the ester oxygen which breaks. Experiments to verify our results are in progress.

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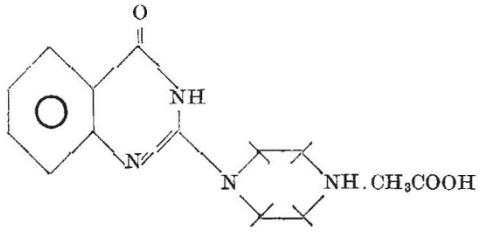
New Potent Blood Sugar Lowering Compound

Hypoglycaemic activity has not so far been reported in any 4-quinazolone derivatives. We have found that 2-piperazino-3H,4-quinazolone monoacetate (I; 68/157) is an effective blood sugar lowering agent (patent pending).



(I; 68/157)

This compound was synthesized by heating 2-ethylthio-3H,4-quinazolone with N-benzylpiperazine followed by debenzylation with H_2 over Pd/C in glacial acetic acid.

The blood sugar lowering action of the compound was studied in male and female albino rats weighing 115–185 g and rabbits weighing 1·41–1·53 kg of C.D.R.I. colony. Blood was collected from the animals after fasting them for 18 h, water being allowed *ad libitum*. The drug, dissolved in water, was fed to the animals by a metal cannula in doses varying from 10 to 100 mg/kg of body weight. Blood was again collected at the second and the fourth hour after feeding. Blood sugar was estimated according to Somogyi's method as modified by Nelson. Results have been expressed as maximum per cent lowering of blood sugar and are given in Table 1.

Table 1. BLOOD SUGAR LOWERING BY 68/157 AND TOLBUTAMIDE

Animal	Dose per kg body weight, given orally	Maximum % lowering of blood sugar between 2–4 hours after (mean ± *S.E.*) 68/157	Tolbutamide
Albino rat	10 mg	27 ± 2·09 (6)	19 ± 4·21 (6)
	25 mg	34 ± 5·4 (6)	24 ± 2·82 (6)
	50 mg	43 ± 7·8 (6)	33 ± 4·9 (4)
	100 mg	50 ± 4·3 (10)	62 ± 7·7 (4)
Rabbit	100 mg	34 ± 3·1 (3)	—

Figures in parentheses indicate number of observations.

It is evident that, dose for dose, I is as potent as tolbutamide in lowering blood sugar in albino rats. It is also effective in lowering the blood sugar of rabbits. The LD_{50} of the compound, given intraperitoneally, in albino mice is above 550 mg/kg, which is higher than the LD_{50} of tolbutamide. An $LD_{50} > 550$ is indicative of a comparatively safe compound. Further work is in progress.

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On Comparison of Interactions of a "Bitter-sensitive Protein" from Porcine Tongues with Human Taste Thresholds

Doig, Lopiekes and I earlier reported the interactions of a porcine protein fraction with bitter compounds[1]. Price has recently commented on the poor agreement of our data with, as he states, "characteristics which might be expected of 'the bitter-receptor protein' "[2]. I would like to make the following comments on comparisons drawn between porcine association constants and human bitter-threshold values.

The apparent contradictions and exceptions in taste response among species as stated by Kare and Ficken[3] allow no such easy correlation even among members of the same species no less than between humans and pigs. It was because of such lack of agreement in the literature concerning threshold values that we did not initially attempt any direct correlation to these *in vivo* values.

Table 1. COMPARISON OF HUMAN BITTER THRESHOLDS WITH DISSOCIATION CONSTANTS FOR BINDING BY THE PORCINE "BITTER-SENSITIVE PROTEIN"

Compound	$1/K^1$ (M)	Thresholds Range (M)	Median (M)
Quinine HCl	$3·9 \times 10^{-3}$	4×10^{-4} (4) 2×10^{-6}	3×10^{-5} (4)
Brucine HCl	$4·6 \times 10^{-3}$	—	—
Naringin	$5·1 \times 10^{-3}$	$1·7 \times 10^{-4}$ 5×10^{-5} (5)	$2·2 \times 10^{-4}$ (5)
Caffeine	$7·8 \times 10^{-3}$	$1·0 \times 10^{-3}$ 3×10^{-4} (4)	$7·0 \times 10^{-4}$ (4)

As for the variance of our data with what might be characteristics of the bitter receptor–taste threshold values, a closer inspection of the reported values for humans, even if one assumes there should be a correlation with pigs, shows no such variance. In Table 1 are the dissociation constants reported by us[1] ($1/K$) from the pigs together with human bitter-taste thresholds reported by others. One can see that no one threshold value represents the population, but instead that there is a rather wide range of values varying from thirty to near a hundred-fold. No values for brucine HCl were found and no assumptions should be made as to its similarity to brucine. There may be as great differences between the different forms of brucine—for example—hydrate, sulphate, hydrochloride, nitrate and so on—as there are between quinine sulphate and quinine HCl. An assumption has been made by Price[2] that the threshold concentration should be one hundred-fold lower than the dissociation constant. I find no evidence to support this guess or any other one as to what might be the correlation between approximate threshold values and *in vitro* dissociation constants. But even if there was such evidence for a hundred-fold difference, the values in Table 1 for the dissociation constants compared with either the range or median of the threshold values do not differ by a hundred-fold.