Drugs 1998 Feb; 55 (2): 268
0012-6667/98/0002-0268/$01.00/0

Rabeprazole

A Viewpoint by Noriaki Takeguchi

Toyama Medical and Pharmaceutical University, Toyama, Japan

The gastric proton pump (H^+,K^+-ATPase) of the parietal cell is involved in the production of acid. Rabeprazole, a proton pump inhibitor, is activated in the gastric lumen and binds extracellularly with a cysteine residue (via *S*-*S* cross-linking) located on the luminal surface of the proton pump.

Rabeprazole was selected for clinical trial because it showed a shorter duration of antisecretory activity than omeprazole in animals and initial clinical trials. The intermediate duration of antisecretory effect of rabeprazole (between that of H_2 receptor antagonists and omeprazole) suggests that rabeprazole is a partially reversible proton pump inhibitor, which may be used over prolonged periods.

Several lines of evidence for the molecular basis of the faster dissociation of rabeprazole from the pump have been presented. The half-life of the proton pump is 72 to 96 hours, so its total replacement would take a week or longer. The complete recovery of acid secretion within 2 days after withdrawing rabeprazole suggests that the *S*-*S* cross-linking between the inhibitor and the pump is dissociated extracellularly (e.g. by glutathione secreted in the lumen) or intracellularly after the internalisation of the pump in the cell. The speed of dissociation may depend on the conformational state of the pump; the rabeprazole-bound conformation was not stabilised to a conformation engaged in the cyclic reaction, whereas the omeprazole-bound conformation was stabilised at a particular E_2 conformation.

In summary, rabeprazole is a novel agent which offers the potential of an improved approach to acid-related disorders. ▲