Supporting Information

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LC-HRMS Based Approach for Identification and Quantification Analysis of Chemical Constituents of Sea Cucumbers from Aegean Sea - Their Cytotoxic and Antiviral Potentials

Nazli Boke Sarikahya[1], Gaye Sumer Okkali[1], Deniz Gunay[2], Ahmet C. Goren[3], Furkan Ozan Coven[4] and Ayse Nalbantsoy[4]

[1]Department of Chemistry, Faculty of Science, Ege University, 35100 Bornova-Izmir, Türkiye
[2]Department of Aquaculture, Faculty of Fisheries, Ege University, 35100 Bornova-Izmir, Türkiye
[3]Department of Chemistry, Faculty of Basic Sciences, Gebze Technical University, Gebze, Kocaeli, Türkiye
[4]Department of Bioengineering, Faculty of Engineering, Ege University, 35100, Bornova, Izmir, Türkiye

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Figure S1: Collecting area of sea cucumbers

Table S1: Mass parameters and linear regression equation of compounds

Compounds	Molecule Formula	m/z	Ionization Mode	Linear	Linear Regression Equation	LOD/ LOQ	r^2	Recovery
Ascorbic acid	$C_6H_8O_6$	175.0248	Negative	0.5-10	y=0.00347x-0.00137	0.39/1.29	0.9988	96.2
Chlorogenic acid	$C_{16}H_{18}O_9$	353.0878	Negative	0.05-10	y=0.00817x+0.000163	0.02/0.06	0.9994	96.7
Fumaric acid	$C_4H_4O_4$	115.0037	Negative	0.1-10	y=0.00061x-0.0000329	0.05/0.17	0.9991	97.1
Orientin	$C_{21}H_{20}O_{11}$	447.0933	Negative	0.1-10	y=0.00757x+0.000347	0.01/0.03	0.9993	96.2
Caffeic acid	$C_9H_8O_4$	179.0350	Negative	0.3-10	y=0.0304x+0.00366	0.08/0.27	0.9993	94.5
Caffeine	$C_8H_{10}N_4O_2$	195.0877	Positive	0.05-7	y=0.122x+0.00366	0.01/0.03	0.9987	92.9
Luteolin-7-rutinoside	$C_{27}H_{30}O_{15}$	593.1512	Negative	0.1-10	y=0.00879x+0.000739	0.01/0.03	0.9988	93.0
Vanilic acid	$C_8H_8O_4$	167.0350	Negative	0.3-10	y=0.00133x+0.0003456	0.1/0.33	0.9997	98.7
Luteolin-7-glucoside	$C_{21}H_{20}O_{11}$	447.0933	Negative	0.1-7	y=0.0162x+0.00226	0.01/0.03	0.9961	96.3
Hyperoside	$C_{21}H_{20}O_{12}$	463.0882	Negative	0.05-10	y=0.0072x-0.00003096	0.01/0.03	0.9995	96.6
Apigenin-7-glucoside	$C_{21}H_{20}O_{10}$	431.0984	Negative	0.3-7	y=0.0246x+0.00306	0.01/0.03	0.9962	96.0
Salicylic acid	$C_7H_6O_3$	137.0244	Negative	0.3-10	y=0.0361x+0.00245	0.01/0.03	0.9982	92.9
Naringenin	$C_{15}H_{12}O_5$	271.0612	Negative	0.1-10	y=0.0281x+0.00182	0.01/0.03	0.9995	86.7
Luteolin	$C_{15}H_{10}O_6$	285.0405	Negative	0.1-10	y=0.117x+0.00848	0.01/0.03	0.9981	96.9
Nepetin	$C_{16}H_{12}O7$	315.0510	Negative	0.05-10	y=0.0853x+0.00269	0.01/0.03	0.9992	97.8
Apigenin	$C_{15}H_{10}O_5$	269.0456	Negative	0.3-10	y=0.104x+0.0199	0.01/0.03	0.9998	81.6
Sinensetin	$C_{20}H_{20}O_7$	373.1282	Positive	0.5-10	y=0.415x+0.0761	0.01/0.03	0.9967	93.3
CAPE	$C_{17}H_{16}O_4$	283.0976	Negative	0.3-7	y=0.255x+0.0477	0.01/0.03	0.9964	94.4
Chrysin	$C_{15}H_{10}O_4$	253.0506	Negative	0.05-7	y=0.0964x-0.0002622	0.01/0.03	0.999	87.9
Cephoside B	$C_{65}H_{106}O_{32}$	1397.659	Negative	0.25-5	y=0.03048x-0.003199	0.08/0.26	0.9988	102.8
Dipsacoside B	$C_{53}H_{86}O_{22}$	1075.568	Positive	0.5-10	y=0.003923x-0.0003301	0.15/0.5	0.9995	108.6
Saponin A	$C_{47}H_{76}O_{18}Na$	952.5002	Positive	0.5-10	y=0.02322x-0.001075	0.11/0.36	0.9995	106.4
Scoposide B	$C_{64}H_{104}O_{30}Na$	1351.654	Negative	0.1-2	y=0.08182x+0.0002178	0.02/0.08	0.9995	98.0
Saponin B	$C_{53}H_{87}O_{23}$	1090.557	Negative	0.2-5	y=0.03348x+-0.002113	0.22/0.73	0.9962	95.5
Aristatoside C	$C_{57}H_{92}O_{25}Na$	1175.585	Negative	0.5-10	y=0.01879x-0.002058	0.13/0.44	0.9994	92.9
Tormentic acid	$C_{30}H_{48}O_5$	511.3394	Positive	0.1-2	y=0.08359x+0.003066	0.03/0.11	0.9983	101.0
Balansoid A	$C_{52}H_{84}O_{20}Na$	1027.548	Negative	0.5-10	y=0.02999x-0.002864	0.19/0.62	0.998	102.3
Macranthoside A	$C_{47}H_{76}O_{17}$	935.4975	Positive	0.5-10	y=0.05647x-0.004836	0.09/0.29	0.9996	102.7
Dipsacus saponin A	$C_{42}H_{69}O_{14}$	796.4615	Negative	0.5-10	y=0.06377x-0.01101	0.2/0.67	0.998	109.4
Pomolic acid	$C_{30}H_{48}O_4$	511.3394	Positive	0.5-10	y=0.005607x-0.001334	0.17/0.56	0.9995	100.9

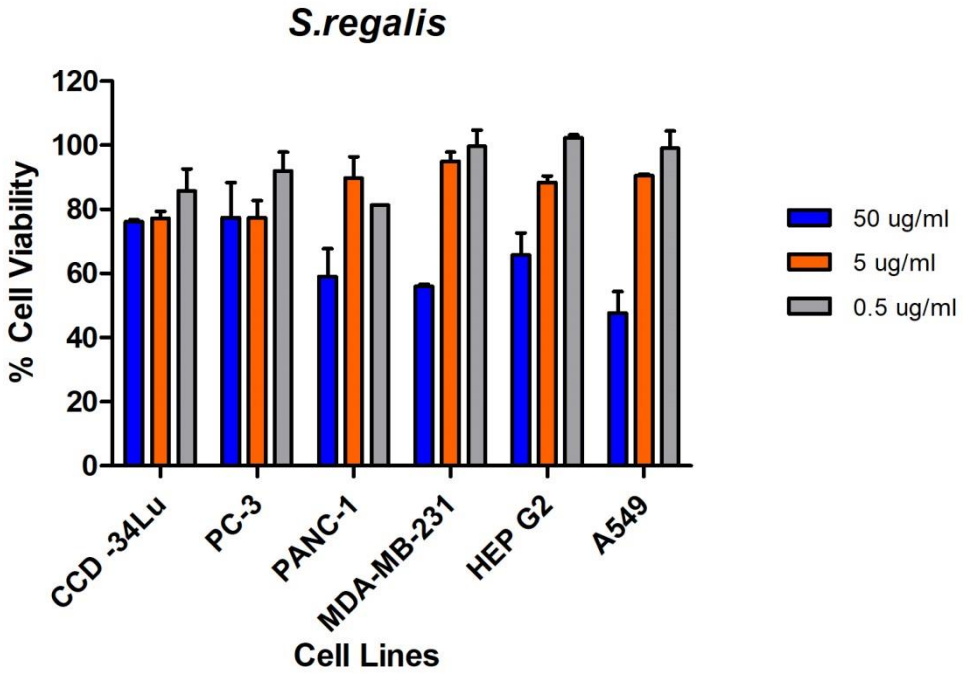

Figure S2: Viability of *S. regalis* against the cell lines.

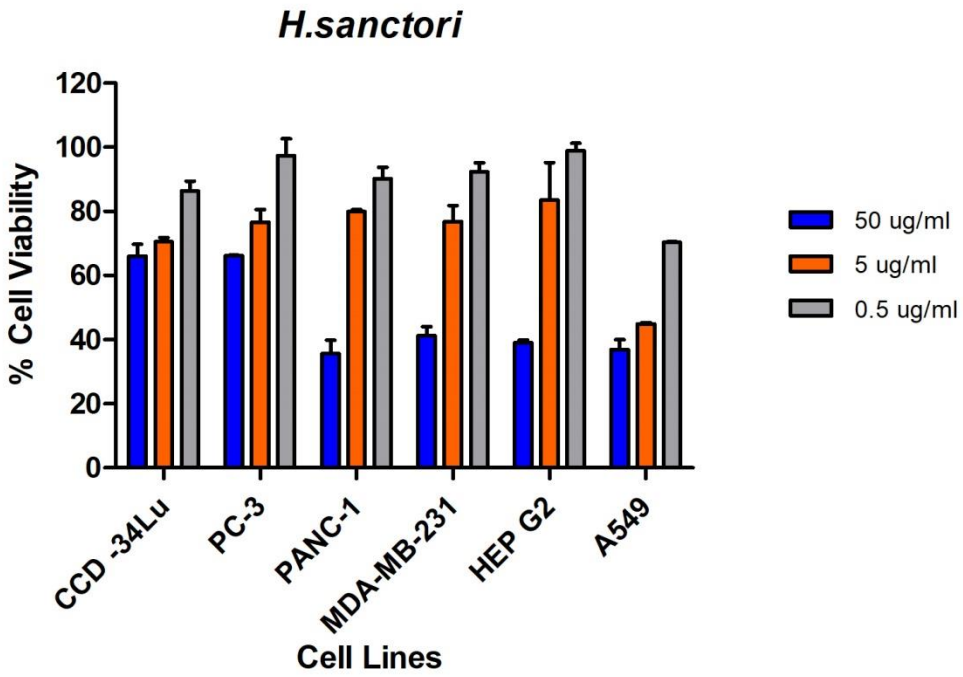

Figure S3: Viability of *H. sanctori* against the cell lines.

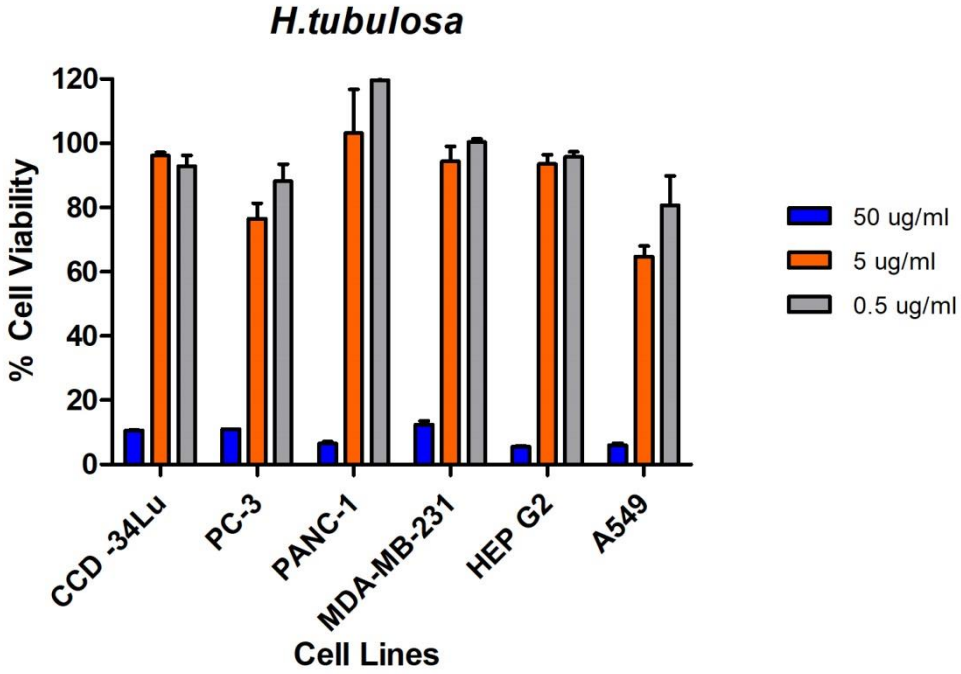

Figure S4: Viability of *H. tubulosa* against the cell lines

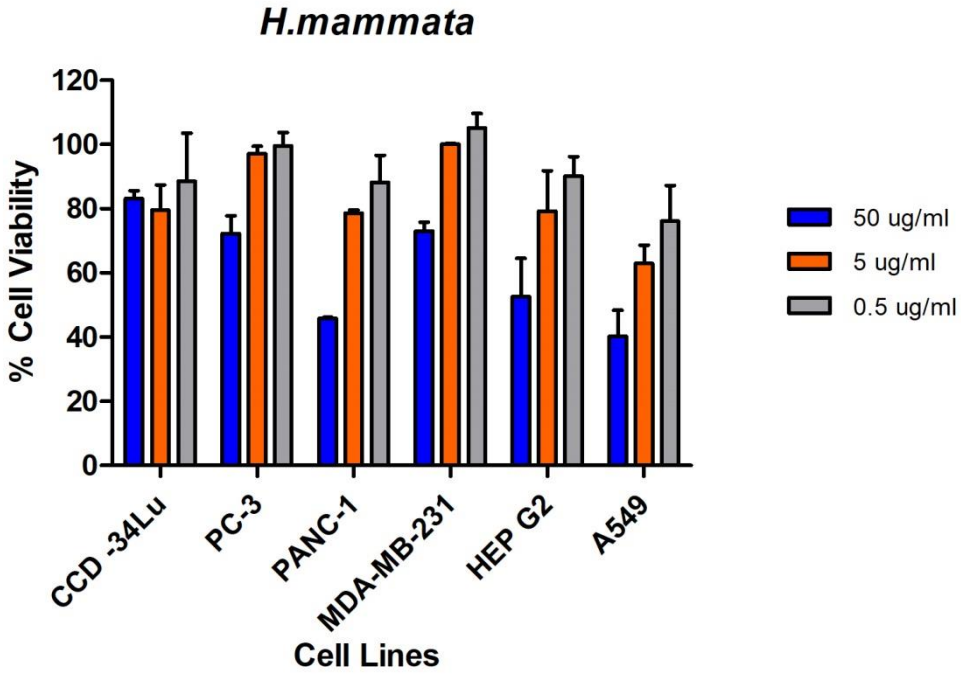

Figure S5: Viability of *H. mammata* against the cell lines

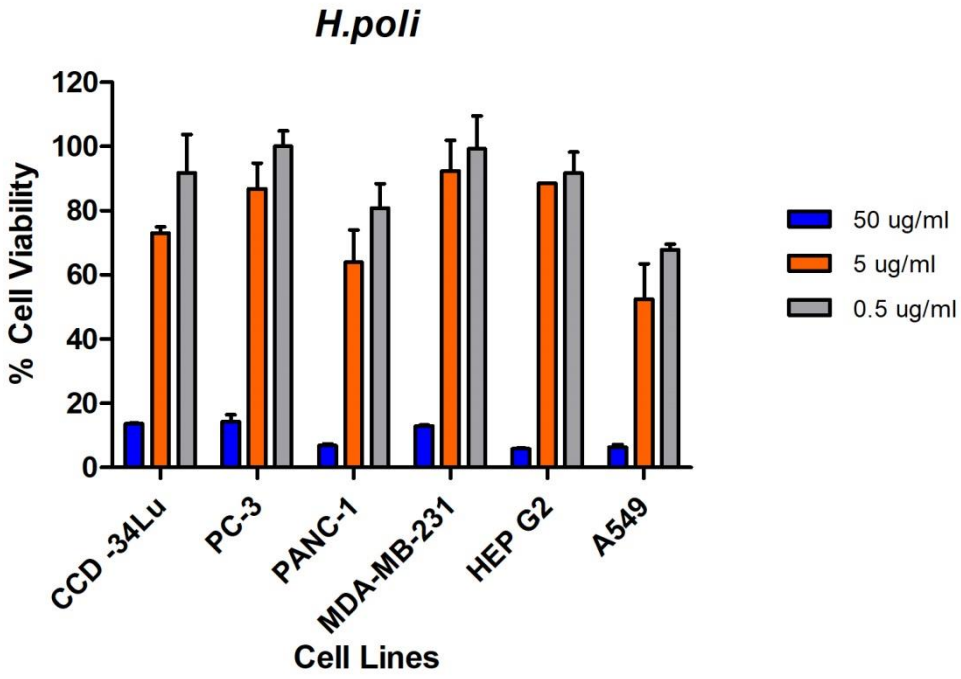

Figure S6: Viability of *H. poli* against the cell lines

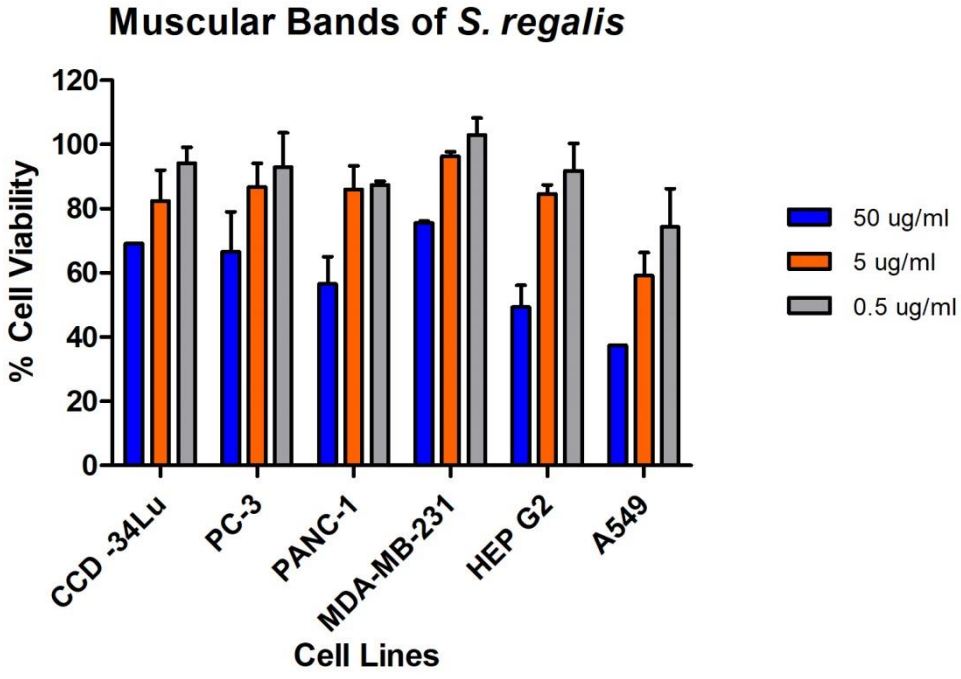

Figure S7: Viability of muscular bands of *S. regalis* against the cell lines

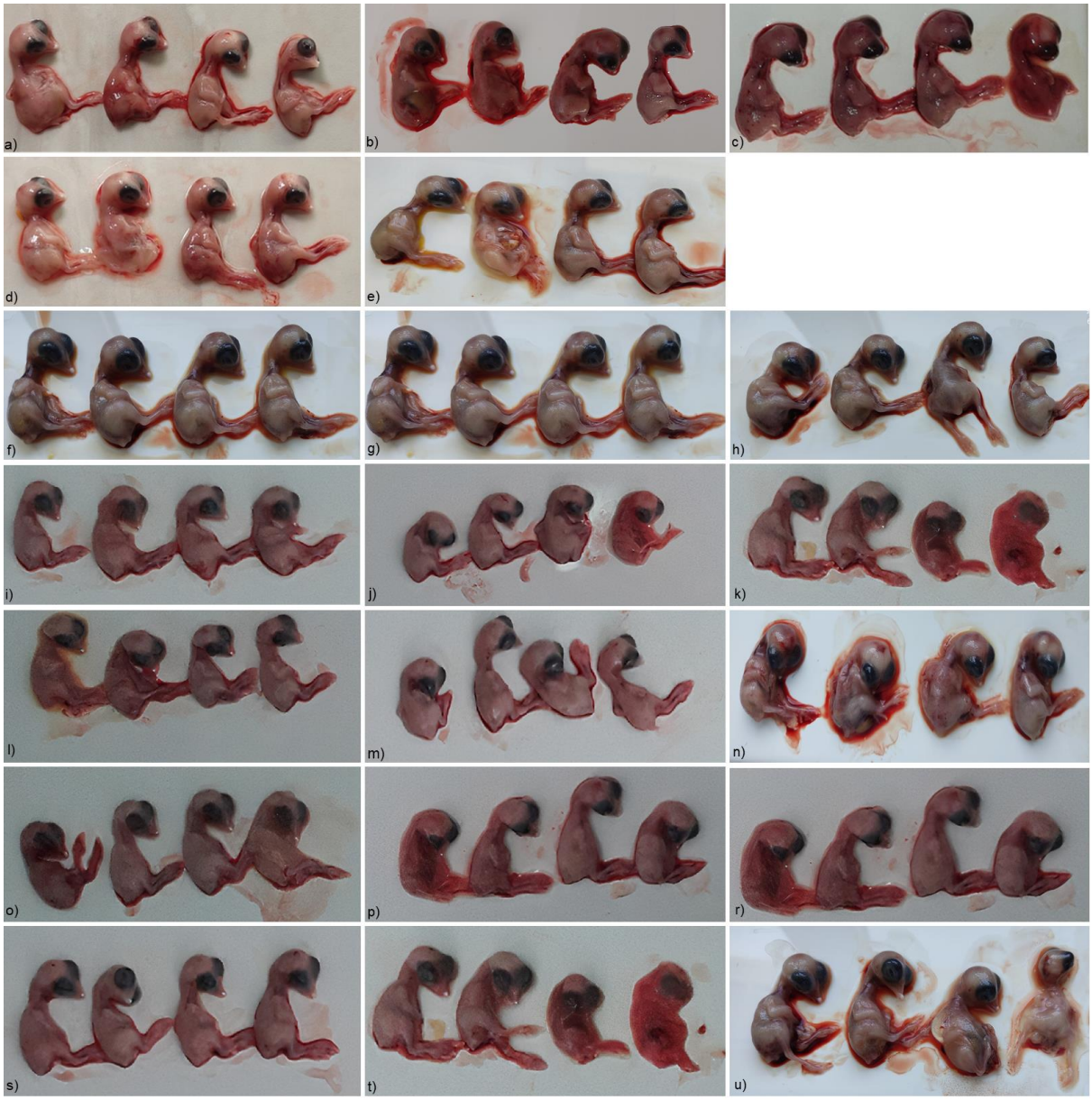

Figure S8: Embryos after 48h incubation with sea cucumber-IBV mixture a) Negative untreated SPF-ECE control b) Negative control, only virus c) Negative vehicle control, treated with %5 DMSO d) Positive antiviral drug control, Favipiravir 10 µg/g e) Positive antiviral drug control, Favipiravir 25 µg/g, f) *S.regalis* sample, 0.01 µg/g, g) *S.regalis* sample, 1 µg/g, h) *S.regalis* sample, 5 µg/g, i) *H.sanctori* sample, 0.01 µg/g, j) *H.sanctori* sample, 1 µg/g, k) *H.sanctori* sample, 5 µg/g, l) *H.tubulosa* sample, 0.01 µg/g, m) *H.tubulosa* sample, 1 µg/g, n) *H.tubulosa* sample, 5 µg/g, o) *H.mammata* sample, 0.01 µg/g, p) *H.mammata* sample, 1 µg/g, r) *H.mammata* sample, 5 µg/g, s) *H.poli* sample, 0.01 µg/g, t) *H.poli* sample, 1 µg/g, u) *H.poli* sample, 5 µg/g.

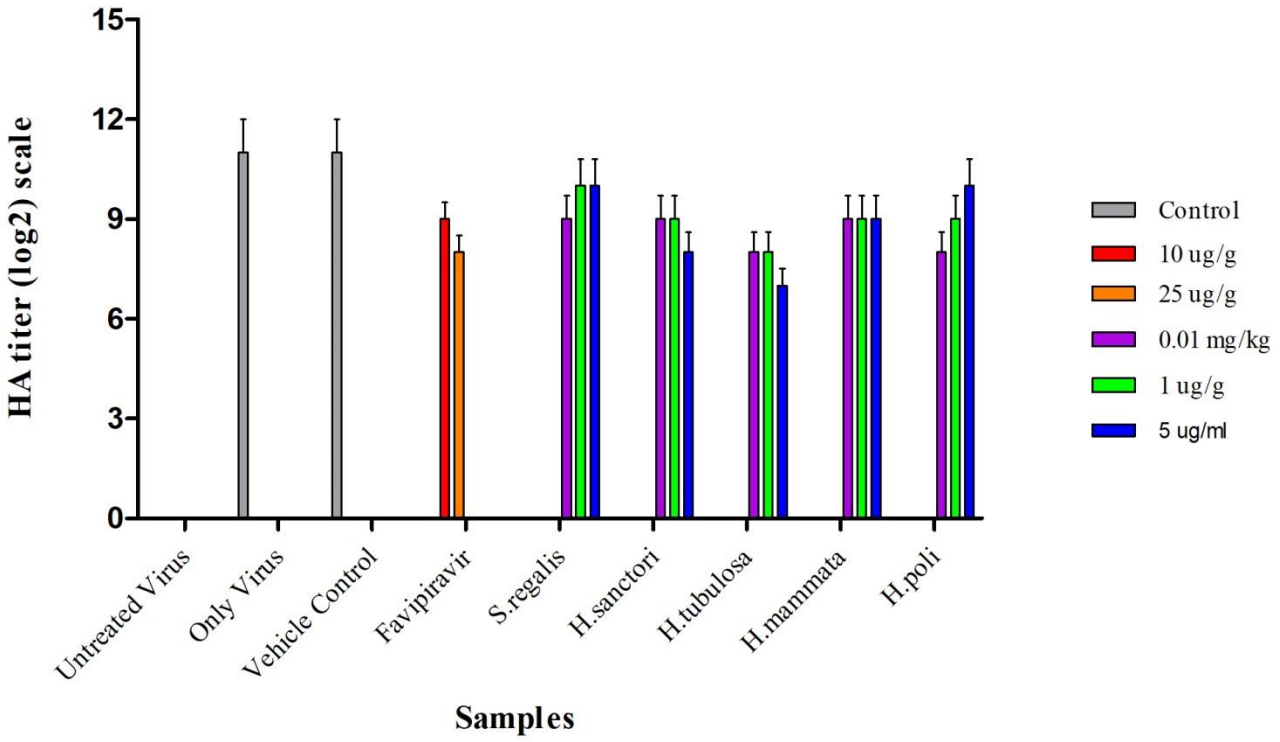

Figure S9: HA titers of SPF-ECE after 1h incubation with IBV-sea cucumber and IBV-favipiravir mixture samples

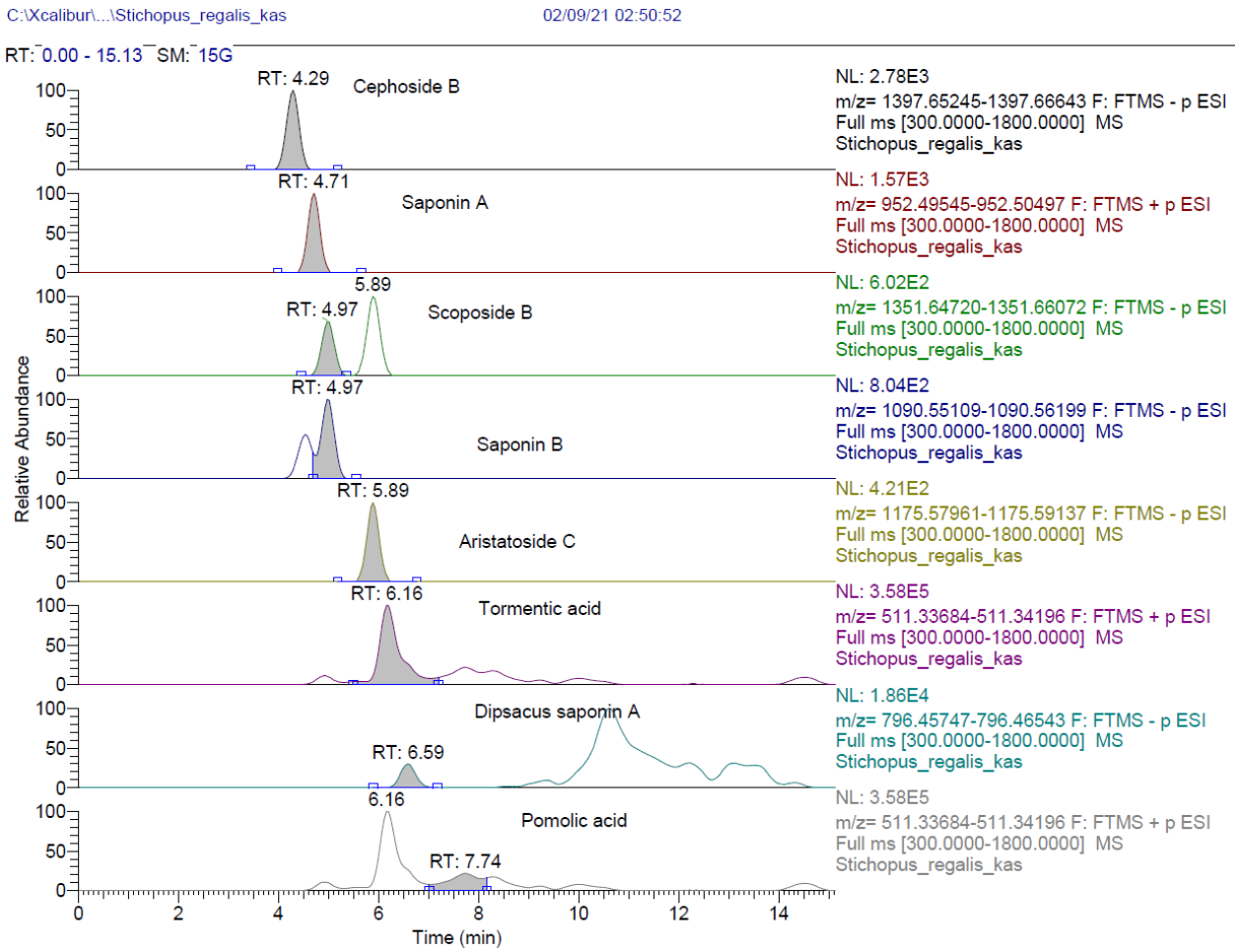

Figure S10: LC-HRMS chromatogram of *n*-butanol extract of *S. regalis*

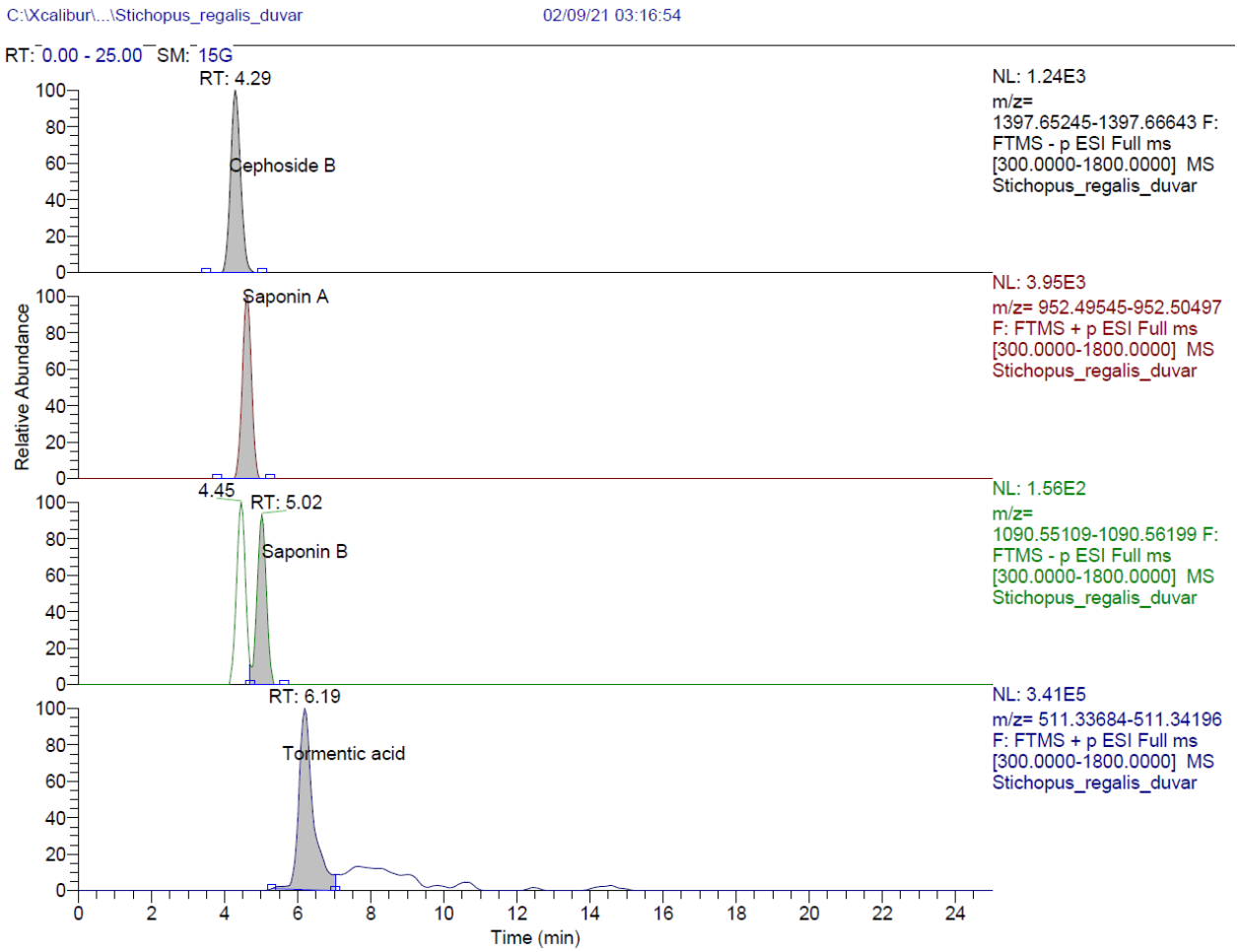

Figure S11: LC-HRMS chromatogram of *n*-butanol extract of muscular bands on *S. regalis*

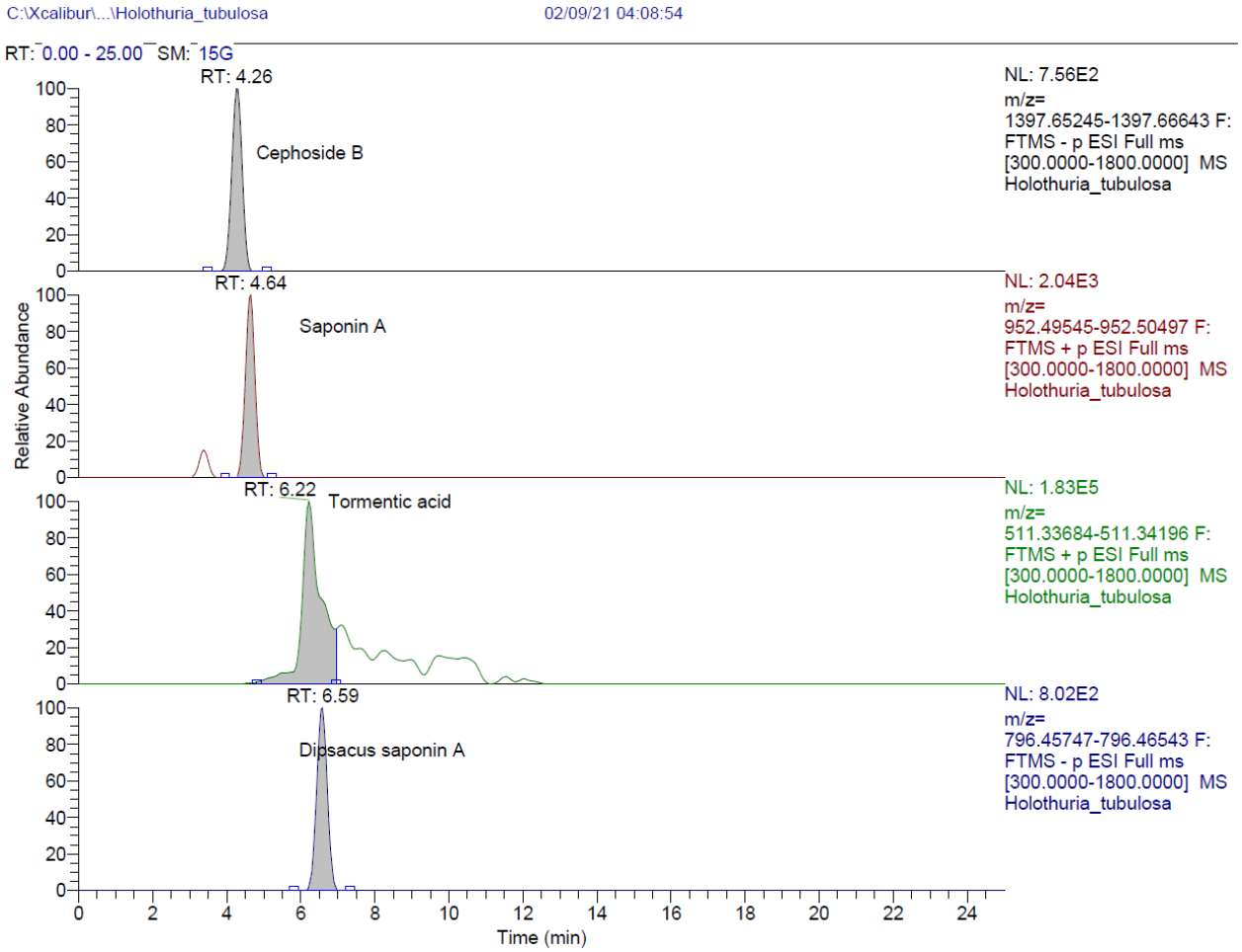

Figure S12: LC-HRMS chromatogram of *n*-butanol extract of *H. tubulosa*

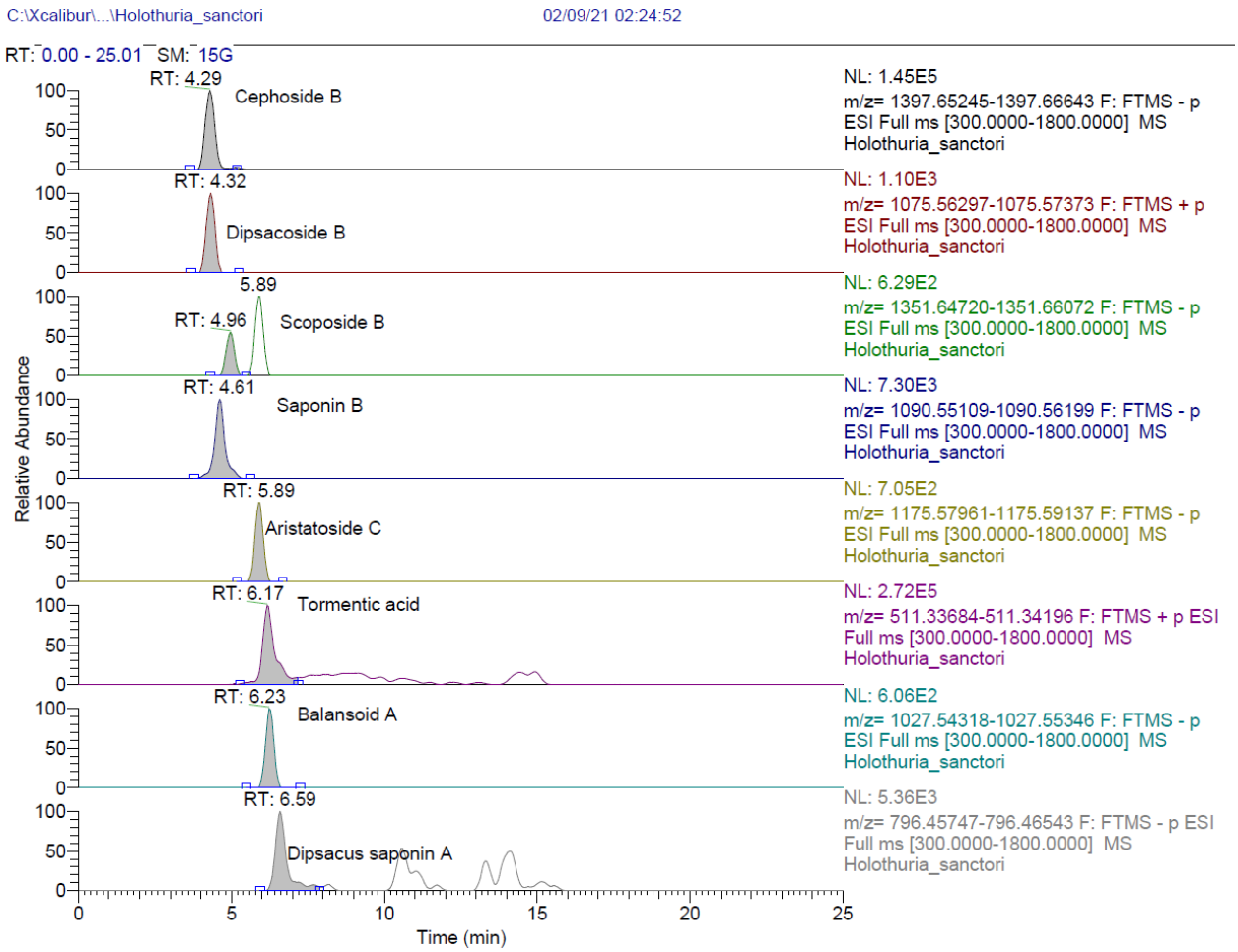

Figure S13: LC-HRMS chromatogram of *n*-butanol extract of *H. sanctori*

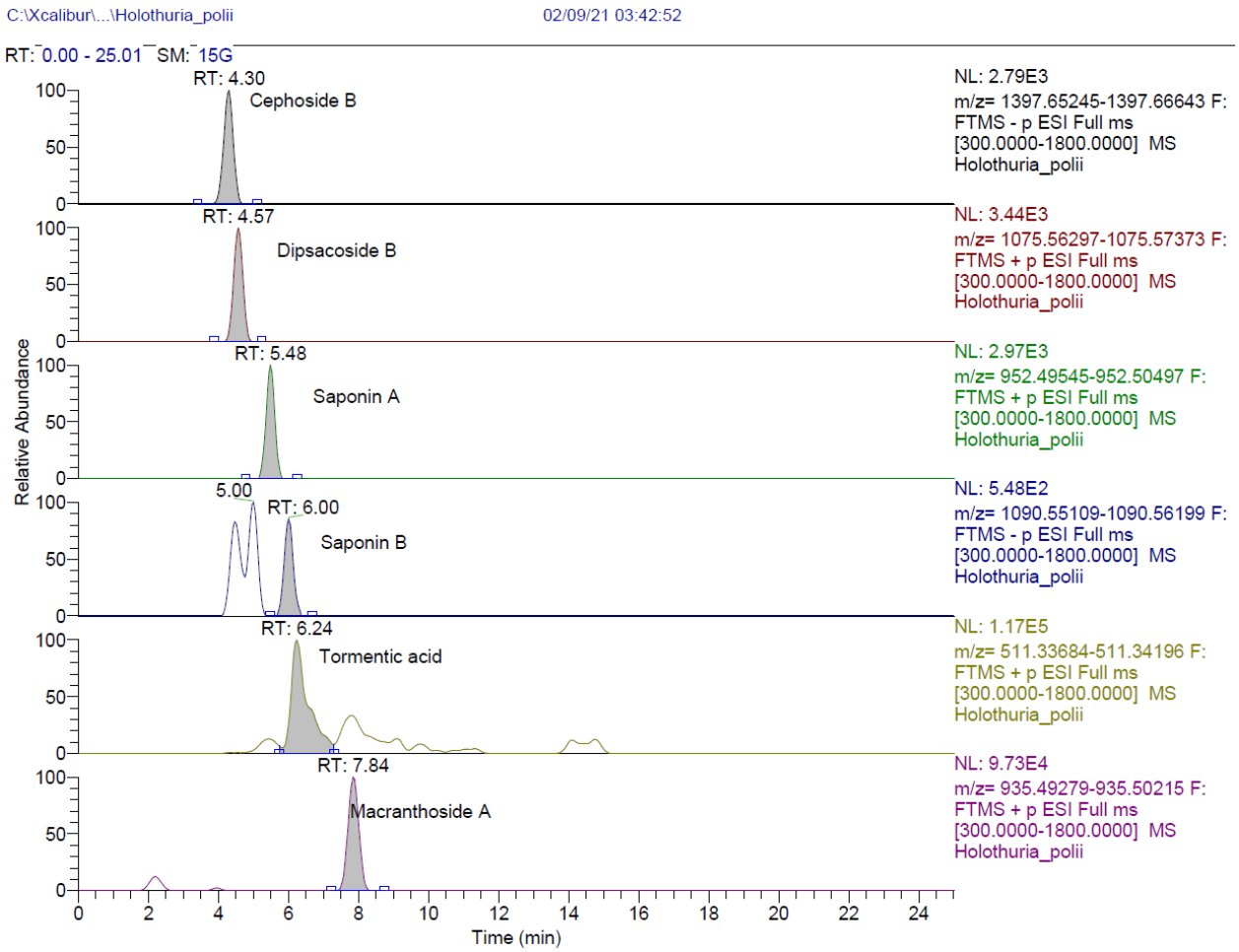

Figure S14: LC-HRMS chromatogram of *n*-butanol extract of *H. poli*

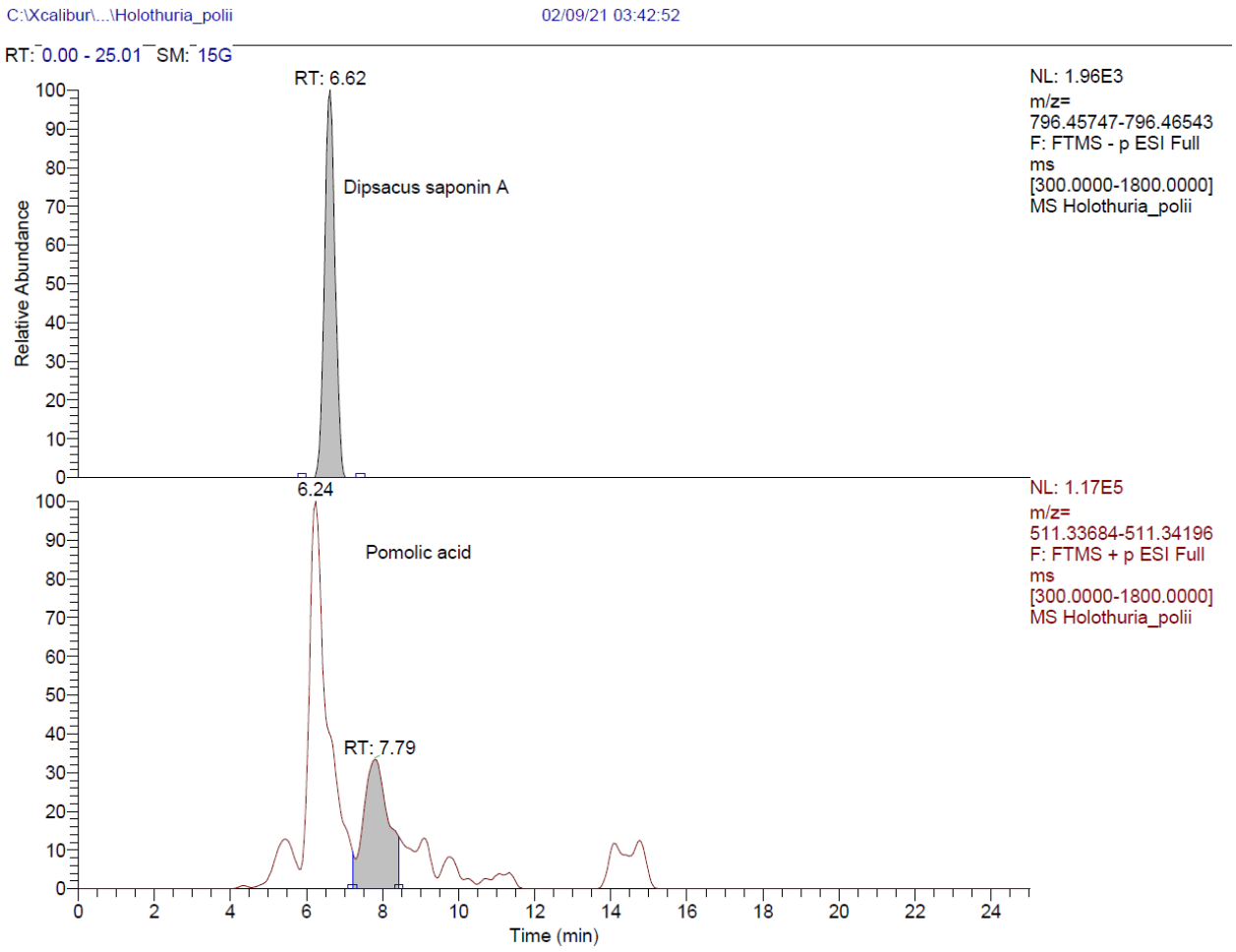

Figure S15: LC-HRMS chromatogram of *n*-butanol extract of *H. poli*

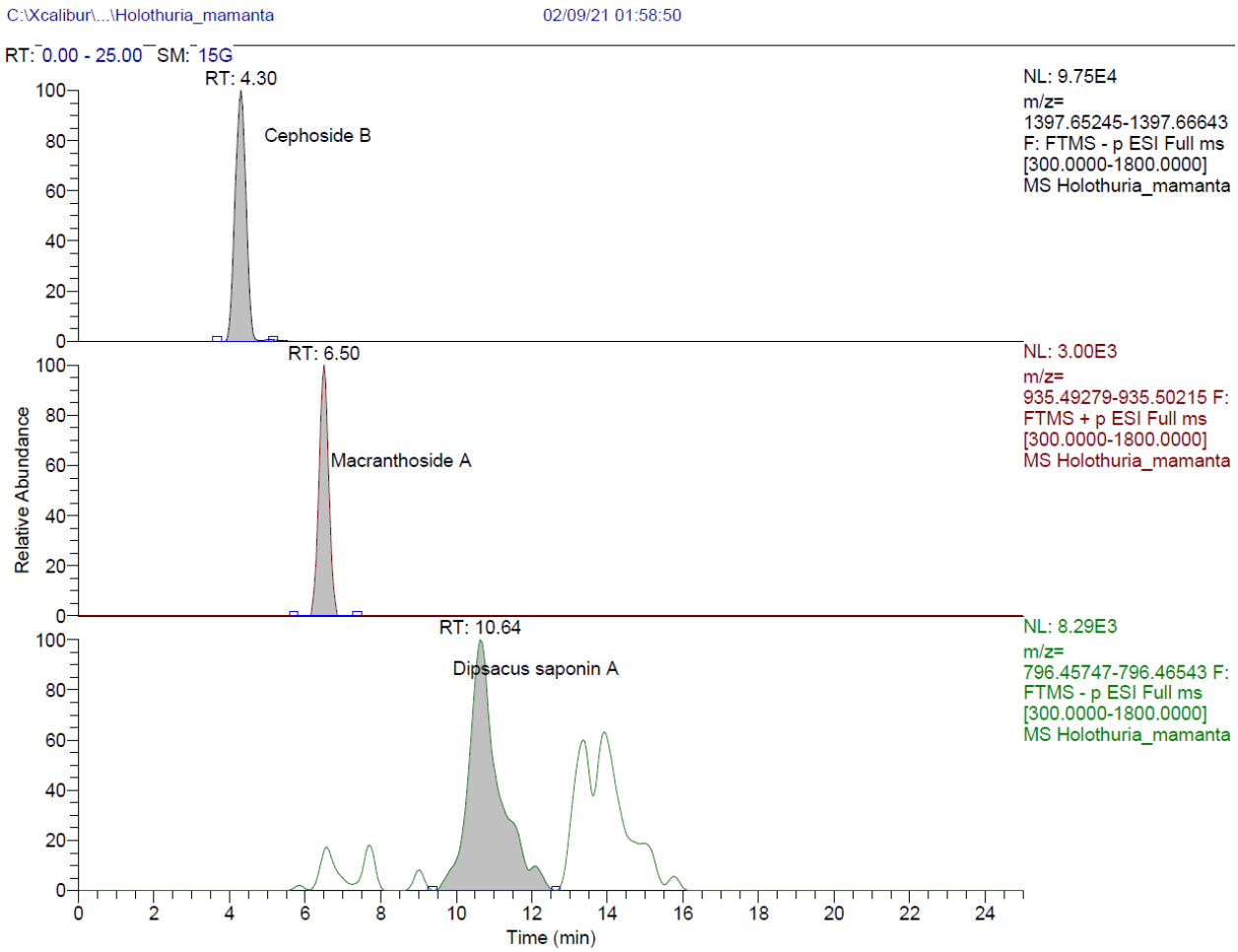

Figure S16: LC-HRMS chromatogram of *n*-butanol extract of *H. mammata*

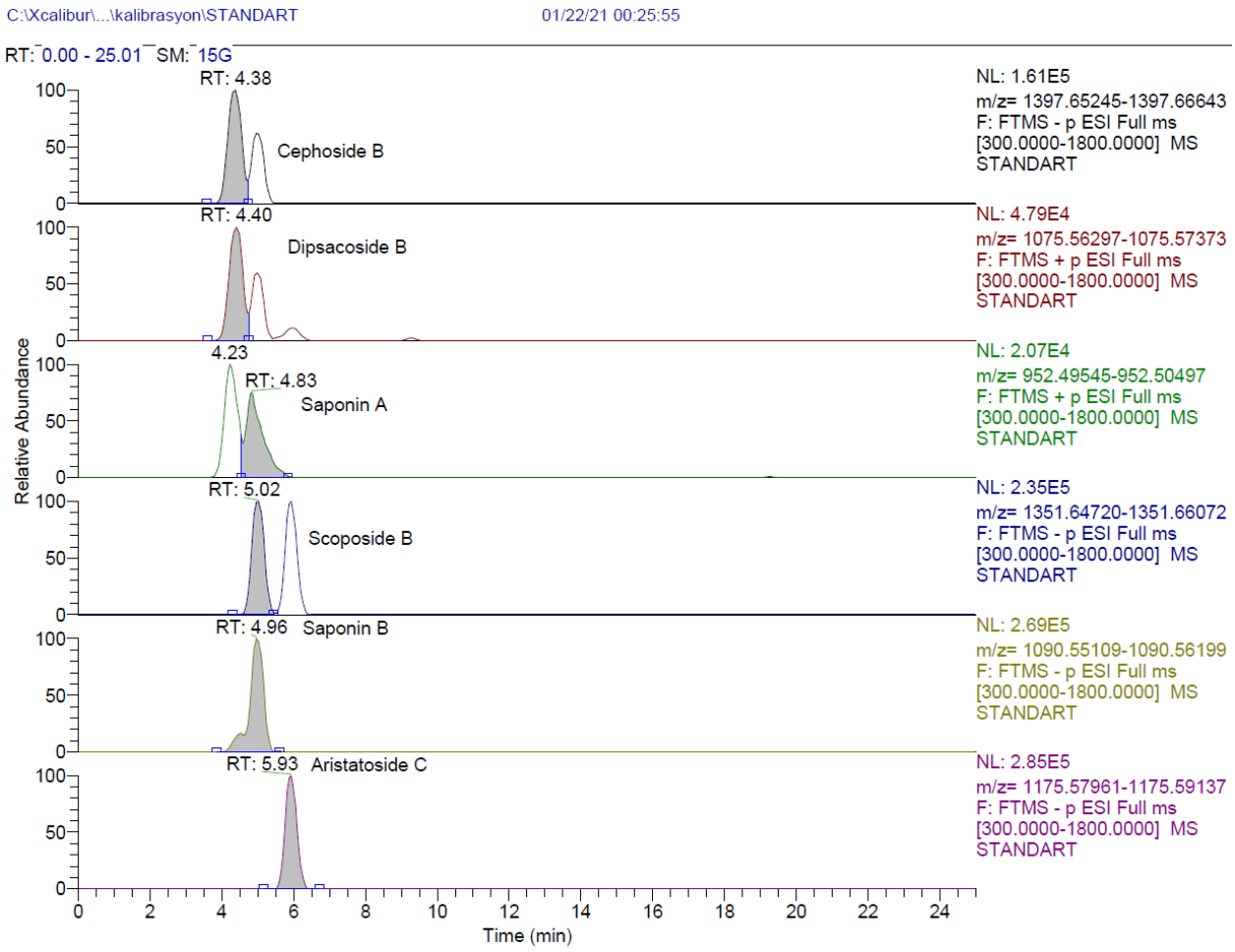

Figure S17: LC-HRMS chromatogram of standard mixture

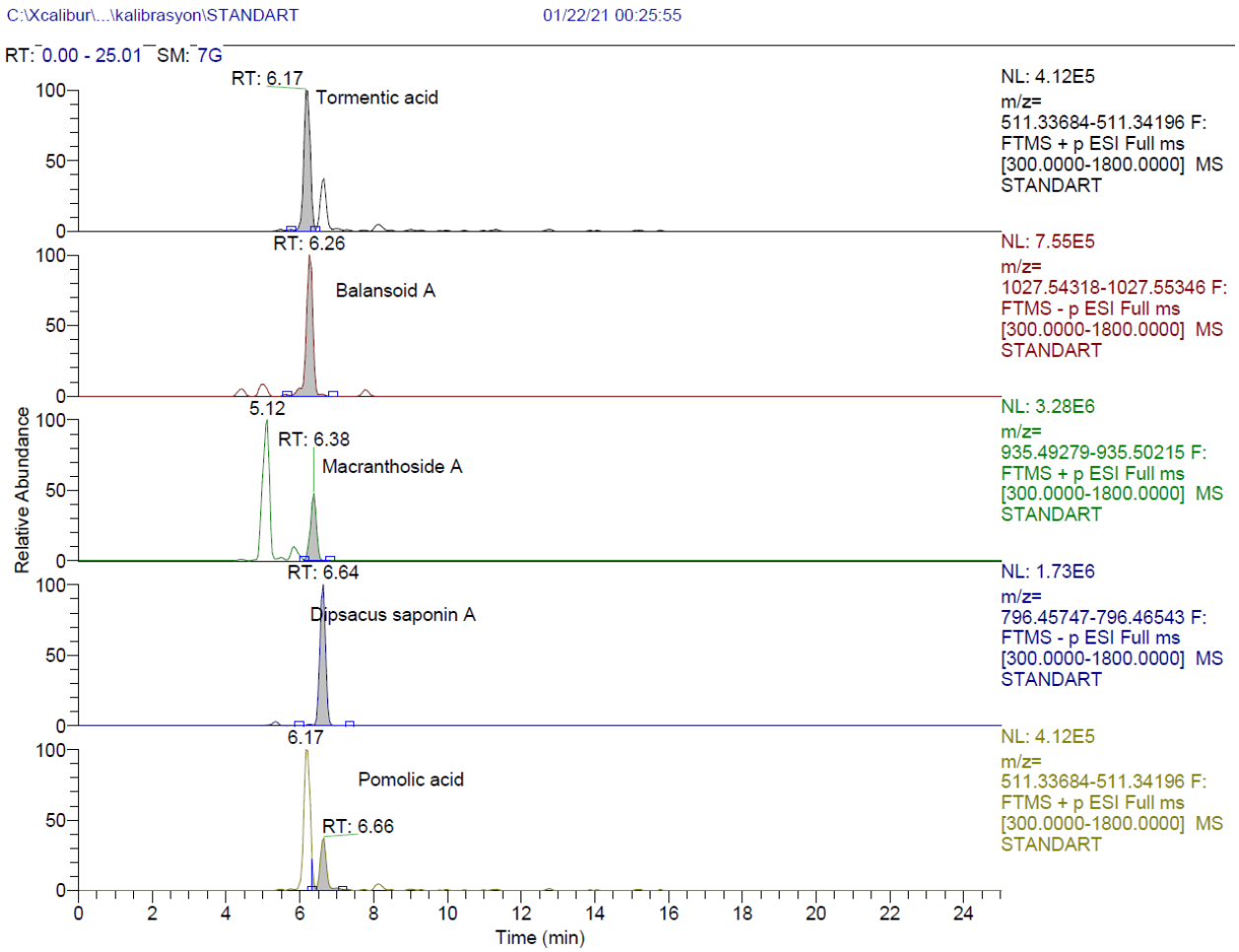

Figure S18: LC-HRMS chromatogram of standard mixture