

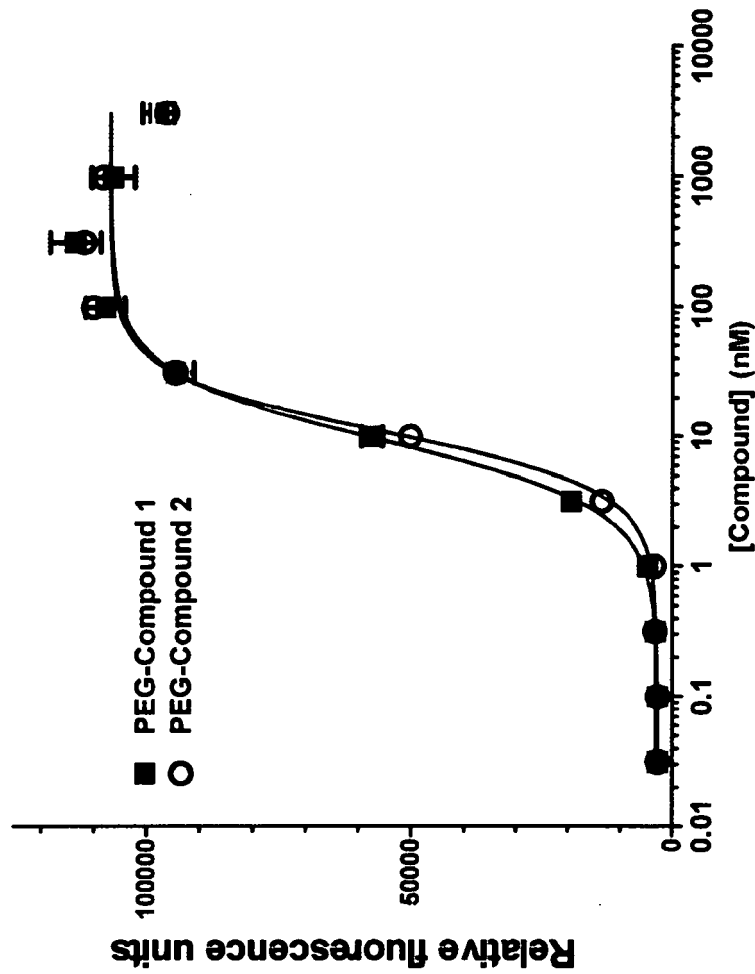
FIG. 1A

Compound Name	SEQ ID NO:	Amino Acid 108	PEG Mol. Wt.	Amino Acids 109-149	Amino Acids 169-181
Compound 1	101	Q	n/a	SEAHGLPLHLPGNKS ^{PHRDPAPRGPARFELPLGLPPAPPEP}	VGPSQGRSPSYAS
Compound 2	102	Q	n/a	SEAHGLPLHL-GSG-----RGPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 3	103	Q	n/a	SEAHGLPLHLPGNKS ^{PHRDPAPRGPARFELPLGLPPAPPEP}	VEPSQGRSPSYAS
Compound 4	104	Q	n/a	SEAHGLPLHLPGKKS ^{PHRDPAPRGPARFELPLGLPPAPPEP}	VEPSQGRSPSYAS
Compound 5	105	Q	n/a	SEAHGLPLHLPGDKS--RDPAPRGPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 6	106	Q	n/a	SEAHGLPLHLPGHKS--RDPAPRGPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 7	107	Q	n/a	SEAHGLPLHLPGDKS ^{PHRDPAPRGPARFELPLGLPPAPPEP}	VEPSQGRSPSYAS
Compound 8	108	Q	n/a	SEAHGLPLHL-GSG-----ARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 9	109	Q	n/a	SEAHGLPLHLPGQKS ^{PHRDPAPRGPARFELPLGLPPAPPEP}	VEPSQGRSPSYAS
Compound 10	110	Q	n/a	SEAHGLPLHL-GSG-----GPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 11	111	Q	n/a	SEAHGLPLHL-GSGH--RDPAPRGPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 12	112	Q	n/a	SEAHGLPLHLPHHSG--RDPAPRGPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 13	113	Q	n/a	SEAHGLPLHLPGKDS--QDPAPRGPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 14	114	Q	n/a	SEAHGLPLHLPGHKS--RDPAPRGPARFELPLGLPPAPPEP	VGPSQGRSPSYAS
Compound 15	115	Q	n/a	SEAHGLPLHLPGHKS--RDPAPRGPARFELPLGLPPAPPEP	VEPSQGREPSYAS
Compound 16	116	Q	n/a	SEAHGLPLHLPGHKS--RDPAPRGPARFELPLGLPPAPPEP	V-PSQGRSPSYAS
Compound 17	117	Q	n/a	SEAHGLPLHLPGHKS--RDPAPRGPARFELPLGLPPAPPEP	VG-SQGRSPSYAS
Compound 18	118	Q	n/a	SEAHGLPLHLPGNKS ^{PHRDPAPRGPARFELPLGLPPAPPEP}	VEP-----
Compound 19	119	Q	n/a	SEAHGLPLHL-GSGP-HRDPAPRGPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 20	120	Q	n/a	SEAHGLPLHL-GGH--RDPAPRGPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 21	121	Q	n/a	SEAHGLPLHL-GSG--RDPAPRGPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 22	122	Q	n/a	SEAHGLPLHLSGG-----PAPRGPARFELPLGLPPAPPEP	VEPSQGRSPSYAS
Compound 23	123	Q	n/a	SEAHGLPLHL-GG-----GPARFELPLGLPPAPPEP	VEPSQGRSPSYAS

FIG. 1B

Compound Name	SEQ ID NO:	Amino Acid 108	PEG Mol. Wt.	Amino Acids 109-149	Amino Acids 169-181
Compound 24	124	Q	n/a	SEAHGLPLHLP-----G--RFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Compound 25	125	Q	n/a	SEAHGLPLHLP-SG-----G--RFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Compound 26	126	Q	n/a	SEAHGLPLH-SGG-----PAPRGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Compound 27	127	Q	n/a	SEAHGLPLH--GSG-----GPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Compound 28	128	Q	n/a	SEAHGLP-H--GG-----RFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Compound 29	129	Q	n/a	SEAHGLP-H-SGG-----RFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Compound 30	130	Q	n/a	SEAHGLP-H--GSG-----RFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Compound 31	131	Q	n/a	SEAHGLPLHL-GSG-----GPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Compound 32	132	Q	n/a	SEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPALPEP	VEPSQGRSPSYAS
Pegylated Compound 1	201	pAF	30 kDa	SEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 2	202	pAF	30 kDa	SEAHGLPLHL-GSG-----RGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 5	205	pAF	30 kDa	SEAHGLPLHLPGDKS--RDPAPRGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 6	206	pAF	30 kDa	SEAHGLPLHLPGHKS--RDPAPRGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 10	210	pAF	30 kDa	SEAHGLPLHL-GSG-----GPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 11	211	pAF	30 kDa	SEAHGLPLHL-GSGH--RDPAPRGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 12	212	pAF	30 kDa	SEAHGLPLHLPHHSG--RDPAPRGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 19	219	pAF	30 kDa	SEAHGLPLHL-GSGP-HRDPAPRGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 20	220	pAF	30 kDa	SEAHGLPLHL-GGH----RDPAPRGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 21	221	pAF	30 kDa	SEAHGLPLHL-GSG----RDPAPRGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 22	222	pAF	30 kDa	SEAHGLPLHLGSG-----PAPRGPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS
Pegylated Compound 23	223	pAF	30 kDa	SEAHGLPLHL-GG-----GPARFLPLPGLPPAPPEP	VEPSQGRSPSYAS

FIG. 2



Summary Data (n=4)			
Parameter	PEG-Compound 1	PEG-Compound 2	
Mean pEC ₅₀ ± S.D. (M)	7.85 ± 0.26	7.74 ± 0.28	
Geo. Mean EC ₅₀ (95% CI) (nM)	14 (5 - 37)	18 (6 - 51)	

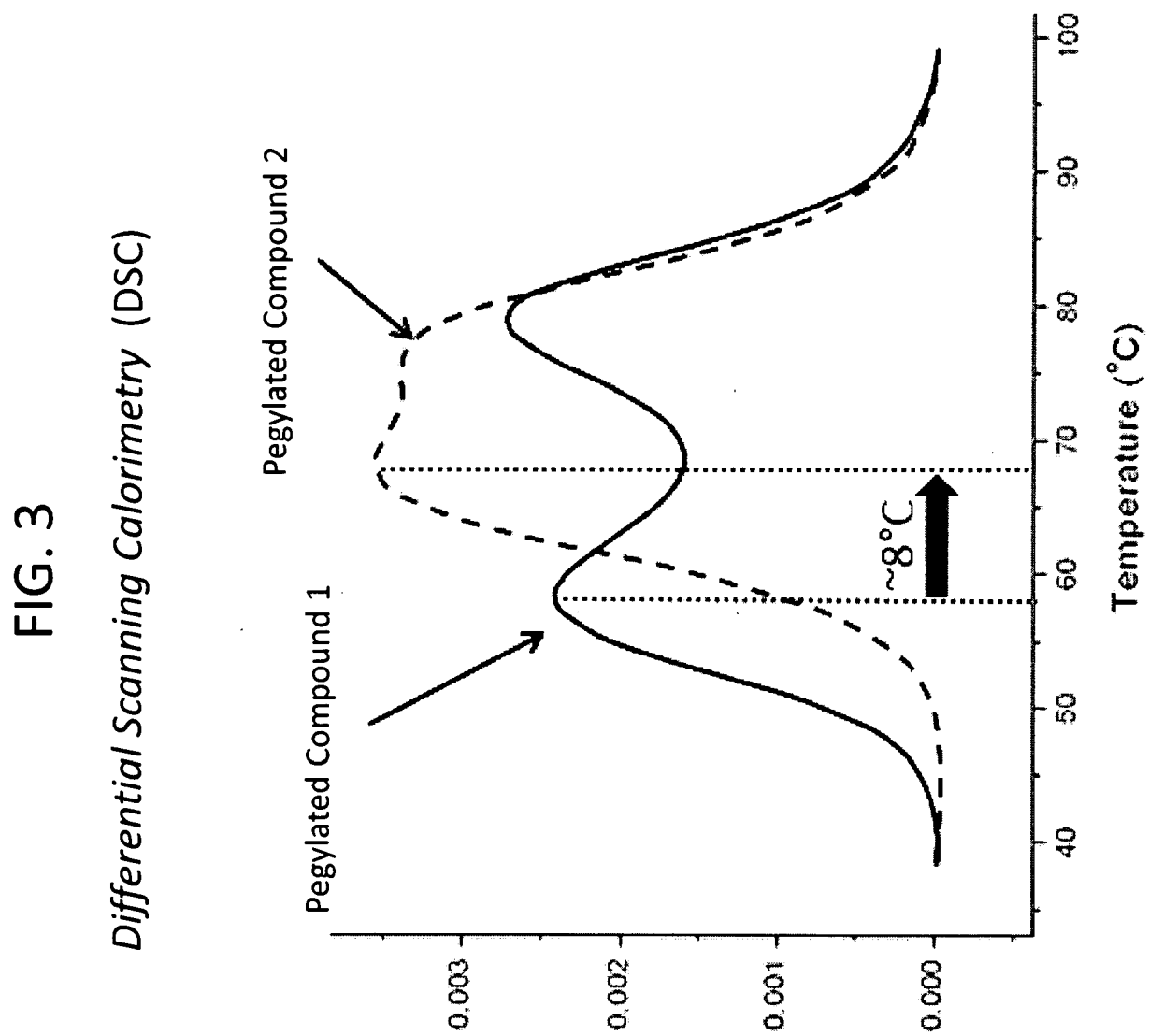


FIG. 4. Thermal Stability by Thermal Scanning Fluorescence (TSF)

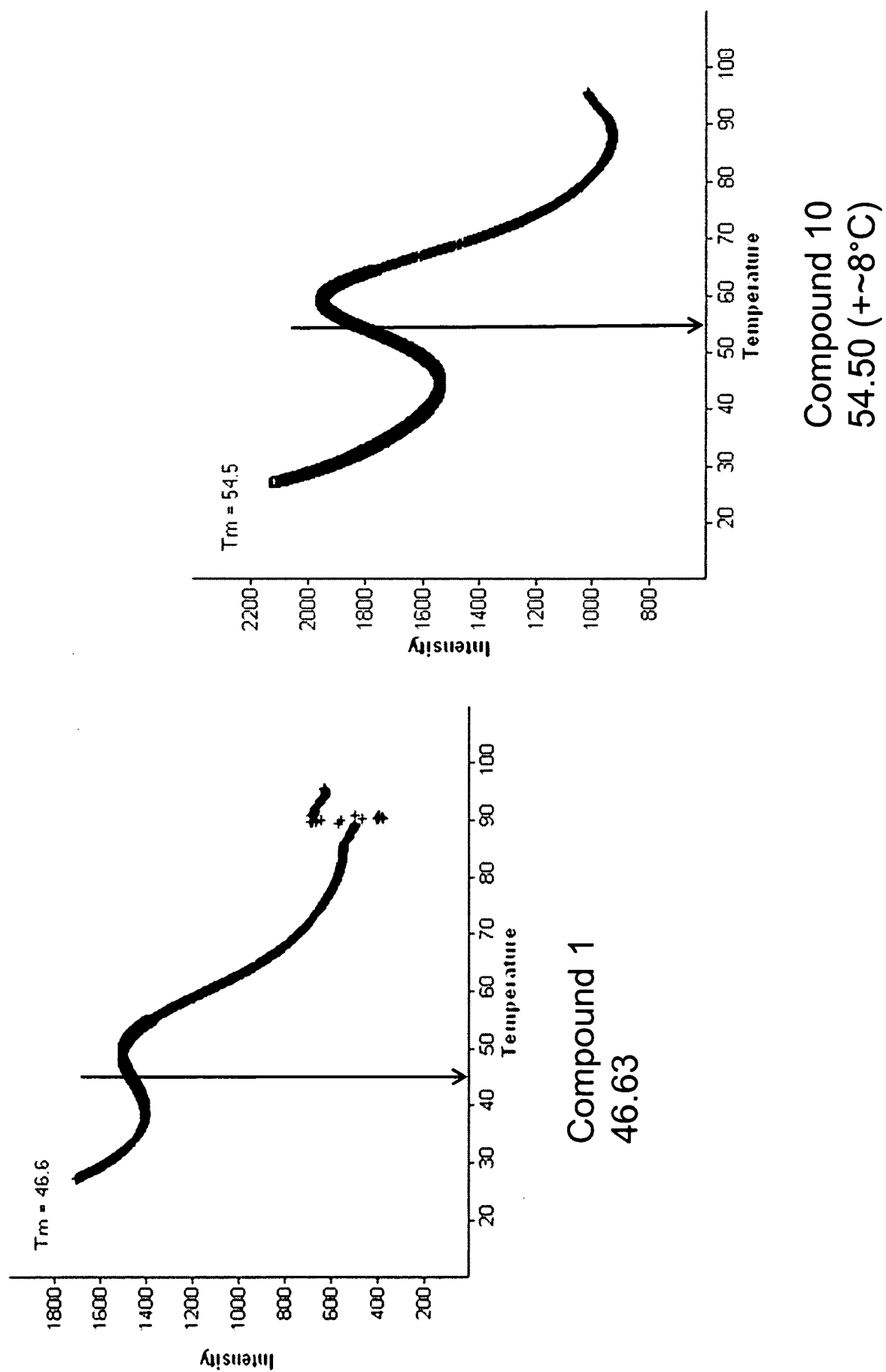
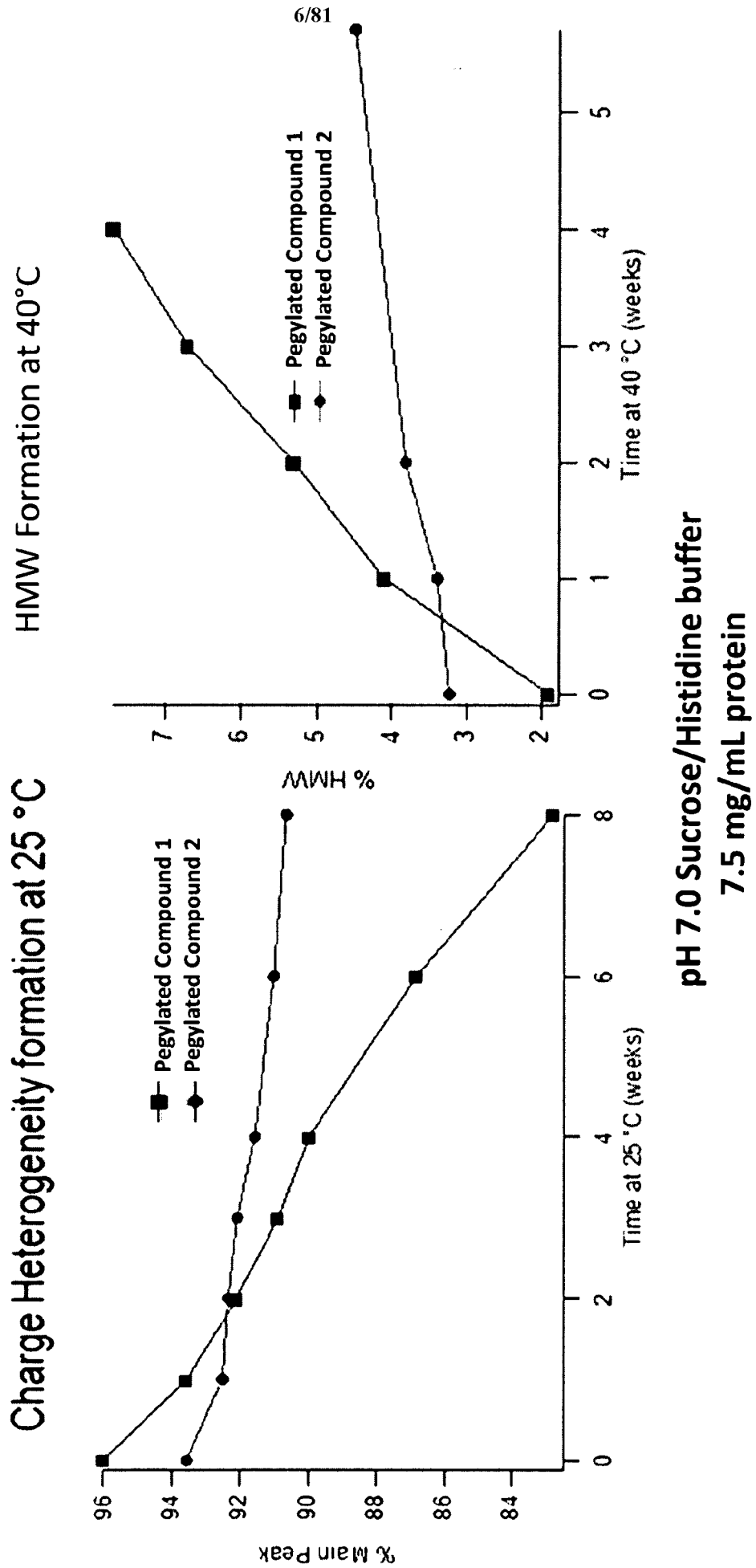
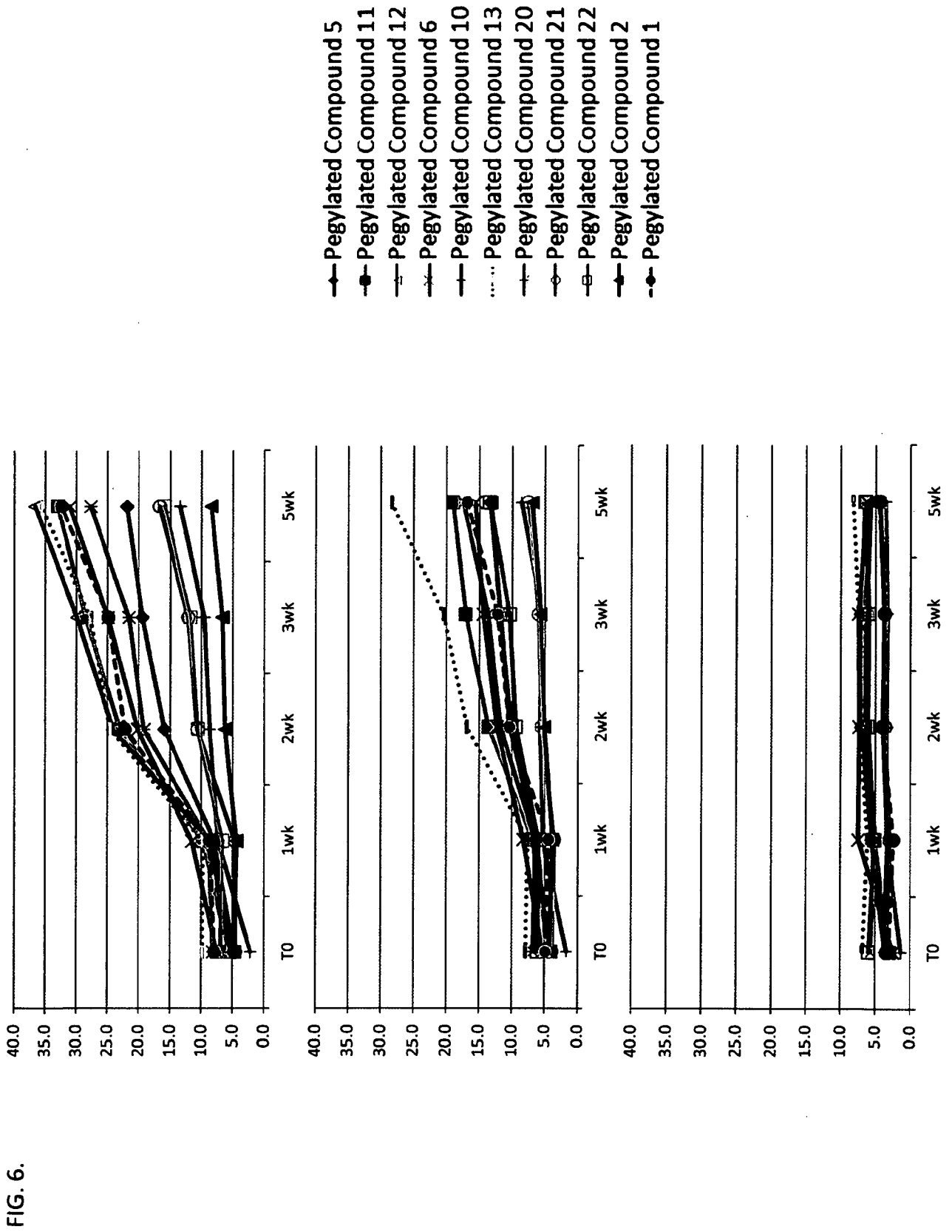


FIG. 5





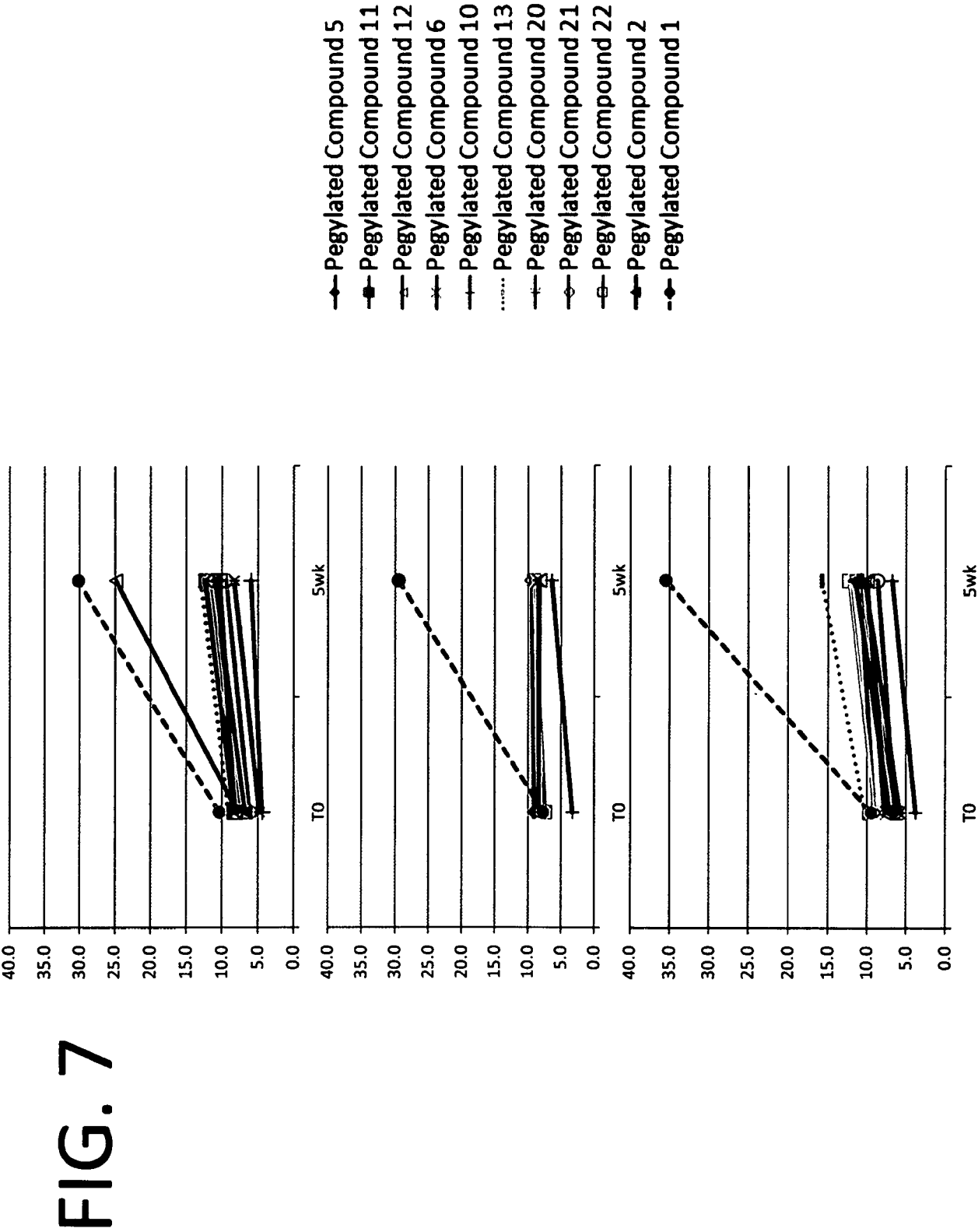


FIG. 8

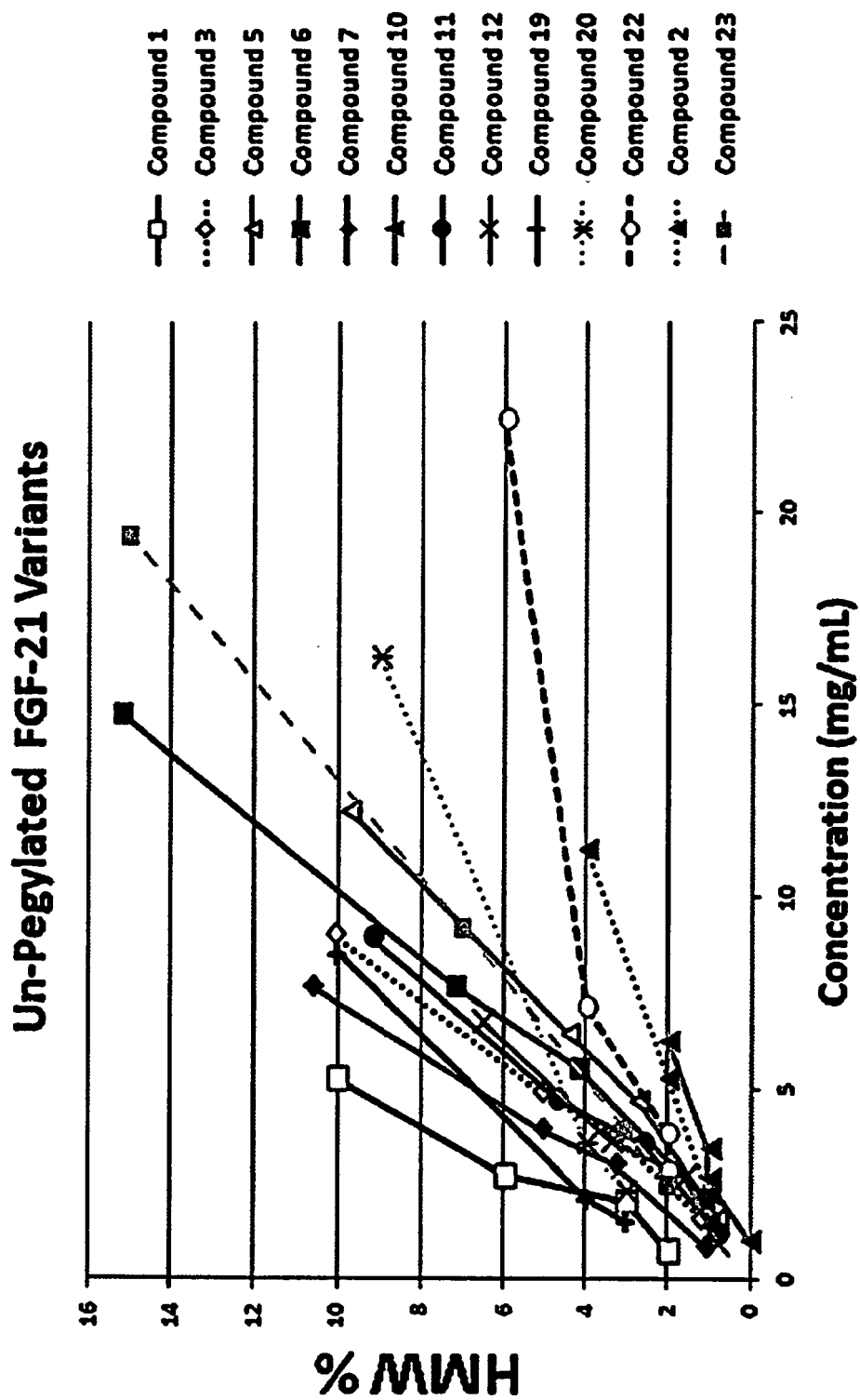


FIG. 9
CD4+ Proliferation Assay Results of
(unPegylated) modified FGF-21 Polypeptides
Percentage Antigenicity Split by Donor

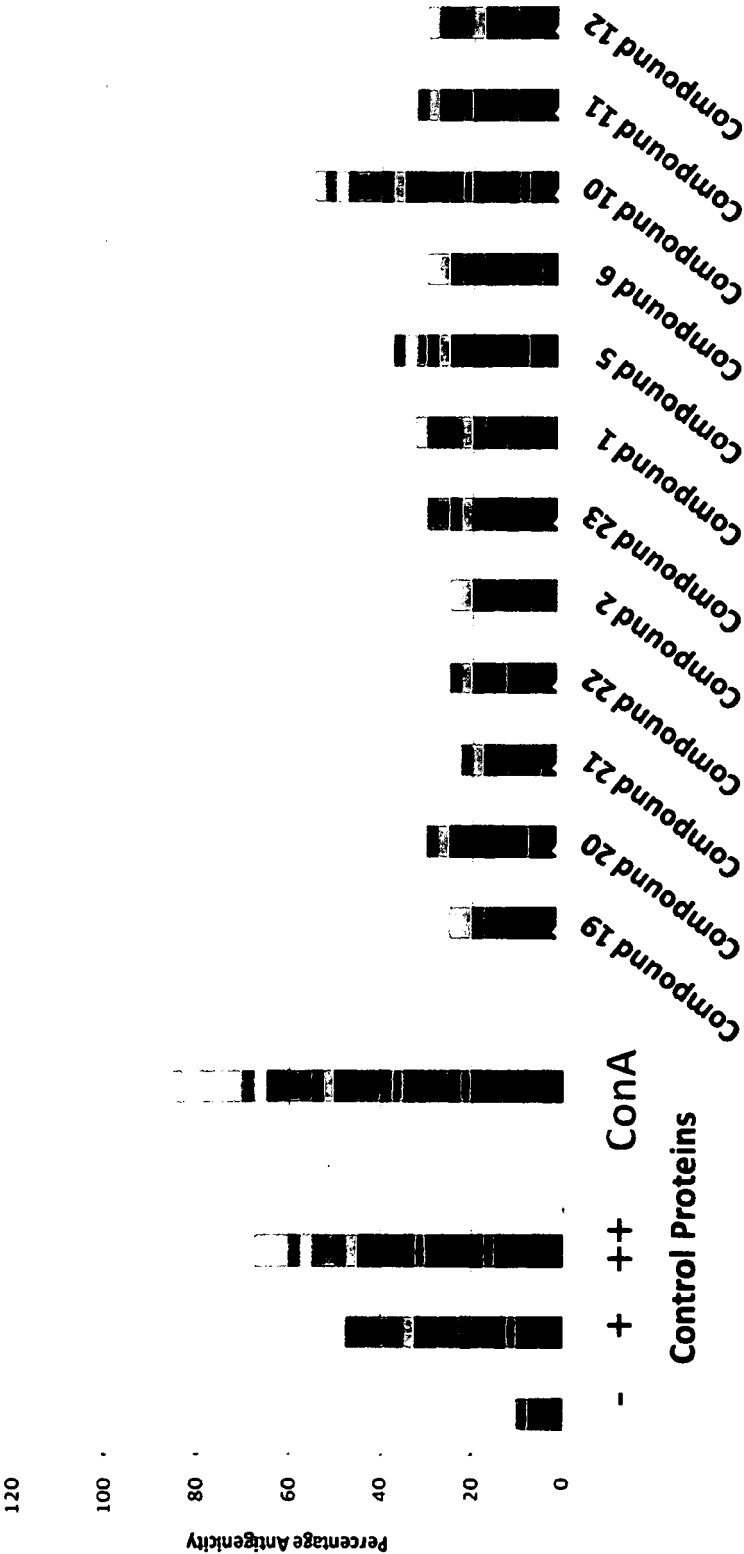
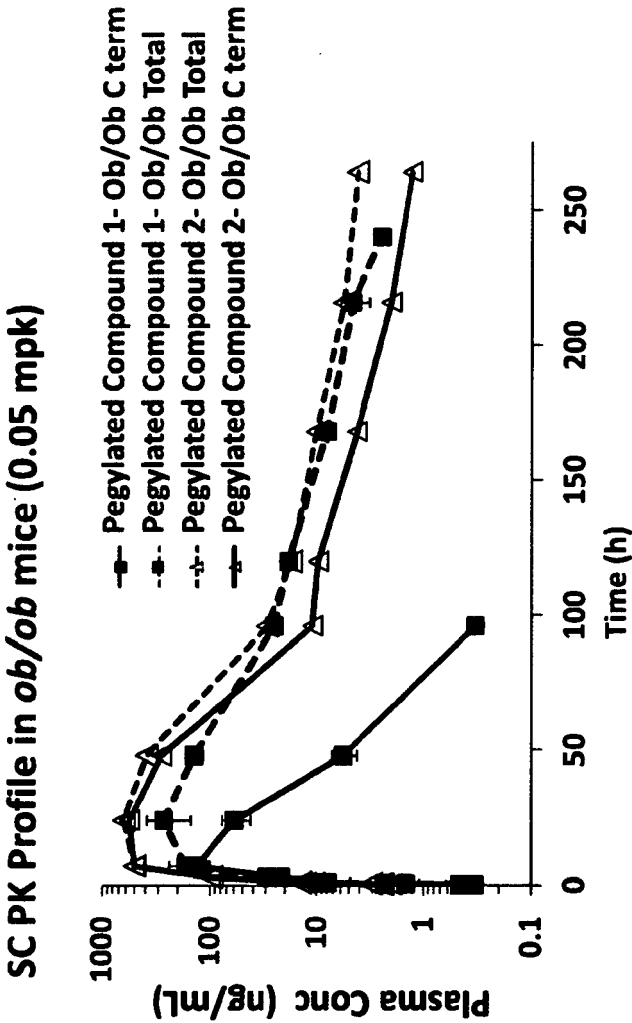


FIG. 10

*Enhanced in vivo (murine
Ob/Ob) Potency Reflects
Increased Exposure to Active
Protein*



Pegylated Compound 1 SC PK Parameters ob/ob mice				
PK Parameters	Units	C term (Active)	Total	
Cmax	ng/mL	133	267.9	
Tmax	h	7	24	
AUCtot	µg/mL*h	2.6	13.8	
AUC Ratio	Active/Total	0.18		

Pegylated Compound 2 SCPK Parameters ob/ob mice				
PK Parameters	Units	C term (Active)	Total	
Cmax	ng/mL	560.5	629	
Tmax	h	24	24	
AUCtot	µg/mL*h	24.9	31.8	
thalf	h	46.1	51.7	
AUC ratio	Active/Total	0.78		

FIG. 11A "Total" Protein PK

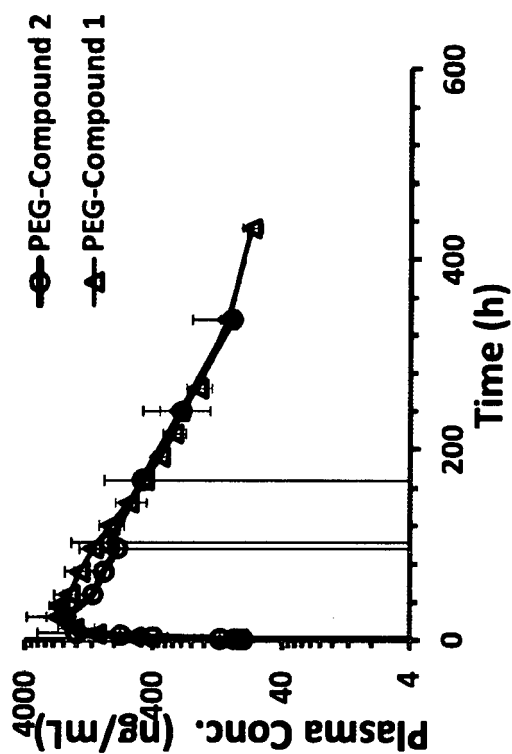


FIG. 11B C-term Intact PK

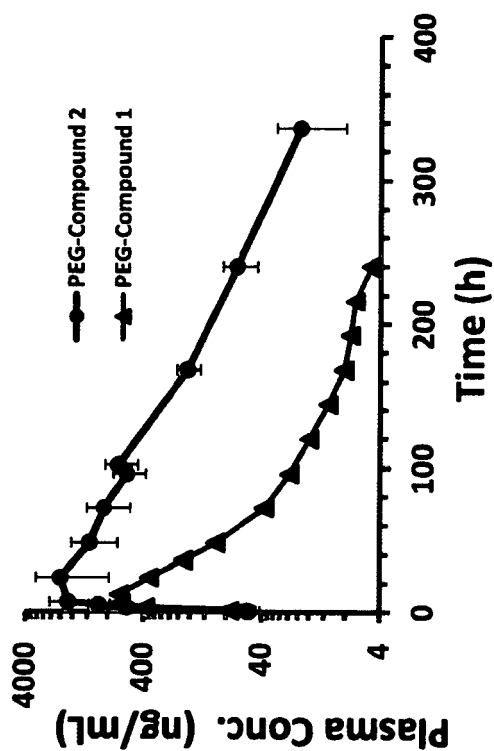


FIG. 12

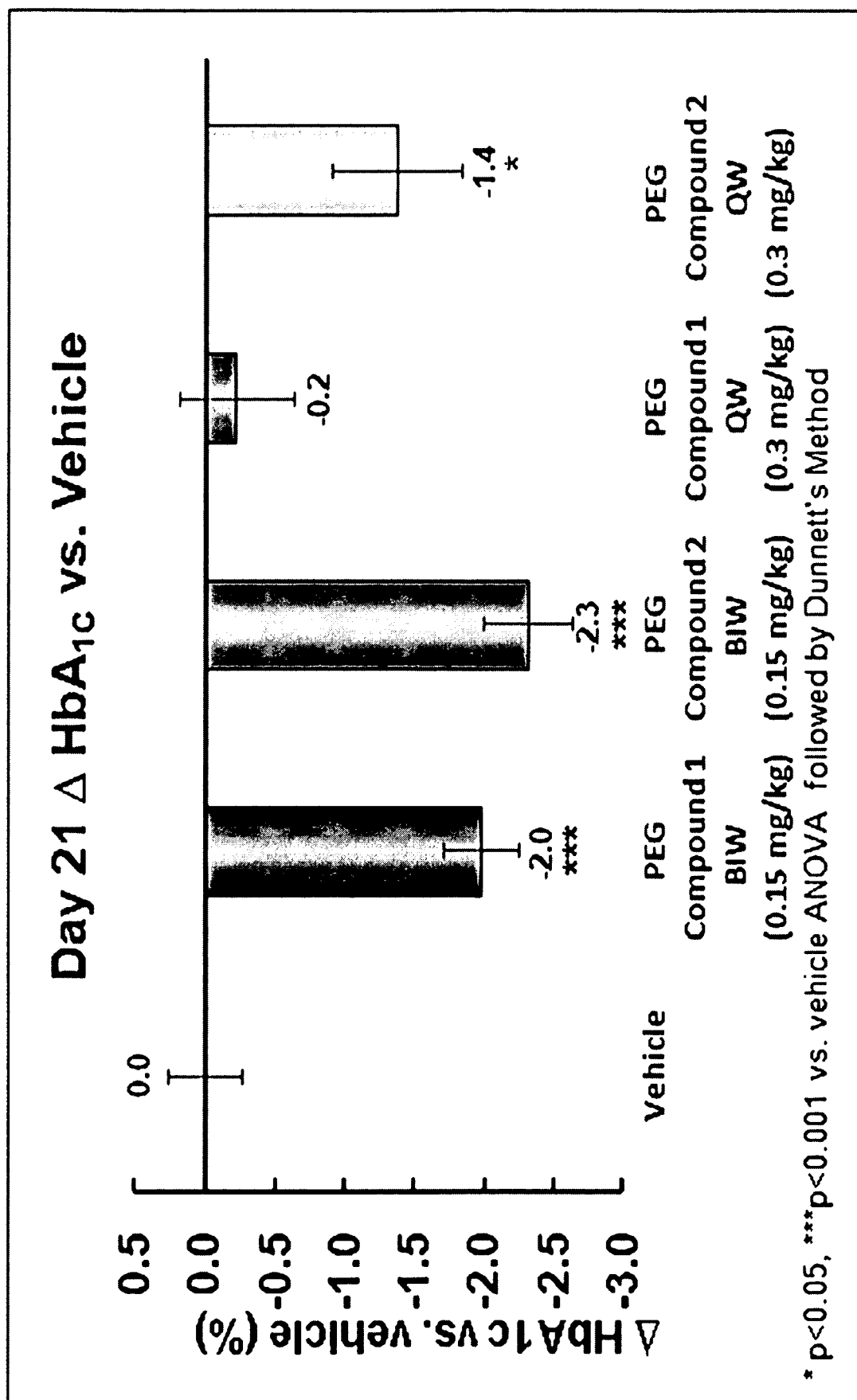


FIG. 13

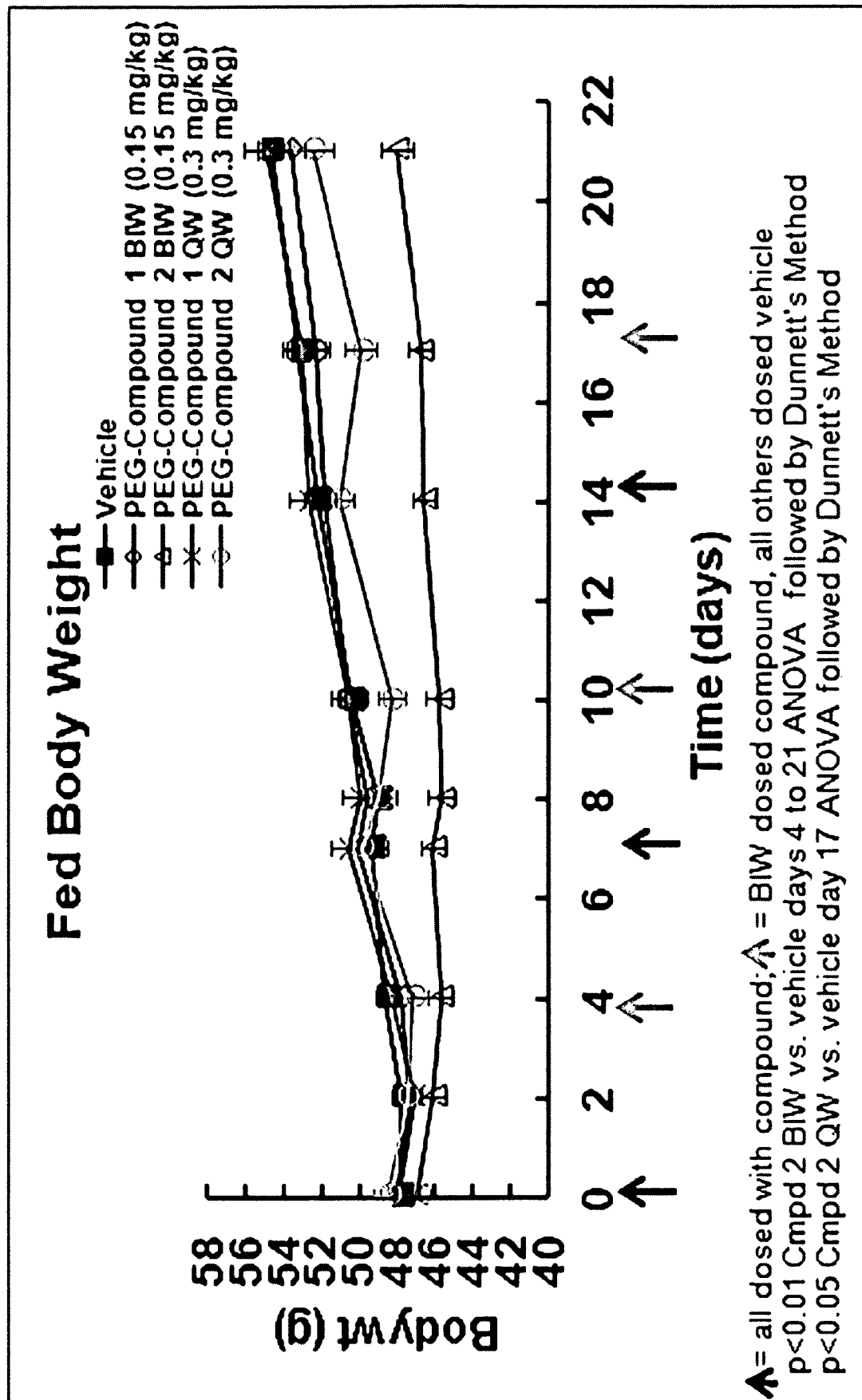


FIG. 14

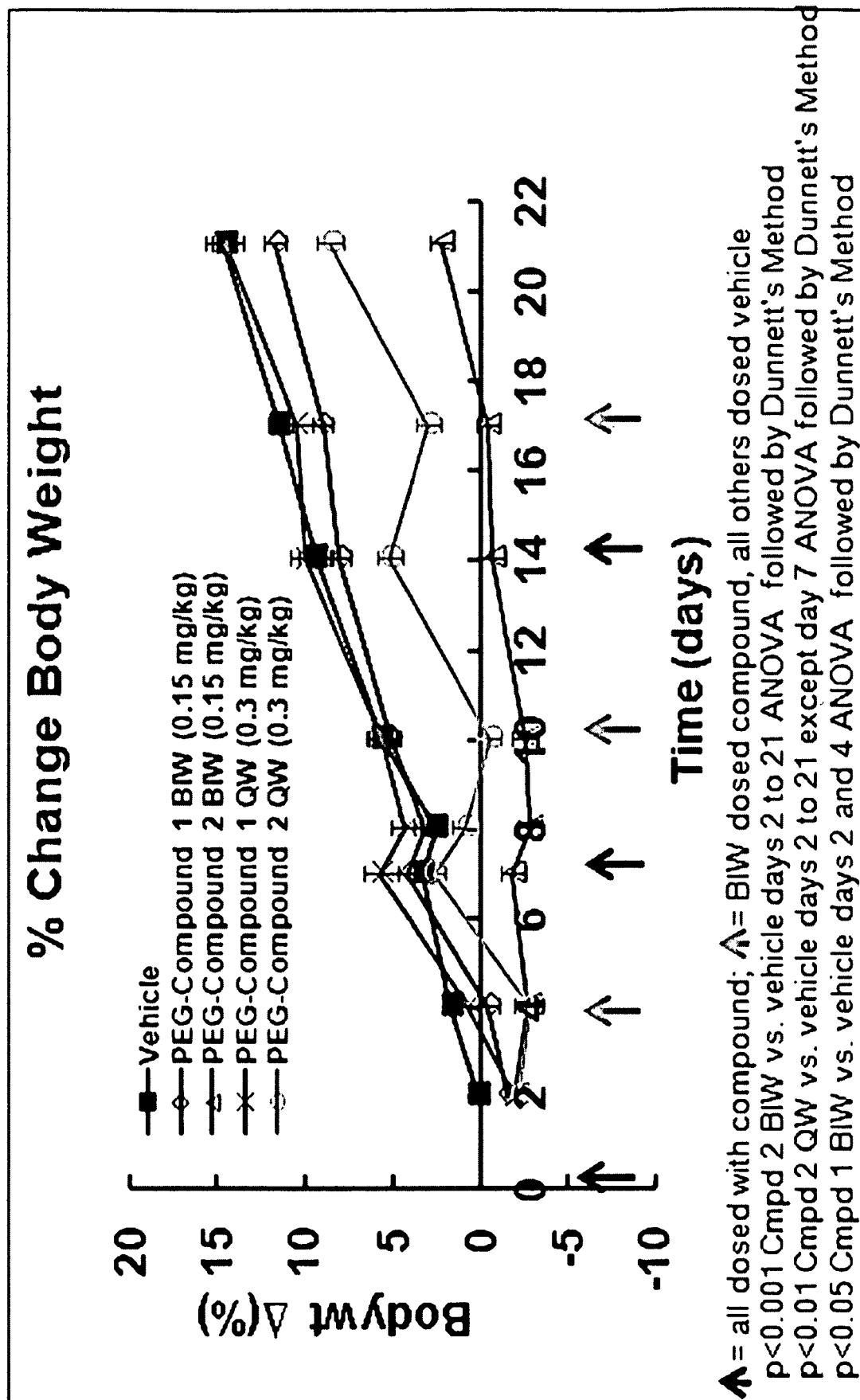


FIG. 15

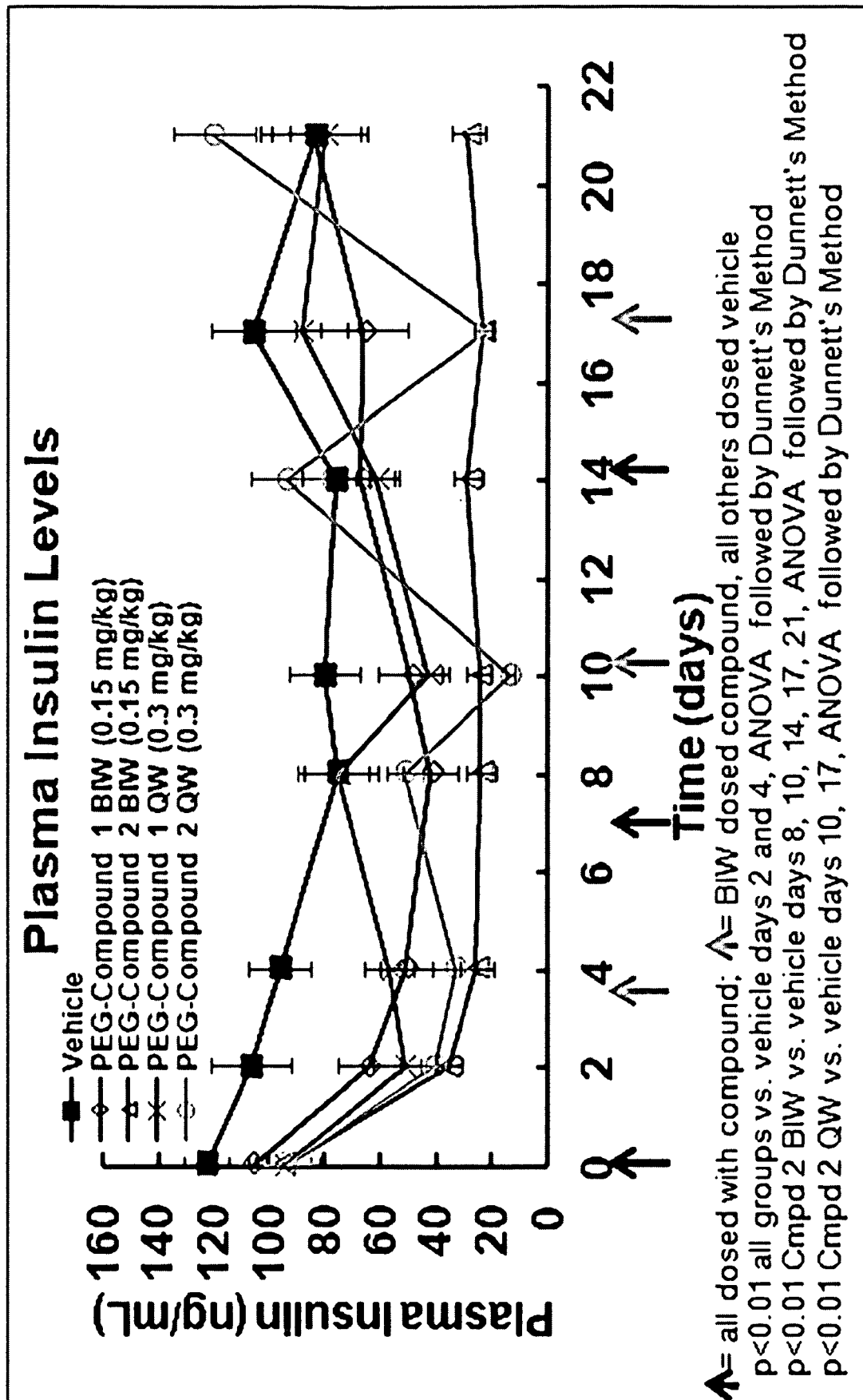


FIG. 16

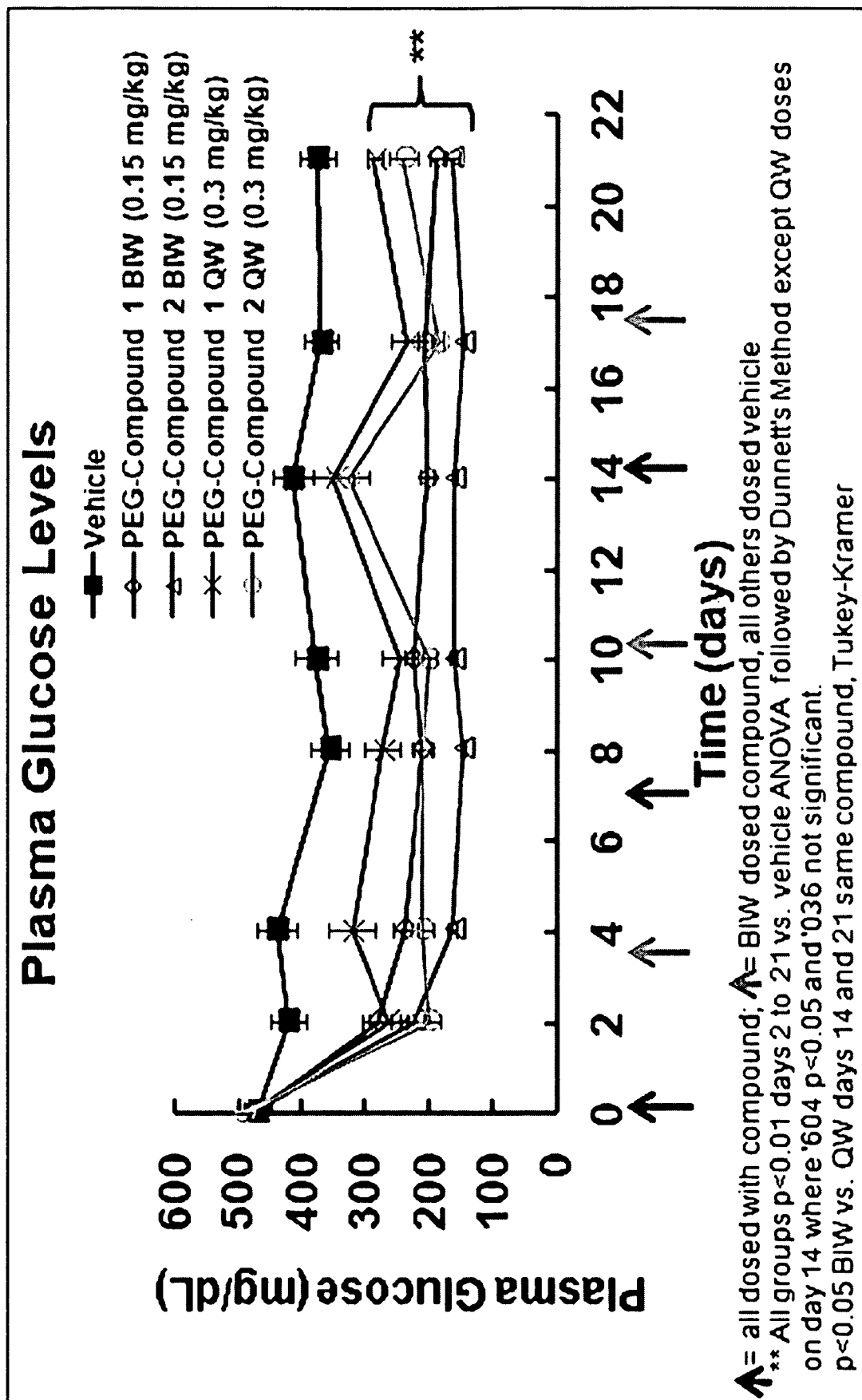


FIG. 17

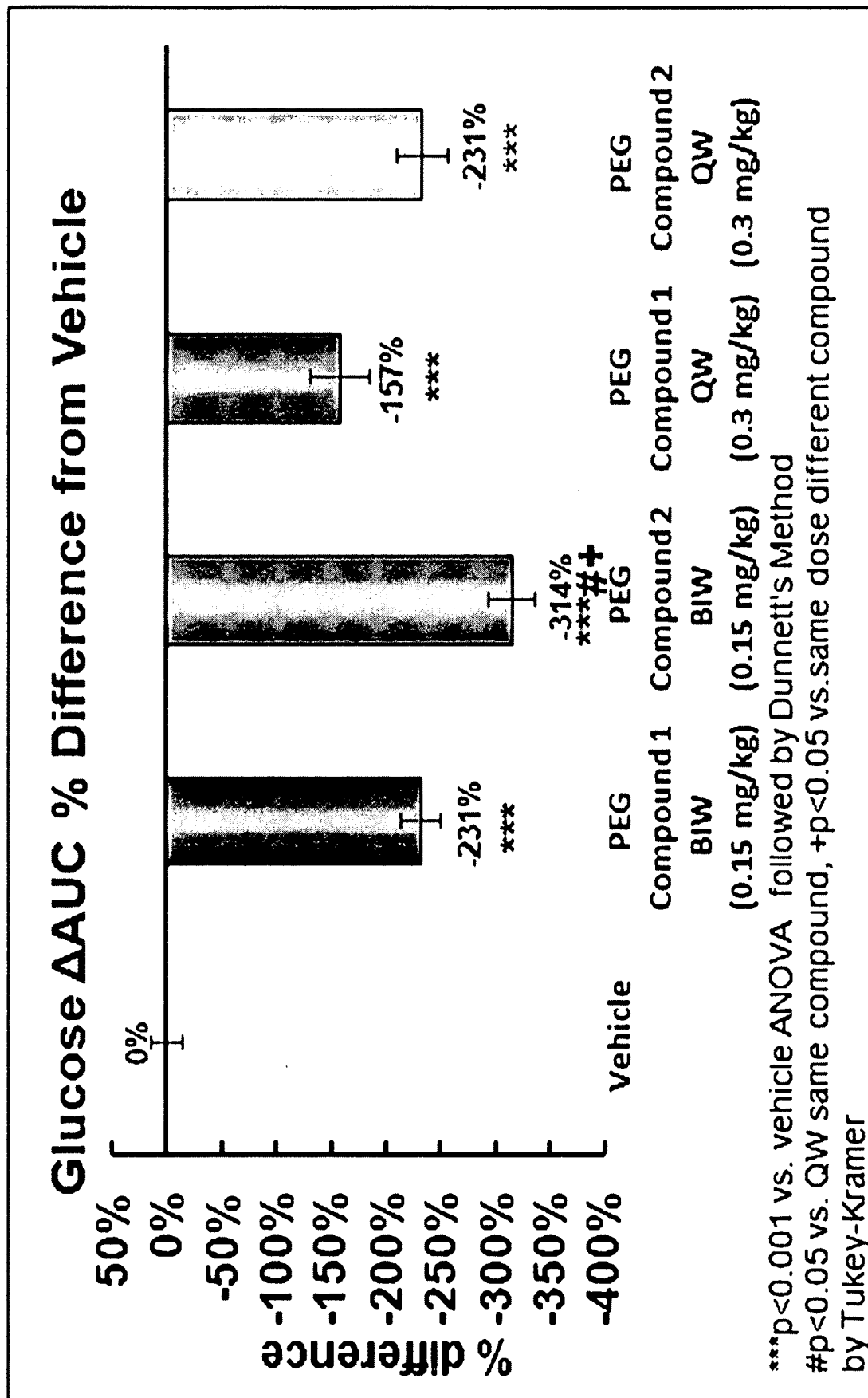


FIG. 18

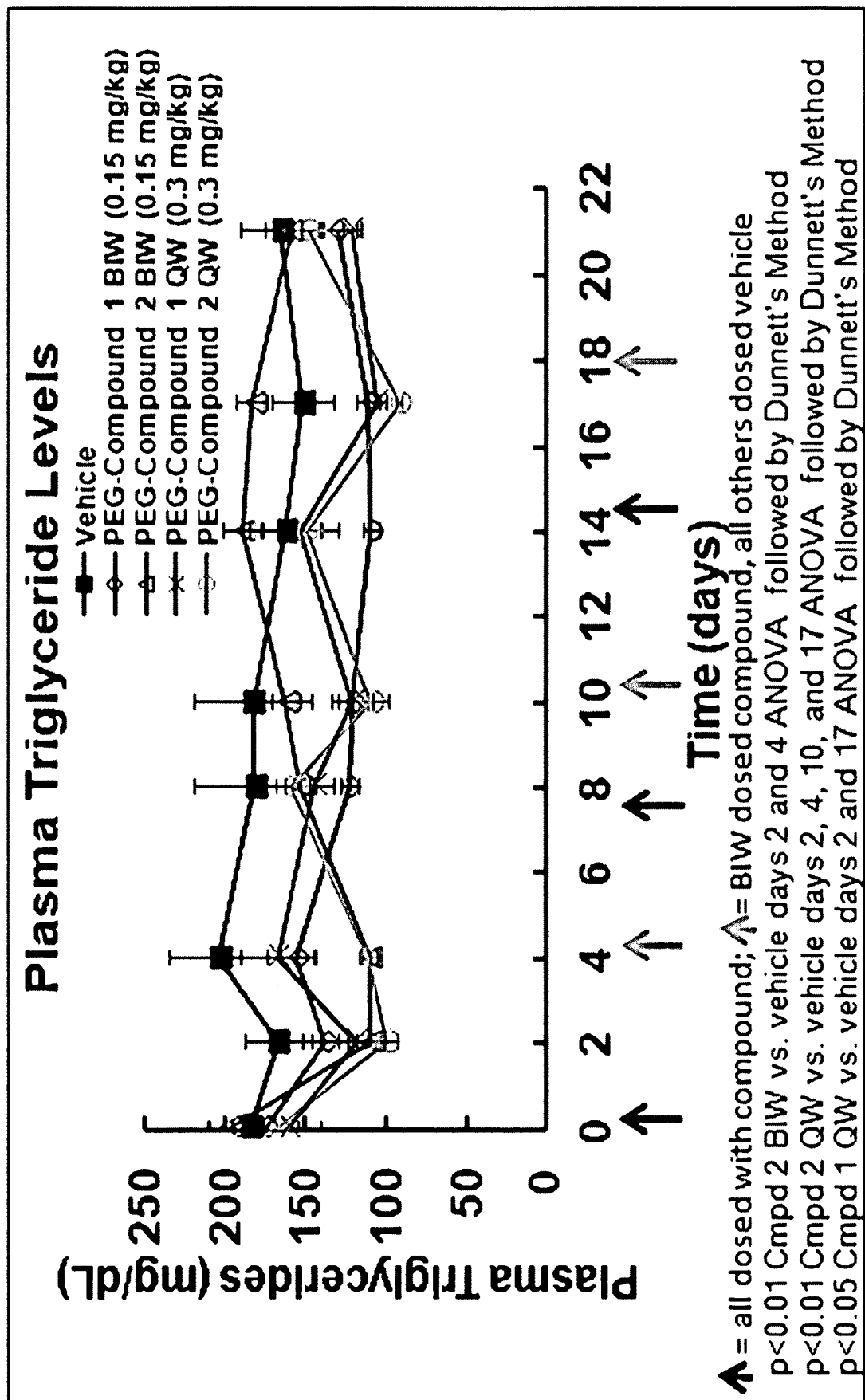


FIG. 19. Body weight changes

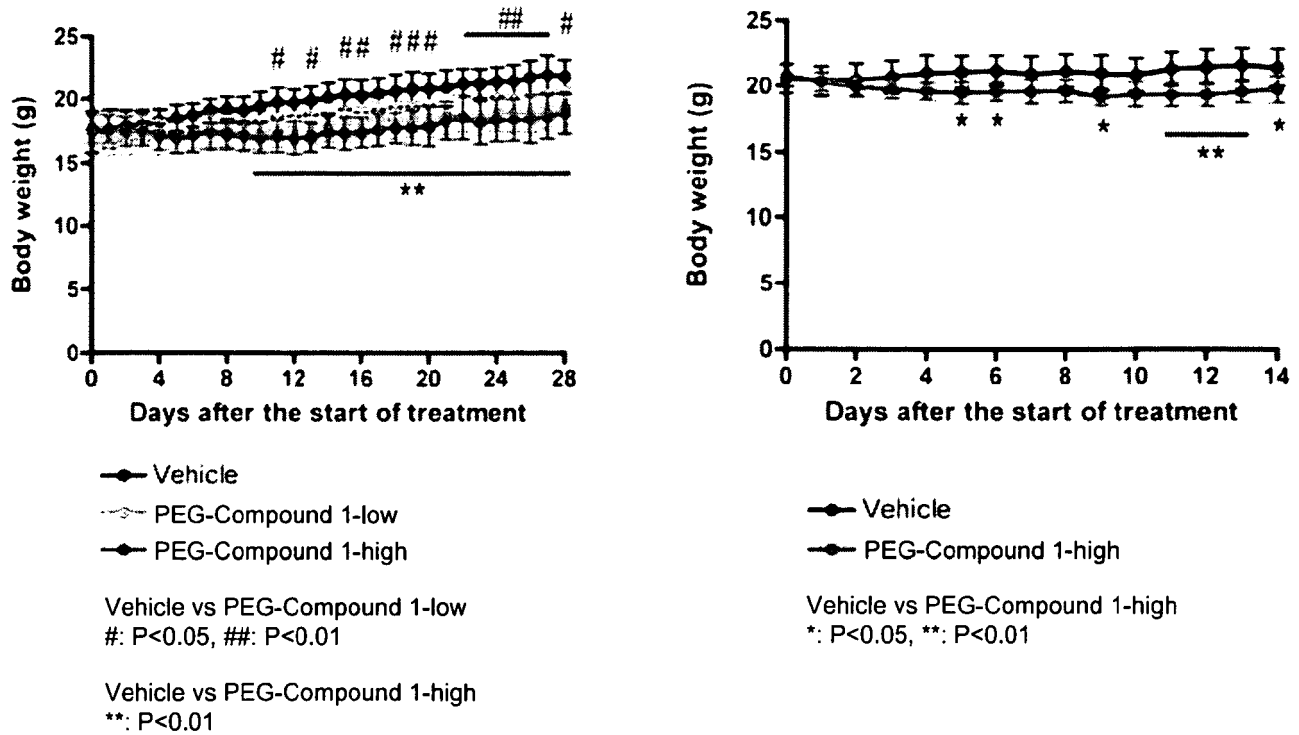


FIG. 20. Total food consumption

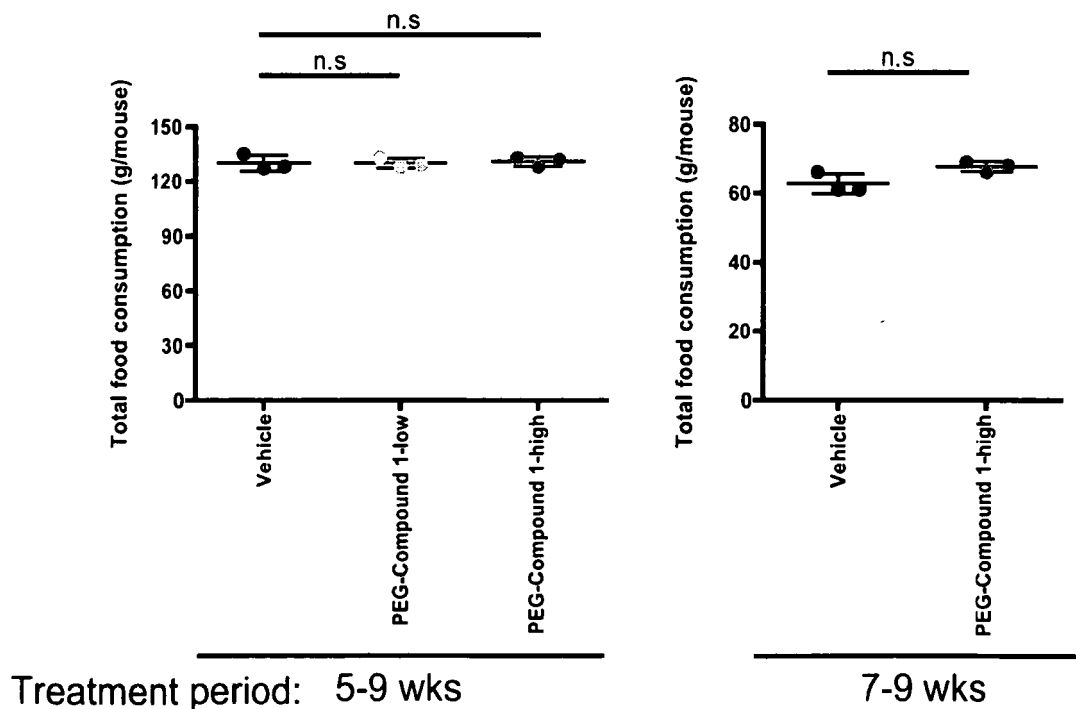


FIG. 21. Body weight

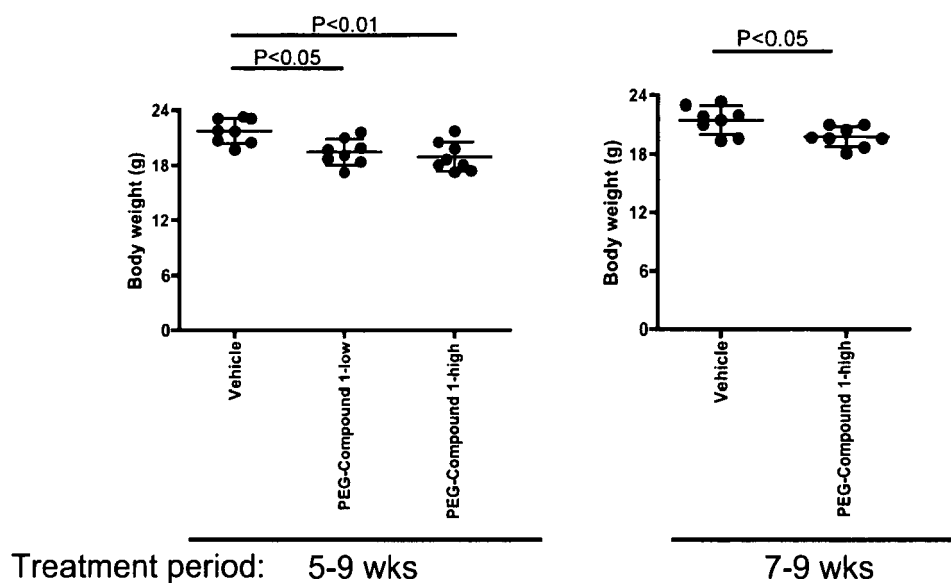


FIG. 22. Liver weight

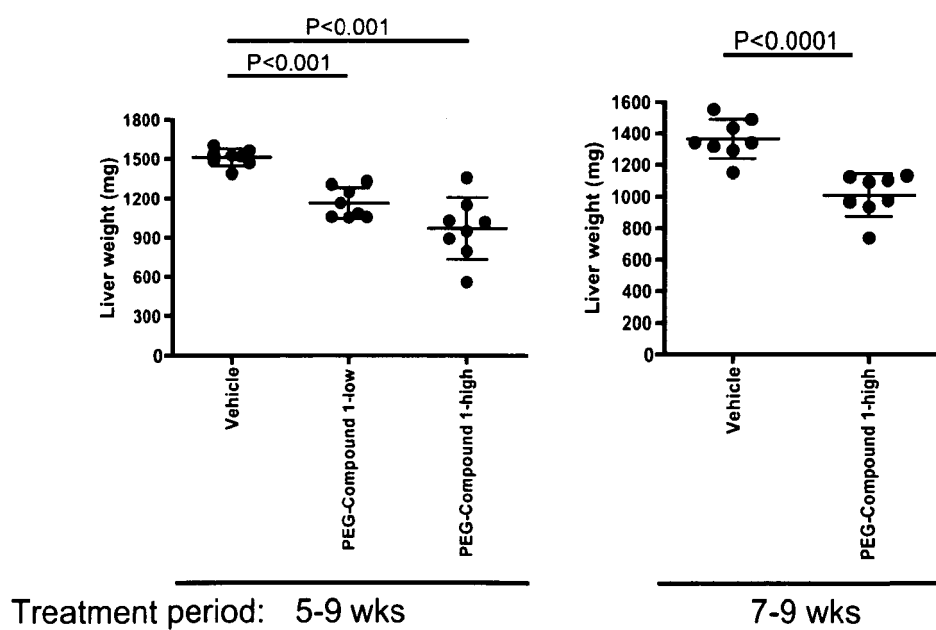


FIG. 23. Liver-to-body weight ratio

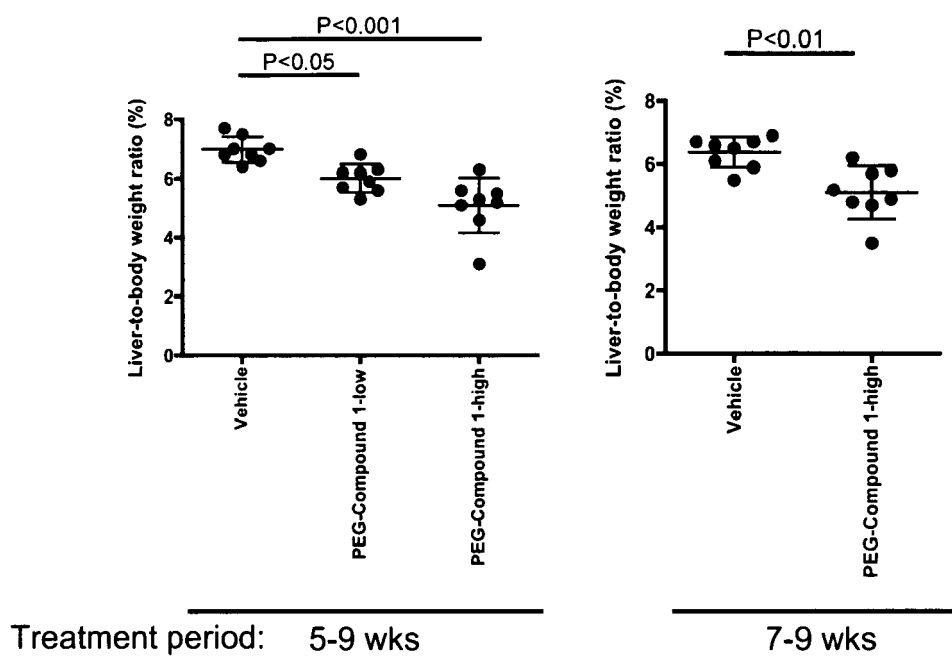


FIG. 24. Whole blood glucose

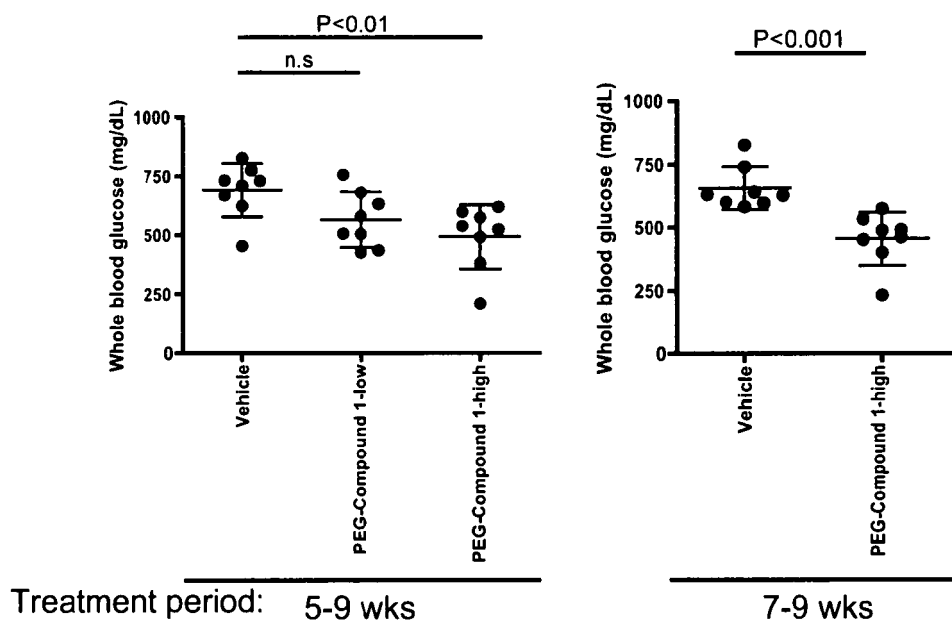


FIG. 25. Plasma ALT

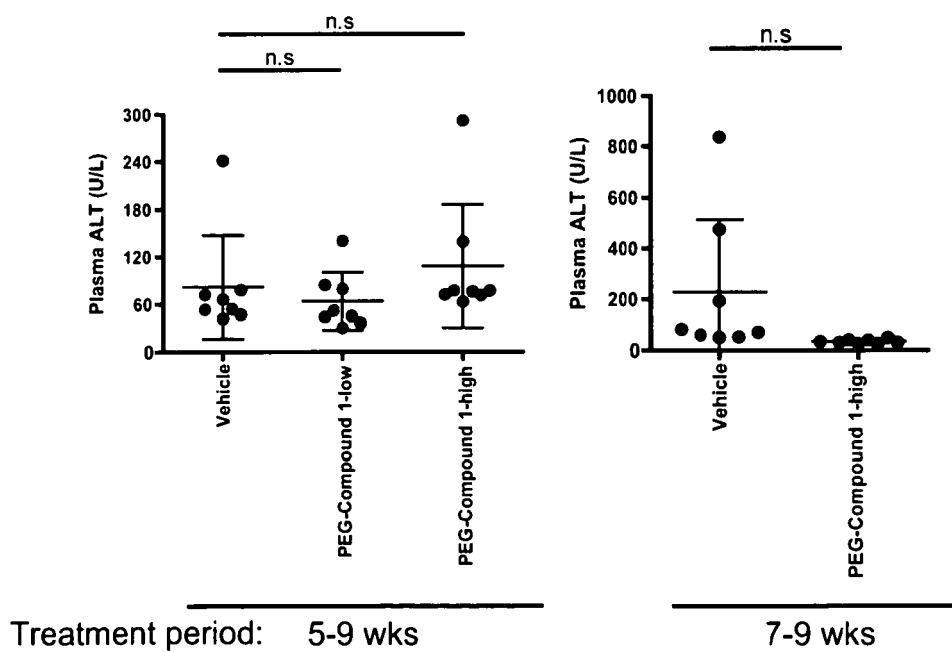


FIG. 26. Plasma triglyceride

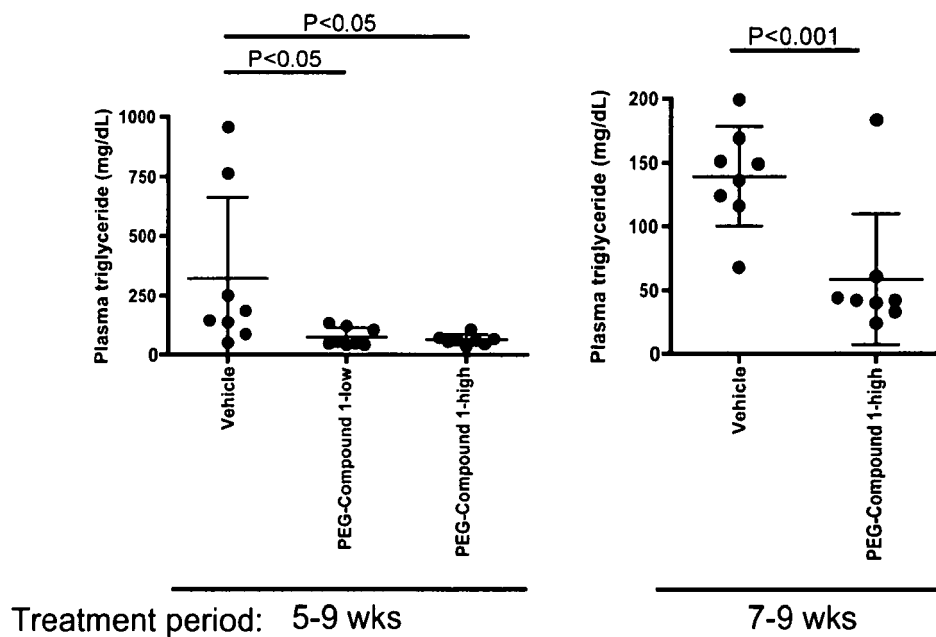


FIG. 27. Plasma total cholesterol

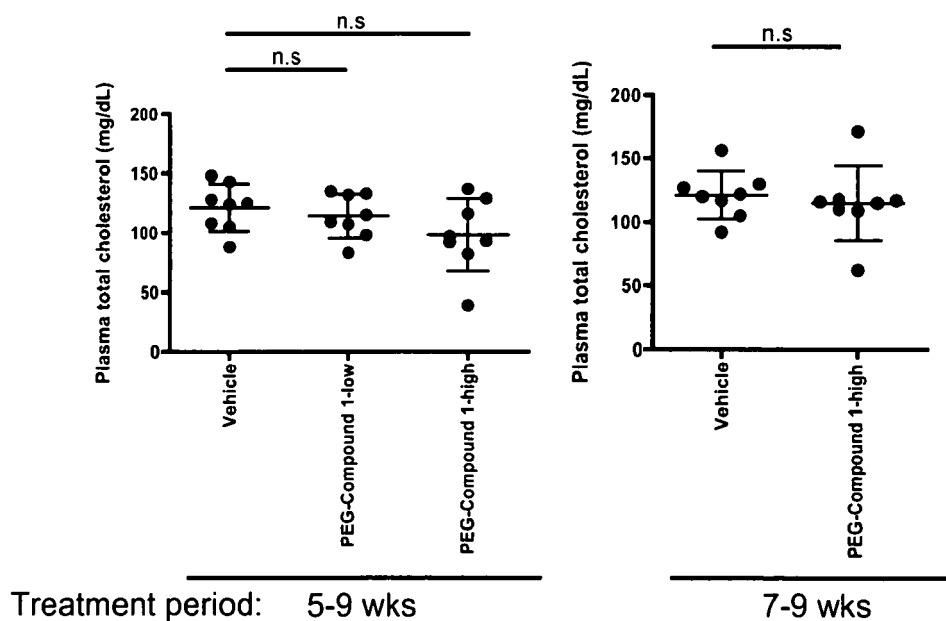


FIG. 28. Liver triglyceride

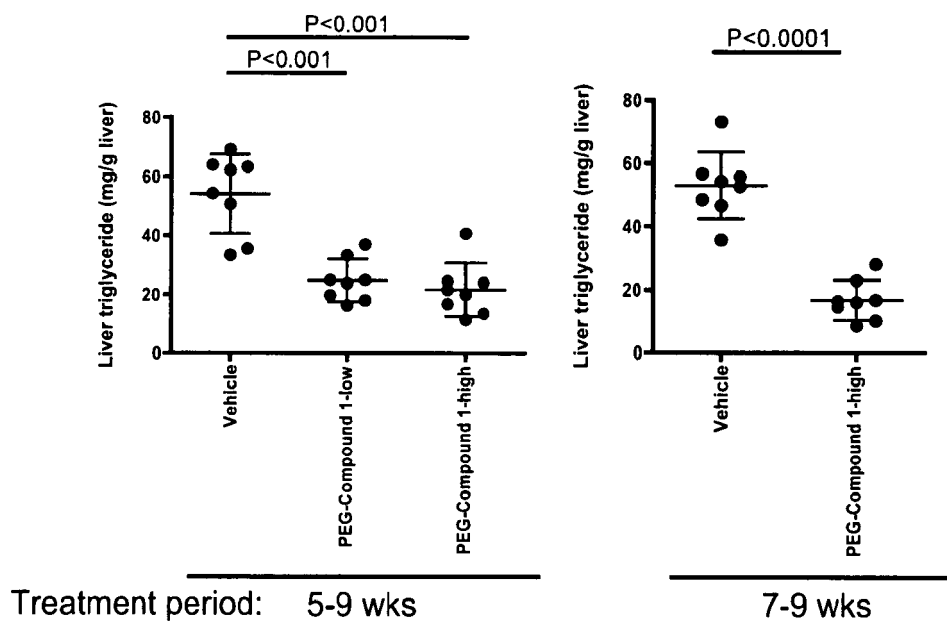


FIG. 29. Liver cholesterol

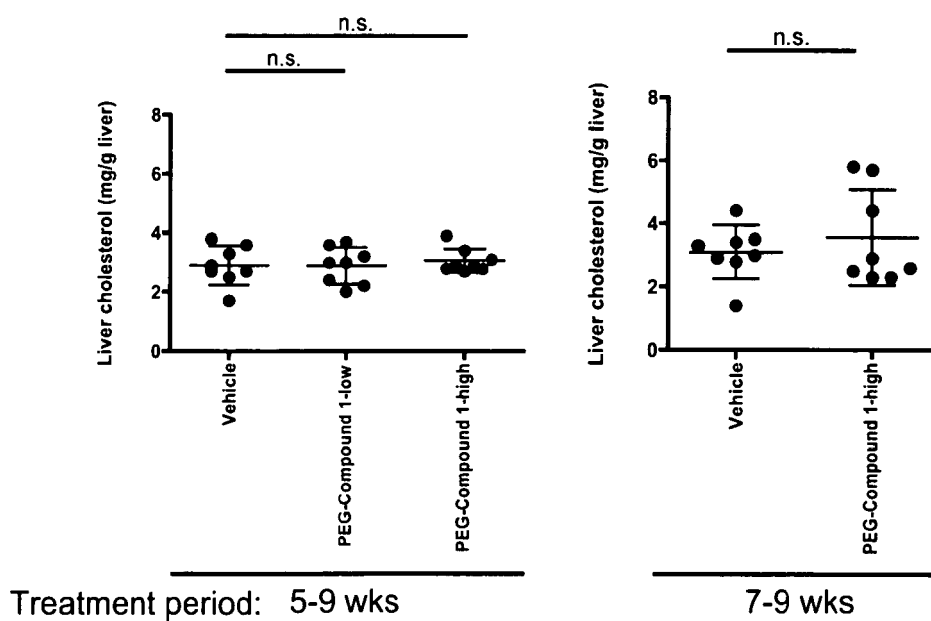


FIG. 30A. Representative photomicrographs of HE-stained liver sections

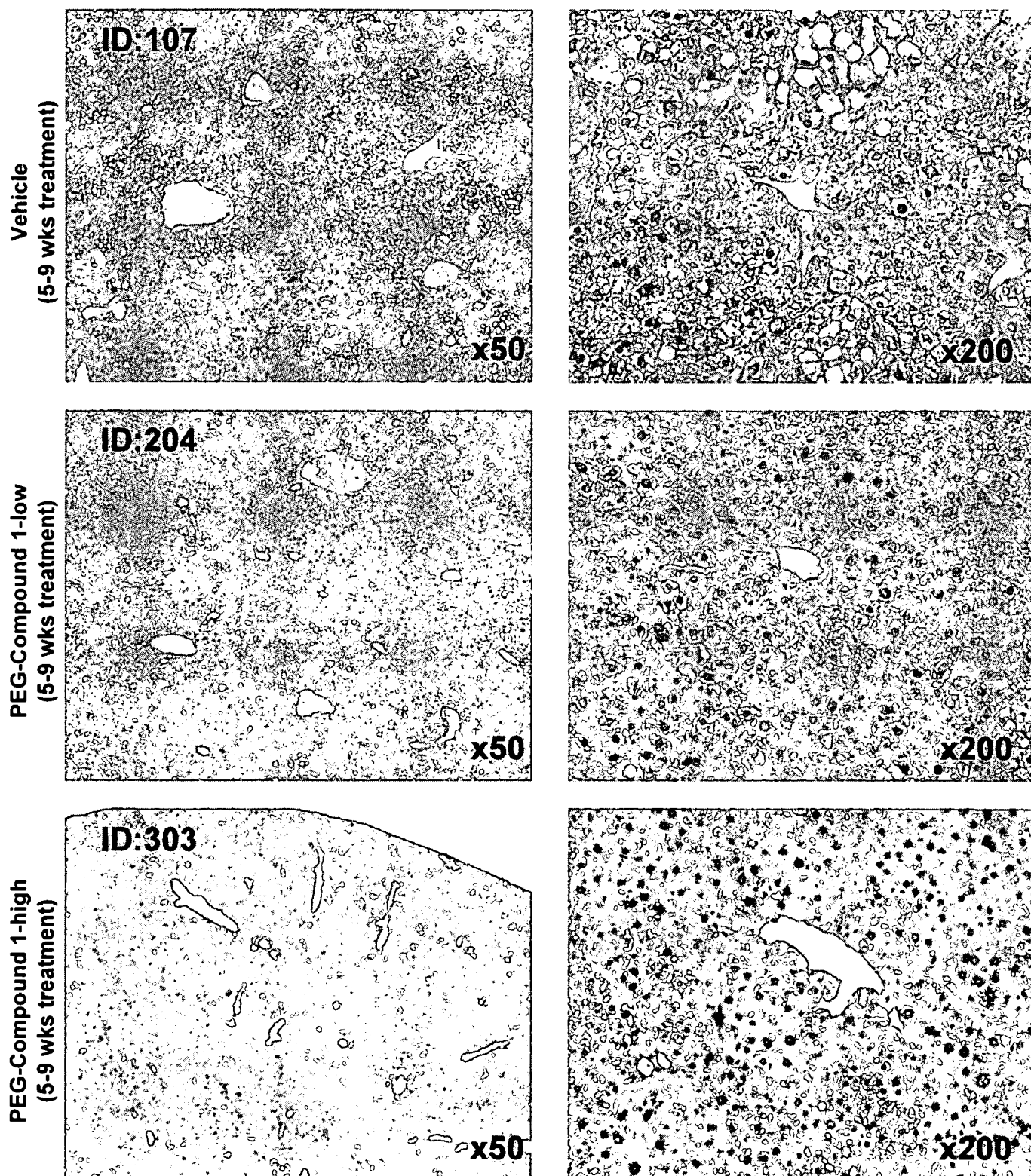
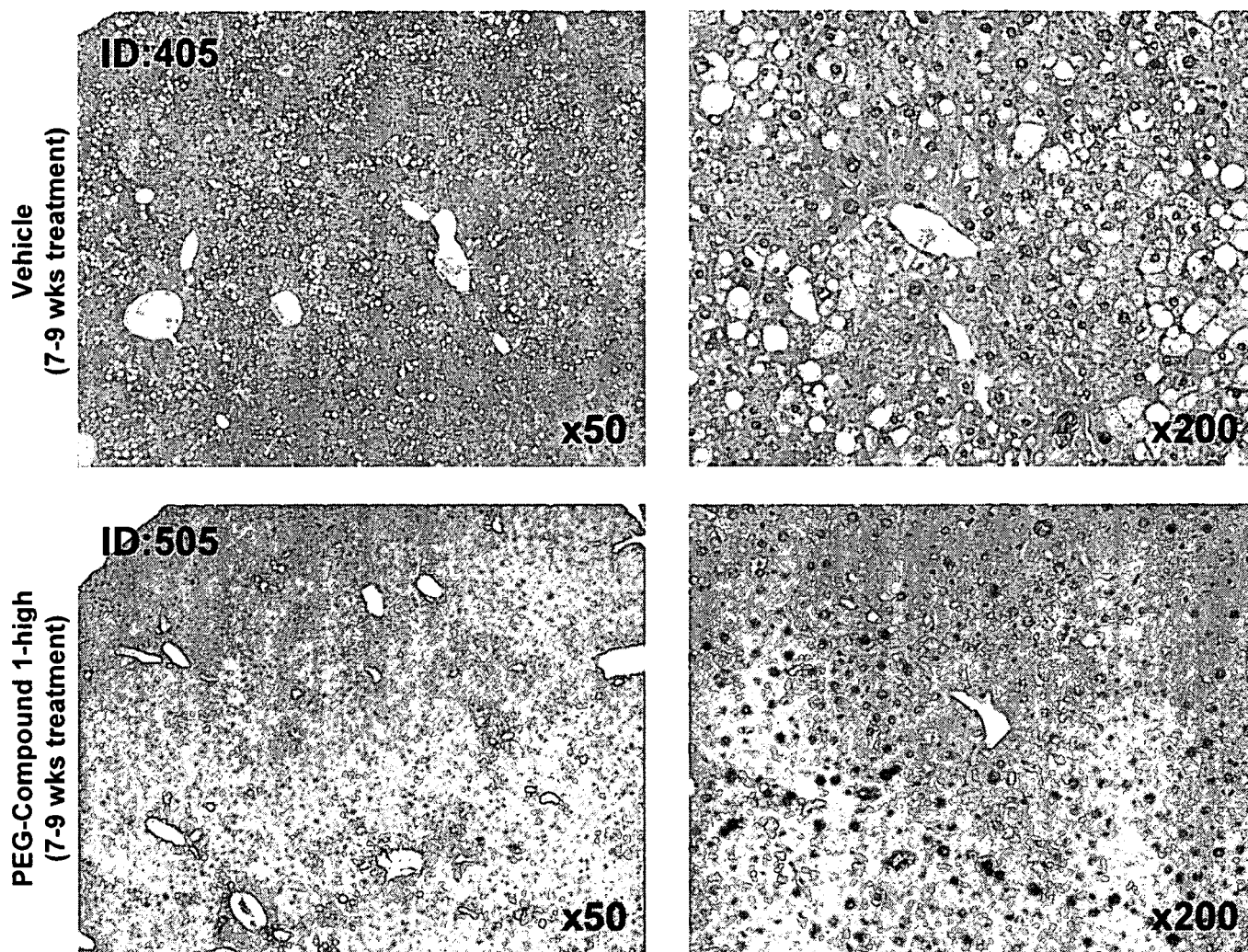


FIG. 30B. Representative photomicrographs of HE-stained liver sections
(continued)



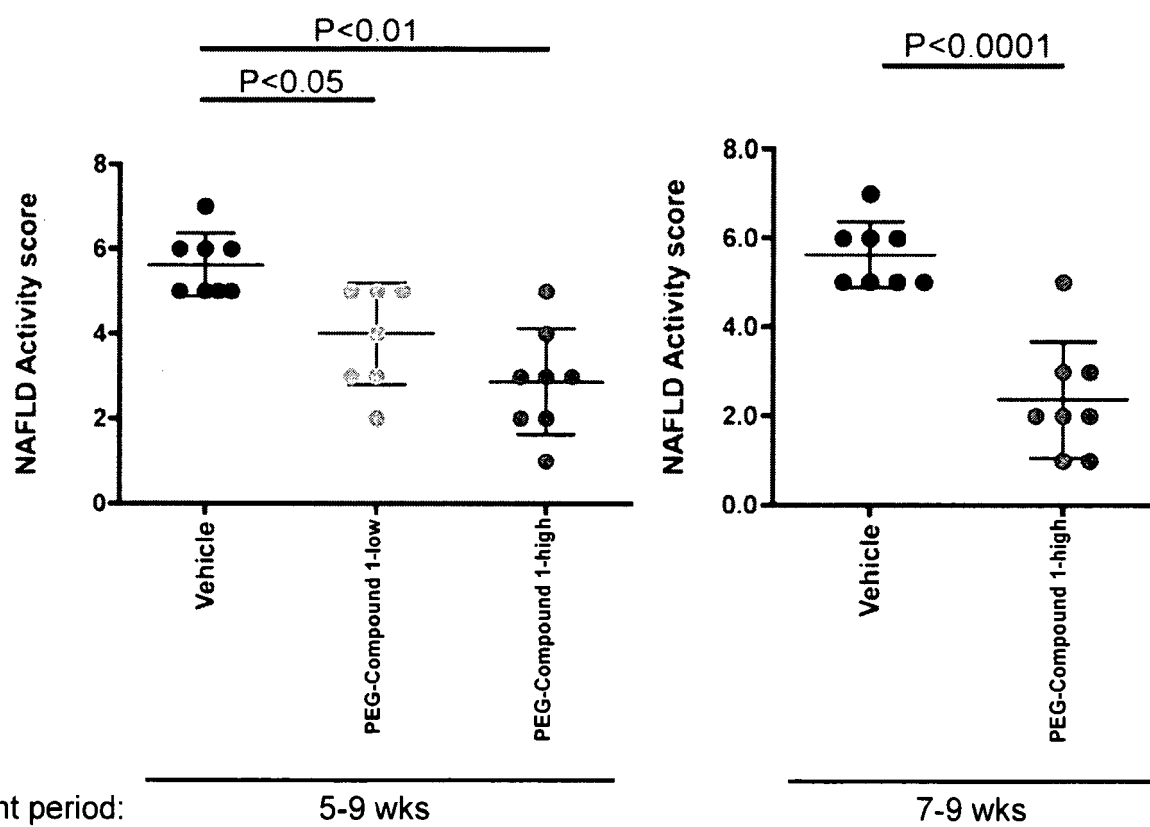


FIG. 32A. Steatosis score

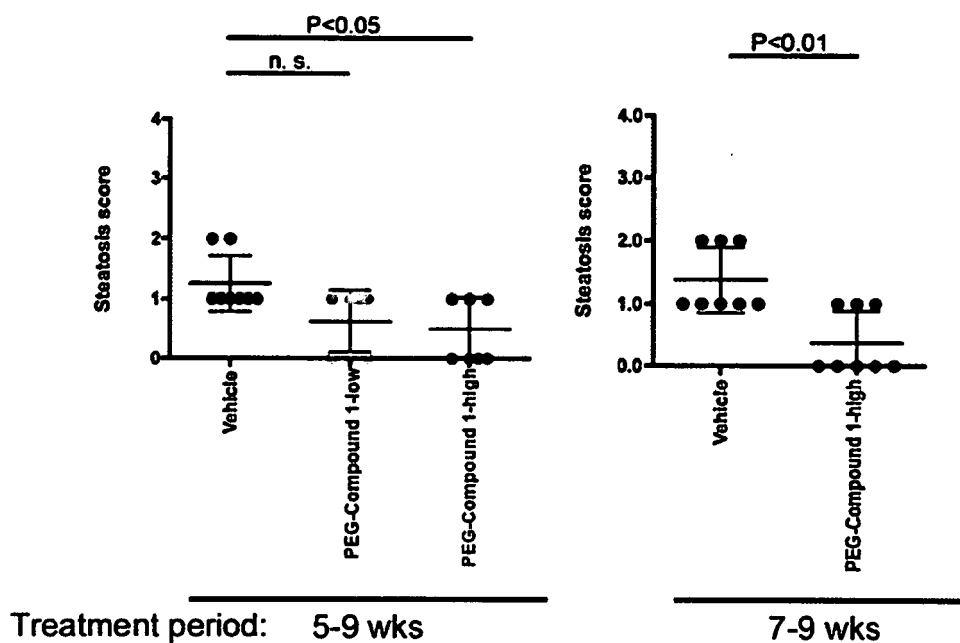


FIG. 32B. Lobular inflammation score

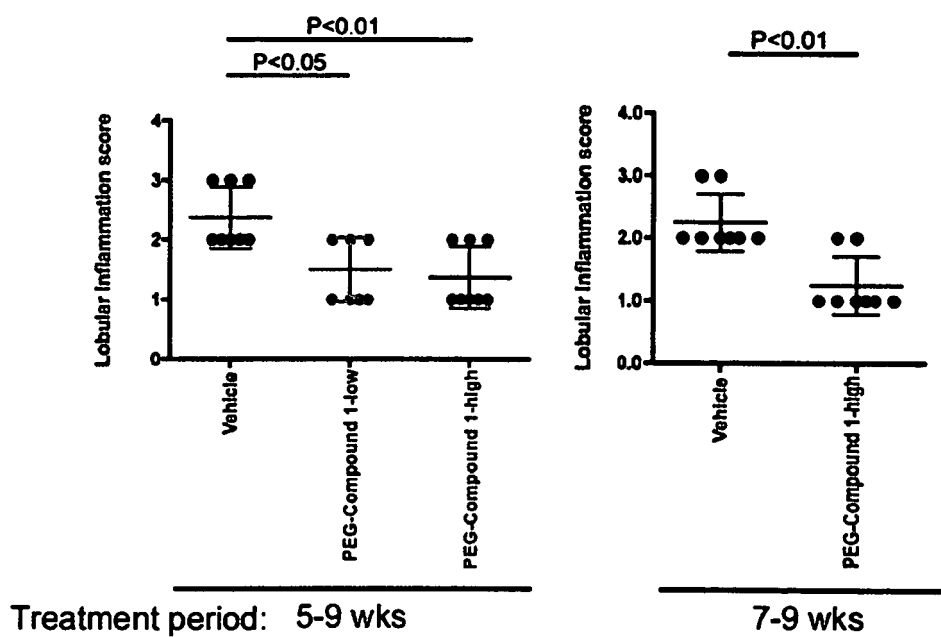


FIG. 32C. Hepatocyte ballooning score

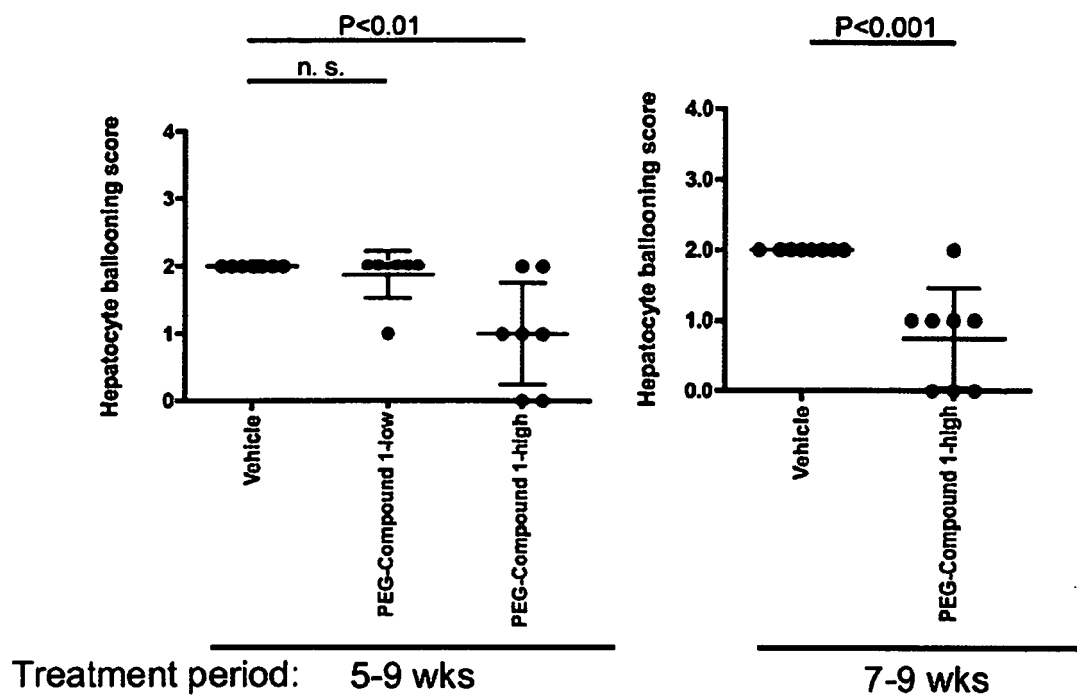


FIG. 33A. Representative photomicrographs of Sirius red-stained liver sections

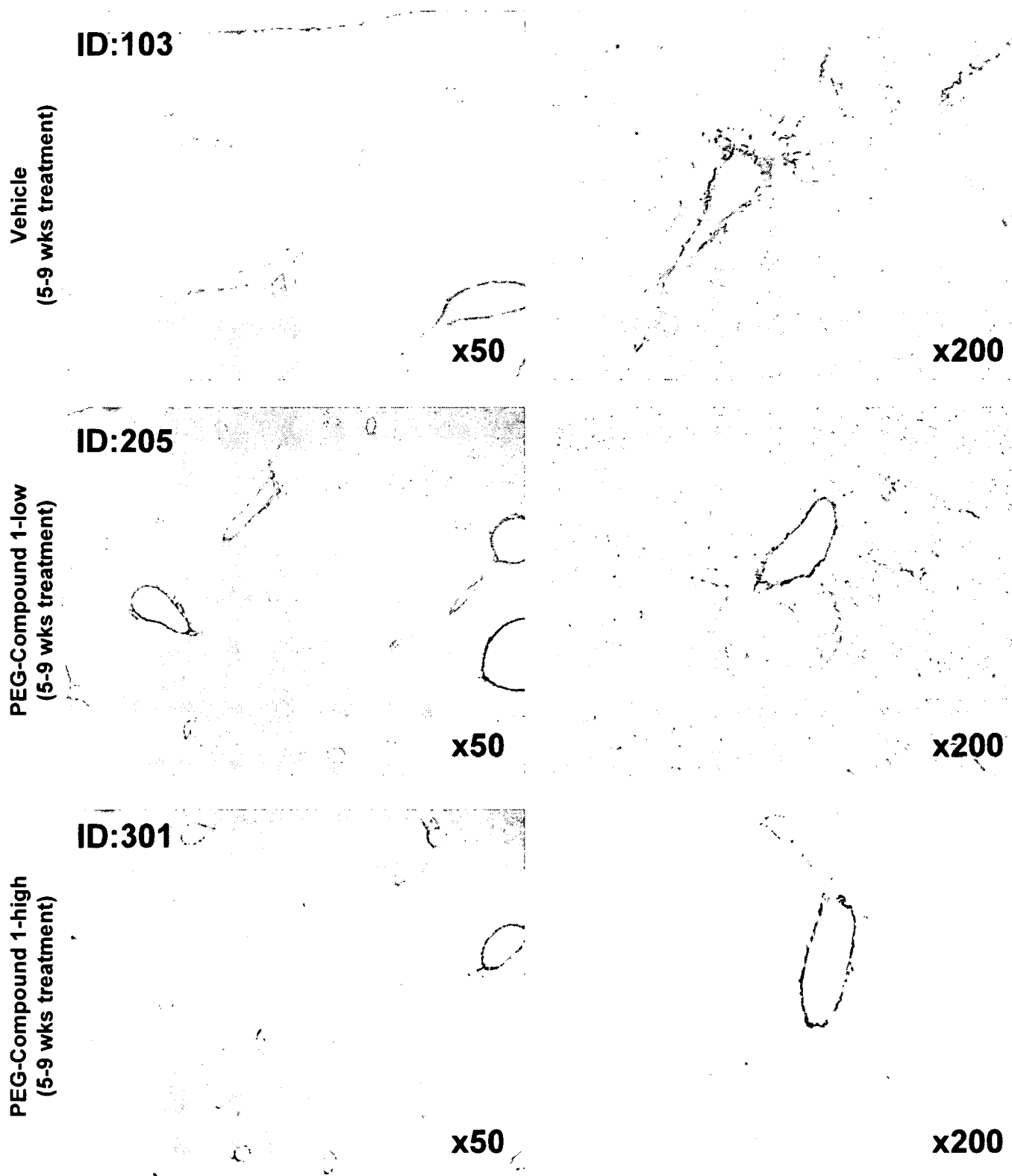


FIG. 33B. Representative photomicrographs of Sirius red-stained liver sections (continued)

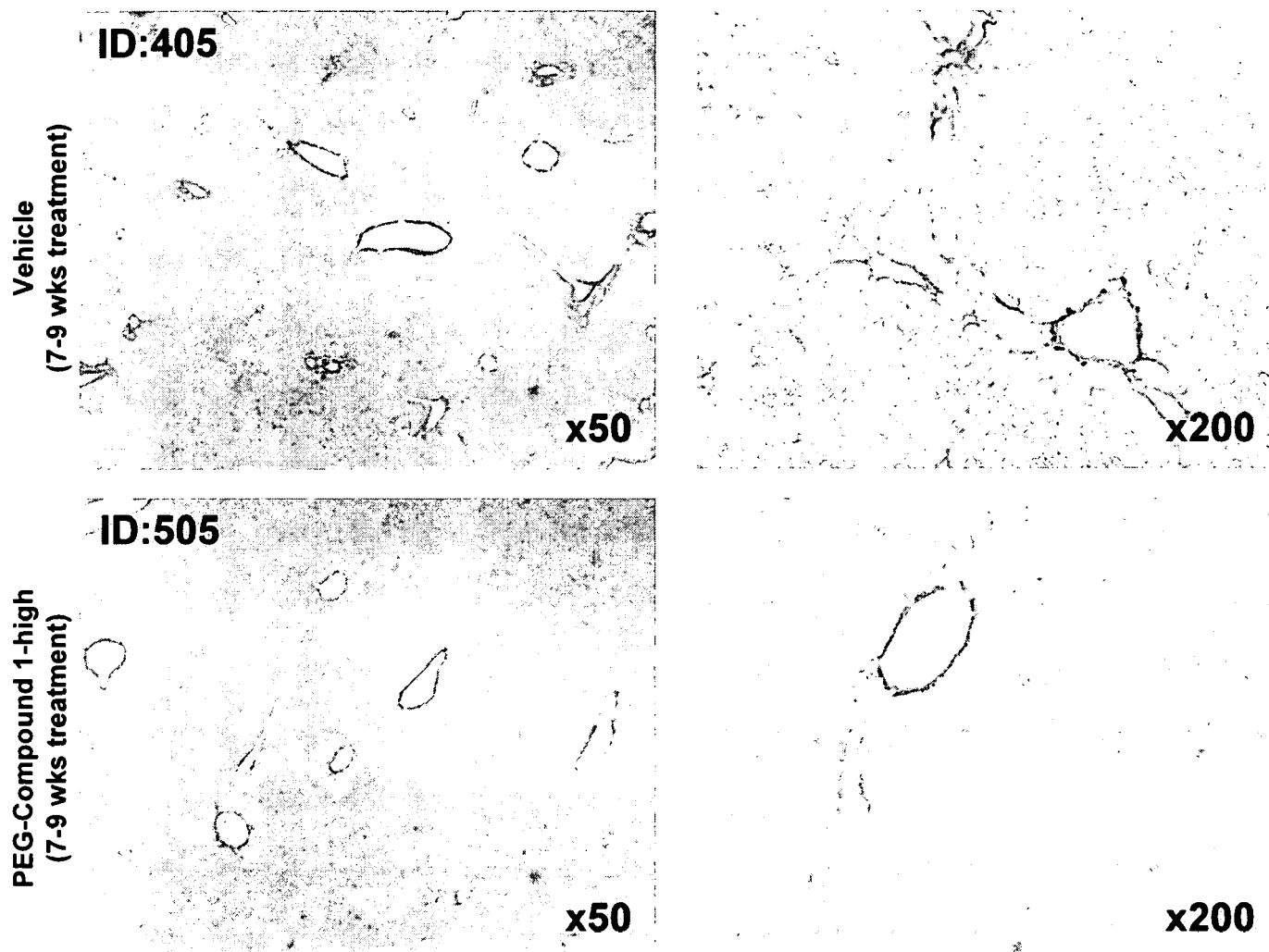


FIG. 34. Fibrosis area

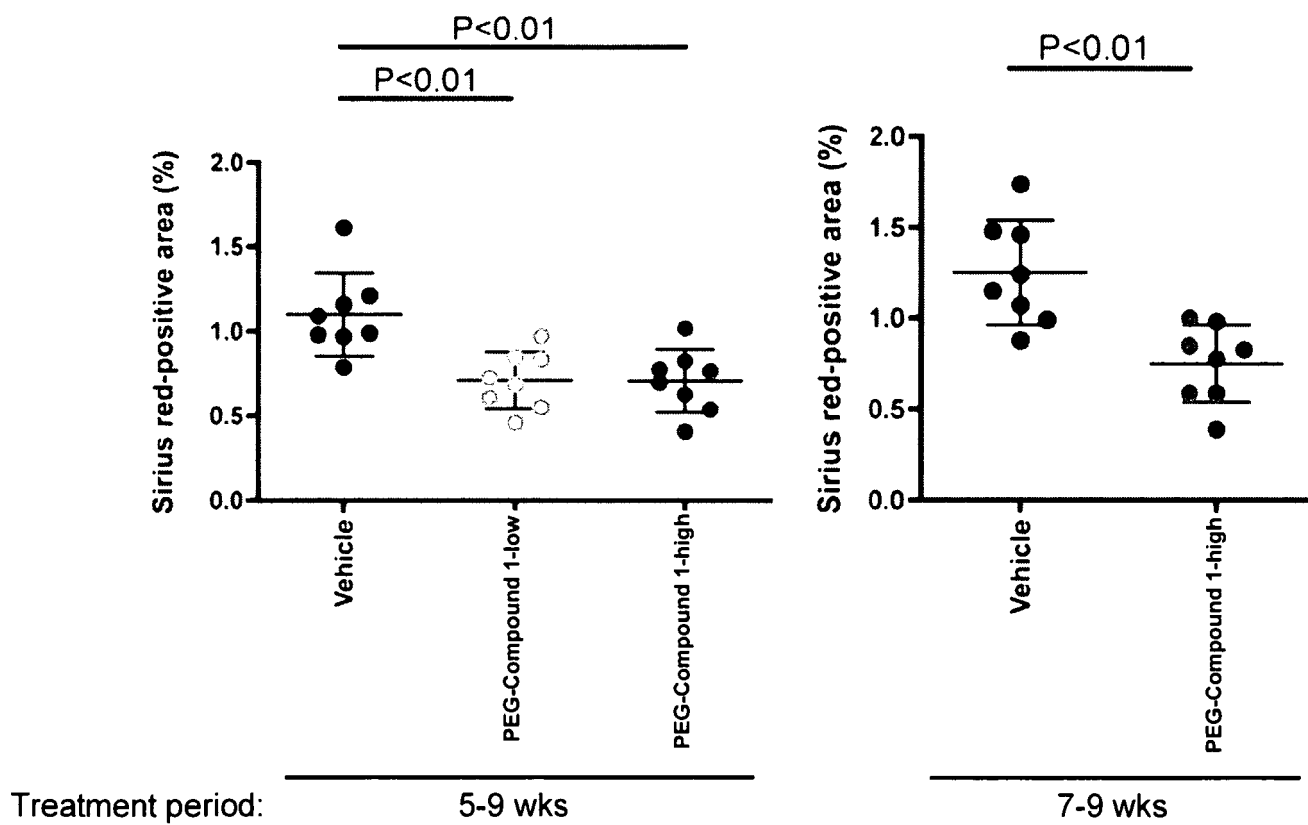


FIG. 35A. Representative photomicrographs of F4/80-immunostained liver sections

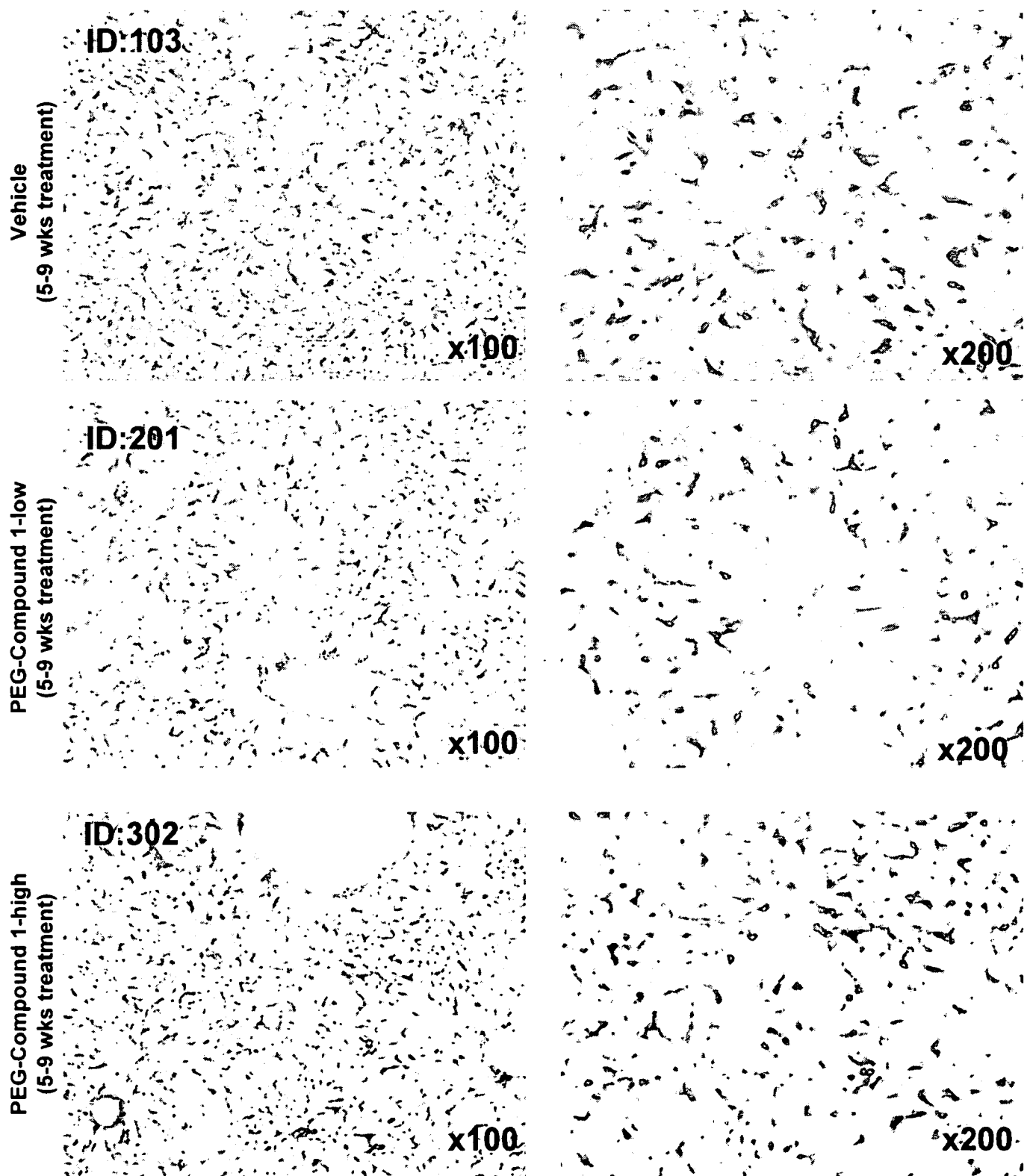


FIG. 35B. Representative photomicrographs of F4/80-immunostained liver sections (continued)

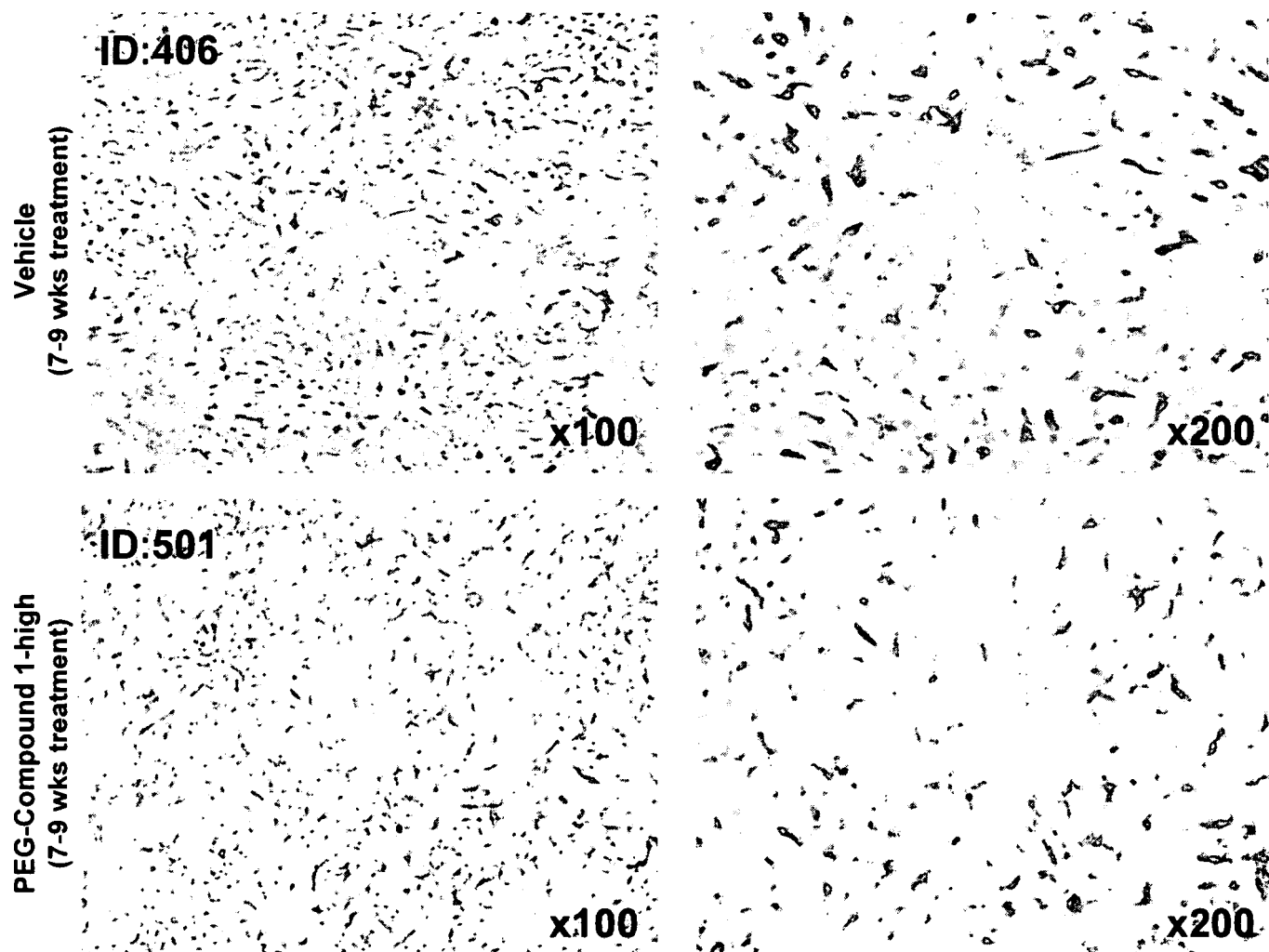


FIG. 36. Inflammation area

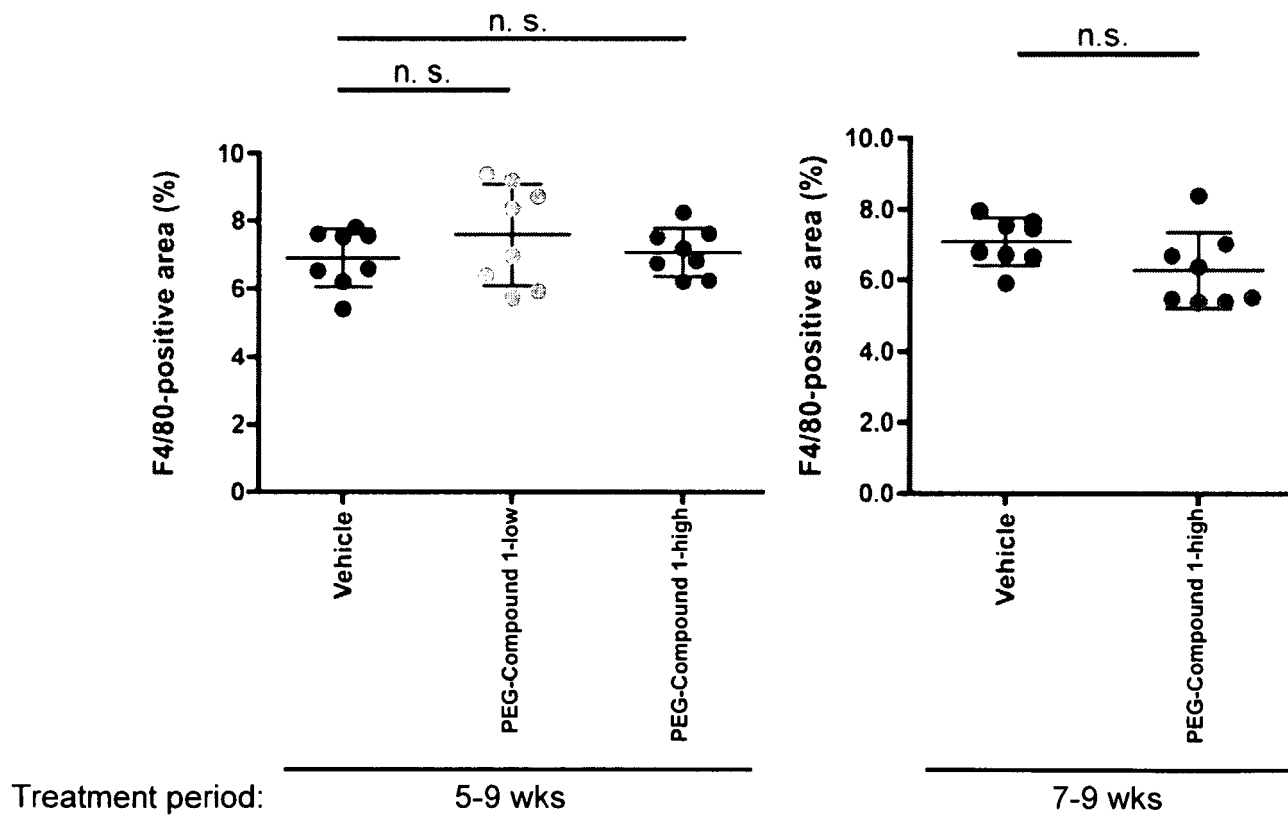


FIG. 37A. Representative photomicrographs of Oil red-stained liver sections

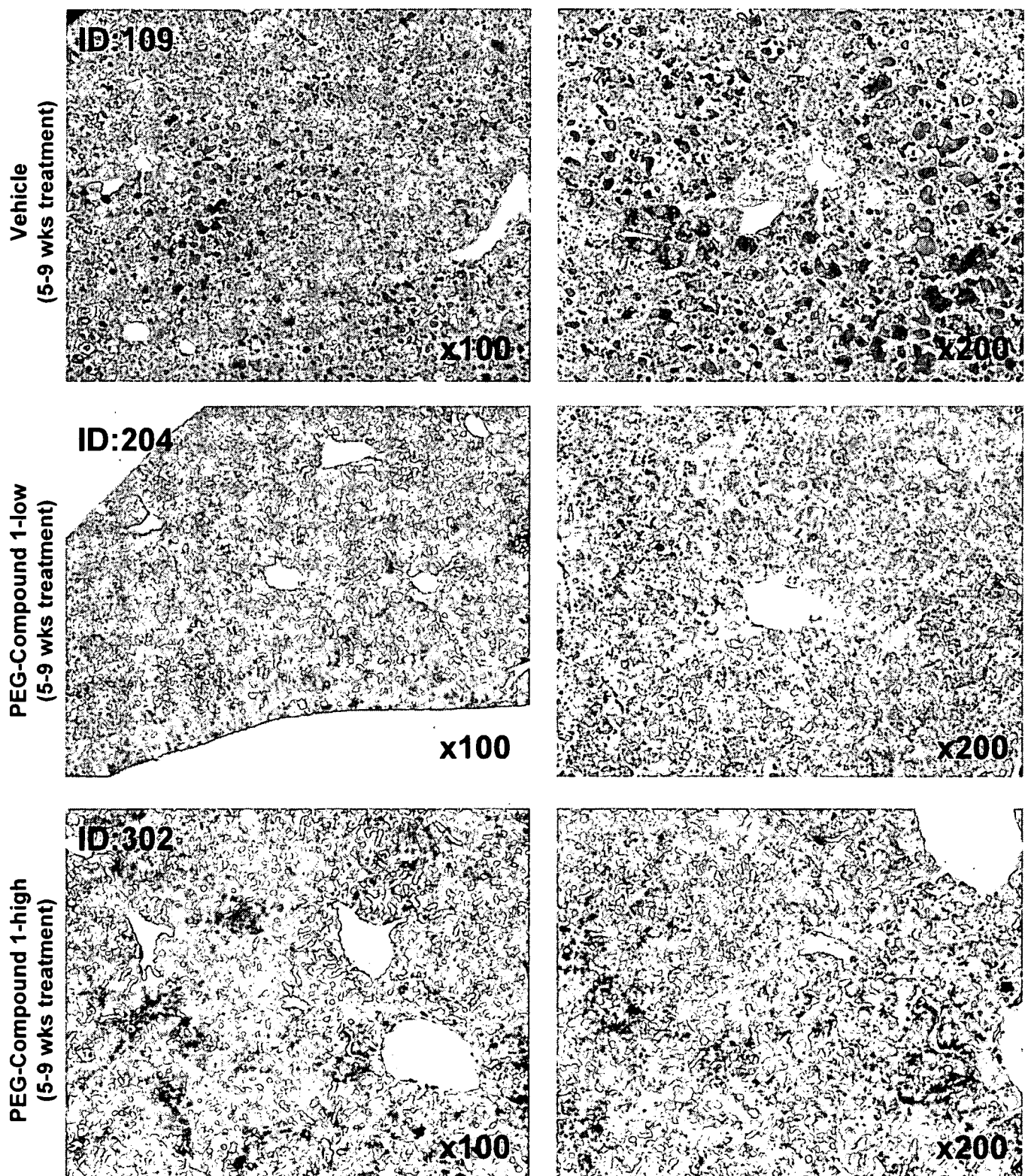


FIG. 37B. Representative photomicrographs of Oil red-stained liver sections (continued)

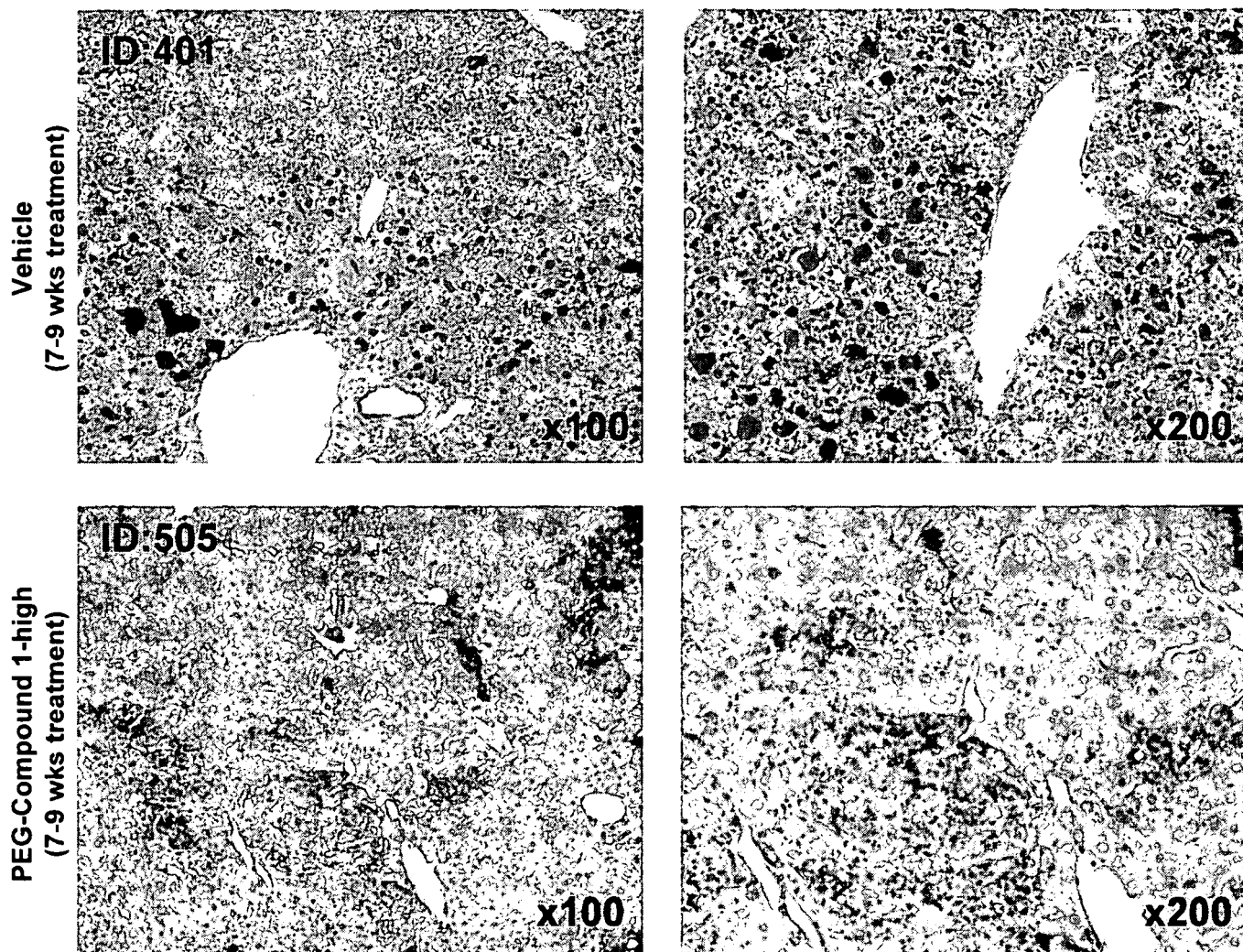


FIG. 38. Fat deposition area

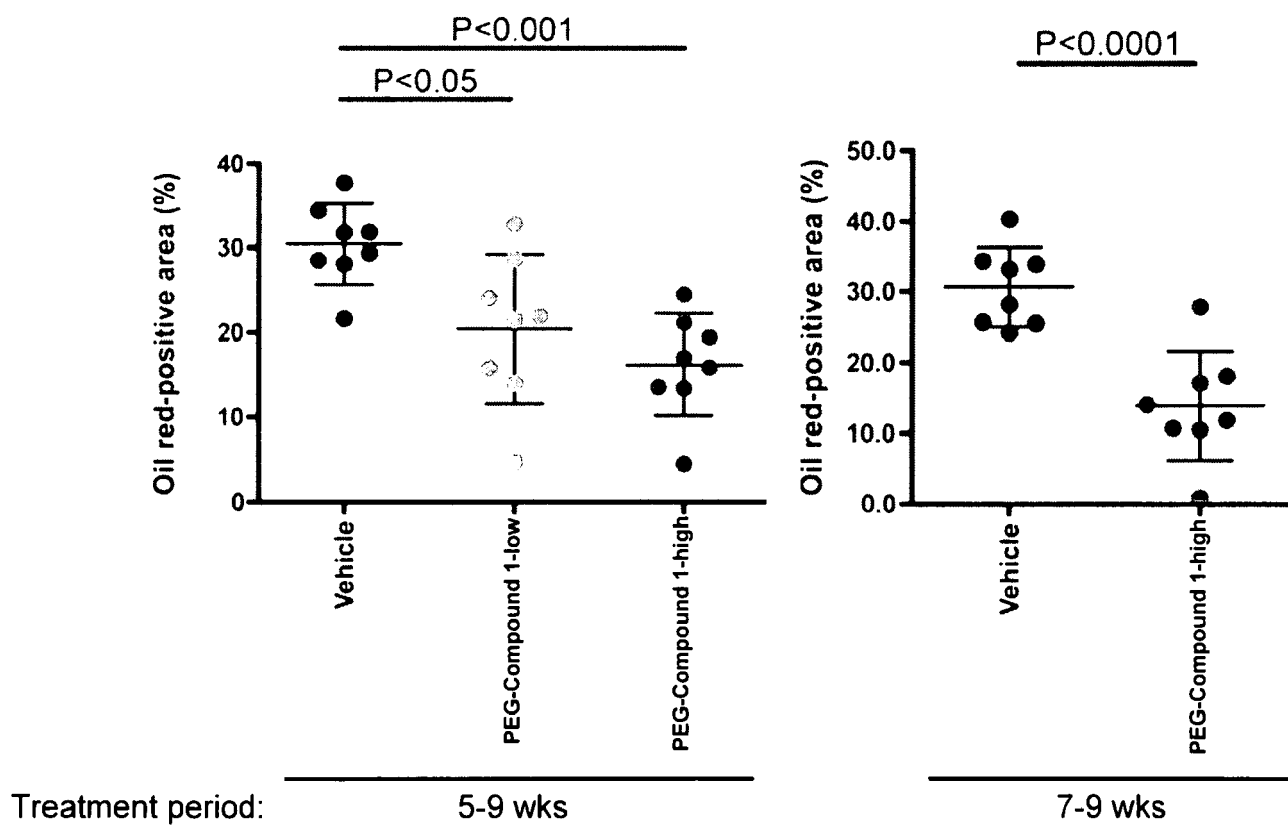


FIG. 39A

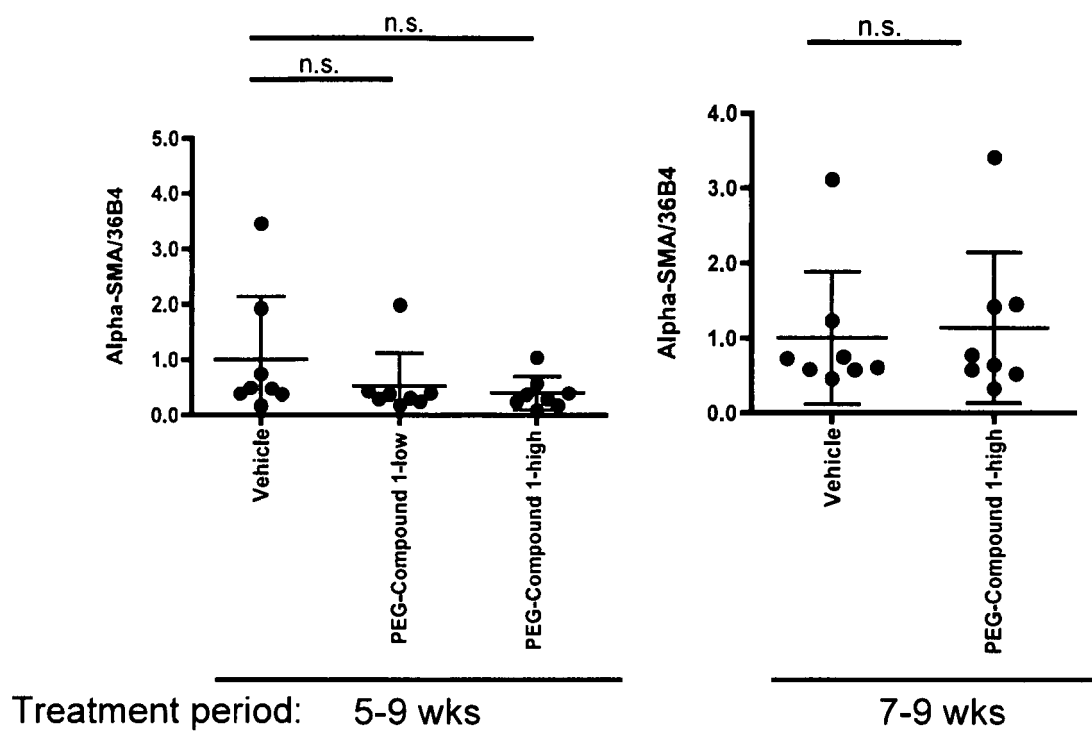
Alpha-SMA

FIG. 39B

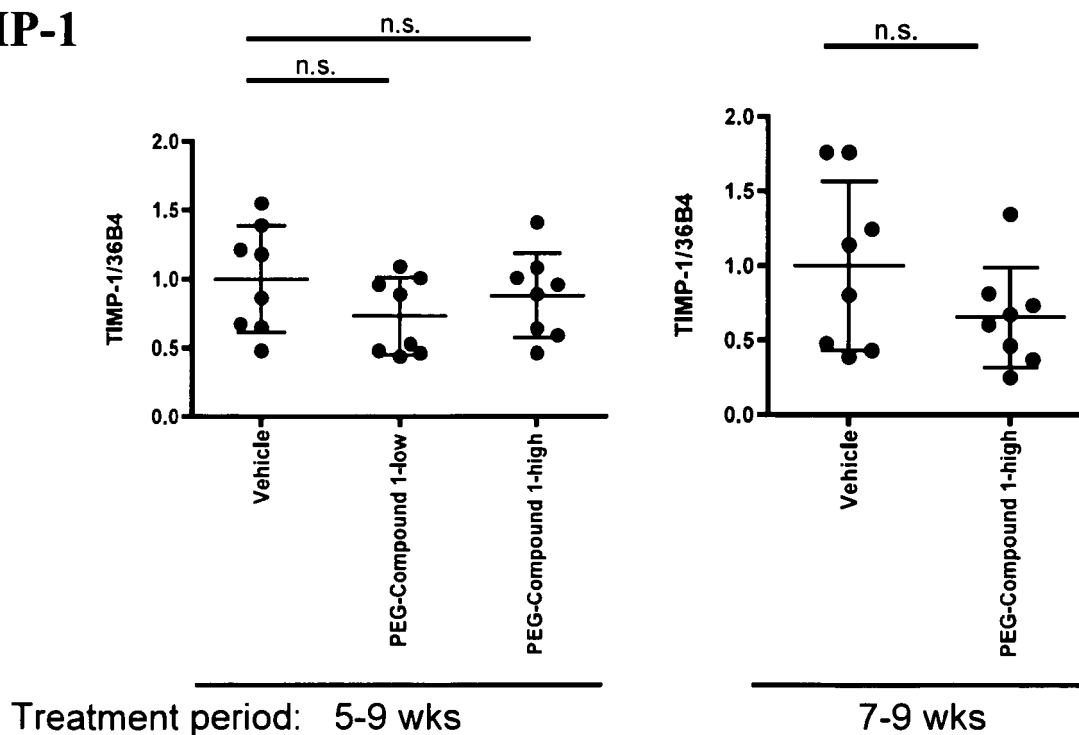
TIMP-1

FIG. 39C

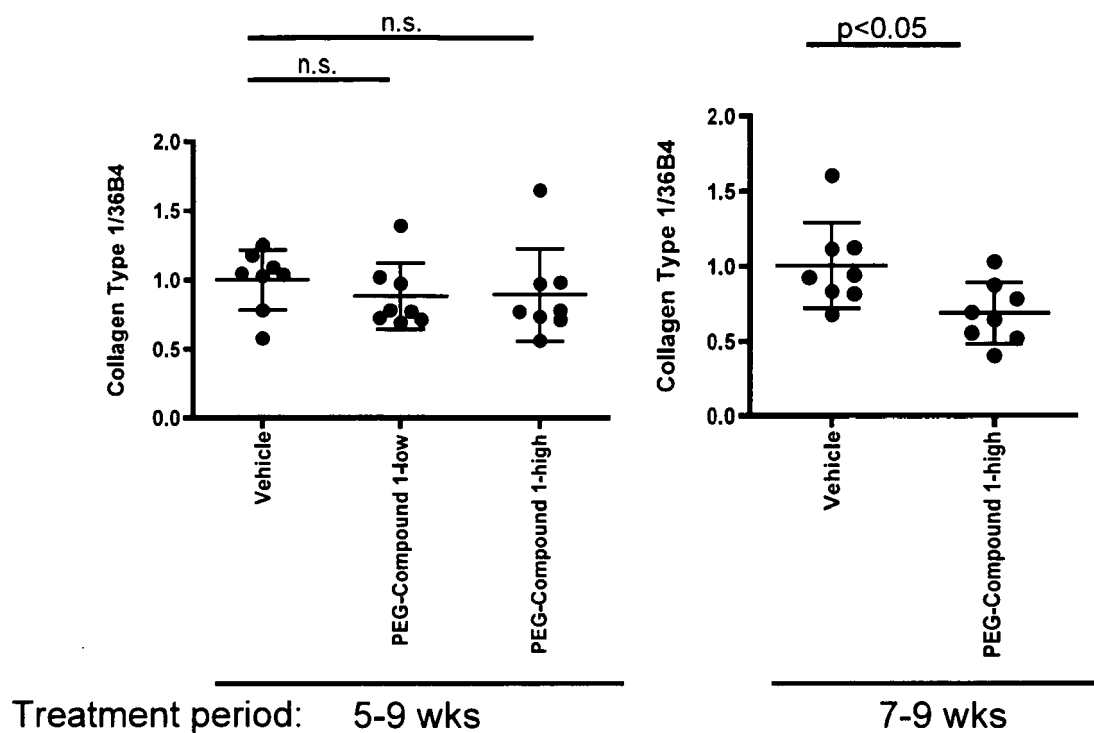
Collagen Type 1

FIG. 39D

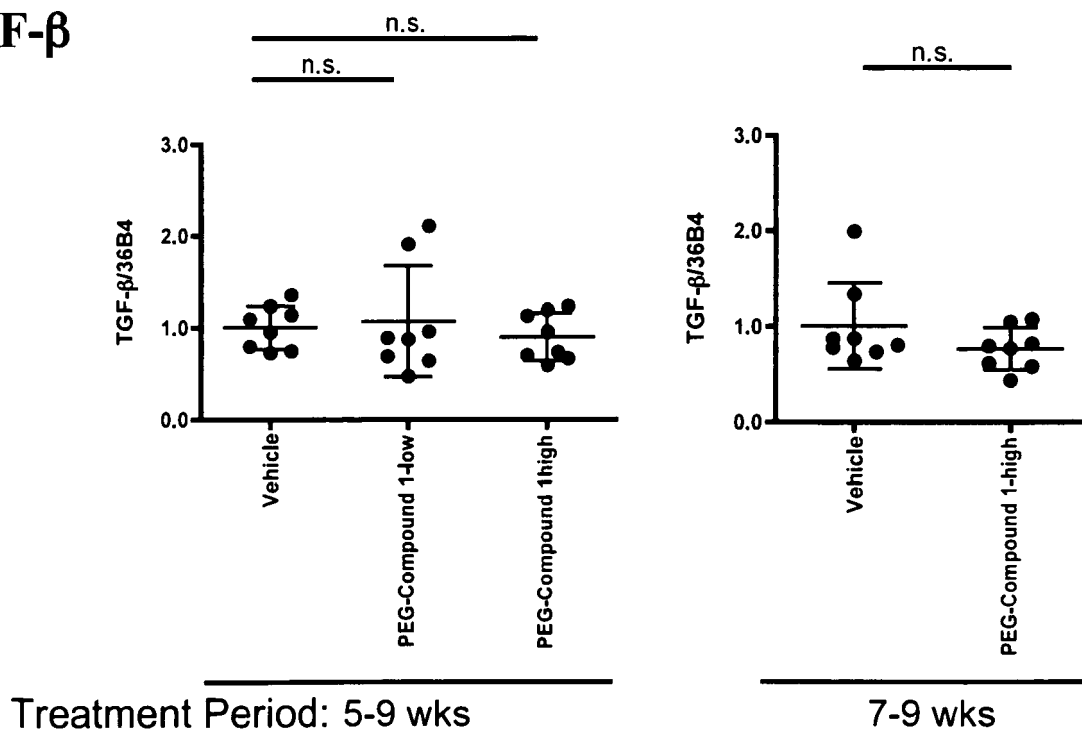
TGF- β 

FIG. 40A. Modified FGF-21 Polypeptide Fusion Proteins

Compound Name	SEQ ID NO:	Fusion Arrangement	Connecting Peptide	SEQ ID NO:
Compound 101	401	PKE(2)-L1-FGF21(Cmp. 2)	GS	354
Compound 102	402	PKE(2)-L2-FGF21(Cmp. 2)	GGGS	355
Compound 103	403	PKE(2)-L3-FGF21(Cmp. 2)	EEEEDEEED	356
Compound 104	404	PKE(2)-L4-FGF21(Cmp. 2)	PSPEPTPEP	357
Compound 105	405	PKE(2)-L5-FGF21(Cmp. 2)	GSHHHHHHHGS	358
Compound 106	406	PKE(2)-L6-FGF21(Cmp. 2)	GGGGGGGGGGGS	359
Compound 107	407	PKE(2)-L7-FGF21(Cmp. 2)	GGGGGGGGGGGS	360
Compound 108	408	PKE(2)-L8-FGF21(Cmp. 2)	GSGSGSGSGSGGS	361
Compound 109	409	PKE(2)-L9-FGF21(Cmp. 2)	PSTPTPSPTPTPS	362
Compound 110	410	PKE(2)-L10-FGF21(Cmp. 2)	RGEEKKKEKEEQEETKTP	363
Compound 111	411	PKE(2)-L11-FGF21(Cmp. 2)	GGGGGGGGGGGGGS	364
Compound 112	412	PKE(2)-L12-FGF21(Cmp. 2)	PSPEPTPEPPSPPTPEPPSPPTPEP	365
Compound 113	413	PKE(2)-L13-FGF21(Cmp. 2)	PSTPTPSPTPTPSPTPTPSPTPTPS	366
Compound 114	414	PKE(2)-L14-FGF21(Cmp. 2)	PSPEP	367
Compound 115	415	PKE(2)-L15-FGF21(Cmp. 2)	PSPEPTPEPPSPPTPEP	368
Compound 116	416	PKE(2)-L16-FGF21(Cmp. 2)	PSPEPTPEPPSPPTPEPPSPPTPEP	369
Compound 117	417	PKE(2)-L17-FGF21(Cmp. 2)	PTPEPPSPPTPEPPSP	370
Compound 118	418	PKE(2)-L18-FGF21(Cmp. 2)	PSPEGGGSPTPEP	371
Compound 119	419	PKE(2)-L19-FGF21(Cmp. 2)	PSPEEEEDPTPEP	372
Compound 120	420	PKE(2)-L20-FGF21(Cmp. 2)	PSPEPTPEEEEDPSPEPTPEP	373
Compound 121	421	PKE(2)-L21-FGF21(Cmp. 2)	PTPEPPSPPTPEEEEDPSPEPTPEPPSP	374
Compound 122	422	PKE(2)-L22-FGF21(Cmp. 2)	PTPEPPSPPTPEGGGSGSPPTPEPPSP	375
Compound 123	423	PKE(2)-L23-FGF21(Cmp. 2)	PSPEPTPEPPSPPTPEP	376

FIG. 40B.

Compound Name	SEQ ID NO:	Fusion Arrangement	Connecting Peptide	SEQ ID NO:
Compound 124	424	HuSA(C34A)-L201-FGF21(Cmp. 2)	GS	354
Compound 125	425	HuSA(C34A)-L202-FGF21(Cmp. 2)	GGGS	355
Compound 126	426	HuSA(C34A)-L203-FGF21(Cmp. 2)	GETGS	377
Compound 127	427	HuSA(C34A)-L204-FGF21(Cmp. 2)	GGGSGGGGS	378
Compound 128	428	HuSA(C34A)-L205-FGF21(Cmp. 2)	GETGSSGEGT	379
Compound 129	429	HuSA(C34A)-L206-FGF21(Cmp. 2)	GGGSGGGSGGGGS	359
Compound 130	430	HuSA(C34A)-L207-FGF21(Cmp. 2)	GETGSSGEGTGSTGS	380
Compound 131	431	HuSA(C34A)-L208-FGF21(Cmp. 2)	GGGSGGGSGGGSGGGGS	381
Compound 132	432	HuSA(C34A)-L209-FGF21(Cmp. 2)	GETGSSGEGTGSTGAGES	382
Compound 133	434	HuSA(C34A, des Leu-585)-L211-FGF21(Cmp. 2)	GGGSGGGSGGGSGGGGS	359
Compound 134	435	HuSA(C34A, des Leu-585)-L207-FGF21(Cmp. 2)	GETGSSGEGTGSTGS	380
Compound 135	436	HuSA(C34A, des Leu-585)-L211-FGF21(Cmp. 1)	GGGSGGGSGGGSGGGGS	359
Compound 136	437	HuSA(C34A, des Leu-585)-L207-FGF21(Cmp. 1)	GETGSSGEGTGSTGS	380
Compound 137	440	FGF21(Cmp. 2)-L205-HuSA(C34A)	GETGSSGEGT	379
Compound 138	441	FGF21(Cmp. 2)-L209-HuSA(C34A)	GETGSSGEGTGSTGAGES	382
Compound 139	442	FGF21(Cmp. 2)-L210-HuSA(C34A)	GETGSSGEGTGSTGAGESGTGSGEGGS	383
Compound 140	443	FGF21(Cmp. 1)-L209-HuSA(C34A)	GETGSSGEGTGSTGAGES	382
Compound 141	446	FGF21(Cmp. 2)-L209-HuSA(C34A)-G4Sx3-FGF21(Cmp. 2)	GETGSSGEGTGSTGAGES	382
Compound 142	447	FGF21(Cmp. 1)-L209-HuSA(C34A)-G4Sx3-FGF21(Cmp. 1)	GETGSSGEGTGSTGAGES	382
Compound 143	448	FGF21(Cmp. 2)-L209-HuSA(C34A, des Leu-585)-G4Sx3-FGF21(Cmp. 2)	GETGSSGEGTGSTGAGES	382
Compound 144	449	FGF21(Cmp. 1)-L209-HuSA(C34A, des Leu-585)-G4Sx3-FGF21(Cmp. 1)	GETGSSGEGTGSTGAGES	382
Compound 145	450	FGF21(Cmp. 2)-L210-HuSA(C34A)-G4Sx3-FGF21(Cmp. 2)	GETGSSGEGTGSTGAGESGTGSGEGGS	383
Compound 146	451	FGF21(Cmp. 1)-L210-HuSA(C34A)-G4Sx3-FGF21(Cmp. 1)	GETGSSGEGTGSTGAGESGTGSGEGGS	383

FIG. 40C

Compound Name	SEQ ID NO:	Fusion Arrangement	Connecting Peptide	SEQ ID NO:
Compound 147	452	PKE(1)-L1-FGF21(Cmp. 2)	GS	354
Compound 148	453	PKE(1)-L2-FGF21(Cmp. 2)	GGGS	355
Compound 149	454	PKE(1)-L3-FGF21(Cmp. 2)	EEEEDEEED	356
Compound 150	455	PKE(1)-L4-FGF21(Cmp. 2)	PSPEPTPEP	357
Compound 151	456	PKE(1)-L5-FGF21(Cmp. 2)	GSHHHHHHHGS	358
Compound 152	457	PKE(1)-L6-FGF21(Cmp. 2)	GGGSGGGSGGGGS	359
Compound 153	458	PKE(1)-L7-FGF21(Cmp. 2)	GGGSGGGSGGGGS	360
Compound 154	459	PKE(1)-L8-FGF21(Cmp. 2)	GSGSGSGSGSGSGS	361
Compound 155	460	PKE(1)-L9-FGF21(Cmp. 2)	PSTPTPSPTPTPS	362
Compound 156	461	PKE(1)-L10-FGF21(Cmp. 2)	RGEEKKKKEKEEERETKTP	363
Compound 157	462	PKE(1)-L11-FGF21(Cmp. 2)	GGGSGGGSGGGSGGGSGGGGS	364
Compound 158	463	PKE(1)-L12-FGF21(Cmp. 2)	PSPEPTPEPPSPPTPEPPSPPTPEP	365
Compound 159	464	PKE(1)-L13-FGF21(Cmp. 2)	PSTPTPSPTPTPSPTPTPSPTPTPS	366
Compound 160	465	PKE(1)-L14-FGF21(Cmp. 2)	PSPEP	367
Compound 161	466	PKE(1)-L15-FGF21(Cmp. 2)	PSPEPTPEPPSPPTPEP	368
Compound 162	467	PKE(1)-L16-FGF21(Cmp. 2)	PSPEPTPEPPSPPTPEPPSPPTPEP	369
Compound 163	468	PKE(1)-L17-FGF21(Cmp. 2)	PTPEPPSPPTPEPPSP	370
Compound 164	469	PKE(1)-L18-FGF21(Cmp. 2)	PSPEPGGSPTEP	371
Compound 165	470	PKE(1)-L19-FGF21(Cmp. 2)	PSPEPEEEDPTPEP	372
Compound 166	471	PKE(1)-L20-FGF21(Cmp. 2)	PSPEPTPEPEEEDPSPEPTPEP	373
Compound 167	472	PKE(1)-L21-FGF21(Cmp. 2)	PTPEPPSPPTPEPEEEDPSPEPTPEPPSP	374
Compound 168	473	PKE(1)-L22-FGF21(Cmp. 2)	PTPEPPSPPTPEPGGGSPSPPTPEPPSP	375
Compound 169	474	PKE(1)-L23-FGF21(Cmp. 2)	PSPEPTPEPPSPPTPEPPSPPTPEP	376

FIG. 40D

Compound Name	SEQ ID NO:	Fusion Arrangement	Connecting Peptide	SEQ ID NO:
Compound 170	475	Fc(hlgG1a_191)-L7-FGF21(Cmp. 2)	GGGGSGGGSGGGGS	360
Compound 171	476	Fc(hlgG1a_191)-L250-FGF21(Cmp. 2)	GGGGSGGGSGGGSGGGSGGGGS	350
Compound 172	477	Fc(hlgG1a_191)-L112-FGF21(Cmp. 2)	PSPEPTPEPPSPPEPTPEPPSPPTPEP	365
Compound 173	478	Fc(hlgG1a_191)-L251-FGF21(Cmp. 2)	PSPEPTPEPPSPPEP	351
Compound 174	479	Fc(hlgG1a_191)-L5-FGF21(Cmp. 2)	GSHHHHHHHHGS	358
Compound 175	480	Fc(hlgG1a_191)-L252-FGF21(Cmp. 2)	ELQLEESAAEAQEGELE	352
Compound 176	481	Fc(hlgG1a_190)-L253-FGF21(Cmp. 2)	SSGGSGGGSGGGSGGGGS	353
Compound 177	482	Fc(hlgG1a_191)-L6-FGF21(Cmp. 2)	GGGGSGGGSGGGGS	359
Compound 178	483	Fc(hlgG1a_189)-L6-FGF21(Cmp. 2)	GGGGSGGGSGGGGS	359
Compound 179	484	Fc(hlgG1a_191)-L7-FGF21-1aa(Cmp. 2)	GGGGSGGGSGGGSGGGGS	360
Compound 180	485	Fc(hlgG1a_191)-L7-FGF21-3aa(Cmp. 2)	GGGGSGGGSGGGSGGGGS	360
Compound 181	486	Fc(hlgG1f_1.1_186)-L7-FGF21(Cmp. 2)	GGGGSGGGSGGGSGGGGS	360
Compound 182	487	Fc(hlgG1a_191b)-L7-FGF21(Cmp. 2)	GGGGSGGGSGGGSGGGGS	360

FIG. 41

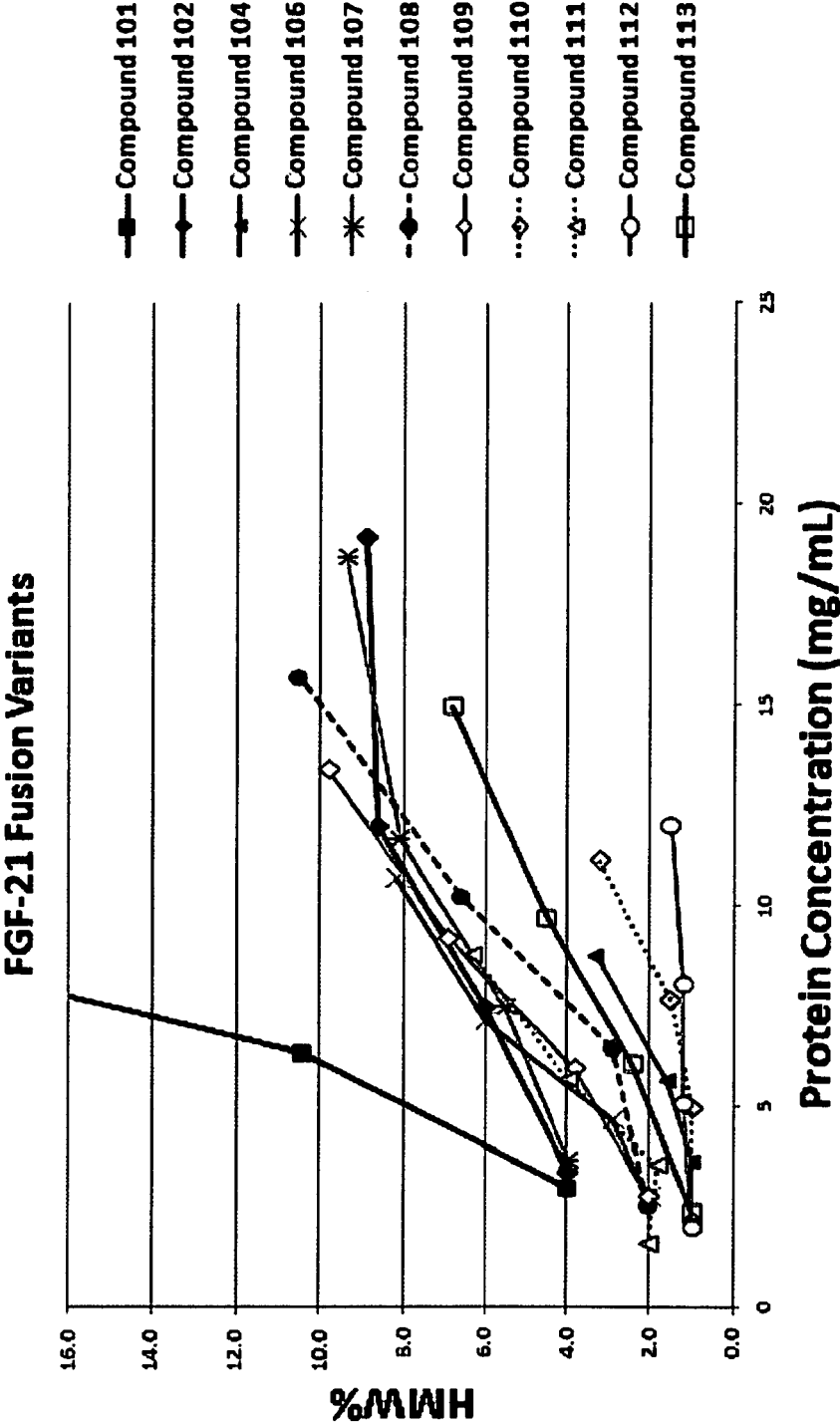


FIG. 42A

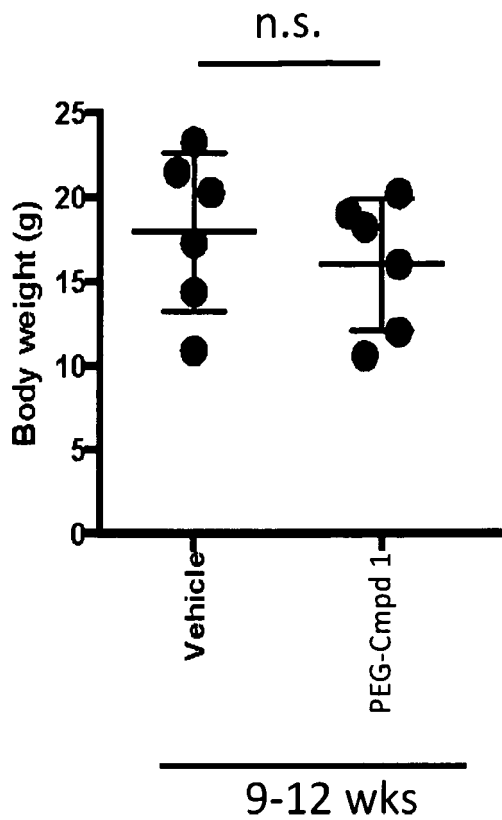
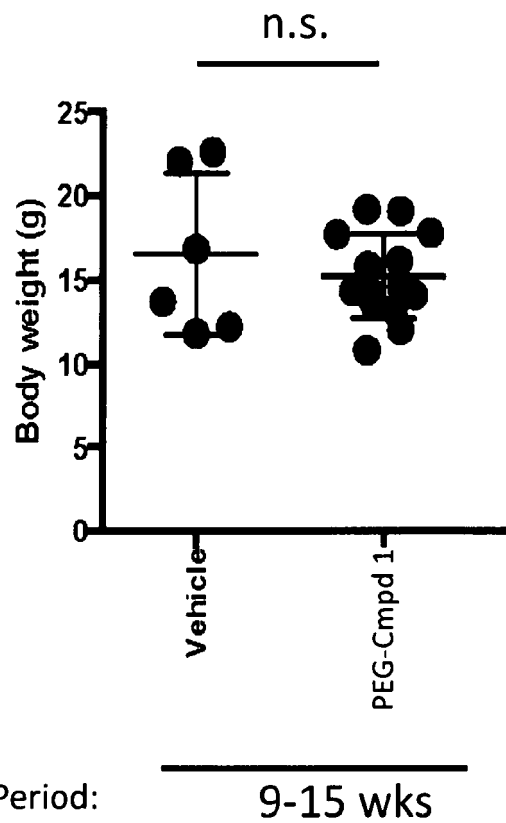


FIG. 42B



Treatment Period:

FIG. 43A

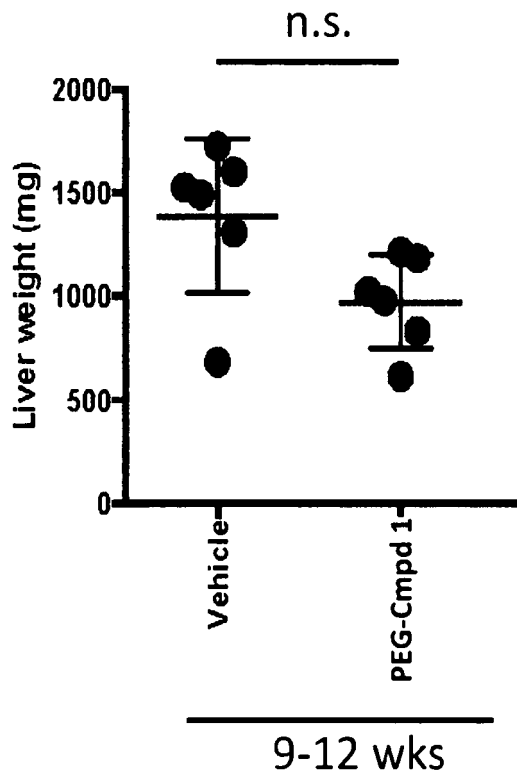
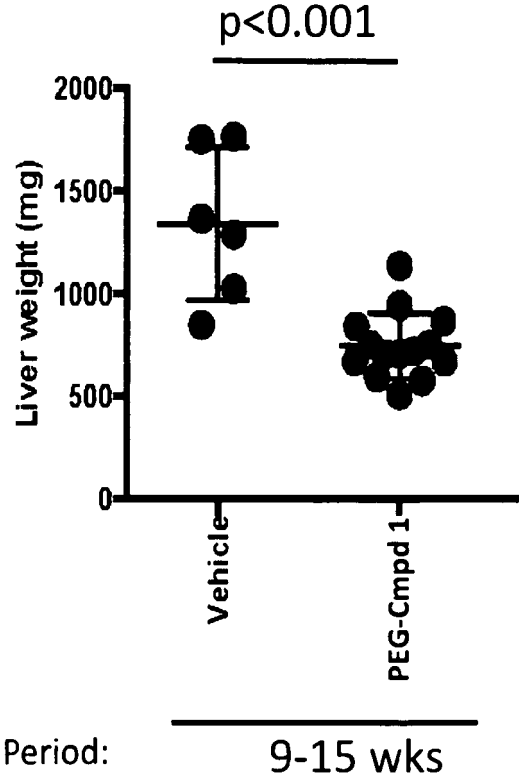


FIG. 43B



Treatment Period:

FIG. 44A

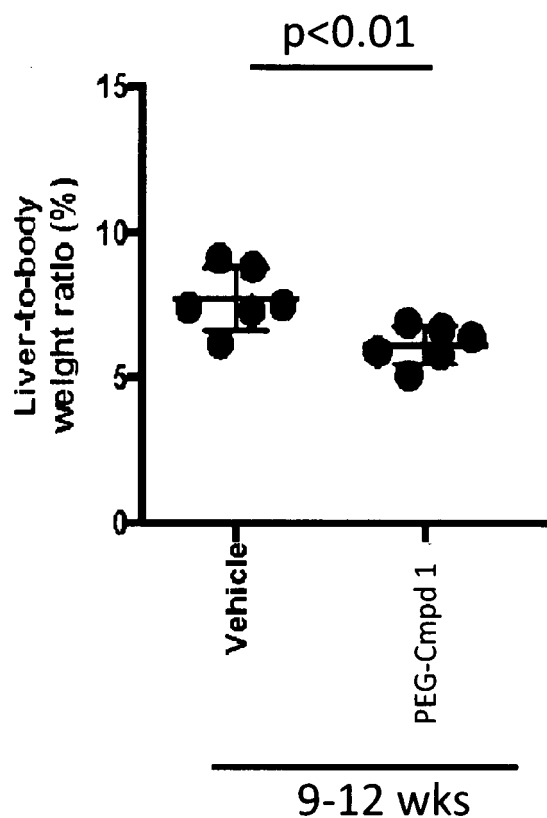


FIG. 44B

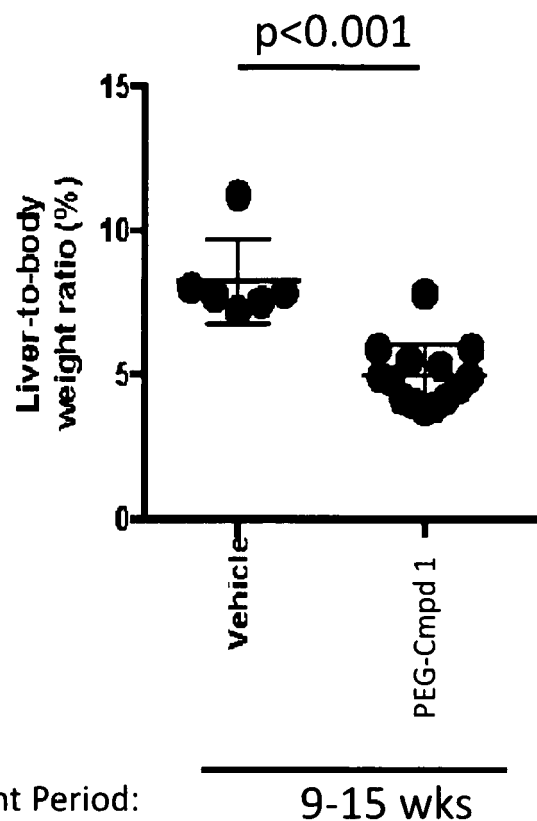


FIG. 45A

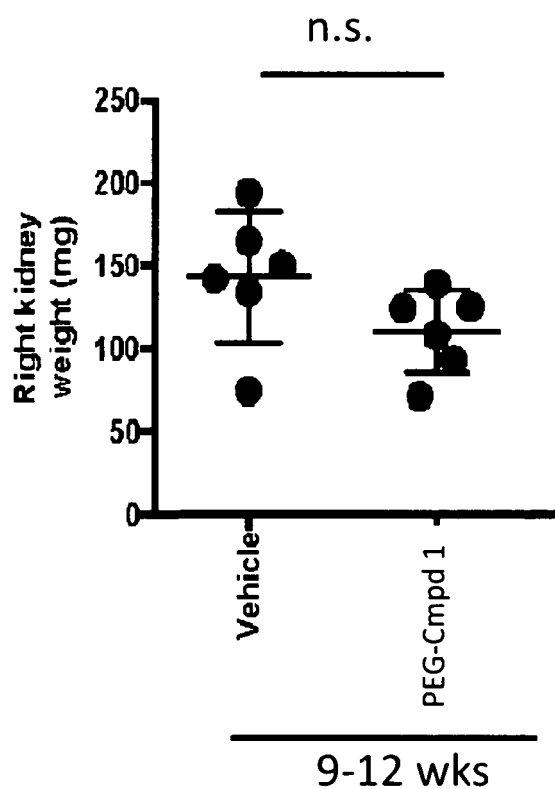


FIG. 45B

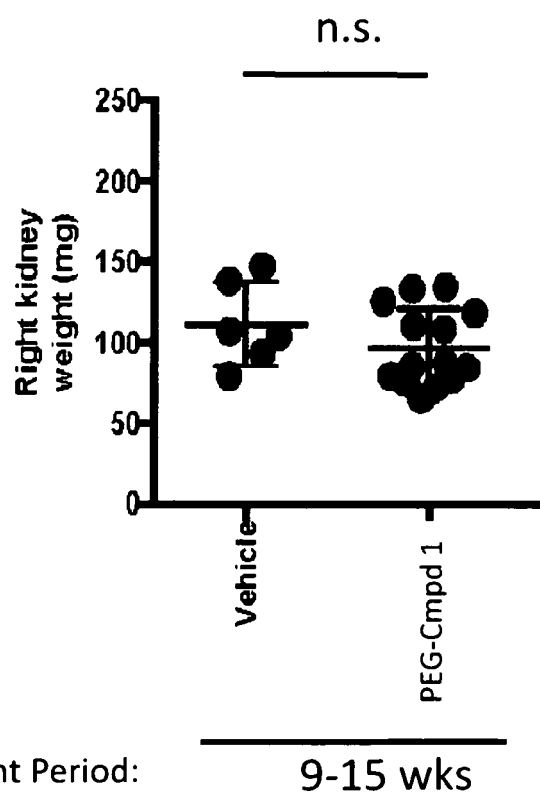
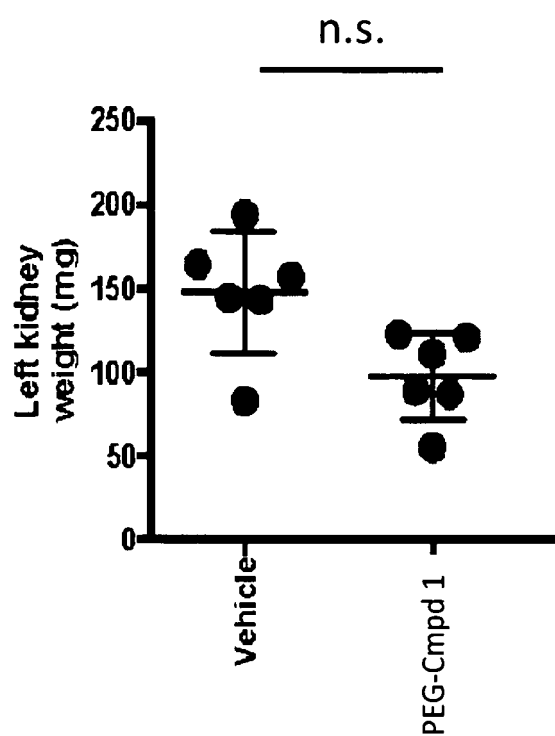


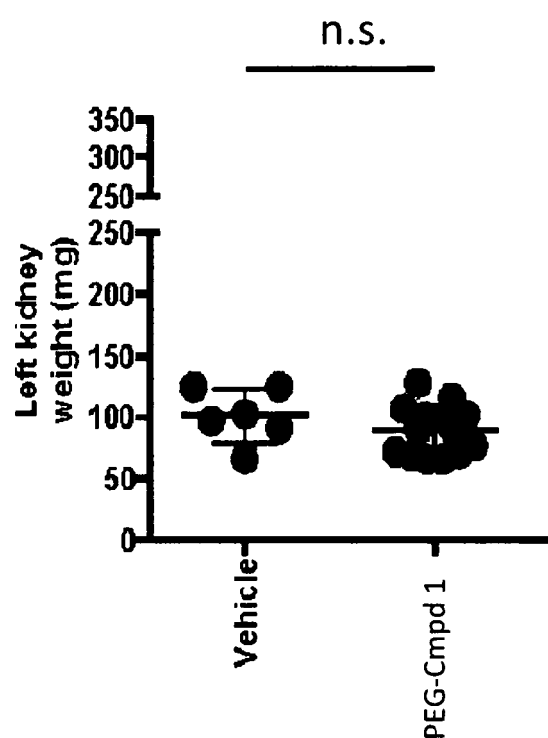
FIG. 46A



9-12 wks

Treatment Period:

FIG. 46B



9-15 wks

FIG. 47A

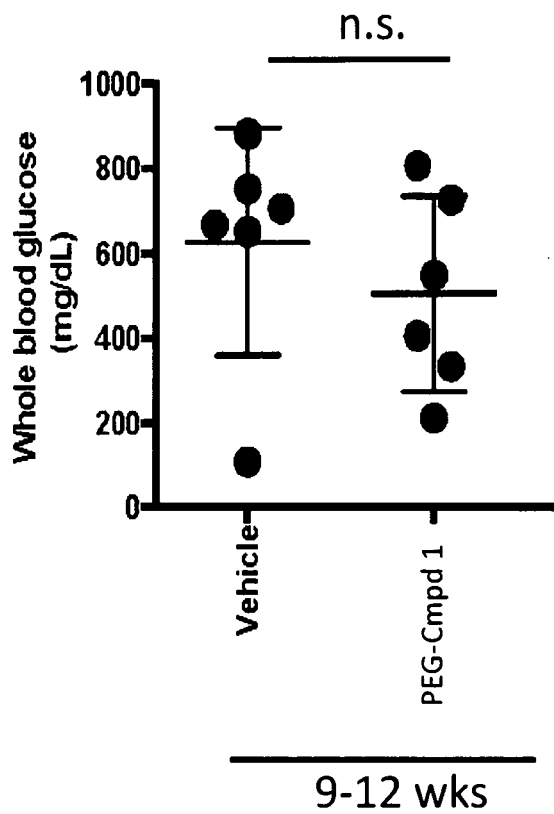
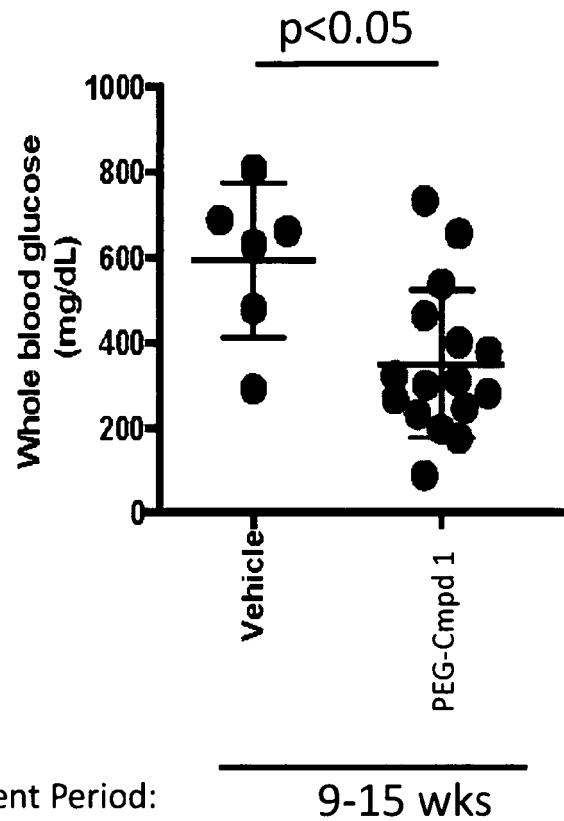


FIG. 47B



Treatment Period:

FIG. 48A

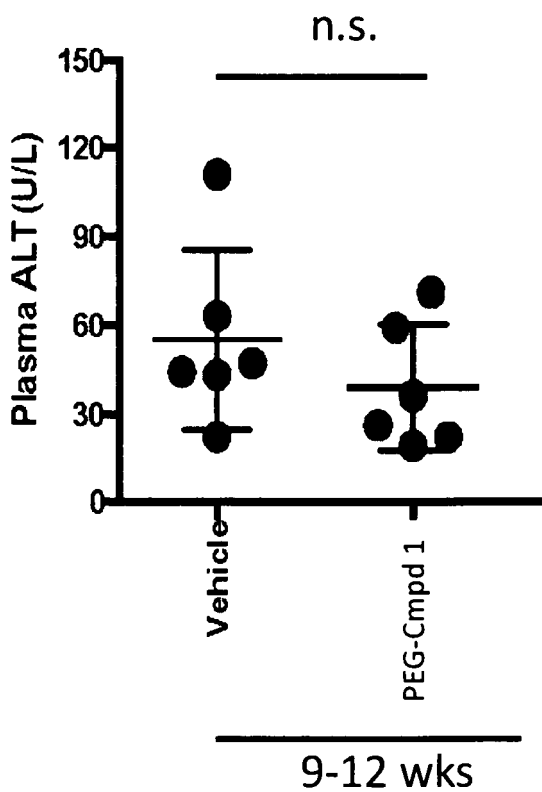
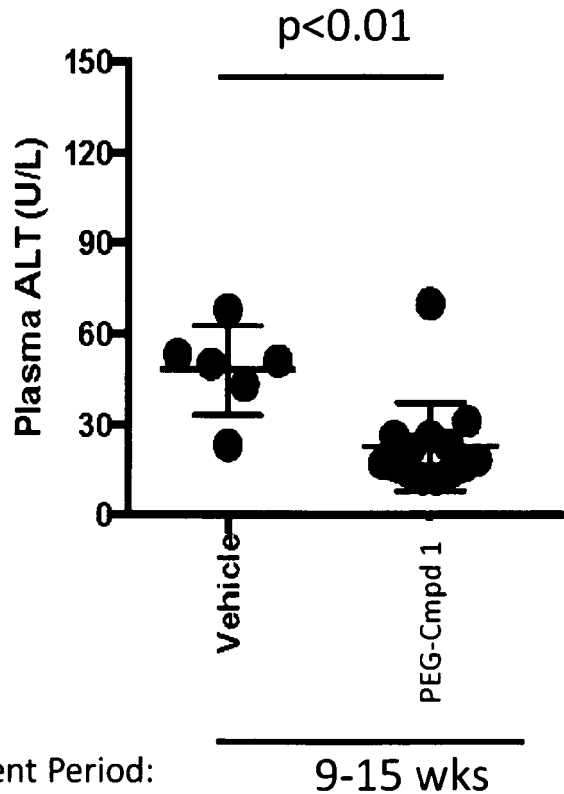


FIG. 48B



Treatment Period:

FIG. 49A

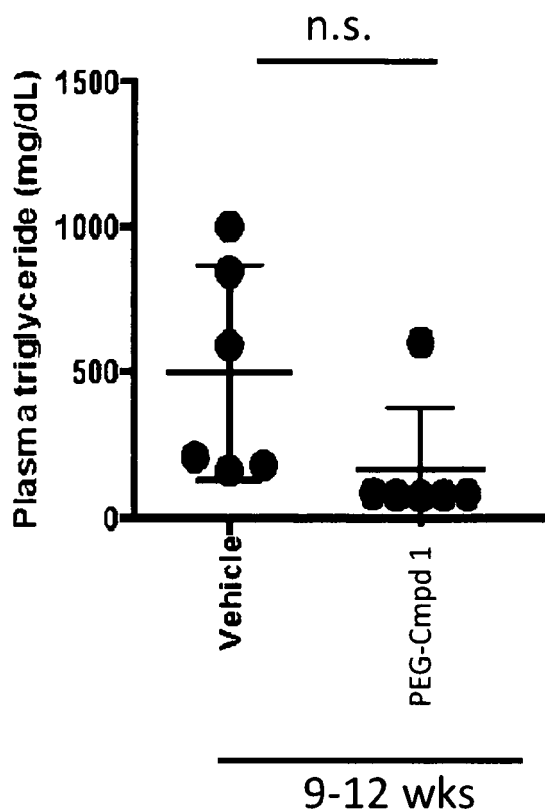


FIG. 49B

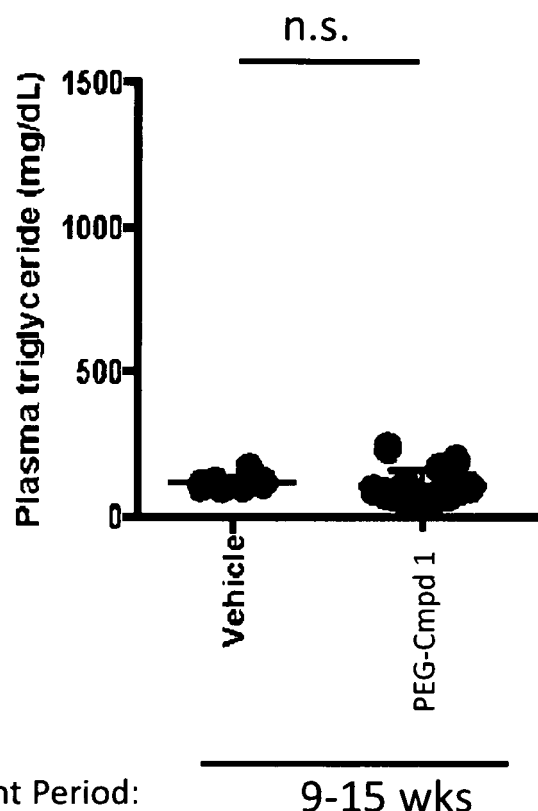


FIG. 50A

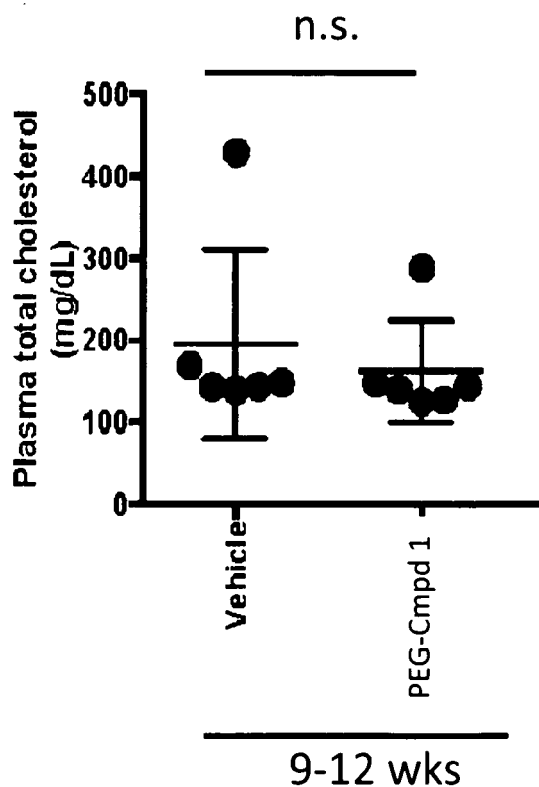


FIG. 50B

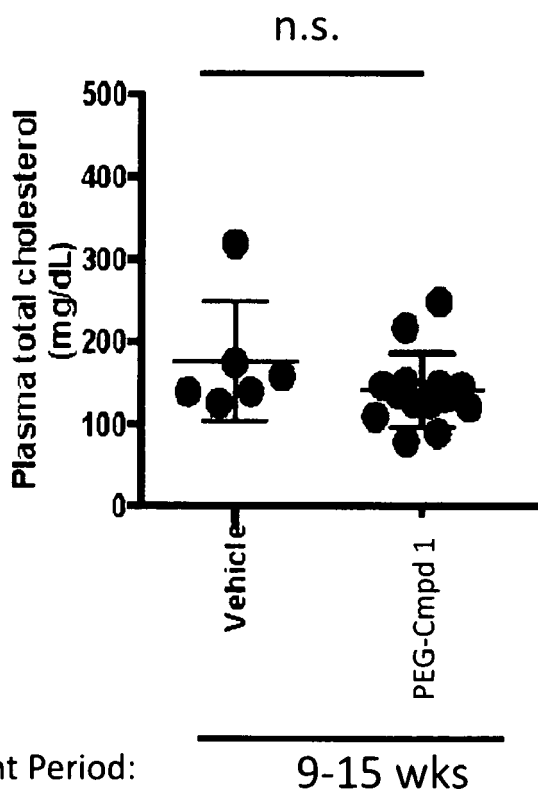


FIG. 51A

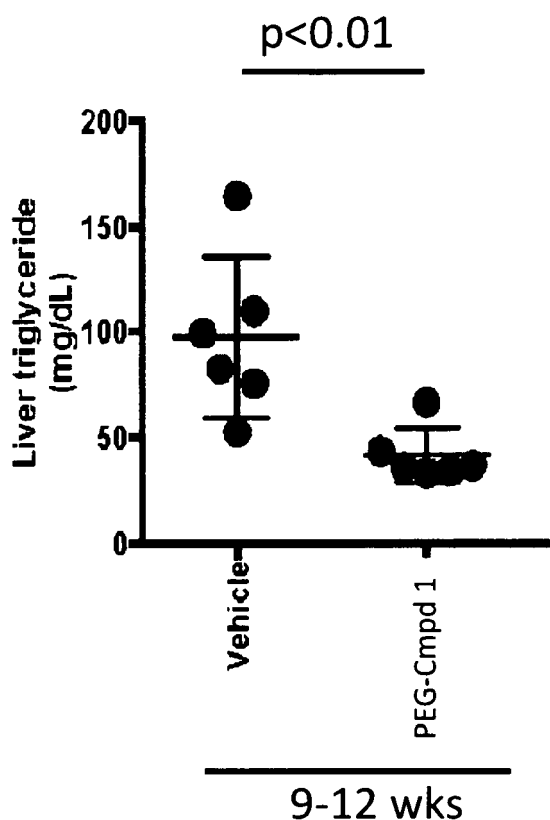


FIG. 51B

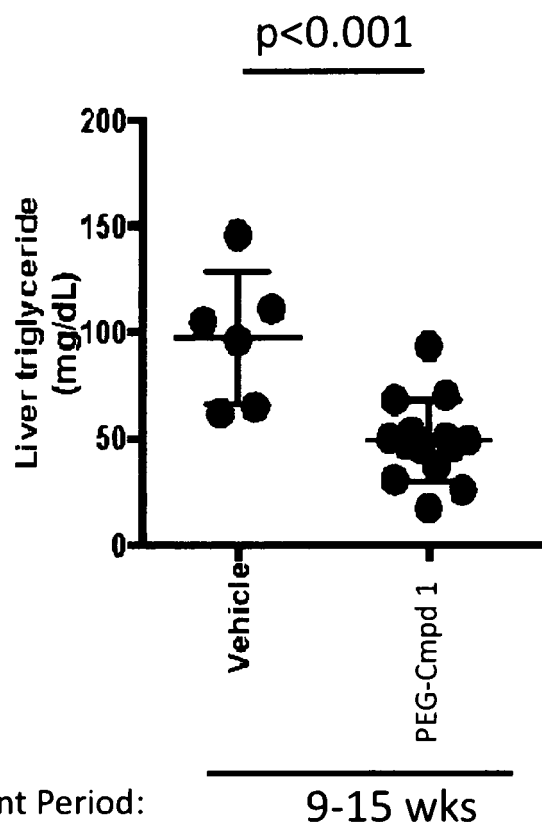


FIG. 52A

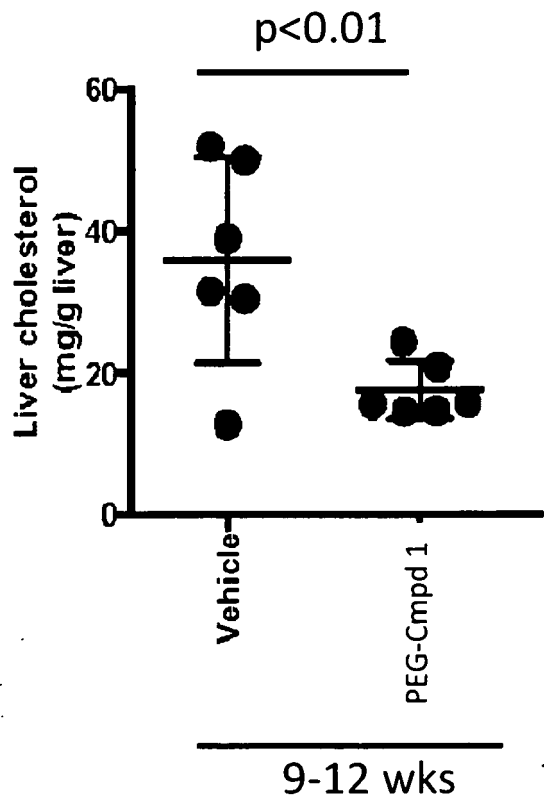
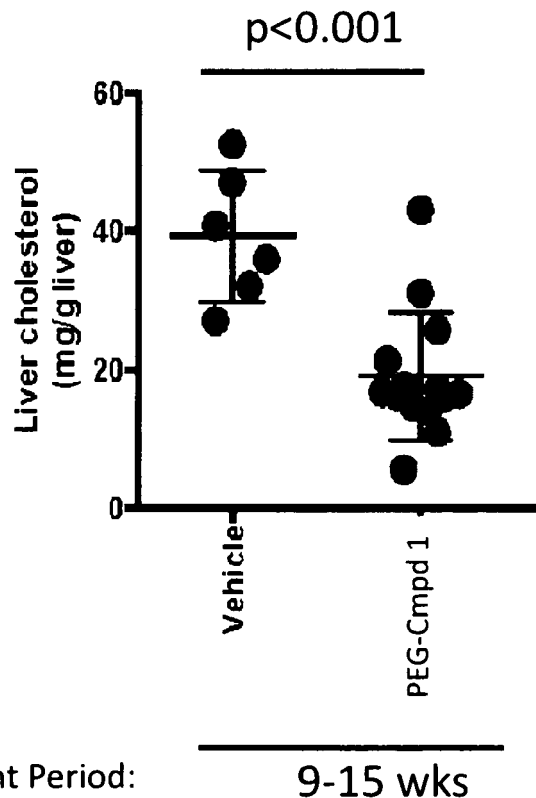


FIG. 52B



Vehicle
(9-12 wks treatment)

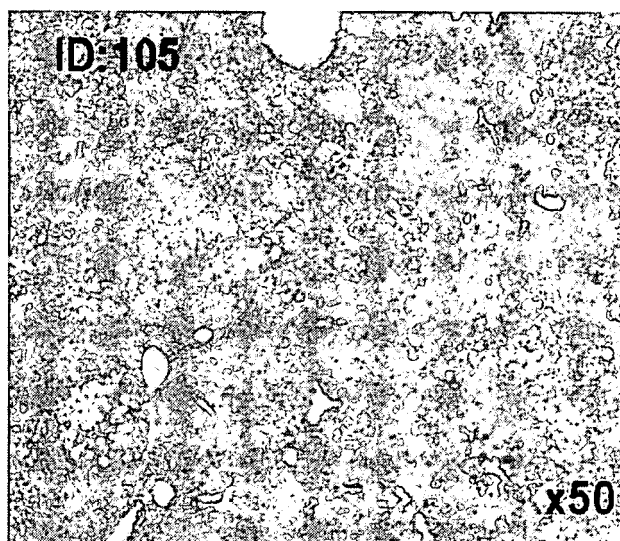


FIG. 53A

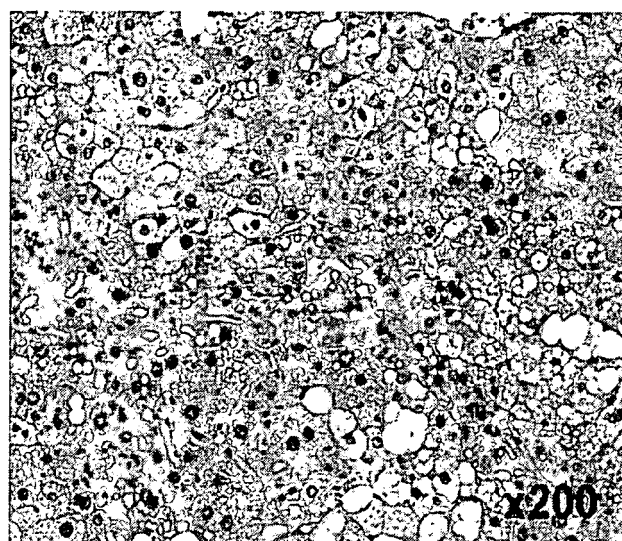


FIG. 53B

PEG-Compound 1
(9-12 wks treatment)



FIG. 53C

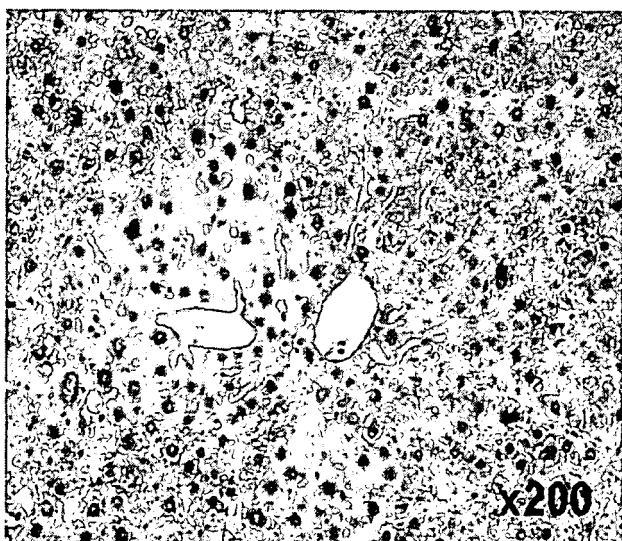


FIG. 53D



FIG. 53E

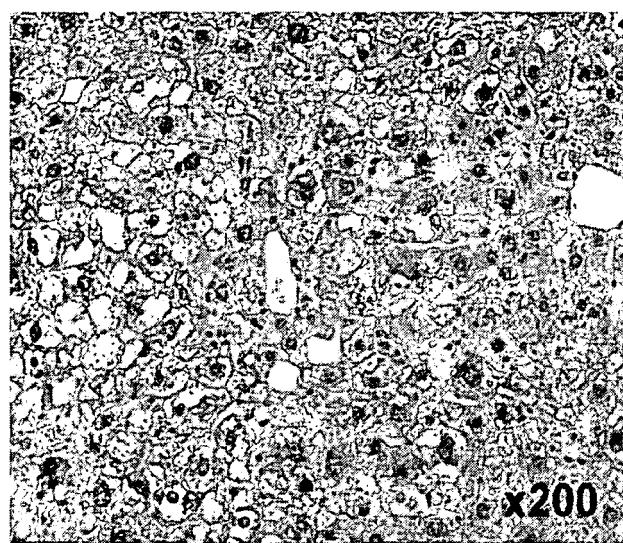


FIG. 53F

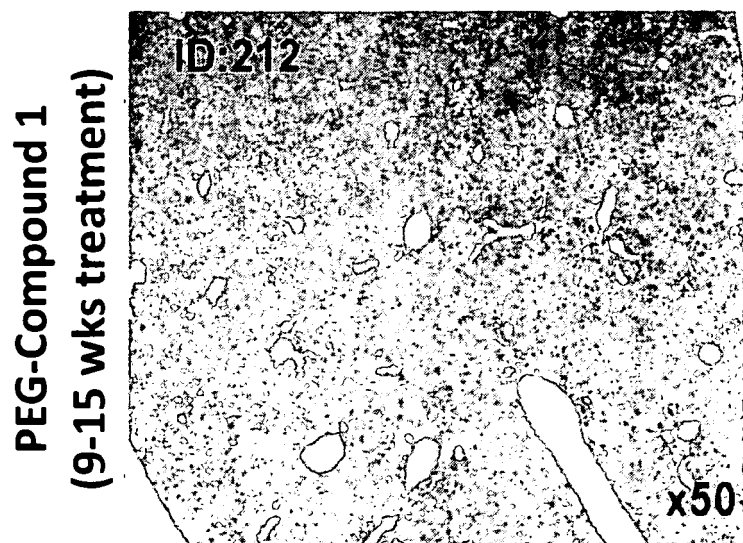


FIG. 53G

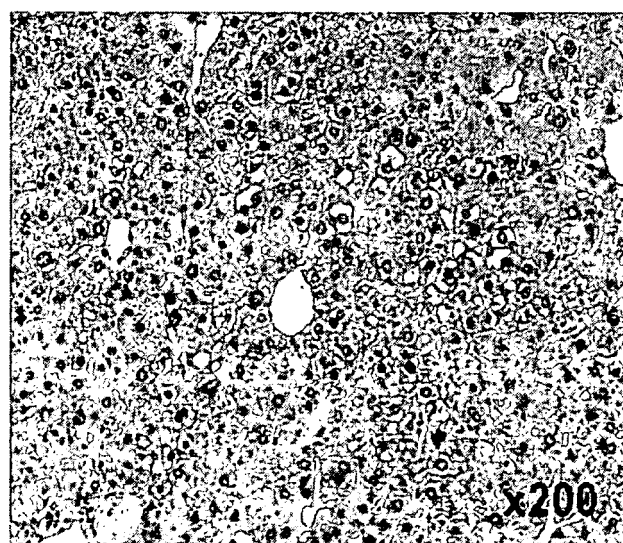
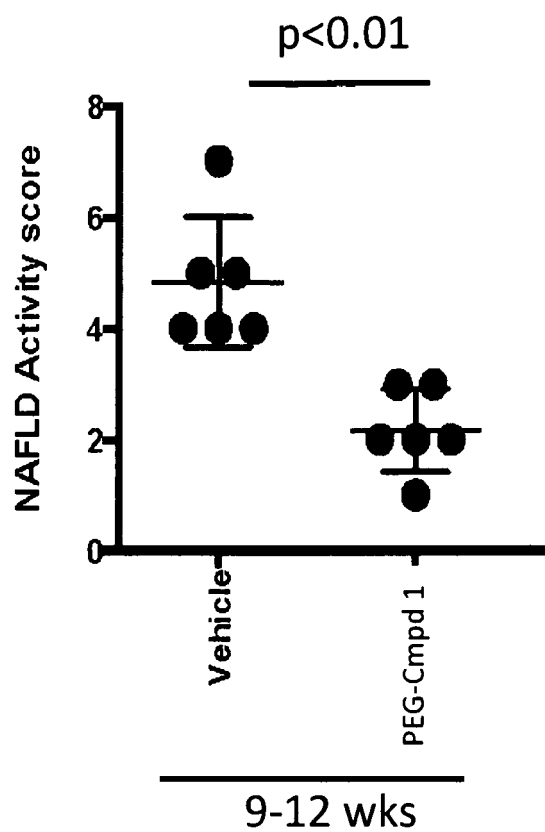


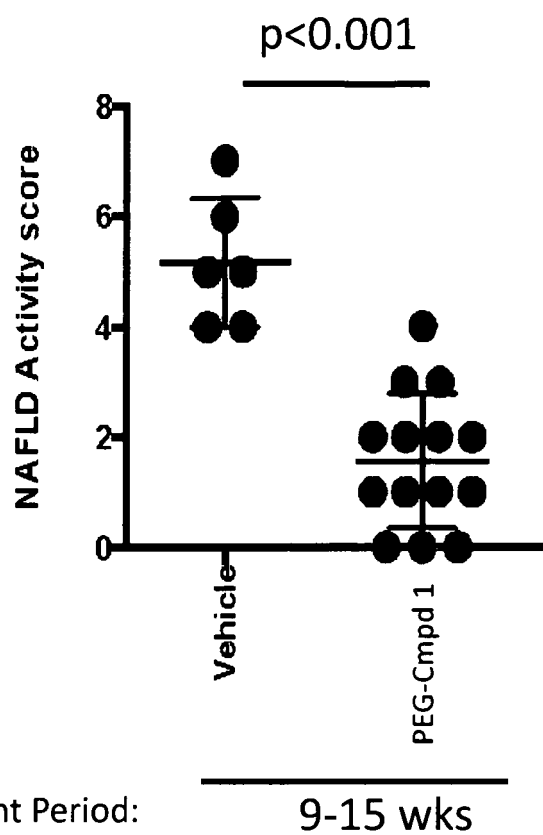
FIG. 53H

FIG. 54A



Treatment Period:

FIG. 54B



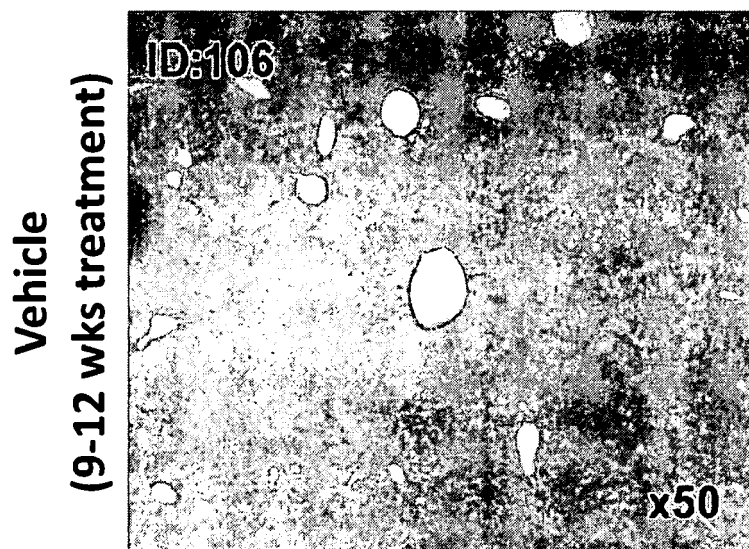


FIG. 55A

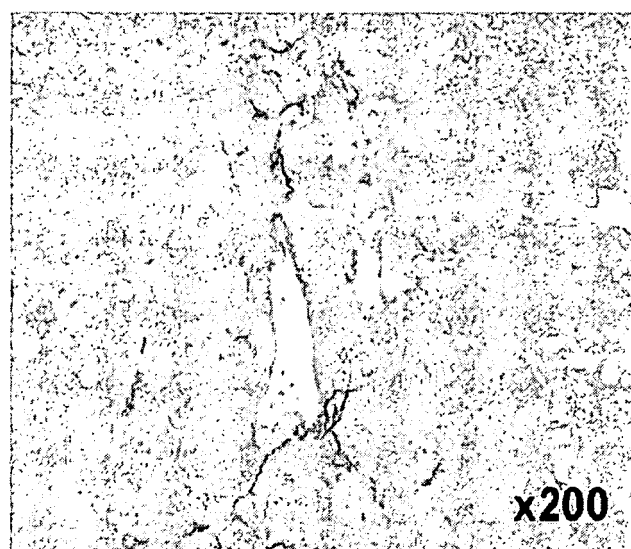


FIG. 55B

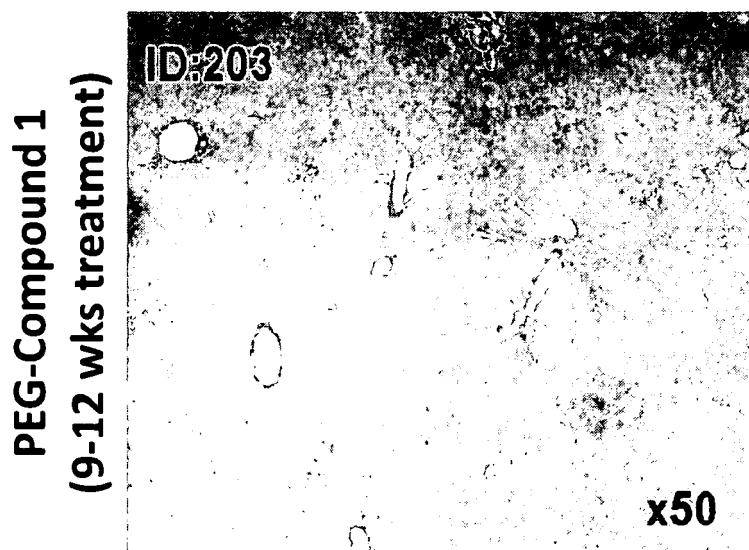


FIG. 55C

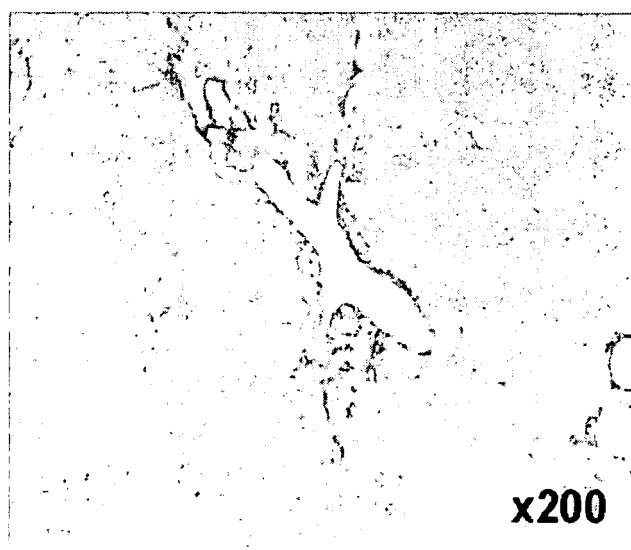


FIG. 55D

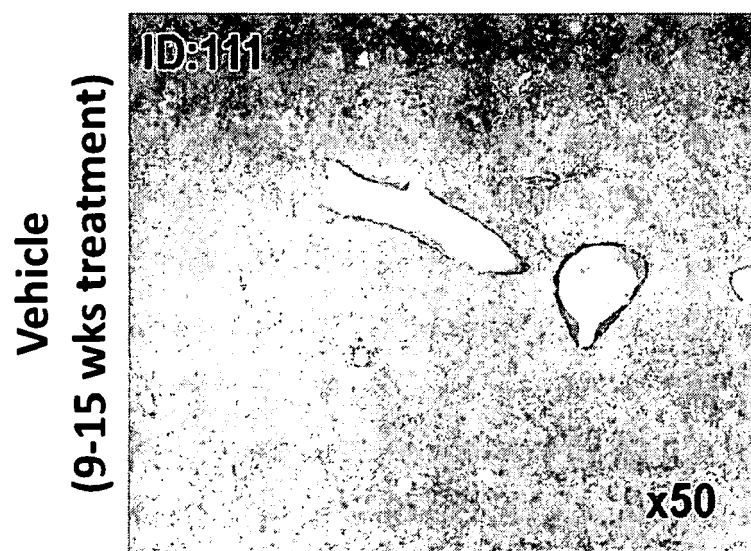


FIG. 55E



FIG. 55F

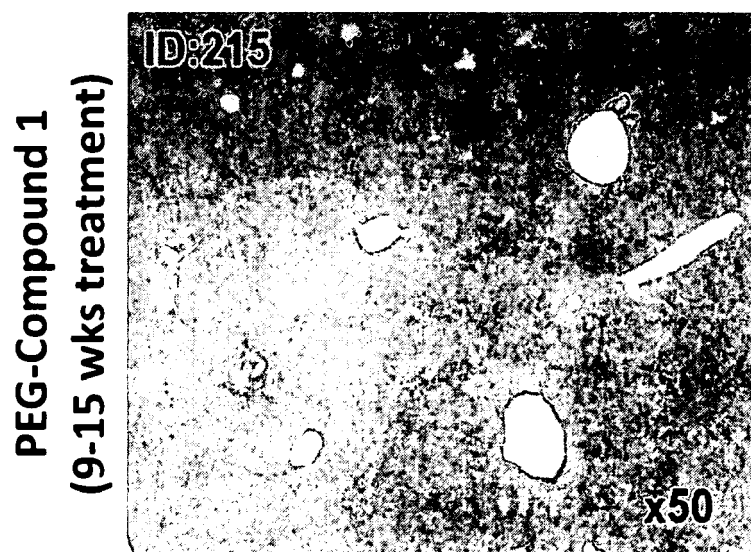


FIG. 55G

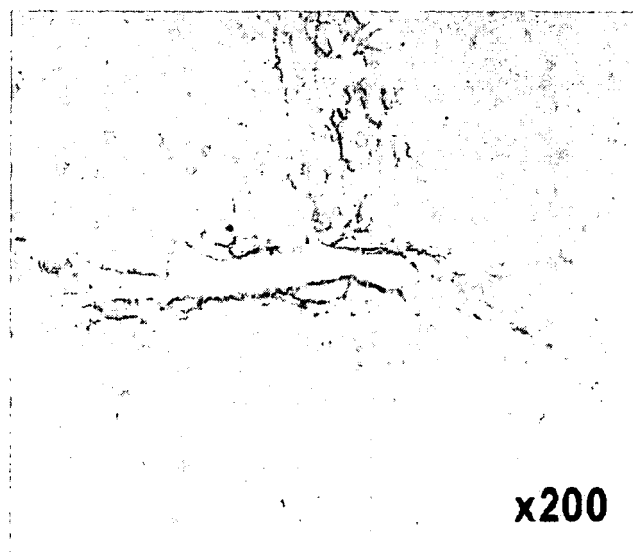


FIG. 55H

FIG. 56A

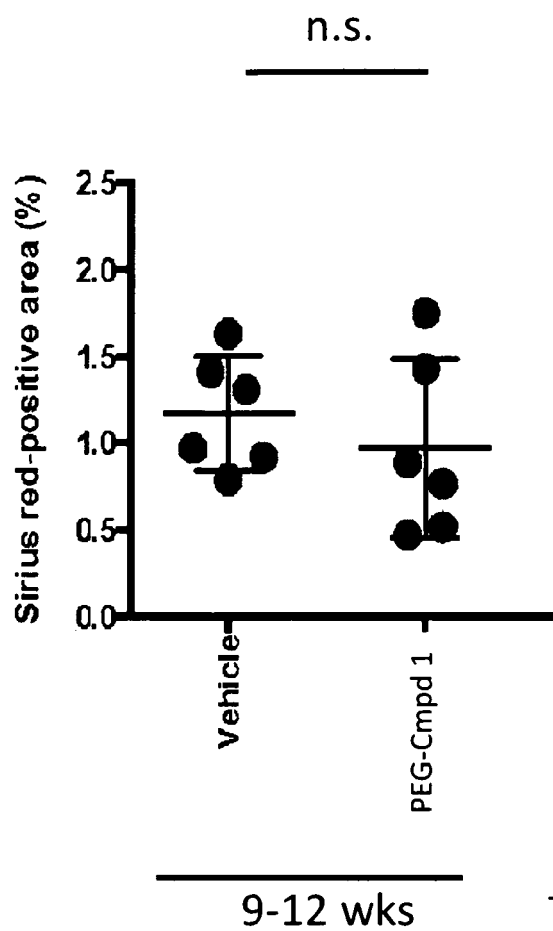
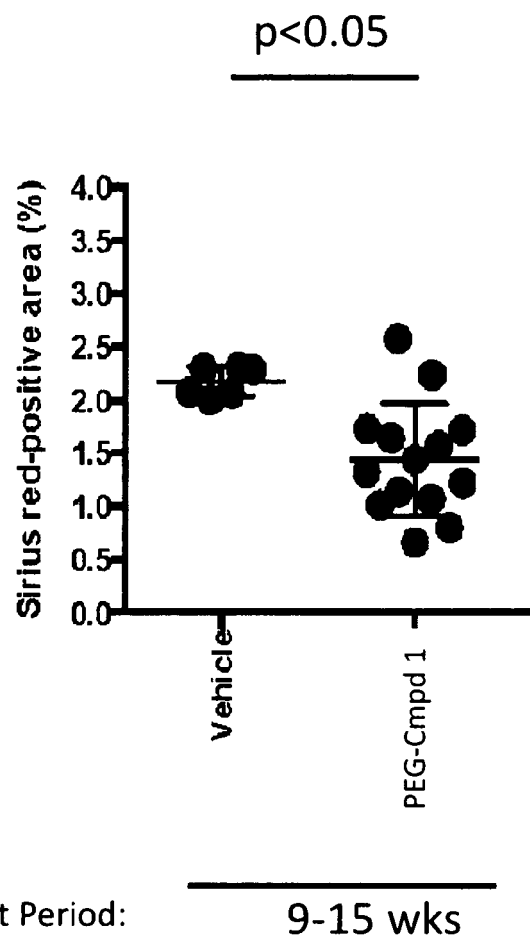


FIG. 56B



Treatment Period:

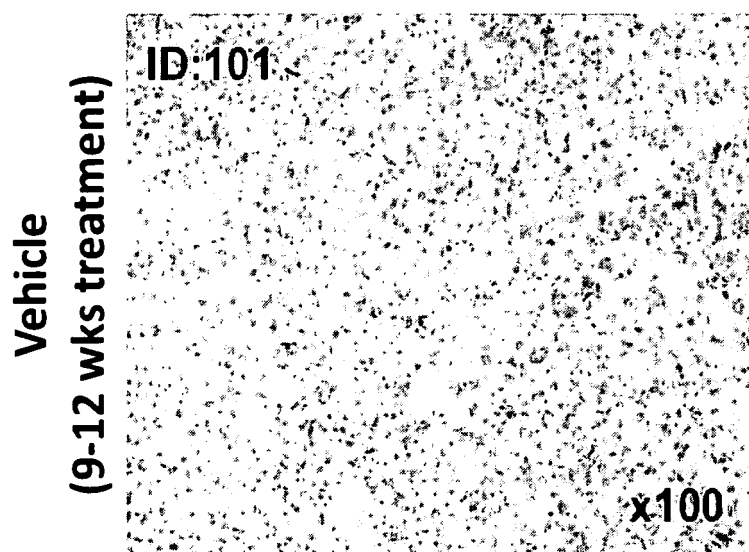


FIG. 57A

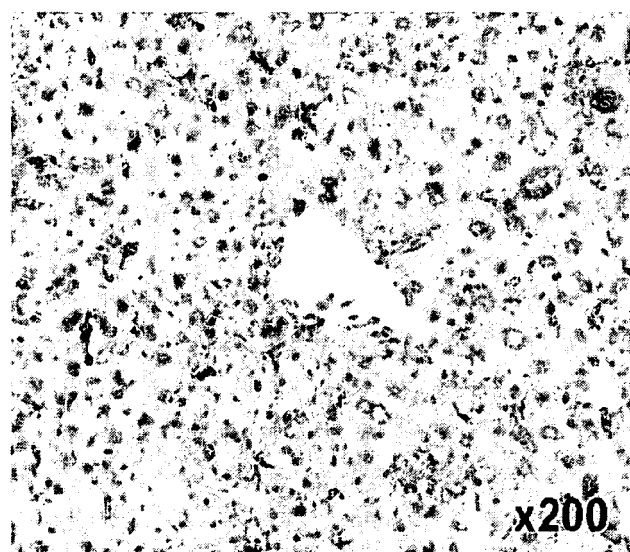


FIG. 57B

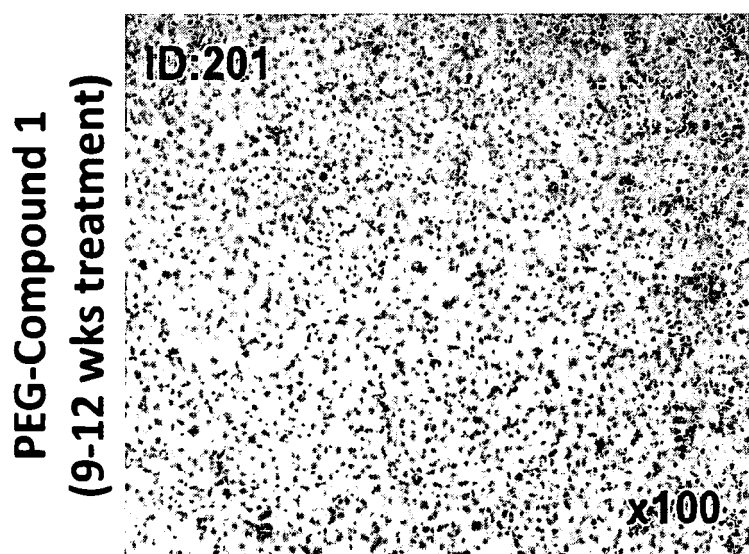


FIG. 57C

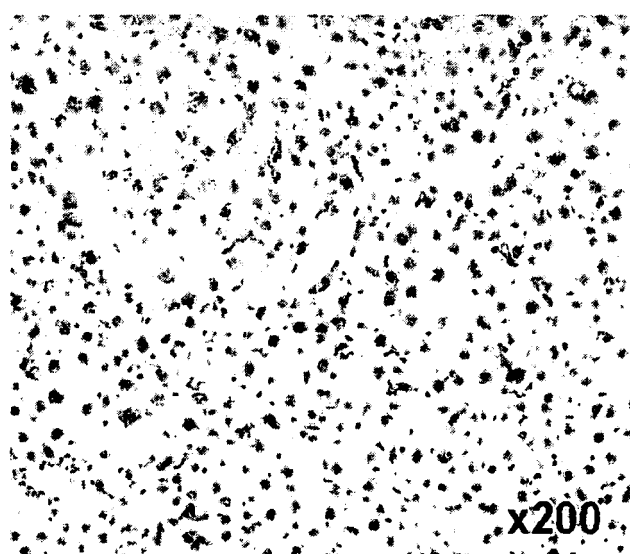


FIG. 57D

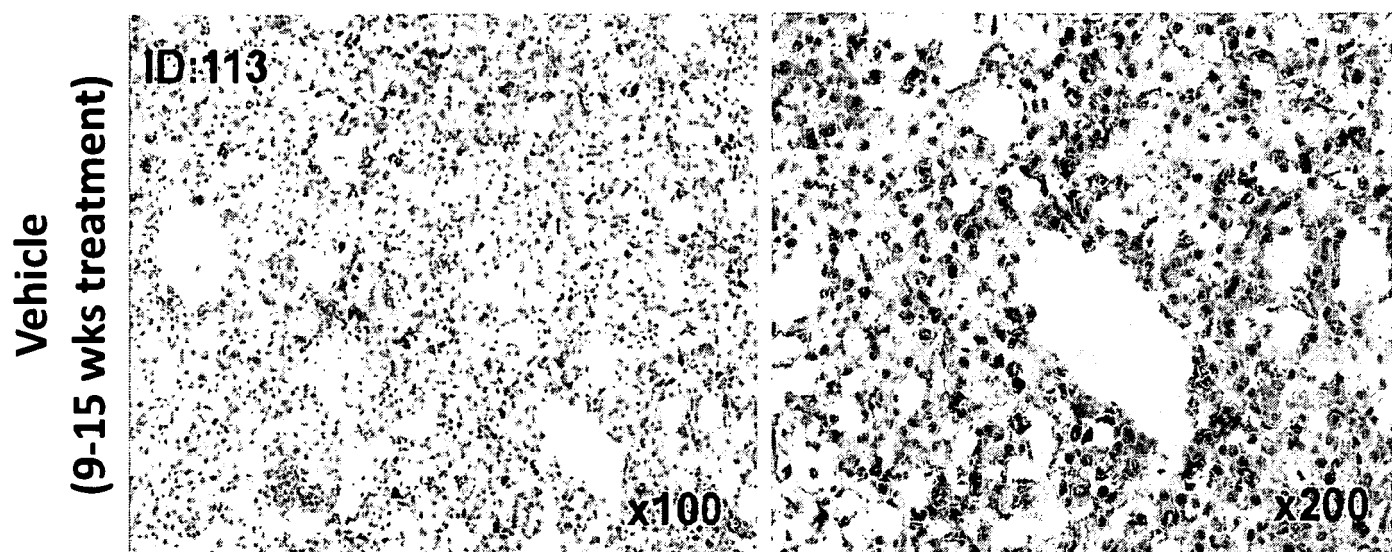


FIG. 57E

FIG. 57F

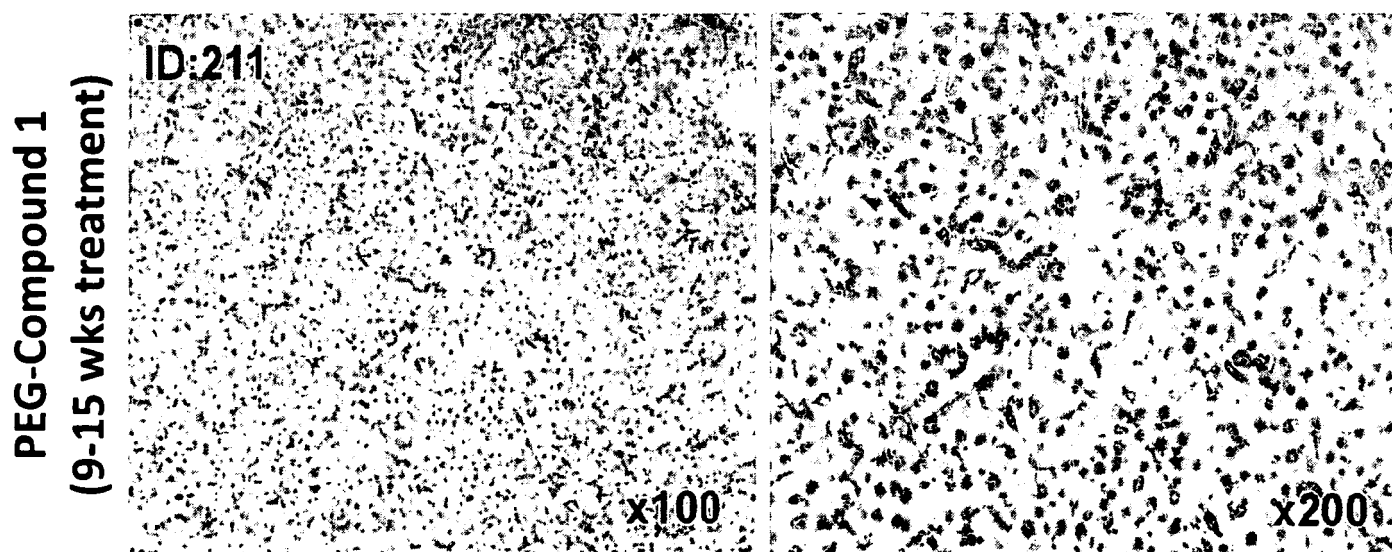
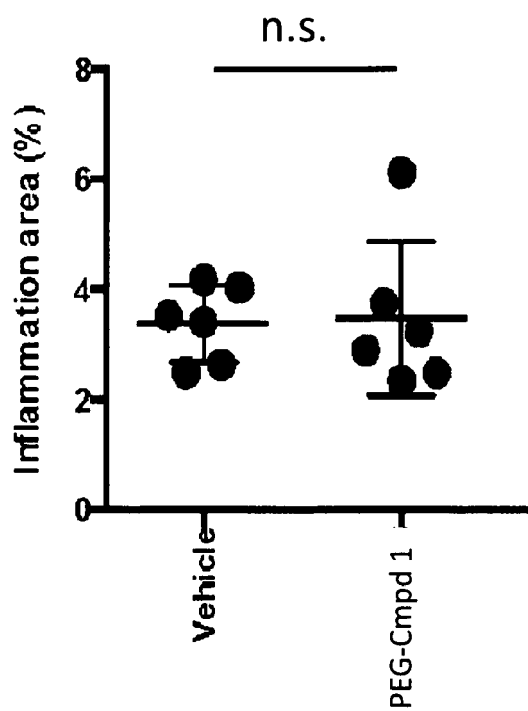


FIG. 57G

FIG. 57H

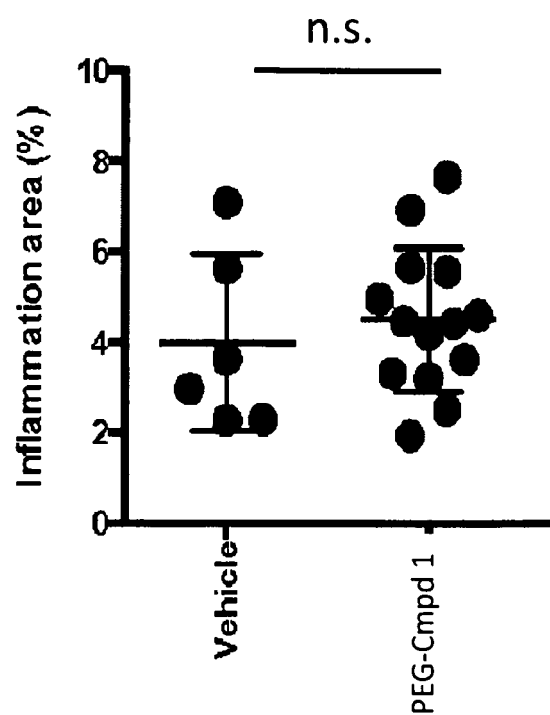
FIG. 58A



9-12 wks

Treatment Period:

FIG. 58B



9-15 wks

**Vehicle
(9-12 wks treatment)**

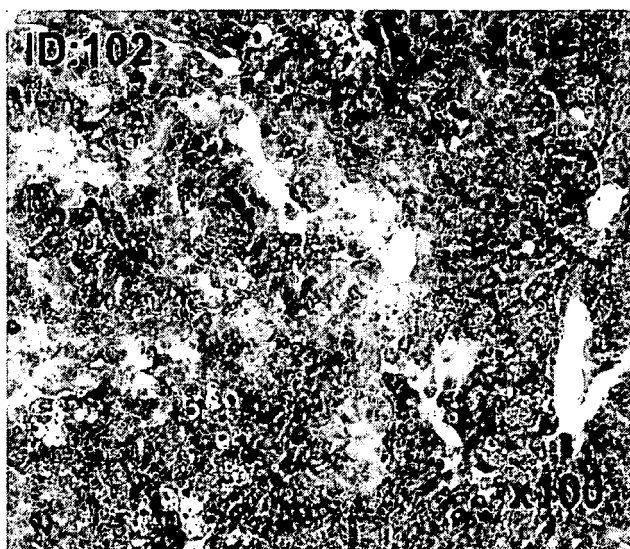


FIG. 59A

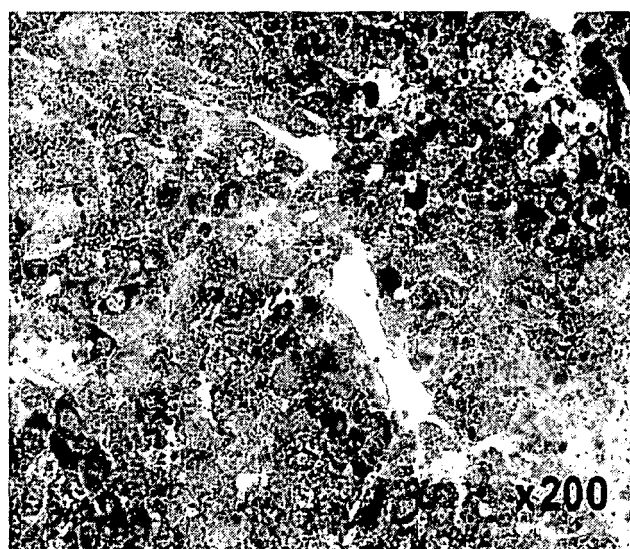


FIG. 59B

**PEG-Compound 1
(9-12 wks treatment)**

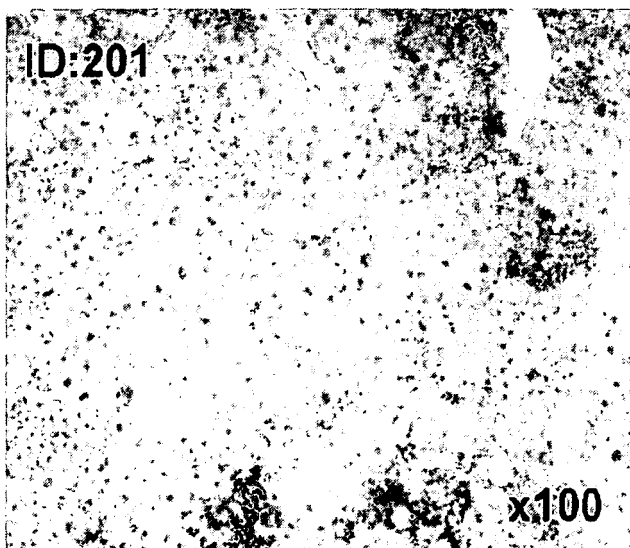


FIG. 59C

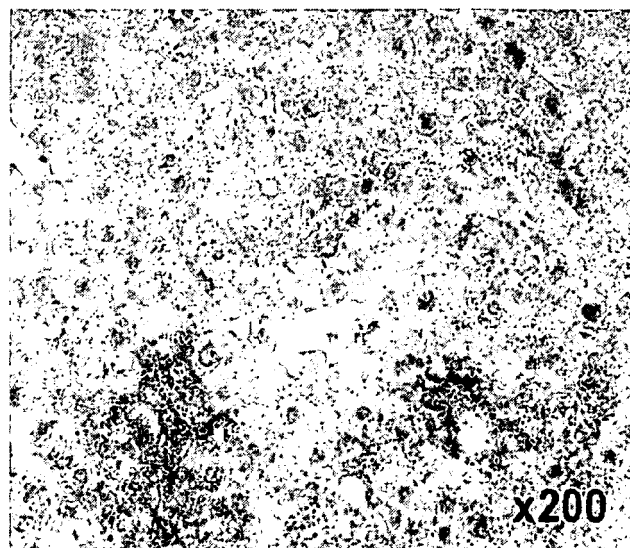


FIG. 59D

Vehicle
(9-15 wks treatment)

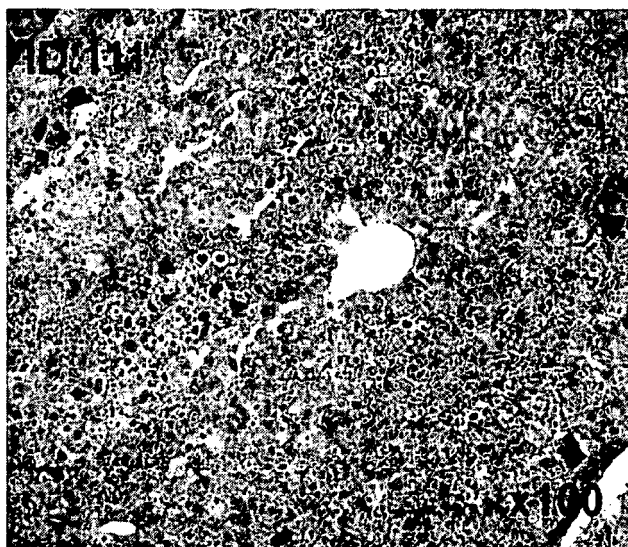


FIG. 59E

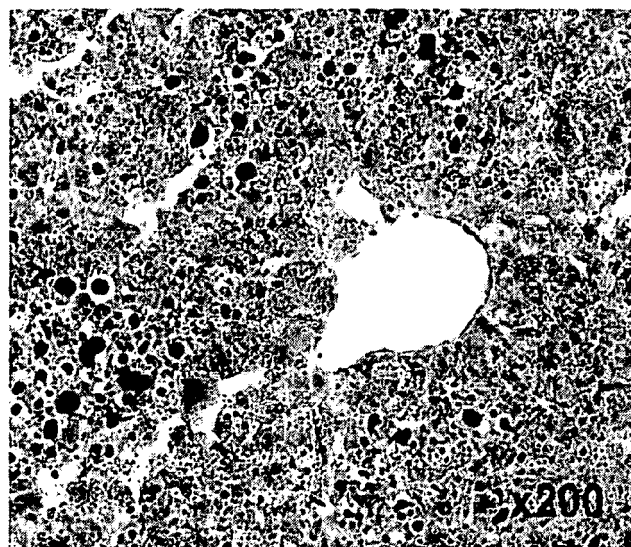


FIG. 59F

PEG-Compound 1
(9-15 wks treatment)

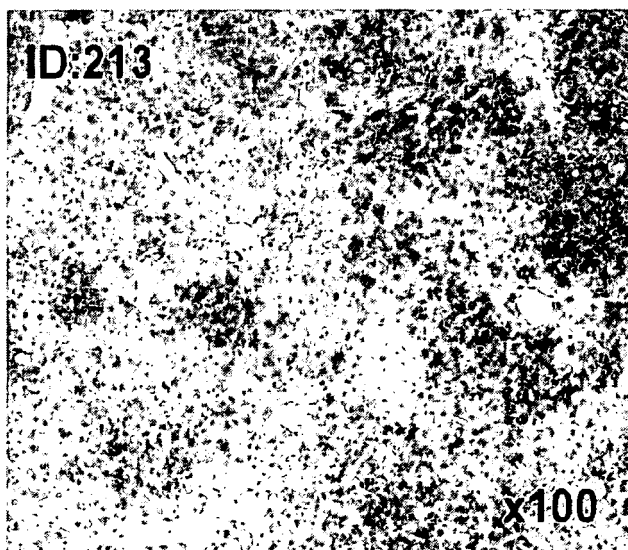


FIG. 59G

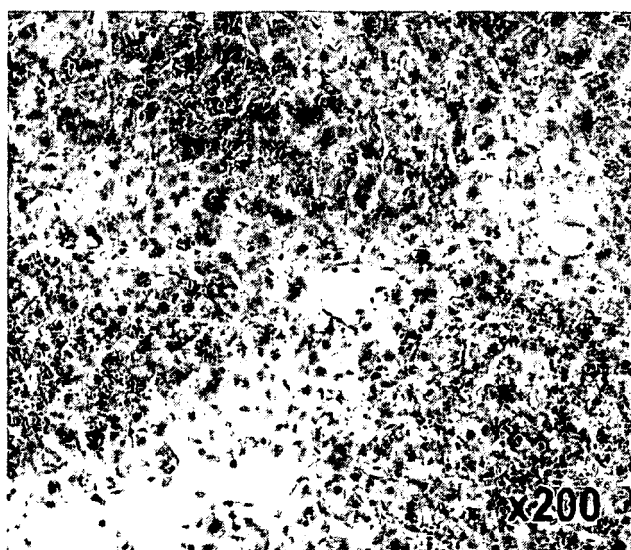
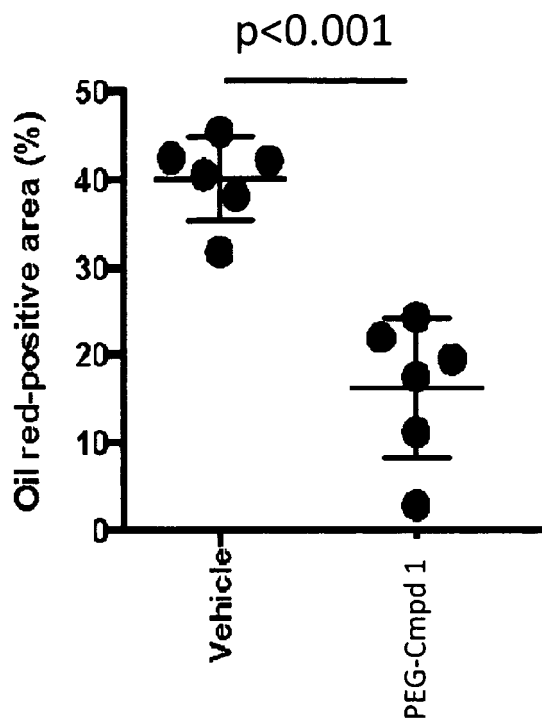


FIG. 59H

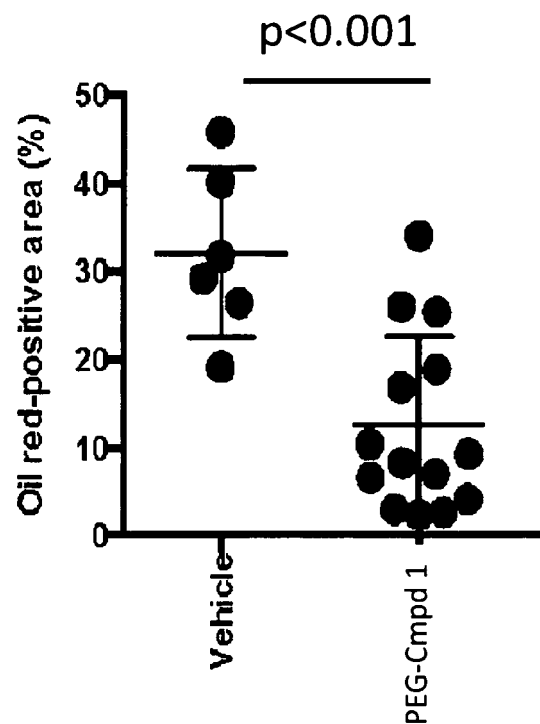
FIG. 60A



9-12 wks

Treatment Period:

FIG. 60B



9-15 wks

FIG. 61

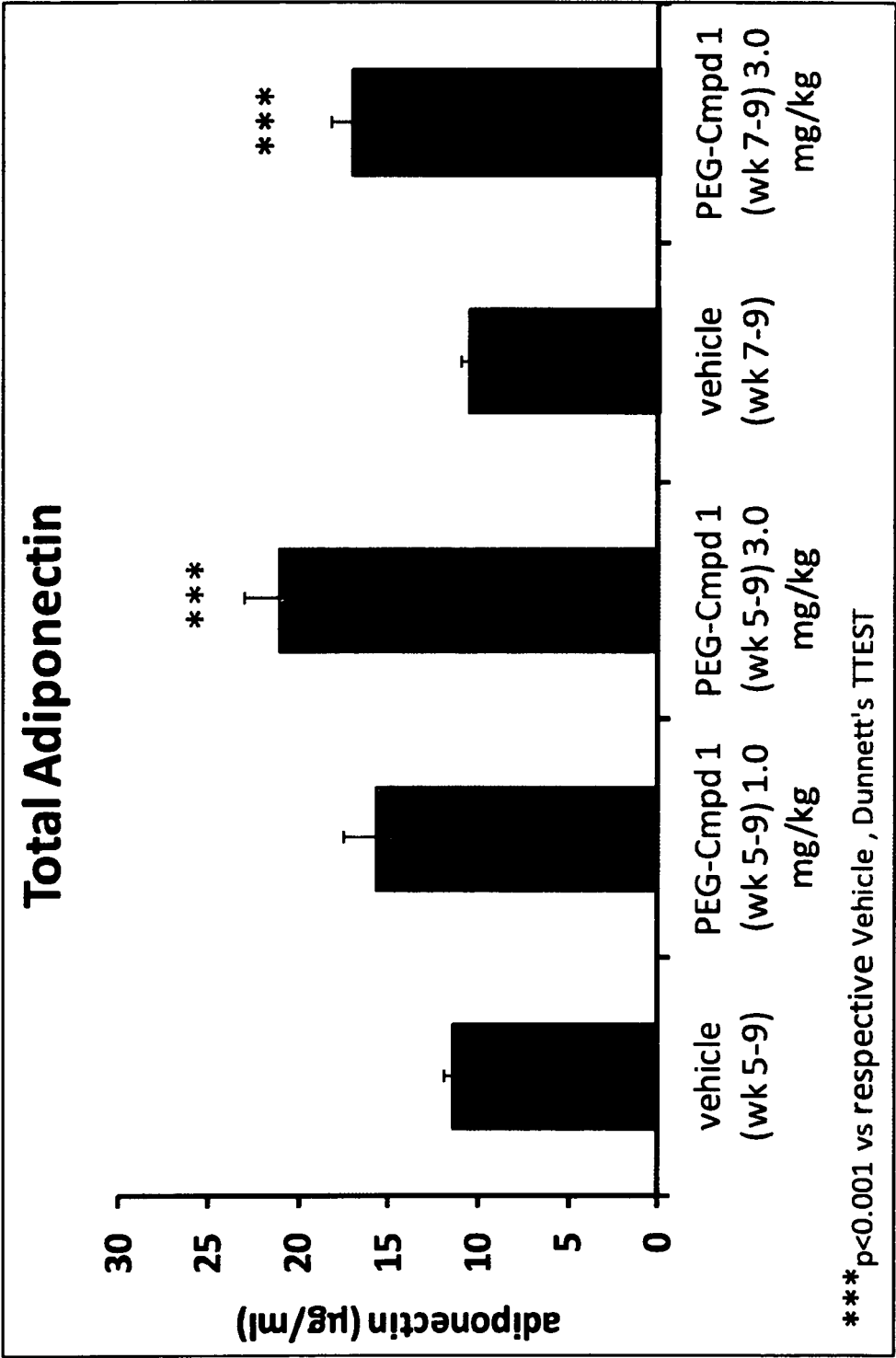


FIG. 62

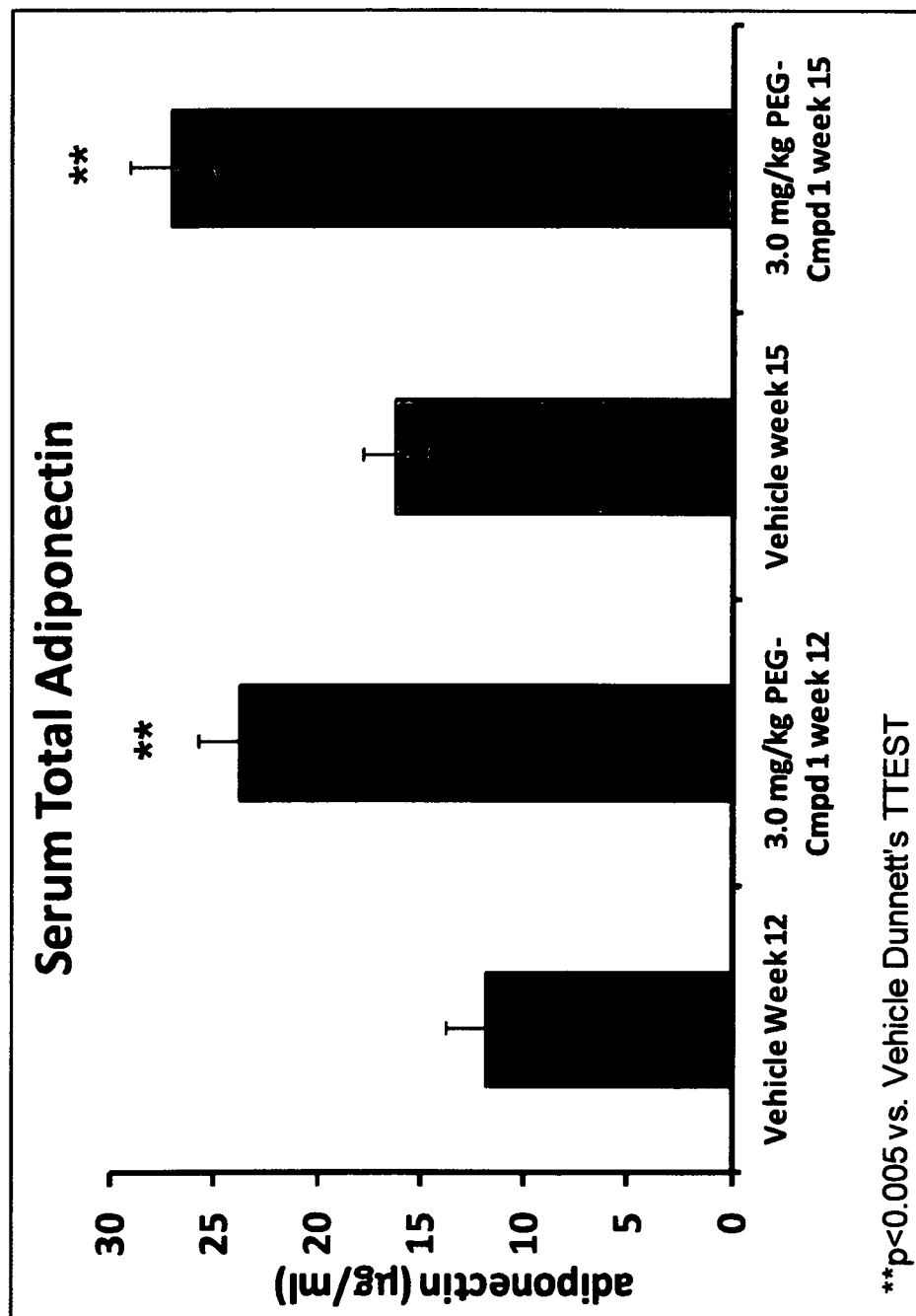


FIG. 63

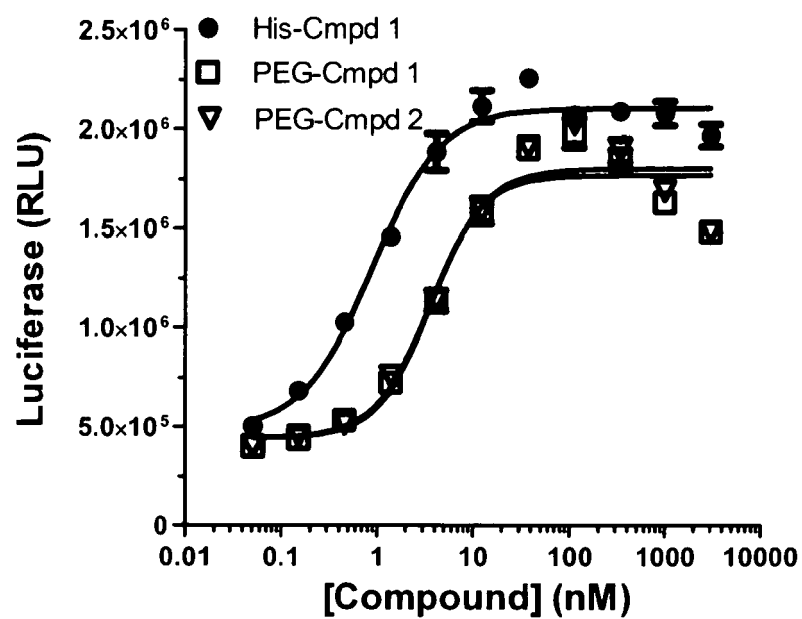


FIG. 64

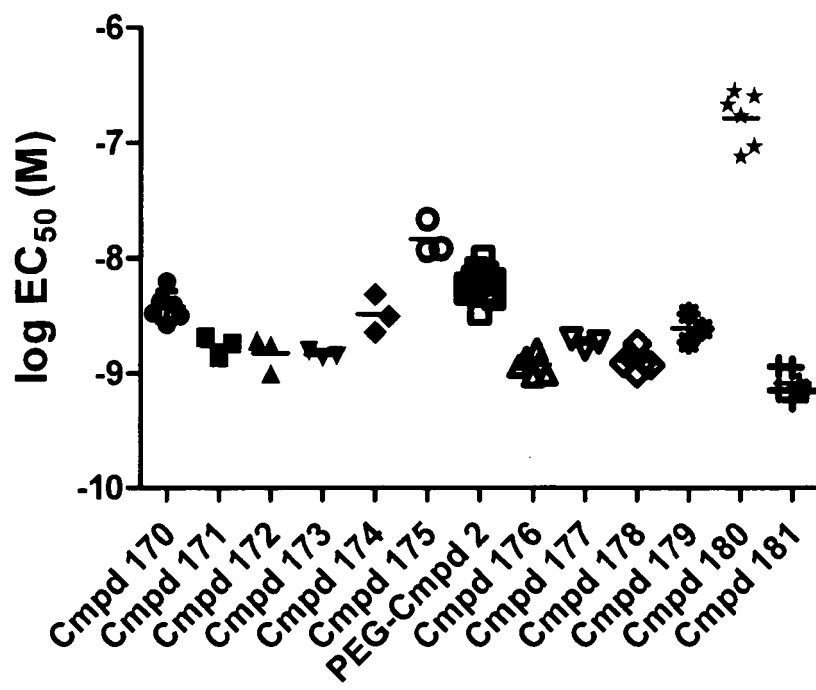


FIG. 65

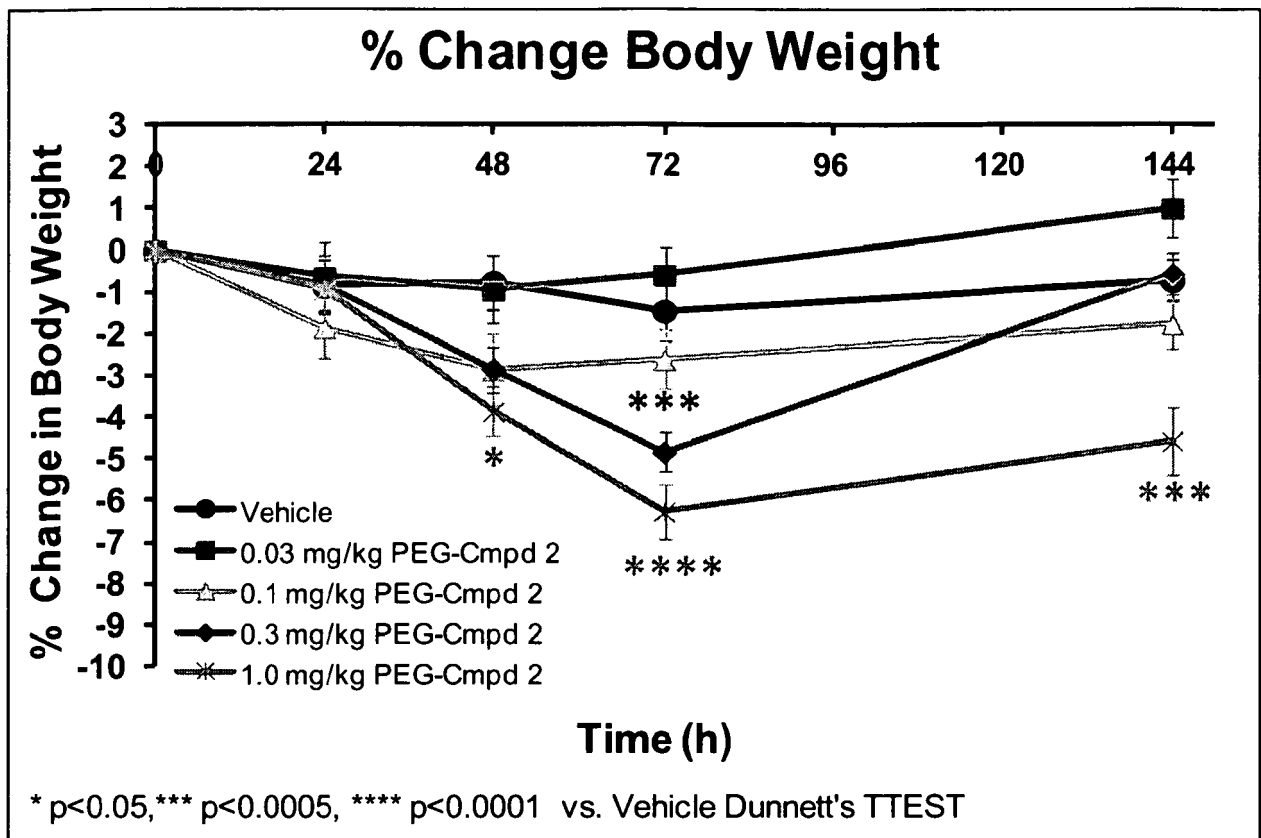


FIG. 66A

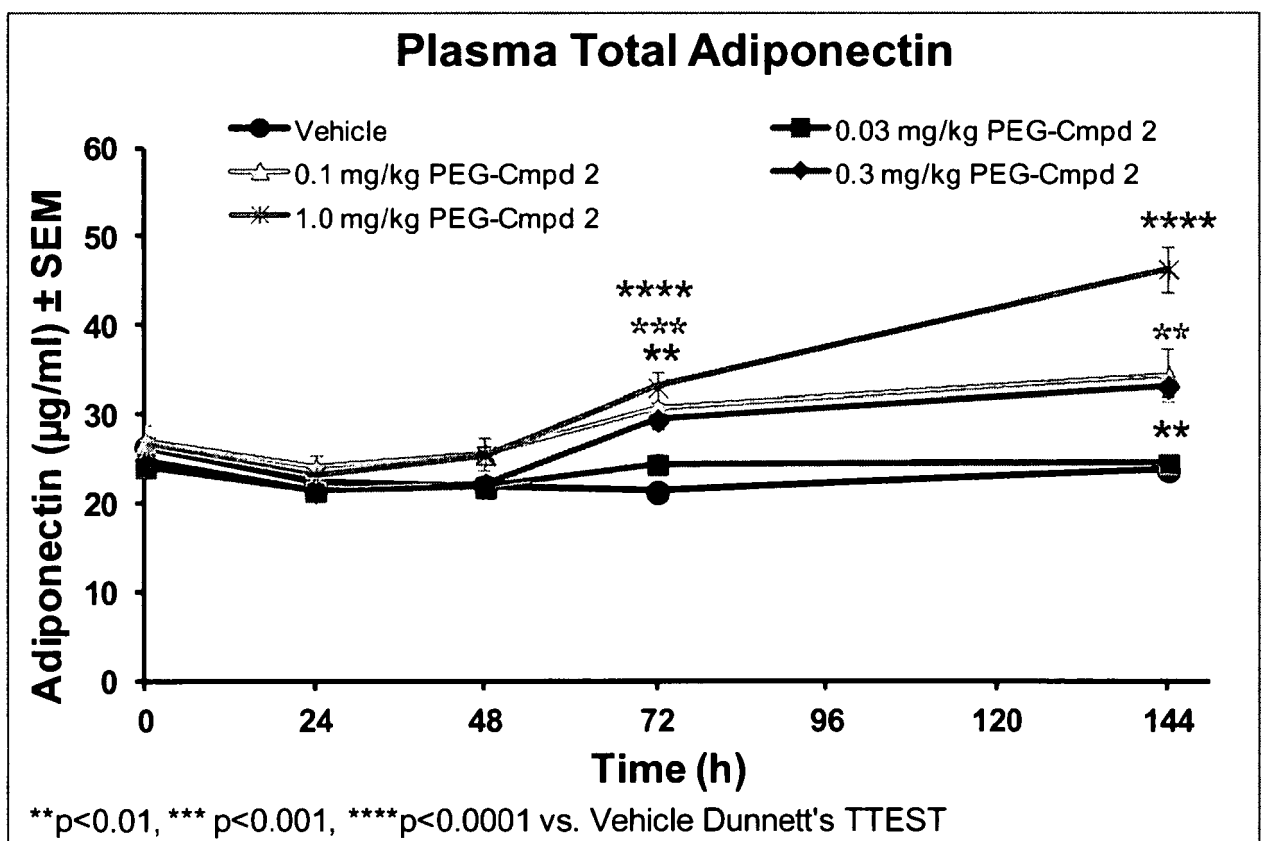


FIG. 66B

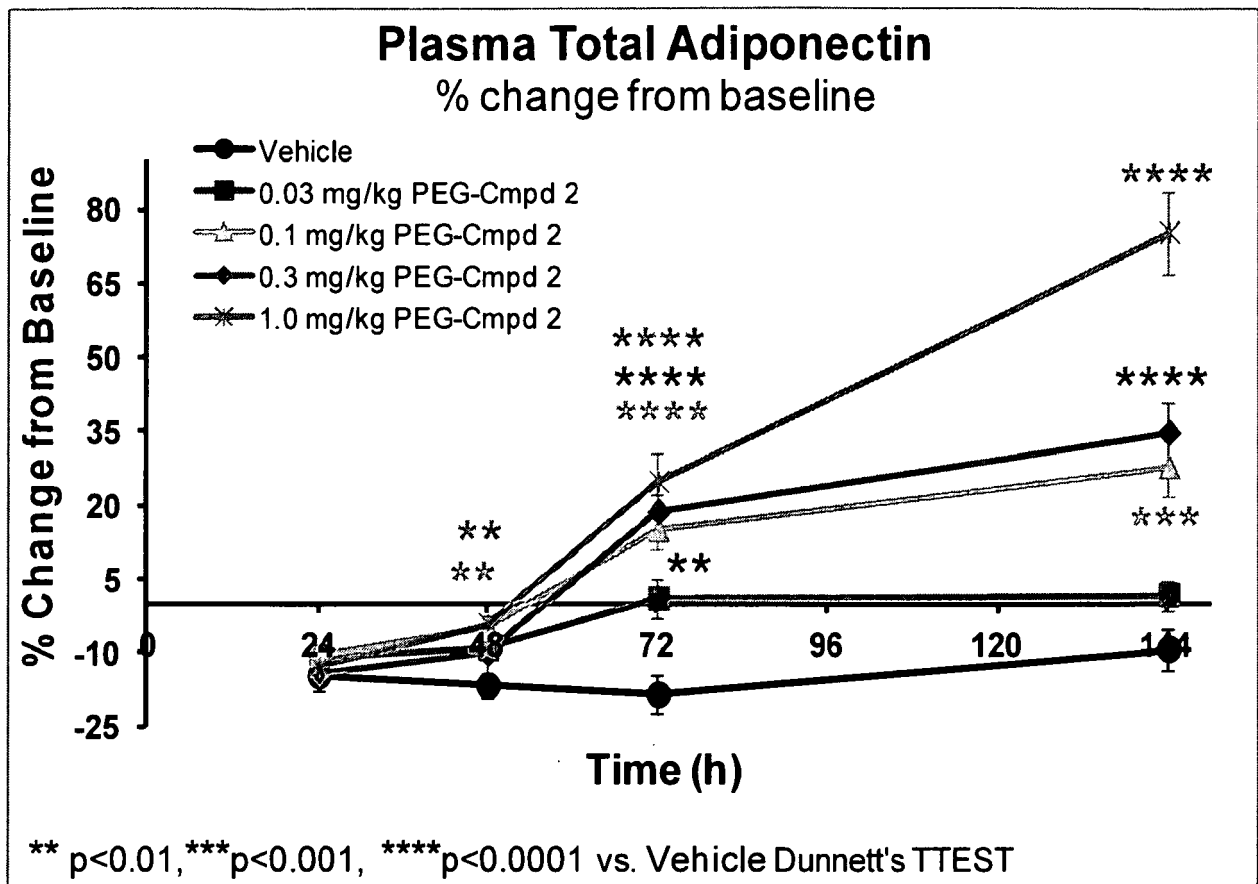


FIG. 67A.

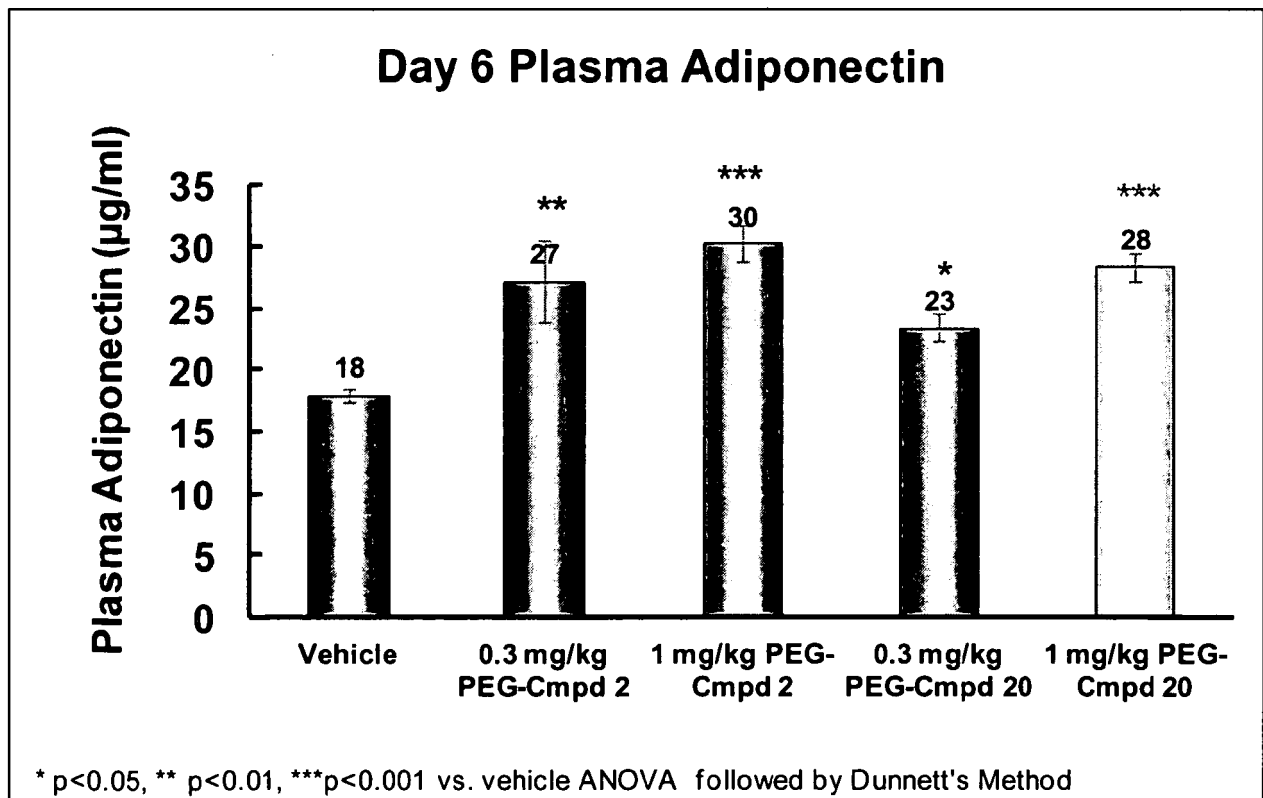


FIG. 67B.

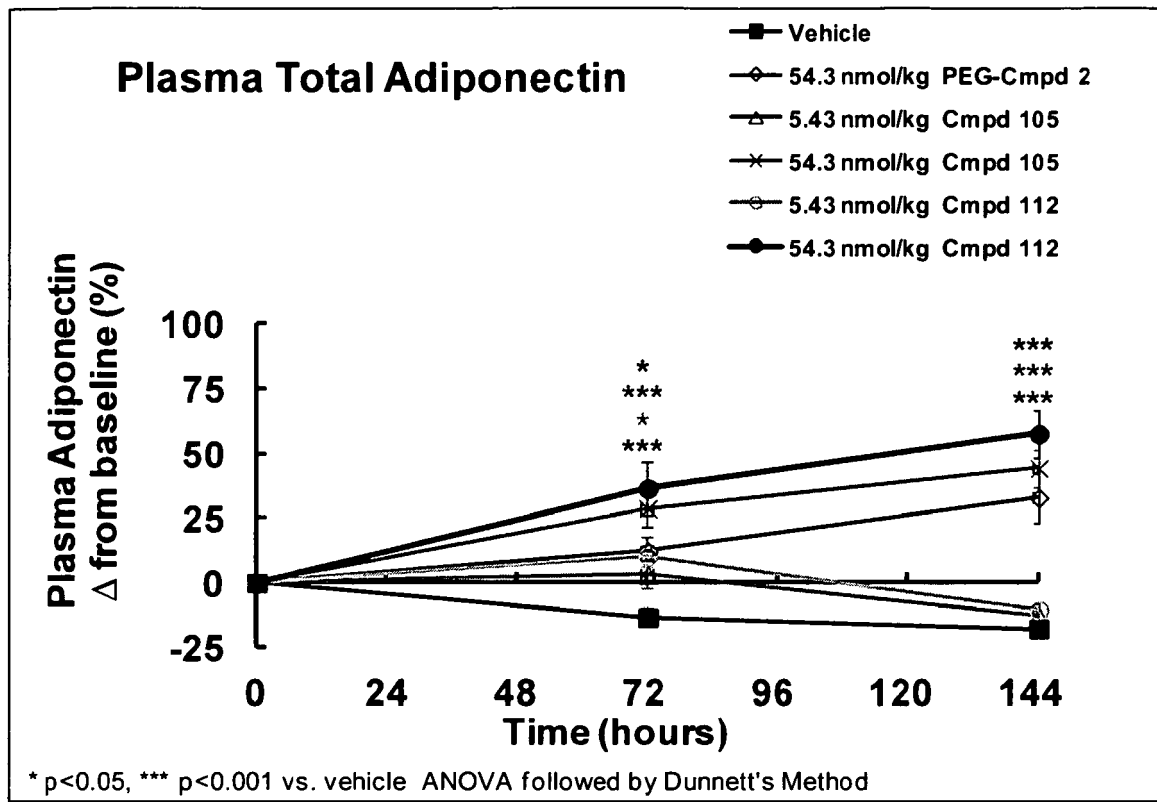


FIG. 67C.

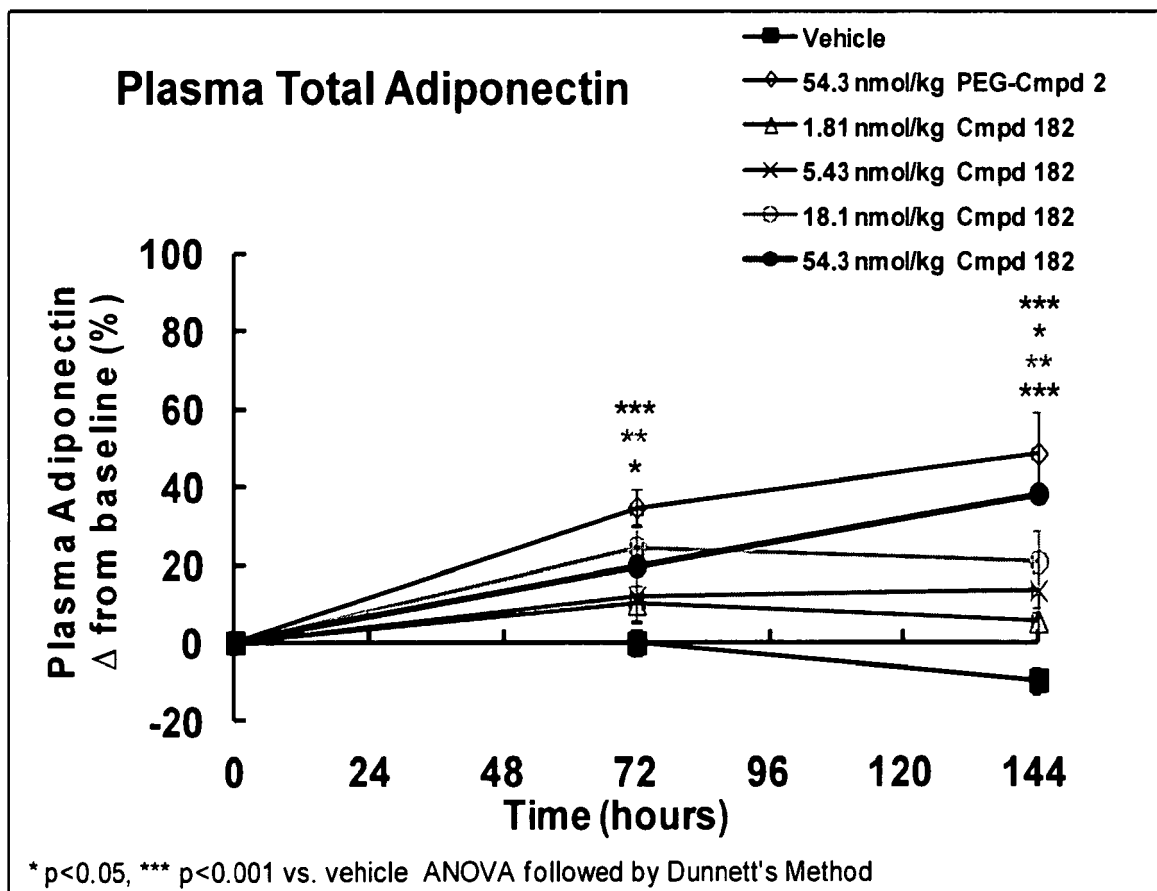


FIG. 67D.

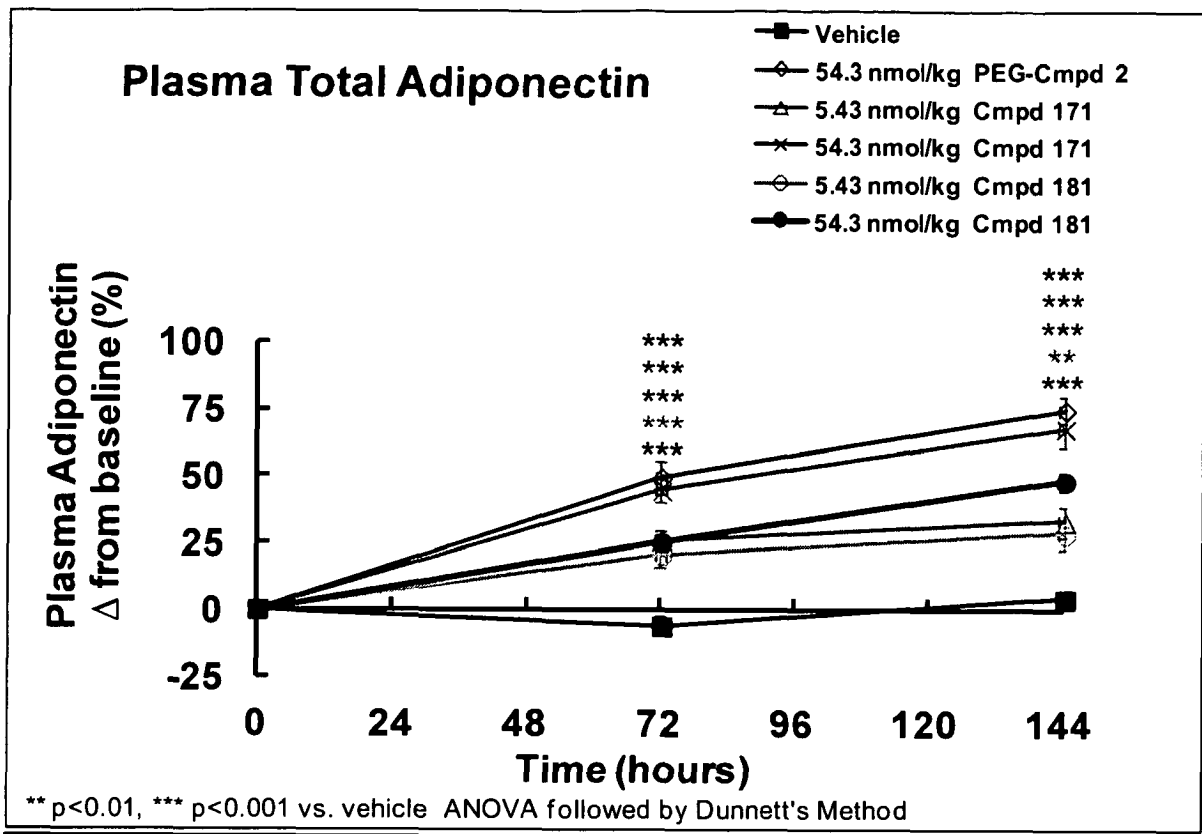


FIG. 67E.

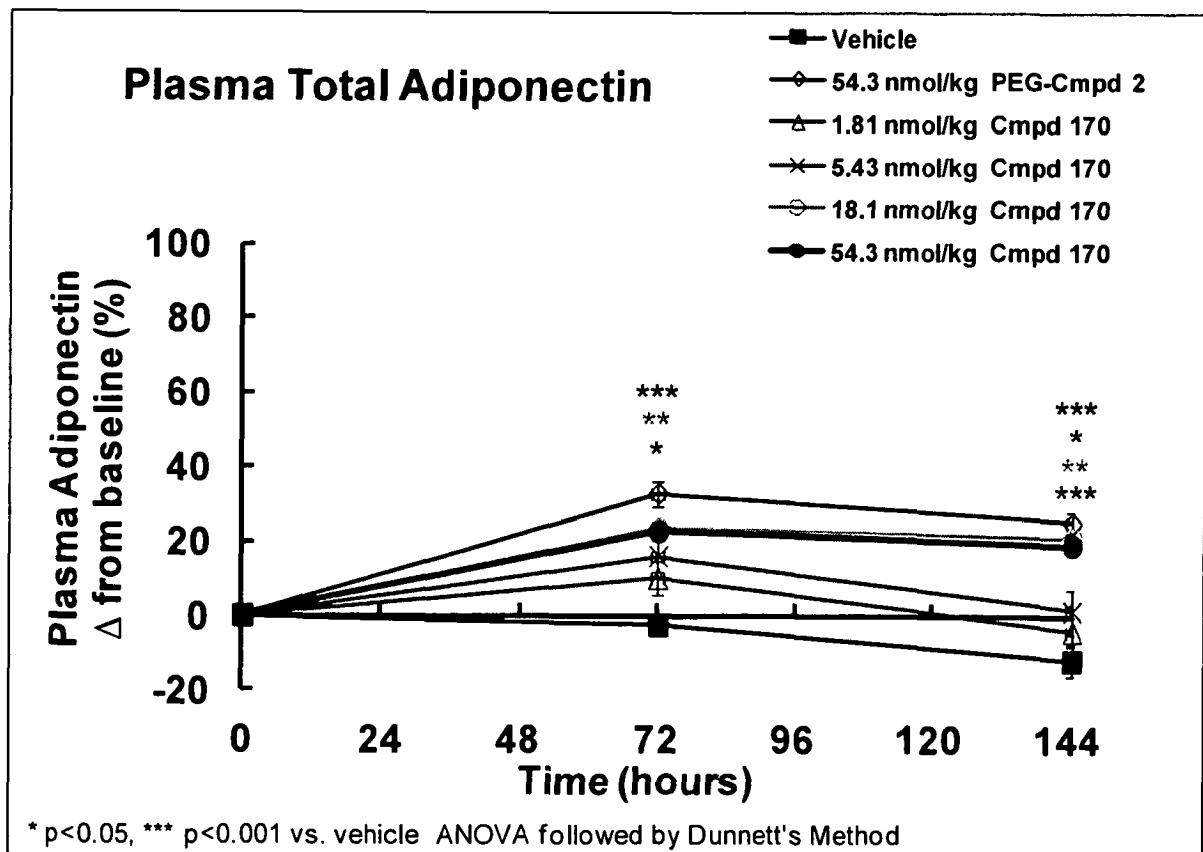


FIG. 67F.

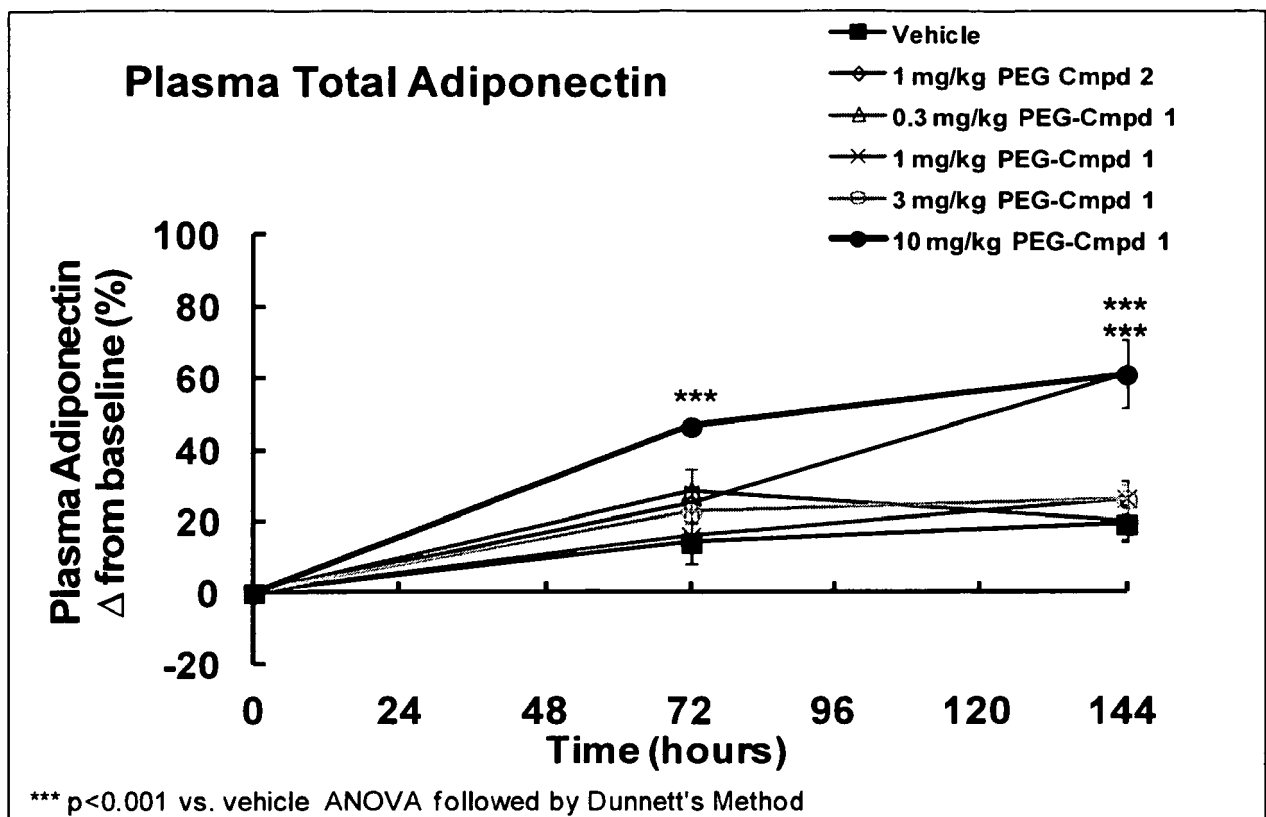


FIG. 68.

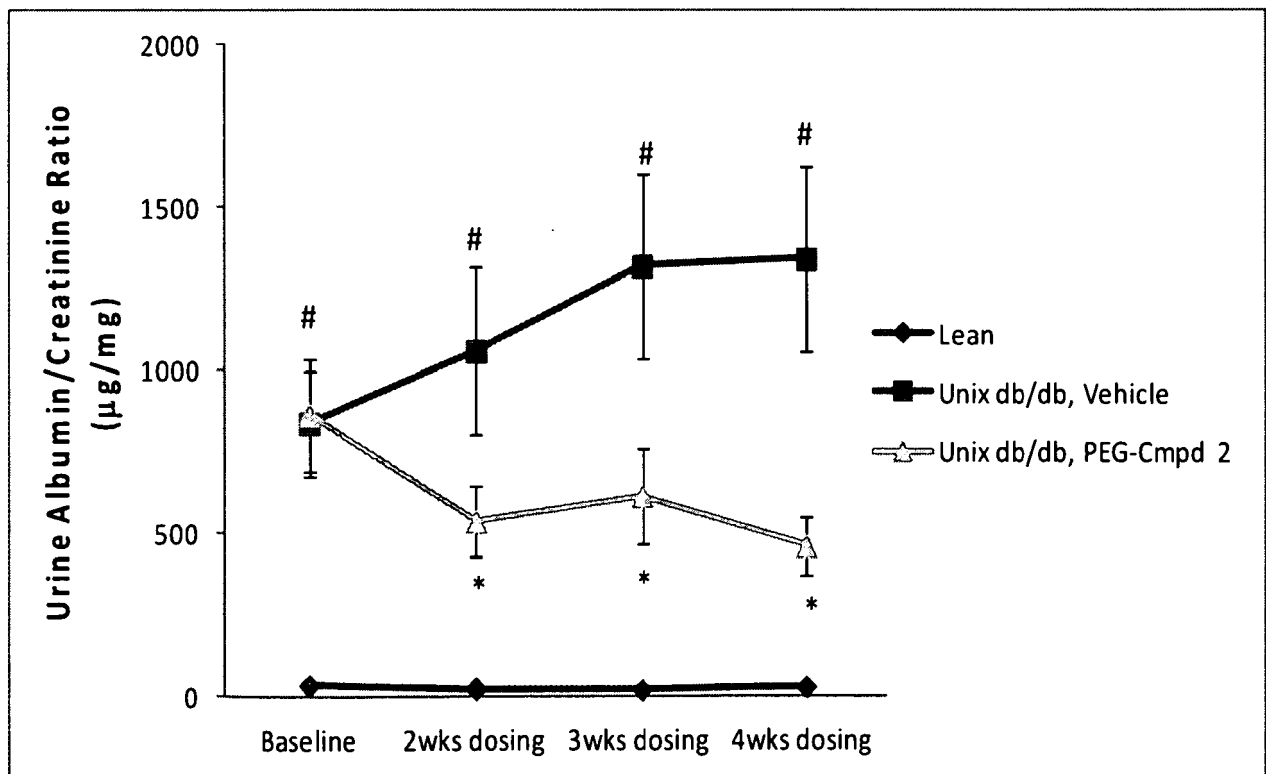


FIG. 69.

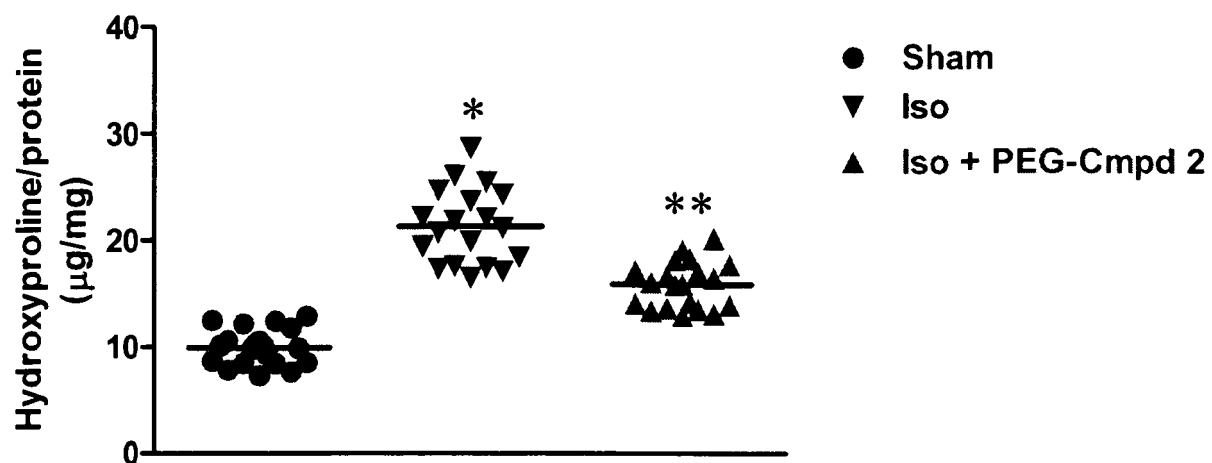


FIG. 70A

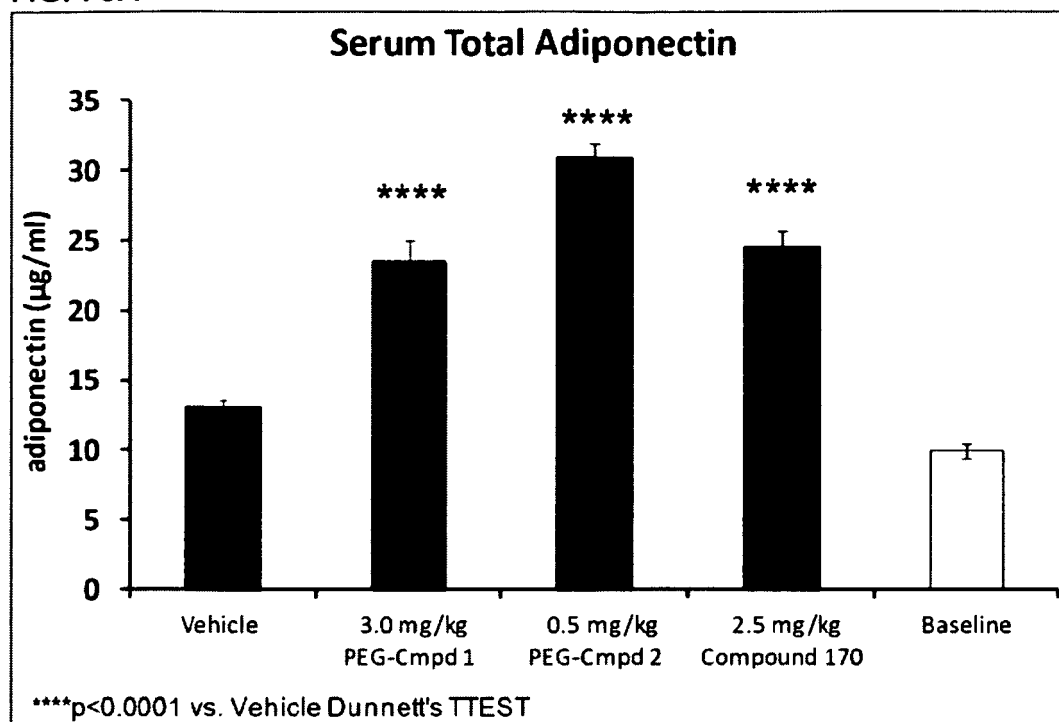


FIG. 70B

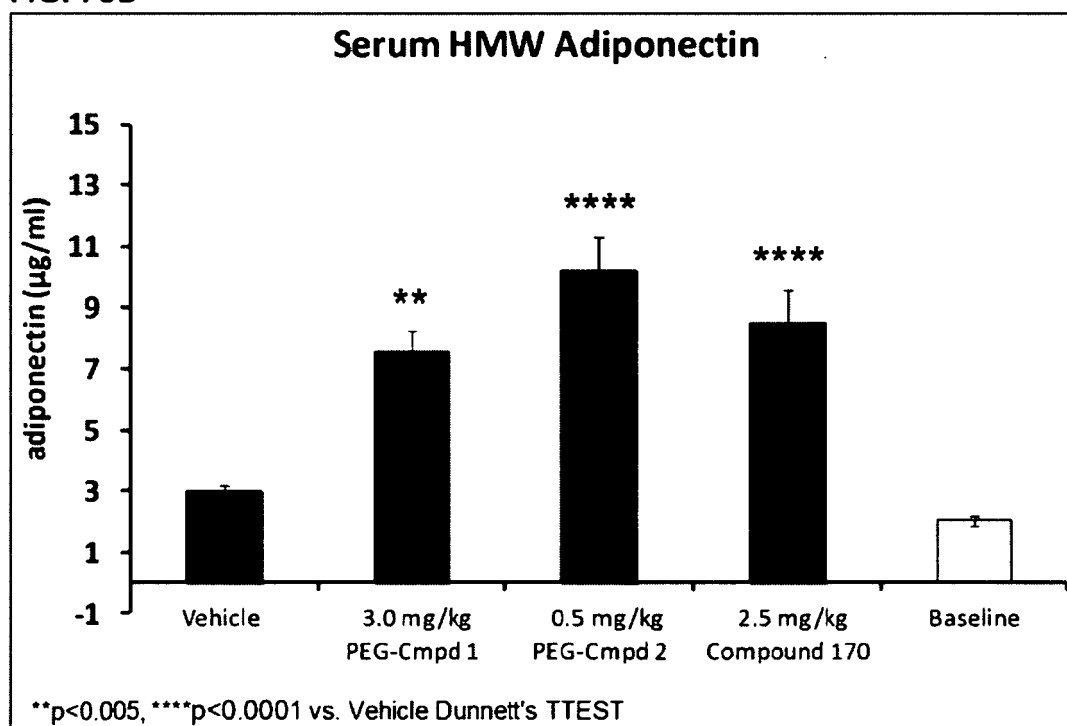


FIG. 70C

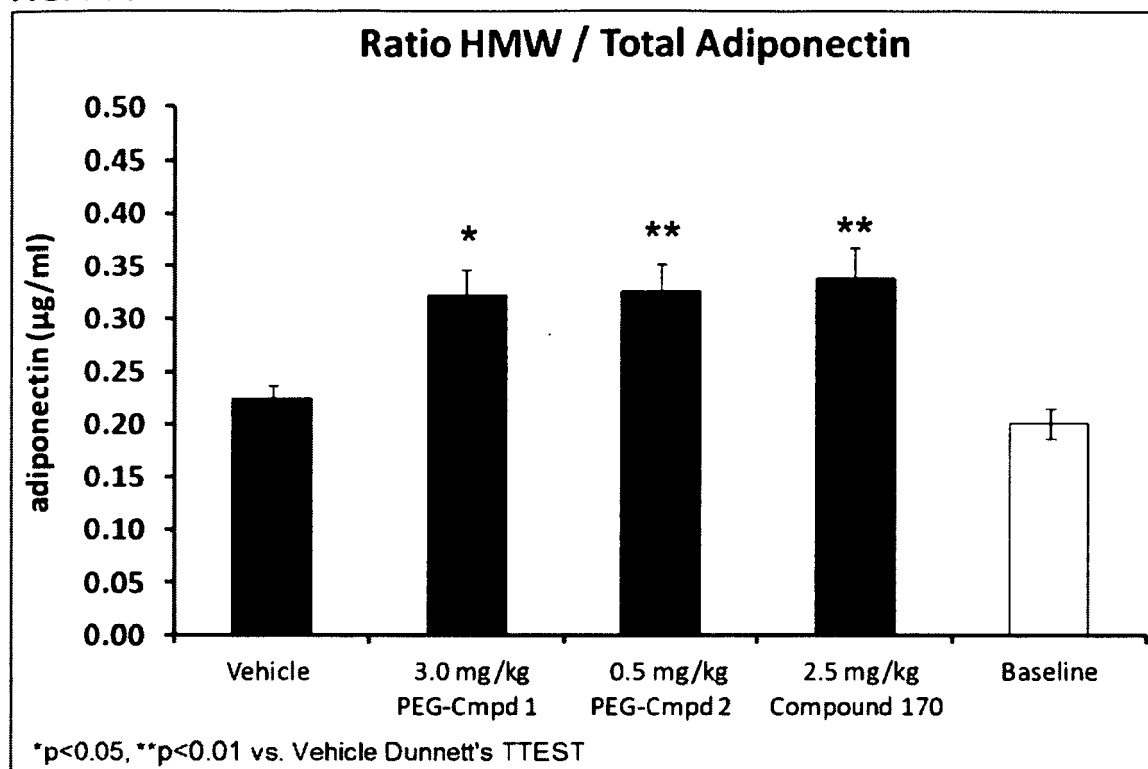


FIG. 71A

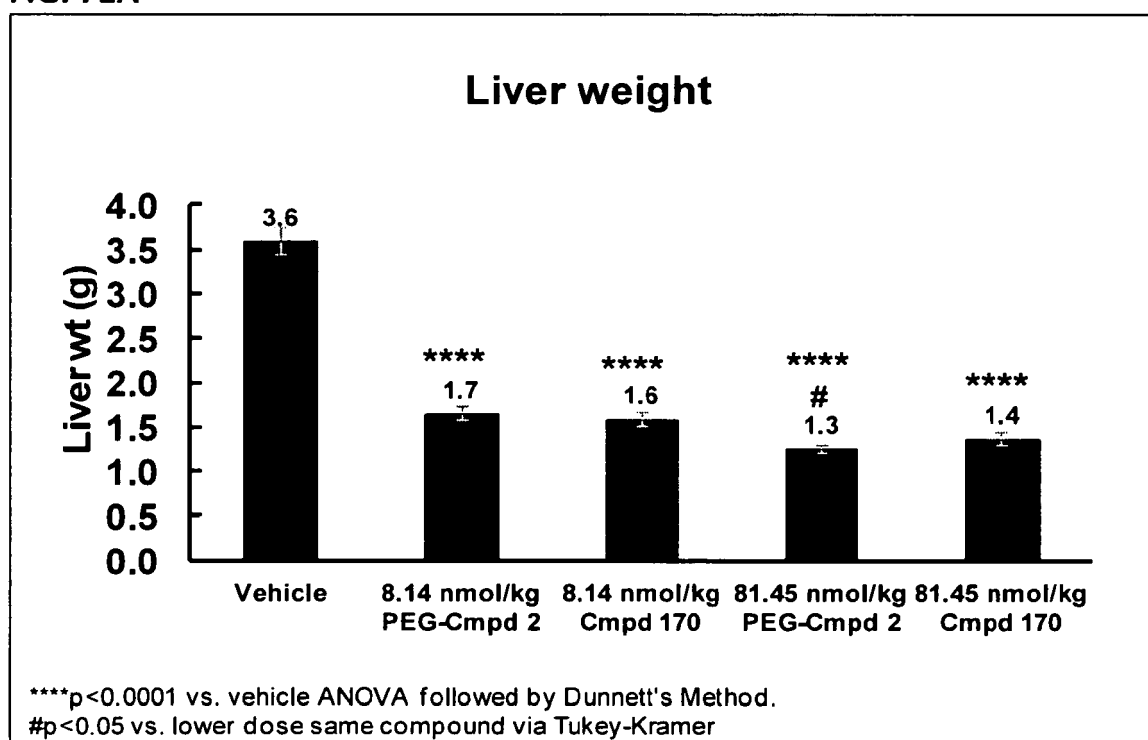


FIG. 71B

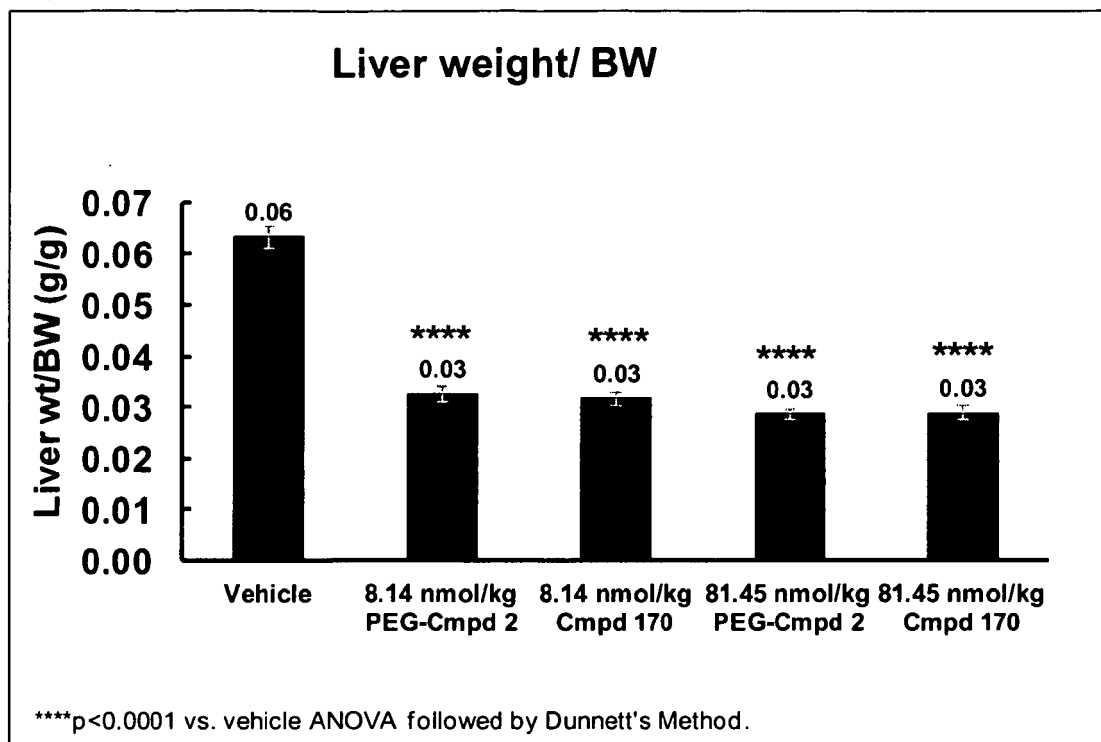


FIG. 72A

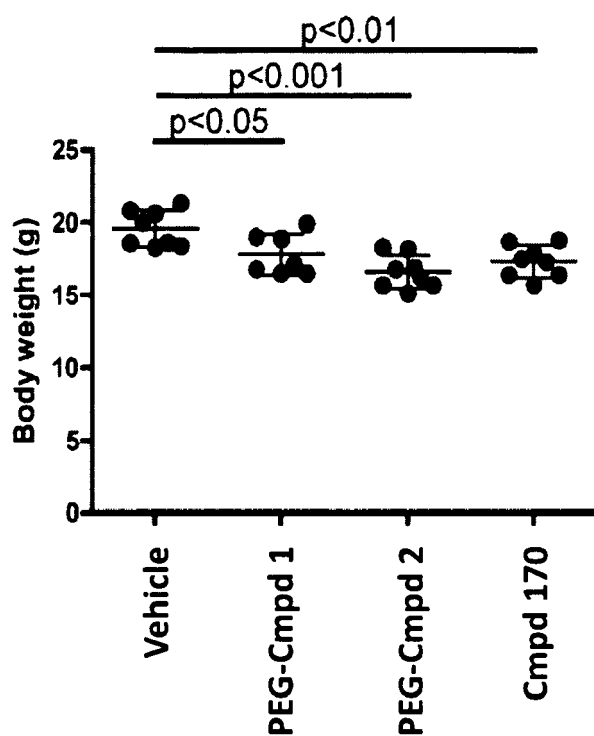


FIG. 72B

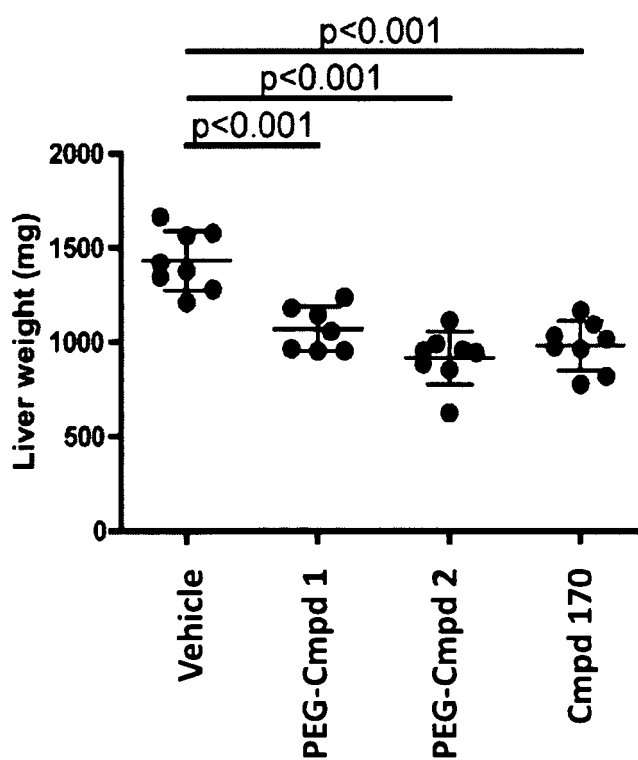


FIG. 72C

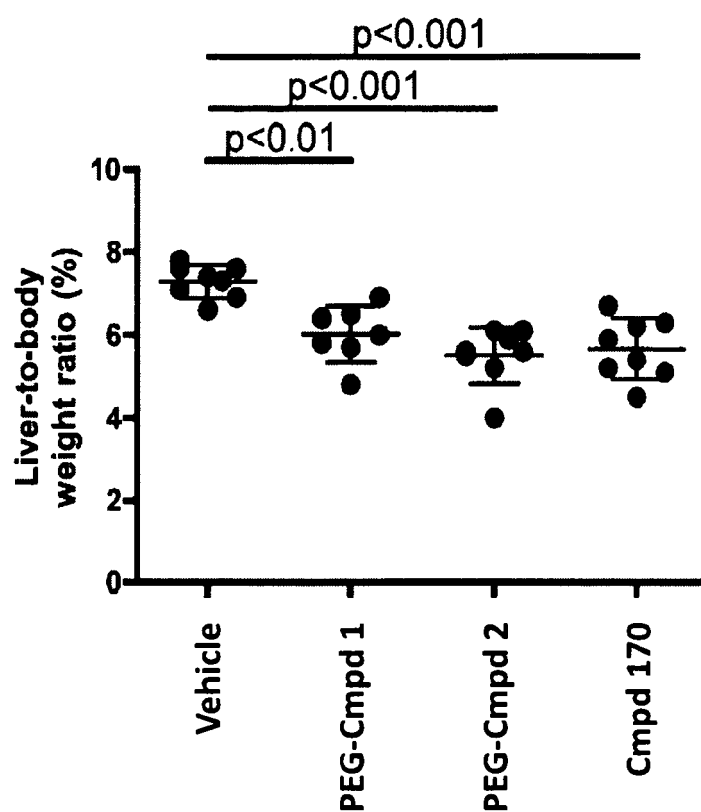


FIG. 72D

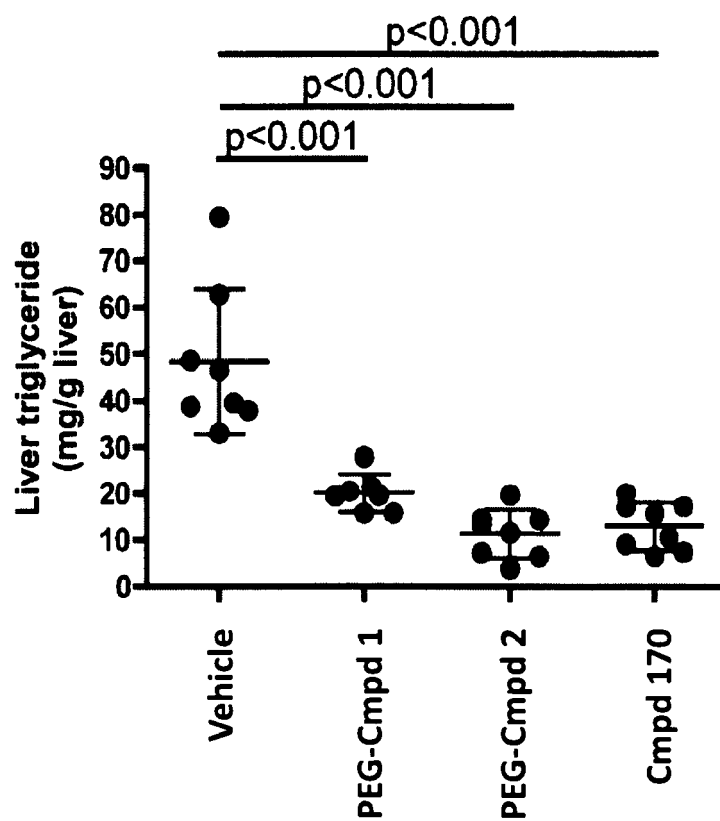


FIG. 72E

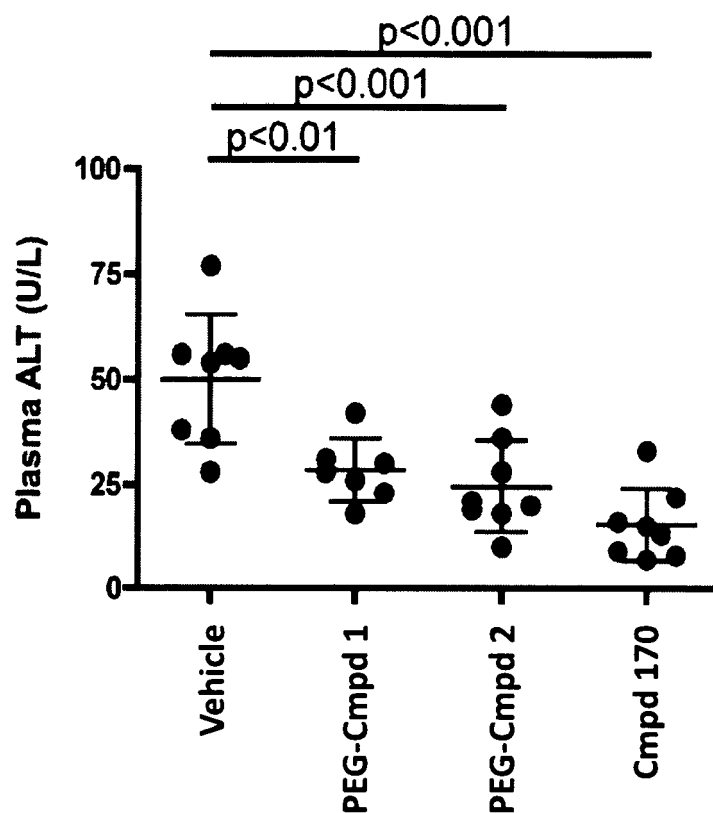


FIG. 72F

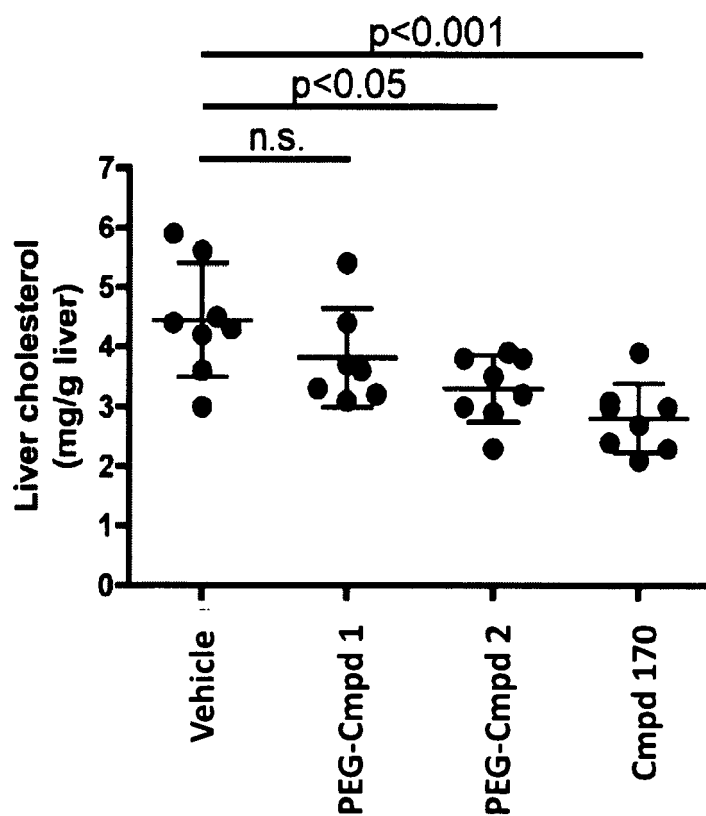


FIG. 72G

