Epidermal Growth Factor: Comparison of Antisecretory and Mitogenic Activities

A.		Gamer
H.		Gregory
S.E.		Hampson
A.M.		Stanier
I.R.		Willshire
J.A.		Young

Bioscience Department, ICI Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, UK

EGF has two distinct actions on the gastrointestinal tract, namely inhibition of acid secretion and stimulation of epithelial proliferation. We have compared the processes of receptor binding and signal transduction associated with these antisecretory and mitogenic activities. Biosynthetic human EGF (uro-gastrone, 1–53) and a series of C-terminal truncated peptides of 48, 47, 46 and 42 amino acids were prepared by progressive enzymic degradation and purified to > 99% by HPLC. Ability of these ligands to bind to the EGF receptor was determined by a radio-receptor assay using A431 cell membranes. Proliferative activity was measured by thymidine incorporation into 3T3 cells in vitro and anti-secretory activity by inhibition of dimaprit-stimulated acid output in rats in vivo. The rank order of potency (URO > 1–48