

***Vulgarin*, a sesquiterpene lactone from *Artemisia judaica* improves the antidiabetic effectiveness of glibenclamide in streptozotocin-induced diabetic rats via modulation of PEPCK and G6Pase genes expression**

Hassan N. Althurwi ^a, Gamal A. Soliman ^{a,b}, Rehab F. Abdel-Rahman ^c, Reham M. Abd-El salam^d, Hanan A. Ogaly ^{e,f}, Mohammed H. Alqarni ^g, Maged S. Abdel-Kader ^{g,h,*}

^a Department of Pharmacology, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-Kharj 11942, Saudi Arabia

^b Department of Pharmacology, College of Veterinary Medicine, Cairo University, Egypt

^c Department of Pharmacology, National Research Centre, Egypt

^d Department of Pathology, College of Veterinary Medicine, Cairo University, Egypt

^e Department of Chemistry, College of Science, King Khalid University, Abha, Saudi Arabia

^f Department of Biochemistry, College of Veterinary Medicine, Cairo University, Egypt

^g Department of Pharmacognosy, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-Kharj 11942, Saudi Arabia

^h Department of Pharmacognosy, College of Pharmacy, Alexandria University, Alexandria 21215, Egypt

Vulgarin (VGN): Colourless crystals, m.p. 175 °C; $[\alpha]_D^{25} = +43$; UV λ_{\max} 216 nm; ^1H and ^{13}C NMR Table S1; HRESIMS $[\text{M}+1]^+ m/z$ 265.1429 (calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4+\text{H}$, 265.1440, 6%), $[\text{M}+\text{Na}]^+ m/z$ 287.1247 (calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4+\text{Na}$, 287.1259, 100%), $[\text{M}-1]^+ m/z$ 263.1287 (calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4-\text{H}$, 263.1283, 100%).

4-Epivulgarin (VGN): Colourless crystals, m.p. 193 °C; $[\alpha]_D^{25} = +82$; UV λ_{\max} 215 nm; ^1H and ^{13}C NMR Table S1; HRESIMS $[\text{M}+1]^+ m/z$ 265.1429 (calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4+\text{H}$, 265.1440, 55%), $[\text{M}+\text{Na}]^+ m/z$ 287.1248 (calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4+\text{Na}$, 287.1259, 100%), $[\text{M}-1]^+ m/z$ 263.1288 (calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4-\text{H}$, 263.1288, 100%).

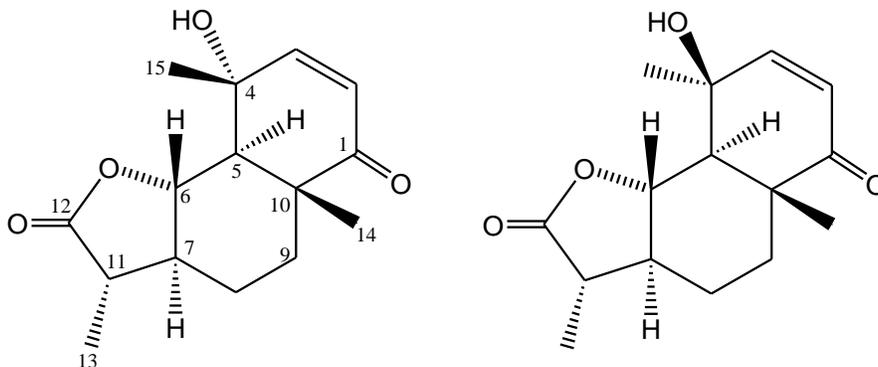


Table S1. ^1H and ^{13}C NMR data for VGN and eVGN (CDCl_3 , δ in ppm).

	Vulgarin (VGN)		4-Epivulgarin (eVGN)	
	^1H	^{13}C	^1H	^{13}C
1	-	201.80	-	203.64
2	5.72 (d, $J= 10.3$ Hz)	125.31	5.72 (d, $J= 10.3$ Hz)	124.64
3	6.47 (d, $J= 10.3$ Hz)	152.03	6.42 (d, $J= 10.3$ Hz)	151.22
4	-	69.91	-	67.76
5	2.27 (d, $J= 10.95$ Hz)	54.39	1.88 (d, $J= 10.95$ Hz)	50.97
6	4.06 (t, $J= 11$ Hz)	79.41	4.25 (t, $J= 10.75$ Hz)	79.34
7	1.54 (m)	52.19	1.55 (m)	52.20
8	1.37 (m), 1.85 (m)	22.53	1.39 (m), 1.81 (m)	22.61
9	1.37 (m), 1.85 (m)	34.01	1.39 (m), 1.81 (m)	32.52
10	-	46.25	-	45.97
11	2.22 (m)	40.39	2.21 (h, $J= 6.85$ Hz)	40.71
12	-	178.43	-	179.46
13	1.09 (d, $J= 6.95$ Hz)	12.39	1.09 (d, $J= 6.95$ Hz)	12.39
14	1.07 (s)	19.71	1.20 (s)	20.65
15	1.41 (s)	23.56	1.44 (s)	31.09
OH	2.95 (s)	-	3.03 (s)	-

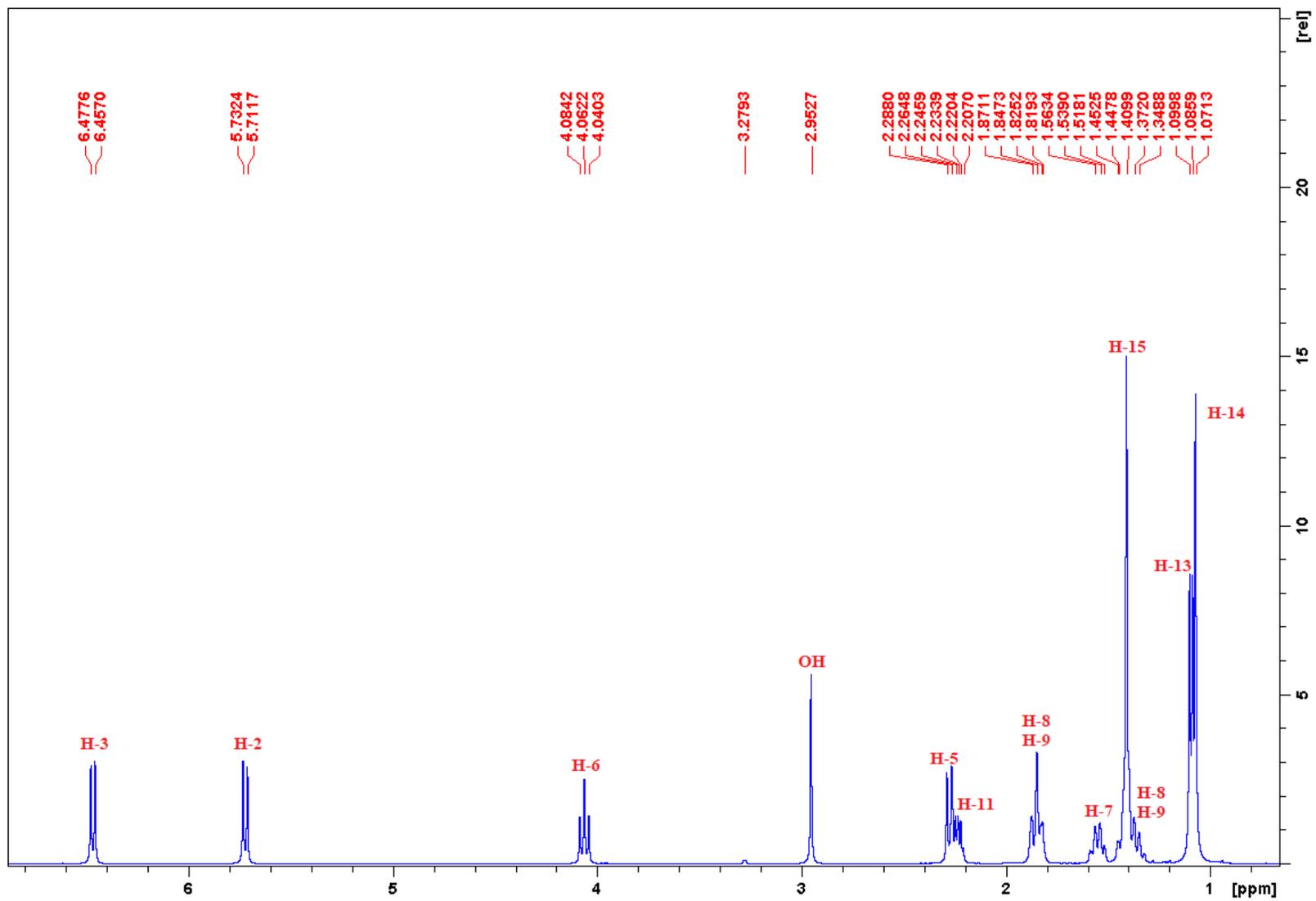


Figure S1: ^1H NMR data for VGN.

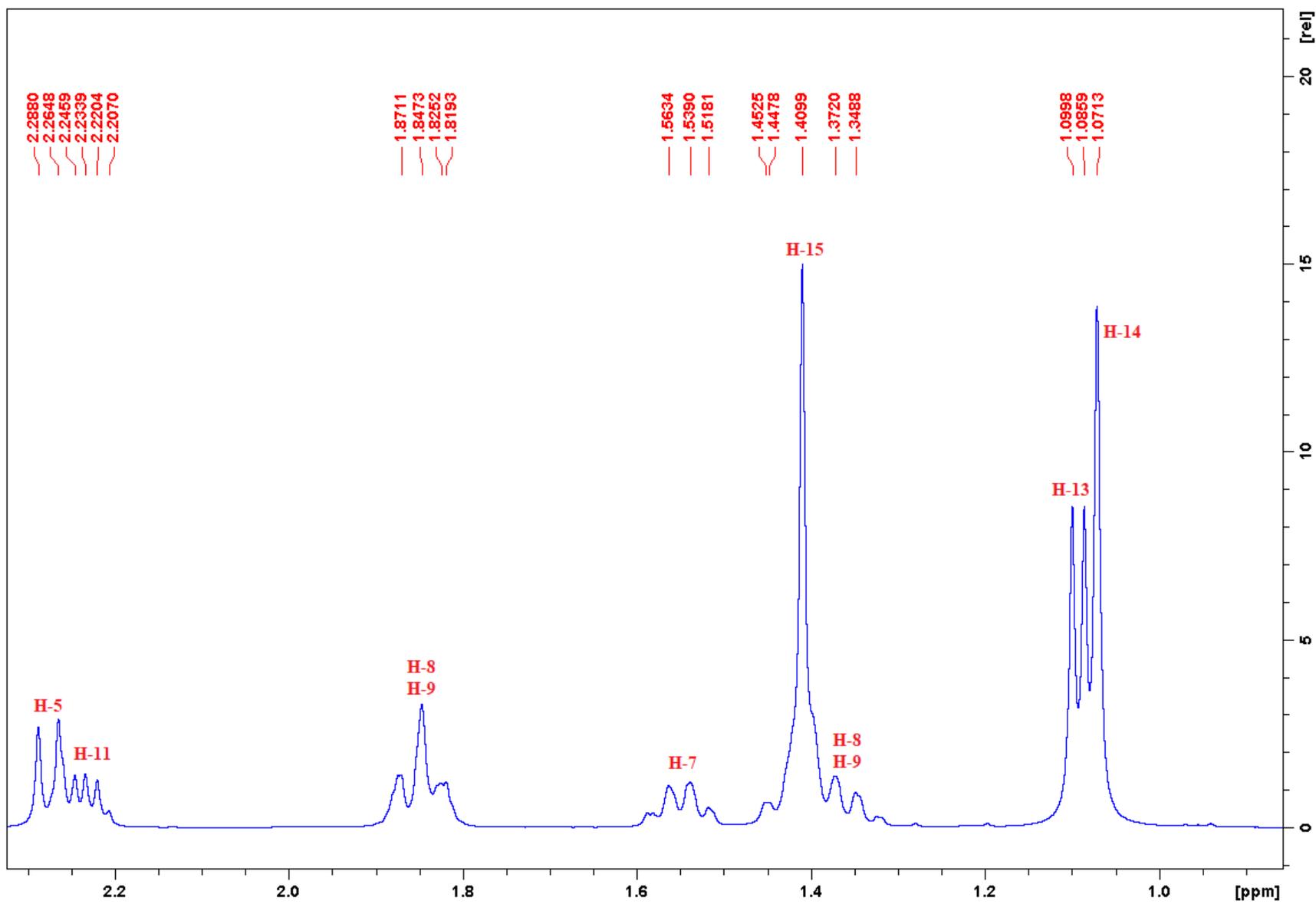


Figure S2: ¹H NMR data for VGN (Exp.).

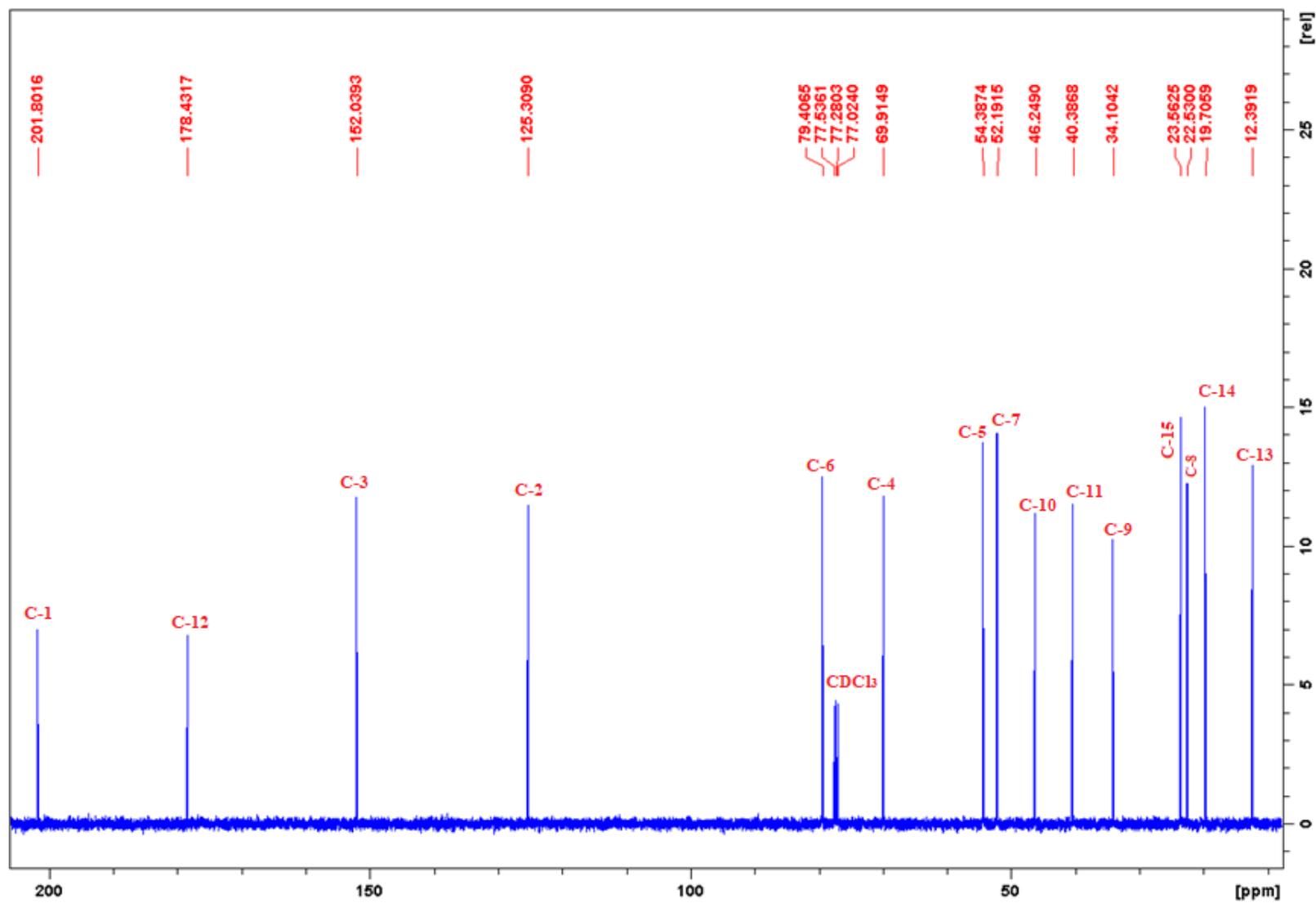


Figure S3: ^{13}C NMR data for VGN.

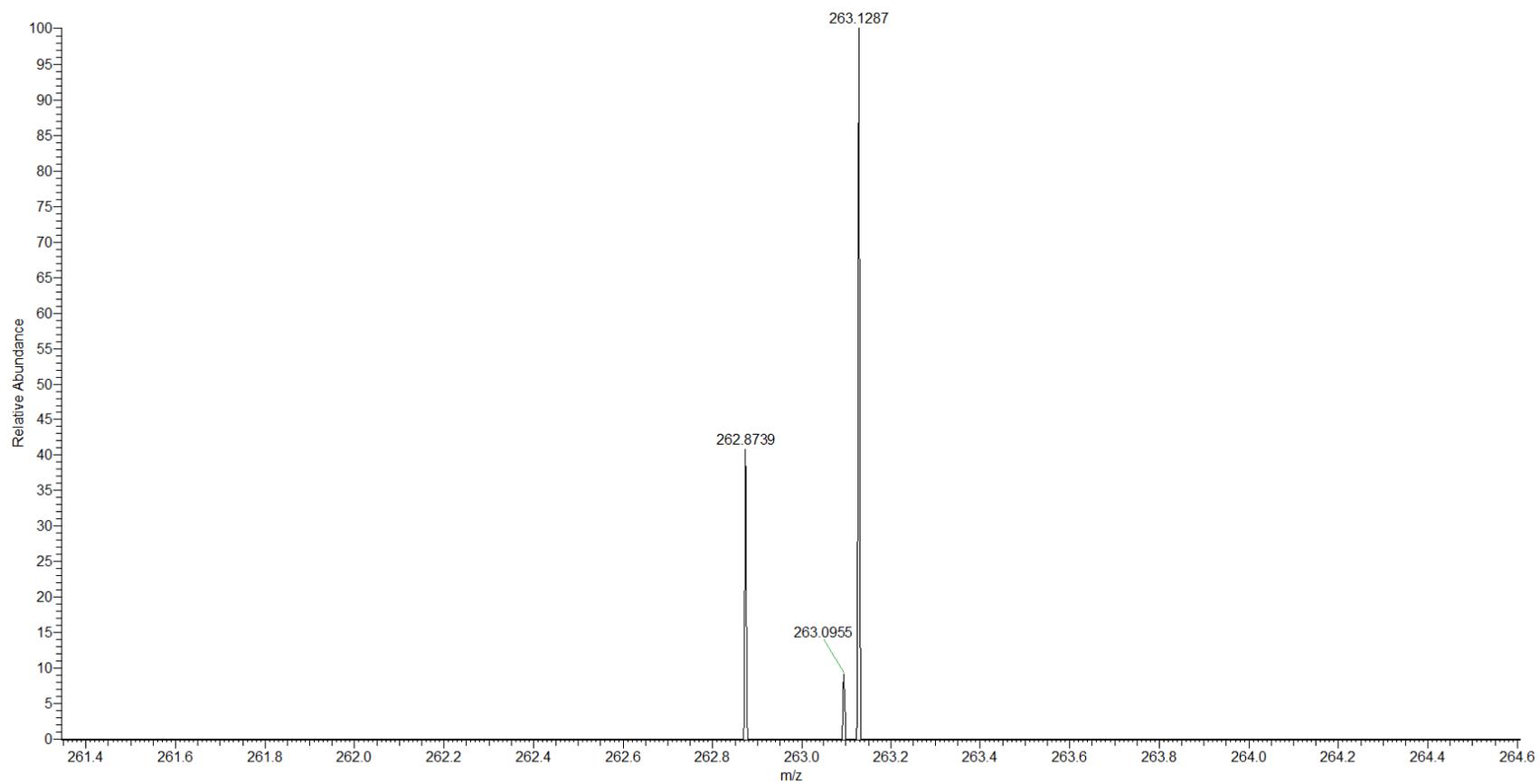


Figure S4: HRESIMS data of VGN (negative mode).

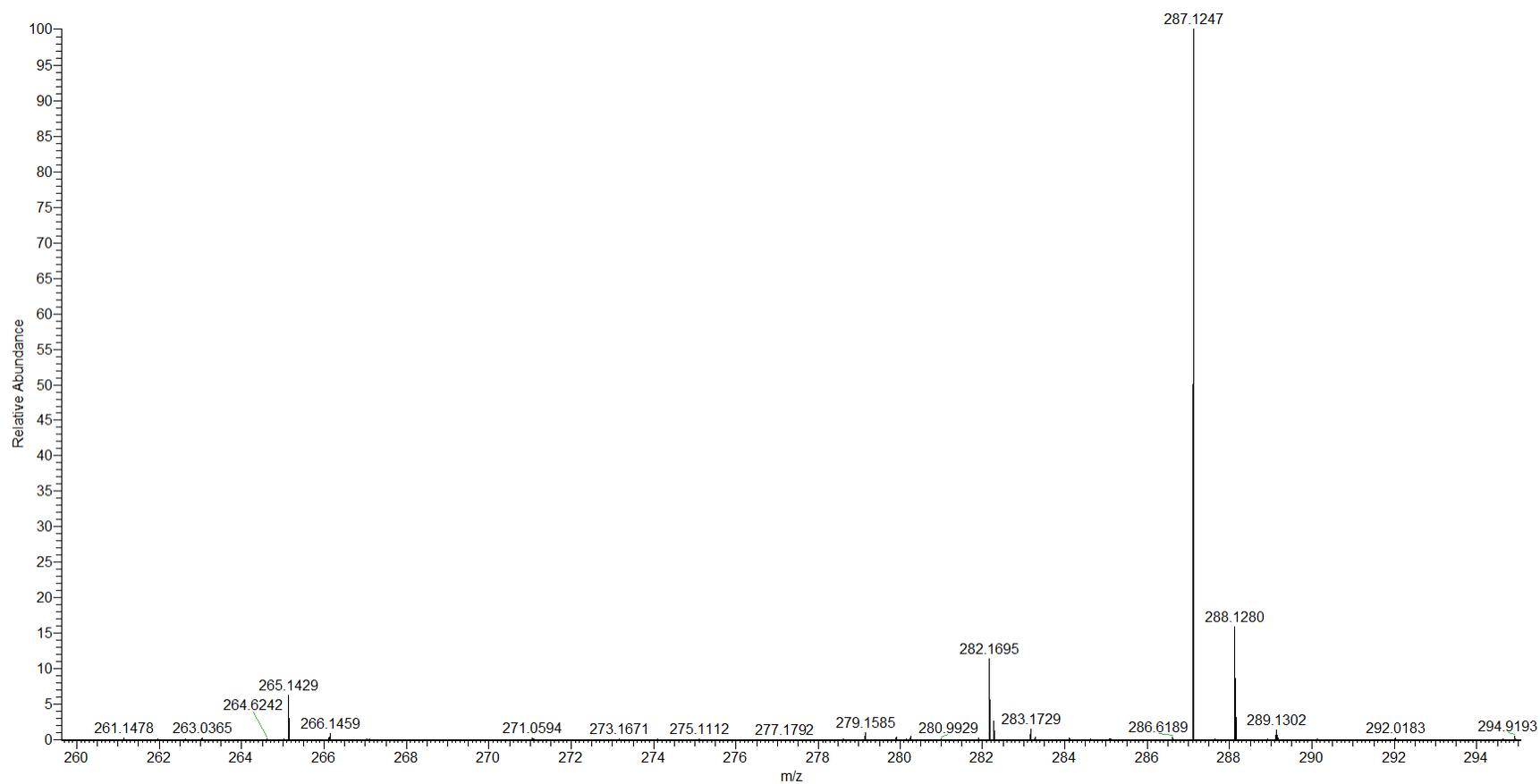


Figure S5: HRESIMS data of VGN (positive mode).

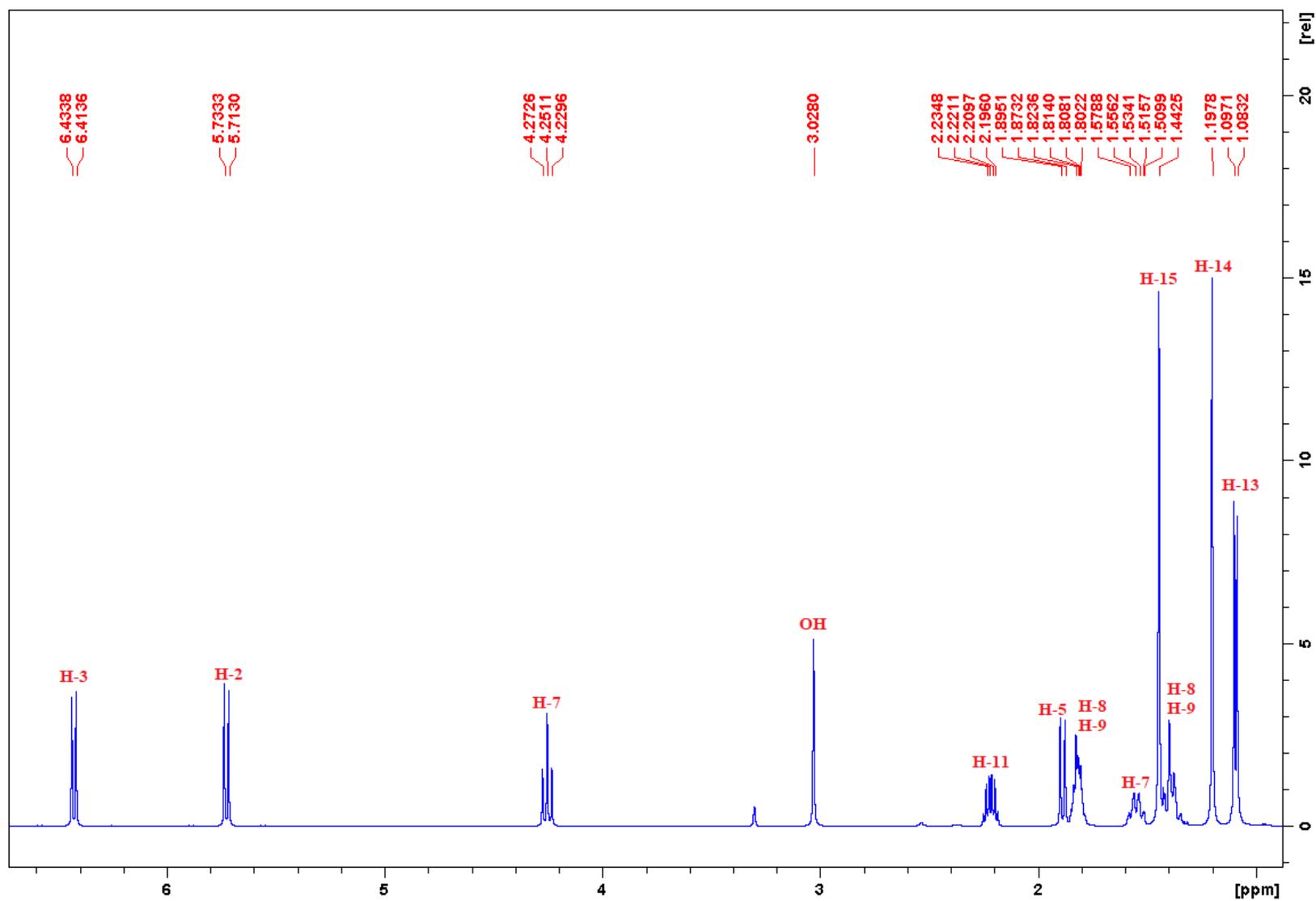


Figure S6: ^1H NMR data for eVGN.

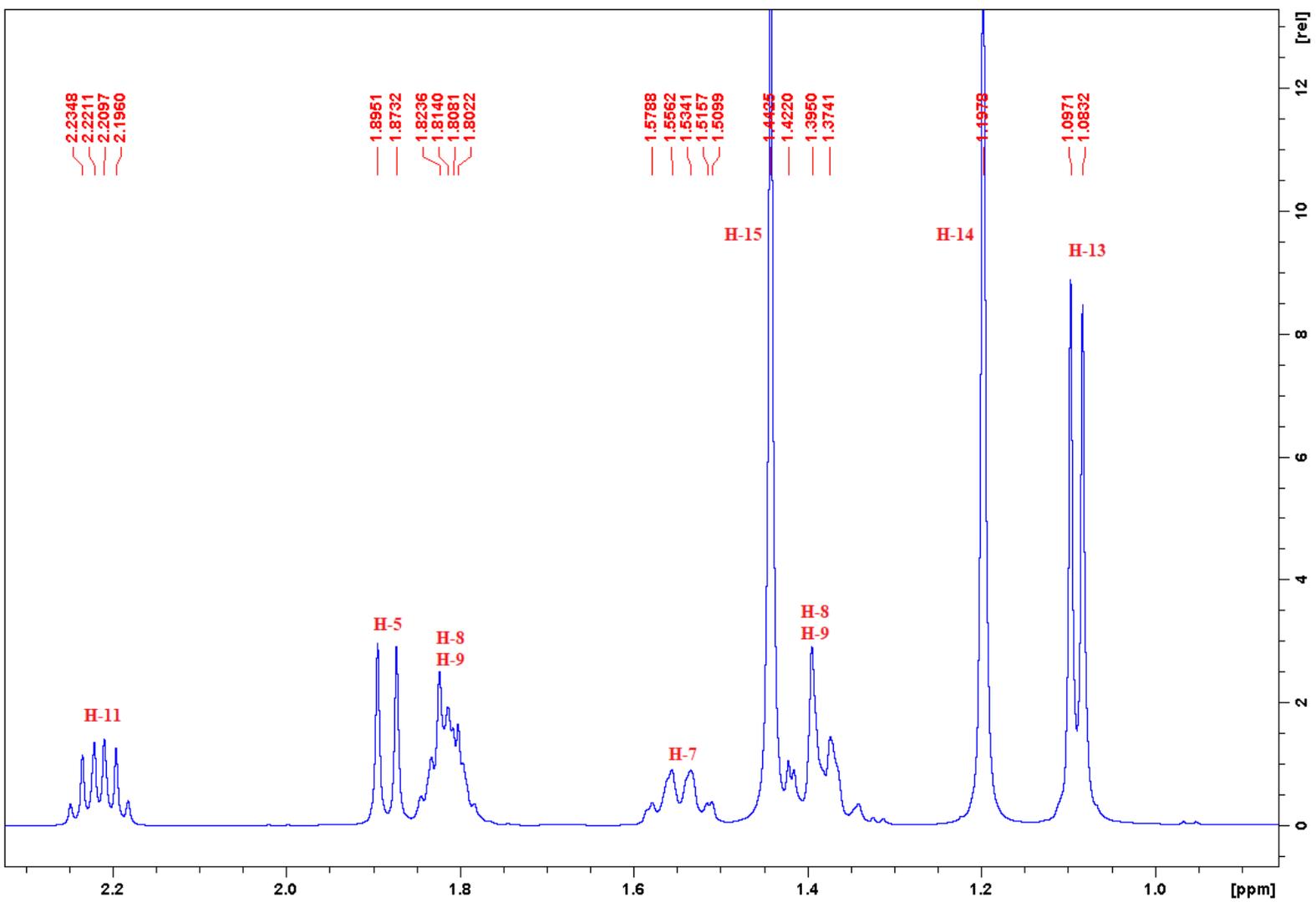


Figure S7: ^1H NMR data for eVGN (Exp.).

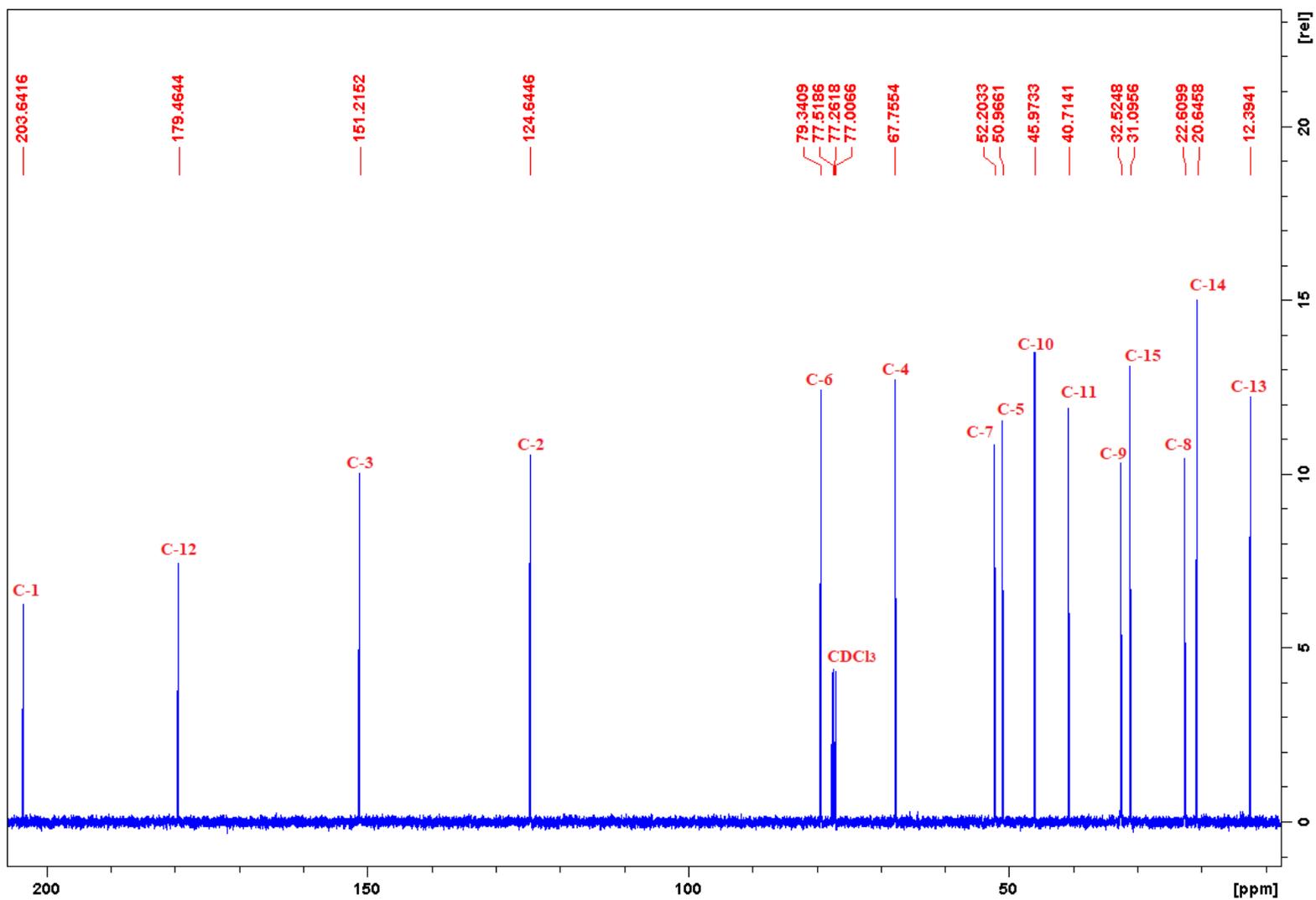


Figure S8: ¹³C NMR data for eVGN.

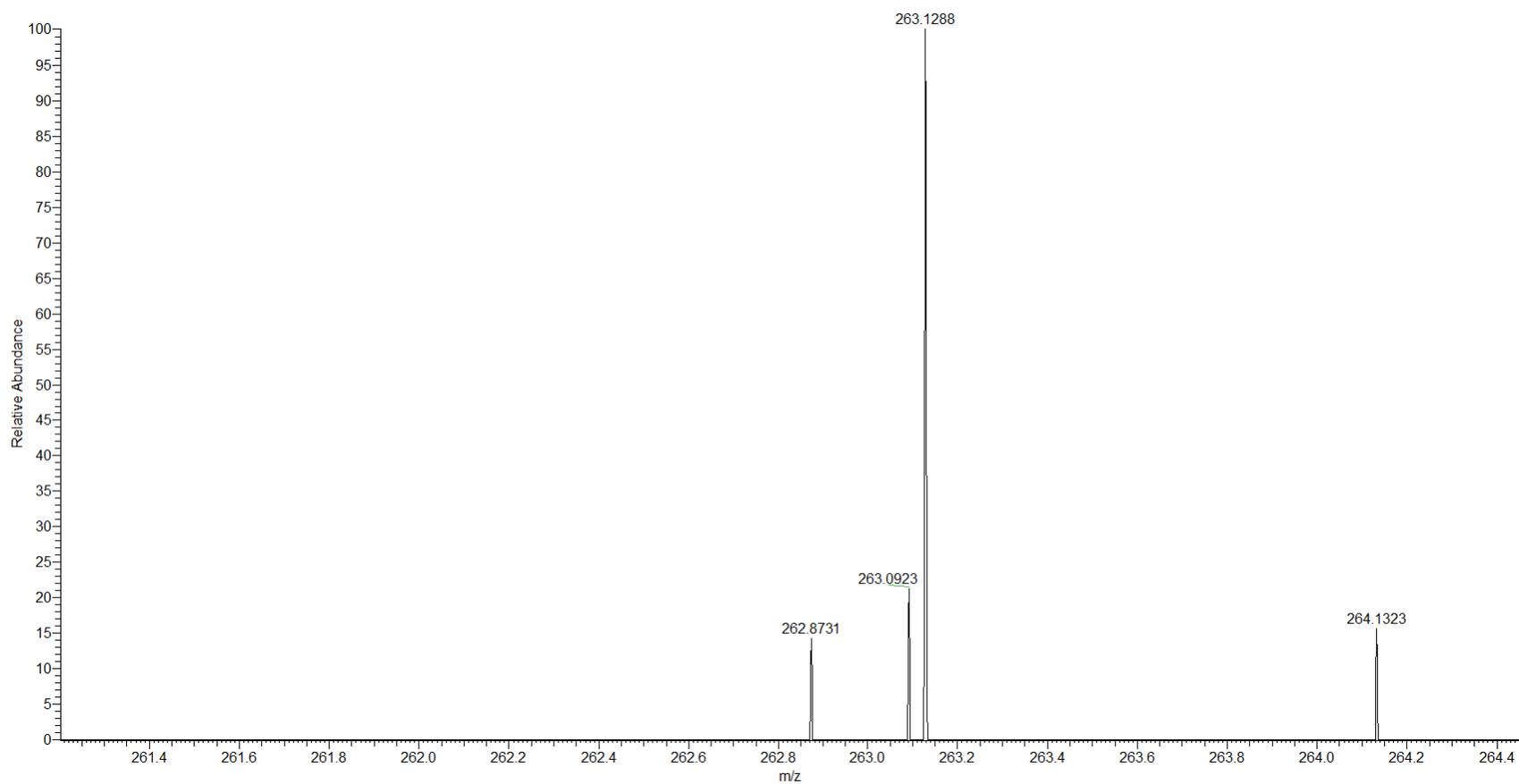


Figure S9: HRESIMS data of eVGn (negative mode).

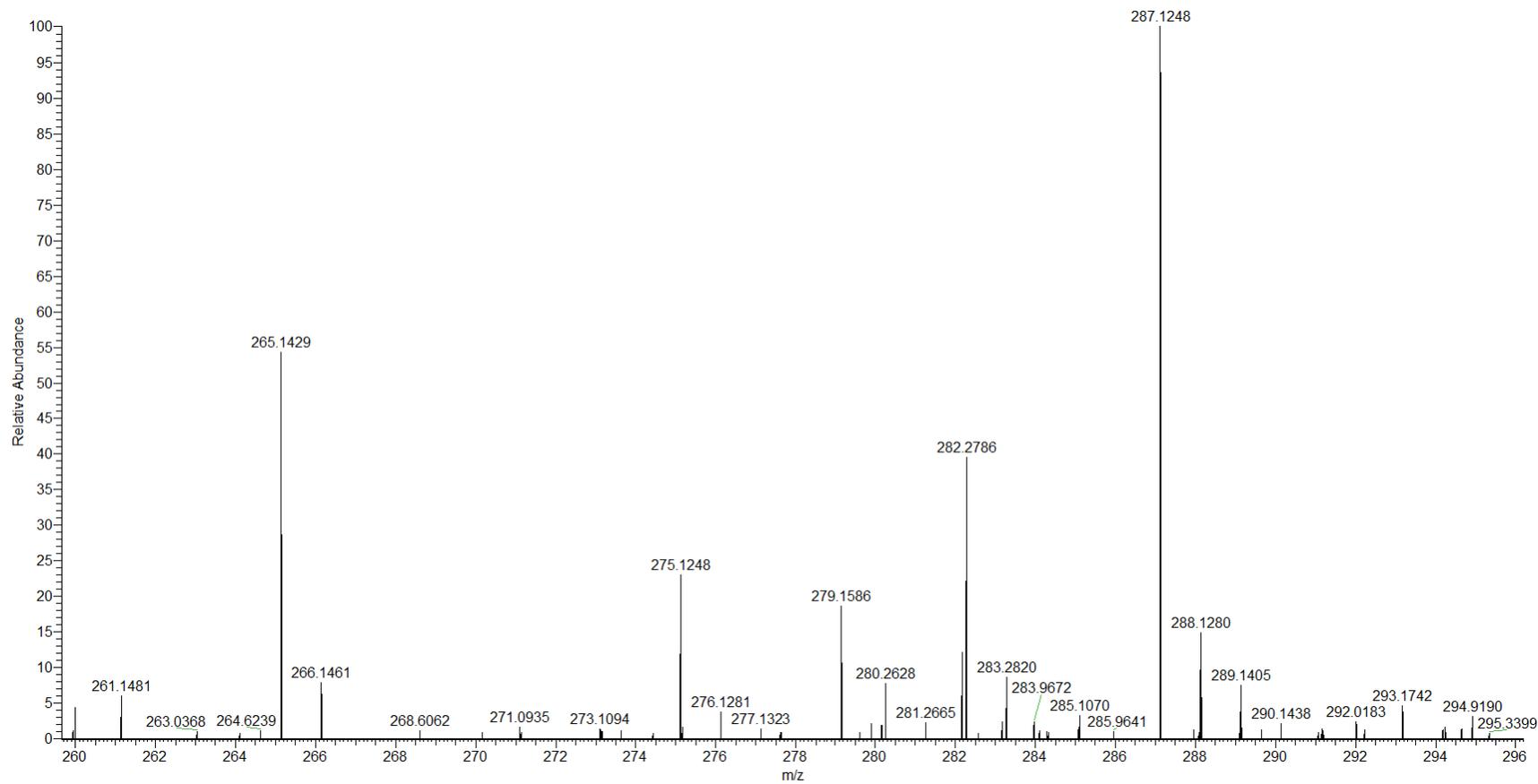


Figure S10: HRESIMS data of eVGN (positive mode).