

Body and organ weights

Body and organ weights are shown in Figure S1 and Tables S1-4 (this supplement). At the first interim sacrifice at week 3, there was a tendency to lower body weight in the vehicle control group and the treated rats compared to the untreated group, however, this decrease was not significant. There were no significant differences in body weight between the treated groups and the vehicle control group throughout the first year of the experimental period (Fig. S1, Table S1, S3).

There were no differences in the weights of the brain, heart, liver, kidneys, spleen, or testes between the treated groups and the vehicle control at week 3 (Table S1), however, there was a slight increase in the relative kidney weight in the 0.50 mg r-nTiO₂ treated group (Table S2), possibly due to the kidney's role in clearance of these particles from the systemic circulation [1]. There was a slight decrease in the absolute weights of the kidneys and spleen in the MWCNT-7 treated group at week 52 (Table S3), but there were no differences in the relative weights of the brain, heart, liver, kidneys, spleen, or testes to body weight in any of the treated groups (Table S4).

At week 3, the relative lung weights were increased in the vehicle control group compared to the untreated group. In addition, in the groups administered 0.50 mg r-nTiO₂, 0.50 mg POT fibers, and 0.50 mg MWCNT-7 there was an increase in relative lung weight compared to the vehicle control group. None of the groups administered either r-nTiO₂ or POT fibers had an increase in the absolute weight of the lung at either 3 or 52 weeks (Table S5). In contrast, at weeks 3 and 52 both the absolute and relative lung weights were increased in the MWCNT-7 group.

- [1] Pujalte I, Dieme D, Haddad S, Serventi AM, Bouchard M. Toxicokinetics of titanium dioxide (TiO₂) nanoparticles after inhalation in rats. *Toxicol Lett.* 2017; 265: 77-85.

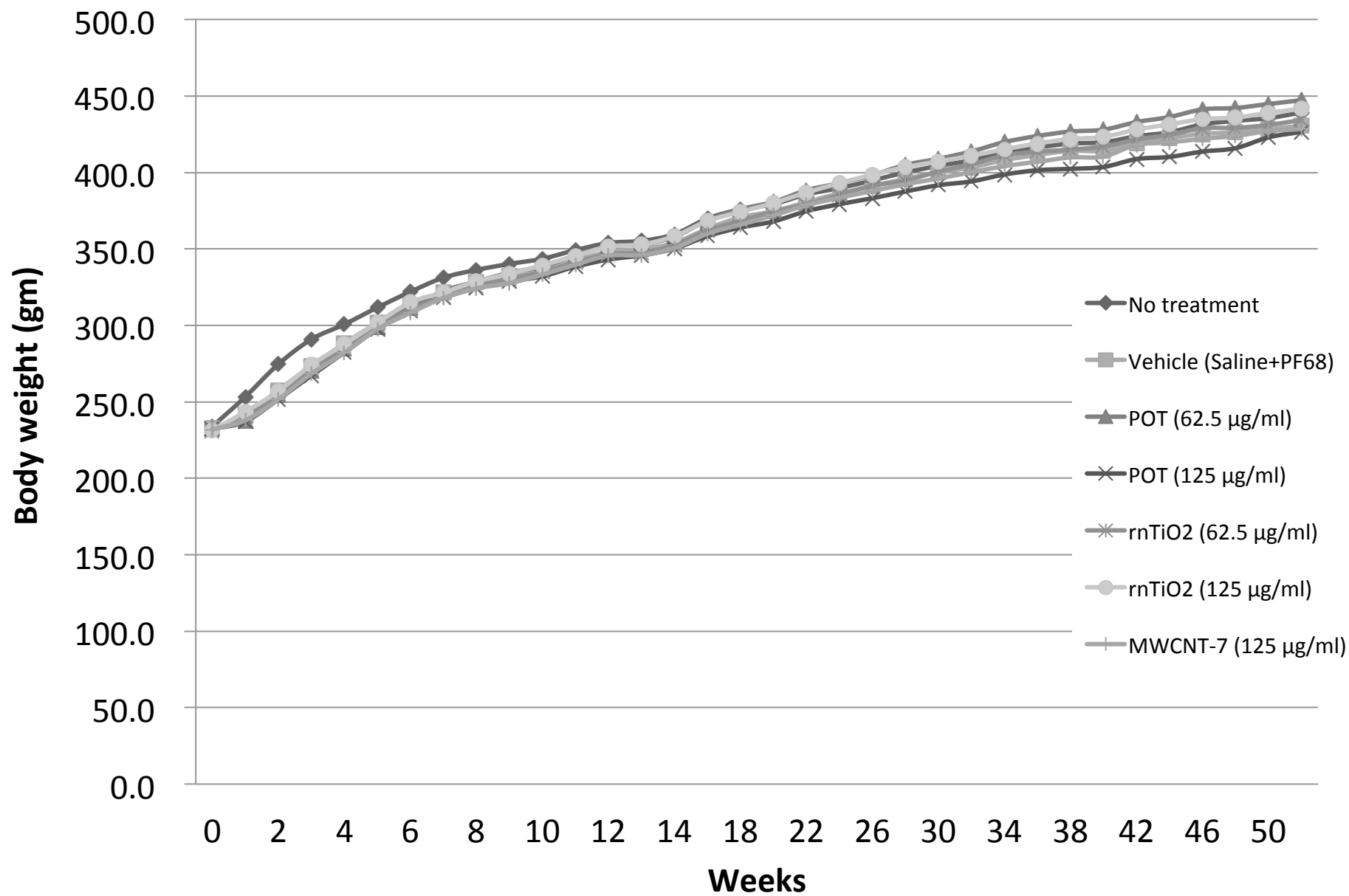


Figure S1. Body weight curves.

Supplementary Table 1. Body and organ weights at week 3

Treatment Group	No. of Rats	Body Weight	Brain	Heart	Liver	Kidneys	Spleen	Testes
No Treatment	5	285.0 ± 13.8	1.878 ± 0.058	0.839 ± 0.061	9.846 ± 0.439	1.917 ± 0.087	0.614 ± 0.033	2.899 ± 0.043
Vehicle	5	269.4 ± 13.2	1.868 ± 0.101	0.792 ± 0.021	8.871 ± 0.523	1.810 ± 0.083	0.608 ± 0.029	2.939 ± 0.103
0.25 mg TiO ₂	5	268.0 ± 16.7	1.903 ± 0.039	0.782 ± 0.045	8.898 ± 0.807	1.798 ± 0.068	0.573 ± 0.026	2.869 ± 0.089
0.50 mg TiO ₂	5	265.8 ± 12.9	1.871 ± 0.022	0.769 ± 0.027	8.562 ± 0.569	1.829 ± 0.110	0.584 ± 0.024	2.960 ± 0.069
0.25 mg POT	5	276.0 ± 9.7	1.926 ± 0.042	0.789 ± 0.043	8.615 ± 0.242	1.840 ± 0.049	0.589 ± 0.025	2.944 ± 0.115
0.50 mg POT	5	275.2 ± 16.0	1.919 ± 0.011	0.811 ± 0.028	9.272 ± 0.895	1.882 ± 0.086	0.583 ± 0.029	2.906 ± 0.109
0.50 mg MWCNT-7	5	265.0 ± 14.6	1.923 ± 0.043	0.803 ± 0.043	8.756 ± 0.556	1.802 ± 0.115	0.587 ± 0.027	2.856 ± 0.074

*, **, ***: p < 0.05, 0.01, and 0.001 vs. vehicle

Supplementary Table 2. Organ to body weight ratio at week 3

Treatment Group	No. of Rats	Brain	Heart	Liver	Kidneys	Spleen	Testes
No Treatment	5	0.659 ± 0.029	0.294 ± 0.010	3.456 ± 0.061	0.673 ± 0.007	0.216 ± 0.010	1.019 ± 0.036
Vehicle	5	0.693 ± 0.020	0.294 ± 0.011	3.293 ± 0.094	0.672 ± 0.007	0.226 ± 0.014	1.092 ± 0.046
0.25 mg TiO ₂	5	0.711 ± 0.033	0.292 ± 0.011	3.316 ± 0.101	0.672 ± 0.028	0.214 ± 0.005	1.073 ± 0.057
0.50 mg TiO ₂	5	0.705 ± 0.031	0.290 ± 0.012	3.220 ± 0.107	0.688 ± 0.011*	0.220 ± 0.008	1.115 ± 0.039
0.25 mg POT	5	0.698 ± 0.021	0.286 ± 0.012	3.123 ± 0.095	0.667 ± 0.018	0.213 ± 0.009	1.068 ± 0.059
0.50 mg POT	5	0.699 ± 0.043	0.295 ± 0.013	3.364 ± 0.148	0.685 ± 0.036	0.212 ± 0.009	1.060 ± 0.099
0.50 mg MWCNT-7	5	0.727 ± 0.035	0.303 ± 0.007	3.303 ± 0.080	0.680 ± 0.014	0.222 ± 0.011	1.079 ± 0.041

*, **, ***: p < 0.05, 0.01, and 0.001 vs. vehicle

Supplementary Table 3. Body and organ weights at week 52

Treatment Group	No. of Rats	Body Weight	Brain	Heart	Liver	Kidneys	Spleen	Testes
No Treatment	5	447.2 ± 17.7	2.096 ± 0.027	1.120 ± 0.051	13.264 ± 0.401	2.637 ± 0.140	0.738 ± 0.030	3.292 ± 0.167
Vehicle	5	439.0 ± 20.5	2.138 ± 0.045	1.108 ± 0.071	12.796 ± 0.945	2.662 ± 0.102	0.732 ± 0.040	3.252 ± 0.151
0.25 mg TiO ₂	5	433.8 ± 10.4	2.092 ± 0.016	1.116 ± 0.028	12.188 ± 0.344	2.520 ± 0.093	0.722 ± 0.034	3.211 ± 0.192
0.50 mg TiO ₂	5	445.4 ± 34.4	2.143 ± 0.047	1.130 ± 0.059	12.879 ± 1.753	2.657 ± 0.148	0.763 ± 0.063	3.229 ± 0.108
0.25 mg POT	5	449.6 ± 18.8	2.100 ± 0.040	1.131 ± 0.032	12.975 ± 0.887	2.612 ± 0.102	0.762 ± 0.065	3.269 ± 0.120
0.50 mg POT	5	433.6 ± 30.3	2.066 ± 0.058	1.100 ± 0.064	12.708 ± 1.338	2.608 ± 0.212	0.696 ± 0.075	3.111 ± 0.560
0.50 mg MWCNT-7	5	424.2 ± 14.5	2.077 ± 0.043	1.081 ± 0.033	12.006 ± 0.935	2.477 ± 0.099*	0.677 ± 0.022*	3.144 ± 0.088

*, **, ***: p < 0.05, 0.01, and 0.001 vs. vehicle

Supplementary Table 4. Organ to body weight ratio at week 52

Treatment Group	No. of Rats	Brain	Heart	Liver	Kidneys	Spleen	Testes
No Treatment	5	0.469 ± 0.020	0.251 ± 0.010	2.968 ± 0.077	0.590 ± 0.025	0.165 ± 0.003	0.736 ± 0.021
Vehicle	5	0.488 ± 0.015	0.252 ± 0.007	2.912 ± 0.104	0.607 ± 0.025	0.167 ± 0.007	0.741 ± 0.014
0.25 mg TiO ₂	5	0.482 ± 0.013	0.257 ± 0.008	2.810 ± 0.083	0.581 ± 0.016	0.166 ± 0.008	0.741 ± 0.039
0.50 mg TiO ₂	5	0.484 ± 0.049	0.254 ± 0.009	2.883 ± 0.208	0.598 ± 0.033	0.172 ± 0.014	0.728 ± 0.042
0.25 mg POT	5	0.468 ± 0.021	0.252 ± 0.016	2.885 ± 0.120	0.581 ± 0.006	0.169 ± 0.012	0.728 ± 0.035
0.50 mg POT	5	0.478 ± 0.026	0.254 ± 0.010	2.925 ± 0.111	0.601 ± 0.021	0.160 ± 0.009	0.717 ± 0.125
0.50 mg MWCNT-7	5	0.490 ± 0.018	0.255 ± 0.013	2.828 ± 0.061	0.584 ± 0.015	0.160 ± 0.005	0.742 ± 0.039

*, **, ***: p < 0.05, 0.01, and 0.001 vs. vehicle

Supplementary Table 5. Lung weights

Treatment group	No. of rats	Absolute Lung Weights		Relative Lung Weights	
		3 weeks	52 Weeks	3 weeks	52 weeks
No Treatment	5	0.934 ± 0.029	1.212 ± 0.049	0.319 ± 0.006	0.271 ± 0.015
Vehicle	5	0.923 ± 0.042	1.183 ± 0.041	0.351 ± 0.006 ^a	0.270 ± 0.007
0.25 mg TiO ₂	5	0.975 ± 0.062	1.209 ± 0.043	0.371 ± 0.013	0.269 ± 0.006
0.50 mg TiO ₂	5	0.978 ± 0.034	1.242 ± 0.079	0.378 ± 0.005 [*]	0.287 ± 0.007
0.25 mg POT	5	0.999 ± 0.035	1.137 ± 0.063	0.362 ± 0.011	0.262 ± 0.013
0.50 mg POT	5	1.003 ± 0.041	1.218 ± 0.080	0.378 ± 0.002 ^{**}	0.274 ± 0.017
0.50 mg MWCNT-7	5	1.278 ± 0.036 ^{***}	1.480 ± 0.101 ^{***}	0.485 ± 0.025 ^{**}	0.349 ± 0.016 ^{***}

^a Significantly different from group 1 (p < 0.01)

*, **, ***: p < 0.05, 0.01, and 0.001.