Discerning the Mauve Factor

Woody McGinnis
London
October 1, 2006

Abram Hoffer    Tapan Audhya    William Walsh
James Jackson    Peter Lauda    Roman Lietha
Douglas Bibus    Frances Jurnak
John McClaren    Howard
Irene (Vicky) Colquhoun

1920-2000
David Horrobin
1939-2003
Mauve History

Discovered in urine in 1958

Named for lilac-colored appearance on paper chromatograms developed with Erhlich's reagent

Labile and elusive

Abram Hoffer is the father of Mauve
Qualitative Mauve assay

All normals Mauve-negative

27/39 early schizophrenics positive

All 7 who recovered on niacinamide converted to negative
Mauve associates with relapses

Apparent role in other behaviors: ETOH, depression

A "mentally retarded" mauve-positive child responded dramatically to niacinamide
Hoffer and Mauve

Relatives should be tested

Preventive potential

10/14 criminal / deviant positives

740 patients: all recovered schizophrenics negative, unrecovered 50% positive
Mauve in Schizophrenia


Yutwiller 1962

O'Reilly 1965

Sohler 1967 x 2
High-Mauve and Behavior

- Down syndrome: 70%
- Schizophrenia: 40-70%
- Autism: 50%
- ADHD: 30%
- ETOH: 20-80%
Donald Irvine and Mauve

Dubbed it “Mauve Factor”

First to extract Mauve from urine

First to suggest pyrrole structure

Mis-identified Mauve twice

Animal experiments
Pfeiffer and Mauve

Introduced the colorimetric assay for Mauve using kryptopyrrole as surrogate standard

**Vitamin B6 and zinc** to suppress Mauve and improve clinical outcome, irrespective of behavioral diagnosis
Mauve is hydroxyhemopyrrolovin-2-one (HPL), **not** kryptopyrrole

![Mauve (HPL) and Kryptopyrrole structures](attachment:image.png)
Validation of Colorimetric Assay

HPL colorimetric equivalents in micrograms / deciliter vs. HPL by HPLC / MS in micrograms / deciliter

n = 54; r = 0.97
Validation of Colorimetric Assay

n 44; r 0.98

HPL Colorimetric Equivalents in micrograms / deciliter

HPL by HPLC / MS in micrograms / deciliter
Mauve Testing

- Levels can fluctuate rapidly during the day, so 24-hour collection.
- Variations in urine volume can affect levels appreciably, so normalize to SG or creatinine.
- Light and temperature labile, so dark techniques, ascorbate preservative, freeze / overnight transport.
HPL and B6 Activity

HPL in micrograms per deciliter

EGOT activity ratio

n 32; r neg 0.77
Mauve Associations

Poor dream recall
Poor breakfast appetite
Nail spots (leukodynia)
Stretch marks (striae)
Pale skin / poor tanning
Acne, allergy, obesity
Mauve Associations

- Course eyebrows
- Knee and joint pain
- Cold hands or feet
- Abdominal tenderness
- Constipation
- Eosinophilia
Mauve Associations

Light / sound / odor intolerance

Tremor / shaking / spasms

Hypoglycemia / glucose intolerance

Delayed Puberty / Impotence

Amenorrhea / irregular periods

B6-responsive anemia
Mauve Associations

Stress intolerance
Emotional lability
Explosive anger
Anxiety / Withdrawal
Pessimism
Depression
Mauve Associations

Familial
Paranoia / Hallucinations
Perceptual disorganization
Crime and deliquency
Substance abuse
Attention deficit / ADHD
Autism
Leukodynia in Zinc Deficiency
Colorimetric Mauve and WBC Zinc

HPL equivalents in micrograms / deciliter

White-cell zinc in nanograms / liter

n 58; r neg 0.54
HPL and RBC Zinc

n 37; r neg 0.69
HPL and Plasma Biotin

$n = 24; \, r = \text{neg} \, 0.74$
Oxidative stress

Poor energetics ↔ Excitotoxicity
Emotional Stress → Oxidative Stress
Emotional stress → Oxidative stress

Tension-anxiety scores correlate with oxidized DNA in blood

Meditation lowers blood lipid peroxides
Immobilization-stress

Increases free radicals and oxidized lipid, protein and DNA

Brain peroxidation prevented by antioxidants
Mauve and Stress

O’Reilly 1965: Hypothesized relationship
Ward 1973: Mauve proportionate to stress
Pfeiffer 1976: Mauve “is induced by stress”
Sohler unpublished animals studies
McCabe 1983: B6 and zinc “stress doses”
Audya 1992: US Navy cold water stress
HPL and Plasma Reduced Glutathione

Plasma GSH in micromoles / liter

HPL in micrograms / deciliter

$n = 30; r_{neg} = 0.85$
HPL and Heme

Graham 1979: HPL injection acutely depresses hepatic microsomal heme and p450 levels

Ames 2002: Experimental heme depression lowers intracellular zinc, induces NOS and increases oxidative stress
Require Heme

Cystathionine synthase
Catalase
Heme-hemopexin for MT translation

Guanylate cyclase
Cytochromes
Sulfite reductase
NOS
Pyrrolase
HPL and RBC Catalase

Catalase units / min / mg of hemoglobin

HPL micrograms / deciliter

n 30; r neg 0.79
HPL and Plasma Nitric Oxide

n 30, r 0.60 improves to 0.96 if exclude outlier
Mauve and Cortisol

• Irvine 1972: corticosteroid administration to rats produced significant Mauve excretion.

• Increased intestinal permeability from psychological stress is mediated via endogenous glucocorticoids

• Administration of corticosteroids experimentally increases intestinal permeability
Mauve from Microbes?

• Irvine 1973: Tetracycline reversibly abolished Mauve excretion in 4 subjects.
  Kanamycin abolished or significantly decreased Mauve in 9 subjects.

• Monopyrroles are generated by various bacteria, including pseudomonas spp.
Colorimetric Mauve and Indicans

Colorimetric Mauve Equivalents in mcg/dl

- indican=0
- indican=1
- indican=2
- indican=3
- indican=4

n 2738
Colorimetric Mauve and Indicans

Ratio of Elevated / Normal Mauve Values

Urinary Indican Measurement

n 2738
Summary

• Mauve levels predict proportionately lower functional B6 and zinc blood levels.
  • Strong relationship to stress.
• Emerging evidence that Mauve is a biomarker for oxidative stress.
  • Possible enteric origin of Mauve.
• Need for prospective laboratory studies and randomized clinical trials