

Supplementary Materials

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Supplementary Table 1. Nutrient Composition of the protein-fortified compound nutritional drink (per 235 ml).

Nutrients	Content	Unit
Protein	15.0	g
Milk protein concentrates and whey protein hydrolysates	13.0	g
Collagen peptide	2.0	g
Fat	5.32	g
Carbohydrate	31.24	g
Dietary fiber	3.6	g
Vitamin A	120	µg
Vitamin C	15	mg
Vitamin D	3	µg
Vitamin E	2.7	mg α -TE
Vitamin B1	0.52	mg
Vitamin B2	0.52	mg
Vitamin B6	0.5	mg
Vitamin B12	0.4	µg
Biotin	11	µg
Niacin	5.5	mg
pantothenic acid	1.2	mg
Taurine	13.6	mg
Calcium	300	mg
Phosphorus	188	mg
Zinc	3.5	mg
Selenium	13	µg

Supplementary Table 2. The toxicology results of MPC, CP, and WPH

Dose ($\mu\text{g/mL}$)	MPC		CP		WPH	
	Exposed	Deaths	Exposed	Deaths	Exposed	Deaths
	number	(%)	number	(%)	number	(%)
0	30	0	30	0	30	0
125	30	0	30	0	30	0
250	30	0	30	0	30	0
300	30	0	/	/	/	/
350	30	0*	/	/	/	/
400	30	4(13.3%)	/	/	/	/
450	30	4(13.3%)	/	/	/	/
500	30	8(26.7%)	30	0	30	12(40%)
1000	30	14(46.7%)	30	0*	30	15(50%)
2000	30	30(100%)	30	0	30	30(100%)

*The status of zebrafish was poor.

Supplementary Table 3. The results of different models for benchmark dose of MPC and WPH

Reagents	Model	Benchmark Dose Lower Bound*	Benchmark Dose	Benchmark Dose Upper Bound*	P-Value	AIC	Scaled Residual for Dose Group near Benchmark Dose	Scaled Residual for Control Dose Group
MPC	Hill	380.518	438.591	498.804	0.1	144.473	0.449	-0.001
	Gamma	379.903	438.544	496.692	0.174	141.66	0.452	-0.001
	LogLogistic	380.518	438.591	498.804	0.1	144.473	0.449	-0.001
	Multistage 1°	163.033	201.33	252.198	<0.001	185.988	-2.048	-0.001
	Multistage 2°	335.508	378.481	429.234	0.364	141.79	0.389	-0.001
	Multistage 3°	370.611	443.164	516.621	0.316	137.927	0.536	-0.001
	Multistage 4°	366.231	442.972	517.212	0.317	137.927	0.534	-0.001
	Multistage 5°	362.813	437.976	517.281	0.349	137.819	0.487	-0.001
	Multistage 6°	360.73	435.48	516.386	0.369	137.672	0.464	-0.001
	Multistage 7°	359.478	434.288	515.564	0.38	137.56	0.453	-0.001
	Multistage 8°#	358.764	433.747	514.98	0.387	137.486	0.447	-0.001
	Weibull	375.253	443.343	513.148	0.245	139.634	0.533	-0.001
	Logistic	431.49	500.407	574.776	0.036	147.205	2.72	-0.608
	LogProbit	382.548	433.393	484.314	0.164	141.983	0.343	-0.001

	Probit	410.01	474.971	543.865	0.073	144.567	0.745	-0.422
	Quantal Linear	163.038	201.33	252.189	<0.001	185.988	-2.048	-0.001
	Hill	263.899	348.377	434.936	0.013	101.092	-1.147	-0.001
	Gamma	258.574	348.029	435.865	0.024	98.681	-1.167	-0.001
	LogLogistic	263.899	348.377	434.936	0.013	101.092	-1.147	-0.001
	Multistage 1°	97.577	122.493	155.847	0.003	116.205	-1.845	-0.001
	Multistage 2°	244.761	326.041	375.507	0.095	94.763	-1.385	-0.001
	Multistage 3°	235.1	337.705	431.478	0.08	94.666	-1.329	-0.001
WPH	Multistage 4°	220.759	340.844	427.52	0.079	94.465	-1.32	-0.001
	Multistage 5° #	213.457	342.214	422.923	0.082	94.177	-1.316	-0.001
	Weibull	247.055	339.75	436.705	0.045	96.69	-1.31	-0.001
	Logistic	332.08	414	506.114	0.001	105.43	3.458	-0.859
	LogProbit	273.473	353.133	432.808	0.025	98.875	-0.983	-0.001
	Probit	314.514	392.833	480.847	0.003	102.782	3.304	-0.67
	Quantal Linear	97.578	122.493	155.844	0.003	116.205	-1.845	-0.001

* Lower and upper bound of the 95% confidence interval for benchmark dose; # Recommended best-fitting model; AIC: Akaike Information Criterion.

Supplementary Table 4. Major baseline characteristics of children after propensity score weighting.

Variable	Control (N=60)	Treatment (N=60)	P value
Age, years	10.46(0.12)	10.37(0.09)	0.552
Weight, kg	31.49(0.75)	31.93(1.17)	0.754
Height, cm	139.05(0.81)	138.84(1.14)	0.884
Body mass index, kg/m ²	16.17(0.26)	16.36(0.35)	0.676

Data are shown as Mean (Standard Error).

Supplementary Table 5. Urinalysis results of children in the RCT at baseline and week 10 of the trial*.

Urinalysis Variables	Group	Baseline			Week 10		
		Control	Treatment	P value #	Control	Treatment	P value #
LEU	Negative (-)	47 (83.93)	50 (89.29)	0.664	40 (88.89)	40 (93.02)	NA
	Borderline Positive (+/-)	2 (3.57)	1 (1.79)		2 (4.44)	1 (2.33)	
	Positive (+)	7 (12.50)	5 (8.93)		3 (6.67)	2 (4.65)	
	Sum	56 (100.00)	56 (100.00)		45 (100.00)	43 (100.00)	
ERY	Negative (-)	48 (85.71)	51 (91.07)	0.684	42 (93.33)	41 (95.35)	NA
	Borderline Positive (+/-)	4 (7.14)	3 (5.36)		2 (4.44)	1 (2.33)	
	Positive (+)	4 (7.14)	2 (3.57)		1 (2.22)	1 (2.33)	
	Sum	56 (100.00)	56 (100.00)		45 (100.00)	43 (100.00)	
PRO	Negative (-)	47 (83.93)	47 (83.93)	0.692	36 (80.00)	39 (90.70)	0.263
	Borderline Positive (+/-)	6 (10.71)	4 (7.14)		4 (8.89)	3 (6.98)	
	Positive (+)	3 (5.36)	5 (8.93)		5 (11.11)	1 (2.33)	
	Sum	56 (100.00)	56 (100.00)		45 (100.00)	43 (100.00)	
BIL	Negative (-)	56 (100.00)	56 (100.00)	NA	45 (100.00)	43 (100.00)	NA
	Sum	56 (100.00)	56 (100.00)		45 (100.00)	43 (100.00)	

	Negative (-)	40 (71.43)	41 (73.21)		31 (68.89)	35 (81.40)	
USCME	Positive (+)	16 (28.57)	15 (26.79)	NA	14 (31.11)	8 (18.60)	0.221
	Sum	56 (100.00)	56 (100.00)		45 (100.00)	43 (100.00)	
	Negative (-)	54 (96.43)	56 (100.00)		45 (100.00)	43 (100.00)	
NIT	Positive (+)	2 (3.57)	0 (0.00)	0.495	0	0	NA
	Sum	56 (100.00)	56 (100.00)		45 (100.00)	43 (100.00)	
	Negative (-)	56 (100.00)	56 (100.00)		42 (93.33)	43 (100.00)	
KET	Borderline Positive (+/-)	0	0	NA	2 (4.44)	0	NA
	Positive (+)	0	0		1 (2.22)	0	
	Sum	56 (100.00)	56 (100.00)		45 (100.00)	43 (100.00)	
	Negative (-)	52 (92.86)	51 (91.07)		36 (80.00)	39 (90.70)	
UBG	Borderline Positive (+/-)	3 (5.36)	3 (5.36)	NA	8 (17.78)	3 (6.98)	0.314
	Positive (+)	1 (1.79)	2 (3.57)		1 (2.22)	1 (2.33)	
	Sum	56 (100.00)	56 (100.00)		45 (100.00)	43 (100.00)	
	Negative (-)	56 (100.00)	56 (100.00)	NA	45 (100.00)	43 (100.00)	NA
GLU	Sum	56 (100.00)	56 (100.00)		45 (100.00)	43 (100.00)	
SG	/	1.020 (0.001)	1.020 (0.001)	0.606	1.021 (0.001)	1.022 (0.001)	0.148

PH	/	6.547 (0.088)	6.584 (0.089)	0.771	6.591 (0.097)	6.366 (0.101)	0.112
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Data are shown as frequency (percentage) for categorical variables or Mean (standard error) for continuous variables.

*For urinalysis, 112 urine samples at baseline and 88 urine samples at week were obtained.

#P values were obtained using Fisher's Exact Test for categorical variables or linear mixed effect model for continuous variables

Abbreviations: LEU, leukocytes; ERY, erythrocytes; PRO, protein; BIL, bilirubin; USCME, urine sediment centrifugation microscopy examination; NIT, nitrite;

KET, ketone bodies; UBG, urobilinogen; GLU, glucose; SG, specific gravity; PH, pondus hydrogenii.

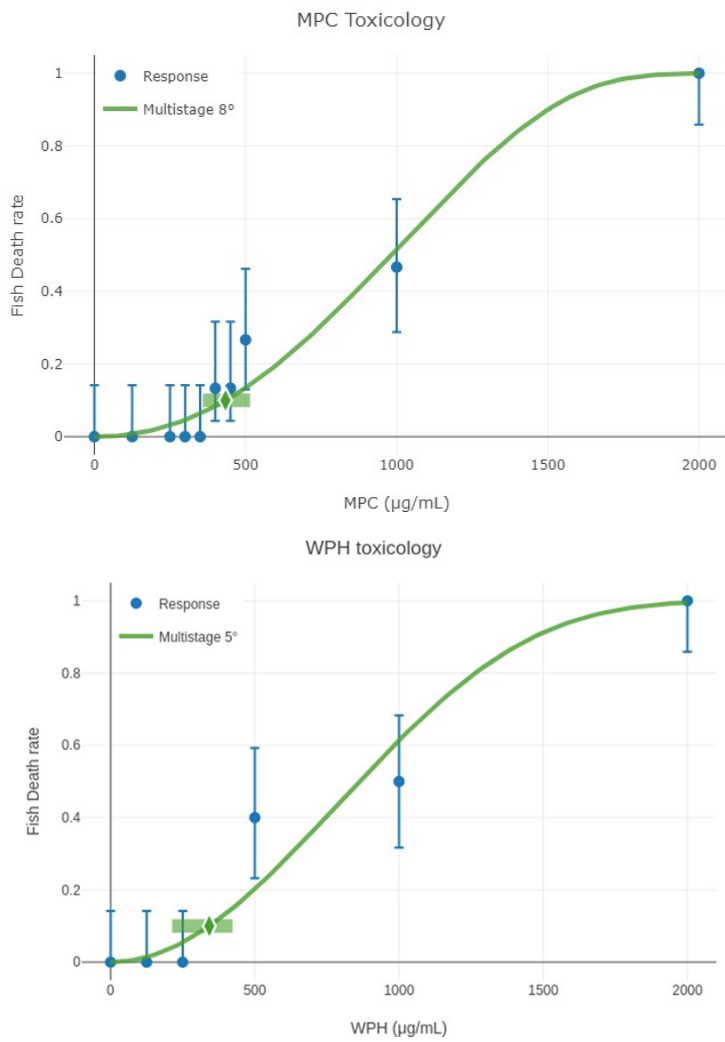
Supplementary Table 6. The mean number of vertebrae, fluorescence intensity, and relative effect at different doses of MPC, CP, and WPH, respectively.

Group	Mean Number of Vertebrae	Fluorescence Intensity	Relative Effect (%)
Blank control	1	18224.27 ± 1815.21	0 ± 20.31
Positive control	2.5	27162.41 ± 2953.24	100±33.04
MPC 30.5 µg/mL	1.6	20528.40 ± 4027.55	25.78 ± 45.06
MPC 61.0 µg/mL	1.7	21997.97 ± 1907.68	42.22 ± 21.34
MPC 122 µg/mL	1.7	24094.65 ± 2189.39	65.68 ± 24.49
CP 70.0 µg/mL	1.6	18787.54 ± 2409.1	6.3 ± 26.95
CP 140 µg/mL	2.4	23911.26 ± 2432.68	63.63 ± 27.22
CP 210 µg/mL	2.5	27116.06 ± 3465.14	99.48 ± 38.77
WPH 50.0 µg/mL	1.2	18876.35 ± 2074.51	7.3 ± 23.21
WPH 100 µg/mL	2.3	21314.26 ± 2332.89	34.57 ± 26.1
WPH 200 µg/mL	2.2	26899.43 ± 3439.26	97.06 ± 38.48

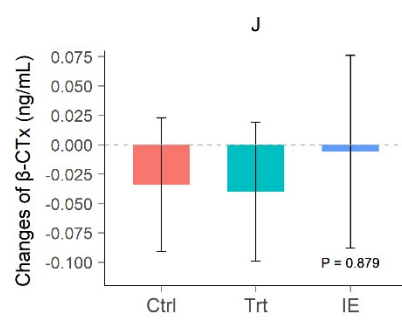
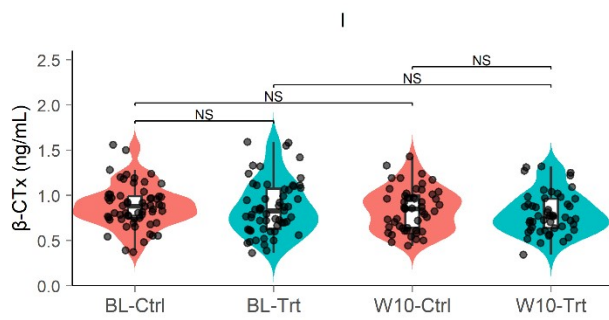
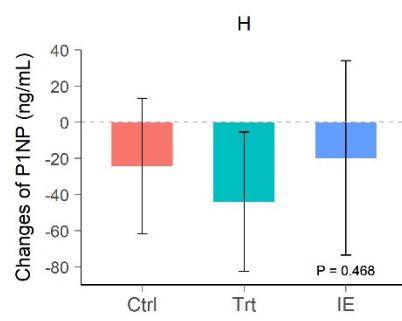
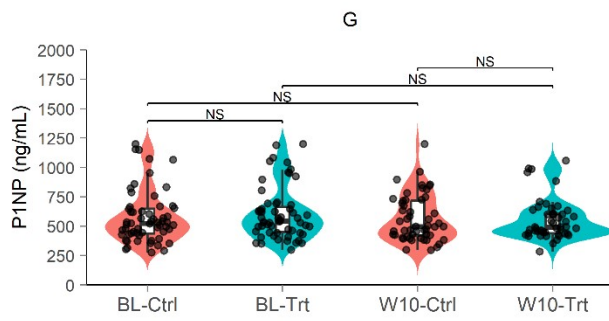
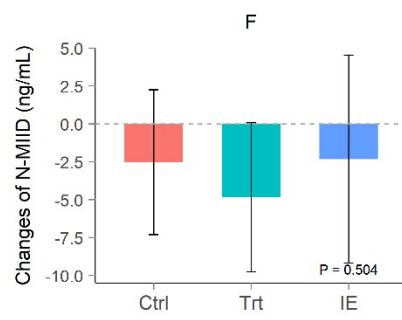
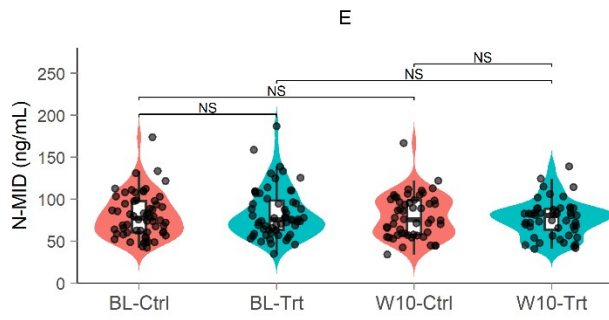
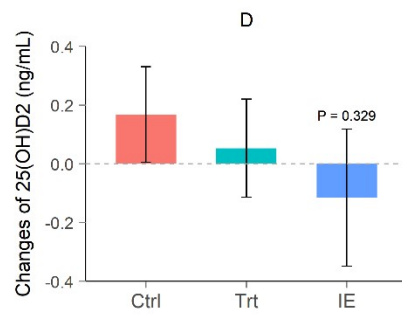
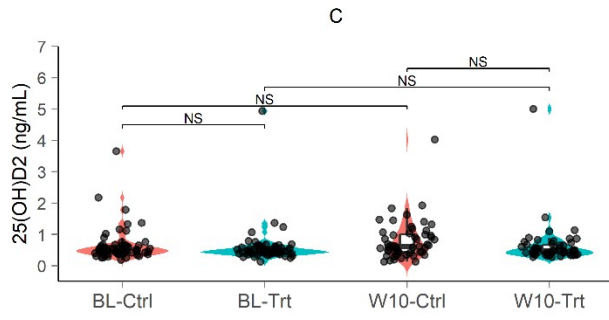
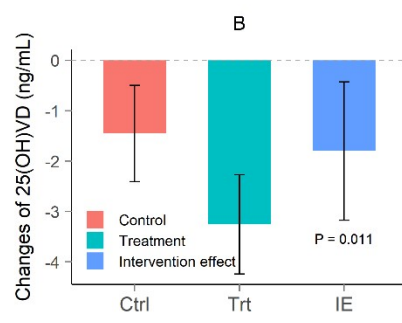
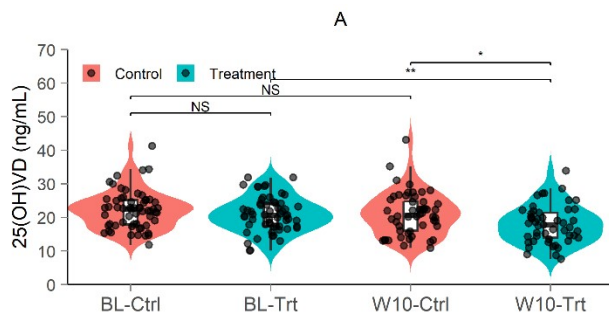
Supplementary Table 7. Changes in BMD and BMC in the treatment and control groups with adjustment for serum calcium concentration.

Variables	Control group (95% CI)	Treatment group (95% CI)	Difference between groups (95% CI)	<i>P</i> for difference
BMD (g/cm ²)	-0.051 (-0.067, -0.035)	-0.025 (-0.043, -0.007)	0.026 (0.003, 0.050)	0.030
BMC (g)*	-0.049 (-0.067, -0.031)	-0.025 (-0.044, -0.005)	0.025 (-0.001, 0.050)	0.057

*For analysis of BMC, bone area was also adjusted.



Supplementary Figure 1. The best-fitting model curve for bench mark dose of MPC and WPH, respectively.



Supplementary Figure 2. Serum 25(OH)VD, 25(OH)D2, and bone turnover biomarkers (N-MID, P1NP, and β -CTX) of children in the RCT. Panel A, C, E, G, and I: Violin plots for biomarkers of children in control and treatment group measured at baseline and week-10 of the trial; the difference between two groups was compared by the Wilcoxon test. Panel B, D, F, H, and J: Bar plots for the changes of bone biomarkers during intervention and the intervention effect analyzed by the mixed effect model. * P < 0.05; ** P < 0.01; *** P < 0.001; NS, not significant; error bars show 95% confidence intervals