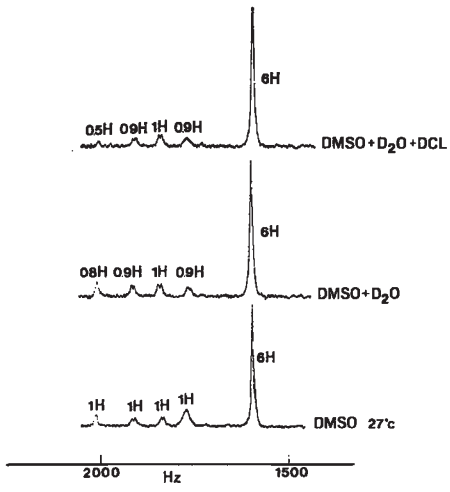

Fig. 4. *HR*/220 NMR spectra of gramicidin *S* in DMSO, DMSO + D_2O, DMSO + D_2O + DCl. The number of protons refer to half molecule.

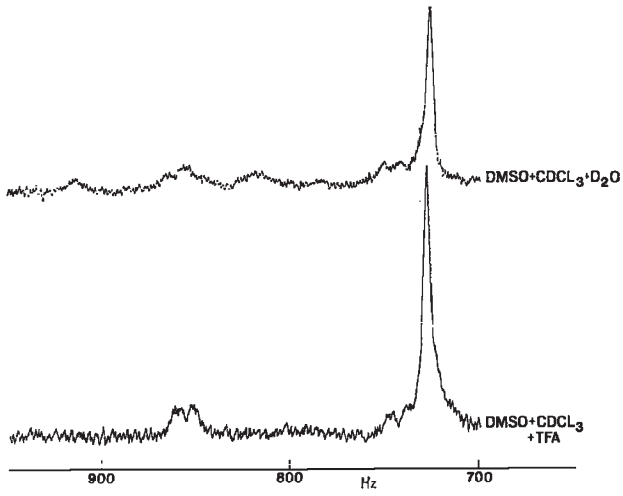

Fig. 5. *HA*/100 NMR spectra of gramicidin *S* in DMSO + $CDCl_3$ (50 per cent) + D_2O and in DMSO + $CDCl_3$ (50 per cent) + TFA.

HA/100 spectrometer, and Professor A. M. Liquori for helpful discussion.

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Putative Bitter-taste Receptor from Porcine Tongues

Dastoli and I reported earlier that we had found a sugar-complexing protein fraction in homogenates of bovine tongue epithelium[1]. Because the interaction of this fraction with sugars resembled in several respects the interactions of taste receptors *in vivo*, we suggested that it contained the chemoreceptor molecule for sweet-tasting compounds. The active component was subsequently purified and was characterized as a cationic protein of high molecular weight[2].

Dastoli *et al.* have recently found a fraction in homogenates of porcine tongue epithelium which forms complexes with bitter-tasting compounds[3]. They refer to this as "the bitter-receptor protein", although their report contains no data justifying reference to the protein in the singular. Moreover, their data show very poor agreement with the characteristics which might be expected of "the bitter-receptor protein".

In Table 1, I have listed the bitter-tasting compounds studied by Dastoli *et al.*[3] and the dissociation constants calculated from their data. The numbers are simply the reciprocals of the association constants which they reported, and represent the concentrations of the stimulus compounds which result in half-saturation of their "receptor". The approximate taste thresholds for these compounds as reported in the literature are given in the right-hand column of Table 1, except for naringen, for which I have been unable to find a reported value.

Table 1. COMPARISONS OF TASTE THRESHOLDS WITH DISSOCIATION CONSTANTS FOR BINDING BY THE "BITTER-SENSITIVE PROTEIN"

Compound	$1/K$*	Approximate threshold†
Quinine·HCl	$3{\cdot}9 \times 10^{-3}$ M	3×10^{-6} M
Brucine·HCl	$4{\cdot}6 \times 10^{-3}$ M	7×10^{-7} M
Naringen	$5{\cdot}1 \times 10^{-3}$ M	—
Caffeine	$7{\cdot}8 \times 10^{-3}$ M	7×10^{-4} M

* Calculated from data in ref. 3.
† From refs. 4 and 5.

With regard to the ranking of the compounds in order of their dissociation constants, Dastoli *et al.* state " . . . this ranking is in excellent accord with the relative bitterness of these compounds"[3]. This is their chief evidence for the identity of their material with the bitter chemoreceptor. But they cite no evidence for this being the order of relative bitterness, and the only published values which I have found (shown in Table 1) are at variance with their statement. Brucine, for example, is reportedly about ten times more bitter than quinine, yet their data seem to indicate that the "bitter-sensitive protein" has a slightly greater affinity for quinine than for brucine. In fact, the association constants reported by Dastoli *et al.* are very nearly the same for three of the four compounds tested, leading one to question the significance of ranking them in any order at all.

Finally, the numerical values of the dissociation constants are far removed from what one might expect on the basis of taste sensitivities *in vivo*. Because the dissociation constant represents the stimulus concentration which saturates one-half of the total receptor sites, one might anticipate that the threshold concentration would be perhaps one hundred-fold lower than the dissociation constant. In other words, about 0·1 per cent to 1 per cent of the sites must be occupied for a response to occur. Only caffeine comes near to meeting this prediction. For brucine, the dissociation constant is some 6,500 times the threshold concentration. Even when one considers the species difference (the thresholds are for humans) this is a remarkable disparity.

In summary, I believe there is no evidence justifying the conclusions drawn by Dastoli *et al.*[3] concerning the identity of their "bitter-sensitive protein" with the *in vivo* receptor for bitter tastes, or even for considering it to be a reasonable model of the receptor. Perhaps they are aware of some *in vivo* data which are in accord with their conclusions. If so, their failure to cite them represents an unfortunate oversight which should be corrected.

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