ORIGIN of FATTY ACIDS

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Of all the questions pertaining to the origins of life, the prebiotic synthesis of fatty acids has given scientists the most difficulty. Indeed, although studies on the synthesis of amino acids, sugars and nucleic acids are very numerous, those on the prebiotic synthesis of fatty acids are very rare. The chemistry is not easy, but we do know that all prebiotic synthesis would have to be simple, fast and possible in vast quantities. In this paper, I will be discussing the elements necessary for the appearance of fatty acids and the interest of these molecules in evolution. We will then turn to the biosynthesis of fatty acids and, finally, the properties of sulfur ylides and the possible prebiotic synthesis of fatty acids from them.

The formation of membranes is one of the most important events in the prebiotic age. Evolution would not have been possible without them. Indeed, membranes permit compartmentalization and define outside and inside. Self and other. These membranes favor the concentration of molecules and facilitate chemical reactions. Some reactions require the participation of two environments: hydrophilic and hydrophobic. Membranes can provide this interface. The prebiotic cell is a unit: an information unit and an energy unit. Life begins with the identification of this unit. It is necessary but not sufficient. To synthesize prebiotic fatty acids, prebiotic matter is needed. The primitive components would have to be very simple and available in vast quantities. We will now turn to the mechanism of fatty acid biosynthesis.

The first cellular component required for fatty acid synthesis is acetylCoA. AcetylCoA is a small molecule which contains an acetyl group, one part cysteamine, one part beta-alanine, one part pantoic acid and one part adenosine 3'-5'diphosphate. The primitive components of acetylCoA could be described as prebiotic, but the acetylCoA resulting from the association of these elements does not at all exhibit a prebiotic molecule profile, because acetylCoA is much too complex. It is likely that billions of years ago cells developed a sophisticated system to synthesize fatty acids from the prebiotic system, but it is unlikely that this system was the primitive system. The biosynthesis of fatty acids has some special features: fixation of the carboxyl group, exchange of this carboxyl group with the aliphatic chain, reduction and dehydration of the new aliphatic chain. In the first step, acetylCoA is converted to malonyl CoA by addition of a carboxyl group from carbon dioxide. This reaction is carried out by acetylCoA carboxylase and requires biotin and ATP. Such a reaction would not be possible in a prebiotic environment. MalonylCoA is introduced in an enzyme to form a malonyl-enzyme complex. The enzyme, which is an acyl synthetase, exchanges the malonyl carboxyl group with an aliphatic chain. Reduction of the new bond requires NADPH and proton. This reaction produces an asymmetric carbon; indeed the hydroxyl group of the butyryl moiety has a D configuration. In a prebiotic environment, the hydrolysis of the thioester link would occur long before reduction and dehydration.

Also, this reaction would be impossible in a prebiotic environment. Synthesis of fatty acids continues with the production of crotonyl derivatives. These components can again react with malonyl-enzyme complex to form unsaturated fatty acids or can be reduced to butyryl derivatives. Afterwards, the reaction can continue again. Generally, the reaction leads to formation of palmitic acid (C16). Mono-, di- and triglycerides are synthesized from phosphoglycerol and fatty acids. These products can evolve to phosphatidylcholine, phosphatidylethanolamine, and phosphatidylerine.

As we have seen, the acetylCoA and malonylCoA pathway raises many questions. In fact, the thioester bond is very unstable in hydrophilic medium. Some steps of the reaction require a highly organized environment. These problems suggest that this pathway is not a prebiotic pathway. Thus, we have to find another pathway for the prebiotic synthesis of fatty acids, a pathway that enables synthesis in a hydrophobic environment, a pathway that does not require reduction and dehydration and which does not need a very organized environment. I suggest that the solution could lie in the sulfonium salts and sulfonium ylides.

Sulfonium salts and sulfonium ylides are very simple molecules endowed with very complex properties. The simplest is the trimethylsulfonium cation. This cation is very volatile. Alone or with a base, it can lose a proton to form a double bond. This bond has very special properties. Indeed, the resonance of this bond allows the formation of a zwitterion. It is anylide. The reactivity of the anionic methylene group is very interesting. It suggests a new pathway for the prebiotic synthesis of fatty acids. Although sulfonium salts are frequently used, most chemists ignore this class of molecules. The most well-known, S-methyl methionine and S-adenosine-methionine, are very potent alkylating agents. Methylene blue is also a sulfonium salt. Sulfonium ylides are synthesized from sulfonium salts by deprotonation. Usually, for the reaction to be very rapid, this deprotonation requires strong base in an organic solvent. But without base we can see that the exchange rate is acceptable, in the hypothesis of a prebiotic environment. Reactivity is increased by temperature and UV light. The problem with these components is that they are destroyed by heavy metal cations and they are relatively sensitive to moisture. As these components are highly volatile, we must imagine that these reactions would have had to occur in the atmospheric phase in the presence of large quantities of radiation and high temperatures.

Sulfonium ylides have the property of decomposing to produce an olefin. This mechanism is very interesting and important because it seems to be the primitive mechanism of aliphatic chain formation in a prebiotic environment. We don't yet know how this reaction occurs. Franzen and his colleagues have proposed this hypothesis about decomposition. An ylide reacts with a sulfonium salt to form a longer sulfonium salt. The second hypothesis was proposed by Wittig. He suggests that carben participates in the elongation reaction. All these pathways require the participation of two or more molecules. In a prebiotic environment, the probability of two reactive molecules encountering each other is low, except if one or both is present in very large quantities. The actual structure of sulfonium salts and sulfonium ylides suggests an internal mechanism of elongation which we will now examine.

During fatty acid biosynthesis we have seen that the growth of the aliphatic chain produces an even number of carbons. I suggest that the growth of the alkyl chain is due