

Dietary Fiber with Functional Properties Counteracts the Thwarting Effects of Copper Nanoparticles on the Microbial Enzymatic Activity and Short-chain Fatty Acid Production in the Feces of Rats

by

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SUPPLEMENTARY MATERIALS

Table S1. Fecal microbial intracellular α -glucosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats. **Table S2.** Fecal microbial total α -glucosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats. **Table S3.** Fecal microbial intracellular β -glucosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats. **Table S4.** Fecal microbial total β -glucosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats. **Table S5.** Fecal microbial intracellular β -glucuronidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats. **Table S6.** Fecal microbial total β -glucuronidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats. **Table S7.** Fecal microbial intracellular α -arabinofuranosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats. **Table S8.** Fecal microbial total α -arabinofuranosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats. **Table S9.** Fecal content ($\mu\text{mol/g}$) of putrefactive short-chain fatty acids (*iso*-butyric+*iso*-valeric+valeric acids) during the experimental feeding period in rats. **Table S10.** Fecal content ($\mu\text{mol/g}$) of total short-chain fatty acids during the experimental feeding period in rats. **Table S11.** Fecal pH values during the experimental feeding period in rats. **Figure S1.** Experimental schema.

Table S1. Fecal microbial intracellular α -glucosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	38.6	38.9	37.8	38.9	44.7	42.1	41.0
Control CH	38.0	39.4	39.0	39.5	43.0	40.0	40.4
2-way ANOVA:							
CN	37.1	32.0 [#]	29.9 [#]	22.3 [#]	14.6 ^{c#}	8.32 ^{e#}	5.90 ^{e#}
CNH	39.1	27.7 ^{&}	28.2 ^{&}	12.0 ^{&}	9.83 ^{c&}	7.71 ^{e&}	5.02 ^{e&}
PN	39.1	43.6	40.4	44.9 [#]	33.7 ^{c#}	32.7 ^{c#}	21.2 ^{c#}
PNH	39.2	36.5	35.4	35.4	24.0 ^{d&}	19.9 ^{d&}	15.3 ^{d&}
JN	40.1	38.5	41.8	50.2 [#]	52.1 ^{b#}	61.4 ^{a#}	61.0 ^{a#}
JNH	39.0	38.7	36.7	37.2	30.3 ^{c&}	30.9 ^{c&}	22.8 ^{c&}
SN	39.1	42.6	41.2	42.4	64.0 ^{a#}	54.5 ^{b#}	48.6 ^{b#}
SNH	38.8	41.4	36.5	33.5 ^{&}	32.5 ^{c&}	29.9 ^{c&}	23.9 ^{c&}
SEM	0.642	0.678	0.680	1.177	1.706	1.813	1.852
Cu-NP dose (D)							
L (6.5 mg/kg)	38.8	39.2 ^a	38.3 ^a	39.9 ^a	41.1	39.2	34.2
H (13 mg/kg)	39.0	36.1 ^b	34.2 ^b	29.5 ^b	24.1	22.1	16.7
P value	0.875	0.010	0.002	<0.001	<0.001	<0.001	<0.001
Fiber type (F)							
C (cellulose)	38.1	29.9 ^b	29.0 ^b	17.1 ^c	12.2	8.01	5.46
P (pectin)	39.1	40.0 ^a	37.9 ^a	40.1 ^{ab}	28.8	26.3	18.2
J (inulin)	39.5	38.6 ^a	39.2 ^a	43.7 ^a	41.2	46.1	41.9
S (psyllium)	38.9	42.0 ^a	38.9 ^a	37.9 ^b	48.3	42.2	36.3
P value	0.910	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Interaction D×F							
P value	0.891	0.133	0.731	0.659	<0.001	<0.001	<0.001

*Control C and CH groups, fed a control diet containing CuCO_3 of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

Table S2. Fecal microbial total α -glucosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	72.6	74.1	72.8	75.1	78.5	77.3	73.8
Control CH	73.3	74.9	74.0	76.1	74.8	72.9	71.7
2-way ANOVA:							
CN	72.1	65.9	60.4 [#]	48.8 ^{c#}	35.5 ^{c#}	34.0 ^{e#}	30.1 ^{d#}
CNH	74.1	60.6 ^{&}	57.1 ^{&}	35.2 ^{d&}	27.8 ^{f&}	26.2 ^{f&}	23.2 ^{e&}
PN	73.7	85.1 [#]	86.5 [#]	94.1 [#]	79.3 ^c	87.4 ^{b#}	77.7 ^b
PNH	73.9	74.8	73.9	75.7 ^b	63.9 ^{d&}	60.2 ^{d&}	56.3 ^{c&}
JN	74.9	75.4	79.5 [#]	97.7 ^{a#}	96.5 ^{b#}	104 ^{a#}	102 ^{a#}
JNH	74.1	74.6	73.2	74.8 ^b	63.3 ^{d&}	66.1 ^{d&}	61.5 ^{c&}
SN	73.4	79.6	84.5 [#]	93.0 ^{a#}	118 ^{a#}	113 ^{a#}	110 ^{a#}
SNH	73.0	77.1	74.2	76.1 ^b	77.4 ^c	77.4 ^c	73.6 ^b
SEM	0.758	0.942	1.033	1.932	2.591	2.683	2.681
Cu-NP dose (D)							
L (6.5 mg/kg)	73.5	76.5 ^a	77.7 ^a	83.4	82.3	84.6	80.2
H (13 mg/kg)	73.8	71.8 ^b	69.6 ^b	65.5	58.1	57.5	53.6
P value	0.883	0.002	<0.001	<0.001	<0.001	<0.001	<0.001
Fiber type (F)							
C (cellulose)	73.1	63.2 ^c	58.7 ^b	42.0	31.6	30.1	26.7
P (pectin)	73.8	79.9 ^a	80.2 ^a	84.9	71.6	73.8	67.0
J (inulin)	74.5	75.0 ^b	76.3 ^a	86.3	79.9	85.2	82.0
S (psyllium)	73.2	78.4 ^{ab}	79.3 ^a	84.6	97.6	95.0	92.1
P value	0.939	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Interaction D×F							
P value	0.948	0.141	0.061	0.046	<0.001	<0.001	<0.001

*Control C and CH groups, fed a control diet containing CuCO_3 of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

Table S3. Fecal microbial intracellular β -glucosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	13.8	15.1	15.1	18.5	20.7	18.2	19.9
Control CH	15.7	15.0	14.2	17.0	17.5	16.6	14.5
2-way ANOVA:							
CN	14.3	13.6	7.90 [#]	7.07 [#]	6.03 [#]	5.84 [#]	8.36 [#]
CNH	14.2	12.7	7.74 ^{&}	4.61 ^{&}	4.32 ^{&}	4.23 ^{&}	5.07 ^{&}
PN	15.0	11.2	11.4	16.5	15.9 [#]	14.1	13.4 [#]
PNH	15.7	10.0	8.20 ^{&}	11.3 ^{&}	12.2	12.6	11.5
JN	15.8	12.3	12.1	10.5 [#]	12.3 [#]	10.9 [#]	12.4 [#]
JNH	15.8	10.8	10.3	8.06 ^{&}	9.94 ^{&}	7.67 ^{&}	10.8 ^{&}
SN	15.6	12.3	11.3	10.6 [#]	13.0 [#]	12.9 [#]	14.9 [#]
SNH	15.9	11.5	9.78	9.36 ^{&}	8.74 ^{&}	10.7 ^{&}	9.73 ^{&}
SEM	0.597	0.539	0.496	0.586	0.639	0.573	0.526
Cu-NP dose (D)							
L (6.5 mg/kg)	15.2	12.3	10.7	11.2 ^a	11.8 ^a	10.9 ^a	12.3 ^a
H (13 mg/kg)	15.4	11.2	8.99	8.34 ^b	8.80 ^b	8.81 ^b	9.28 ^b
P value	0.865	0.355	0.051	<0.001	<0.001	0.022	0.001
Fiber type (F)							
C (cellulose)	14.2	13.1	7.82 ^b	5.83 ^c	5.17 ^c	5.03 ^c	6.71 ^b
P (pectin)	15.3	10.6	9.82 ^{ab}	13.9 ^a	14.0 ^a	13.3 ^a	12.4 ^a
J (inulin)	15.8	11.5	11.1 ^a	9.26 ^b	11.1 ^b	9.30 ^b	11.6 ^a
S (psyllium)	15.7	11.9	10.5 ^a	10.0 ^b	10.8 ^b	11.8 ^{ab}	12.3 ^a
P value	0.849	0.488	0.041	<0.001	<0.001	<0.001	<0.001
Interaction D×F							
P value	0.997	0.995	0.651	0.339	0.695	0.901	0.476

*Control C and CH groups, fed a control diet containing CuCO_3 of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

Table S4. Fecal microbial total β -glucosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	29.8	31.3	31.2	36.3	38.1	35.0	37.8
Control CH	31.9	30.9	29.7	34.6	35.7	33.2	31.6
2-way ANOVA:							
CN	30.4	28.3	21.5 [#]	19.6 [#]	18.1 [#]	17.8 [#]	20.8 [#]
CNH	30.5	26.9	20.9 ^{&}	15.4 ^{&}	13.9 ^{&}	14.4 ^{&}	14.8 ^{&}
PN	31.6	29.8	31.9	44.0 [#]	44.3 [#]	43.5 [#]	41.9
PNH	31.9	27.5	25.8	36.5	35.9	37.0	34.3
JN	31.8	28.4	29.2	29.6 [#]	35.1	34.8	36.9
JNH	32.1	26.0	25.6	24.1 ^{&}	27.0 ^{&}	27.0 ^{&}	32.2
SN	31.5	28.3	28.7	32.5	37.5	39.6	41.9
SNH	32.4	27.3	24.7	27.6 ^{&}	31.1	34.5	33.2
SEM	0.957	0.725	0.736	0.985	1.056	0.998	0.957
Cu-NP dose (D)							
L (6.5 mg/kg)	31.4	28.7	27.8 ^a	31.4 ^a	33.7 ^a	33.9 ^a	35.4 ^a
H (13 mg/kg)	31.7	26.9	24.2 ^b	25.9 ^b	27.0 ^b	28.2 ^b	28.6 ^b
P value	0.869	0.245	0.005	<0.001	<0.001	<0.001	<0.001
Fiber type (F)							
C (cellulose)	30.5	27.6	21.2 ^b	17.5 ^c	16.0 ^c	16.1 ^c	17.8 ^b
P (pectin)	31.8	28.6	28.9 ^a	40.3 ^a	40.1 ^a	40.2 ^a	38.1 ^a
J (inulin)	32.0	27.2	27.4 ^a	26.8 ^b	31.0 ^b	30.9 ^b	34.5 ^a
S (psyllium)	32.0	27.8	26.7 ^a	30.0 ^b	34.3 ^b	37.0 ^a	37.6 ^a
P value	0.952	0.926	<0.001	<0.001	<0.001	<0.001	<0.001
Interaction D×F							
P value	0.999	0.986	0.483	0.782	0.572	0.574	0.628

*Control C and CH groups, fed a control diet containing CuCO_3 of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

Table S5. Fecal microbial intracellular β -glucuronidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	49.4	46.3	47.6	49.8	50.8	48.9	47.9
Control CH	46.8	47.6	47.6	44.6	46.6	42.5	45.5
2-way ANOVA:							
CN	46.4	44.8	41.4 ^{cd#}	34.0 ^{d#}	38.3 ^{c#}	39.1 ^{b#}	34.5 ^{c#}
CNH	46.2	44.3	39.1 ^{d&}	27.3 ^{e&}	25.5 ^{d&}	23.4 ^{c&}	23.0 ^{d&}
PN	48.3	50.4	53.6 ^a	47.9 ^{bc}	44.8 ^{b#}	40.0 ^{b#}	38.7 ^{bc#}
PNH	48.7	51.0	46.8 ^b	43.7 ^c	40.2 ^{bc&}	40.4 ^b	39.5 ^{bc&}
JN	45.8	48.0	54.1 ^{a#}	58.7 ^{a#}	52.5 ^a	45.8 ^a	47.1 ^a
JNH	46.9	46.1	40.7 ^{cd&}	41.9 ^c	40.9 ^{bc&}	46.2 ^a	43.9 ^{ab}
SN	49.9	51.6	51.0 ^{ab}	51.0 ^{ab}	42.4 ^{bc#}	40.5 ^{b#}	34.8 ^{c#}
SNH	50.4	51.3	44.7 ^{bc}	46.4 ^{bc}	37.2 ^{c&}	36.4 ^{b&}	38.8 ^{bc&}
SEM	0.667	0.538	0.705	1.044	0.888	0.862	0.868
Cu-NP dose (D)							
L (6.5 mg/kg)	47.6	48.7	50.1	47.9	44.5	41.4	38.7
H (13 mg/kg)	48.1	48.2	42.8	39.9	36.0	36.6	36.3
P value	0.765	0.617	<0.001	<0.001	<0.001	<0.001	0.052
Fiber type (F)							
C (cellulose)	46.3	44.6 ^c	40.3	30.7	31.9	31.2	28.7
P (pectin)	48.5	50.7 ^a	50.2	45.8	42.5	40.2	39.1
J (inulin)	46.4	47.0 ^b	47.4	50.3	46.7	46.0	45.5
S (psyllium)	50.2	51.5 ^a	47.9	48.7	39.8	38.5	36.8
P value	0.232	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Interaction D×F							
P value	0.993	0.881	0.007	0.015	0.028	<0.001	<0.001

*Control C and CH groups, fed a control diet containing CuCO_3 of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

Table S6. Fecal microbial total β -glucuronidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	71.4	69.5	70.4	72.3	76.0	72.5	68.7
Control CH	70.0	70.1	68.3	65.1	71.4	64.5	64.1
2-way ANOVA:							
CN	68.8	63.9 [#]	60.4 ^{d#}	51.3 ^{e#}	56.5 ^{e#}	56.7 ^{d#}	51.1 ^{f#}
CNH	69.2	61.9 ^{&}	56.5 ^{e&}	44.2 ^{f&}	40.3 ^{f&}	37.8 ^{e&}	38.4 ^{g&}
PN	71.3	77.0 [#]	81.5 ^{a#}	86.1 ^{a#}	86.2 ^{a#}	83.2 ^{a#}	81.2 ^{a#}
PNH	70.9	74.7	72.7 ^{b&}	76.3 ^{b&}	76.0 ^{b&}	74.7 ^{b&}	73.9 ^{bc&}
JN	68.4	68.8	73.6 ^b	78.9 ^{b#}	78.8 ^b	73.1 ^b	74.8 ^{bc#}
JNH	69.4	65.7 ^{&}	59.8 ^{de&}	61.9 ^d	63.6 ^{d&}	70.5 ^b	69.2 ^{de&}
SN	72.6	74.6 [#]	75.6 ^{b#}	78.7 ^b	76.0 ^b	75.1 ^b	71.7 ^{cd#}
SNH	72.4	69.9	64.6 ^c	71.5 ^{c&}	68.8 ^c	64.9 ^c	66.1 ^e
SEM	0.732	0.625	0.865	1.337	1.329	1.305	1.249
Cu-NP dose (D)							
L (6.5 mg/kg)	70.3	71.1 ^a	72.7	73.7	74.4	72.0	69.7
H (13 mg/kg)	70.5	68.1 ^b	63.4	63.5	62.1	62.0	61.9
P value	0.907	0.002	<0.001	<0.001	<0.001	<0.001	<0.001
Fiber type (F)							
C (cellulose)	69.0	62.9 ^c	58.5	47.7	48.4	47.2	44.8
P (pectin)	71.1	75.9 ^a	77.1	81.2	81.1	79.0	77.6
J (inulin)	68.9	67.3 ^b	66.7	70.4	71.2	71.8	72.0
S (psyllium)	72.5	72.2 ^{ab}	70.1	75.1	72.4	70.0	68.9
P value	0.412	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Interaction D×F							
P value	0.991	0.767	0.003	0.009	0.013	<0.001	0.021

*Control C and CH groups, fed a control diet containing CuCO_3 of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

Table S7. Fecal microbial intracellular α -arabinofuranosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	2.30	2.23	2.22	2.14	2.29	2.19	2.13
Control CH	2.26	2.31	2.25	1.96	2.06	1.98	2.07
2-way ANOVA:							
CN	2.25	1.84 [#]	1.46 [#]	1.13 [#]	0.919 [#]	0.879 ^{d#}	0.735 ^{c#}
CNH	2.23	1.71 ^{&}	1.21 ^{&}	0.680 ^{&}	0.460 ^{&}	0.310 ^{e&}	0.335 ^{d&}
PN	2.26	1.96	2.05	1.99	1.79 [#]	1.61 ^{a#}	1.43 ^{a#}
PNH	2.27	2.18	1.85	1.80	1.51 ^{&}	1.16 ^{c&}	1.18 ^{b&}
JN	2.24	1.88	1.86 [#]	1.77 [#]	1.67 [#]	1.39 ^{abc#}	1.18 ^{b#}
JNH	2.25	1.83 ^{&}	1.59 ^{&}	1.45 ^{&}	1.45 ^{&}	1.42 ^{abc&}	1.37 ^{ab&}
SN	2.24	1.99	2.00	1.62 [#]	1.40 [#]	1.46 ^{ab#}	1.38 ^{ab#}
SNH	2.30	2.08	1.64 ^{&}	1.62 ^{&}	1.42 ^{&}	1.26 ^{bc&}	1.28 ^{ab&}
SEM	0.034	0.039	0.050	0.053	0.058	0.058	0.057
Cu-NP dose (D)							
L (6.5 mg/kg)	2.25	1.92	1.84 ^a	1.63 ^a	1.45 ^a	1.34	1.18
H (13 mg/kg)	2.26	1.95	1.57 ^b	1.39 ^b	1.21 ^b	1.04	1.04
P value	0.877	0.692	0.003	0.004	<0.001	<0.001	0.012
Fiber type (F)							
C (cellulose)	2.24	1.77 ^b	1.33 ^b	0.904 ^c	0.689 ^c	0.595	0.535
P (pectin)	2.27	2.07 ^a	1.95 ^a	1.90 ^a	1.65 ^a	1.39	1.31
J (inulin)	2.25	1.86 ^{ab}	1.73 ^a	1.61 ^b	1.56 ^{ab}	1.41	1.28
S (psyllium)	2.27	2.04 ^a	1.82 ^a	1.62 ^b	1.41 ^b	1.36	1.33
P value	0.988	0.029	<0.001	<0.001	<0.001	<0.001	<0.001
Interaction D×F							
P value	0.991	0.413	0.922	0.248	0.113	0.011	0.002

*Control C and CH groups, fed a control diet containing CuCO_3 of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

Table S8. Fecal microbial total α -arabinofuranosidase activity ($\mu\text{mol/h/g}$) during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	3.77	3.70	3.79	3.63	3.84	3.76	3.67
Control CH	3.70	3.79	3.77	3.37	3.51	3.42	3.52
2-way ANOVA:							
CN	3.73	3.16 [#]	2.63 [#]	2.20 [#]	2.03 [#]	1.96 [#]	1.78 ^{d#}
CNH	3.69	3.01 ^{&}	2.19 ^{&}	1.48 ^{&}	1.31 ^{&}	1.14 ^{&}	1.16 ^{e&}
PN	3.72	3.73	4.09	4.41 [#]	4.29 [#]	4.31 [#]	4.17 ^{a#}
PNH	3.73	3.79	3.83	3.93 ^{&}	3.78 ^{&}	3.41	3.31 ^b
JN	3.70	3.38	3.58	3.54	3.53 [#]	3.41 [#]	3.25 ^{b#}
JNH	3.71	3.17 ^{&}	3.11 ^{&}	3.04 ^{&}	2.93 ^{&}	2.71 ^{&}	2.79 ^{c&}
SN	3.72	3.71	3.81	3.90 [#]	3.80	4.03 [#]	4.04 ^{a#}
SNH	3.79	3.70	3.34 ^{&}	3.43	3.42	3.32	3.43 ^b
SEM	0.040	0.043	0.071	0.088	0.091	0.096	0.094
Cu-NP dose (D)							
L (6.5 mg/kg)	3.72	3.50	3.53 ^a	3.51 ^a	3.41 ^a	3.43 ^a	3.31
H (13 mg/kg)	3.73	3.42	3.11 ^b	2.97 ^b	2.86 ^b	2.64 ^b	2.68
P value	0.871	0.307	<0.001	<0.001	<0.001	<0.001	<0.001
Fiber type (F)							
C (cellulose)	3.71	3.09 ^b	2.41 ^c	1.84 ^d	1.67 ^d	1.55 ^c	1.47
P (pectin)	3.73	3.76 ^a	3.96 ^a	4.17 ^a	4.04 ^a	3.86 ^a	3.75
J (inulin)	3.71	3.28 ^b	3.34 ^b	3.29 ^c	3.23 ^c	3.06 ^b	3.03
S (psyllium)	3.76	3.71 ^a	3.57 ^b	3.67 ^b	3.61 ^b	3.67 ^a	3.74
P value	0.982	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Interaction D×F							
P value	0.987	0.567	0.824	0.581	0.282	0.674	0.038

*Control C and CH groups, fed a control diet containing CuCO_3 of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

Table S9. Fecal content ($\mu\text{mol/g}$) of putrefactive short-chain fatty acids (*iso*-butyric+*iso*-valeric+valeric acids) during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	6.92	6.23	6.44	7.08	7.12	6.85	6.52
Control CH	6.35	6.01	6.06	6.85	7.03	6.55	6.97
2-way ANOVA:							
CN	6.69	5.42	5.64 [#]	5.66 [#]	6.22 ^{b#}	5.99 ^{b#}	6.05 ^{b#}
CNH	6.31	4.15 ^{&}	3.99 ^{&}	4.23 ^{&}	3.22 ^{e&}	3.32 ^{f&}	3.37 ^{f&}
PN	6.76	5.51	6.33	7.00	7.37 ^a	7.43 ^a	6.89 ^a
PNH	6.57	4.85	5.52 ^{&}	5.41 ^{&}	5.90 ^{b&}	5.03 ^{c&}	5.08 ^{c&}
JN	6.69	5.34	5.49 [#]	5.30 [#]	5.17 ^{c#}	4.72 ^{cd#}	4.26 ^{de#}
JNH	6.13	4.29 ^{&}	4.02 ^{&}	4.06 ^{&}	4.01 ^{d&}	4.16 ^{e&}	4.04 ^{e&}
SN	6.16	5.04 [#]	5.40 [#]	5.47 [#]	5.02 ^{c#}	4.78 ^{cd#}	4.48 ^{de#}
SNH	6.20	4.43 ^{&}	3.86 ^{&}	3.63 ^{&}	3.54 ^{e&}	4.35 ^{de&}	4.53 ^{d&}
SEM	0.112	0.113	0.111	0.131	0.152	0.138	0.134
Cu-NP dose (D)							
L (6.5 mg/kg)	6.58	5.33 ^a	5.71 ^a	5.86 ^a	5.94	11.0	8.55
H (13 mg/kg)	6.29	4.42 ^b	4.31 ^b	4.31 ^b	4.13	7.73	6.09
P value	0.214	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Fiber type (F)							
C (cellulose)	6.50	4.79	4.82 ^b	4.95 ^b	4.72	4.66	4.71
P (pectin)	6.66	5.19	5.93 ^a	6.26 ^a	6.69	6.28	5.98
J (inulin)	6.41	4.82	4.76 ^b	4.68 ^b	4.59	4.44	4.15
S (psyllium)	6.18	4.73	4.63 ^b	4.55 ^b	4.28	4.56	4.50
P value	0.539	0.492	<0.001	<0.001	<0.001	<0.001	<0.001
Interaction D×F							
P value	0.821	0.635	0.234	0.548	<0.001	<0.001	<0.001

*Control C and CH groups, fed a control diet containing CuCO_3 of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

Table S10. Fecal content ($\mu\text{mol/g}$) of total short-chain fatty acids during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	77.7	75.5	76.9	81.6	81.0	85.0	82.0
Control CH	78.5	74.4	77.2	79.1	78.8	84.8	79.2
2-way ANOVA:							
CN	79.5	65.8 [#]	62.4 [#]	58.3 [#]	51.8 ^{d#}	47.9 ^{f#}	45.2 ^{g#}
CNH	75.7	58.8 ^{&}	53.6 ^{e&}	50.1 ^{f&}	43.8 ^{e&}	40.1 ^{g&}	36.4 ^{h&}
PN	77.3	67.8 [#]	70.6 ^b	79.0 ^b	81.8 ^a	88.6 ^{a#}	87.6 ^{a#}
PNH	78.8	61.3 ^{&}	59.6 ^{cd&}	60.5 ^{e&}	64.0 ^{c&}	64.0 ^{d&}	63.8 ^{d&}
JN	78.1	71.4 [#]	75.0 ^a	84.3 ^a	83.0 ^a	82.6 ^b	83.9 ^b
JNH	76.1	60.1 ^{&}	62.4 ^{c&}	74.6 ^{c&}	74.8 ^{b&}	71.7 ^{c&}	70.2 ^{c&}
SN	76.8	64.5 [#]	60.5 ^{cd#}	67.3 ^{d#}	60.8 [#]	54.9 ^{e#}	53.5 ^{e#}
SNH	77.8	60.0 ^{&}	57.1 ^{de&}	51.0 ^{f&}	51.0 ^{d&}	49.6 ^{f&}	48.4 ^{f&}
SEM	0.468	0.739	0.909	1.284	1.482	1.750	1.790
Cu-NP dose (D)							
L (6.5 mg/kg)	77.9	67.4 ^a	67.1	72.2	69.3	68.5	67.5
H (13 mg/kg)	76.7	60.1 ^b	58.2	59.1	58.2	56.1	54.4
P value	0.211	<0.001	<0.001	<0.001	<0.001	0.001	<0.001
Fiber type (F)							
C (cellulose)	77.6	62.3	58.0	54.1	47.8	44.0	40.8
P (pectin)	77.7	64.9	65.4	70.5	73.2	76.8	76.3
J (inulin)	77.1	65.8	68.7	79.5	78.9	77.2	77.1
S (psyllium)	76.9	62.2	58.8	59.2	55.9	52.2	50.9
P value	0.927	0.167	<0.001	<0.001	<0.001	<0.001	<0.001
Interaction D×F							
P value	0.299	0.147	0.006	<0.001	0.002	<0.001	<0.001

*Control C and CH groups, fed a control diet containing CuCO_3 of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

Table S11. Fecal pH values during the experimental feeding period in rats*.

	Day 0	Day 1	Day 2	Day 7	Day 14	Day 21	Day 42
Control C	7.36	7.31	7.29	7.29	7.30	7.28	7.30
Control CH	7.37	7.37	7.32	7.34	7.36	7.33	7.34
2-way ANOVA:							
CN	7.36	7.36	7.33	7.34	7.34	7.33	7.33
CNH	7.37	7.37	7.32	7.34	7.36	7.33	7.34
PN	7.37	7.28	7.25	7.23 [#]	7.22	7.23	7.24
PNH	7.37	7.35	7.27	7.25	7.24	7.26	7.27
JN	7.36	7.30	7.20 [#]	7.15 [#]	7.25	7.28	7.29
JNH	7.37	7.31	7.24 ^{&}	7.21 ^{&}	7.28	7.30	7.30
SN	7.38	7.37	7.32	7.24	7.20 [#]	7.23	7.23
SNH	7.37	7.38	7.30	7.24	7.24	7.25	7.26
SEM	0.012	0.009	0.008	0.010	0.010	0.009	0.010
Cu-NP dose (D)							
L (6.5 mg/kg)	7.37	7.33	7.27	7.24	7.25	7.27	7.27
H (13 mg/kg)	7.37	7.35	7.28	7.26	7.28	7.29	7.29
P value	0.922	0.266	0.680	0.334	0.176	0.316	0.315
Fiber type (F)							
C (cellulose)	7.36	7.37 ^a	7.32 ^a	7.34 ^a	7.35 ^a	7.33 ^a	7.33 ^a
P (pectin)	7.37	7.31 ^{ab}	7.26 ^{bc}	7.24 ^b	7.23 ^b	7.25 ^b	7.26 ^b
J (inulin)	7.36	7.30 ^b	7.22 ^c	7.18 ^c	7.26 ^b	7.29 ^{ab}	7.30 ^{ab}
S (psyllium)	7.38	7.37 ^a	7.31 ^{ab}	7.24 ^b	7.22 ^b	7.24 ^b	7.25 ^b
P value	0.982	0.034	<0.001	<0.001	<0.001	0.007	0.032
Interaction D×F							
P value	0.985	0.717	0.572	0.692	0.983	0.939	0.979

*Control C and CH groups, fed a control diet containing CuCO₃ of 6.5 and 13 mg/kg, respectively and 8% of cellulose ($n=10$ per group); groups CN and CNH, fed diets containing Cu-nanoparticle (Cu-NP) of 6.5 and 13 mg/kg from, respectively, and 8% of cellulose ($n=10$ per group); groups PN and PNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of pectin ($n=10$ per group); groups JN and JNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of inulin ($n=10$ per group); groups SN and SNH, fed diets containing Cu-NP of 6.5 and 13 mg/kg, respectively, 2% of cellulose and 6% of psyllium ($n=10$ per group); L, treatment with diets containing Cu-NP of 6.5 mg/kg ($n=40$); H, treatment with diets containing Cu-NP of 13 mg/kg dose ($n=40$); C, treatment with cellulose ($n=20$); P, treatment with pectin ($n=20$); J, treatment with inulin ($n=20$); S, treatment with psyllium ($n=20$). Significant differences among the CN, CNH, PN, PNH, JN, JNH, SN, SNH groups are indicated with different superscript letters (a–f), only in the case of a significant interaction D×F ($p<0.05$). Significant differences between each group fed diet containing Cu-NP of 6.5 mg/kg (CN, PN, JN, SN) and the control C are indicated by # (t -test, $p<0.05$). Significant differences between each group fed diet containing Cu-NP of 13 mg/kg (CNH, PNH, JNH, SNH) and the control CH are indicated by & (t -test, $p<0.05$). SEM, pooled standard error of mean (standard deviation for all rats divided by the square root of rat number, $n=100$).

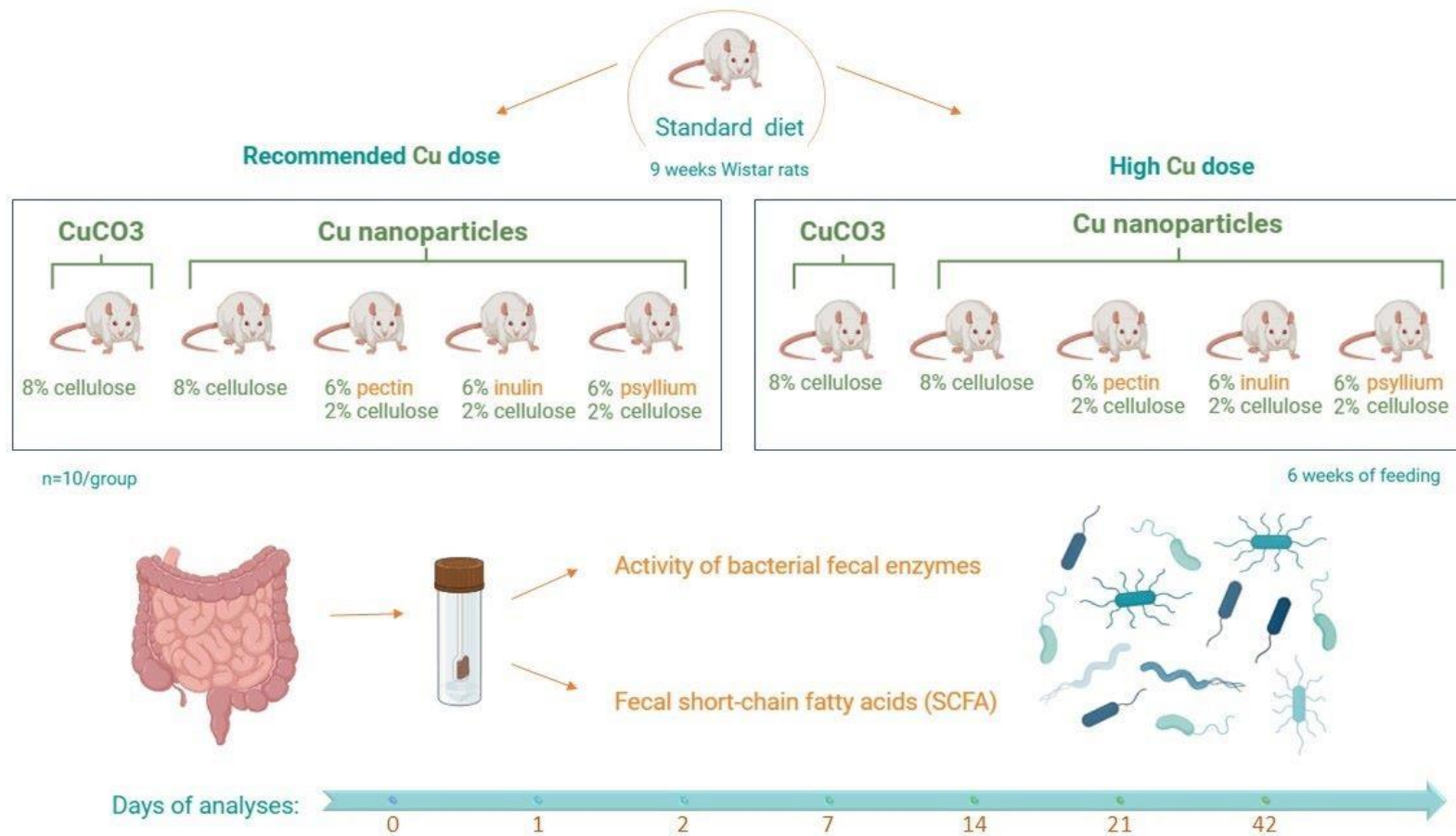


Figure S1. Experimental schema.