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# Allantoin and Urate as Suppressors of the Genotoxic Effects of 300–400 nm Ultraviolet Irradiation

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**Abstract**—The genotoxicity of ultraviolet radiation with a wavelength of 300–400 nm (sunlight UVR) is mediated by the generation of reactive oxygen species (ROSs). Research carried out on the basis of a bacterial model developed by us earlier indicated the existence of UV-protecting activity of allantoin, formed from uric acid in organisms of all vertebrates except human and anthropoid apes. Uric acid, which is the end product of purine catabolism in anthropoid apes, does not possess a statistically significant protective effect. The safety of allantoin makes it a promising component for sunscreens.

**Keywords:** UV, reactive oxygen species, genotoxicity, SOS response, allantoin, uric acid.

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Near the surface of the Eearth, the ultraviolet (UV) part of the spectrum with a wavelength of 300–400 nm is known to be a strong inducer of human skin cancer despite its lower quantum energy compared to short-wavelength ultraviolet light (Kligman, 1989). Although there are a number of publications on UV-protectors, sunscreen products, i.e., substances applied to the skin to either absorb or reflect part of the light's energy, are used in practice. It has been suggested that the efficacy of protecting mixtures can be significantly increased by substances that are capable of either stimulating DNA repair or inhibiting its damage. Therefore, the search for natural substances capable of protecting a cell from the genotoxic effects of sunlight UVR is considered important.

The present work aimed to study the capacity of allantoin and its catabolic precursor urate to suppress the genotoxic effects of sunlight UVR near the Earth's surface.

We used the SOS–lux test system, previously used for assessment of the antimutagenic effects of a series of natural substances (Guskov et al., 2002, 2004), to estimate the genotoxicity of the studied treatment. Lux–operon was considered as an SOS-response reporter. To perform the test, we used the *E. coli C 600* strain, transformed with the *pPLS–1* plasmid, where the bioluminescence operon is under control of an SOS promoter (*C600(pPLS–1)*) (Ptitsin, 1996). The experimental protocol is described in detail in (Chistyakov et al., 2009). The obtained data were analyzed using a standard statistical analysis (Vladimirsky, 1983; Glants, 1998).

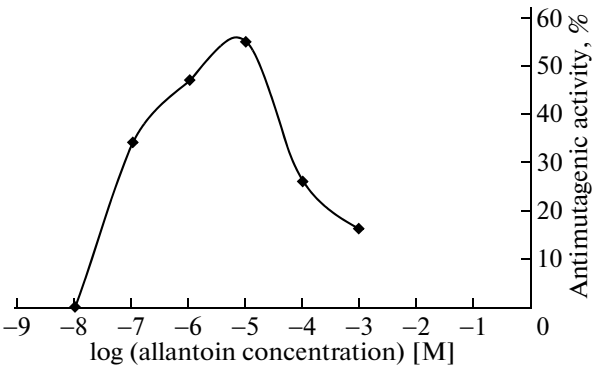
Our experiments have shown (see the table) that allantoin provides antimutagenic effects in a concentration range of $10^{7}$–$10^{4}$ M, with the maximum value of this effect (55%) observed at a concentration of $10^{5}$ M. The dose-dependent manner of the antimutagenic activity of allantoin was shown to be characterized by a bell-shaped curve (see the figure). At the same time, no statistically significant protector activity of urate was found in our experimental model.

Therefore, it was shown that allantoin is capable of decreasing UV-mediated genotoxicity near the Earth's surface by almost two times. These observations are consistent with the previously obtained data (Zhdanov, 2002; Guskov, 2004), which showed the

Induced SOS response in *E. coli* using 300–400 nm UVR in the presence of allantoin

| Allantoin concentration, M | Inducement factor, arbitrary units | Antimutagenic activity, % |
|---|---|---|
| 0 | 7.6 ± 0.4 | 0 |
| $10^{-9}$ | 7.8 ± 0.8 | −3 ± 11** |
| $10^{-8}$ | 7.4 ± 0.6 | 3 ± 8 |
| $10^{-7}$ | 5.0 ± 0.4* | 34 ± 5 |
| $10^{-6}$ | 4.0 ± 0.3* | 47 ± 4 |
| $10^{-5}$ | 3.4 ± 0.3* | 55 ± 4 |
| $10^{-4}$ | 5.6 ± 0.4 | 26 ± 5 |
| $10^{-3}$ | 6.4 ± 0.6 | 16 ± 8 |

Note: *—statistically significant differences with respect to control values, $p < 0.05$ (multiple comparison Dannet test). Hereafter, the value and standard error of the inducement factor were calculated from the data of three independent experiments.
**—Antimutagenic activity error was calculated as the result of indirect measurement division error (Atsukovsky, 2005).




Dynamics of the dose-dependent antimutagenic activity of allantoin.

capacity of allantoin to inhibit the development of a series of destructive processes caused by ROSs. The antioxidative properties of urate, as well as its capacity to protect cellular structures from ROSs, were demonstrated in a series of studies, the most accurate of which is the study conducted by Ames et al. (1981). Nevertheless, it was shown that urate, when oxidized to allantoin in the presence of metals with variable valence, is capable of starting a chain of reactions which leads to hydroxyl radical generation (Filipe et al., 2004). These processes are suggested to compensate for the antioxidative effects.

The obtained data raise a further question regarding the reproduction of the observed photoprotector effect in mammalian skin cells.

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