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Commentary

Significance and Application of Pyrroles as Possible Biomarkers in Stress Disorders

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DESCRIPTION

Pyrrole, which represents a class of five-membered nitrogen heterocycles, can be found as a chemical subunit of porphyrin systems such as vitamin B12, bile pigments (biliverdin and bilirubin), heme and chlorophyll also known as ' Crypto Pyrrole', later hydroxyhemopyrrolenone, it is found in urine and is associated with psychiatric disorders such as schizophrenia, anxiety, and depression. Mauve factor is another term used for pyrrole and crypto pyrrole, a term coined to reflect the mauve complex formed when active pyrrole derivatives react with urine extracts.

Here we propose that most previous urine tests for pyrrole detected urobilinogen. This has been characterized by spectroscopy and confirmed by laboratory interference studies, including spike recovery experiments in pure urobilinogen. This ambiguity may be due to the fact that pyrrole and urobilinogen react similarly to urine extract by forming mauve complexes at different wavelengths. Pyrrole is elevated when physical and psychological stress leads to overproduction of peroxides. This process, termed oxidative burst, is followed by increased regulatory heme fragmentation and pyrrole accumulation. As already mentioned, the by-product urobilinogen is formed in a completely different way. Since psychiatric disorders are associated with markers of oxidative stress, it is important to distinguish between the two different by-products. This is particularly important in diagnosing psychosis, as patients with biliary tract disease may have a similar ethology as psychosis. Mental disorders are complex, have much comorbidity and are often associated with deteriorating physical health. Management of biliary tract-related disorders is also quite different compared to oxidative stress disorders, so it is important to distinguish between the two different pathophysiology's to ensure proper patient management.

Our laboratory-established method physically separates water-soluble pyrroles such as zwitter ionic porphobilinogen and spectrophotometrically distinguishes between urobilinogen and reactive pyrrole fractions. Both by-products can be measured separately. Quantification of urobilinogen levels is useful as it is an indicator of bile flow and renal function. Absence of urobilinogen indicates obstructed bile flow, and urobilinogen >16-33 mol/L indicates kidney damage or impaired kidney function. Measurement of pyrrole levels is used as a marker of the degree of oxidative stress or regulatory heme damage.

A redox imbalance or oxidative stress resulting from both environmental and genetic factors is observed in patients with schizophrenia. Therefore, identifying markers of oxidative stress in the early stages of psychosis and using antioxidant therapy as an adjunct to antipsychotic drugs has important implications. The reaction of p-N, N-Di Methyl Amino Benzaldehyde (DMAB) with pyrrole moieties has been well studied as a marker of oxidative stress dysregulation for over a century. During this time, pyrrole in urine extracts was tested with varying precision to identify elevated levels in patients diagnosed with schizophrenia. The substances from this reaction have not been fully elucidated, but an objective look at most studies suggests that urobilinogen is likely one of them.

There are examining the chemistry of HPL, DMAB and pyrrole. However, the date remains controversial. There are many anecdotal comments suggesting that B6 and pyrrole form complexes. Such a chemical structure (without confirming spectroscopic data such as NMR chemical shift data) and the correctness of these hypotheses are questionable. This is unusual since pyridoxal is a pyridine derivative. To confirm this, we used 3-ethyl-2, 4-dimethylpyrrole and the pyridoxal vitamin B6 (aldehyde DMAB was used in place of aldehyde pyridoxal) to reproduce conditions suitable for the DMAB reaction and UV-Reaction progress was monitored by Vis and LC-MS. without success. This suggests that the assumption that pyridoxal is quenched by pyrrole substances *in vivo* is weak.

It is well known that vitamin B6 does not bind to pyrrole due to incompatibility of the chemicals involved. The potential benefits of B6 treatment may be due to its antioxidant properties. However, further research is needed to identify other antioxidants such as N-acetylcysteine. Understanding biochemistry and the role of biomarkers promises objective scientific methods to help diagnose and treat psychiatric disorders.

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