

[This article was published in the NEMSN Newsletter, November-December 2021.]

Other L-Tryptophan-Like Supplements to Avoid

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The Eosinophilia-Myalgia Syndrome (EMS) epidemic of 1998-90 was caused by the consumption of contaminated Showa Denko L-Tryptophan. However, over the past thirty years there have been a number of sporadic patient reports of EMS-like symptoms from individuals taking other L-Tryptophan-like supplements. These include a number of patients who have self-reported through NEMSN, and this is detailed more in the article written by Nancy Grant and Lois Vierk entitled “Contacts from Epidemic Patients and Possible New EMS Cases” published in the NEMSN December 2019 newsletter.

5-Hydroxytryptophan & Melatonin: After the temporary withdrawal of L-Tryptophan due to the EMS epidemic, 5-Hydroxytryptophan (5-HTP) was promoted and marketed as a safer, superior replacement. The increased usage of 5-HTP and vigilance over the possible role of contaminants in EMS onset prompted a report in 1994 that three members of a Canadian family using 5-HTP manifested EMS-like symptoms. Analysis of the case-implicated product in 1994 revealed the presence of a unique contaminant, designated as Peak X. My research group in association with Dr. Gleich ultimately identified case-associated Peak X as 4,5-tryptophan-dione (4,5-TD) and detected its presence in a number of commercially available 5-HTP supplement brands. Our findings were subsequently confirmed by independent analyses carried out by the US FDA.

There have been numerous reports from a variety of sources, including NEMSN, that taking Melatonin can also cause EMS-like symptoms. In a clinical study in 1993, Melatonin was being evaluated as an anti-cancer agent; several patients developed eosinophilia. Based on these reports my group at Mayo Clinic analyzed three commercially available Melatonin supplements bought from a local pharmacy in Rochester, Minnesota. Analysis of these Melatonin tablets enabled us to determine the chemical structures of seven contaminants. The structural similarity to the case-associated contaminants found in Showa Denko L-Tryptophan was striking. Two of these contaminants were identified as Peak C (L-Tryptophan case-associated contaminant) analogs. The other Melatonin contaminants were identified as Peak E (L-Tryptophan case-associated contaminant) analogs.

Chemical Structure of Contaminants: The contaminants found in L-Tryptophan, 5-HTP and Melatonin all have complex names and chemical structures. The determination of these structures is both expensive and complicated. These efforts require access to analytical instrumentation that can cost millions of dollars and requires many years of specialized training. So why go to such efforts to determine the structures of these contaminants? The structure of a molecule, particularly a contaminant, can provide valuable insight into how disease symptoms such as those in EMS occur. In other instances the structure and shape of a molecule determines how it interacts with the body. For example, everybody is familiar with the analgesic Aspirin, as well as the cholesterol lowering Statin drugs. These widely used chemical compounds have very different chemical structures and thus react with different parts of your body in order to bring about the effects we are all familiar with after taking them. The same principle applies to

contaminants; by determining their structures it may be possible to unravel the mechanism by which they harm your body. Once we have such an understanding then it is both possible to prevent further damage as well as possibly treat the effects of the contaminant(s).

L-Tryptophan, 5-HTP and Melatonin Same or Different? All three supplements have been used to facilitate sleep, control weight gain, aid in the relief of depression and other assorted maladies. Many people who take L-Tryptophan, 5-HTP and/or Melatonin believe that they are unrelated, and very different supplements. So why has each one of these supplements been associated with EMS-like symptoms after consumption by individuals? Organic Chemists and Toxicologists would inform you that *all three supplements are closely related based on their chemical structures*. As an analogy, think about if you were evaluating three different houses, one of which will be purchased. All three houses have an identical foundation and structural framework. However, they differ in color and type of siding, window frames and door entrance ways. Those minor changes can elicit very different responses from potential buyers, but to the building constructor they are essentially the same type of house with cosmetic changes

In the case of L-Tryptophan, 5-HTP and Melatonin the structural framework is identical, and consists of what organic chemists call an indole ring system. However, just like the house analogy, some of the appendages (called functional groups) are different. These minor structural changes determine how each of these compounds can react differently in the human body. But, L-Tryptophan, 5-HTP and Melatonin also react with other molecules in such a way that produces structurally similar contaminants that may induce identical symptoms of a disease like EMS. More recently, in 2015 a peer-reviewed case report entitled “Drug rash with eosinophilia and systemic symptoms caused by the dietary supplement Diindolylmethane” was published in the *Journal of Allergy and Clinical Immunology*. Diindolylmethane (DIM) is sold as a supplement for the potential treatment of hormone-related conditions, including acne, menopause symptoms, prostate issues, and certain forms of cancer. Please note there is no clinical evidence to support such overly optimistic claims for the use of DIM. In this case a 36 year-old woman presented with an itching, painful rash and facial edema after taking DIM. She was diagnosed with “Drug Rash with Eosinophilia and Systemic Symptoms” (DRESS). DRESS is a closely related eosinophilic mediated disease to EMS. The structure of DIM contains two indole rings joined together, and “coincidentally” resembles the structure of the case-associated contaminant Peak E found in Showa Denko L-Tryptophan.

All individuals should remember that L-Tryptophan, 5-HTP and Melatonin are very similar from a chemical structure perspective and this must be considered the next time you think about purchasing a supplement for personal consumption. Not only should you be cautious in considering the use of 5-HTP and Melatonin, but also any supplement containing an indole ring, as in the case of DIM.

(Please note the opinions expressed in this article are solely those of the author and do not necessarily reflect the views of NEMSN.)