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Review

A comprehensive review on the colorless carotenoids phytoene and phytofluene

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ABSTRACT

Carotenoids and their derivatives are versatile isoprenoids involved in many varied actions, hence their importance in the agri-food industry, nutrition, health and other fields. All carotenoids are derived from the colorless carotenes phytoene and phytofluene, which are oddities among carotenoids due to their distinct chemical structure. They occur together with lycopene in tomato and other lycopene-containing foods. Furthermore, they are also present in frequently consumed products like oranges and carrots, among others. The intake of phytoene plus phytofluene has been shown to be higher than that of lycopene and other carotenoids in Luxembourg. This is likely to be common in other countries. However, they are not included in food carotenoid databases, hence they have not been linked to health benefits in epidemiological studies. Interestingly, there are evidences *in vitro*, animal models and humans indicating that they may provide health benefits. In this sense, the study of these colorless carotenes in the context of food science, nutrition and health should be further encouraged. In this work, we review much of the existing knowledge concerning their chemical characteristics, physico-chemical properties, analysis, distribution in foods, bioavailability and likely biological activities.

Introduction

Phytoene (7,8,11,12,7′,8′,11′,12′-octahydro-ψ, ψ-carotene, PT[1]) and phytofluene (7,8,11,12,7′,8′-hexahydro-ψ, ψ-carotene, PTF) were already studied in the 1940s, with a wealth of dedicated investigations in the 1950s [1–7]. They can be considered as rarities within the "Carotenoid Kingdom" as they are colorless. However, they are key carotenoids because they are precursors of all the others. This is why they have been extensively studied in investigations dealing with the biosynthesis of these compounds. Surprisingly, they have been largely neglected as compared to other carotenoids in other kinds of studies, despite they are known to occur in widely consumed foods. Likewise they are among the predominant carotenoids in human plasma and tissues. In this work, aspects like chemical features, properties, analysis, occurrence in foods, bioavailability and likely biological activities of PT and PTF are reviewed.

Chemical structure and physico-chemical properties

PT and PTF are linear hydrocarbons with molecular formulae $C_{40}H_{64}$ (MW = 544 Da) and $C_{40}H_{62}$ (MW = 542 Da), respectively. More specifically, they are alkenes with 9 and 10 double bonds, respectively. In the case of PT, three of the double bonds are conjugated, whereas PTF has five conjugated double bonds (c.d.b.) (Fig. 1) [8]. The system of alternating double and single bonds is one of the main structural characteristics of carotenoids. This is an electron-rich conjugated system in which the π-electrons are delocalized and is considered the structural feature mainly related to the light-absorbing properties, reactivity and shape of carotenoids [9]. The system of c.d.b. in PT and PTF is clearly shorter compared to other dietary carotenoids (for instance, lycopene, another linear carotene, contains 11 c.d.b.) (Fig. 2), so both PT and PTF are

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[1] *Abbreviations used:* ABA, abscisic acid; ABTS, [2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid)]; ACC-1, acetyl-CoA carboxylase; CD, control diet; CD36, cluster of differentiation 36; CPT-1, carnitine palmitoyltransferase ; CRTISO, carotenoid isomerase; DGAT, diacylglycerol acyltransferase; DMAPP, dimethylallyl diphosphate; DXP, 1-deoxy-D-xylulose-5-phosphate; E, energy; FFA, free fatty acid; FPP, farnesyl pyrophospate; GGPP, geranylgeranyl pyrophosphate; GPP, geranyl pyrophospate; HDL, high density lipoprotein; HFD, high-fat diet; IPP, isopentenyl diphosphate; LDL, low density lipoprotein; LYC, lycopene; MeOH, methanol; MEP, methylerythritol 4-phosphate; MTBE, methyl-tert-butyl ether; MVA, mevalonic acid; PDS, phytoene desaturase; PPAR, peroxisome proliferator-activated receptors; PPARγ, peroxisome proliferator-activated receptor gamma; PT, phytoene; PTF, phytofluene; SREBP-1, sterol-regulatory element binding protein; TEAC, trolox equivalent antioxidant capacity; VLDL, very low density lipoprotein; ZDS, ζ-carotene desaturase; ZISO, ζ-carotene isomerase; c.d.b., conjugated double bonds.

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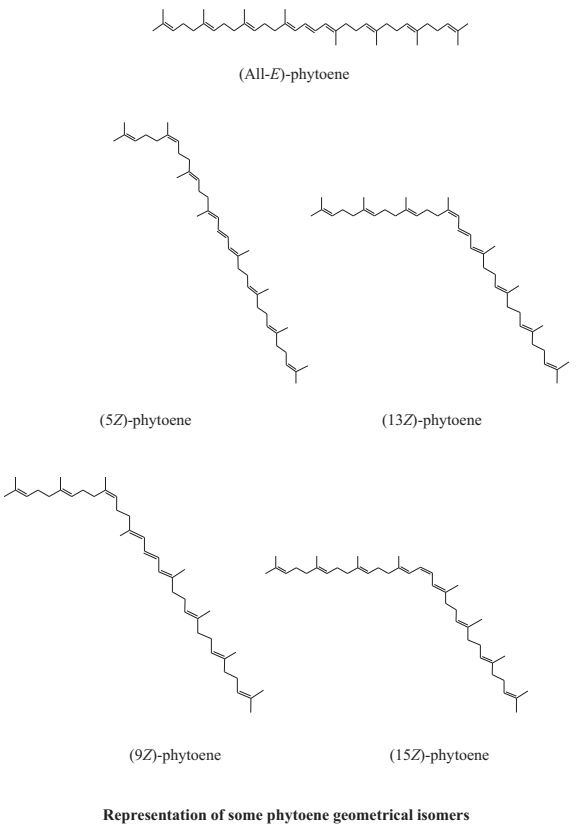

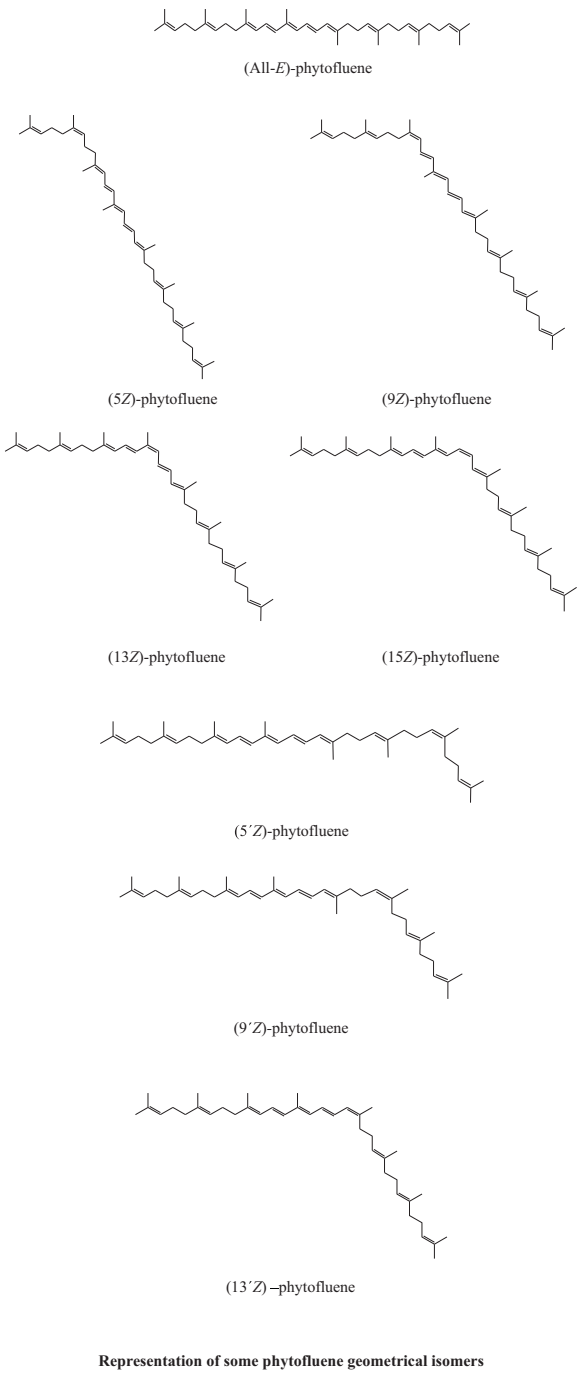

Fig. 1. Chemical structures of geometrical isomers of phytoene, phytofluene and lycopene.

Fig. 1 (*continued*)

expected to exhibit important differences in some physico-chemical properties compared to other carotenoids.

Light absorbing properties

According to the data tabulated in reference books, PT absorbs maximally at 286 nm and the spectrum also exhibit two shoulders at 276 and 297 nm in petroleum ether, its fine structure being low (%III/II = 10). In the case of PTF, the λ_{max} is 348 in petroleum ether. The spectrum has sharp absorption bands (%III/II = 90) with other absorption maxima at 331 and 367 nm [10,11]. The relationships between the length and arrangement of the system of c.d.b. of common dietary carotenoids on the color parameters of the CIELAB uniform space is well understood. Although the color of carotenoids is dependent on factors others than just their chemical structure (like concentration and interaction with other molecules, among others), it is considered that at least 7 c.d.b. are needed for a carotenoid to exhibit color [12], hence PT and PTF are considered colorless carotenoids. On the other hand PTF is known to fluorescence at around 510 nm when it is excited with near-UV light [13]. This property can be certainly used to enhance its detection or for other analytical purposes.

Reactivity

In contrast to other carotenoids, there are not many specific data relative to the susceptibility of PT and PTF to oxidation in model systems. In a recent study, this was compared in PT, PTF and LYC by *in silico* strategies and the ABTS radical cation decoloration assay. The theoretical and experimental results were found to agree well and indicated that, as it could be presumed from their chemical structures, PT and PTF were not as effective antiradicals as LYC. However, the comparison of the experimental TEAC with those reported for other carotenoids by other authors indicated that PT and PTF seem to be better scavengers of the ABTS radical cation than it may be expected beforehand [14]. Interestingly, and contrary to what it could be expected from its structure, PTF is known to be very unstable in the presence of oxygen [8]. More studies assessing the behavior of these carotenoids under different oxidation conditions and by other approaches are warranted.

Shape

The study of the geometry of molecules as well as their size or presence of functional groups is important to help understand where they can fit in structures or how they interact with other