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The Effect of Onion Peel Extract on Inflammatory Mediators in Korean Overweight and Obese Women

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Conflict of Interest
The authors have no potential conflicts of interest to disclose.

ABSTRACT

Quercetin, found abundantly in onion peel, has been known to have antioxidant and anti-obesity effects and improves endothelial function. The purpose of this study was to evaluate the effects of a quercetin-rich onion peel extract (OPE) on the inflammatory mediators in overweight and obese women. This study was a randomized double-blind, placebo-controlled study. Thirty-seven healthy overweight and obese women were randomly assigned to two groups, and one group was given a soft capsuled OPE (100 mg quercetin/day, n = 18) and the other group a same capsuled placebo (n = 19) for 12 weeks. Fat mass was measured by bioimpendance method at baseline and after 12 weeks of intervention. The levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured with colorimetric assay kits. The concentrations of leptin, adiponectin, visfatin, tumor necrosis factor (TNF)-α and interleukin (IL)-4 in plasma were determined by using enzyme-linked immunosorbent assay kits. Baseline characteristics of anthropometric indicators and blood metabolic profiles were not significantly different between placebo and OPE groups. Compared with baseline value, both placebo and OPE supplementation significantly decreased the percent of body fat mass and induced plasma adiponectin levels while ALT and AST activities as well as leptin, visfatin, TNF-α, and IL-4 levels in plasma were not significantly different between two groups after 12 weeks of the supplementation. These findings suggest that 12-week supplementation of OPE do not affect modulators of systemic inflammation in overweight and obese women.

Keywords: Onion peel extract; Quercetin; Obesity; Inflammation; Adiponectin

INTRODUCTION

The prevalence of overweight and obesity is increasing at an alarming rate worldwide. In the analyses for the Global Burden of Disease Study, Ng et al. [1] reported that about 37% of men and 27% of women were obese (body mass index [BMI] ≥ 25 kg/m^2) in South Korea. Obesity and its associated metabolic alterations are linked with a chronic low-grade systemic inflammatory response, which is characterized by abnormal production of pro-inflammatory cytokines and activation of inflammatory signaling pathways [2]. Extensively reviewed evidences demonstrate that adipose tissue plays an important role in inflammation and thus acts as a major contributor to the elevation of inflammatory activity [3]. Indeed, various

Author Contributions

Kyung-Ah Kim was responsible for experimental anaysis and writing of manyscript and Jung-Eun Yim was responsible for study design, experimental anaysis, and writing of manuscript.

secreted products from adipocytes/adipose tissue, so called adipokines or adipocytokines, have been characterized. Adipokines, adiponectin, leptin, resistin, and visfatin are considered as an important link between obesity and related inflammatory diseases [4]. Furthermore, the infiltration of macrophages in adipose tissue and then altered production of inflammatory cytokines such as tumor necrosis factor (TNF)-α and interleukin (IL)-4 may contribute to the mechanisms underlying the development of inflammation [5,6]. Therefore, the application of natural resources such as vegetables has recently become a focus of interest as potential source of anti-inflammatory substances to prevent obesity and its associated metabolic diseases.

Quercetin, found abundantly in onion peel, is one of the major plant-derived flavonoids. It has been known to have anti-diabetes, anti-obesity, and anti-hypertensive effects in animal and human studies [7-10]. Recently, we reported that 12-week supplementary intake of quercetin-rich onion peel extract (OPE) significantly decreased body weight and percentage of body fat in overweight and obese adults [11]. We also have demonstrated that quercetin-rich OPE consumption for 12 weeks may exert antioxidative activity by preventing the reduction of superoxide dismutase (SOD) activity as well as the production of reactive oxygen species (ROS) in obese women [12]. In addition, several recent studies have demonstrated that OPE has anti-inflammatory property in vitro as well as in animal models [13,14]. However, little has been known about the effect of OPE on the inflammatory mediators in obese human. Therefore, the aim of this study was for the first time to examine the effect of quercetin-rich OPE supplementation on the pro- and anti-inflammatory mediators in overweight and obese women.

MATERIALS AND METHODS

Subjects

This study was a 12-week, randomized, double-blind, placebo-controlled study. Thirty-seven overweight and obese women were recruited (BMIs > 23 kg/m^2). The study was approved and conducted by the institutional review board of Kyung Hee Medical Center (KMC IRB 1304-03-C1), and all subjects agreed to participate in this study and signed written informed consents forms. Subjects who had psychological disease, hypertension, diabetes mellitus, infectious diseases, and medical or surgical illness within 3 months of enrollment were excluded from the study.

Study design

We randomly assigned using a computerized random allocation sequence of thirty-seven subjects of whom nineteen were assigned to a placebo and another eighteen were assigned to an OPE. The OPE was acquired from Changnyeong between August and September 2012, and passed through an OPE powder manufacturing process [15]. The OPE group was received 100 mg of quercetin [15] daily for 12 weeks, while placebo group was treated with identically-packaged soft capsules containing lactose mixture [16].

Anthropometric analysis

Anthropometric measurements were measured at baseline and at 12th week of intervention. Body weight and height were measured twice by a single trained registered dietitian. BMI was calculated as weight in kg divided by height in meters squared. Fat free mass (FFM), body fat mass (BFM), and percent of body fat mass (PBFM) were measured by bioimpedance analysis (Inbody 3.0; Biospace, Seoul, Korea).

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Biochemical analysis

The blood samples of subjects were taken baseline and at 12 weeks of intervention, and were collected after a 12-hour overnight fasting. The samples were centrifuged and plasma were frozen and stored at −60°C. Plasma levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured with colorimetric method using enzymatic analysis kits (Asan Phamaceuticals Co., Ltd., Hwasung, Korea). Plasma levels of adiponectin and leptin were measured by an enzyme-linked immunosorbent assay (ELISA) using Alpco kits (ALPCO Diagnostics; Salem, NH, USA). Visfatin was analyzed by a sandwich ELISA using kits from LifeSpan BioSciences, Inc. (Seattle, WA, USA). TNF-α and IL-4 levels were determined using ELISA kits from Enzo Life Sciences, Inc. (Farmingdale, NY, USA).

Statistical analysis

The data in this study were statistically analyzed with the Statistical Analysis System software package (SAS 9.1; SAS Institute Inc., Cary, NC, USA). Data were expressed as means and standard deviation values. The anthropometric data and biochemical data from placebo and OPE-treated groups before and after the intervention were analyzed by a paired t-test. The difference between the placebo and OPE-treated groups was analyzed by a t-test. All statistical results were defined as a p value less than 0.05.

RESULTS

Effects of OPE on anthropometric measurements

Baseline characteristics of anthropometric indicators were not significantly different between the two groups. On assessing body weight, BMI, FFM, and BFM after 12 weeks of supplementation, no significant difference was found between the placebo and OPE-treated groups. Compared with baseline values, both placebo and OPE significantly reduced PBFM while no significant inter-group difference was found (**Table 1**).

Effects of OPE on plasma metabolic parameters

The activities of ALT and AST before and after the 12-week treatment were not significantly different between the two groups (**Table 2**).

Plasma adipokines, adiponectin levels were increased in placebo and OPE-treated groups compared with baseline values. However, no significant differences were found between the two groups (**Table 3**). Compared with baseline values, the levels of IL-4 and TNF-α were

Table 1. Anthropometric measurement of subjects during 12 weeks of intervention

Variables	Placebo (n = 19)			OPE (n = 18)		
	Baseline	12 wk	Change, %	Baseline	12 wk	Change, %
Age, yr	45.4 ± 9.5	-	-	44.6 ± 7.6	-	-
Height, cm	159.0 ± 6.3	-	-	159.2 ± 4.1	-	-
Weight, kg	67.2 ± 6.8	67.2 ± 6.6	0.02 ± 3.90	65.9 ± 9.2	65.4 ± 8.9	−0.68 ± 1.80
BMI, kg/m^2	26.6 ± 2.5	26.6 ± 2.4	0.02 ± 3.90	26.0 ± 3.8	25.8 ± 3.6	−0.68 ± 1.80
FFM, kg	43.7 ± 3.9	23.8 ± 4.2	0.30 ± 3.10	42.1 ± 4.4	22.0 ± 4.5	−0.30 ± 2.30
BFM, kg	23.6 ± 4.5	23.4 ± 4.1	0.20 ± 5.20	23.7 ± 6.3	23.4 ± 5.9	−1.10 ± 5.50
PBFM, %	34.9 ± 4.1	34.7 ± 3.8*	−0.30 ± 5.20	39.0 ± 15.3	35.4 ± 4.6*	−4.00 ± 14.80

Values are mean ± standard deviation (SD).

OPE, onion peel extract; BMI, body mass index; FFM, fat free mass; BFM, body fat mass; PBFM, percent of body fat mass.

*p value < 0.05, significant difference before and after placebo or OPE intakes by paired t-test.

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Table 2. Changes in AST and ALT activities

Variables	Placebo (n = 19)			OPE (n = 18)		
	Baseline	12 wk	Change, %	Baseline	12 wk	Change, %
AST, IU/L	21.9 ± 5.5	18.4 ± 3.5	−13.0 ± 18.0	25.3 ± 12.4	23.4 ± 16.5	−3.3 ± 35.0
ALT, IU/L	16.1 ± 5.0	14.2 ± 4.9	−7.4 ± 29.6	22.9 ± 16.3	22.0 ± 22.4	0.0 ± 39.5

Values are mean ± standard deviation (SD).

OPE, onion peel extract; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

*p value < 0.05, significant difference before and after placebo or OPE intakes by paired t-test.

Table 3. Changes in plasma adipokines

Variables	Placebo (n = 19)			OPE (n = 18)		
	Baseline	12 wk	Change, %	Baseline	12 wk	Change, %
Leptin, ng/mL	15.2 ± 7.8	12.8 ± 6.1	−12.6 ± 30.9	16.9 ± 11.6	13.3 ± 7.3	−7.3 ± 51.0
Adiponectin, μg/mL	3.8 ± 1.5	6.4 ± 1.8*	94.1 ± 47.0	3.6 ± 2.0	6.9 ± 2.3*	118.5 ± 114.2
Visfatin, ng/mL	0.9 ± 0.6	0.6 ± 0.4	−9.3 ± 73.5	1.0 ± 0.7	1.0 ± 1.1	−22.0 ± 66.0
TNF-α, pg/mL	201.3 ± 18.2	203.9 ± 22.4	2.6 ± 23.2	201.6 ± 22.7	207.3 ± 22.9	5.6 ± 27.2
IL-4, pg/mL	11.7 ± 5.1	15.5 ± 6.8	3.7 ± 8.7	12.0 ± 7.2	18.4 ± 10.5	6.4 ± 14.4

Values are mean ± standard deviation (SD).

OPE, onion peel extract; TNF, tumor necrosis factor; IL, interleukin.

*p value < 0.05, significant difference before and after placebo or OPE intakes by paired t-test.

increased while those of leptin and visfatin were decreased in placebo and OPE-treated groups, although these results did not reach statistical significance in intra-group as well as inter-group comparison.

DISCUSSION

The aim of this randomized, double-blind, placebo-controlled study was to examine for the first time effects of a 12-week supplementation with quercetin-rich OPE on the inflammatory mediators in overweight and obese women. In the present study, we found that OPE supplementation significantly decreased the PBFM and induced plasma adiponectin levels compared with baseline values, while no significant difference was found between placebo and OPE-treated groups. In addition, leptin, visfatin, TNF-α, and IL-4 levels in plasma were not significantly different between the two groups before and after 12 weeks of supplementation.

Several recent studies suggest the suppressive effects of quercetin and quercetin-rich OPE against obesity in cell lines and animal models. In 3T3-L1 cells, quercetin and quercetin-rich OPE attenuated adipogenesis [17,18] and decreased liver fat accumulation in mice fed a Western diet or high-fat diet (HFD) [7,9]. Recently, Yang and Kim [19] demonstrated that the obesity index (% fat, BMI, waist circumstance) were significantly decreased by OPE intake for 12 weeks in obese university women. Previously, we reported that OPE supplementation significantly reduced the weight and percentage of body fat in overweight and obese adults [11]. We also reported that OPE supplementation significantly reduced waist and hip circumferences compared with baseline values while the changes observed in body weight and BMI were not statistically significant after 12 weeks of supplementation [12]. However, another study reported that no significant difference was observed in body weight and BMI in healthy young women with OPE supplementation for 2 weeks [15]. In the present study, we observed that OPE supplementation significantly decreased the PBFM but without a significant effect in inter-group comparison. Smaller pool of subjects in this study was a

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probable reason of different results in body weight and PBFM compared with other studies which found anti-obesity effect of OPE.

It is widely accepted that obesity is associated with low-grade chronic inflammatory responses, characterized by abnormal cytokine production and the activation of pro-inflammatory signaling pathways [2]. Numerous studies suggest that adipocytes and diverse types of infiltrated immune cells such as macrophages and T lymphocytes in adipose tissue play a vital role in inflammation by releasing bioactive inflammatory mediators so called adipokines [4]. These include highly active cytokines, mainly produced by adipocytes like adiponectin, leptin, resistin, and visfatin, as well as some more classical cytokines produced by infiltrated inflammatory cells like TNF-α, IL-6, and IL-4.

Adiponectin is the most abundant adipokine and serum levels of adiponectin are markedly decreased in individuals with visceral obesity and adiponectin levels correlate inversely with insulin resistance [20]. Adiponectin has been demonstrated to have anti-inflammatory effects by inhibiting NF-κB activation in endothelial cells and inducing the production of the anti-inflammatory cytokines in human leukocytes [21,22]. In animal models of liver inflammation, adiponectin exerts anti-inflammatory effects by suppressing the expression of TNF-α and attenuating liver fibrosis [23,24]. Recently, Kim et al. [14] reported that quercetin-rich OPE supplementation increased the adiponectin production at a transcription level in the high fat diet-induced obese animal model, suggesting that quercetin-rich OPE has modulatory effect on the inflammatory processes in obesity. Furthermore, quercetin increased levels of secreted adiponectin in TNF-α-treated 3T3-L1 adipocytes [25] as well as in obese Zucker rats [8] and diet-induced obese mice [26]. In the present study, adiponectin levels in placebo and OPE-treated groups were increased compared with baseline values. However, no significant differences were found between the two groups. This finding is consistent with the study conducted by Brüll et al. [27] which reported that 6-week treatment with quercetin did not significantly affect serum concentrations of adiponectin and leptin, compared to placebo in obese humans.

Similar to adiponectin, leptin is produced by adipocytes. It is involved mainly in the regulation of food intake and serum levels of leptin are proportional to adipose tissue mass in both animals and humans [28,29]. In contrast to adiponectin, leptin is generally considered to be a pro-inflammatory cytokine. The concentration of leptin is increased in inflammatory conditions in animal model [30,31] and in rheumatoid arthritis patients [32]. In animal model, quercetin reduced both plasma leptin and expression of leptin in adipose tissue from mice fed the Western diet for 18 weeks [26]. However, we observed that neither placebo nor OPE supplementation significantly changed the concentration of leptin. Wein et al. [33] also reported that quercetin feeding for 4 weeks did not affect plasma leptin levels in HFD fed rats.

Visfatin, originally identified as a growth factor for early B-cells, is up-ragulated in obese patients with metabolic syndrome and also implicated in generally atherosclerotic-related diseases [34,35]. Furthermore, visfatin has an immunomodulatory effect by increasing the levels of pro-inflammatory cytokines such as TNF-α and IL-6 [36]. According to the report of Derdemezis et al. [37], visfatin secretion was inhibited by quercetin in human Simpson-Golabi-Behmel syndrome (SGBS) adipocytes. In our study, we did not find significant differences in the plasma levels of visfatin after 12 weeks of OPE supplementation. Indeed, Kim et al. [14] also reported that quercetin-rich OPE did not alter the mRNA levels of visfatin from mesenteric fats.

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Unlike TNF-α, a potent inflammatory marker, IL-4 is the biologic anti-inflammatory mediator. It is known to originate from T-cell and plays biologic anti-inflammatory roles through inhibition of the production and release of pro-inflammatory mediators such as TNF-α [38]. In the present study, we observed that placebo or OPE supplementation increased plasma IL-4 levels without statistically significant differences between the two groups.

To the best of our knowledge, no previous human study investigated the effects of quercetin-rich OPE on inflammatory mediators in obese women. There are several reasons that may explain the lack of effects on these modulators of systemic inflammation. First, the anti-inflammatory properties of quercetin or quercetin-rich OPE are clearly seen in in vitro studies and these effects are also different between results from human and animal studies which may associated with difference of physiology in humans and animals as well as difference in the levels of inflammation status. In addition, there are only few studies examined the effect of OPE supplementation in humans. Second, although the participants of this study were overweight and obese, most of them were relatively healthy individuals with very low levels of inflammation since subjects with hypertension or diabetes were excluded from this study. The effect of OPE supplementation may be more visible in individuals with high levels of inflammation. Third, our 12-week administration of OPE was probably not long enough to find differences in the inflammatory mediators production. In addition, a large biological variation in measured parameters, evident from high standard deviations reduced the power to detect significant changes in the inflammatory mediators. Furthermore, we observed a significant reduction in the PBFM and an increase in adiponectin concentration in the placebo group which may occur due to the psychological effect of placebo intake.

In conclusion, our findings demonstrated that 12-week supplementation of OPE did not affect modulators of systemic inflammation in overweight and obese women. We could not find any significant adverse effect of OPE supplementation on the hepatic biomarkers such as AST and ALT compared with placebo. It seems that further studies are required with various doses of OPE and/or a large number of subjects to determine the effect of OPE supplement on the inflammation more extensively.

REFERENCES

1. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, Mullany EC, Biryukov S, Abbafati C, Abera SF, Abraham JP, Abu-Rmeileh NM, Achoki T, AlBuhairan FS, Alemu ZA, Alfonso R, Ali MK, Ali R, Guzman NA, Ammar W, Anwari P, Banerjee A, Barquera S, Basu S, Bennett DA, Bhutta Z, Blore J, Cabral N, Nonato IC, Chang JC, Chowdhury R, Courville KJ, Criqui MH, Cundiff DK, Dabhadkar KC, Dandona L, Davis A, Dayama A, Dharmaratne SD, Ding EL, Durrani AM, Esteghamati A, Farzadfar F, Fay DF, Feigin VL, Flaxman A, Forouzanfar MH, Goto A, Green MA, Gupta R, Hafezi-Nejad N, Hankey GJ, Harewood HC, Havmoeller R, Hay S, Hernandez L, Husseini A, Idrisov BT, Ikeda N, Islami F, Jahangir E, Jassal SK, Jee SH, Jeffreys M, Jonas JB, Kabagambe EK, Khalifa SE, Kengne AP, Khader YS, Khang YH, Kim D, Kimokoti RW, Kinge JM, Kokubo Y, Kosen S, Kwan G, Lai T, Leinsalu M, Li Y, Liang X, Liu S, Logroscino G, Lotufo PA, Lu Y, Ma J, Mainoo NK, Mensah GA, Merriman TR, Mokdad AH, Moschandreas J, Naghavi M, Naheed A, Nand D, Narayan KM, Nelson EL, Neuhouser ML, Nisar MI, Ohkubo T, Oti SO, Pedroza A, Prabhakaran D, Roy N, Sampson U, Seo H, Sepanlou SG, Shibuya K, Shiri R, Shiue I, Singh GM, Singh JA, Skirbekk V, Stapelberg NJ, Sturua L, Sykes BL, Tobias M, Tran BX, Trasande L, Toyoshima H, van de Vijver S, Vasankari TJ, Veerman JL, Velasquez-Melendez G, Vlassov VV, Vollset SE, Vos T, Wang C, Wang X, Weiderpass E, Werdecker A, Wright JL, Yang YC, Yatsuya H, Yoon J, Yoon SJ, Zhao Y, Zhou M, Zhu S, Lopez AD, Murray CJ, Gakidou E. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014;384:766-81.
PUBMED | CROSSREF

https://doi.org/10.7762/cnr.2016.5.4.261

2. Wellen KE, Hotamisligil GS. Obesity-induced inflammatory changes in adipose tissue. J Clin Invest 2003;112:1785-8.
PUBMED | CROSSREF
3. Greenberg AS, Obin MS. Obesity and the role of adipose tissue in inflammation and metabolism. Am J Clin Nutr 2006;83:461S-465S.
PUBMED
4. Tilg H, Moschen AR. Adipocytokines: mediators linking adipose tissue, inflammation and immunity. Nat Rev Immunol 2006;6:772-83.
PUBMED | CROSSREF
5. Weisberg SP, McCann D, Desai M, Rosenbaum M, Leibel RL, Ferrante AW Jr. Obesity is associated with macrophage accumulation in adipose tissue. J Clin Invest 2003;112:1796-808.
PUBMED | CROSSREF
6. Xu H, Barnes GT, Yang Q, Tan G, Yang D, Chou CJ, Sole J, Nichols A, Ross JS, Tartaglia LA, Chen H. Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. J Clin Invest 2003;112:1821-30.
PUBMED | CROSSREF
7. Jung CH, Cho I, Ahn J, Jeon TI, Ha TY. Quercetin reduces high-fat diet-induced fat accumulation in the liver by regulating lipid metabolism genes. Phytother Res 2013;27:139-43.
PUBMED | CROSSREF
8. Rivera L, Morón R, Sánchez M, Zarzuelo A, Galisteo M. Quercetin ameliorates metabolic syndrome and improves the inflammatory status in obese Zucker rats. Obesity (Silver Spring) 2008;16:2081-7.
PUBMED | CROSSREF
9. Kobori M, Masumoto S, Akimoto Y, Oike H. Chronic dietary intake of quercetin alleviates hepatic fat accumulation associated with consumption of a Western-style diet in C57/BL6J mice. Mol Nutr Food Res 2011;55:530-40.
PUBMED | CROSSREF
10. Duarte J, Pérez-Palencia R, Vargas F, Ocete MA, Pérez-Vizcaino F, Zarzuelo A, Tamargo J. Antihypertensive effects of the flavonoid quercetin in spontaneously hypertensive rats. Br J Pharmacol 2001;133:117-24.
PUBMED | CROSSREF
11. Lee JS, Cha YJ, Lee KH, Yim JE. Onion peel extract reduces the percentage of body fat in overweight and obese subjects: a 12-week, randomized, double-blind, placebo-controlled study. Nutr Res Pract 2016;10:175-81.
PUBMED | CROSSREF
12. Kim KA, Yim JE. Antioxidative activity of onion peel extract in obese women: a randomized, double-blind, placebo controlled study. J Cancer Prev 2015;20:202-7.
PUBMED | CROSSREF
13. Kim J, Kim JS, Park E. Cytotoxic and anti-inflammatory effects of onion peel extract on lipopolysaccharide stimulated human colon carcinoma cells. Food Chem Toxicol 2013;62:199-204.
PUBMED | CROSSREF
14. Kim OY, Lee SM, Do H, Moon J, Lee KH, Cha YJ, Shin MJ. Influence of quercetin-rich onion peel extracts on adipokine expression in the visceral adipose tissue of rats. Phytother Res 2012;26:432-7.
PUBMED
15. Kim J, Cha YJ, Lee KH, Park E. Effect of onion peel extract supplementation on the lipid profile and antioxidative status of healthy young women: a randomized, placebo-controlled, double-blind, crossover trial. Nutr Res Pract 2013;7:373-9.
PUBMED | CROSSREF
16. Kang HJ, Baik HW, Kim SJ, Lee SG, Ahn HY, Park JS, Park SJ, Jang EJ, Park SW, Choi JY, Sung JH, Lee SM. Cordyceps militaris enhances cell-mediated immunity in healthy Korean men. J Med Food 2015;18:1164-72.
PUBMED | CROSSREF
17. Bae CR, Park YK, Cha YS. Quercetin-rich onion peel extract suppresses adipogenesis by down-regulating adipogenic transcription factors and gene expression in 3T3-L1 adipocytes. J Sci Food Agric 2014;94:2655-60.
PUBMED | CROSSREF
18. Moon J, Do HJ, Kim OY, Shin MJ. Antiobesity effects of quercetin-rich onion peel extract on the differentiation of 3T3-L1 preadipocytes and the adipogenesis in high fat-fed rats. Food Chem Toxicol 2013;58:347-54.
PUBMED | CROSSREF
19. Yang YK, Kim SP. The effect of onion extract intake for 12 weeks on blood lipid and obesity index in obese university women. Korean J Sports Sci 2013;22:955-62.

20. Arita Y, Kihara S, Ouchi N, Takahashi M, Maeda K, Miyagawa J, Hotta K, Shimomura I, Nakamura T, Miyaoka K, Kuriyama H, Nishida M, Yamashita S, Okubo K, Matsubara K, Muraguchi M, Ohmoto Y, Funahashi T, Matsuzawa Y. Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. Biochem Biophys Res Commun 1999;257:79-83.
PUBMED | CROSSREF

21. Ouchi N, Kihara S, Arita Y, Maeda K, Kuriyama H, Okamoto Y, Hotta K, Nishida M, Takahashi M, Nakamura T, Yamashita S, Funahashi T, Matsuzawa Y. Novel modulator for endothelial adhesion molecules: adipocyte-derived plasma protein adiponectin. Circulation 1999;100:2473-6.
PUBMED | CROSSREF

22. Wolf AM, Wolf D, Rumpold H, Enrich B, Tilg H. Adiponectin induces the anti-inflammatory cytokines IL-10 and IL-1RA in human leukocytes. Biochem Biophys Res Commun 2004;323:630-5.
PUBMED | CROSSREF

23. Xu A, Wang Y, Keshaw H, Xu LY, Lam KS, Cooper GJ. The fat-derived hormone adiponectin alleviates alcoholic and nonalcoholic fatty liver diseases in mice. J Clin Invest 2003;112:91-100.
PUBMED | CROSSREF

24. Kamada Y, Tamura S, Kiso S, Matsumoto H, Saji Y, Yoshida Y, Fukui K, Maeda N, Nishizawa H, Nagaretani H, Okamoto Y, Kihara S, Miyagawa J, Shinomura Y, Funahashi T, Matsuzawa Y. Enhanced carbon tetrachloride-induced liver fibrosis in mice lacking adiponectin. Gastroenterology 2003;125:1796-807.
PUBMED | CROSSREF

25. Yen GC, Chen YC, Chang WT, Hsu CL. Effects of polyphenolic compounds on tumor necrosis factor-α (TNF-α)-induced changes of adipokines and oxidative stress in 3T3-L1 adipocytes. J Agric Food Chem 2011;59:546-51.
PUBMED | CROSSREF

26. Kobori M, Takahashi Y, Sakurai M, Akimoto Y, Tsushida T, Oike H, Ippoushi K. Quercetin suppresses immune cell accumulation and improves mitochondrial gene expression in adipose tissue of diet-induced obese mice. Mol Nutr Food Res 2016;60:300-12.
PUBMED | CROSSREF

27. Brüll V, Burak C, Stoffel-Wagner B, Wolffram S, Nickenig G, Müller C, Langguth P, Alteheld B, Fimmers R, Stehle P, Egert S. No effects of quercetin from onion skin extract on serum leptin and adiponectin concentrations in overweight-to-obese patients with (pre-)hypertension: a randomized double-blinded, placebo-controlled crossover trial. Eur J Nutr. Forthcoming 2016.
PUBMED

28. La Cava A, Matarese G. The weight of leptin in immunity. Nat Rev Immunol 2004;4:371-9.
PUBMED | CROSSREF

29. Friedman JM, Halaas JL. Leptin and the regulation of body weight in mammals. Nature 1998;395:763-70.
PUBMED | CROSSREF

30. Grunfeld C, Zhao C, Fuller J, Pollack A, Moser A, Friedman J, Feingold KR. Endotoxin and cytokines induce expression of leptin, the ob gene product, in hamsters. J Clin Invest 1996;97:2152-7.
PUBMED | CROSSREF

31. Sarraf P, Frederich RC, Turner EM, Ma G, Jaskowiak NT, Rivet DJ 3rd, Flier JS, Lowell BB, Fraker DL, Alexander HR. Multiple cytokines and acute inflammation raise mouse leptin levels: potential role in inflammatory anorexia. J Exp Med 1997;185:171-5.
PUBMED | CROSSREF

32. Lee SW, Park MC, Park YB, Lee SK. Measurement of the serum leptin level could assist disease activity monitoring in rheumatoid arthritis. Rheumatol Int 2007;27:537-40.
PUBMED | CROSSREF

33. Wein S, Behm N, Petersen RK, Kristiansen K, Wolffram S. Quercetin enhances adiponectin secretion by a PPAR-gamma independent mechanism. Eur J Pharm Sci 2010;41:16-22.
PUBMED | CROSSREF

34. Filippatos TD, Derdemezis CS, Kiortsis DN, Tselepis AD, Elisaf MS. Increased plasma levels of visfatin/pre-B cell colony-enhancing factor in obese and overweight patients with metabolic syndrome. J Endocrinol Invest 2007;30:323-6.
PUBMED | CROSSREF

35. Filippatos TD, Randeva HS, Derdemezis CS, Elisaf MS, Mikhailidis DP. Visfatin/PBEF and atherosclerosis-related diseases. Curr Vasc Pharmacol 2010;8:12-28.
PUBMED | CROSSREF

36. Moschen AR, Kaser A, Enrich B, Mosheimer B, Theurl M, Niederegger H, Tilg H. Visfatin, an adipocytokine with proinflammatory and immunomodulating properties. J Immunol 2007;178:1748-58.
PUBMED | CROSSREF

37. Derdemezis CS, Kiortsis DN, Tsimihodimos V, Petraki MP, Vezyraki P, Elisaf MS, Tselepis AD. Effect of plant polyphenols on adipokine secretion from human SGBS adipocytes. Biochem Res Int 2011;2011:285618.
PUBMED | CROSSREF

38. Schuerwegh AJ, Dombrecht EJ, Stevens WJ, Van Offel JF, Bridts CH, De Clerck LS. Influence of pro-inflammatory (IL-1 α, IL-6, TNF-α, IFN-γ) and anti-inflammatory (IL-4) cytokines on chondrocyte function. Osteoarthritis Cartilage 2003;11:681-7.
PUBMED | CROSSREF

https://doi.org/10.7762/cnr.2016.5.4.261