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DISTINGUISHING FEATURES OF TOCOPHERYL PHOSPHATES AND PHOSPHOLIPIDS

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Abstract - Natural form of vitamin E is composed of eight different analogues, the α-, β-, γ-, and δ-tocopherols and the α-, β-, γ-, and δ-tocotrienols. However, only α-tocopherol is selectively enriched by the liver while the other vitamin E analogues as well as excess α-tocopherol are converted to several metabolites and are subsequently eliminated. A new phosphorylated form of tocopherol, i.e. α-tocopheryl phosphate, has been shown to occur naturally in animal and human tissues as well as in foods. Two derivatives of vitamin E, i.e. α-tocopheryl phosphate (TP) and di-α-tocopheryl phosphate (T_2P) possess many useful properties such as atherosclerotic-preventing effects, anti-inflammatory properties and cardioprotective ability. There are ambiguities with respect of classification of these molecules and in some literature they are referred to as phospholipids. This report aims to bring evidence that TP and T_2P molecules are not phospholipids.
Index Terms - α-tocopheryl phosphate, liposome, tocopherol derivatives, tocosome, Vitamin E.

1. INTRODUCTION

Alpha-tocopheryl phosphate (also called α-tocopheryl phosphate ester or tocopherol phosphate, abbreviated as TP) is a phosphoric acid ester of alpha-tocopherol, with the hydroxyl group of tocopherol, a form of vitamin E [1]. Like vitamin E, it can exist in either the synthetic allracemic (dl) or natural RRR (d) form. The phosphate ester of alpha-tocopherol is found in some plant and animal tissues [2,3]. Another tocopherol derivative has also been described recently: the bis-tocopheryl phosphate ester, or di-α-tocopheryl phosphate (T_2P). T_2P is obtained by esterification of two tocopherol moieties with one phosphate molecule [4]. Several synthetic vitamin E derivatives have been synthesized that are either converted by esterases to the natural form, or exert novel or vitamin E related biological activities. During the last years, specific cellular effects for each individual vitamin E analogue have been described that are the consequence of modulating signal transduction and gene expression. These effects possibly reflect specific interactions of each of the vitamin E analogues with enzymes, structural proteins, lipids and transcription factors. In this review, the different aspects of vitamin E analogues and lipid and phospholipid molecules including their chemical structures, thermal behaviour and polymorphism are explained.

Chemical structures (Fig. 1.1 and 1.2) and some of the characteristics of TP and T_2P molecules are outlined below (Table 1.1).

Chemical Structures of TP and T_2P

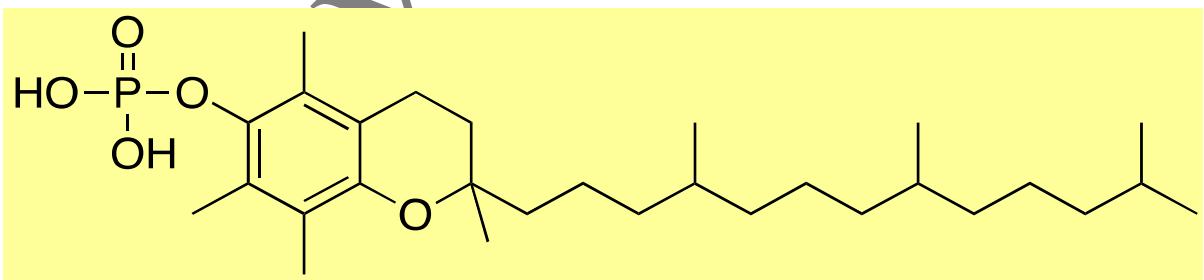

Fig 1.1 Alpha Tocopheryl Phosphate

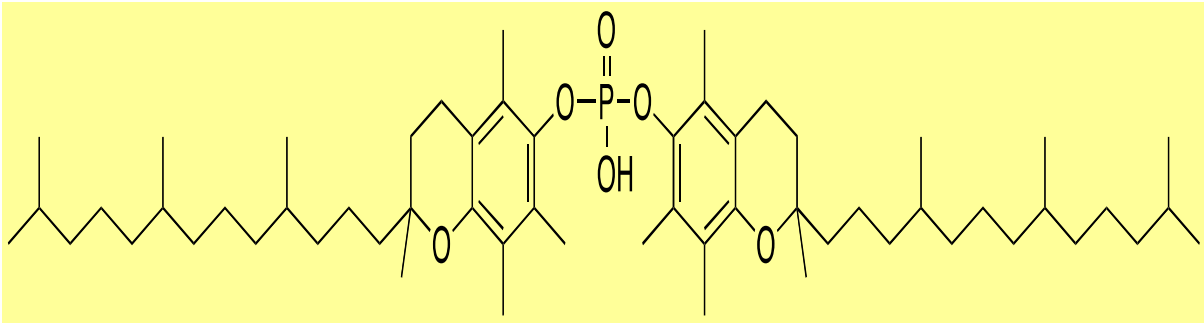

Fig. 1.2 Di Alpha Tocopheryl Phosphate

Table-1.1 Chemical Characteristics of TP and T_2P Molecules

Molecular Formula and Weight		
Compound	**Formula**	**Molecular Weight**
Alpha-tocopheryl Phosphate	$C_{29}H_{51}O_5P$	510.69
Di-alpha-tocopheryl Phosphate	$C_{58}H_{99}O_6P$	923.38

As explained in the next sections there are scientific evidences that show TP and T_2P molecules cannot be classified as phospholipids.

2. DEFINITION OF LIPIDS AND PHOSPHOLIPIDS

Some definitions for lipid and phospholipid molecules are listed below:

Lipids are fatty acid derivatives with various head group moieties. They are widely occurring in nature and have been the subject of various chemical manipulations, for instance to prepare liposomes with certain physico-chemical characteristics (e.g. fluidity, shelf-life, blood circulation time, rate of drug release, etc.). When taken orally, lipids are subject to conversion by gastrointestinal lipases to their constituent fatty acids and head groups. Triglycerides are lipids made from three fatty acids and a glycerol molecule (a three-carbon alcohol with a hydroxyl [OH] group on each carbon atom). Mono- and diglycerides are glyceryl mono- and diesters of fatty acids.

Phospholipids are similar to triglycerides except that the first hydroxyl of the glycerol molecule has a polar phosphate-containing group in place of the fatty acid. Phospholipids are amphipathic (amphiphilic), being both hydrophilic and hydrophobic. The head group of a phospholipid is hydrophilic (water-loving) and its fatty acid tail (acyl chain) is hydrophobic (water hating). The phosphate moiety of the head group is negatively charged [5]. Phospholipids are a class of lipids and are a major component of all biological membranes. All phospholipids contain a diglyceride, a phosphate group, and a simple organic molecule such as choline [6]. A phospholipid molecule can also be defined as a lipid that in its simplest form is composed of glycerol bonded to two fatty acids and a phosphate group [7].

Chemical structure of a phospholipid molecule with its main parts is shown in Figure 3 below. It is clear that while definition of phospholipid necessitates presence of a phosphate group, fatty acid tails and a glycerol linker, structurally, the tocopherols can be viewed as consisting of a chroman head (with two rings: one phenolic and one heterocyclic) and a phytyl tail [8,9]. Furthermore, tocopherols and their derivatives TP and T_2P do not possess glycerol group, which is an essential chemical part of phospholipids.

The other difference between the tocopheryl phosphates and phospholipids is their thermal behaviour. It is well known that amphipathic molecules such as soaps and phospholipids can undergo a thermotropic phase transition at temperatures much lower than their final melting point [5]. This is while TP and T_2P molecules do not possess any phase transition temperature – when assessed by DSC within a very broad temperature range (ca. subzero to 400 °C) – and only have melting points.

In summary

1. Phospholipids by definition are esters of glycerol. TP and T_2P are derivatives of Vitamin E or can be thought as phosphate salts of tocopherol. In TP and T_2P molecules there is not any glycerol unit and there is no aliphatic fatty acid component.
2. Phospholipid molecules form lyotropic liquid crystalline systems upon hydration. However, they exhibit phase transtion due to their huge polymorphism and they transit from one molecular orientation to another due to their polymorphism. In other words, phospholipids have phase transition due to their polymorphism, especially lyotropic polymorphism upon hydration. TP and T_2P molecules are not phospholipid and they do not have any phase transition.

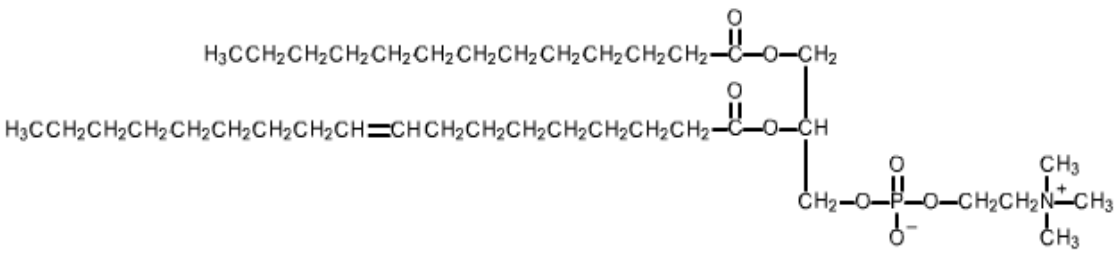

Fig. 3 A Different Representations of Chemical Structure of a Phospholipid Molecule

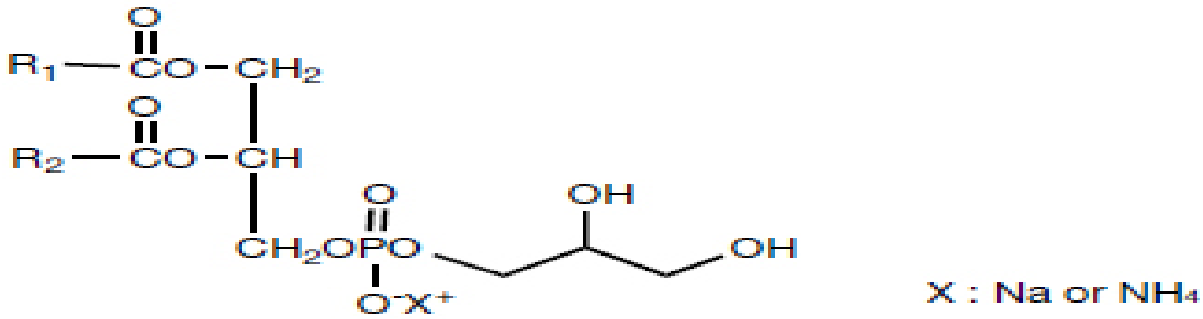

Fig. 3 B Different Representations of Chemical Structure of a Phospholipid Molecule

Due to significant biological and medical properties as well as noticeable health benefits [10] TP and T_2P molecules merit special scientific attention and have huge potential to be applied in various fields including food, nutrition, pharmaceutics, skin-care and drug delivery [11].

CONCLUSION

Based on the facts and evidences presented in this report, considering disagreements between the definition of phospholipids and tocopherols, in addition to main differences in their chemical structures along with major differences in their thermal behaviour, the derivatives of vitamin E (i.e. TP and T_2P molecules) cannot be classified as phospholipids.

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