Title: Hemiterpene compound, 3,3-dimethylallyl alcohol promotes longevity and neuroprotection in *Caenorhabditis elegans*

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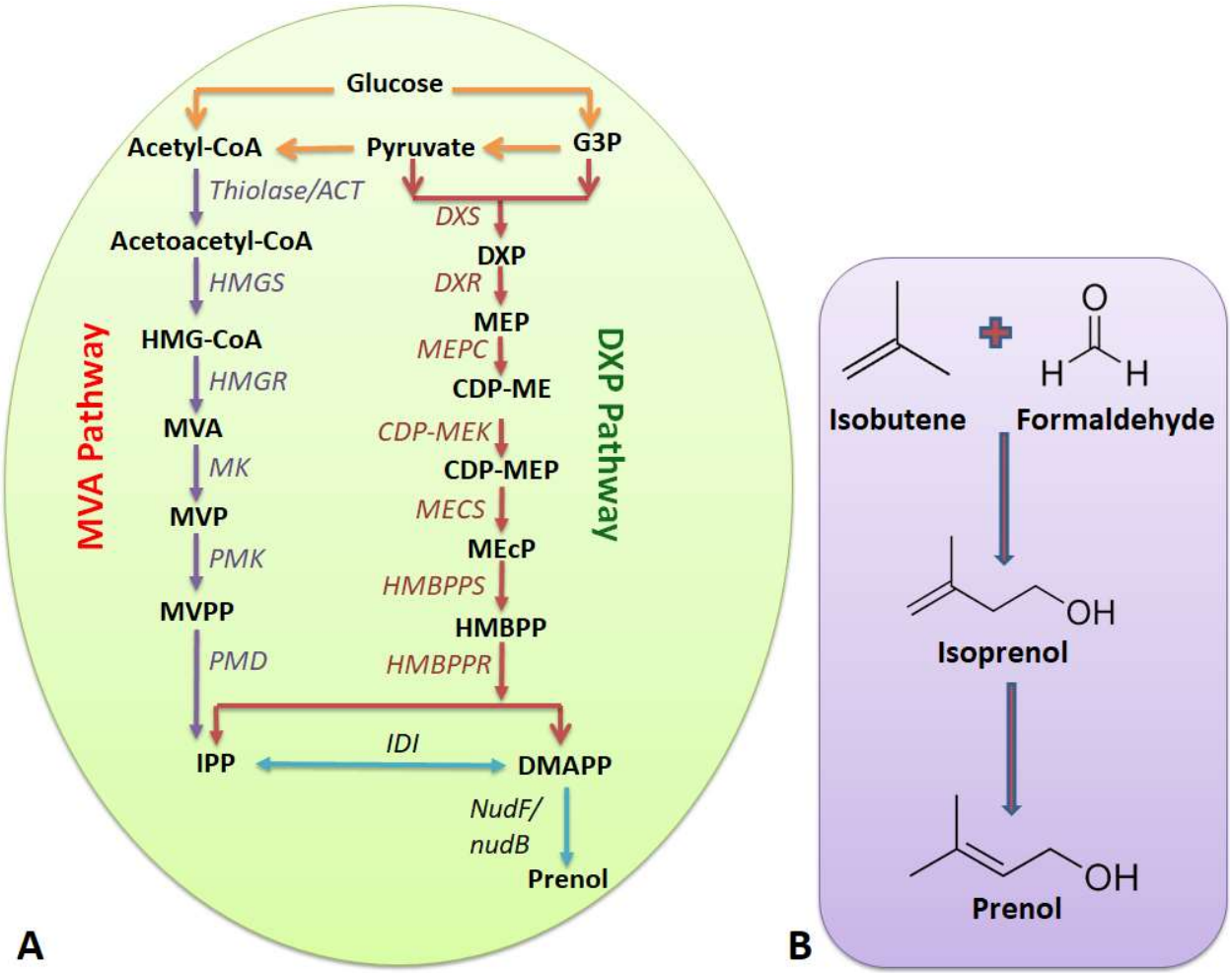
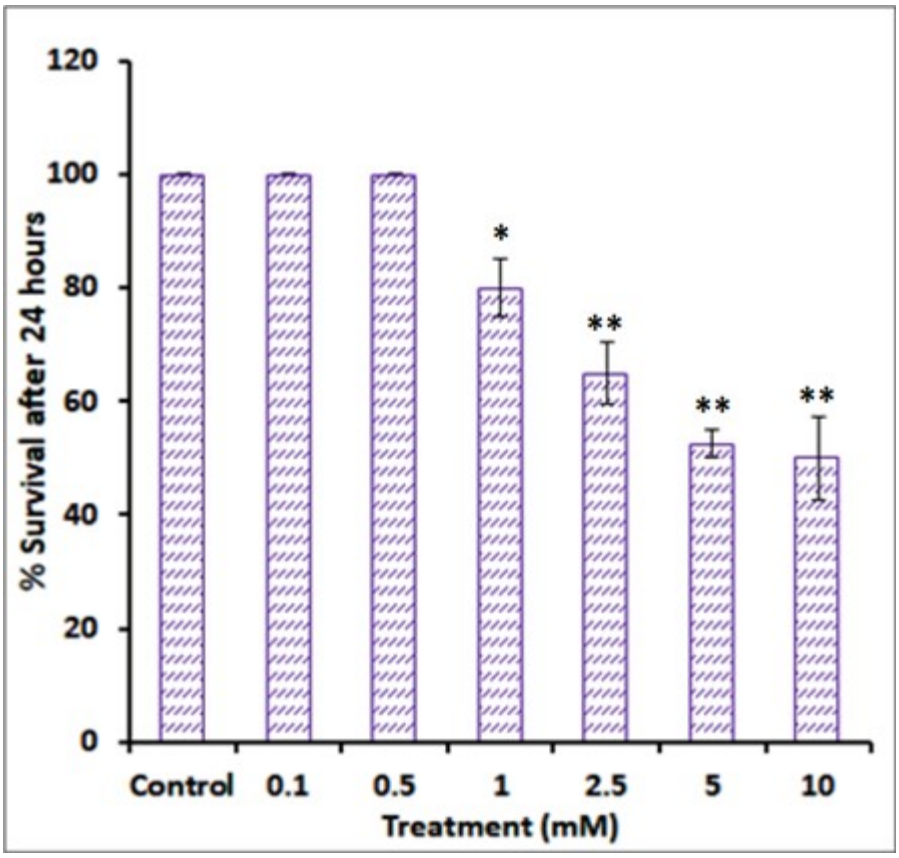
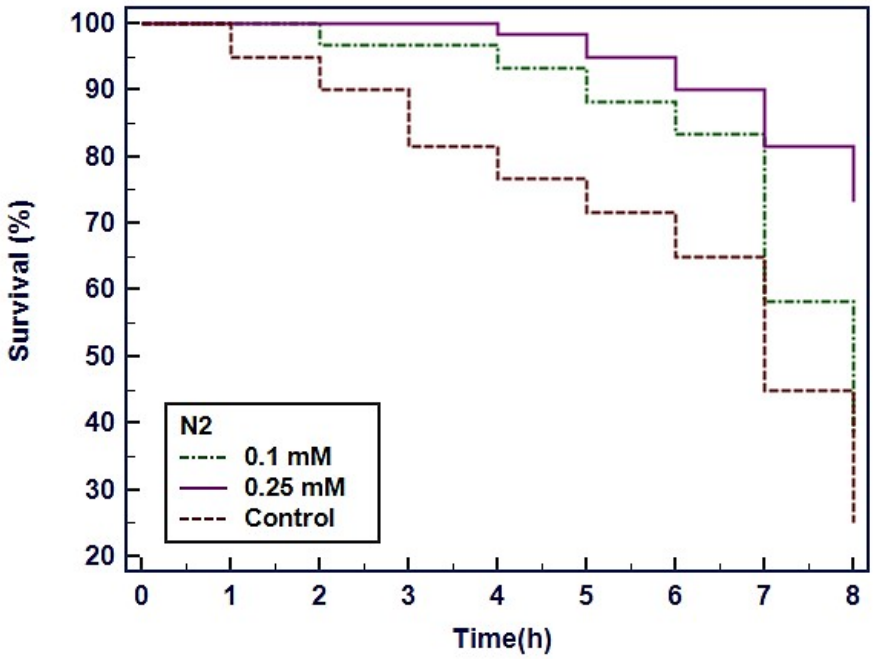


Supplementary Fig. S1. Synthesis of Prenol**A.** Biosynthesis of Prenol from acetyl-CoA via MVA pathway and from glyceraldehyde-3-phosphate and pyruvate via DXP pathway.G3P, glyceraldehyde-3-phosphate; ACT, Acetoacetyl-CoA transferase; HMG-CoA, 3-hydroxy-3-methylglutaryl-CoA; HMGS, HMG-CoA synthase; HMGR, HMG-CoA reductase; MVA, mevalonate; MK, mevalonate kinase; MVP, mevalonate-5-phosphate; MVAPP, mevalonate pyrophosphate; PMK, phosphomevalonate kinase; PMD, pyrophosphomevalonatedecarboxylase; DXP, deoxyxylulose-5-phosphate; DXS, DXP; DXR, DXPreductoisomerase; MEP, 2C-methyl-D-erythritol-4-phosphate; MEPC, MEPcytidyltransferase; CDP-ME, 4-(Cytidine-5′-diphospho)-2-C-methylerythritol; CDP-MEK, CDP-ME kinase; CDP-MEP, 2-Phospho-4-(cytidine-5′-diphospho)-2-C-methylerythritol; MEcP, 2-CMethylerythritol-2,4-cyclodiphosphate;MECS, MEcP synthase; HMBPP, 1-hydroxy-2-methyl-2-(E)-butenyl-4-diphosphate; HMBPPS, HMBPPsyhthase; HMBPPR, HMBPPreductase; IPP, isopentenyl pyrophosphate; DMAPP, dimethylallyl pyrophosphate; IDI, isoprenyldiphosphateisomerase; NudF, ADP ribose pyrophosphatase.**B.** Chemical synthesis of Prenol from isobutene and formaldehyde

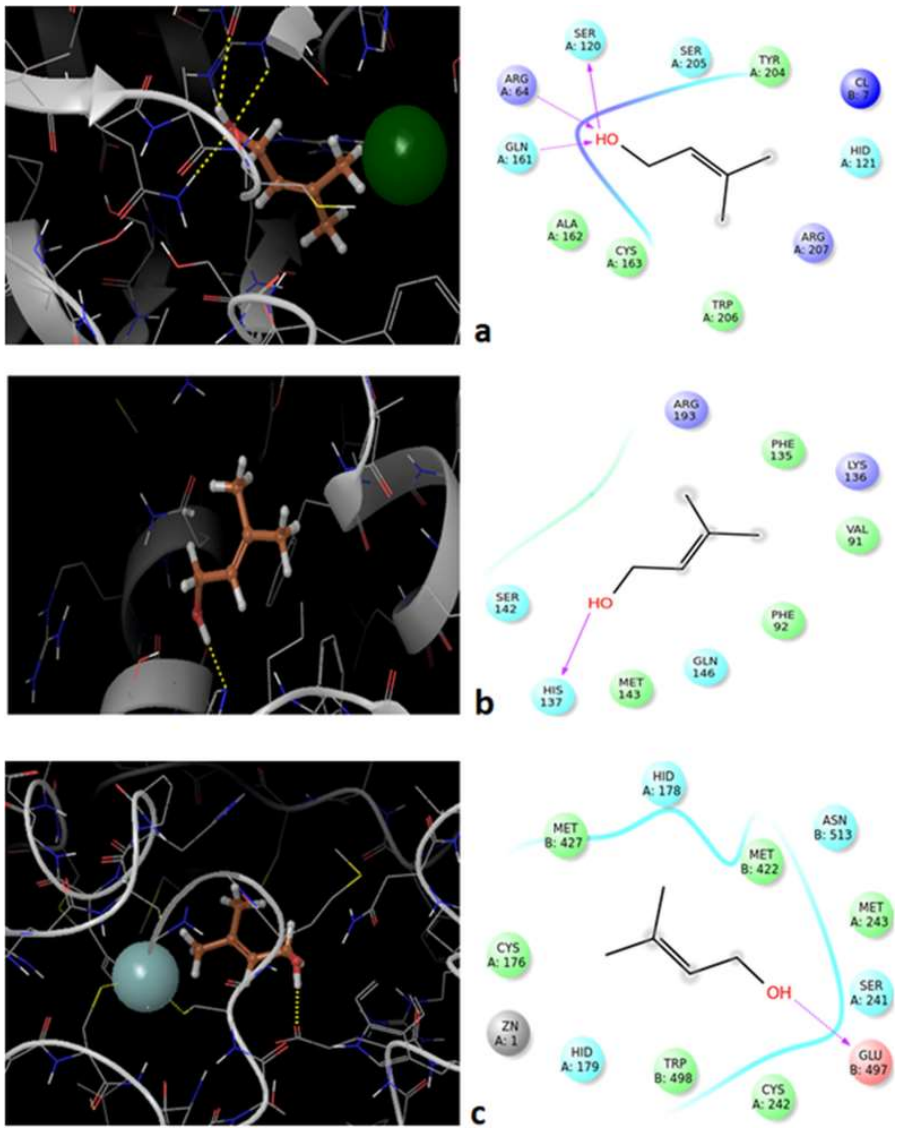


Supplementary Fig. S2. Toxicity assessment of Prenol in *C. elegans*.Higher concentrations [1 mM (n=169), 2.5 mM (n=172), 5 mM (n=178) and 10 mM (n=164)] of Prenol were found to be toxic to wild type worms, whereas, no obvious toxicity was observed at 0.1 mM (n=178) and 0.5 mM (n=172) concentrations. Data were considered significant at $p \leq 0.05$. Error bars represent the standard error of the mean.*$p < 0.01$, **$p < 0.001$.

n is the cumulative number of worms from two independent trials.



Supplementary Fig. S3. Survival of the worm under juglone-induced oxidative stress. Worms were synchronized on NGM plates treated with and without test concentration of Prenol. On adult day 2, the worms were transferred to fresh NGM plates treated with 250 µM juglon to induce oxidative stress. Survival of the worms was measured after every 2 h until 8 h of continuous exposure to juglone. Worms treated with Prenol showed enhanced resistance to juglone-induced oxidative stress compared to untreated control worms. Experiments were performed in 3 independent trials for each test concentration. The data were processed using the Kaplan–Meir survival analysis in Medcalc17.9.7 software.



Supplementary Fig. S4 *In-silico* prediction of molecular docking of Prenol on proteins DAF-16, HSF-1, and SKN-1. The figure indicates molecular docking between target proteins **a.** DAF-16, **b.** HSF-1, and **c.** SKN-1 with Prenol, respectively. Discontinuous yellow lines in left panel represent hydrogen bond interactions

Table S1. Effect of Prenol on the thermal stress tolerance in *C. elegans*.

Strain	Prenol Treatment	No. of worms	Mean lifespan ± SE (Days)	% Change	p value
N2	Control	110	7.07 ± 0.175		
	0.1 mM	118	8.04 ± 0.20	13.7 %	= 0.0004
	0.25 mM	117	9.37 ± 0.28	32.53 %	< 0.0001