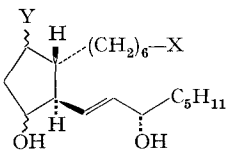
which is at least as potent as *rac*-PG(E$\beta\beta$)$_1$ on the rat uterus. The synthesis proceeds from *enantio*-9$\beta$-nitro-11$\beta$, 15$\alpha$-dihydroxy-*trans*-13-prostenonitrile (recovered from an incubation of the racemic compound with the swine lung dehydrogenase) by steps already outlined[10].

Some comments on the relationship between smooth muscle stimulating activity and dehydrogenase activity appear warranted. A 15(S)-hydroxyl group appears to be the major stereostructural requirement for both. The dehydrogenase system is less sensitive to the stereochemistry at C-11 whereas smooth muscle stimulating activity appears to be enhanced markedly by buttressing hydroxyl groups (formally *cis* at C-11 and even C-9, unpublished data) and only slightly affected by the back-bone stereochemistry in the most favorable cases (*ent*-PG(E$\beta\beta$)$_1$ as an example). This difference in sensitivity to the back-bone stereochemistry (inversion at C-8 and C-12) has allowed us to partially realize our original objective. Thus pure *ent*-PG(E$\beta\beta$)$_1$ should be at least as potent as *nat*-PGE$_1$ on the rat uterus and far more potent on other tissue preparations but would be degraded at only 15% of the rate of *nat*-PGE$_1$.

Finally the dehydrogenase accommodates major changes at positions remote from C-15 and C-12. The functionality present at C-1, C-9 and C-11, as well as the configuration of these groups, can be varied within the limits shown below without altering the rate of the enzymic reaction substantially. The 9-formamidoprostanes are not dehydrogenated, apparently due to a greatly reduced affinity for the enzyme – they show no inhibitory effect on the reaction of *nat*-PGE$_1$[19], [20].




X = –$CO_2H$, –CN
Y = =O, –OH, –$NH_2$, –$NO_2$
Y ≠ –NHCHO

*Zusammenfassung.* Die stereochemischen Voraussetzungen der Prostaglandin-15-Dehydrogenase aus Schweinelunge werden im Hinblick auf die pharmakologische Aktivität anhand einer Reihe synthetischer Prostaglandin E$_1$-Präparate abgeklärt.

H. Shio, P. W. Ramwell,
N. H. Andersen and E. J. Corey

*Worcester Foundation for Experimental Biology, Shrewsbury (Massachusetts 01545, USA), and Department of Chemistry, Harvard University, Cambridge (Massachusetts 02138, USA),*
*20 October 1969.*

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## Endocrine Cells in Mammalian Gastric Mucosa: Possible Storage Sites for Vitamin $B_{12}$-Binding Proteins

Very little is known of the cellular localization of the gastric antipernicious principle (the intrinsic factor, IF). The first cell to be implicated as the source of IF was the argentaffin (enterochromaffin) cell[1–3]. This hypothesis fell into disrepute because of a poor correlation between the distribution of these cells and of IF in many species[4]. In the rat, the chief cell has been proposed as the storage site for IF[5]. It is quite evident from the literature that in several other species the chief cell is not the cellular storage site for IF[6–8] and both the oxyntic cell and the pyloric gland cell have been advocated. Current opinion appears to locate IF to different cells in different species[8, 9]. From pure speculation it appears likely that a compound with such a specific function as IF should be produced and stored in the same type of cell in all species. Recently, it was reported that in the rat the regional and topographical distribution of vitamin $B_{12}$-binding proteins, associated with IF activity, coincided with the distribution of a system of histamine-containing enterochromaffin-like cells[10], which are believed to have an endocrine function[11–16]. The enterochromaffin (argentaffin) and enterochromaffin-like (argyrophil, non-argentaffin) cells have the morphological characteristics of polypeptide- or protein-secreting endocrine cells, and it has been suggested that they are active in the formation and secretion of gastrointestinal polypeptide hormones[11–16]. Enterochromaffin cells are recognized by their intense yellow formaldehyde-induced fluorescence, which reflects their content of 5-HT[17]. Enterochromaffin-like cells are devoid of 5-HT but can be demonstrated in L-DOPA-treated animals by their green formaldehyde-induced dopamine fluorescence[17]. Enterochromaffin cells usually retain their yellow fluorescence also after L-DOPA treatment, which

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permits the simultaneous detection of both enterochromaffin and enterochromaffin-like cells in one and the same section[17]. In the rat and mouse the enterochromaffin-like cells contain histamine[18–20]; in all other species studied, including man, histamine cannot be demonstrated in such cells[17, 21, 22].

A series of investigations has been initiated to establish the cellular storage site of IF. The present study compares the regional and topographical distribution of vitamin $B_{12}$-binding proteins with that of the gastric enterochromaffin and enterochromaffin-like cells in the mouse, hamster, guinea-pig and rabbit. Vitamin $B_{12}$-binding proteins were quantitated radiometrically after conjugation with $^{57}$Co-cyanocobalamin followed by Sephadex gel chromatography[10]. The number of enterochromaffin and enterochromaffin-like cells was calculated as previously described[23, 10, 17] in 6 $\mu$ transverse sections, taken from

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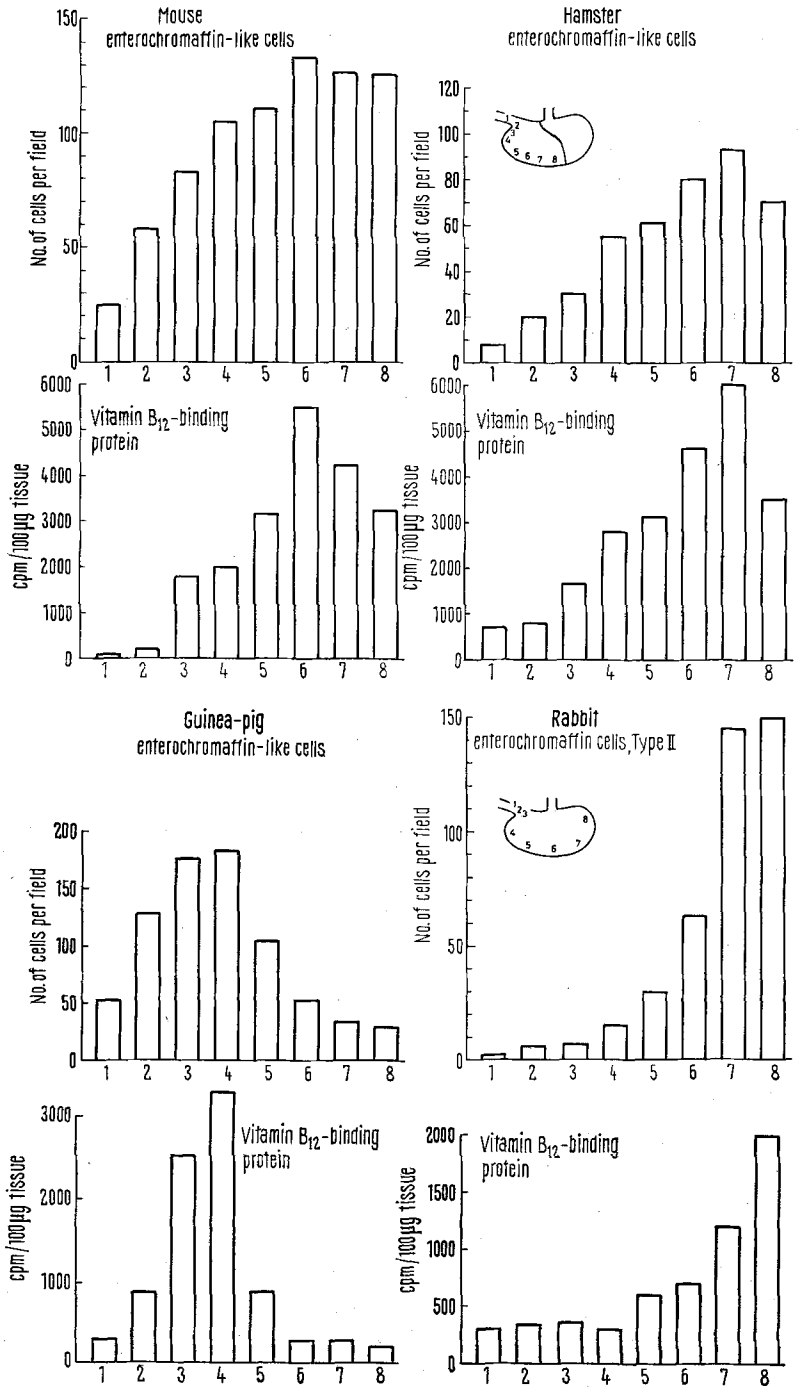


Fig. 1. Regional distribution of $B_{12}$-binders and gastric endocrine cells. The locations of the tissue samples analyzed are indicated in the inserted drawings. The top drawing refers to both mouse and hamster; the drawing below refers to guinea-pig and rabbit. Cells were counted in 6 $\mu$ transverse sections at × 125 magnification. Enterochromaffin-like cells were detected by their green formaldehyde-induced fluorescence observed after the administration of L-DOPA. The enterochromaffin cells referred to in the diagram were of a special, markedly reserpine-resistant type[17]. The amount of vitamin $B_{12}$-binding proteins was determined as described elsewhere[10] and given as cpm/100 $\mu$g tissue (wet weight). (Mouse and hamster: whole stomach wall; guinea-pig and rabbit: mucosa only). Each value is the mean of 3–6 experiments.

various locations along the major curvature (to establish their regional distribution); or in 20 μ horizontal serial sections (to establish their topographical distribution).

The regional distribution of gastric vitamin $B_{12}$-binding proteins was found to follow the distribution of the enterochromaffin-like cells in mouse, rat and hamster very closely (Figure 1 and Ref. [10]). In these species, enterochromaffin cells are almost exclusively found in the pyloric gland area, whereas the enterochromaffin-like cells occur in the oxyntic gland area.

Also in the guinea-pig, the distribution of the vitamin $B_{12}$-binding proteins was well correlated with that of the enterochromaffin-like cells, which occurred in the pyloric gland area and in the adjacent portion of the oxyntic gland area (Figure 1, see also Ref. [17]). There was no correlation between vitamin $B_{12}$-binders and chief cells.

The rabbit was exceptional in that the distribution of the vitamin $B_{12}$-binging proteins closely agreed with a rich population of markedly reserpine-resistant 5-HT-containing enterochromaffin cells (referred to as enterochromaffin cells, Type II[17]) in the oxyntic gland area (Figure 1), which is poor in enterochromaffin-like cells[17]. It could be shown that in this region the vitamin $B_{12}$-binging proteins were restricted to the basal layer of the mucosa, a topographical distribution which corresponds closely to that of the enterochromaffin cells (Figure 2).

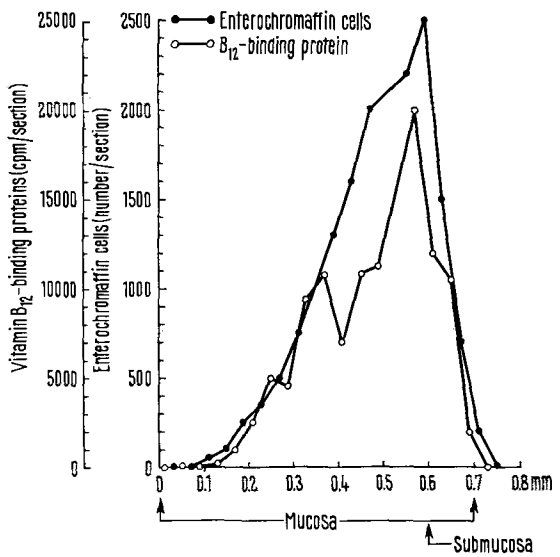


Fig. 2. Topographical distribution of $B_{12}$-binders and enterochromaffin cells in the oxyntic gland area of the rabbit. Serial sectioning. Each cryostat section (— 36 °C) 20 μ thick, 4 × 4 mm. The content of vitamin $B_{12}$-binding protein in single sections was determined as described elsewhere[10]. Each value is the mean of 4 experiments.

A high vitamin $B_{12}$-binding capacity is a basic requirement for IF activity[24,25]. It should be noted, however, that vitamin $B_{12}$-binders other than IF have been recognized in both gastric juice and gastric mucosa[24-29]. The vitamin $B_{12}$-binding capacity is thus not by itself a measure of IF content; the estimation of IF levels must be based on the capacity of gastric vitamin $B_{12}$-binders to facilitate the intestinal absorption of cyanocobalamin. This will be the subject of a separate study.

It is evident that gastric vitamin $B_{12}$-binding proteins are not regularly associated with one particular region of the stomach and that no previously proposed cell type can be the single cellular storage site for such proteins. It is suggested that the enterochromaffin-like cells in the mouse, rat, hamster and guinea-pig, and the enterochromaffin cells in the rabbit contain gastric vitamin $B_{12}$-binding proteins. This may indicate some functional similarity between these cells inspite of species-dependent differences as regards their amine storage mechanisms[30].

*Zusammenfassung.* Es wird angenommen, dass in Maus, Ratte, Hamster und Meerschweinchen Vitamin $B_{12}$-bindende Proteine sich mit enterochromaffinähnlichen (argyrophilen, nichtargentaffinen) Zellen und im Kaninchen mit einer bestimmten Art enterochromaffiner (argentaffiner) Zellen verbinden.

R. Håkanson, G. Liedberg and K. Lindstrand

*Departments of Pharmacology, Histology, Surgery and Hematology, University of Lund, Lund (Sweden), 5 November 1969.*

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## 5-Hydroxytryptophan-Decarboxylase Activity in the Decapod Crustacean *Upogebia littoralis*

Serotonin is widely distributed in the animal kingdom. All major groups of animals have been found to contain this amine[1].

The occurrence and the physiological role of serotonin in crustacea is very little known, although the plexuses of nerve fibres and the pericardial organs of certain decapods crustaceans have been known to contain appreciable amounts of serotonin[1,2]. More recently, Elofsson et al.[3] have found one pair of large yellow fluorescing cells, which indicate the presence of serotonin in the 'brain' of the crayfish *Astacus astacus*, while later, the same authors[4] could not detect a yellow fluorescence in the nerve fibres of the hind gut.

For a better understanding of serotonin role in crustacea, more information must be obtained about its distribution in various tissues of different species. In the present study, we have undertaken the further investigation of this problem by measuring the activity of serotonin-producing enzyme in various tissues of the abovementioned decapod crustacean.