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THE IMPACT OF MANGIFERIN AND TRANS-CINNAMIC ACID ON THE SURVIVAL AND LIFESPAN OF WILD TYPE N2 BRISTOL AND AAK-2 *CAENORHABDITIS ELEGANS* MUTANT STRAINS UNDER OXIDATIVE STRESS *

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Abstract

Reactive oxygen (ROS) and nitrogen species (RNS) are generated during cellular metabolism. These ROS and RNS, in turn, cause oxidative damage to DNA and proteins. As a survival mechanism, these stressors modulate gene expression and various signalling pathways in *Caenorhabditis elegans* [1]. Furthermore, it has been demonstrated that environmental changes have an impact on lifespan and health span [2]. The ability of humans and animals to remain viable under different environmental conditions is called stress tolerance, wherein the resistance to multiple types of stress peaks during early adulthood and then declines with age [3]. AAK-2, an AMP-activated protein kinase isoform in *C. elegans*, has a role in stress responses, germ cell cycle arrest following dauer formation, and maintenance of life span [4].

In this study, we evaluated the effect of mangiferin and trans-cinnamic acid (at 10, 50, 100 and 200 µM) on percentage survival ratio and lifespan of hydrogen peroxide-treated *C. elegans* in a well-known *in vivo* model of resistance to oxidative stress. The nematodes (wild-type N2 Bristol and AAK-2 mutant strains) were exposed to 3 % H_2O_2 corresponding to 1:10 v/v for 2 hours. Thereafter, the H_2O_2-stressed nematodes were observed using ZEISS LSM 900 Confocal Microscope for the computation of % survival ratio and continued to be monitored until the last nematode alive (maximum lifespan).

The treatment of oxidatively challenged wild-type N2 *C. elegans* with trans-cinnamic acid at 50, 100 and 200 µM significantly ($p < 0,05$) increased the survival ratio and maximum lifespan of the nematodes compared to the control (Table 1). Furthermore, mangiferin at all doses investigated significantly ($p < 0,05$) improved the survival ratio and extended the lifespan of H_2O_2-stressed N2 nematodes (see Table 1).

H_2O_2-treated AAK-2 mutant strains demonstrated a dose-dependent increase in survival ratio and lifespan following the administration of mangiferin and trans-cinnamic acid (Table 2). The 200 µM of mangiferin was particularly commendable as it improved the survival ratio from 5 % in the control group to 52 %, and lifespan from 2 — 118 hours (see Table 2).

Our findings suggests that trans-cinnamic acid and more importantly, mangiferin markedly enhanced lifespan and stress tolerance in *in vivo* model of hydrogen peroxide-treated *C. elegans*. These beneficial effects highlight the potential of using them in combating oxidative stress-related diseases and aging.

Table 1

Effect of trans-cinnamic acid and mangiferin on 3 % H_2O_2-treated N2 wild-type *C. elegans*

Group	Dose (µmoL)	Number of nematodes	Survival ratio (%)	Maximum lifespan (hrs)
Control		21,40 ± 1,05 [a]	2,75	2,00 ± 0,51 [a]
Trans-cinnamic acid	10	21,80 ± 2,77 [a]	3,82	2,50 ± 0,20 [a]
	50	19,80 ± 0,09 [a]	15,79	3,50 ± 0,46 [b]
	100	16,80 ± 2,33 [b]	13,65	3,25 ± 0,11 [b]
	200	27,80 ± 2,05 [c]	16,66	3,30 ± 0,38 [b]
Mangiferin	10	22,20 ± 1,97 [a]	15,41	7,25 ± 0,44 [c]
	50	18,40 ± 1,10 [b]	14,95	8,10 ± 0,98 [c]
	100	21,50 ± 0,83 [a]	17,83	8,97 ± 0,52 [c]
	200	20,00 ± 1,22 [a]	28,67	68,20 ± 5,67 [d]

Values are means ± standard error of means for 5 replicates, $p < 0.05$. Values with the same superscript implies the absence of a statistically significant difference.

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Table 2

Effect of trans-cinnamic acid and mangiferin on 3 % H_2O_2-treated AAK-2 *C. elegans* mutant strain

Group	Dose (μmoL)	Number of nematodes	Survival ratio (%)	Maximum lifespan (hrs)
Control		18,20 ± 0,67 [a]	4,37	2,00 ± 0,30 [a]
Trans-cinnamic acid	10	17,40 ± 2,17 [a]	3,45	2,00 ± 0,01 [a]
	50	16,80 ± 1,02 [a]	3,57	2,50 ± 0,50 [a]
	100	19,40 ± 2,68 [a]	5,15	10,54 ± 0,33 [d]
	200	19,40 ± 3,31 [a]	7,22	12,11 ± 0,48 [e]
Mangiferin	10	16,20 ± 0,43 [a]	4,94	4,59 ± 0,22 [b]
	50	20,20 ± 1,65 [a]	6,93	7,40 ± 0,05 [c]
	100	19,60 ± 2,51 [a]	8,16	12,00 ± 0,11 [e]
	200	16,20 ± 1,37 [a]	51,85	118,30 ± 0,25 [f]

Values are means ± standard error of means for 5 replicates, $p < 0.05$. Values with the same superscript implies the absence of a statistically significant difference.

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