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Review

Vegetable tannins – Lessons of a phytochemical lifetime

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Dedicated to the scientific legacies of E.C. Bate-Smith and Tony Swain, founding fathers of the Plant Phenolics Group later to become the Phytochemical Society of Europe.

Abstract

After the early encouragement from the outstanding contribution in the early 1900s of Emil Fischer to an understanding of vegetable tannins the work of the following half-century had simply exemplified the complexity of the problems they presented. It was generally recognised [Freudenberg, 1920. Die Chemie der Natürliche Gerbstoffe. Springer, Berlin] that there was a broad division into *condensed* or *non-hydrolysable* and *hydrolysable* tannins but much else remained vague and untidy. In the 1950s Bate-Smith and Swain gave the lead into totally new ways of looking at these substances. They drew aside for the first time the curtains on the botanical aspects of these substances to reveal the rich vistas which lay beyond. It was to initiate remarkable progress in the next fifty years in the understanding of their chemistry and biochemistry; some of the principal developments of this work are reviewed herein.

Keywords: Vegetable tannins; Galloyl and hexahydroxydiphenoyl esters; Condensed proanthocyanidins; Structure and biosynthesis; Comparative biochemistry; Astringency

Contents

1. Introduction and occurrence

Progress in scientific research hinges on the continual discovery of new methods and techniques. The discovery in 1943 by Martin and Synge of paper chromatography

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provided for the first time the means of surveying the phenolic constituents of plants and for their separation and identification. There was an explosion of activity in this field after 1945, none more so than that of Bate-Smith and Tony Swain. Bate-Smith's own surveys of the commoner phenolic constituents from over 1500 species of plants from nearly one half of the known plant families (dicotyledons; Bate-Smith, 1962) is a lasting testament – a work for all ages and affectionately known in some quarters as 'Bate-Smithery'. As a result of this and the work of others, the occurrence of vegetable tannins in over 80 dicotyledonous plant families has been described and the greater preponderance amongst these of those referred to as condensed tannins noted. Detailed studies have also been reported on the presence of particular groups of hydrolysable tannins in members of the orders Hammamelidales, Fagales, Dilleniales, Theales, Ericales, Rosales, Myrtales, Cornales, Proteales, Sapindales, Geraniales and Juglandales. Of equal importance however was that this work signposted directions for future researches in this area and away from those simply associated with the processes of vegetable tannage and leather manufacture.

Substantial accumulations of vegetable tannins may occur in almost any part of a plant – seeds, fruit, leaves, wood, bark, root. Increased tannin production is often associated with a particular pathological condition; the most familiar is that of plant galls caused by insect attack. Leaves of sumach (*Rhus typhina)* thus contain some 12% (dry weight) of a tannin based on gallic acid, most commonly referred to as tannic acid. The hard carapace of Chinese galls (leaves, *Rhus semialata*) contains up to 70% of the same tannin. However the level of vegetable tannins normally found in most plant tissues, such as fruit and leaves, is in the range 2–5% of the fresh weight. A comprehensive and detailed 'hands on' review of the methods available for the detection and measurement of tannins in plants is available (Waterman and Mole, 1994).

2. Structure and biosynthesis

According to Bate-Smith three classes of phenolic constituent overwhelmingly predominate in the leaves of vascular plants, leucoanthocyanins, flavonol glycosides and various derivatives of the hydroxycinnamic acids – principally *p*-coumaric, caffeic, ferulic and sinapic acids.

Leucoanthocyanins were originally described by Sir Robert and Lady Robinson in the 1930s and named in the belief that these compounds were colourless 'leuco' forms of the parent anthocyanins. Bate-Smith observed that their distribution in plants was very strongly correlated with that of condensed vegetable tannins. They are now invariably referred to as *proanthocyanidins*. One further observation which emerged from these studies and to which Bate-Smith repeatedly drew attention was the enigma of gallic acid. The occurrence of individual hydroxybenzoic acids (*o* and *p*-hydroxybenzoic acids, vanillic, protocatechuic) in plants is sporadic and idiosyncratic; in certain taxa however that of gallic acid is widespread and it is often found in high concentrations. He noted that 3,4,5-trihydroxycinnamic acid had not been encountered in his taxonomic work and speculated that *gallic acid* was the real taxonomic equivalent of the 'missing' 3,4,5-trihydroxycinnamic acid. Bate-Smith also concluded that the synthetic capabilities to metabolise leucoanthocyanins and the vic-trihydroxyaryl grouping (e.g. esters of gallic acid; gallotannins and ellagitannins) were 'primitive' ones and that once these synthetic capabilities had been lost during the course of evolution these changes were irreversible. He concluded that *the capacity of plants to synthesise vegetable tannins – both condensed and hydrolysable – was therefore a primitive one*.

2.1. Gallotannins and ellagitannins

Hydrolysable tannins are a classic example of secondary metabolism (Haslam, 1995) and are characterised by a number of distinctive features of which three are summarised below; a fourth is noted but for which important questions remain.

(i) *Structural diversity*. Hydrolysable tannins are based upon the fundamental structural unit of gallic acid and are almost invariably found as multiple esters with D-glucose (gallotannins). Derivatives of hexahydroxydiphenic acid (ellagitannins) are assumed to be derived by oxidative coupling of adjacent galloyl ester groups in a polygalloyl D-glucose ester, (Schmidt and Mayer, 1956), Fig. 1.

Metabolites number over 1000; principally described by Okuda (Okuda et al., 1989, 1990, 1993) and Nishioka (Nishioka et al., 1985, 1990) in Japan. Structural diversity is invariably accomplished by different chemical embellishment, usually (*vide supra*) dehydrogenation or oxygenation, of a key metabolite such as β-1,2,3,4,6-penta-*O*-galloyl-D-glucose (Cai and Haslam, 1994; Haslam, 1998); an indication of nature's economy or her unrestrained prodigality.

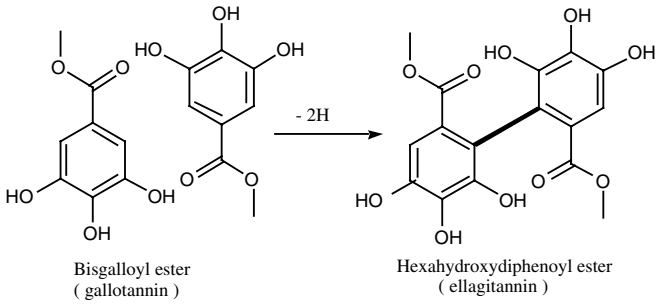

Fig. 1. Derivation of ellagitannins by oxidative coupling.

(ii) *Taxonomic distribution* – Hydrolysable tannins have a very restricted taxonomic distribution; they are associated principally with woody and herbaceous dicotyledonous plants (Bate-Smith and Metcalfe, 1957).

(iii) *Accumulation and storage* – Hydrolysable tannins are regularly characterised by substantial accumulations of particular metabolites in certain tissues. Examples are legion; the fresh leaves of *Rhus typhina* contain some 12–15% of a hepta- to octagalloyl glucose derivative (*syn*. tannic acid) based upon the further galloylation of the key metabolite β-1,2,3,4,5-penta-*O*-galloyl-D-glucose; the young leaves (flush) of the tea plant (*Camellia sinensis*) contains 3–4% caffeine and ~20–25% of the phenols (−)-epicatechin and (−)-epigallocatechin and their galloyl ester derivatives (Lunder, 1988).

(iv) *Induction and regulation* – Although Gross and his group (Gross, 1999; Haslam, 1998) have made substantial progress towards an understanding of the mechanisms involved in the formation of the pivotal metabolite β-1,2,3,4,6-penta-*O*-galloyl-D-glucose and the various gallotannins from glucose and gallic acid, so far as induction and regulation of gallic acid metabolism are concerned large and significant gaps in our knowledge remain. Indeed, they begin with the biosynthesis of gallic acid itself. Two pathways, *a* and *b*, Fig. 2, have been suggested and the weight of experimental evidence favours the former route *a*, namely direct dehydrogenation of an intermediate in the shikimate pathway and retention of the oxygen atoms of the alicyclic precursor (Conn and Swain, 1961; Knowles et al., 1961; Dewick and Haslam, 1969; Cornthwaite and Haslam, 1965; Werner et al., 1997). However, this places gallic acid in a potentially unique position when compared to the majority of other plant phenols which more generally derive from end-products of the pathway (as in route *b*, Zenk, 1964) and the phenolic groups are derived by direct oxygen insertion into the aromatic nucleus. Clearly work at the enzymic and/or genetic level is necessary to resolve this question.

2.2. Proanthocyanidins

Of all the changes which Bate-Smith and Swain prompted in the 1950s it was that towards the condensed tannins which was to have the greatest impact. They thus directed attention away from the variously intractable commercial extracts, particularly those from the bark and wood of trees – mangrove, oak, hemlock, quebracho, chestnut and cutch – to the invariably more amenable living tissues of plants. It was revolutionary. They confirmed that the condensed tannins were identical with the leucoanthocyanins/leucoanthocyanidins, (first recorded by Sir Robert and Lady Robinson in the 1930s) and that these latter groups of compound were most commonly responsible for the range of reactions in plant tissues attributed to condensed tannins. The fundamental structural unit in this group is the phenolic flavan-3-ol ('catechin') nucleus. Condensed proanthocyanidins exist as oligomers (water soluble), containing two to ten or more 'catechin' units, and polymers (water insoluble). The flavan-3-ol units are linked principally through the 4 and the 8 positions. The nomenclature derives from the property which they

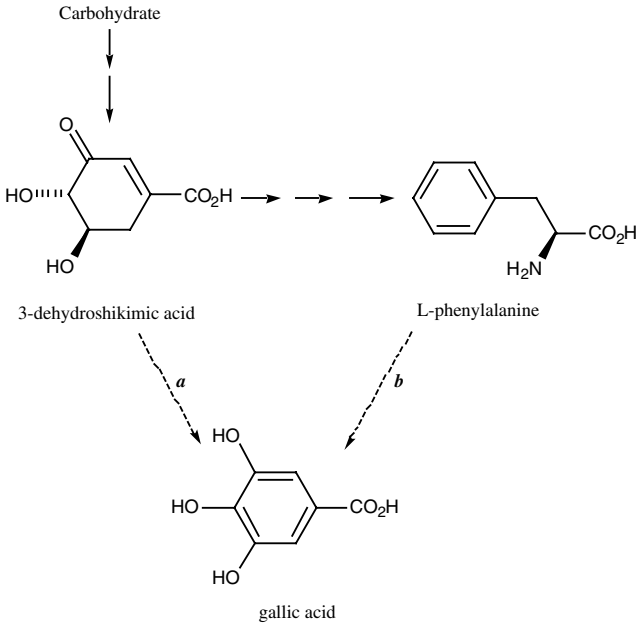

Fig. 2. Suggested pathways for the biosynthesis of gallic acid.

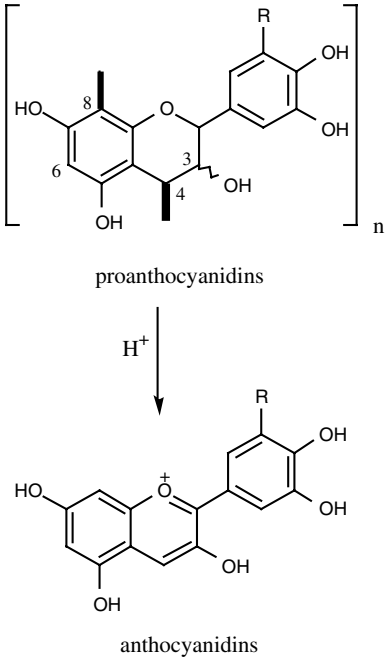

Fig. 3. Acid-catalysed degradation of proanthocyanidins.

possess of degradation in strong acid to give the corresponding anthocyanidin, generally cyanidin and/or delphinidin, Fig. 3. Procyanidins (R = H) and prodelphinidins (R = OH) are the most commonly found types of condensed proanthocyanidins and they are generally associated with plants which possess a woody habit of growth. In so far as the total complement of condensed proanthocyanidins found in plant tissues is concerned, the soluble oligomeric forms (dimers, trimers...) are in metabolic terms but the 'tip of the iceberg', but they provided the ideal substrates for chemical structure evaluation (Weinges et al., 1968, 1969; Haslam, 1977, 1998; Porter, 1988, 1989; Balas and Vercauteren, 1994). However, for the generality of plants it is now quite clear that condensed proanthocyanidins, which are totally insoluble or are insoluble in organic solvents such as ethanol, overwhelmingly predominate. They are, metaphorically speaking, the base of the 'metabolic iceberg'. Indeed in the tissues of some plants such as the Leguminosae (Bate-Smith, 1973) ferns and fruit such as the persimmon (*Diospyros kaki*) there is a preponderance of these forms. They are also of frequent occurrence in plant gums and exudates such as *Butea frondosa* gum. To date their exact structures are not known although, because of their properties, they are presumed to contain the typical proanthocyanidin units which give rise to anthocyanidins on treatment with acid.

Current lines of thought suggest that the proanthocyanidins are formed, in some way, (again as with gallic acid still not clearly defined at the biochemical level), as by-products of the processes in which the parent flavan-3-ols are biosynthesised from flavan-3,4-diols, (Stafford and Lester, 1982, 1984, 1985; Stafford et al., 1985; Tanner and Kristiansen, 1993). Chemists, familiar with Sir Robert Robinson's famous dictum that 'cells obey the laws of chemistry' (Robinson, 1955), have suggested (Haslam, 1977, 1998; Fig. 4) that the reduction of the flavan-3,4-diol to the flavan-3-ol proceeds by a *two* step process *via* the corresponding quinone methide. Invoking the nucleophilic capture of this intermediate by, for example, the flavan-3-ol then makes possible a wholly reasonable (chemically that is!) route to the proanthocyanidins. Strong support

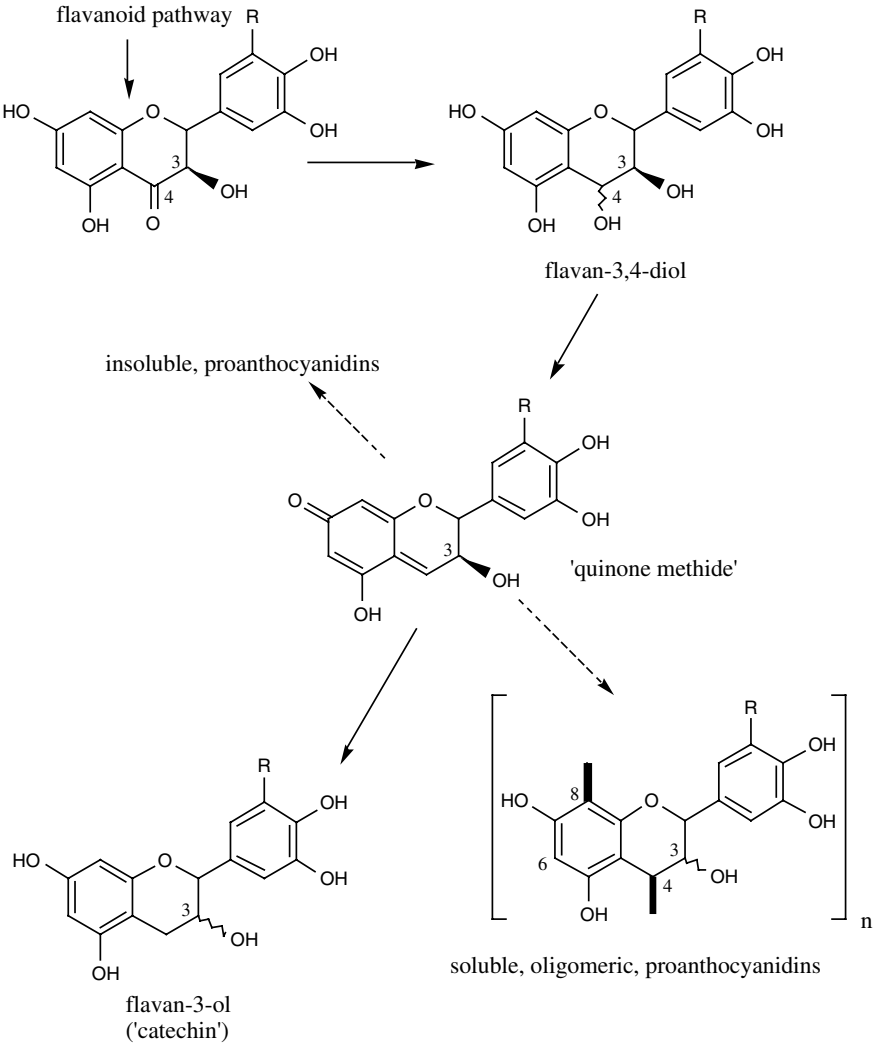

Fig. 4. Proanthocyanidin metabolism – suggested pathways.

for this idea derives from the fact that this rationale provides the basis for the efficient biomimetic synthesis of proanthocyanidins (Haslam, 1974; Hemingway and Foo, 1983).

Participation of the quinone methide as an intermediate also then makes possible the rationalisation of the epimerisation at C-3, necessary to explain the formation of the flavan-3-ol (−)-epicatechin and analogously derived procyanidins.

2.3. Metabolic comparisons and relationships

Both major groups of vegetable tannins are characterised by complex structures bearing a multiplicity of phenolic groups and by relative molecular masses which, for secondary metabolites, are very high – regularly in excess of 10^3. Bate-Smith also often stated that, in his view, the capacity of plants to synthesise vegetable tannins – condensed and hydrolysable – were 'primitive' ones and once these synthetic capabilities had been lost during the course of evolution these changes were irreversible. A question well worthy of further consideration in the future is whether these two groups of polyphenolic metabolites, despite their acknowledged very distinctive origins (*vide supra*, Figs. 2 and 4), have metabolic or other relationships which extends this kinship further. Two circumstantial pointers in this direction are outlined below.

(i) Plants which have a strong capacity to synthesise proanthocyanidins generally do not metabolise substantial quantities of esters of gallic and hexahydroxydiphenic acids, and vice-versa. In this context it should also be noted that for the very few plants which biosynthesise galloyl esters of flavan-3-ol substrates then very little, if any, proanthocyanidins are found co-occuring. The best known example of this phenomenon is the tea plant (*Camellia sinensis*) where the metabolic profile is dominated by ~20–25% of the phenols (−)-epicatechin and (−)-epigallocatechin and their galloyl ester derivatives (Lunder, 1988; Nonaka et al., 1983).

(ii) Leaves of plants, in the Northern hemisphere, which synthesise substantial quantities of condensed or hydrolysable tannins during normal growth *generally*, and under the right external conditions, produce strong anthocyanin pigmentation during autumnal senescence.

Each autumn millions of tons of chlorophyll are destroyed in the Northern hemisphere. Accompanying this there are dramatic changes in the colour of the leaves of

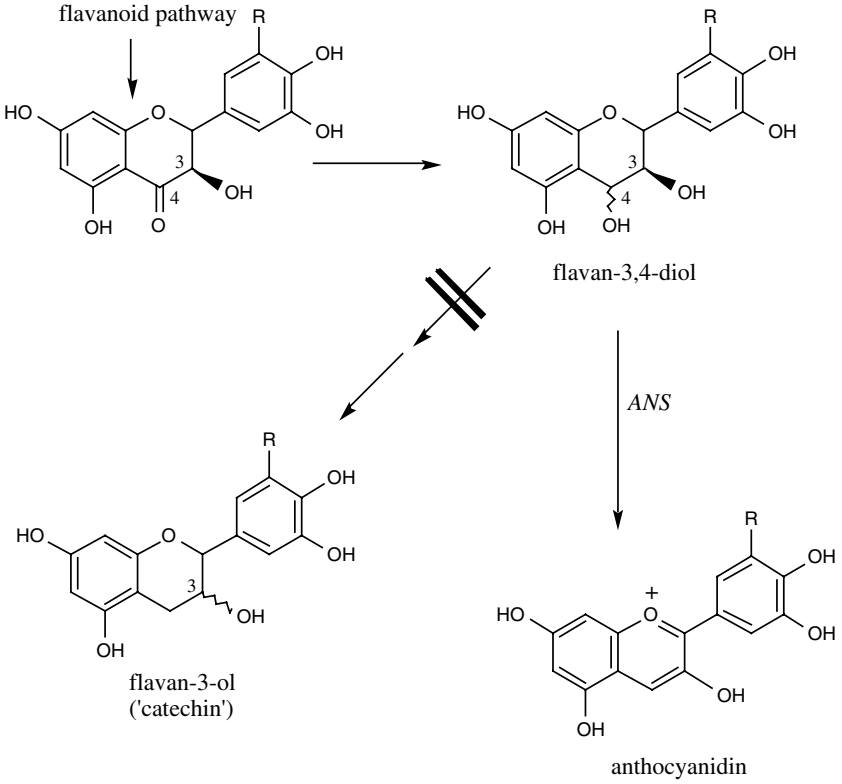

Fig. 5. Autumnal colouration - metabolic diversion at senescence from flavan-3-ol formation (reduction) to anthocyanidin synthesis (oxidation): a possible rationale.

plants from green to the yellow, red and browns of the dying year. In the New England States of America the 'fall' generates over 1 billion$ from tourism in the space of just three weeks. In a wet autumn most leaves do not colour strongly and the journalist Alistair Cooke in his 'Letter from America' (October, 1970) stated that the essentials for good autumn colours are 'a poor soil, slight frost and warm sun – in that order'. For a great many plants the leaves, once the chlorophyll has been oxidatively degraded, remain yellow-brown as a result of the presence of residual xanthophylls, etc. However some give spectacular displays as the yellow pigmentation gives way to a rich deep red of anthocyanin pigmentation: invariably, in this context the good performers are those whose normal metabolism gives high levels of proanthocyanidins: however, the very finest performers are without doubt those plants which during normal growth produce high levels of gallic acid and its derivatives. *Rhus typhina* is one such example. It metabolises some 12–15% of a hepta- to octa galloyl glucose derivative in its leaves.

Anthocyanidin synthase is a 2-oxoglutarate iron-dependent oxygenase (Schofield et al., 2002) which catalyses anthocyanidin formation from the natural flavan-3,4-diol substrate by a mechanism involving stereoselective C-3 hydroxylation.

Rationalisation of the case of anthocyanidin formation during senescence in proanthocyanidin producing plants (e.g. *Prunus* sp.) might therefore be visualised as a metabolic diversion from reduction at the terminal flavan-3,4-diol stage to oxidation (Fig. 5). However, a corresponding metabolic rationalisation of autumnal anthocyanin pigmentation in plants such as *Rhus typhina* is on this basis very far from clear, a mystery in fact. Yet such plants producing gallic acid and its derivatives are quite the most outstanding examples in this respect.

Recent work by Walker et al. (2007) points however to another possible explanation of this phenomenon. The Australian group showed that anthocyanin production in grapes is controlled by two separate but related VvMYBA genes and that white grapes only arise where there have been mutations in both of these genes. It has long been known that all wild species of *Vitis* have dark coloured grapes and this research on the genes of white grapes provides a probable explanation of their origin. In this context one might argue (*á la* Bate-Smith) that anthocyanidin formation in grapes is a primitive characteristic of *Vitis* species, lost over the course of evolution. Likewise autumnal anthocyanin synthesis in leaves might well be a similarly primitive characteristic of plants. Moreover if it is also linked to vegetable tannin formation then one might speculate that it has, likewise, been lost, along with the tannins, during the course of evolution. Its retention in those plants which metabolise vegetable tannins could therefore be viewed as evidence that it is a metabolic process entirely complimentary to tannin synthesis.

3. Protein – vegetable tannin interactions

Vegetable tannage of animal skins represents just one specific example of a physical phenomenon which is widespread, namely the association (complexation) of vegetable tannins with natural macromolecules and a range of small molecules (Haslam, 1998). These interactions are of considerable technical significance in areas as diverse as agriculture, ecology and food selection, foodstuffs and nutrition, the taste of beverages (astringency), herbal medicines, floral pigmentation, and the formation of natural glues and varnishes. Pre-eminent amongst these phenomena are those which derive primarily from the interaction with proteins. Considerable progress has been made in recent years in the understanding and application of many of these properties at the molecular level, (Haslam, 1998). However, in so far as their participation in all these phenomena is concerned, it is that group of polyphenolic compounds described by the initial phrase in Bate-Smith and Swain's (1962) original description of vegetable tannins, upon which attention should be primarily focussed: – *'Water soluble phenolic compounds having molecular weights between 500 and 3000 and, besides giving the usual phenolic reactions, they have special properties such as the ability to precipitate alkaloids, gelatin and other proteins'*.

3.1. Taste and astringency

Saliva is produced by the salivary glands which empty their secretions into the oral cavity and contains a group of unique proteins which are usually referred to as 'proline-rich proteins': PRPs. Proline accounts for 25–42% of the amino acids in isolated PRPs. In addition there are high contents of glutamine (glutamic acid) and glycine and these three residues account for 70–88% of all amino acids in the proteins (Fig. 6; Bennick, 1982). The phenomenon of astringency – a desirable characteristic of many beverages such as wines, ciders, teas, etc. – is believed to be associated specifically with the interaction of polyphenols with PRPs.

Astringency is generally recognised as a loss of lubrication, a feeling of extreme puckeriness and dryness in the palate. It is not confined to a particular region but is experienced as a diffuse stimulus which invariably takes a finite time to develop fully (Joslyn and Goldstein, 1964). The

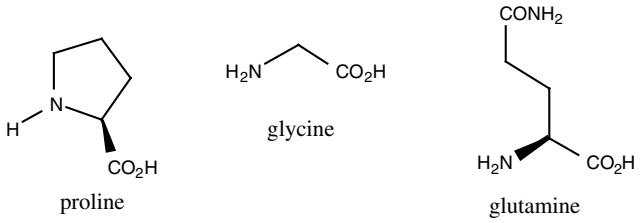

Fig. 6. Proline-rich proteins – principal amino acids.

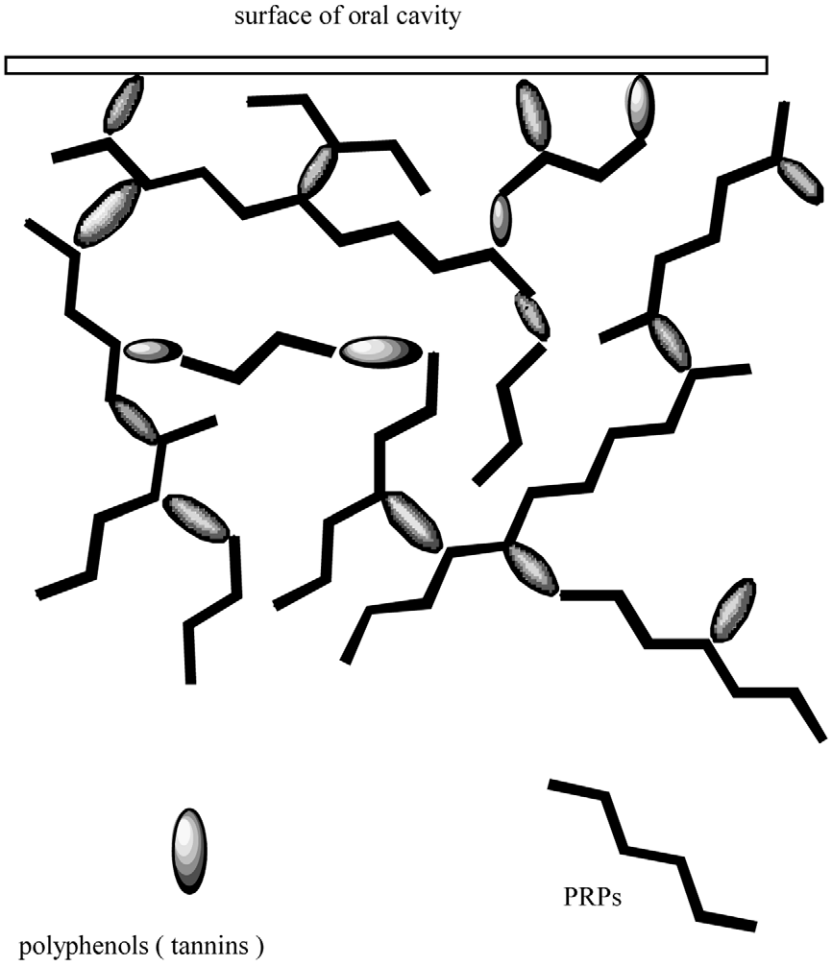

Fig. 7. Multidentate cross-linking of PRP molecules by polyphenolic molecules (tannins) with concomitant loss of lubrication and development of the astringent response.

primary reaction is thought to be *via* the precipitation of proteins and mucopolysaccharides in the mucous secretions caused by the astringent principles. A pictorial representation of the process whereby polyphenols (tannins) are envisaged to act at the molecular level to complex with salivary PRPs and bring about the astringent response is depicted in Fig. 7. An essential feature is the cross-linking of adjacent polypeptide chains of the PRPs by polyphenol molecules giving rise to the formation of aggregates and precipitation of the salivary PRPs. In turn, this leads to the loss of lubrication in the palate and the sensation of astringency. The whole process is a time dependent and dynamic one and requires a period of time to develop fully. A necessary feature of this model is that the polyphenol should be of sufficient size and composition to bring about, by polydentate binding, the cross-linking process. Studies show that the strong affinity which polyphenols have towards PRPs also derives from the loose, random coil structures of the PRPs which afford a large surface area for complexation and from a specific complexation of the phenolic nuclei with the proline residues in the PRPs.

The pyrrolidine rings of the prolyl residues provide a multiplicity of binding sites ('hydrophobic sticky patches') on the PRPs and exert a strong, selective influence on the complexation process. The extensive data compiled by Williamson and his colleagues (Murray and Williamson, 1994; Murray et al., 1994; Luck et al., 1994) suggest that there is 'face-to-face' hydrophobic stacking of the prolyl and aromatic groups, with subsequent hydrogen bonding of one or more phenolic hydroxyl groups to the tertiary amide group N-terminal to the prolyl residue. Preferential binding occurs at the N-terminal prolyl group in an oligoproline sequence.

4. Reflections

The researches of Bate-Smith and Swain in the 1950s and beyond initiated remarkable progress in the next fifty years in the understanding of the chemistry and biochemistry of vegetable tannins; for those who have followed in their pioneering footsteps a minor transcription of the words of Sir Isaac Newton (1675) 'If we have seen further

it is by standing on the shoulders of giants' eloquently expresses this debt. However, it is also important to recall the benefits which Bate-Smith and Swain themselves derived from the optimism and scientific ethos of those days, namely that fundamental studies 'of those things not yet considered important' were encouraged. It is an argument with which scientists have been faced repeatedly over the past 250 years, for as many of the subsequent developments in this particular field amply demonstrate yet again 'There are no such things as applied sciences, only applications of science', (Pasteur, 1872).

References

Balas, L., Vercauteren, J., 1994. Extensive high resolution reverse 2D NMR analysis allows structural elucidation of procyanidin oligomers. Mag. Res. Chem. 33, 386–393.

Bate-Smith, E.C., 1962. The phenolic constituents of plants and their taxonomic significance. I. Dicotyledons. J. Linn. Soc. (Bot.) 58, 95–173.

Bate-Smith, E.C., 1973. Tannins of herbaceous Leguminosae. Phytochemistry 12, 1809–1812.

Bate-Smith, E.C., Metcalfe, C.R., 1957. Leucoanthocyanins 3. The nature and systematic distribution of tannins in dicotyledonous plants. J. Linn. Soc. (Bot.) 55, 669–705.

Bate-Smith, E.C., Swain, T., 1962. In: Mason, H.S., Florkin, A.M. (Eds.), Comparative Biochemistry. Springer, Berlin, p. 764.

Bennick, A., 1982. Salivary proline-rich proteins. Mol. Cell. Biochem. 45, 83–99.

Cai, Y., Haslam, E., 1994. Plant polyphenols (vegetable tannins): gallic acid metabolism. Nat. Prod. Rep. 11, 41–66.

Conn, E.E., Swain, T., 1961. Biosynthesis of gallic acid in higher plants. Chem. Ind., 592–593.

Cornthwaite, D.C., Haslam, E., 1965. Gallotannins 9. The biosynthesis of gallic acid in *Rhus typhina*. J. Chem. Soc., 3008–3011.

Dewick, P.M., Haslam, E., 1969. The biosynthesis of gallic acid in higher plants. Biochem. J. 113, 537–542.

Freudenberg, K., 1920. Die Chemie der Natürliche Gerbstoffe. Springer, Berlin.

Gross, G.G., 1999. Biosynthesis of hydrolysable tannins. In: Pinto, B.M. (Ed.), Comprehensive Natural Products Chemistry, vol. 3. Elsevier, Amsterdam, pp. 799–826.

Haslam, E., 1974. Biogenetically patterned synthesis of procyanidins. J. Chem. Soc., Chem. Comm., 594–595.

Haslam, E., 1977. Symmetry and promiscuity in proanthocyanidin biochemistry. Phytochemistry 16, 1625–1640.

Haslam, E., 1995. Secondary metabolism – evolution and function; products or processes? Chemoecology 5 (6), 89–95.

Haslam, E., 1998. Practical polyphenolics: from structure to molecular recognition and physiological action. Cambridge University Press, Cambridge, New York, Melbourne.

Hemingway, R.W., Foo, L.Y., 1983. Quinone methide intermediates in procyanidin synthesis. J. Chem. Soc., Chem. Comm., 1035–1036.

Joslyn, M.A., Goldstein, J.L., 1964. Astringency of fruits and fruit products in relation to phenolic content. Adv. Food Res. 13, 179–217.

Knowles, P.F., Haworth, R.D., Haslam, E., 1961. Gallotannins IV. The biosynthesis of gallic acid. J. Chem. Soc., 1854–1859.

Luck, G., Liao, H., Murray, N.J., Grimmer, H.R., Warminski, E.E., Williamson, M.P., Lilley, T.H., Haslam, E., 1994. Polyphenols, astringency and proline-rich proteins. Phytochemistry 37, 357–371.

Lunder, T.V., 1988. Tea. Nestle, Nestec Ltd. Company, Vevey, Suisse.

Murray, N.J., Williamson, M.P., 1994. Conformational study of a salivary proline-rich protein repeat sequence. Eur. J. Biochem. 219, 915–921.

Murray, N.J., Williamson, M.P., Lilley, T.H., Haslam, E., 1994. Study of the interaction between proline-rich proteins and a polyphenol by ^{1}H NMR spectroscopy. Eur. J. Biochem. 219, 923–935.

Nishioka, I., Nonaka, G., Ageta, M., 1985. Tannins and related compounds. 25. A new class of gallotannins possessing a (−)-shikimic acid core from *Castanopsis cuspidata* var. *sieboldii Nakai*.. Chem. Pharm. Bull. 33, 96–101.

Nishioka, I., Nonaka, G., Tanaka, T., Sakai, T., Mihashi, K., 1990. Tannins and related compounds. 97. Structural revision of C-glycosidic ellagitannins, castalagin, vescalagin, casuarinin and stachyurin and related hydrolysable ellagitannins. Chem. Pharm. Bull. 38, 2151–2156, and references therein.

Nonaka, G.-I., Kawahara, O., Nishioka, I., 1983. Tannins and related compounds XV. A new class of dimeric flavan-3-ol gallates, theasinensins A and B, and proanthocyanidin gallates from green tea leaf. Chem. Pharm. Bull. 31, 61–65.

Okuda, T., Hatano, T., Yoshida, T., 1989. New methods of analysing tannins. J. Nat. Prod. 52, 1–31.

Okuda, T., Hatano, T., Yoshida, T., 1990. Oligomeric hydrolysable tannins, a new class of plant polyphenols. Heterocycles 30, 1195–1218.

Okuda, T., Hatano, T., Yoshida, T., 1993. Polyphenols of new types and their correlation with plant systematics. Phytochemistry 32, 507–522.

Porter, L.J., 1988. Flavans and proanthocyanidins. In: Harborne, J.B. (Ed.), The Flavanoids: Advances in Research Since 1980. Chapman and Hall, London, pp. 21–62.

Porter, L.J., 1989. Tannins. In: Harborne, J.B. (Ed.), Methods in Plant Biochemistry, Plant Phenolics, Vol. 1. Academic Press, London and New York, pp. 389–419.

Robinson, R., 1955. The Structural Relationships of Natural Products. Clarendon Press, Oxford, 150.

Schmidt, O.Th., Mayer, W., 1956. Natürliche gerbstoffe. Angewandte Chemie 68, 103–115.

Schofield, C.J., Wilmouth, R.C., Turnbull, J.J., Welford, R.W.D., Clifton, I.J., Prescott, A.G., 2002. Structure and mechanism of anthocyanidin synthase from *Arabidopsis thaliana*. Structure 10, 93–103.

Stafford, H.A., Lester, H.H., 1982. Enzymatic and non-enzymatic reduction of (+)-dihydroquercetin to its 3,4-diol. Plant Physiol. 70, 695–698.

Stafford, H.A., Lester, H.H., 1984. Flavan-3-ol biosynthesis. The conversion of (+)-dihydroquercetin and flavan-3,4-diol (leucocyanidin) to (+)-catechin by reductases from cell suspension cultures of Douglas fir. Plant Physiol. 76, 184–186.

Stafford, H.A., Lester, H.H., 1985. Flavan-3-ol biosynthesis. The conversion of (+)-dihydromyricetin and its flavan-3,4-diol (leudelphinidin) to (+)-gallocatechin by reductases extracted from tissue cultures of *Gingko biloba* and *Pseudotsuga menziesii*. Plant Physiol. 78, 791–794.

Stafford, H.A., Lester, H.H., Porter, L.J., 1985. Chemical and enzymic synthesis of monomeric procyanidins (leucocyanidins) from 2*R*,3*R*-dihydroquercetin. Phytochemistry 24, 333–338.

Tanner, G.J., Kristiansen, K.N., 1993. Synthesis of 3,4-*cis*-leucocyanidin and enzymatic reduction to catechin. Anal. Biochem. 209, 274–277.

Walker, A.R., Lee, E., Bogs, J., McDavid, D.A.J., Thomas, M.R., Robinson, S.P., 2007. White grapes arose through the mutation of two similar and adjacent regulatory genes. Plant J. 49, 772–785.

Waterman, P.G., Mole, S., 1994. Analysis of Plant Phenolic Metabolites. Blackwell, London, Edinburgh and Boston.

Weinges, K., Marx, H.-D., Kaltenhauser, W., Nader, E., Nader, F., Perner, J., Seiler, D., 1968. Procyanidine aus früchten. Liebigs Ann. 711, 184–204.

Weinges, K., Bahr, W., Ebert, W., Goritz, K., Marx, H.-D., 1969. Konstitution enstehung und bedeutung der flavonoid-gerbstoffe. Fortschrit Chem. Org. Nat. 27, 158–260.

Werner, I., Bacher, A., Eisenreich, W., 1997. Retrobiosynthetic NMR studies with ^{13}C labelled glucose. Formation of gallic acid in plants and fungi. J. Biol. Chem. 272, 25474–25482.

Zenk, M.H., 1964. Zur frage der biosynthese von gallussäure. Z. Naturforsch. 19b, 83–84.

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