Cyclodextrin therapy for Ischemic Heart Disease (IHD).

The repurposing of an old and widely used pharmacological substance is about to alter the approach to the management of ischemic heart disease (heart attacks and angina).

Hydroxypropyl beta cyclodextrin (HP-β CD) is a 'sugar soap' that has been widely used for many decades as an ingredient of therapeutic formulations, generally to assist in the absorption of other drugs. Animal and other laboratory studies over the last decade have shown that HP-β CD can remove cholesterol from areas of inflammation in blood vessel walls, called plaques, that occur in response to the toxic effects of cholesterol that finds its way into the wall of arteries prom the bloodstream. Plaques block arteries producing heart attacks and angina. Editorials in scientific journals have emphasised the potential importance of the findings of HP-β CD induced plaque regression, or shrinking, of plaques as a treatment to reduce IHD and called for urgent studies to determine whether HP-β CD can cause plaque regression in humans with IHD and reduce heart attacks and angina. Until recently a move from animal studies to studies in humans (called translational research) has been conspicuous by its absence.

A small Australian pharmaceutical company, Cholrem Pty Ltd, has produced and marketed a formulation of HP-β CD for use in humans called Cavadex. Preliminary results of Cavadex used to treat humans with IHD indicate that similar effects of plaque regression occur to those observed in animal studies. The rate of plaque regression induced by HP-β CD appears to be much greater than can be achieved by any other pharmacological treatment.

IHD is the number one cause of death globally, costing over US$818 billion each year for treatment in the US alone. The development of a drug therapy that reduces plaque size rapidly (over several months) would lead to a major rethink about the strategy for treating IHD and I believe would be the most important advance in IHD therapy since the introduction of statins.

Cyclodextrins are complex molecules with many different subtypes, each with their own properties. HP-β CD therapy appears to be very safe and many decades of its use in drug formulations in man support its safety. It is therefore likely that this form of cyclodextrin will be the initial focus of clinical development. The observations of beneficial effects on plaque regression associated with HP-β CD have been made outside of the usual restraints of formal clinical trials, and high-quality clinical trials must now be performed as a crucial component of the development of this novel therapeutic approach. The use of HP-β CD in IHD brings the promise of a movement towards the management of IHD by pharmacological methods with less reliance on interventional and surgical procedures.

Professor Laurence Guy Howes MB BS PhD FRACP FCSANZ
Clinical Pharmacologist and Toxicologist,
Preeminent Consultant Physician in Cardiology and Internal Medicine.