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Metformin's Potential as a Form of Anti-Aging Therapy

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Introduction

- Metformin is an oral medication used to treat Type II Diabetes and is the first-line drug for treatment.
- Metformin is the fourth most prescribed medication in the United States and has been prescribed to over 78 million patients since 2017¹.
- Metformin increases glucose uptake of cells and decreases hepatic glucose production, leading to lower blood glucose levels².
- Metformin may help prevent cancer, improve cardiovascular health, and protect against inflammation, therefore focus has been directed on its potential to be an anti-aging drug³.

Research Focus

The research was centered primarily around examining the following questions:






1. What effect does metformin have on aging and lifespan?
2. Does metformin promote health and longevity?
3. What metabolic side effects (on stress response, body weight, or feeding) does metformin cause?

Methods

- Conducted a literature review analyzing published primary research articles about metformin and its effects on lifespan and healthspan in various model organisms.
- Analyzed preliminary data from *Drosophila melanogaster* lifespan and feeding assays.

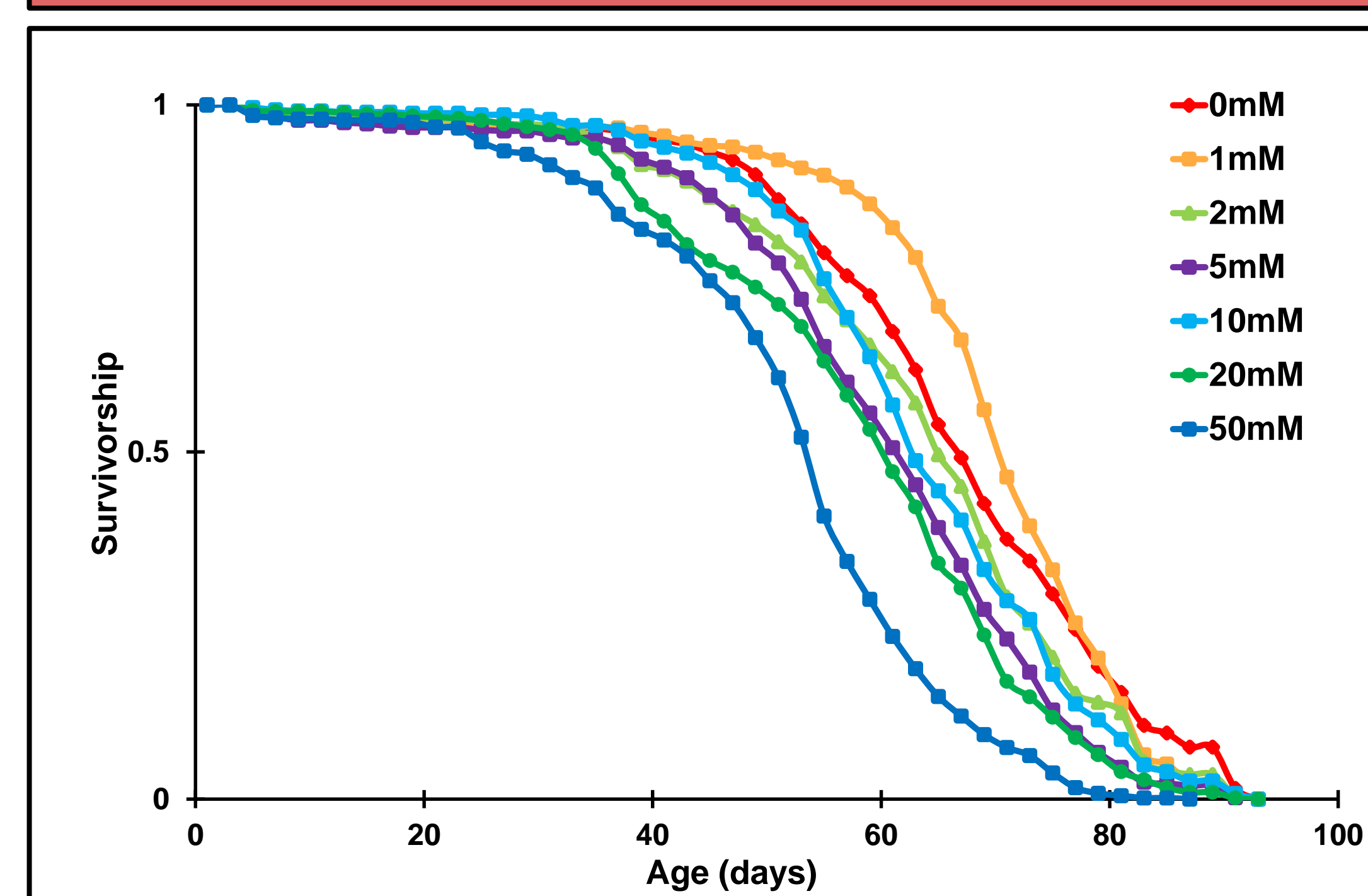
Results

Table 1: Literature Survey of Metformin and Aging Studies

Model Organism	Lifespan Extension with Metformin Treatment	Significant Healthspan Markers	Papers Cited
<i>C. elegans</i> 	Increased mean lifespan	↑ youthful locomotor ability; ↓ levels of stored fat; ↑ B-oxidation; Altered microbial folate and methionine metabolism; Displayed a younger cuticle	4, 5, 6
<i>Drosophila melanogaster</i> 	No significant effect on lifespan; Decreased lifespan at higher concentrations	↓ levels of triglycerides at 10 mM and 100 mM; At 25 mM, female flies laid more eggs than control at 7 days; At 50 mM, female flies laid more eggs than control at 7 days, but fewer at 14 days.	7, 8
<i>Bombyx mori</i> 	Increased lifespan in male silkworms; No significant effect on lifespan of female silkworms	↑ survival rate of silkworms subjected to feeding stress by 13.46% but did not increase thermotolerance; ↓ silk production; ↓ fecundity in female silkworms	9
<i>Mus musculus</i> 	Increased mean lifespan	↑ B-oxidation of fatty acids; ↓ lipid synthesis; ↑ fitness performance in male C57BL/6 strain; ↓ age-related switch-off of estrous function; ↓ mean size and accumulation of mammary adenocarcinomas in female HER-2/Neu strain; ↓ the first tumor detection by 22% and 25% when started at 3 and 9 months	10, 11, 12, 13, 14, 15, 16
<i>Rattus norvegicus</i> 	No significant effect on lifespan	↓ mean body weight compared to the control group during weeks 48-74; Food consumption was similar to control group	17

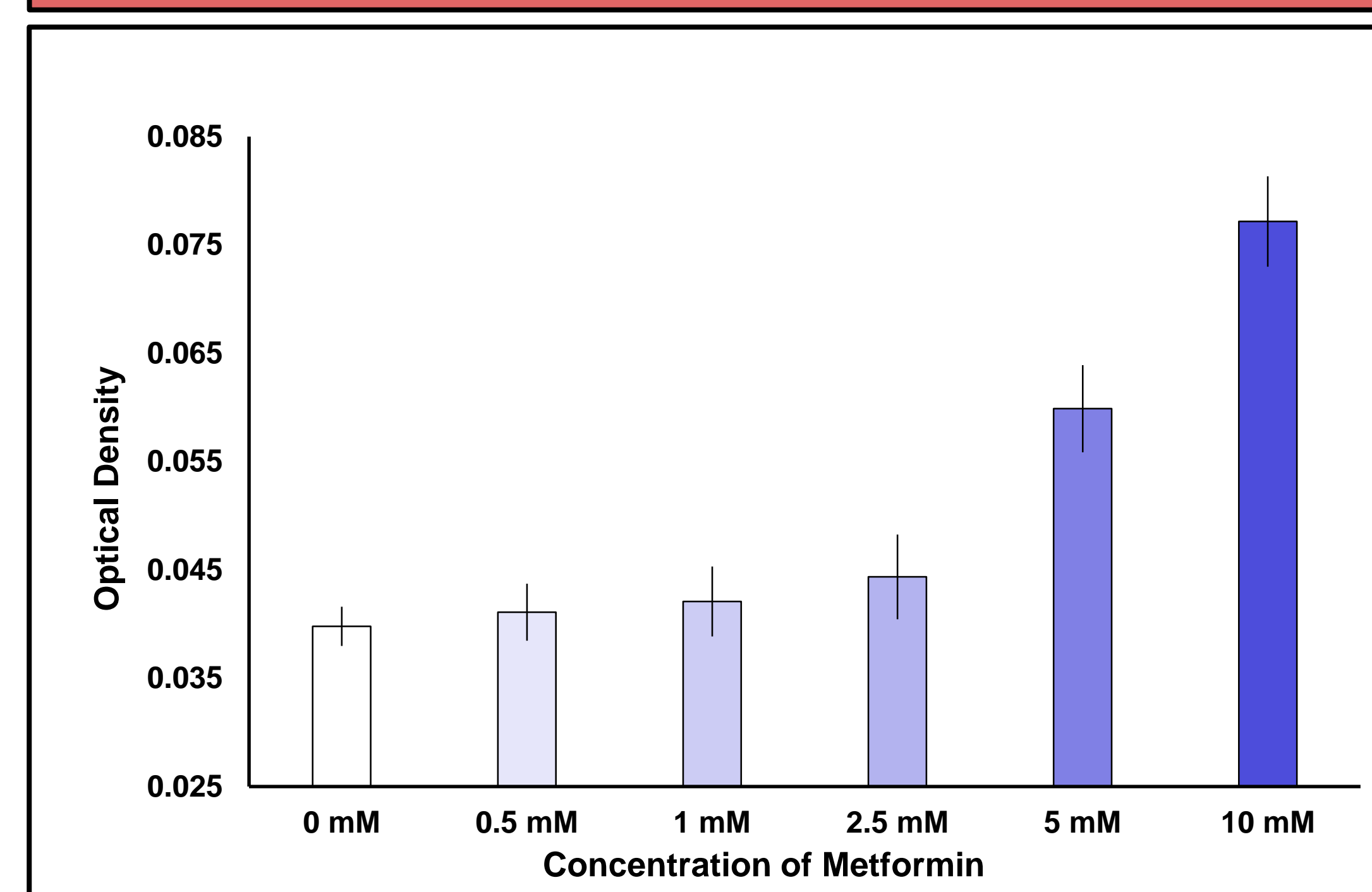
Images were adopted from public sources and are available upon request.

Figure 1: The Effect of Metformin Treatment on *Drosophila* Lifespan



- Survivorship curve of wild-type flies fed diets with concentrations of 1-50 mM of metformin.
- Lifespan extension was observed in flies when supplemented with 1 mM of metformin ($p < 0.05$ by log-rank test).
- Flies maintained on diets with concentrations of metformin higher than 10 mM experienced lifespan reduction.

Figure 2: Metformin Increased Food Intake in *Drosophila*



- Food consumption measured in wild-type flies using the Con-Ex method.
- This graph represents absorbance density vs. different metformin concentrations administered in diet.
- Higher concentrations of metformin increased food intake in flies ($p < 0.05$ by t-test for 5mM and 10mM compared to control).

Discussion

- The literature survey indicates that metformin treatment extends lifespan in *C. elegans*, *Mus musculus*, and *Bombyx mori* (male), though it has the opposite effect in *Drosophila* (Table 1).
- Additionally, metformin treatment affects several metabolic parameters, such as triglyceride levels, in *C. elegans*, *Drosophila*, and *Mus musculus* (Table 1).
- Our data shows that lifespan extension was observed in *Drosophila* treated with a low dose of metformin. These results demonstrate that metformin has the potential to extend lifespan, contrary to previous *Drosophila* lifespan studies (Fig 1).
- Higher concentrations of metformin in diet appear to increase feeding behavior in *Drosophila*, which may have a negative impact on lifespan extension (Fig 2).
- Future studies will involve conducting experiments with *Drosophila* to verify these preliminary results and to identify the molecular mechanisms that mediate lifespan extension and increase food intake by metformin.

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