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Teasaponin improves leptin sensitivity in the prefrontal cortex of obese mice

Yinghua Yu  
*University of Wollongong, yinghua@uow.edu.au*

Hongqin Wang  
*University of Wollongong, hongqin@uow.edu.au*

Yizhen Wu  
*University of Wollongong, yw903@uowmail.edu.au*

Alexander M. Szabo  
*University of Wollongong, aszabo@uow.edu.au*

Christopher Bell  
*University of Wollongong, cjb692@uowmail.edu.au*

*See next page for additional authors*

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**Authors**
Yinghua Yu, Hongqin Wang, Yizhen Wu, Alexander M. Szabo, Christopher Bell, and Xu-Feng Huang

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Teasaponin improves leptin sensitivity in the prefrontal cortex of obese mice

Yu YH 1,2, Wang HQ1, Wu YZ 1, Szabo A 1, Bell CJ 1, Huang XF1,2

School of Medicine, IHMRI, University of Wollongong, NSW 2522

Schizophrenia Research Institute (SRI), 405 Liverpool St, Sydney, NSW 2010, Australia

**Purpose:** Obesity impairs cognition, and leptin-induced increases in neurogenesis and expression of brain-derived neurotrophic factor (BDNF). Tea consumption improves cognition and increases brain activation in the prefrontal cortex. This study examined whether teasaponin, an active ingredient in tea, could improve memory and central leptin effects on neurogenesis in the prefrontal cortex.

**Methods:** C57/B6 mice were divided into lab chow fed control (LC) and high fat diet-induced obesity (DIO) groups. A subgroup of DIO mice was treated orally with teasaponin to examine recognition memory with novel object recognition (NOR) tests. Another subgroup of DIO mice was injected intraperitoneally with teasaponin to test its effects on leptin signaling and leptin-induced neurogenesis in the prefrontal cortex by Western blot. Cultured prefrontal cortical neurons pre-treated with leptin to induce BDNF expression and neurogenesis were treated with either palmitic acid or a combination of teasaponin and palmitic acid, and then examined by IHC and RT-PCR.

**Results:** Oral teasaponin treatment significantly improved the memory of DIO mice ($p=0.027$) in the NOR test. Intraperitoneal teasaponin improved downstream leptin signaling in the JAK2 and STAT3 pathways, and leptin-induced BDNF expression in the prefrontal cortex of DIO mice. Cultured prefrontal cortical neurons pre-treated with leptin showed increased neurite outgrowth, and expression of post-synaptic density protein 95 (PSD-95) and BDNF. Treatment with palmitic acid abrogated the leptin-induced effects. However, treatment with teasaponin significantly increased the leptin effects on neurite outgrowth ($p<0.05$), and PSD-95 ($p<0.05$) and BDNF expression ($p<0.05$).

**Conclusion:** Teasaponin improves obesity associated memory deficit and central leptin effects in the prefrontal cortex *in vivo*. Furthermore, *in vitro* observations show that teasaponin sensitizes leptin activity within the prefrontal cortex. Therefore, teasaponin supplementation may be useful for treating obesity-associated neurodegenerative disorders by improving prefrontal cortical function.