

## **Design and development of novel compounds for the treatment of nephropathic cystinosis**

At the moment, the only drug treatment for nephropathic cystinosis is cysteamine (marketed as Cystagon). This drug is effective in lowering the high levels of cystine found in cystinotic cells, but cysteamine has an unpleasant taste and smell and when taken orally can cause stomach upsets, nausea, diarrhoea as well as more serious side effects. As a result, some patients do not take their cysteamine as often as they should. We now know that most of these unpleasant side effects arise because of the large amounts of cysteamine present in the stomach and gut when Cystagon is taken.

In an attempt to overcome these problems, we have made a number of prodrugs of cysteamine. Prodrugs are pharmacologically inert i.e. they themselves do not work in the body, but once they have been absorbed, the prodrug decomposes to release cysteamine. The prodrug approach has been used successfully in a number of therapeutic areas including antibiotics, antihistamines and ulcer treatments. The advantage of using prodrugs is that the cysteamine is chemically 'camouflaged' and no cysteamine is released until the drug has passed out of the gut and into the cells of the body. We hope that in this way the stomach upsets, bad breath etc. associated with cysteamine will be minimised or even abolished entirely.

So far about twenty prodrugs have been made and tested for their ability to lower the high levels of cystine found in cystinosis. Some of the prodrugs worked very well in cell culture assays, but as yet, we have little or no results from animal studies. We are currently designing new types of prodrug which, we hope, will be as good, if not better than cysteamine. Our aim is to produce an odourless, tasteless and orally active treatment for cystinosis, although, that goal remains some time in the future. We believe, however, that the prodrug approach offers the real possibility of an effective oral therapy for cystinosis.

If you would like more information on the prodrug work, please feel free to contact me at the address or e-mail below.

Dr. Donald Cairns  
School of Pharmacy  
The Robert Gordon University  
Schoolhill  
Aberdeen  
AB10 1FR  
Scotland  
Tel 44 (0)1224 262530  
E mail [d.cairns@rgu.ac.uk](mailto:d.cairns@rgu.ac.uk)