

Investigation of Melanocyte Cytotoxicity to Phenolic Compounds in Vitiligo

Raymond E. Boissy, Ph.D.

*Assoc. Prof of Dermatology & Cell Biology, Neurobiology & Anatomy
University of Cincinnati Medical Center*

There have been anecdotal reports of "occupational" vitiligo developing at a relatively high frequency in people who work with or are exposed to phenolic and catecholic derivatives. It had been suggested that environmental toxins may be very damaging to melanocytes and could lead to cell death after excessive exposure in skin. We have continued to investigate whether and how phenolic derivatives (specifically 4-tert butylphenol; TBP), found in rubbers and industrial oils, can cause the destruction of melanocytes. We had previously demonstrated that cultured melanocytes derived from human skin were indeed cytotoxic to melanocytes in a time- and dosage- dependent manner. We have recently assessed the cytotoxicity of a panel of melanocytes cultured from over one dozen individuals and demonstrated that viability of melanocytes after exposure to 50 uM TBP ranged from relatively unresponsive (i.e., a 15% decrease in cell viability) to extremely susceptible (i.e., a 72% reduction in cell viability). This suggests that the population on the whole vary in their sensitivity to this toxic agent. We would expect that people who develop vitiligo after exposure to phenolic derivatives are individuals most sensitive to the compound. We are currently investigating the relative effect of TBP on melanocytes cultured from patients with vitiligo.

As it turns out, 4-tert butylphenol is structurally similar to tyrosine, the substrate used by the melanocyte to synthesize melanin. It has been proposed in the literature that the vulnerability of melanocytes to TBP damage occurs because the cells erroneously begin to use TBP to make melanin which results in the generating of toxic reactive oxygen metabolites as a consequence. However, our current research demonstrated that activity of making melanin is independent of the cytotoxic affects of TBP. This data consist of: 1.) The relative cytotoxicity among cultured melanocytes did not correlate with their tyrosinase activity or melanin content. 2.) Melanocytes from individuals with albinism were moderately sensitive to TBP. 3.) Analogues of TBP less similar to tyrosine were equal in cytotoxicity as TBP. 4.) Fibroblasts cultured from numerous individuals were dramatically more sensitive to TBP than melanocytes. This suggests that melanocytes are not selective targets of this environmental toxin. Yet, we are still perplexed as to why only melanocytes can be destroyed after exposure to TBP resulting in "occupational" vitiligo.

However, 4-tert butylphenol still has the potential to be converted into reactive oxygen metabolites (i.e., free radicals, superoxides, etc.) by the melanocytes by a more conventional pathway. Therefore, we have begun to test the effect of therapeutic antioxidants on the effect of cytotoxicity by TBP. In our pilot study, Vitamin E as opposed to catalase has a minimal effect in inhibiting the cellular damage caused by TBP. However, further studies are indeed warranted in order to validate the effect of Vitamin E on the consequence of exposure to phenolic derivatives.