Dietary Spermidine Depletes the Fat Stores in *Drosophila melanogaster* Fed High-Sugar Low-Protein Diets

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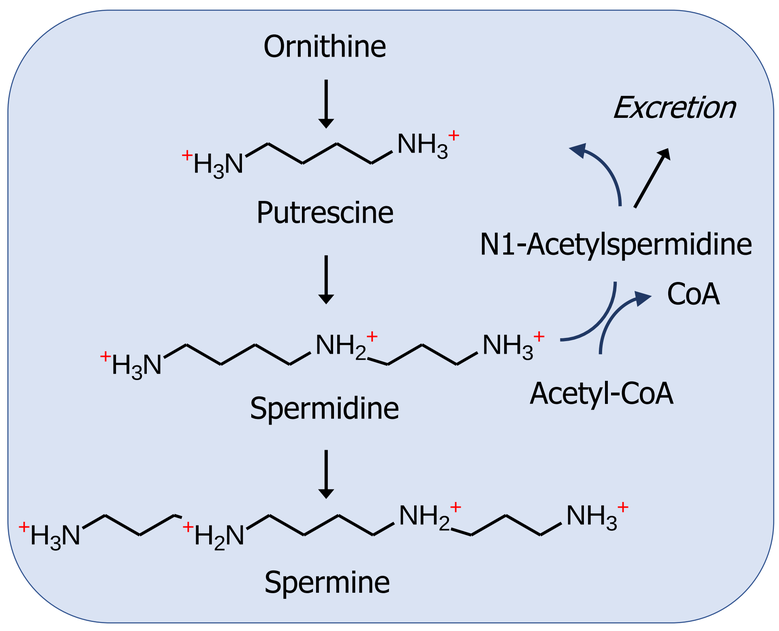
BACKGROUND

Spermidine (Spd) is a naturally occurring polyamine. Its endogenous pool is replenished by biosynthesis from amino acids and intestinal uptake from the diet and microbiota [1]. Dietary Spd has been suggested to promote healthy aging [2]. Moreover, genetic models indicate that the polyamine metabolism interacts with the triacylglyceride (TAG) metabolism in mammals and invertebrates, including the fruit fly *Drosophila melanogaster* [3-5]. Here, we used the fruit fly model to examine the impact of Spd supplementation on body composition and elucidate the underlying molecular mechanism.

Polyamine synthesis and catabolism



METHODS

Nutritional & genetic phenotyping

using the fruit fly model *D. melanogaster*

Control diet

Assessment of:

- Body composition
- Polyamine content
- Food intake
- Starvation resistance
- Egg laying
- *akh* and *bmm* mutants

Spd diet

CONCLUSION

- Dietray Spd induces endogenous Spd catabolism
- The TAG-lowering effect of dietary Spd depends on the protein-to-carbohydrate ratio of the *Drosophila* diet
- The Akh-Bmm signaling pathway is required to deplete the fat store through dietary Spd
- Further studies are needed to clarify whether the anti-obesity activity of Spd can be utilized in human nutrition

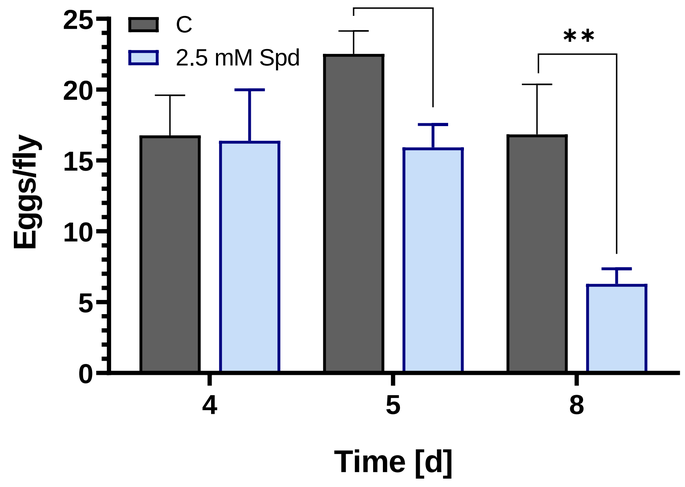
RESULTS

Dietary Spd led to increased levels of catabolic polyamines in female fruit flies

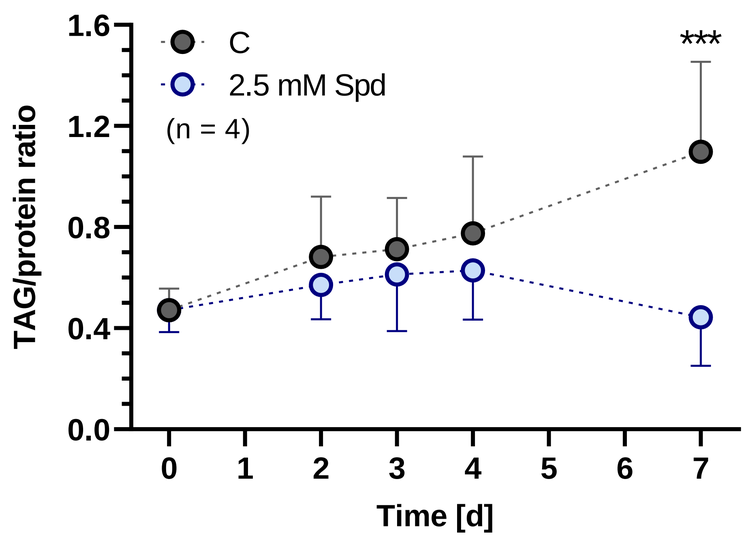
	Polyamines [nmol/mg BW]			
Diet	Put	N1AcSpd	Spd	Spm
CT	0.045 ± 0.007	0.030 ± 0.003	0.833 ± 0.145	0.093 ± 0.014
CT-Spd	0.328 ± 0.056 ***	0.098 ± 0.028 ***	0.802 ± 0.100	0.068 ± 0.003 ***
CT_{10}	0.046 ± 0.008	0.022 ± 0.004	1.960 ± 0.252	0.139 ± 0.022
CT_{10}-Spd	0.131 ± 0.033 ***	0.053 ± 0.006 ***	2.291 ± 0.161 **	0.161 ± 0.087

Put, putrescine; N1AcSpd, N1-acetylspermidine; Spd, spermidine; Spm, spermine
** p < 0.01; *** p < 0.001 (t-test); n = 9

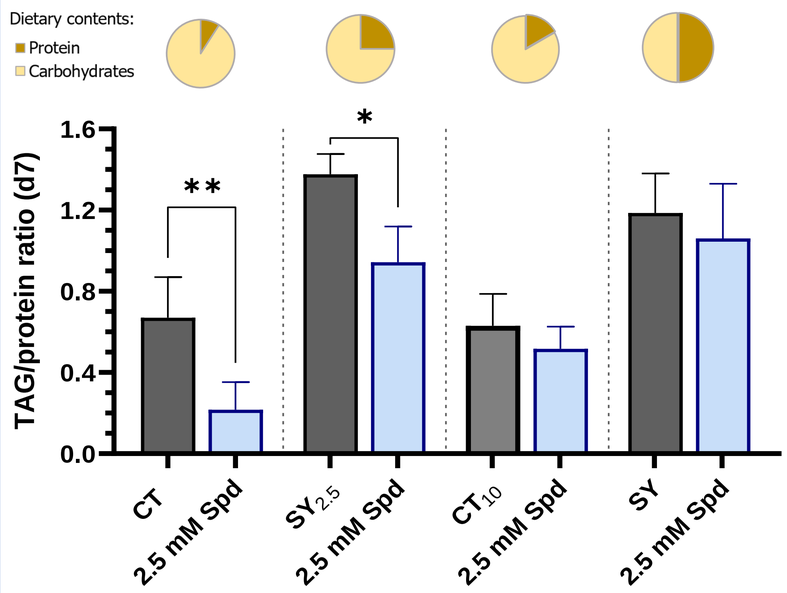
Dietary Spd led to a decreased egg production in *D. melanogaster*



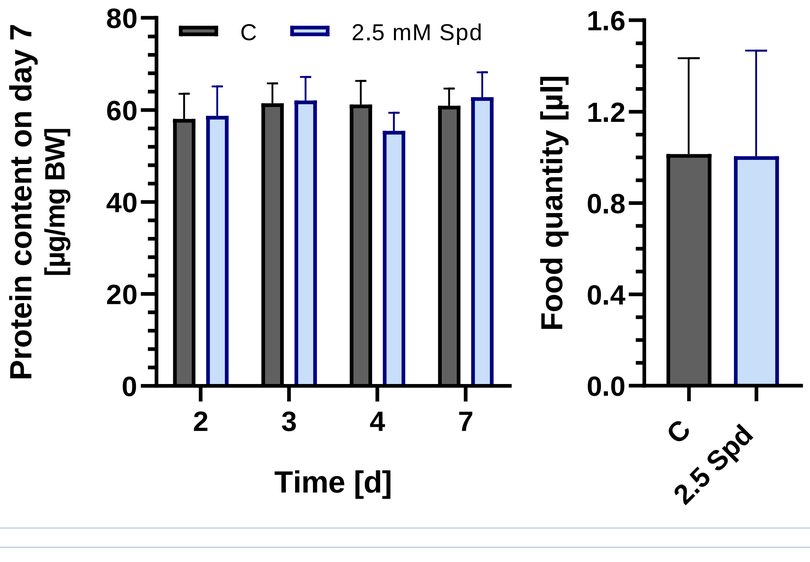
Dietary Spd led to decreased TAG level in female fruit flies



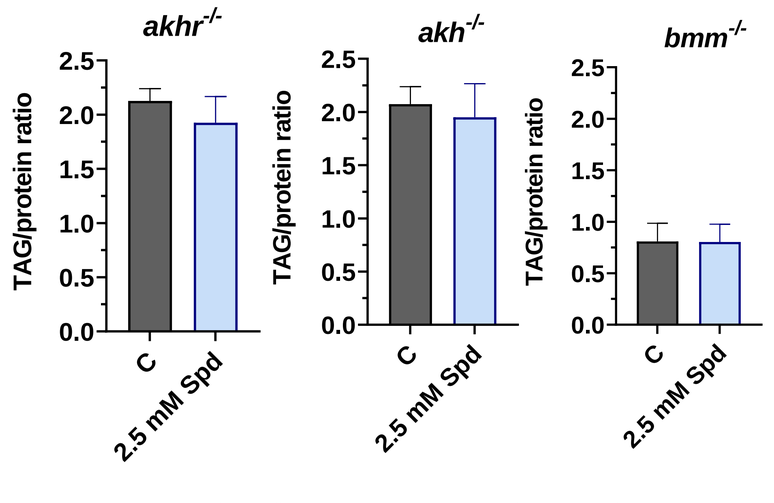
The protein content of the diet determines the Spd effect on TAG level



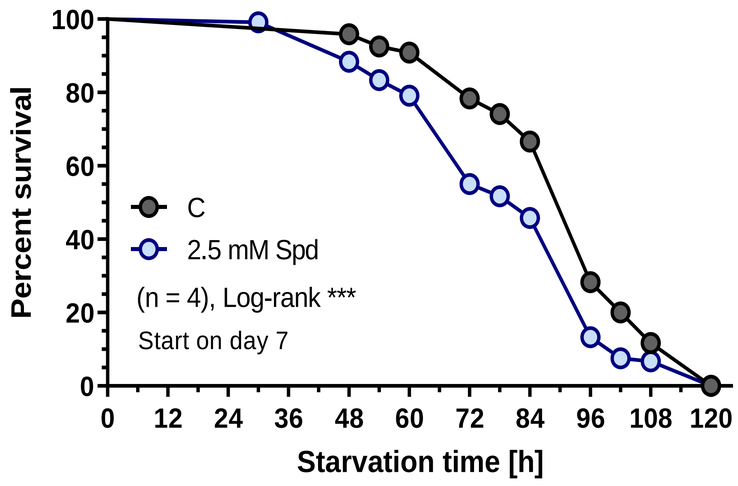
Dietary Spd did not affect the protein level and food intake of female fruit flies



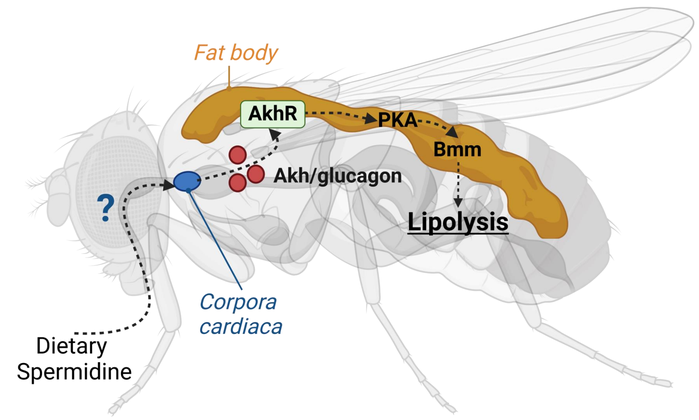
Akh-Bmm signalling pathway is required to reduce fat storage by dietary Spd



Reduced fat stores of Spd-fed flies are associated with increased starvation sensitivity



Dietary Spd triggers the Akh pathway to promote lipolysis in female fruit flies



AkhR, Akh receptor; PKA, protein kinase A; Bmm, TAG lipase (Created with BioRender.com)

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