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Abstract

TITLE: Protective role of flavonoids against colonic motor dysfunctions associated with high fat diet-induced obesity

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ABSTRACT BODY:

Abstract Body: Introduction. Obesity is a chronic disease characterized by low-grade systemic inflammation and by alteration in gastrointestinal motility. Recently, the beneficial effects of flavonoids in the prevention of some comorbidities associated with obesity have been reported. However, their putative effects in counteracting the enteric functional disorders related to obesity have not been investigated. This study examines the effect of dietary supplementation with luteolin, apigenin and naringenin on colonic motor and inflammatory abnormalities in a mouse model of diet-induced obesity.

Methods. C57BL/6 mice (n=5/group) were fed with standard diet (SD, 18% calories from fat) or a high-fat diet (HFD, 60% calories from fat) for 8 weeks. Subgroups of mice on SD or HFD were treated for 8 weeks with luteolin (10 mg/Kg/die), apigenin (10 mg/Kg/die) and naringenin (10 mg/Kg/die). At the end of the treatments, body and epididymal fat weight, as well as blood cholesterol, triglycerides and glucose levels were evaluated. Malondialdehyde (MDA), IL-1β and IL-6 levels in colonic tissue were also examined. Colonic longitudinal muscle strips (LMS) were set up in organ baths with Krebs solution and connected to isometric transducers to record contractions elicited by electrical stimulation (ES, 10 Hz, 0.5 msec, 30 mA). N^{ω}-nitro-L-arginine methylester, alone or in combination with guanethidine, atropine, NK_2 and NK_3 receptor antagonists were used to record nitrergic and NK_1 receptor-mediated tachykininergic motor responses.

Results. When compared with SD mice, HFD animals displayed an increase in body and epididymal fat weight with alterations of blood metabolic indexes (Table 1). Colonic tissues from HFD mice showed also an increase in MDA, IL-1β and IL-6 levels versus SD mice (Table 1). Colonic LMS obtained from obese mice displayed an enhancement of electrically evoked nitrergic and tachykininergic responses (+48% and +126% vs SD mice, respectively). Dietary supplementation with luteolin, apigenin, and naringenin counteracted the increase of body and epididymal fat weight, as well as the alterations of metabolic indexes in HFD-fed mice (Table 1). In addition, flavonoids administration reduced MDA, IL-1β, IL-6 tissue levels in obese animals (Table 1). Luteolin, apigenin and naringenin treatment normalized the enhancement of colonic nitrergic and tachykininergic contractions. Of note, treatment with flavonoids did not induce significant changes in metabolic, inflammatory and functional parameters in SD-fed animals, in comparison with untreated mice.

Conclusion. Diet-supplementation with luteolin, apigenin and naringenin prevented metabolic alterations associated with obesity. Moreover, flavonoids administration resulted in a reduction of intestinal inflammation and in counteract the colonic contractile dysfunctions associated with obesity.

TABLE:

Table of the results

.	SD	HFD	HFD+luteolin	HFD+apigenin	HFD+naringenin
Body and epididymal fat weight	.				
Body weight gain (%)	36±2	74±2.6a	46±2*	20±1.8#	28±3.3*
Epididymal fat weight (g)	0.3±0.02	1.8±0.1c	0.9±0.08*	0.5±0.03$	0.6±0.09$
Metabolic indexes	.				
Cholesterol (mg/dL)	145±5.4	182±7.7a	146±7.5*	142±5.3*	134±3.2#
Triglycerides (mg/dL)	118±2.4	149.5±0.03a	143±8.5	109±6.8*	112±2.8*
Glucose (mg/dL)	128±7	166±4.8a	133±6*	120±7.3*	116±8.1*
Inflammatory parameters	.				
MDA (nmol/mg tissue)	21 ± 2	59 ± 3.1c	33.5 ± 3.9*	29 ± 2.3*	36.4 ± 4 #
IL-1β (pg/mg tissue)	3.6±0.04	7.6±0.4c	2.1±0.6#	3.3±0.2#	1.8±0.1#
IL-6 (pg/mg tissue)	0.08±0.01	0.38 ± 0.05a	0.06±0.01*	0.1±0.07*	0.12±0.02*
aP < 0.05, cP < 0.001 versus SD *P < 0.05, $P < 0.01, #P < 0.001 versus HFD					

(No Image Selected)