VIII is even more labile in purified preparations[2,4], addition of glycerol may facilitate further purification of this coagulation factor as it has done in the case of certain labile enzymes[6].

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Dependence of Relative Sweetness on Hydrophobic Bonding

MANY differing types of sweet compounds have been known for some time, but it is only in recent years that an extensive investigation of the subject has been undertaken. Ferguson and his co-workers[1-5] examined the physiological aspects of taste and attempted to correlate relative sweetness with certain physical properties.

We have been able to correlate biological activity in many systems[6] using the following equation:

$$\log BR = -k\pi^2 + k'\pi + k''\sigma + k''' \qquad (1)$$

BR is the biological response which could be applied in this case to RS, the measured relative sweetness, σ is the Hammett constant and π is the hydrophobic bonding constant[7]. π is defined as $\log P_X/P_H$ where P_H is the partition coefficient of the parent compound between octanol and water, and P_X that of a derivative.

The relative sweetnesses of some derivatives of 2-amino-4-nitrobenzene with respect to cane sugar were measured by Blanksma and Hoegen[8] and are shown in Table 1. The following equations were calculated from their data by the method of least squares:

$$\log RS = 1{\cdot}214\pi + 1{\cdot}970 \qquad 0{\cdot}766\,(r)\ 0{\cdot}476\,(s) \quad (2)$$

$$\log RS = 1{\cdot}610\pi - 1{\cdot}831\sigma + 1{\cdot}729 \qquad 0{\cdot}936\,(r)\ 0{\cdot}282\,(s) \quad (3)$$

$$\log RS = 0{\cdot}119\pi^2 + 1{\cdot}485\pi - 1{\cdot}848\sigma + 1{\cdot}742 \qquad 0{\cdot}936\,(r)\ 0{\cdot}308\,(s) \quad (4)$$

r is the multiple correlation coefficient and s is the standard deviation. Equation (2) shows the high dependence of relative sweetness on hydrophobic bonding, and equation (3) confirms the observation of Lawrence and Ferguson that sweetness increases as the basicity of the derivative rises. F tests show that the π term in equation (2) is significant at $> 0{\cdot}975$ and that the addition of the σ term is significant at $> 0{\cdot}99$. Equation (3) accounts for 88 per cent of the variance in the data. Since the correlation is not improved by the addition of a π^2 term in equation (4), we can assume that the π values investigated are relatively low and fall in the "linear" portion of the parabolic curve.

Table 1. RELATIVE SWEETNESS OF 2-AMINO-4-NITROBENZENES (Ref. 8)

Group	σ	π	log RS Obs.	log RS Calc.*	Δlog RS
H	0	0	1·602	1·729	−0·127
1-OMe	−0·27	−0·02	2·519	2·192	0·327
1-OEt	−0·24	0·48	3·146	2·942	0·205
1-OPr	−0·24	0·98	3·699	3·746	−0·047
1-F	0·06	0·14	1·602	1·845	−0·243
1-Cl	0·23	0·71	2·602	2·451	0·151
1-Br	0·23	0·86	2·903	2·693	0·120
1-I	0·28	1·20	3·097	3·149	−0·052
1-Me	−0·17	0·56	2·519	2·942	−0·424

* log RS was calculated from equation (3).

The substituents methoxy, ethoxy and propoxy are an excellent example of the dependence of relative sweetness on π. It can be seen from Table 1 that their σ values are approximately constant, whereas their π values parallel the increase in sweetness. However, if π is further increased by the addition of CH_2 groups, the compounds will become less soluble in water and eventually tasteless. Kaufmann and Schweitzer[9] report the sweetness of the butoxy derivative as much less than that of the propoxy.

An important prerequisite for sweetness is high anionic character or the ability to form hydrogen bonds with water. Once the compound is in the aqueous phase, its sweetness will then be determined by favourable partitioning on to the receptor sites on the tongue. This step may depend on hydrophobic bonding, degree of polarity, distance of charge separation in the molecule, electron density at a specific point in the molecule as measured by σ, and steric effects.

It can be inferred from equation (3) that the receptor site consists of an area for hydrophobic bonding coupled with a site for electronic bonding.

Sugars are known to be very soluble in water, but are rather low on the relative sweetness scale, so that their attachment to the receptor sites is weak and critically dependent on their stereochemistry. Saccharin is used commercially as the sodium or calcium salt so that it will be readily soluble in water. Its sweetness decreases if the dissociation is inhibited by increasing the concentration in water or by the addition of sodium ions[10]. Any substitution on the isothiazole nucleus which causes loss of solubility also causes loss of sweetness[11]. The benzene ring presumably plays a part in the hydrophobic bonding to the receptor site. The sweetness of the 2-amino-4-nitrobenzenes is very dependent on the position of the substituent and its effect on the electrons of the ring. A distribution of charge occurs when an electron donating group is in a *para* position to the nitro group, as in the derivatives in Table 1, or when an electron attracting group is in a *para* position to the amino group. Examples of this type are the substituents —COOH and —SO_2NH_2 which Ferguson and Childers[5] reported as being sweet. Other sweet compounds such as sucaryl, 5-benzyl-2-furfuraldoxime and dulcin also fall into the general pattern of requiring charge separation for solubility and sufficient hydrophobic bonding power.

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Precursor–Product Relationship between Nuclear and Cytoplasmic Ribonucleic Acid

IN a previous communication[1] a simple kinetic model for the incorporation of radioactive adenine into the purine bases of nuclear and cytoplasmic ribonucleic acid (RNA) of exponentially growing cells was proposed. This was used in the evaluation of kinetic data reported by Harris and Watts[2]. Harris[3], in questioning the validity of the model, raised objections based on his interpretation of an equation derived from considerations of our model.