Reports

On the Use of -tropin or -trophin in Connection with Anterior Pituitary Hormones

Abstract. The divergent usage that has persisted in the literature in connection with the terminology of anterior pituitary hormones is discussed, and the reasons for proposing the acceptance of *-tropins* and *tropic hormones* for standard use are outlined.

In arriving at final acceptance of terminology for any set of objects or materials or substances coming newly into use after their discovery, a veering course is always steered between the Scylla of logical etymology and the Charybdis of common usage. It often takes some deliberate act of common consent, for the sake of international communication, to decide finally among various alternatives which have grown up along with a particular field of investigation. A good example is furnished by the anterior pituitary hormones, which generically have been called either *tropic* or *trophic* hormones and individually have been designated either *-tropins* or *-trophins*, according to geographic location and personal preference. This has been going on now for well over a decade, and practice is still equally divided, with, on the whole, endocrinologists and biochemists on the other side of the Atlantic preferring the suffix *-trophin* and those on this continent adhering to *-tropin*; indeed, the editors of a recent volume, *Hormones in Blood* (*1*), say in the preface: "Our decision to use the suffix -trophin rather than -tropin was not made because we necessarily accepted the claimed etymological legitimacy of either, but simply because in our estimate most British endocrinologists favour the former."

It is certainly true that usage is a prime determinant of language, but it is our opinion in this laboratory (see *2*, *3*) that language must also be used with an awareness of its precise connotations and associations, when these are present; otherwise we are throwing away the real value of meaning. For this reason, we have preferred through the years the term *tropic* to *trophic*, and the suffix *-tropin* to *-trophin*, for these adenohypophyseal hormones, not just on puristic grounds of "legitimacy" but on the basis of signification. We feel that the use of one or the other of these suffixes is not just an idiosyncratic matter but, rather, that the terminology is intimately connected in this instance with the concept of the action of these hormones.

If we review for a moment the derivation of these suffixes, we recall that *-tropin* comes from the Greek *tropos*, used to denote turning, changing, or tending to turn or change, especially in a specified manner or in response to a specified stimulus, as in *heliotropic, isotropic, phototropic*. Thus, terminology with this suffix implies the stimulating effect of the hormone on its target organ which is characteristic of all these adenohypophyseal hormones [with, perhaps, the exception of growth hormone, which has no one target organ, although here the soma, the whole body, can be viewed as the "target" for the hormonal action (see *3*)]. The suffix *-trophin*, on the other hand, derives from the Greek *trophé* (from *trephein*, to nourish) and in its combining form denotes nutrition, nourishment, nurture—a meaning which is misleading in the light of our present knowledge of these pituitary hormones. We have had no evidence up to now that these tropic hormones have any function as nourishing agents to the endocrine glands. In the future, when we have unlocked the actual mechanism of action of these hormones, it may turn out that there is a nourishing function involved and we may have to revise our concepts, but right now we do not know that the tropic hormones are utilized in any way by their target organs. What we do know is that the hormones from the pituitary stimulate, in vivo and in vitro, other endocrine organs to produce and to secrete hormonal substances or to change or react in certain ways, as well as accelerating various metabolic processes in the body. The terminology *trophic* and *-trophin* has really come to be used by analogy with many of the very familiar scientific terms which do accurately imply a nourishing mechanism—terms such as *neurotrophy, embryotrophy*, and many more. We need not labor the point; the distinction is very clearly evident in certain roots that use both suffixes with the two separate meanings—for example, *phototropism* and *phototrophism*.

The acceptance of terminology on the basis of familiarity and currency of usage is certainly valid, but only so long as no confusion or irrelevance or ambiguity is introduced by the underlying established meaning of the term. It would perhaps be easy enough to become accustomed to calling the adrenal-stimulating hormone "adrenocorticotrophin" or the melanocyte-stimulating hormone "melanotrophin" if these terms were used often enough for the eye and ear to adjust to them, but when we employ this form adjectivally and refer to the "trophic hormones," the difficulty really becomes clear. For it is then, especially, that the established signification intrudes itself upon the reader or auditor, and an association connected with nourishment comes automatically to mind.

Thus, although we realize that the suffix *-trophin* has come to be used in the literature, particularly in Europe, we would very much prefer to retain the original implication of the other suffix. We wish to propose a standardization of the terminology used for the adenohypophyseal hormones, and the adoption of the suffix *-tropin* and the adjectival designation *tropic hormones* in future use.

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Type manuscripts double-spaced and submit one ribbon copy and two carbon copies.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each. Submit three copies of illustrative material.

For further details see "Suggestions to contributors" [*Science* **125**, 16 (1957)].

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Carbonic Anhydrase and the Precipitation of Apatite

Abstract. On theoretical grounds it is unlikely that the catalytic action of the enzyme carbonic anhydrase would be required for the precipitation of apatite in vitro. The presence of carbonic anhydrase in either active or inactivate form did not initiate precipitation in a metastable calcifying solution. It is unlikely that carbonate (or bicarbonate) ions are essential for the precipitation of apatite in vitro or in vivo.

In a recent paper by McConnell *et al.* the conclusion was drawn: ". . . that the carbonate ion is essential to precipitation of bone mineral and that the principal biochemical catalyst in vivo is carbonic anhydrase" (*1*). This conclusion was based on results obtained in experiments in which apatite was deposited in vitro on glass plummets immersed intermittently into saliva or into solutions containing sodium phosphate and calcium chloride. It was claimed that under their experimental conditions (which were not specified in sufficient detail by the authors) the catalytic activity of carbonic anhydrase was necessary to elicit this precipitation. In view of the known properties of this enzyme, their interpretation of the experimental results seems surprising.

The uncatalyzed hydration of CO_2 to carbonic acid is an extremely rapid process (*2*). Hence rapid recording methods are required to demonstrate the enzymatic activity of carbonic anhydrase (*3*). The uncatalyzed reaction goes to completion in a matter of a few minutes.

In mammals the enzyme is found particularly in tissues and cells (for example, red blood cells, stomach wall, kidney tubules, pancreas) where large amounts of CO_2 must be hydrated in fractions of a second, and the speed of the uncatalyzed reaction would be insufficient (*4*). This situation clearly does not exist in the experiments of McConnell *et al.*, in which it took up to 5 days to develop a precipitate of calcium phosphate. The CO_2 molecules slowly diffusing into the solution from the outside atmosphere do not require the activity of the enzyme over such an extended period, particularly not at a *p*H as high as 7.5.

Another interpretation of the results of McConnell *et al.* suggested itself. Carbonic anhydrase is known to be strongly adsorbed to glass surfaces (*5*), and it is conceivable that the added enzyme, in either active or inactivate form, was adsorbed to the glass plummets and became firmly attached to them during the intermittent immersions. The adsorbed carbonic anhydrase might then have caused the deposition of apatite in a way unrelated to its activity in the hydration of CO_2. Adsorbed films can subsequently be calcified by placing them in a calcifying solution. Such plaques can be produced on filter paper disks by intermittent immersion into saliva (*6*).

In order to test whether carbonic anhydrase will initiate deposition of apatite we performed a number of experiments with a metastable calcifying solution which does not deposit any solid in 2 or 3 days, unless initiators like apatite or collagen are present (*7*). The solutions contained the following concentrations (in millimoles) of ions: Na, 145; Cl, 133; total carbonate, 22; K, 5; Ca, 3.75 (150 mg/l); phosphate, 1.6 (50 mg of P per liter). The ionic strength was approximately 0.16. After first bubbling CO_2 through the solution in order to lower the *p*H to about 6.0 and thus prevent spontaneous precipitation upon addition of the calcium solution, we then removed the excess CO_2 by shaking and in this way adjusted the *p*H to 7.3 ± 0.05. Quantities up to 1 mg of the crystalline enzyme (Sigma Chemical Co.) were placed in 50 ml glass erlenmeyer flasks. Then the flasks were filled with the calcifying solution and closed with paraffinized cork stoppers held in place by rubber bands. After 3 days' incubation at 37°C no precipitation had occurred. Even after 1 week the activity of the enzyme, as measured by the method of Philpot and Philpot (*8*), had not decreased. In other experiments as much as 1 mg of the enzyme was dissolved in small amounts of distilled water in the erlenmeyer flasks, and the solutions were evaporated to dryness in an oven at 110°C. This treatment completely inactivated the enzyme. The flasks containing the inactivated enzyme were filled with calcifying solution. As in the case of the active enzyme, no precipitation occurred during 3 days' incubation at 37°C.

When the calcification experiments were carried out for periods longer than 3 days a film gradually formed on the surface of the solutions, even in flasks containing only calcifying solution. This film consisted mainly of apatite (determined from the chemical composition and the x-ray diffraction pattern). It also contained some organic material of bacterial and fungal origin. The addition of a crystal of thymol, a drop of chloroform, or up to 5 mg of sulfanilamide to the calcifying solutions did not prevent the formation of this film. Therefore, it is thought likely that the effect was due to a slow loss of CO_2 through the stoppers or to nucleation in the surface layer of the solution, rather than to the presence of microorganisms. Carbonic anhydrase seemed to have no perceptible influence on the rate of film formation. We conclude that the presence of carbonic anhydrase in either active or inactivate form did not initiate precipitation in the metastable calcifying solution.

Our findings do not provide an explanation of the results reported by McConnell *et al.* Perhaps a clearer picture of the mechanism of precipitation will emerge when a more detailed account of their experimental conditions is available.

The negative results of our attempts to obtain precipitates in vitro from metastable physiological calcifying solutions under the influence of carbonic anhydrase, together with the knowledge of the rapidity of the uncatalyzed CO_2 hydration, argue against the function of carbonic anhydrase as the "principal biochemical catalyst in vivo" for the precipitation of apatite. Moreover, our many experiments on the precipitation of calcium phosphates in the presence of carbonate (*9*) demonstrate that the carbonate ion interferes with or even inhibits apatite precipitation rather than initiates it (*10*).

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References and Notes

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