Dr John Walshe and the treatment of Wilson’s disease

Dr Rupert Purchase
Wilson’s Disease Support Group – UK

Background: Copper and Wilson’s disease

- 1785: First description of copper intoxication (Thomas Percival, MD, FRS).
- 1948: Elevated copper (and iron) levels found in brain and liver samples from Wilson’s disease patients. Significance of reducing copper levels in Wilson’s disease patients realised.
- 1948: Elevated copper (and iron) levels found in brain and liver samples from Wilson’s disease patients. Significance of reducing copper levels in Wilson’s disease patients realised.
- 1948: Elevated copper (and iron) levels found in brain and liver samples from Wilson’s disease patients. Significance of reducing copper levels in Wilson’s disease patients realised.
- 1952: PENICILLAMINE (penicillamine) first synthesized by John Cornforth. Identified as the D-isomer by Dorothy Crowfoot et al. Found to be a chemical degradation product of penicillins (1943).
- 1955: D-penicillamine identified as a copper-binding agent following observations of depletion of copper levels in cinnamon caused by dietary molybdenum (1943-1975).
- 1951: D-Penicillamine identified as a potential metal chelating agent. In particular, for removing copper in a patient with Wilson’s disease.
- 1951: D-penicillamine (for the first time) as a potential metal chelating agent. In particular, for removing copper in a patient with Wilson’s disease.
- 1952: PENICILLAMINE (penicillamine) first synthesized by John Cornforth. Identified as the D-isomer by Dorothy Crowfoot et al. Found to be a chemical degradation product of penicillins (1943).
- 1955: D-penicillamine identified as a copper-binding agent following observations of depletion of copper levels in cinnamon caused by dietary molybdenum (1943-1975).
- 1955: D-penicillamine first synthesized by John Cornforth. Identified as the D-isomer by Dorothy Crowfoot et al. Found to be a chemical degradation product of penicillins (1943).

Background: Ligand chemistry

- PENICILLAMINE (penicillamine) first synthesized by John Cornforth. Identified as the D-isomer by Dorothy Crowfoot et al. Found to be a chemical degradation product of penicillins (1943).
- D-Penicillamine first synthesized by John Cornforth (1951). Identified as a copper-binding agent following observations of depletion of copper levels in cinnamon caused by dietary molybdenum (1943-1975).
- PENICILLAMINE (penicillamine) first synthesized by John Cornforth. Identified as the D-isomer by Dorothy Crowfoot et al. Found to be a chemical degradation product of penicillins (1943).
- PENICILLAMINE (penicillamine) first synthesized by John Cornforth. Identified as the D-isomer by Dorothy Crowfoot et al. Found to be a chemical degradation product of penicillins (1943).

Summary

Treatment of Wilson’s disease was transformed in the 20th century by the introduction of four drugs, which could be administered orally: D-penicillamine, triethylenetetramine (trientine) dihydrochloride, zinc acetate and ammonium tetrathiomolybdate.

Three of these four oral treatments – D-penicillamine, trientine and tetrathiomolybdate – owe their provenance to the diligence, perspicacity and intuition of the English physician, Dr John Walshe.