Supplemental material to

Aqueous extracts of lingonberry and blackberry leaves identified by high-content screening beneficially act on cholesterol metabolism.

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Table S1. Screening results for top-extracts. Extracts giving positive results in both screening rounds are displayed. SRE-activity is given as mean from both screening rounds. For methodological details, see main manuscript.

rank	systematic name	common name	SRE-activity
1	Vaccinium vitis-idaea	lingonberry	3,16
2	Poterium spinosum	thorny burnet	2,73
3	Anagallis arvensis	scarlet pimpernel	2,55
4	Chondrodendron tomentosum	pareira	2,51
5	Peumus boldus	boldo	2,42
6	Agrimonia	agrimony	2,29
7	Sarsaparillae	sarsaparilla	2,15
8	Myrtus communis	myrtle	2,14
9	Viburnum prunifolium	blackhaw, blackhaw viburnum, sweet haw, stag bush	2,03
10	Cusparia febrifuga	angostura	2,02
11	Daucus carota	carrot	2,00
12	Rubus fructicosus	blackberry	1,78
13	Satureja hortensis	summer savory	1,75
14	Pyrus	pear	1,75
15	Aronia × prunifolia	purple chokeberry	1,69
16	Tussilago farfara	coltsfoot	1,67
17	Allium sativum	garlic	1,66
18	Agrimonia	agrimony	1,66
19	Echinacea purpurae	purple coneflower	1,64
20	Geranium robertianum	herb-Robert	1,58
21	Dipteryx odorata	cumaru	1,53
22	Passiflora caerulea	passionflower	1,53
23	Lycopodium clavatum	common/stag's-horn/running clubmoss, ground pine	1,51
24	Filipendula ulmaria	meadowsweet, mead wort	1,50
25	--	flower pollen, Spanish	1,48
26	Artemisia absinthium	wormwood	1,45
27	Sambucus nigra	elderberry	1,42
28	Fagopyrum	buckwheat	1,35

Table S2. LC-MS analysis of lingonberry leaf extract. Compounds were assigned according a recently published analysis (Marsol-Vall et al. 2021; Food Chem, 2021, 339, 128052). This table shows the same results as table 1 in the main manuscript, but also includes compounds that could not be assigned as well as MS^2 fragments.

compound name	**t_R (UV) [min]**	**exact mass m/z $[MH]^+$**	**fragment(s)**
unknown	8,07	577,1335	425,0863; 289,0702
unknown	8,19	325,0913	307,2546; 163,0387
unknown	8,87	611,1599	465,1184; 303,0493
quercetin-hexoside	9,01	465,1015	303,0490
quercetin-hexoside	9,20	465,1015	303,0490
quercetin-pentoside	9,57	435,0918	303,0493
quercetin-pentoside	9,77	435,0918	303,0493
quercetin-pentoside	9,96	435,0918	303,0493
unknown	10,22	453,1175	303,0493
quercetin-3-O-rhamnoside	10,28	449,1072	303,0493
unknown	10,98	367,0991	163,0347
quercetin-3-*O*-4``-(3-hydroxy-3-methylglutaroyl)-rhamnoside	11,53	593,1433	303,0463
kaempferol-3-hydroxy-3-methylglutaroyl-rhamnoside	12,25	577,1262	287,0514

Table S3. LC-MS analysis of blackberry leaf extract. Compounds were assigned according a previously published analysis (Pavlović et al. 2016; Industrial Crops and Products, 2016, 87, 304–314). This table shows the same results as table 1 in the main manuscript, but also includes compounds that could not be assigned as well as MS^2 fragments.

Compound name	**t_R (UV) [min]**	**exact mass m/z $[M-H]^-$**	**exact mass m/z $[MH]^+$**	**fragment(s) of $[MH]^+$**
caffeoylquinic acid isomer	3,31	353,0886	355,1025	163,0026
caffeic acid hexoside isomer	4,65	341,0887	343,1022	325,0918
apigenin 7- *O* -hexuronide	5,23	445,0423	447,0560	-*
caffeoylquinic acid isomer	5,76	353,0886	355,1024	163,0389
unknown	6,20	300,9993	303,0135	-
unknown	6,27	291,0160	293,0291	275,0615
caffeoylquinic acid isomer	6,50	353,0889	355,1024	-
unknown	6,66	301,0002	303,0135	-
apigenin 7- *O* -hexuronide	7,15	443,0272	445,0403	-
unknown	7,33	300,9999	303,0135	-
unknown	7,59	300,9999	303,0135	-
valoneic acid dilactone isomer	7,82	469,0059	471,0195	-
unknown, probably valoneic acid dilactone isomer	8,18	469,0059	471,0195	-
unknown, probably valoneic acid dilactone isomer	8,30	469,0058	471,0196	-
unknown, probably valoneic acid dilactone isomer	8,48	469,0052	471,0197	-
ellagic acid	9,24	300,9990	303,0136	-
quercetin-hexuronide	9,64	477,0669	479,0819	303,1645
kaempferol 7- *O* -hexuronide	9,90	461,0749	463,0871	287,1495
quercetin 3- *O* -pentoside	10,24	433,0792	435,0923	-
kaempferol 7- *O* -hexuronide	10,58	461,0725	463,0869	-
apigenin 7- *O* -hexuronide	10,98	445,0770	447,0922	271,1529
kaempferol hexoside isomer	12,53	593,1321	595,1443	287,1073

* … mother ions were too small for automated MS^2 experiments

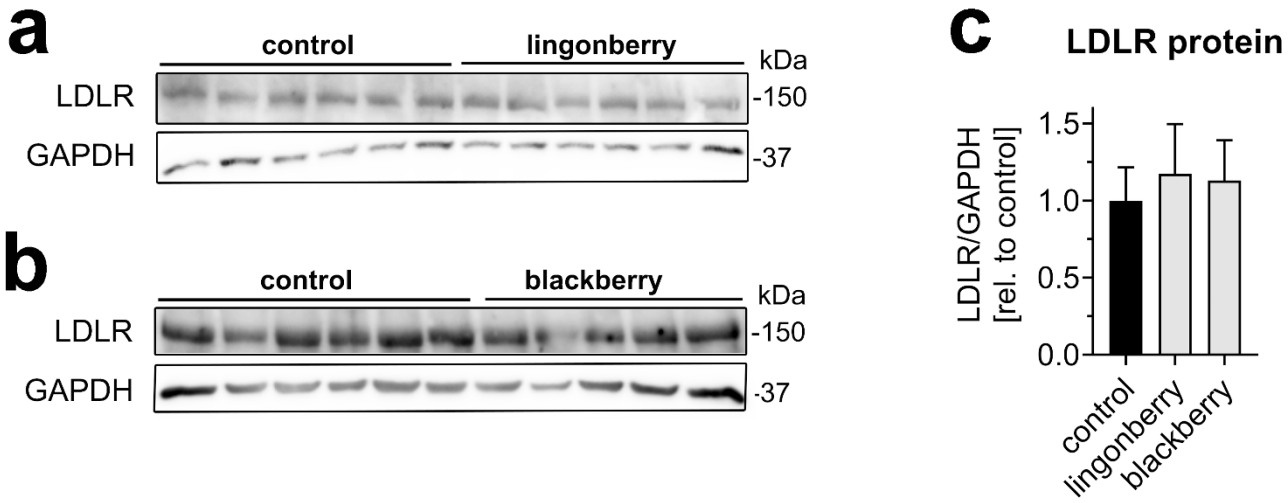


Figure S1. Effect of lingonberry and blackberry leaf extracts on hepatic LDLR protein expression. Plant extracts were applied to C57bl/6 mice for five consecutive days as described in the main manuscript. LDLR expression in liver tissue was detected by immunoblot (a, b). Semi-quantitative analysis by densitometry is depicted in panel c.

Figure legends for supplemental figures S2 and S3 (below):

Figure S2. LC-MS analysis of lingonberry leaf extract. Upper panel: Chromatogram with PDA detector. Lower panel: Chromatogram with APCI(pos)-MS detector in TIC mode. For methodological details, see main manuscript.

Figure S3. LC-MS analysis of blackberry leaf extract. Upper panel: Chromatogram with PDA detector. Lower panel: Chromatogram with APCI(pos)-MS detector in TIC mode. For methodological details, see main manuscript.

Figure S2

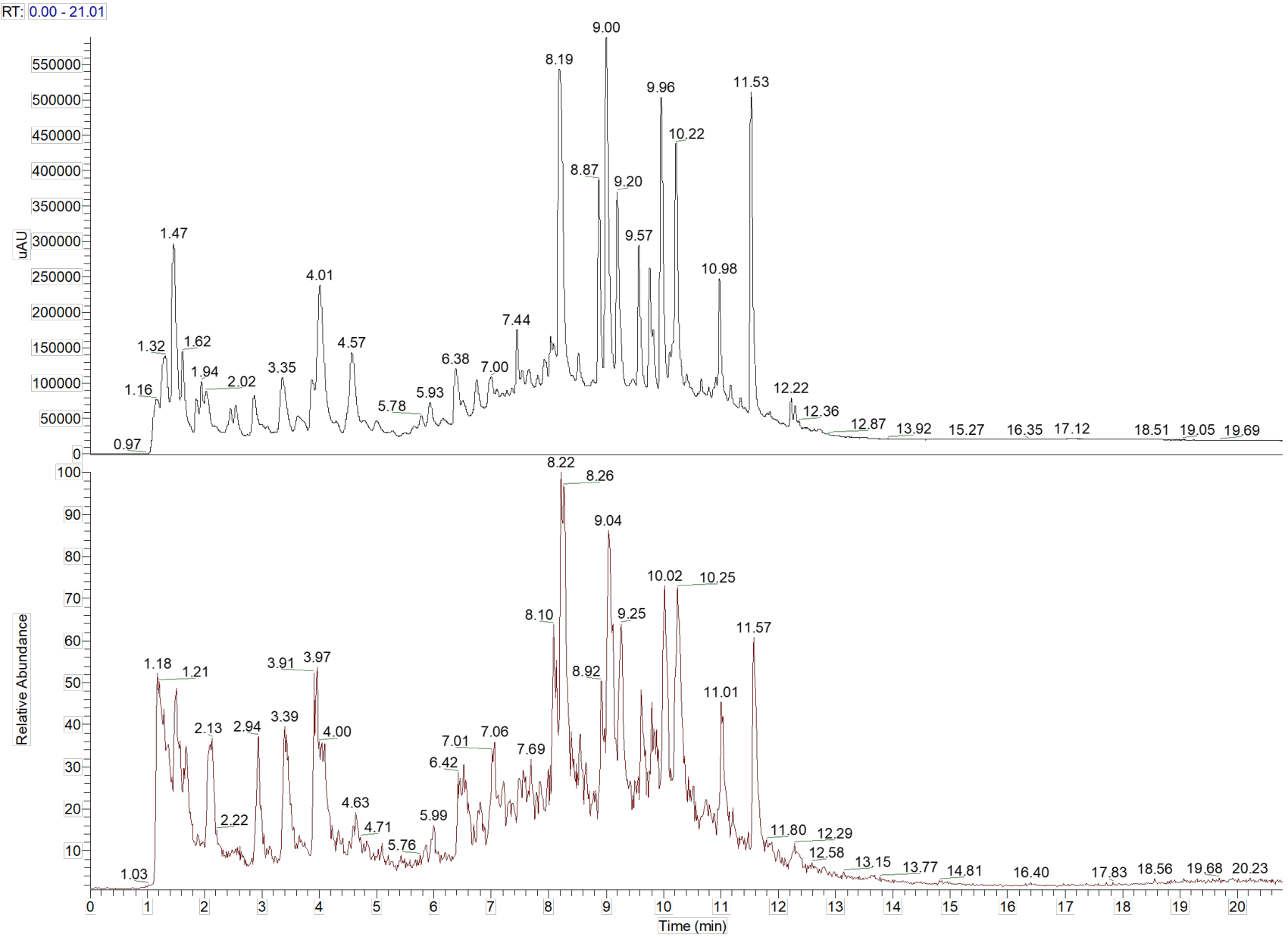
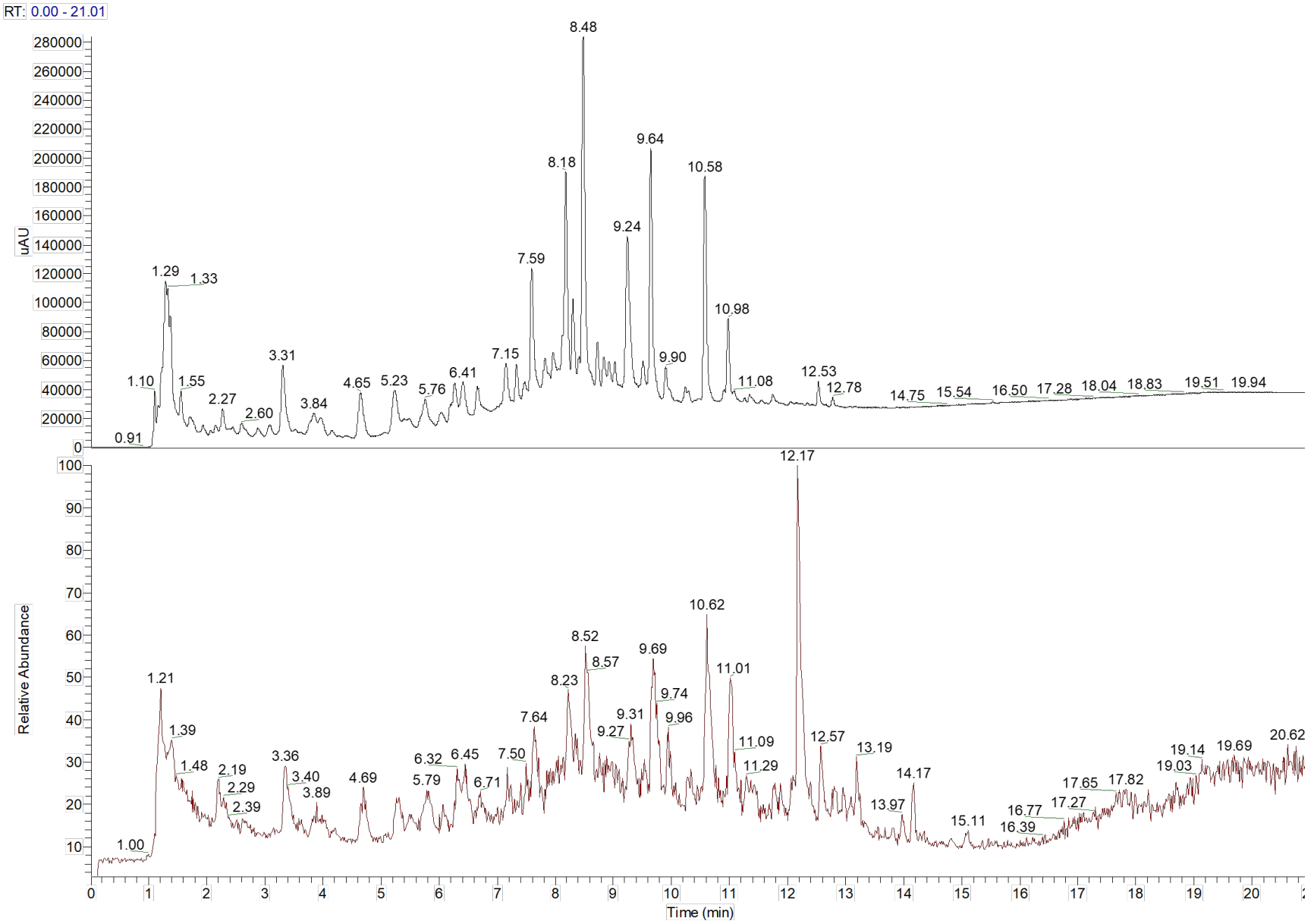


Figure S3



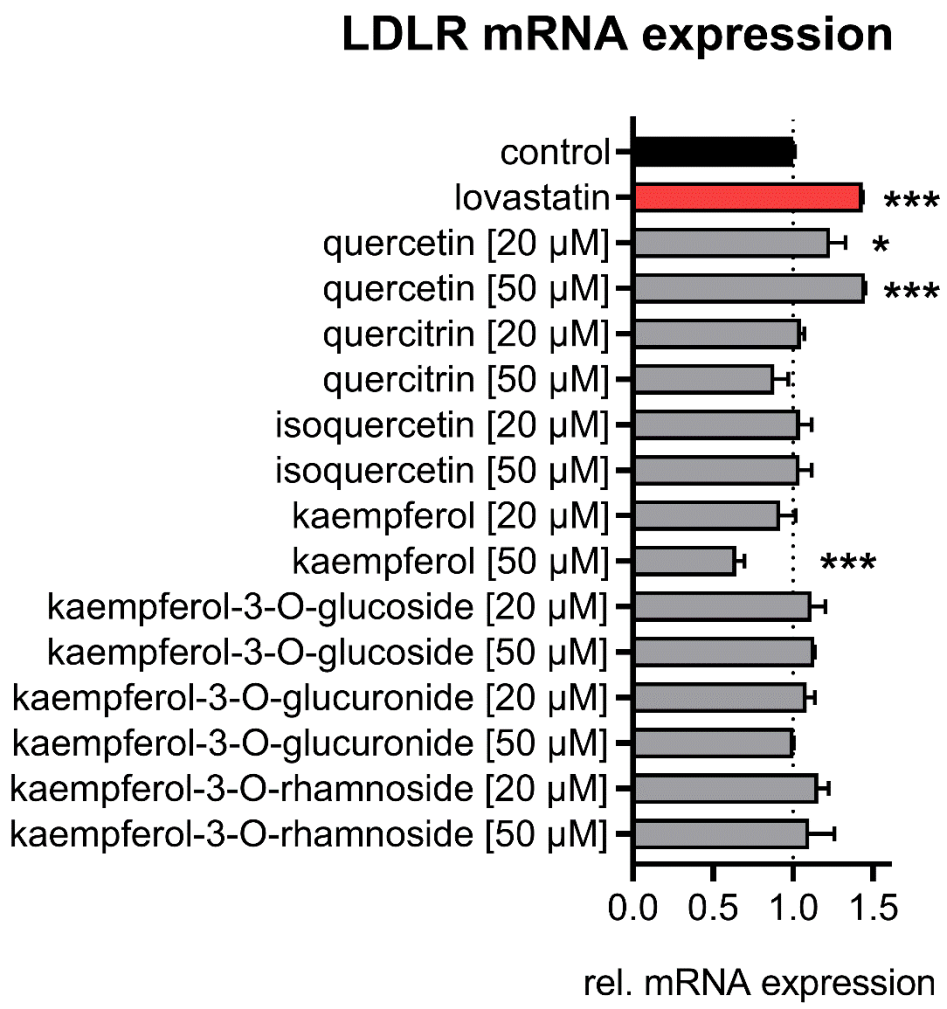


Figure S4. Impact of quercetin, kaempferol, and its glycosides on LDLR expression. Huh-7 cells were treated with the indicated compounds under serum-reduced conditions (1% FBS) for 24 hrs. Lovastatin [10 µM] was used as positive control. LDLR mRNA expression was measured by qRT-PCR and relative expression was normalized to two housekeeping genes (β-actin and GAPHD); n=2.