

Supporting Information

Investigation of Chemical Compositions and Biological Activities of *Ajuga pyramidalis* – Isolation of Iridoids and Phenylethanoid Glycosides

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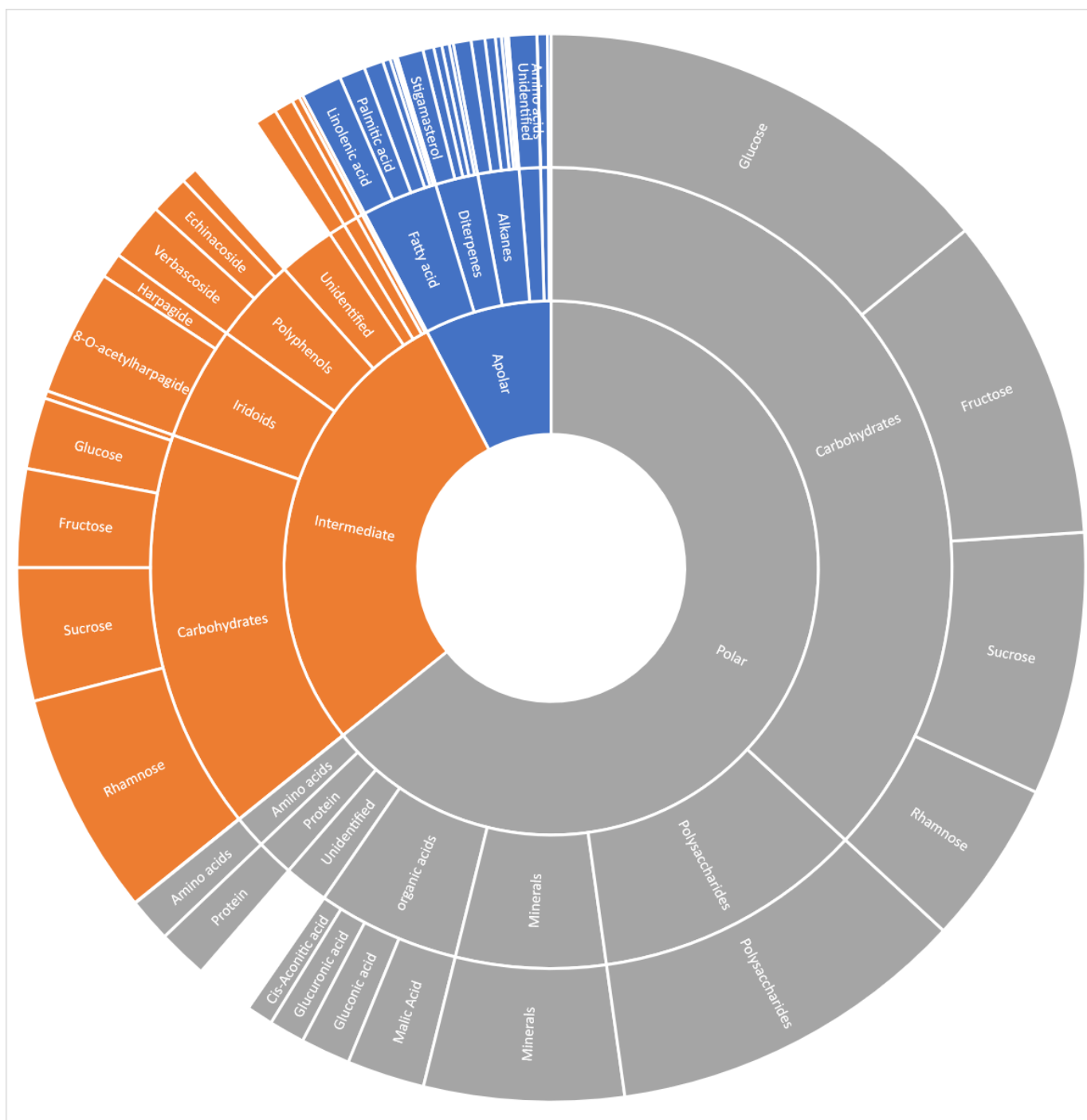


Figure S1. Global composition of the extracts of *A. pyramidalis* (in blue: the apolar extract, in orange: the intermediate extract and in grey: the polar extract).

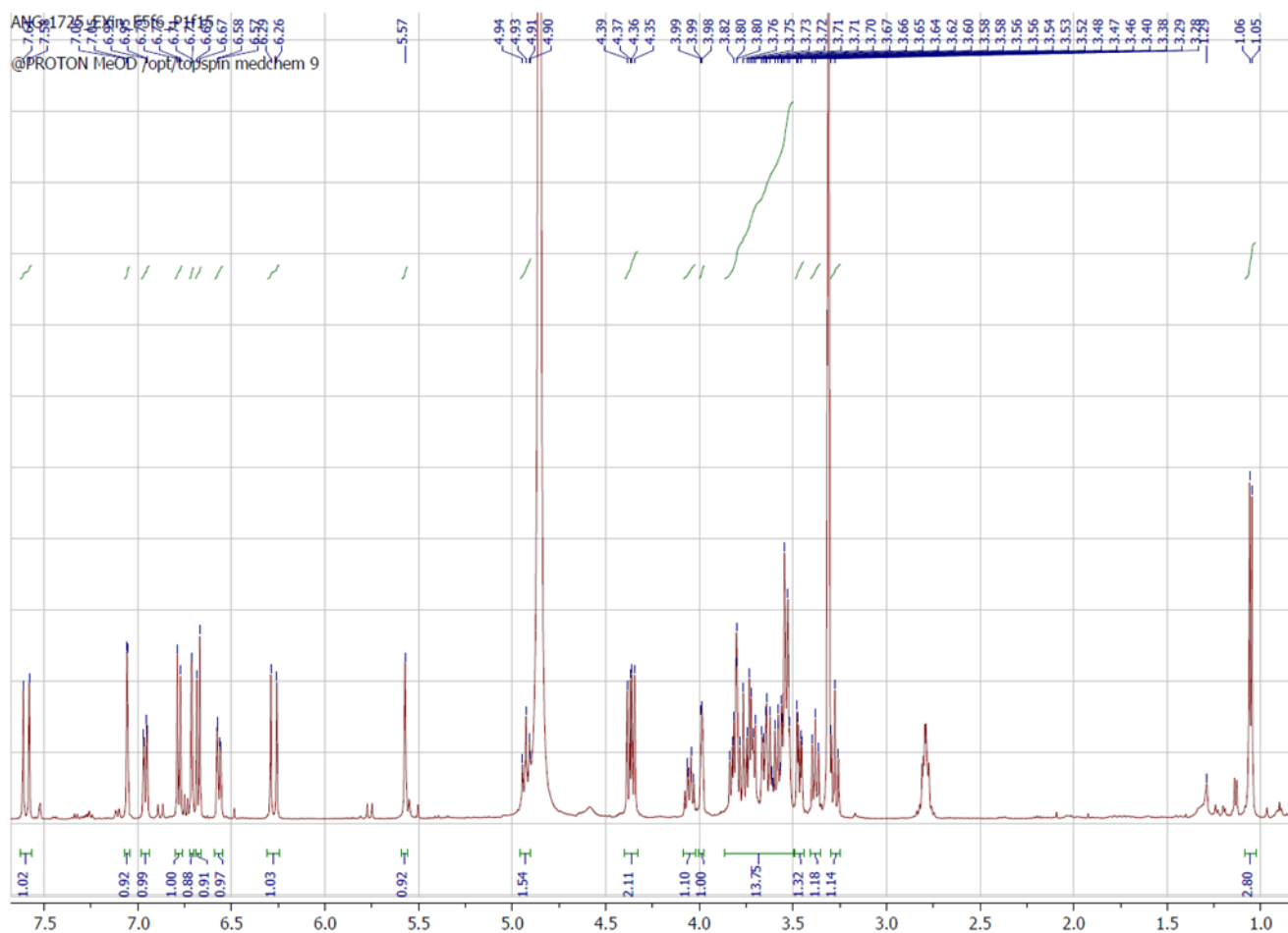


Figure S2. ^1H NMR spectrum of echinacoside (CD_3OD , 500 MHz)

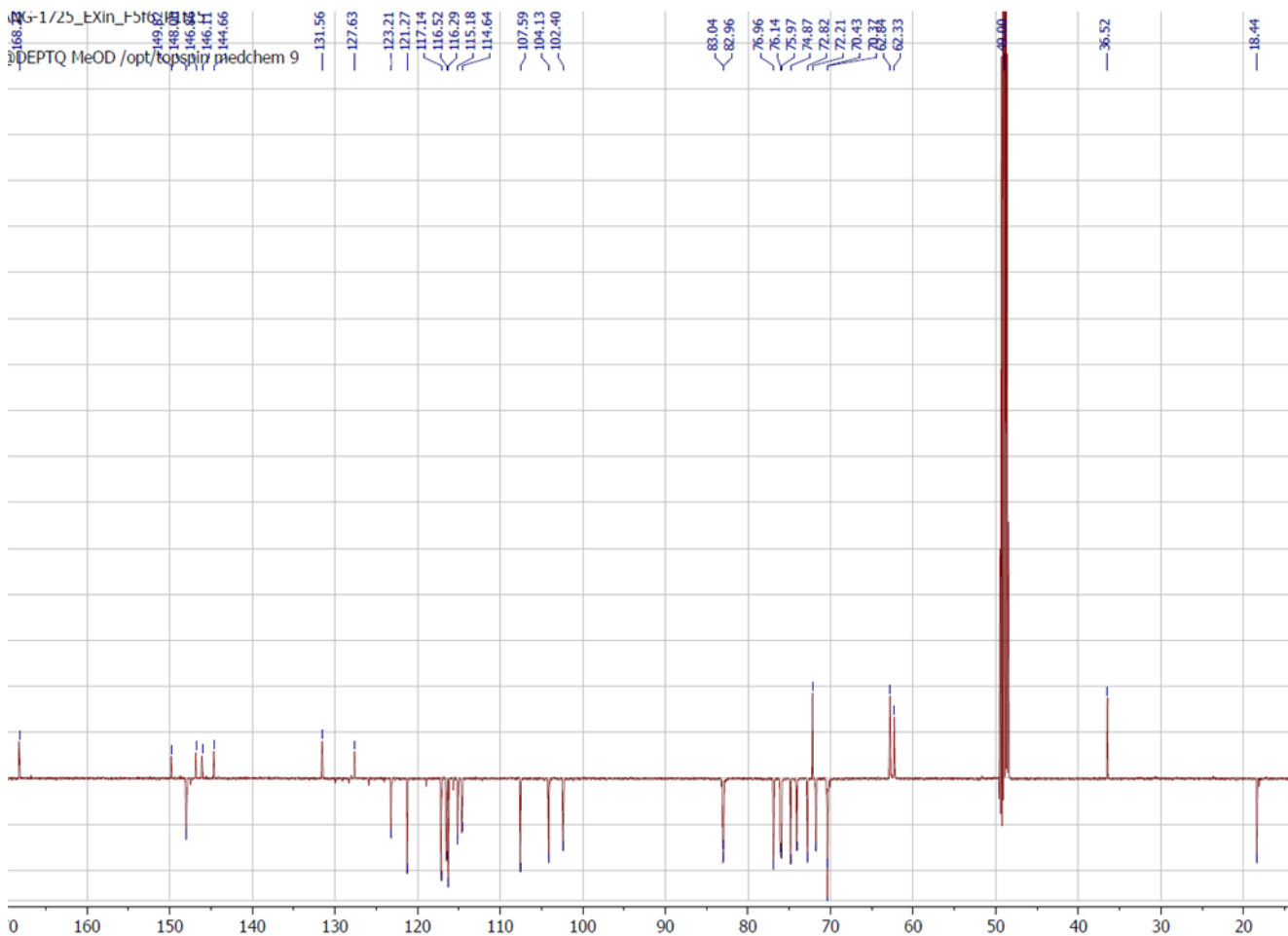


Figure S3. ^{13}C NMR spectrum of echinacoside (CD_3OD , 125 MHz)

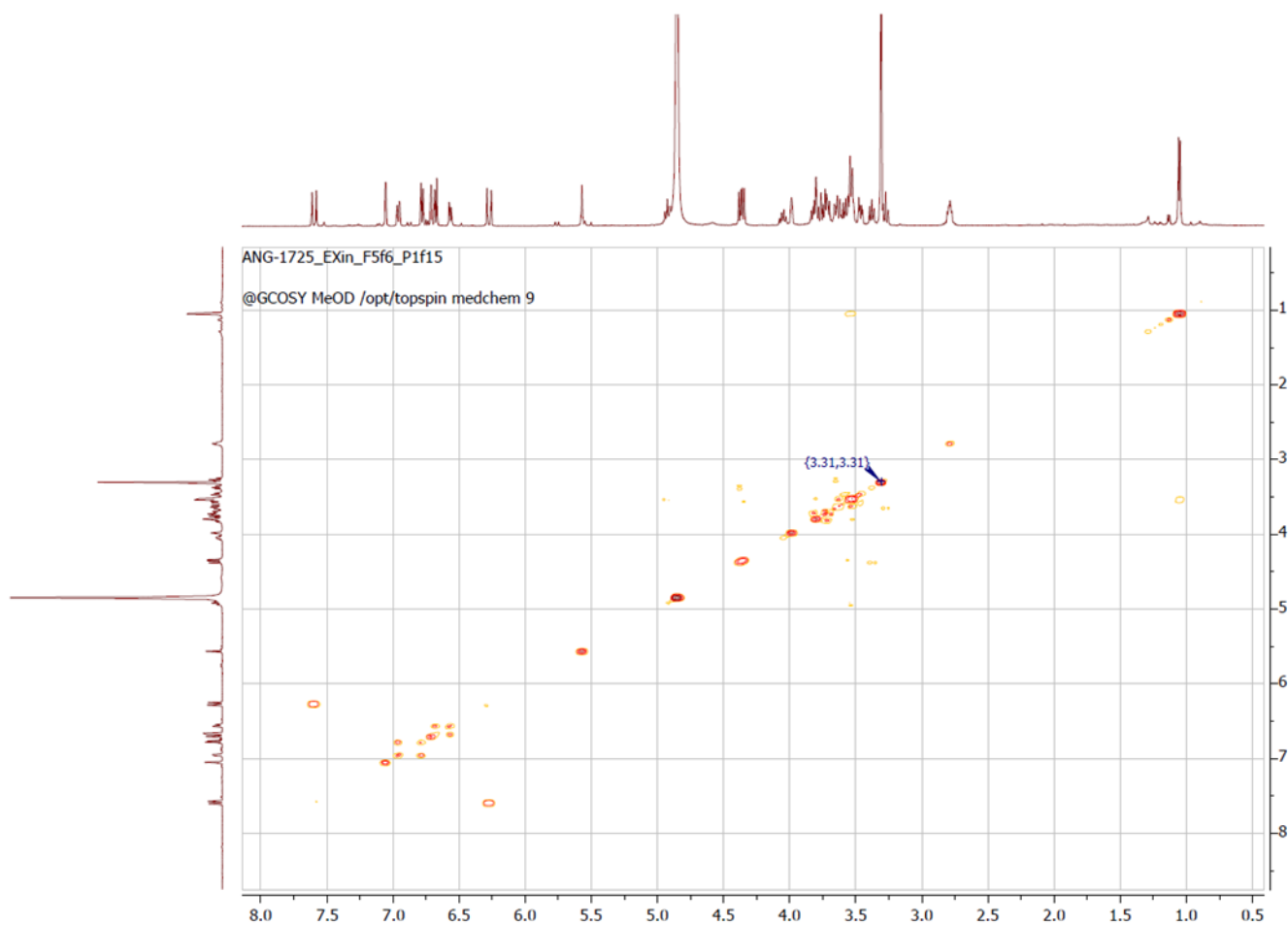


Figure S4. COSY spectrum of echinacoside (CD_3OD)

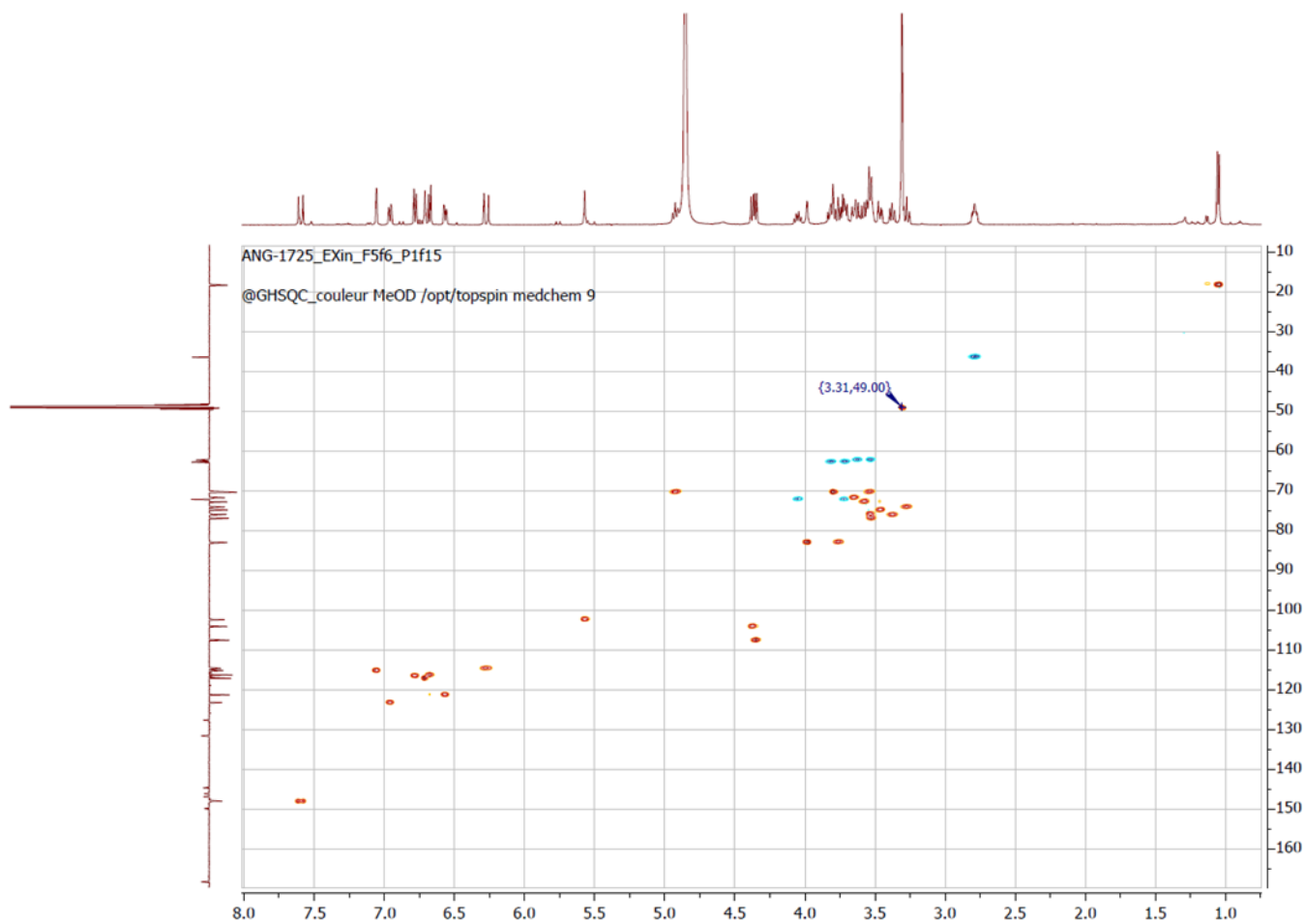


Figure S5. HSQC spectrum of echinacoside (CD_3OD)

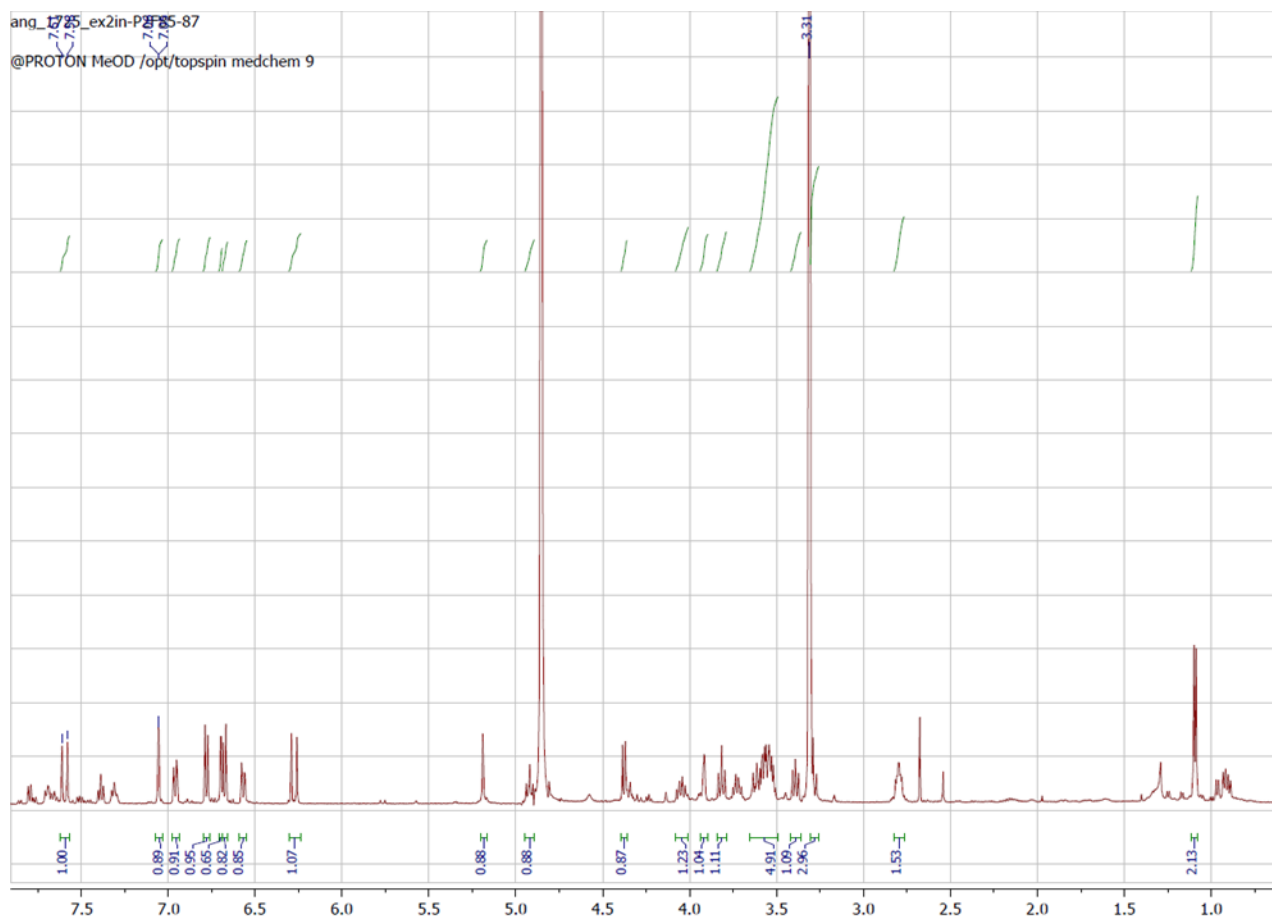


Figure S6. ^1H NMR spectrum of verbascoside (CD_3OD , 500 MHz)

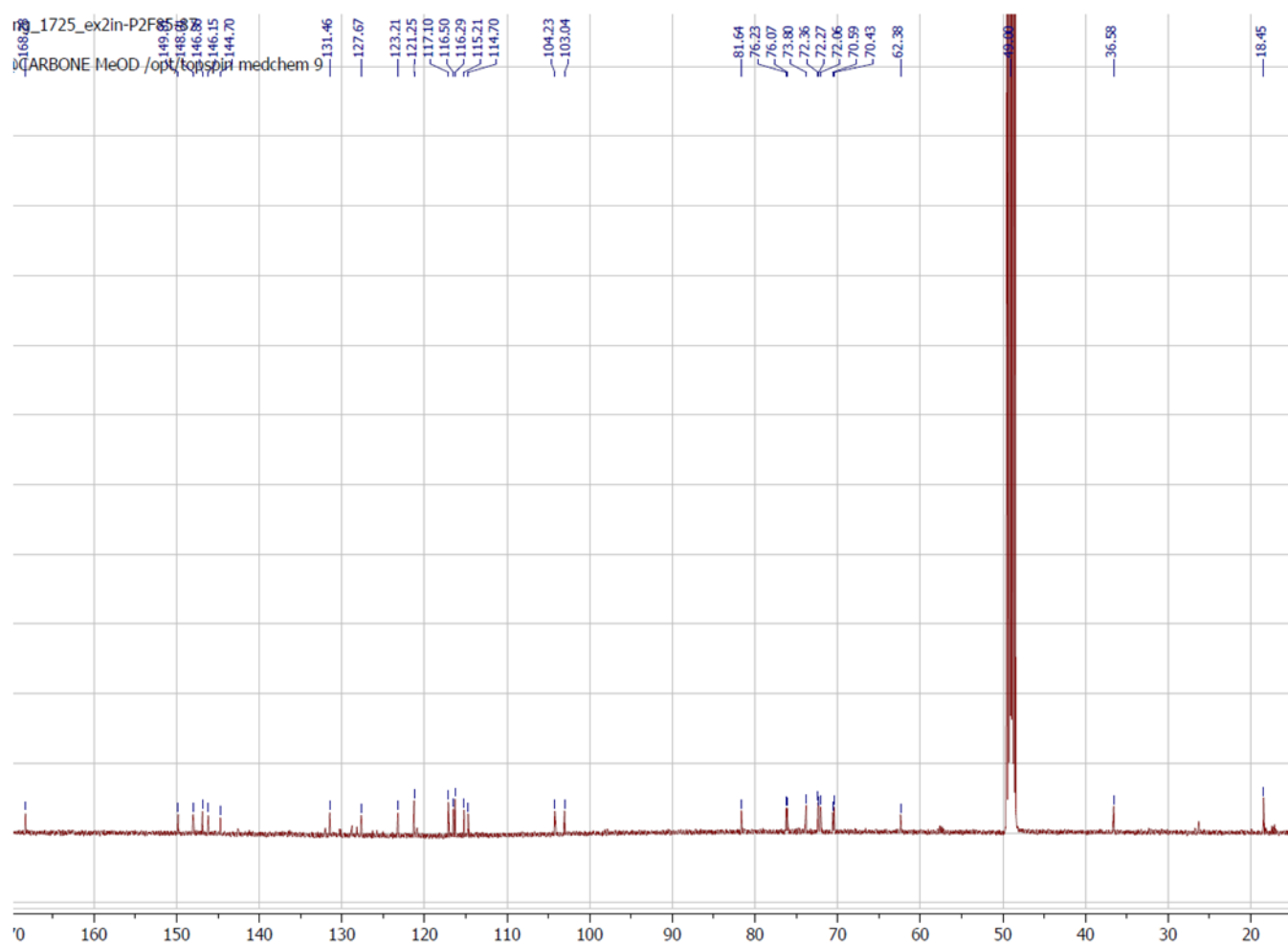


Figure S7. ^{13}C NMR spectrum of verbascoside (CD_3OD , 125 MHz)

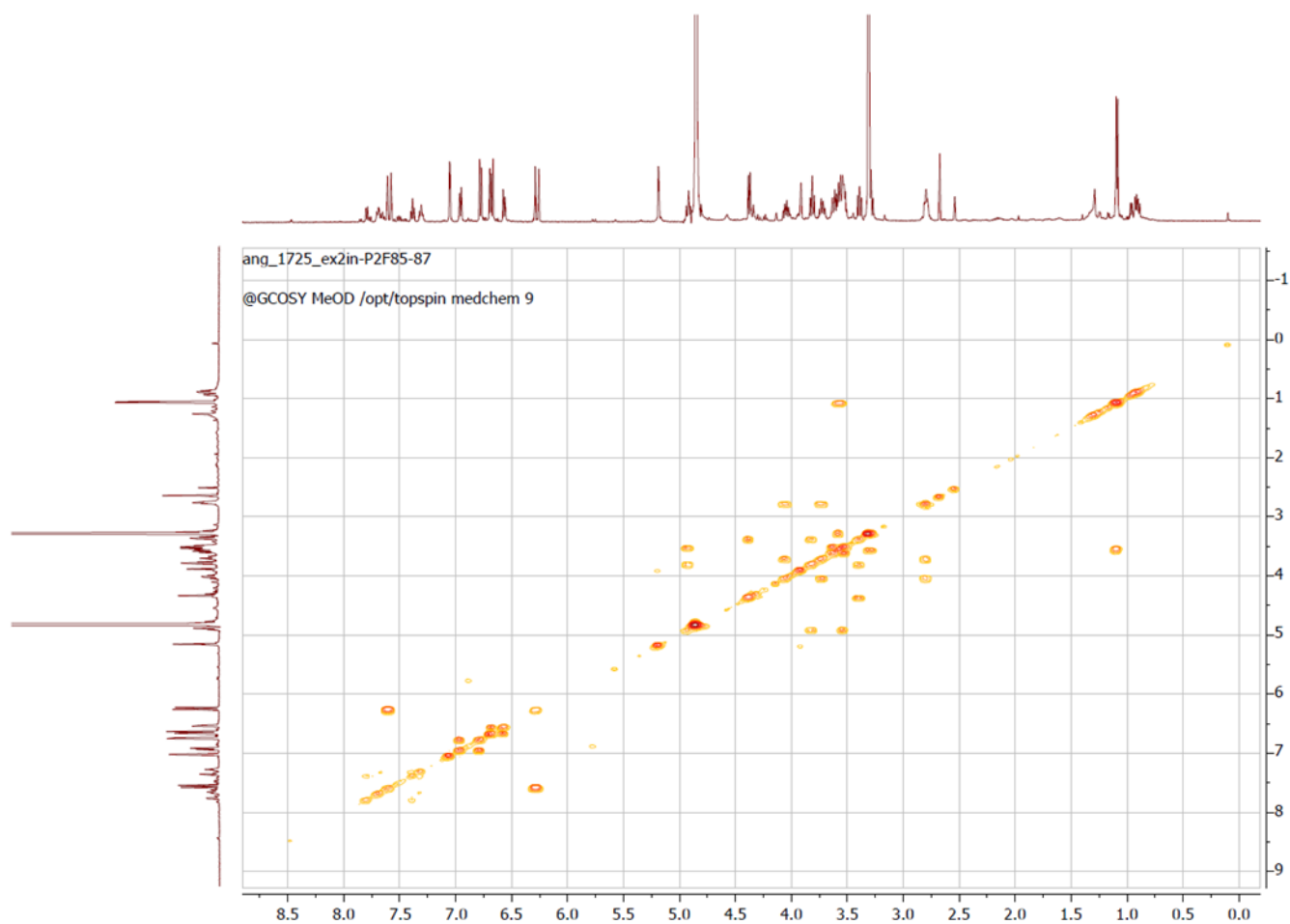


Figure S8. COSY spectrum of verbascoside (CD₃OD)

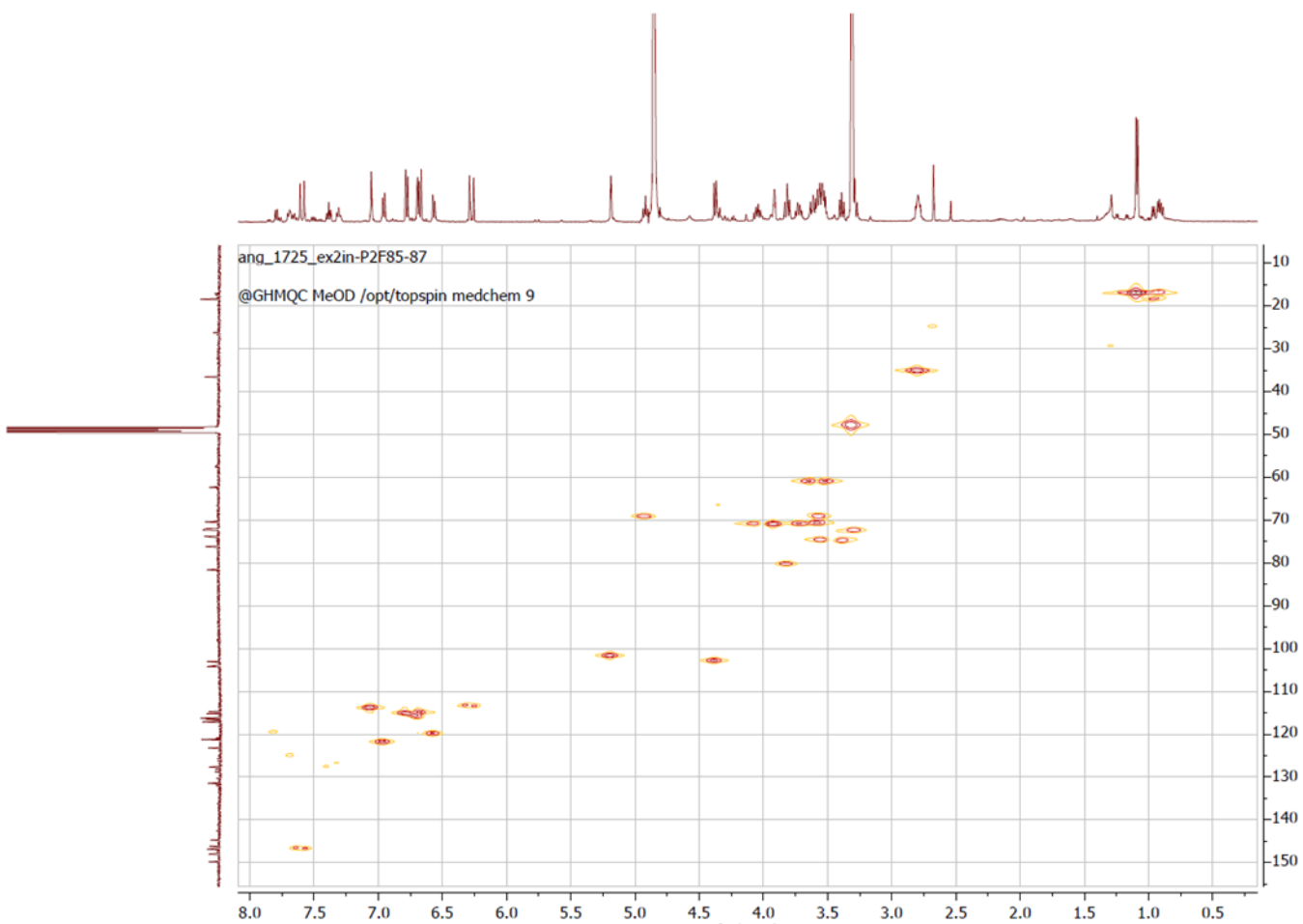


Figure S9. HSQC spectrum of verbascoside (CD₃OD)

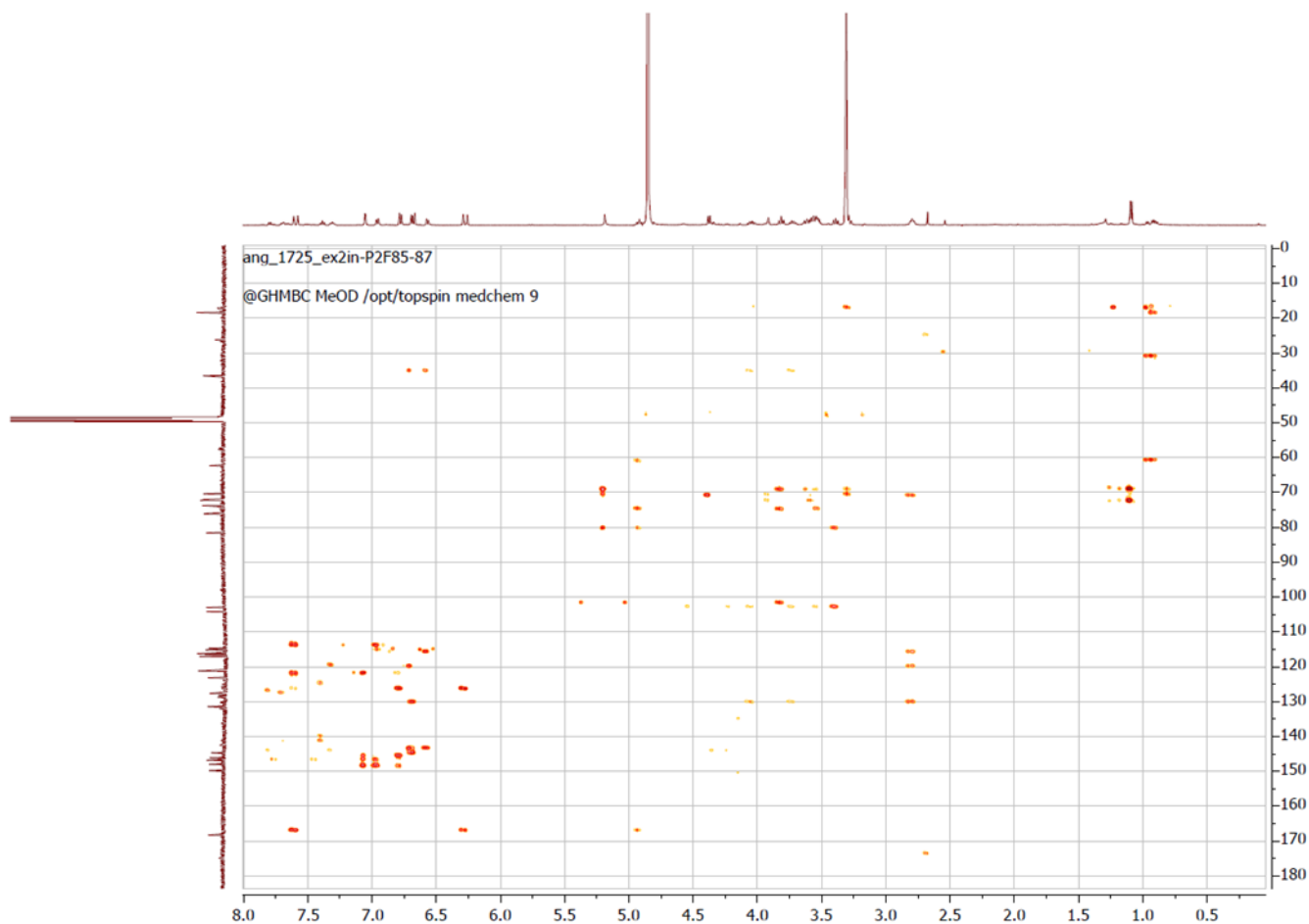


Figure S10. HMBC spectrum of verbascoside (CD_3OD)

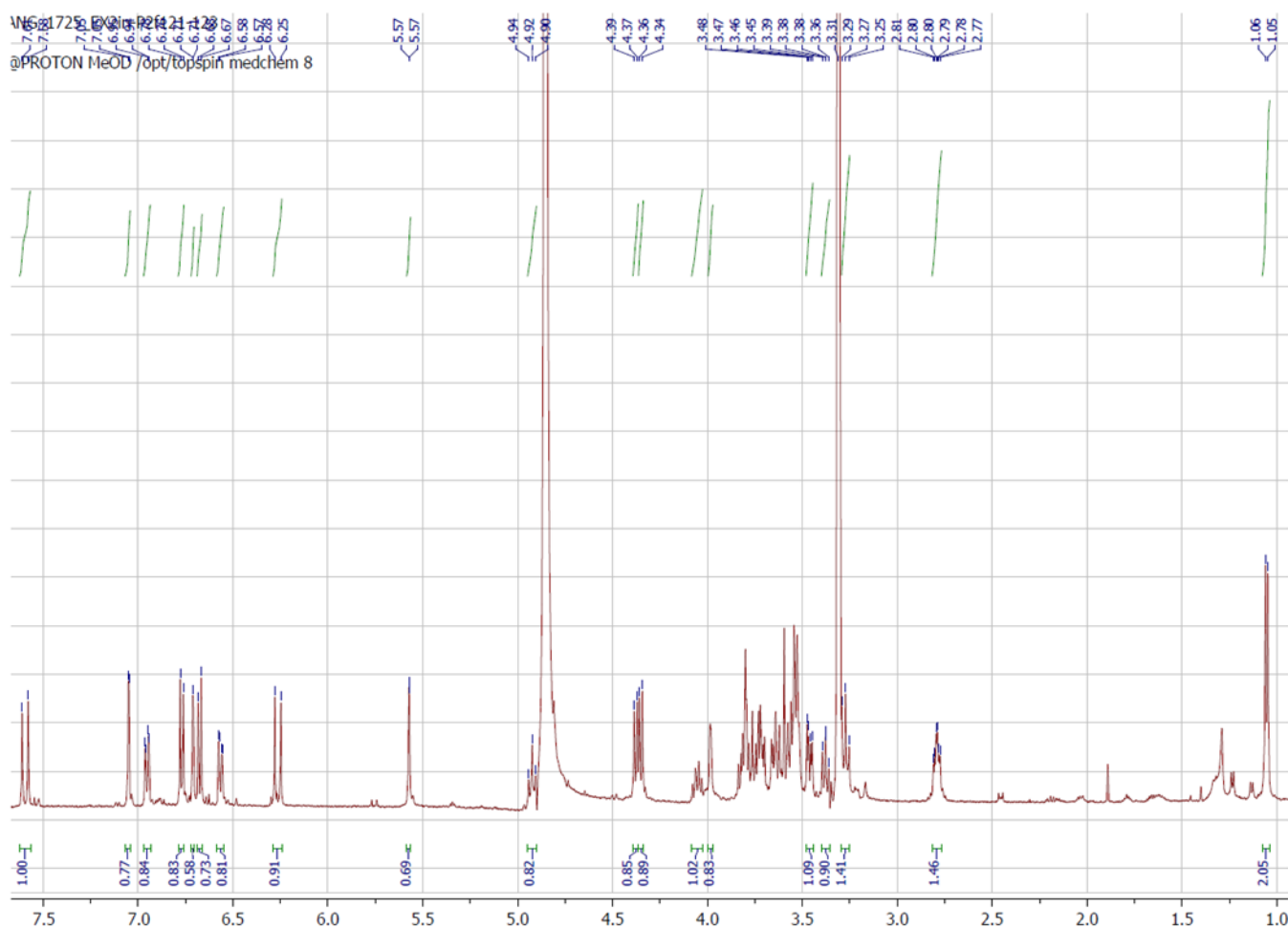


Figure S11. ^1H NMR spectrum of teupolioside (CD_3OD , 500 MHz)

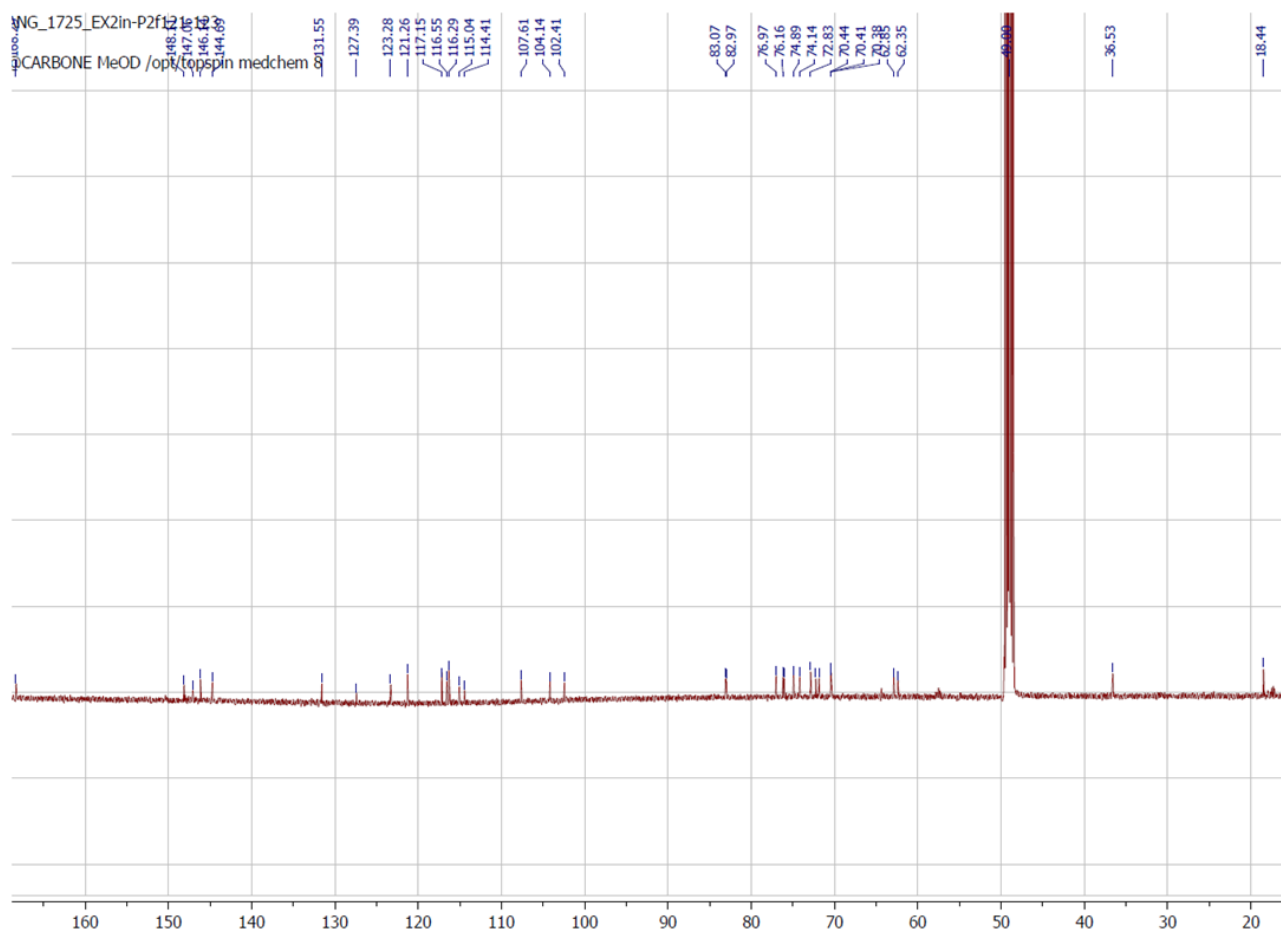


Figure S12. ^{13}C NMR spectrum of teupolioside (CD_3OD , 125 MHz)

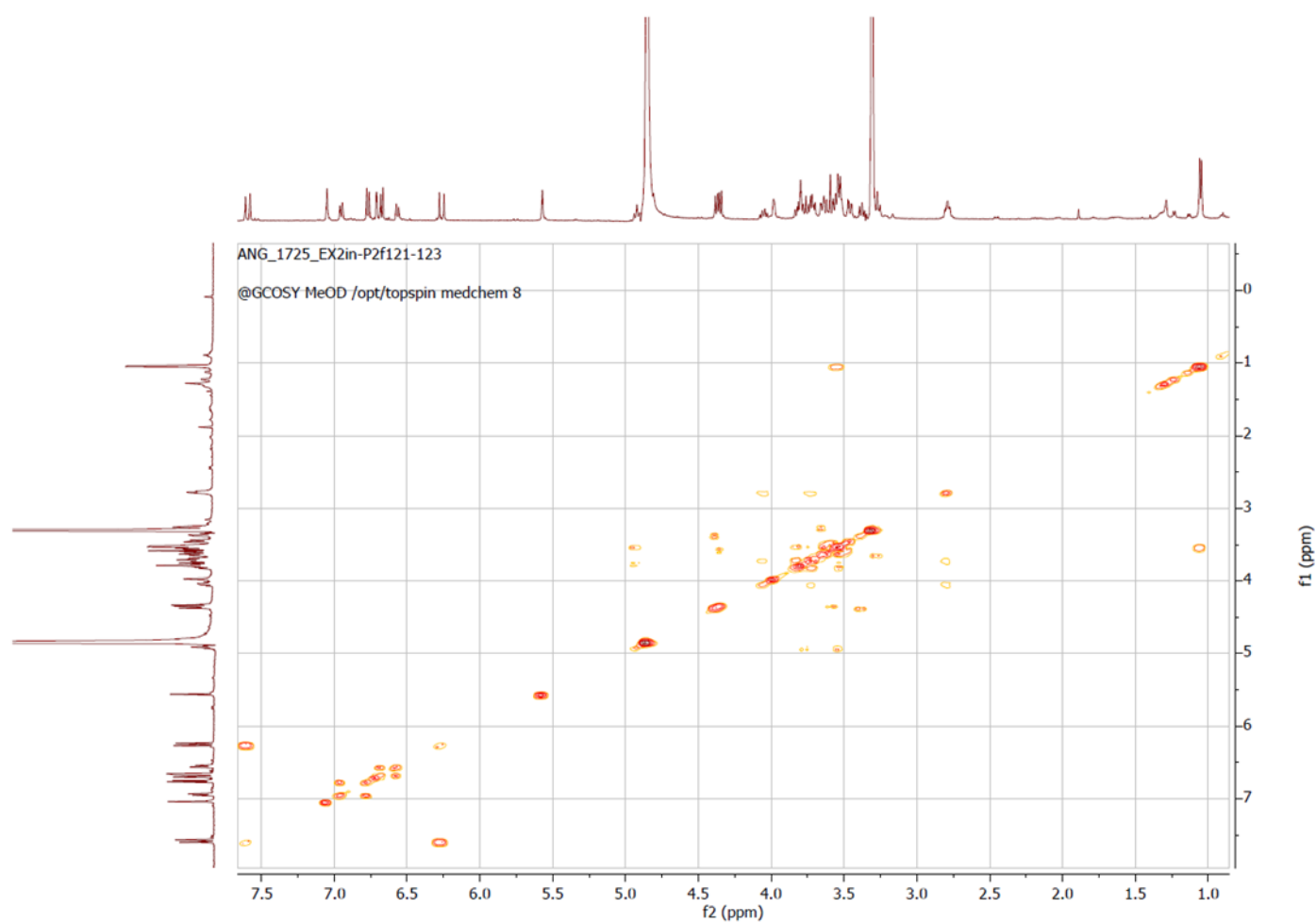


Figure S13. COSY spectrum of teupolioside (CD_3OD)

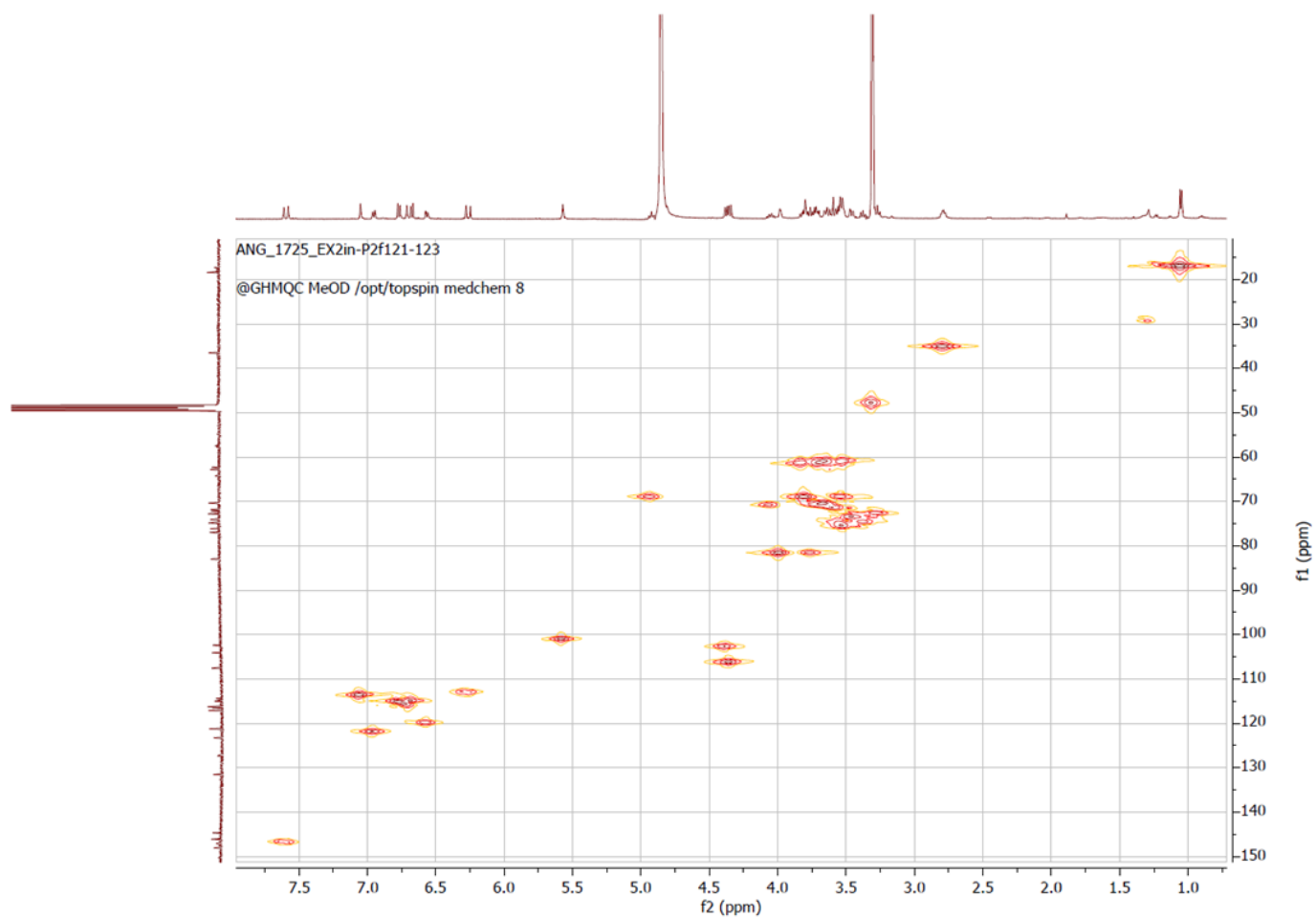


Figure S14. HSQC spectrum of teupolioside (CD₃OD)

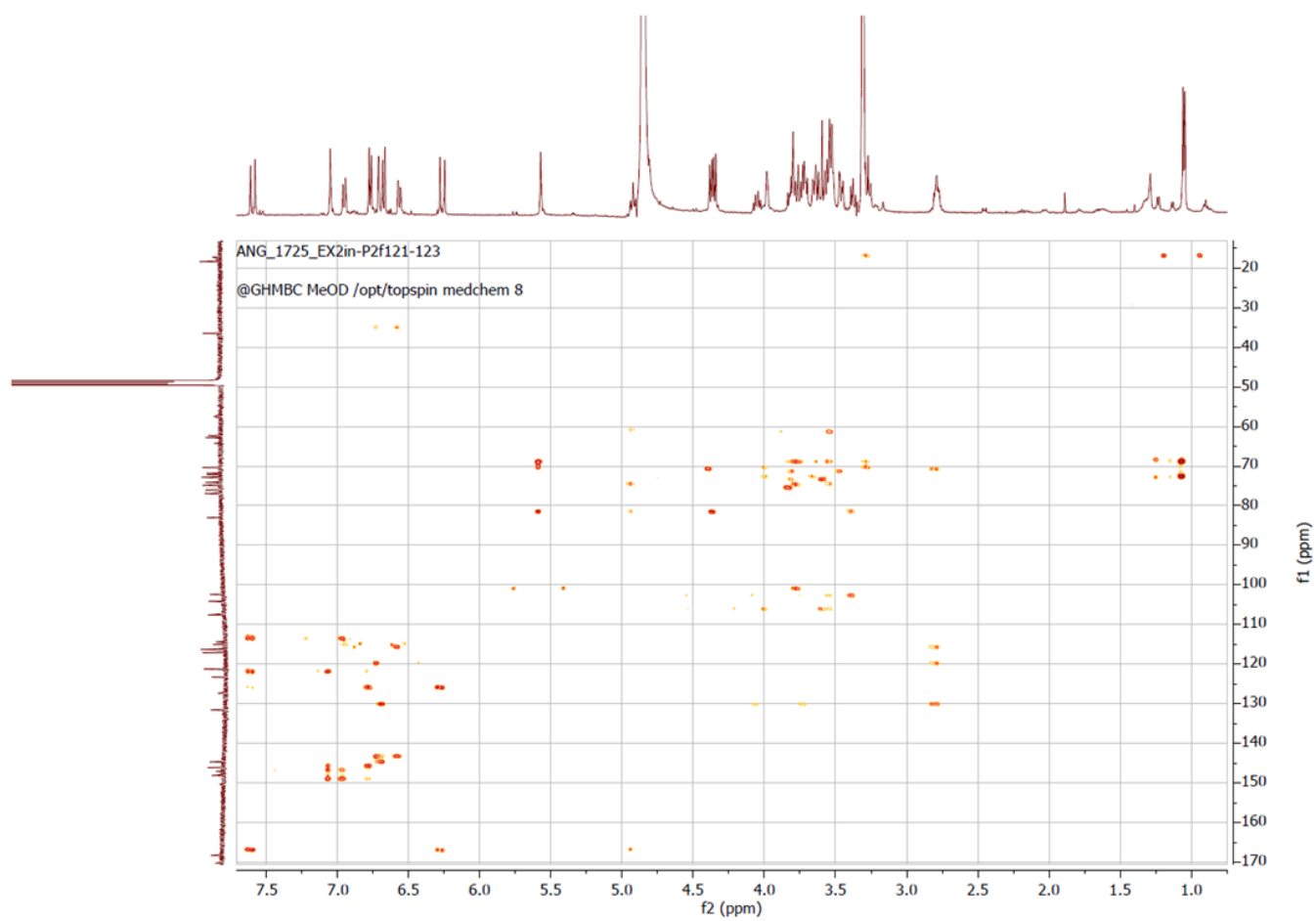


Figure S15. HMBC spectrum of teupolioside (CD₃OD)

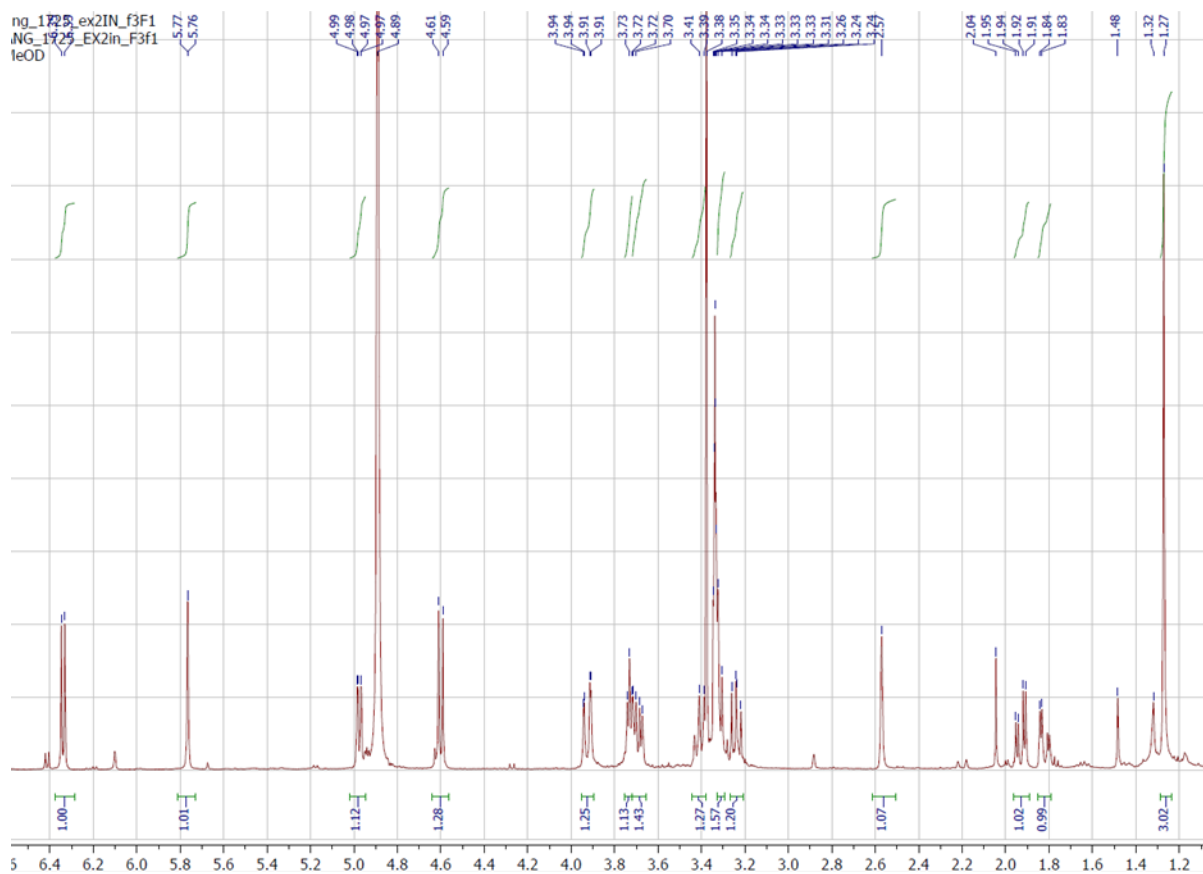


Figure S16. ^1H NMR spectrum of harpagide (CD_3OD , 400 MHz)

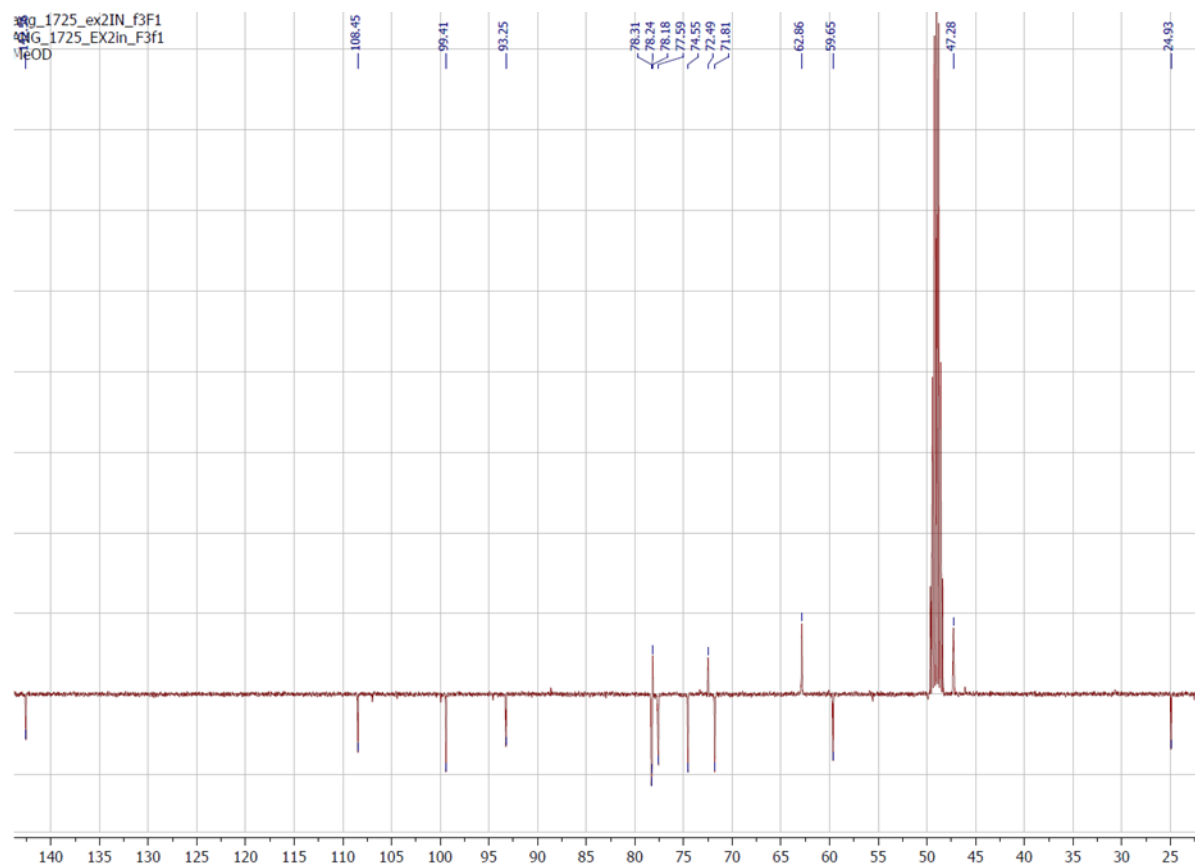


Figure S17. ^{13}C NMR spectrum of harpagide (CD_3OD , 100 MHz)

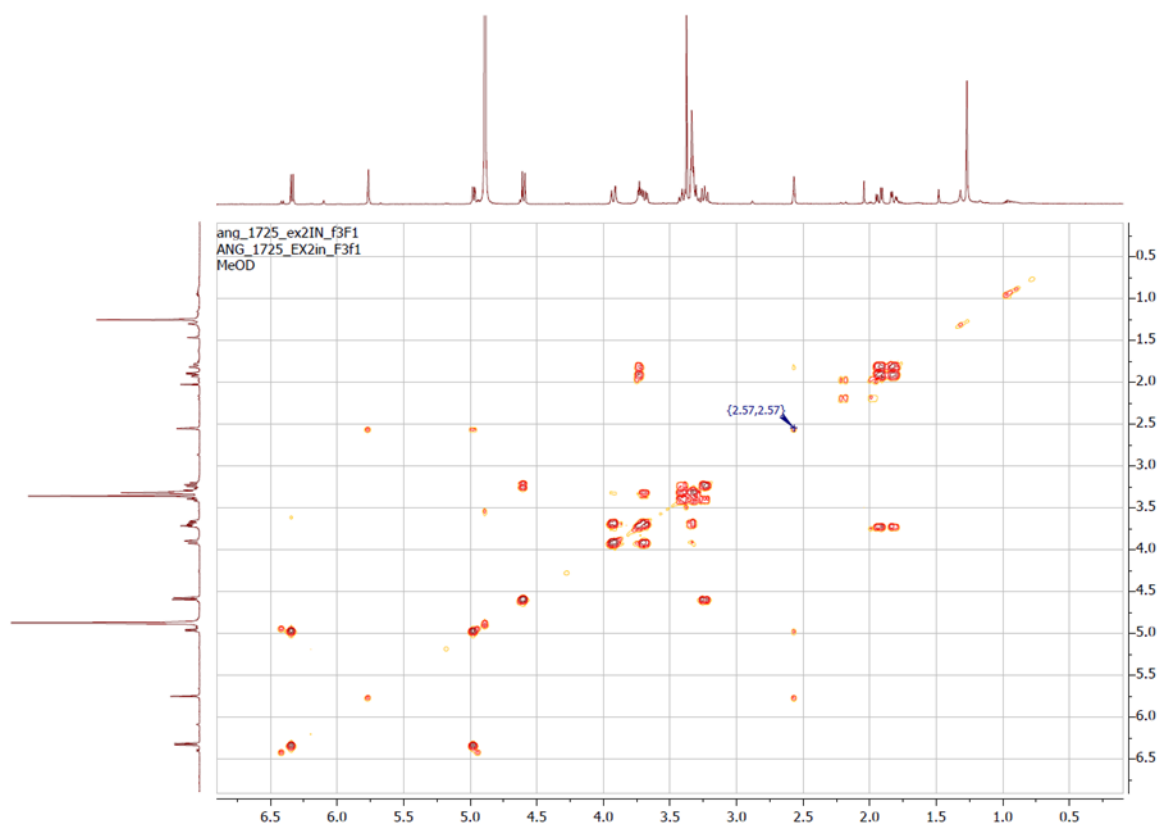


Figure S18. COSY spectrum of harpagide (CD_3OD)

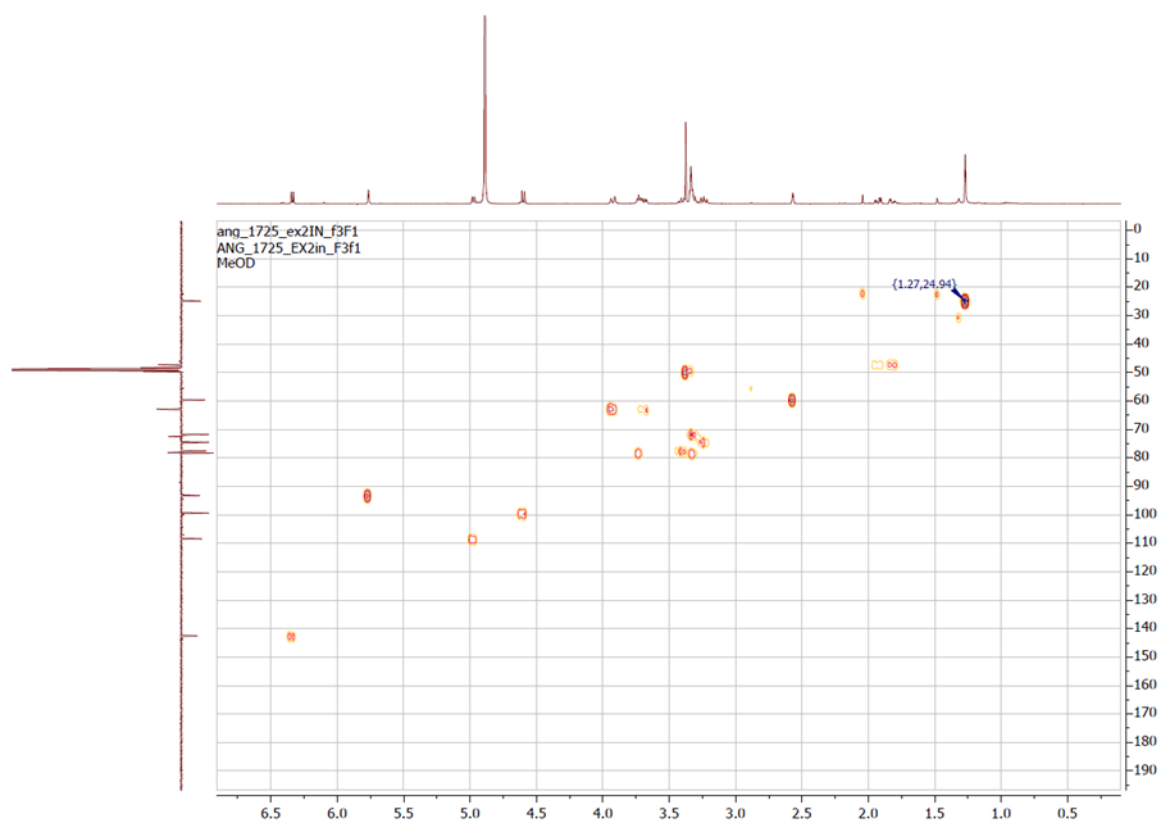


Figure S19. HSQC spectrum of harpagide (CD_3OD)

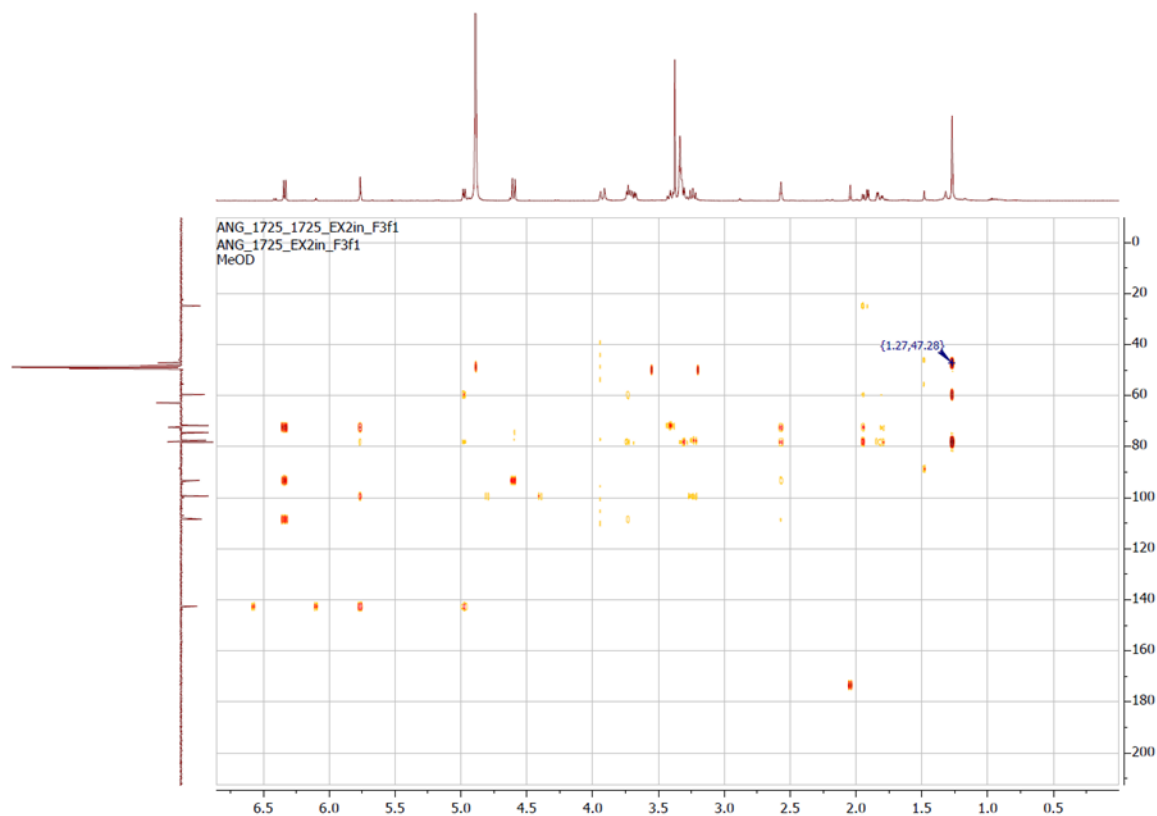


Figure S20. HMBC spectrum of harpagide (CD_3OD)

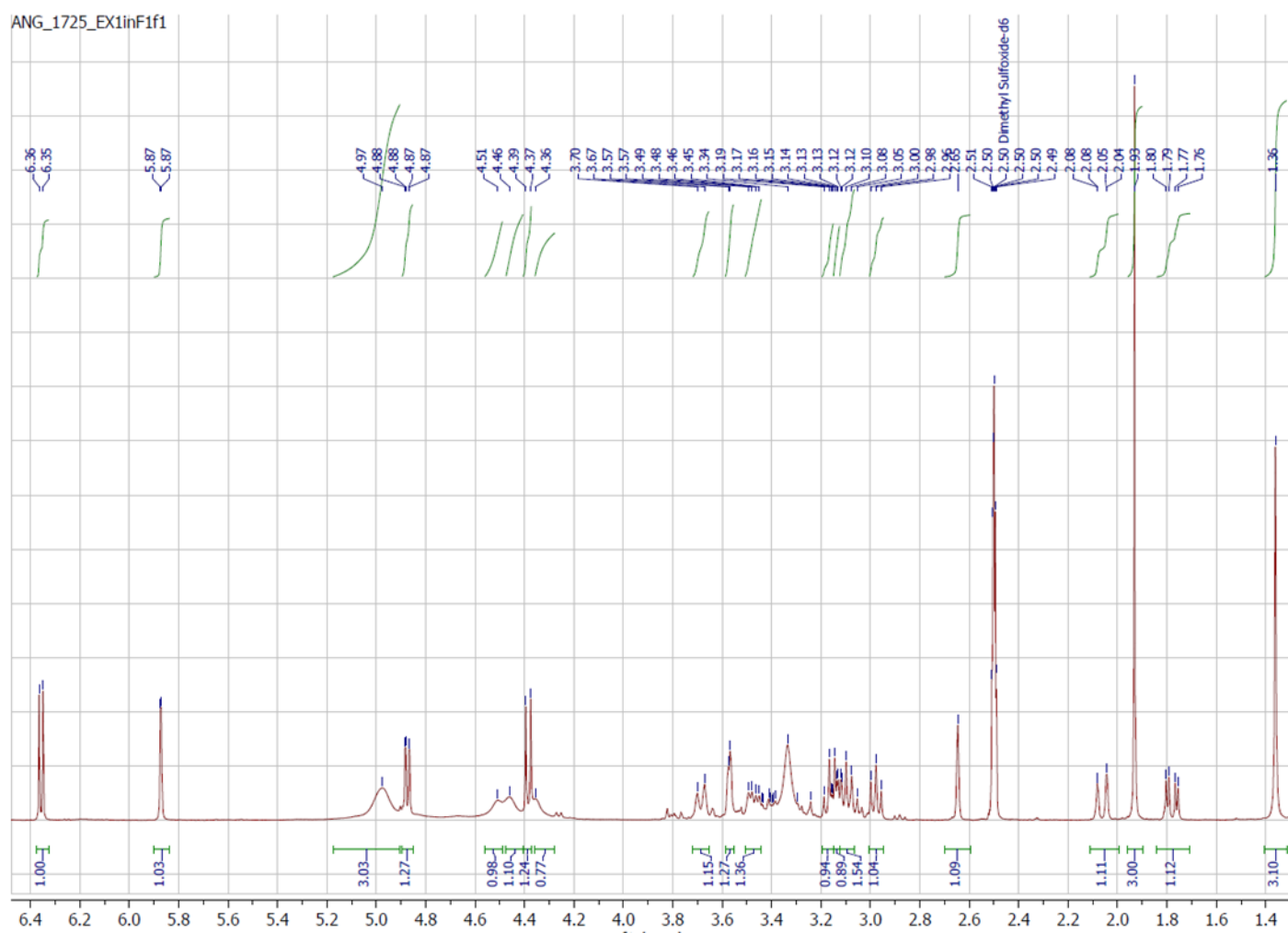


Figure S21. ^1H NMR spectrum of 8-*O*-acetylharpagide ($\text{DMSO}-d_6$, 400 MHz)

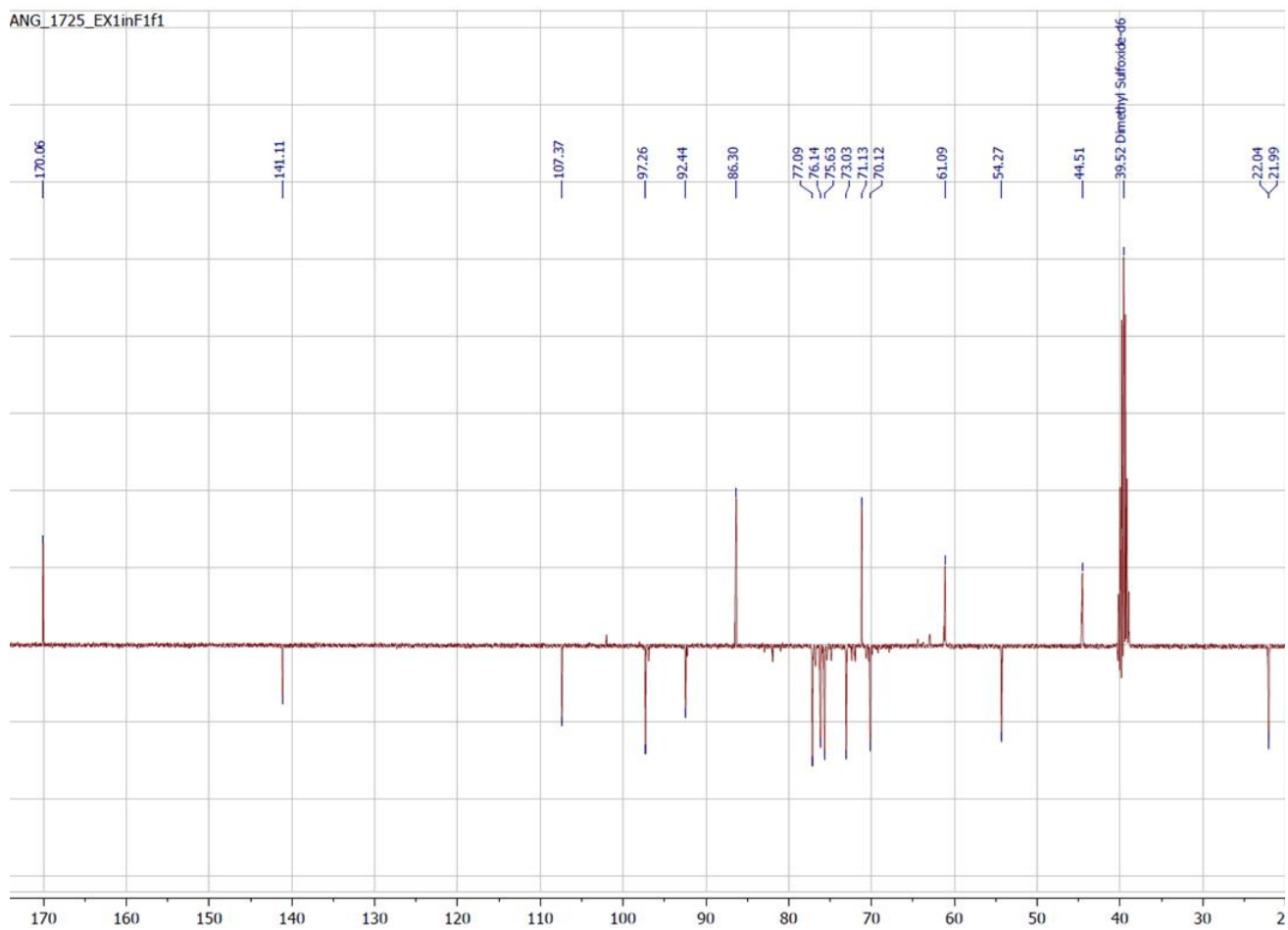


Figure S22. ^{13}C NMR spectrum of 8-*O*-acetylharpagide ($\text{DMSO}-d_6$, 100 MHz)

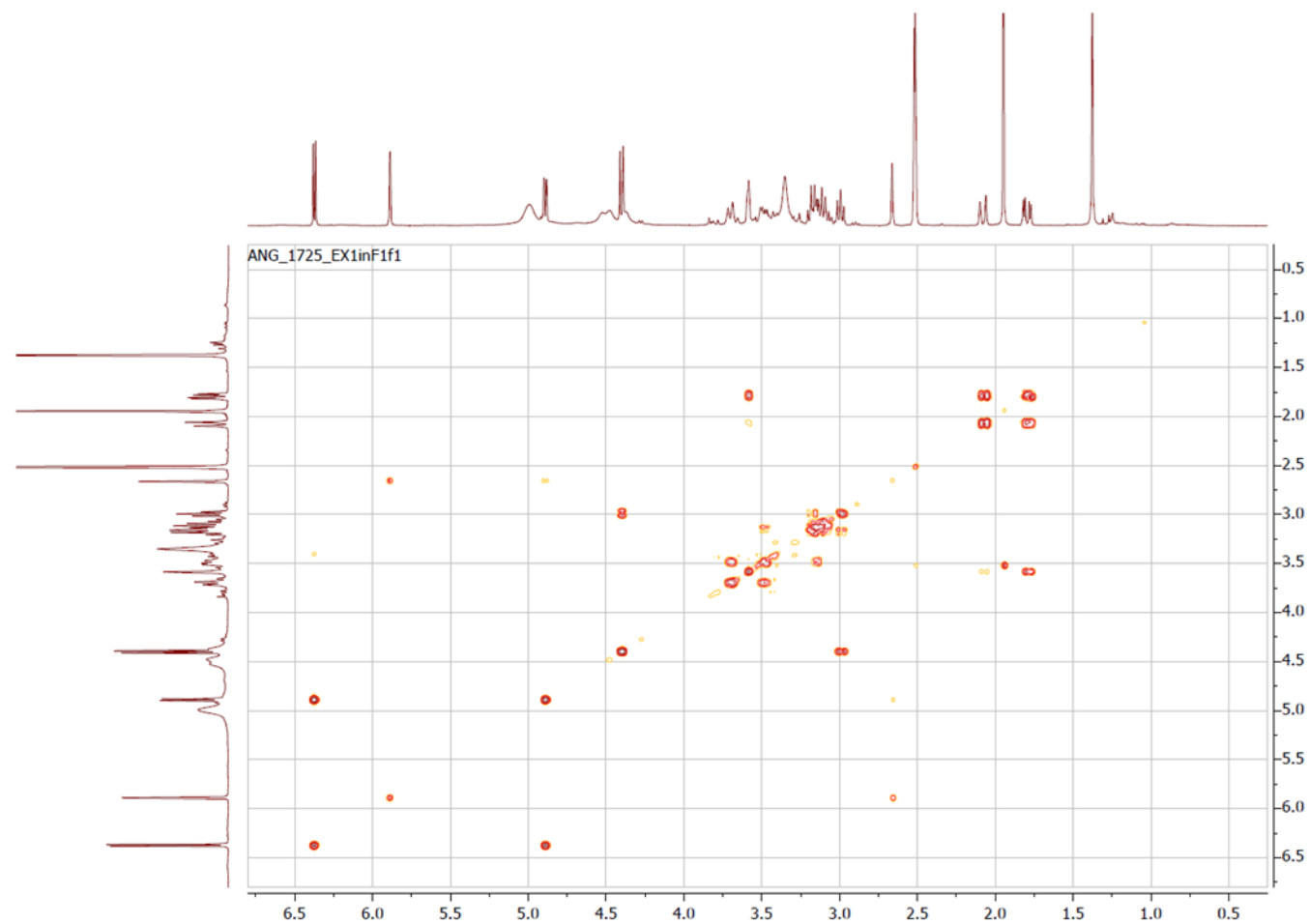


Figure S23. COSY spectrum of 8-*O*-acetylharpagide ($\text{DMSO}-d_6$)

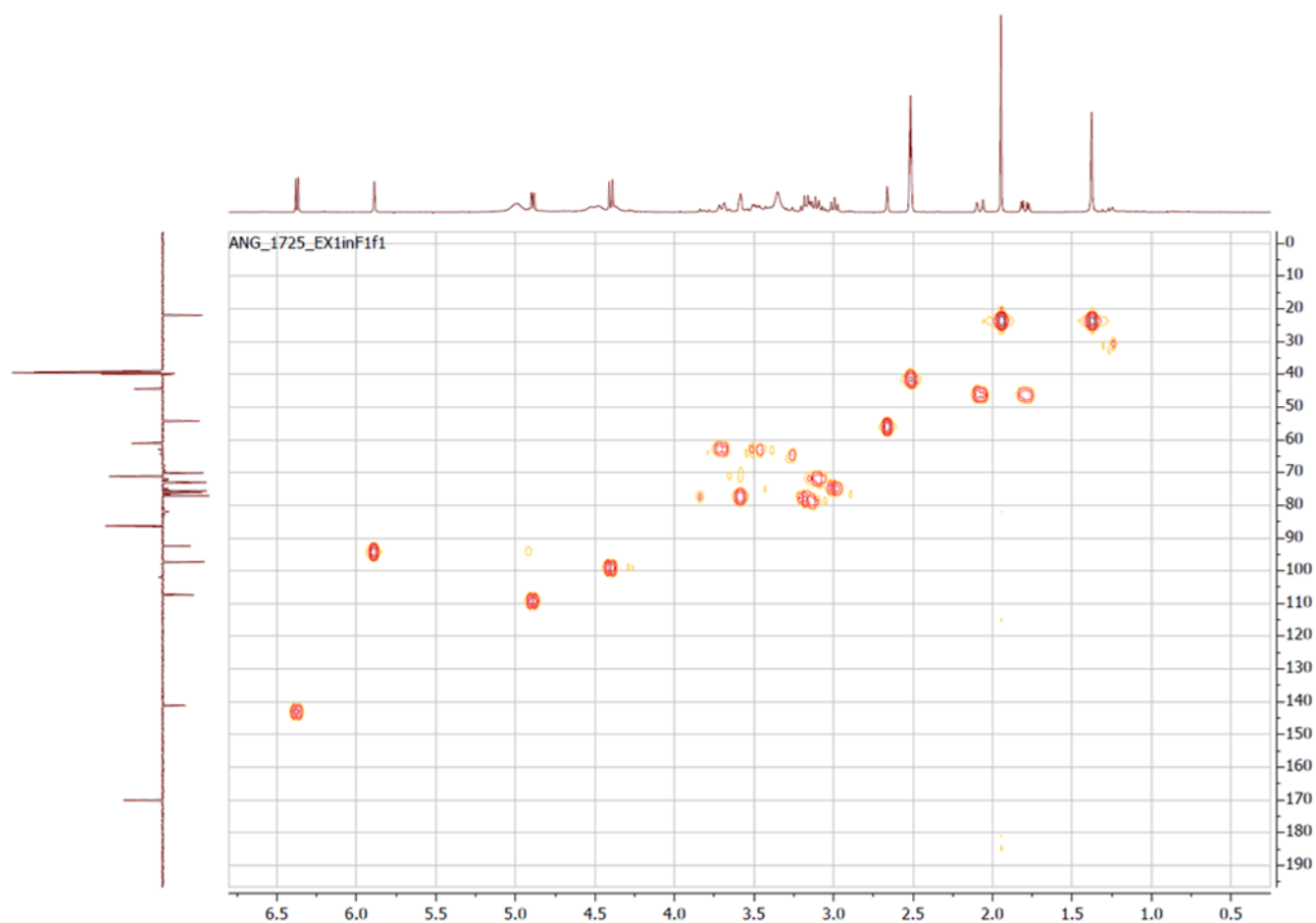


Figure S24. HSQC spectrum of 8-*O*-acetylharpagide (DMSO- d_6)

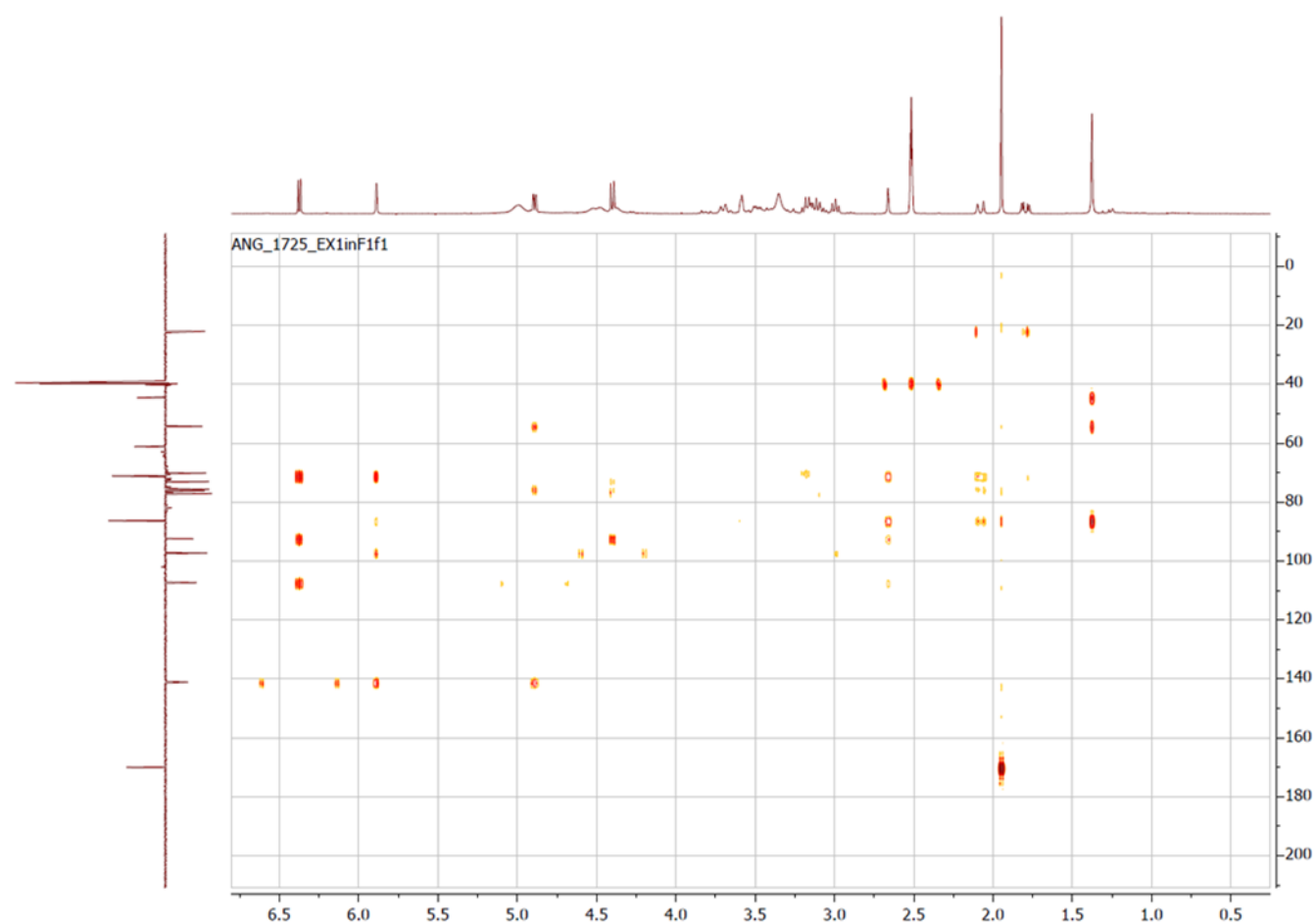


Figure S25. HMBC spectrum of 8-*O*-acetylharpagide (DMSO- d_6)

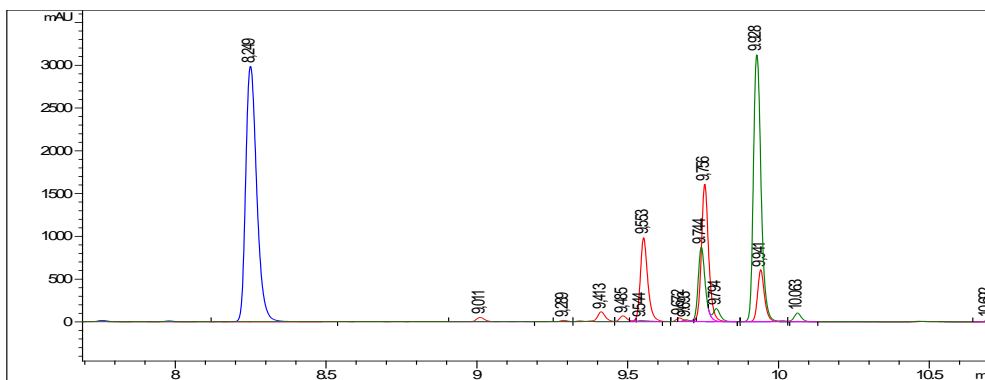


Figure S26. Acetylation reaction: HPLC chromatograms of harpagoside (blue), after 24 h of reaction (4 h at 70 °C and 20 h at room temperature, red) and after 6 more days of reaction (green)

Figure S27. Expression analysis of selected RNA for keratinocytes (NHEK) from sample 1

SPL-0005 : Expression analysis of selected RNA

FD190914 - mQPA 43 genes	Genes	Abbreviation	Control		Apolar extract		Intermediate extract		Polar extract		8-O-acetyltharpagide		Polyphenols fraction		Iridoids fraction	
			-		2.74 x 10 ⁻⁴ %		0.0025%		0.06%		0.0024%		0.0024%		0.0226%	
			Cycles		% control Mean HK		Cycles		% control Mean HK		Cycles		% control Mean HK		Cycles	
Housekeeping	GAPDH	Glyceraldehyde-3-phosphate dehydrogenase	17,92 18,00	18,10 17,98	99	17,80 17,74	103	18,01 17,97	109	18,33 18,08	99	17,94 17,85	102	18,04 17,93	119	
	B2M	Beta-2-microglobulin	25,16 24,82	24,50 24,23	161	25,72 25,24	65	25,64 25,13	86	24,58 24,62	153	25,89 25,48	60	25,46 25,34	91	
	RPLP0	Ribosomal protein, large, P0	18,96 18,86	18,88 18,80	110	18,73 18,75	102	19,14 19,09	97	18,99 18,94	113	18,84 18,80	103	19,44 19,34	87	
	RPS28	Ribosomal protein S28	19,23 19,30	19,49 19,50	89	19,25 19,26	91	19,68 19,74	82	19,74 19,74	84	19,37 19,30	93	20,12 20,02	69	
	FLG	Filaggrin	26,74 26,89	26,58 26,71	118	26,87 26,78	90	26,73 26,88	112	27,09 27,09	97	27,00 26,78	92	27,29 27,50	81	
Keratinocytes differentiation	IVL	Involucrin	27,12 27,11	26,80 27,06	119	27,44 27,47	71	25,76 25,83	278	27,50 27,28	97	27,68 27,65	66	27,59 27,49	90	
	KRT10	Keratin 10	23,67 23,79	23,94 24,05	87	24,14 24,36	63	23,21 23,18	161	24,36 24,35	76	23,90 23,98	84	24,26 24,22	85	
	KRT5	keratin 5, type II	20,54 20,68	20,78 20,94	88	21,18 21,18	61	20,97 20,95	87	21,07 21,09	85	21,30 21,39	58	22,62 22,55	31	
	LOR	Loricrin	27,01 27,08	26,57 26,70	139	26,91 26,85	101	27,20 27,52	90	27,08 27,19	110	26,93 26,96	104	27,19 27,21	109	
	TGM1	transglutaminase 1	23,77 23,83	23,90 24,04	93	25,63 25,60	26	23,71 23,67	120	24,59 24,31	75	26,01 25,97	21	27,42 27,50	10	
	MMP1	matrix metalloproteinase 1	26,58 26,70	26,72 26,99	90	26,99 26,28	105	26,73 26,60	110	26,87 26,76	98	26,87 26,76	104	24,99 25,04	374	
	MMP9	matrix metalloproteinase 9	30,56 30,56	30,43 30,51	111	30,28 30,80	93	29,89 29,80	183	30,06 29,83	180	29,74 29,50	187	28,62 28,62	465	
Extracellular matrix degradation	TIMP1	TIMP metalloproteinase inhibitor 1	20,63 20,56	20,95 20,84	85	21,44 21,28	53	21,23 21,14	74	21,08 21,11	83	21,01 20,92	75	19,75 19,61	229	
	TIMP2	TIMP metalloproteinase inhibitor 2	29,10 29,31	29,21 29,34	99	29,64 29,43	72	29,83 29,63	77	29,55 29,64	89	29,50 29,80	72	29,61 29,79	86	
	AKT1	V-akt murine thymoma viral oncogene homolog 1	26,58 26,82	26,78 26,75	100	26,83 26,85	82	26,97 27,00	91	26,99 26,99	98	26,98 26,80	85	26,76 26,87	112	
	BAX	BCL2-associated X protein	27,77 28,00	27,81 27,75	112	27,72 27,85	101	27,76 27,68	129	27,61 27,73	127	27,51 27,74	116	26,09 26,53	88	
Apoptosis	CASP3	Caspase 3, apoptosis-related cysteine peptidase	26,65 26,84	26,44 26,62	121	26,86 26,70	88	26,83 26,88	103	26,89 26,90	105	26,56 26,66	106	26,52 26,52	140	
	FOS	FBJ murine osteosarcoma viral oncogene homolog	28,69 28,85	28,96 29,10	87	28,47 28,29	118	28,01 28,19	177	28,48 28,55	140	27,94 28,12	162	28,80 28,99	111	
	TP53	Tumor protein p53	26,68 26,71	26,55 26,87	104	26,34 26,45	111	26,93 26,82	98	26,75 26,82	110	26,70 26,52	103	28,02 28,11	47	
	CDH1	cadherin 1, type 1	23,49 23,13	23,91 24,14	63	23,60 23,82	68	23,27 23,05	123	23,28 23,43	113	23,04 23,59	98	22,85 22,75	171	
	CLDN1	claudin 1	23,11 23,21	23,31 23,30	94	23,78 23,74	60	23,27 23,21	105	23,23 23,23	112	24,04 23,92	55	25,48 25,44	25	
Cell-cell interactions	DSC1	desmocollin 1	26,68 30,13	29,94 30,20	92	30,46 30,68	56	28,61 28,73	259	30,62 30,65	70	29,94 30,54	81	32,14 32,06	26	
	DSP	desmoplakin	22,82 22,68	22,63 22,20	133	23,60 23,28	56	22,65 22,48	127	22,73 22,64	123	23,51 23,34	61	23,75 23,72	61	
	ITGA6	Integrin, alpha 6	24,69 24,69	24,67 24,87	99	24,89 24,72	84	24,80 24,82	103	24,83 24,70	111	24,77 24,56	99	24,78 24,66	119	
	ITGB1	Integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)	20,66 20,63	20,72 20,63	102	20,79 20,63	87	20,88 20,89	94	21,03 20,96	92	20,56 20,49	106	20,60 20,53	128	
	LGALS1	Lectin, galactoside-binding, soluble, 1	21,32 21,24	21,58 21,54	86	21,46 21,37	82	22,95 22,92	35	22,02 22,02	70	21,52 21,51	82	22,36 22,29	59	
	LGALS7	lectin, galactoside-binding, soluble, 7	23,53 23,60	23,75 23,83	89	23,73 23,72	81	23,88 23,94	88	24,55 24,52	60	23,86 23,91	81	25,58 25,64	29	
	GPX1	glutathione peroxidase 1	22,32 22,29	22,32 22,29	105	21,79 21,79	129	22,97 22,96	71	22,62 22,59	95	22,05 21,97	119	22,48 22,48	106	
	HIF1A	Hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)	24,69 24,86	24,62 24,67	114	24,84 24,83	87	25,05 25,02	93	25,05 25,03	97	24,91 24,94	87	25,10 25,14	95	
	HMOX1	Heme oxygenase (decycling) 1	27,61 27,79	27,16 27,62	131	27,74 27,86	84	27,91 27,99	94	27,57 27,80	119	28,02 27,90	81	27,52 27,68	130	
	HSPB1	heat shock 27kDa protein 1	18,64 18,71	18,97 18,93	86	20,01 20,00	36	19,12 19,13	82	19,53 19,53	65	19,99 20,00	39	21,24 21,27	20	
Response to oxidative and et cellular stress	NFKB1	Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1	25,30 25,51	25,18 25,23	120	25,50 25,47	85	25,29 25,36	118	25,48 25,32	118	25,37 25,38	99	25,32 25,31	129	
	NQO1	NAD(P)H dehydrogenase, quinone 1	26,61 26,74	26,45 26,36	126	26,81 26,79	83	26,04 25,88	183	26,07 25,85	193	26,85 27,06	80	25,99 25,71	216	
	SOD1	Superoxide dismutase 1, soluble	22,94 22,98	22,90 22,90	109	22,91 22,72	100	23,03 22,94	110	23,10 23,06	108	23,07 22,85	97	23,23 23,20	102	
	IL1A	Interleukin 1, alpha	23,80 23,91	23,79 23,59	117	23,55 23,15	129	23,58 23,45	141	23,53 23,29	160	23,88 23,53	108	23,23 23,05	199	
	IL6	Interleukin 6	nd nd	nd nd	-	nd nd	-	nd nd	-	nd nd	-	nd nd	-	nd nd	-	
Translation regulation	MAPK1	mitogen-activated protein kinase 1	25,52 25,73	25,51 25,66	107	25,66 25,62	89	25,67 25,63	109	25,83 25,83	101	25,62 25,57	99	25,65 25,70	117	
	MAPK14	mitogen-activated protein kinase 14	26,79 27,02	26,91 27,08	98	27,03 27,05	82	26,96 27,03	104	27,16 27,18	97	27,09 27,16	83	27,47 27,32	86	
	EGFR	epidermal growth factor receptor	23,87 23,81	23,92 23,81	103	23,82 23,77	93	24,56 24,48	70	24,20 24,02	97	24,14 24,03	82	24,58 24,43	77	
Cellular cycle / Growth factor / Transcription factors	JUN	Jun proto-oncogene	28,53 28,93	28,10 28,30	150	28,42 28,57	105	28,61 28,69	117	28,56 28,43	137	28,58 28,71	102	28,62 28,79	122	
	NOTCH1	Notch 1	27,88 28,27	28,05 28,50	91	28,86 28,98	50	29,00 28,91	60	28,45 28,29	95	29,15 29,42	42	30,13 30,03	30	
	TGFB1	Transforming growth factor, beta 1	23,86 23,93	23,98 23,92	101	23,95 23,91	88	24,13 23,98	100	24,10 24,06	103	24,09 24,09	85	23,87 23,75	129	
	TP63	Tumor protein p63	26,02 26,14	26,04 26,22	101	26,58 26,27	81	26,50 26,43	83	26,50 26,49	88	26,32 26,25	84	26,89 26,89	69	
	FOXO1	Forkhead box O1	26,56 26,66	26,21 26,28	135	26,71 26,81	81	26,93 26,86	91	26,68 26,76	109	26,88 26,98	78	27,10 27,14	85	
Stimulation (Arbitrary selection): % > 200																
Inhibition (Arbitrary selection): % < 50																
Results to be interpreted with caution (high cycle count indicating low relative expression, close to detection limit) > 31																
Not detected or non-compliant melting curve																
nd																

Figure S28. Expression analysis of selected RNA for keratinocytes (NHEK) from sample 2

SPL-0005 : Expression analysis of selected RNA

			Control	Apolar extract		Intermediate extract		Polar extract		8-O-acetyltharpagide		Polyphenols fraction		Iridoids fraction	
FD190914 - mQPA 43 genes	Genes		-	2.74 x 10 ⁻⁴ %		0.0025%		0.06%		0.0024%		0.0024%		0.0226%	
	Abbreviation		Cycles	Cycles	% control Mean HK	Cycles	% control Mean HK	Cycles	% control Mean HK	Cycles	% control Mean HK	Cycles	% control Mean HK	Cycles	% control Mean HK
Housekeeping	GAPDH	Glyceraldehyde-3-phosphate dehydrogenase	18,16 18,14	18,58 18,53	97	18,43 18,55	98	18,52 18,49	109	18,30 18,17	106	18,15 18,00	104	18,89 18,97	97
	B2M	Beta-2-microglobulin	25,59 25,58	26,09 25,65	106	26,80 26,50	60	24,99 25,09	203	25,60 25,84	103	25,80 25,87	83	25,89 26,05	128
	RPLP0	Ribosomal protein, large, P0	19,90 18,83	19,08 19,19	106	19,03 19,10	108	19,51 19,38	93	19,13 19,14	93	18,89 18,89	97	19,53 19,49	107
	RPS28	Ribosomal protein S28	19,36 19,38	19,69 19,80	99	19,78 19,83	92	20,00 20,03	89	19,62 19,59	96	19,48 19,37	95	20,18 20,17	96
	FLG	Filaggrin	27,06 26,92	27,20 27,27	108	26,91 27,09	124	27,27 27,20	117	26,74 26,94	125	26,58 26,81	121	26,75 26,76	197
	IVL	Involucrin	27,67 27,70	27,76 27,73	123	27,75 27,67	122	26,53 26,53	309	27,35 27,44	137	27,33 27,21	132	27,18 27,13	242
Keratinocytes differentiation	KRT10	Keratin 10	24,59 24,51	24,81 24,79	108	24,67 24,70	113	23,84 23,93	220	24,42 24,59	116	24,02 24,05	141	24,53 24,58	167
	KRT5	keratin 5, type II	21,51 21,53	22,02 22,03	90	22,17 22,05	83	22,36 22,31	79	22,11 21,95	79	21,94 21,85	76	23,84 23,88	33
	LOR	Loricrin	26,61 26,87	26,92 27,06	107	26,77 26,97	114	27,09 27,28	102	26,49 26,53	131	26,46 26,52	117	26,44 26,49	202
	TGM1	transglutaminase 1	24,93 24,85	25,51 25,51	83	26,47 26,49	41	25,29 25,23	107	24,99 25,09	101	27,09 27,03	22	28,11 28,03	18
	MMP1	matrix metalloproteinase 1	26,00 26,01	25,98 26,11	125	25,12 25,08	233	25,51 25,54	194	26,08 26,04	108	24,99 25,03	197	24,96 24,98	343
	MMP9	matrix metalloproteinase 9	30,90 30,58	30,63 31,07	119	31,26 31,19	88	29,77 30,09	243	30,61 30,59	123	30,05 29,89	167	29,86 30,07	285
Extracellular matrix degradation	TIMP1	TIMP metalloproteinase inhibitor 1	21,02 20,96	21,61 21,59	84	21,69 21,56	80	21,66 21,57	90	21,34 21,21	92	21,14 21,13	89	19,85 19,82	372
	TIMP2	TIMP metalloproteinase inhibitor 2	28,96 29,23	29,15 29,57	107	29,30 29,50	101	29,97 30,08	73	29,41 29,43	89	29,21 29,52	82	30,57 30,54	61
	AKT1	V-akt murine thymoma viral oncogene homolog 1	26,71 26,85	26,97 27,18	104	26,83 27,14	109	27,20 27,19	104	27,02 27,20	89	26,56 26,70	109	27,84 27,81	81
	BAX	BCL2-associated X protein	27,58 27,82	27,53 27,64	138	27,94 28,04	102	27,81 28,05	118	27,85 28,03	95	27,58 27,45	112	28,66 28,71	84
	CASP3	Caspase 3, apoptosis-related cysteine peptidase	26,85 26,87	26,80 27,04	123	26,78 26,90	126	26,82 26,83	142	27,00 27,23	94	26,68 26,51	119	27,49 27,30	116
	FOS	FBJ murine osteosarcoma viral oncogene homolog	28,10 28,50	28,45 28,59	109	28,10 28,47	126	28,22 27,99	158	28,03 28,19	127	27,82 27,88	134	29,82 29,60	63
Apoptosis	TP53	Tumor protein p53	26,33 26,61	26,78 26,99	96	26,97 27,03	86	26,75 26,89	109	26,74 26,83	90	26,55 26,59	92	29,04 28,93	29
	CDH1	cadherin 1, type 1	23,43 23,89	23,01 23,03	197	22,51 23,21	220	22,94 22,83	235	23,01 23,74	140	23,10 22,52	179	23,21 23,79	188
	CLDN1	claudin 1	23,94 23,90	24,52 24,64	81	24,80 24,83	67	23,72 23,61	166	23,95 23,91	112	24,97 25,00	47	26,24 26,46	31
	DSC1	desmocollin 1	32,13 32,54	31,19 31,10	289	32,05 31,97	155	31,52 31,44	249	32,01 32,46	121	31,55 31,62	164	32,27 32,42	165
	DSP	desmoplakin	23,51 23,65	23,63 23,72	120	23,64 23,96	107	23,21 23,24	177	23,90 23,64	99	23,71 23,44	99	25,02 24,90	64
	ITGA6	Integrin, alpha 6	24,71 24,78	24,80 24,87	120	24,67 24,65	132	24,72 24,81	137	25,13 24,92	93	24,42 24,17	135	25,64 25,56	92
Cell-cell interactions	ITGB1	Integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)	20,83 20,81	21,07 21,01	110	20,98 20,99	111	21,10 21,05	116	21,17 21,02	93	20,50 20,45	125	21,01 21,00	147
	LGALS1	Lectin, galactoside-binding, soluble, 1	20,25 20,28	20,65 20,62	99	20,60 20,60	99	21,54 21,51	58	20,75 20,74	81	20,10 20,10	111	21,14 21,08	93
	LGALS7	lectin, galactoside-binding, soluble, 7	24,03 24,09	24,79 24,91	74	25,05 25,17	60	25,23 25,25	61	24,84 24,79	67	24,50 24,49	73	26,30 26,49	33
	GPX1	glutathione peroxidase 1	22,19 22,13	22,61 22,51	97	22,28 22,23	117	22,50 22,69	93	22,50 22,44	91	21,96 21,92	115	22,78 22,79	108
	HIF1A	Hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)	24,81 24,91	24,91 25,05	118	24,91 24,97	118	24,91 24,98	131	24,93 24,94	107	24,68 24,72	110	25,09 25,21	137
	HMOX1	Heme oxygenase (decycling) 1	27,62 28,08	27,93 28,07	114	27,90 28,01	114	28,16 28,02	116	27,57 27,68	130	27,66 27,65	112	27,48 27,44	216
Response to oxidative and et cellular stress	HSPB1	heat shock 27kDa protein 1	19,74 19,83	20,34 20,37	86	20,98 21,04	53	20,38 20,38	92	20,30 20,33	78	20,92 20,97	44	22,34 22,31	29
	NFKB1	Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1	25,26 25,30	25,58 25,56	105	25,51 25,46	108	24,68 24,66	212	25,55 25,48	96	25,05 25,01	117	25,29 25,28	167
	NQO1	NAD(P)H dehydrogenase, quinone 1	27,61 27,44	27,18 27,49	147	26,69 26,83	212	26,32 26,49	302	27,01 26,96	163	27,09 26,88	144	25,99 25,89	501
	SOD1	Superoxide dismutase 1, soluble	23,14 23,19	23,53 23,47	101	23,21 23,19	122	23,65 23,55	103	23,54 23,31	94	23,02 22,96	111	23,64 23,64	120
	IL1A	interleukin 1, alpha	23,70 23,66	23,88 23,83	113	23,36 23,28	160	22,32 22,10	386	23,88 23,64	107	23,21 23,05	145	23,65 23,62	173
	IL6	interleukin 6	nd nd	nd nd	-	nd nd	-	nd nd	-	nd nd	-	nd nd	-	nd nd	-
Translation regulation	MAPK1	mitogen-activated protein kinase 1	25,57 25,80	25,90 25,86	111	25,92 26,10	99	25,90 25,80	123	25,89 25,95	95	25,58 25,58	106	26,23 26,44	107
	MAPK14	mitogen-activated protein kinase 14	27,21 27,28	27,21 27,59	116	27,33 27,51	110	27,15 27,15	148	27,56 27,28	100	26,90 27,00	121	27,81 27,99	106
	EGFR	epidermal growth factor receptor	24,04 24,01	24,42 24,24	104	24,25 24,23	107	24,25 24,06	127	24,67 24,53	76	24,11 24,04	95	24,84 24,85	95
Cellular cycle / Growth factor / Transcription factors	JUN	Jun proto-oncogene	28,63 28,83	28,55 28,56	144	28,52 28,68	136	28,76 28,91	129	28,50 28,59	128	27,82 28,09	169	27,85 28,17	277
	NOTCH1	Notch 1	28,78 28,69	28,89 29,01	110	29,01 29,26	95	29,02 29,10	111	29,02 29,08	90	29,49 29,57	57	30,99 31,52	30
	TGFB1	Transforming growth factor, beta 1	24,07 24,08	24,50 24,30	102	24,22 24,17	115	24,46 24,28	113	24,35 24,29	95	23,96 23,98	106	24,83 24,78	101
	TP63	Tumor protein p63	26,31 26,57	26,78 26,86	98	26,75 26,81	98	26,94 26,98	193	26,66 26,77	93	26,57 26,59	89	28,29 28,29	46
	FOXO1	Forkhead box O1	26,74 26,83	26,77 26,84	124	26,84 26,84	120	26,83 26,82	135	26,64 26,80	118	26,58 26,52	116	26,58 26,53	196
Simulation (Arbitrary selection): % > 200			200												
Inhibition (Arbitrary selection): % < 50			50												
Results to be interpreted with caution (high cycle count indicating low relative expression, close to detection limit) > 31			31												
Not detected or non-compliant melting curve / nd			nd												

Figure S29. Expression analysis of selected RNA for keratinocytes (NHEK) from sample 3

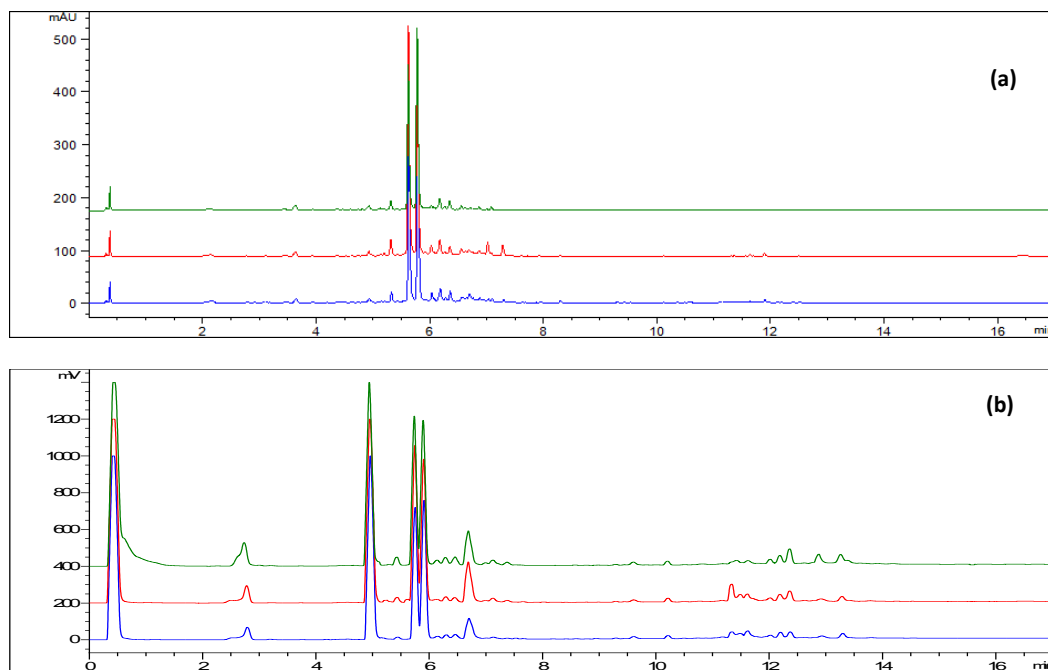


Figure S30. Interannual variability study on *Ajuga pyramidalis* ethanolic extracts, samples collected in 2017 (blue), 2018 (red), 2019 (green): **(a)** HPLC-DAD and **(b)** HPLC-ELSD chromatograms.