



Linking carbohydrate science and health longevity

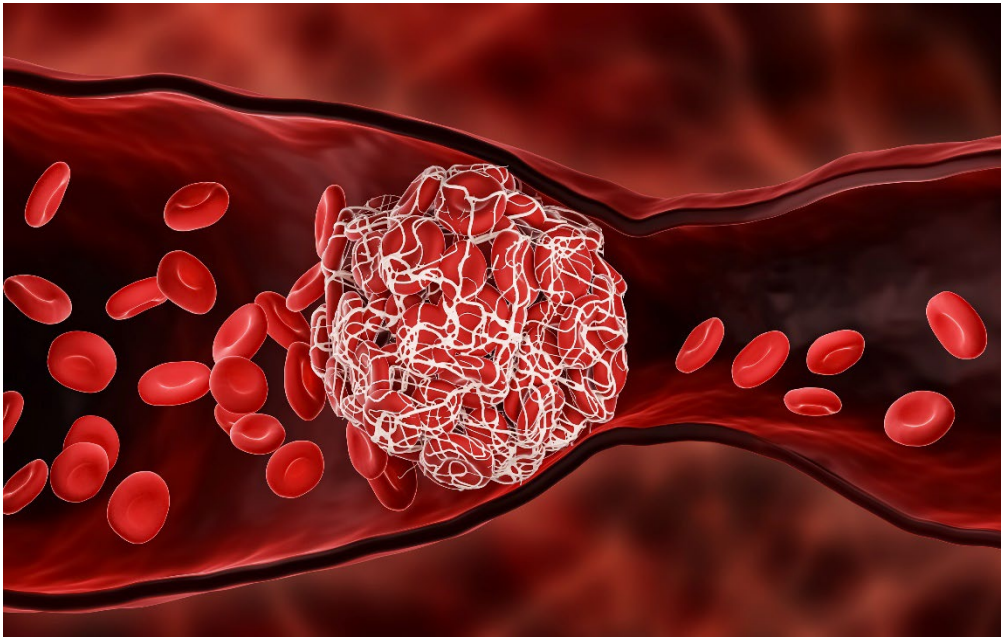
MARUKYOU BIO FOODS Co.

Nano247

**A new hypertension remedy using
chondroitin sulfate oligosaccharide**

What is hypertension?

Hypertension is also known as a silent killer, as it gradually damages tissues without causing any subjective symptoms, and can eventually lead to serious conditions such as cerebral infarction and myocardial infarction.



The causes of hypertension are not uniform, and are extremely diverse. Excess salt intake, obesity, arteriosclerosis, stress, etc. are all factors, but the main cause is still excessive salt intake in the diet.



Countermeasures for hypertension

Excessive salt intake, which is the cause of most cases, occurs when the blood volume expands because the salt absorbed into the blood is diluted and water is also absorbed to lower the osmotic pressure.

Therefore, in order to improve this,

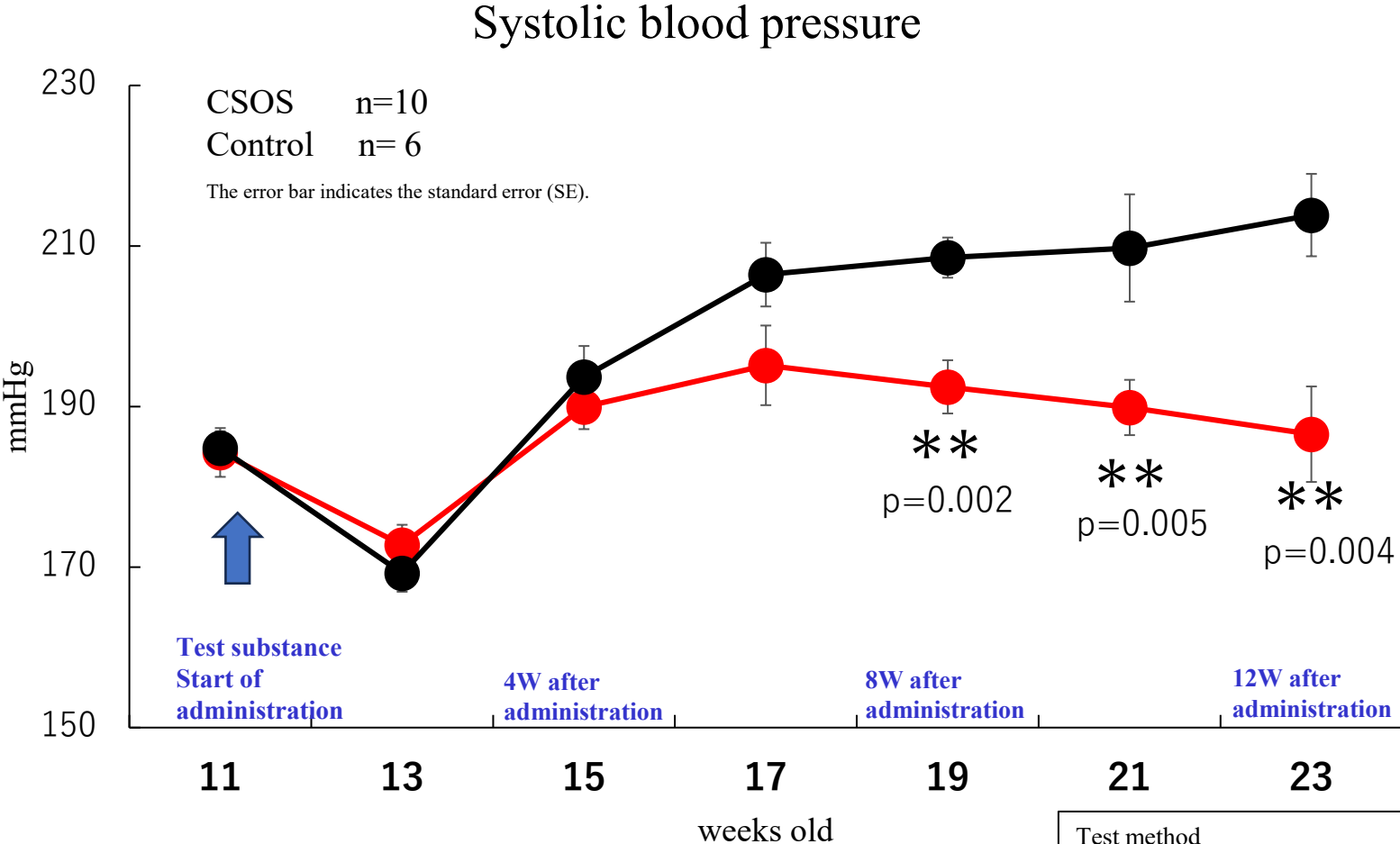
- (1) the amount of salt intake must be reduced**
- (2) the amount of salt reabsorption must be reduced**

1. Administration test on hypertensive model rats

Animals used	Spontaneously hypertensive rats (SHR)
Test substance	Nano247 chondroitin sulfate oligosaccharide (Mw.2000)
Dose	20 mg / head / day (equivalent to 800 mg / man / day in humans)
Administration method	Mixed feed administration
Group composition	10 test substance administration group, 6 non-administration group
Evaluation items	Blood pressure (once every two weeks)
Duration of administration	12 weeks (23 weeks old)

Spontaneously hypertensive rats (SHR) are a strain of rat that develops hypertension with age without any artificial treatment, and have a genetic characteristic. Their systolic blood pressure rises to over 200.

1. Test results



Test method
Comparison of two samples: Test for difference in mean
One-sided t-test for each week
Alternative hypothesis: Active < Placebo
Significance level < 0.05

The administration of CS oligosaccharides significantly suppressed the increase in systolic blood pressure.

Conclusion

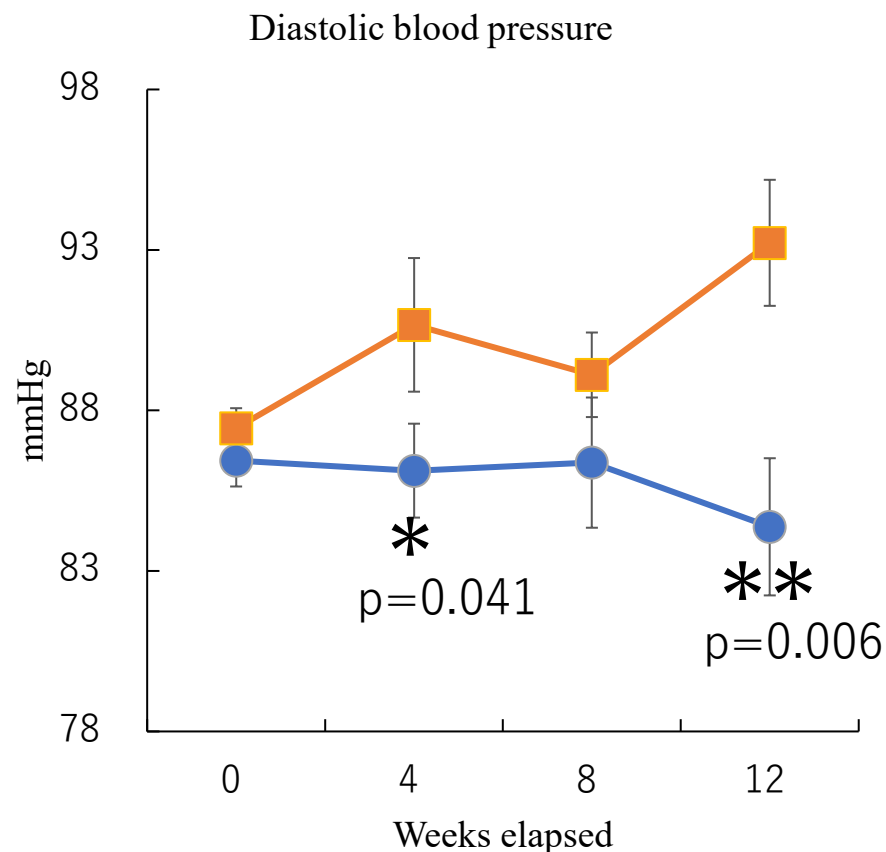
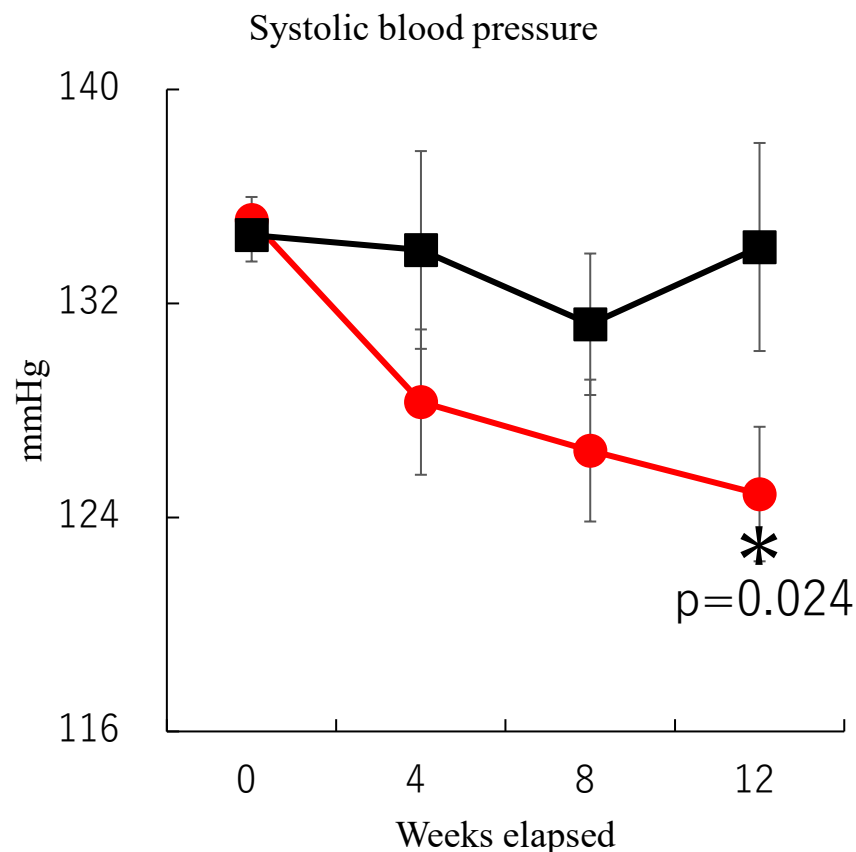
**Chondroitin sulfate oligosaccharides
inhibit the rise in blood pressure in
hypertensive model rats when
administered orally.**

2. Human intervention study

Test Subject Title	A placebo-controlled, randomized, double-blind, parallel-group comparative study of the effect of continuous intake of chondroitin sulfate oligosaccharide on blood pressure improvement
Test Purpose	To investigate the effect of continuous intake of chondroitin sulfate oligosaccharide on blood pressure improvement and safety in a placebo-controlled, randomized, double-blind, parallel-group comparative study.
Subjects	Adult men and women aged 40 to 65 years with a systolic blood pressure of 130 to 139 mmHg and a diastolic blood pressure of 89 mmHg or less at the time of visit
Study design	Placebo-controlled, randomized, double-blind, parallel-group comparative study
Group composition	Placebo food intake group and test food intake group (Dose : 100 mg / head / day/ human)
Registered users	70 (35 in each group)
Number of participants enrolled	69 (34 in the placebo food intake group, 35 in the test food intake group)
Intake period	12 weeks
Evaluation period	Before intake, 4 weeks after intake, 8 weeks after intake, 12 weeks after intake
Main evaluation items	① Blood pressure (systolic blood pressure, diastolic blood pressure) at the time of visit Secondary evaluation items
Secondary evaluation items	① Blood glucose (blood glucose level, HbA1c) ② FMD (Flow-mediated dilatation) (only before the start of intake and 12 weeks after intake) ③ CAVI (Cardio-ankle vascular index) (only before the start of intake and 12 weeks after intake)

2-1. Test results: Human intervention study: Blood pressure

(Subclass analysis: males with T-Chol of 200 or more)



● Active-H ■ Placebo-H

● Active-L ■ Placebo-L

Active n=16

Placebo n= 9

The error bar indicates the standard error (SE).

Test method

Comparison of two samples: Test for difference in population means (one-sided t-test for each week)

Alternative hypothesis: Active < Placebo

Significance level < 0.05

Blood pressure in the CSOS group was significantly lower than in the placebo group.

2-2. Human Intervention Study: Blood Test Results

(Subclass analysis: males with T-Cho of 200 or more)

項目	treat	0W	12W	差
White blood cell count	Active	5,786	5,306	-480
	Placebo	5,784	5,068	-716
Red blood cell count	Active	492	482	-10
	Placebo	477	473	-4
Hemoglobin level	Active	15.1	14.7	0
	Placebo	13.2	13.1	0
hematocrit	Active	45	45	0
	Placebo	45	45	0
MCV	Active	92	94	2
	Placebo	95	95	0
MCH	Active	30.7	30.4	0
	Placebo	31.8	31.7	0
MCHC	Active	33.3	32.4	-1
	Placebo	33.4	33.2	0
Platelet count	Active	26.6	25.2	-1
	Placebo	25.3	23.1	-2
TP	Active	7.3	7.1	0
	Placebo	7.4	7.1	0
ALB_BCP	Active	4.5	4.4	0
	Placebo	4.6	4.4	0
T_Bil	Active	0.6	0.7	0
	Placebo	0.8	0.8	0
ALP	Active	69.5	68.0	-2
	Placebo	75.5	73.9	-2
LD	Active	175.3	173.4	-2
	Placebo	197.0	191.8	-5

項目	treat	0W	12W	差
AST	Active	21.6	21.7	0
	Placebo	22.1	24.4	2
ALT	Active	21.6	21.0	-1
	Placebo	18.8	20.3	2
g_GT	Active	28.7	29.8	1
	Placebo	51.0	45.8	-5
CK	Active	153.9	118.1	-36
	Placebo	133.6	149.0	15
T-Cho	Active	231.3	230.8	-1
	Placebo	224.1	226.5	2
neutral fat	Active	123.5	130.3	7
	Placebo	120.1	125.5	5
HDL_C	Active	66.1	64.1	-2
	Placebo	66.8	63.6	-3
LDL_C	Active	142.8	142.8	0
	Placebo	136.8	140.9	4
urea nitrogen	Active	13.8	13.5	0
	Placebo	13.0	15.3	2
Creatinine	Active	0.8	0.9	0
	Placebo	0.8	0.8	0
UA	Active	5.9	6.1	0
	Placebo	6.3	6.5	0
blood sugar_fasting	Active	98.9	97.4	-2
	Placebo	103.0	99.3	-4
HbA1c_NGSP	Active	5.5	5.6	0
	Placebo	5.3	5.4	0

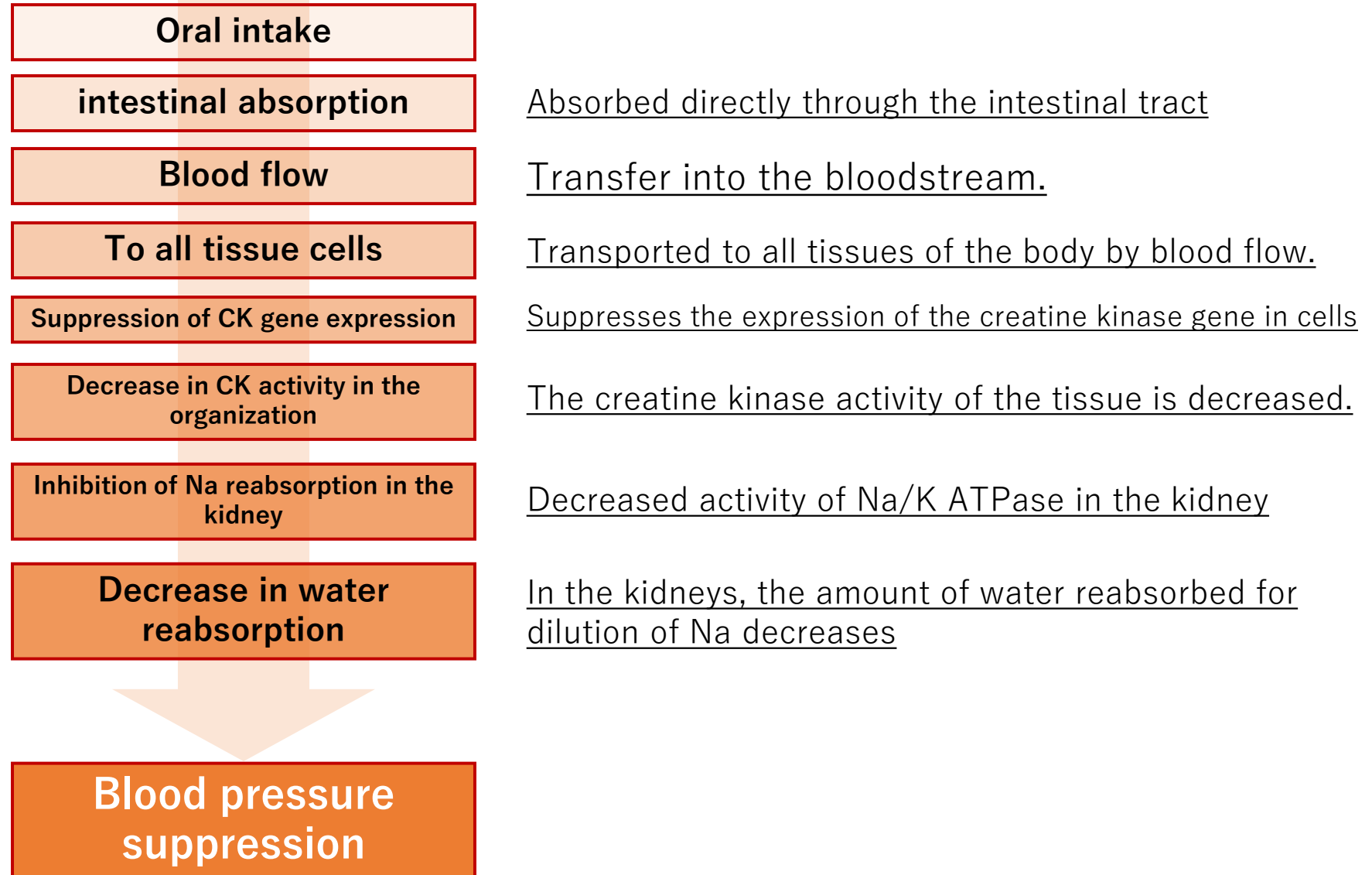
Chondroitin sulfate oligosaccharides significantly reduce blood CK levels.

Conclusion

**Chondroitin sulfate oligosaccharides
suppress hypertension in humans
when taken orally
and their effects can be measured
using blood markers.**

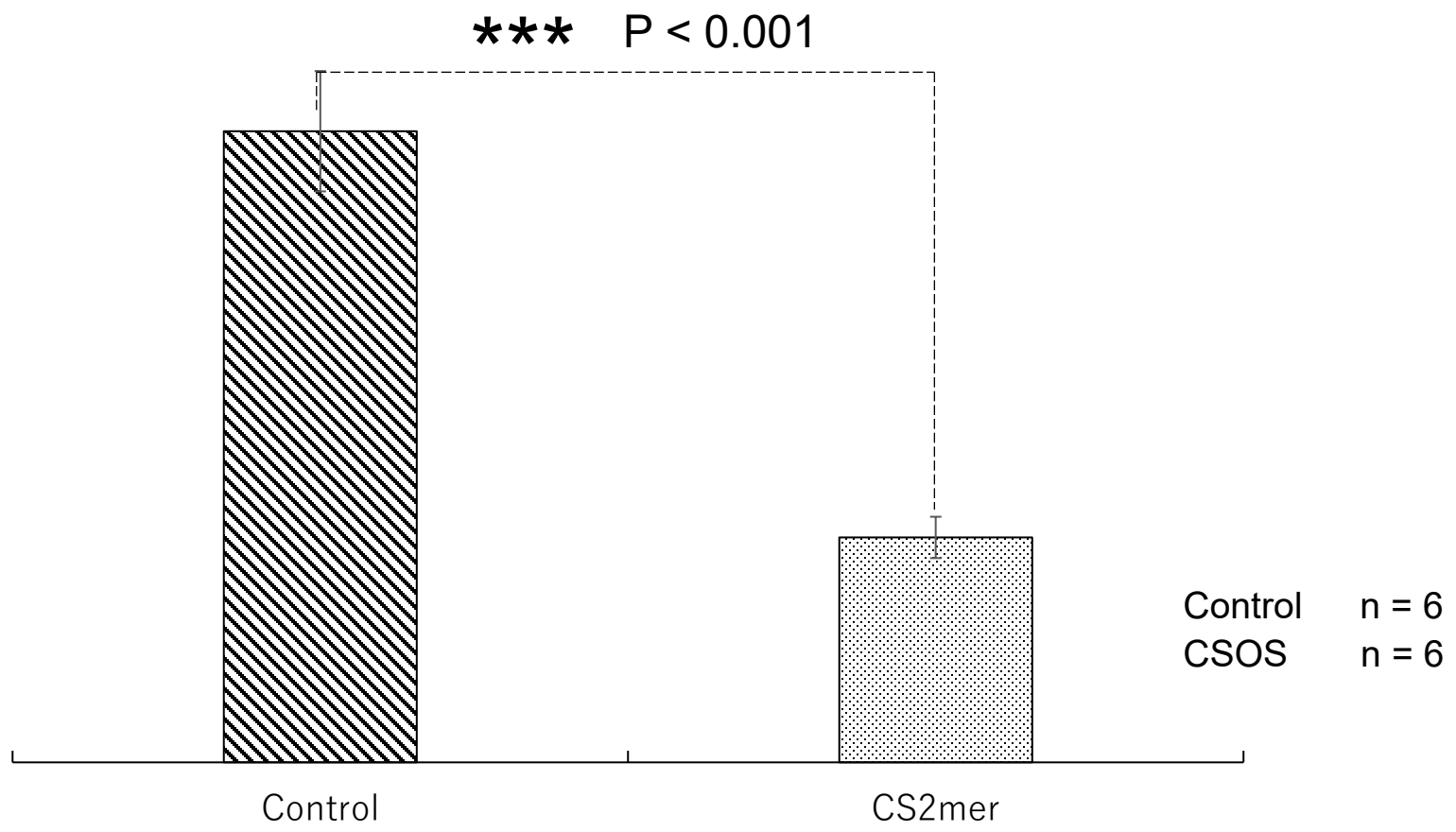
The mechanism of blood pressure suppression by chondroitin sulfate oligosaccharides

chondroitin sulfate oligosaccharides



3. Supplementary data: Verification in Cell Tests

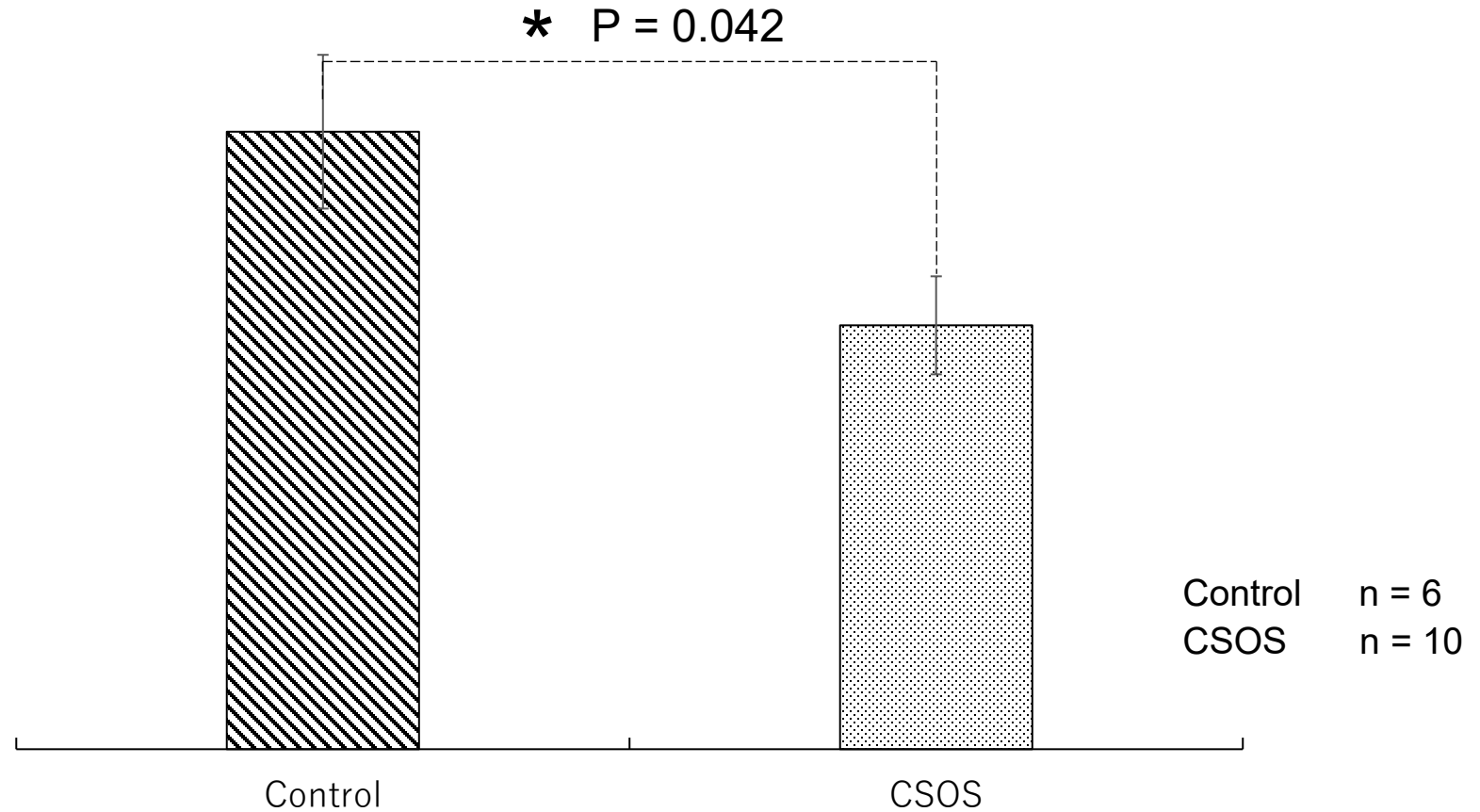
Amount of creatine kinase gene expression in cultured cells



CS oligosaccharides addition significantly suppresses CK-B gene expression

3. Supplementary data: Verification in animal tissue (hypertension model rats)

Amount of creatine kinase gene expression in rat kidneys



CS oligosaccharides administration significantly suppresses CK-B gene expression