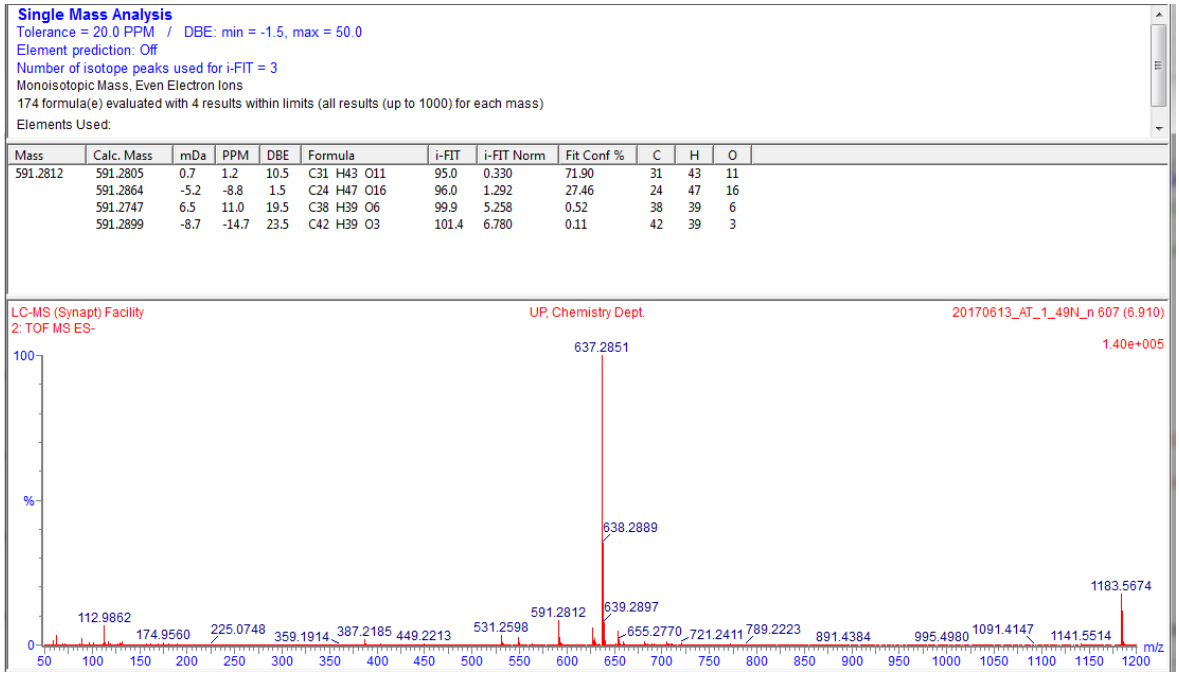
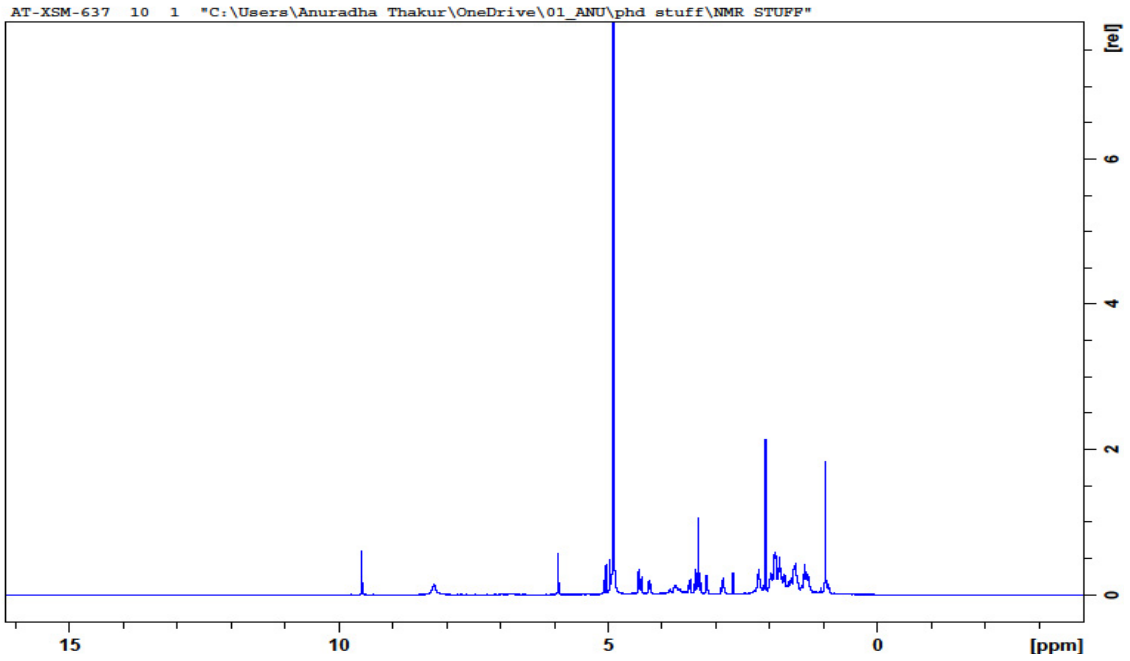
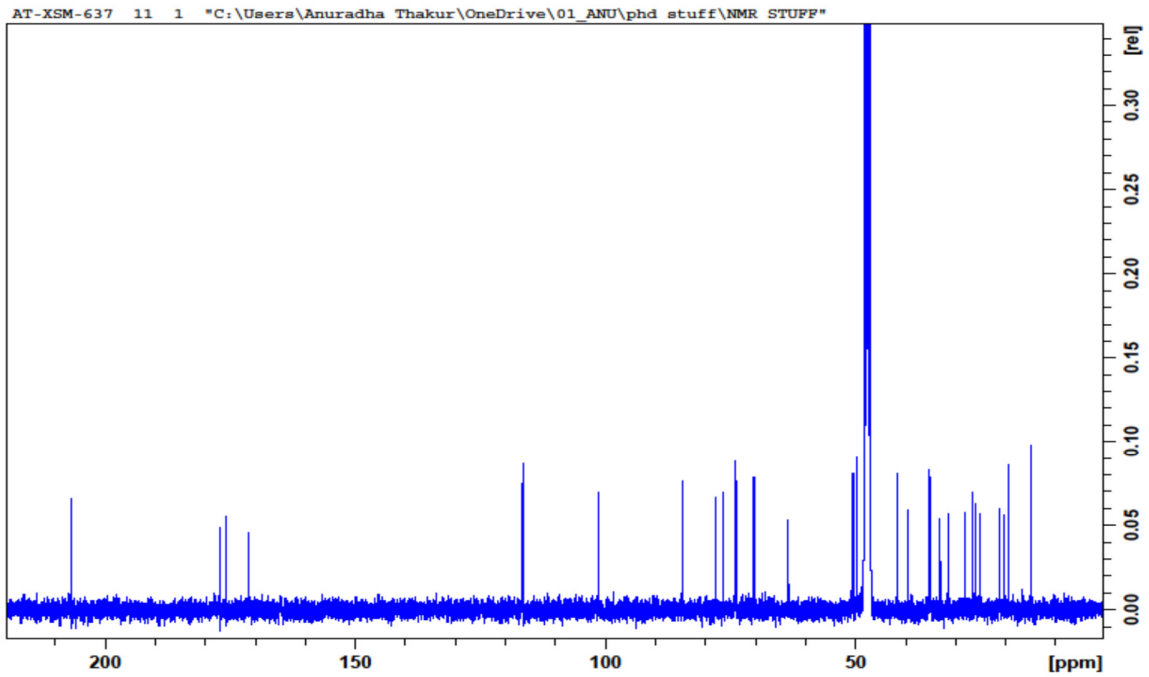
Supplementary Materials:



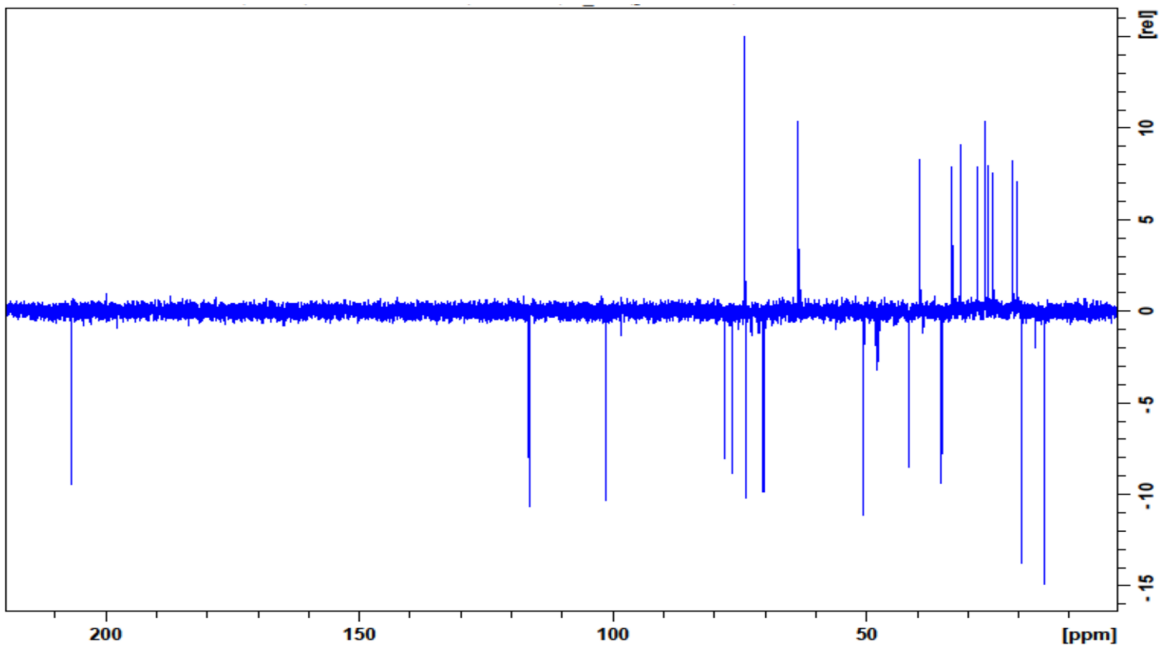
Supplementary Figure S1. iFit value of acetylated glycosydated crotoxigenin **1** in *X. undulatum* leaves extracted with DCM:MeOH



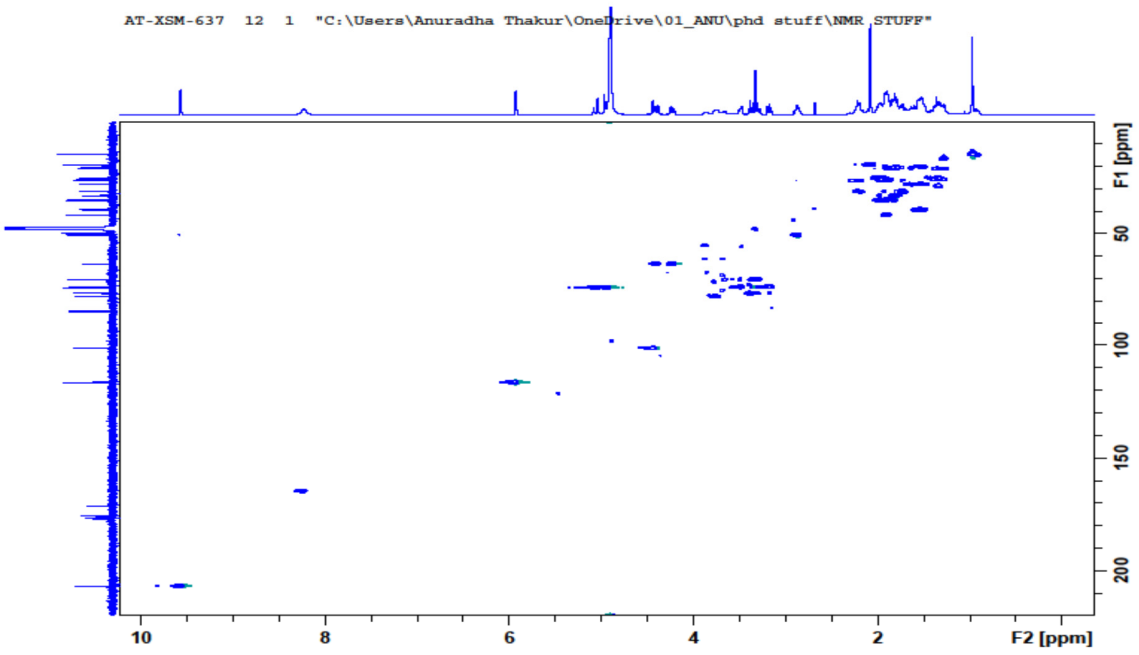
Supplementary Figure S2. ^{1}H NMR for acetylated glycosydated crotoxigenin **1** in MeOD-*d4*



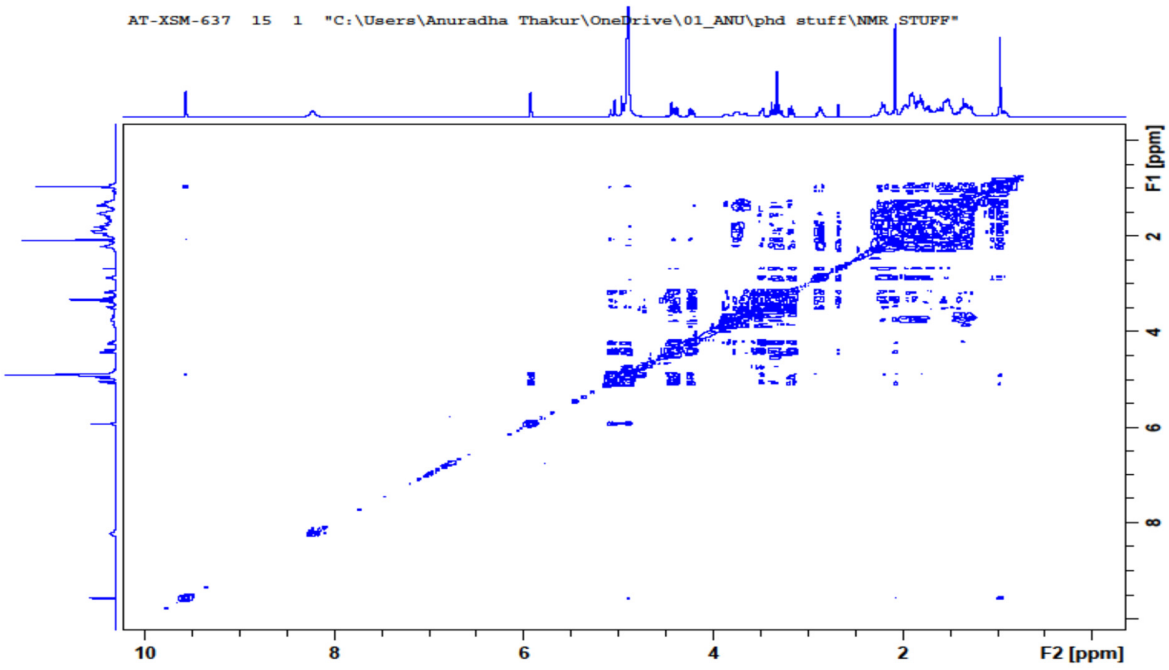
Supplementary Figure S3. ^{13}C NMR for acetylated glycosydated crotoxigenin **1** in MeOD-*d4*



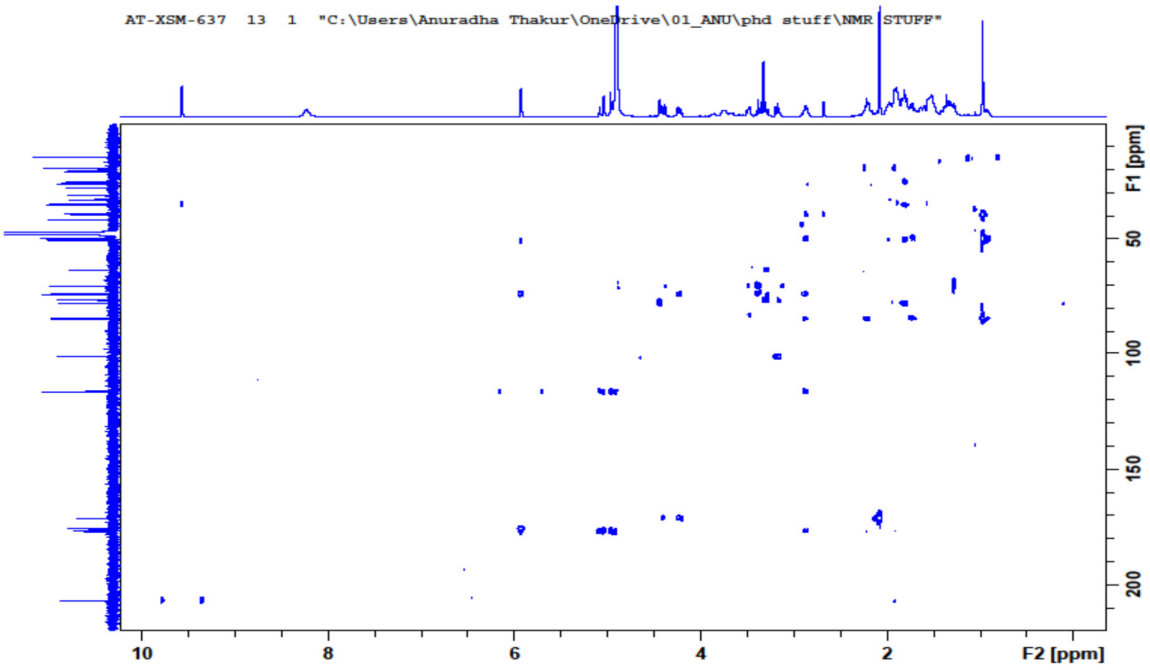
Supplementary Figure S4. DEPT 135 for acetylated glycosydated crotoxigenin **1** in MeOD-*d4*



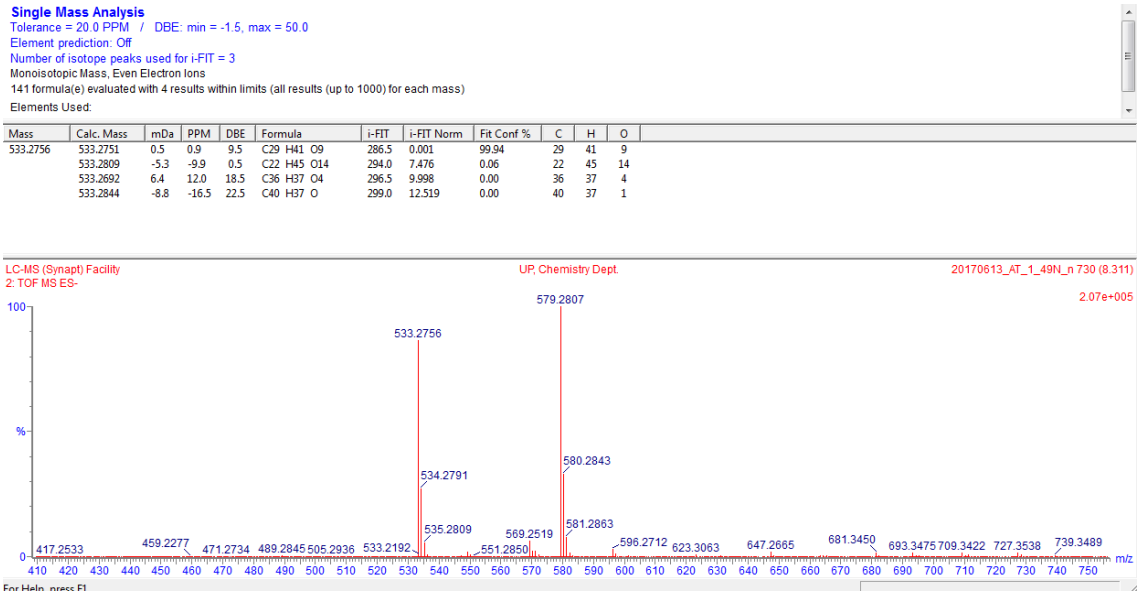
Supplementary Figure S5. HSQC spectrum for acetylated glycosydated crotoxogenin **1** in MeOD-*d4*



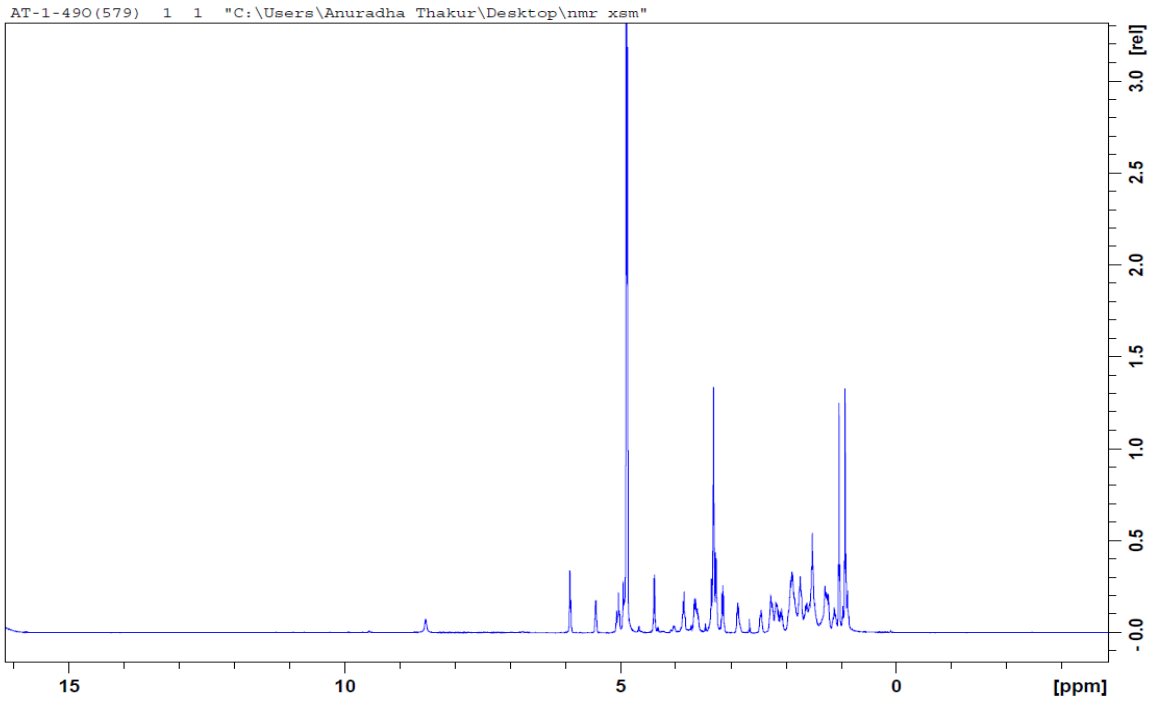
Supplementary Figure S6. COSY spectrum for acetylated glycosydated crotoxogenin **1** in MeOD-*d4*



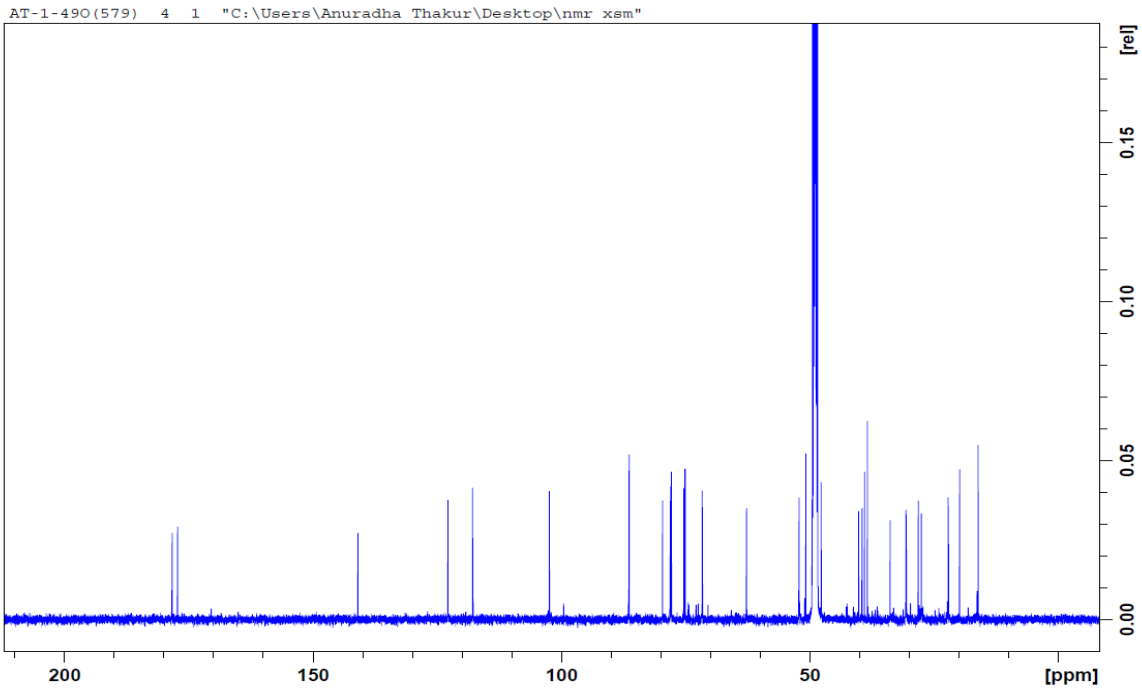
Supplementary Figure S7. HMBC for acetylated glycosydated crotoxigenin **1** in MeOD-*d4*



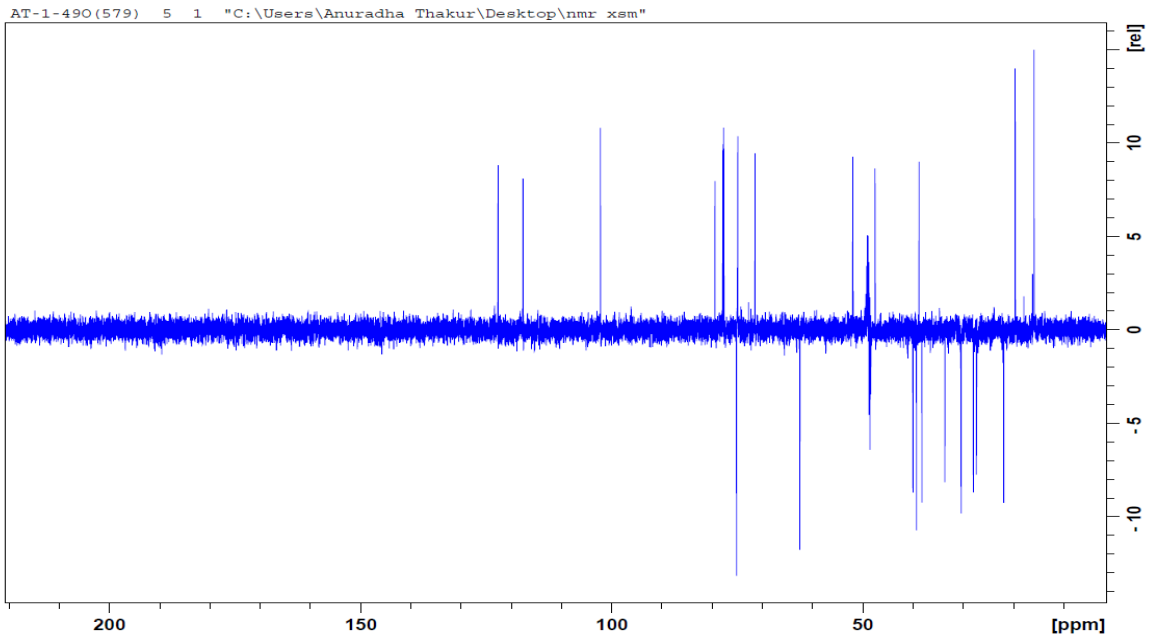
Supplementary Figure S8. iFit value of Xysmalogenin-3, β-D-glucopyranoside **2** in *X. undulatum* leaves extracted with DCM:MeOH



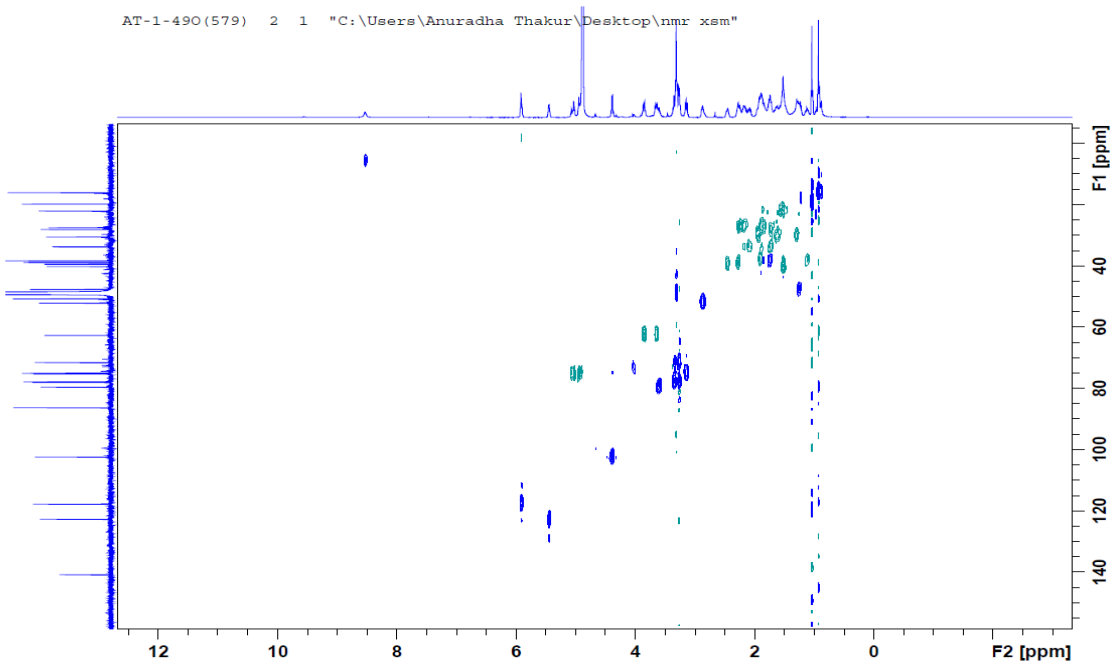
Supplementary Figure S9. ^{1}H NMR for Xysmalogenin-3, β-D-glucopyranoside **2** in MeOD-*d4*



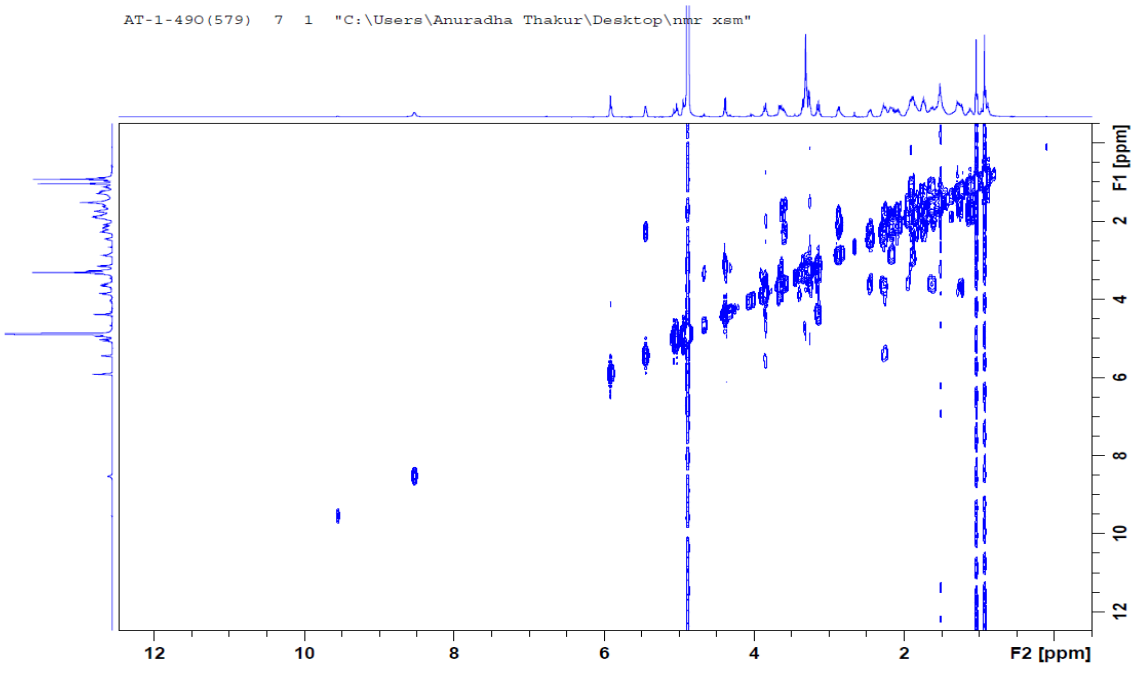
Supplementary Figure S10. ^{13}C NMR for Xysmalogenin-3, β-D-glucopyranoside **2** in MeOD-*d4*



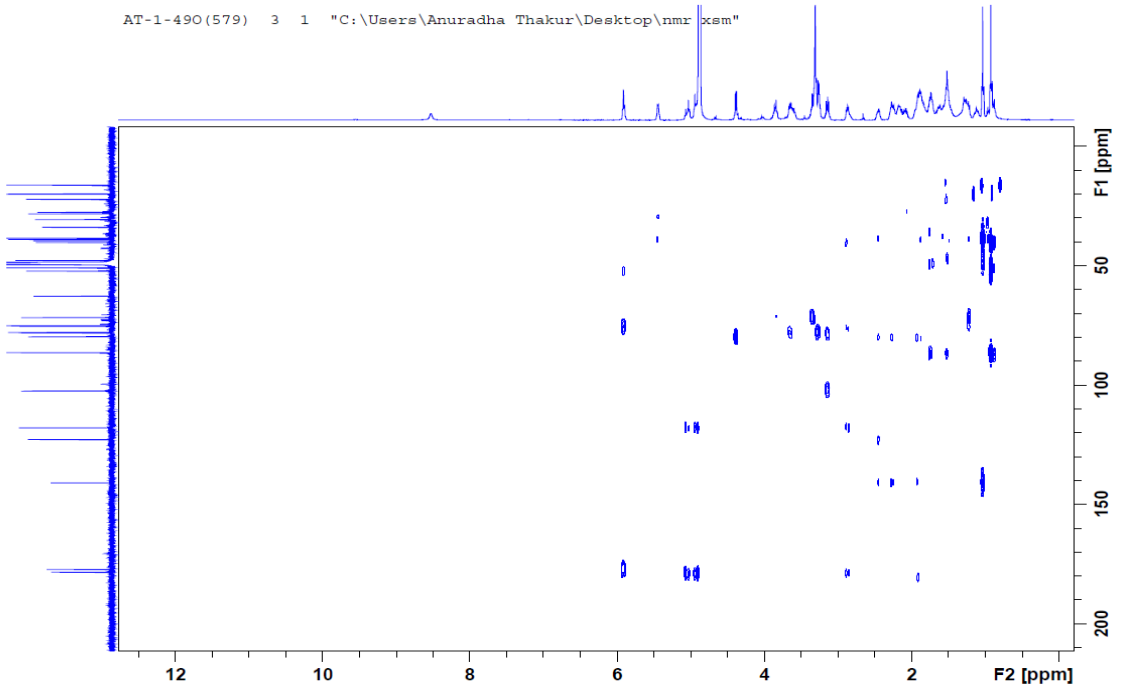
Supplementary Figure S11. DEPT 135 for Xysmalogenin-3, β-D-glucopyranoside **2** in MeOD-*d4*



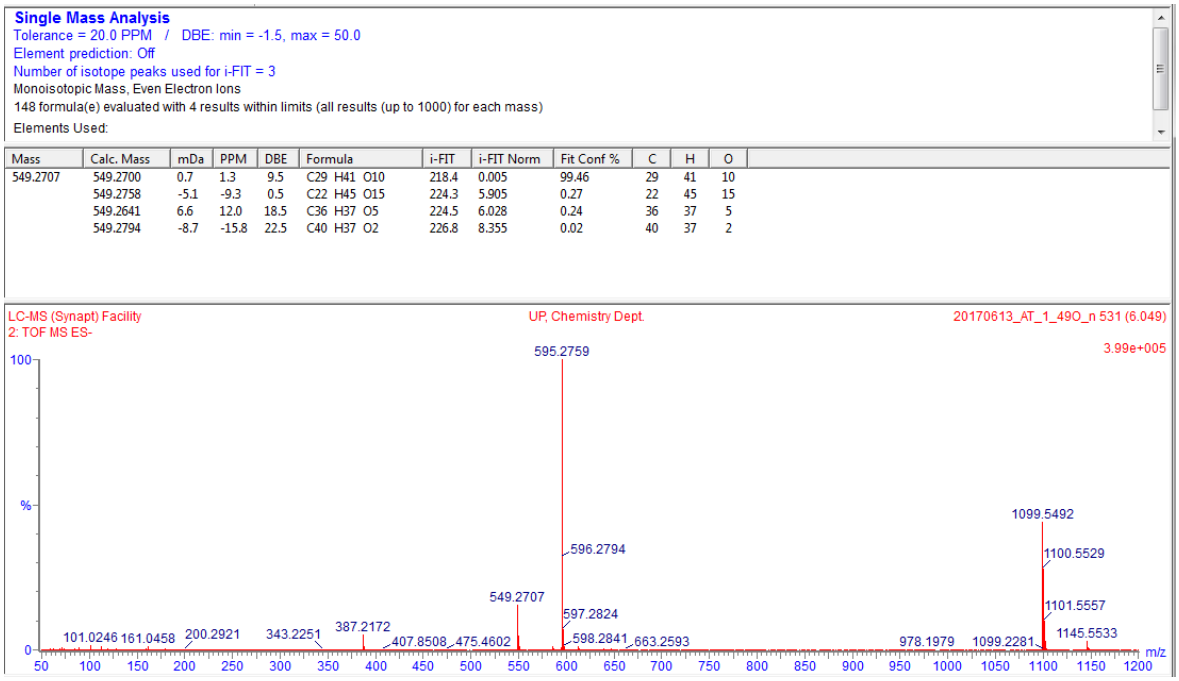
Supplementary Figure S12. HSQC for Xysmalogenin-3, β-D-glucopyranoside **2** in MeOD-*d4*



Supplementary Figure S13. COSY spectrum for Xysmalogenin-3, β-D-glucopyranoside **2** in MeOD-*d4*



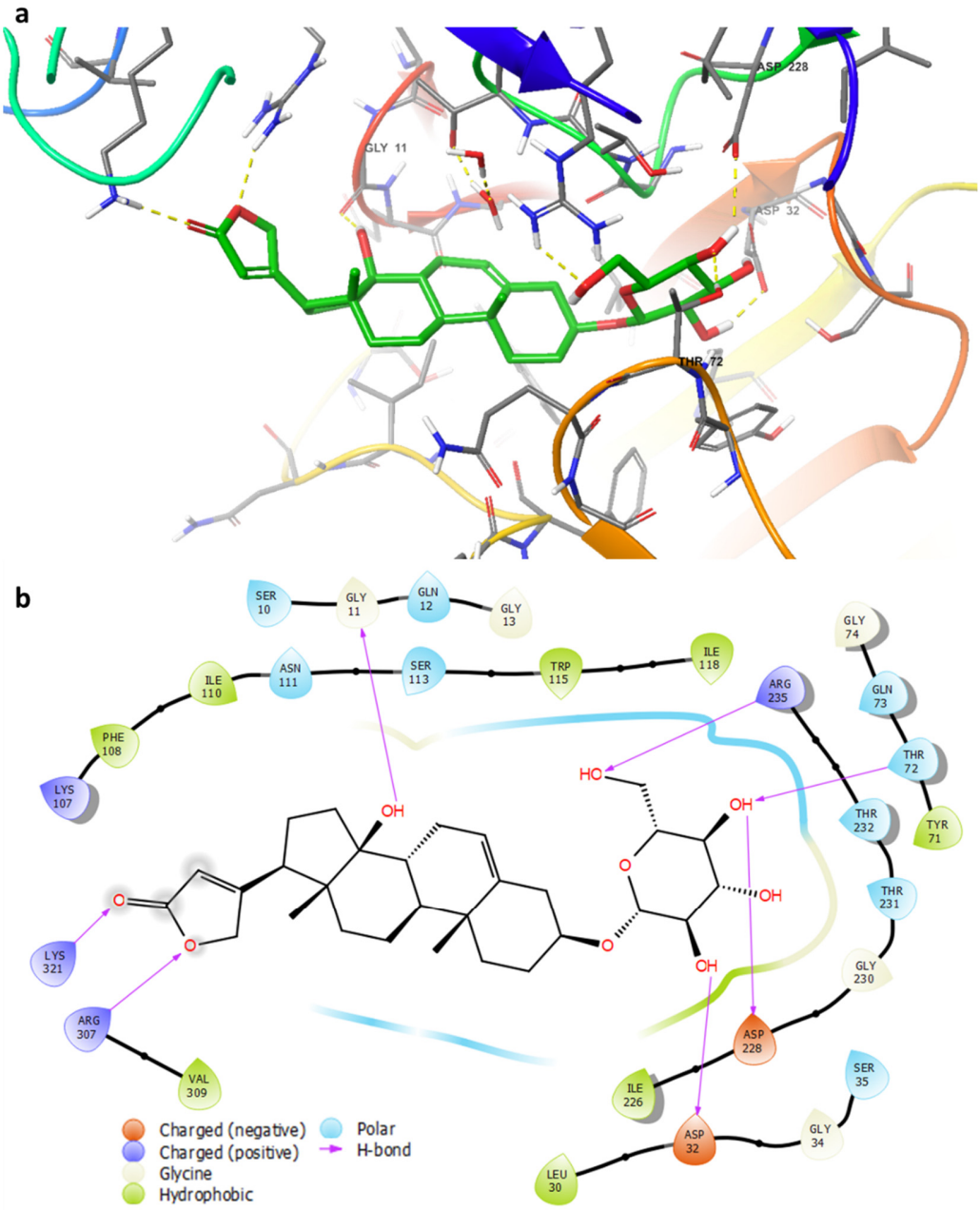
Supplementary Figure S14. HMBC spectrum for Xysmalogenin-3, β-D-glucopyranoside **2** in MeOD-*d4*



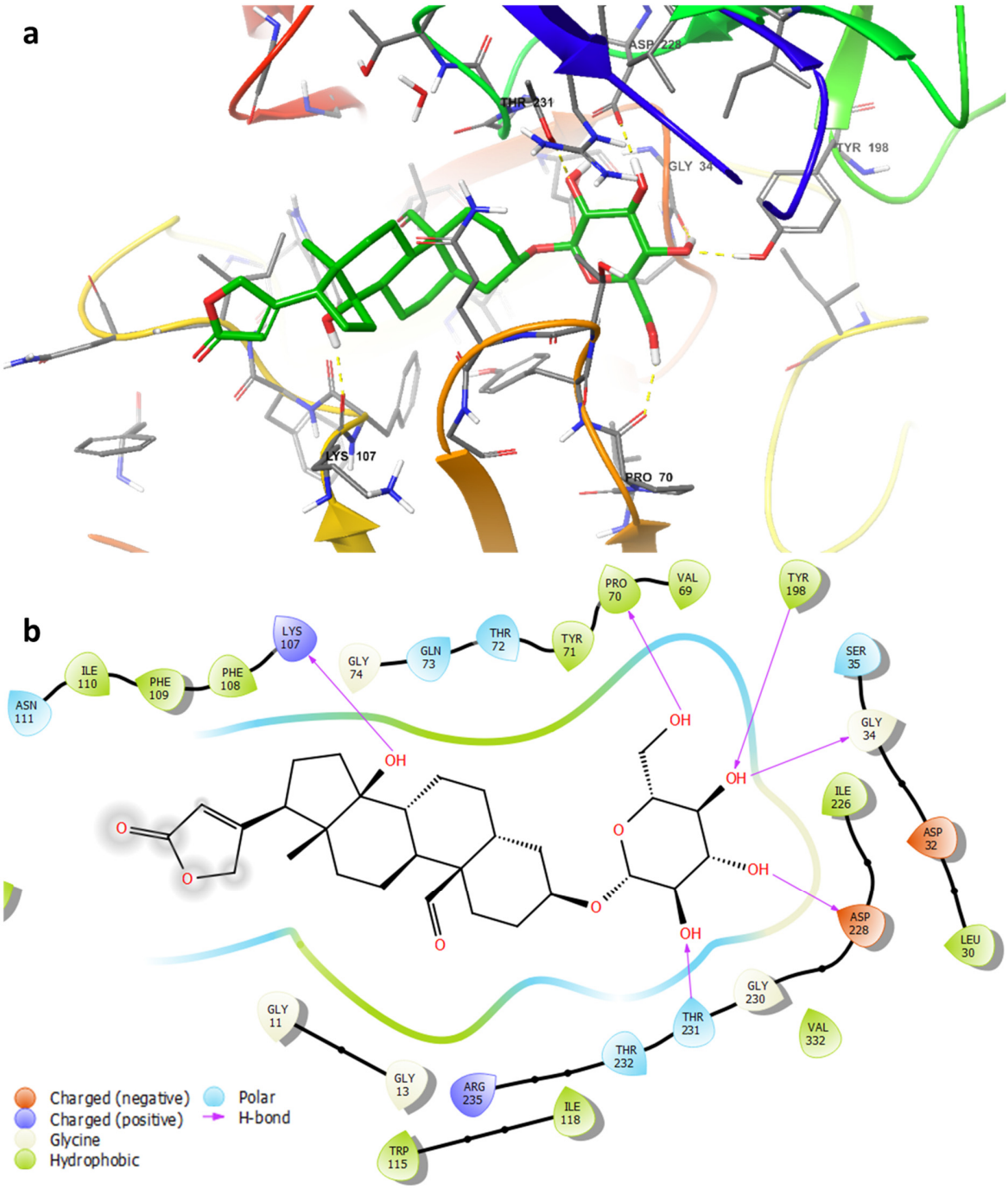
Supplementary Figure S15. iFit value of crotoxigenin 3-O-glucopyranoside **3** in *X. undulatum* leaves extracted with DCM:MeOH

Supplementary Table S1. ^{1}H NMR and ^{13}C NMR data for crotoxogenin 3-*O*-glucopyranoside **3** in MeOD-*d4* compared to literature reports [1] for the compound in DMSO-*d6*.

Isolated Crotoxogenin 3-O-glucopyranoside (18)			**^{1}H NMR and ^{13}C NMR literature data for compound (59) in DMSO-d6**	
Position	**^{13}C (ppm)**	**^{1}H (ppm), *J* (Hz)**	**^{13}C (ppm)**	**^{1}H (ppm), *J* (Hz)**
1	28.0	1.83 m, 1.54 m	28.03	1.85 m,1.50 m
2	31.3	1.85 m	30.36	1.80 m
3	77.0	3.82 m	76.78	3.05 m
4	25.9	1.85 m, 1.33 m	30.20	1.82 m, 1.14 m
5	41.6	1.89 m	42.03	1.45 m
6	24.9	1.76 m	26.27	1.74 m
7	20.3	1.48 m	21.41	1.60 m
8	35.2	1.96 m	47.57	1.43 m
9	35.0	1.79 m	35.49	1.81 m
10	50.4	-	49.99	-
11	21.2	1.82 m, 1.32 m	21.41	1.60 m
12	39.4	1.51 m	42.18	1.44 m
13	49.6	-	49.19	-
14	84.5	-	83.37	-
15	32.9	1.71 m	31.59	1.94 m, 1.55 m
16	26.5	2.16 m	27.17	2.13 m
17	50.5	2.8 (q, 14.6)	51.23	2.72 m
18	14.8	0.95 s	15.54	0.69 s
19	206.8	9.54 s	209.66	9.94 s
20	175.8	-	173.96	-
21	73.7	5.04 (d, 1.65), 4.92 (dd, 18.5, 1.74)	73.48	4.90 dd
22	116.4	5.91 s	116.38	5.89 s
23	176.9	-	176.31	-
1′	100.8	4.42 d (7.80)	100.71	4.20 d
2′	73.9	3.14 (dd, 9.03, 1.07)	75.75	3.59 m
3′	76.5	3.26	73.23	2.85 m
4′	70.3	3.27 m	70.11	3.02 m
5′	76.7	3.35m	76.78	3.06 m
6′	61.4	3.87 m, 3.65 m	61.14	3.64m, 3.40m



Supplementary Figure S16. (a) Predicted binding pose from induced fit docking for **2**, shown in green, bound to BACE1. Hydrogen bonds are shown in yellow dashed lines. Only selected residues are shown for clarity. (b) 2D ligand interaction diagram for the binding pose of **2**.



Supplementary Figure S17. (a) Predicted binding pose from induced fit docking for **3**, shown in green, bound to BACE1. Hydrogen bonds are shown in yellow dashed lines. Only selected residues are shown for clarity. (b) 2D ligand interaction diagram for the binding pose of **3**.

References:

[1] L. Rascón-Valenzuela, C. Velázquez, A. Garibay-Escobar, L. A. Medina-Juárez, W. Vilegas, and R. E. Robles-Zepeda, "Antiproliferative activity of cardenolide glycosides from Asclepias subulata," *J. Ethnopharmacol.*, vol. 171, pp. 280–286, 2015, doi: 10.1016/j.jep.2015.05.057.