COMPARATIVE NMR STUDIES OF THE DRUG INTERACTION WITH SYNTHETIC DOPA MELANIN AND THE NEW MELANIN FROM *Bacillus thuringiensis*

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The soluble synthetic melanin prepared at the near saturating concentration of (-)-Dopa in 0.1M potassium phosphate deuterium oxide buffer exhibited characteristic NMR signal at ppm 6.45-6.75, of small unconverted (-)-Dopa in the pigment but none from the dark polymer. Signals of N-methyl protons (2.57 ppm) and aromatic group (7.28 ppm) of (-)-ephedrine (1.5 mM), however, were altered when the alkaloid was mixed with the melanin. Even at 1:1280 dilution of the melanin, T_2 values of protons were altered. The line broadening of the signals indicated the suspected interaction of the ephedrine with the pigment. The line width measurement of N-methyl protons of (-)ephedrine with the melanin provided two binding constants; k_d, 2.08 mM and k_{d2} >20 mM. Similar measurements of atropine melanin interactions were k_d, 0.79 mM and k_{d2} >6mM[1]. The biologic significance of the drug: melanin interaction is well known.[2, 3] Recently pure water soluble bacterial melanin has been isolated from Bacillus thuringiensis and partially characterized by Professor Ashot Saghiyan, et al. of Armenia[4].

The bacterial melanin was examined for its drug interacting characteristics by 400MHz NMR spectroscopy. In D_2O buffer 1-3 mM melanin showed characteristic signals at 0.7 - 2.5 ppm attributed to aliphatic groups and dense overlapping signals at 2.5 - 4.5 ppm arising from heteroaliphatic groups. When ephedrine or atropine ≤3mM was combined with the melanin, the spectral characteristics of the pigment or the aromatic or N-methyl group signals of the drugs were not altered. This finding is in contrast to that reported for (-)-dopa melanin. The pigment lacks significant interaction with the drugs, perhaps due to low content of paramagnetic centers. Pharmacologic evaluation of the melanin (≤0.3 mg/ml) on the isolated frog skeletal muscle, rat aorta, vas deferens, guinea pig ileum, tracheal smooth muscle and heart, did not interfere with the activities of agonists. On the ileum, however, the melanin produced small contraction. Thus physical and physiological properties of two types of melanins differ. Vertebrates and bacteria need two different types of melanins for different reasons. Many new functions and uses of melanins are discovered.

References:

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