

Figure S1.

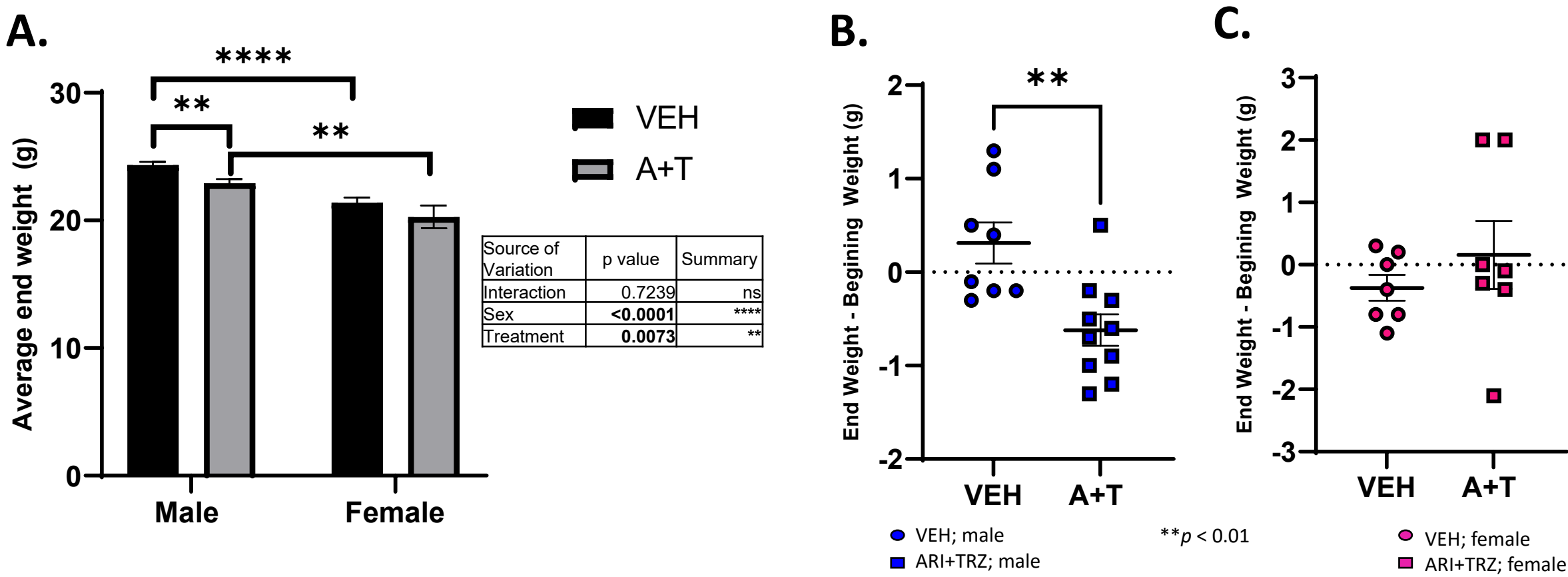


Table S1.

	VEH			ARI + TRZ			
A. Mouse Weights	Mean	SEM	N	Mean	SEM	N	t-test
male (grams)	24.3375	0.0685	8	22.91	0.9586	10	0.0041 **
female (grams)	21.3857	0.9906	7	20.2714	2.1618	7	0.2734

	VEH			VEH			t-test
male vs female (grams)	24.3375	0.0685	8	21.3857	0.9906	7	<0.0001 ****

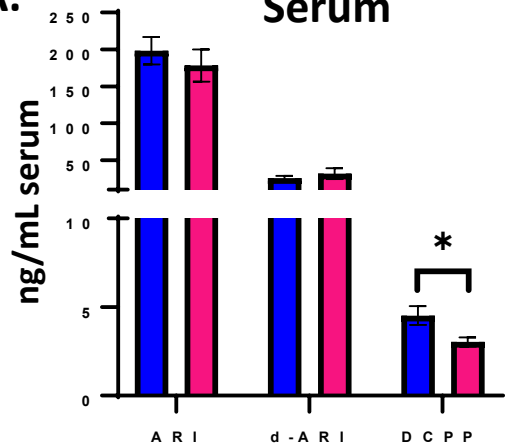
	ARI + TRZ			ARI + TRZ			t-test
male vs female (grams)	22.9100	0.9586	10	20.2714	2.1618	7	0.0059 **

	VEH			ARI + TRZ			
B. Delta mouse weight	Mean	SEM	N	Mean	SEM	N	t-test
male (grams)	0.3130	0.2200	8	-0.6200	0.1690	10	0.0035 **
female (grams)	-0.3710	0.2080	7	0.1570	0.5450	7	0.3830

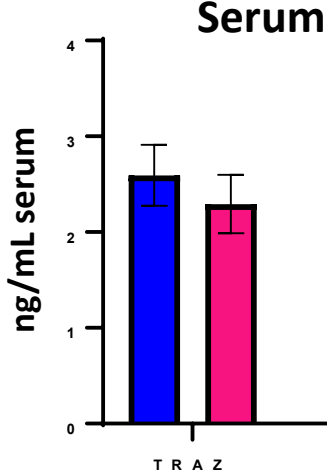
Table S1. Mouse weights.

A. Serum

Figure S2.

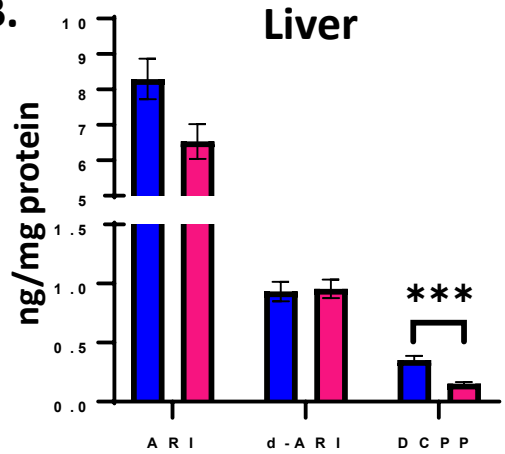


Source of Variation	p value	summary
Interaction	0.5503	ns
Drug and metabolites	<0.0001	****
Sex	0.5981	ns

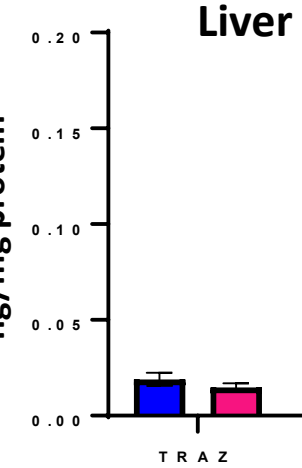


Source of Variation	p value	summary
Interaction	0.4182	ns
Drug and metabolite	0.5726	ns
Sex	0.0597	ns

B. Liver

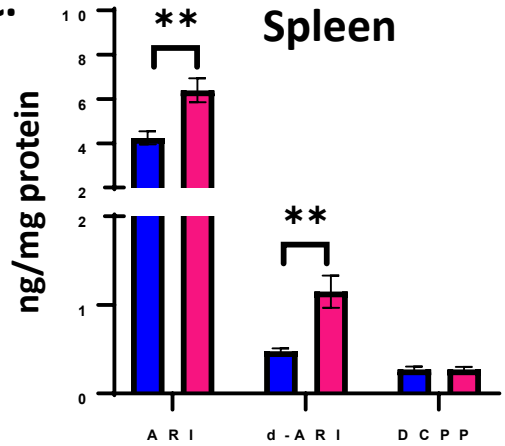


Source of Variation	p value	summary
Interaction	0.0219	*
Drug and metabolites	<0.0001	****
Sex	0.0228	*

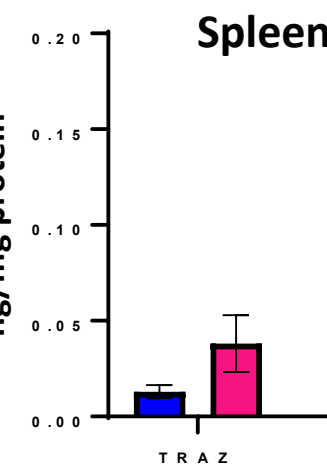


Source of Variation	p value	summary
Interaction	0.0003	***
Drug and metabolite	<0.0001	****
Sex	<0.0001	****

C. Spleen



Source of Variation	p value	summary
Interaction	0.0004	***
Drug and metabolites	<0.0001	****
Sex	<0.0001	****



Source of Variation	p value	summary
Interaction	0.9438	ns
Drug and metabolite	<0.0001	****
Sex	0.0861	ns

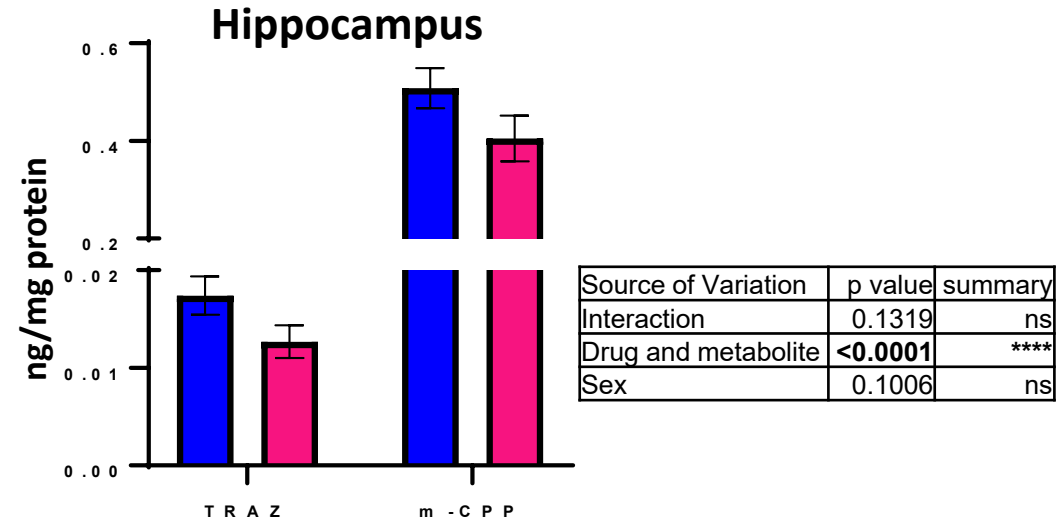
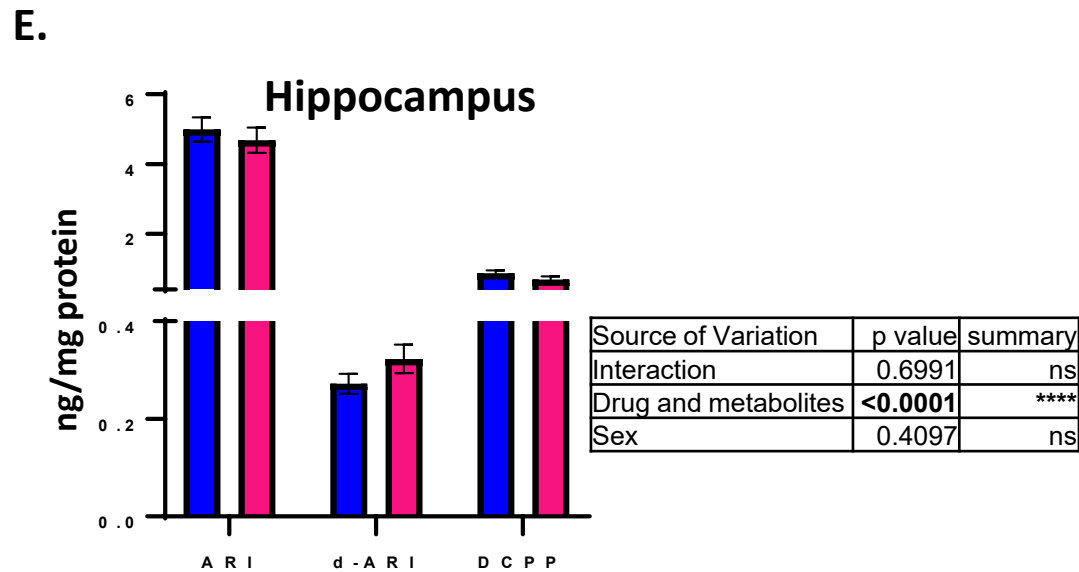
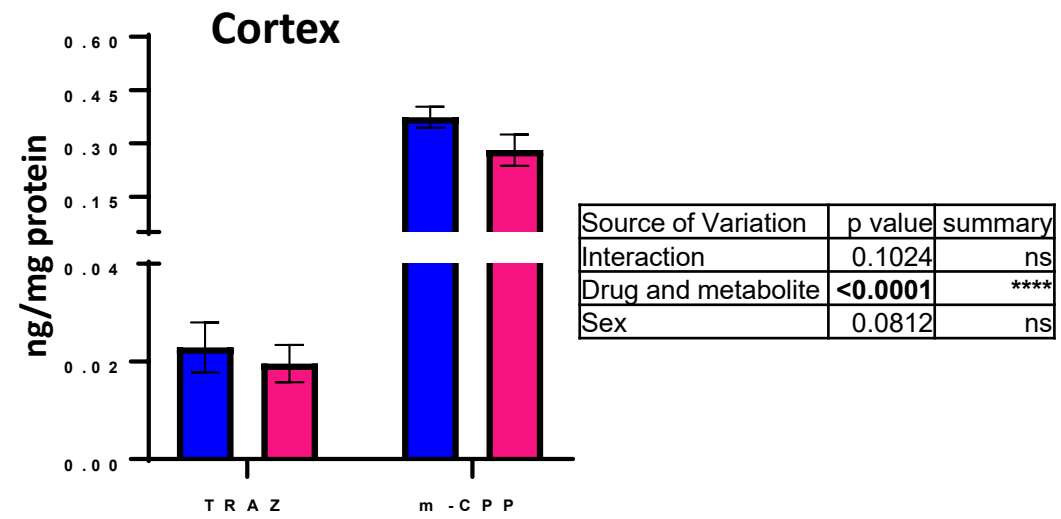
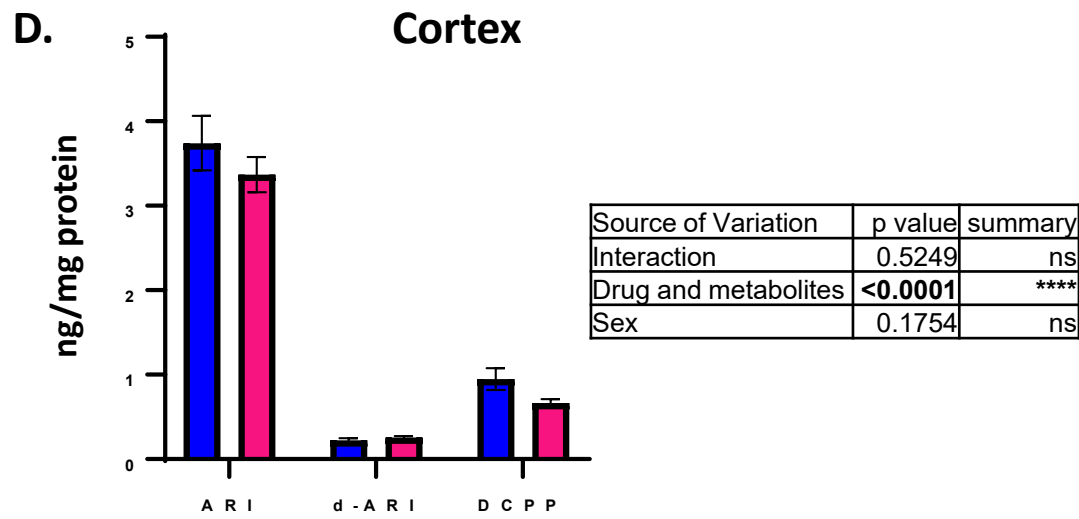


Figure S2. Aripiprazole with its metabolites and trazadone with its metabolite in serum and organs. Average ARI, d-ARI, DCPP TRZ, and m-CPP in males (blue) and females (red) exposed to ARI + TRZ for 21 days with 2-way ANOVA. A) Serum. B) Liver. C) Spleen. D) Cortex. E) Hippocampus. Statistical details are in Table S2.

Table S2.

Supplemental Table 2.							
Drug and metabolites							
A. Serum	Male			Female			t-test
	Mean	SEM	N	Mean	SEM	N	
ARI	198.4275	18.51573	5	178.2413	21.83032	5	0.5007
d-ARI	25.9348	2.812522	5	31.75601	7.309506	5	0.4786
DCPP	4.521948	0.532209	5	3.029276	0.266929	5	0.0365
TRZ	2.592502	0.317946	5	2.291929	0.305047	5	0.5144
m-CPP	2.656606	0.220812	5	1.938147	0.099891	5	0.018
B. Liver							
	Mean	SEM	N	Mean	SEM	N	t-test
ARI	8.29639	0.574082	7	6.532194	0.488176	5	0.0517
d-ARI	0.932552	0.083375	7	0.956004	0.078767	5	0.8483
DCPP	0.353251	0.03387	7	0.153476	0.012421	5	0.0008
TRZ	0.018997	0.003472	7	0.014792	0.002055	5	0.3721
m-CPP	0.151327	0.00736	7	0.099285	0.005533	5	0.0004
C. Spleen							
	Mean	SEM	N	Mean	SEM	N	t-test
ARI	4.24814	0.295182	7	6.395561	0.542897	5	0.0038
d-ARI	0.4768	0.033389	7	1.151228	0.181938	5	0.0015
DCPP	0.27137	0.033933	7	0.270561	0.028594	5	0.9866
TRZ	0.012984	0.003413	7	0.038095	0.014815	5	0.0809
m-CPP	0.132545	0.015146	7	0.155746	0.017851	5	0.3454
D. Cortex							
	Mean	SEM	N	Mean	SEM	N	t-test
ARI	3.741342	0.321441	7	3.368334	0.208558	5	0.4640
d-ARI	0.224507	0.023396	7	0.254657	0.019557	5	0.4167
DCPP	0.948305	0.128026	7	0.663347	0.045321	5	0.1340
TRZ	0.02285	0.005115	6	0.019558	0.00381	5	0.6576
m-CPP	0.373692	0.029433	6	0.280919	0.044326	5	0.1195
E. Hippocampus							
	Mean	SEM	N	Mean	SEM	N	t-test
ARI	4.993539	0.347217	7	4.681363	0.363649	5	0.5572
d-ARI	0.271794	0.020703	7	0.322675	0.029317	5	0.1737
DCPP	0.868674	0.077229	7	0.687621	0.091685	5	0.1617
TRZ	0.017395	0.001962	7	0.012677	0.001682	5	0.1152
m-CPP	0.508085	0.04104	7	0.40506	0.046523	5	0.1304

Table S2. Drugs and metabolites in serum and organs.

Figure S3.

Figure S3. Comparison of ARI and TRZ turnover in males and females across tissues. A) D-ARI/ARI ratio is higher in females than in males in all organs. The serum values did not reach statistical significance but showed the same trend as in other organs. B) DCP/ARI ratio is higher in males than in females. The hippocampus values did not reach statistical significance but showed the same trend as in other organs. C) m-CPP/TRZ ratio is similar in males and females across all organs. Statistical details are in Table S3.

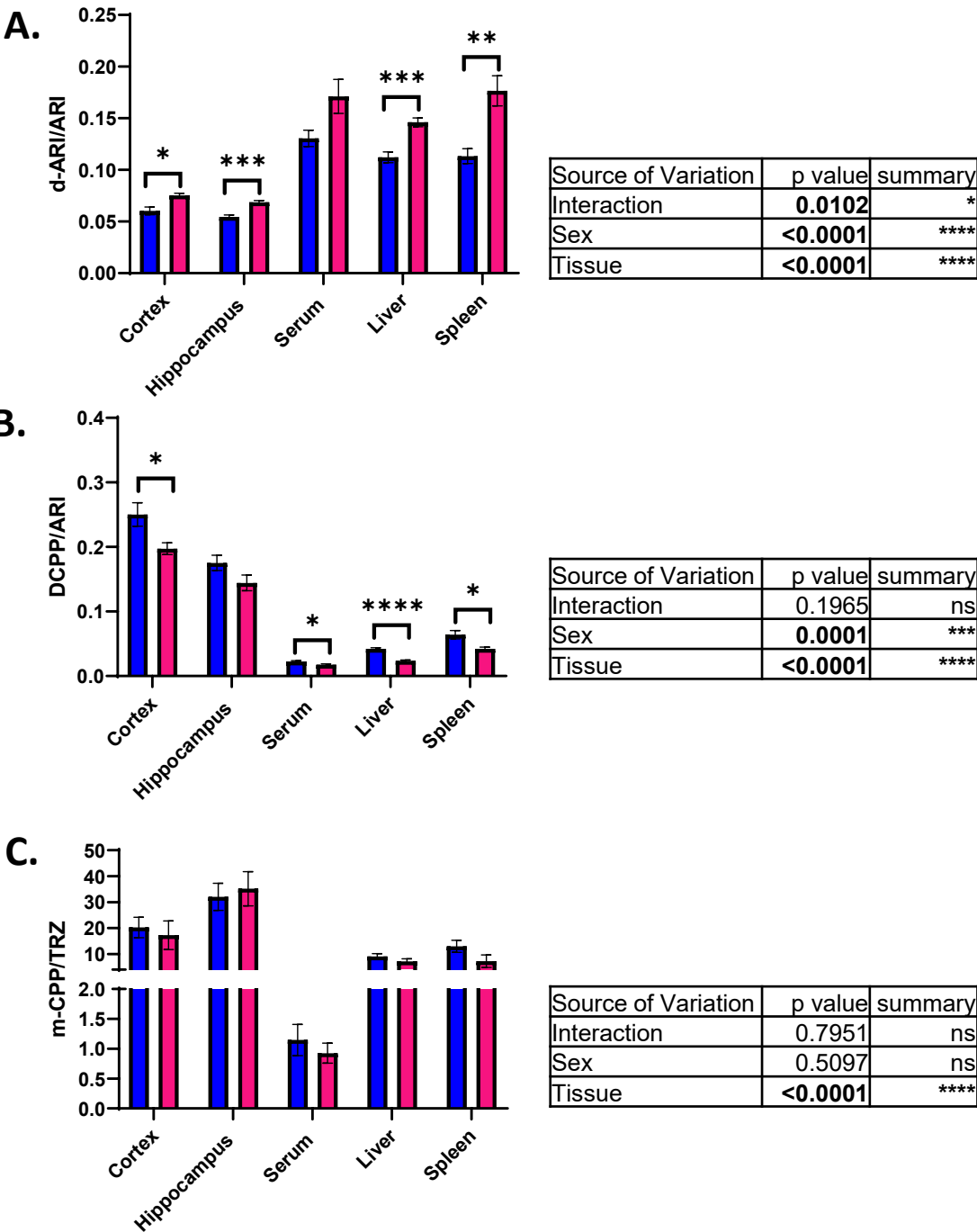


Table S3.

Drug Turnover (au)	Male			Female			t-test
A. Serum	Mean	SEM	N	Mean	SEM	N	
d-ARI/ARI	0.1305	0.0079	5	0.1711	0.0164	5	0.0566
DCPP/ARI	0.0226	0.0011	5	0.0174	0.0014	5	0.0198
d-ARI+DCPP/ARI	0.1531	0.0074	5	0.1886	0.0153	5	0.0711
m-CPP/TRZ	1.1474	0.2612	5	0.9257	0.1681	5	0.4957

B. Liver	Mean	SEM	N	Mean	SEM	N	t-test
d-ARI/ARI	0.1122	0.0052	7	0.1461	0.0042	5	0.0009
DCPP/ARI	0.0421	0.0017	7	0.0235	0.0013	5	<0.0001
d-ARI+DCPP/ARI	0.1544	0.0051	7	0.1696	0.0055	5	0.0726
m-CPP/TRZ	9.0809	1.1129	7	7.2052	0.9435	5	0.2533

C. Spleen	Mean	SEM	N	Mean	SEM	N	t-test
d-ARI/ARI	0.1133	0.0072	7	0.1766	0.0146	5	0.0016
DCPP/ARI	0.0640	0.0065	7	0.0422	0.0027	5	0.0231
d-ARI+DCPP/ARI	0.1773	0.0095	7	0.2188	0.0144	5	0.0305
m-CPP/TRZ	13.0021	2.3042	7	7.2849	2.3885	5	0.1235

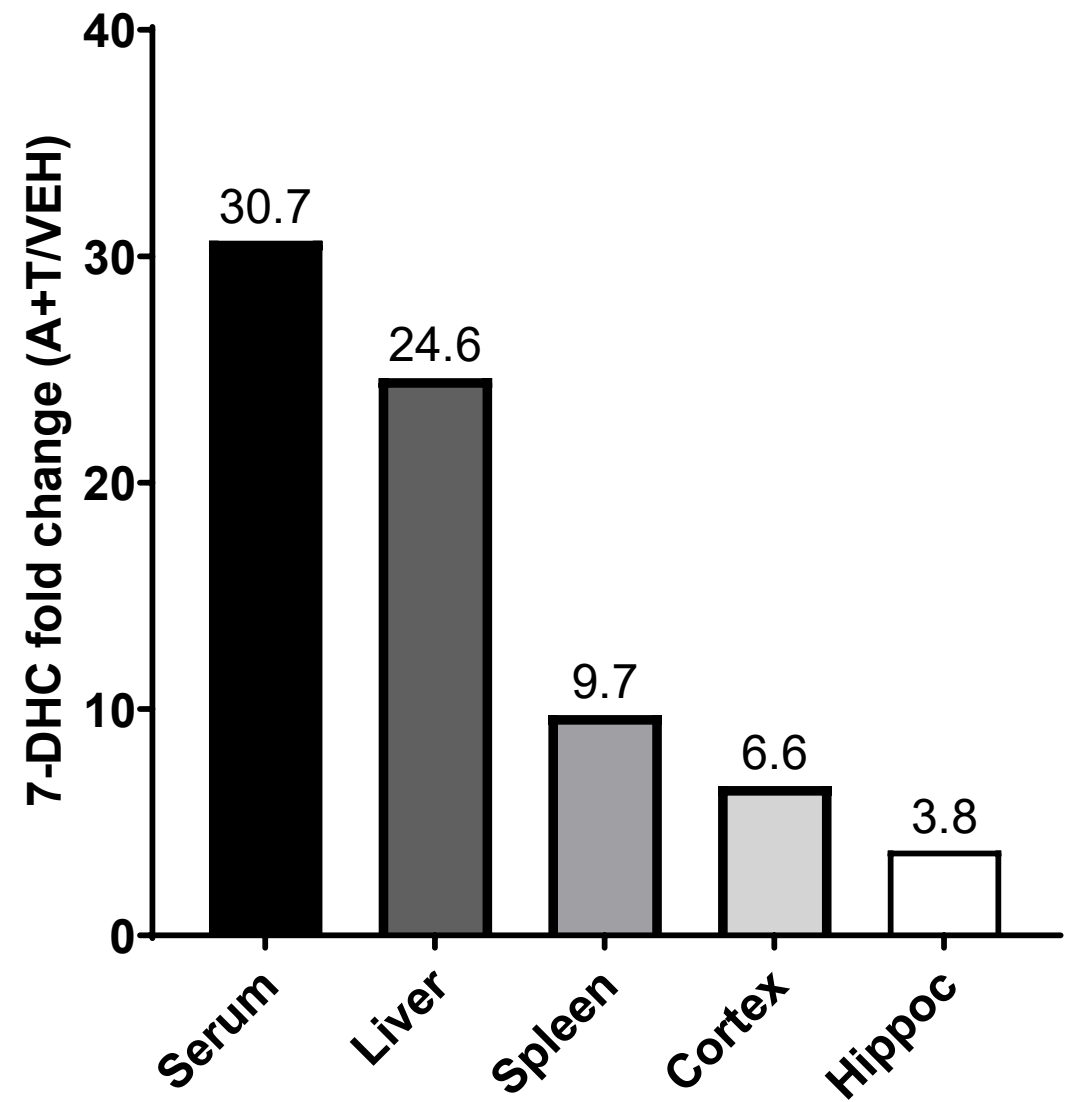
D. Cortex	Mean	SEM	N	Mean	SEM	N	t-test
d-ARI/ARI	0.0603	0.0038	7	0.0754	0.0020	5	0.0113
DCPP/ARI	0.2503	0.0181	7	0.1973	0.0091	5	0.0441
d-ARI+DCPP/ARI	0.3106	0.0211	7	0.2727	0.0084	5	0.1798
m-CPP/TRZ	20.2527	3.9339	6	17.2839	5.5079	5	0.6637

E. Hippocampus	Mean	SEM	N	Mean	SEM	N	t-test
d-ARI/ARI	0.0544	0.0020	7	0.0686	0.0016	5	0.0004
DCPP/ARI	0.1753	0.0120	7	0.1443	0.0122	5	0.1073
d-ARI+DCPP/ARI	0.2297	0.0121	7	0.2129	0.0132	5	0.3753
m-CPP/TRZ	32.0681	5.2047	7	35.1763	6.6177	5	0.7162

Table S3. Drugs turnover in serum and organs.

Figure S4.

Figure S4. 7-DHC fold increase in response to ARI+TRZ exposure. Compared to the levels of 7-DHC in VEH exposed mice, the levels of 7-DHC in ARI+TRZ exposed mice were significantly increased in all analyzed tissues.



Serum

Figure S5.

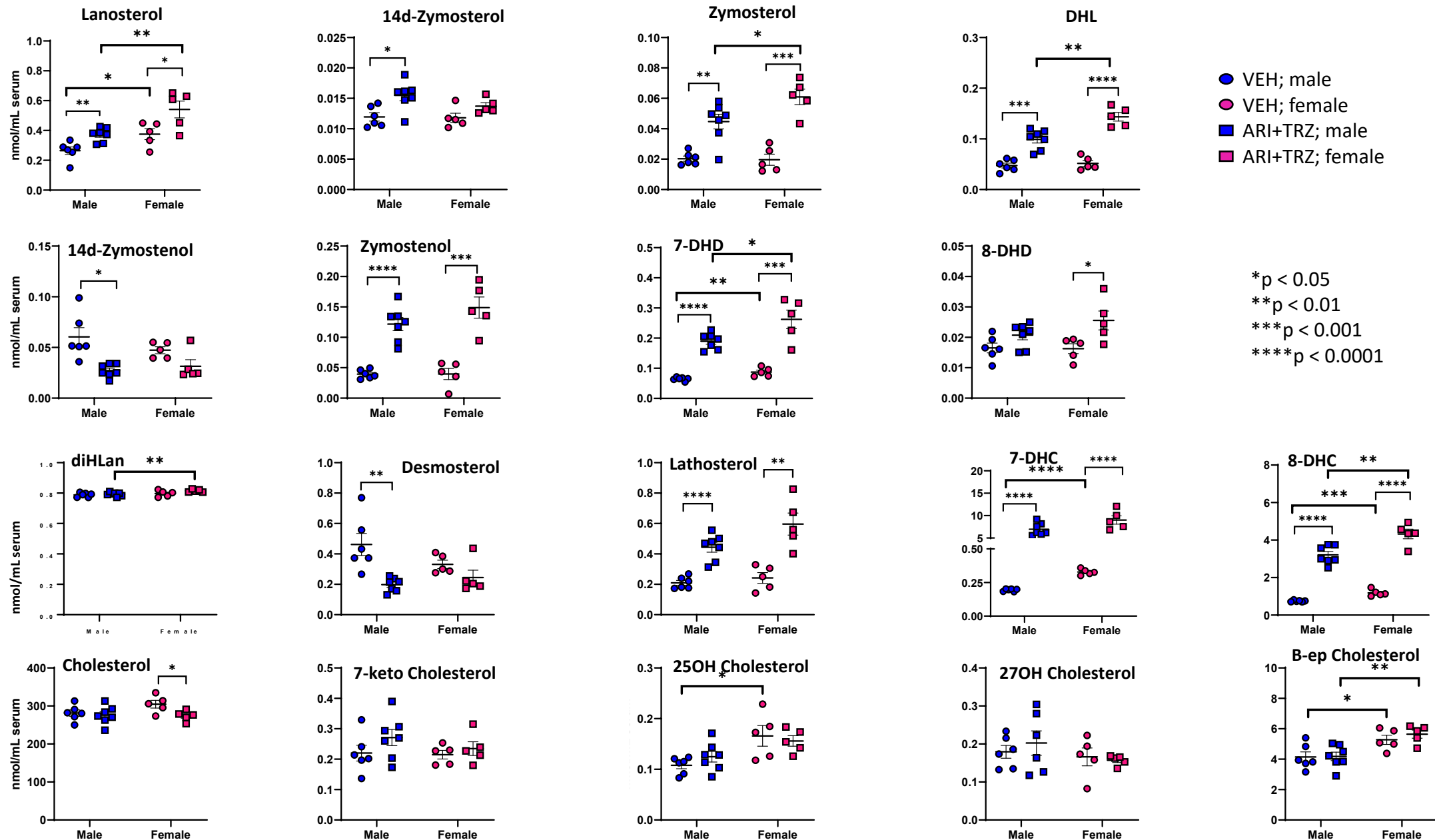


Figure S5. Comparison of sterols and oxysterols between males and females within the serum. Graphs show levels of sterols and oxysterols in males (blue) and females (red) under control (circles) and experimental (squares) conditions. Two-tailed unpaired t-tests were used to determine significance.

Liver

Figure S6.

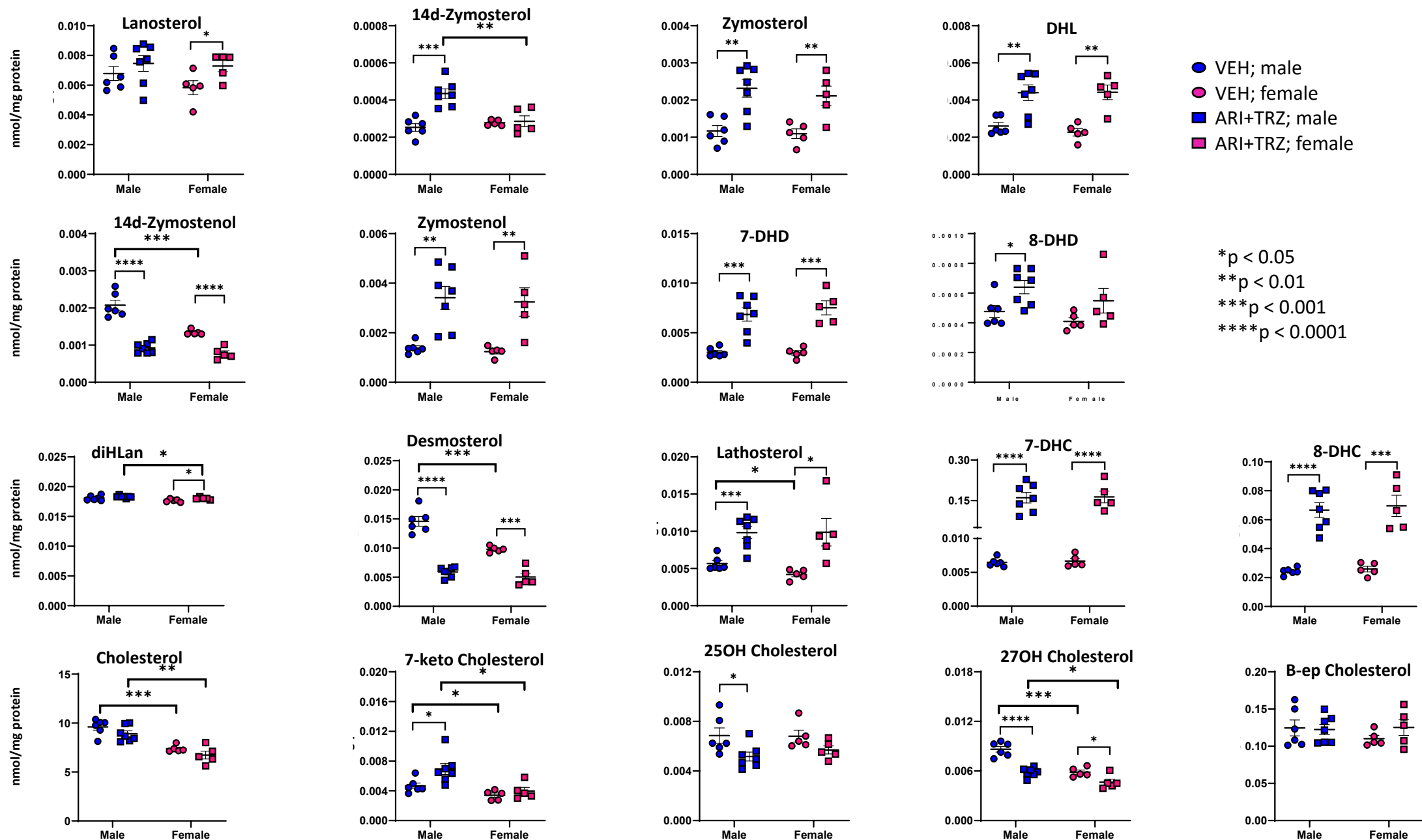


Figure S6. Comparison of sterols and oxysterols between males and females within liver. Graphs show levels of sterols and oxysterols in males (blue) and females (red) under control (circles) and experimental (squares) conditions. Two-tailed unpaired t-tests were used to determine significance.

Figure S7.

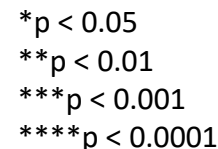


Figure S7. Comparison of sterols and oxysterols between males and females within spleen. Graphs show levels of sterols and oxysterols in males (blue) and females (red) under control (circles) and experimental (squares) conditions. Two-tailed unpaired t-tests were used to determine significance.

Figure S8. Cortex

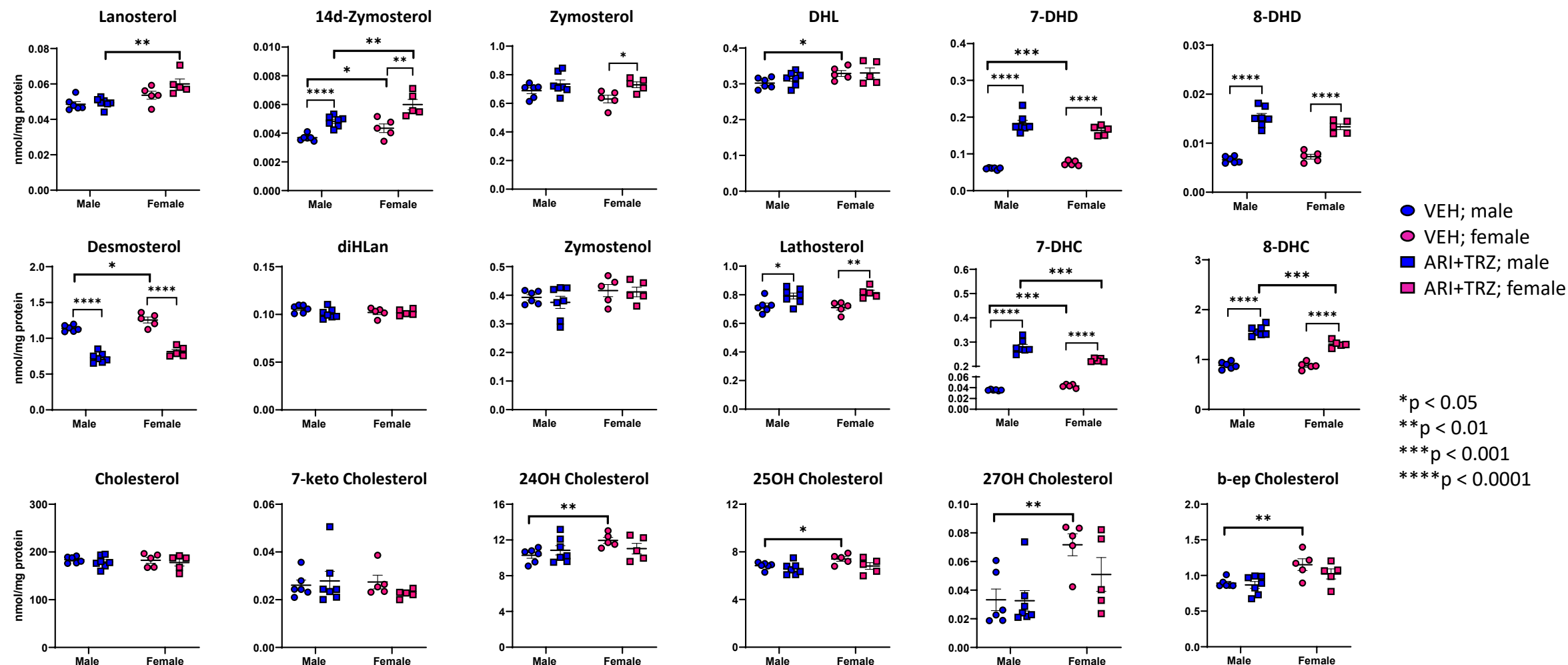


Figure S8. Comparison of sterols and oxysterols between males and females within cortex. Graphs show levels of sterols and oxysterols in males (blue) and females (red) under control (circles) and experimental (squares) conditions. Two-tailed unpaired t-tests were used to determine significance.

Figure S9. Hippocampus

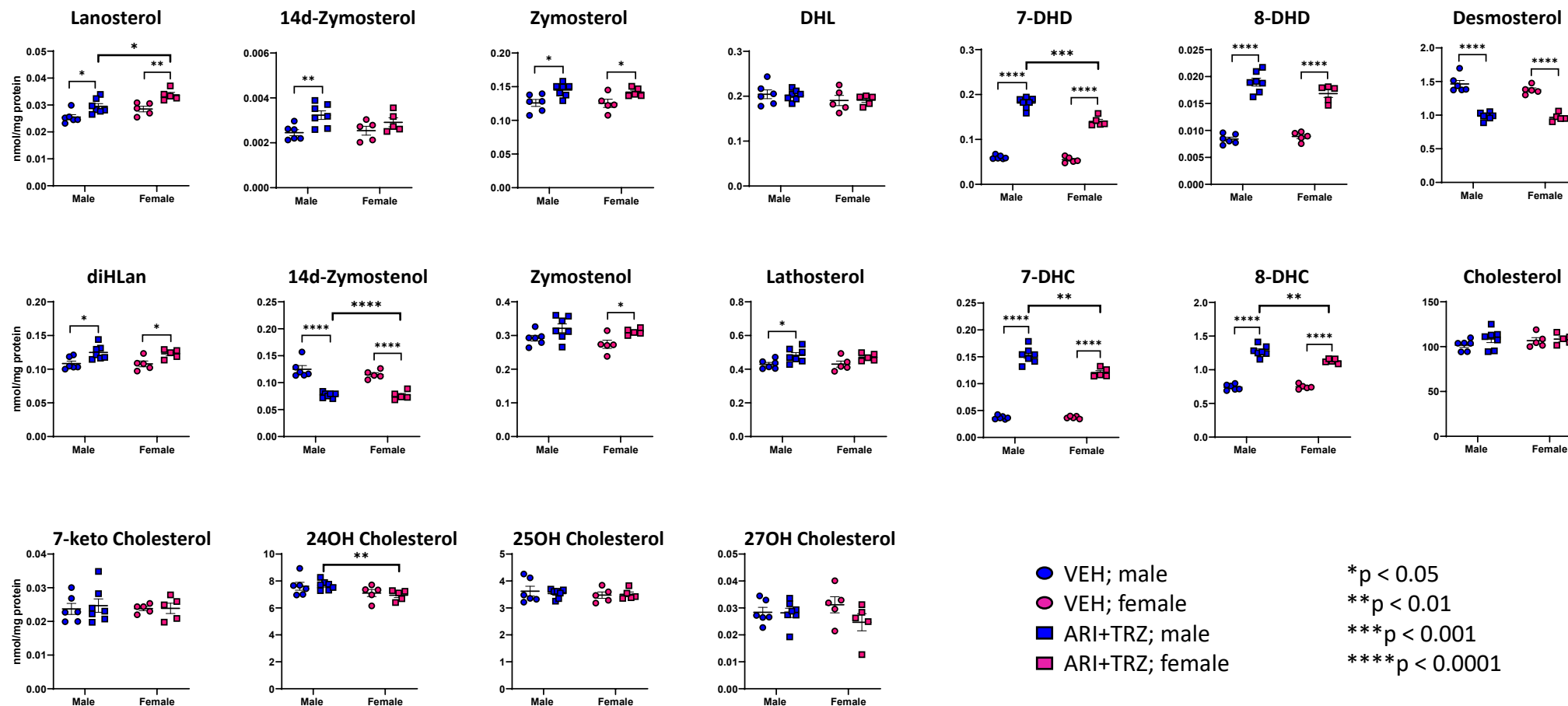
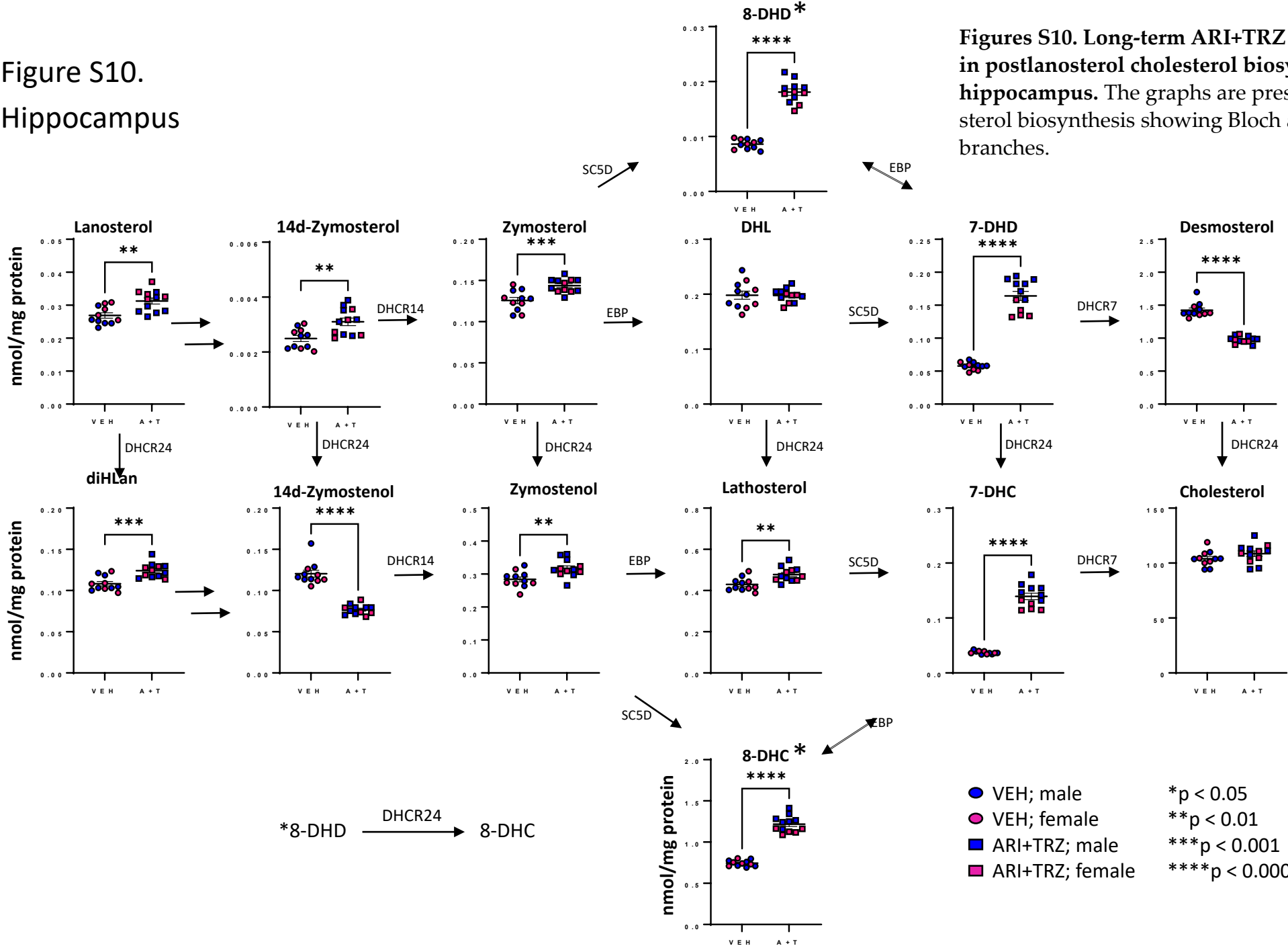


Figure S9. Comparison of sterols and oxysterols between males and females within hippocampus. Graphs show levels of sterols and oxysterols in males (blue) and females (red) under control (circles) and experimental (squares) conditions. Two-tailed unpaired t-tests were used to determine significance.

Figure S10.
Hippocampus



Figures S10. Long-term ARI+TRZ inhibits multiple enzymes in postlanosterol cholesterol biosynthesis pathway within hippocampus. The graphs are presented to coincide with the sterol biosynthesis showing Bloch and Kandutsch-Russell branches.

Table S4.

TABLE S4.		SERUM					SPLEEN					LIVER					CORTEX					HIPPOCAMPUS						
	DMG Sterols	Abbr.	VEH		ARI + TRZ		t-test	VEH		ARI + TRZ		t-test	VEH		ARI + TRZ		t-test	VEH		ARI + TRZ		t-test	VEH		ARI + TRZ		t-test	
			mean	SEM	mean	SEM		p value	mean	SEM	mean		SEM	p value	mean	SEM		mean	SEM	p value	mean		SEM	mean	SEM	p value		mean
Bloch	Lanosterol	LAN	0.3149	0.0269	0.4425	0.0348	0.0092 **	0.0056	0.0002	0.0052	0.0002	0.1866	0.0064	0.0004	0.0074	0.0003	0.0452 *	0.0509	0.0015	0.0538	0.0020	0.2514	0.0269	0.0008	0.0313	0.0009	0.0019 **	
	14-dehydrozymosterol	14-DZYM	0.0119	0.0005	0.0148	0.0006	0.0014 **	0.0003	0.0000	0.0003	0.0000	0.2203	0.0003	0.0000	0.0004	0.0000	0.0028 **	0.0040	0.0002	0.0053	0.0002	0.0002 ***	0.0002	0.0001	0.0031	0.0001	0.0029 **	
	Zymosterol	ZYM	0.0200	0.0018	0.0515	0.0041	<0.0001 ****	0.0015	0.0002	0.0019	0.0002	0.1973	0.0011	0.0001	0.0022	0.0002	<0.0001 ****	0.6622	0.0180	0.7330	0.0178	0.0109 *	0.1257	0.0037	0.1438	0.0024	0.0005 ****	
	24-dehydrolathosterol	DHL	0.0493	0.0035	0.1177	0.0085	<0.0001 ****	0.0067	0.0004	0.0080	0.0007	0.1175	0.0024	0.0001	0.0044	0.0003	<0.0001 ****	0.3145	0.0063	0.3215	0.0072	0.4746	0.1981	0.0074	0.1976	0.0036	0.9456	
	8-dehydrodesmosterol	8-DHD	0.0164	0.0011	0.0227	0.0016	0.0047 **	0.0011	0.0001	0.0017	0.0001	<0.0000 ****	0.0004	0.0000	0.0006	0.0000	0.0063 **	0.0069	0.0003	0.0145	0.0006	<0.0001 ****	0.0086	0.0003	0.0181	0.0006	<0.0001 ****	
	7-dehydrodesmosterol	7-DHD	0.0750	0.0047	0.2200	0.0171	<0.0001 ****	0.0053	0.0003	0.0174	0.0012	<0.0001 ****	0.0030	0.0001	0.0071	0.0005	<0.0001 ****	0.0668	0.0027	0.1746	0.0064	<0.0001 ****	0.0578	0.0018	0.1641	0.0069	<0.0001 ****	
Kandutsch Russell	Desmosterol	DES	0.4025	0.0447	0.2172	0.0223	0.0010 **	0.0311	0.0015	0.0128	0.0011	<0.0001 ****	0.0124	0.0009	0.0055	0.0003	<0.0001 ****	1.1920	0.0272	0.7646	0.0227	<0.0001 ****	1.4240	0.0327	0.9781	0.0155	<0.0001 ****	
	dihydrolanosterol	DIHLAN	0.7923	0.0051	0.8021	0.0046	0.1661	0.0199	0.0002	0.0197	0.0002	0.4357	0.0179	0.0001	0.0182	0.0001	0.0389 *	0.1041	0.0014	0.1014	0.0013	0.1654	0.1082	0.0027	0.1241	0.0025	0.0003 ****	
	14-dehydrozymostenol	14-DZYME	0.0544	0.0054	0.0290	0.0029	0.0004 ***	0.0041	0.0001	0.0018	0.0001	<0.0001 ****	0.0017	0.0001	0.0009	0.0000	<0.0001 ****						0.1204	0.0042	0.0769	0.0002	<0.0001 ****	
	Zymostenol	ZYME	0.03964	0.0042	0.1330	0.0100	<0.0001 ****	0.0015	0.0001	0.0023	0.0002	0.0020 **	0.0013	0.0001	0.0033	0.0003	<0.0001 ****	0.4034	0.0109	0.3904	0.0147	0.4903	0.2838	0.0074	0.3171	0.0077	0.0052 **	
	Lathosterol	LATH	0.2244	0.0180	0.5073	0.0405	<0.0001 ****	0.0093	0.0005	0.0118	0.0009	0.0337 *	0.0050	0.0003	0.0099	0.0009	<0.0001 ****	0.7172	0.0132	0.8012	0.0138	0.0003 ***	0.4296	0.0096	0.4780	0.0099	0.0022 **	
	7-dehydrocholesterol	7-DHC	0.2550	0.0216	7.8250	0.5568	<0.0001 ****	0.0086	0.0008	0.0834	0.0073	<0.0001 ****	0.0066	0.0002	0.1614	0.0140	<0.0001 ****	0.0390	0.0014	0.2576	0.0101	<0.0001 ****	0.0371	0.0008	0.1393	0.0059	<0.0001 ****	
Oxysterols	8-dehydrocholesterol	8-DHC	0.9467	0.0768	3.6740	0.2192	<0.0001 ****	0.0382	0.0040	0.0748	0.0067	0.0002 ***	0.0250	0.0010	0.0678	0.0041	<0.0001 ****	0.8802	0.0204	1.4650	0.0461	<0.0001 ****	0.7439	0.0116	1.2170	0.0284	<0.0001 ****	
	Cholesterol	CHOL	292.0000	7.1940	275.2000	5.7090	0.0790	10.9600	0.5030	9.4480	0.3723	0.0231 *	8.5990	0.3961	7.9970	0.3965	0.2964	183.2000	3.0090	178.6000	3.8490	0.3616	104.0000	2.1100	108.5000	2.5010	0.1800	
	7-keto cholesterol	7-KETO	0.2177	0.0149	0.2560	0.0183	0.1228	0.0123	0.0009	0.0093	0.0005	0.0073 **	0.0041	0.0003	0.0057	0.0006	0.0387 *	0.0267	0.0017	0.0257	0.0024	0.7336	0.0238	0.0009	0.0244	0.0013	0.7163	
	24OH-cholesterol	24OH-CHOL																11.0400	0.3447	10.9200	0.3755	0.8174	7.3830	0.2066	7.3750	0.1477	0.9747	
	25OH-cholesterol	25OH-CHOL	0.1343	0.0131	0.1379	0.0086	0.8173	0.0058	0.0004	0.0050	0.0003	0.1329	0.0068	0.0004	0.0054	0.0003	0.0042 **	7.0980	0.1348	6.6850	0.1566	0.0609	3.5570	0.1101	3.5240	0.0496	0.7817	
	27OH-cholesterol	27OH-CHOL	0.1733	0.0135	0.1818	0.0185	0.7146	0.0034	0.0002	0.0032	0.0002	0.5372	0.0074	0.0005	0.0053	0.0003	0.0011 **	0.0508	0.0079	0.0403	0.0067	0.3206	0.0297	0.0017	0.0267	0.0017	0.2238	
		β-epoxycholesterol	β-EP CHOL	4.6600	0.2818	4.7910	0.2879	0.7495	0.1708	0.0147	0.1579	0.0139	0.5277	0.1180	0.0063	0.1236	0.0058	0.5162	1.0100	0.0555	0.9317	0.0451	0.2821					
these numbers are males and females combined (NOT SEPARATE)																												

Table S4. Sterols and oxysterol levels (Mean±SEM) in serum, and organs in VEH and ARI+TRZ exposed mice.

Table S5.

SERUM												
VEH			VEH			ARI + TRZ			ARI + TRZ			
SEX			SEX			SEX			SEX			
Male			Female			VEH			Male			A+T
mean			SEM			p value			mean			p value
Bloch	DMG Sterols	Abbr.	mean	SEM	mean	SEM	p value		mean	SEM	SEM	
	Lanosterol	LAN	0.2645	0.0254	0.3753	0.0364	0.0306		0.3721	0.0176	0.5412	0.0562
	14-dehydrozymosterol	14-DZYM	0.0120	0.0007	0.0118	0.0008	0.8825	0.0155	0.0009	0.0137	0.0006	0.1567
	Zymosterol	ZYM	0.0203	0.0017	0.0196	0.0036	0.8555	0.0447	0.0048	0.0610	0.0051	0.0469
	24-dehydrolathosterol	DHL	0.0474	0.0047	0.0516	0.0058	0.5776	0.0991	0.0073	0.1436	0.0085	0.0027
	8-dehydrosdesmosterol	8-DHD	0.0165	0.0016	0.0163	0.0016	0.9160	0.0207	0.0015	0.0255	0.0031	0.1550
	7-dehydrosdesmosterol	7-DHD	0.0647	0.0024	0.0874	0.0066	0.0068	0.1898	0.0100	0.2622	0.0309	0.0284
	Desmosterol	DES	0.4619	0.0727	0.3312	0.0272	0.1544	0.1977	0.0171	0.2447	0.0485	0.3220
Kandutsch Russell	dihydrolanosterol	DIHLAN	0.7880	0.0057	0.7972	0.0092	0.4045	0.7928	0.0048	0.8152	0.0041	0.0073
	14-dehydrozymosterol	14-DZYME	0.0604	0.0092	0.0473	0.0034	0.2463	0.0272	0.0024	0.0315	0.0064	0.4973
	Zymosterol	ZYME	0.0395	0.0029	0.0398	0.0092	0.9793	0.1217	0.0108	0.1489	0.0174	0.1913
	Lathosterol	LATH	0.2097	0.0161	0.2420	0.0354	0.4013	0.4439	0.0325	0.5962	0.0723	0.0588
	7-dehydrocholesterol	7-DHC	0.1940	0.0040	0.3281	0.0098	<0.0001	6.9694	0.5152	9.0219	0.9349	0.6510
	8-dehydrocholesterol	8-DHC	0.7491	0.0173	1.1838	0.0787	0.0002	3.2080	0.1825	4.3260	0.2547	0.0043
	Cholesterol	CHOL	281.4323	8.5194	304.6943	10.0970	0.1097	276.1044	9.1612	273.9122	6.1786	0.8601
	7-keto cholesterol	7-KETO	0.2200	0.0260	0.2149	0.0142	0.8735	0.2710	0.0268	0.2349	0.0224	0.3541
Oxysterols	24OH-cholesterol	24OH-CHOL										
	25OH-cholesterol	25OH-CHOL	0.1078	0.0068	0.1660	0.0203	0.0165	0.1249	0.0105	0.1560	0.0104	0.0699
	27OH-cholesterol	27OH-CHOL	0.1793	0.0169	0.1661	0.0235	0.6510	0.2024	0.0323	0.1572	0.0059	0.2425
	β-epoxycholesterol	β-EP CHOL	4.1464	0.3352	5.2763	0.3066	0.0372	4.1819	0.2798	5.6430	0.2668	0.0046

SPLEEN												
VEH			VEH			ARI + TRZ			ARI + TRZ			
SEX			SEX			SEX			SEX			
Male			Female			VEH			Male			A+T
mean			SEM			p value			mean			p value
0.0051	0.0003	0.0061	0.0001	0.0382	0.0047	0.0002	0.0057	0.0003	0.0079			
0.0003	0.0000	0.0003	0.0000	0.0232	0.0003	0.0000	0.0004	0.0000	0.0966			
0.0010	0.0001	0.0020	0.0002	0.0003	0.0015	0.0002	0.0024	0.0004	0.0459			
0.0058	0.0003	0.0078	0.0005	0.0044	0.0067	0.0007	0.0098	0.0008	0.0124			
0.0009	0.0000	0.0013	0.0001	0.0005	0.0017	0.0001	0.0019	0.0001	0.2958			
0.0046	0.0002	0.0062	0.0004	0.0048	0.0155	0.0012	0.0201	0.0017	0.0464			
0.0287	0.0013	0.0340	0.0024	0.0732	0.0103	0.0006	0.0164	0.0015	0.0019			
0.0195	0.0001	0.0203	0.0002	0.0045	0.0193	0.0001	0.0202	0.0001	0.0007			
0.0039	0.0001	0.0042	0.0002	0.3260	0.0015	0.0001	0.0021	0.0002	0.0110			
0.0012	0.0001	0.0019	0.0001	<0.0001	0.0020	0.0002	0.0027	0.0003	0.0486			
0.0062	0.0005	0.0105	0.0006	0.0171	0.0098	0.0010	0.0146	0.0007	0.0039			
0.0068	0.0002	0.0107	0.0011	0.0054	0.0704	0.0090	0.1015	0.0064	0.0278			
0.0290	0.0021	0.0492	0.0052	0.0038	0.0599	0.0045	0.0956	0.0081	0.0020			
10.0537	0.4909	12.0562	0.6952	0.0039	8.6837	0.4030	10.5178	0.2883	0.0068			
0.0119	0.0015	0.0127	0.0010	0.7016	0.0091	0.0005	0.0094	0.0010	0.7875			
0.0052	0.0003	0.0065	0.0006	0.0911	0.0043	0.0003	0.0060	0.0002	0.0005			
0.0034	0.0003	0.0033	0.0004	0.7681	0.0028	0.0001	0.0037	0.0002	0.0026			
0.1406	0.0155	0.2071	0.0149	0.0137	0.1231	0.0072	0.2066	0.0119	<0.0001			

LIVER												
VEH			VEH			ARI + TRZ			ARI + TRZ			
SEX			SEX			SEX			SEX			
Male			Female			VEH			Male			A+T
mean			SEM			p value			mean			p value
0.0068	0.0005	0.0058	0.0005	0.1943	0.0075	0.0005	0.0073	0.0004	0.8159			
0.0003	0.0000	0.0003	0.0000	0.3224	0.0004	0.0000	0.0003	0.0000	0.0036			
0.0012	0.0001	0.0011	0.0001	0.7265	0.0023	0.0002	0.0021	0.0003	0.5810			
0.0026	0.0002	0.0023	0.0002	0.2657	0.0044	0.0004	0.0044	0.0004	0.9694			
0.0005	0.0000	0.0004	0.0000	0.2213	0.0006	0.0000	0.0005	0.0001	0.3208			
0.0030	0.0002	0.0030	0.0002	0.8432	0.0068	0.0007	0.0075	0.0007	0.5126			
0.0146	0.0008	0.0098	0.0002	0.0007	0.0059	0.0003	0.0050	0.0007	0.2239			
0.0181	0.0002	0.0177	0.0001	0.0793	0.0183	0.0001	0.0180	0.0001	0.0036			
0.0021	0.0001	0.0013	0.0000	0.0009	0.0009	0.0001	0.0008	0.0001	0.1174			
0.0014	0.0001	0.0012	0.0001	0.3201	0.0034	0.0005	0.0032	0.0006	0.8175			
0.0057	0.0004	0.0042	0.0003	0.0185	0.0098	0.0008	0.0099	0.0019	0.9784			
0.0065	0.0002	0.0067	0.0004	0.6749	0.1601	0.0195	0.1631	0.0220	0.9229			
0.0243	0.0010	0.0258	0.0020	0.4868	0.0666	0.0051	0.0695	0.0073	0.7446			
9.6096	0.3305	7.3852	0.1565	0.0003	8.9033	0.3001	6.7287	0.3982	0.0012			
0.0047	0.0004	0.0034	0.0003	0.0344	0.0069	0.0007	0.0040	0.0005	0.0128			
0.0069	0.0006	0.0068	0.0005	0.9531	0.0052	0.0004	0.0057	0.0003	0.3184			
0.0086	0.0003	0.0059	0.0002	0.0002	0.0058	0.0002	0.0046	0.0004	0.0119			
0.1246	0.0106	0.1100	0.0045	0.2722	0.1224	0.0069	0.1253	0.0108	0.8159			

			CORTEX									
			VEH		VEH			ARI + TRZ		ARI + TRZ		
			SEX		SEX			SEX		SEX		
			Male		Female		VEH	Male		Female		A+T
	DMG Sterols	Abbr.	mean	SEM	mean	SEM	p value	mean	SEM	mean	SEM	p value
Bloch	Lanosterol	LAN	0.0486	0.0015	0.0536	0.0022	0.0846	0.0494	0.0010	0.0600	0.0028	0.0022
	14-dehydrozymosterol	14-DZYM	0.0037	0.0001	0.0043	0.0003	0.0476	0.0048	0.0001	0.0060	0.0004	0.0073
	Zymosterol	ZYM	0.6886	0.0203	0.6307	0.0267	0.1125	0.7353	0.0281	0.7299	0.0203	0.8885
	24-dehydrolathosterol	DHL	0.0070	0.0003	0.0070	0.0005	0.0256	0.0150	0.0007	0.0130	0.0006	0.3000
	8-dehydrosdesmosterol	8-DHD	0.0066	0.0003	0.0073	0.0005	0.2560	0.0153	0.0007	0.0133	0.0006	0.0783
	7-dehydrosdesmosterol	7-DHD	0.0603	0.0010	0.0747	0.0030	0.0008	0.1824	0.0093	0.1637	0.0059	0.1548
	Desmosterol	DES	1.1392	0.0174	1.2561	0.0420	0.0223	0.7297	0.0259	0.8135	0.0310	0.0641
	dihydrolanosterol	DIHLAN	0.3023	0.0062	0.3291	0.0081	0.1866	0.3149	0.0074	0.3307	0.0137	0.6843
Kandutsch Russell	14-dehydrozymostenol	14-DZYME										
	Zymostenol	ZYME	0.3926	0.0093	0.4164	0.0212	0.3015	0.3751	0.0212	0.4118	0.0169	
	Lathosterol	LATH	0.7225	0.0200	0.7108	0.0182	0.6809	0.7914	0.0205	0.8148	0.0169	0.4281
	7-dehydrocholesterol	7-DHC	0.0356	0.0004	0.0431	0.0015	0.0004	0.2804	0.0103	0.2256	0.0033	0.0015
	8-dehydrocholesterol	8-DHC	0.8833	0.0288	0.8765	0.0323	0.8774	1.5750	0.0372	1.3115	0.0314	0.0005
	Cholesterol	CHOL	183.7624	2.7001	182.6276	6.2187	0.8623	179.1427	4.6799	177.9157	7.1826	0.8837
Oxysterols	7-keto cholesterol	7-KETO	0.0261	0.0021	0.0274	0.0029	0.7118	0.0279	0.0040	0.0226	0.0008	0.3012
	24OH-cholesterol	24OH-CHOL	10.2862	0.3264	11.9475	0.3425	0.0068	10.8461	0.5226	11.0270	0.5935	0.0741
	25OH-cholesterol	25OH-CHOL	6.8419	0.1186	7.4049	0.1887	0.0278	6.5908	0.1886	6.8170	0.2822	0.5027
	27OH-cholesterol	27OH-CHOL	0.0333	0.0075	0.0717	0.0077	0.0063	0.0326	0.0071	0.0510	0.0118	0.1868
	β-epoxycholesterol	β-EP CHOL	0.8922	0.0248	1.1515	0.0827	0.0098	0.8677	0.0486	1.0214	0.0706	0.0924

Table S5.

SERUM			p value VEH vs ARI+TRZ		SPLEEN			p value VEH vs ARI+TRZ		LIVER			p value VEH vs ARI+TRZ		CORTEX			p value VEH vs ARI+TRZ		HIP			p value VEH vs ARI+TRZ	
	DMG Sterols		Males	Females	DMG Sterols	Males	Females			DMG Sterols	Males	Females			DMG Sterols	Males	Females			DMG Sterols	Males	Females		
Bloch	Lanosterol	LAN	0.0044**	0.0383*	LAN	0.2856	0.2478			LAN	0.3689	0.0443*			LAN	0.6450	0.1099			LAN	0.0156*	0.0054**		
	14-dehydrozymosterol	14-DZYM	0.0104*	0.0756	14-DZYM	0.0313*	0.8996			14-DZYM	0.0002***	0.7814			14-DZYM	<0.0001****	0.0081**			14-DZYM	0.0078**	0.2151		
	Zymosterol	ZYM	0.0010**	0.0002***	ZYM	0.0979	0.3563			ZYM	0.0023**	0.0084**			ZYM	0.2187	0.0183			ZYM	0.0105*	0.039*		
	24-dehydrolathosterol	DHL	0.0001***	<0.0001****	DHL	0.2457	0.0584			DHL	0.0038**	0.0012**			DHL	0.2237	0.9234			DHL	0.8234	0.9566		
	8-dehydrodesmosterol	8-DHD	0.0817	0.0289*	8-DHD	0.0002***	0.0094**			8-DHD	0.0219*	0.1488			8-DHD	<0.0001****	<0.0001****			8-DHD	<0.0001****	<0.0001****		
	7-dehydrodesmosterol	7-DHD	<0.0001****	0.0006***	7-DHD	<0.0001****	<0.0001****			7-DHD	0.0004***	0.0003***			7-DHD	<0.0001****	<0.0001****			7-DHD	<0.0001****	<0.0001****		
	Desmosterol	DES	0.0029**	0.1585	DES	<0.0001****	0.0003***			DES	<0.0001****	0.0002***			DES	<0.0001****	<0.0001****			DES	<0.0001****	<0.0001****		
Kandutsch Russell	dihydrolanosterol	DIHLAN	0.5432	0.1130	DIHLAN	0.2767	0.7318			DIHLAN	0.2216	0.0348*			DIHLAN	0.0865	0.9878			DIHLAN	0.0121*	0.0224*		
	14-dehydrozymostenol	14-DZYME	0.0031**	0.0619	14-DZYME	<0.0001****	<0.0001****			14-DZYME	<0.0001****	<0.0001****			14-DZYME					14-DZYME	<0.0001****	<0.0001****		
	Zymostenol	ZYME	<0.0001****	0.0005***	ZYME	0.0024**	0.0213*			ZYME	0.0020**	0.0086**			ZYME	0.4914	0.8678			ZYME	0.0974	0.0195*		
	Lathosterol	LATH	<0.0001****	0.0023**	LATH	0.2013	0.0027**			LATH	0.0010***	0.0165*			LATH	0.0363*	0.0030**			LATH	0.0226*	0.0784		
	7-dehydrocholesterol	7-DHC	<0.0001****	<0.0001****	7-DHC	<0.0001****	<0.0001****			7-DHC	<0.0001****	<0.0001****			7-DHC	<0.0001****	<0.0001****			7-DHC	<0.0001****	<0.0001****		
	8-dehydrocholesterol	8-DHC	<0.0001****	<0.0001****	8-DHC	0.0001***	0.0013**			8-DHC	<0.0001****	0.0004***			8-DHC	<0.0001****	<0.0001****			8-DHC	<0.0001****	<0.0001****		
	Cholesterol	CHOL	0.6821	0.0316*	CHOL	0.052	0.0752			CHOL	0.1413	0.1635			CHOL	0.4317	0.6333			CHOL	0.1941	0.6886		
Oxysterols	7-keto cholesterol	7-KETO	0.2030	0.4716	7-KETO	0.0888	0.0568			7-KETO	0.0255*	0.3572			7-KETO	0.7164	0.1415			7-KETO	0.7205	0.9739		
	24OH-cholesterol	24OH-CHOL			24OH-CHOL					24OH-CHOL					24OH-CHOL	0.4020	0.2160			24OH-CHOL	0.8268	0.6244		
	25OH-cholesterol	25OH-CHOL	0.2170	0.6723	25OH-CHOL	0.0573	0.5319			25OH-CHOL	0.0318*	0.0949			25OH-CHOL	0.3028	0.1215			25OH-CHOL	0.6335	0.8319		
	27OH-cholesterol	27OH-CHOL	0.5418	0.7223	27OH-CHOL	0.0527	0.3227			27OH-CHOL	<0.0001****	0.0265*			27OH-CHOL	0.9488	0.1789			27OH-CHOL	0.9336	0.1760		
	β-epoxycholesterol	β-EP CHOL	0.9362	0.3933	β-EP CHOL	0.3049	0.9782			β-EP CHOL	0.8614	0.2290			β-EP CHOL	0.6782	0.2660			β-EP CHOL				

t-test here comparing Male VEH vs Male ARI+TR and Female VEH vs Female ARI+TRZ

Table S5. Sterols and oxysterol levels (Mean±SEM) in serum and organs in male and female VEH and ARI+TRZ exposed mice.