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Photooxidation of Tetrahydrobiopterin Underlies Vitiligo Phototherapy

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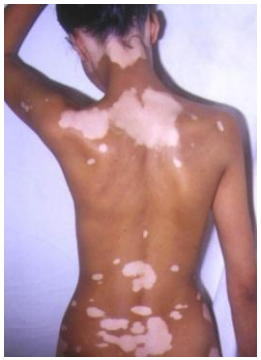
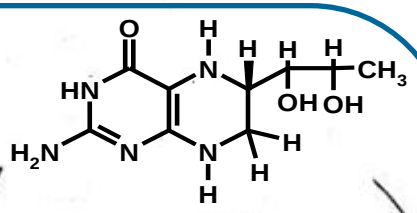
Melanogenesis disorders in vitiligo associated with H_4Bip





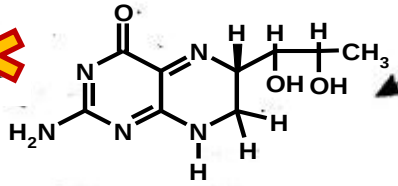
5,6,7,8-tetrahydrobiopterin (H_4Bip)

NADP⁺

Dihydropteridine reductase

NADPH+H⁺

vitiligo

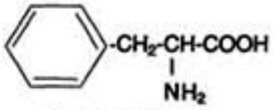


quinonoid 6,7-dihydrobiopterin (qH_2Bip)

7,8-dihydrobiopterin (H_2Bip), biopterin (Bip), H_2O_2

H_2O_2 stimulates *de novo* biosynthesis of excessive H_4Bip through the induction of GTF-cyclohydrolase

Melanogenesis

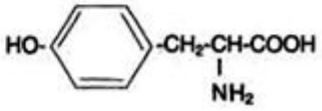


Phenylalanine

O_2

Phenylalanine hydroxylase, Fe^{2+}

H_2O



Tyrosine

Tyrosinase

DOPA

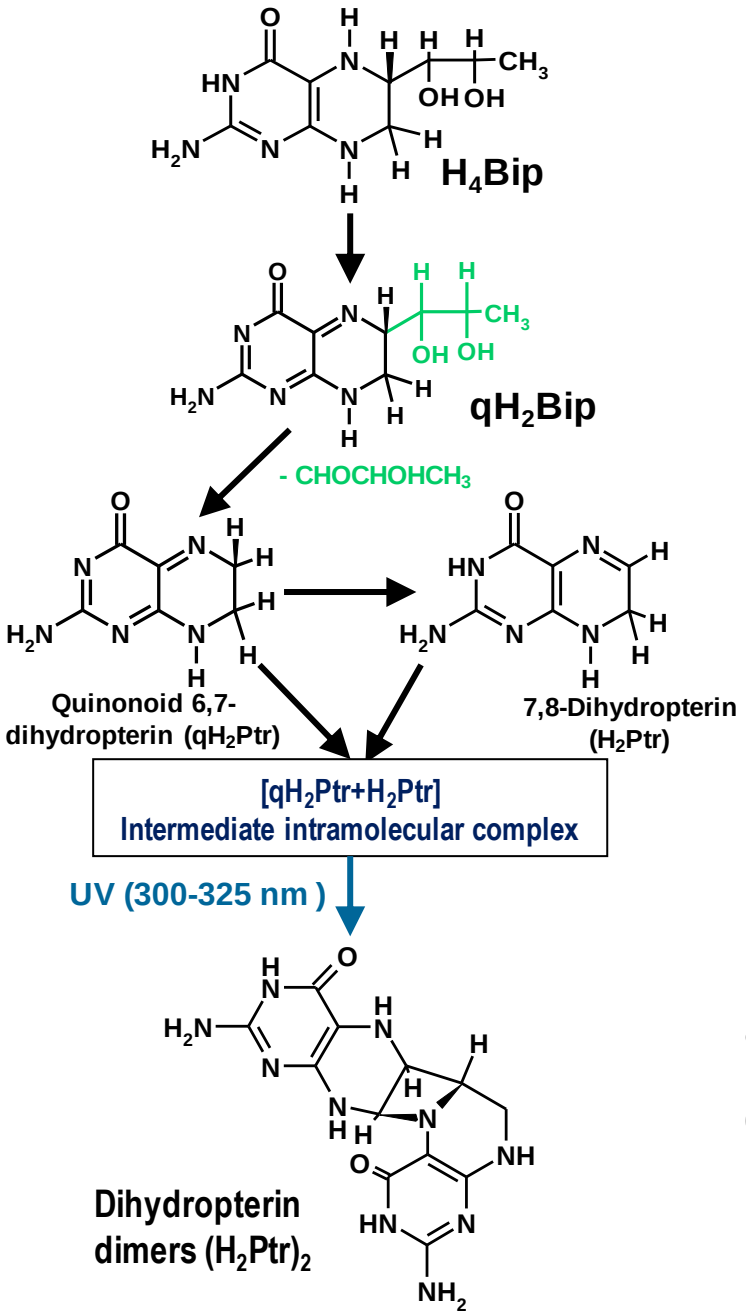
Dopachrome

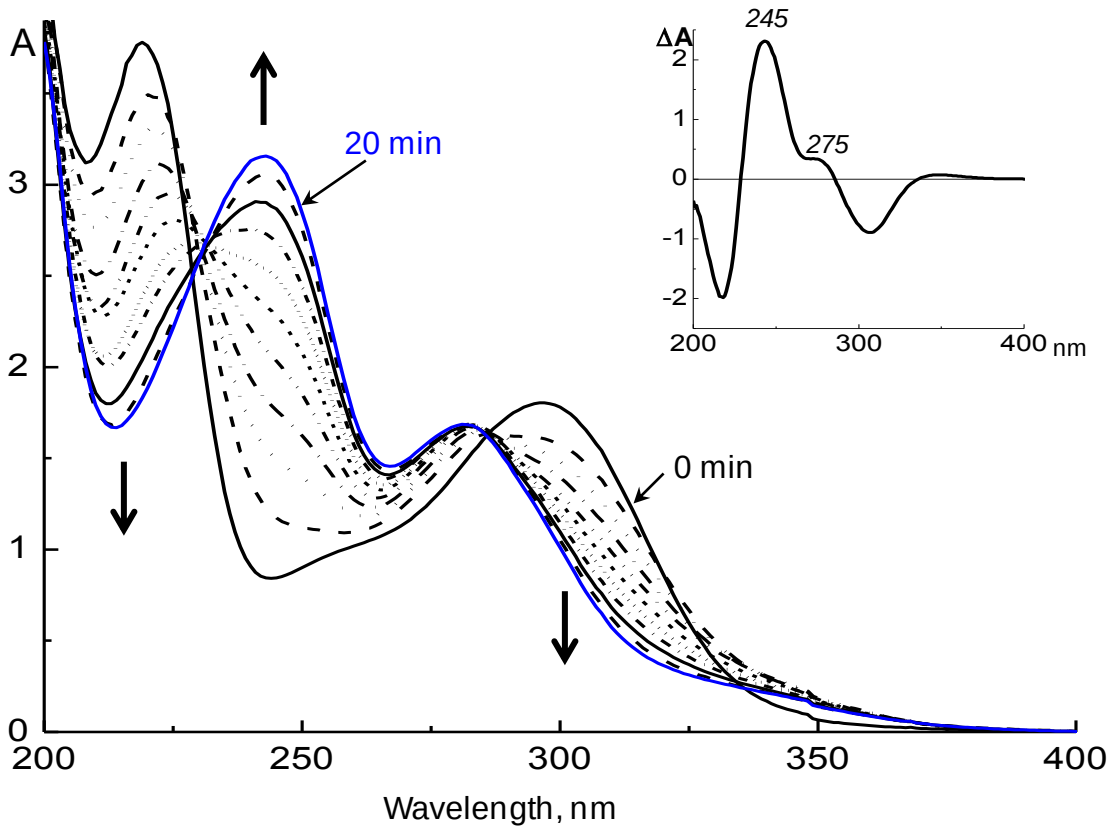
Melanin

The starting point of melanogenesis disorders in melanocytes is apparently associated with metabolic reactions of tetrahydrobiopterin (H_4Bip), a coenzyme of phenylalanine hydroxylase, the first enzyme in the metabolic chain of melanin biosynthesis. During vitiligo, H_4Bip is present in a 3-5-fold excess and inhibits tyrosinase (a key enzyme of melanogenesis). UVB phototherapy (308 and 311 nm) is used to treat vitiligo, but the mechanism of the therapeutic effect remains unclear.

In the present work, the mechanism of H_4Bip photooxidation was studied and the action spectrum of UV radiation was constructed, which sheds light on vitiligo phototherapy mechanism

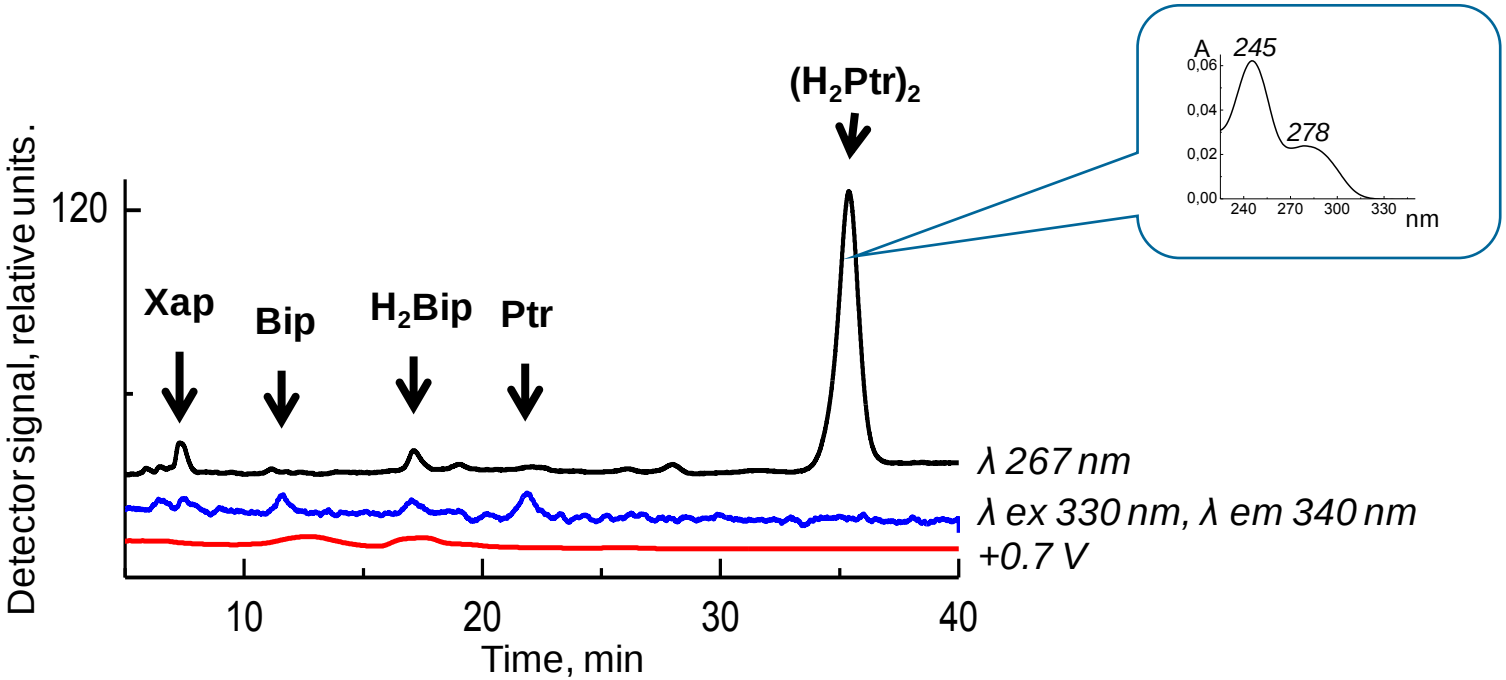
Kinetics and mechanism of H_4Bip photooxidation



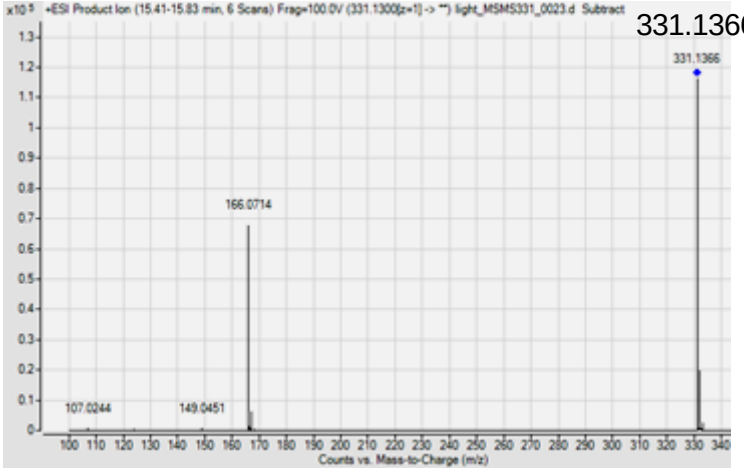


Changes in the absorption spectra monitored upon irradiation at 320 10 nm (11.5 mW cm^{-2}) H_4Bip (1.77 10^{-4}M) in 0.1 M phosphate buffer, pH 7.2. Arrows indicate the changes observed at different wavelengths. Insets show the difference spectrum between the final spectrum (20 min) and the initial one (0 min).

Analysis of the H_4Bip photooxidation products

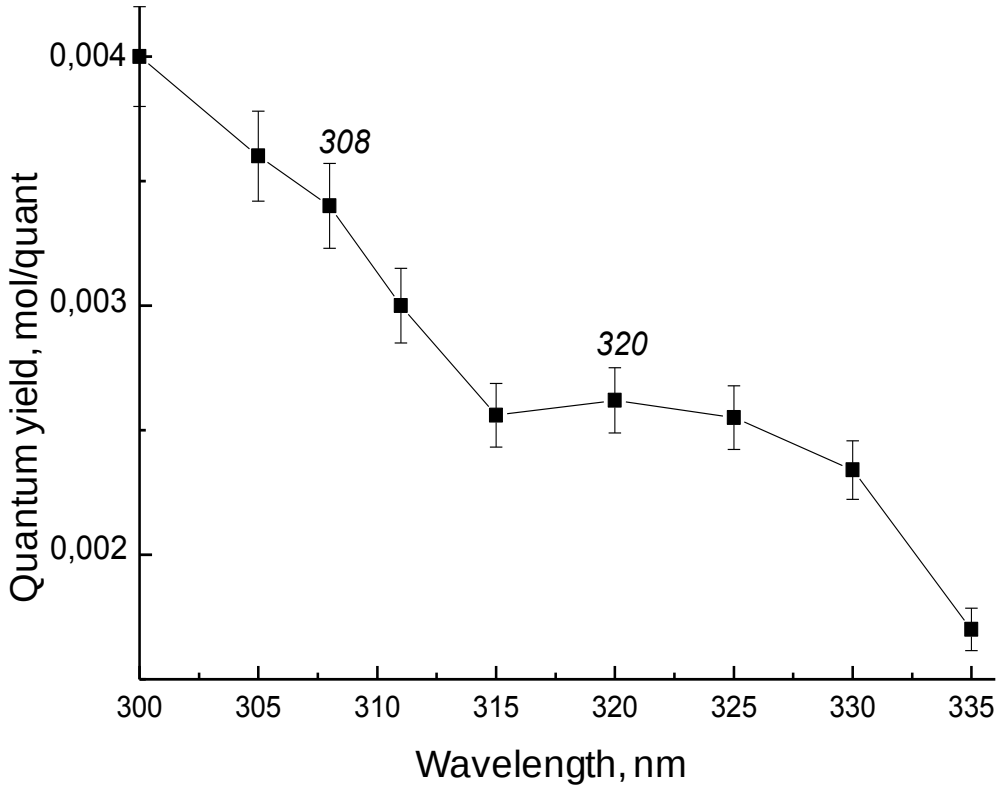


HPLC analysis of photooxidation products with H_4Bip (0.1 M Tris-HCl buffer, pH 7.2) at 320 10 nm irradiation for 16 min, on cation-exchange column Luna 5u SCX 100A (0.1 M Na-citrate buffer pH 2.7).



The HPLC-MS/MS mass spectrum of the photooxidation products contained the dominant signal MH^+/z = 331, that corresponds to mass of the dimer $(H_2Ptr)_2$ – 330 Da.

Dependence of the quantum yield of the formation of dihydropterin dimers on the wavelength of UV radiation



Based on the quantum yields data, the action spectrum of UV radiation was designated, demonstrating that the effective spectral range for the vitiligo phototherapy lies in the range of 300-325 nm. The obtained data and the action spectrum will expand the range of UV light sources for the treatment of vitiligo.

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Thank you for your attention!