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Discovery of varlaxins, new aeruginosin-type inhibitors of human trypsins

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Table S1. Subunits of aeruginosins, dysinosins, oscillarins, pseudoaeruginosins, spumigins, pseudospumigins, suomilide, banyaside and nostosins and structurally similar commercial trypsin inhibitors leupeptin and antipain. Mgs= 2-O-methylglyceric acid 3-O-sulfate, MgA = 2-O-methylglyceric acid, Hpla = 4-hydroxyphenyllactic acid, Pla = phenyllactic acid, Hhpba = 2-hydroxy-4-(4-hydroxyphenyl)butanoic acid, Choi = 2-carboxy-6-octahydroindole, Agma = 4-amidinobutylamide, Aaep = 1-amidino-3-(2-aminoethyl)-3-pyrroline, Ddha = didehydroaraginal. Subunits matching with varlaxin 1046A marked with green and possibly matching with red.

No	Name	Number of subunits matching with varlaxins	Subunits 1	2	3	4	DOI
1	Chlorodysinosin A	2	Mgs	L-Cleu	L-Choi-OH	Aaep	10.1021/ja0625834
2	Dysinosin A	2	Mgs	D-Leu	L-Choi-OH	Aaep	10.1021/ja020814a
3	Dysinosin B	2	Mgs	Val	L-Choi-OH-Glc	Aaep	10.1021/np049968p
4	Dysinosin C	2	Mgs	Val	L-Choi-OH	Aaep	10.1021/np049968p
5	Suomilide	2	Mgs	*allo*-Ile	Abn	Aaep	10.1016/S0040-4039(97)01193-3
6	Banyaside A	2	Mgs	D-Leu	Abn-Glc-Hex-Carb	Aaep	10.1016/j.tet.2004.11.016
7	Banyaside B	2	Mgs	D-Leu	Abn-Glc-Hex	Aaep	10.1016/j.tet.2004.11.016
8	Aeruginosin	1/2	Pla	Ile/Leu	Choi	Aaep	10.1007/s00203-014-1008-9
9	Aeruginosin	1/2	Hpla	Ile/Leu	Choi-Pentose	Aaep	10.1007/s00203-014-1008-12
10	Aeruginosin	1/2	Hpla-Cl	Ile/Leu	Choi-Pentose	Aaep	10.1016/j.foodres.2012.12.028
11	Aeruginosin 663	1/2	Pla	Ile/Leu	Choi-S	Aaep	Found by K Sivonen group, Unpublished
12	Oscillarin 748	1/2	Pla-Cl	Ile/Leu	Choi-Pentose	Aaep	10.1007/s00203-014-1008-13
13	Oscillarin 816A	1/2	Pla	Ile/Leu	Choi-Pentose-SO_3Na	Aaep	Found by K Sivonen group, Unpublished
14	Aeruginoside 126A	1	D-Pla	D-Leu	Choi-Xyl	Aaep	10.1016/j.chembiol.2007.04.006
15	Aeruginosin 632	1	Hpla	Phe	Choi	Aaep	Found by K Sivonen group, Unpublished
16	Aeruginosin 828A	1	D-Pla	L-Cleu	L-Choi	Aaep	10.1016/j.hal.2014.07.003
17	Dysinosin D	1	MgA	Val	L-Choi-OH	Aaep	10.1021/np049968p
18	Oscillarin	1	D-Pla	D-Phe	L-Choi	Aaep	patentti WO1996011941 A1 / 10.1021/ja030669g
19	Aeruginosin KY608	1	L-Hpla-Cl	D-Ile	L-Choi-6-αOH	Agma	10.1016/j.phytol.2008.10.002
20	Aeruginosin KY642	1	L-Hpla-2Cl	D-Ile	L-Choi	Agma	10.1016/j.phytol.2008.10.002
21	Nostosin C	1	doHhpba	Ile	-	Argal	10.1021/np500106w
22	Nostosin E	1	doHhpba	Ile	-	Argol	10.1021/np500106w
23	Aeruginoside 126B	0/1	Pla	Ile/Leu	Choi-Xyl	Agma	10.1016/j.chembiol.2007.04.006
24	Aeruginosin	0/1	Hpla-Cl	Ile/Leu	Choi	Argal	10.1007/s00203-014-1008-10
25	Aeruginosin	0/1	Hpla	Ile/Leu	Choi-Pentose	Agma	10.1007/s00203-014-1008-11
26	Aeruginosin	0/1	Pla-Cl	Ile/Leu	Choi-Pentose	Agma	10.1007/s00203-014-1008-14
27	Aeruginosin	0/1	Hpla	Ile/Leu	Choi-Hex	Agma	10.3390/md13063892
28	Aeruginosin	0/1	Hpla-Cl	Ile/Leu	Choi-Pentose	Agma	10.1016/j.foodres.2012.12.028
29	Aeruginosin	0/1	Hpla	Ile/Leu	Choi-OH-Hex	Agma	10.3390/md13063892
30	Aeruginosin	0/1	Hpla	Ile/Leu	Choi-OH-HexA	Agma	10.3390/md13063892
31	Aeruginosin	0/1	Hpla	Ile/Leu	Choi-OH-Hex-BuA	Agma	10.3390/md13063892
32	Aeruginosin	0/1	Hpla	Ile/lLeu	Choi-OH-HexA-BuA	Agma	10.3390/md13063892
33	Aeruginosin	0/1	Pla	Ile/Leu	Choi-OH-HexA-HeA	Agma	10.3390/md13063892
34	Aeruginosin	0/1	Hpla	Ile/Leu	Choi-OH-Hex-HeA	Agma	10.3390/md13063892
35	Aeruginosin	0/1	Hpla	Ile/Leu	Choi-OH-HexA-OcA	Agma	10.3390/md13063892
36	Oscillarin 838A	0/1	Pla	Ile/Leu	Choi-Pentose-SO_3H	Agma-prenyl	Found by K Sivonen group, Unpublished
37	Aeruginosin K-139	0/1	Hpla	Ile/Leu	Choi	Argal	10.2323/jgam.53.17
38	Aeruginosin 602	0/1	Hpla	Ile/Leu	Choi	Argal	10.1016/j.peptides.2006.03.014
39	Aeruginosin 638	0/1	Pla	Ile/Leu	Choi-S	Agma	Found by K Sivonen group, Unpublished
40	Aeruginosin 670	0/1	Hpla-2Cl	Ile/Leu	Choi	Argal	10.1016/j.peptides.2006.03.014
41	Aeruginosin	0	Hpla-Cl	Phe	Choi	Argal	10.1016/j.foodres.2012.12.028
42	Aeruginosin	0	Hpla-Cl	MePhe	Choi	Argal	10.1016/j.foodres.2012.12.028
43	Aeruginosin	0	Hpla	Me(Ile/Leu)	Choi-OH-HexA-HeA	Agma	10.3390/md13063892
44	Aeruginosin	0	Hpla	Me(Ile/Leu)	Choi-OH-HexA-HepA	Agma	10.3390/md13063892
45	Aeruginosin 101	0	D-Hpla-2Cl	D-*allo*-Ile	L-Choi-S	Agma	10.1016/S0040-4020(99)00621-3
46	Aeruginosin 102-A	0	D-Hpla-S	D-Tyr	L-Choi	L-Argal	10.1016/0040-4020(96)00890-3
47	Aeruginosin 102-B	0	D-Hpla-S	D-Tyr	Choi	D-Argal	10.1016/0040-4020(96)00890-3
48	Aeruginosin 103-A	0	D-Hpla	D-Tyr	Choi	Aeap	10.1021/np980106w
49	Aeruginosin 205-A	0	L-Pla	D-Cleu	L-Choi-Xyl-S	Agma	10.1021/jo961902e / 10.1021/ol901702k
50	Aeruginosin 205-B	0	D-Pla	L-Cleu	L-Choi-Xyl-S	Agma	10.1021/jo961902e / 10.1021/ol901702k
51	Aeruginosin 298-A	0	D-Hpla	D-Leu	L-Choi	L-Argol	10.1016/S0040-4039(00)76848-1
52	Aeruginosin 298-B	0	D-Hpla	D-Leu	L-Choi-NH_2	-	10.1016/S0040-4020(99)00621-3
53	Aeruginosin 592	0	Pla	Phe	Choi	Agma	Found by K Sivonen group, Unpublished
54	Aeruginosin 686	0	Hpla-Cl	Tyr	Choi	Argal	10.1016/j.peptides.2006.03.014
55	Aeruginosin 865	0	Hpla	D-Leu	Choi-OH-ManA-HeA	Agma	10.1002/cbic.201300246 / doi.org/10.1016/j.toxic
56	Aeruginosin 89-A	0	D-Hpla-Cl-S	D-Leu	L-Choi	L-Argal	10.1016/S0040-4020(99)00621-3
57	Aeruginosin 89-B	0	D-Hpla-Cl-S	D-Leu	L-Choi	D-Argal	10.1016/S0040-4020(99)00621-3
58	Aeruginosin 98-A	0	D-Hpla-Cl	D-*allo*-Ile	L-Choi-S	Agma	10.1016/0040-4039(95)00396-T
59	Aeruginosin 98-B	0	D-Hpla	D-*allo*-Ile	L-Choi-S	Agma	10.1016/0040-4039(95)00396-T
60	Aeruginosin 98-C	0	D-Hpla-Br	D-*allo*-Ile	L-Choi-S	Agma	10.1016/S0040-4020(99)00621-3
61	Aeruginosin DA495A	0	D-Hpla	D-Phe	L-6-*epi*-Choi-NH_2	-	10.1021/np4006844
62	Aeruginosin DA495B	0	D-Hpla-Cl	D-Leu	L-Choi-NH_2	-	10.1021/np4006844
63	Aeruginosin DA511	0	D-Hpla	D-Tyr	L-6-*epi*-Choi-NH_2	-	10.1021/np4006844
64	Aeruginosin DA642A	0	L-Hpla-Cl	L-Phe	L-Choi	Agma	10.1021/np4006844

65	Aeruginosin DA642B	0	D-Hpla-Cl	L-Phe	L-Choi	Agma	10.1021/np4006844
66	Aeruginosin DA688	0	D-Hpla-Cl	D-Leu	L-Choi-SO_3H	Agma	10.1021/np4006844
67	Aeruginosin DA722	0	D-Hpla-2Cl	D-Leu	L-Choi-SO_3H	Agma	10.1021/np4006844
68	Aeruginosin EI461	0	L-Hpla	D-Leu	L-3a,7a-diepiChoi-NH_2	-	10.1021/ol0273250 / 10.1021/ol0273250
69	Aeruginosin GE642	0	D-Hpla-2Cl	D-Leu	L-Choi	Agma	10.1021/np3005612
70	Aeruginosin GE686	0	D-Hpla-Cl-Br	D-*allo*-Ile	L-Choi	Agma	10.1021/np3005612
71	Aeruginosin GE730	0	D-Hpla-2Br	D-*allo*-Ile	L-Choi	Agma	10.1021/np3005612
72	Aeruginosin GE766	0	D-Hpla-Cl-Br	D-*allo*-Ile	L-Choi-S	Agma	10.1021/np3005612
73	Aeruginosin GE810	0	D-Hpla-2Br	D-*allo*-Ile	L-Choi-S	Agma	10.1021/np3005612
74	Aeruginosin GH553	0	L-Hpla	D-Tyr	AcO-D-*diepi* Choi-NH_2	-	10.1021/np200909x
75	Aeruginosin IN608	0	D-Hpla-Cl	D-Leu	L-Choi	Agma	10.1021/np4001152
76	Aeruginosin IN652	0	D-Hpla-Br	D-Leu	L-Choi	Agma	10.1021/np4001152
77	Aeruginosin KB676	0	D-Hpla	D-Phe	L-6-epi-Choi	Agma-prenyl	10.3390/md13042347
78	Aeruginosin KT608A	0	L-Hpla	D-Phe	D-*diepi* Choi	Agma	10.1021/np200909x
79	Aeruginosin KT608B	0	D-Hpla	D-Phe	D-*diepi* Choi	Agma	10.1021/np200909x
80	Aeruginosin KT650	0	D-Hpla-Ac	D-Phe	D-*diepi* Choi	Agma	10.1021/np200909x
81	Aeruginosin LH606	0	D-Hpla-Cl	D-Leu	L-6α-Choi	Aap	10.1016/j.tet.2014.07.057
82	Aeruginosin LH650A	0	D-Hpla-Cl	D-Leu	L-6α-Choi	(2R,3S)-Amap	10.1016/j.tet.2014.07.057
83	Aeruginosin LH650B	0	D-Hpla-Cl	D-Leu	L-6α-Choi	(2S,3S)-Amap	10.1016/j.tet.2014.07.057
84	Aeruginosin NAL1	0	Bu	Tyr	Choi	Argal	10.1371/journal.pone.0073618
85	Aeruginosin NAL2	0	Hex	L-Tyr	L-Choi	Argal	10.1371/journal.pone.0073618
86	Aeruginosin NAL3	0	Oct	Tyr	Choi	Argal	10.1371/journal.pone.0073618
87	Aeruginosin NAL4	0	Oct	Tyr	Choi-P	Argal	10.1371/journal.pone.0073618
88	Aeruginosin NOL1	0	Ac	Tyr	Choi	Argol	10.1371/journal.pone.0073618
89	Aeruginosin NOL2	0	Bu	Tyr	Choi	Argol	10.1371/journal.pone.0073618
90	Aeruginosin NOL3	0	Hex	Tyr	Choi	Argol	10.1371/journal.pone.0073618
91	Aeruginosin NOL4	0	Oct	Tyr	Choi	Argol	10.1371/journal.pone.0073618
92	Aeruginosin NOL5	0	Hex	Tyr	Choi-P	Argol	10.1371/journal.pone.0073618
93	Aeruginosin NOL6	0	Oct	Tyr	Choi-P	Argol	10.1371/journal.pone.0073618
94	Aeruginosin NOL7	0	Dec	Tyr	Choi-P	Argol	10.1371/journal.pone.0073618
95	Aeruginosin TR642	0	Hpla	D-*allo*-Ile	Choi-Oac	Ddha	10.3390/md15120371
96	Aeruginosin 19	0	N/D	N/D	Choi	Arg	10.3390/md11010001
97	Aeruginosin 20	0	N/D	N/D	Choi	Argol	10.3390/md11010002
98	Aeruginosin 21	0	N/D	N/D	Choi	Argal	10.3390/md11010003
99	Aeruginosin 22	0	N/D	N/D	Choi	Agm	10.3390/md11010004
100	Antipain	0	-CO-N-L-Phe	L-Arg	L-Val	L-Argal	10.7164/antibiotics.25.267
101	Leupeptin	0	Ac	L-Leu	L-Leu	L-Argal	10.7164/antibiotics.22.283
102	Microcin SF608	0	L-Hpla	L-Phe	L-Choi	Agma	10.1016/S0040-4020(99)00597-9
103	Nostosin A	0	Hhpba	L-Ile	-	L-Argal	10.1021/np500106w
104	Nostosin B	0	Hhpba	L-Ile	-	Argol	10.1021/np500106w
105	Nostosin D	0	Hhpba	Val	-	Argal	10.1021/np500106w
106	Nostosin F	0	Hhpba	Val	-	Argol	10.1021/np500106w
107	Pseudoaeruginosin KT554	0	D-Hpla	D-Leu	L-Phe	Agma	10.1021/np200909x
108	Pseudoaeruginosin NS1	0	Hex	L-Tyr	L-mPro	Argal	10.1021/cb5004306
109	Pseudoaeruginosin NS2	0	Hex	L-Tyr	L-mPro	Argol	10.1021/cb5004306
110	Pseudospumigin A	0	Hpla	D-Hty	L-Ile	Argal	10.3389/fmicb.2017.01963
111	Pseudospumigin B	0	Hpla	Hty	Leu	Argal	10.3389/fmicb.2017.01963
112	Pseudospumigin C	0	Hpla	Hty	Val	Argal	10.3389/fmicb.2017.01963
113	Pseudospumigin D	0	Hpla	Hph	Ile	Argal	10.3389/fmicb.2017.01963
114	Pseudospumigin E	0	Hpla	Hph	Leu	Argal	10.3389/fmicb.2017.01963
115	Pseudospumigin F	0	Hpla	Hph	Val	Argal	10.3389/fmicb.2017.01963
116	Spumigin A	0	D-Hpla	D-Hty	L-MePro	L-Argol	10.1016/S0040-4039(97)01192-1
117	Spumigin B1	0	D-Hpla	D-Hty	L-MePro	L-Arg	10.1016/S0040-4039(97)01192-1
118	Spumigin B2	0	D-Hpla	D-Hty	L-mPro	D-Arg	10.1016/S0040-4039(97)01192-1
119	Spumigin C	0	D-Hpla	D-Hty	L-Pro	D,L-Arg	10.1016/S0040-4039(97)01192-1
120	Spumigin D	0	Hpla	Hty	Pro	Argol	10.1111/j.1365-2958.2009.06816.x
121	Spumigin E	0	D-Hpla	D-Hty	L-mPro	L-Argal	10.1111/j.1365-2958.2009.06816.x
122	Spumigin F	0	Hpla	Hty	Pro	Argal	10.1111/j.1365-2958.2009.06816.x
123	Spumigin G	0	Hpla	Hph	mPro	Argal	10.1111/j.1365-2958.2009.06816.x
124	Spumigin H	0	Hpla	Hph	Pro	Argal	10.1111/j.1365-2958.2009.06816.x
125	Spumigin I	0	Hpla	Leu	Pro	Argol	10.1111/j.1365-2958.2009.06816.x
126	Spumigin J	0	R-Hpla	D-Hty	mPro	Nme-D-Lys	10.1021/np300282a
127	Spumigin 1	0	Hpla-Ac	Hty	Pro	Arg	10.3390/md11010001
128	Spumigin 2	0	Hpla-Ac	Hty	mPro	Argal	10.3390/md11010001
129	Spumigin 3	0	Hpla-Ac	Hty	Pro	Argol	10.3390/md11010001
130	Spumigin 4	0	Hpla-Ac	Hty	Pro	Argal	10.3390/md11010001
131	Spumigin 12	0	Hpla	Tyr	Pro	Argal	10.3390/md11010001
132	Spumigin 13	0	Hpla	Hty	mPro	Agma	10.3390/md11010001
133	Spumigin 15	0	Hpla-Ac	Leu	Pro	Argal	10.3390/md11010001
134	Spumigin 17	0	Hpla	Hty	mPro-NH2	-	10.3390/md11010001
135	Spumigin 18	0	Hpla	Hty	Pro-OH	-	10.3390/md11010001
136	Spumigin 596	0	Hhpba	Tyr	Pro	Argal	10.1016/j.toxicon.2015.09.019
137	Spumigin 598	0	Hhpba	Tyr	Pro	Argol	10.1016/j.toxicon.2015.09.019
138	Spumigin 610	0	Hhpba	Tyr	mPro	Argal	10.1016/j.toxicon.2015.09.019
139	Spumigin 612	0	Hhpba	Tyr	mPro	Argol	10.1016/j.toxicon.2015.09.019

Table S2. Trypsin (animal origin) inhibition (IC_{50}) by aeruginosins, structurally similar compounds and structurally similar commercial trypsin inhibitors leupeptin and antipain.

No	Name	IC_{50} (μM)	DOI
1	Chlorodysinosin A	0.037	10.1021/ja0625834
2	Oscillarin	0.04	patent WO1996011941 A1 / 10.1021/ja030669g
3	Aeruginosin 205-A	0.09	10.1021/jo961902e / 10.1021/ol901702k
4	Aeruginosin 205-B	0.09	10.1021/jo961902e / 10.1021/ol901702k
5	Spumigin E	0.1	10.1111/j.1365-2958.2009.06816.x
6	Aeruginosin 828A	0.11	10.1016/j.hal.2014.07.003
7	Aeruginosin 102-A	0.27	10.1016/0040-4020(96)00890-3
8	Nostosin A	0.35	10.1021/np500106w
9	Antipain	0.43	10.7164/antibiotics.25.267
10	Leupeptin	0.5	10.7164/antibiotics.22.283
11	Aeruginosin 89-A	0.56	10.1016/S0040-4020(99)00621-3
12	Microcin SF608	0.82	10.1016/S0040-4020(99)00597-9
13	Aeruginosin 98-B	0.9	10.1016/0040-4039(95)00396-T
14	Aeruginosin 98-A	0.9	10.1016/0040-4039(95)00396-T
15	Aeruginosin KT608B	1.3	10.1021/np200909x
16	Aeruginosin 102-B	1.4	10.1016/0040-4020(96)00890-3
17	Banyaside A	1.5	10.1016/j.tet.2004.11.016
18	Aeruginosin 298-A	1.7	10.1016/S0040-4039(00)76848-1
19	Suomilide	1.8	10.1016/S0040-4039(97)01193-3
20	Aeruginosin KT608A	1.9	10.1021/np200909x
21	Aeruginosin KY642	2.2	10.1016/j.phytol.2008.10.002
22	Aeruginosin GE730	2.3	10.1021/np3005612
23	Aeruginosin KY608	2.8	10.1016/j.phytol.2008.10.002
24	Aeruginosin GE686	3.2	10.1021/np3005612
25	Aeruginosin TR642	3.8	10.3390/md15120371
26	Aeruginosin IN652	4.1	10.1021/np4001152
27	Aeruginosin 101	4.2	10.1016/S0040-4020(99)00621-3
28	Aeruginosin IN608	4.3	10.1021/np4001152
29	Aeruginosin 98-C	5.3	10.1016/S0040-4020(99)00621-3
30	Pseudospumigin A	6.5	10.3389/fmicb.2017.01963
31	Aeruginosin DA722	7.3	10.1021/np4006844
32	Aeruginosin GE642	8.5	10.1021/np3005612
33	Aeruginosin 89-B	9.2	10.1016/S0040-4020(99)00621-3
34	Aeruginosin DA688	9.5	10.1021/np4006844
35	Aeruginosin GE766	12.2	10.1021/np3005612
36	Aeruginosin GE810	18.2	10.1021/np3005612
37	Aeruginosin LH606	18.5	10.1016/j.tet.2014.07.057
38	Aeruginosin DA642B	19.0	10.1021/np4006844
39	Aeruginosin KT650	19.9	10.1021/np200909x
40	Spumigin A	26.3	10.1016/S0040-4039(97)01192-1
41	Aeruginosin DA642A	30.8	10.1021/np4006844
42	Spumigin B1	33.1	10.1016/S0040-4039(97)01192-1
43	Aeruginosin LH650B	35.3	10.1016/j.tet.2014.07.057
44	Aeruginosin LH650A	37.9	10.1016/j.tet.2014.07.057
45	Aeruginosin KB676	40.0	10.3390/md13042347
46	Aeruginosin GH553	45.5	10.1021/np200909x
47	Pseudoaeruginosin KT554	45.5	10.1021/np200909x
48	Nostosin B	55	10.1021/np500106w
49	Aeruginosin 103-A	75	10.1021/np980106w
50	Aeruginoside 126A	94	10.1016/j.chembiol.2007.04.006
51	Aeruginosin DA495A	>45.5	10.1021/np4006844
52	Aeruginosin DA511	>45.5	10.1021/np4006844
53	Aeruginosin EI461	>>100	10.1021/ol0273250 / 10.1021/ol0273250
54	Aeruginosin 298-B	>220	10.1016/S0040-4020(99)00621-3

Table S3. Parameters for NMR data collection.

Experiment	Complex points in (t_1) t_2	Acquisition time in (t_1) t_2 [s]	Number of scans
^{1}H	16k	1.28	16
^{13}C	48k	1.0	8k
2D TOCSY	(256) 2048	(0.0231) 0.183	8
2D DQF-COSY	(256) 1024	(0.0246) 0.098	16
2D ^{13}C HSQC	(200) 1024	(0.005) 0.0799	16
2D ^{13}C HMBC	(512) 1024	(0.0115) 0.1278	32
2D ^{15}N HSQC	(128) 1024	(0.0128) 0.0799	80

Table S4. Annotation of product ions from protonated, desulfated (−SO_3) varlaxin variants 10465, 1022A , 912, 888B, 778, 764 and 754 from *Nostoc* UHCC strains 0870, 0840 and 0758. Mgs = 2-O-methylglyceric acid 3-O-sulfate, MgA = 2-O-methylglyceric acid, Choi = 2-carboxy-6-octahydroindole, Agma = 4-amidinobutylamide, Aaep = 1-amidino-3-(2-aminoethyl)-3-pyrroline, Hpaa = 2-(4-hydroxyphenyl)acetic acid. Δ = difference in parts per million (ppm) between calculated and experimental *m/z* values.

			UHCC 0870		UHCC 0840		UHCC 0758									
			Varlaxin 1046A–SO_3		Varlaxin 1022A–SO_3		Varlaxin 912A–SO_3		Varlaxin 888B–SO_3		Varlaxin 778–SO_3		Varlaxin 764–SO_3		Varlaxin 754–SO_3	
			X2 = Ile, X4 = Aaep, A = 2		X2 = Ile, X4 = Agma, A = 2		X2 = Ile, X4 = Aaep, A = 1		X2 = Ile, X4 = Agma, A = 1		X2 = Ile, X4 = Aaep, A = 0		X2 = Val, X4 = Aaep, A = 0		X2 = Ile, X4 = Agma, A = 0	
	Ion assignment		Calc	Δ	Calc	Δ	Calc	Δ	Calc	Δ	Calc	Δ	Calc	Δ	Calc	Δ
No	Ion assignment without NL	Neutral loss (NL)	*m/z*	(ppm)	*m/z*	(ppm)	*m/z*	(ppm)	*m/z*	(ppm)	*m/z*	(ppm)	*m/z*	(ppm)	*m/z*	(ppm)
1	$[M+H]^+$	-	967.46589	-3.1	943.46589	-1.6	833.42911	-1.6	809.42911	-1.7	699.39233	-2.1	685.37668	-1.6	675.39233	-2.3
2	$[M+H]^+$	H_2O	949.45533	-0.9	925.45533	-12.3	815.41855	-3.1	791.41855	-6.9	681.38177	-1.9	667.36612	8.4	657.38177	-9.5
3	$[M+H]^+$	CH_2O	937.45533	-8.5	913.45533	-4.6	803.41855	-2.2	779.41855	-8.6	669.38177	-3.5	655.36612	-6.1	645.38177	-1.3
4	$[M+H]^+$	HN=C=NH	925.44409	-11.6	901.44409	-5.9	791.40731	-0.7	767.40731	-	657.37053	-1.9	643.35488	11.5	633.37053	-3.6
5	$[M+H]^+$	MgA	865.43240	-0.6	841.43240	9.0	731.39742	-1.6	707.39562	-	597.36064	-7.2	583.34499	-	573.36064	-8.9
6	$[M+H]^+$	MgA, H_2O	847.42363	-	823.42363	-	713.38685	-2.5	689.38685	-	579.35007	-3.0	565.33442	-	555.35007	-6.5
7	$[M+H]^+$	Hpaa	833.42911	-	809.42911	8.1	699.39233	-4.4	675.39233	-	-	-	-	-	-	-
8	$[M+H]^+$	Hpaa, H_2O	815.41855	-8.7	791.41855	-	681.38177	-5.3	657.38177	-	-	-	-	-	-	-
9	$[M+H]^+$	MgA-X2	752.35013	-2.1	728.35013	-0.9	618.31335	-1.6	594.31335	-2.5	484.27658	-2.1	484.27658	-2.7	460.27658	2.3
10	$[M+H]^+$	MgA-X2, NH_3	735.32358	3.0	711.32358	-1.3	601.28681	-1.1	577.28680	-0.6	467.25003	-3.4	467.25003	4.5	443.25003	-7.4
11	$[M+H]^+$	MgA-X2, HN=C=NH	710.32834	-4.9	686.32834	-3.0	576.29156	-0.4	552.29156	6.5	442.25478	-1.2	442.25478	-2.8	418.25478	-6.5
12	$[M+H]^+$	MgA-X2, HN=C=NH, H_2O	692.31777	-	668.31777	4.5	558.28099	2.8	534.28099	-10.2	424.24421	-1.1	424.24421	-11.5	400.24421	-
13	$[M+H]^+$	MgA-X2, HN=C=NH, $2xH_2O$	674.30721	-	650.30721	-	540.27043	8.0	516.27043	-	406.23365	-0.7	406.23365	-	382.23365	-9.9
14	$[M+H]^+$	MgA, Hpaa, 2 x CH_2O from Glc	671.37629	-1.3	647.37629	-	537.33951	-2.3	513.33951	0.5	-	-	-	-	-	-
15	$[M+H]^{\cdot+}$	A x Hpaa, $\cdot C_4H_5$, HN=C=NH	600.30011	1.2	576.30011	3.0	600.30011	-7.8	576.30011	-	600.30011	-	600.30011	-	576.30011	-
16	Choi(Glc-AxHpaa) + H^+	CO	570.23337	0.0	570.23337	-1.3	436.19659	0.8	436.19659	-6.5	302.15981	-1.9	302.15981	-3.5	302.15981	2.4
17	MgA-X2-Choi-X4 + H^+	-	537.33951	-2.5	513.33951	1.4	537.33951	-2.3	513.33951	0.5	537.33951	-2.2	523.32386	-5.0	513.33951	-3.4
18	MgA-X2-Choi-X4 + H^+	H_2O	519.32894	-2.9	495.32894	-2.4	519.32894	-3.3	495.32894	3.5	519.32894	-2.1	505.31329	3.7	495.32894	-2.8
19	MgA-X2-Choi-X4 + H^+	CH_2O	507.32894	3.0	483.32894	4.6	507.32894	-4.5	483.32894	0.4	507.32894	-2.5	493.31329	-	483.32894	-3.3
20	MgA-X2-Choi-X4 + H^+	HN=C=NH	495.31771	0.1	471.31771	-12.6	495.31771	-3.1	471.31771	-3.3	495.31771	-1.7	481.30206	-7.9	471.31771	-1.0
21	MgA-X2-Choi-X4 + H^+	CH_2O, H_2O	489.31838	-	465.31838	-	489.31838	-0.9	465.31838	-	489.31838	-4.1	475.30273	-	465.31838	2.7
22	MgA-X2-Choi-X4 + H^+	HN=C=NH, H_2O	477.30715	0.0	453.30715	-8.2	477.30715	-1.5	453.30715	-	477.30715	-3.1	463.29150	-10.3	453.30715	7.9
23	Choi(Glc)-X4 + H^+	H_2O	466.26601	-	442.26601	-	466.26601	-3.1	442.26601	-	-	-	-	-	442.26601	-4.4
24	MgA-X2-Choi-X4 + H^+	HN=C=NH, CH_2O	465.30715	2.8	441.30715	-	465.30715	-	441.30715	-	465.30715	-5.4	451.29150	-0.1	441.30715	-
25	Glc-AxHpaa + H^+	-	431.13366	-6.1	431.13366	0.9	297.09688	-0.1	297.09688	-	163.06010	-	163.06010	-	163.06010	-
26	Glc-AxHpaa + H^+	H_2O	413.12309	-6.9	413.12309	-0.6	279.08631	-0.6	279.08631	-1.6	-	-	-	-	-	-
27	Choi(Glc)-X4 + H^+	$4xCH_2O$ from Glc	364.23432	-	340.23432	-	364.23432	-12.8	340.23432	-2.9	364.23432	-1.3	364.23432	10.5	340.23432	1.9
28	Choi(Glc)-X4 + H^+	$4xCH_2O$ from Glc, NH_3	347.20777	9.7	323.20777	5.8	347.20777	4.0	323.20777	-0.4	347.20777	-2.1	347.20777	-6.7	323.20777	-5.3
29	Choi-X4 + H^+	-	322.22375	-4.0	298.22375	-6.7	322.22375	-1.9	298.22375	-1.0	322.22375	-5.9	322.22375	-2.2	298.22375	-4.0
30	Choi-X4 + H^+	NH_3	305.19720	12.0	281.19720	-2.0	305.19720	1.1	281.19720	-0.9	305.19720	-1.8	305.19720	-3.1	281.19720	-2.7
31	Choi-X4 + H^+	H_2O	304.21319	-3.7	280.21319	0.2	304.21319	-2.1	280.21319	3.8	304.21319	-4.7	304.21319	-3.7	280.21319	-2.6
32	Choi-X4 + H^+	H_2O, NH_3	287.18664	-4.1	263.18664	-0.3	287.18664	-2.1	263.18664	0.8	287.18664	-2.4	287.18664	-4.5	263.18664	-1.1
33	Choi-X4 + H^+	HN=C=NH	280.20195	-6.1	256.20195	-7.4	280.20195	-4.6	256.20195	0.8	280.20195	-2.5	280.20195	-3.9	256.20195	0.4
34	CO-Choi-X4 + H^+	HN=C=NH, $2xH_2O$, 2H	270.16009	-0.1	246.16009	-0.2	270.16009	-6.8	246.16009	3.5	270.16009	-3.8	270.16009	-	246.16009	0.6
35	Choi-X4 + H^+	HN=C=NH, H_2O	262.19139	-2.1	238.19139	-3.5	262.19139	-2.1	238.19139	-3.5	262.19139	-2.4	262.19139	-3.2	238.19139	-3.1
36	Choi-X4 + H^+	$H_2NC(=NH)NH_2$, H_2O	245.16484	-8.5	221.16484	0.5	245.16484	-2.0	221.16484	-0.9	245.16484	-4.4	245.16484	-9.7	221.16484	-1.8
37	Choi-X4 + H^+	HN=C=NH, $2xH_2O$	244.18082	8.3	220.18082	-1.7	244.18082	-3.6	220.18082	-5.3	244.18082	-1.9	244.18082	-	220.18082	-2.1
38	Choi-X4 + H^+	HN=C=NH, $2xH_2O$, 2H	242.16517	-3.4	218.16517	-0.1	242.16517	-4.6	218.16517	2.2	242.16517	1.2	242.16517	-	218.16517	1.7
39	X2-Choi + H^+	$2xH_2O$, NH_3	228.13829	-5.4	228.13829	-	228.13829	-1.5	228.13829	-	228.13829	-1.5	214.12264	-	228.13829	-
40	X2-Choi + H^+	CO, $2xH_2O$	217.16993	-4.1	217.16993	-	217.16993	-0.4	217.16993	-	217.16993	-3.1	203.15428	-	217.16993	-0.8
41	$C_{10}H_{16}N_3O_2^+$ (from CO-Choi-X4)	-	-	-	210.12370	-1.7	-	-	210.12370	-1.2	-	-	-	-	210.12370	-0.2
42	HC_2=CHCO-X4 + H^+	-	209.13969	-9.3	185.13969	6.3	209.13969	-2.1	185.13969	-	209.13969	-0.7	209.13969	-	185.13969	-
43	HN=CHCO-X4 + H^+	NH_3	193.10839	5.0	169.10839	-	193.10839	0.3	169.10839	-2.0	193.10839	1.3	193.10839	-1.8	169.10839	-9.7
44	CH_2CHCO-X4	NH_3	192.11314	5.3	168.11314	-	192.11314	-1.0	168.11314	-	192.11314	0.1	192.11314	1.6	168.11314	-
45	$C_{10}H_{14}N_3O^+$ (from X2-Choi-X4)	-	192.11314	5.3	192.11314	1.1	192.11314	-1.0	192.11314	1.1	192.11314	0.1	192.11314	1.6	192.11314	1.6
46	Choi-X4 + H^+	C_6H_8, $2xH_2O$, NH_3	189.11347	-	165.11347	-3.1	189.11347	-	165.11347	1.1	-	-	189.11347	-1.7	165.11347	-5.0
47	MgA-X2 + H^+	CO	188.12812	0.2	188.12812	-0.9	188.12812	-0.4	188.12812	-0.4	188.12812	-0.9	174.11247	-1.8	188.12812	0.2
48	X2-Choi + H^+	C_4H_8, CO, H_2O	179.11789	12.6	179.11789	-3.0	179.11789	10.9	179.11789	-10.8	179.11789	-	179.11789	-	179.11789	-0.2
49	OC=X4 + H^+	-	181.10839	-14.0	157.10839	8.7	181.10839	-0.2	157.10839	-7.3	181.10839	-1.9	181.10839	11.4	157.10839	3.6
50	Choi + 2H + H^+	-	170.11756	-	170.11756	1.7	170.11756	-1.8	170.11756	6.4	170.11756	-0.1	170.11756	-2.4	170.11756	-0.6
51	$C_7H_{10}N_3O^+$ (from X2-Choi-X4)	-	-	-	152.08184	1.4	-	-	152.08184	2.7	-	-	-	-	152.08184	2.7
52	CO-X4 + H^+	H_2O	165.11347	-	141.11347	1.3	165.11347	-3.1	141.11347	-	165.11347	-	165.11347	-2.5	141.11347	-8.6
53	X4 + H^+	-	155.12912	2.8	131.12912	-8.9	155.12912	1.5	131.12912	-8.2	155.12912	-0.5	155.12912	5.4	131.12912	-4.3
54	Choi-NH_2 + H^+	$2xH_2O$	149.10732	-	149.10732	2.2	149.10732	6.2	149.10732	6.2	149.10732	-	149.10732	-	149.10732	2.2
55	Glc	2 x H_2O	145.04954	-5.4	145.04954	-0.6	145.04954	0.1	145.04954	6.3	145.04954	-2.0	145.04954	-	145.04954	-
56	Choi + H^+	CO	140.10699	0.4	140.10699	2.6	140.10699	1.9	140.10699	4.7	140.10699	1.1	140.10699	-0.3	140.10699	1.1
57	X4 + H^+	NH_3	138.10257	4.2	114.10257	6.8	138.10257	-2.3	114.10257	3.3	138.10257	-8.1	138.10257	-6.7	114.10257	2.5
58	MgA-X2 + 2H + H^+	C_4H_8, CH_2O	132.06552	0.2	132.06552	10.1	132.06552	-2.0	132.06552	1.7	132.06552	-0.5	118.04987	-	132.06552	7.0
59	Glc + H^+	3 x H_2O	127.03897	-7.2	127.03897	3.0	127.03897	1.4	127.03897	7.7	127.03897	-0.9	127.03897	-6.5	127.03897	-0.2
60	Choi + 2H + H^+	CO, H_2O	124.11208	-0.2	124.11208	-5.9	124.11208	-1.9	124.11208	-	124.11208	1.4	124.11208	-5.1	124.11208	3.0
61	Choi + H^+	CO, H_2O	122.09643	1.8	122.09643	0.2	122.09643	1.0	122.09643	2.6	122.09643	1.0	122.09643	-0.7	122.09643	1.0
62	X4 + H^+	$2xNH_2$	121.07602	-	97.07602	-3.8	121.07602	-1.4	97.07602	-5.9	121.07602	-1.4	121.07602	-12.1	97.07602	-5.9
63	MgA-NH_2 + H^+	-	120.06552	-0.6	120.06552	2.7	120.06552	1.9	120.06552	5.2	120.06552	1.1	120.06552	-	120.06552	1.1
64	X4 + H^+	HN=C=NH	113.10732	4.7	89.10732	8.2	113.10732	-0.6	89.10732	-0.8	113.10732	2.9	113.10732	-	89.10732	5.9
65	$C_7H_7O^+$	-	107.04914	2.9	107.04914	1.0	107.04914	1.0	107.04914	0.1	107.04914	-	107.04914	-	107.04914	-
66	$C_8H_9^+$	-	105.06988	8.3	105.06988	-6.0	105.06988	1.6	105.06988	-4.1	105.06988	-0.3	105.06988	-5.0	105.06988	1.6
67	X4 + H^+	$H_2NC(=NH)NH_2$	96.08078	4.9	72.08078	-4.6	96.08078	1.8	72.08078	-1.8	96.08078	-0.3	96.08078	2.8	72.08078	-6.0
68	$C_6H_8N^+$	-	94.06513	8.7	94.06513	-	94.06513	1.3	94.06513	1.3	94.06513	0.2	94.06513	3.4	94.06513	8.7
69	X2 + H^+	CO	86.09643	-4.4	86.09643	3.7	86.09643	-2.1	86.09643	-2.1	86.09643	-3.3	72.08078	3.7	86.09643	-4.4
70	$C_5H_8N^+$	-	82.06513	-4.6	82.06513	6.3	82.06513	-2.2	82.06513	-2.2	82.06513	-2.2	82.06513	-4.6	82.06513	-3.4
71	$C_5H_6N^+$	-	80.04948	-	80.04948	4.6	80.04948	4.6	80.04948	-0.4	80.04948	-2.9	80.04948	-10.4	80.04948	-4.1
72	$C_6H_7^+$	-	79.05423	-13.7	79.05423	-3.5	79.05423	-3.5	79.05423	-1.0	79.05423	-4.8	79.05423	-2.3	79.05423	1.5
73	$C_6H_5^+$	-	77.03858	-10.8	77.03858	-5.6	77.03858	-0.4	77.03858	3.5	77.03858	-9.5	77.03858	-	77.03858	-5.6
74	MgA + H^+	CO	75.04406	-12.1	75.04406	-2.8	75.04406	-1.5	75.04406	-4.1	75.04406	-5.5	75.04406	-1.5	75.04406	-4.1
75	$C_4H_{10}N^+$ (from Agma)	-	-	-	72.08078	-4.6	-	-	72.08078	-1.8	-	-	-	-	72.08078	-6.0
76	$C_4H_8N^+$ (e.g. from Agma)	-	-	-	70.06513	-	-	-	70.06513	-5.4	70.06513	3.1	70.06513	-	70.06513	4.6
77	$C_5H_9^+$ (e.g. from Ile)	-	69.06988	-6.2	69.06988	-4.8	69.06988	-7.7	69.06988	2.5	69.06988	-4.8	69.06988	-	69.06988	-1.9
78	$C_5H_7^+$ (e.g. from Agma)	-	-	-	67.05423	-	67.05423	-	67.05423	-10.1	67.05423	-4.2	67.05423	-4.2	67.05423	-2.7

Table S5. NMR data of Varlaxins 1022A and 1046A in DMSO-d_6.

	Varlaxin 1022A				Varlaxin 1046A			
	trans (3/5)		*cis* (2/5)		*trans* (3/5)		*cis* (2/5)	
Subunit	**$\delta_{C/N}$**	**δ_H**	**$\delta_{C/N}$**	**δ_H**	**$\delta_{C/N}$**	**δ_H**	**$\delta_{C/N}$**	**δ_H**
Mgs, 1	169.0	-	169.1	-	169.0	-	169.2	-
2	80.2	3.92	79.9	3.90	80.3	3.91	79.8	3.90
2-OCH_3	57.1	3.22	57.0	3.22	57.1	3.23	56.9	3.21
3	66.5	3.73	65.6	3.81	66.2	3.73	65.6	3.79
3'		3.92		3.94		3.95		3.91
Ile, 1	169.2	-	169.3	-	169.2	-	169.3	-
2	54.2	4.35	53.4	4.10	54.1	4.36	53.4	4.05
3	36.7	1.65	35.6	1.83	36.8	1.65	35.6	1.84
4	24.0	1.08	23.6	0.96	24.2	1.07	23.9	0.91
4'		1.50		1.50		1.50		1.49
5	11.0	0.82	10.8	0.78	11.0	0.82	10.8	0.78
6	15.1	0.81	15.4	0.78	15.0	0.81	15.3	0.78
2-NH	120.0	7.77	121.0	7.81	119.0	7.62	121.7	7.90
Choi, 1	171.3	-	172.0	-	171.2	-	172.1	-
2	59.7	4.24	59.6	4.61	59.7	4.23	59.5	4.61
3	30.2	2.06	33.3	2.25	30.3	2.05	33.3	2.26
3'		1.86		1.87		1.82		1.86
3a	35.9	2.24	34.2	2.12	35.9	2.26	34.2	2.13
4	19.6	1.93	19.6	1.91	19.5	1.93	19.7	1.93
4'		1.45		1.45		1.45		1.45
5	24.1	1.56	24.8	1.47	24.1	1.56	24.8	1.47
5'		1.43				1.43		
6	72.9	3.77	72.5	3.76	72.8	3.76	72.5	3.75
7	30.2	2.30	29.3	1.93	30.1	2.29	29.3	1.92
7'		1.61		1.62		1.61		1.59
7a	54.3	4.00	53.4	4.40	54.3	4.00	53.4	4.39
Agma/Aaep,								
1	38.0	3.03	38.3	3.00	36.5	3.13	37.2	3.14
1'		3.07		3.24		3.29		3.38
2	26.2	1.42	26.0	1.48	28.3	2.26	28.0	2.31
2'						2.29		2.34
3	25.6	1.47	25.9	1.53	136.1	-	135.9	-
4	40.4	3.09	40.5	3.09	54.1	4.11	54.1	4.13
5	156.7	-	156.7	-	154.1	-	154.1	-
6	-	-	-	-	55.3	4.14	55.5	4.16
7	-	-	-	-	119.0	5.64	119.6	5.69
1-NH	113.7	7.62	116.1	8.05	112.7	7.70	114.2	8.10
4-NH	85.5	7.58	85.5	7.58	-	-	-	-
5-NH					77.1	7.23	77.1	7.23
5-NH2					77.1	7.23	77.1	7.23
Glc, 1	95.1	5.01	94.5	4.91	95.1	5.02	94.6	4.91

2	73.3	4.50	73.4	4.42	73.3	4.50	73.4	4.42
3	70.2	3.65	70.0	3.69	70.2	3.66	70.0	3.69
4	70.4	3.17	70.4	3.16	70.3	3.18	70.3	3.16
5	70.2	3.67	70.0	3.71	70.2	3.66	70.0	3.71
6	64.0	4.01	63.8	4.03	64.0	4.01	63.8	4.03
6'		4.37		4.33		4.36		4.33
3-OH	-	5.21	-	5.25	-	5.21	-	5.25
4-OH	-	5.39	-	5.34	-	5.39	-	5.34
Hpaa1, 1	171.3	-	171.9	-	171.3	-	171.9	-
2	39.1	3.59	38.6	3.60	39.1	3.59	38.6	3.60
2'		3.59		3.91				3.91
3	124.2	-	124.2	-	124.2	-	124.5	-
4,4'	130.3	7.06	130.7	7.12	130.3	7.07	130.7	7.12
5,5'	115.0	6.67	114.8	6.66	115.0	6.67	114.8	6.66
6	156.0	-	156.0	-	156.0	-	156.0	-
6-OH		9.23		9.21		9.23		9.21
Hpaa2, 1	171.3	-	171.4	-	171.3	-	171.3	-
2	39.3	3.52	39.3	3.51	39.2	3.52	39.2	3.52
2'		3.52		3.51				3.52
3	124.2	-	124.2	-	124.2	-	124.2	-
4,4'	130.1	7.03	130.1	7.03	130.1	7.03	130.1	7.03
5,5'	115.0	6.68	115.0	6.68	115.0	6.68	115.0	6.68
6	156.2	-	156.2	-	156.1	-	156.1	-
6-OH		9.26		9.26		9.25		9.25

Table S6. DQF-COSY and ^{1}H-^{13}C HMBC correlations of Varlaxins 1022A and 1046A in DMSO-d_6.

	Varlaxin 1022A				Varlaxin 1046A			
	trans (3/5)		*cis* (2/5)		*trans* (3/5)		*cis* (2/5)	
Subunit	**DQF-COSY**	**HMBC**	**DQF-COSY**	**HMBC**	**DQF-COSY**	**HMBC**	**DQF-COSY**	**HMBC**
Mgs, 1								
2		1, 3, 2-OCH_3		1, 3, 2-OCH_3		1, 3, 2-OCH_3		1, 3, 2-OCH_3
2-OCH_3		2		2		2		2
3		1, 2		1, 2		1, 2		1, 2
3'		2-OCH_3		2-OCH_3		1		2-OCH_3
Ile, 1								
2	3, 2-NH	1, 3, 4, 6, Mgs-1	3, 2-NH	1, 3, 4, 6, Mgs-1	3, 2-NH	1, 3, 4, 6	3, 2-NH	1, 3, 6
3	2, 4, 6		2, 4, 6		2, 4, 6		2, 4, 6	
4	3, 4', 5	3, 5, 6	3, 4', 5	3, 5, 6	3,4', 5	3, 5, 6	3,4', 5	3, 6
4'	4, 5		4, 5		4, 5		4, 5	
5	4	2, 3, 4	4	2, 3, 4	4, 4'	2, 3, 4	4, 4'	2, 3, 4
6	3	2, 3, 4	3	2, 3, 4	3	2, 3, 4	3	2, 3, 4
2-NH	2	Mgs-1	2	Mgs-1	2	Mgs-1	2	Mgs-1
Choi, 1								
2	3, 3'	1, 3/7	3, 3'	3	3, 3'	1, 3	3, 3'	3
3	2, 3', 3a	7a	2, 3', 3a		2, 3', 3a	7a	2, 3a	
3'	2, 3, 3a	1, 2	2, 3a	1, 2	2, 3, 3a	1	2, 3, 3a	1
3a	3, 4, 7a	3/7, 5, 7a	3, 7a		3, 3', 4, 7a	3, 7a	3, 3', 4, 7a	
4	3a, 4'		3a		3a, 4', 5'		3a, 4'/5	
4'	4		4		4		4	
5	4, 5', 6		4, 6		5', 6		6	
5'	4, 5'				4, 5			
6	5, 5', 7, 7'		5, 7, 7'		5, 5', 7, 7'		5, 7, 7'	
7	6, 7', 7a		6, 7', 7a		6, 7', 7a		6, 7', 7a	
7'	6, 7, 7a		6, 7', 7a		7', 7a		7', 7a	
7a	3a, 7, 7'	2, 3, 7	3a, 7, 7'	3	3a/7, 7'	2, 3	3a, 7, 7'	
Agma/Aaep, 1	2, 1-NH	3, Choi-1	1', 2, 1-NH	Choi-1	2/2', 1-NH	2, 3, Choi-1	1', 2/2', 1-NH	2, 3, Choi-1
1'	2, 1-NH	Choi-1	1, 2, 1-NH	Choi-1	1, 2/2', 1-NH	2, 3, Choi-1	1, 2/2', 1-NH	2, 3, Choi-1
2		1, 3, 4	1, 1'		1, 1'	1, 3, 6, 7	1, 1'	3, 6, 7
2'					1, 1'	1, 3, 6, 7	1, 1'	3
3	4		4	3, 4				
4	3		3			3, 7		3, 7
5								
6					7	3, 7		3, 7
7					6	2, 3, 4, 6	6	6
1-NH	1, 1'	1, Choi-1	1, 1'	Choi-1	1	Choi-1	1, 1'	Choi-1
4-NH	4		4					
5-NH								
5-NH_2								
Glc, 1	2	3/4/5, Choi-6	2	3/4/5, Choi-6	2	3/4/5, Choi-6	2	3/4/5
2	1, 3	3/4/5	1, 3	3/4/5	1, 3	3/4/5, Hpaa1/2-1	1, 3	
3	2, 4, 3-OH	2, 3/4/5	2, 4, 3-OH	3/4/5, 6	2, 4, 3-OH	3/4/5	2, 4, 3-OH	
4	3/5, 4-OH	3/4/5	3, 5, 4-OH	3/4/5	3/5, 4-OH	3/4/5	3/5, 4-OH	3/4/5
5	4, 6		4, 6	3/4/5	4, 6	3/4/5	4, 6	
6	5, 6'	3/4/5, Hpaa1/2-1	5, 6'	3/4/5, Hpaa1/2-1	5, 6'	Hpaa1/2-1	5, 6'	Hpaa2-1
6'	6	Hpaa1/2-1	6	Hpaa2-1	6	Hpaa1/2-1	6	Hpaa2-1
3-OH	3	2, 3/4/5	3		3	3/4/5	3	3/4/5
4-OH	4	3/4/5	4	3/4/5	4	3/4/5	4	
Hpaa1, 1								
2		1, 3, 4		1		1, 3, 4		1, 3, 4
2'		3, 4		1, 3, 4, Glc-6				1
3								
4,4'	5, 5'	2, 4, 5, 6	5, 5'	2, 4, 5, 6	5, 5'	2, 4, 5, 6	5, 5'	2, 4, 6
5,5'	4, 4'	3, 5, 6	4, 4'	3, 5, 6	4, 4'	3, 5, 6	4, 4'	3, 5, 6
6								
6-OH				5				
Hpaa2, 1								
2		1, 3, 4		1, 3, 4		1, 3, 4		1, 3, 4
2'		3, 4		3, 4		1, 3, 4		1, 3, 4
3								
4,4'	5, 5'	2, 4, 5, 6	5, 5'	2, 4, 5, 6	5, 5'	2, 4, 5, 6	5, 5'	2, 4, 5, 6
5,5'	4, 4'	3, 5, 6	4, 4'	3, 5, 6	4, 4'	3, 5, 6	4, 4'	3, 5, 6
6								
6-OH		5		5				

= overlapping correlations x/x/x = overlapping correlations

Table S7. The substrate specificity of aeruginosin NRPS adenylation domains.

Protein	Strain	Residue								Proposed substrate
		235	**236**	**239**	**278**	**299**	**301**	**322**	**330**	
aerB	*Microcystis aeruginosa* NIES-98	D	A	F	F	L	G	V	T	Ile
	Nodularia sphaerocarpa UHCC 0038	D	A	F	F	L	G	V	T	Ile
	Nostoc sp. UHCC 0870	D	A	L	W	M	G	G	V	*allo*-Ile
	Hormoscilla sp. GM7CHS1pb	D	A	L	F	I	G	I	I	Val
	Nostoc sp. UIC10630	D	A	W	F	L	G	N	V	Leu
	Microcystis aeruginosa PCC 7806	D	A	S	T	I	A	A	V	Tyr
	Microcystis aeruginosa NIES-843	D	A	S	T	I	A	A	V	Tyr
	Planktothrix agardhii CYA 126-8	D	A	W	F	L	G	N	V	Leu
	Nodularia spumigena CCY 9414	D	A	S	T	I	A	A	v	Tyr
aerG	NIES-98	D	V	H	I	I	A	Y	I	Choi
	UHCC 0038	D	V	H	F	I	C	L	L	Choi
	UHCC 0870	D	V	H	F	I	C	-	-	Choi
	GM7CHS1pb	D	V	H	I	I	C	F	L	Choi
	UIC10630	D	V	H	F	I	C	-	-	Choi
	PCC 7806	D	V	H	I	I	A	Y	I	Choi
	NIES-843	D	V	H	I	I	A	F	I	Choi
	CYA 126-8	D	V	H	I	I	A	F	L	Choi
	CCY 9414	D	V	H	I	C	A	F	L	Choi
aerM	PCC 7806	D	V	E	N	A	G	V	V	Arg
	NIES-843	D	V	E	N	I	G	A	I	Arg
	CCY 9414	D	V	E	N	V	G	A	I	Arg

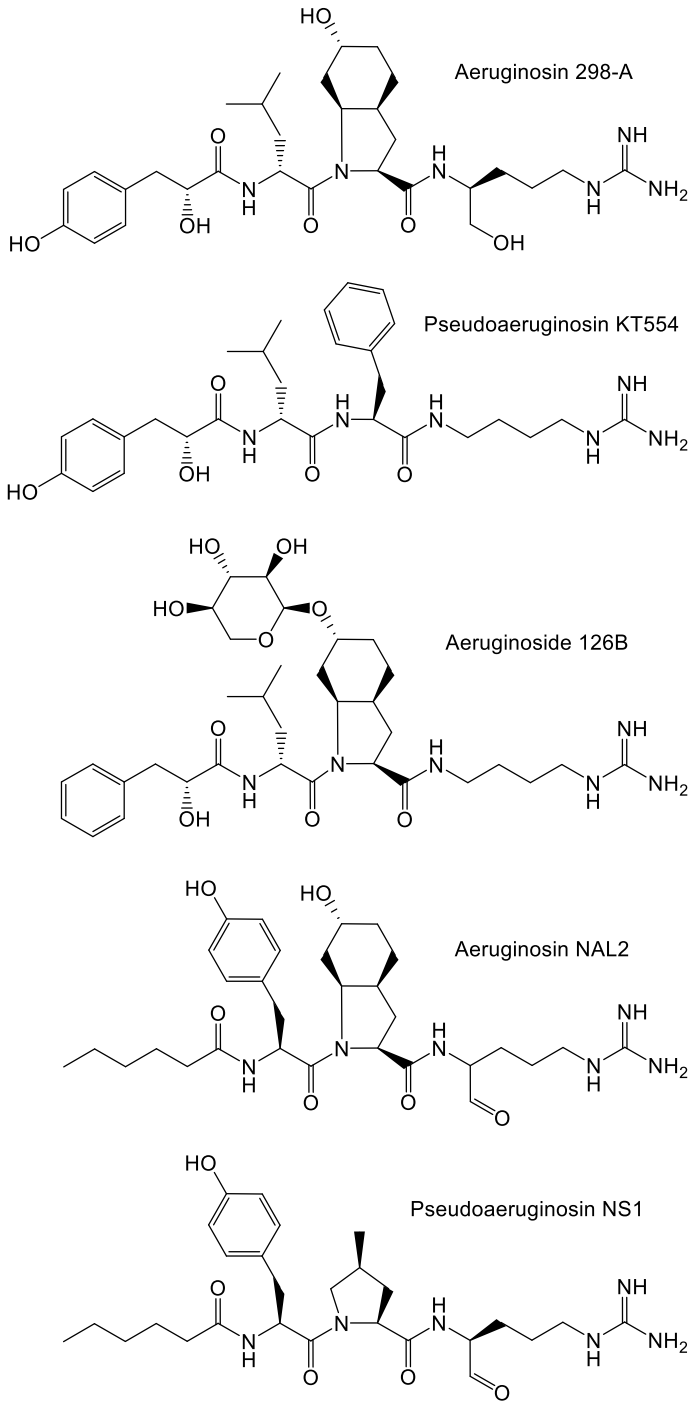


Figure S1. Structures of aeruginosin 298-A from *Microcystis aeruginosa* NIES-298, pseudoaeruginosin KT554 from *M. aeruginosa* IL-347, aeruginoside 126B from *Planktothrix agardhii* CYA 126/8, aeruginosin NAL2 and pseudoaeruginosin NS1 from *Nodularia spumigena* AV1.

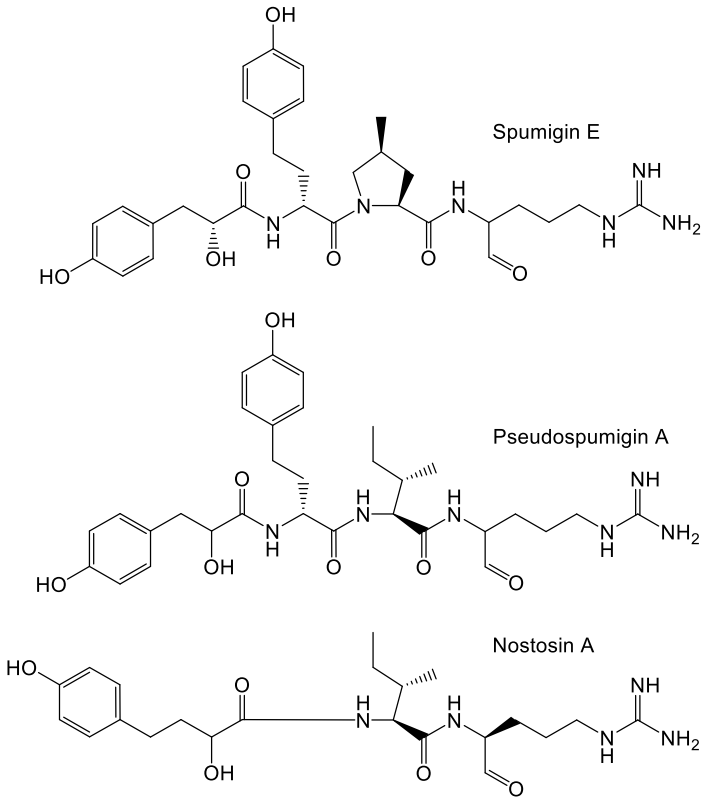


Figure S2. Structures of spumigin E from *N. spumigena* AV1, pseudospumigin from *Nostoc* sp. CENA 543 and nostosin A from *Nostoc* sp. FSN.

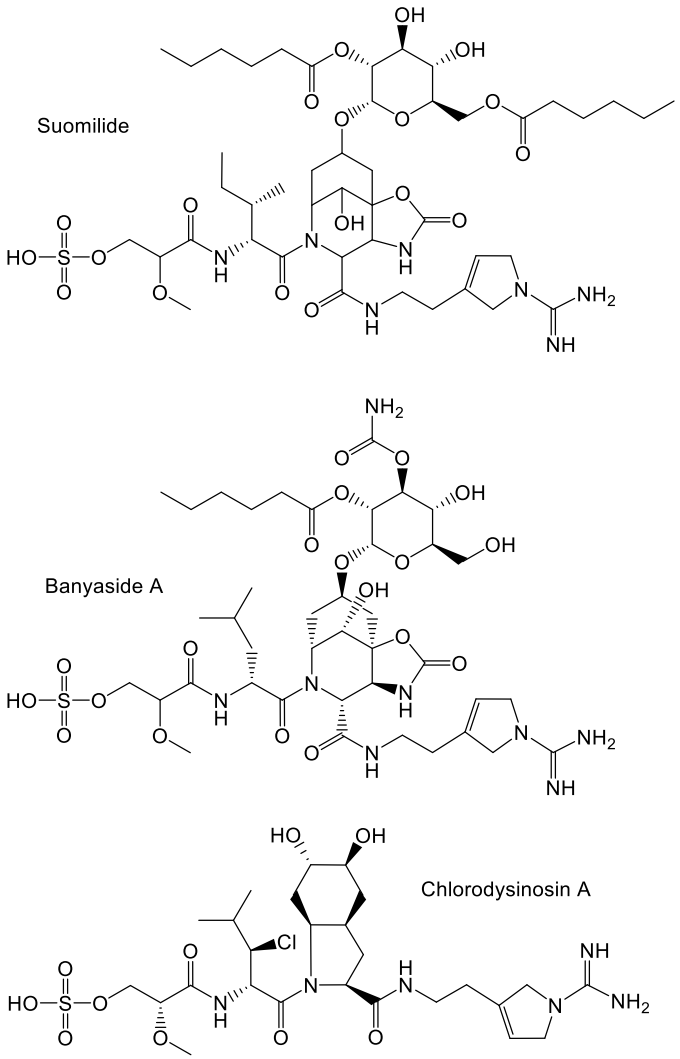


Figure S3. Structures of suomilide from *N. sphaerocarpa* HKVV, banyaside A from *Nostoc* sp. IL-235 and chlorodysinosin A from sponge, family *Dysideidae*.

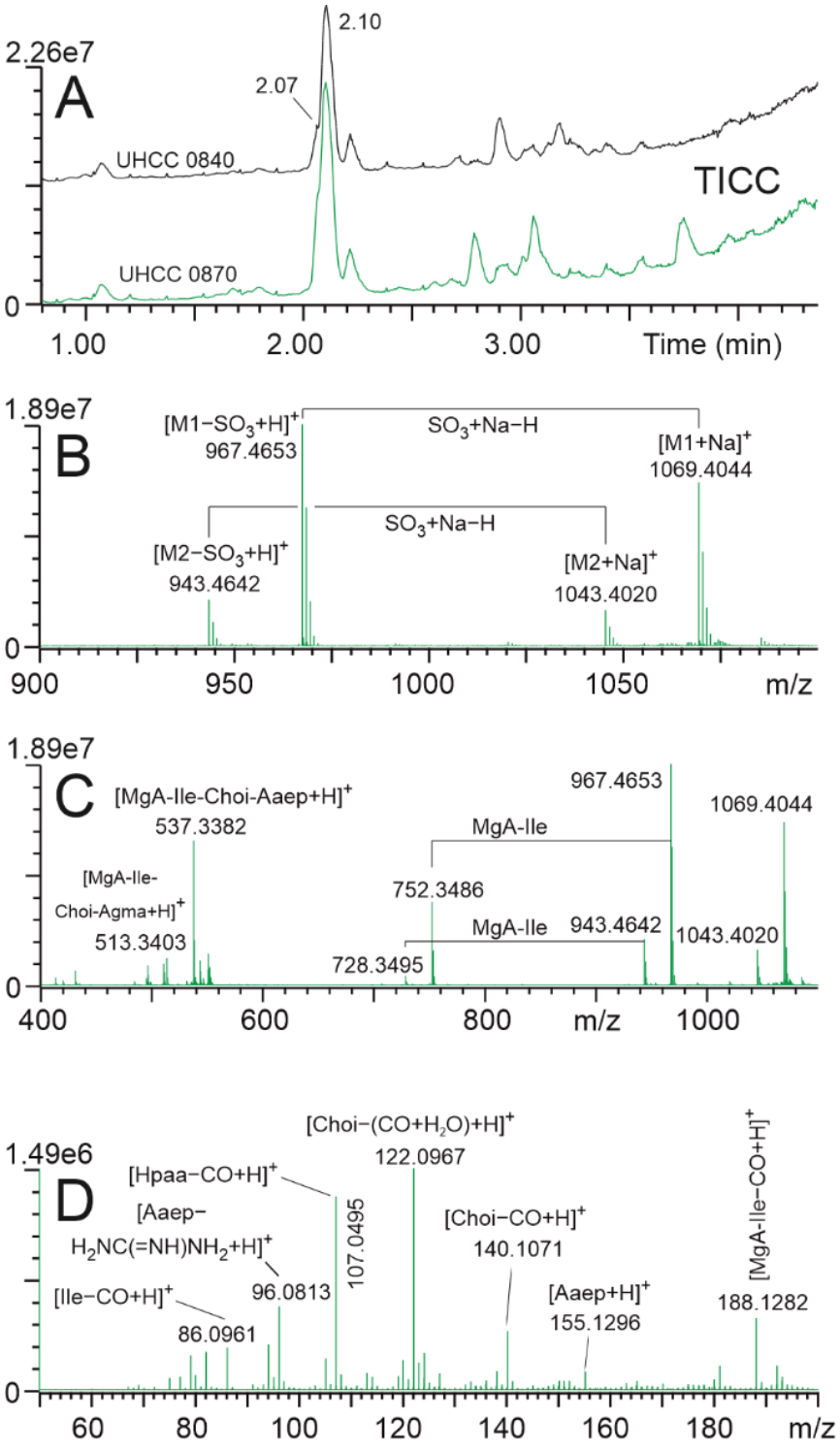


Figure S4. UPLC-QTOFMS analysis of varlaxin producers *Nostoc* sp. UHCC 0870 MeOH extracts. A: Total ion current chromatograms (TICC) showing varlaxin 1046A (2.10 min) and 1022A (2.07 min) peaks. B: Mass spectrum of the merged peaks 2.07 and 2.10 min showing peak patterns of sodiated and desulfated protonated varlaxins 1046A (M1) and 1022A (M2). C: Mass spectrum from *m/z* 400 to 1100 show ions typical for aeruginosins. D: MS^E mass spectrum of the merged peaks 2.07 and 2.10 min from *m/z* 50 to 200 show low mass diagnostic ions for aeruginosins. MgA = 2-O-methylglyceric acid, Choi = 2-carboxy-6-octahydroindole, Agma = 4-amidinobutylamide, Aaep = 1-amidino-3-(2-aminoethyl)-3-pyrroline, Hpaa = 4-hydroxyphenylacetic acid.

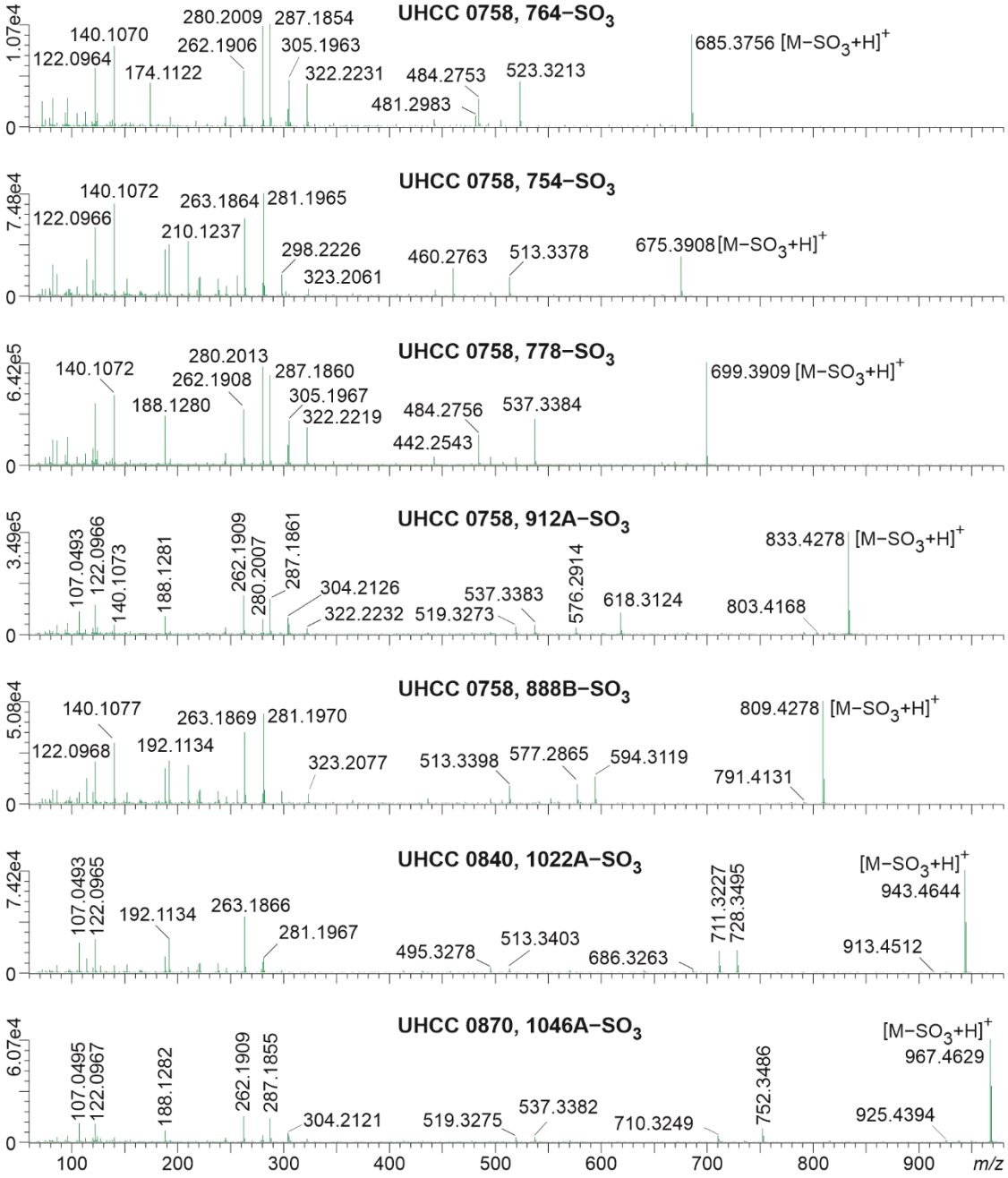


Figure S5. Product ion spectra (MS^2) of protonated desulfated varlaxins 764, 754, 778, 912A, 888B, 1022A and 1046A in MeOH extracts from *Nostoc* sp. UHCC strains 0758, 0840 and 0870. Annotation of ions in Table 2.

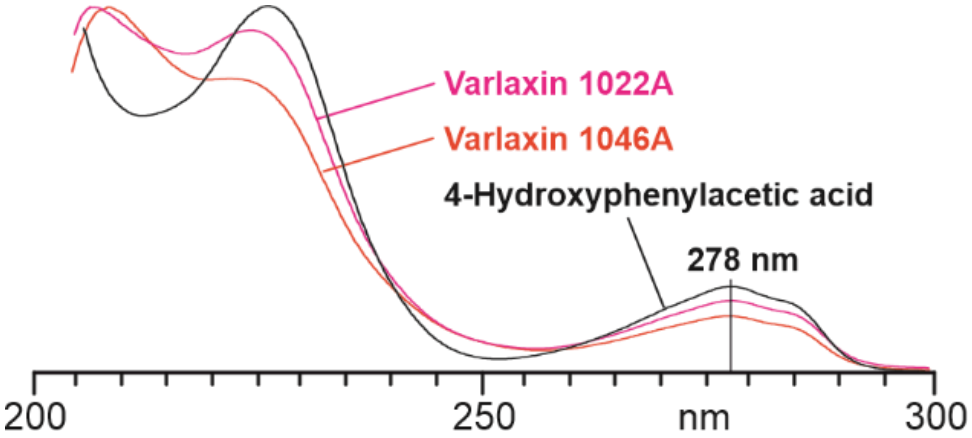
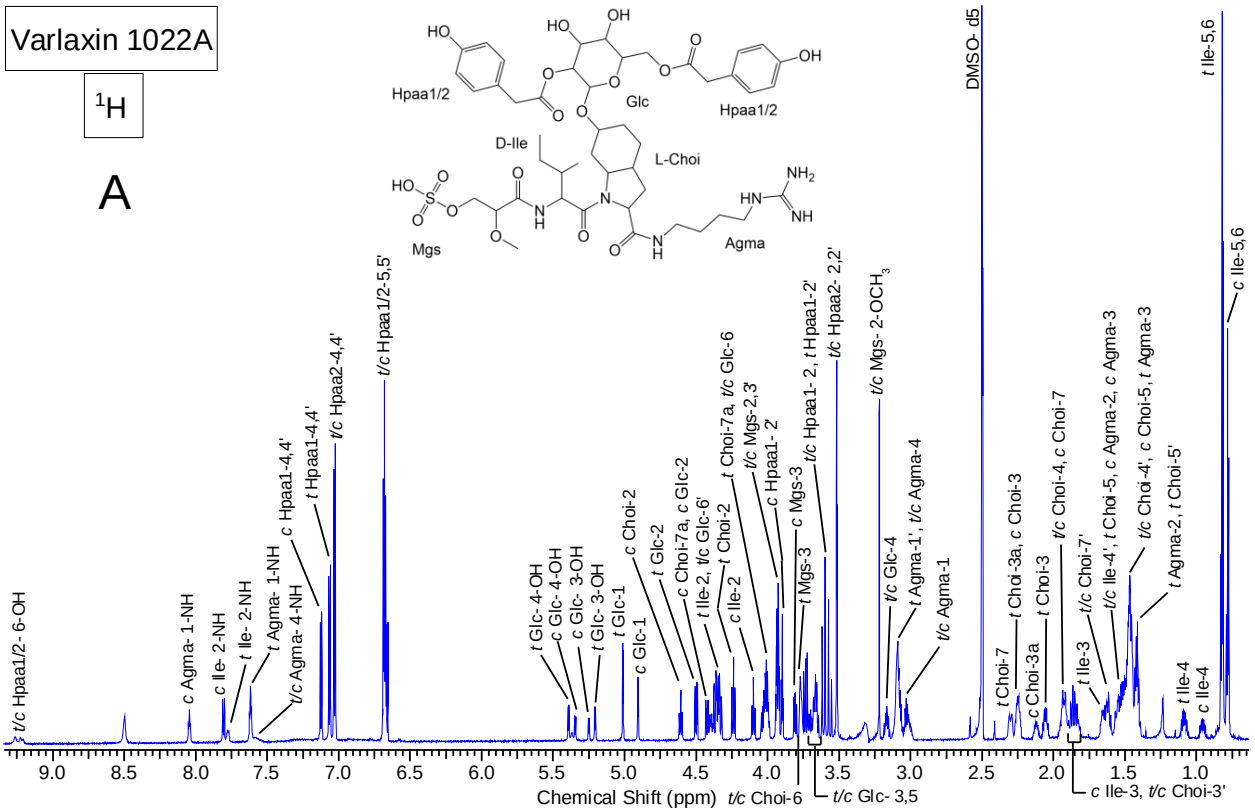
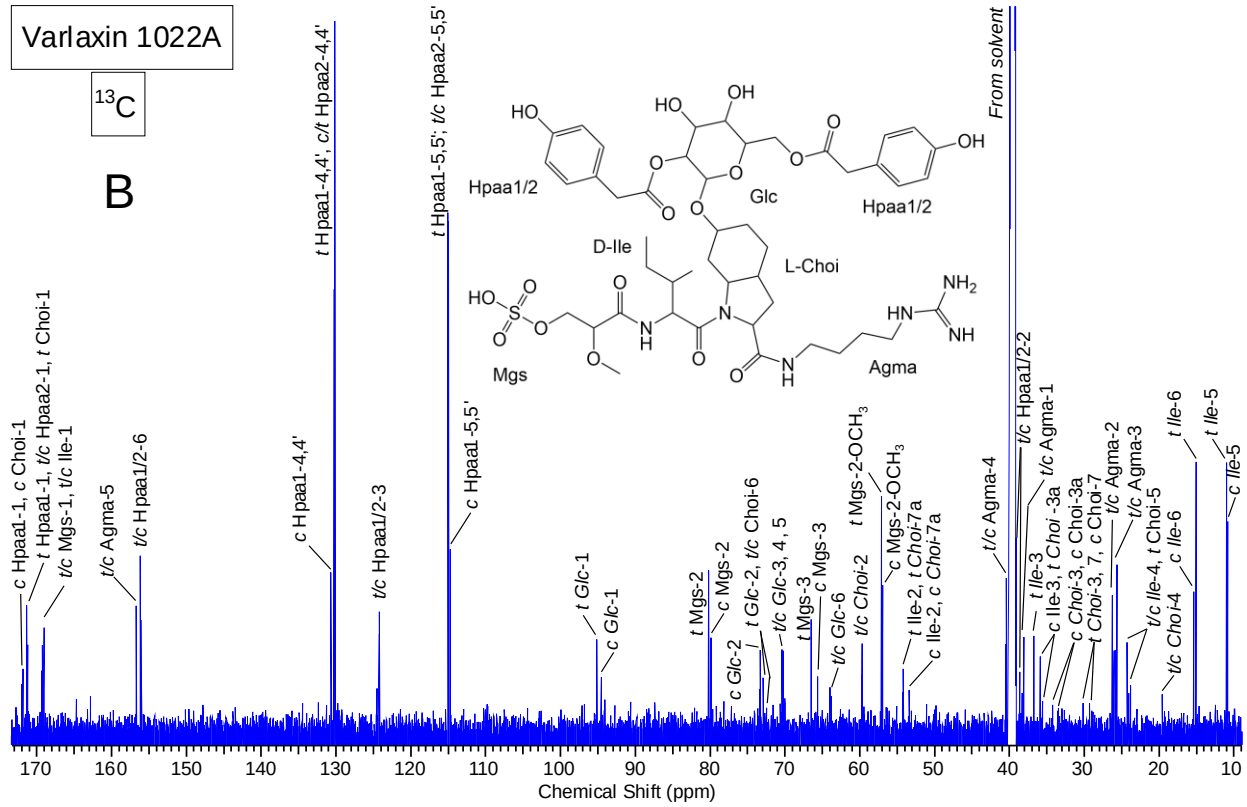
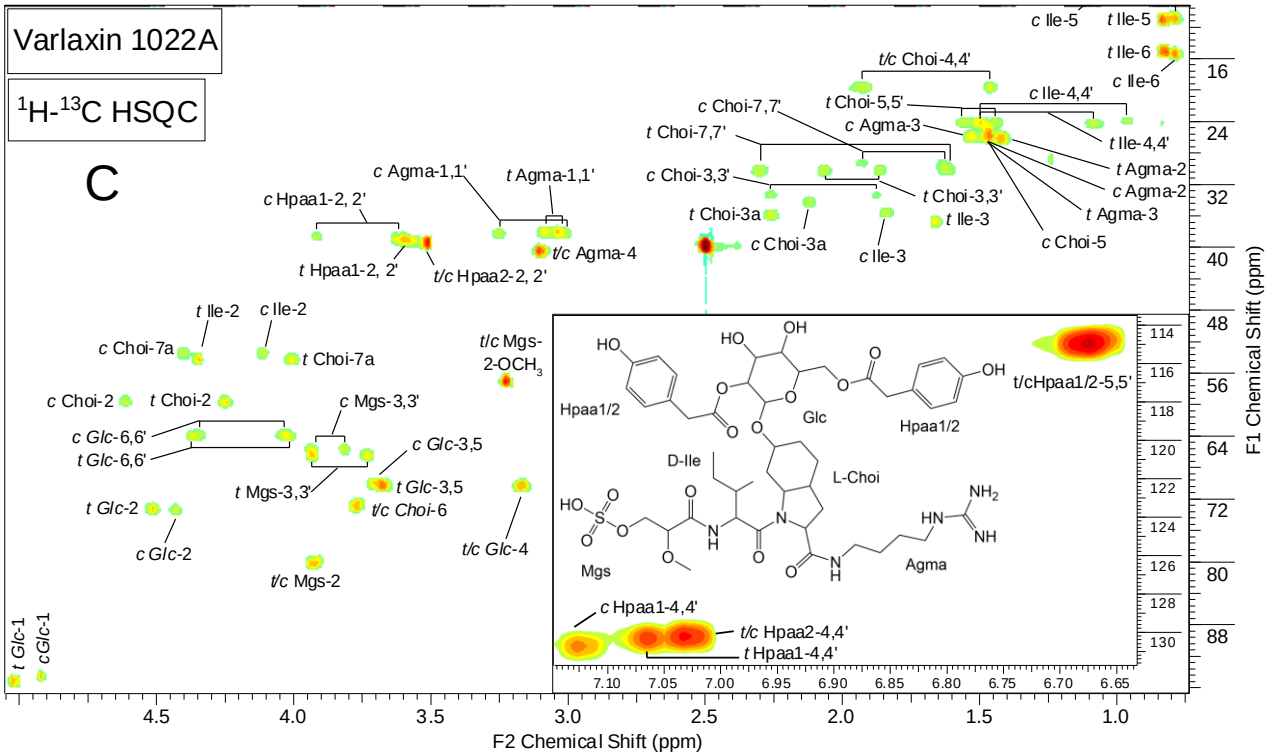
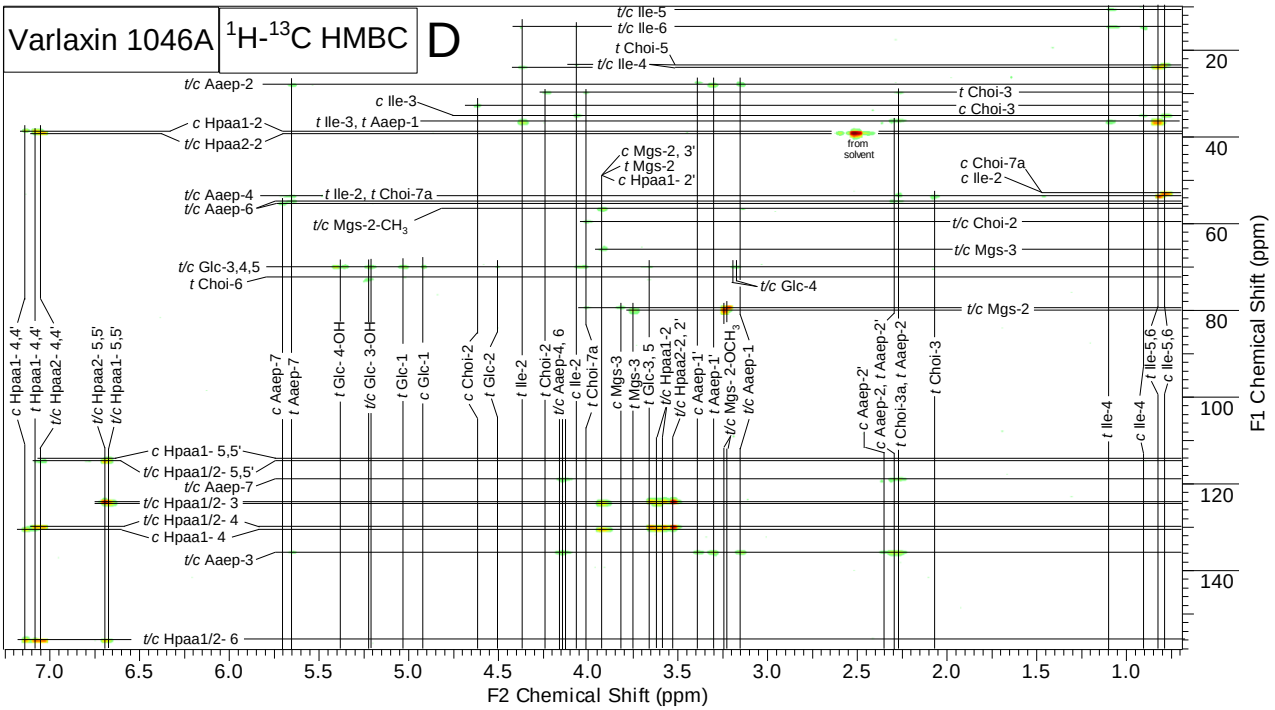


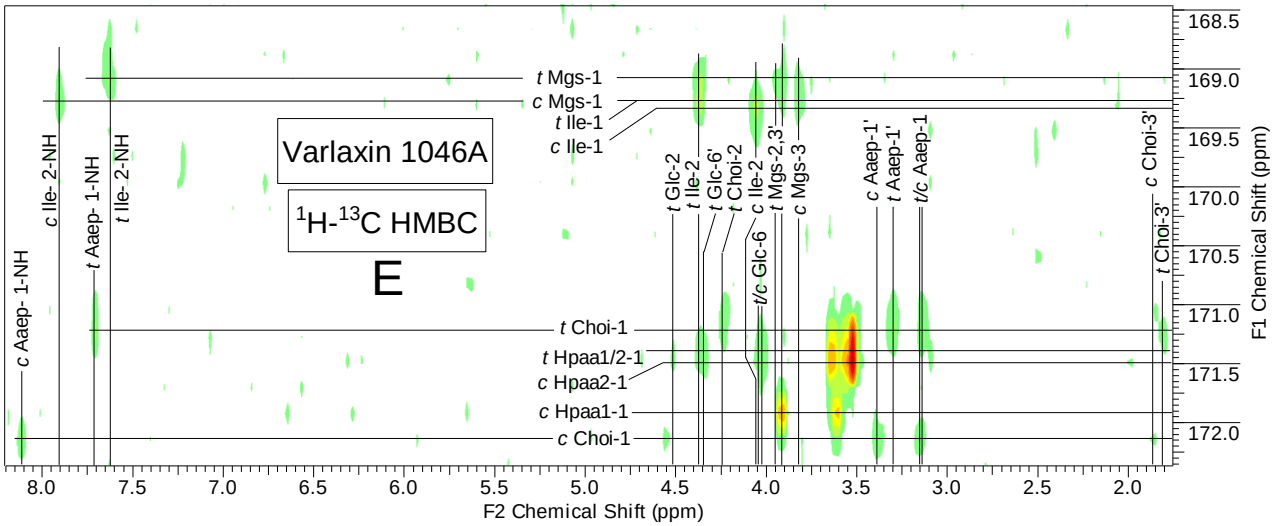
Figure S6. UV spectra of varlaxins 1022A and 1046A and a reference compound 4-hydroxyphenylacetic acid.

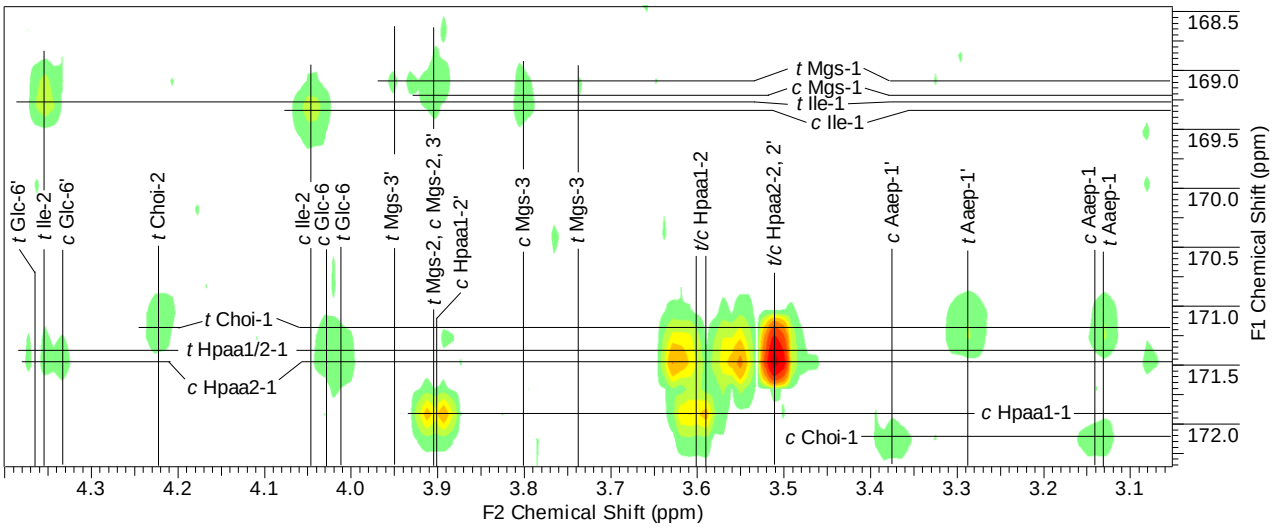


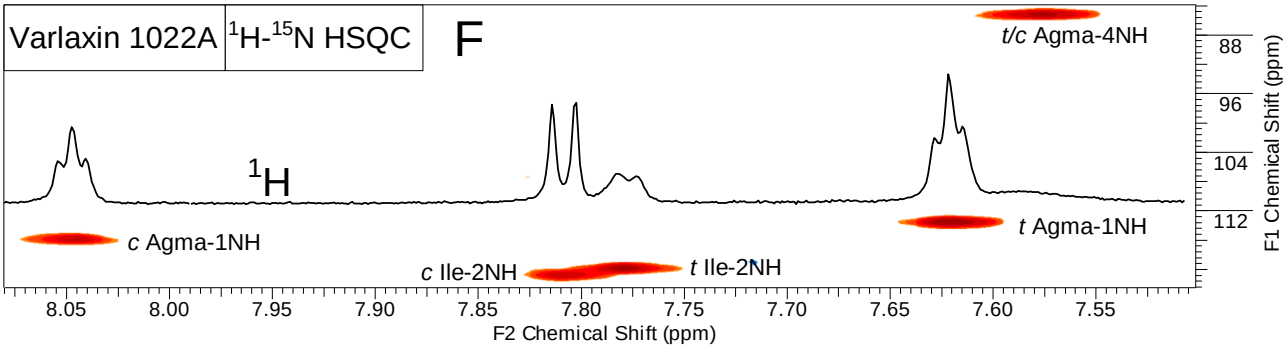

Varlaxin 1022A
13C
B
Hpaa1/2
Glc
Hpaa1/2
D-Ile
L-Choi
Mgs
Agma
c Hpaa1-1, c Choi-1
t Hpaa1-1, t/c Hpaa2-1, t Choi-1
t/c Mgs-1, t/c Ile-1
t/c Agma-5
t/c Hpaa1/2-6
t Hpaa1-4,4'; c/t Hpaa2-4,4'
c Hpaa1-4,4'
t/c Hpaa1/2-3
t Hpaa1-5,5'; t/c Hpaa2-5,5'
c Hpaa1-5,5'
t Glc-1
c Glc-1
t Mgs-2
c Mgs-2
c Glc-2
t Glc-2, t/c Choi-6
t/c Glc-3, 4, 5
t Mgs-3
c Mgs-3
t/c Glc-6
t/c Choi-2
t Mgs-2-OCH3
c Mgs-2-OCH3
t Ile-2, t Choi-7a
c Ile-2, c Choi-7a
t/c Agma-4
From solvent
t/c Hpaa1/2-2
t/c Agma-1
t Ile-3
t/c Agma-3a
c Ile-3, t Choi -3a
c Choi-3, c Choi-3a
c Choi-3, 7, c Choi-7
t/c Agma-2
t/c Agma-3
t Ile-6
t Ile-5
t/c Ile-4, t Choi-5
c Ile-6
t/c Choi-4
c Ile-5
Chemical Shift (ppm)

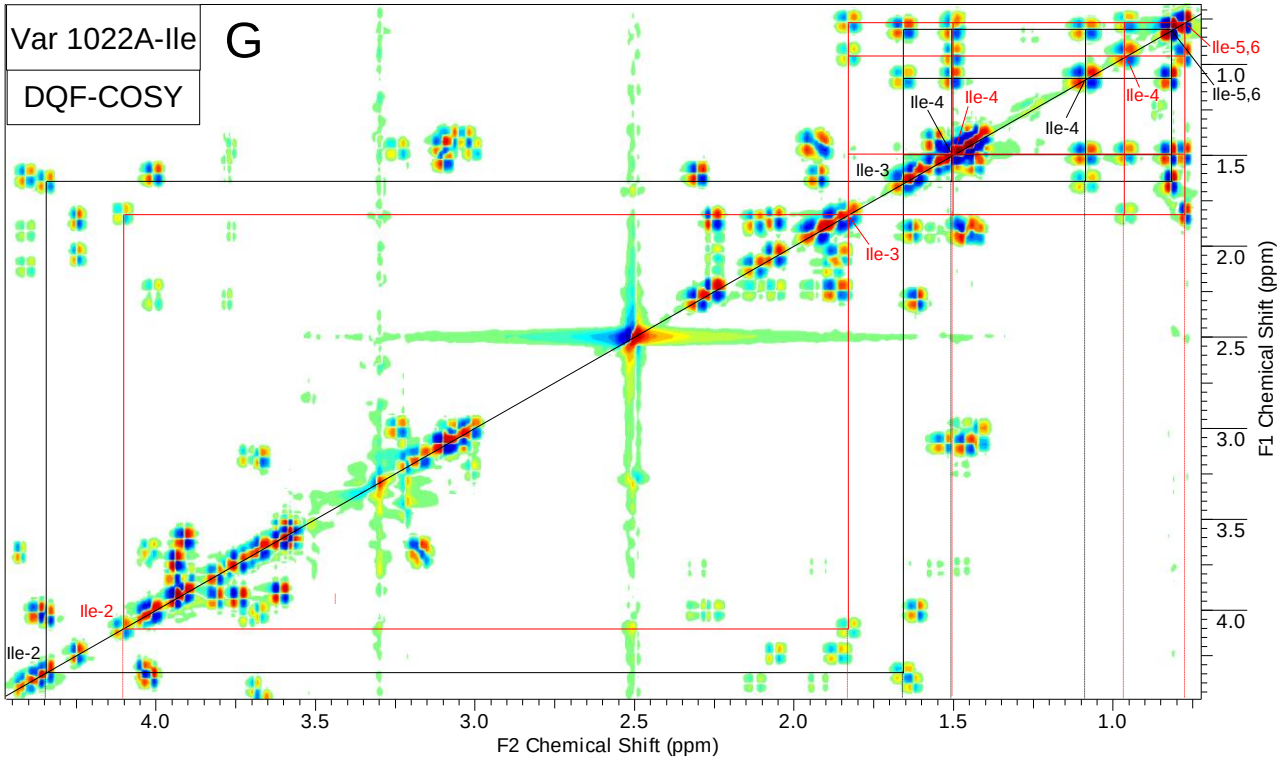

Varlaxin 1022A
1H-13C HSQC
C
c Agma-1,1'
t Agma-1,1'
c Hpaa1-2, 2'
t Hpaa1-2, 2'
t/c Hpaa2-2, 2'
t/c Agma-4
t Ile-2
c Ile-2
c Choi-7a
t Choi-7a
c Choi-2
t Choi-2
c Mgs-3,3'
c Glc-6,6'
t Glc-6,6'
c Glc-3,5
t Mgs-3,3'
t Glc-3,5
t/c Choi-6
t Glc-2
c Glc-2
t/c Mgs-2
t/c Glc-4
t/c Mgs-2-OCH3
t Glc-1
c Glc-1
c Ile-5
t Ile-5
t/c Choi-4,4'
t Ile-6
c Ile-6
t Choi-5,5'
c Ile-4,4'
c Choi-7,7'
t Choi-7,7'
c Agma-3
t Ile-4,4'
c Choi-3,3'
t Agma-2
t Choi-3,3'
c Agma-2
t Choi-3a
t Ile-3
t Agma-3
c Choi-3a
c Ile-3
c Choi-5
t/cHpaa1/2-5,5'
c Hpaa1-4,4'
t/c Hpaa2-4,4'
t Hpaa1-4,4'
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

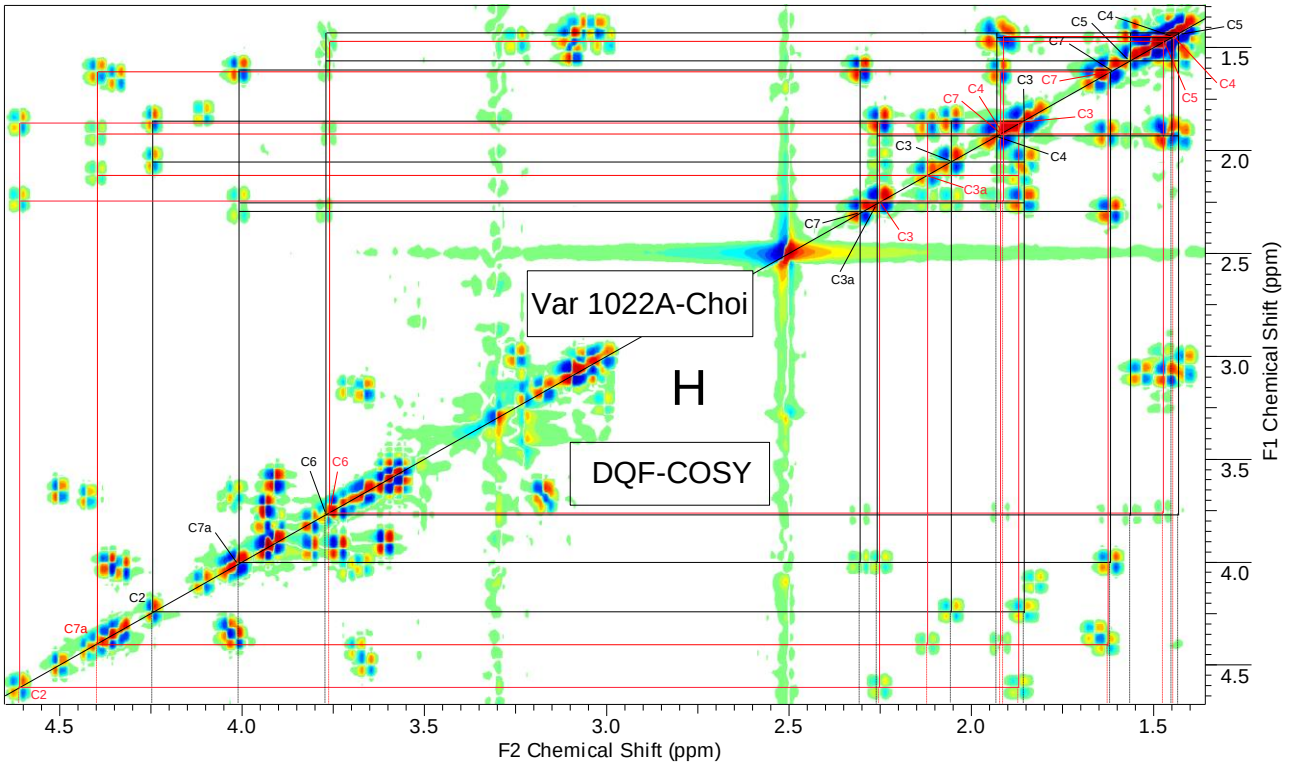

Varlaxin 1046A
^{1}H-^{13}C HMBC
D
t/c Ile-5
t/c Ile-6
t Choi-5
t/c Ile-4
t/c Aaep-2
c Ile-3
t Choi-3
c Choi-3
c Hpaa1-2
t/c Hpaa2-2
t Ile-3, t Aaep-1
from solvent
c Mgs-2, 3'
t Mgs-2
c Hpaa1- 2'
c Choi-7a
c Ile-2
t/c Aaep-4
t/c Aaep-6
t Ile-2, t Choi-7a
t/c Mgs-2-CH$_3$
t/c Choi-2
t/c Mgs-3
t/c Glc-3,4,5
t Choi-6
t/c Glc-4
t/c Mgs-2
c Hpaa1- 4,4'
t Hpaa1- 4,4'
t/c Hpaa2- 4,4'
t/c Hpaa2- 5,5'
t/c Hpaa1- 5,5'
c Aaep-7
t Aaep-7
t Glc- 4-OH
t/c Glc- 3-OH
t Glc-1
c Glc-1
c Choi-2
t Glc-2
t Ile-2
t Choi-2
t/c Aaep-4, 6
c Ile-2
t Choi-7a
c Mgs-3
t Mgs-3
t Glc-3, 5
t/c Hpaa1-2
t/c Hpaa2-2, 2'
c Aaep-1'
t Aaep-1'
t/c Mgs- 2-OCH$_3$
t/c Aaep-1
c Aaep-2'
c Aaep-2, t Aaep-2'
t Choi-3a, t Aaep-2
t Choi-3
t Ile-4
c Ile-4
t Ile-5,6
c Ile-5,6
c Hpaa1- 5,5'
t/c Hpaa1/2- 5,5'
t/c Aaep-7
t/c Hpaa1/2- 3
t/c Hpaa1/2- 4
c Hpaa1- 4
t/c Aaep-3
t/c Hpaa1/2- 6
20
40
60
80
100
120
140
F1 Chemical Shift (ppm)
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
F2 Chemical Shift (ppm)

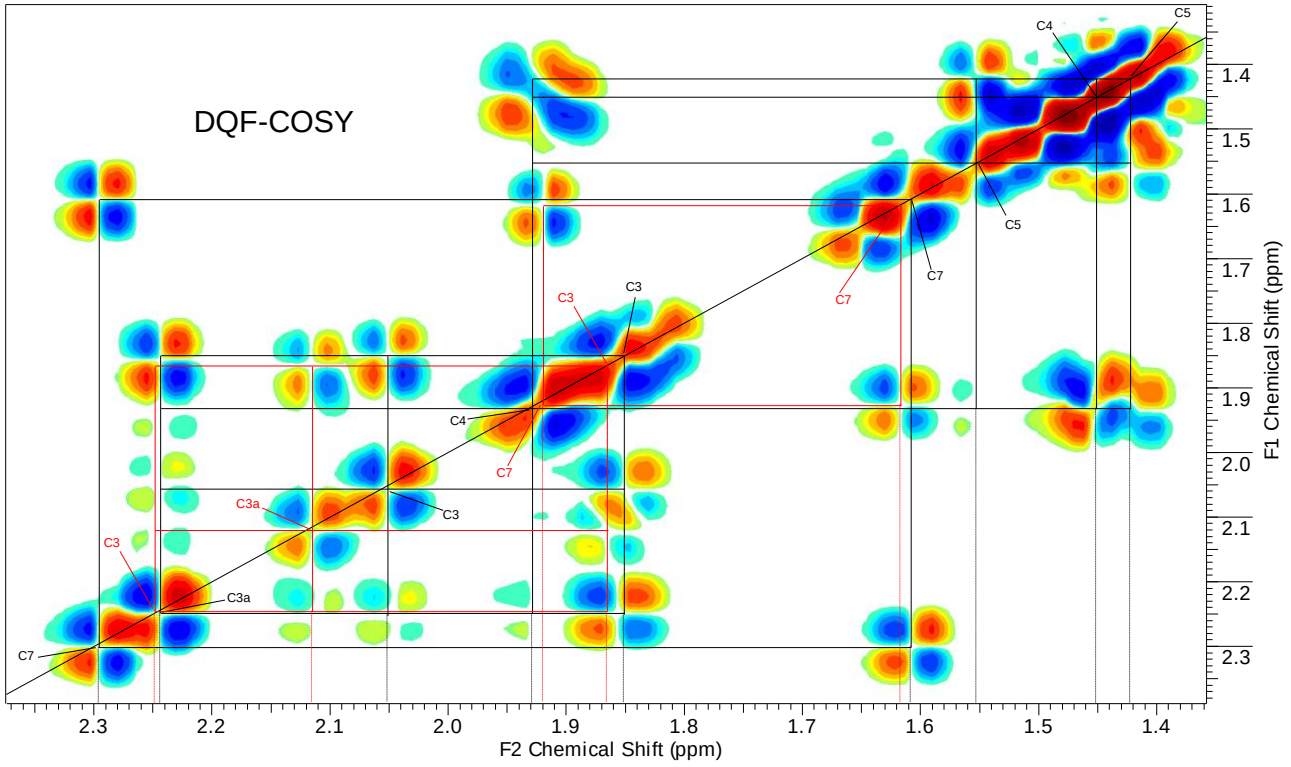

Varlaxin 1046A
^{1}H-^{13}C HMBC
E
t Mgs-1
c Mgs-1
t Ile-1
c Ile-1
t Choi-1
t Hpaa1/2-1
c Hpaa2-1
c Hpaa1-1
c Choi-1
c Ile- 2-NH
t Aaep- 1-NH
t Ile- 2-NH
c Aaep- 1-NH
t Glc-2
t Ile-2
t Glc-6'
t Choi-2
c Ile-2
t Mgs-2,3'
c Mgs-3
t/c Glc-6
c Aaep-1'
t Aaep-1'
t/c Aaep-1
c Choi-3'
t Choi-3'
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

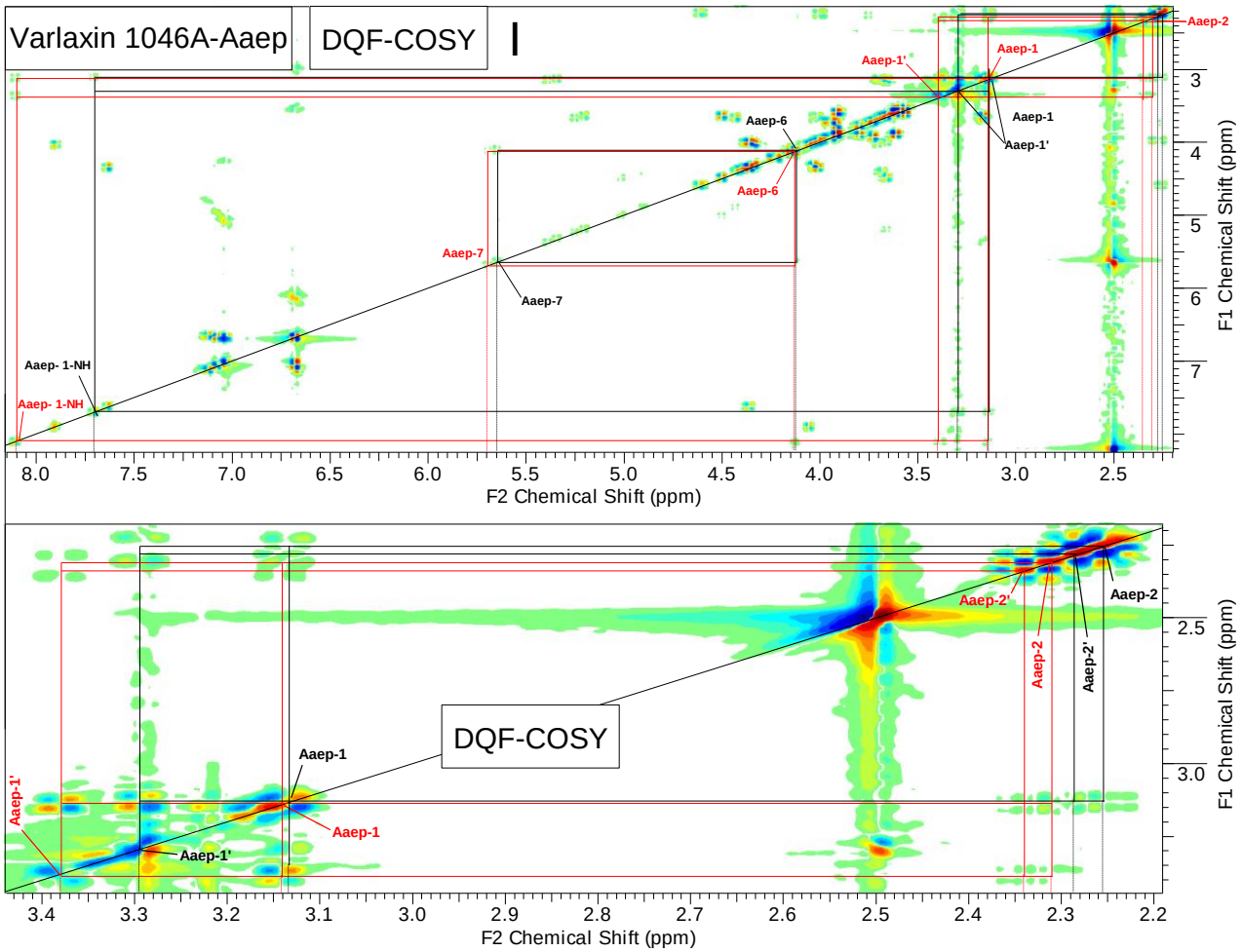

t Mgs-1
c Mgs-1
t Ile-1
c Ile-1
t Choi-1
t Hpaa1/2-1
c Hpaa2-1
c Hpaa1-1
c Choi-1
t Glc-6'
t Ile-2
c Glc-6'
t Choi-2
c Ile-2
c Glc-6
t Glc-6
t Mgs-3'
t Mgs-2, c Mgs-2, 3'
c Hpaa1-2'
c Mgs-3
t Mgs-3
t/c Hpaa1-2
t/c Hpaa2-2, 2'
c Aaep-1'
t Aaep-1'
c Aaep-1
t Aaep-1
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

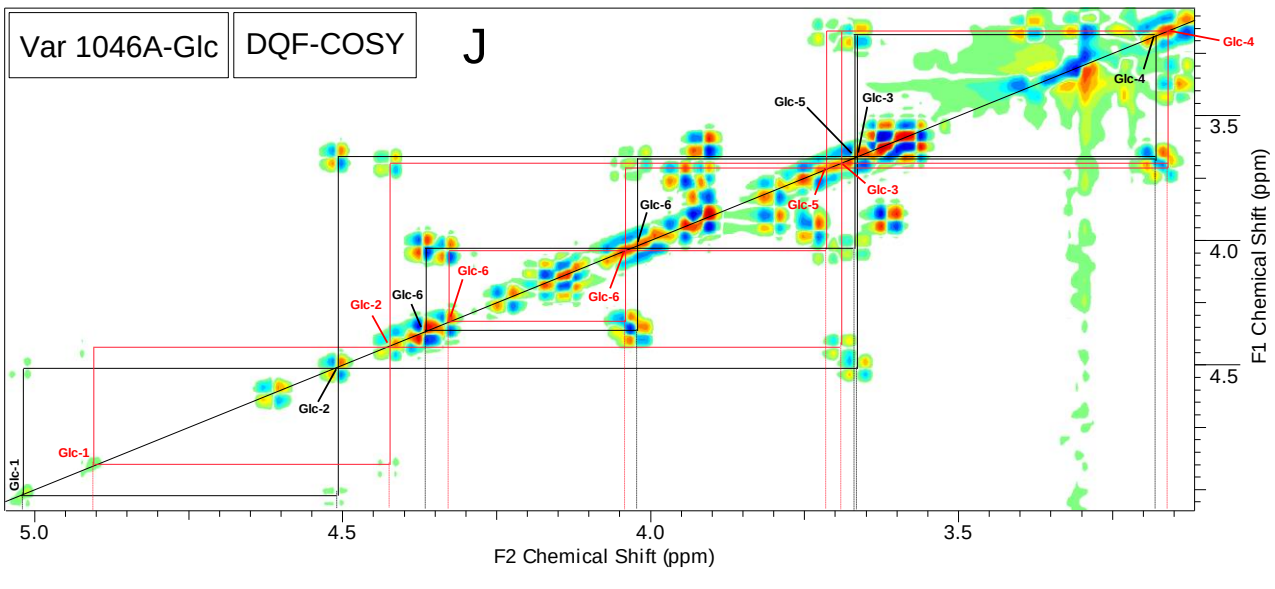

Varlaxin 1022A
^{1}H-^{15}N HSQC
F
^{1}H
t/c Agma-4NH
t Agma-1NH
c Agma-1NH
c Ile-2NH
t Ile-2NH
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

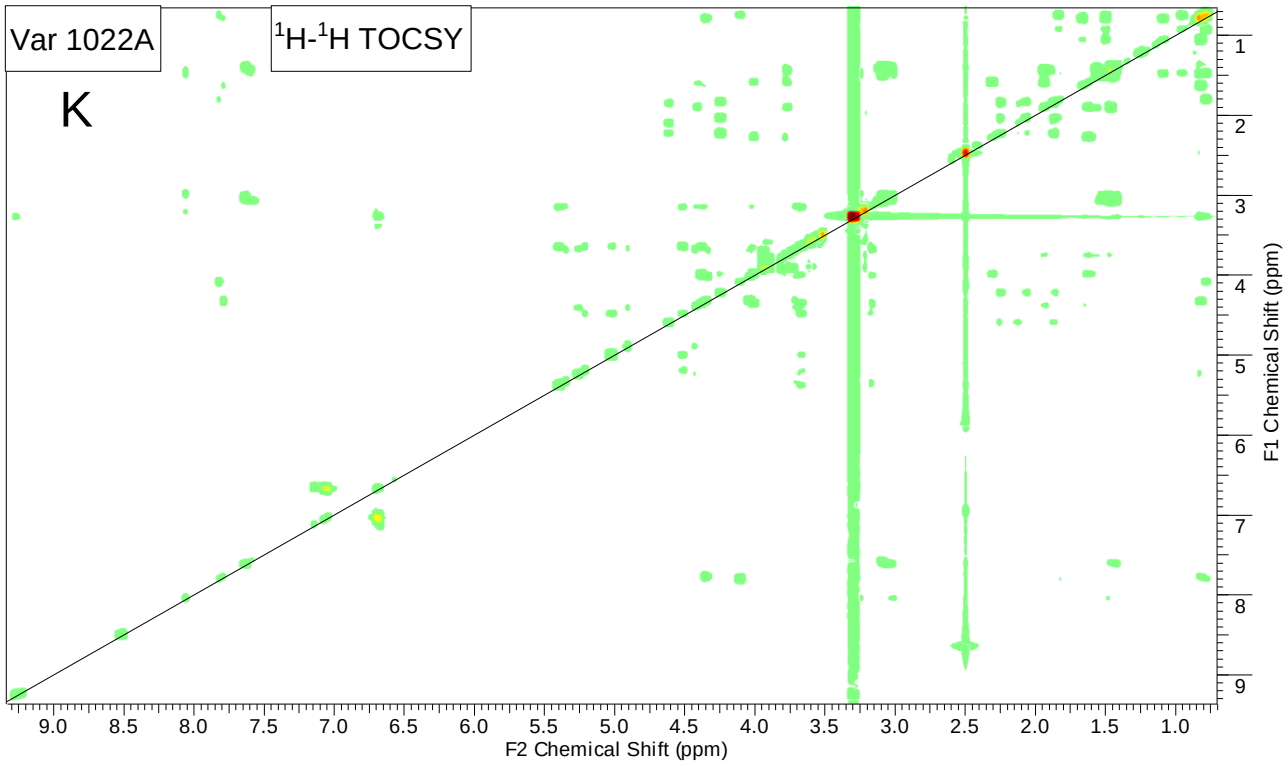

Var 1022A-Ile
DQF-COSY
G
Ile-5,6
Ile-5,6
Ile-4
Ile-4
Ile-4
Ile-4
Ile-3
Ile-3
Ile-2
Ile-2
1.0
1.5
2.0
2.5
3.0
3.5
4.0
F1 Chemical Shift (ppm)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
F2 Chemical Shift (ppm)

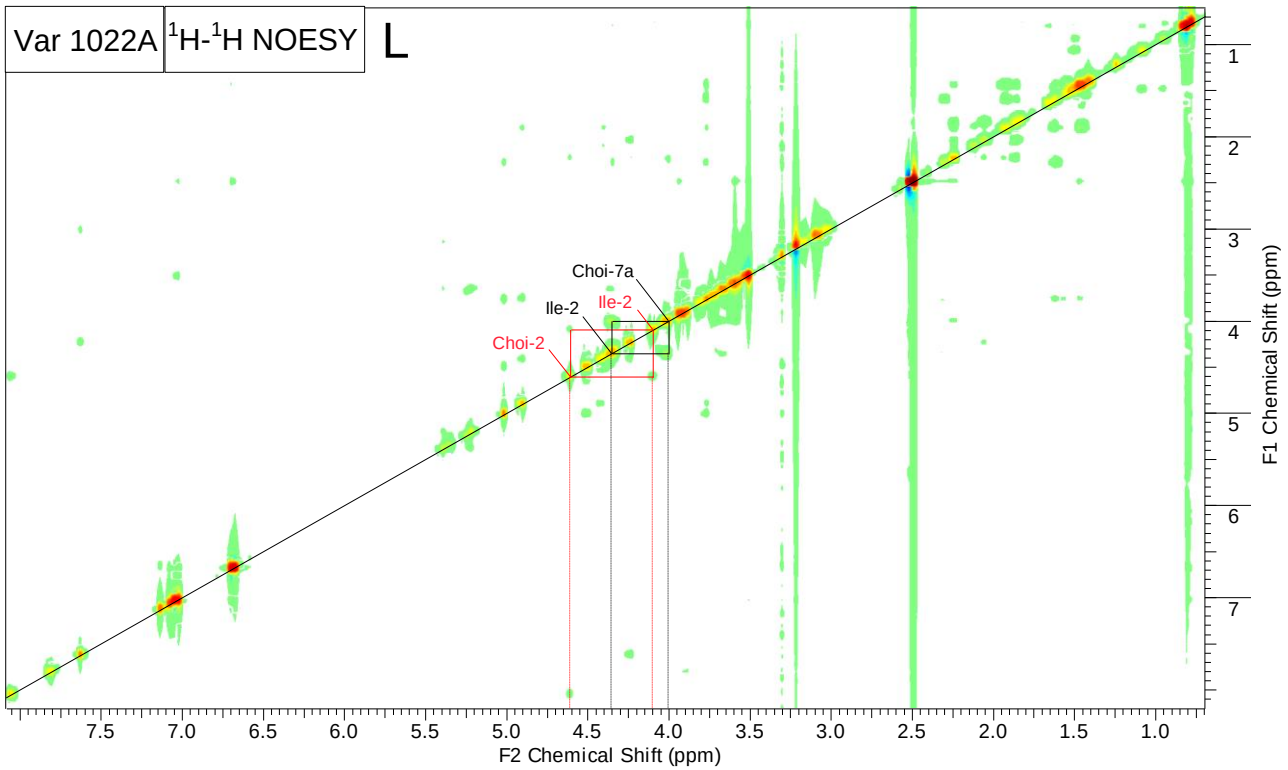

Var 1022A-Choi
H
DQF-COSY
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)


DQF-COSY
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)


Varlaxin 1046A-Aaep
DQF-COSY
I
Aaep-2
Aaep-1'
Aaep-1
Aaep-6
Aaep-7
Aaep- 1-NH
F1 Chemical Shift (ppm)
F2 Chemical Shift (ppm)
DQF-COSY
Aaep-2'
Aaep-1
Aaep-1'


Var 1046A-Glc
DQF-COSY
J
Glc-4
Glc-5
Glc-3
Glc-6
Glc-2
Glc-1
F1 Chemical Shift (ppm)
F2 Chemical Shift (ppm)


Var 1022A
^{1}H-^{1}H TOCSY
K
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)


Var 1022A
^{1}H-^{1}H NOESY
L
Choi-7a
Ile-2
Ile-2
Choi-2
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

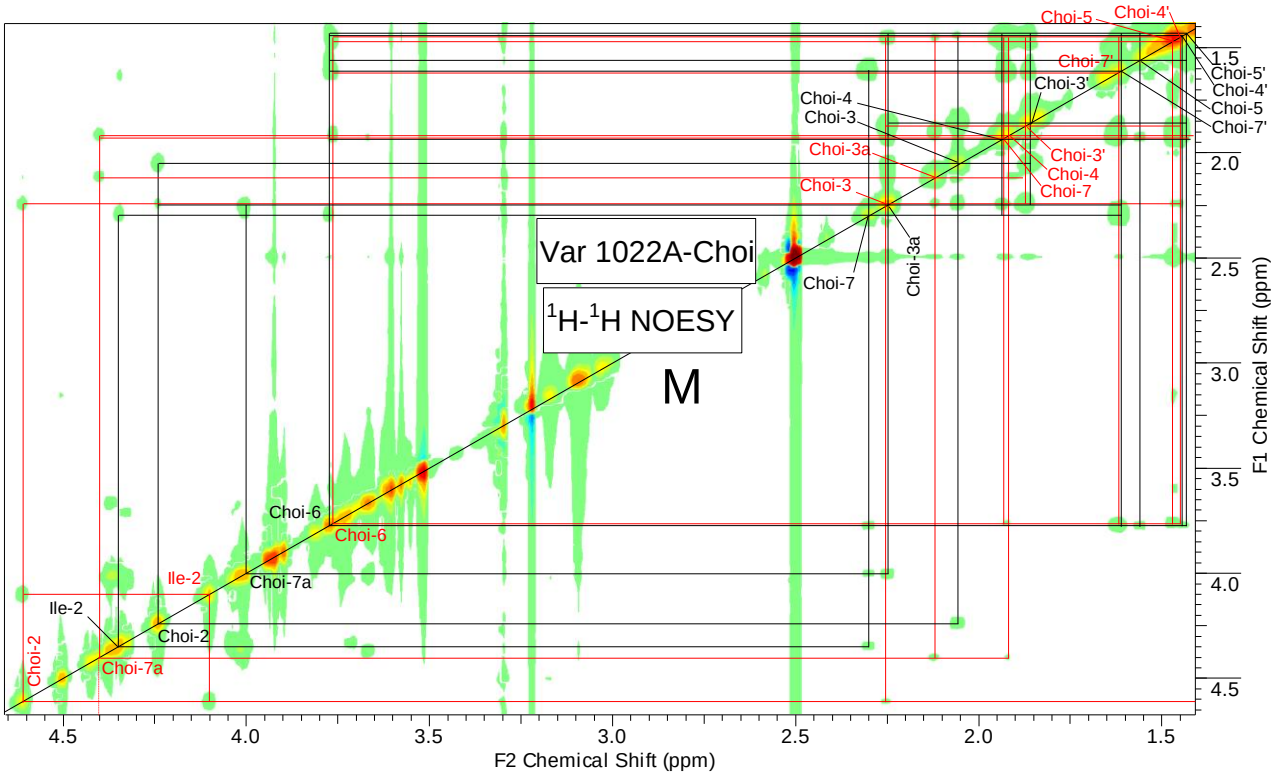
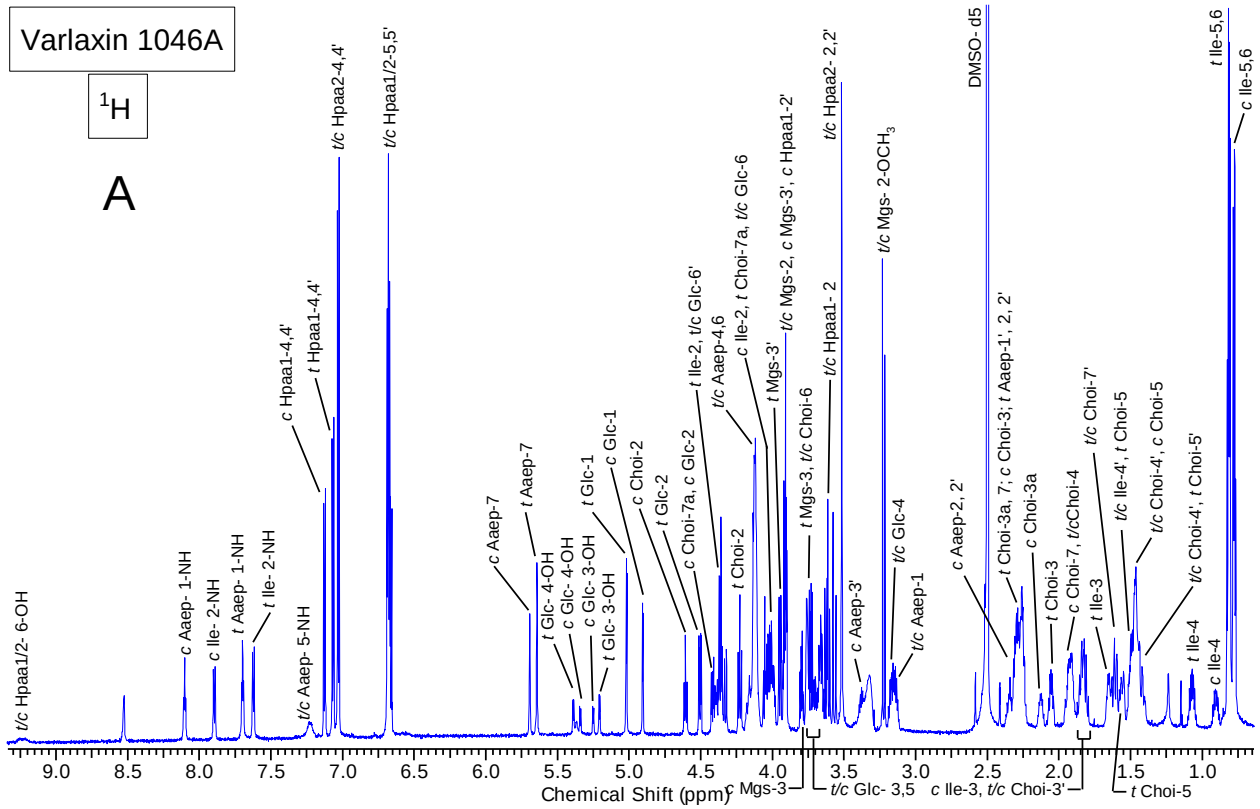
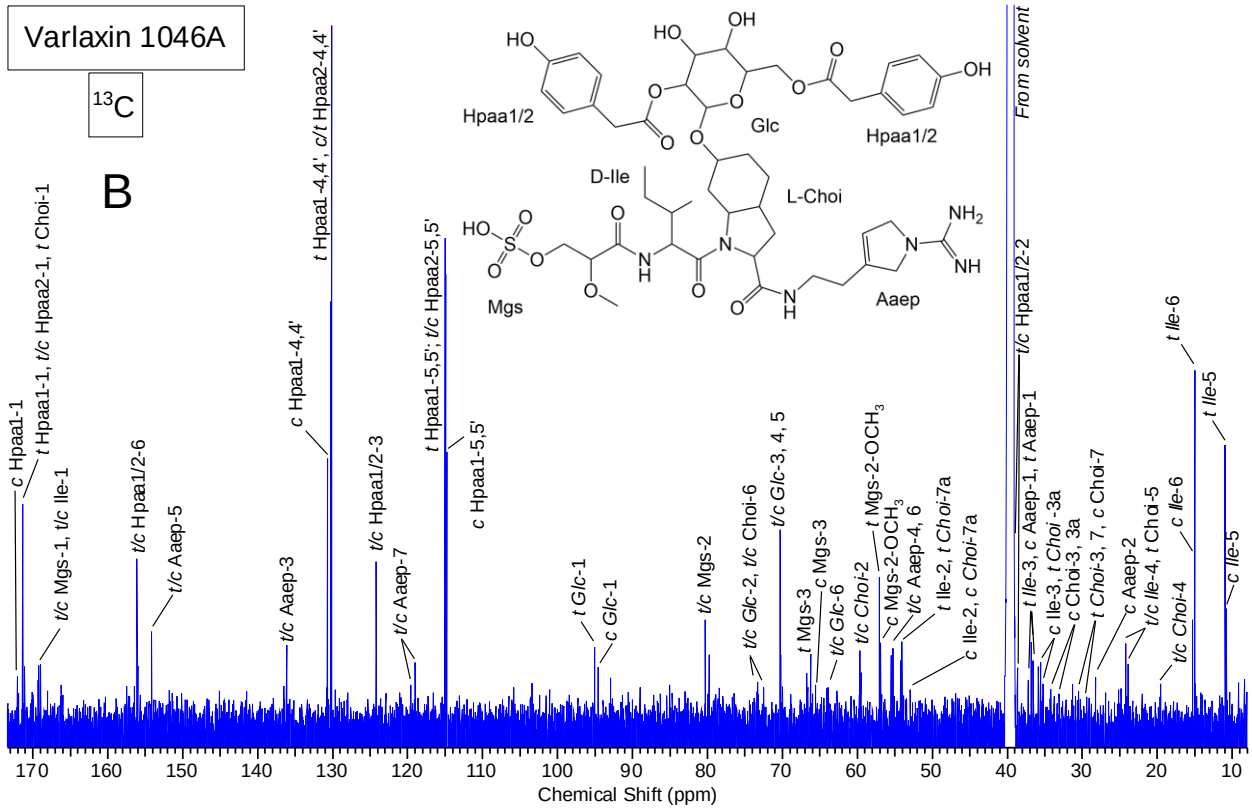
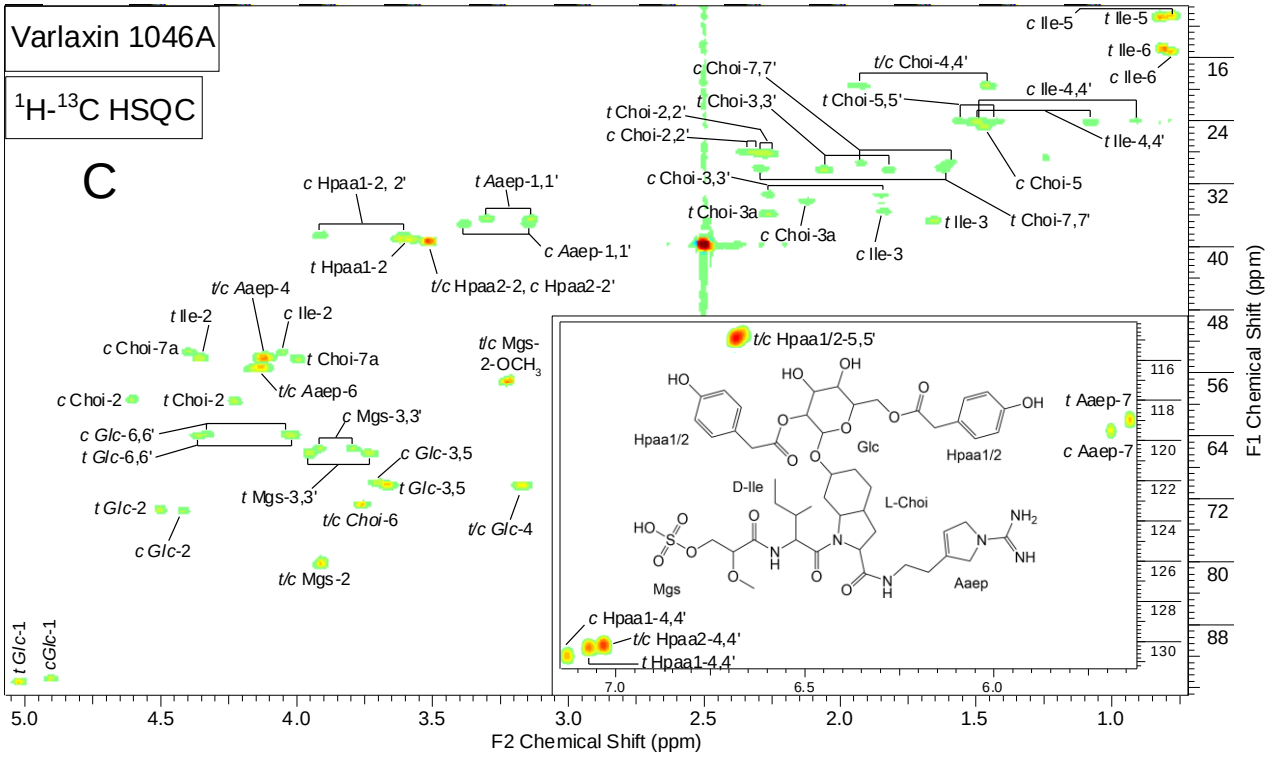
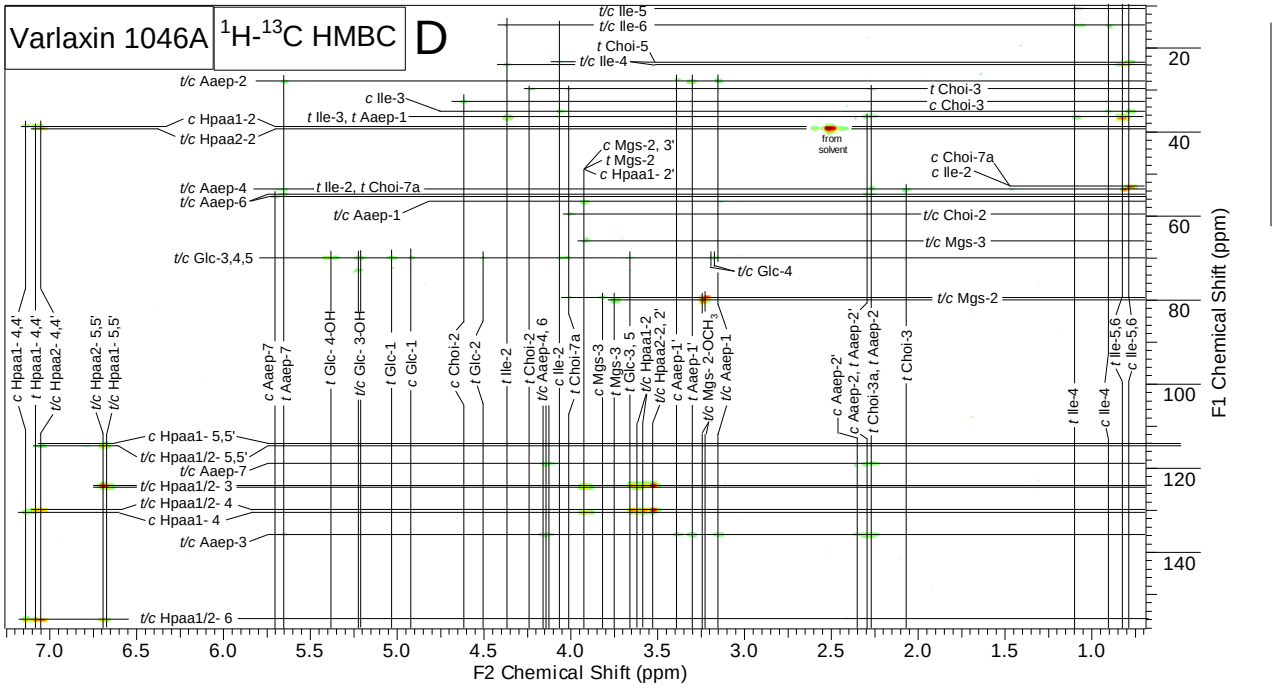


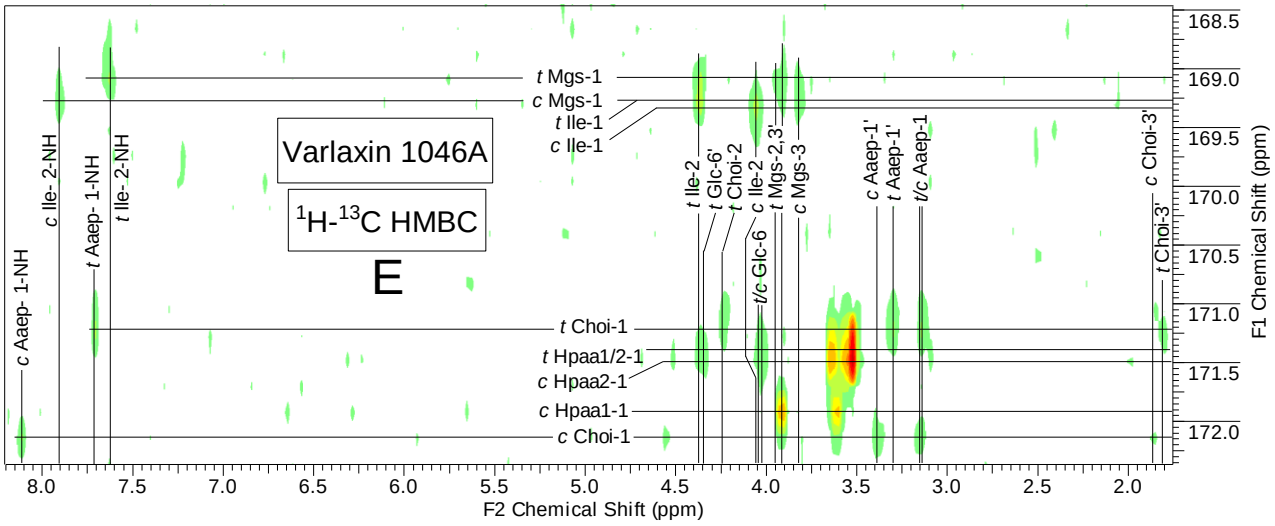
Figure S7. 800 MHz NMR spectra of the varlaxin 1022A isolated from *Nostoc* sp. CENA543. A: ^{1}H, B: ^{13}C, C: ^{1}H-^{13}C HSQC, D: ^{1}H-^{13}C HMBC, E: ^{1}H-^{13}C HMBC from the carbonyl region, F: ^{1}H-^{15}N HSQC, G-J: DQF-COSY of Ile, Choi, Agma and Glucopyranose (Glc), K: ^{1}H-^{1}H TOCSY (60 ms), L: ^{1}H-^{1}H NOESY and M: ^{1}H-^{1}H NOESY of Choi. Trans correlations are in black and cis correlations in red. t/c = trans/cis.

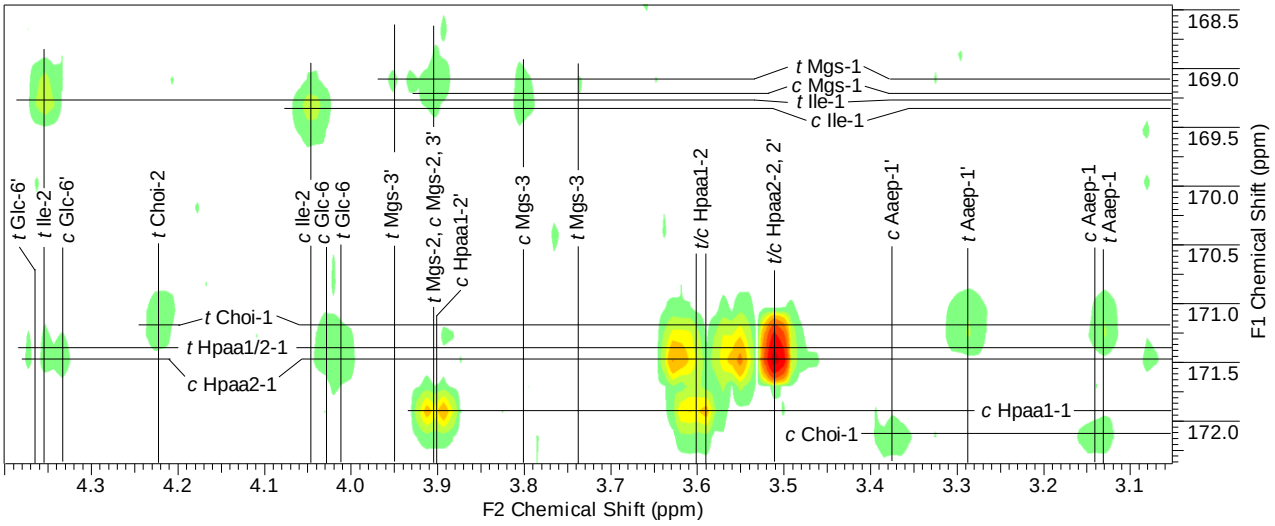

Varlaxin 1046A
^{1}H
A
t/c Hpaa1/2- 6-OH
c Aaep- 1-NH
c Ile- 2-NH
t Aaep- 1-NH
t Ile- 2-NH
c Hpaa1-4,4'
t Hpaa1-4,4'
t/c Aaep- 5-NH
t/c Hpaa2-4,4'
t/c Hpaa1/2-5,5'
c Aaep-7
t Aaep-7
t Glc- 4-OH
c Glc- 4-OH
c Glc- 3-OH
t Glc- 3-OH
t Glc-1
c Glc-1
c Choi-2
t Glc-2
c Choi-7a, c Glc-2
t Ile-2, t/c Glc-6'
t/c Aaep-4,6
t Choi-2
c Ile-2, t Choi-7a, t/c Glc-6
t Mgs-3'
t/c Mgs-2, c Mgs-3', c Hpaa1-2'
t Mgs-3, t/c Choi-6
t/c Hpaa1- 2
t/c Hpaa2- 2,2'
c Aaep-3'
t/c Mgs- 2-OCH$_3$
t/c Glc-4
t/c Aaep-1
c Aaep-2, 2'
t Choi-3a, 7; c Choi-3; t Aaep-1', 2, 2'
DMSO- d5
c Choi-3a
t Choi-3
c Choi-7, t/cChoi-4
t Ile-3
t/c Choi-7'
t/c Ile-4', t Choi-5
t/c Choi-4', c Choi-5
t Ile-4
c Ile-4
t/c Choi-4', t Choi-5'
t Ile-5,6
c Ile-5,6
Chemical Shift (ppm)
c Mgs-3
t/c Glc- 3,5
c Ile-3, t/c Choi-3'
t Choi-5

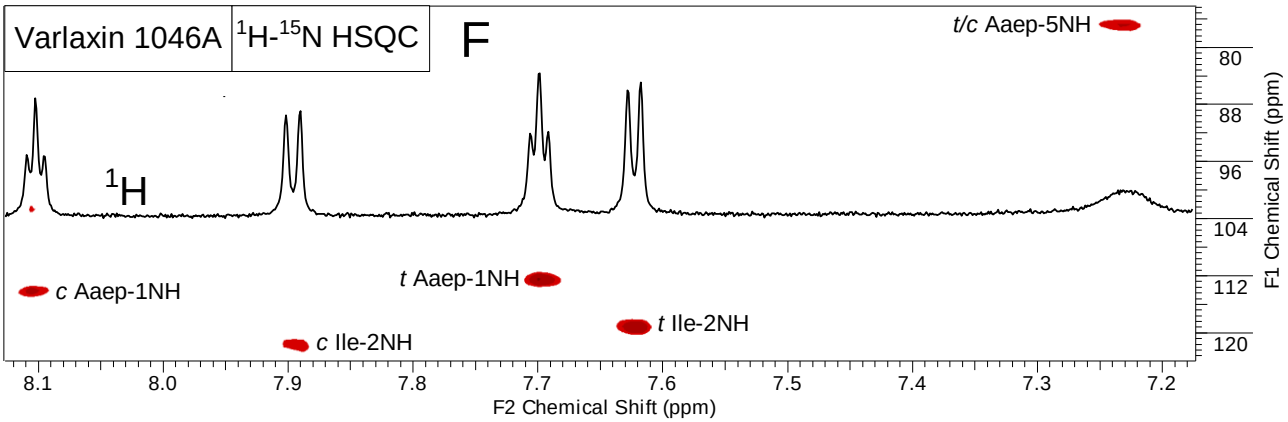

Varlaxin 1046A
^{13}C
B
Hpaa1/2
Glc
Hpaa1/2
D-Ile
L-Choi
Mgs
Aaep
c Hpaa1-1
t Hpaa1-1, t/c Hpaa2-1, t Choi-1
t/c Mgs-1, t/c Ile-1
t/c Hpaa1/2-6
t/c Aaep-5
t/c Aaep-3
c Hpaa1-4,4'
t Hpaa1-4,4'; c/t Hpaa2-4,4'
t/c Hpaa1/2-3
t/c Aaep-7
t Hpaa1-5,5'; t/c Hpaa2-5,5'
c Hpaa1-5,5'
t Glc-1
c Glc-1
t/c Mgs-2
t/c Glc-2, t/c Choi-6
t/c Glc-3, 4, 5
t Mgs-3
c Mgs-3
t/c Glc-6
t/c Choi-2
t Mgs-2-OCH$_3$
c Mgs-2-OCH$_3$
t/c Aaep-4, 6
t Ile-2, t Choi-7a
c Ile-2, c Choi-7a
From solvent
t/c Hpaa1/2-2
t Ile-3, c Aaep-1, t Aaep-1
c Ile-3, t Choi -3a
c Choi-3, 3a
t Choi-3, 7, c Choi-7
c Aaep-2
t/c Ile-4, t Choi-5
t/c Choi-4
c Ile-6
t Ile-6
t Ile-5
c Ile-5
Chemical Shift (ppm)

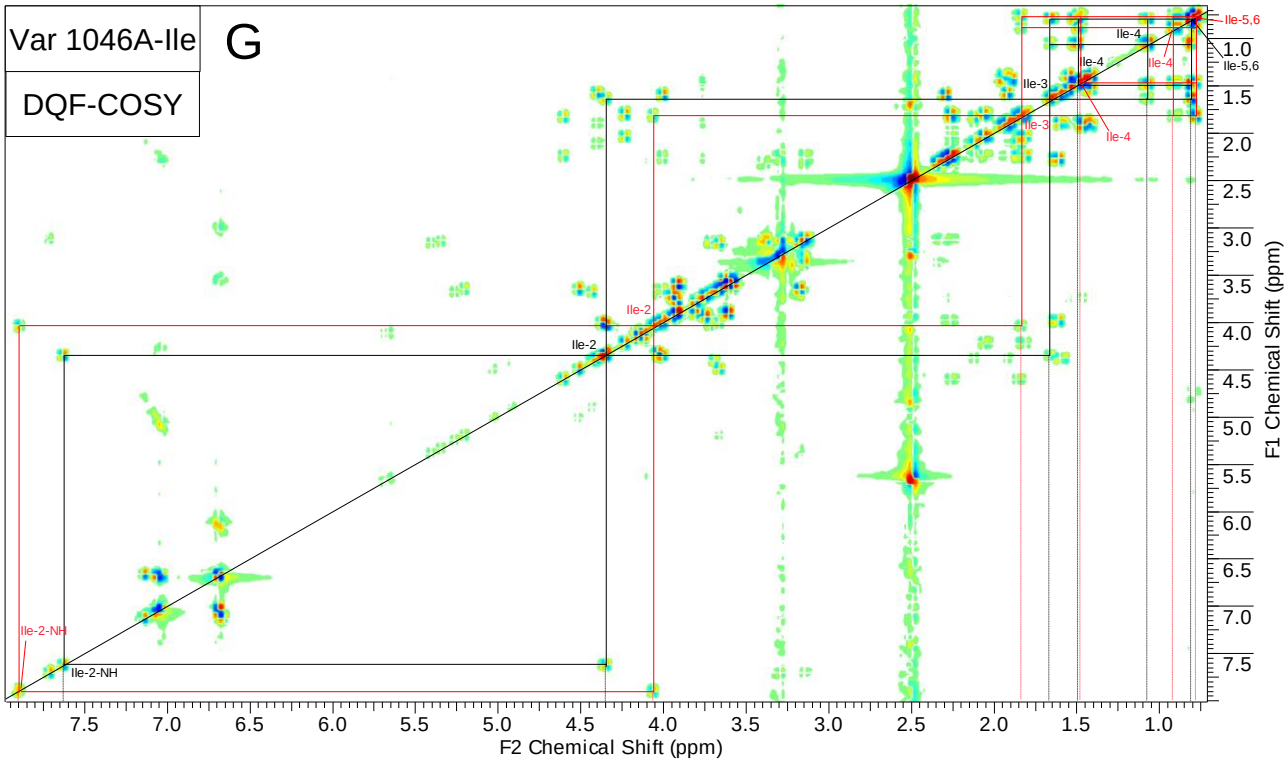

Varlaxin 1046A
^{1}H-^{13}C HSQC
C
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)
Hpaa1/2
Glc
D-Ile
L-Choi
Mgs
Aaep

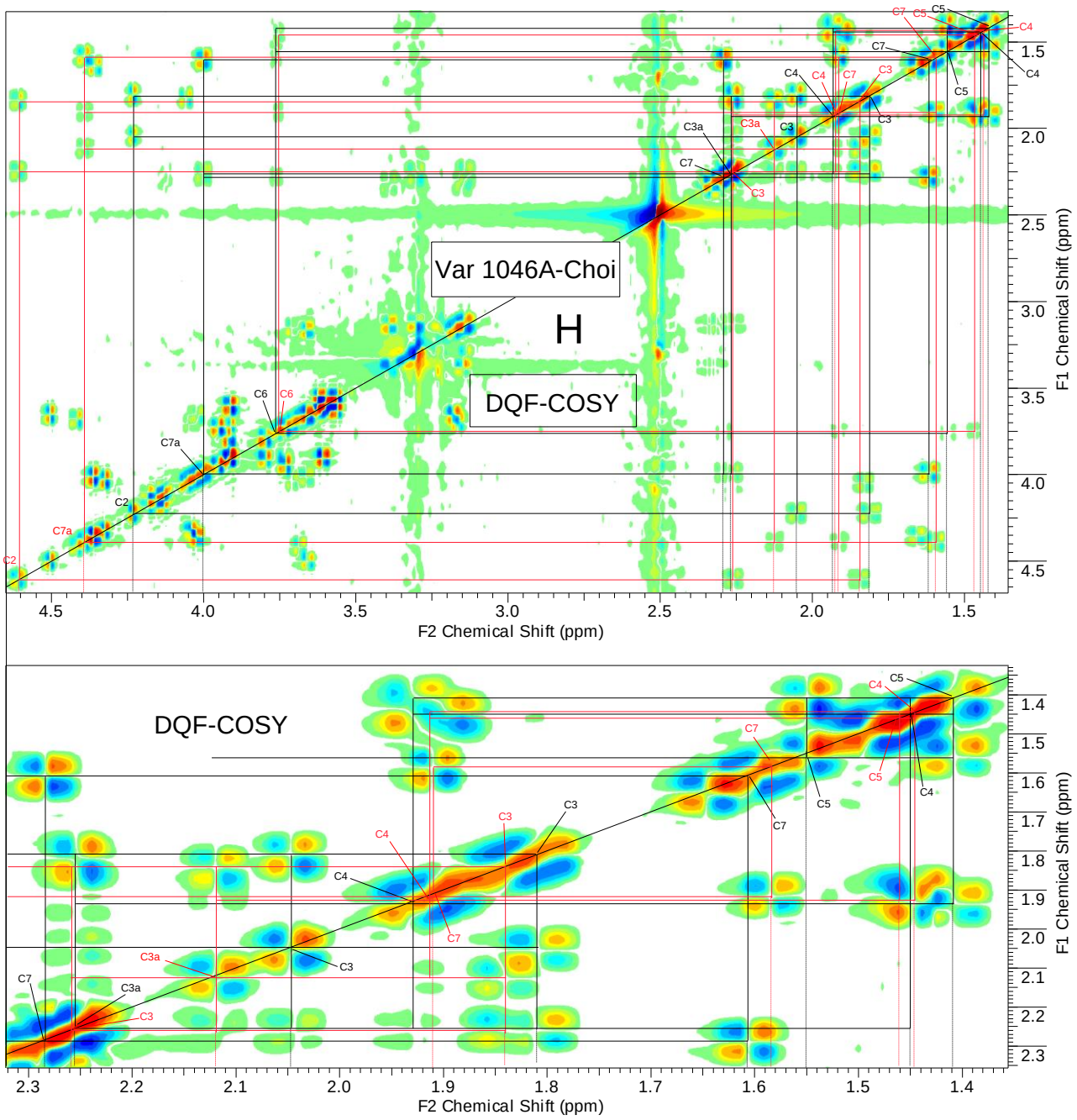

Varlaxin 1046A
^{1}H-^{13}C HMBC
D
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)
from solvent

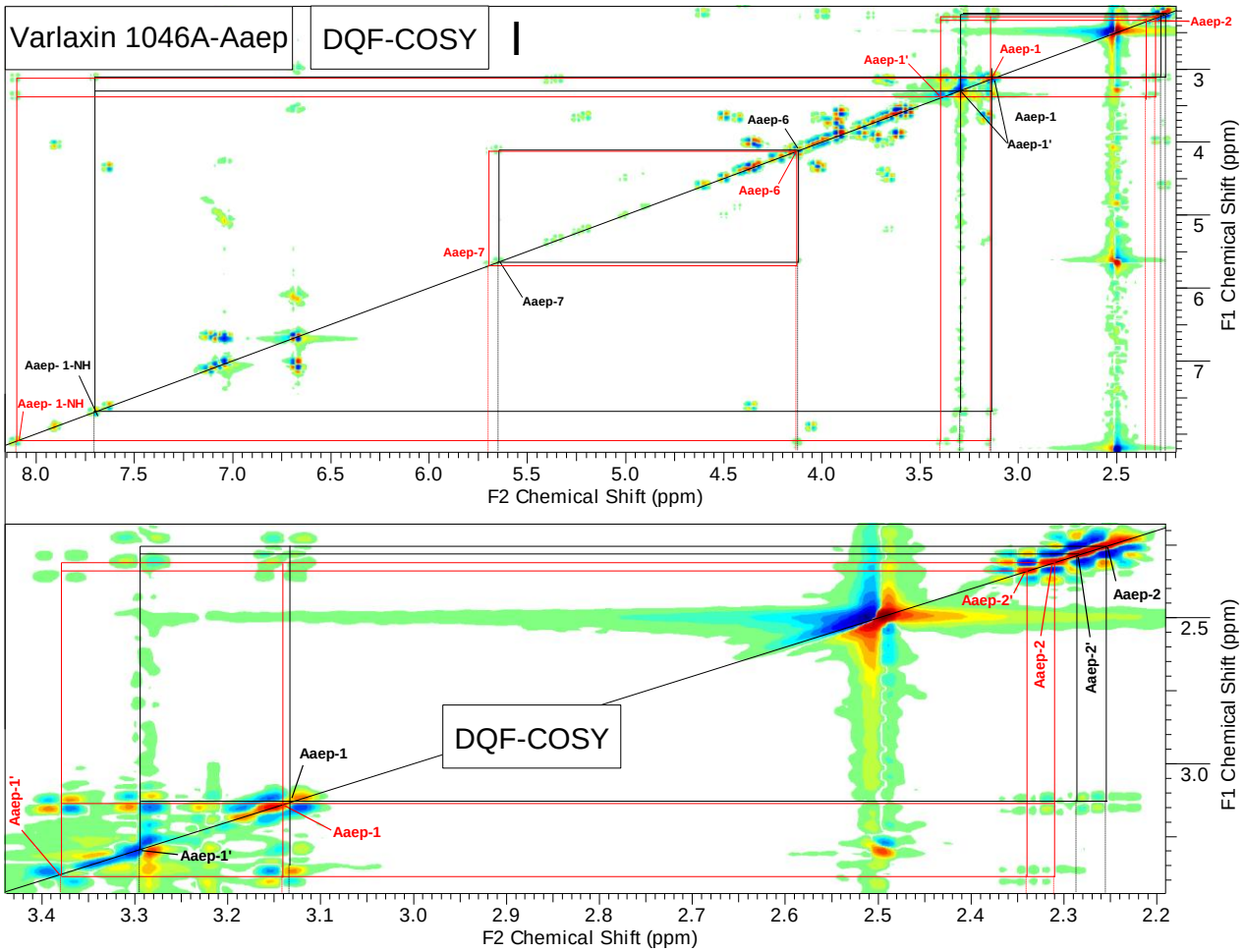

Varlaxin 1046A
^{1}H-^{13}C HMBC
E
t Mgs-1
c Mgs-1
t Ile-1
c Ile-1
c Aaep- 1-NH
c Ile- 2-NH
t Aaep- 1-NH
t Ile- 2-NH
t Ile-2
t Glc-6'
t Choi-2
c Ile-2
t Mgs-2,3'
c Mgs-3
t/c Glc-6
c Aaep-1'
t Aaep-1'
t/c Aaep-1
c Choi-3'
t Choi-3'
t Choi-1
t Hpaa1/2-1
c Hpaa2-1
c Hpaa1-1
c Choi-1
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

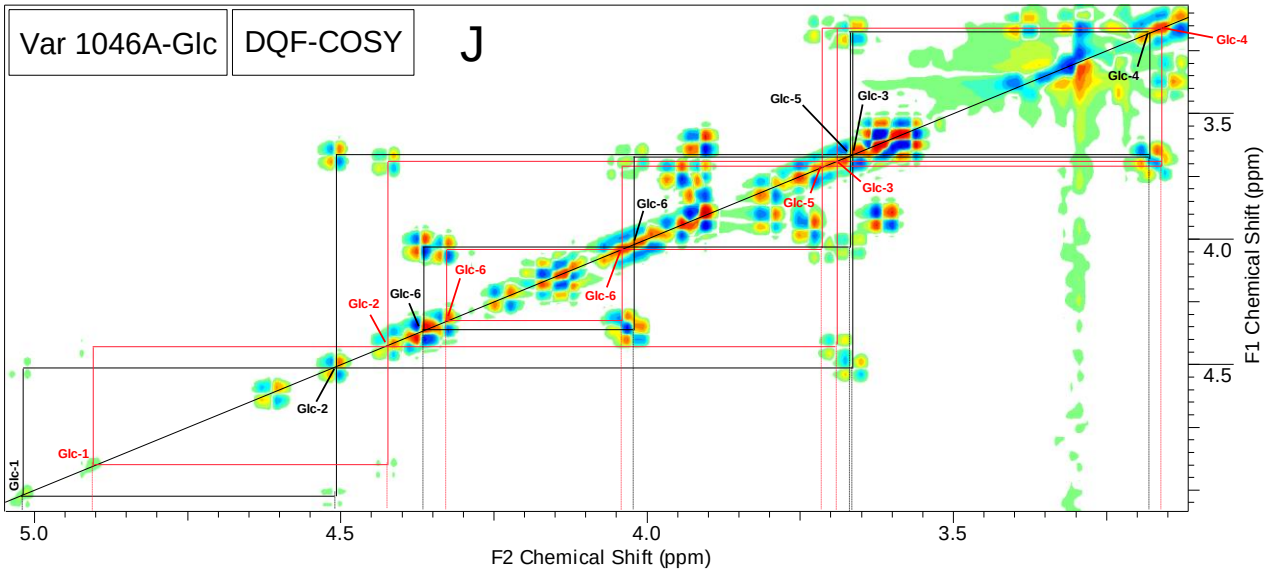

t Glc-6'
t Ile-2
c Glc-6'
t Choi-2
c Ile-2
c Glc-6
t Glc-6
t Mgs-3'
t Mgs-2, c Mgs-2, 3'
c Hpaa1-2'
c Mgs-3
t Mgs-3
t/c Hpaa1-2
t/c Hpaa2-2, 2'
c Aaep-1'
t Aaep-1'
c Aaep-1
t Aaep-1
t Mgs-1
c Mgs-1
t Ile-1
c Ile-1
t Choi-1
t Hpaa1/2-1
c Hpaa2-1
c Hpaa1-1
c Choi-1
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

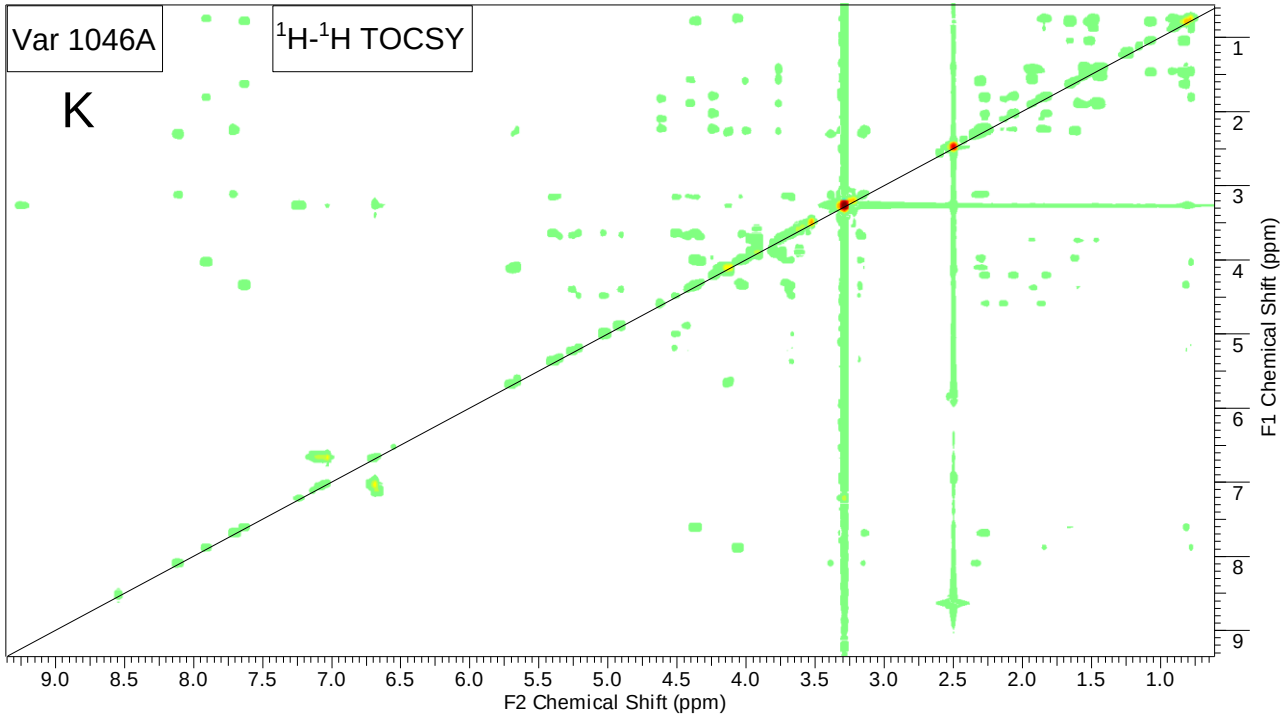

Varlaxin 1046A
^{1}H-^{15}N HSQC
F
^{1}H
t/c Aaep-5NH
c Aaep-1NH
t Aaep-1NH
t Ile-2NH
c Ile-2NH
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

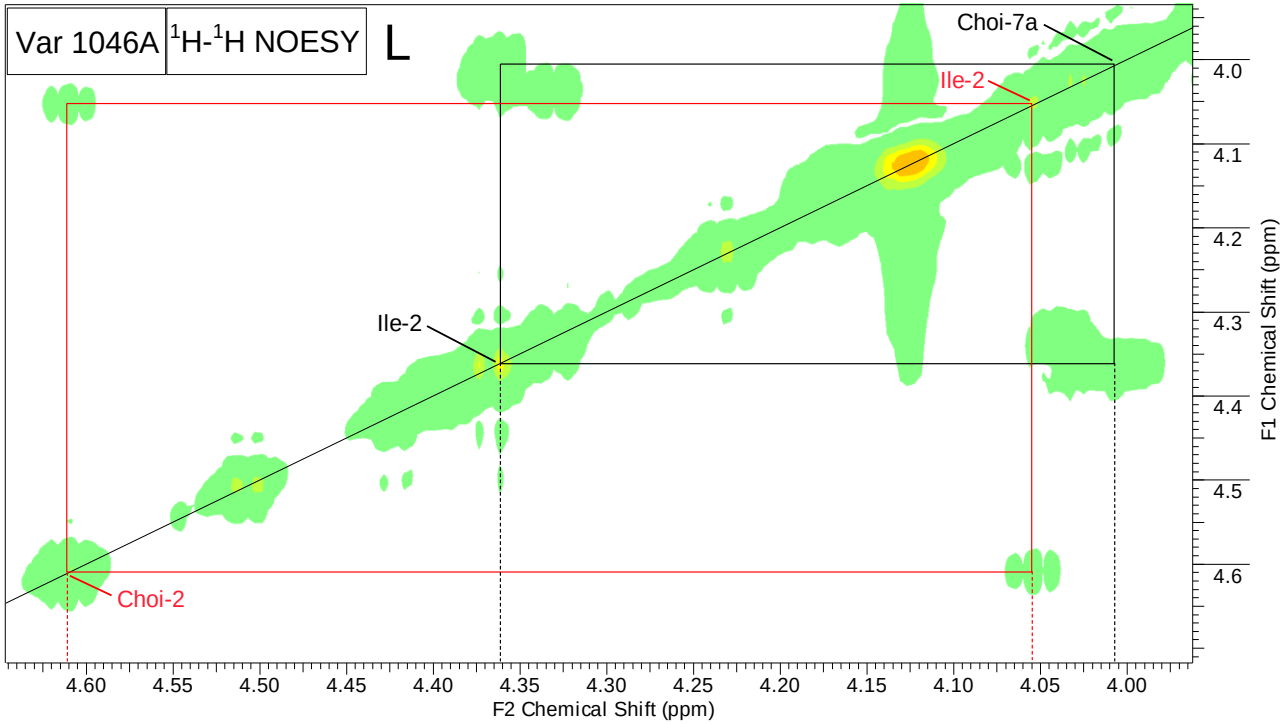

Var 1046A-Ile
DQF-COSY
G
Ile-5,6
Ile-4
Ile-4
Ile-4
Ile-3
Ile-3
Ile-4
Ile-2
Ile-2
Ile-2-NH
Ile-2-NH
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

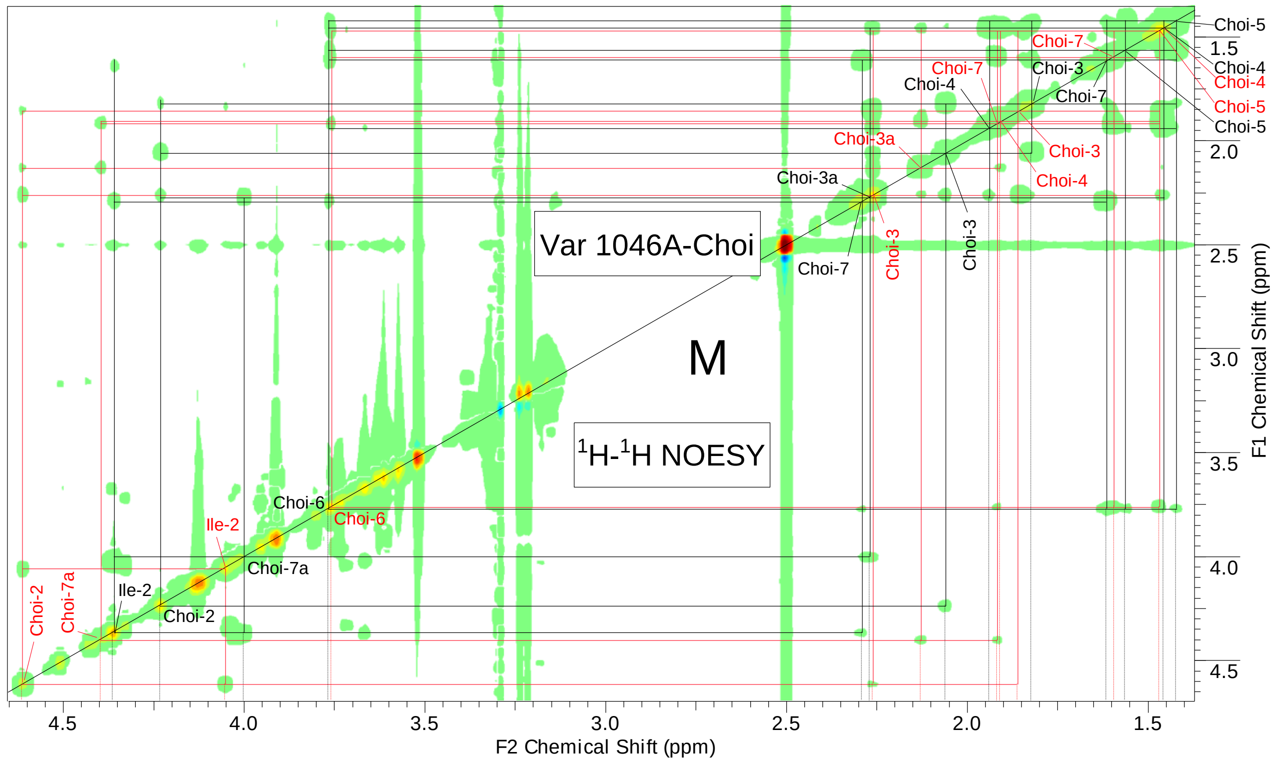

Var 1046A-Choi
H
DQF-COSY
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)
DQF-COSY
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)


Varlaxin 1046A-Aaep
DQF-COSY
I
Aaep-2
Aaep-1'
Aaep-1
Aaep-6
Aaep-7
Aaep- 1-NH
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)
DQF-COSY
Aaep-2'
Aaep-1
Aaep-1'

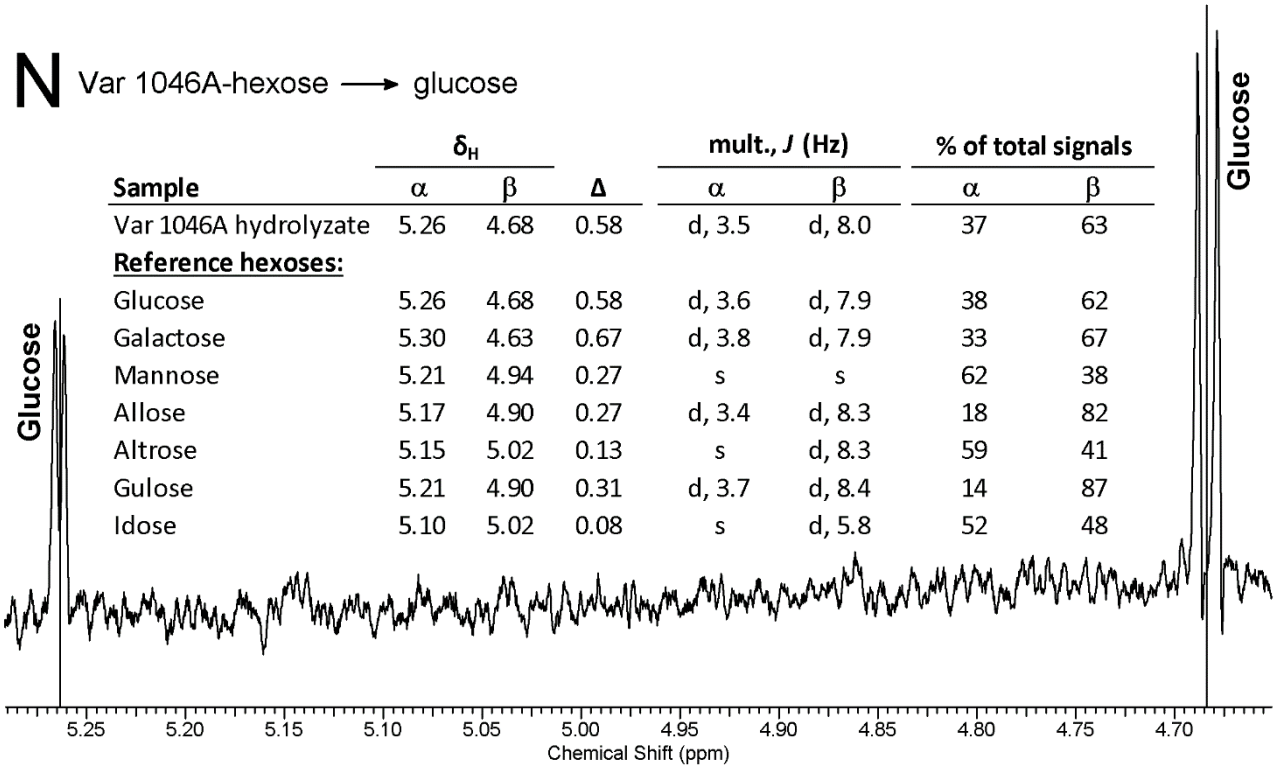

Var 1046A-Glc
DQF-COSY
J
Glc-4
Glc-5
Glc-3
Glc-6
Glc-2
Glc-1
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)


Var 1046A
^{1}H-^{1}H TOCSY
K
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)


Var 1046A
^{1}H-^{1}H NOESY
L
Choi-7a
Ile-2
Ile-2
Choi-2
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)



Var 1046A-Choi
M
^{1}H-^{1}H NOESY
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)
Choi-5
Choi-7
Choi-4
Choi-5
Choi-5
Choi-3
Choi-7
Choi-4
Choi-7
Choi-3
Choi-4
Choi-3a
Choi-3a
Choi-7
Choi-3
Choi-3
Choi-6
Choi-6
Ile-2
Choi-7a
Ile-2
Choi-2
Choi-2
Choi-7a



Sample	δ_H α	δ_H β	Δ	mult., *J* (Hz) α	mult., *J* (Hz) β	% of total signals α	% of total signals β
Var 1046A hydrolyzate	5.26	4.68	0.58	d, 3.5	d, 8.0	37	63
Reference hexoses:							
Glucose	5.26	4.68	0.58	d, 3.6	d, 7.9	38	62
Galactose	5.30	4.63	0.67	d, 3.8	d, 7.9	33	67
Mannose	5.21	4.94	0.27	s	s	62	38
Allose	5.17	4.90	0.27	d, 3.4	d, 8.3	18	82
Altrose	5.15	5.02	0.13	s	d, 8.3	59	41
Gulose	5.21	4.90	0.31	d, 3.7	d, 8.4	14	87
Idose	5.10	5.02	0.08	s	d, 5.8	52	48

Figure S8. 800 MHz NMR spectra of the varlaxin 1046A isolated from *Nostoc* sp. CENA543. A: ^{1}H, B: ^{1}H-^{13}C HSQC, D: ^{1}H-^{13}C HMBC, E: ^{1}H-^{13}C HMBC from the carbonyl region, F: ^{1}H-^{15}N HSQC, G-J: DQF-COSY of Ile, Choi, Aaep and glucopyranose (Glc), K: ^{1}H-^{1}H TOCSY, L: ^{1}H-^{1}H NOESY and M: ^{1}H-^{1}H NOESY of Choi. Trans correlations are in black and cis correlations in red. t/c = trans/cis, N: Partial ^{1}H spectra of Varlaxin 1046A acid hydrolysate in 2 M D_2SO_4 (in D_2O) showing the match of anomeric protons signals to reference compounds presented in the table which values are from Giner et al., J Nat Prod 2016, 79, 2413-2417.

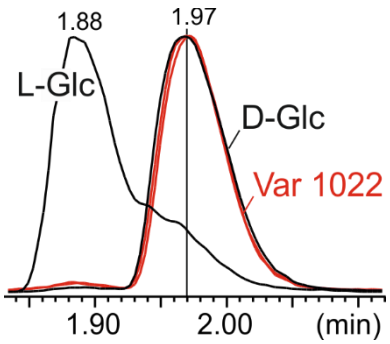


Figure S9. Monosaccharide D/L analysis of varlaxin 1022A . Ion chromatograms *m/z* 447.13 ([M+H]$^{+}$) of derivatized monosaccharide standards D- and L-Glc, and hydrolyzed varlaxin 1022A **.**

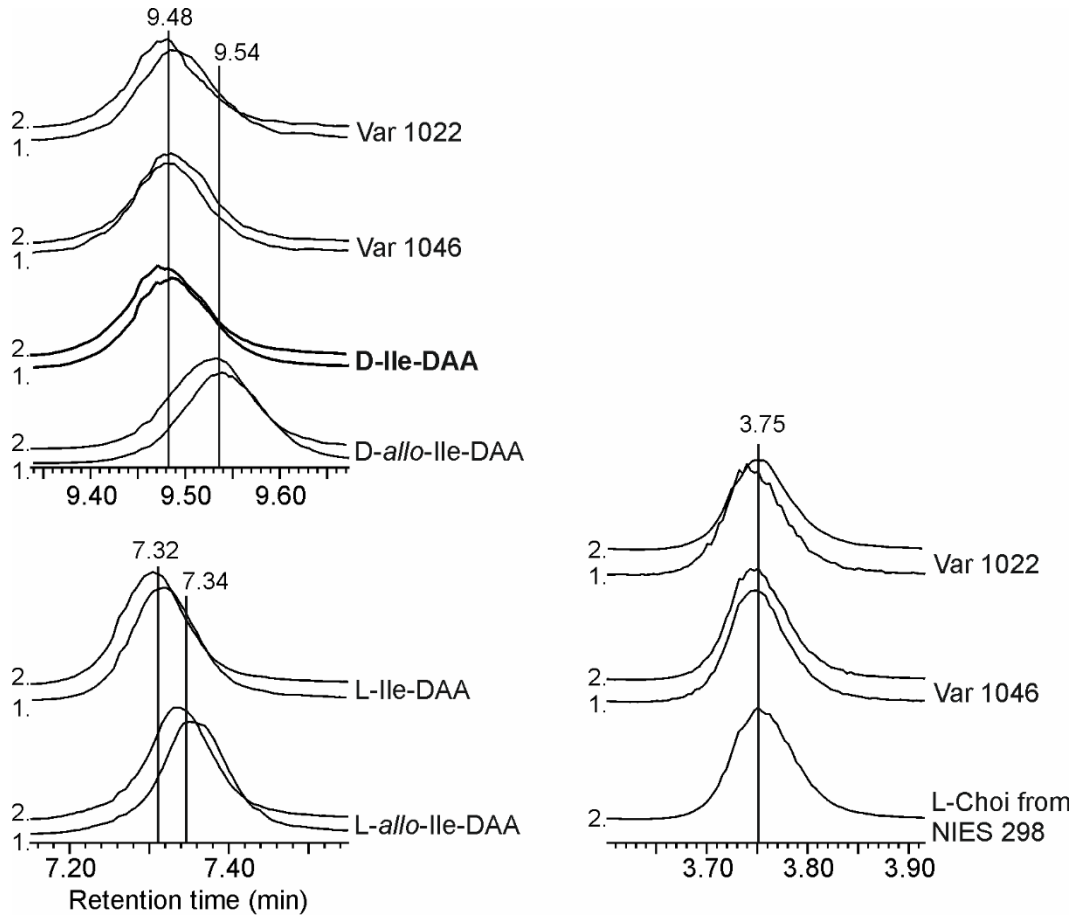


Figure S10. Amino acid analysis of varlaxins 1022A and 1046A . EIC's (*m/z* 384.15, $[M+H]^+$ of Ile-DAA, *m/z* 438.16, $[M+H]^+$ of Choi-DAA) of the DAA derivatives of the reference amino acids L-, D-, L-*allo*- and D-*allo*-Ile and L-Choi-DAA (from NIES 298) and acid hydrolyzates of purified varlaxins 1022A and 1046A . Chromatograms from 1. and 2. injections show some shifting but without effecting to the fact that in both varlaxins 1022A and 1046A Ile was in D- configuration and Choi was L-.