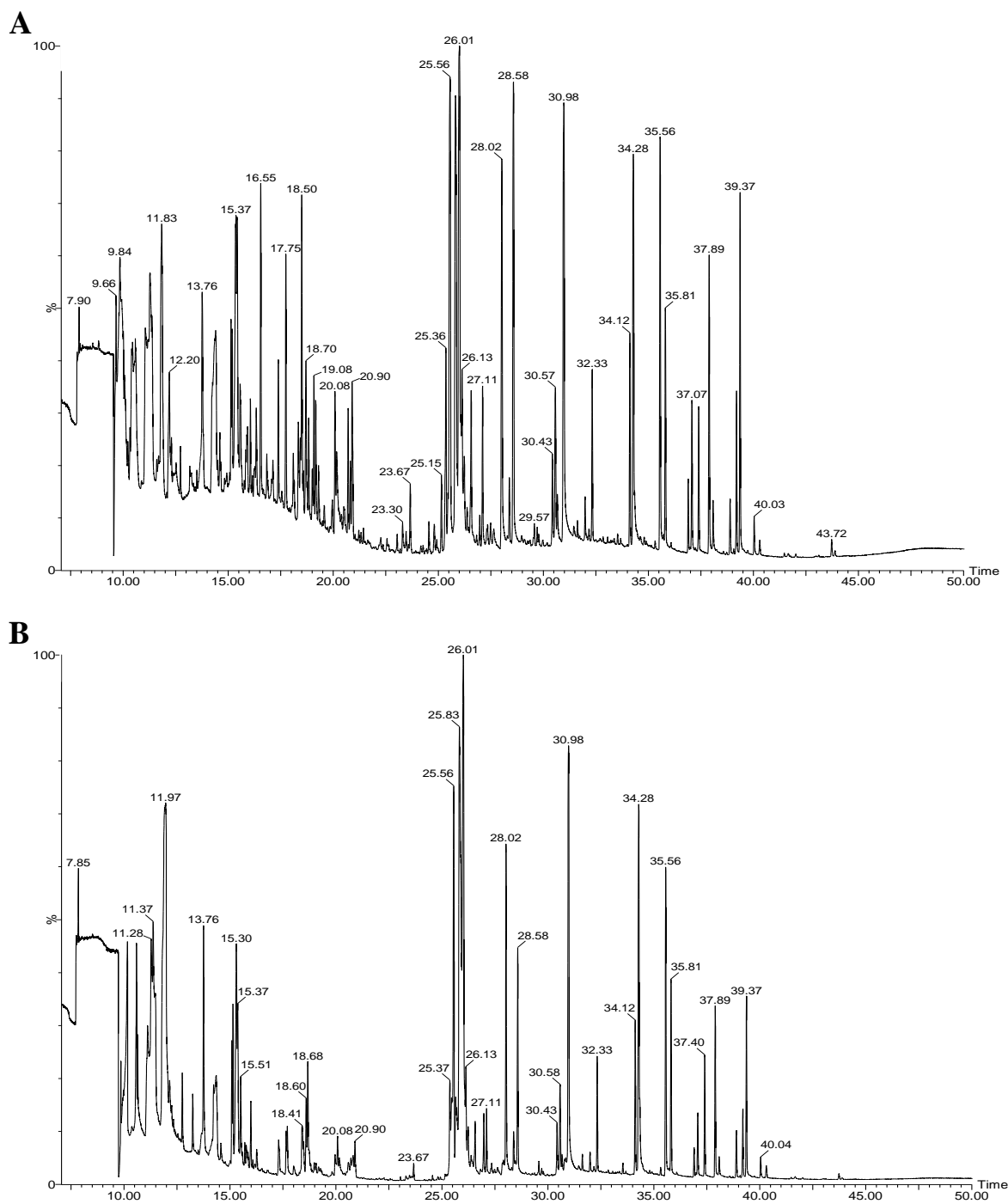
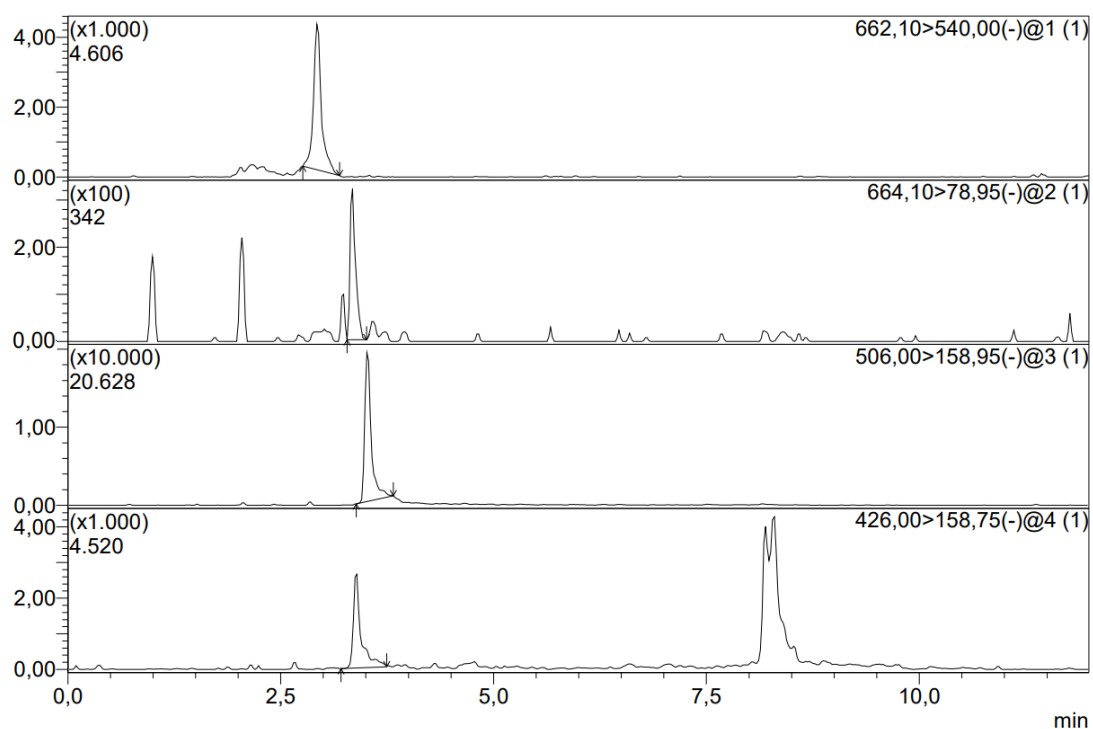
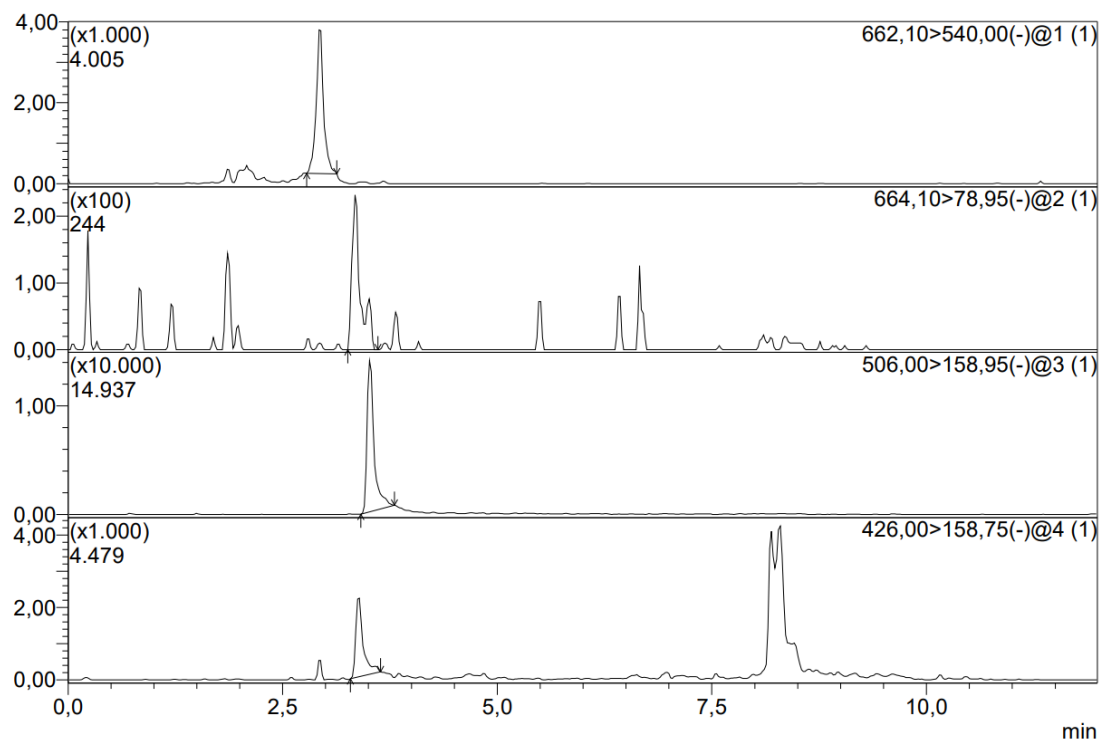


**Supplemental Figure 1.** TEM micrograph of RhNPs on aqueous suspension. Image was obtained using a JEOL JEM 1400 PLUS microscope.



**Supplemental Figure 2.** Representative chromatograms obtained in TIC mode for metabolite extracts from control (A) and treated (B) samples.

**A****B**

**Supplemental Figure 3.** Representative chromatograms from control (A) and treated (B) samples obtained by LC-QqQ-MS operating in MRM mode for NAD<sup>+</sup>, NADH, ATP and ADP, respectively.

**Supplemental table S1.** Transitions and collision energies used for the quantification of ATP, ADP, NADH and NAD<sup>+</sup> by LC-QqQ-MS working in MRM mode.

Metabolite	Precursor ion [M-H] <sup>+</sup> (m/z)	Product ion (m/z)	Collision energy (eV)
ATP	506.00	426.00	30
ADP	426.00	158.75	26
NADH	664.10	78.95	54
NAD <sup>+</sup>	662.10	540.00	16

**Supplemental table S3.** Common metabolites identified in control and treated samples by GC-TOF-MS with a minimum NIST Rmatch value of 700.

Number	Metabolite	Retention time (min)	NIST Rmatch
1	Acetate	12.293	709
2	L-valine	12.371	902
3	Serine	13.446	769
4	L-isoleucine	14.144	907
5	Pyruvate	14.484	778
6	Propanedionate	14.743	813
7	Propionate	14.872	835
8	Butanoate	15.047	739
9	Nonanoate	15.425	778
10	L-threonine	15.978	833
11	Pentanedionate	16.319	801
12	Cyclohexanamine	16.587	921
13	B-alanine	16.795	811
14	Decanoate	17.451	805
15	Malate	18.056	865
16	L-proline	18.468	888
17	L-aspartate	18.665	890
18	Creatinine	19.198	735
19	Cytein	19.394	750
20	Dodecanoate	21.197	852
21	D-xylofuranose	21.684	851
22	Pyrimidine	21.766	733
23	Phosphate	23.296	905
24	Azelate	23.807	826
25	Propanetricarboxylate	24.278	823
26	Tetradecanoate	24.696	865
27	Fructose	25.022	837
28	Galactose	25.430	857
29	Glucose	25.575	709
30	Hexadecanenitrile	25.580	900
31	D-mannitol	25.864	713
32	N-pentadecanoate	26.324	823
33	Gluconate	26.562	778
34	Hexadecanoate	27.885	826
35	Oleanitrile	28.417	930
36	Myo-inositol	28.438	814
37	Octadecanenitrile	28.830	880

38	Heptadecanoate	28.975	863
39	11-trans-octadecenoate	30.546	864
40	Oleate	30.671	791
41	Dehydroabietate	32.711	748
42	Mystirate	32.938	889
42	Eicosanoate	33.553	845
44	Monopalmitoglycerol	35.026	826
45	2- monostearin	37.367	831
46	Octadecanoate	37.574	879
47	Decanedionate	38.081	844
48	Cholesterol	41.615	895

Supplemental Table S4. Pearson’s correlation matrix data for the 48 identified metabolites.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48					
1	1																																																				
2	0.7885	1																																																			
3	-0.1752	-0.0524	1																																																		
4	0.5042	0.6641	0.2869	1																																																	
5	0.1986	0.3224	0.3033	0.3247	1																																																
6	-0.0647	-0.0720	-0.0784	-0.3252	0.1201	1																																															
7	0.1918	0.2615	-0.4781	-0.1908	0.2586	0.6497	1																																														
8	-0.0649	0.1360	-0.0796	0.1246	0.0462	0.4306	0.6288	1																																													
9	-0.4384	-0.1702	0.6791	0.0812	-0.0723	-0.1230	-0.3929	0.2223	1																																												
10	-0.1079	0.0532	0.7602	0.3227	0.4298	0.4470	0.0422	0.2424	0.3341	1																																											
11	0.1707	-0.0369	0.0239	0.1522	0.0902	0.4299	0.1892	0.1984	-0.0221	0.3173	1																																										
12	0.0818	0.0533	-0.0380	0.0220	-0.0492	-0.1189	-0.2114	-0.5502	-0.1471	-0.1139	-0.2582	1																																									
13	0.0443	0.0692	0.1746	0.1653	0.5902	0.3683	0.1449	-0.0562	0.0059	0.4081	0.6404	0.2094	1																																								
14	0.2380	0.4135	0.3323	0.3869	0.6377	0.5478	0.2812	0.1853	0.0107	0.6922	0.4258	0.1717	0.5644	1																																							
15	-0.2261	-0.0924	-0.0966	-0.2470	0.2084	0.3999	-0.5523	0.3609	-0.0353	0.2043	0.1983	-0.2564	0.1988	0.1419	1																																						
16	0.0642	0.4941	0.4764	0.5515	0.4112	-0.0249	0.2086	0.5496	0.4251	0.5222	-0.2332	-0.2933	-0.0962	0.3671	0.2262	1																																					
17	0.2462	0.4233	0.4703	0.3189	0.6051	0.2801	0.5387	0.4801	0.1457	0.6601	0.0960	-0.3011	0.1892	0.4902	0.4152	0.7628	1																																				
18	0.2148	0.5711	-0.0532	0.1769	0.2925	0.4191	0.5938	0.4966	0.0160	0.2735	0.0075	-0.1743	0.0948	0.5027	0.6282	0.5765	0.5491	1																																			
19	0.0051	0.1328	0.2783	0.1682	0.6456	0.4835	0.2332	0.2401	-0.0406	0.6246	0.4267	-0.3678	0.6309	0.7176	0.4251	0.2959	0.4963	0.3828	1																																		
20	0.2304	0.1229	-0.1414	-0.2732	0.1539	0.4350	0.4429	-0.0761	-0.1608	0.0376	0.5493	-0.0537	0.4136	0.3515	0.4192	-0.2717	0.1754	0.3397	0.1525	1																																	
21	0.1581	0.3725	0.0693	0.3083	0.5900	0.4960	0.4265	0.4674	0.0445	0.4066	0.3903	-0.4524	0.4642	0.8143	0.0846	0.3941	0.4091	0.4019	0.6781	0.1902	1																																
22	-0.2106	-0.0609	-0.4518	-0.4467	0.0449	0.0546	0.5011	0.1271	-0.3837	-0.3260	-0.4088	-0.0944	-0.2619	-0.2164	0.1027	-0.0386	0.0633	0.0658	-0.1766	0.0830	-0.0076	1																															
23	0.2342	0.4949	-0.0480	0.2538	0.6338	0.3264	0.5532	0.4871	-0.0064	0.2032	0.1280	-0.5262	0.2286	0.6550	0.3364	0.5460	0.5220	0.6288	0.5806	0.2266	0.8647	0.1240	1																														
24	-0.0399	0.1472	0.0852	0.2906	0.3030	0.5511	0.4176	0.4275	-0.0164	0.5938	0.7289	-0.2971	0.6121	0.6727	0.4881	0.2394	0.3948	0.4478	0.6758	0.3981	0.6017	-0.1306	0.4201	1																													
25	0.3279	0.3887	0.3155	0.2155	0.3451	0.1293	-0.1099	-0.0169	0.3123	0.1874	0.1178	-0.2917	0.1551	0.5301	-0.1430	0.2771	0.2126	0.2002	0.3437	0.1715	0.6040	-0.3917	0.6157	0.0227	1																												
26	0.1976	0.2322	-0.1495	0.1695	0.5096	0.7071	0.6523	0.3939	-0.3527	0.4235	0.5610	-0.2188	0.5928	0.7252	0.2265	0.1165	0.3822	0.3025	0.6721	0.3198	0.8105	0.1036	0.6075	0.7409	0.2129	1																											
27	0.0130	-0.0784	0.1600	-0.1160	0.3936	0.3924	0.1224	-0.0582	0.1392	0.2589	0.7371	-0.0263	0.8726	0.4214	0.2542	-0.2545	0.1201	0.0319	0.5404	0.6288	0.3909	-0.2824	0.2075	0.4980	0.3072	0.4412	1																										
28	0.0843	0.2090	-0.4090	-0.1318	-0.3486	-0.0725	0.1547	-0.0366	-0.4106	-0.2660	-0.2324	-0.1206	-0.3574	-0.2701	0.3670	0.0011	-0.0368	0.3213	0.0316	0.0014	-0.2736	0.2898	-0.0426	0.0390	-0.2597	-0.1311	-0.3290	1																									
29	0.1783	0.3789	0.3725	0.4206	0.6845	0.3439	0.1013	0.1723	0.0096	0.6542	0.3283	-0.2039	0.6325	0.7814	0.1974	0.4144	0.5111	0.4056	0.9329	0.0338	0.6900	-0.2680	0.5617	0.6041	0.4151	0.6101	0.4525	-0.0212	1																								
30	-0.2938	-0.3214	0.1186	-0.3356	-0.1466	0.4214	0.3151	0.1538	0.2222	0.2724	0.5432	-0.0400	0.3707	-0.0204	0.4979	-0.1229	0.2105	0.0219	0.1325	0.5328	-0.0462	-0.0247	-0.1411	0.4720	-0.1475	0.2123	0.5480	0.0434	-0.0584	1																							
31	0.2309	0.4402	0.2187	0.5046	0.1167	0.4527	0.2619	0.2273	-0.0093	0.6238	0.2501	0.0992	0.1605	0.6863	0.0919	0.4220	0.3602	0.4945	0.2427	0.1463	0.4084	-0.2539	0.2682	0.5887	0.1737	0.4843	-0.0690	-0.0190	0.3585	0.0748	1																						
32	-0.3329	-0.1538	-0.3613	-0.4695	-0.0421	0.2515	0.5172	0.2048	-0.2540	-0.1601	-0.3107	0.0495	-0.1534	-0.1353	0.0360	-0.0655	0.0292	0.0479	-0.2001	0.0815	0.0167	0.9257	0.0049	-0.0250	-0.4622	0.1786	-0.2172	0.1194	-0.2704	0.0990	-0.0821	1																					
33	-0.0568	0.1015	-0.3728	-0.0886	0.3501	0.4397	0.5671	0.2480	-0.3752	0.0785	0.1465	-0.1515	0.2935	0.3504	0.8112	0.1250	0.2026	0.6476	0.5541	0.2957	0.3382	0.1349	0.5317	0.5213	-0.0248	0.4834	0.1889	0.4021	0.3928	0.1216	0.2220	0.0439	1																				
34	-0.0089	0.0435	0.2065	0.0005	0.2513	0.2593	0.3691	0.0209	-0.1498	0.4517	0.3446	-0.2313	0.1918	0.3896	0.3034	0.1329	0.4967	0.1613	0.2323	0.5640	0.2028	0.3388	0.1598	0.5387	-0.1041	0.3927	0.2028	0.0825	0.1383	0.4871	0.3787	0.3388	0.1285	1																			
35	-0.2548	-0.0125	0.0005	0.0813	0.2220	0.4503	0.6016	0.6435	0.1615	0.3992	0.5465	-0.2795	0.4649	0.3299	0.6251	0.3097	0.4479	0.4515	0.3882	0.3774	0.3946	0.1402	0.3326	0.8195	-0.2394	0.5235	0.4059	-0.0367	0.2655	0.6152	0.3148	0.2560	0.4474	0.4916	1																		
36	0.2815	0.2755	-0.3815	-0.2350	0.4151	0.3894	0.8608	0.4020	-0.3643	-0.1210	-0.0458	-0.0460	0.1130	0.1216	0.3757	0.1348	0.4735	0.4539	0.0795	0.4170</																																	

**Supplemental Table S5.** PCA score values for controls and treated samples on the PC3.

<b>Samples</b>	<b>PC3 (11%)</b>
Control 1 (C1)	-0.415
Control 2 (C2)	-1.820
Control 3 (C3)	-1.175
Control 4 (C4)	-2.041
Control 5 (C5)	-4.537
Control 6 (C6)	-2.156
Control 7 (C7)	-0.643
Treated 1 (R1)	1.915
Treated 2 (R2)	2.129
Treated 3 (R3)	1.576
Treated 4 (R4)	0.803
Treated 5 (R5)	0.429
Treated 6 (R6)	5.753
Treated 7 (R7)	0.182