

## **Urinary Pyrrole (Maue Factor): Metric for Oxidative Stress in Behavioral Disorders**

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Urinary pyrrole, "Maue Factor" for its chromatographic appearance, was found elevated in 60% of schizophrenics four decades ago by Hoffer, who reported that high doses of niacinamide lowered pyrrole levels, and that symptoms improved accordingly. Pfeiffer introduced successful treatment with zinc, vitamin B6 and generous anti-oxidants. Many thousands of patients have responded to these approaches, often dramatically.

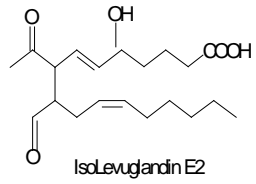
The frequency of elevated pyrrole is 70% in Down syndrome (Jackson, Riordan), 50% in autism (Audhya), 40% in alcoholism (Mathews-Larson), and 30% in ADHD (Walsh). Irrespective of behavioral diagnosis, elevation is associated with poor tolerance of physical and emotional stress, which increases urinary levels and necessitates dosing adjustments. Low red cell (Audhya) and white cell (McLaren-Howard) zinc levels correlate with pyrrole levels, as do zinc (and B6) requirements, which may be great.

Maue Factor is unstable in presence of light, and was misidentified as kryptopyrrole (KP) until improved technology in 1976 established that hydroxyhemopyrrolin-2-one (HPL), a hydroxylactam of hemopyrrole, is Maue Factor, or at least its key moiety. Laboratories use KP or HPL as standard for this economical test.

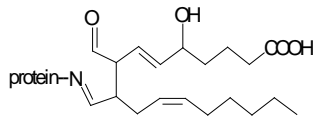
HPL inhibits heme synthesis (Graham). Experimentally, heme inhibition results in lower cellular zinc, and higher iron and oxidativestress levels (Ames). Heme-dependent enzymes, which play key roles in anti-oxidant defense, include catalase, peroxidase, NO-synthase, cystathionine synthase, heme-hemopexin (synthesis of metallothionein), p450, and cytochromes for energy production.

Maue Factor is strongly associated with depletion of arachidonic acid (Bibus), which is attacked by free radicals to form levuglandins and isolevuglandins, which in turn produce pyrrolic tissue adducts. These pyrrolic adducts consistently auto-oxidize to form a hydroxylactam (Salomon), and the pyrrolic moiety of these adducts corresponds precisely to the structure of HPL. Urinary pyrroles are known to result from the formation of pyrrolic tissue adducts (Batoreu).

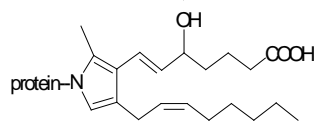
Thus, Maue Factor appears to derive from oxidative injury to lipid and protein. Current research seeks to correlate Maue Factor with glutathione with glutathione, GSH-peroxidase, lipoperoxide, isoprostane, and apoptosis levels. The clinical experience with Maue Factor in the abnormal behaviors should heighten interest in the causal role of oxidative stress and advance treatment for these disorders.



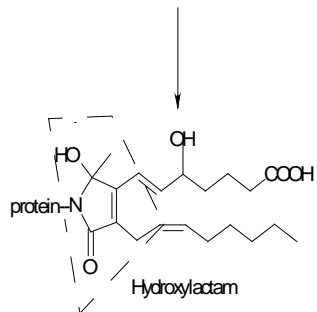
protein-NH



Schiff base



Pyrrole



Boxed-area is HPL (Hydroxyhemopyrrolin-2-one), putative Mauve Factor