ELSEVIER

FEBS Letters 342 (1994) 103

FEBS 13830

FEBS LETTERS

Retraction

Retraction concerning an endothelin B receptor-selective antagonist: Urade, Y., Fujitani, Y., Oda, K., Watakabe, T., Umemura, I., Takai, M., Okada, T., Sakata, K. and Karaki, H. (1992) FEBS Lett. 311, 12–16.

An endothelin B receptor-selective antagonist: IRL 1038, [Cys^{11}-Cys^{15}]-endothelin-1(11–21)

Yoshihiro Urade[a], Yasushi Fujitani[a], Kyoko Oda[a], Tadashi Watakabe[a], Ichiro Umemura[a], Michihiro Takai[a], Toshikazu Okada[a,*], Kiyoshi Sakata[b] and Hideaki Karaki[b]

[a]*International Research Laboratories, Ciba-Geigy Japan Ltd., 10-66 Miyuki-cho, Takarazuka 665, Japan*
[b]*Department of Veterinary Pharmacology, Faculty of Agriculture, The University of Tokyo, Bunkyo-ku, Tokyo 113, Japan*

Received 14 February 1994

The article describes the synthetic peptide IRL 1038 as having a much higher affinity to ET_B receptors (K_i = 6–11 nM) than to ET_A receptors (K_i = 400–700 nM) in various tissue membranes. It was also shown that this peptide antagonized the ET_B-mediated contraction of guinea pig ileal and tracheal smooth muscles. Since the publication of the data, we have synthesized more than 20 different batches of IRL 1038, some of which showed potencies and selectivities almost equivalent to the published data. However, the other batches, including batches synthesized by external suppliers, exhibited significantly higher K_i of 50–400 nM for the binding to ET_B receptors in porcine lung membranes.

We have very carefully investigated the physico-chemical properties of IRL 1038 in aqueous solutions at different pH (pH 7–10) and peptide concentrations, using fluorescence and proton NMR spectroscopy. At high pH (pH 10), the peptide does not aggregate and two kinds of non-aggregated states were observed by NMR spectroscopy. There was, however, no evident correlation between the two non-aggregated states and binding affinity to ET_B receptors. On the other hand, at lower pH, the NMR and fluorescence data strongly indicate that intermolecular association and/or irreversible aggregation occur. The state and degree of aggregation also vary as a function of peptide concentration and ionic strength. The state of aggregation is not consistent in all batches investigated. Hence, one possible explanation for the variation of the K_i values might be attributed to these different molecular states and the degree of aggregation.

Based on the biological data obtained with the active batches, we believe that IRL 1038 has the potential to be a good and useful tool for the investigation of ET_B receptor-mediated functions. However, since we have not been able to reproducibly synthesize IRL 1038 having the claimed potency and selectivity, and no active compound is available to further investigate this problem, we regrettably retract the above article.

We deeply apologize to researchers who have spent time and effort attempting to reproduce the data claimed in our publication.

A note from the Managing Editor

At a time when competition occasionally degenerates in to fierce polemics (into which some authors try to involve even the Managing Editors), I am grateful to those authors for whom truth has premium over ill-understood personal prestige.

G. Semenza
Zurich, 19 February 1994

*Corresponding author.

SSDI 0014-5793(94)00215-H