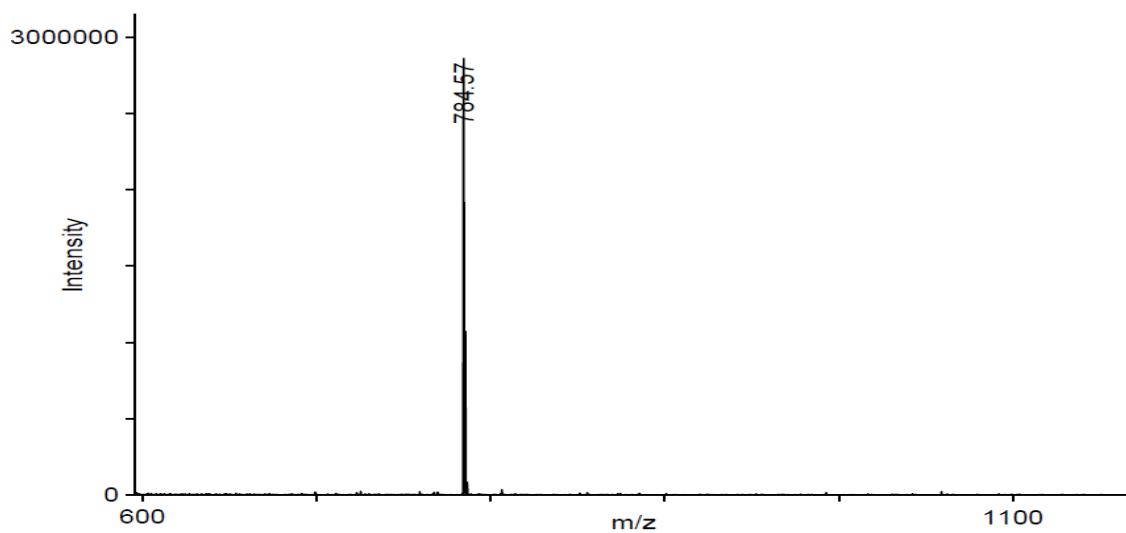
### 11 Ala-Gly



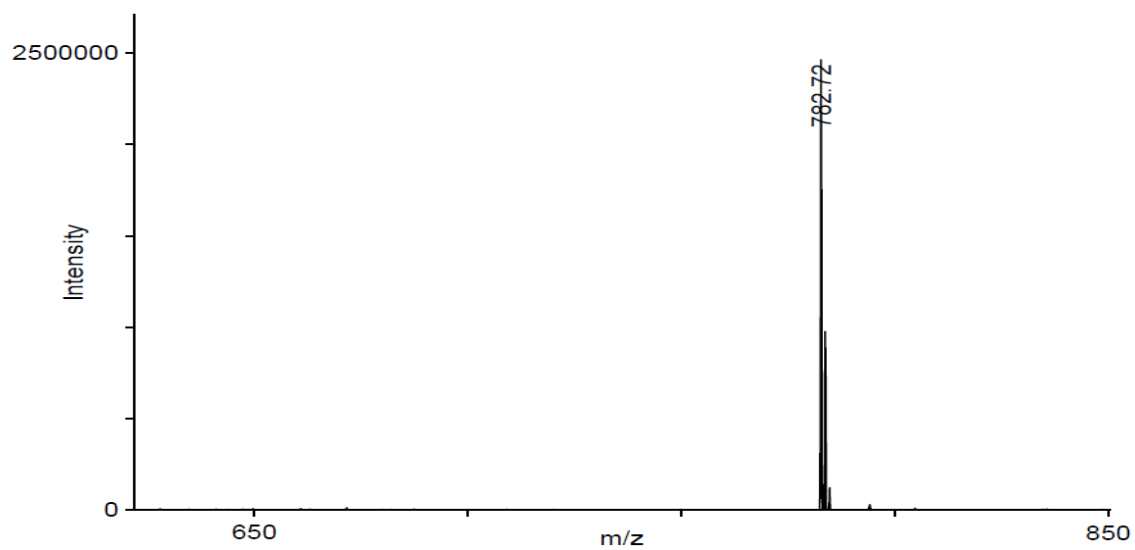
### 11 Ala-Ala



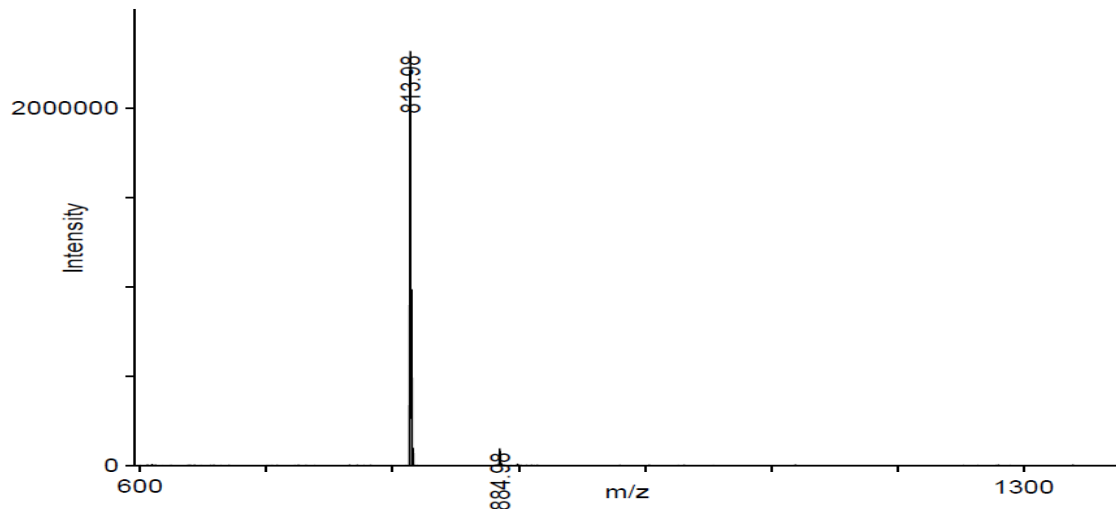
### 11 Ala-D-Val



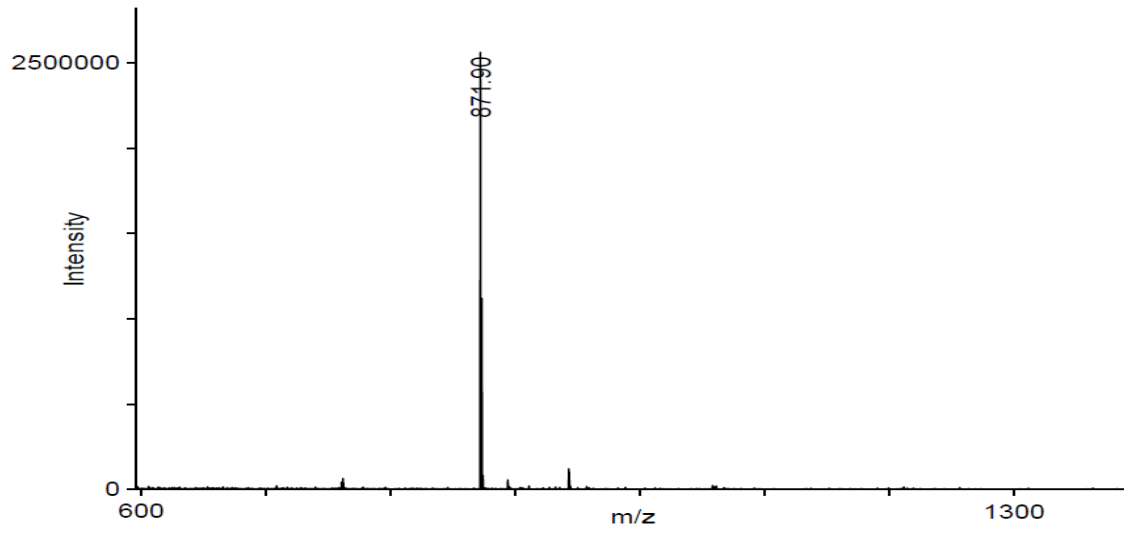
### 11 Ala-Pro



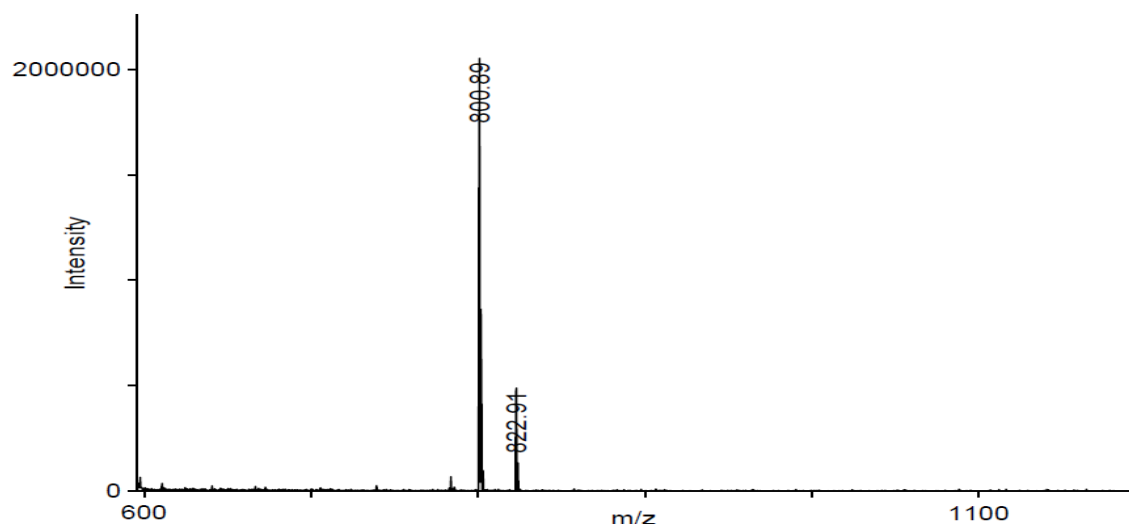
### 11 Ala-Lys



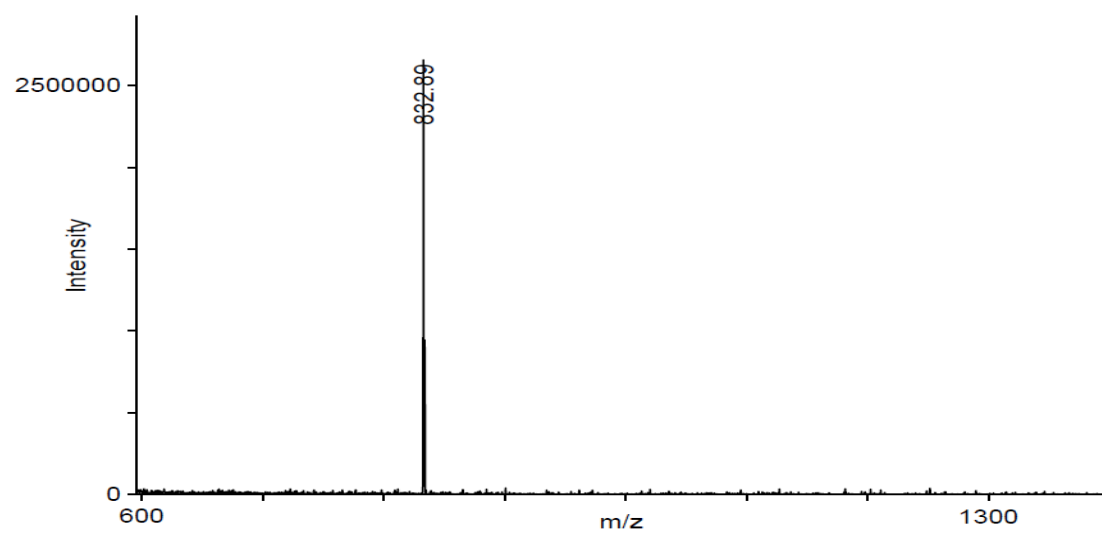
### 11 Ala-Trp



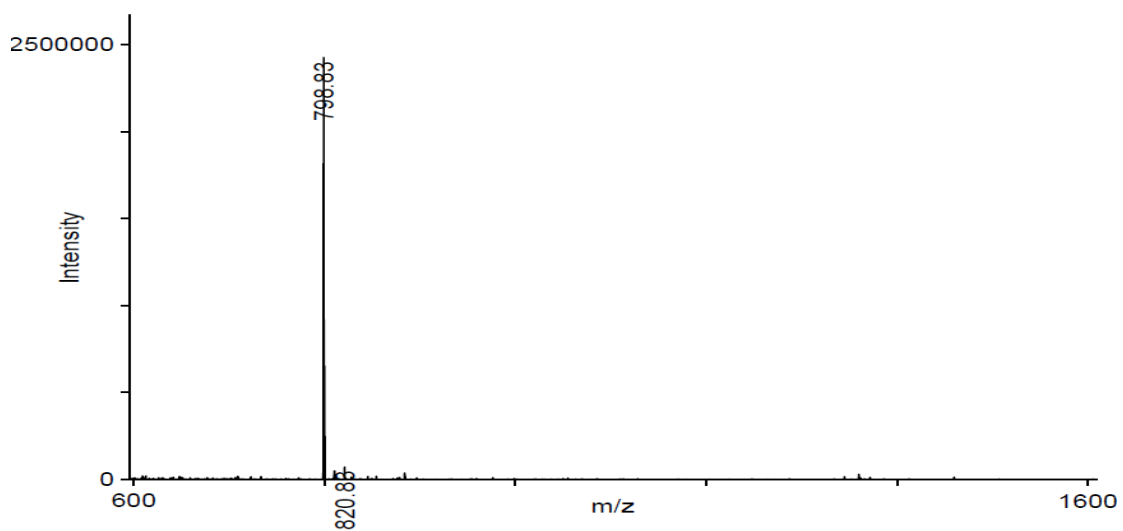
### 11Ala-Asp



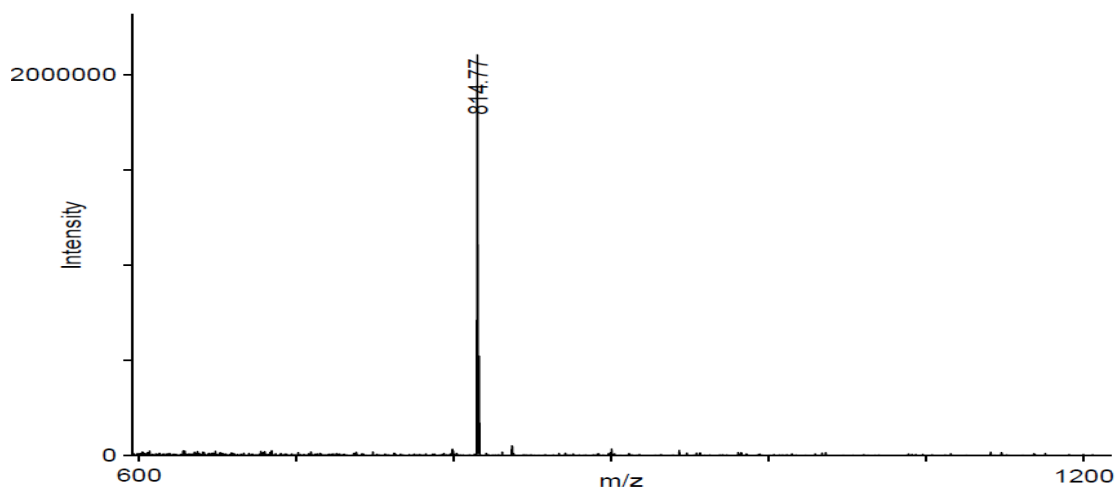
**11 Ala-D-Phe**



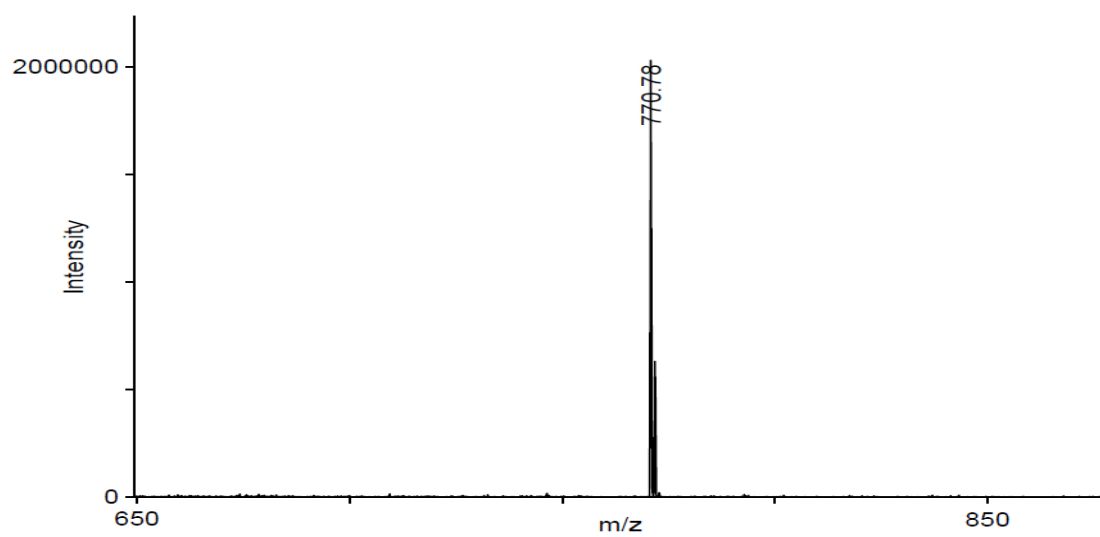
**11 Ala-Nle**



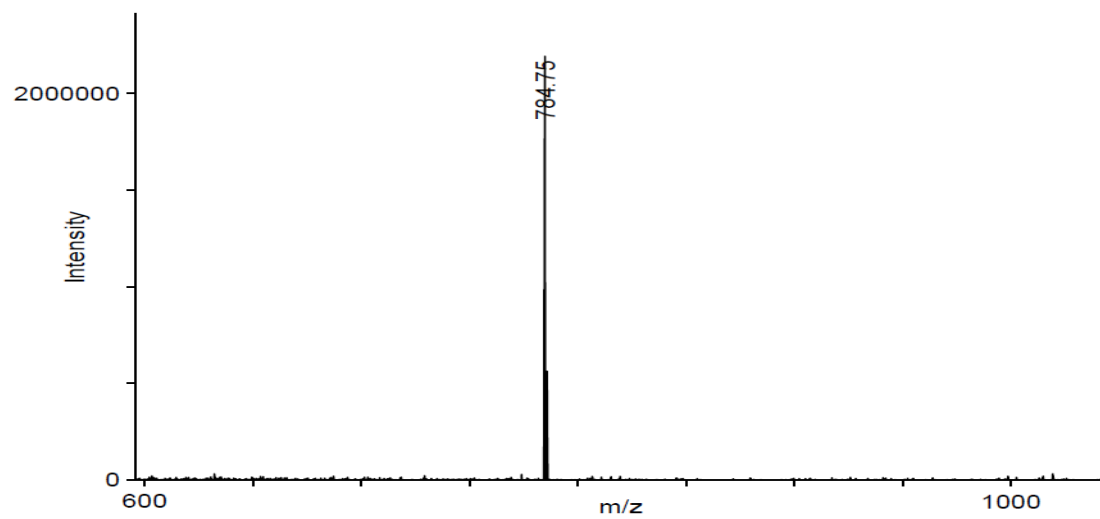
**11 D-Val-D-Thr**



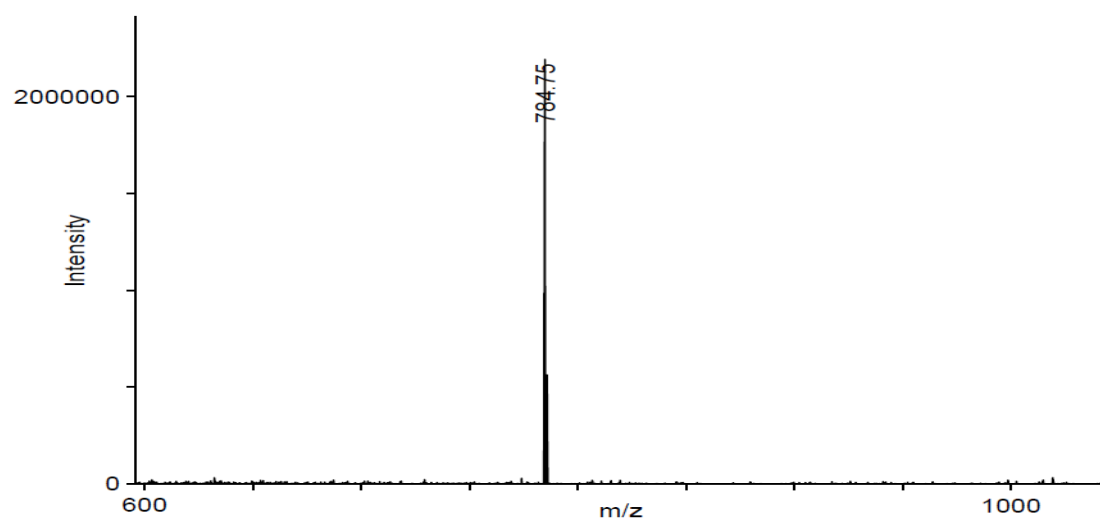
### 11 D-Val-Gly



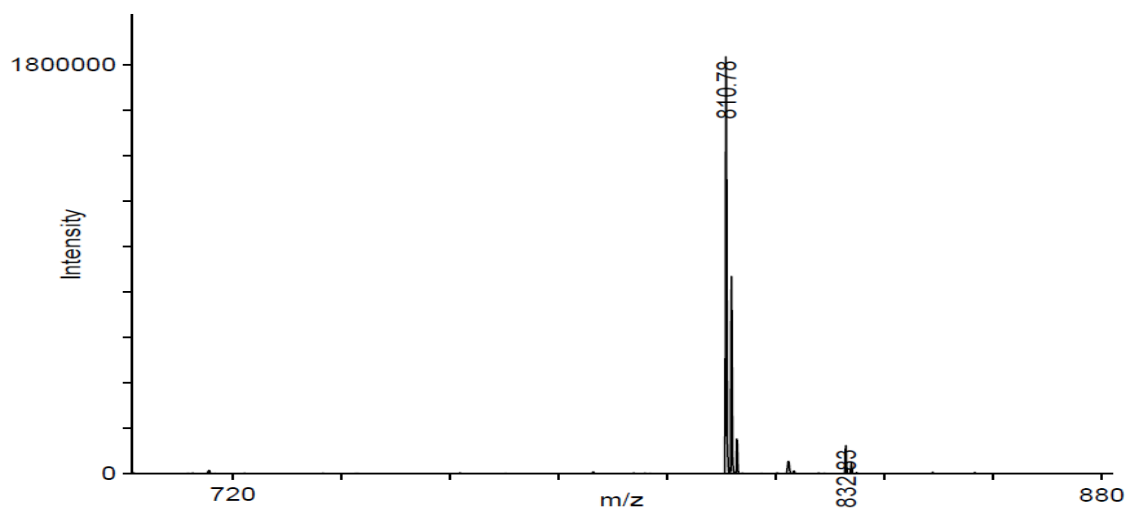
### 11 D-Val-Ala



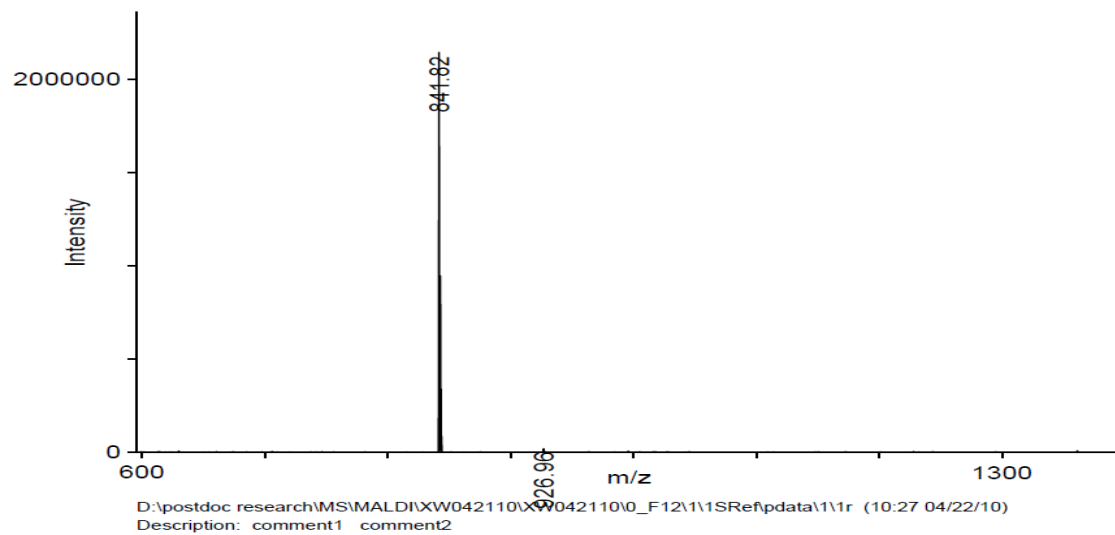
### 11 D-Val-D-Val



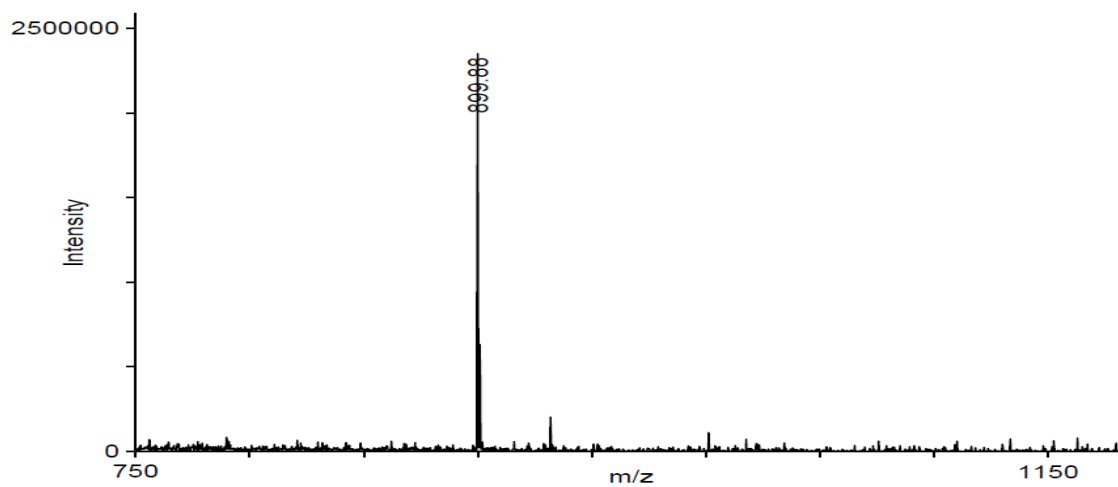
### 11 D-Val-Pro



### 11 D-Val-Lys

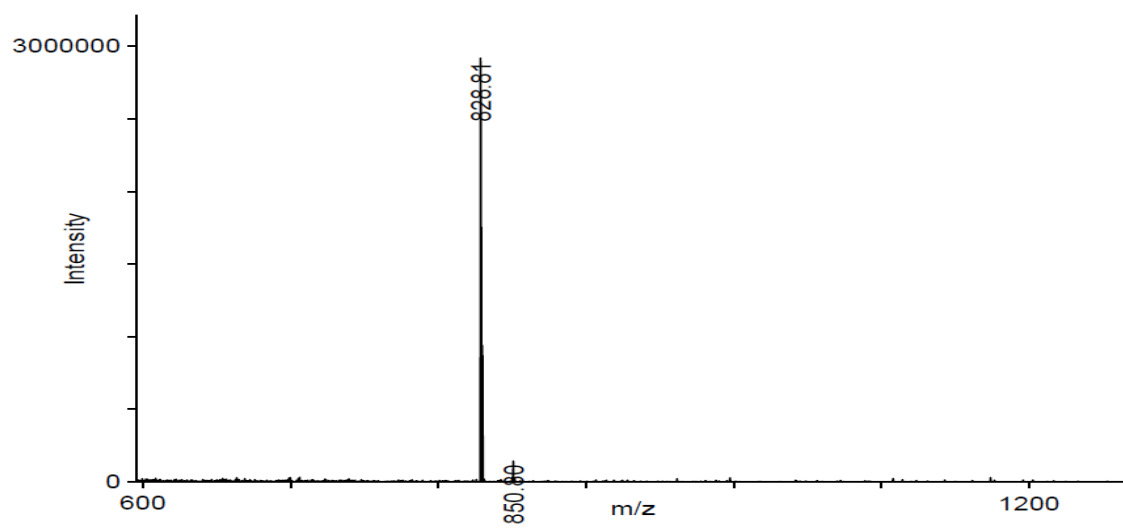


### 11 D-Val-Trp

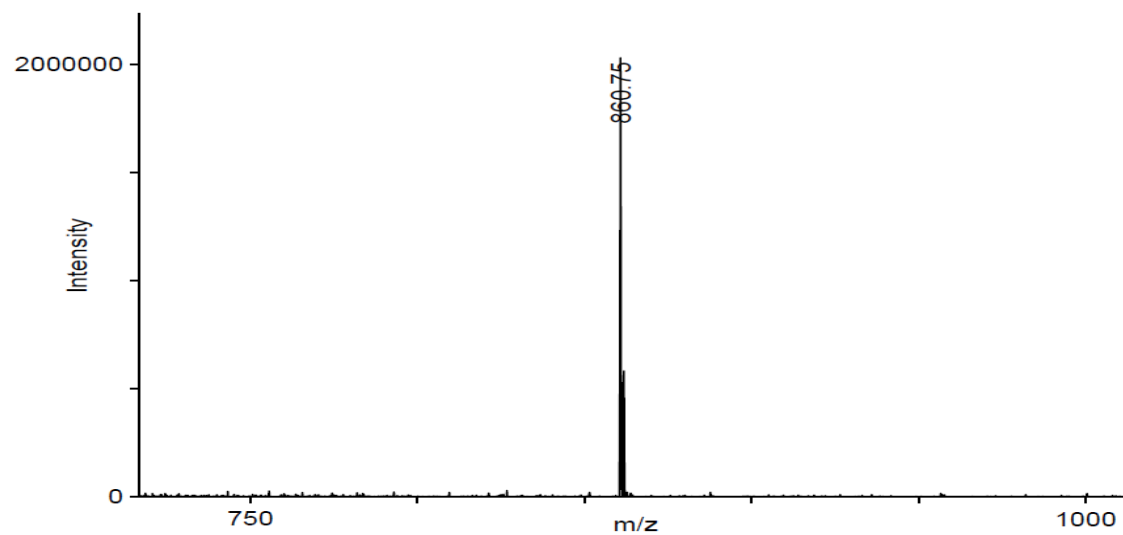




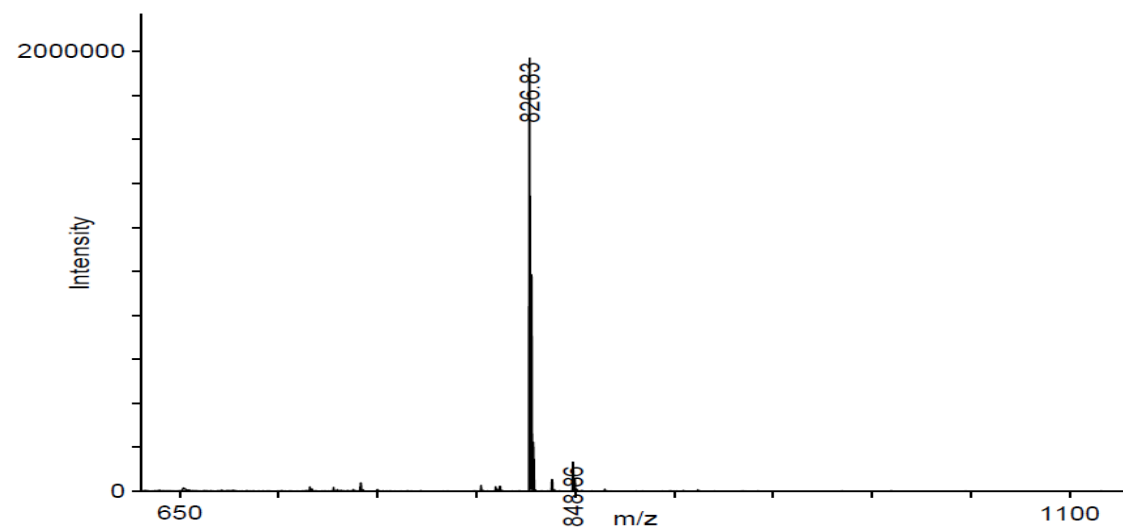
### 11 D-Val-Asp



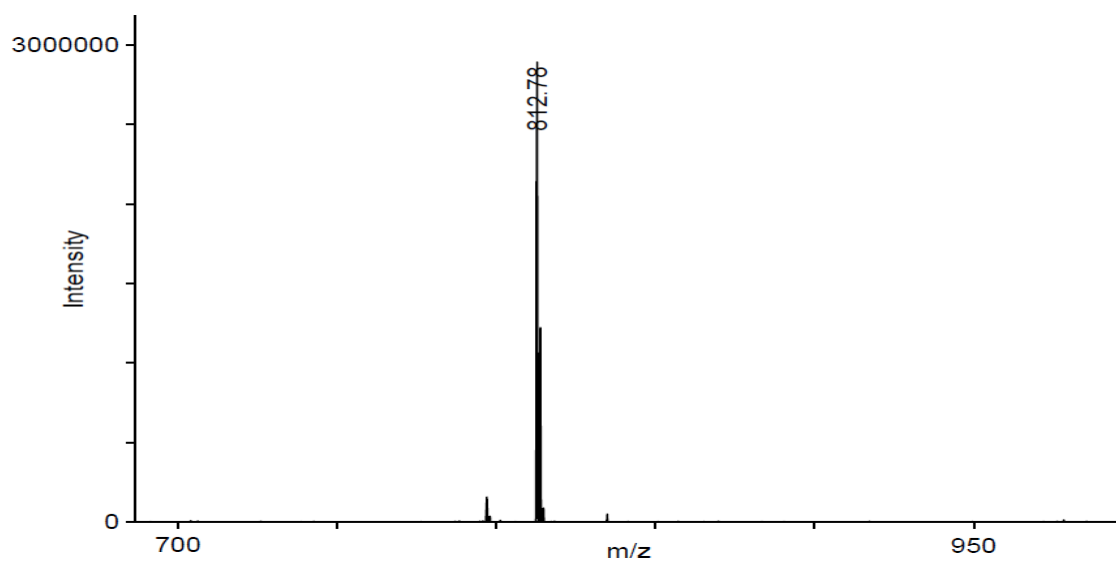
### 11 D-Val-D-Phe



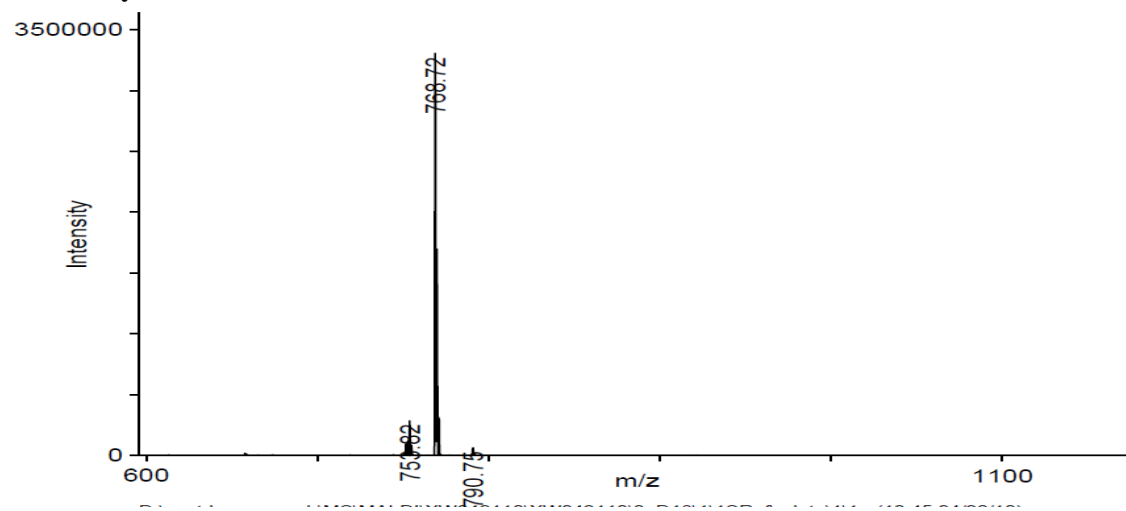
### 11 D-Val-Nle



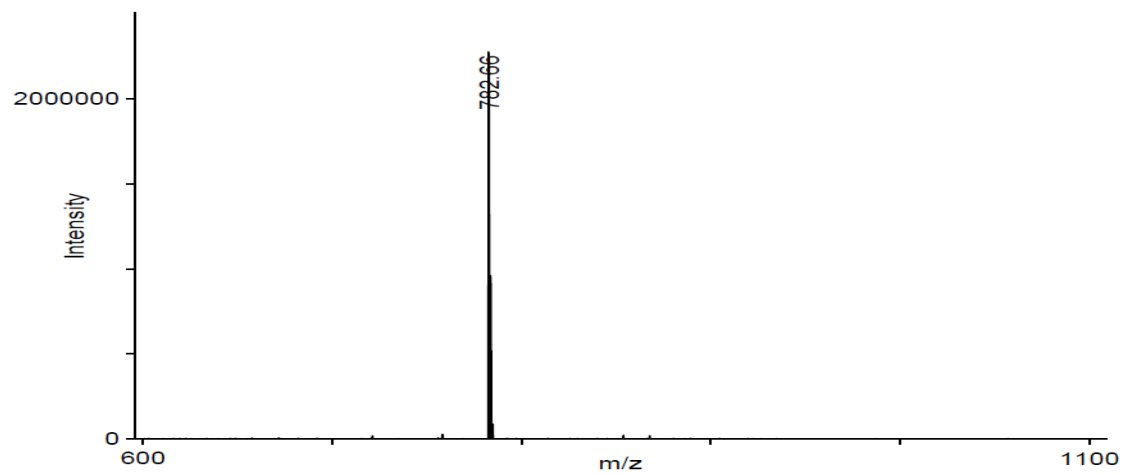
### 11 Pro-D-Thr



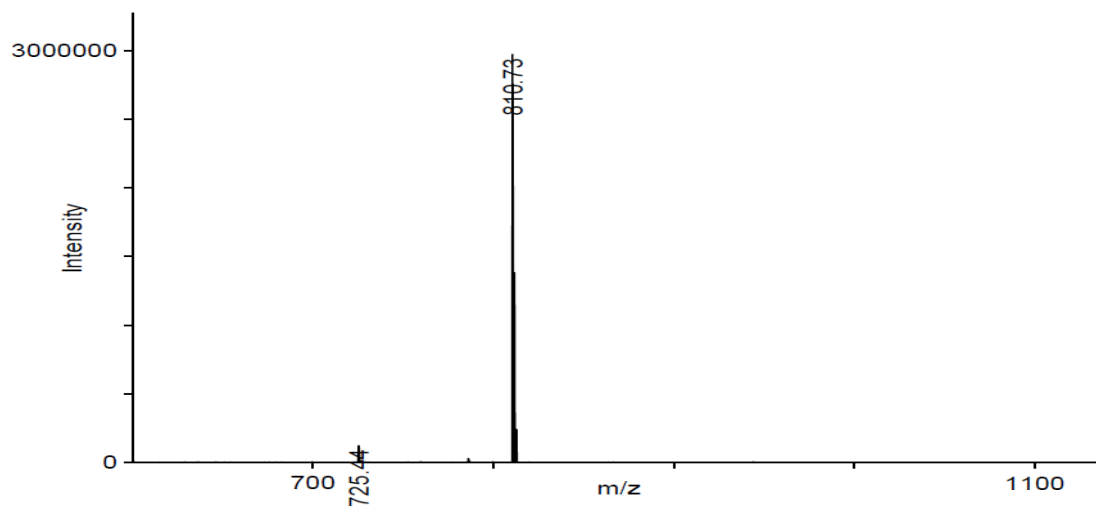
### 11 Pro-Gly



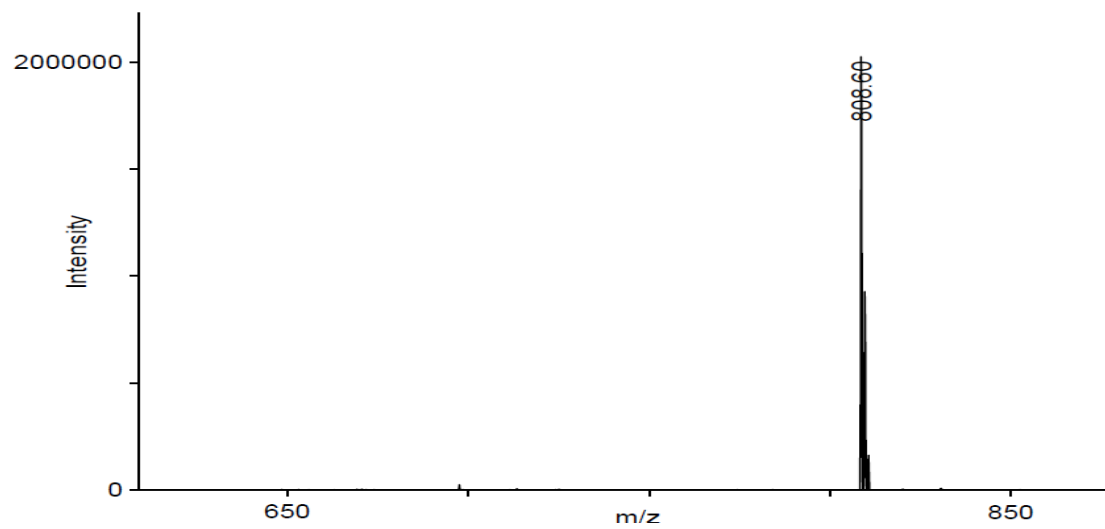
### 11 Pro-Ala



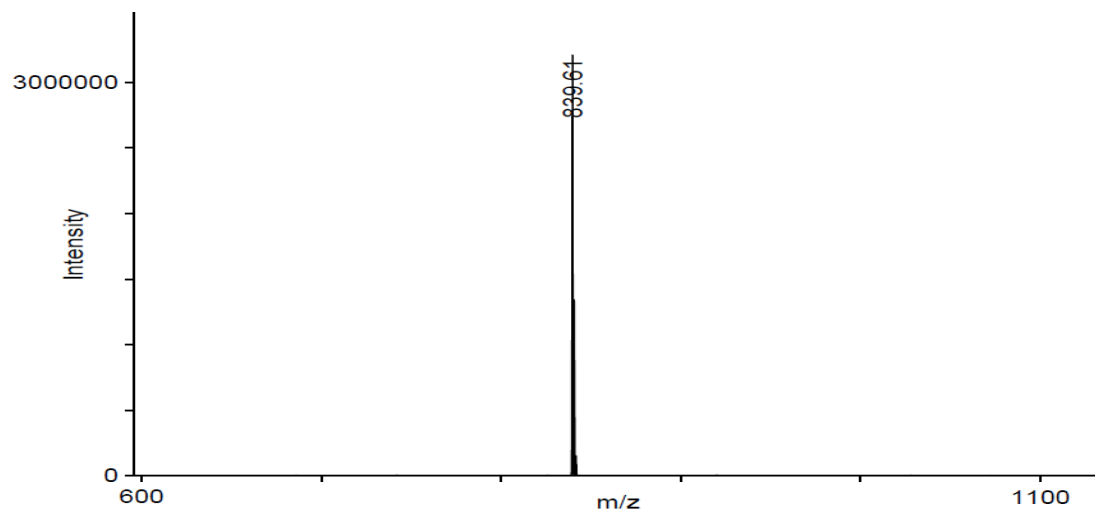
### 11 Pro-D-Val



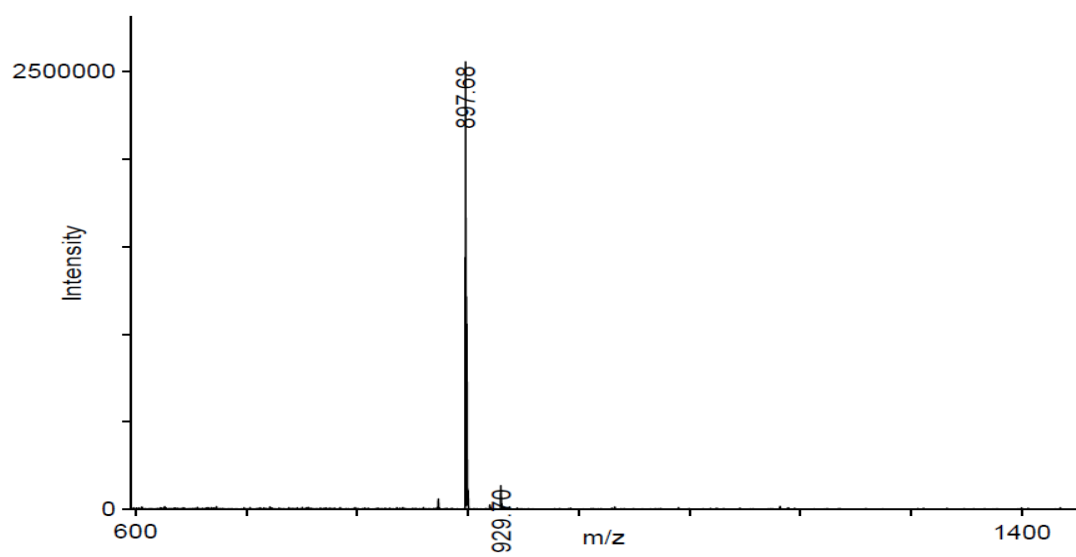
### 11 Pro-Pro



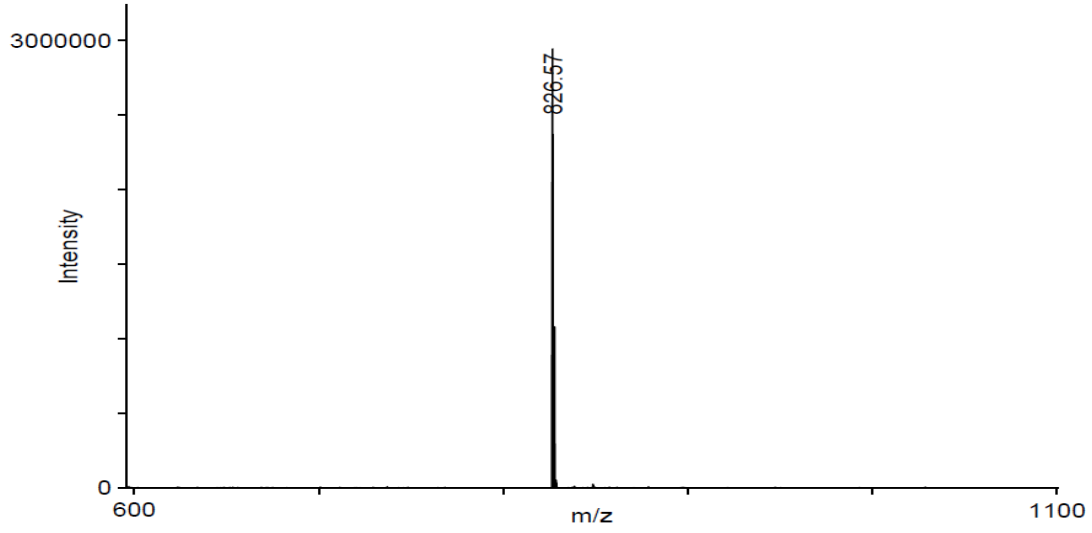
### 11 Pro-Lys



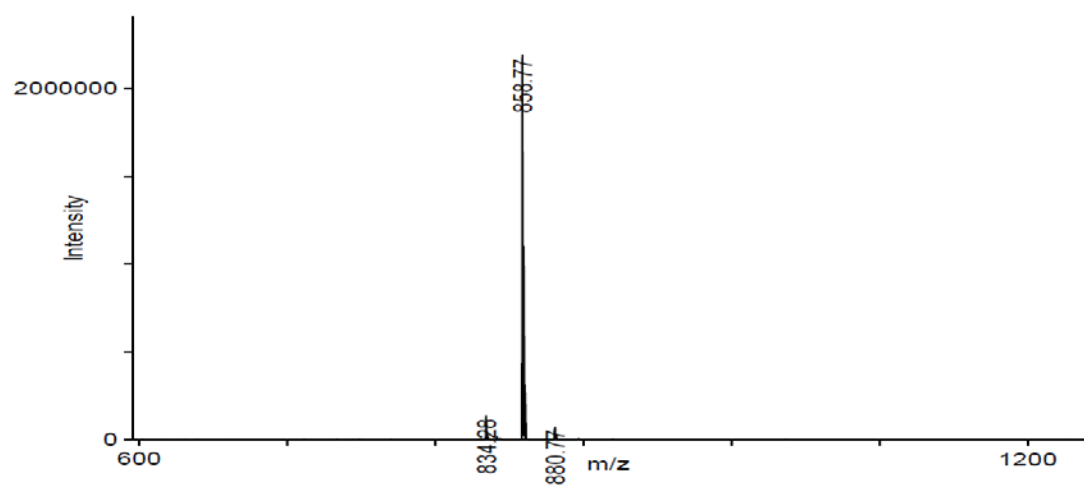
### 11 Pro-Trp



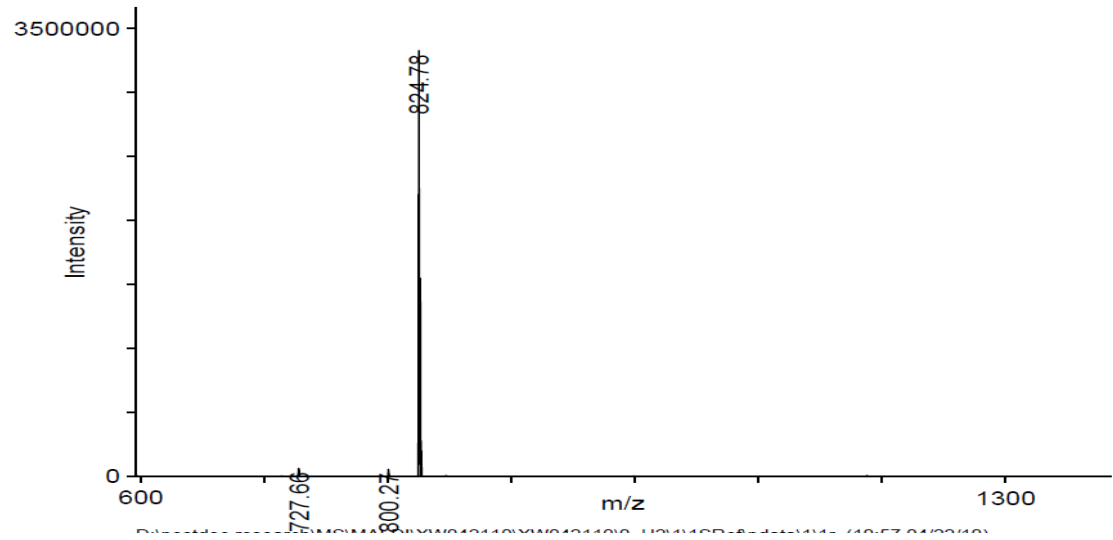
### 11 Pro-Asp



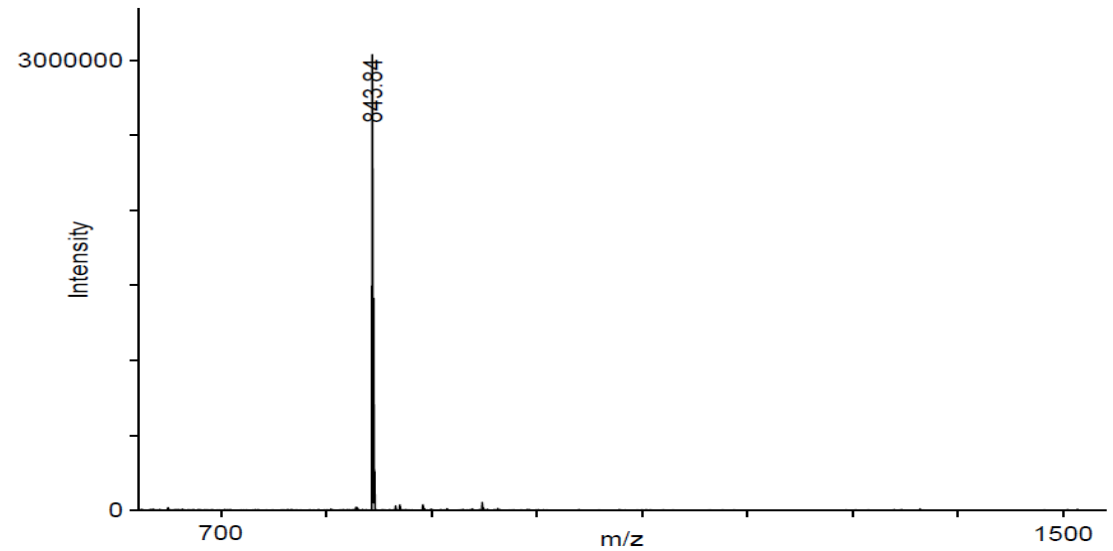
### 11 Pro-D-Phe



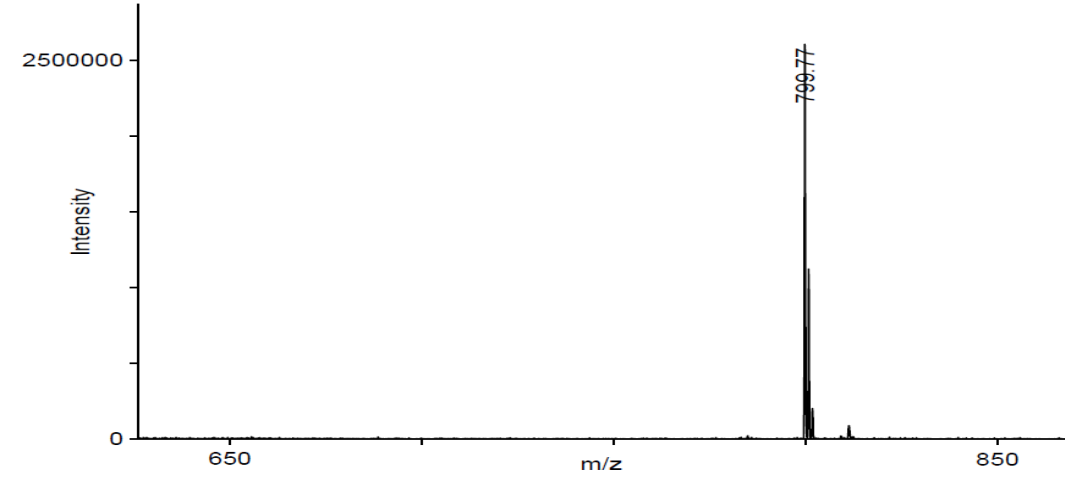
### 11 Pro-Nle



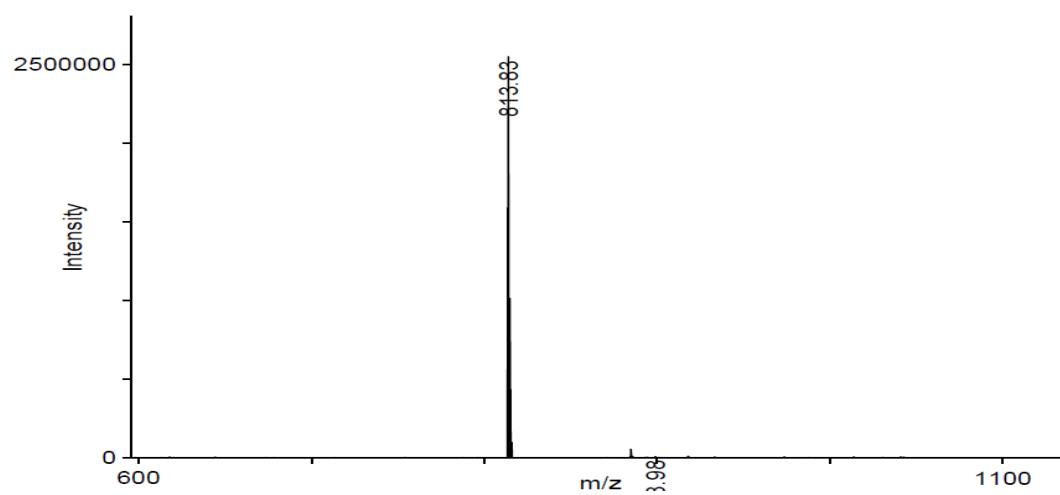
### 11 Lys-D-Thr



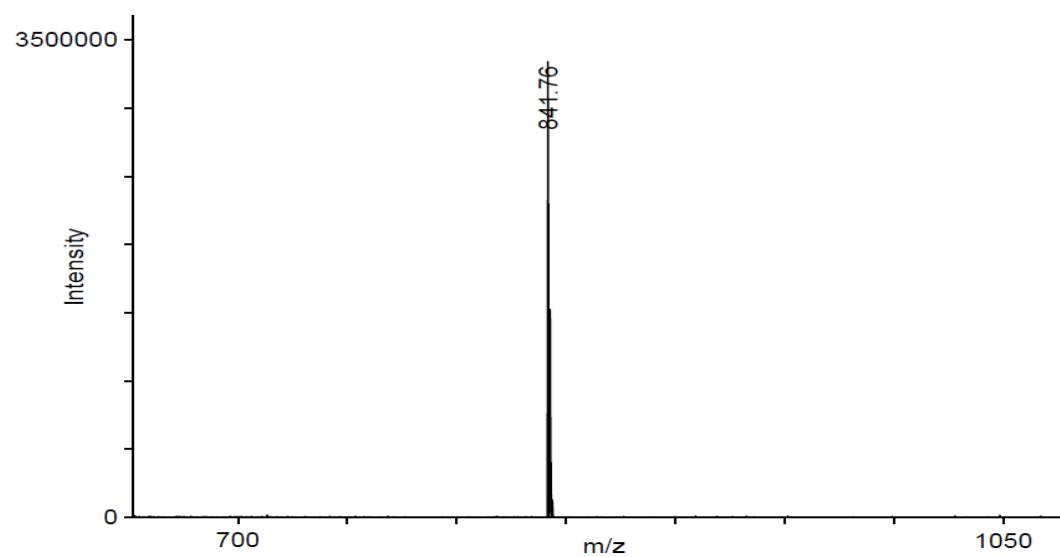
### 11 Lys-Gly



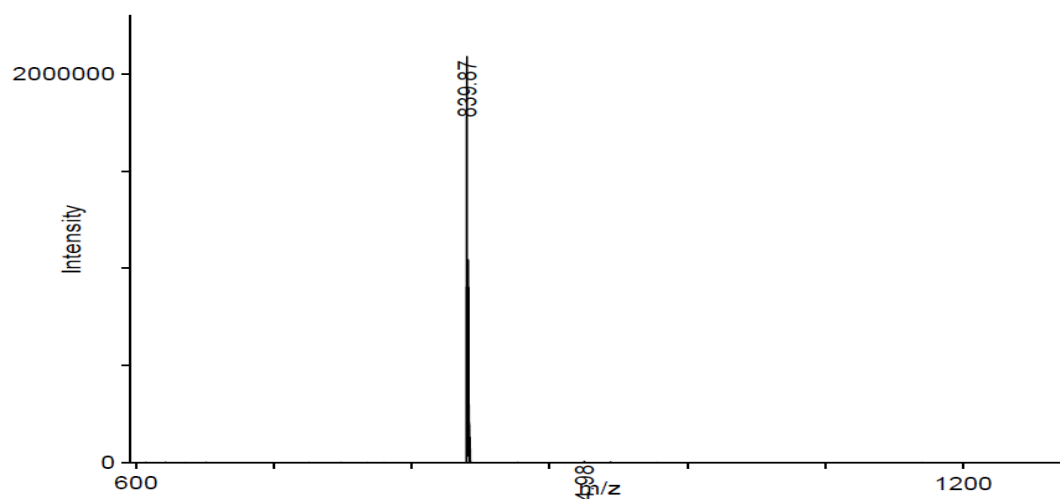
### 11 Lys-Ala



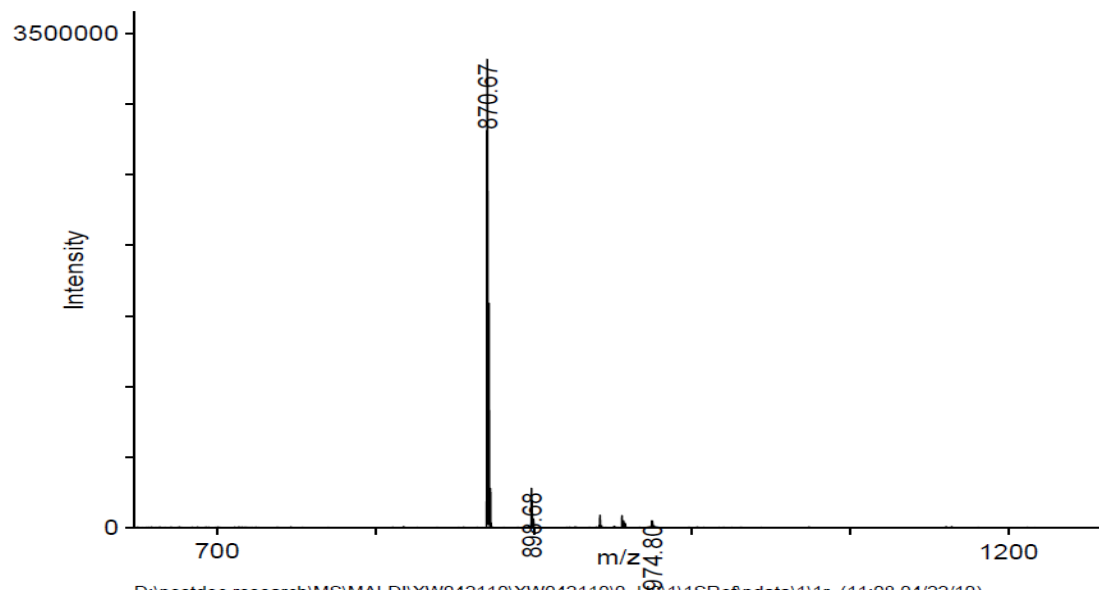
### 11 Lys-D-Val



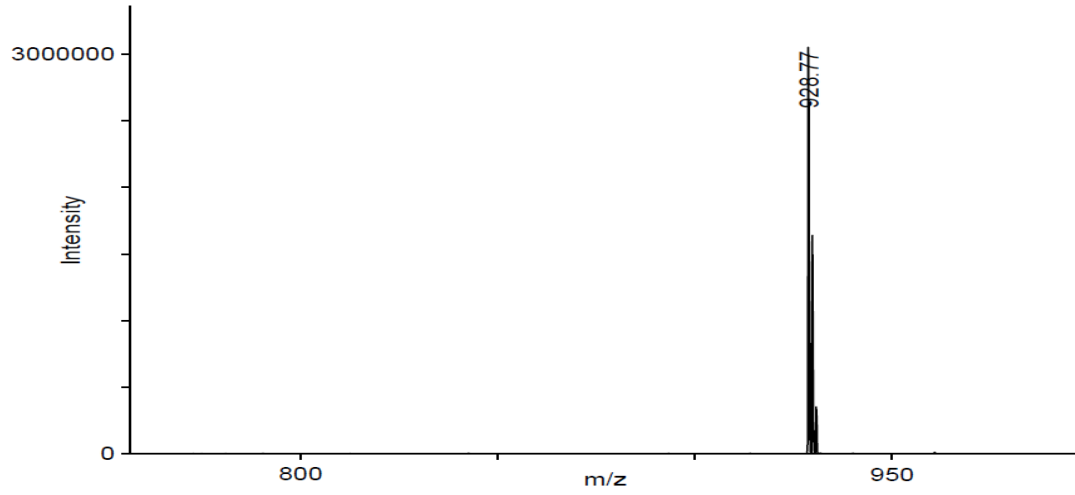
### 11 Lys-Pro



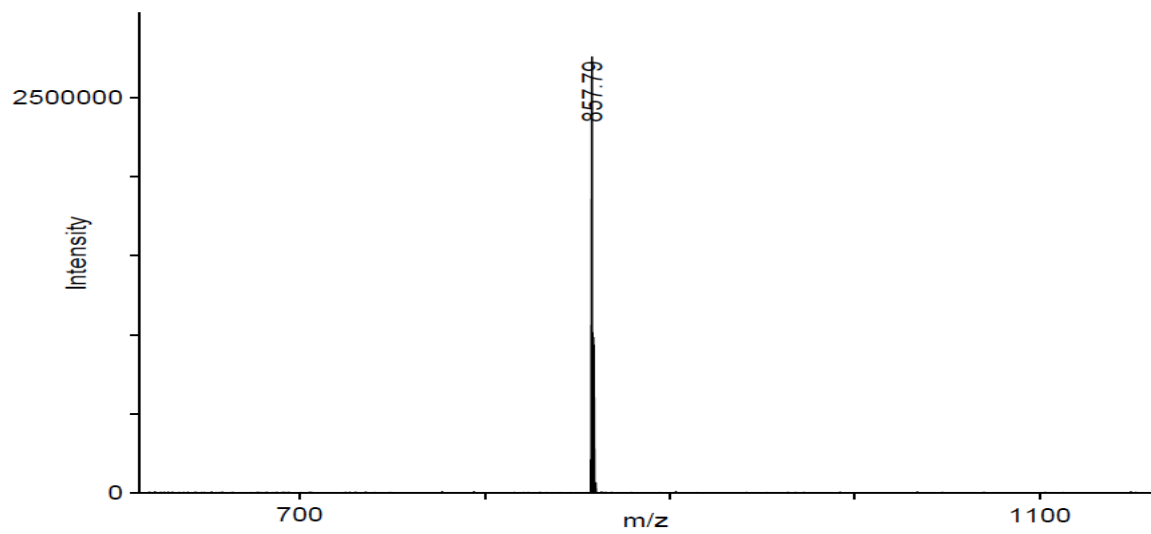
### 11 Lys-Lys



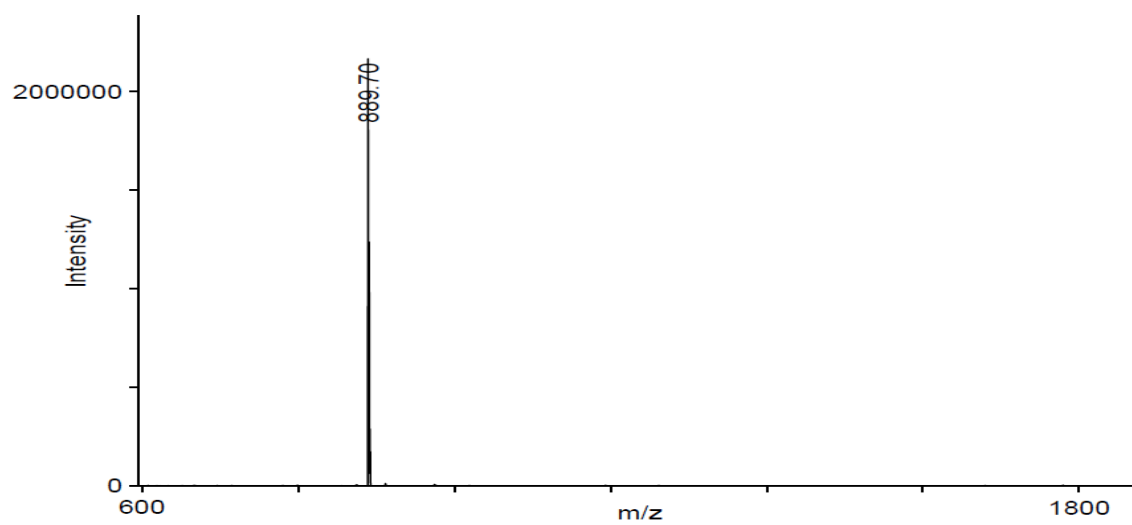
### 11 Lys-Trp



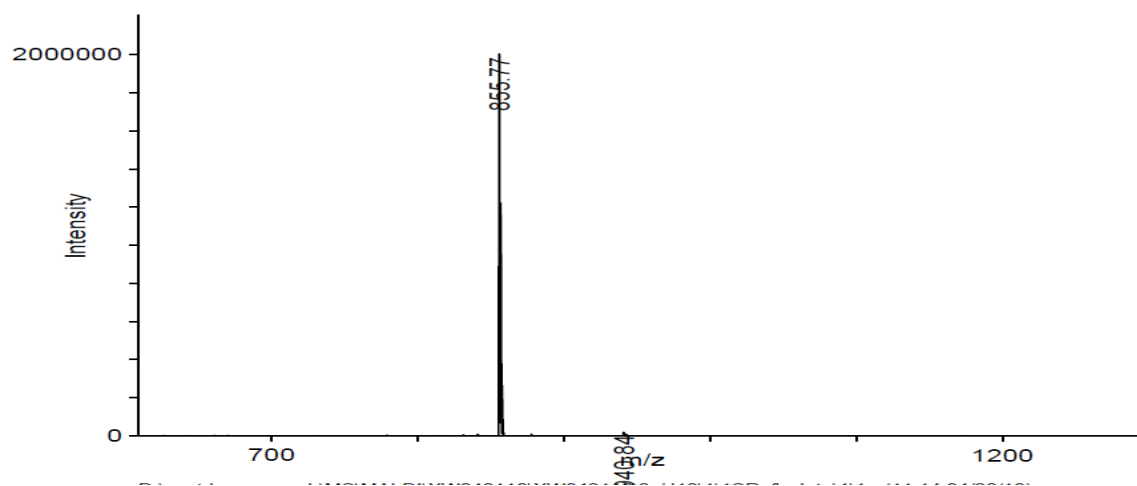
### 11 Lys-Asp



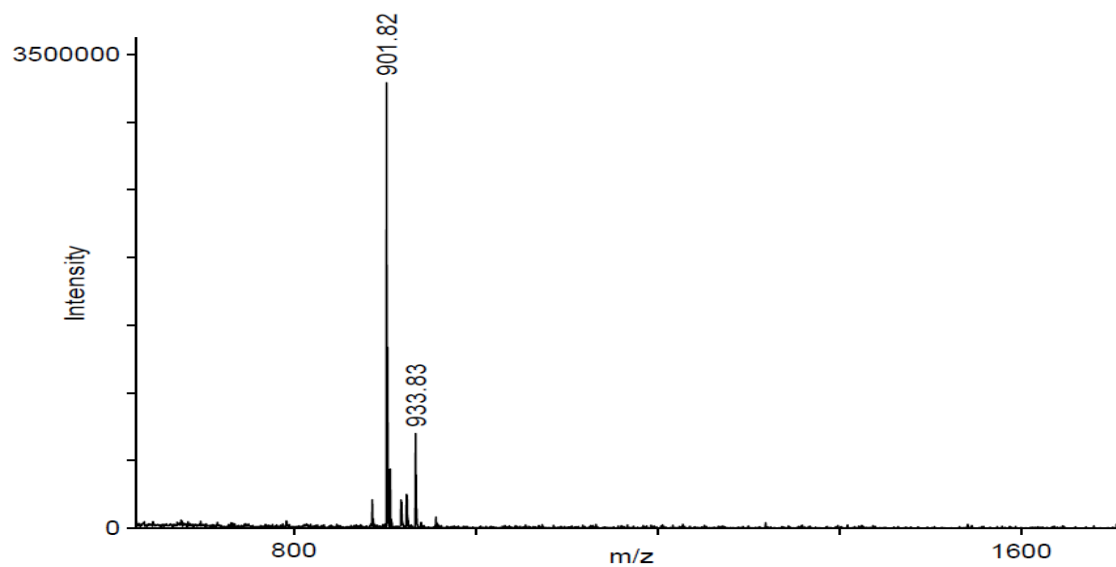
### 11 Lys-D-Phe



### 11 Lys-Nle

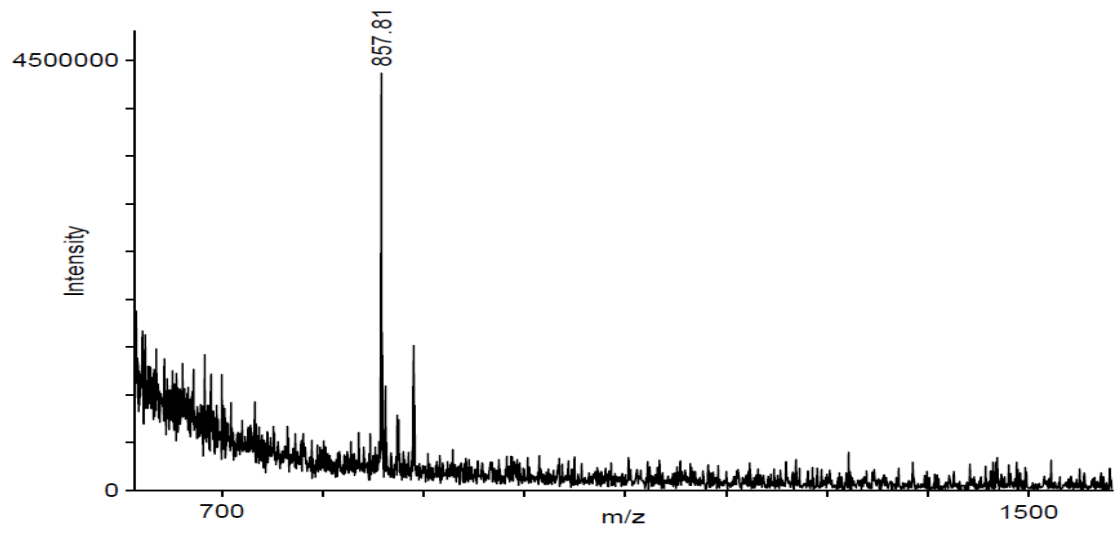


### 11 Trp-D-Thr

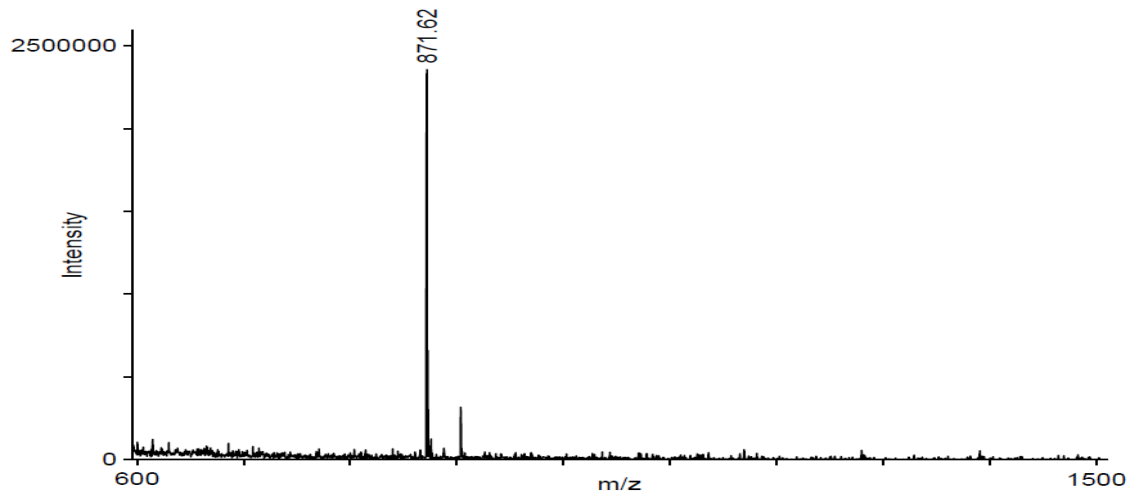




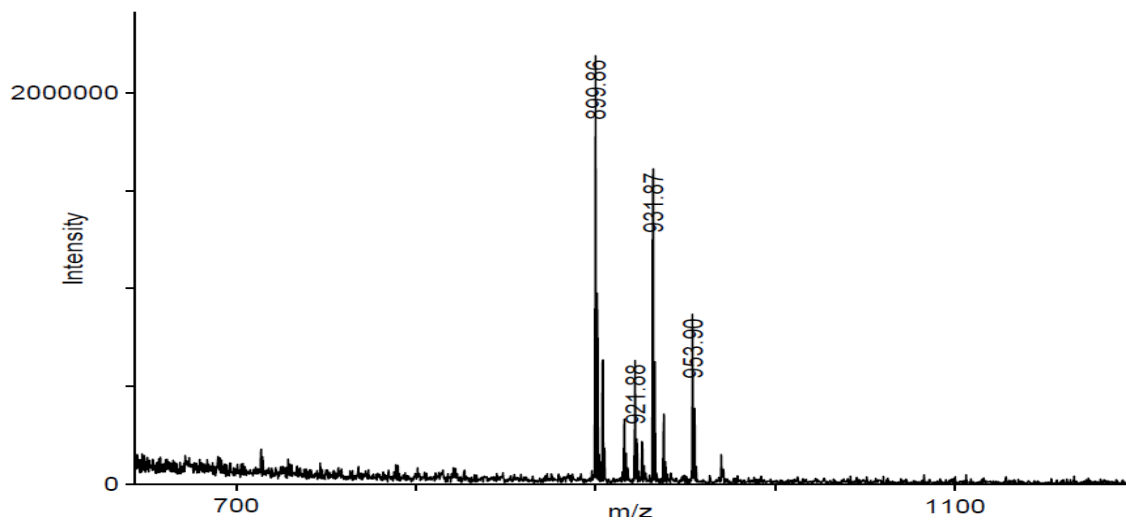
### 11 Trp-Gly



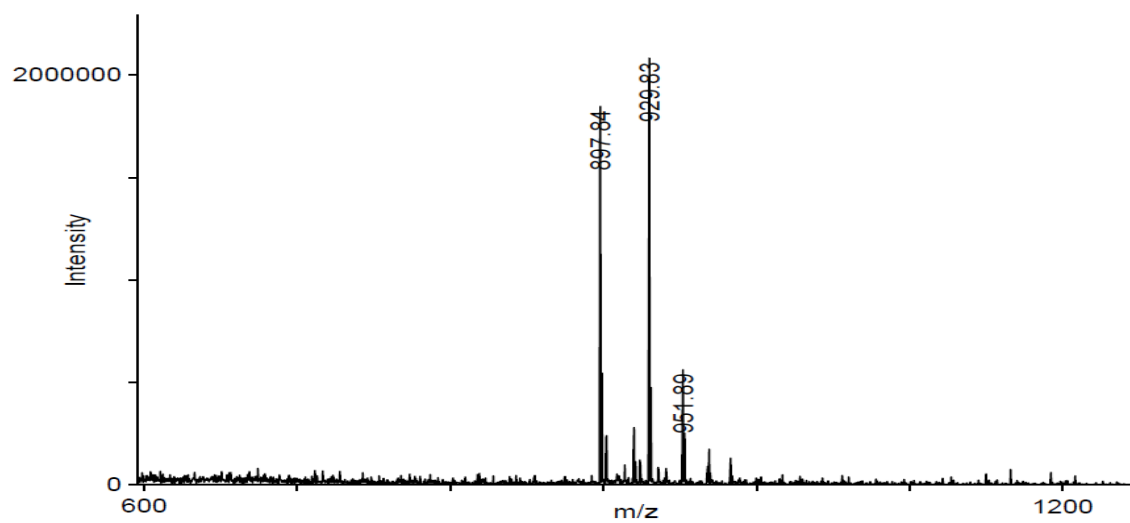
### 11 Trp-Ala



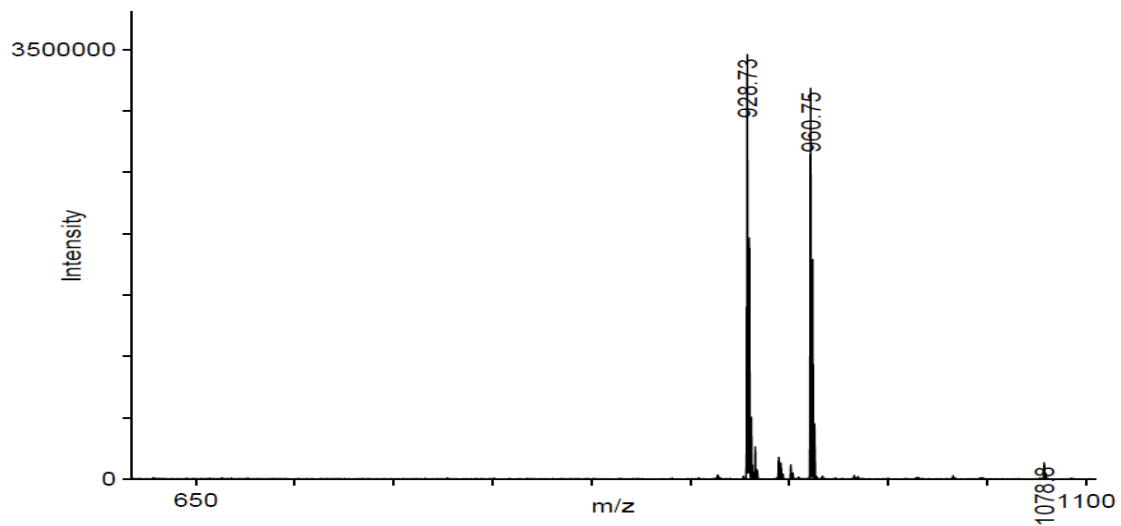
### 11 Trp-D-Val



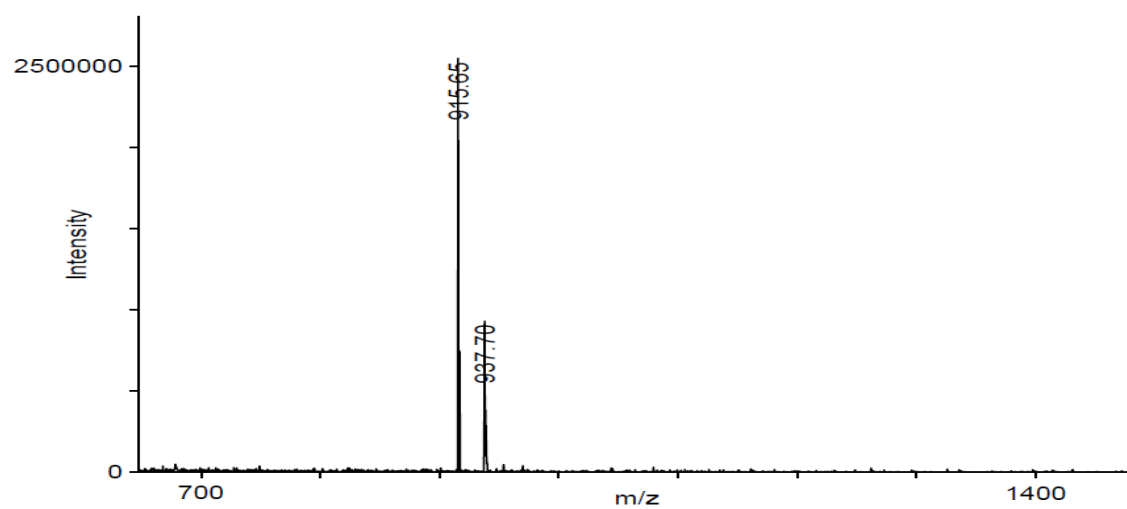
### 11 Trp-Pro



### 11 Trp-Lys



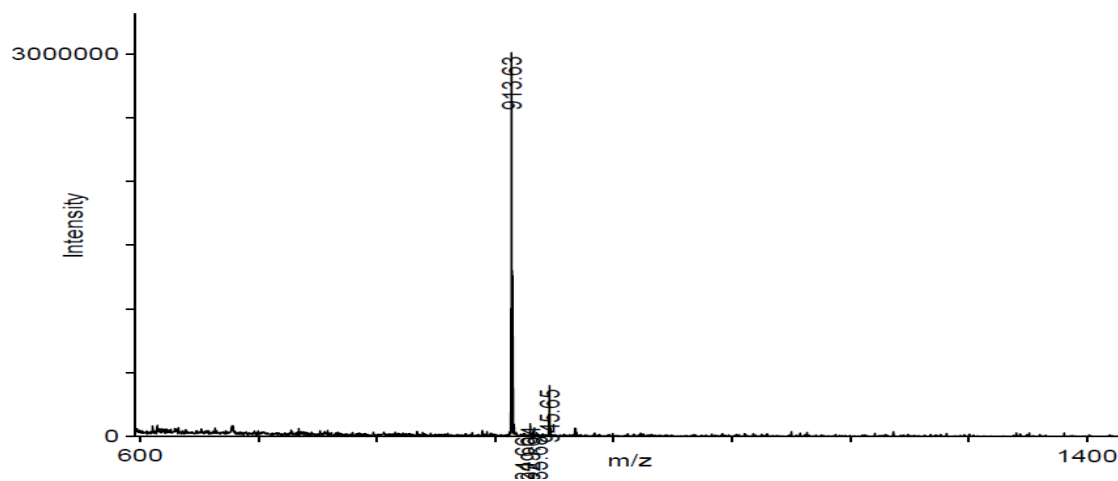
### 11 Trp-Asp



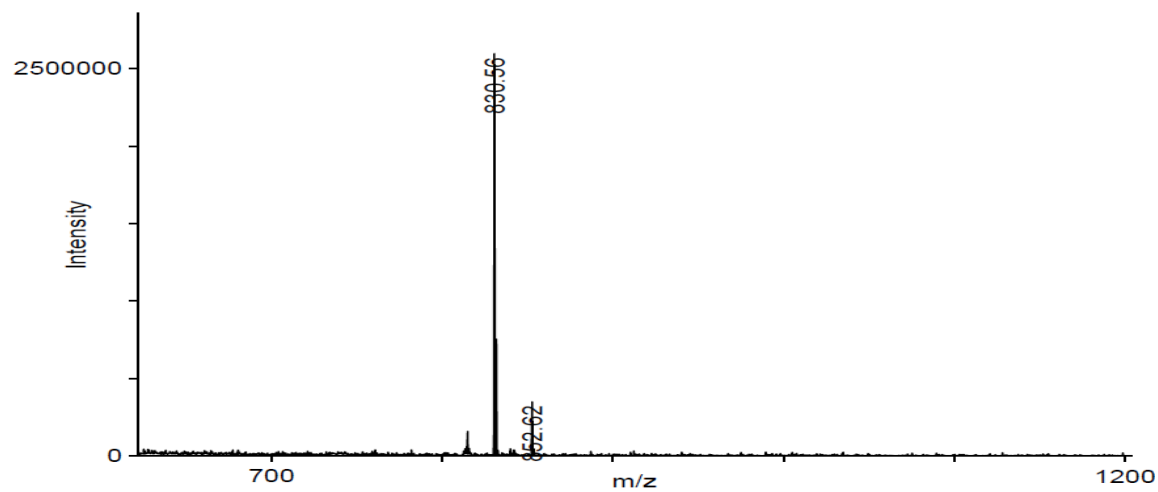
### 11 Trp-D-Phe



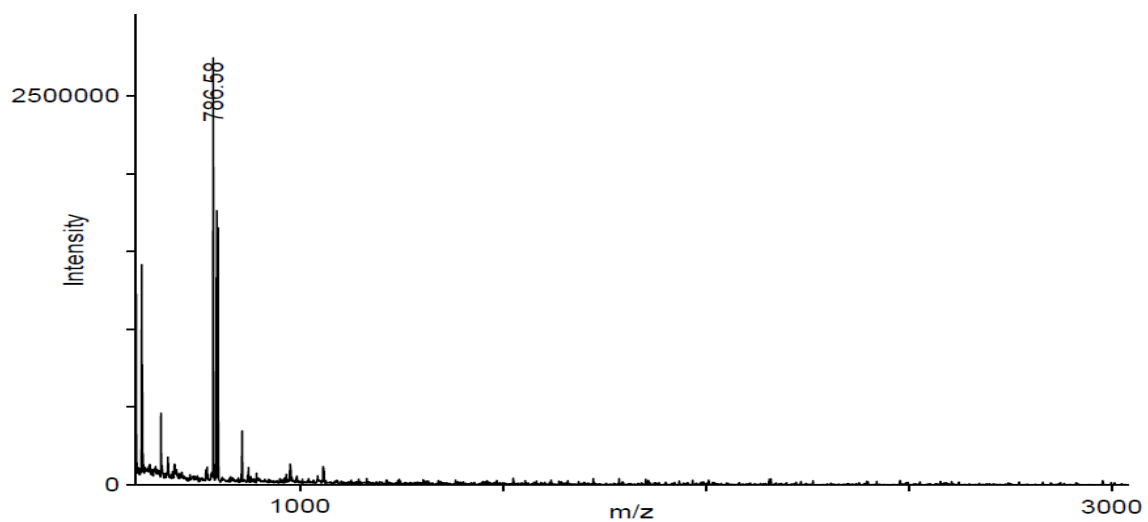
### 11 Trp-Nle



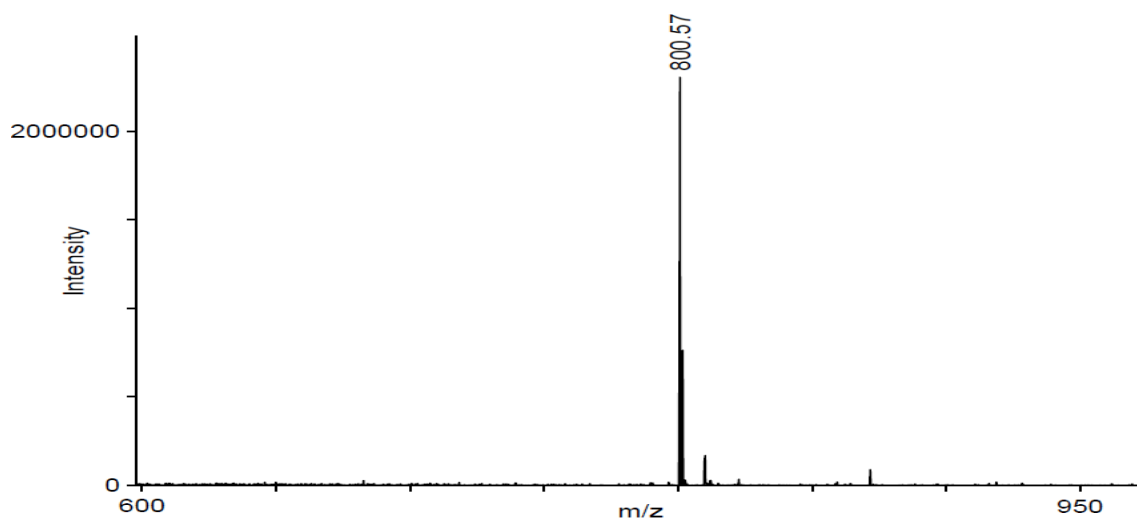
### 11 Asp-D-Thr



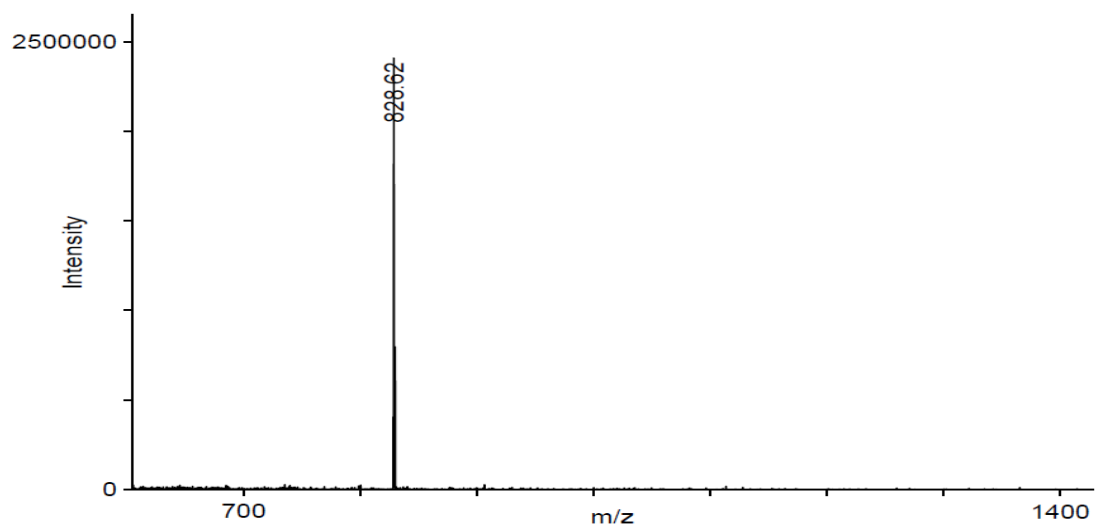
### 11 Asp-Gly



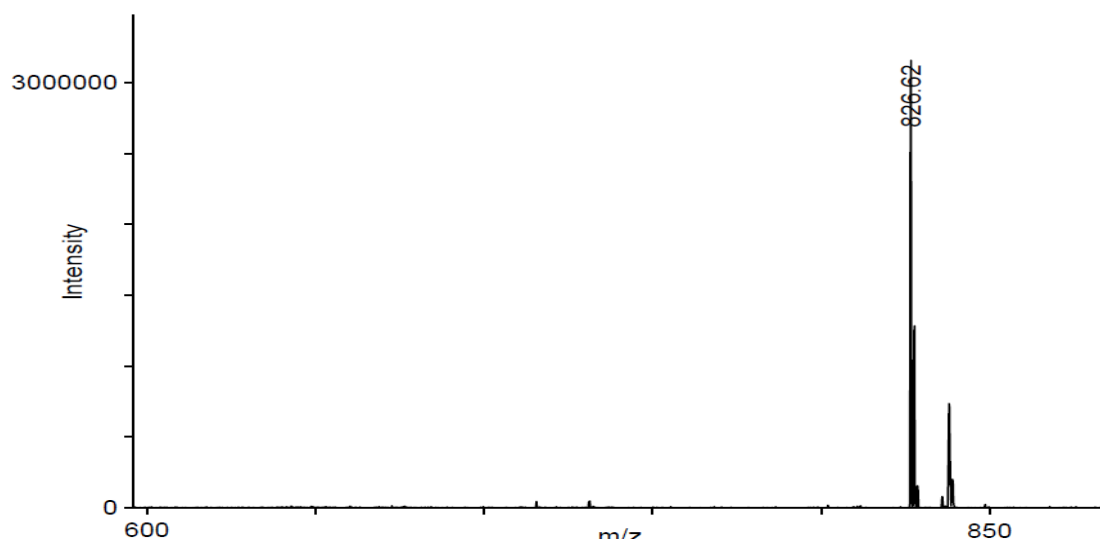
### 11 Asp-Ala



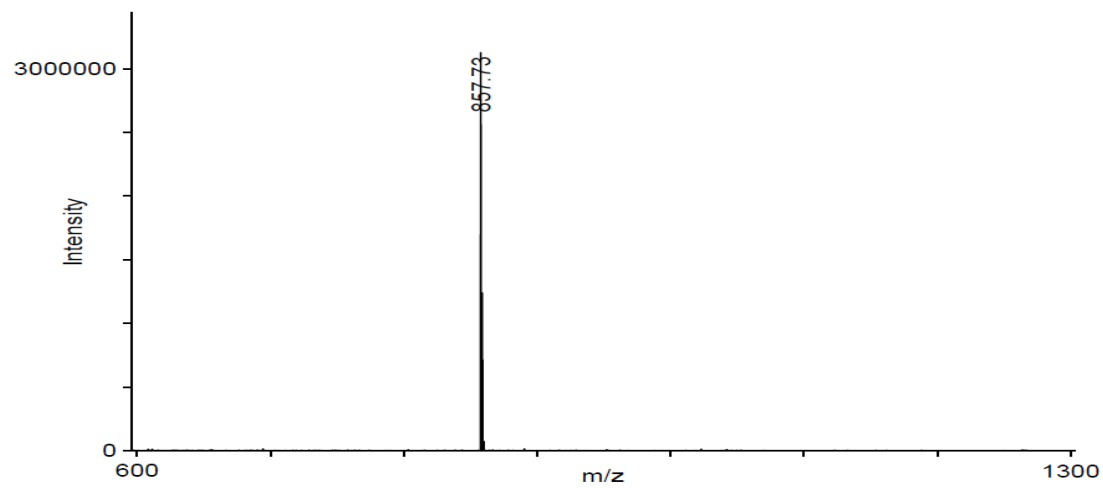
### 11 Asp-D-Val



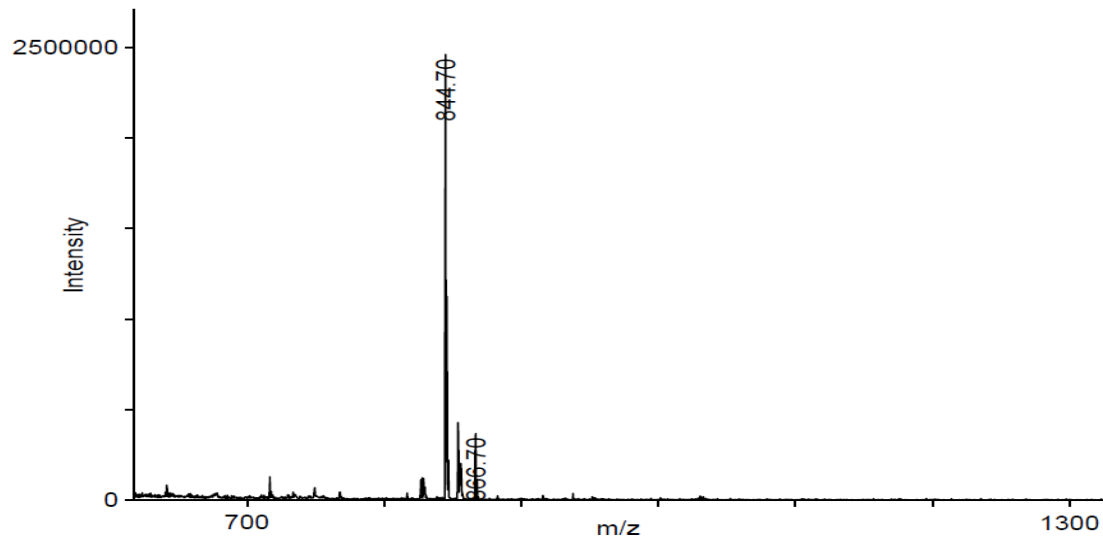
### 11 Asp-Pro



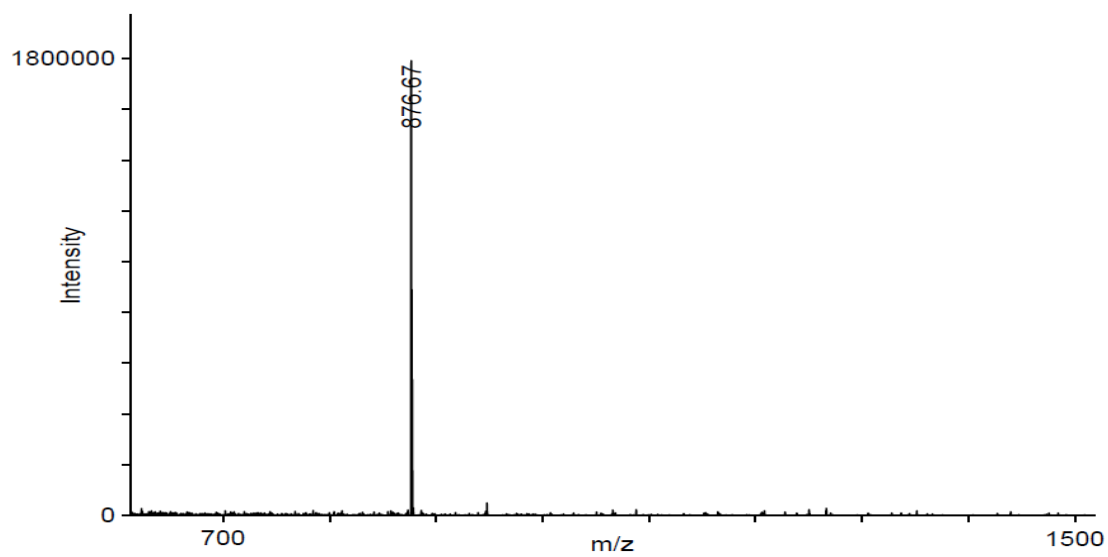
### 11 Asp-Lys



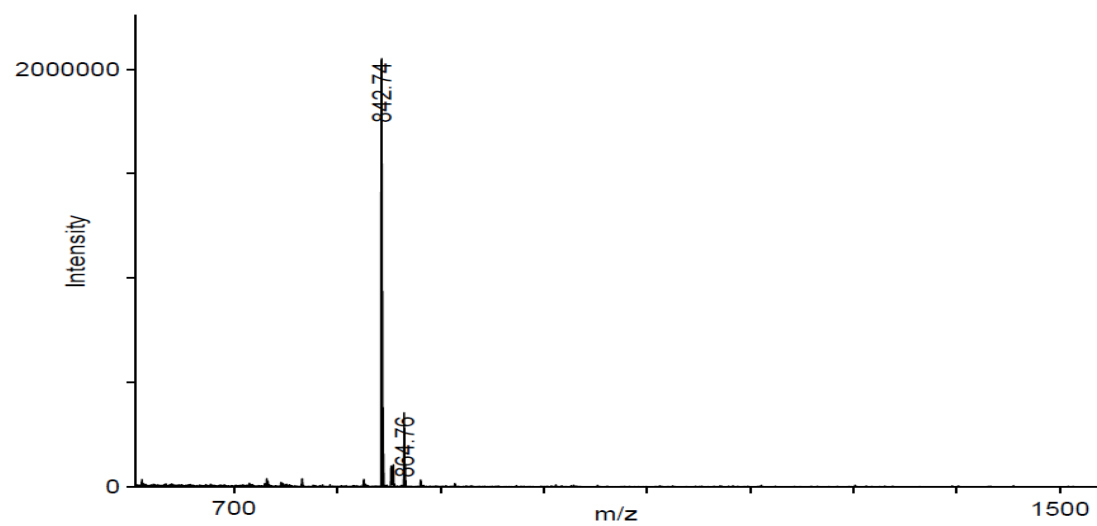
### 11 Asp-Asp



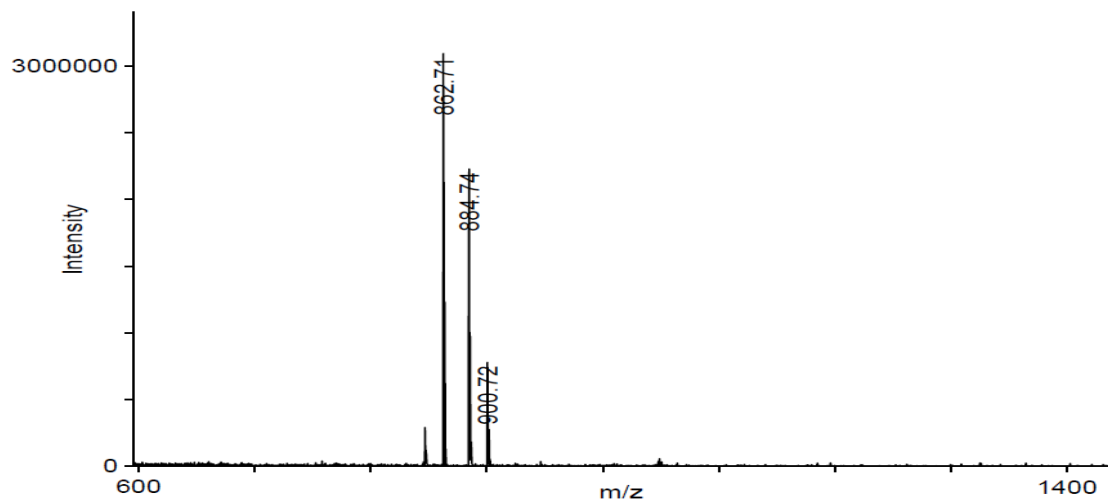
### 11 Asp-D-Phe



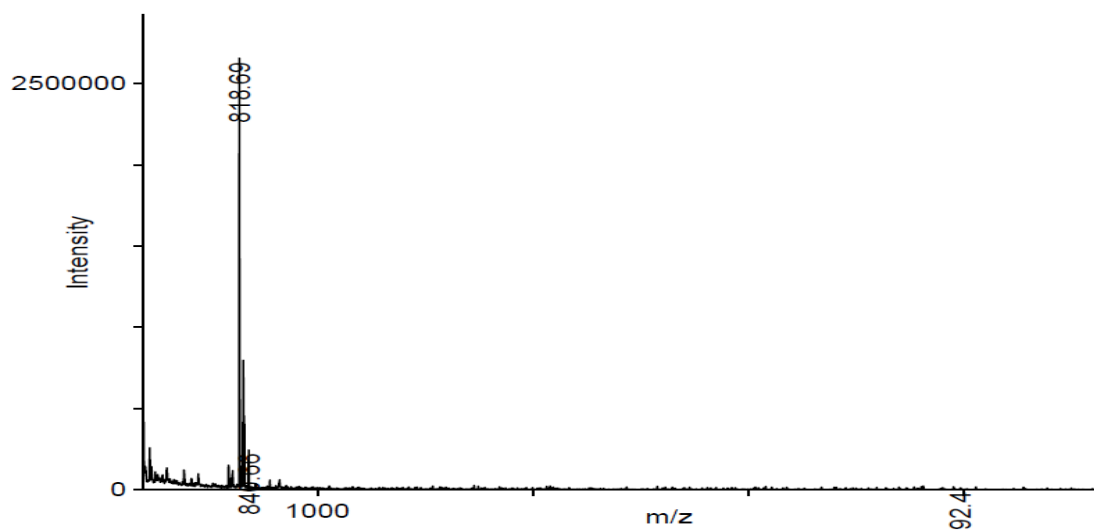
### 11 Asp-Nle



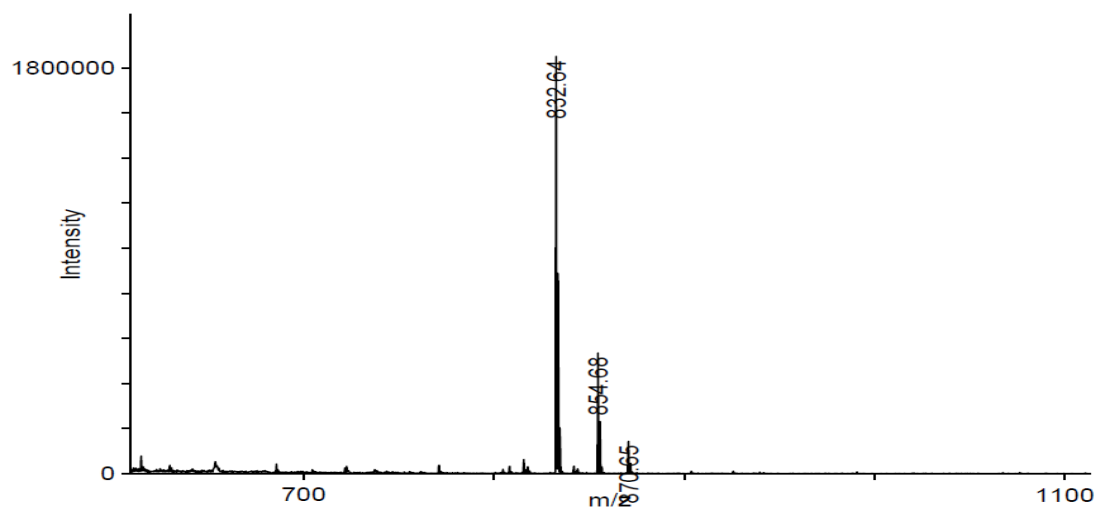
### 11 D-Phe-D-Thr



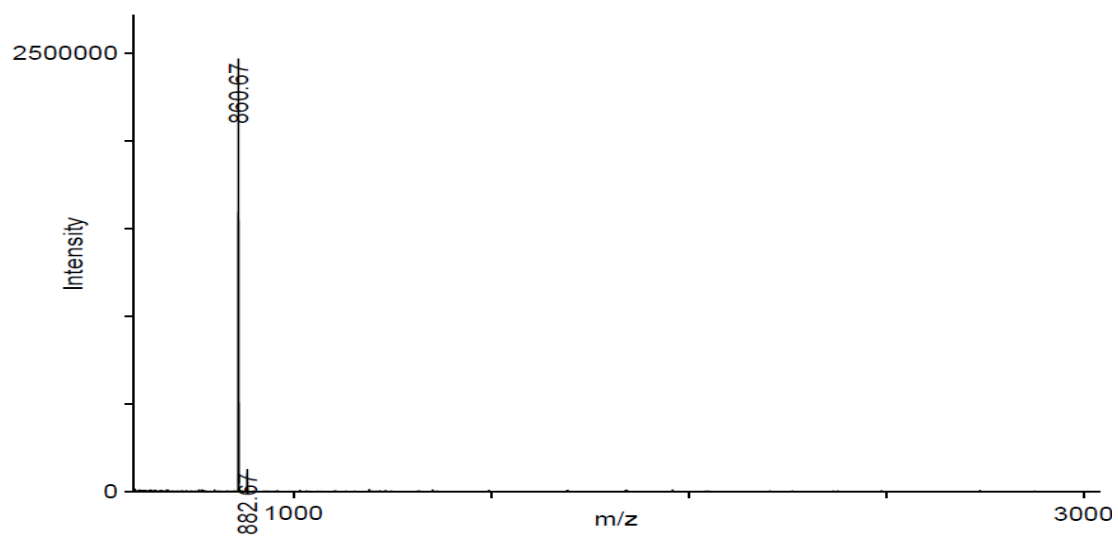
### 11 D-Phe-Gly



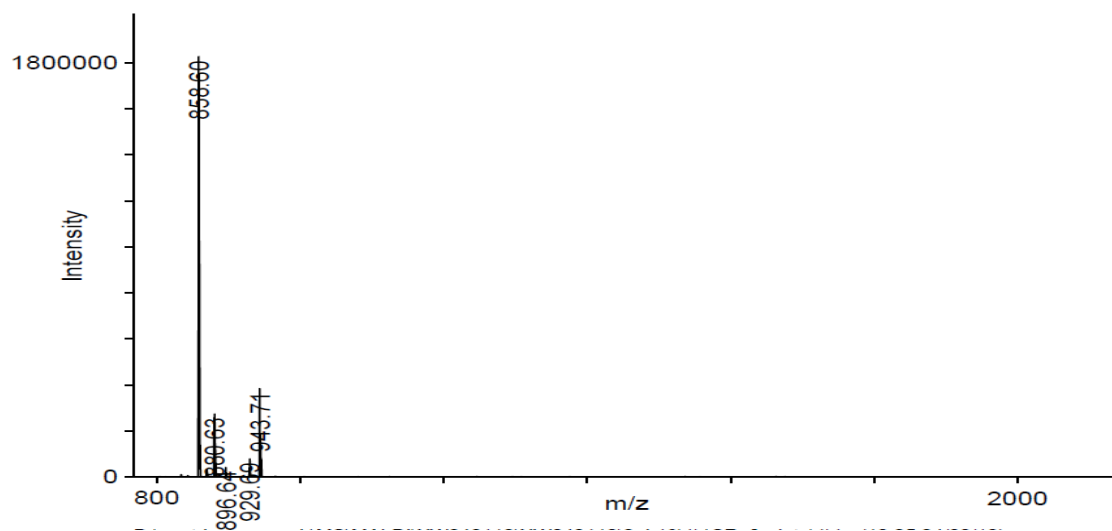
### 11 D-Phe-Ala



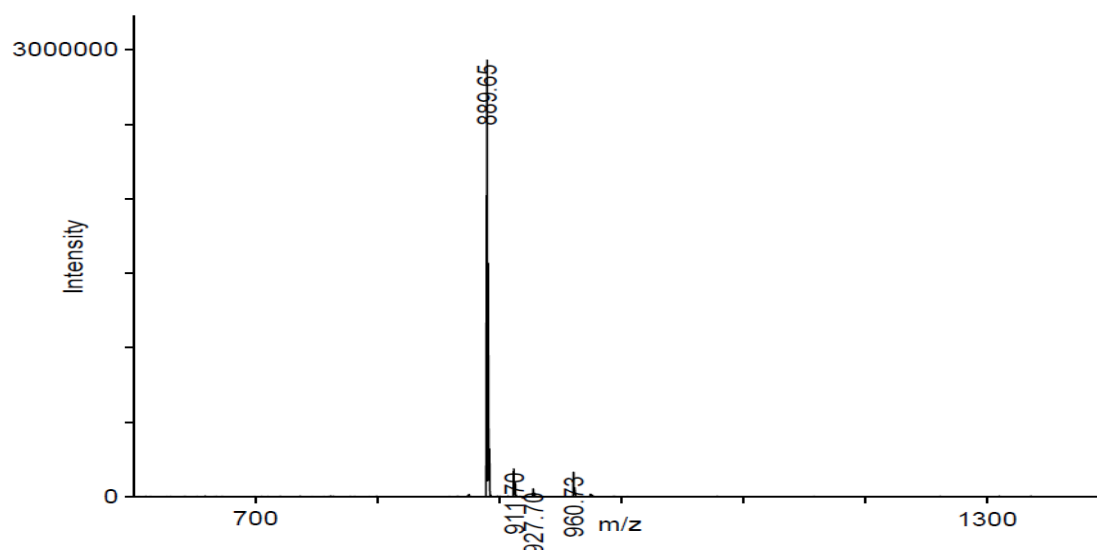
### 11 D-Phe-D-Val



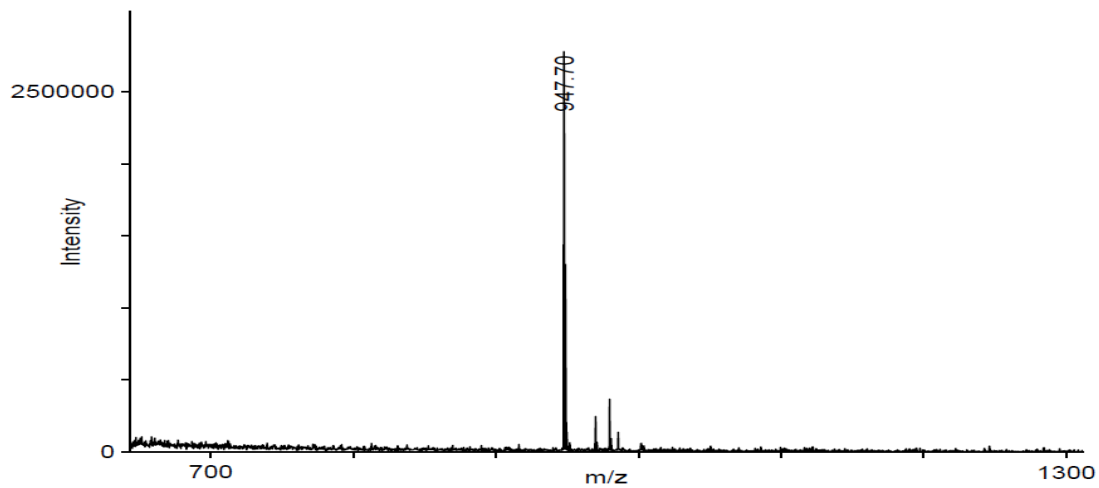
### 11 D-Phe-Pro



### 11 D-Phe-Lys

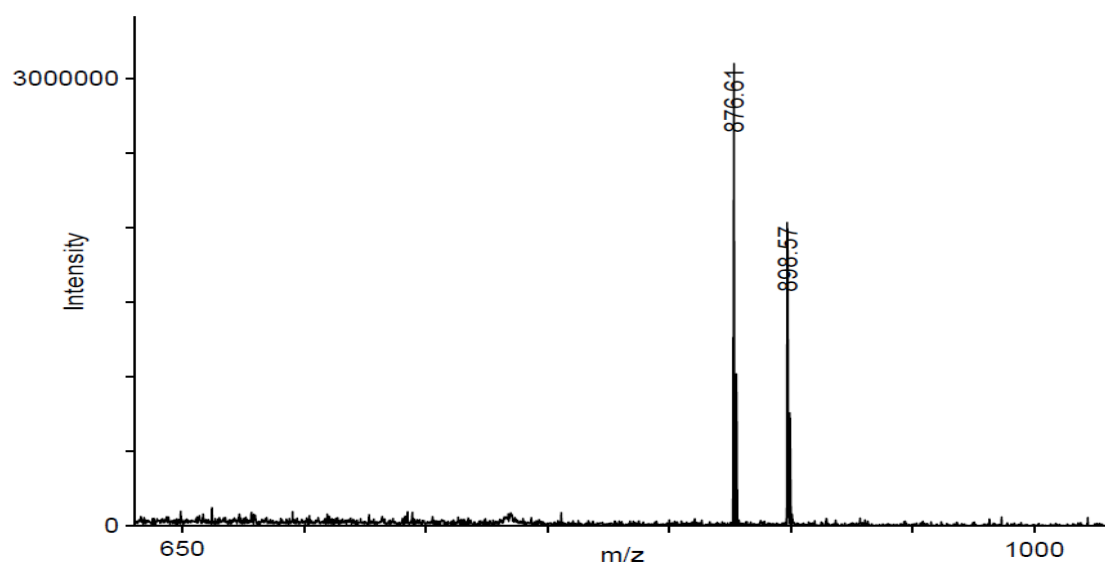


### 11 D-Phe-Trp

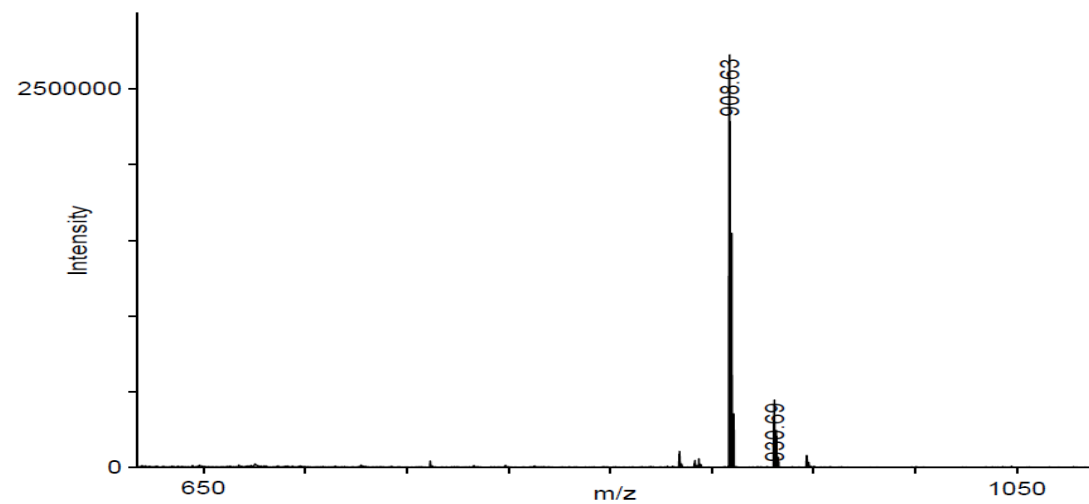




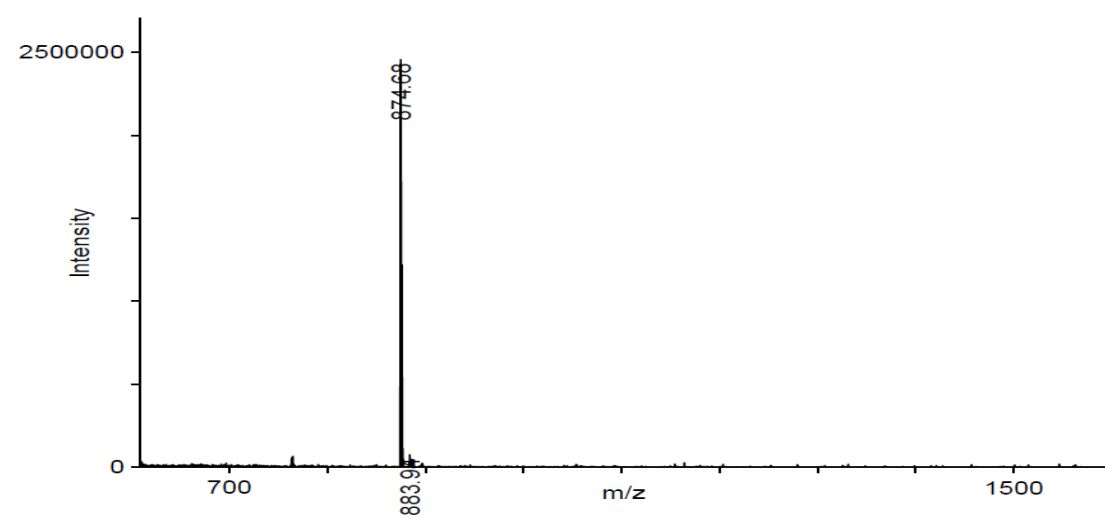
### 11 D-Phe-Asp



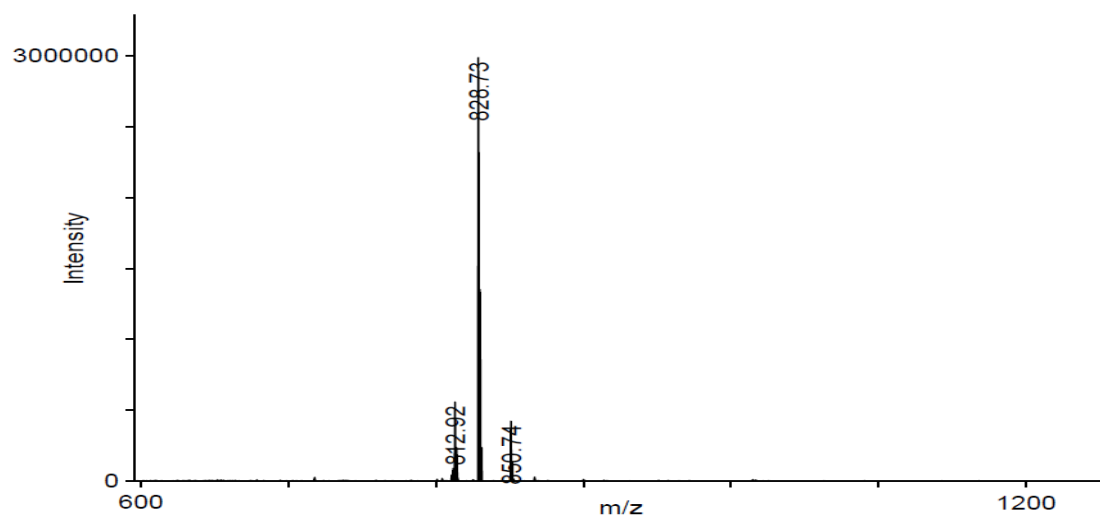
### 11 D-Phe-D-Phe



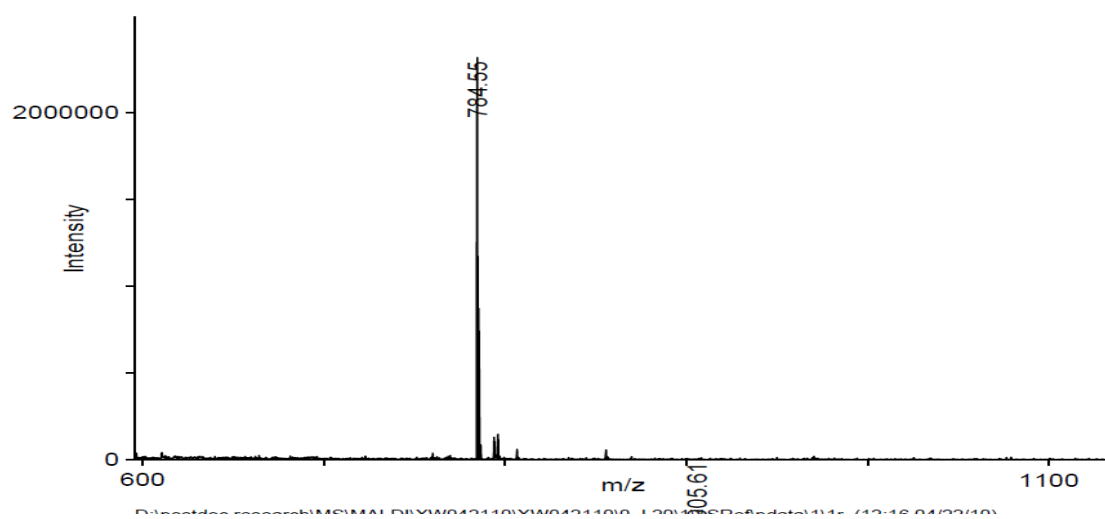
### 11 D-Phe-Nle



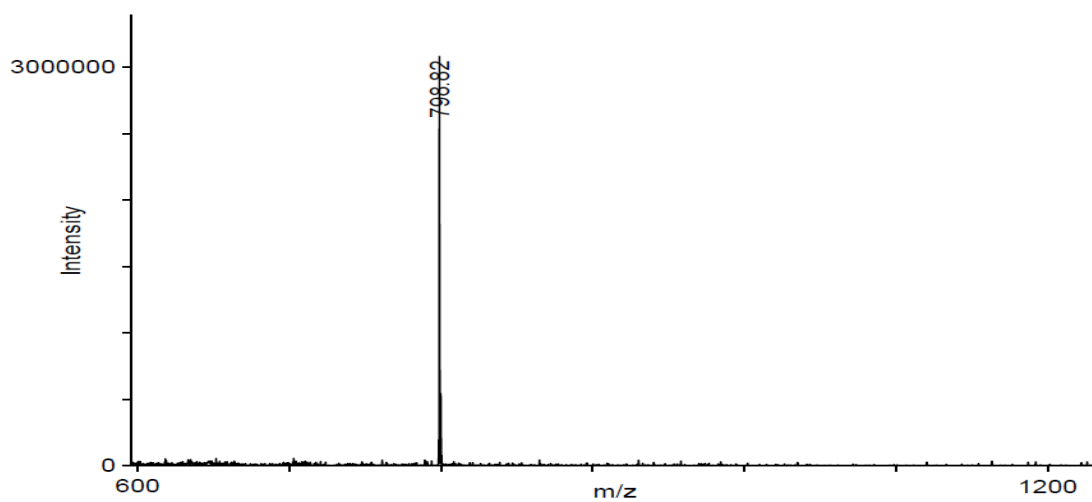
### 11 Nle-D-Thr



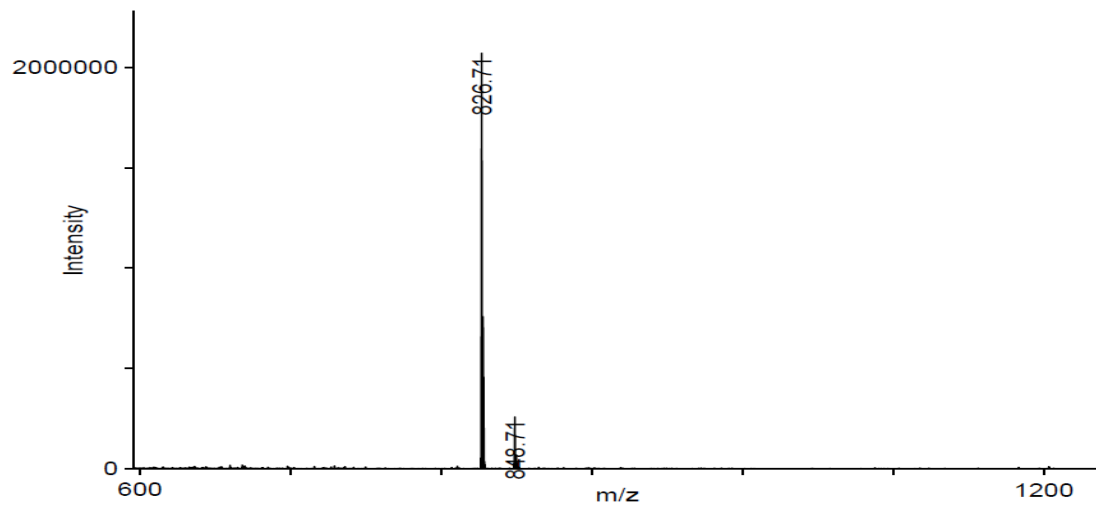
### 11 Nle-Gly



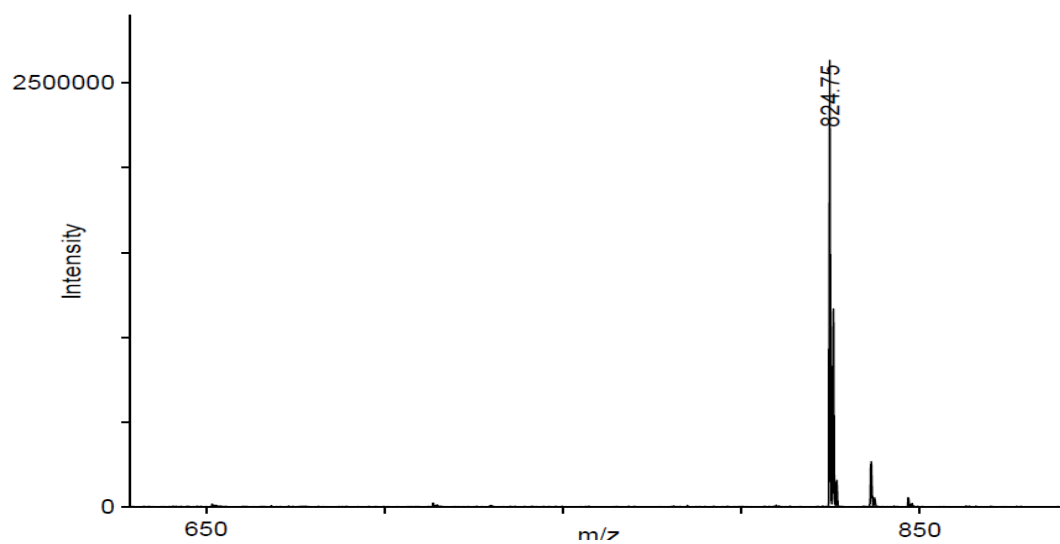
### 11 Nle-Ala



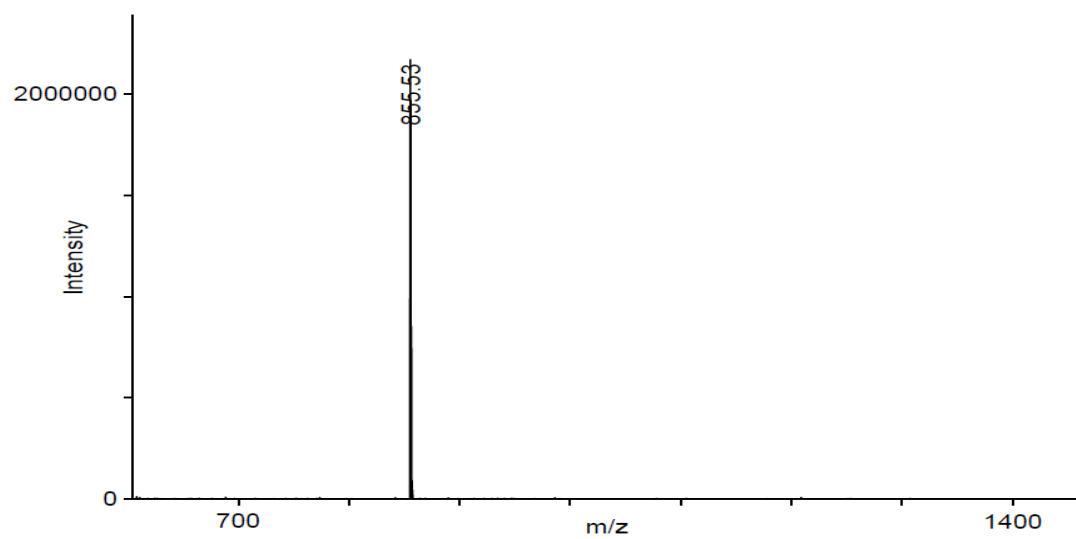
### 11 Nle-D-Val



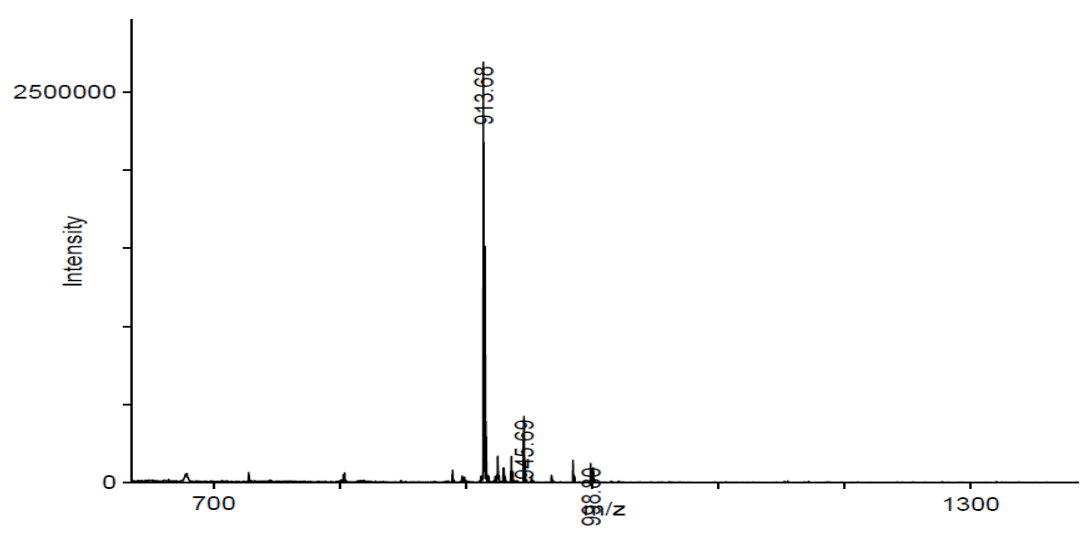
### 11 Nle-Pro



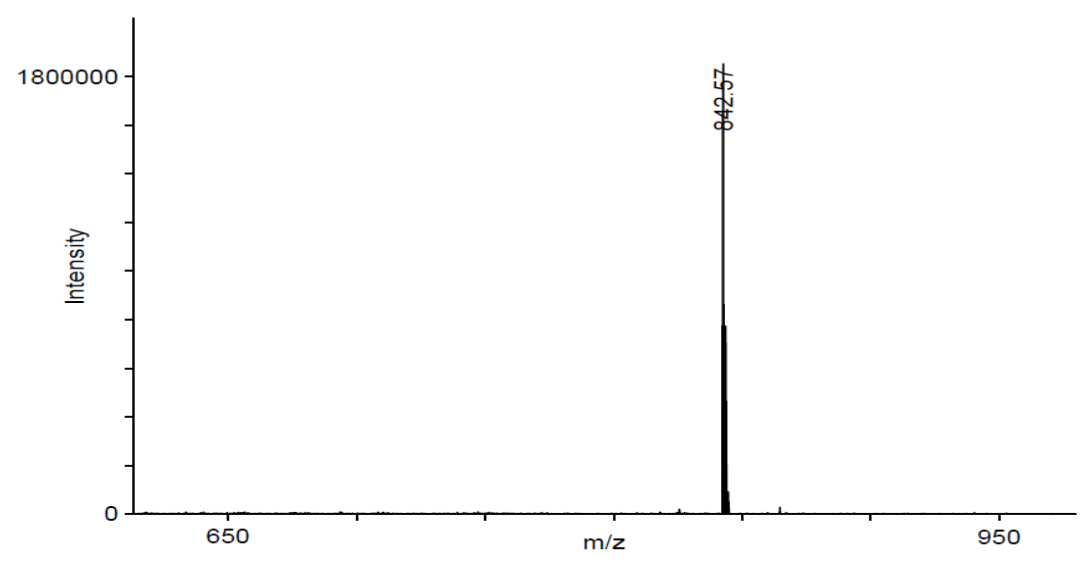
### 11 Nle-Lys



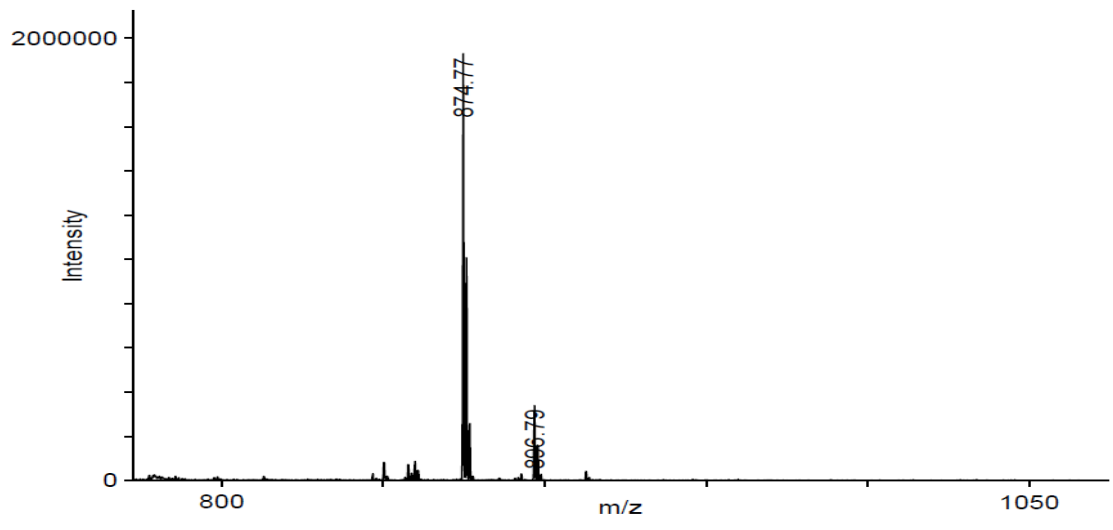
### 11 Nle-Trp



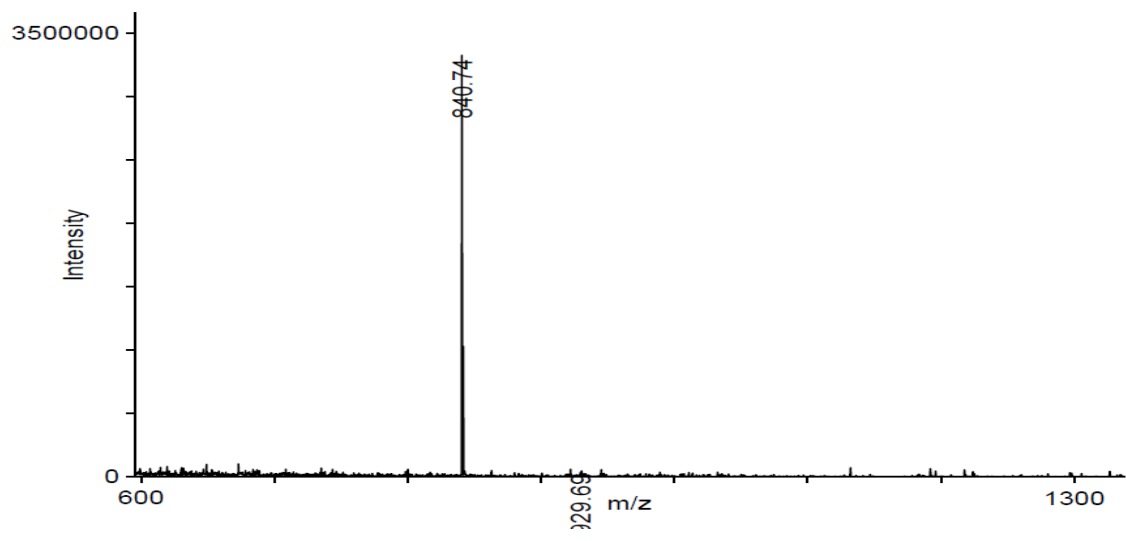
### 11 Nle-Asp



### 11 Nle-D-Phe

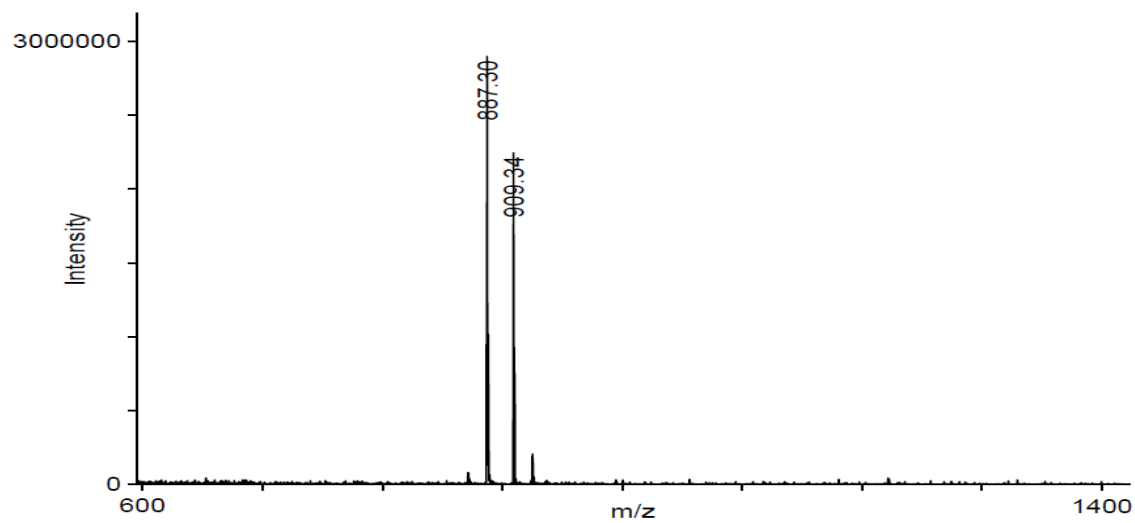


11 Nle-Nle

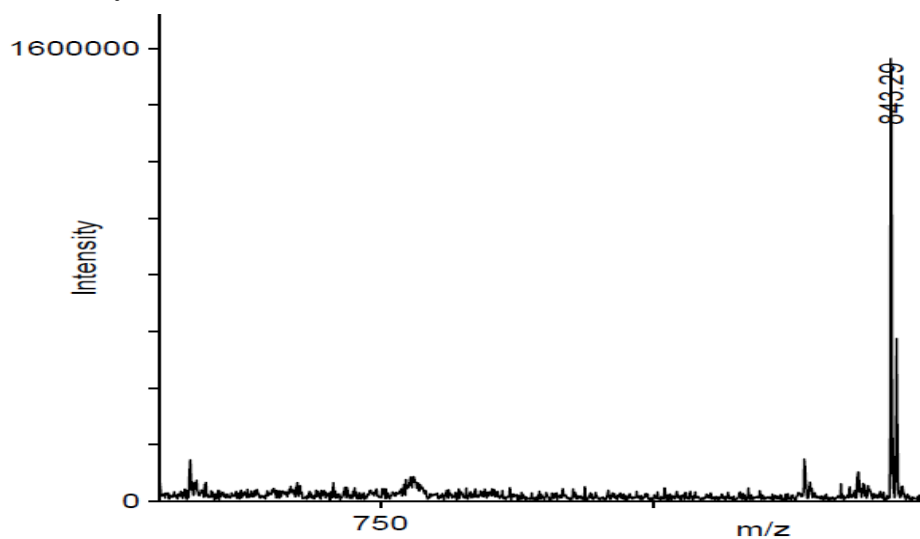


**Figure S4.** MALDI-TOF MS of Rapalogs **12** in Table 2

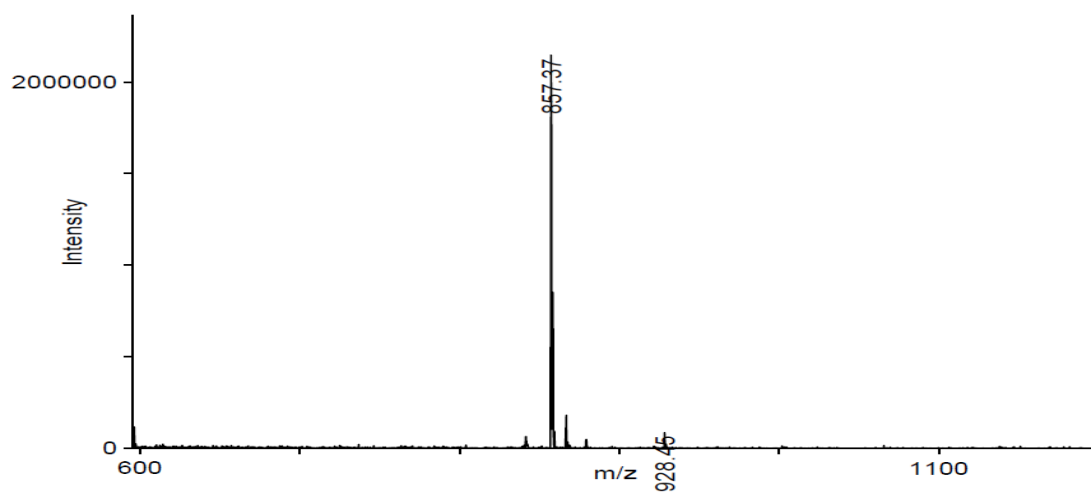
**12 D-Thr-D-Thr**



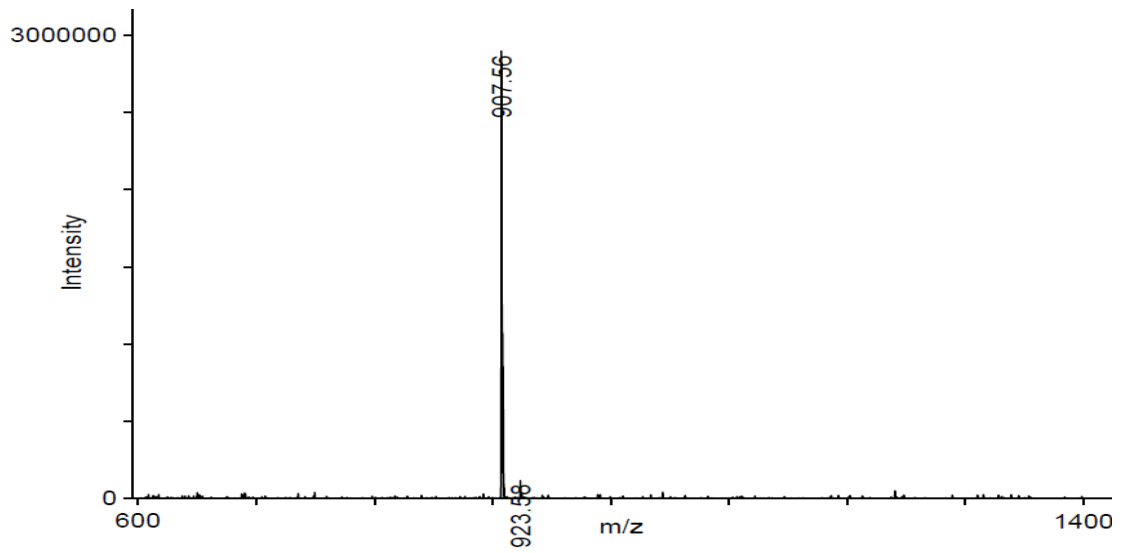
**12 D-Thr-Gly**



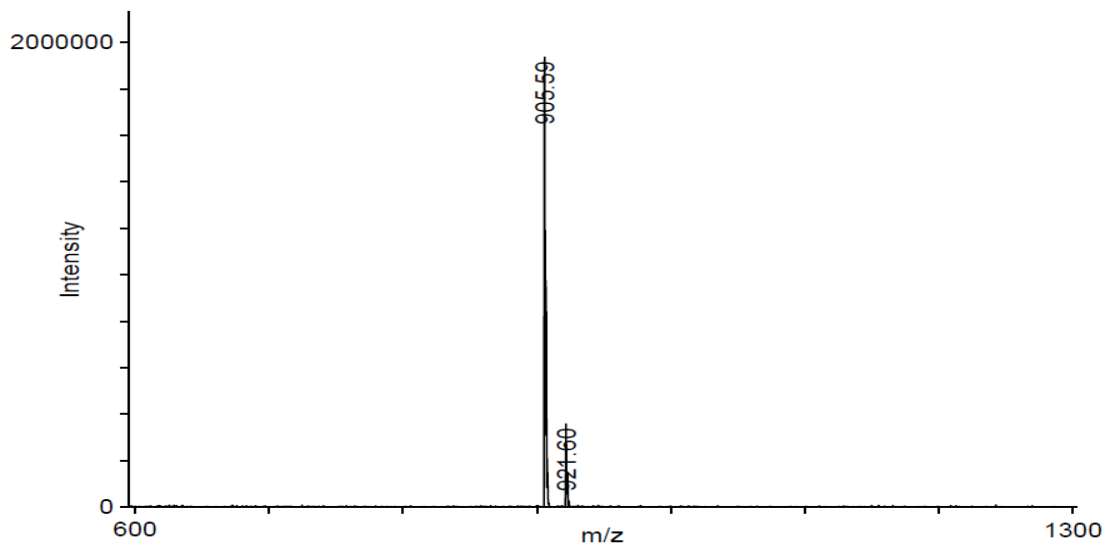
**12 D-Thr-Ala**



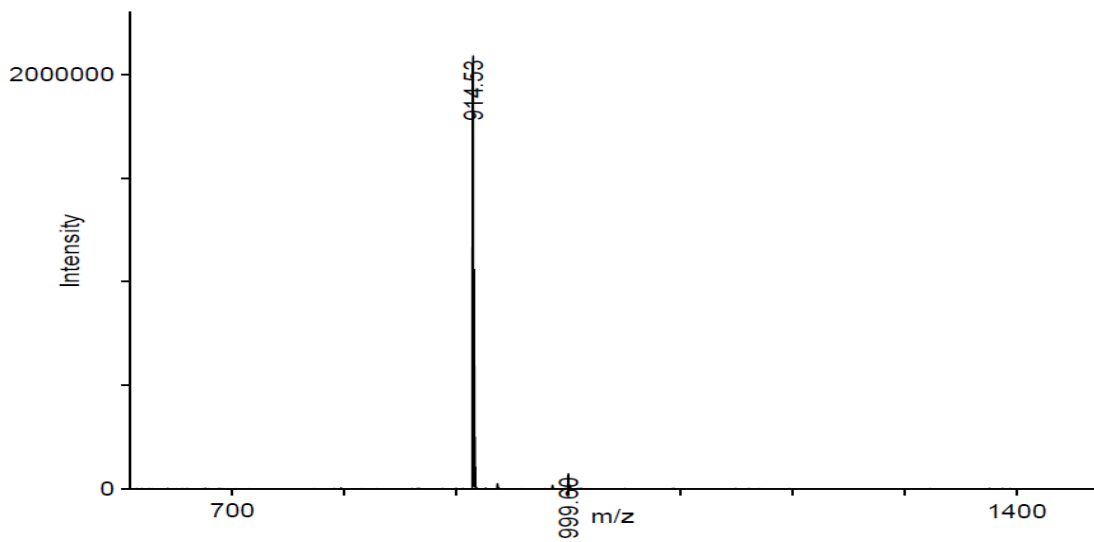
**12**  
**D-Thr-D-**  
**Val**



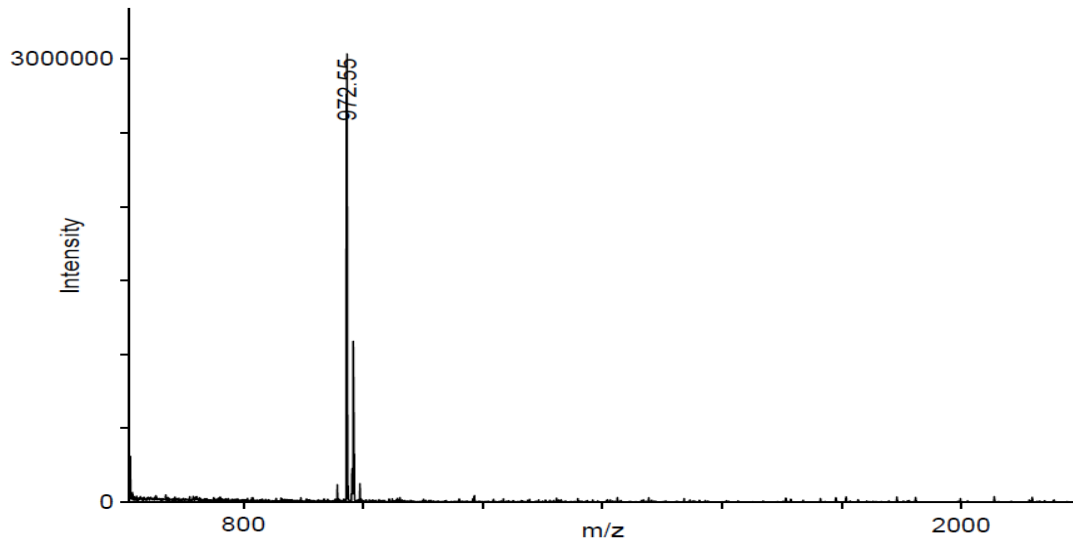
**12 D-Thr-Pro**



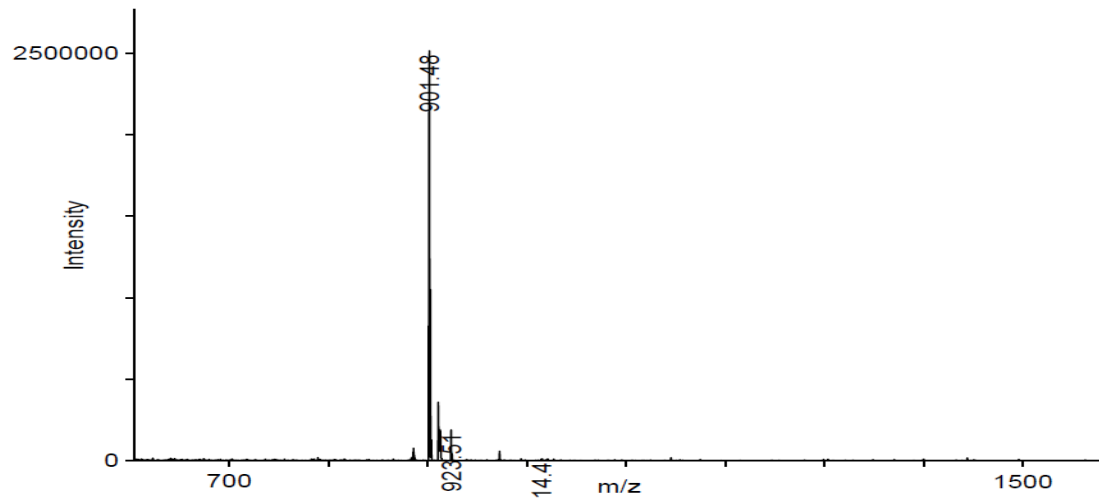
**12 D-Thr-Lys**



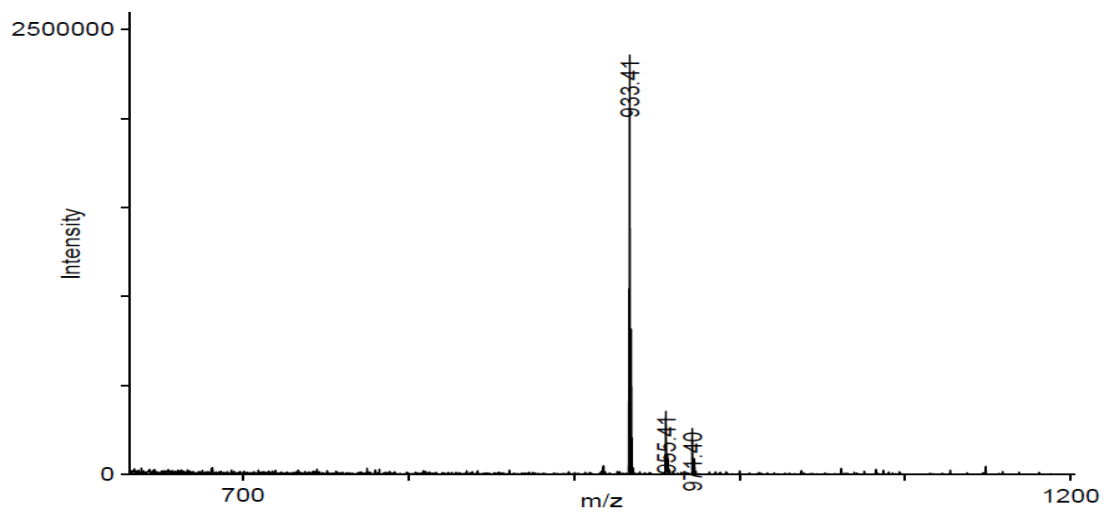
**12 D-Thr-Trp**



**12 D-Thr-Asp**

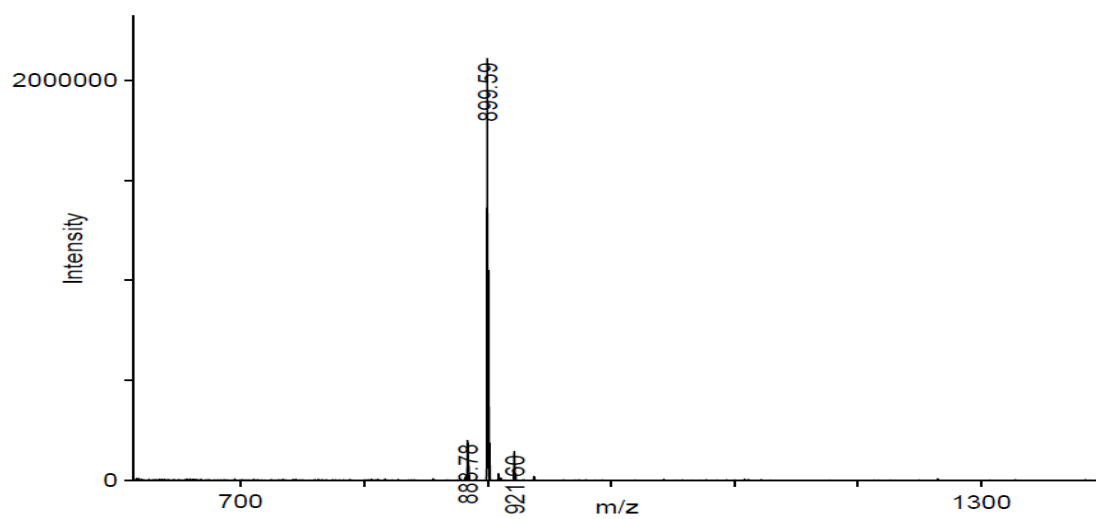


**12 D-Thr-D-Phe**

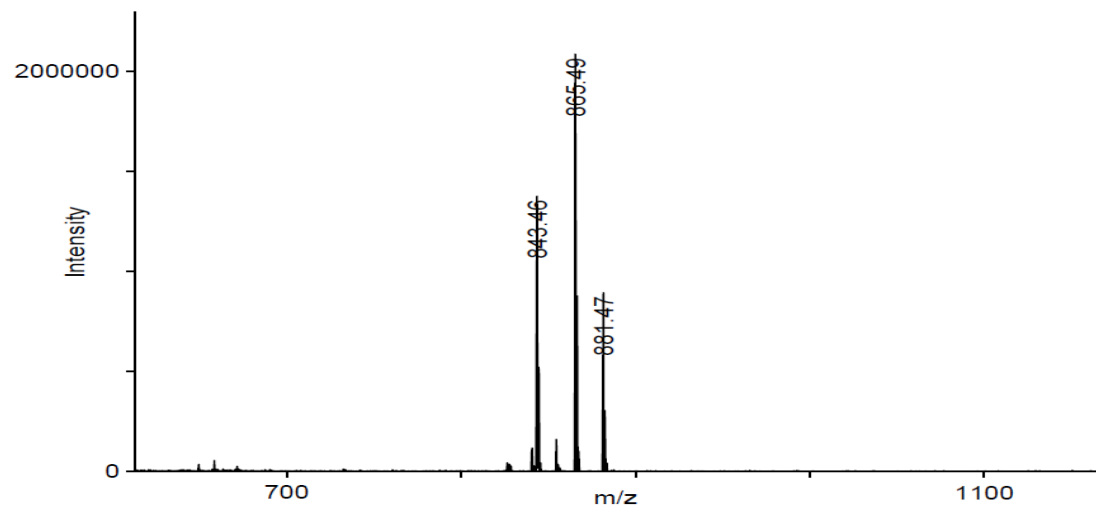




### 12 D-Thr-Nle

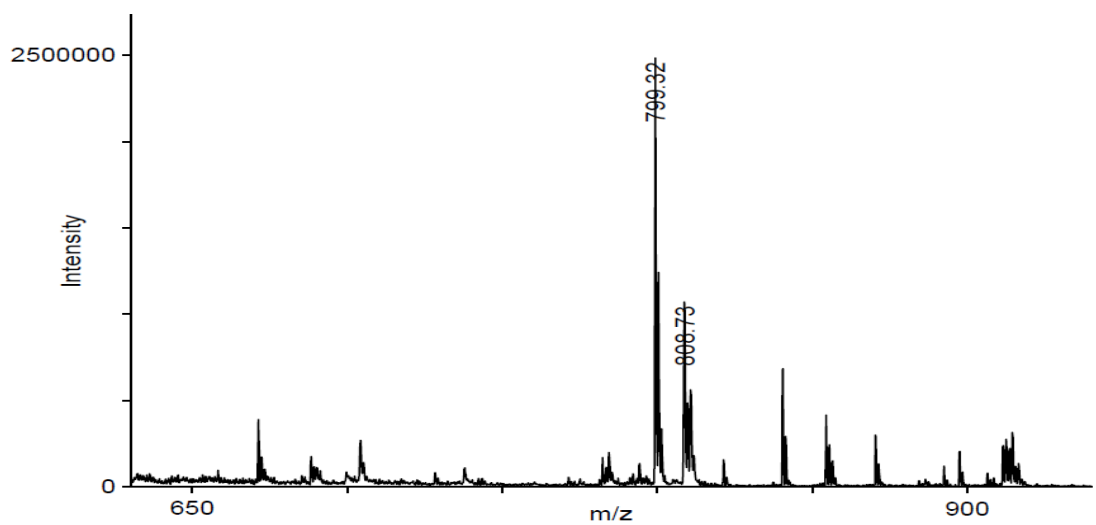


### 12 Gly-D-Thr

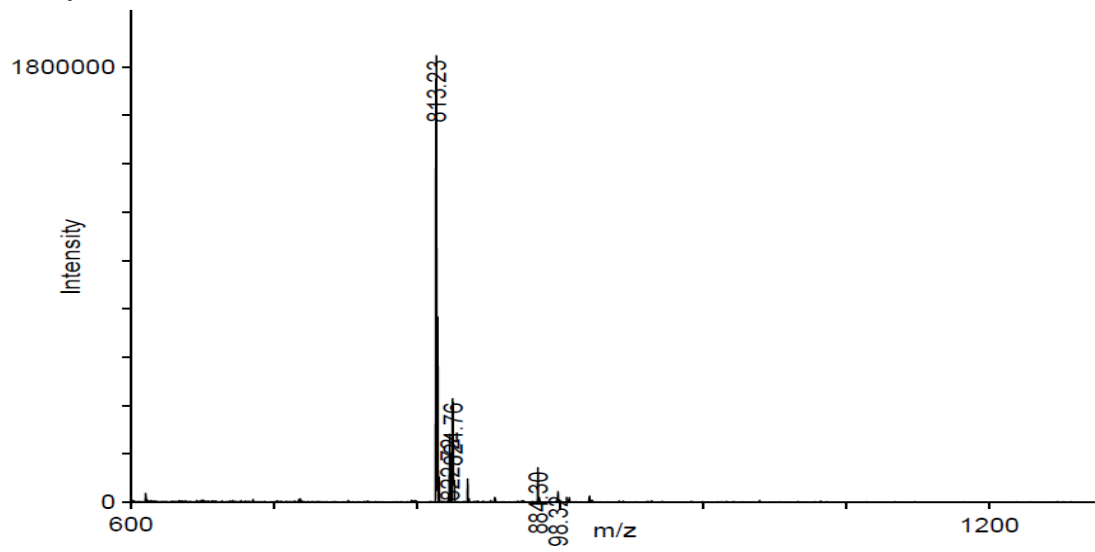


843(MW+H<sup>+</sup>); 865(MW+Na<sup>+</sup>), 881(MW+K<sup>+</sup>)

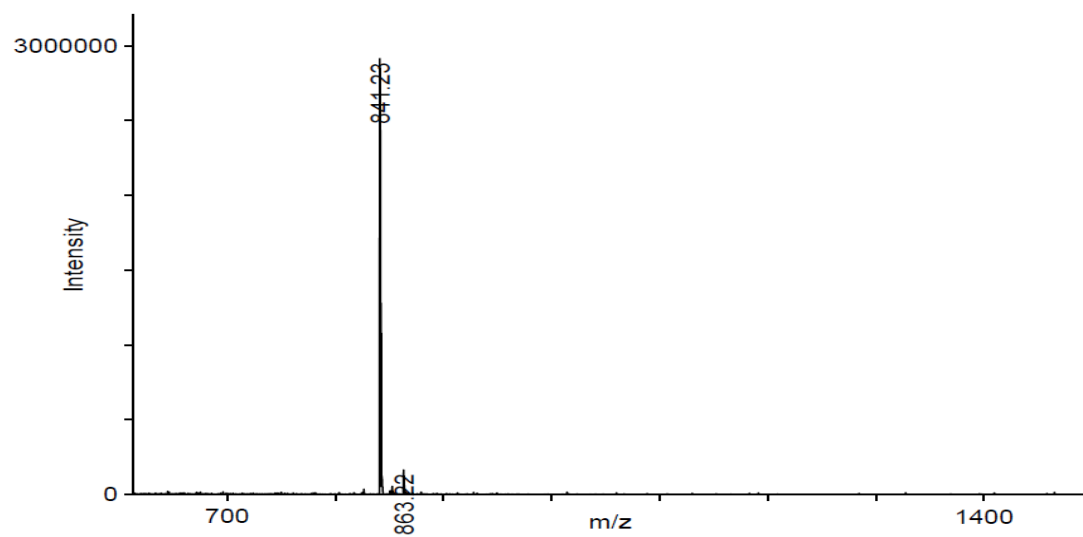
### 12 Gly-Gly



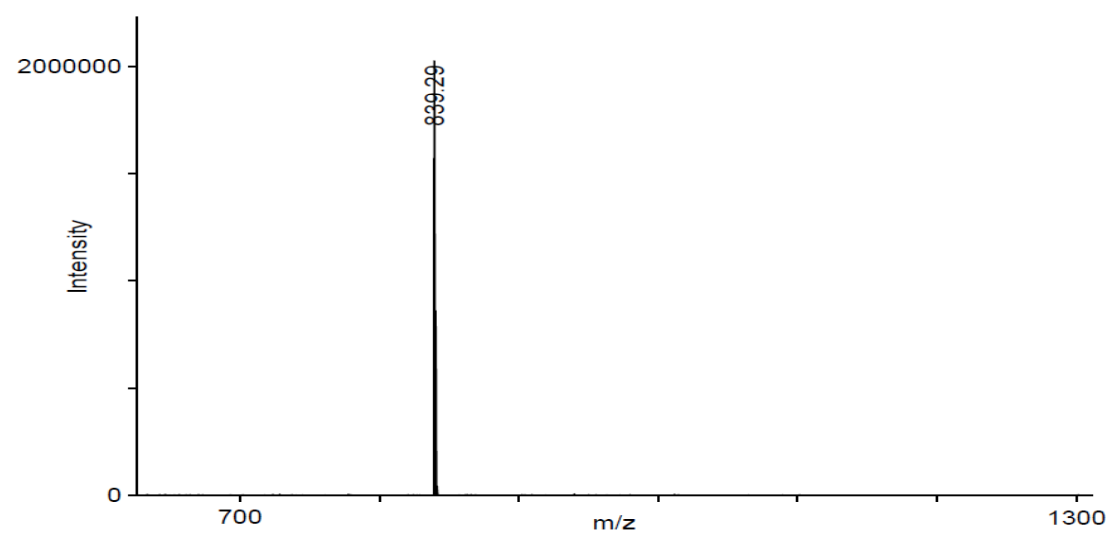
### 12 Gly-Ala (12b)



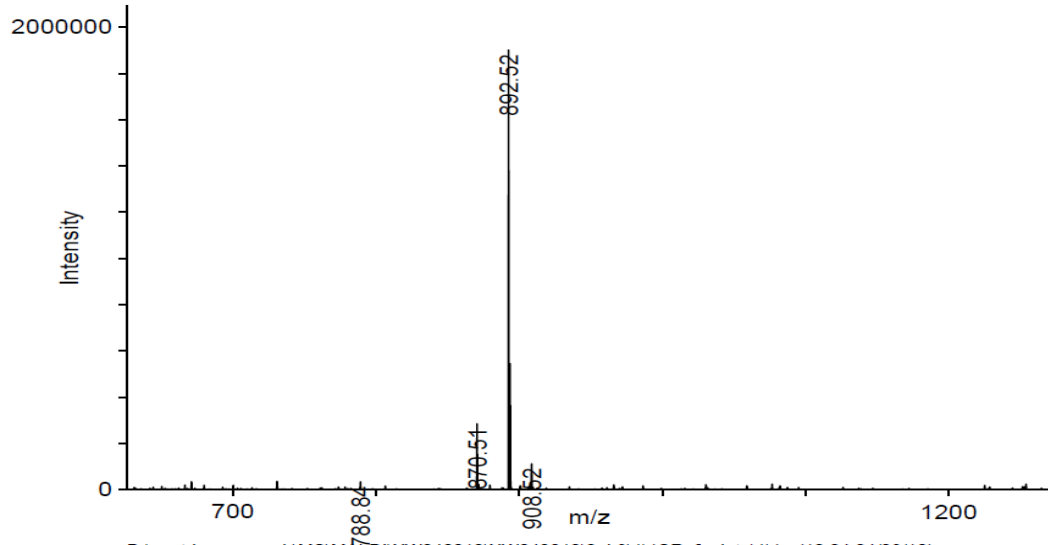
### 12 Gly-D-Val



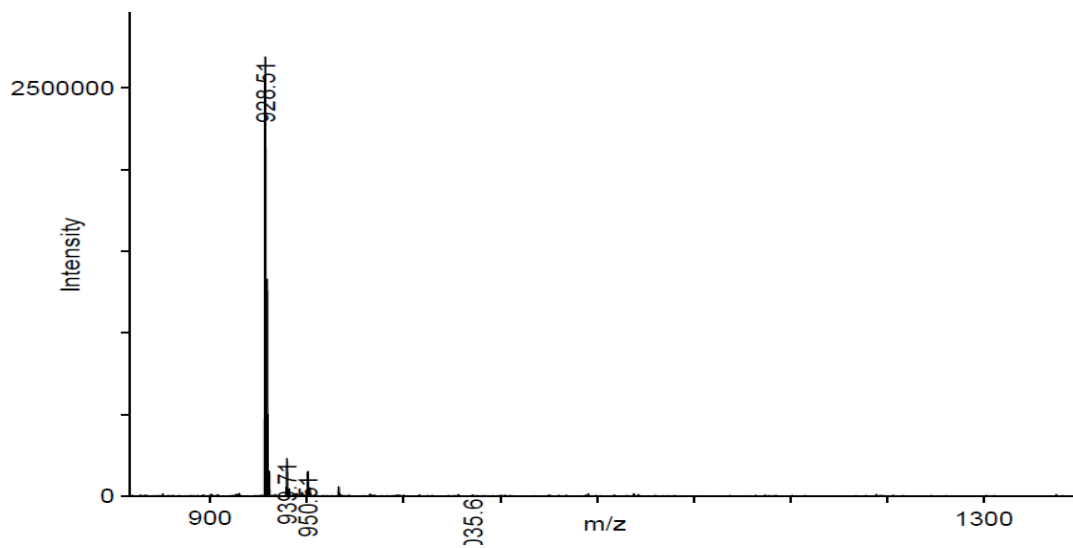
### 12 Gly-Pro



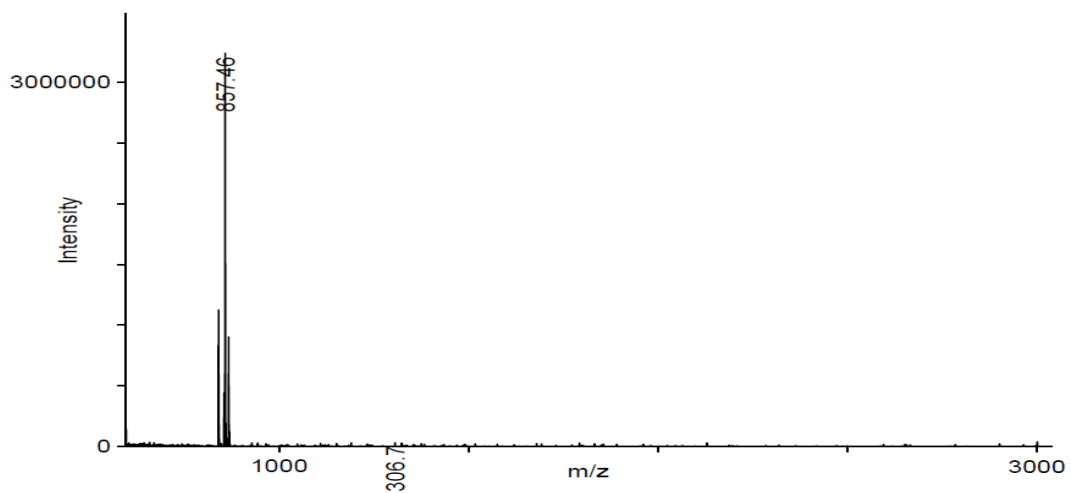
### 12 Gly-Lys



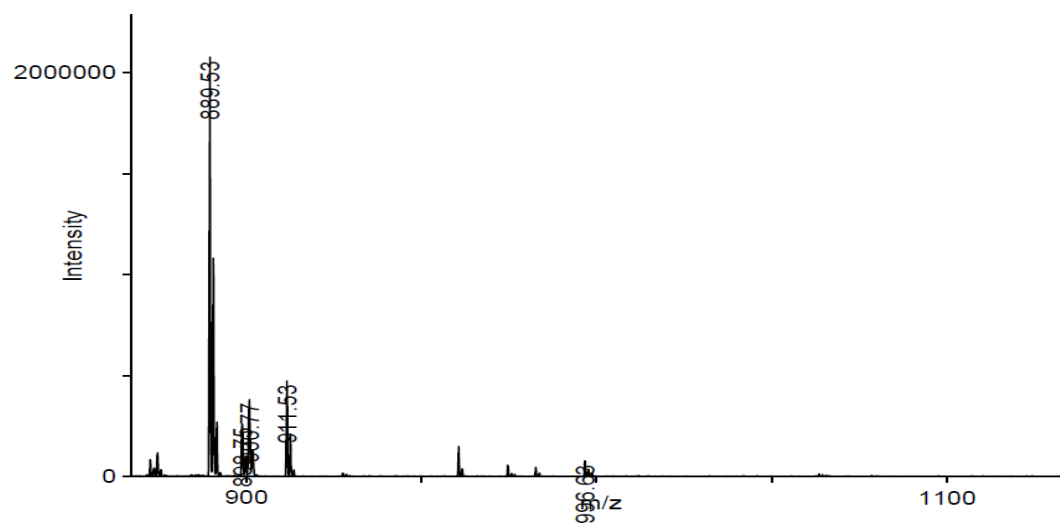
### 12 Gly-Trp



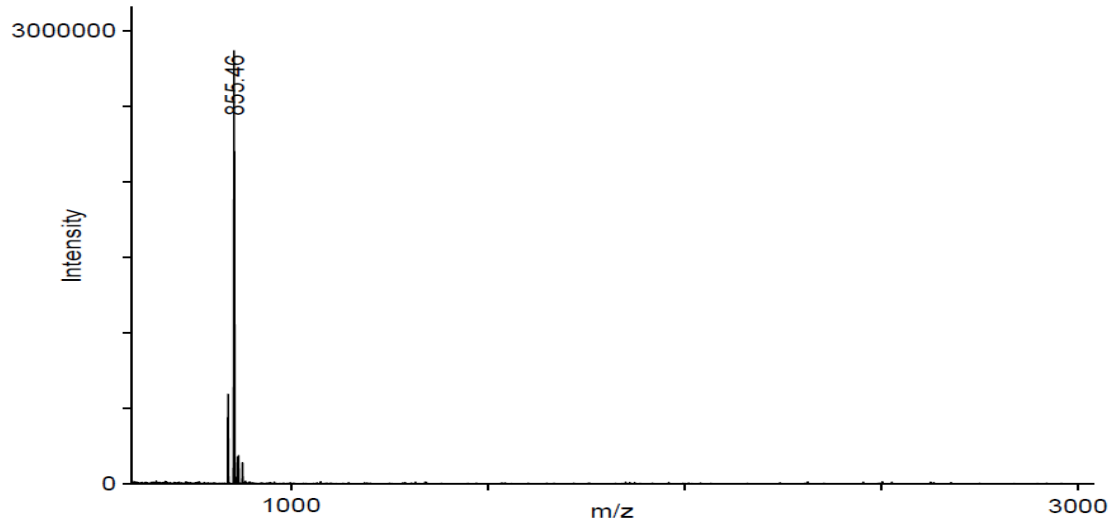
### 12 Gly-Asp



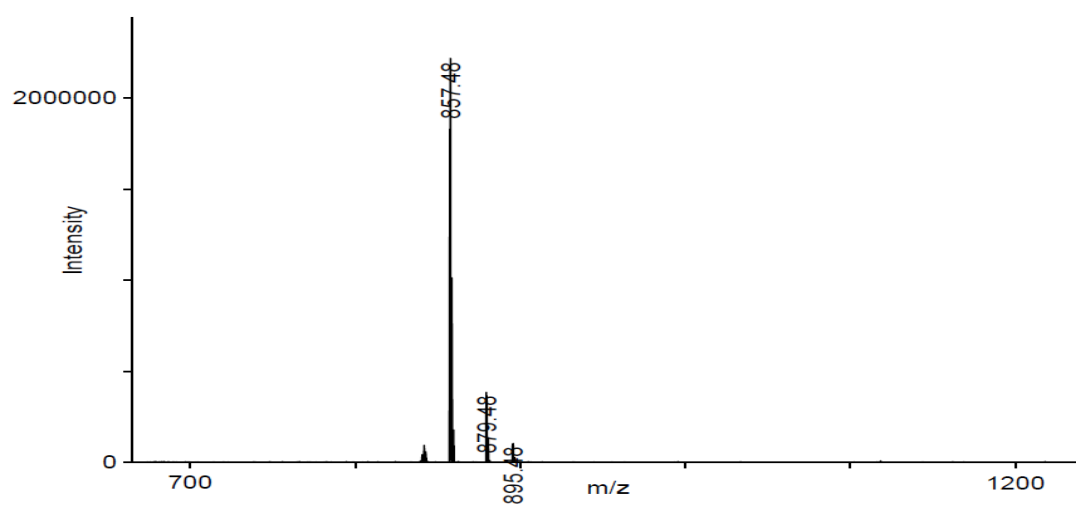
### 12 Gly-D-Phe



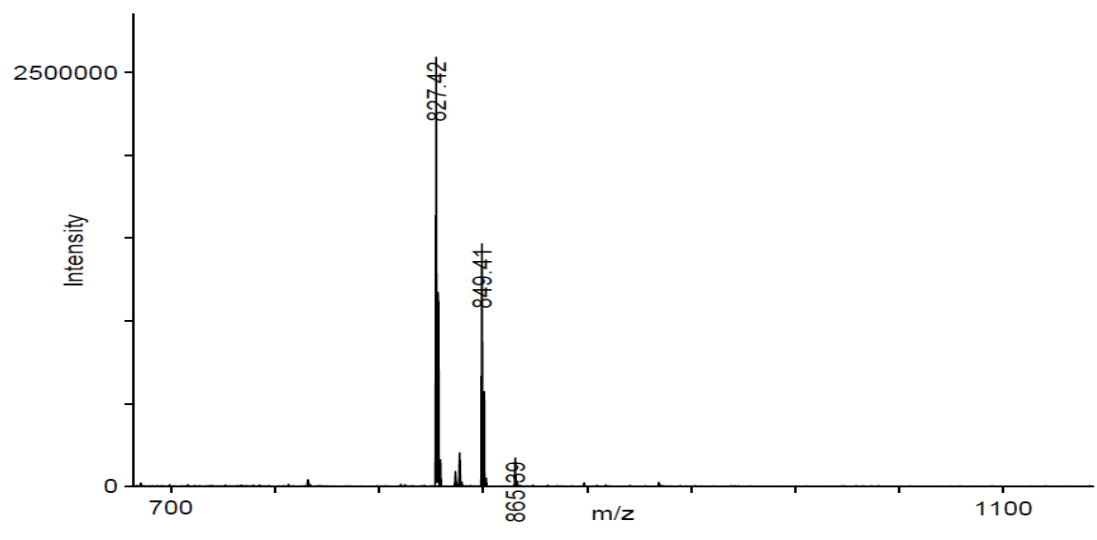
### 12 Gly-Nle



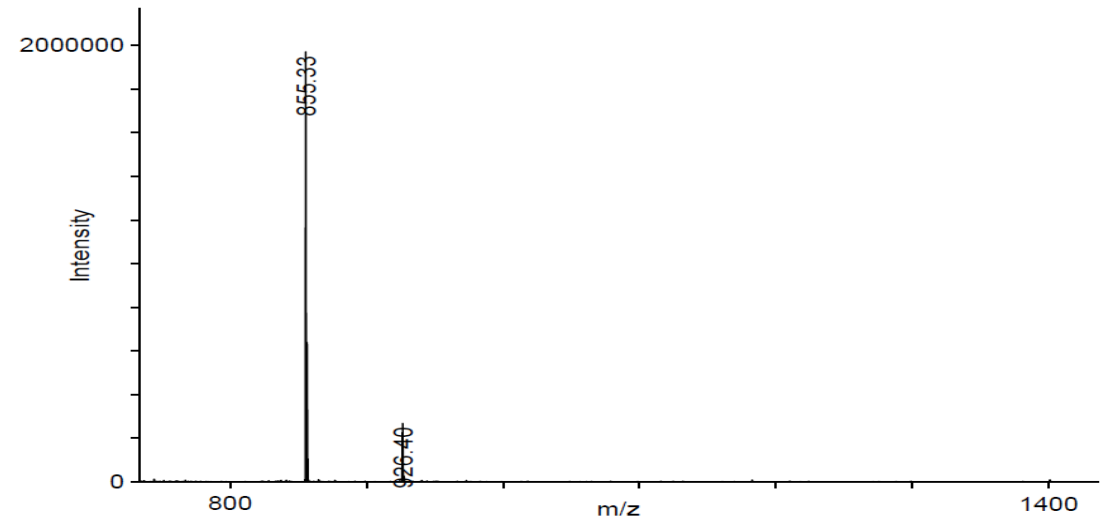
### 12 Ala-D-Thr



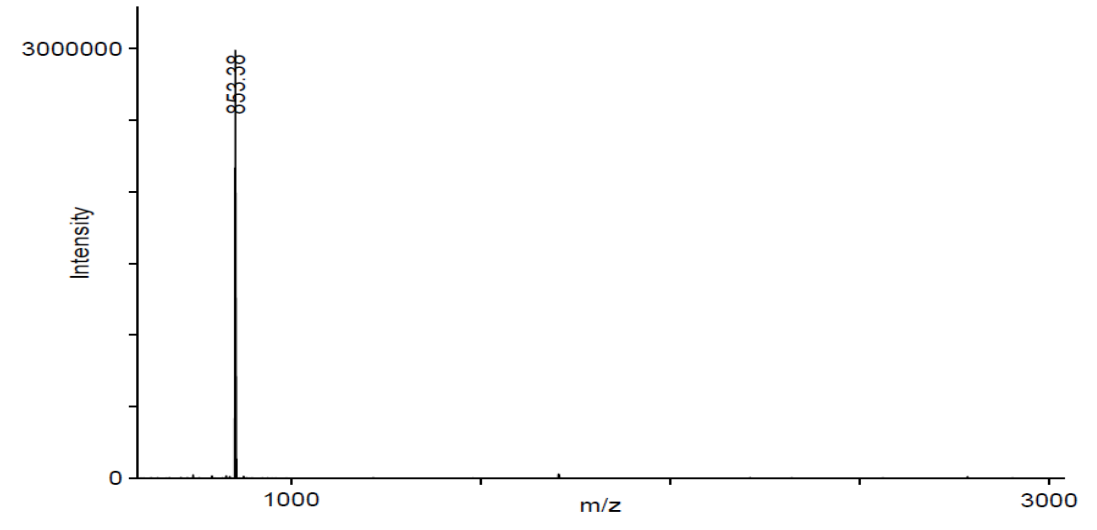
**12 Ala-Ala**



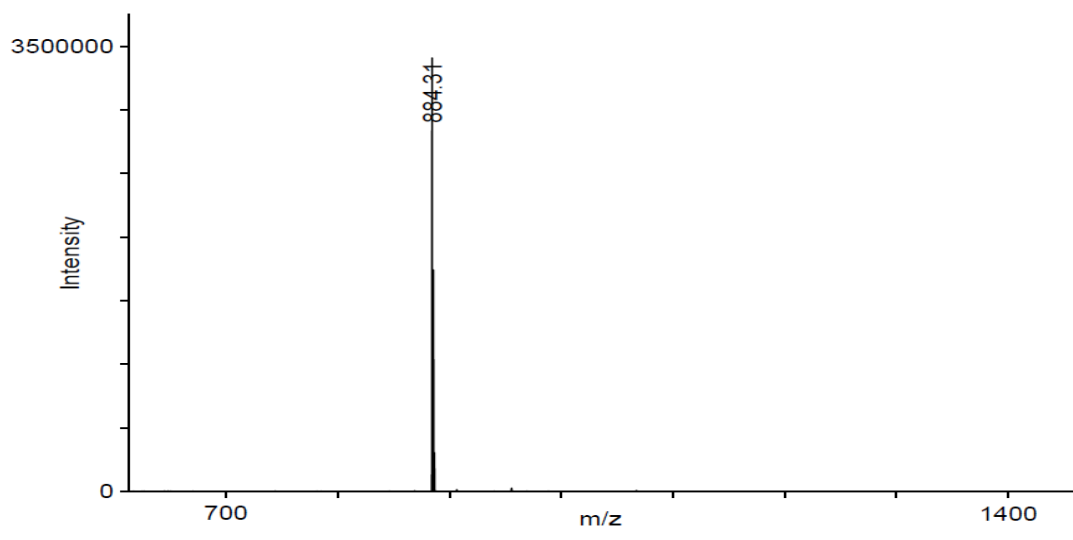
**12 Ala-D-Val**



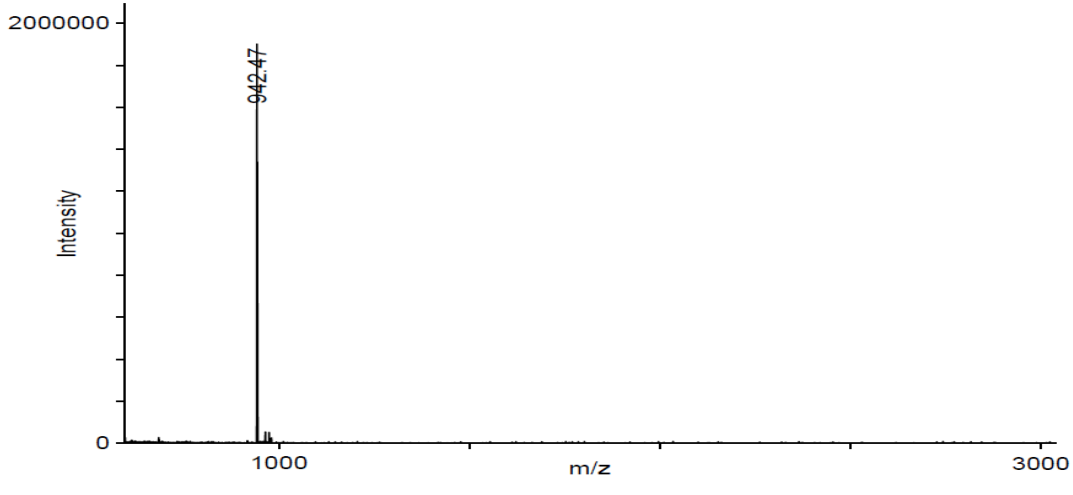
**12 Ala-Pro**



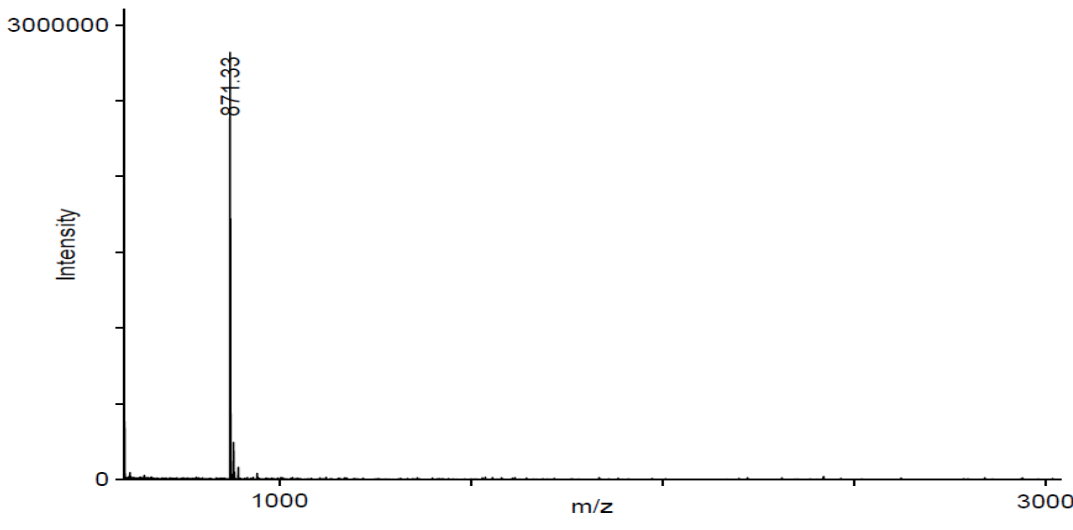
### 12 Ala-Lys



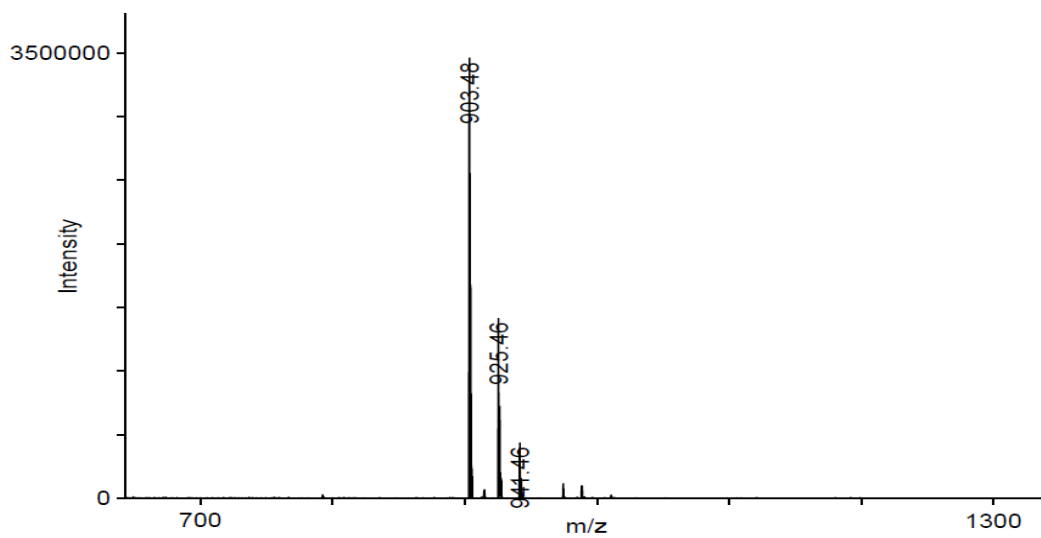
### 12 Ala-Trp



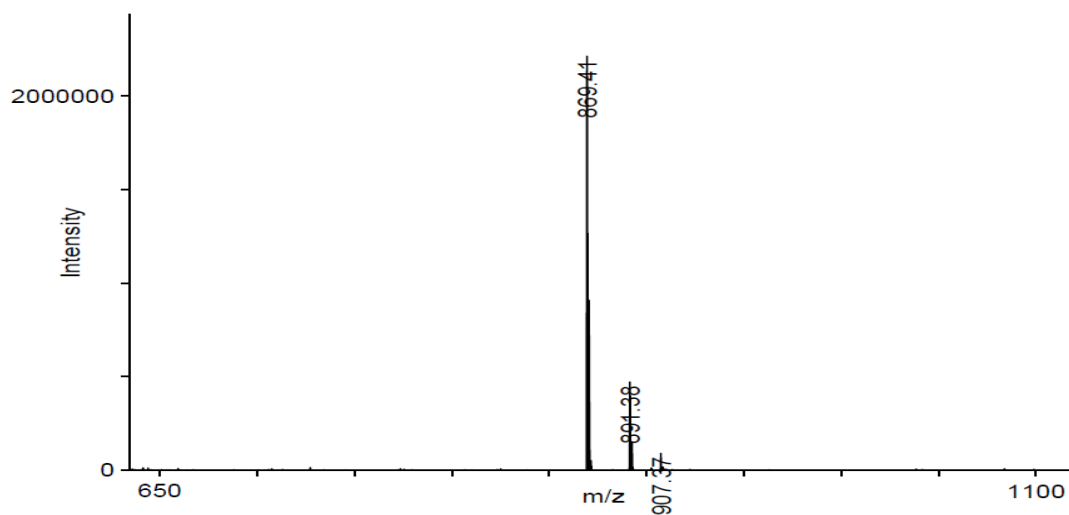
### 12 Ala-Asp



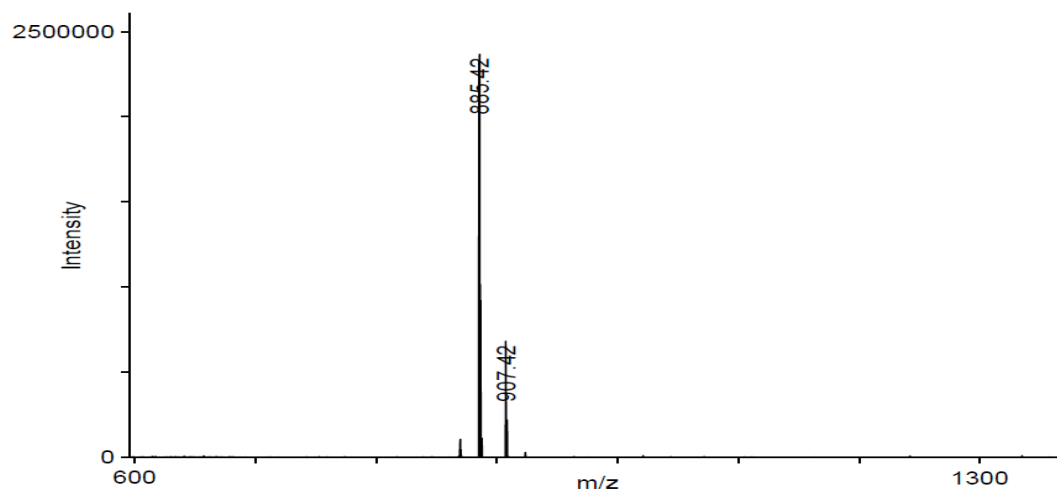
### 12 Ala-D-Phe



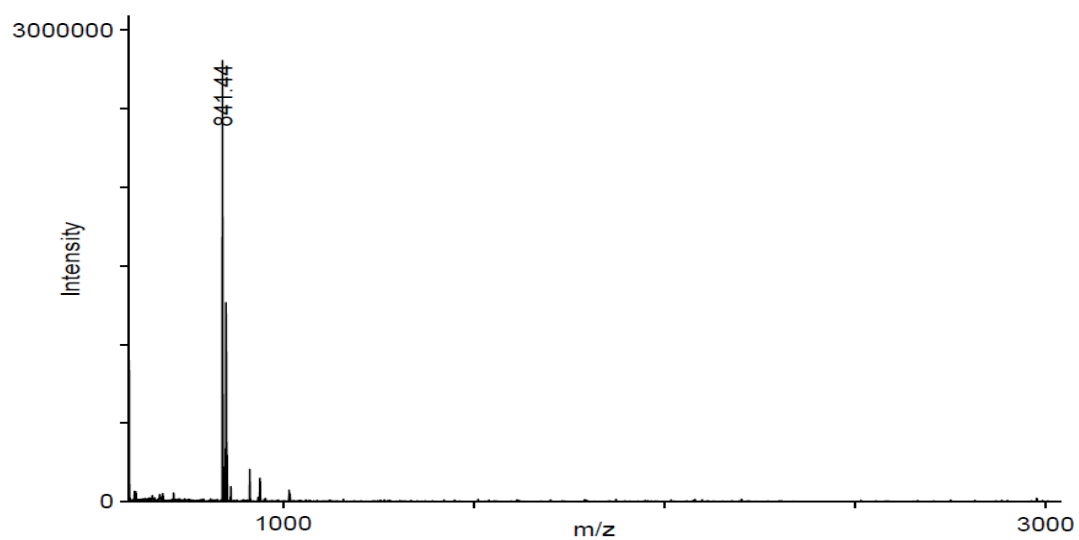
### 12 Ala-Nle



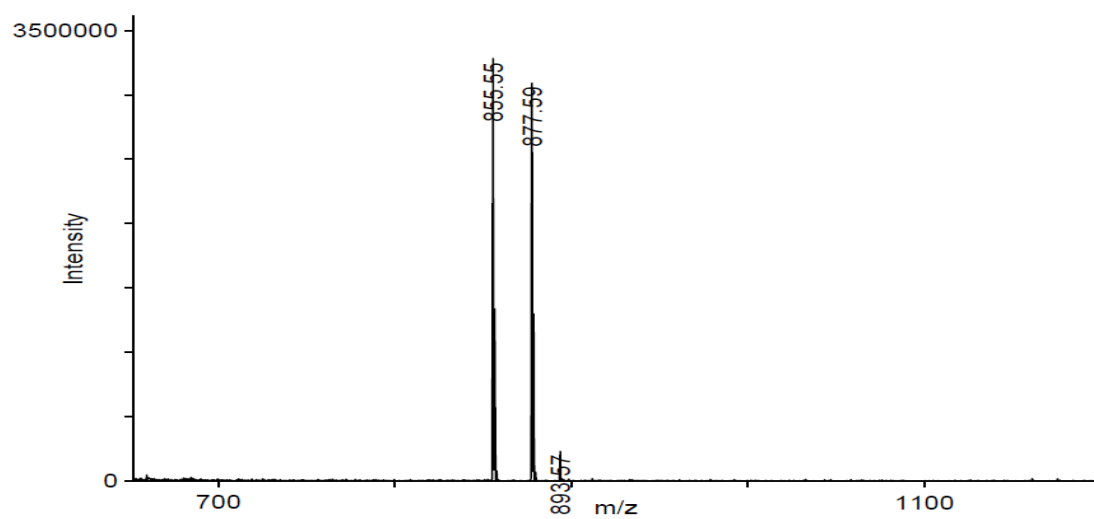
### 12 D-Val-D-Thr



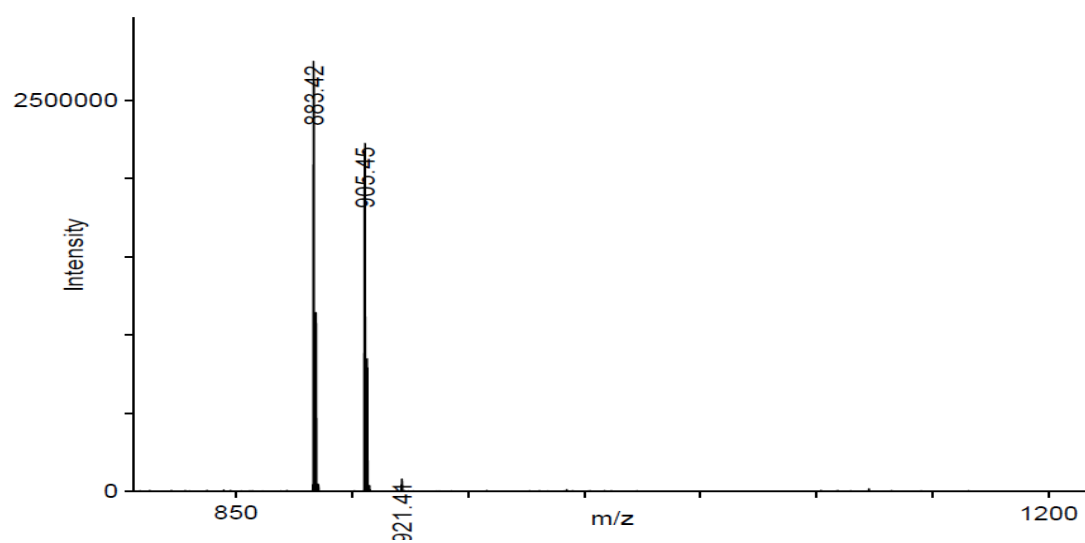
**12 D-Val-Gly (12c)**



**12 D-Val-Ala**

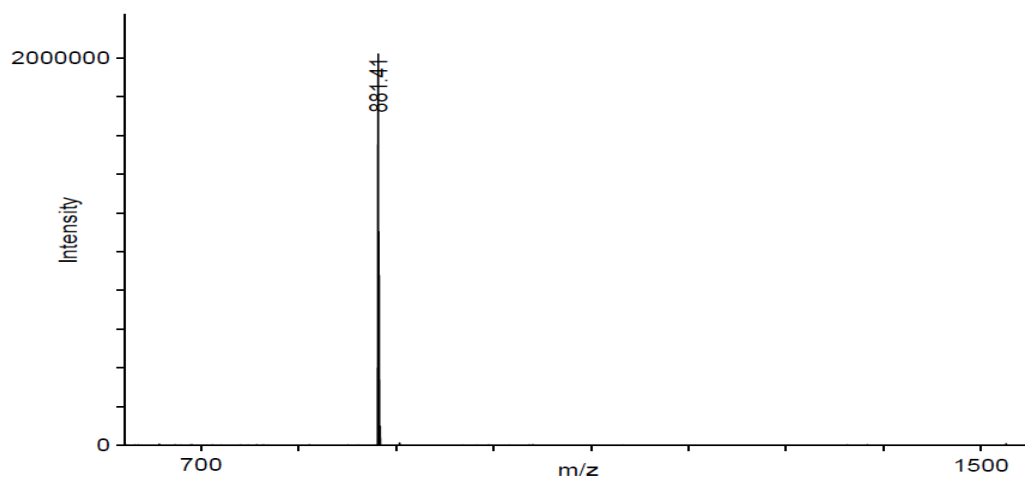


**12 D-Val-D-Val**

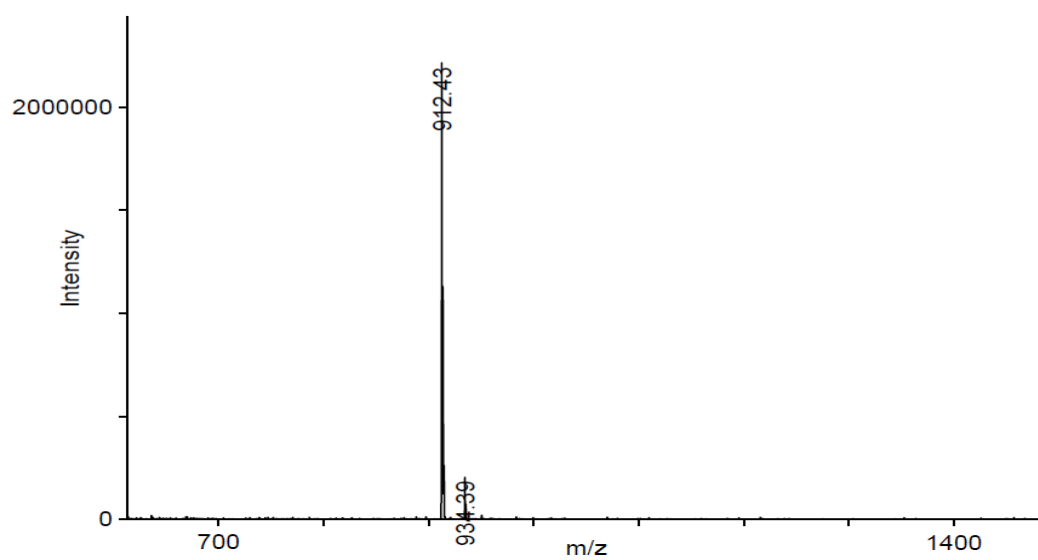




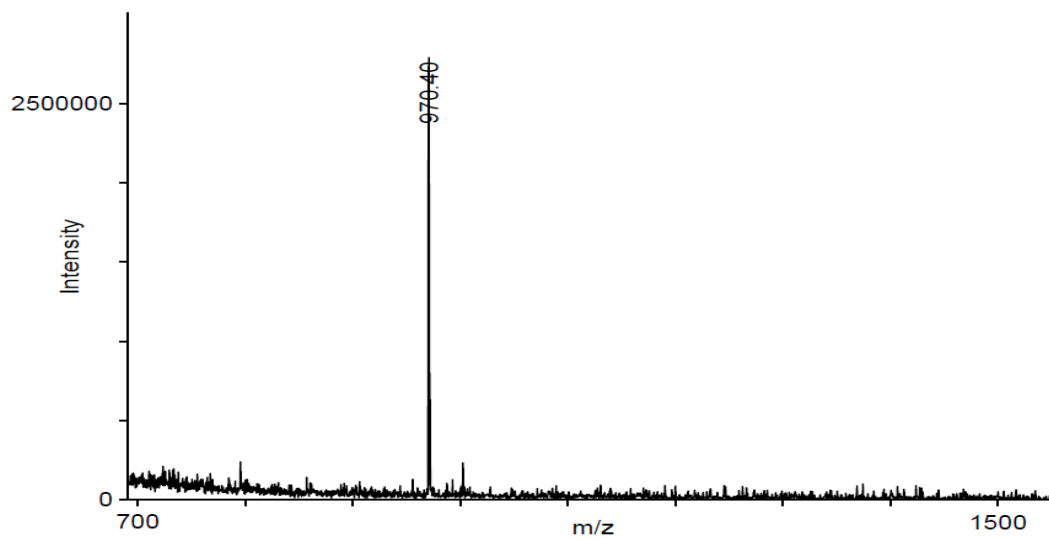
### 12 D-Val-Pro



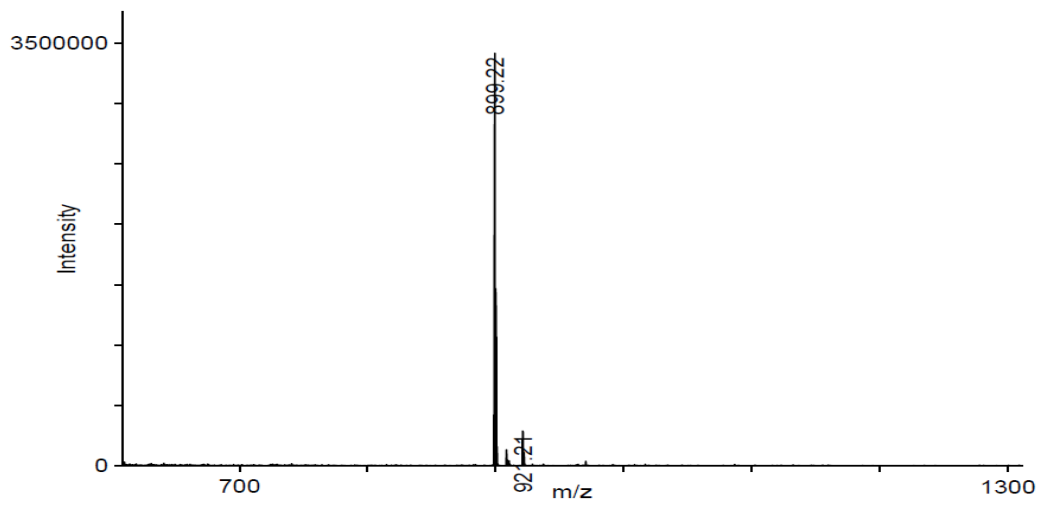
### 12 D-Val-Lys



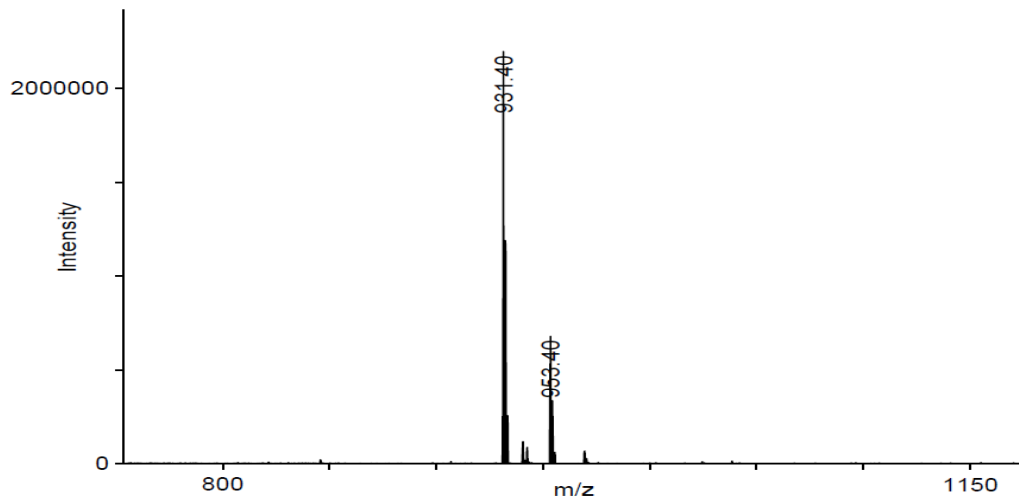
### 12 D-Val-Trp



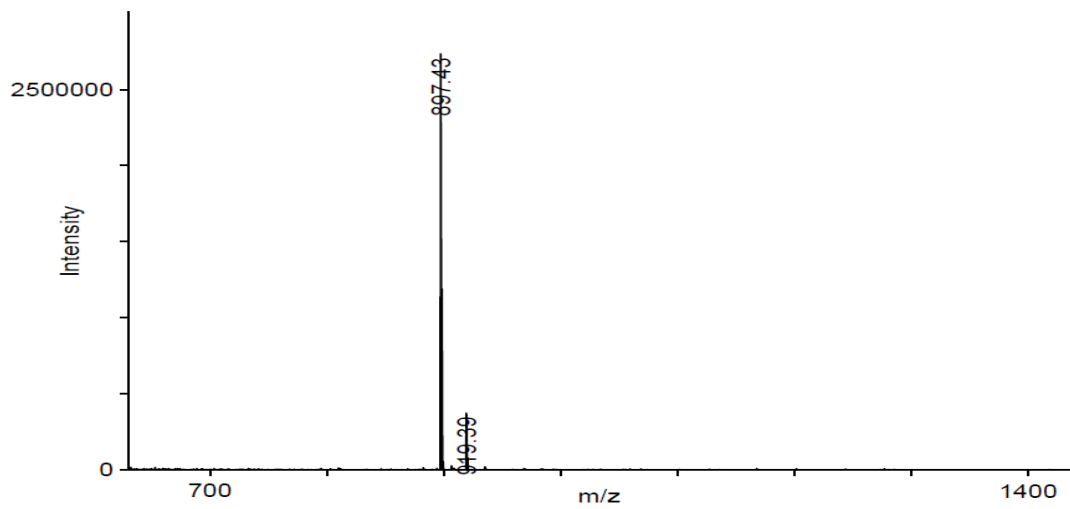
### 12 D-Val-Asp



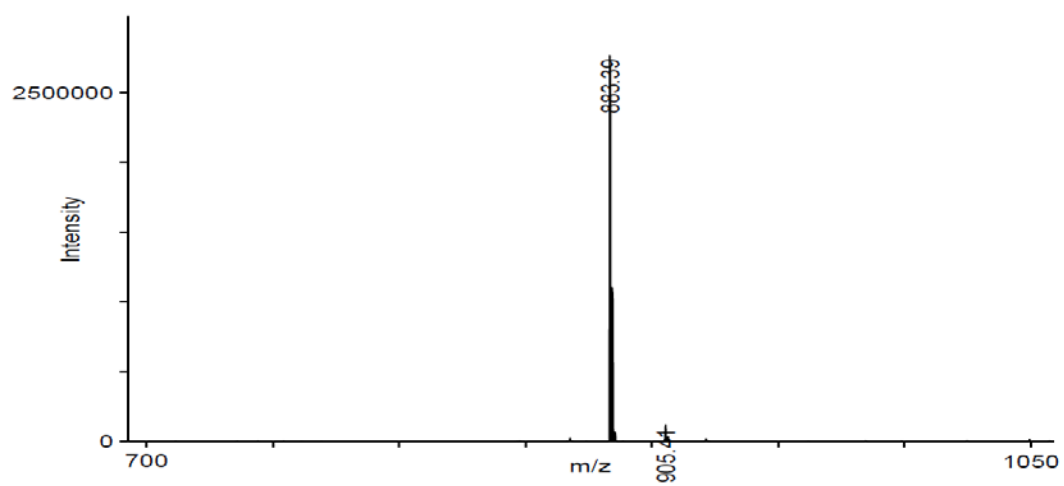
### 12 D-Val-D-Phe



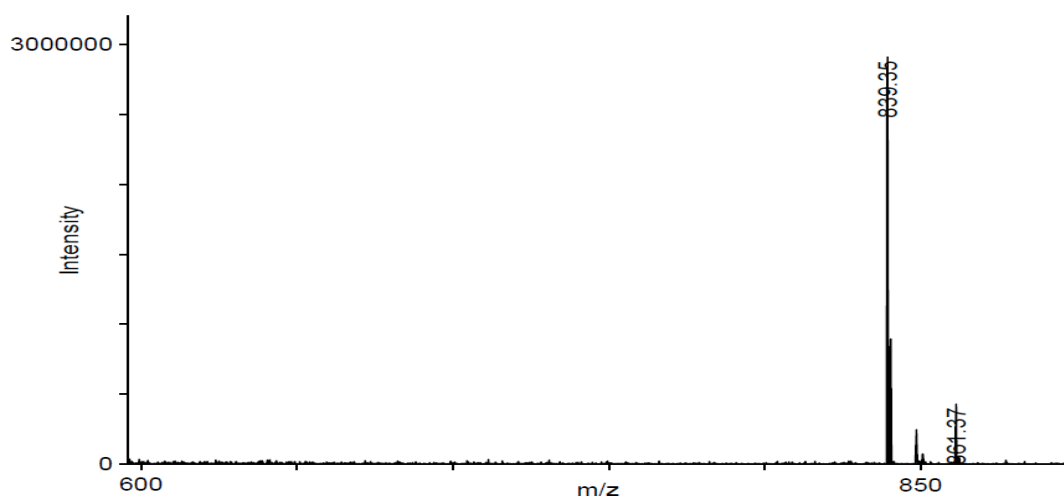
### 12 D-Val-Nle



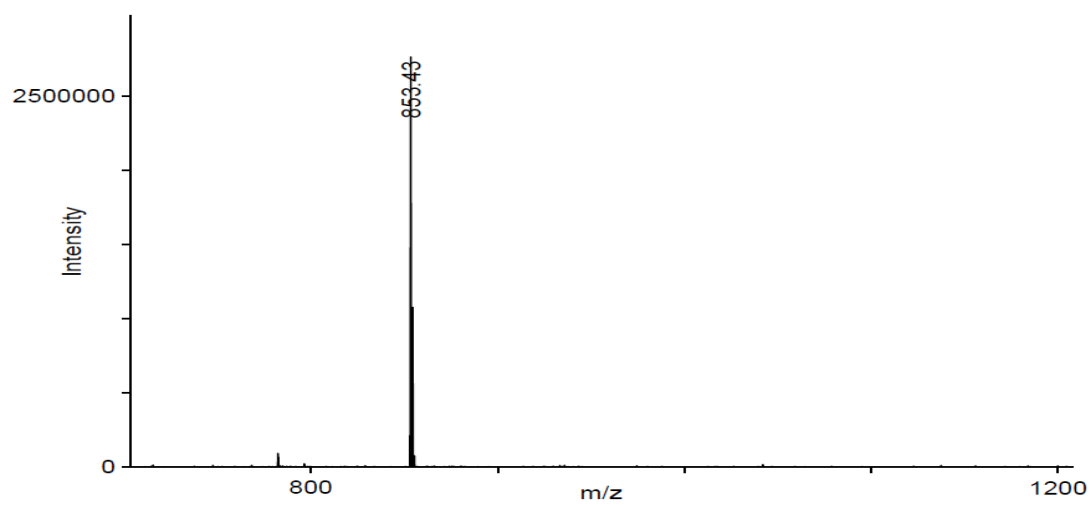
### 12 Pro-D-Thr



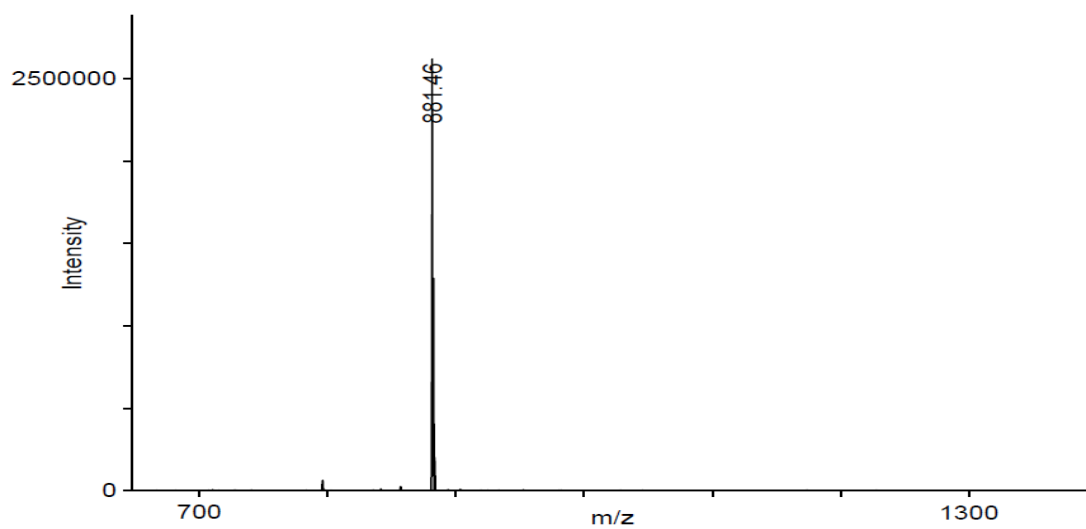
### 12 Pro-Gly



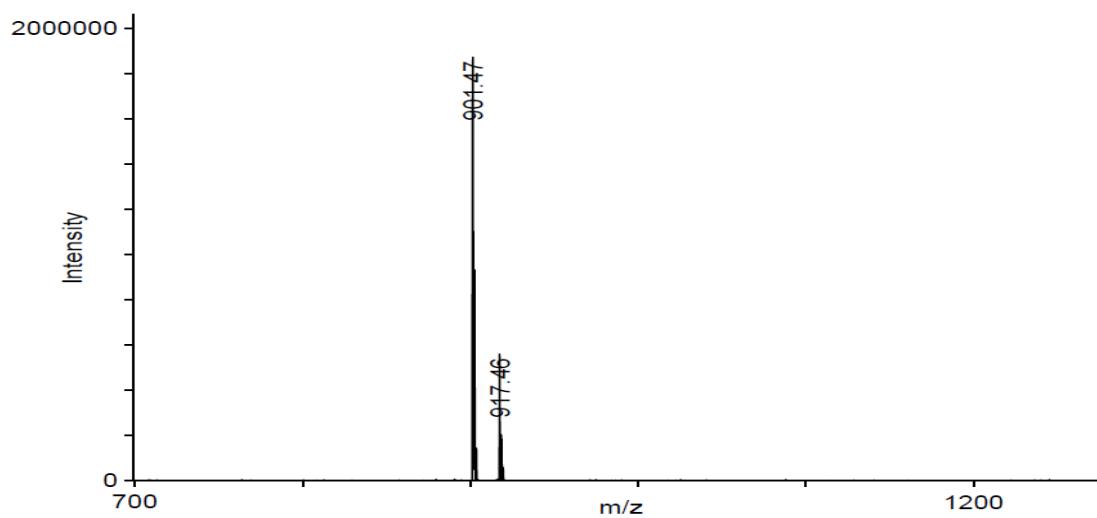
### 12 Pro-Ala



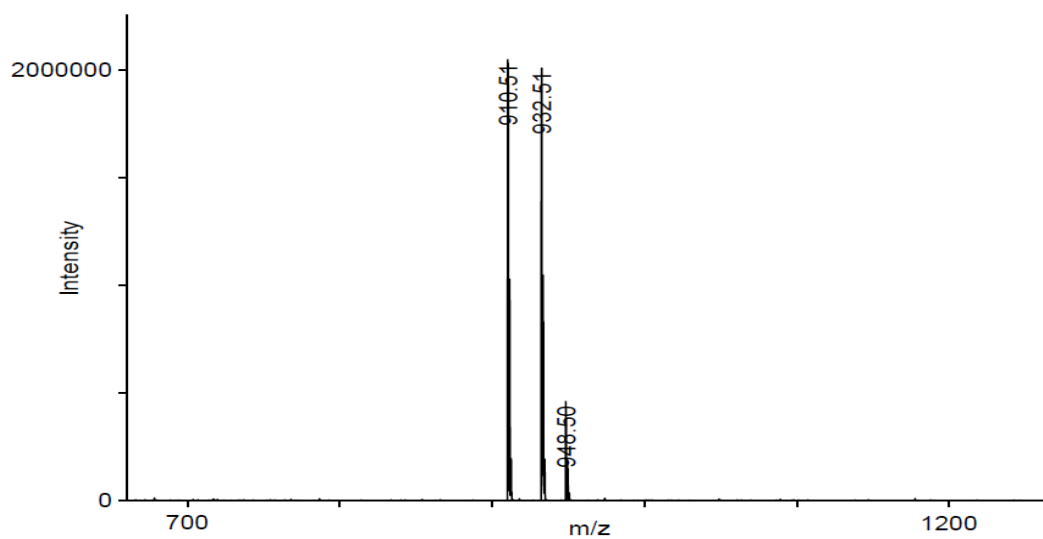
### 12 Pro-D-Val



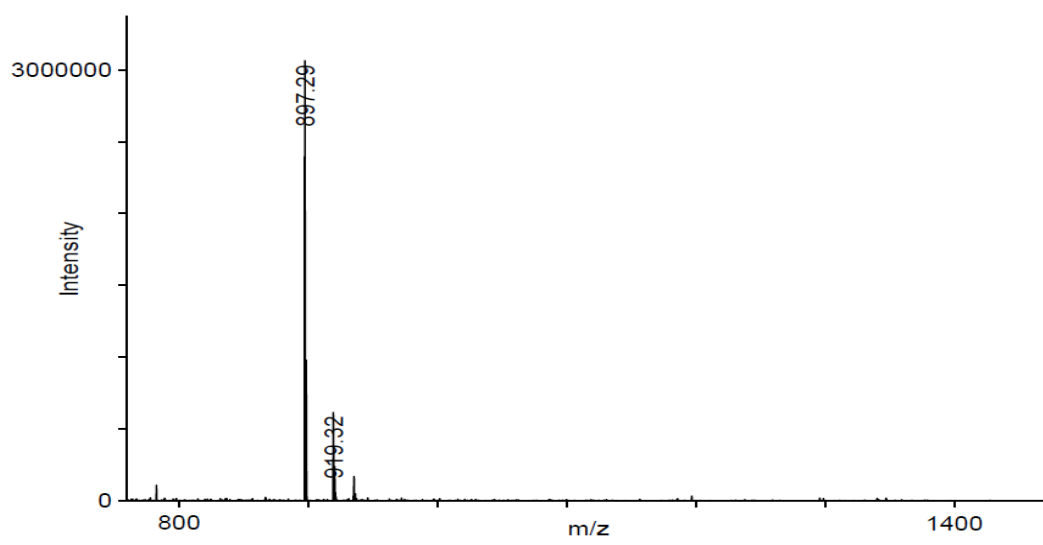
### 12 Pro-Pro



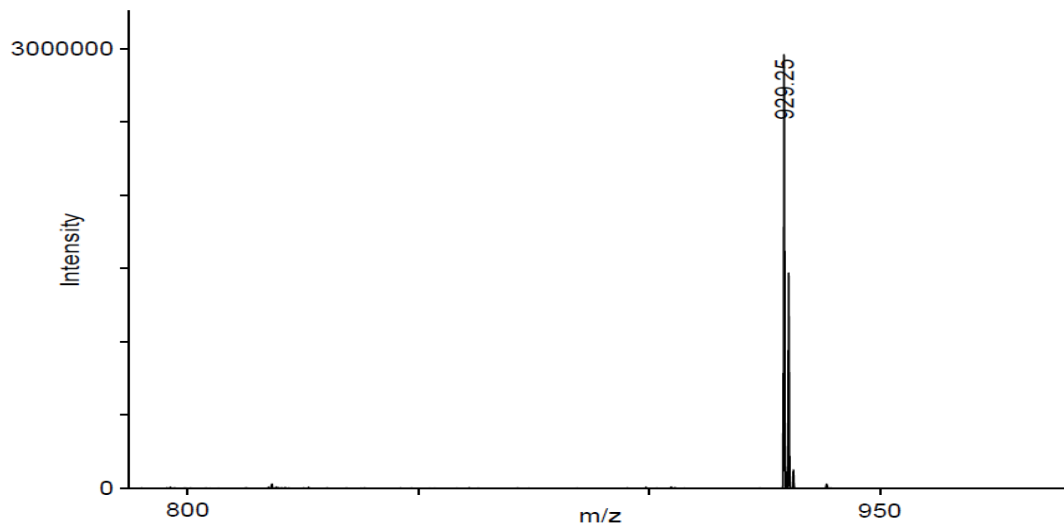
### 12 Pro-Lys



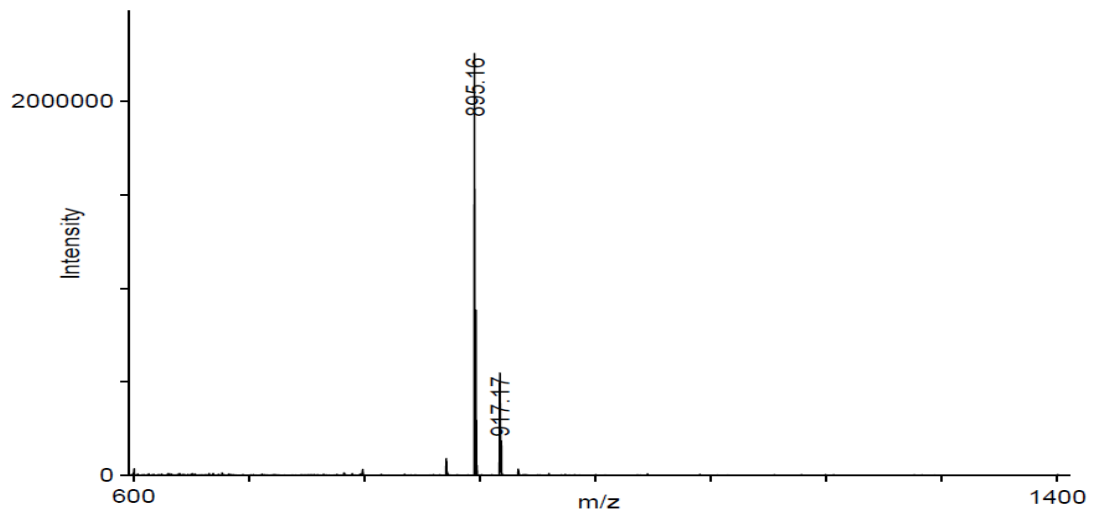
### 12 Pro-Asp



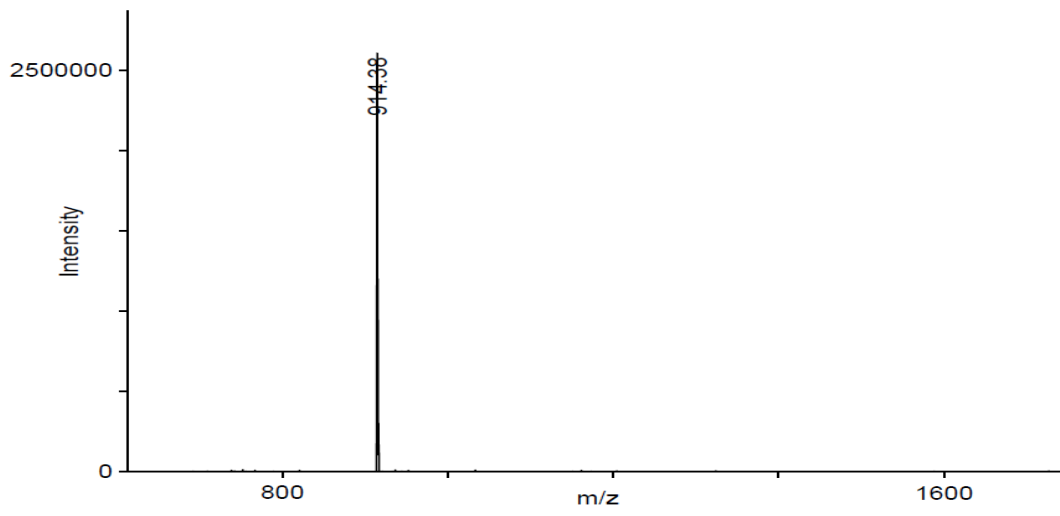
### 12 Pro-D-Phe



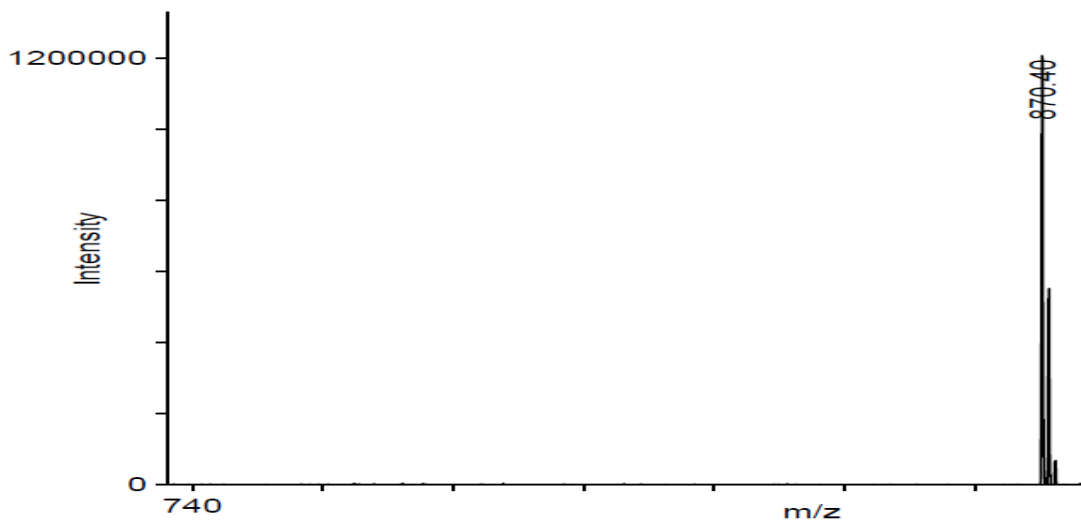
### 12 Pro-Nle



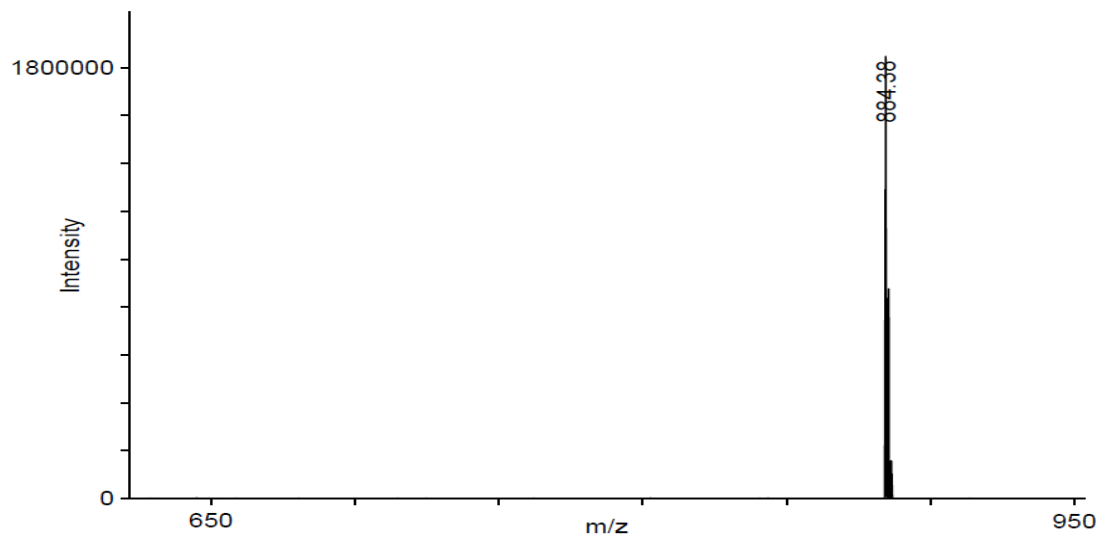
### 12 Lys-D-Thr



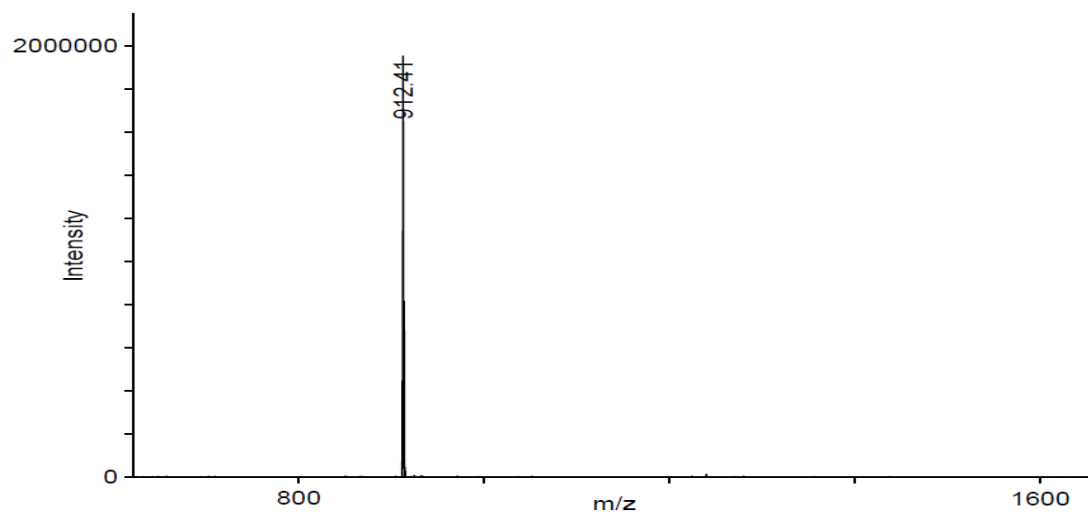
### 12 Lys-Gly



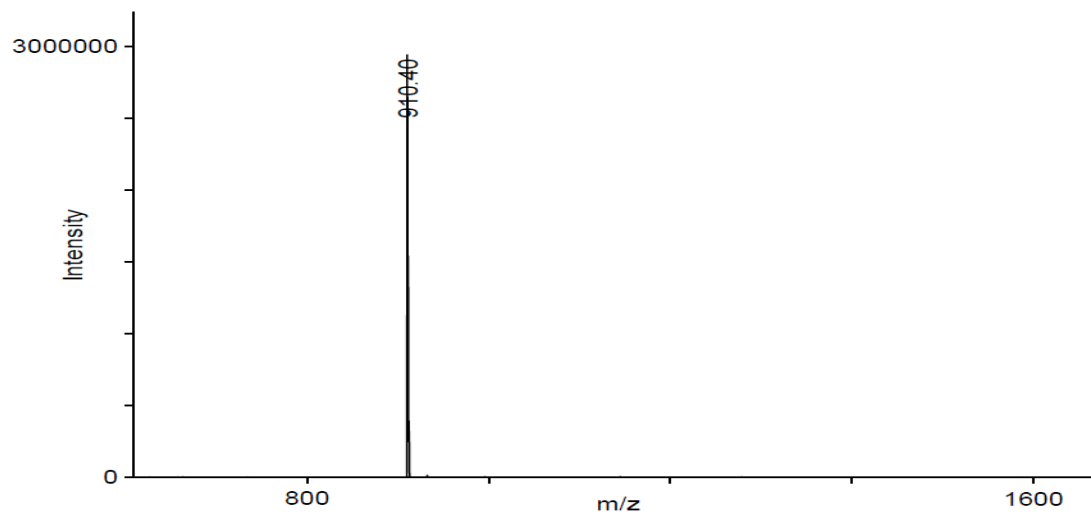
### 12 Lys-Ala



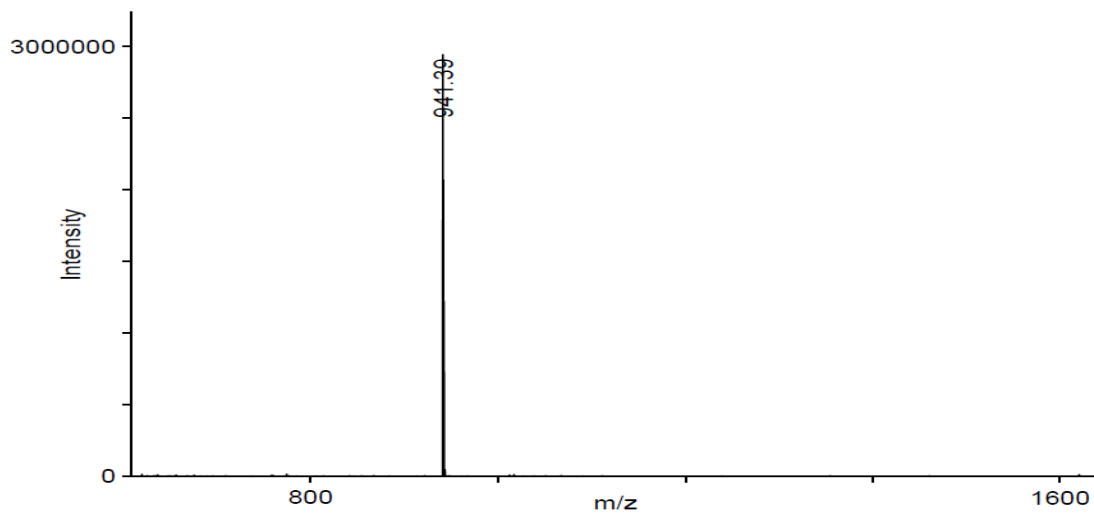
### 12 Lys-D-Val



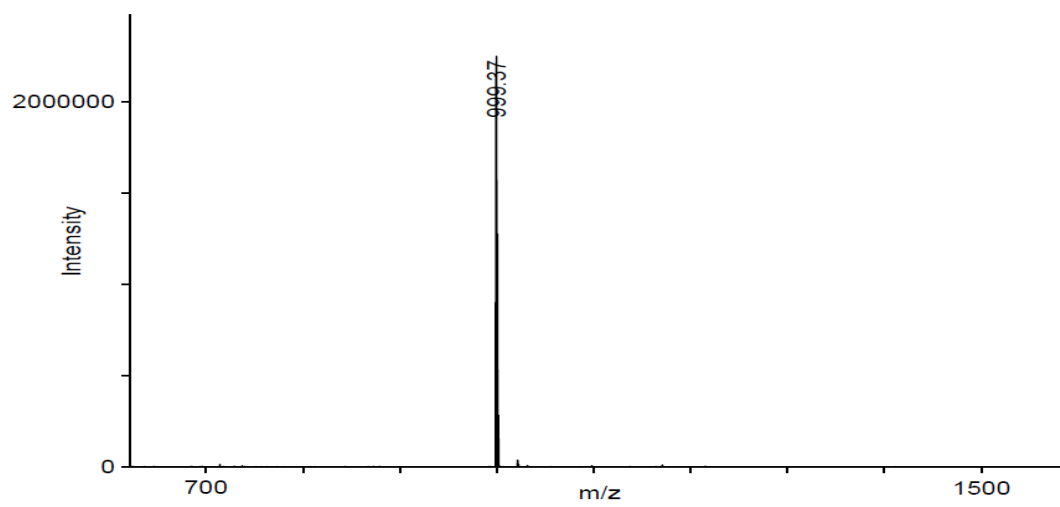
### 12 Lys-Pro



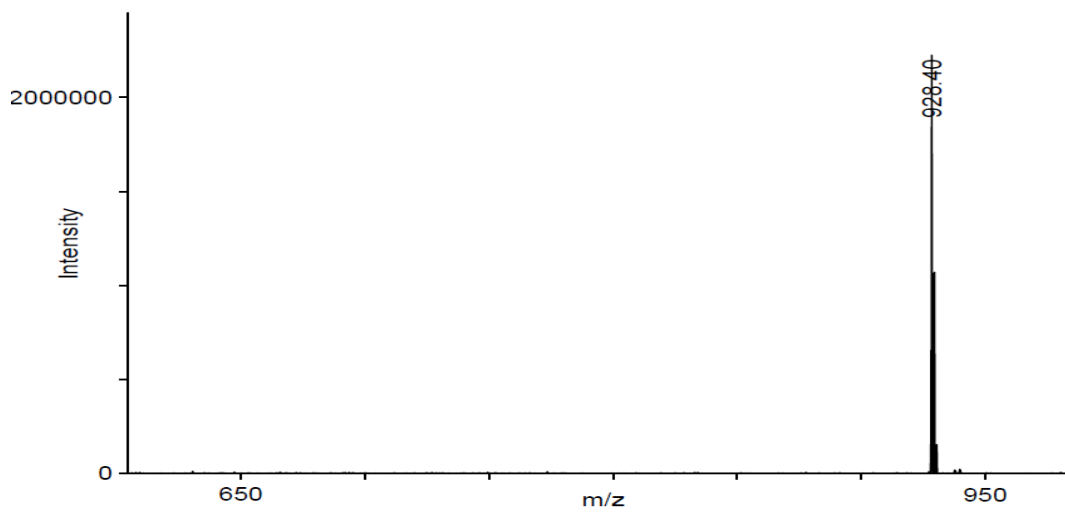
### 12 Lys-Lys



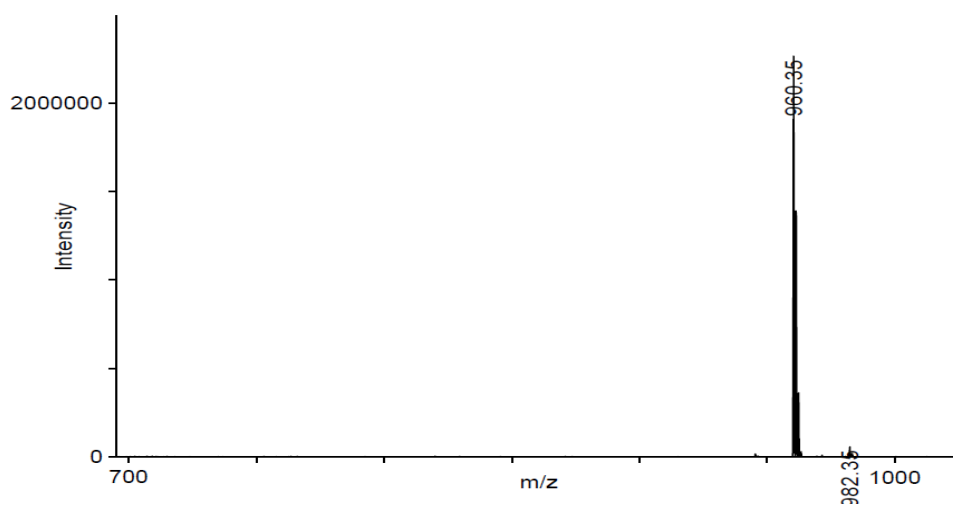
### 12 Lys-Trp



### 12 Lys-Asp

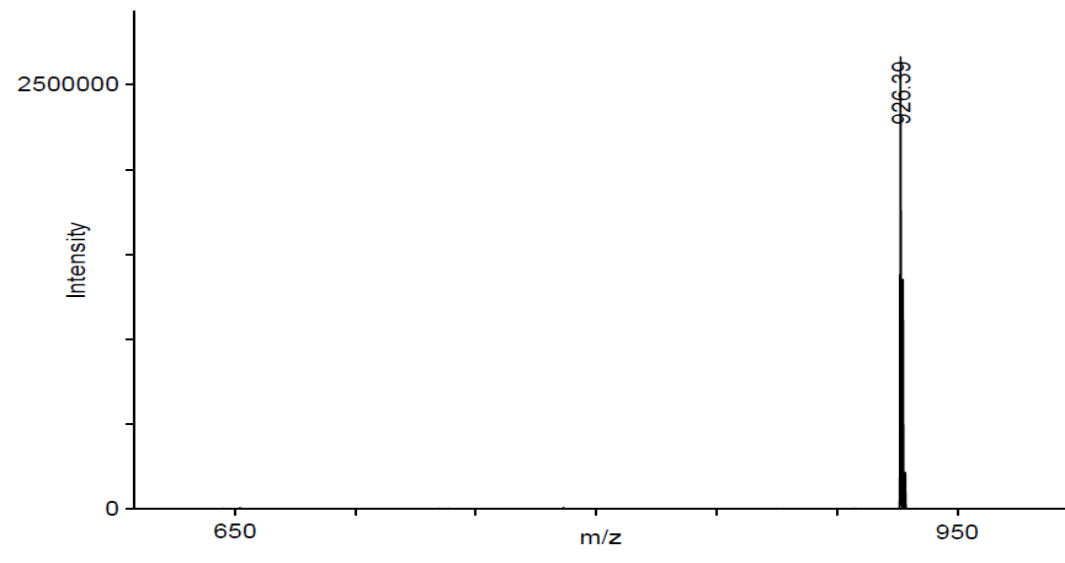


### 12 Lys-D-Phe

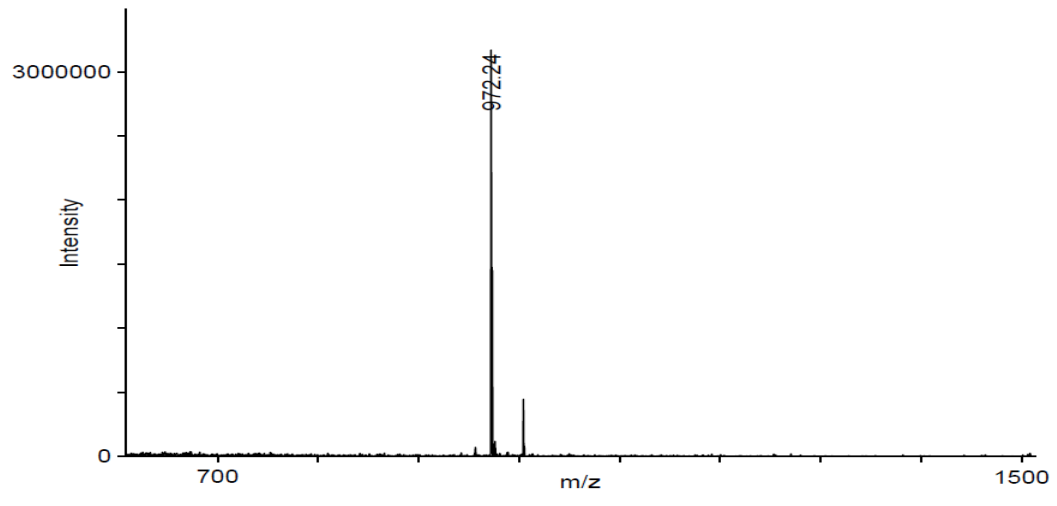




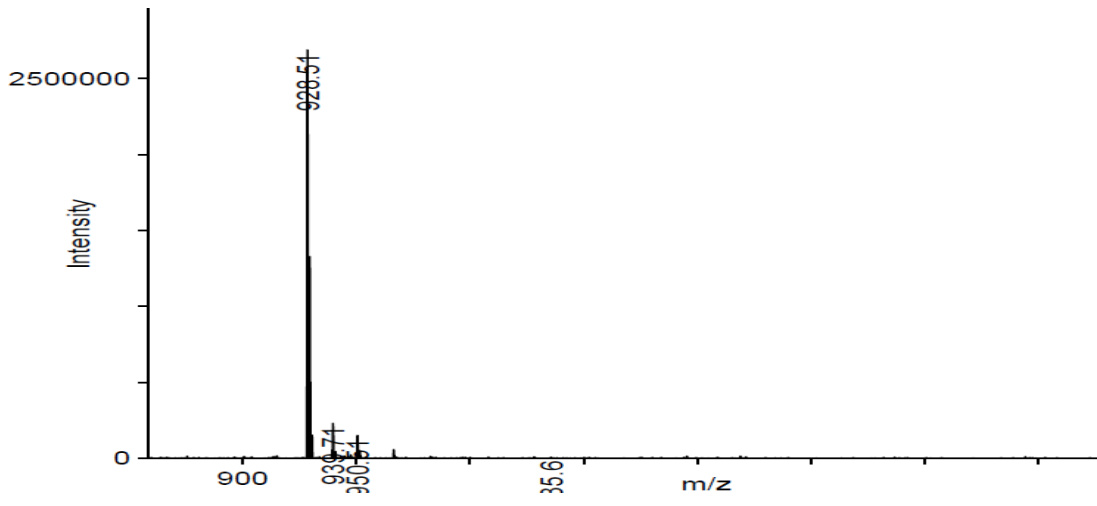
### 12 Lys-Nle



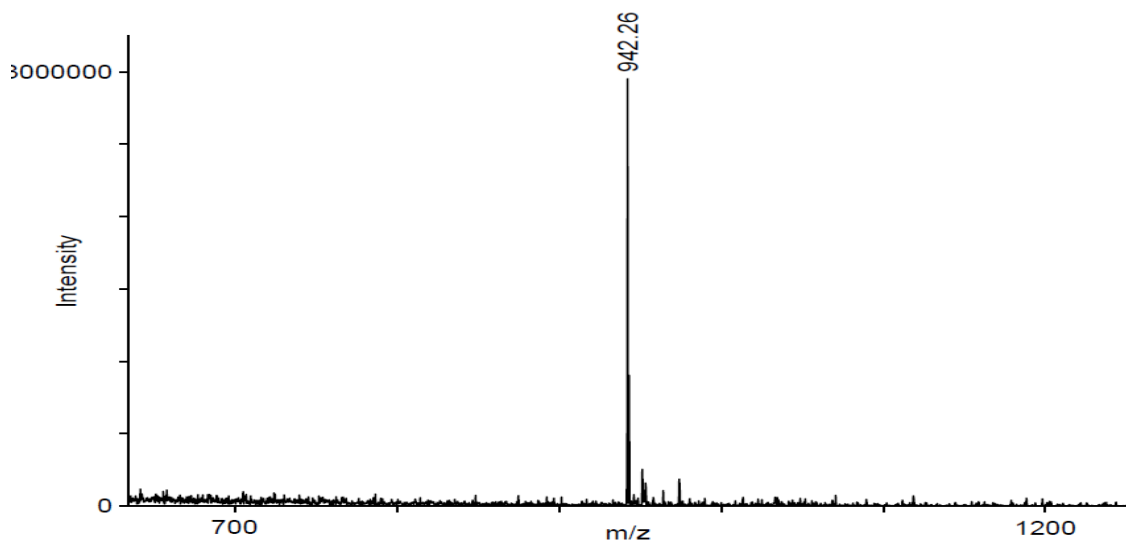
### 12 Trp-D-Thr



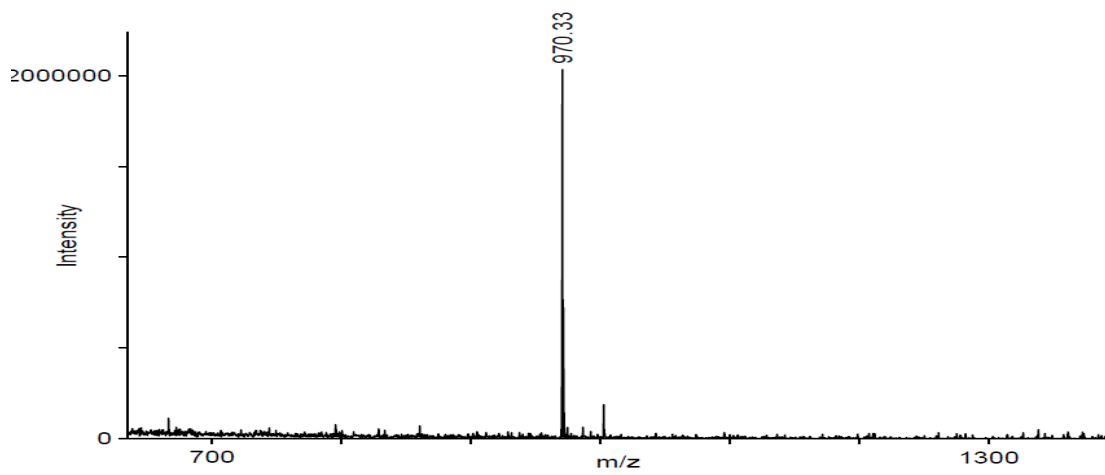
### 12 Trp-Gly



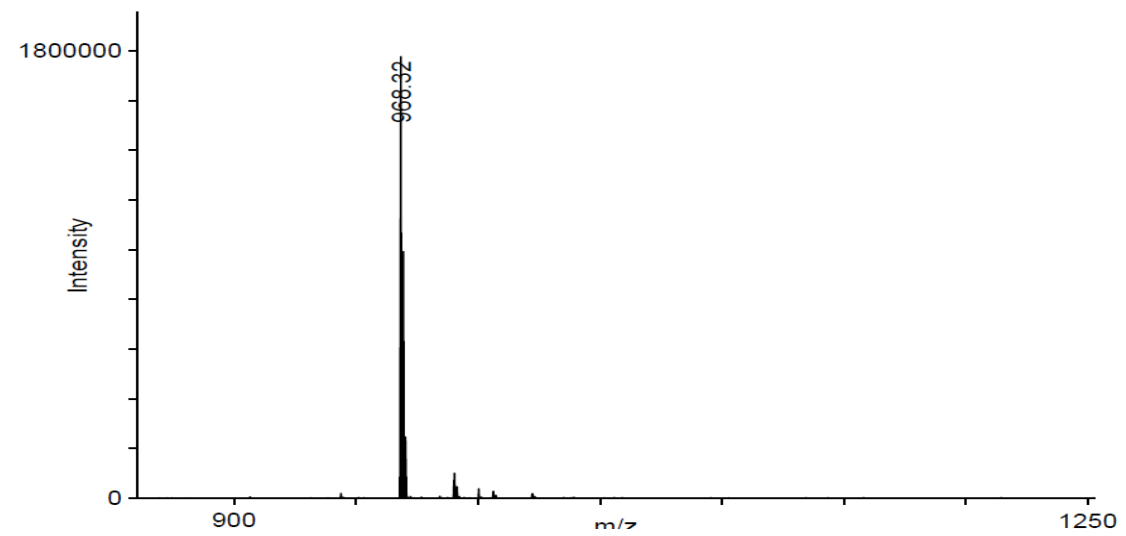
### 12 Trp-Ala



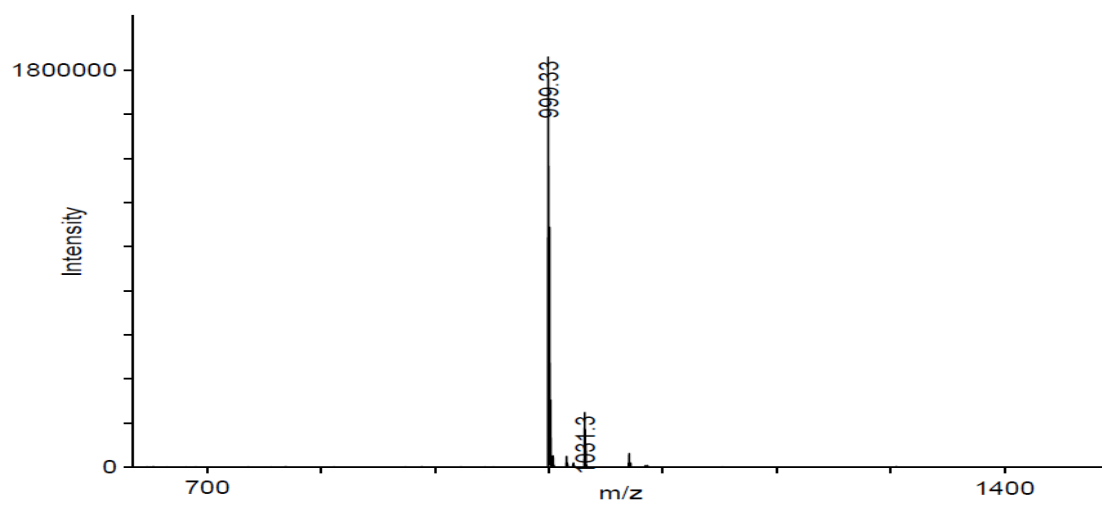
### 12 Trp-D-Val



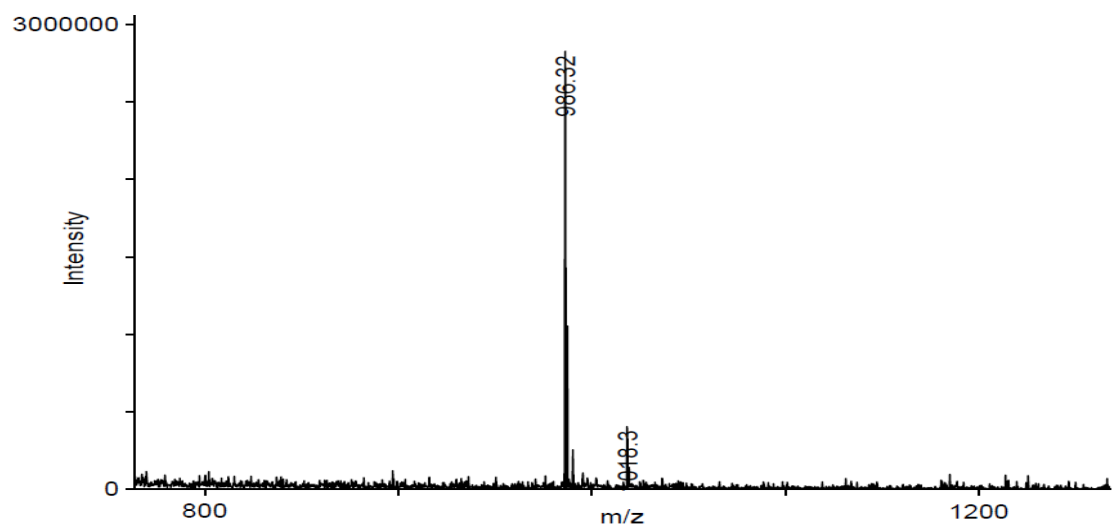
### 12 Trp-Pro



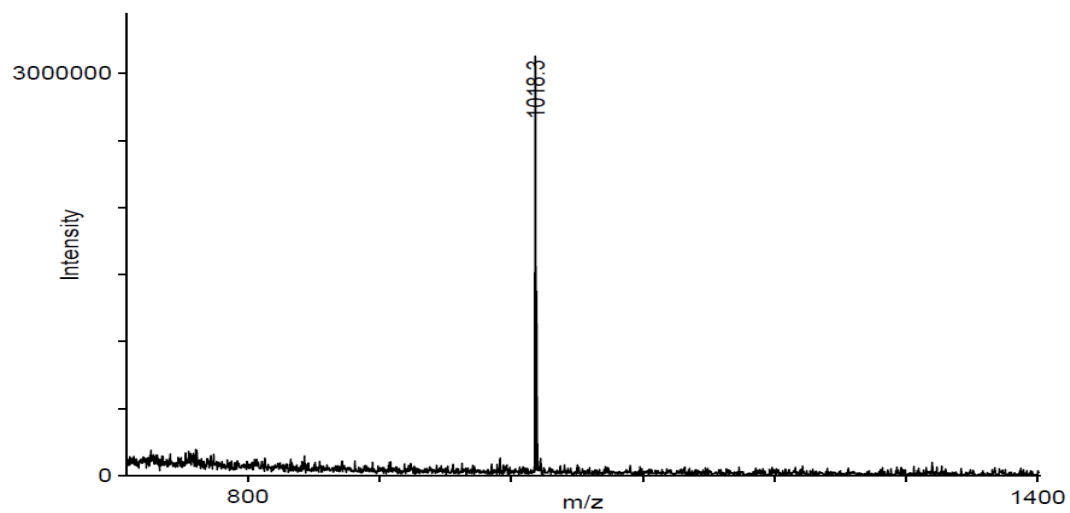
### 12 Trp-Lys



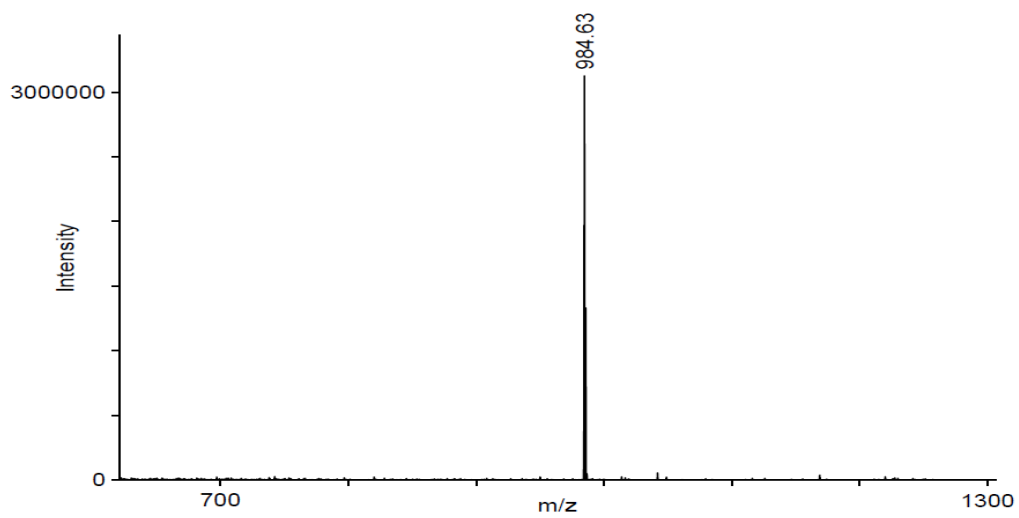
### 12 Trp-Asp



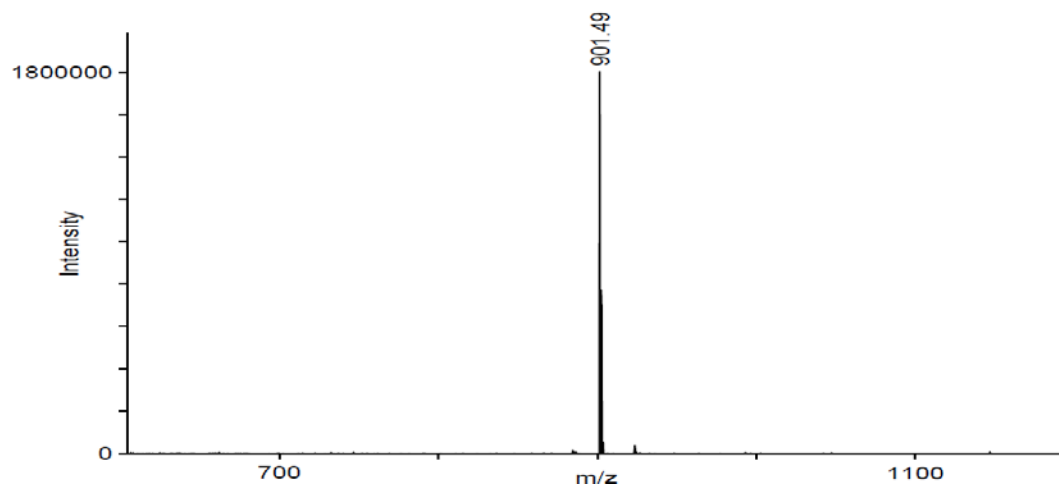
### 12 Trp-D-Phe



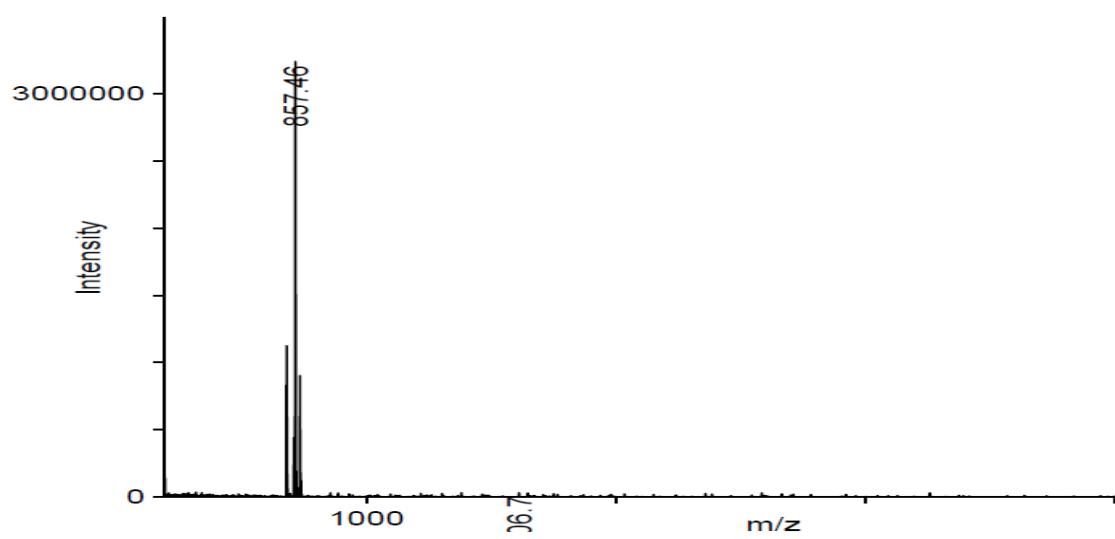
### 12 Trp-Nle



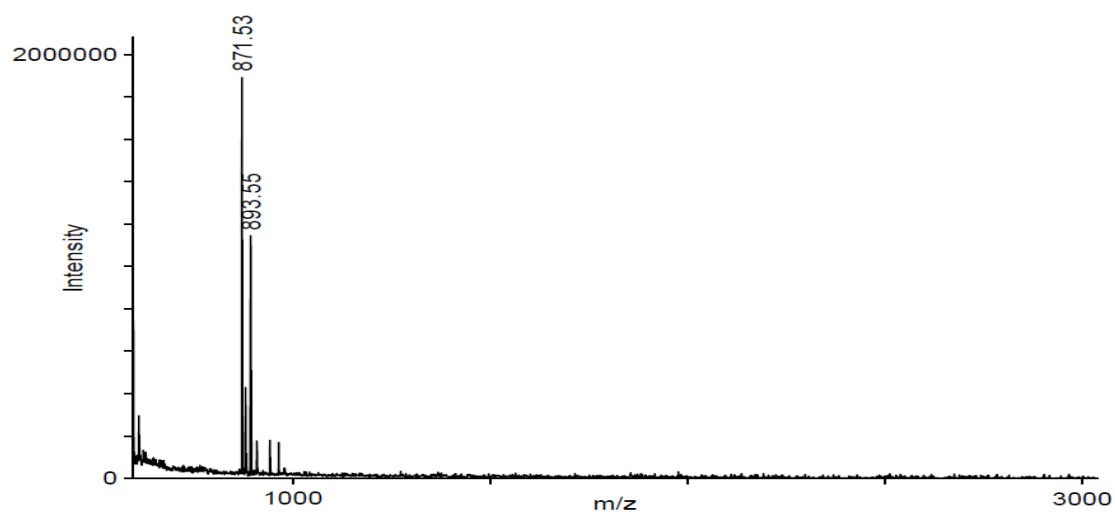
### 12 Asp-D-Thr



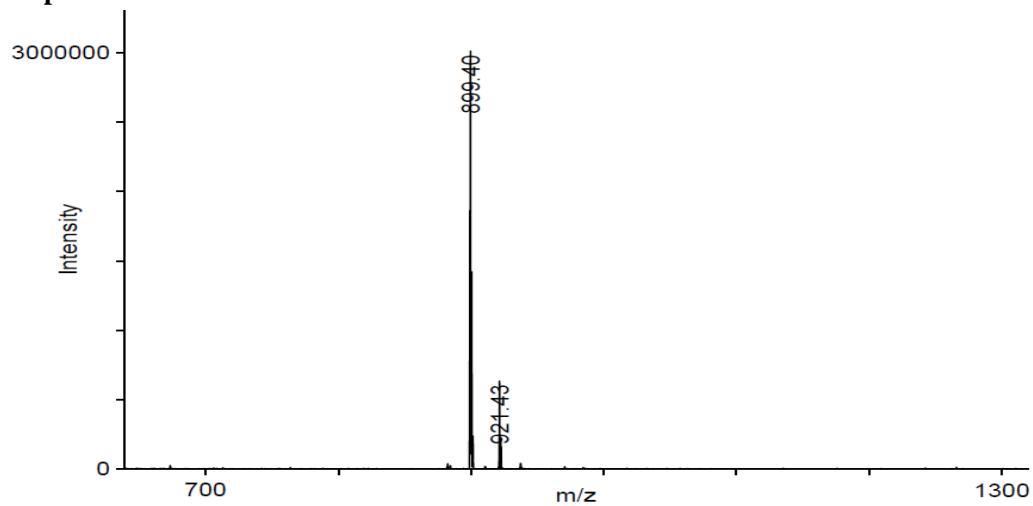
### 12 Asp-Gly



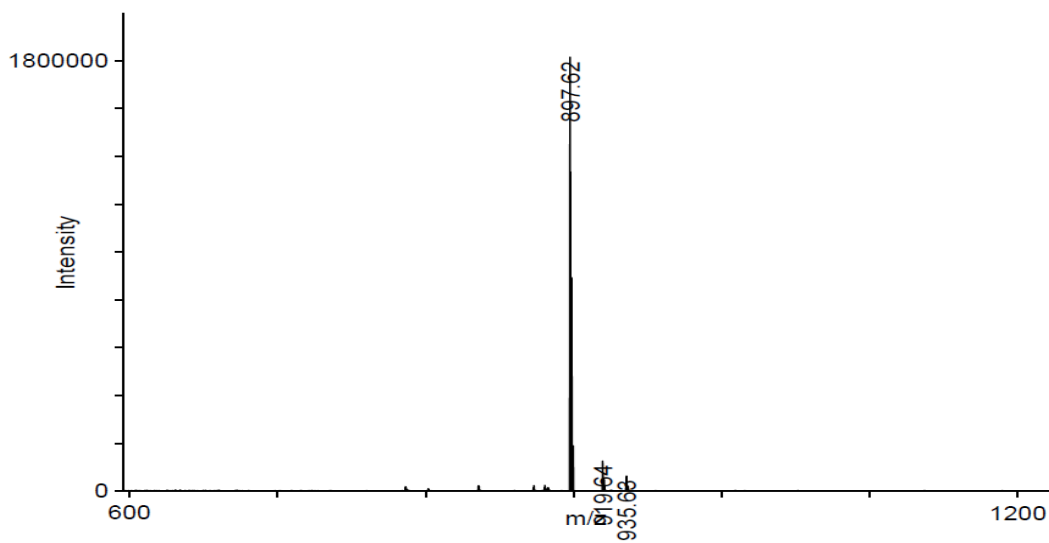
### 12 Asp-Ala (12a)



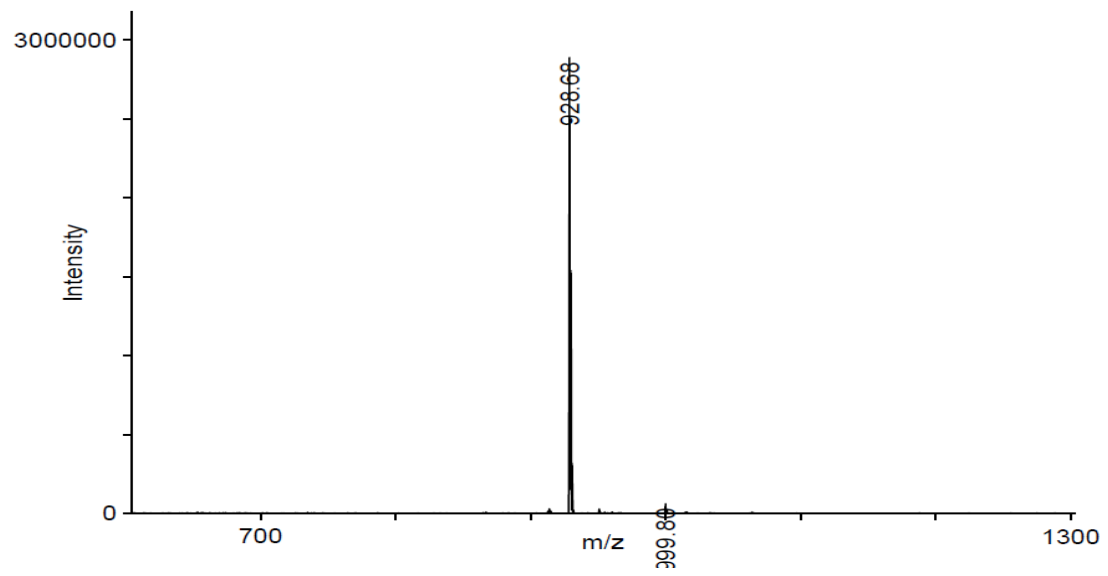
### 12 Asp-D-Val



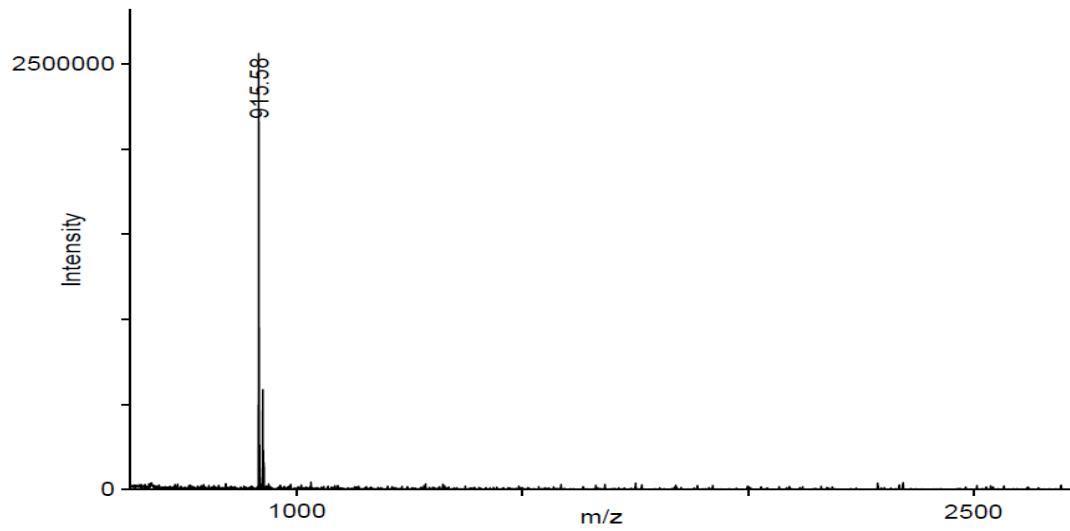
### 12 Asp-Pro



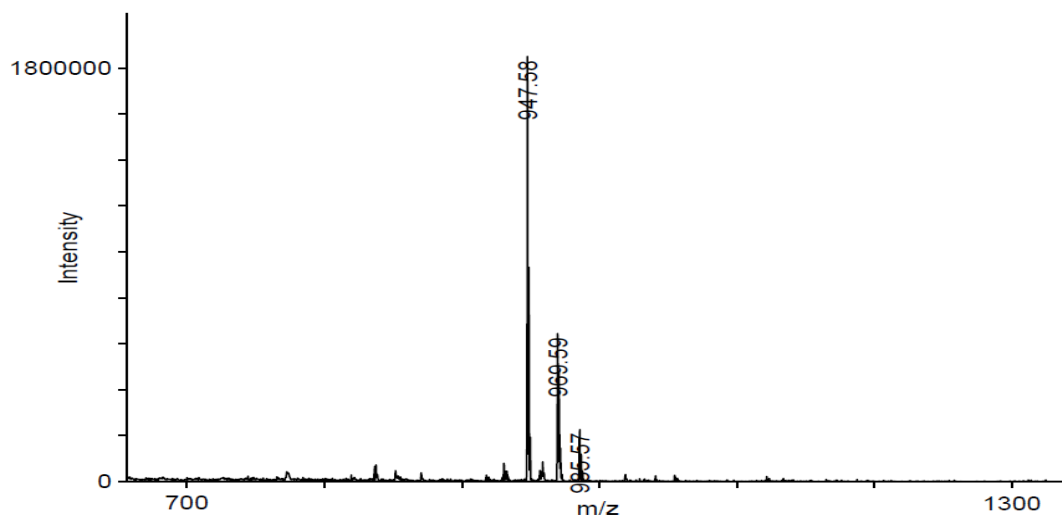
### 12 Asp-Lys



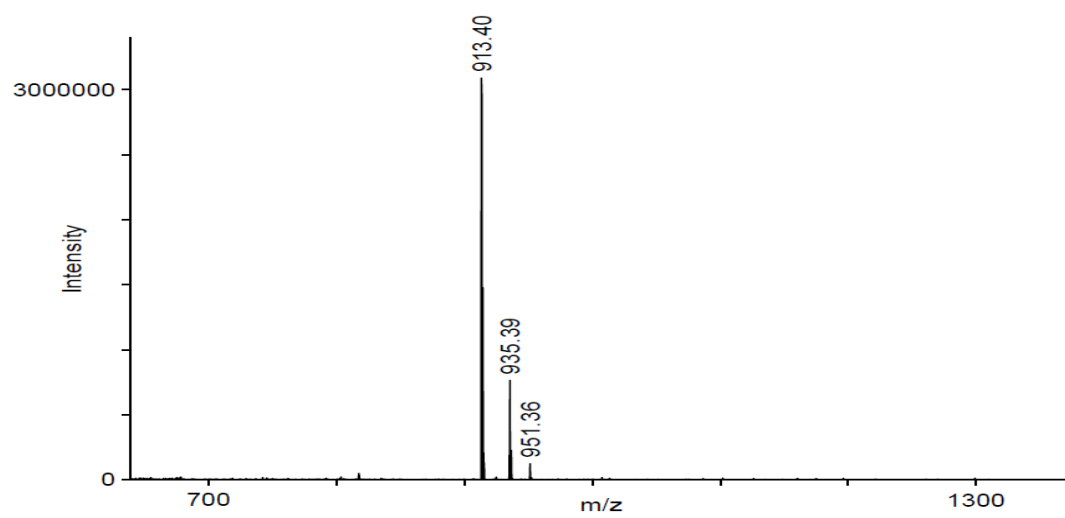
### 12 Asp-Asp



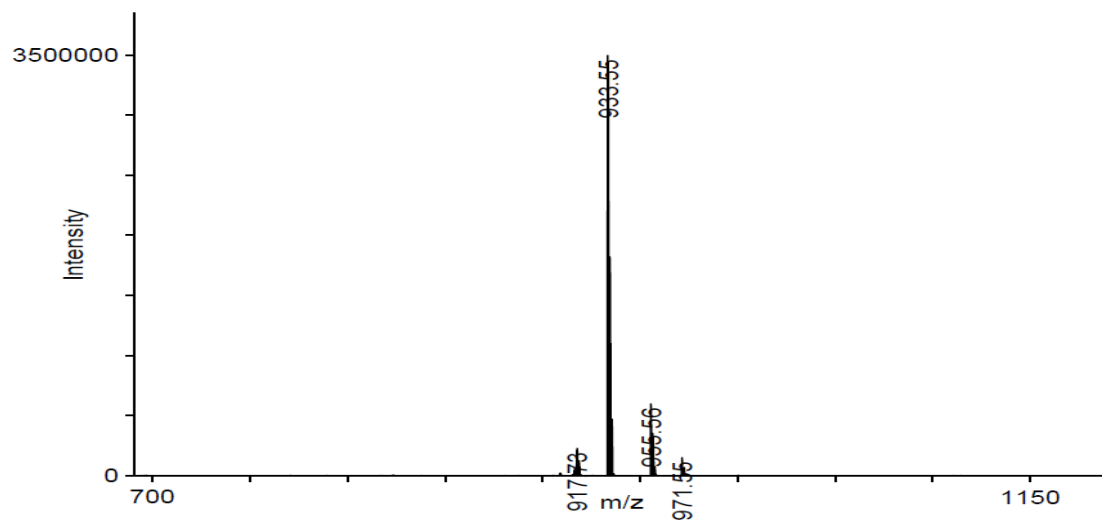
### 12 Asp-D-Phe



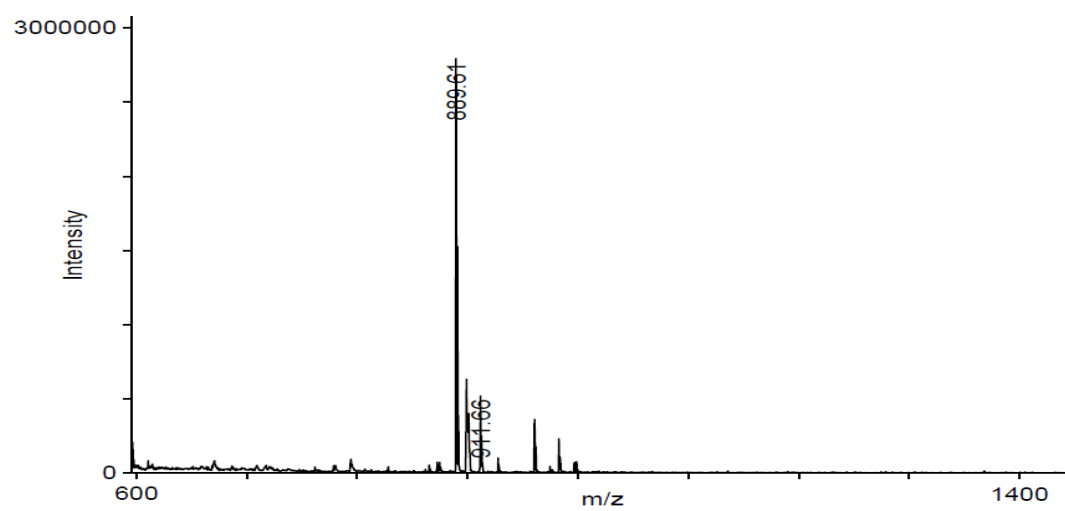
### 12 Asp-Nle



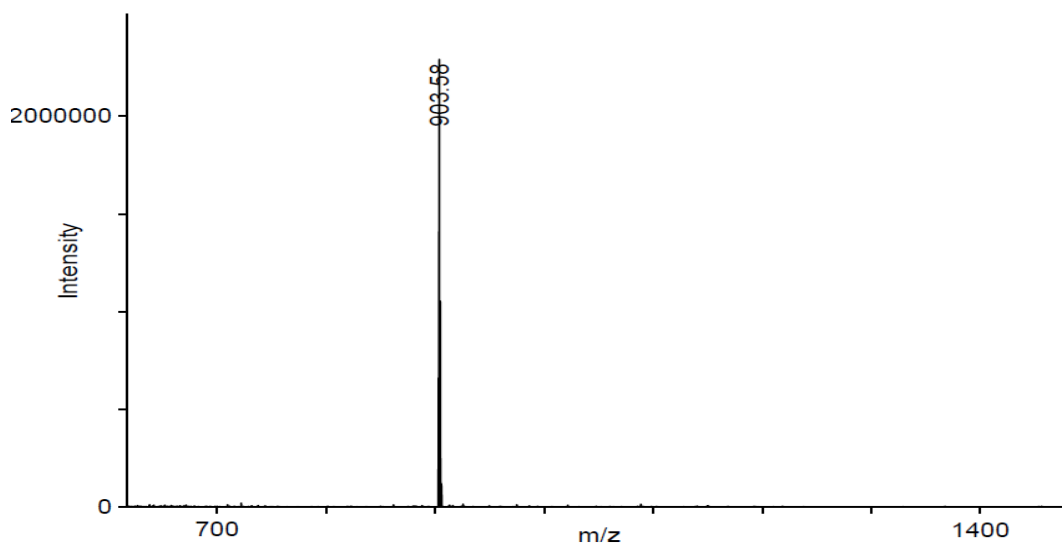
### 12 D-Phe-D-Thr



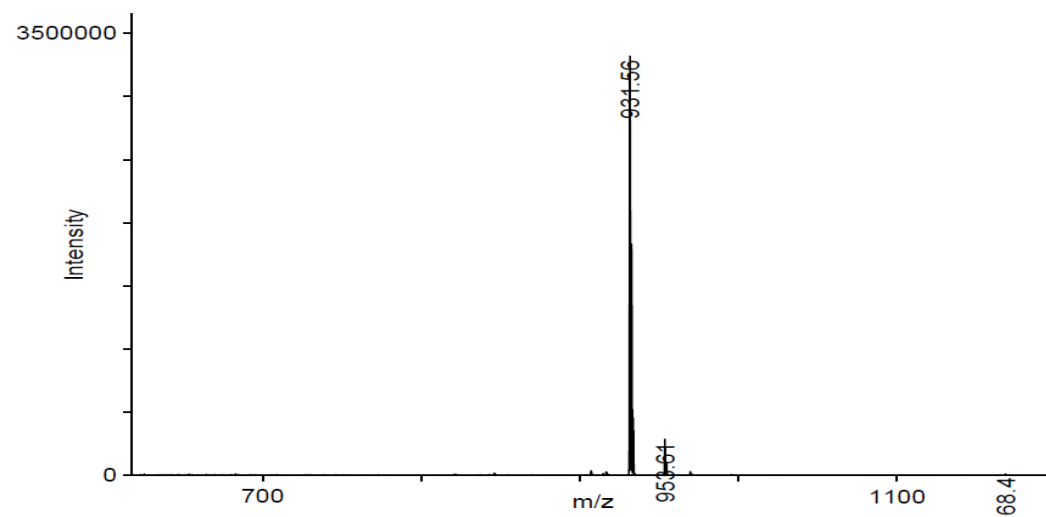
### 12 D-Phe-Gly



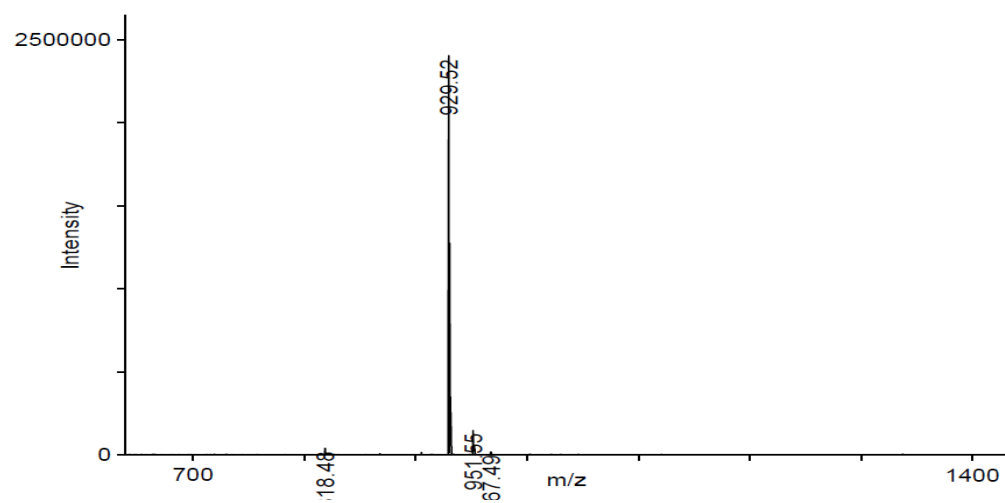
### 12 D-Phe-Ala



### 12 D-Phe-D-Val

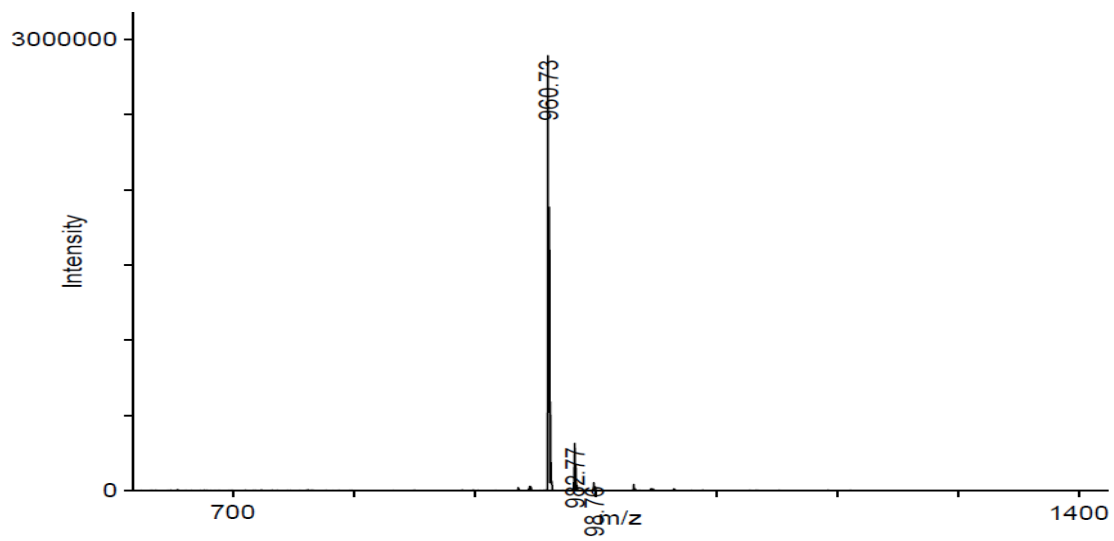


### 12 D-Phe-Pro

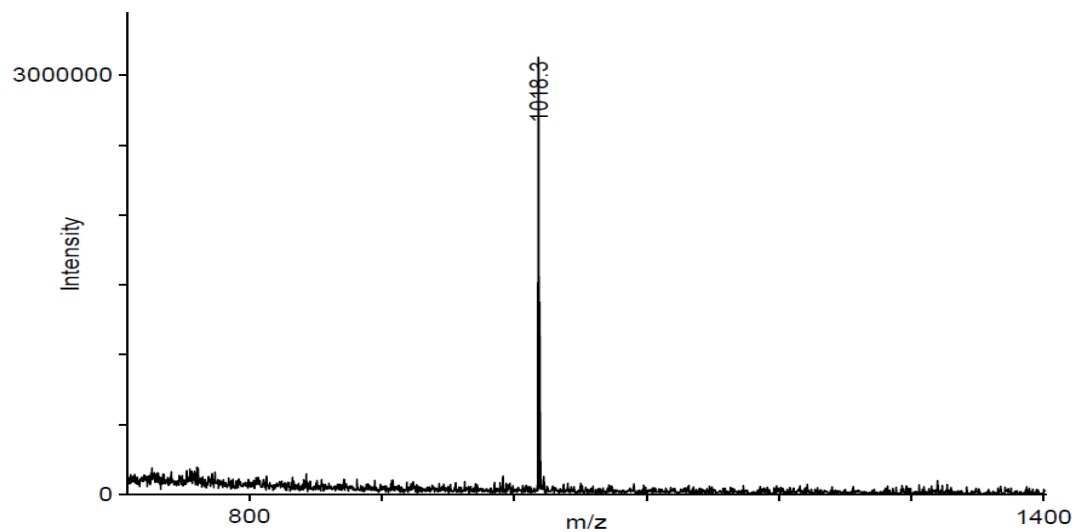




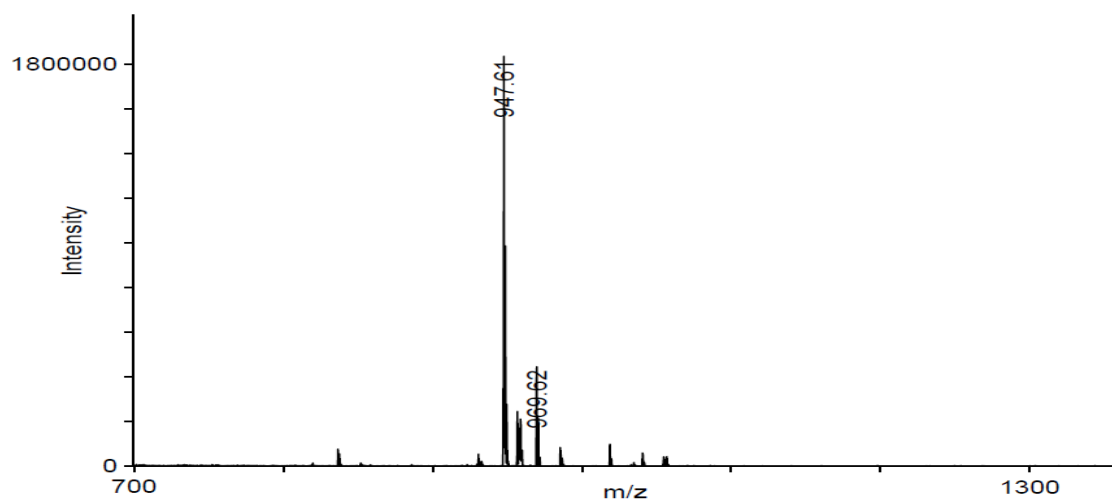
### 12 D-Phe-Lys



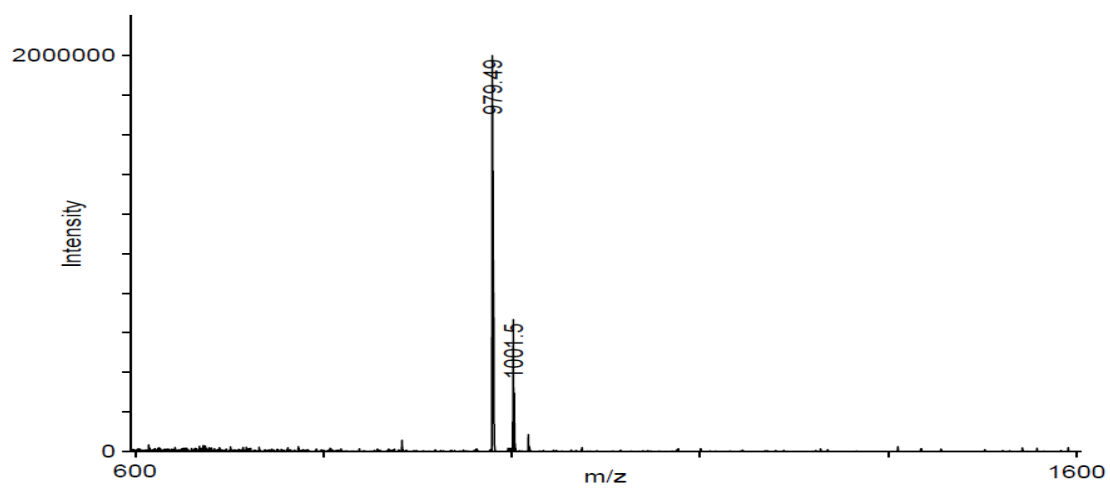
### 12 D-Phe-Trp



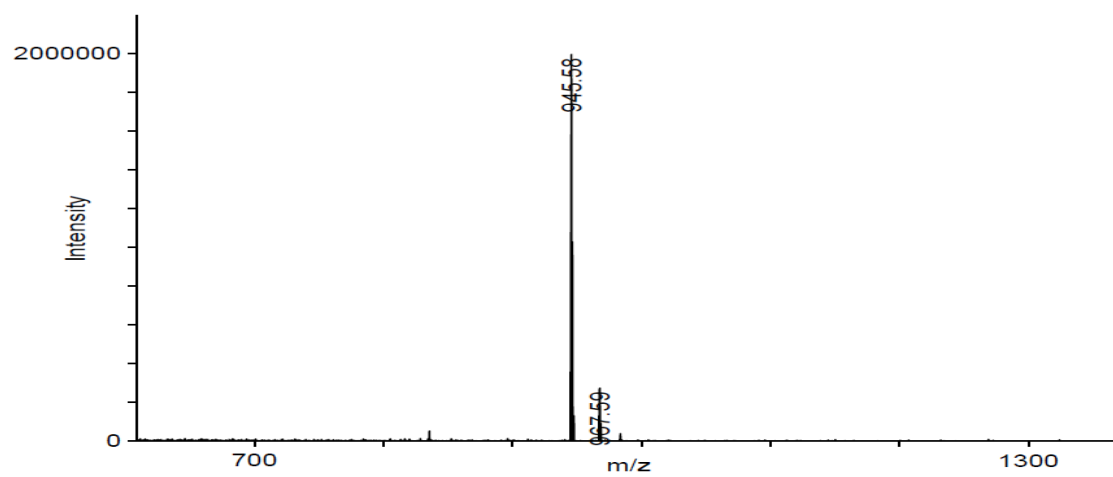
### 12 D-Phe-Asp



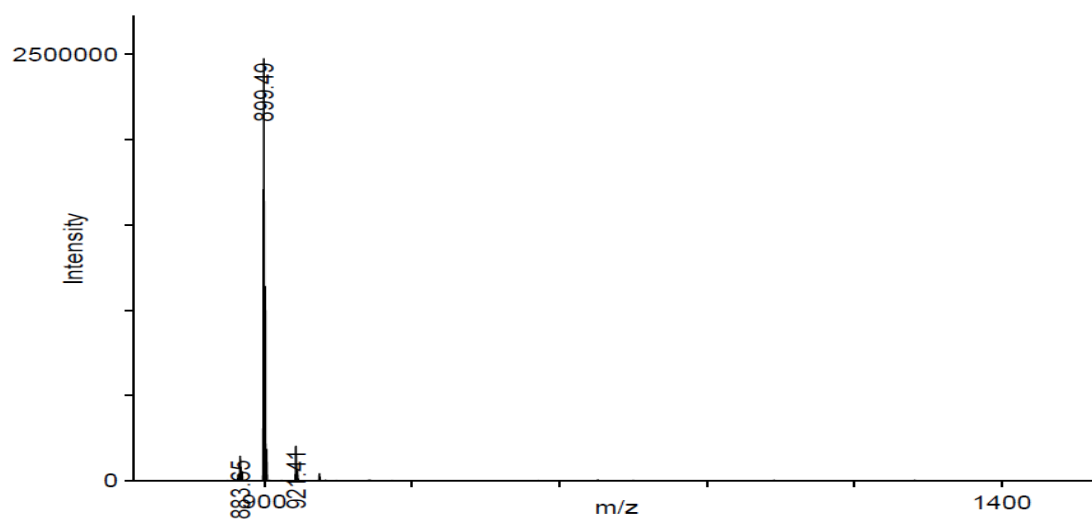
### 12 D-Phe-D-Phe



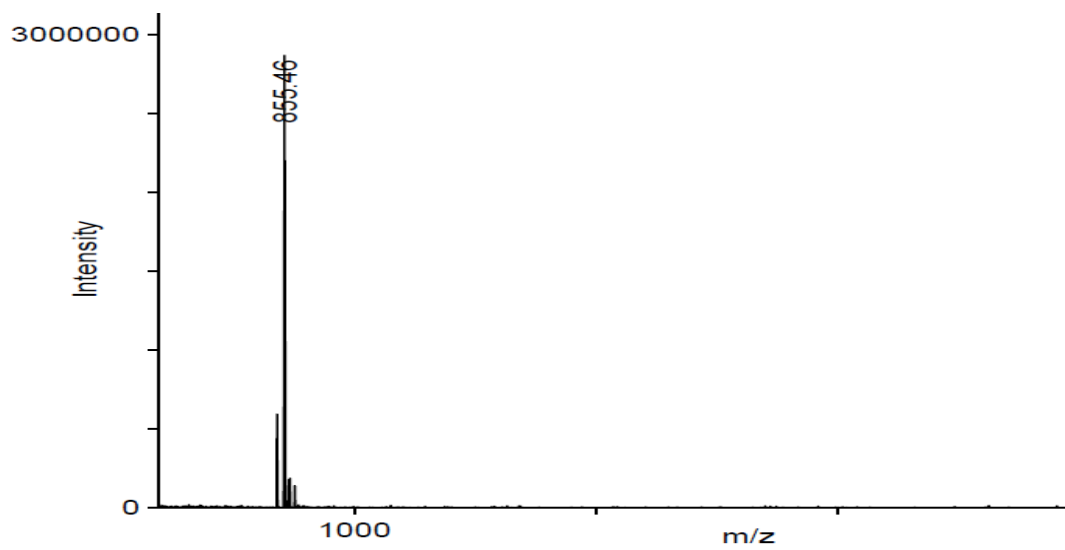
### 12 D-Phe-Nle



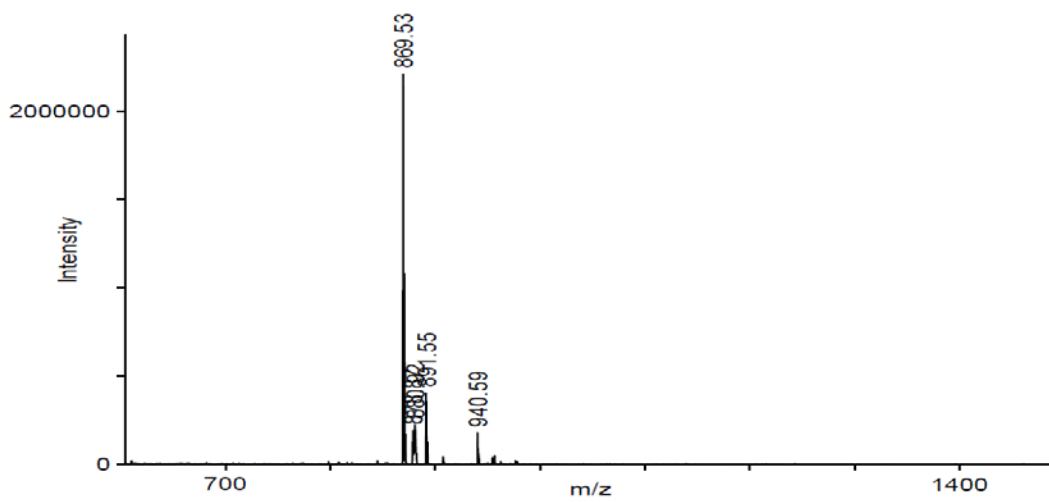
### 12 Nle-D-Thr



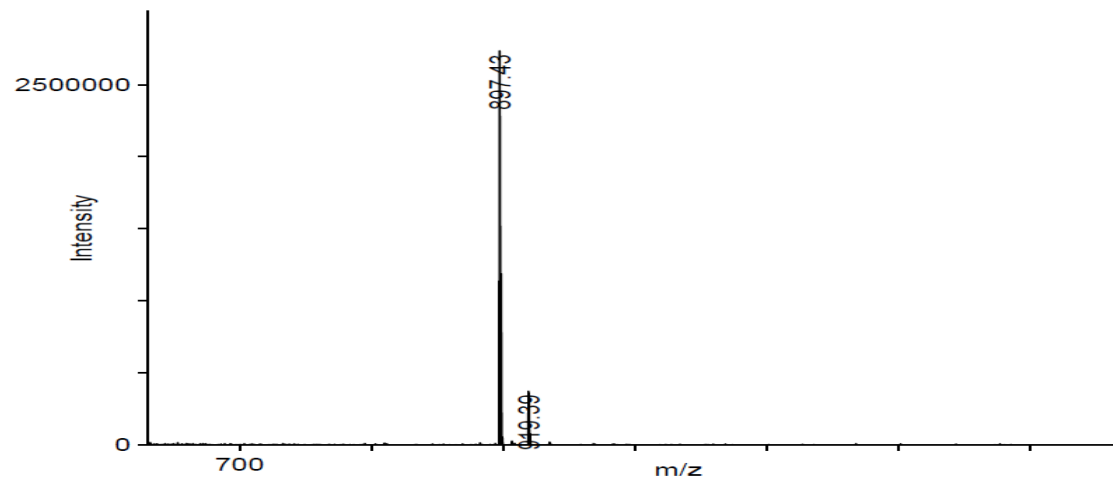
### 12 Nle-Gly



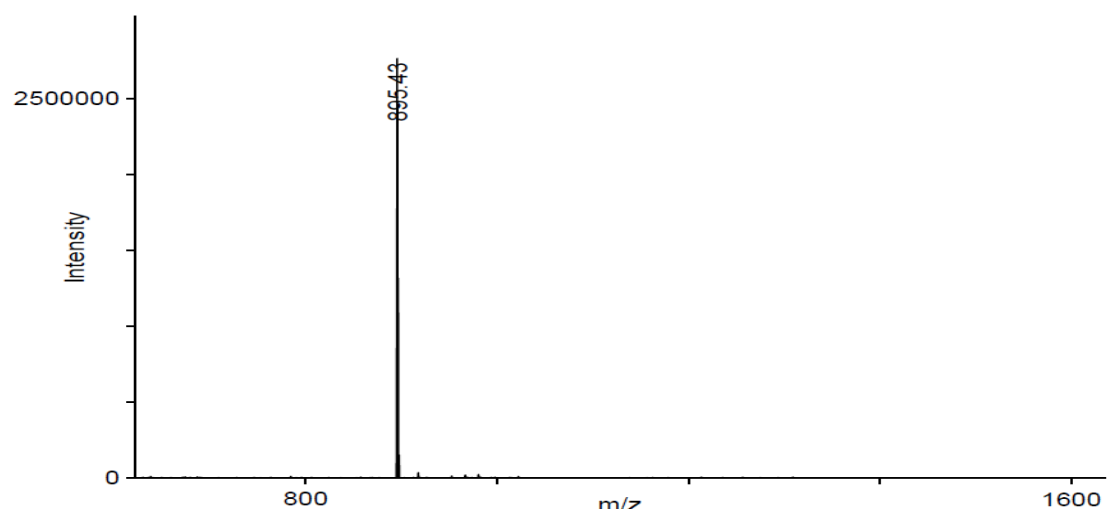
### 12 Nle-Ala



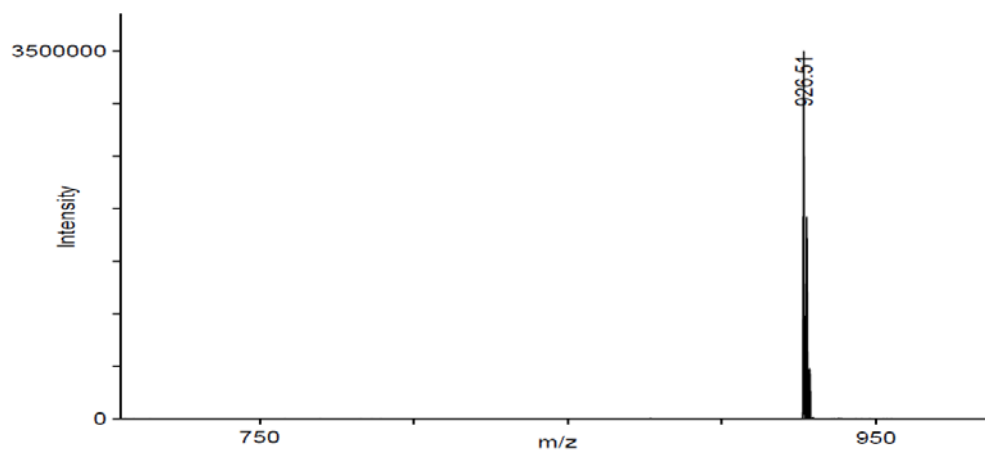
### 12 Nle-D-Val



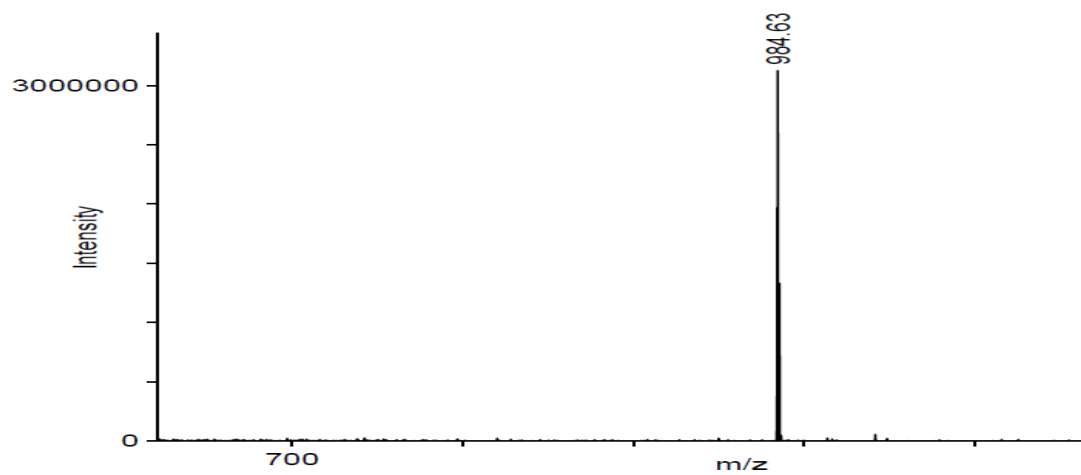
### 12 Nle-Pro



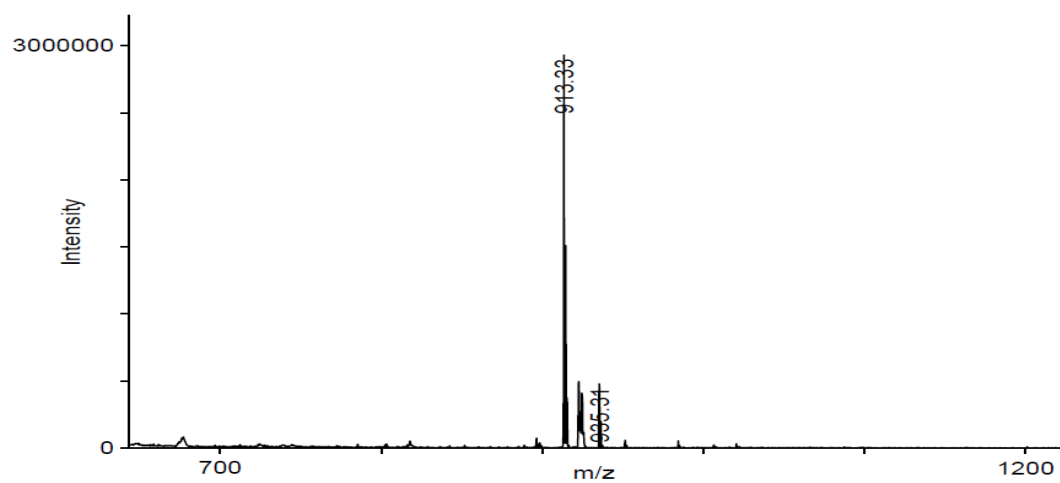
### 12 Nle-Lys



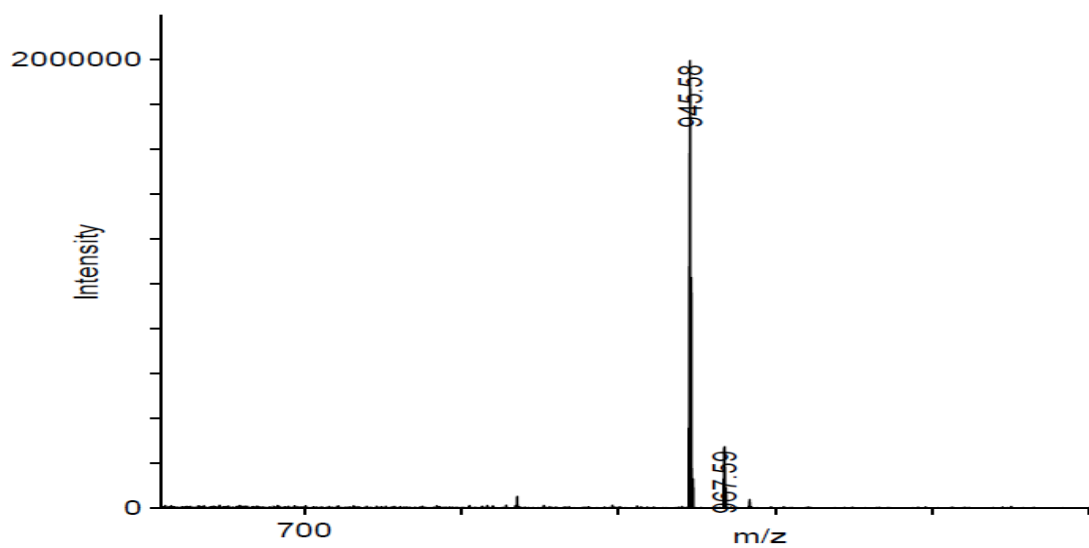
### 12 Nle-Trp



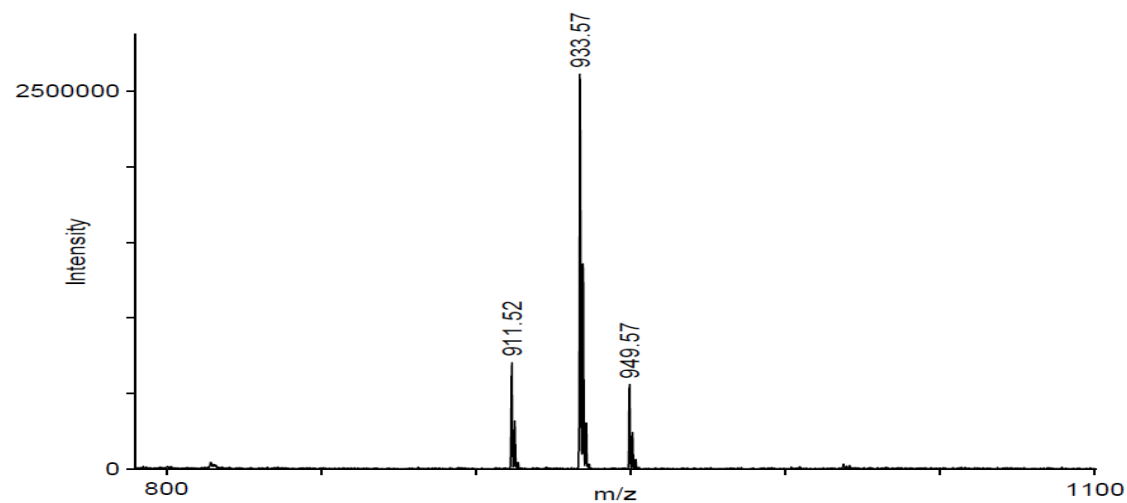
### 12 Nle-Asp



### 12 Nle-D-Phe



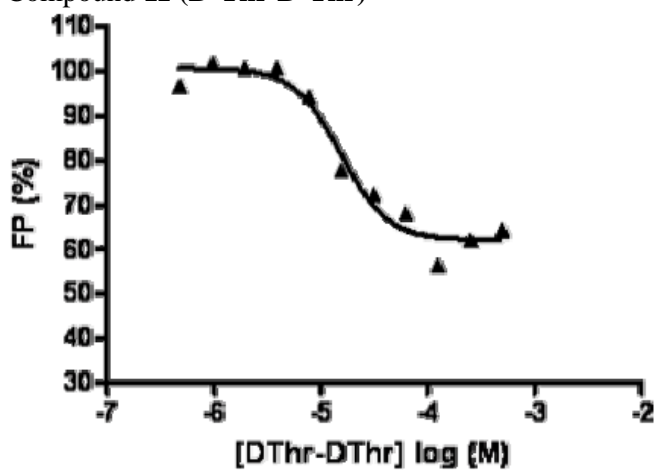
### 12 Nle-Nle



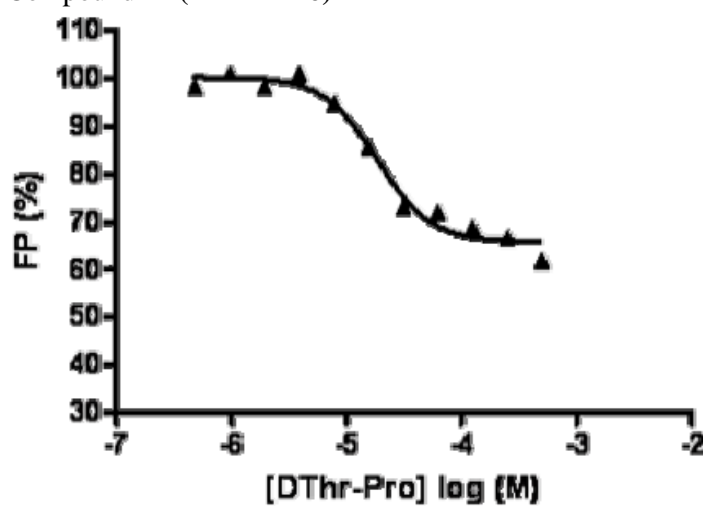
(911 MW+H<sup>+</sup>, 933 MW+Na<sup>+</sup>, 949 MW+K<sup>+</sup>)

**Figure S5.** Additional representative titration curves derived from fluorescence anisotropy (FA) competition assay of rapalogs. The percentage of FA was plotted against the rapalog concentration.

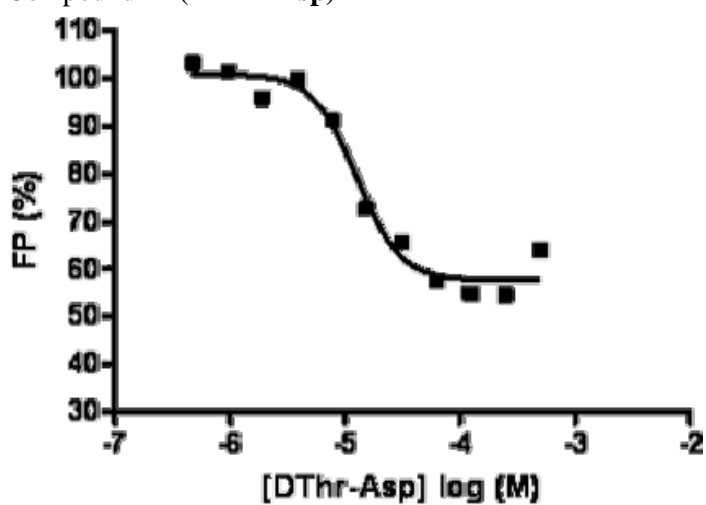
**Compound 11 (D-Thr-D-Thr)**



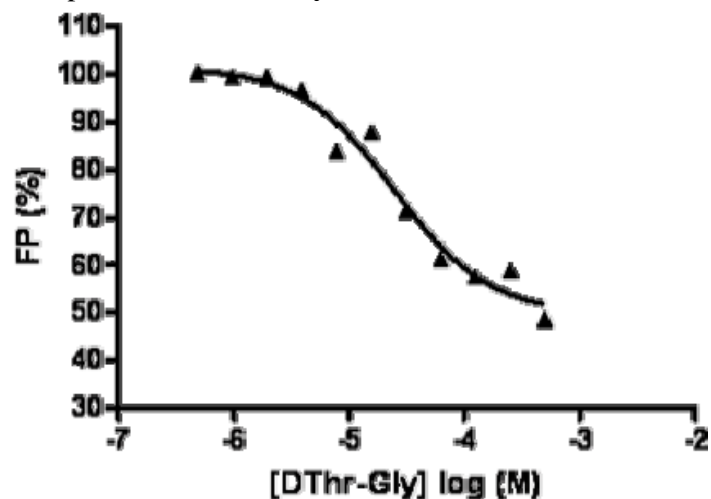
**Compound 11 (D-Thr-Pro)**



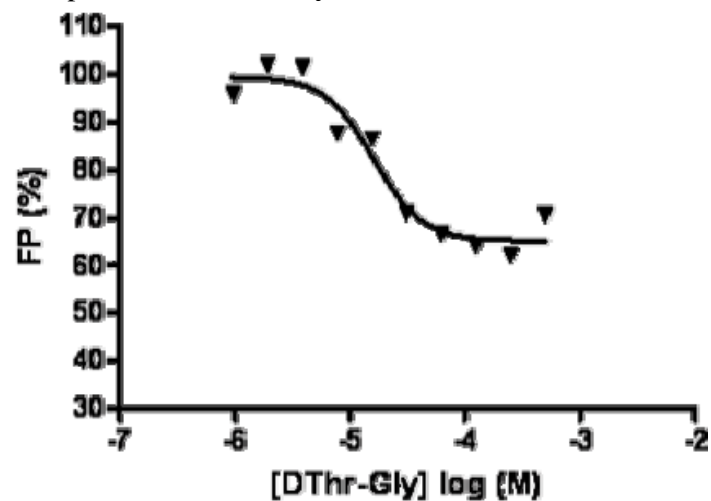
**Compound 11 (D-Thr-Asp)**



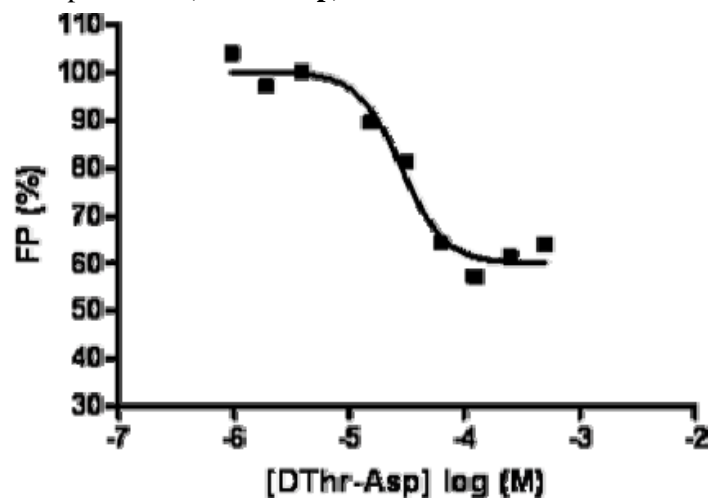
Compound 11 (D-Thr-Gly)



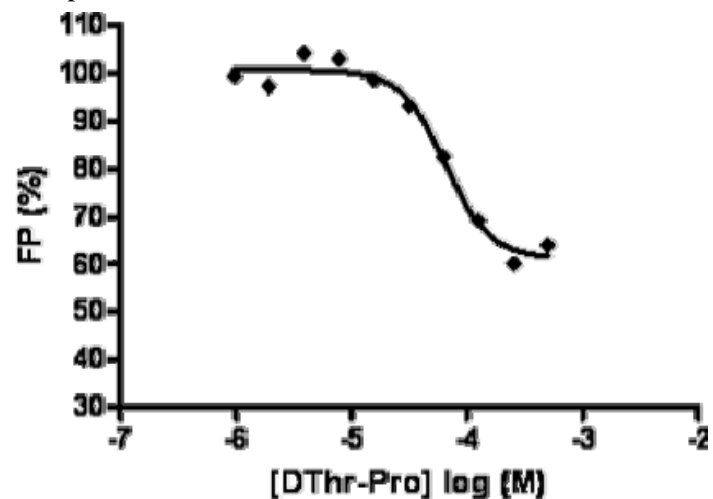
Compound 12 (D-Thr-Gly)



Compound 12 (D-Thr-Asp)



Compound 12 (D-Thr-Pro)



Compound 12 (D-Thr-Trp)

