

Cell Biology of ageing. IV. Effect of Nordihydro-guaiaretic acid(NDGA) and cortisone on the ageing syndromes of early senescent mutants of N. crassa

less biomass formation (in some cases), (v) increased accumulation of 'Lipofuscin' - age pigment (in some cases), and (vi) increased malondialdehyde formation - a product of lipid peroxidation. In an attempt to overcome the deleterious effects of 'free radicals' which were believed to be the primary cause of early senescence in these mutants, we previously studied the effects of some antioxidants (free radical scavengers) like vitamin E, vitamin C and sodium selenite (Islam and Nessa 1983 Cell Biol. Int. Rep. 7:404. More recently, the effects of NDGA and cortisone, which are also known to be potent antioxidant and membrane stabilizer, respectively (Rana and Munkres 1978 Mach. Ageing and Dev. 7:241-272) were investigated. The results are shown in Table 1 and Table 2. The results indicated that NDGA had a significant positive effect on 377 and cortisone on 270 in the case of malondialdehyde formation i.e. less of the aldehyde was found to accumulate in the supplemented cultures than in the controls (measured according to Heath and Packer 1968; see Islam and Nessa 1984 Cell Biol. Int. Rep. 8:373-377). For other mutants NDGA had either significantly negative or very little negative effect, while cortisone had very little positive effect. In the case of other syndromes of early senescence, NDGA or cortisone had very little or no beneficial effect (Table 1 and 2). The results indicate that cortisone could be a more potent quencher of excessive lipid peroxidation than NDGA as all the mutants tested responded to some extent positively to it with respect to malondialdehyde formation. But, since for the other syndromes of early senescence cortisone had very little beneficial effect, its overall role in ageing could not be proved unambiguously.

Table 1. Effect of Nordihydroguaiaretic acid (NDGA; 20uM) on Ageing mutants of N. crassa

strain	Malondialdehyde formation after 72 hrs. (O.D. 535nm-600nm) Mean ^a + S.D.	UV-fluorescence of culture filtrate after 7 days	Biomass production after 7 days (mg/10ml)	Linear growth up to 14th day (in cm)	Growth potentialities in liquid media (No. of subcultures survived)	Conidial viability after 15 days (Survival percentage)
270	Cont. 0.76* + 0.14 NDGA 0.96* + 0.04	Light green Light green	25.0 35.0	107.1 102.7	16 13	0 0.44
345	Cont. 0.74 + 0.06 NDGA 0.79 + 0.07	No fluorescence No fluorescence	52.5 60.0	86.9 79.2	6 4	0 0
377	cont. 1.09** + 0.05 NDGA 0.89** + 0.01	Light green Light green	45.0 42.5	23.3 21.3	4 4	0 0
448	cont. 0.81 + 0.16 NDGA 0.96 + 0.10	Very lt. green Very lt. green	50.0 50.0	32.5 35.4	13 13	2.0 1.1
EmA	cont. 0.04* + 0.03 NDGA 0.1* + 0.03	No fluorescence No fluorescence	45.0 53.75	132.5 129.5	>18 13	100 100

a: Average of two independent experiments

*: Significant at 5% level

**: Significant at 1% level

Table 2. Effect of Cortisone (20uM) on Ageing mutants of N. crassa

Strain	Malondialdehyde formation after 72 hrs. (O.D. 535nm-600nm)	UV-fluorescence of culture filtrate after 7 days	Biomass production after 7 days (mg/10ml)	Linear growth up to 14th day (in cm)	Growth potentialities in liquid media (No. of subcultures survived)	Conidial viability after 15 days (Survival percentage)
	Mean ^a + S.D.					
270	Cont. 1.17* + 0.13	Light green	52.5	79.4	18	0
	Cort. 1.01* + 0.02	Light green	55.0	76.9	18	0
345	Cont. 1.09 + 0.24	No fluorescence	67.5	73.2	4	0.52
	Cort. 0.94 + 0.08	No fluorescence	70.0	69.4	4	0
377	cont. 1.35 + 0.20	Light green	50.0	20.5	5	0.66
	Cort. 1.14 + 0.02	Light green	50.0	20.1	5	0
448	cont. 1.07 + 0.07	Very lt. green	60.0	27.1	12	15.8
	Cort. 0.99 + 0.06	Very lt. green	62.5	29.8	12	4.0
EmA	cont. 0.07 + 0.01	Very lt. green	65.0	108.3	>19	100
	Cort. 0.07 + 0.01	Very lt. green	62.5	106.9	>19	100

a: Average of two independent experiments

*: Significant at 5% level

From these results, we conclude that ageing is a stochastic process in which several molecular mechanisms work together, and that the concept of 'free radical' theory cannot be applied in every case as the only phenomenon responsible for ageing. - - - Division of Genetics, Institute of Food and Radiation Biology, Bangladesh Atomic Energy Commission, G.P.O. Box 3787, Dhaka, Bangladesh.