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Bitterness of Peptides: Amino Acid Composition and Chain Length

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During our work on taste of foods we synthesized a series of peptides and soon came to the opinion, that the bitterness of peptides is caused by the hydrophobic action of amino acid side chains.

Here I think some remarks on hydrophobic interactions (1) would be appropriate. It is generally accepted now, that hydrophobic interactions are a contributing factor to protein behaviour and esp. to the formation of the secondary structure, e.g. helix. This means, that as shown in Figure 1 hydrophobic residues of the amino acids in a peptide are driven together by clusters of water molecules and so the secondary structure of a peptide or protein is formed. For the transfer from the helical to the stretched form, Tanford (2) found that the transfer free energy of the total protein results from the sum of the contributions of the single amino acid residues.

$$\triangle F = \sum \triangle f$$

The $\triangle f$ values of the single amino acids given in Table I were determined by Tanford (2) from solubility data and they represent a measure of the hydrophobicity of an amino acid residue. Please note, that the values are relative to the methyl groups of glycine which is taken to be 0. In Table II the taste of some "isomeric"-dipeptides is described. All the dipeptides are composed of the natural l-amino acids, as are all the examples, that will follow later. It is interesting to note, that the position of the amino acid has no influence on bitterness (3).

The value Q given represents the average hydrophobicity of a peptide and is obtained by summing the $\triangle f$-values of the amino acid residues of a peptide and dividing by the number of the amino acid residues.

$$Q = \frac{\sum \triangle f}{n}$$

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In Food Taste Chemistry; Boudreau, J.;
ACS Symposium Series; American Chemical Society: Washington, DC, 1979.

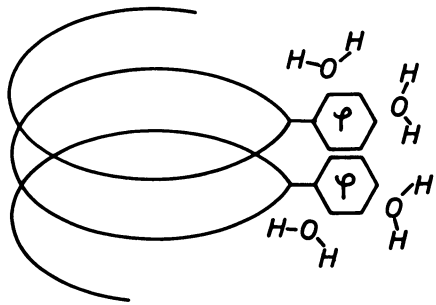


Figure 1. Hydrophobic interactions

Table I

△f-values of the side chains of amino acids, representing their hydrophobicity, according to Tanford

Amino acid	△ f-value cal/mol
Glycine	0
Serine	40
Threonine	440
Histidine	500
Aspartic acid	540
Glutamic acid	550
Arginine	730
Alanine	730
Methionine	1300
Lysine	1500
Valine	1690
Leucine	2420
Proline	2620
Phenylalanine	2650
Tyrosine	2870
Isoleucine	2970
Tryptophan	3000

Table II

Taste and Q-value of "Isomeric" dipeptides

Peptide	bitter	non-bitter	Q
Gly-Ala		x	365
Ala-Gly		x	365
Glu-Ala		x	640
Ala-Glu		x	640
Met-Ala		x	1015
Ala-Met		x	1015
Leu-Met	x		1860
Met-Leu	x		1860
Ala-Phe	x		1690
Phe-Ala	x		1690

You will have noticed in Table II, that the Q-values are much higher in the case of bitter dipeptides compared with the non-bitter dipeptides.

Table III shows a series of non-bitter dipeptides. It should be noted here that the Q-values are all below 1300. We can compare this with values of the following Table IV,

which lists a series of bitter dipeptides with Q-values above 1400.

Table III

Q-values of further non-bitter dipeptides

Peptide	non-bitter	Q
Glu-Val	x	1120
Glu-Lys	x	1025
Gly-Gly	x	0
Gly-Asp	x	270
Ala-Asp	x	635
Ser-Asp	x	290
Ser-Glu	x	295
Val-Asp	x	1115
Val-Glu	x	1120
Ala-Ala	x	730
Asp-Asp	x	540
Glu-Asp	x	545
Glu-Gly	x	225
Gly-Ser	x	20
Gly-Thr	x	220
Val-Gly	x	845
Lys-Glu	x	1025

Table IV

Q-values of further bitter dipeptides

Peptide	bitter	Q
Leu-Tyr	x	2645
Leu-Leu	x	2420
Arg-Pro	x	1665
Asp-Phe	x	1595
Asp-Tyr	x	1705
Val-Leu	x	2055
Gly-Ile	x	1485
Gly-Phe	x	1325
Gly-Try	x	1500
Val-Val	x	1690
Glu-Phe	x	1600
Gly-Tyr	x	1435
Ala-Leu	x	1575

On Table V a series of bitter di- and tripeptides synthesized by Shiraishi (68) is given.

It follows therefore, that in the case of peptides from the natural l-amino acids no bitterness occurs when Q is

below 1300, bitterness occuring only when the value Q exceeds 1400 (3).

Table V

Q-values of further bitter di- and tripeptides

Peptide	Q
Pro-Ala	1665
Ala-Pro	1665
Pro-Pro	2600
Val-Val	1690
Val-Pro	2145
Pro-Val	2145
Leu-Pro	2510
Pro-Leu	2510
Ile-Pro	2785
Pro-Ile	2785
Tyr-Pro	2735
Pro-Tyr	2735
Arg-Pro	1665
Lys-Pro	2050
Pro-Phe	2625
Phe-Pro	2625
Gly-Phe-Pro	1750
Phe-Pro-Gly	1750

If the Q-values lie between 1300 and 1400 no prediction can be made of the peptides bitterness.

It was interesting to see if our method can also be applied to individual l-amino acids. This means, that n = 1 and consequently in

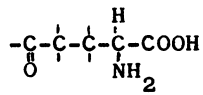
$$Q = \frac{\sum \triangle f}{n}$$

Q equals $\triangle$ f.

As can be seen from Table VI, the individual l-amino acids also follow the rule. The only exceptions are lysine and proline, which have too high Q-values for non-bitter amino acids. However, a slight bitter note is detectable in the otherwise sweetish taste of lysine and proline.

In this context it is worth taking a brief look at the question of flavour enhancing qualities of glutamate, generally substances of the UMAMI-type as described by Shizuko Yamaguchi in her contribution to this symposium.

Kuninaka (4) proposed the following structural element for flavour intensifiers:



but he pointed out, that the element is not absolute, as otherwise glutamine would have been a flavour enhancer.

Table VI

Q-values and taste of individual l-amino acids

l-Amino-Acid	bitter	non-bitter	Q
Glycine (opt. non active)		x	0
Serine		x	40
Threonine		x	440
Histidine		x	500
Aspartic acid		x	540
Glutamic acid		x	550
Arginine		x	730
Alanine		x	730
Methionine		x	1300
Lysine		x	1500
Valine	x		1690
Leucine	x		2420
Proline		x	2620
Phenylalanine	x		2650
Isoleucine	x		2970
Tryptophan	x		3000

Based on a series of examples from publications and patents, I would like to discuss, however, the hypothesis, that in order to achieve flavour enhancing, glutamate-like effect, a compound must have two negative charges. These should be located 3 to 9, preferably 4 to 6 C-atoms from one another. Instead of a C-atom, a S-atom can also occur. The presence of an α-amino group in l-configuration has additional flavour enhancing effect (5):

$$\ominus\ OOC[-\overset{|}{\underset{|}{C}}-]_n COO\ \ominus \qquad n = 1\text{-}7$$

The facts, on which our assumption is based, are given in Table VII.

An extension of our hypothesis to flavour-active nucleotides seems to be possible because these compounds also have negative charges at two different points of the molecule: in addition to the acidic phosphate group, they also possess a phenolic hydrogen.

It seems that the negative charges can also be on a peptide chain. Fujimaki describes the bitter masking action of peptides rich in glutamyl residues (29) and the isolation and identification of acidic oligopeptides from a flavour-intensifying fraction from fish protein hydrolysate (30).

Table VII

Facts on which our hypothesis is based

No.	Fact	Lit.
1)	Acc. to J. Solms only the dissociated form of l-glutamic acid is flavour-active	(6,92)
2)	l-Cystein-S-sulfonic acid has a similar effect to that of MSG	(7,8)
3)	l-Homocysteic acid has a similar effect to that of MSG	(9,10,11)
4)	l-Aspartic acid has a similar effect to that of MSG	(12)
5)	l-α-Aminoadipic acid has a similar effect to that of MSG	(11)
6)	Adipic acid makes the bitter after-taste of sweetners	(13,14,15)
7)	Succinic acid is comparable in its effect with that of MSG	(11,16)
8)	The flavour enhancing properties of the fruit acids - viz. malic acid, tartaric acid and citric acid - are known	(17,18,19,20)
9)	Lemon juice intensifies the flavour of strawberries	(21)
10)	The tastes of leguminose products are improved by treating with solutions of more than two of the following acids: malic acid, lactic acid, tartaric acid, citric acid	(22)
11)	The odour of garlic can be reduced by adding fumaric acid or maleic acid	(23)
12)	Glutathione (γ-glutamylcysteinyl-glycine) is reported to contribute towards the flavour of meat as an enhancer	(24)
13)	The diammonium salts of the dicarb-oxylic acids from malonic to sebacic acid are used as table salt-substitutes	(25)

Furthermore, it may be, that the well known action of polyphosphates in increasing the taste of chicken meat (31) or processed cheese (32) can be traced back on the negative charges of the polyphosphates.

Asparagine, unlike aspartic acid is completely lacking any flavour intensifying property, because one of the acidic groups was eliminated.

Also the findings on the derivatives of glutamic (33) acid are very interesting: if the glutamic acid is

esterified or amidified, the flavour intensifying properties are lost.

I would like now to return to the topic of the Q-values dimensions. Since Tanford gave his $\triangle$ f-values in calories, the dimension of the Q-value is cal res^{-1}. All the Q-values mentioned in this paper are given in these dimensions.

Up to this point only amino acids, di- and tripeptides had been considered. However, we wanted to see if the Q-concept could be extended to higher peptides as well. Stepwise we synthesized a heptapeptide and followed the change of the taste. The following Table VIII shows this synthesis (5).

Table VIII

Peptide	bitter	non-bitter	Q
Glu-Lys		x	1025
Met-Glu-Lys		x	1116
Ala-Met-Glu-Lys		x	1020
Ile-Ala-Met-Glu-Lys	x		1410
Asp-Ile-Ala-Met-Glu-Lys		x	1265
Glu-Asp-Ile-Ala-Met-Glu-Lys		x	1163

As you can see, the di-, tri- and tetrapeptides have Q-values below 1300 and are not bitter. In the step leading to the pentapeptide the introduction of the strong hydrophobic isoleucine with its high $\triangle$f-value of 2970 confers a bitterness and correspondingly a Q-value of 1410. When aspartic acid with its low $\triangle$ f-value of 540 is added, in the next step, the hexapeptide again becomes non-bitter with a Q-value of 1265. Glutamic acid - with a low $\triangle$ f-value of 550 - added in the final step gives a non-bitter heptapeptide with a Q-value of 1163. This example shows the influence of the amino acid residues as a polypeptide is synthesized and it gives a good demonstration of the possibilities of the method and we regarded it as a crucial experiment. Whereas in this example the bitter taste during the synthesis of peptides was followed, Table IX gives according to Minamiura (34) the degradation of a bitter peptide obtained from the action of Bacillus subtilis on casein.

Table IX

Degradation of a bitter peptide obtained from the action of Bacillus subtilis on Casein

Peptide	Q
Arg-Gly-Pro-Pro-Phe-Ile-Val	1891
Gly-Pro-Pro-Phe-Ile-Val	2085
Arg-Gly-Pro-Pro-Phe	1716
Gly-Pro-Pro-Phe	1963

We now wanted to extend the range to peptides of longer chain length. As you see from Table X, the Q-method works well up to eikosapeptides.

Table X

Q-values and taste of tri- to eikosapeptides

Peptide	bitter	non-bitter	Q
Val-Val-Val	x		1690
Ala-Ser-Phe		x	1140
Val-Val-Glu		x	1310
Pro-Gly-Gly-Glu		x	787
Ser-Pro-Pro-Pro-Gly	x		1508
Gly-Pro-Phe-Pro-Val-Ile	x		2085
Val-Ser-Glu-Glu-Glu-Asp-Ile-Ala-Met-Glu-Lys		x	815
Lys-Asp-Glu-Glu-Glu-Glu-Val-Glu-Ser-Gly-Pro-Asp-Ala-Pro-Leu-Pro-Ala-Glu		x	1121
Phe-Phe-Val-Ala-Pro-Phe-Pro-Glu-Val-Phe-Glu-Lys-Phe-Ala-Leu-Pro-Glu-Tyr-Leu-Lys	x		1912

Kauffmann and Kossel (35) isolated a series of oligopeptides from spinach and these are shown in Table XI.

Table XI

Q-values of non-bitter oligopeptides from spinach

Peptide	Q
Glu-Gly	225
Glu-(Gly,Ser)	196
Gly-(Glu,Ser)	196
Ala-(Glu,Gly-Ser)	330
Glu-(Gly,Gly,Ala)	320
Asp-(Glu,Gly,Ser,Ser)	234
Ser-(Gly,Gly,Thr)	120
Ala-(Glu,Glu,Gly,Ser)	374

As you see, the Q-values are extremely low and therefore the peptides non bitter.

As given in Table XII the Q-method was also successfully applied in the case of bitter peptides from the rennet-sensitive sequence of K-casein (36).

We published the Q-hypothesis in 1971 (3) and thus established for the first time a quantitative relationship between the amino acid composition of a peptide and its bitterness, as we introduced the Tanford values and so

opened the way for a calculation of bitterness.

Table XII

Bitter peptides synthesized acc. to the rennet-sensitive sequence of K-Casein

Peptide	Q
Ser-Leu-Phe-Met-Ala	1428
Lys-His-Pro-Pro-His-Leu-Ser-Phe	1726
Lys-His-Pro-Pro-His-Leu-Ser-Phe-Met-Ala-Ile-Pro-Pro-Lys-Lys	2001

In Table XIII we have collated other former postulates for bitterness of peptides. The results are in agreement with the Q-rule, for example the sequence Gly-Pro-Pro-Phe postulated by Minamiura (34) to be the core of the bitterness has a high Q-value of 1963.

Table XIII

Former postulated requirements for bitterness of peptides

Amino acid or sequence inducing bitterness	Lit.	Q
-Leucine-	37,38,39	2420
-Try-Phe-Leu-	40	2647
-Gly-Pro-Pro-Phe-	34	1963
-2 neutral amino acids with large alkyl groups C ⩾ 3	41	high
-1 neutral amino acid with a large alkyl group C ⩾ 3 with a short alkyl group		high
-1 neutral amino acid + 1 aromatic amino acid		high
-1 neutral amino acid + 1 basic amino acid		open

The same holds for the sequence Tyr-Phe-Leu, postulated by Fujimaki (40) to be essential for bitterness, here the Q-value is 2647. Also leucine, postulated earlier by Fujimaki (37,38,39) to be essential for bitterness, has a $\triangle$ f-value of 2420 and therefore contributes considerably to the Q-value of any peptide of which it forms a part.

Also the postulates of Kirimura (41) correspond to our theory.

It follows that the Q-concept represents a general rule for predicting bitterness under which the previously cited postulates are special cases.

The dipeptide glutamyl-tyrosine is bitter below pH 10,

and not bitter above pH 10. This coincides with the dissociation of the phenolic hydroxyl group of tyrosine. The corresponding dipeptide glutamyl-phenylalanine has no phenolic group, and is bitter over the whole pH-range. Q of this compound is 1660 (42).

The Q-concept has been assessed and accepted by the scientists (43-61) working in this field.

Series of bitter peptides have been isolated from enzymatic hydrolysates of proteins, esp. casein and soybean protein.

Figure 2 gives the sequence (61,62,63) of α_{s1} - casein - which represents about 40 % of casein - and shows the bitter peptides, that have been isolated. According to Mercier (63) the polypeptide chain of α_{s1} - casein contains 3 hydrophobic regions, viz. 1-44, 90-113 and 132-199. It is very interesting that all bitter peptides derived from α_{s1} - casein and isolated by the groups of Mercier (63), Matoba (65), Belitz (66), Solms (47), Hill (67) are located in these hydrophobic regions and have Q-values above 1400.

Figure 3 gives the sequence of β-casein - which represents 30 % of casein - and the bitter peptides derived from it and isolated by the groups of Clegg (49), Klostermeyer (46), Gordon (64). Here also the Q-values of the bitter peptides are above 1400. Please note, that no special single amino acid or sequence is needed to impart the bitter taste.

From soybean protein hydrolysates several series of bitter peptides have been isolated. As an example Table XIV shows bitter peptides isolated by Fujimaki (69,70). As before the high Q-values are evident.

Table XIV

Bitter peptides from peptic soya protein hydrolysates

Peptide	Q
Leu-Phe	2535
Leu-Lys	1960
Arg-Leu	1575
Arg-Leu-Leu	1856
Phe-Ile-Ile-Glu-Gly-Val	1766

From peptic Zein hydrolysates, Wieser and Belitz (71) isolated bitter peptides which are given in Table XV together with the corresponding high Q-values.

Regarding the whole picture of enzymatic hydrolysates we came to the conclusion, that certain proteins are more prone to yield bitter peptides than others. Therefore we tried to transfer our method also to proteins as well. This would enable a prediction to be made as to whether in the

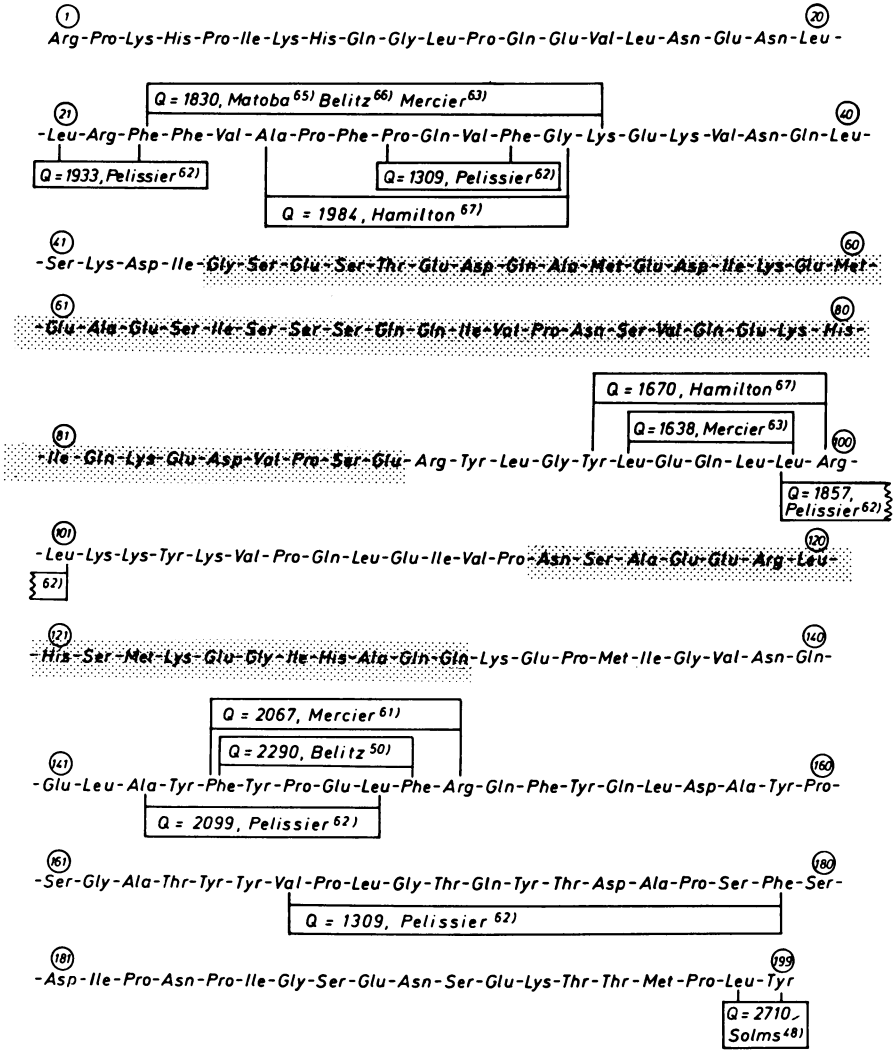


Figure 2. Bitter peptides from α_{s1}-casein ( ) = hydrophilic regions

In Food Taste Chemistry; Boudreau, J.;
ACS Symposium Series; American Chemical Society: Washington, DC, 1979.

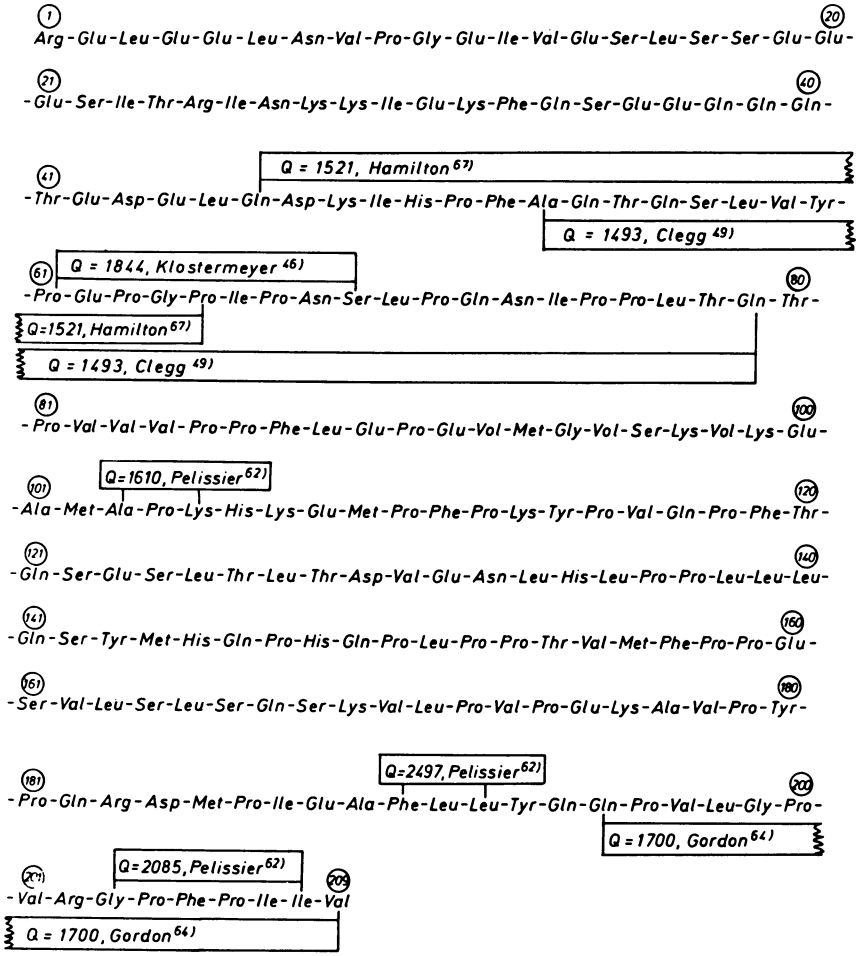


Figure 3. Bitter peptides from β-casein

Table XV

Bitter peptides from peptic Zein hydrolysates

Peptide	Q
Ala-Ile-Ala	1477
Ala-Ala-Leu	1293
Leu-Gln-Leu	1613
Leu-Glu-Leu	1797
Leu-Val-Leu	2177
Leu-Pro-Phe-Asn-Glu-Leu	1682
Leu-Pro-Phe-Ser-Glu-Leu	1688

course of a hydrolysis of a protein, bitter peptides would be formed (72). Generally pure proteins are considered to be without any taste. Secondary, tertiary and quaternary structures generally prevent a taste impression being obtained. The following Table XVI gives the Q-values of some proteins.

Table XVI

Q-values of proteins and bitter hydrolysates derived

Protein	Q	Bitter hydrolysates known
Collagen	1280	no
Gelatin	1280	no
Bovine muscular tissue	1300	no
Wheat Gluten	1420	yes
Zein	1480	yes
Soybean protein	1540	yes
Potato protein	1567	yes
Casein	1600	yes

It is interesting to see that proteins with high Q-values above 1400 as e.g. soybean protein, casein wheat gluten, potato protein, Zein are the "parents" of bitter peptides, whereas no bitter peptides have been isolated from hydrolysates prepared from collagen or gelatin, proteins with Q-values below 1300.

Petrischek (74) confirmed that the protein and not the protease is responsible for the occurence of bitter peptides. However, when the "parent" proteins are not bitter but the peptides derived from them are bitter, the questions arise as to why this is so and as to where we must place the molecular weight limits of peptides with $Q > 1400$ that are also not bitter.

An indication of the values to be expected can be obtained from the results of our synthesis of bitter peptides with $Q > 1400$ and molecular weights up to 2000 Dalton. Fujimaki (75) isolated from the peptic hydrolysate of soybean protein a non-dialysable bitter peptide of a molecular weight of about 2800 Dalton. Pilnik (76) found by the proteolysis of soybean protein in a membrane-filtration apparatus that no bitter peptides existed with molecular weights above 6000 Dalton. Clegg (49) obtained from digests of Casein with Papain a bitter peptide having a molecular weight of about 3000 Dalton.

Fujimaki (77,78) condensed bitter soybean protein hydrolysates in a Plastein-Reaction (79) and obtained non-bitter protein-like products, unfortunately without determination of molecular weights.

We studied the influence of chain length on the bitterness of peptides by gel permeation chromatography of

enzymatic protein hydrolysates (80).

Table XVII sums up the results of these experiments. We can conclude, that a limit of about 6000 Dalton can be placed on the molecular weight.

Table XVII

Molecular weights and tastes of enzymatic hydrolysates

Parent Protein	Q	Molecular weight of hydrolysate in Dalton	Taste	
			bitter	non-bitter
Soybean protein	1540	4000	x	
Soybean protein	1540	12500		x
Casein	1605	4000	x	
Casein	1605	8000		x
Wheat Gluten	1420	5000	x	
Potato protein	1567	400	x	
Potato protein	1567	8000		x
Gelatine	1280	3000		x

Above this molecular weight, also peptides with a Q-value above 1400 will no longer exhibit bitter taste. It is clear therefore, that 2 ways exist to come to non-bitter protein hydrolysates. As demonstrated in Figure 4

a) choice of the starting material, this means proteins with Q-values below 1300
b) choice of the working conditions, this means, if the Q-value of the starting protein is above 1400, careful hydrolysis to obtain peptides with main molecular weights of above 6000 Dalton.

It should be pointed out, that we were concerned with presence or absence of bitterness. Bitterness in terms of sensory threshold values or bitterness ratings was not assessed.

What is now the current state of affairs of the Q-rule? As mentioned it has been accepted and applied by the scientists working in this field. The most comprehensive and careful assessment of the Q-rule has been carried out by Guigoz and Solms (54). They found that the rule can be applied to the majority of the bitter peptides known and observed, that only peptides containing glycine sometime do not comply fully with the rule. They therefore propose, that glycine should be left out of the calculations, which then gives Q-values higher than 1400 for all bitter peptides. Guigoz and Solms conclude that the Q-values should be a useful assessment of the relationship between amino acid composition and the bitter taste of peptides. Wieser and Belitz (81) have suggested a very interesting extension of the rule. They obtained the bitterness threshold values of

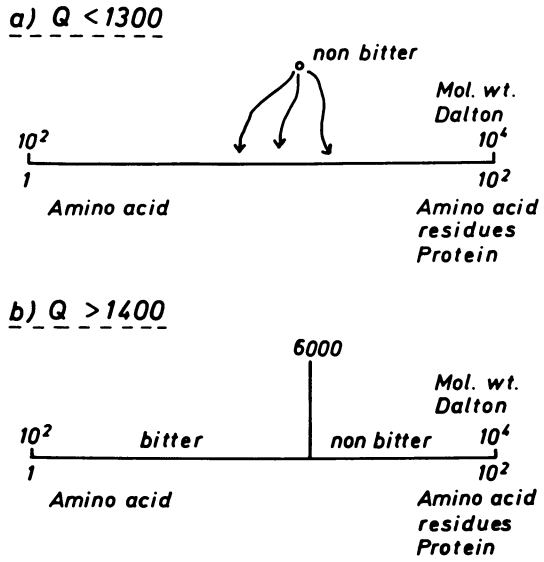


Figure 4. Molecular weight, average hydrophobicity Q, and bitter taste of peptides

di- and tripeptides by calculating the sum of the hydrophobicity of the "backbone" peptide consisting only of glycine residues adding to it the hydrophobicities of the side chains. In this way an estimation of the threshold values of di- and tripeptides was obtained.

We now investigated the hypothesis if the bitterness of lipids - and carbohydrates - could also be linked to hydrophobic interactions (82,83). Let us look first at the questions of hydroxylated fatty acids.

By the action of lipoxygenase and peroxydase on linolenic acid Grosch (84) obtained an intensively bitter tasting trihydroxyoctadecenoic acid. On the other hand, it is well known that monohydroxystearic acid and dihydroxystearic acid do not exhibit a bitter taste. We know from our studies on proteins that hydrophobicity plays a key role in determining bitterness. Lipids are, however, too hydrophobic to be bitter and bitterness here increases with increasing hydrophilicity. As a criterion for this diminution of hydrophobicity we applied the ratio of the number of carbon atoms of a molecule to the number of its hydroxyl groups. So the value $\frac{n_C}{n_{OH}}$ is obtained, which we have called the "R-value".

In Table XVIII the R-values for the hydroxylated C_{18} fatty acids are given.

Table XVIII

Bitterness of Hydroxy acids

Substance	n_C	n_{OH}	bitter	non-bitter	sweet	$\frac{n_C}{n_{OH}}=R$
Monohydroxystearic acid	18	1		x		18.00
Dihydroxystearic acid	18	2		x		9.00
Trihydroxyoctadecenoic acid	18	3	x			6.00

As the number of the hydroxyl groups changes, it is evident, that the accumulation of the 3 hydroxyl groups induces a bitterness: it can be seen that the R-value of the bitter substance is 6.00.

Wieske and Guhr investigated the taste properties of monoglycerides, diglycerides and phosphatides. We refer here to their findings (85).

As can be seen from Table XIX the R-values of bitter mono- and diglycerides are below 7.00.

In the case of phosphatides, we have made the assumption that one phosphatidyl-choline is equivalent to 2 hydroxyl groups. The following Table XX gives the results of

phosphatides.

Table XIX

Bitterness of mono- and diglycerides

Substance	n_C	n_{OH}	bitter	non-bitter	sweet	$\frac{n_C}{n_{OH}}$ =R
Monobutyrin	7	2	x			3.50
Monocaprin	13	2	x			6.50
Monolaurin	15	2		x		7.50
Monomyristin	17	2		x		8.50
Monoglyceride of linseed oil	20	2		x		10.00
1,3 Dicaprylin	19	1		x		19.00
Tetraglycerolmono-caprylate	20	5	x			4.00
Tetraglycerolmono-laurate	24	5	x			4.80

Table XX

Bitterness of phosphatides

Substance	n_C	n_{OH}	bitter	non-bitter	sweet	$\frac{n_C}{n_{OH}}$ =R
1,2 Dicaprinoylphos-phatidylcholine	28	2		x		14.00
1,2 Dilauroylphos-phatidylcholine	32	2		x		16.00
Lyso-Laurophosphati-dylcholine	20	3	x			6.66
Lyso-Oleylphosphati-dylcholine	26	3		x		8.25

Similarly, we can see here, that above R = 7.00 no bitterness occurs.

Bitterness in terms of sensory threshold values or bitterness ratings was not assessed.

Having previously considered the glycerides we then studied glycerol itself and related compounds.

The following Table XXI gives the results. Here we found an interesting fact that - outside the fat area - with R = 1 sweet taste occurred and we therefore included sugars and derivatives in our considerations. The occurrence of monofunctional substituents like the hydroxyl groups always

raises the question of stereochemistry, if the substituents are different. This question was not taken into consideration for the moment.

Table XXI

Bitterness of glycerol and derivatives

Substance	n_C	n_{OH}	bitter	non-bitter	sweet	$\frac{n_C}{n_{OH}}$ =R
Ethylene glycol	2	2			x	1.00
Glycerol	3	3			x	1.00
2,3 Dihydroxypropionic acid ethyl ester	5	2	x			2.50

According to Birch and Lindley (86) the sweetness of sugars decreases with increasing molecular weight. We therefore considered only mono- and disaccharides. Table XXII gives the results.

Table XXII

Bitterness of sugars and derivatives

Substance	n_C	n_{OH}	bitter	non-bitter	sweet	$\frac{n_C}{n_{OH}}$ =R
Glukose	6	5			x	1.20
Galaktose	6	5			x	1.20
Fruktose	6	5			x	1.20
Tetramethylglucose	6	1	x			6.00
Lactose	12	8			x	1.50
Saccharose	12	8			x	1.50
Cellobiose	12	8			x	1.50
Maltose	12	8			x	1.50
Trehalose	12	8			x	1.50
Arabinose	5	4			x	1.25
Xylose	5	4			x	1.25
Ribose	5	4			x	1.25
Desoxyribose	5	3			x	1.66
Methylglucopyranose	7	4			x	1.75
Athylglucopyranose	8	4	x			2.00
Propylglucopyranose	9	4	x			2.25
Butylglucopyranose	10	4	x			2.50
Phenylglucopyranose	12	4	x			3.00
Benzylglucopyranose	14	4	x			2.50
Inositol	6	6			x	1.00
Xylitol	5	5			x	1.00

As can be seen from the table, a sweet taste occurs when R has a value between 1.00 and 1.99; bitter compounds having R-values between 2.00 and 6.99. This is in full agreement with the finding of Birch and Lee (87) that reactions, which increase the hydrophobicity of sugars, generally lead to bitter products.

Bitterness of terpenoids, of purines like coffein, and of glucosides (88,89) may also be derived from hydrophobic interactions. See also the contribution of Belitz to this symposium.

A complete different mechanism seems to be present in the bitterness of salts , as two bitter sensations are differentiated (90): bitter I as elicited by stimuli like l-tryptophan, this would correspond to our "hydrophobic bitterness" and bitter II, elicited e.g. by $MgSO_4$. This bitter II seems to be triggered by ions. Kionka and Strätz (91) comparing 1 n solutions of the different alkali halogenides made a separation in three groups as shown in Table XXIII: salty, salty + bitter, bitter.

Table XXIII

Bitterness of salts

a) salty taste dominates. NaCl, KCl, LiCl, RbCl, NaBr, LiBr, NaJ, LiJ
b) salty and bitter: KBr
c) bitter dominates: CsCl, RbBr, CsBr, KJ, RbJ, CsJ

We give in Table XXIV the salts ordered in increasing sum of the ionic diameter and compare also the solubility in water. As can be derived from the Table, there is no relationship between the solubility of the salts in water and the taste. Molecular weights show a certain parallel: with increasing molecular weight the salts became bitter. An exception is KBr, which is bitter and salty, but according to the molecular weight should only be salty. A clear relation, however, exists between the sum of the ionic diameter of a salt and its bitterness. From LiCl with 4.98 Å to RbCl with 6.56 Å the salty taste dominates. KBr with 6.58 Å is salty and bitter and from RbBr with 6.86 Å to CsI with 7.74 Å the bitter taste dominates. It should be mentioned that $MgCl_2$ with 8.50 Å is also bitter, the same holds for $MgSO_4$.

Table XXIV

Relations between the bitterness of salts and their ionic diameter

Salt	Sum of the ionic diameter (Å)	Taste bitter	Taste salty	Solubility (g/100ml H_2O)	Molecular weight
LiCl	4.98		+	63.7	42.39
LiBr	5.28		+	145.0	86.85
NaCl	5.56		+	35.7	58.44
LiJ	5.76		+	151.0	133.84
NaBr	5.86		+	116.0	102.90
KCl	6.28		+	34.7	74.56
NaJ	6.34		+	184.0	148.89
RbCl	6.56		+	77.0	120.92
KBr	6.58	+	+	53.5	119.01
RbBr	6.86	+		98.0	165.38
CsCl	6.96	+		162.2	168.36
KJ	7.06	+		127.5	166.01
CsBr	7.26	+		124.3	212.81
RdJ	7.34	+		152.0	212.37
CsJ	7.74	+		44.0	259.81

Summary

Bitterness of a peptide is caused by the hydrophobic action of its amino acid side chains. By summing the hydrophobicities of the amino acid side chains of a peptide and dividing by the number of the amino acid residues, an average hydrophobicity Q is obtained. Peptides with Q-values below 1300 are not bitter, whereas peptides with Q-values higher than 1400 are bitter. This principle is valid for molecular weights up to approximately 6000 Dalton, above this limit peptides with Q 1400 are also not bitter.

Practically all known peptides with defined amino acid composition, chain length and flavour, whether isolated or synthetic, follow this principle and they number about 200 in 1978. It is therefore possible to predict the bitterness of any new peptide simply from its amino acid composition and chain length. Furthermore the danger of obtaining bitter peptides from enzymatic hydrolysis of a protein can also be predicted. For example, casein and soy protein, having high Q-values, are prone to produce bitter peptides on enzymatic hydrolysis, whereas collagen having a low Q-value does not give bitter peptides.

Hydrophobic interactions can also be used to provide information on the bitterness of lipids.

Bitterness of salts seems to be triggered by another mechanism.

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