

The Protective Impact of *Aronia melanocarpa* L. Berries Extract against Prooxidative Cadmium Action in the Brain – A Study in an In Vivo Model of Current Environmental Human Exposure to this Harmful Element

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Table S1. The concentration of cadmium (Cd) in the brain.

Group	Experiment Duration			
	3 Months	10 Months	17 Months	24 Months
Control	0.026	0.028	0.017	0.025
	0.014–0.041	0.022–0.039	0.012–0.026	0.014–0.038
AE	0.028	0.029	0.018	0.026
	0.014–0.038	0.022–0.036	0.010–0.025	0.015–0.034
Cd ₁	0.042 ^{a*}	0.044 ^{a‡}	0.031 ^{a*}	0.048 ^{a‡}
	0.027–0.057 ↑ 62%	0.037–0.056 ↑ 57%	0.017–0.060 ↑ 82%	0.026–0.071 ↑ 92%
Cd ₁ + AE	0.044 ^{a*}	0.043 ^{a‡}	0.030 ^{a*}	0.048 ^{a‡}
	0.021–0.062 ↑ 69%	0.034–0.060 ↑ 54%	0.011–0.065 ↑ 77%	0.027–0.067 ↑ 92%
Cd ₅	0.075 ^{a‡}	0.051 ^{a‡}	0.051 ^{a‡}	0.056 ^{a‡}
	0.043–0.097 ↑ 2.9x	0.039–0.065 ↑ 82%	0.040–0.068 ↑ 3x	0.050–0.065 ↑ 2.3x
Cd ₅ + AE	0.061 ^{a‡}	0.043 ^{a‡}	0.040 ^{a‡e*}	0.045 ^{a‡e*}
	0.041–0.122 ↑ 2.4x	0.035–0.056 ↑ 54%	0.036–0.046 ↑ 2.4x ↓ 22%	0.038–0.055 ↑ 80% ↓ 20%

The table was prepared based on: Brzóska, M.M.; Gałażyn-Sidorczuk, M.; Jurczuk, M.; Tomczyk, M. Protective effect of *Aronia melanocarpa* polyphenols on cadmium accumulation in the body: A study in a rat model of human exposure to this metal. *Curr. Drug Targets* **2015**, *16*, 1470–1487. <https://doi.org/10.2174/1389450116666150102121708>. Rats were administered with 0, 1, or 5 mg Cd/kg of diet (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value. The statistically significant differences compared to: a – Control group, and e – Cd₅ group are marked as * $p < 0.05$ and ‡ $p < 0.001$. ↑ – higher vs Control group, ↓ – lower vs Cd₅ group.

Table S2. The absolute and relative weights of the brain of female rats.

Group	Experiment Duration			
	3 Months	10 Months	17 Months	24 Months
Absolute Weight of the Brain (g)				
Control	1.721 1.380–1.943	1.894 1.798–2.038	2.017 1.844–2.250	2.055 1.846–2.096
AE	1.763 1.683–1.898	1.904 1.742–1.990	1.991 1.724–2.194	1.993 1.319–2.112
Cd ₁	1.798 1.727–1.903	1.928 1.789–2.052	1.905 1.748–2.208	2.070 1.990–2.217
Cd ₁ + AE	1.732 1.587–1.913	1.935 1.765–2.047	1.964 1.875–2.002	1.903 1.793–2.081
Cd ₅	1.723 1.559–1.917	1.968 1.834–2.060	1.899 1.543–2.068	2.020 1.915–2.123
Cd ₅ + AE	1.926 1.758–2.114	1.918 1.779–1.979	2.017 1.731–2.018	2.027 1.868–2.205
Relative Weight of the Brain (g/100 g b.w.)				
Control	0.552 0.399–0.604	0.433 0.421–0.509	0.411 0.301–0.517	0.313 0.267–0.381
AE	0.539 0.486–0.727	0.435 0.352–0.497	0.349 0.320–0.486	0.351 0.240–0.430
Cd ₁	0.631 0.525–0.667	0.426 0.369–0.483	0.413 0.272–0.531	0.289 0.252–0.459
Cd ₁ + AE	0.560 0.527–0.686	0.454 0.311–0.495	0.396 0.365–0.445	0.344 0.299–0.495
Cd ₅	0.605 0.471–0.715	0.441 0.386–0.491	0.358 0.267–0.609	0.349 0.304–0.439
Cd ₅ + AE	0.614 0.542–0.687	0.473 0.366–0.559	0.403 0.310–0.494	0.349 0.314–0.490

Rats were administered with 0, 1, or 5 mg of cadmium (Cd)/kg of diet (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (AE) (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value for 8 rats in each group, except for 7 females in the AE, Cd₁, and Cd₅ groups after 24 months. No statistically significant differences (non-parametric Kruskal-Wallis test) between groups were noted.

Table S3. The activities of superoxide dismutase (SOD) and catalase (CAT) in the brain of female rats.

Group	Experiment Duration			
	3 Months	10 Months	17 Months	24 Months
SOD (U/mg protein)				
Control	0.932 0.303–1.734	0.732 0.196–0.835	1.321 1.037–1.674	1.360 1.071–1.653
AE	0.913 0.651–2.118	0.743 0.570–1.222	1.355 1.086–2.366	1.393 0.954–2.445
Cd ₁	0.505 0.247–0.909	0.633 0.168–0.849	1.284 0.994–2.101	1.326 0.805–2.027
Cd ₁ + AE	0.872 0.554–1.312	0.869 0.567–1.104	1.178 0.985–1.815	1.270 1.094–2.067
Cd ₅	0.721 0.293–1.190	0.608 0.158–0.934	0.880 ^{a* b† c*} 0.662–1.094	0.680 ^{a* b† c* d*} 0.644–0.928
Cd ₅ + AE	1.078 ^{c*} 0.776–1.429	0.920 ^{e*} 0.689–1.164	1.195 ^{e*} 1.024–2.449	1.292 ^{e*} 1.056–2.060
Effect size (η^2)	0.193	0.176	0.298	0.330
CAT (mU/mg protein)				
Control	17.71 13.77–38.571	13.59 8.54–21.85	15.17 8.97–24.50	16.34 11.91–20.50
AE	24.91 14.91–51.99	15.99 7.69–29.06	21.43 10.273–30.636	22.25 12.14–34.59
Cd ₁	8.574 ^{a* b†} 7.003–11.93	6.490 ^{a# b†} 4.388–10.635	9.052 ^{b†} 5.342–14.76	7.330 ^{a# b†} 3.623–9.596
Cd ₁ + AE	21.05 ^{c†} 12.20–33.38	14.08 ^{c*} 8.602–18.53	17.51 9.265–30.41	19.07 ^{c*} 11.35–24.32
Cd ₅	12.38 ^{b*} 9.92–18.75	6.893 ^{b*} 4.091–11.57	6.580 ^{a* b† d†} 4.377–8.028	6.020 ^{a* b† d†} 4.012–7.136
Cd ₅ + AE	25.66 ^{c† e*} 16.62–27.18	18.75 ^{c† e†} 10.73–23.68	16.58 ^{e*} 11.01–20.37	16.39 ^{c* e*} 13.31–20.72
Effect size (η^2)	0.595	0.608	0.622	0.624

Rats were administered with 0, 1, or 5 mg of cadmium (Cd)/kg of diet (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (AE) (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value for 8 rats in each group, except for 7 females in the AE, Cd₁, and Cd₅ groups after 24 months. The statistically significant differences (non-parametric Kruskal-Wallis test) compared to: a – Control group, b – AE group, c – Cd₁ group, d – Cd₁ + AE group, and e – Cd₅ group are marked as * $p < 0.05$, † $p < 0.01$, ‡ $p < 0.001$, and # $p = 0.07$ – 0.08 . To evaluate the effect size for the differences between the experimental groups, eta squared (η^2) was calculated (for $\eta^2 \geq 0.14$ the effect size is large).

Table S4. The activities of glutathione peroxidase (GPx) and glutathione reductase (GR) in the brain of female rats.

Group	Experiment Duration			
	3 Months	10 Months	17 Months	24 Months
GPx (mU/mg protein)				
Control	21.98 18.35–57.47	27.08 14.23–40.61	27.79 20.03–33.49	29.36 15.74–39.66
AE	22.08 14.05–30.43	43.41 19.00–46.75	26.50 20.92–32.59	29.71 21.46–35.14
Cd ₁	15.34 10.47–20.12	13.55 ^{b*} 6.509–16.85	14.24 9.665–23.59	15.97 11.31–25.71
Cd ₁ + AE	22.33 12.05–35.27	12.11 8.85–20.64	22.30 11.80–33.67	22.48 14.33–34.15
Cd ₅	19.89 10.34–39.25	4.000 ^{a†b†} 2.310–5.650	13.91 ^{a*b*} 8.122–18.00	10.78 ^{a†b†} 7.190–13.69
Cd ₅ + AE	30.22 ^{c†} 21.41–44.14	11.13 ^{b*} 10.58–20.28	31.74 ^{c†e†} 23.25–37.20	27.62 ^{e†} 22.51–38.17
Effect size (η^2)	0.278	0.730	0.553	0.538
GR (mU/mg protein)				
Control	8.791 4.144–14.121	6.530 4.923–12.16	8.659 7.140–16.01	7.018 3.469–7.871
AE	6.783 3.006–9.830	5.772 3.401–9.760	2.205 ^{a†} 1.360–3.610	2.617 ^{a*} 1.114–3.131
Cd ₁	7.729 3.860–10.28	4.225 ^{a†} 2.450–4.859	3.589 ^{a*} 2.190–6.910	7.078 ^{b*} 4.475–9.443
Cd ₁ + AE	9.808 5.330–16.20	7.818 ^{c†} 4.542–9.462	3.732 ^{a*} 3.193–6.500	6.801 ^{b*} 5.702–10.31
Cd ₅	5.170 4.680–11.76	5.779 4.283–8.231	8.205 ^{b†c*} 6.850–9.030	9.943 ^{a*b†} 8.296–14.15
Cd ₅ + AE	6.534 4.320–9.280	5.851 4.616–10.71	3.614 ^{a*e*} 3.100–7.830	5.386 ^{e†} 2.679–7.357
Effect size (η^2)	-	0.270	0.709	0.618

Rats were administered with a diet containing 0, 1, or 5 mg of cadmium (Cd)/kg (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (AE) (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value for 8 rats in each group, except for 7 females in the AE, Cd₁, and Cd₅ groups after 24 months. The statistically significant differences (non-parametric Kruskal-Wallis test) compared to: a – Control group, b – AE group, c – Cd₁ group, and e – Cd₅ group are marked as * $p < 0.05$, † $p < 0.01$, and ‡ $p < 0.001$. To evaluate the effect size for the differences between the experimental groups, eta squared (η^2) was calculated (for $\eta^2 \geq 0.14$ the effect size is large).

Table S5. The concentrations of thioredoxin (Trx), thioredoxin reductase (TrxR), and thioredoxin peroxidase (TPx) in the brain of female rats.

Group	Experiment Duration			
	3 Months	10 Months	17 Months	24 Months
Trx (ng/mg protein)				
Control	0.959 0.492–1.679	0.788 0.481–1.242	0.693 0.482–0.976	0.519 0.353–0.792
AE	0.868 0.680–2.282	0.807 0.565–1.297	0.715 0.541–0.944	0.503 0.305–0.798
Cd ₁	0.762 0.545–0.790	0.661 0.564–0.947	0.388 ^{a†b*} 0.298–0.563	0.225 ^{a†b†} 0.152–0.315
Cd ₁ + AE	0.755 0.645–2.389	0.667 0.473–1.004	0.459 0.392–0.766	0.381 0.131–0.680
Cd ₅	0.951 0.717–1.350	0.724 0.533–1.006	0.516 0.093–0.871	0.455 0.116–0.669
Cd ₅ + AE	1.027 ^{c*} 0.837–3.877	0.776 0.587–0.888	0.463 0.329–0.913	0.371 0.254–0.561
Effect size (η^2)	0.130	-	0.300	0.270
TrxR (ng/mg protein)				
Control	1.283 0.771–2.641	1.147 0.692–3.955	1.699 0.944–2.314	1.582 0.983–3.528
AE	2.063 1.293–3.686	1.012 0.633–1.748	1.370 1.004–2.115	1.734 0.568–2.386
Cd ₁	1.174 0.577–2.392	0.881 0.383–1.391	1.596 1.232–3.893	1.486 1.275–2.019
Cd ₁ + AE	1.898 1.310–5.288	1.014 0.264–1.657	1.679 1.094–2.424	1.463 1.119–1.868
Cd ₅	1.834 0.769–2.340	0.699 0.421–2.048	1.872 1.058–3.194	1.608 0.904–2.447
Cd ₅ + AE	1.590 0.725–2.883	0.712 0.346–0.972	1.693 1.376–1.855	0.599 ^{a*b*c*d*et†} 0.108–0.820
Effect size (η^2)	-	-	-	0.330
TPx (ng/mg protein)				
Control	2.774 1.832–19.28	2.579 1.500–6.679	3.360 2.193–3.687	3.232 2.415–4.988
AE	2.567 1.433–8.158	1.026 ^{a†} 0.691–1.568	1.793 0.405–7.117	2.951 1.971–4.112
Cd ₁	1.166 0.628–4.344	1.326 0.922–4.835	1.093 ^{a†} 0.338–1.772	1.389 ^{a*} 1.120–1.982
Cd ₁ + AE	4.821 1.373–7.572	1.737 0.923–4.132	3.098 ^{c†} 2.363–4.840	3.649 ^{c†} 2.572–4.748
Cd ₅	2.597 1.444–4.972	1.959 0.888–3.264	2.256 1.616–2.667	2.294 1.566–2.751
Cd ₅ + AE	2.703 1.879–6.734	1.560 1.319–2.372	2.857 ^{c*} 1.942–4.871	4.501 ^{c†et†} 3.205–6.618
Effect size (η^2)	-	0.290	0.380	0.640

Rats were administered with a diet containing 0, 1, or 5 mg of cadmium (Cd)/kg (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (AE) (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value for 8 rats in each group, except for 7 females in the AE, Cd₁, and Cd₅ groups after 24 months. The statistically significant differences (non-parametric Kruskal-Wallis test) compared to: a – Control group, b – AE group, c – Cd₁ group, d – Cd₁ + AE group, and e – Cd₅ group are marked as * $p < 0.05$, † $p < 0.01$, and ‡ $p < 0.001$. To evaluate the effect size for the differences between the experimental groups, eta squared (η^2) was calculated (for $\eta^2 \geq 0.14$ the effect size is large, for $0.01 < \eta^2 < 0.14$ it is medium).

Table S6. The concentrations of reduced glutathione (GSH) and oxidized glutathione (GSSG) and their ratio (GSH/GSSG) in the brain of female rats.

Group	Experiment Duration			
	3 Months	10 months	17 Months	24 Months
GSH (nmol/mg protein)				
Control	4.090 2.741–5.520	2.247 1.530–3.381	1.472 1.323–2.195	0.869 0.845–1.252
AE	2.159 1.276–4.809	2.428 1.778–3.198	1.358 0.913–1.642	2.178 ^{a*} 1.596–4.228
Cd ₁	1.046 ^{a†} 0.464–2.214	2.088 1.120–3.301	1.323 0.735–1.905	0.545 ^{b† c†} 0.475–0.691
Cd ₁ + AE	2.370 1.038–4.586	2.079 1.518–3.155	1.502 1.195–2.635	2.010 ^{c†} 1.424–4.172
Cd ₅	2.032 1.323–3.871	1.288 0.498–4.810	1.454 0.767–1.592	0.499 ^{b† d†} 0.325–1.131
Cd ₅ + AE	4.000 ^{c†} 3.339–6.165	4.438 ^{a* c† d† e†} 3.496–5.806	2.525 ^{a* b† c† e*} 2.200–3.251	1.866 ^{c† e†} 1.165–3.704
Effect size (η^2)	0.505	0.370	0.361	0.773
GSSG (nmol/mg protein)				
Control	2.796 2.402–5.520	1.596 1.054–2.306	0.692 0.560–1.033	0.722 0.570–1.993
AE	1.010 ^{a*} 0.568–1.899	1.178 1.042–1.706	0.628 0.393–1.075	0.380 0.243–0.550
Cd ₁	1.046 ^{a†} 0.522–1.388	1.385 1.063–1.741	0.791 0.330–1.230	2.215 ^{b†} 0.825–2.553
Cd ₁ + AE	0.486 ^{a†} 0.201–2.118	0.780 ^{a*} 0.452–1.521	0.666 0.549–1.122	0.311 ^{c†} 0.177–0.751
Cd ₅	1.410 ^{a*} 0.605–2.390	1.550 ^{d*} 1.042–2.546	1.166 ^{a*} 0.857–1.540	0.721 0.451–2.162
Cd ₅ + AE	1.613 0.946–2.036	1.831 ^{d†} 1.367–2.439	1.053 ^{b† d*} 0.337–2.633	0.229 ^{a† c† e*} 0.126–0.475
Effect size (η^2)	0.503	0.392	0.297	0.717
GSH/GSSG				
Control	1.000 1.000–2.122	1.311 1.000–2.602	2.188 1.839–2.679	1.204 0.430–2.089
AE	2.138 2.073–3.451	2.093 1.042–2.133	2.108 1.527–2.989	7.345 2.901–12.88
Cd ₁	1.451 0.396–2.192	1.567 1.027–2.117	2.144 0.843–2.229	0.297 ^{b†} 0.202–0.635
Cd ₁ + AE	2.527 ^{a*} 1.417–7.472	2.486 2.046–5.982	2.137 2.018–3.711	7.314 ^{c†} 4.579–9.628
Cd ₅	2.267 0.838–6.584	0.971 ^{d*} 0.334–3.496	1.214 ^{a* d*} 0.632–1.765	0.722 ^{b* d†} 0.231–1.415
Cd ₅ + AE	2.259 2.109–6.383	2.565 ^{e*} 1.874–2.944	2.333 ^{e†} 1.235–7.626	8.300 ^{a* c† e†} 6.052–11.53
Effect size (η^2)	0.300	0.264	0.322	0.789

Rats were administered with a diet containing 0, 1, or 5 mg of cadmium (Cd)/kg (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (AE) (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value for 8 rats in each group, except for 7 females in the AE, Cd₁, and Cd₅ groups after 24 months. The statistically significant differences (non-parametric Kruskal-Wallis test) compared to: a – Control group, b – AE group, c – Cd₁ group, d – Cd₁ + AE group, and e – Cd₅ group are marked as * $p < 0.05$, † $p < 0.01$, and ‡ $p < 0.001$. To evaluate the effect size for the differences between the experimental groups, eta squared (η^2) was calculated (for $\eta^2 \geq 0.14$ the effect size is large).

Table S7. The concentration of total thiol groups (t-SH) in the brain of female rats.

Group	Experiment Duration			
	3 Months	10 Months	17 Months	24 Months
	t-SH (nmol/mg protein)			
Control	89.44 53.41–154.1	63.31 39.39–74.43	51.33 43.51–64.62	62.53 45.21–92.53
AE	21.27 ^{a†} 10.58–125.6	32.39 20.78–77.09	43.22 34.34–75.51	28.07 14.68–145.3
Cd ₁	32.60 ^{a†} 19.79–40.86	22.54 ^{a†} 15.42–47.54	27.73 ^{a† b*} 18.65–34.02	20.15 ^{a*} 10.28–25.97
Cd ₁ + AE	62.10 37.84–113.9	51.42 ^{c†} 40.08–84.94	44.48 ^{c*} 35.31–79.39	81.49 ^{c†} 50.41–107.3
Cd ₅	64.11 21.47–116.7	27.18 ^{a† d*} 17.66–51.13	25.32 ^{a† b* d*} 19.17–34.52	21.52 ^{a* d†} 13.54–25.09
Cd ₅ + AE	56.36 42.89–71.34	42.30 36.10–69.51	52.66 ^{c† e†} 43.97–75.79	88.71 ^{c† e†} 42.01–116.9
Effect size (η^2)	0.430	0.490	0.650	0.620

Rats were administered with a diet containing 0, 1, or 5 mg of cadmium (Cd)/kg (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (AE) (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value for 8 rats in each group, except for 7 females in the AE, Cd₁, and Cd₅ groups after 24 months. The statistically significant differences (non-parametric Kruskal-Wallis test) compared to: a – Control group, b – AE group, c – Cd₁ group, d – Cd₁ + AE group, and e – Cd₅ group are marked as * $p < 0.05$, and † $p < 0.01$. To evaluate the effect size for the differences between the experimental groups, eta squared (η^2) was calculated (for $\eta^2 \geq 0.14$ the effect size is large).

Table S8. The total antioxidative status (TAS), total oxidative status (TOS), and the oxidative stress index (OSI) in the brain of female rats.

Group	Experiment Duration			
	3 Months	10 Months	17 Months	24 Months
TAS (μmol/g protein)				
Control	135.3	96.70	61.18	55.81
	121.1–247.6	82.04–149.6	50.49–98.18	40.89–74.97
AE	136.7	100.0	85.32	52.55
	106.0–340.5	80.70–137.3	61.59–107.2	44.28–97.41
Cd ₁	108.4 ^{a*}	98.53	54.10	31.01 ^{a*}
	84.26–128.1	88.96–124.0	46.05–73.98	15.96–34.45
Cd ₁ + AE	109.3	94.53	69.80	88.65 ^{c†}
	100.7–311.3	80.44–143.6	58.10–104.9	80.92–110.3
Cd ₅	133.0	94.71	44.60 ^{a* b† d*}	28.50 ^{a† d‡}
	105.3–183.7	80.12–130.2	28.97–47.68	8.996–45.807
Cd ₅ + AE	130.4	105.4	87.10 ^{e†}	46.23 ^{e*}
	127.0–173.7	57.85–131.6	54.75–95.16	33.90–95.49
Effect size (η ²)	0.198	-	0.564	0.697
TOS (μmol/g protein)				
Control	3.780	2.535	2.268	1.963
	2.138–4.934	1.892–3.530	1.734–4.439	1.284–3.595
AE	2.637	2.222	2.363	1.697
	1.985–4.207	1.873–2.670	1.427–3.099	0.577–1.871
Cd ₁	7.308	18.14 ^{a† b†}	13.85 ^{a† b†}	9.893 ^{a* b†}
	5.357–9.292	3.272–53.94	8.168–26.10	7.583–14.16
Cd ₁ + AE	6.044	3.875	3.622 ^{c†}	2.470 ^{c*}
	4.552–10.52	1.137–16.64	2.174–6.139	1.295–3.450
Cd ₅	37.11 ^{a† b†}	17.69 ^{a† b†}	17.38 ^{a† b†}	14.79 ^{a† b† d*}
	10.76–89.60	6.555–41.34	10.65–30.77	10.43–23.61
Cd ₅ + AE	12.65 ^{a* b† e*}	9.447 ^{b*}	3.053 ^{c* e†}	1.897 ^{e†}
	1.660–18.10	5.015–16.62	1.461–4.791	0.968–3.683
Effect size (η ²)	0.747	0.626	0.709	0.688
OSI				
Control	0.021	0.024	0.034	0.038
	0.017–0.037	0.019–0.042	0.019–0.076	0.018–0.071
AE	0.022	0.023	0.025	0.032
	0.010–0.025	0.014–0.028	0.015–0.037	0.010–0.038
Cd ₁	0.071	0.151 ^{a* b†}	0.252 ^{a* b†}	0.319 ^{a* b†}
	0.048–0.073	0.037–0.606	0.131–0.465	0.248–0.887
Cd ₁ + AE	0.051	0.041 ^{c*}	0.050 ^{c†}	0.025 ^{c†}
	0.020–0.097	0.014–0.178	0.026–0.100	0.015–0.040
Cd ₅	0.281 ^{a† b†}	0.159 ^{a† b†}	0.418 ^{a† b† d†}	0.643 ^{a† b† d†}
	0.062–0.659	0.117–0.331	0.252–0.697	0.229–2.368
Cd ₅ + AE	0.098 ^{a* b*}	0.098 ^{b* e*}	0.038 ^{e†}	0.037 ^{e†}
	0.010–0.138	0.048–0.156	0.015–0.056	0.029–0.056
Effect size (η ²)	0.660	0.656	0.735	0.684

Rats were administered with a diet containing 0, 1, or 5 mg of cadmium (Cd)/ kg (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (AE) (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value for 8 rats in each group, except for 7 females in the AE, Cd₁, and Cd₅ groups after 24 months. The statistically significant differences (non-parametric Kruskal-Wallis test) compared to: a – Control group, b – AE group, c – Cd₁ group, d – Cd₁ + AE group, and e – Cd₅ group are marked as * $p < 0.05$, † $p < 0.01$, and ‡ $p < 0.001$. To evaluate the effect size for the differences between the experimental groups, eta squared (η²) was calculated (for η² ≥ 0.14 the effect size is large).

Table S9. The concentrations of hydrogen peroxide (H₂O₂), myeloperoxidase (MPO), and xanthine oxidase (XOD) in the brain of female rats.

Group	Experiment Duration			
	3 Months	10 Months	17 Months	24 Months
H₂O₂ (nmol/mg protein)				
Control	4.251	3.684	3.374	3.830
	1.297–8.331	2.047–4.870	2.814–5.460	2.754–4.309
AE	4.436	3.206	3.460	2.848
	3.072–4.852	1.737–3.554	2.747–4.006	2.428–3.331
Cd ₁	4.283	3.501	3.504	4.064 ^{b†}
	2.989–7.202	3.247–4.856	1.552–5.736	3.584–4.581
Cd ₁ + AE	1.748 ^{a†b†c†}	2.357 ^{a†c†}	2.848	2.244 ^{a†c†}
	0.652–2.823	0.573–3.697	1.610–3.976	1.616–3.588
Cd ₅	3.634	2.195 ^{c†}	4.640 ^{a†b†c†d†}	4.629 ^{a†d†}
	2.095–5.555	1.559–4.103	3.887–5.084	3.418–5.189
Cd ₅ + AE	2.065	1.717 ^{a†b†c†}	2.045 ^{a†b†c†e†}	1.849 ^{a†c†e†}
	0.941–4.555	0.158–2.957	1.496–2.212	1.059–2.502
Effect size (η ²)	0.410	0.380	0.490	0.750
MPO (ng/mg protein)				
Control	1.369	1.117	0.961	1.018
	0.679–2.192	0.728–1.411	0.780–1.182	0.692–1.429
AE	1.215	1.091	0.928	1.171
	1.089–2.260	0.447–1.520	0.732–1.261	0.719–1.282
Cd ₁	1.171	1.507	1.250	1.918 ^{a†}
	1.008–1.401	1.005–2.756	0.717–1.380	1.659–2.549
Cd ₁ + AE	1.149	0.974	0.746	0.932 ^{c†}
	0.628–3.700	0.500–1.469	0.598–1.160	0.561–1.288
Cd ₅	1.364	1.795 ^{a#d†}	1.431 ^{d†}	1.824 ^{a†d†}
	0.918–1.908	1.192–4.796	1.060–1.909	1.684–2.367
Cd ₅ + AE	1.284	1.336	0.871 ^{e†}	1.064 ^{c†e†}
	0.851–1.675	0.740–2.271	0.539–0.998	0.879–1.246
Effect size (η ²)	-	0.300	0.410	0.600
XOD (ng/mg protein)				
Control	1.459	0.683	0.535	0.470
	0.717–2.526	0.589–1.006	0.183–1.050	0.197–0.639
AE	1.209	0.640	0.598	0.502
	0.688–2.565	0.553–0.965	0.141–0.736	0.261–1.584
Cd ₁	1.495	0.722	0.665	0.841 ^{a#}
	0.901–2.162	0.643–1.427	0.394–2.621	0.714–1.997
Cd ₁ + AE	1.100	0.793	0.447	0.288 ^{c†}
	0.946–2.613	0.600–1.036	0.141–1.147	0.123–0.533
Cd ₅	1.307	0.803	0.965 ^{d†}	0.950 ^{a#d†}
	0.964–2.129	0.708–1.062	0.622–2.684	0.672–1.182
Cd ₅ + AE	1.062	0.794	0.289 ^{e†}	0.411 ^{c†e†}
	0.568–1.208	0.349–0.923	0.136–0.869	0.146–0.538
Effect size (η ²)	-	-	0.340	0.580

Rats were administered with a diet containing 0, 1, or 5 mg of cadmium (Cd)/ kg (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (AE) (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value for 8 rats in each group, except for 7 females in the AE, Cd₁, and Cd₅ groups after 24 months. The statistically significant differences (non-parametric Kruskal-Wallis test) compared to: a – Control group, b – AE group, c – Cd₁ group, d – Cd₁ + AE group, and e – Cd₅ group are marked as * $p < 0.05$, † $p < 0.01$, ‡ $p < 0.001$, and # $p = 0.05–0.08$. To evaluate the effect size for the differences between the experimental groups, eta squared (η²) was calculated (for η² ≥ 0.14 the effect size is large).

Table S10. The concentrations of lipid peroxides (LPO) and 8-isoprostane (8-iso) in the brain of female rats.

Group	Experiment Duration			
	3 Months	10 Months	17 Months	24 Months
LPO ($\mu\text{mol}/\text{mg}$ protein)				
Control	0.787 0.490–0.925	0.598 0.351–1.103	0.678 0.532–0.709	0.573 0.487–0.646
AE	0.609 0.286–0.795	0.733 0.487–1.051	0.632 0.410–1.138	0.223 ^{a*} 0.165–0.275
Cd ₁	1.256 ^{b*} 0.686–1.812	1.181 0.534–1.722	0.940 0.663–1.619	0.808 ^{b†} 0.719–1.211
Cd ₁ + AE	0.684 0.448–1.472	0.465 ^{c*} 0.203–1.204	0.581 ^{c*} 0.469–0.796	0.320 ^{c#} 0.209–0.449
Cd ₅	1.589 ^{b† d*} 0.716–2.353	1.015 ^{d*} 0.521–1.926	0.984 ^{a* d†} 0.876–1.348	1.502 ^{b† d†} 1.332–2.172
Cd ₅ + AE	1.420 ^{b†} 0.741–2.514	0.983 0.451–1.272	0.662 ^{e*} 0.327–0.915	0.307 ^{c* e†} 0.190–0.559
Effect size (η^2)	0.510	0.240	0.390	0.820
8-iso (pg/mg protein)				
Control	12.99 10.63–19.79	15.32 12.63–20.88	17.66 14.83–20.57	9.943 9.483–11.81
AE	12.02 7.715–17.20	14.08 10.95–25.70	18.91 9.557–21.06	18.94 11.50–21.70
Cd ₁	11.97 9.776–14.63	18.21 15.60–24.08	28.30 ^{a† b*} 27.01–46.02	28.49 ^{a*} 23.84–31.81
Cd ₁ + AE	11.02 10.61–15.74	11.83 ^{c*} 9.303–24.25	16.04 ^{c†} 11.85–17.05	9.630 ^{c†} 7.492–11.59
Cd ₅	15.73 12.77–20.70	19.11 13.58–24.91	26.02 ^{d†} 21.00–29.09	30.18 ^{a† d†} 25.61–36.40
Cd ₅ + AE	11.38 10.50–18.71	14.89 9.614–17.85	17.87 ^{c† e*} 8.483–19.77	9.694 ^{c† e†} 8.344–11.72
Effect size (η^2)	-	0.210	0.700	0.770

Rats were administered with a diet containing 0, 1, or 5 mg of cadmium (Cd)/kg (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (AE) (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value for 8 rats in each group, except for 7 females in the AE, Cd₁, and Cd₅ groups after 24 months. The statistically significant differences (non-parametric Kruskal-Wallis test) compared to: a – Control group, b – AE group, c – Cd₁ group, d – Cd₁ + AE group, and e – Cd₅ group are marked as * $p < 0.05$, † $p < 0.01$, ‡ $p < 0.001$, and # $p = 0.05$. To evaluate the effect size for the differences between the experimental groups, eta squared (η^2) was calculated (for $\eta^2 \geq 0.14$ the effect size is large).

Table S11. The concentrations of 3-nitrotyrosine (3-NT), protein carbonyl groups (PC), and γ -H2A histone family member X (γ -H2AX) in the brain of female rats.

Group	Experiment Duration			
	3 Months	10 Months	17 Months	24 Months
3-NT (ng/mg protein)				
Control	101.1	71.05	75.76	47.61
	17.05–122.5	56.72–125.5	23.59–87.31	33.15–61.64
AE	96.34	72.77	77.25	49.29
	26.64–294.4	54.04–95.23	75.49–97.30	32.85–77.49
Cd ₁	92.67	78.00	89.75	100.9 ^{a*}
	81.16–112.0	56.80–100.9	60.65–178.5	61.26–107.4
Cd ₁ + AE	69.00	71.89	65.28	47.68 ^{c*}
	28.03–237.5	45.98–102.4	34.93–74.01	28.84–63.81
Cd ₅	94.39	87.42	88.63 ^{d*}	93.35 ^{a* d*}
	41.80–169.1	63.67–115.2	66.64–109.3	65.47–114.1
Cd ₅ + AE	86.51	68.64	52.05 ^{b* c† e†}	47.44 ^{c* e*}
	55.24–147.6	58.98–102.5	36.68–63.20	33.38–66.44
Effect size (η^2)	-	-	0.420	0.520
PC (nmol/mg protein)				
Control	10.44	6.659	4.845	11.53
	8.332–14.90	4.400–7.130	4.047–5.739	10.16–16.19
AE	9.393	7.808	5.097	10.83
	6.815–16.53	5.798–8.759	4.295–8.959	9.722–14.42
Cd ₁	9.407	6.372	10.88 ^{a*}	21.76 ^{b*}
	7.393–21.10	5.459–10.76	5.316–16.94	16.48–29.70
Cd ₁ + AE	8.495	5.144	4.677	17.96
	6.546–11.82	3.842–8.789	3.908–7.967	10.53–29.38
Cd ₅	13.34	10.97 ^{a* c* d†}	23.44 ^{a† b† d†}	48.71 ^{a† b†}
	8.564–17.15	7.030–14.09	17.72–30.20	29.60–52.89
Cd ₅ + AE	8.455	7.663	5.905 ^{e*}	14.96 ^{e†}
	6.406–10.12	5.998–8.638	5.202–7.623	8.750–16.89
Effect size (η^2)	-	0.390	0.640	0.650
γ-H2AX (ng/mg protein)				
Control	1.007	0.873	0.992	0.777
	0.371–1.425	0.638–1.009	0.752–1.369	0.489–0.986
AE	1.194	0.840	0.920	0.919
	0.368–3.263	0.697–1.226	0.658–1.084	0.251–1.087
Cd ₁	0.836	0.835	1.016	1.534 ^{a#}
	0.326–1.160	0.673–1.282	0.888–1.819	1.191–2.111
Cd ₁ + AE	0.979	0.851	0.817	0.635 ^{c†}
	0.888–1.362	0.637–1.276	0.697–1.343	0.249–1.002
Cd ₅	1.141	0.783	1.147	1.622 ^{a* d†}
	0.457–1.341	0.647–1.120	0.781–1.813	1.299–1.915
Cd ₅ + AE	0.944	0.867	0.777	0.616 ^{c† e†}
	0.480–1.122	0.726–0.946	0.276–1.009	0.483–0.694
Effect size (η^2)	-	-	-	0.640

Rats were administered with a diet containing 0, 1, or 5 mg of cadmium (Cd)/kg (groups: Control, Cd₁, and Cd₅) and/or 0.1% extract from *Aronia melanocarpa* L. berries (AE) (groups: AE, Cd₁ + AE, and Cd₅ + AE) for 3, 10, 17, and 24 months. Data are presented as a median and minimum and maximum value for 8 rats in each group, except for 7 females in the AE, Cd₁, and Cd₅ groups after 24 months. The statistically significant differences (non-parametric Kruskal-Wallis test) compared to: a – Control group, b – AE group, c – Cd₁ group, d – Cd₁ + AE group, and e – Cd₅ group are marked as * $p < 0.05$, † $p < 0.01$, ‡ $p < 0.001$, and # $p = 0.05$. To evaluate the effect size for the differences between the experimental groups, eta squared (η^2) was calculated (for $\eta^2 \geq 0.14$ the effect size is large).