Baicalein reduces fat accumulation in *Caenorhabditis elegans*

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ABSTRACT

Baicalein (5,6,7-trihydroxyflavone), a type of flavonoid, is typically found in roots of Scutellaria and *Scutellaria lateriflora*, *Oroxylum indicum* (Indian trumpetflower) and thyme. Baicalein is one of active ingredients in some Asian traditional medicine. It has been reported with anti-cancer, anti-inflammation, and possible anti-depressant effects. Previously, baicalin, the glucuronide of baicalein, showed anti-obesity and anti-insulin resistance effects. Though study showed baicalin has promising reduction on fat accumulation in high-fat diet fed mice, there is limited reports examining baicalein regarding anti-obesity effects. Thus, the goal of this study was to examine the effect of baicalein on fat metabolism and to determine its underlying mechanisms using *Caenorhabditis elegans* as a living model system. *C. elegans* is a eukaryotic, multi-organ nematode that can be easily maintained in the laboratory with non-pathogenic bacterial *Escherichia coli* OP50 as a food source. *C. elegans* is significantly anatomically simpler than many of living models and share almost 65% homology with human disease related genes, including those of lipid metabolism. Treatment of baicalein for 48 hours, at 100 μM, significantly decreased the triglyceride levels compared to the control in wild-type *C. elegans* by ~10% (p= 0.0054). Baicalein had no effects on pumping rate, suggesting baicalein had no effect on food intake. Furthermore, we examined baicalein in three mutants with key genes of lipid metabolism knocked out to determine the pathways of baicalein on fat accumulation. Baicalein had no effect on triglyceride accumulation in *daf-16, fat-6, or sbp-1* null mutants. These suggest that baicalein reduced fat accumulation via *daf-16, sbp-1,* and/or *fat-6*-dependent mechanisms in *C. elegans*.

METHODS

Materials

- Wild-type (N2), *daf-16* (GR1307), *sbp-1* (CE541) *and fat-6* (BX106) null mutant *C. elegans* were obtained from the *Caenorhabditis* Genetics Center. (Minneapolis, MN)
- Infinity™ Triglycerides Reagent and Pierce™ BCA Protein Assay Kit from Fisher Diagnostics Thermo Fisher Scientific (Middletown, VA) Bio-Rad DC protein assay kit from Bio-Rad Co. (Hercules, CA)

Treatment

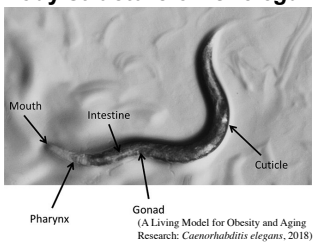
- Control solution prepared with 0.1% dimethyl sulfoxide (DMSO)
- Baicalein treated at 50 μM, 100 μM and 200 μM dissolved in 0.1% DMSO
- Wild-type, *daf-16, sbp-1 and fat-6 C. elegans* synchronized and incubated at 20°C
- Treatment was administrated to early adult worms for 48 hours

Measurement

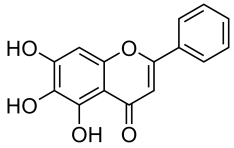
- Triglyceride: Measured by a commercial kit, then normalized by protein level. *Values represent means ± S.E.* (n = 4, each had about 1,000 worms). Means with different letters are significantly different at *P<0.05.*
- Pumping rate: Measured by counting pharyngeal contractions of randomly selected 12 worms from each group for 30 seconds.

RESULTS

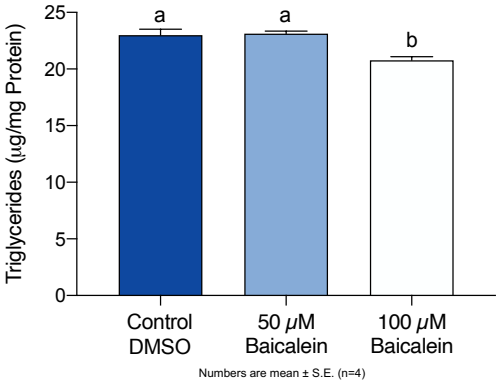
Body structure of *C. elegans*



Baicalein

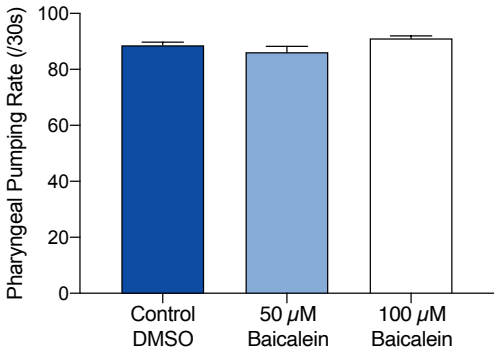


Baicalein at 100 μM reduced fat accumulation in wild-type *C. elegans*



Numbers are mean ± S.E. (n=4)

Baicalein had no effect on pumping rate

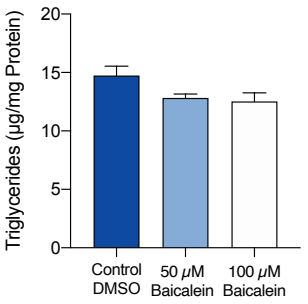


Numbers are mean ± S.E. (n=12)

RESULTS

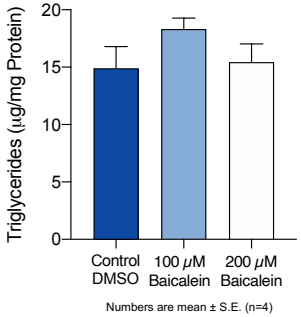
Baicalein had no significant effect on *daf-16, sbp-1 or fat-6* null mutant

daf-16 null mutant



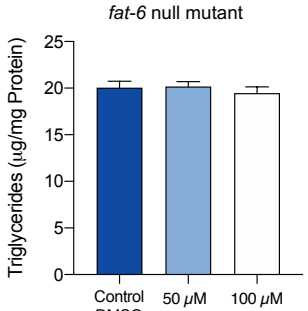
Numbers are mean ± S.E. (n=4)

sbp-1 null mutant



Numbers are mean ± S.E. (n=4)

fat-6 null mutant



Numbers are mean ± S.E. (n=4)

- ***daf-16*** (abnormal **DA**uer **F**ormation)
  - Homolog of human mammalian Forkhead box O transcription factor
  - Involved in regulation of metabolism via insulin/ insulin-like growth factor pathway
- ***sbp-1*** (**S**terol regulatory element **B**inding **P**rotein)
  - Homolog of human SREBF2 (sterol regulatory element binding transcription factor 2)
  - Involved in lipogenesis
- ***fat-6*** (**FAT**ty acid desaturase)
  - Homolog of human SCD (stearoyl-CoA desaturase).
  - Involved in monounsaturated fatty acid biosynthesis.

CONCLUSION

- Baicalein at 100 μM reduced fat accumulation without affecting pumping rate.
- Baicalein had no significant effect on *daf-16, sbp-1,* or *fat-6* null mutants *C. elegans,* suggesting baicalein reduces fat accumulation via *daf-16, sbp-1,* and/or *fat-6*-dependent mechanism.
- Additional studies using different *C. elegans* mutants related fat metabolisms are needed to further determine the exact mechanisms of baicalein on anti-obesity effect.

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