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

We have been investigating the molecular mechanisms of cellular ageing using Neurospora crassa as the test organism. By subjecting the conidia to gamma radiation a number of early senescent mutants showing varied ageing syndromes have been isolated and characterized (Islam et al. 1981 Cell Biol. Int. Rep. 5:1005-1017). In general, these mutants show (i) decreased extensional growth, (ii) low replication potentials, (iii) less conidial viability, (iv) 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	Light green	25.0	107.1	16	0
	NDGA	0.96* + 0.04	Light green	35.0	102.7	13	0.44
345	Cont.	0.74 + 0.06	No fluorescence	52.5	86.9	6	0
	NDGA	0.79 + 0.07	No fluorescence	60.0	79.2	4	0
377	cont.	1.09** + 0.05	Light green	45.0	23.3	4	0
	NDGA	0.89** + 0.01	Light green	42.5	21.3	4	0
448	cont.	0.81 + 0.16	Very lt. green	50.0	32.5	13	2.0
	NDGA	0.96 + 0.10	Very lt. green	50.0	35.4	13	1.1
EmA	cont.	0.04* + 0.03	No fluorescence	45.0	132.5	>18	100
	NDGA	0.1* + 0.03	No fluorescence	53.75	129.5	13	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) 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)
	Cont.	1.17* + 0.13	Light green	52.5	79.4	18	0
270	Cort.	1.01* + 0.02	Light green	55.0	76.9	18	0
	Cont.	1.09 + 0.24	No fluorescence	67.5	73.2	4	0.52
345	Cort.	0.94 + 0.08	No fluorescence	70.0	69.4	4	0
	cont.	1.35 + 0.20	Light green	50.0	20.5	5	0.66
377	Cort.	1.14 + 0.02	Light green	50.0	20.1	5	0
	cont.	1.07 + 0.07	Very lt. green	60.0	27.1	12	15.8
448	Cort.	0.99 + 0.06	Very lt. green	62.5	29.8	12	4.0
	cont.	0.07 + 0.01	Very lt. green	65.0	108.3	>19	100
EmA	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.