Fig. 3. Possible alternative pathways for the early stages of linoleic acid conversion

It is suggested that the provision of high concentrations of arachidonic acid in youth is accomplished by the simultaneous existence of both the $A_1-A_2$ and the $B$ pathways, the latter only being retained during adulthood.

and docosapentaenoic acid. This has, however, been determined by studies on mature animals and it is possible that both the $C_{18:2}-C_{18:3}-C_{20:3}$ and the $C_{18:2}-C_{20:3}-C_{20:3}$ pathways (Fig. 3) are operative in the earliest age group studied here. Once the demand by the developing testis for more highly unsaturated fatty acids declines with maturity, the additional $C_{18:2}-C_{20:2}-C_{20:3}$ pathway is dispensed with, leading to a lowered metabolic turnover of linoleic acid between $7\frac{1}{2}$ and $17\frac{1}{2}$ months. The even more marked decrease in polyunsaturated fatty acid requirements, consequent on the total failure of reproductive capacity of the animal, results in the switching off of the main pathway involving the $C_{18:3}-C_{20:3}$ step.

References


Age-Related Changes during the Biosynthesis and Maturation of Collagen Fibres

ALLEN J. BAILEY

Department of Biochemistry, Agricultural Research Council Meat Research Institute, Langford, Bristol BS18 7DY, U.K.

In contrast with the majority of proteins the biological half-life of collagen is very long, and as a result time-dependent changes in its physical properties are possible. Indeed, changes occurring in the collagen of connective tissues, particularly the dermis, with increasing age are readily demonstrable and have made it an obvious target for studies of aging. Arguments for its importance in aging are based on its potential ability to cause abnormal physiological functions, such as diffusion of nutrients, oxygen and catabolized products leading to cell death, that could occur as a consequence of changes in physical properties of the collagen fibres. These changes in the physical properties of the collagenous tissues, usually based on mechanical stability, have been attributed to increased
aggregation and excessive cross-linking of the collagen fibres (for reviews see Engel & Larsson, 1970; Sinex, 1967).

The processes leading to the formation of the collagen fibril and subsequent stabilization by cross-linking constitute a complex sequence of events occurring both intra- and extra-cellularly (Grant & Prockop, 1972; Traub & Piez, 1971; Tanzer, 1973; Bailey et al., 1974). Hence, changes with age in the structural organization of collagen may possibly be brought about by cellular differentiation or they may be a result of changes taking place in the extracellular milieu.

The collagen initially synthesized in many embryonic tissues is genetically distinct from collagen of adult tissues (Chung & Miller, 1974; Epstein, 1974). The embryonic collagen, known as Type III, possesses three identical α chains and is stabilized by intramolecular disulphide cross-links. In addition the more usual collagen intermolecular cross-links based on reactions of hydroxylysine aldehydes are also formed. The aldimine cross-link initially formed spontaneously undergoes an Amadori rearrangement to produce the more stable hydroxylysino-5-oxonorleucine (Robins & Bailey, 1973). The embryonic-type collagen is subsequently replaced, or possibly diluted out, during the rapid post-natal growth period by the synthesis of Type I collagen. The latter is the normal collagen of adult skin, tendon and bone, and possesses two identical α chains, the third chain differing slightly in amino acid composition. The Type I collagen present in the adult dermis is stabilized by dehydrohydroxylysino-norleucine, the aldimine cross-links being derived from lysine aldehyde rather than hydroxylysine aldehyde (Bailey et al., 1974). The latter cross-link, in contrast with the one present in embryonic collagen, is chemically and thermally unstable, thus accounting for the higher solubility of young dermal collagen.

The cross-link of both Type I and Type III collagen in embryonic skin exists in vivo as a highly glycosylated derivative. This glucosyl-galactosyl derivative is bound O-glycosidically to the hydroxylysine moiety. In contrast the cross-link in adult Type I collagen is only glycosylated to a small extent. The role of these saccharides in the cross-linking process is not at present known.

In addition to these cell-mediated changes in the type of collagen synthesized, extracellular changes occur during maturation. First, there is a progressive increase in the proportion of some of the reducible components. However, these have been characterized as condensation products of lysine and hydroxylysine with glucose and mannose. Their structure clearly indicates that they can neither be involved in collagen cross-linking nor can they bind collagen to glycoprotein (Robins & Bailey, 1972). Although the presence of these compounds might alter the charge profile of the fibres, the physiological implications, if any, are as yet unknown.

More importantly the proportion of the reducible cross-links present in rapidly developing tissues decreases as the growth rate slows down towards maturation. The bonds present in mature tissue are thermally and chemically stable, and since the proportion of these bonds increases during maturation this would account for the decreasing solubility with age. Although the nature of these cross-links has not been elucidated the most likely explanation of the presently available evidence suggests that they are derived in some way from the reducible cross-links. We have proposed therefore that there is a spontaneous conversion of the labile bonds into stable bonds, rather than invoking the formation of additional new cross-links with all the attendant difficulties of enzyme accessibility within the fibre. This time-dependent conversion is the normal pattern of maturation and should not be confused with senescence. At the present time it is not possible to demonstrate chemical changes that may be taking place after maturation.


Vol. 3
THE BIOCHEMISTRY OF 1,6-α-GLUCOSIDIC LINKAGES: a Colloquium organized on behalf of the Carbohydrate Biochemistry Group by T. N. Palmer (London) and Brenda E. Ryman (London)

The Mechanism of Branching Enzyme Action and Its Influence on the Structure of Amylopectin

DOV BOROVSKY, ERIC E. SMITH and WILLIAM J. WHELAN

Department of Biochemistry, University of Miami School of Medicine, P.O. Box 520875, Miami, Fla. 33152, U.S.A.

The 1,6-branch linkages that interlink the unit chains of amylopectin are formed by the action of Q-enzyme (Drummond et al., 1972). The most extensively studied variety of this enzyme is from potato, also the subject of this report. The enzyme acts by transglycosylation and we have demonstrated that this event can occur by inter-chain transfer from a donor chain to an acceptor chain. A 1,4-bond in the former is split and that portion of the donor chain from the point of scission to the non-reducing terminus is transferred to the acceptor chain with the formation of a 1,6-bond. (Intra-chain transfer, in which a single chain acts as donor and acceptor, has not been excluded.)

The concept that branching occurs after two 1,4-linked α-glucan chains have come into association is thought to explain an old and puzzling finding that at 35°C Q-enzyme does not act rapidly on such chains unless they are about 40 glucose units or more in length (Peat et al., 1954). Such a chain would be 17 nm in extended length, considerably longer than the maximum possible size of the combining site of the enzyme (mol.wt. 85000; Borovsky, 1972). However, if branching requires inter-chain association, and if this association occurs through hydrogen bonds, then one can postulate that a minimum and significant length of chain will be necessary before an association of sufficient stability occurs to permit branching action.

Experimental verification for this idea has come from the demonstration of temperature dependence of the minimum length of chain that Q-enzyme will branch. If the temperature of incubation is lowered to 4°C, this minimum length falls to about 10.

A second test of the idea of chain association came from the postulate that once a branch point is formed between a donor and acceptor chain, the covalent branch link now established should greatly assist the maintenance of an association between the two chains favourable for further branching. In a test of this hypothesis, Q-enzyme was allowed to act on amylose in the presence and absence of an excess of a debranching enzyme (pullulanase) that would hydrolyse the branch linkages as rapidly as they were formed. The experimental finding, in agreement with the hypothesis, was that branching was much more rapid and extensive in the absence of debranching enzyme.

Thirdly, the behaviour of Q-enzyme towards a starch fraction supplied by Dr. D. French and Dr. S. Kikumoto (Iowa State University) confirms the results of this last experiment. This fraction consists of two 1,4-α-glucan chains of around 11–14 glucan units in length joined by a branch point near the reducing end of the chain whose primary hydroxyl group is substituted. Q-Enzyme branches this material at 35°C, but does not act on it after debranching.