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A MINI REVIEW ON CAROTENOIDS FROM THERMOPHILES- STRUCTURAL FEATURES AND ITS BIOLOGICAL ADVANTAGES

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ABSTRACT

Microbial carotenoids offer several advantages such as ready accessibility and reproducibility than plants, with no seasonal-dependence to limit their availability. The carotenoid producing microbes are found in varied sources, of which, those isolated from extremophilic conditions show intense coloration and their resistance to extreme conditions makes them valuable during industrial production. The present review focuses on the core structural features and the possible modifications in carotenoids from thermophiles that renders functionality and survival advantage thus making them best candidate for future applications.

Keywords: Carotenoids, Thermophiles, Structural features, Biological advantages.

1. INTRODUCTION

Carotenoids are among the most vibrant and diverse pigments that hold a platter of red, yellow, and orange shades [1]. The carotenoids' market has grown substantially in the last few years which can be credited to the growing use of natural carotenoids as food colorants and advances in the methods used for their extraction. Carotenoids extracted from the plants are rather expensive as they have to cope with the various disadvantages such as instability, limited range, non-availability throughout the year, difficult extraction procedures and low bioavailability [2]. Thus, carotenoids commercialized as food color additives and supplements continue to be mostly products of chemical synthesis. The chemical synthesis of carotenoids is a well-established process, contributing to the majority of the global market, but its safety to human direct consumption is questionable [3]. Owing to concern over the health impacts of chemical additives, finding alternative sources for sustainable procurement of carotenoids has become need of the hour.

Extremophiles produce intense pigments as a part of their survival mechanism. Interestingly, for survival in extreme environments, the membranes of extremophiles especially thermophiles have been stabilized by carotenoid pigments [4]. Studies have shown that the carotenoids form an integral part of thermophiles' membrane with distinct structural features [5] and positioning thereby imparting strength, rigidity and oxidative stability [6] implying their role in adaptation to high temperatures and oxidative stress. This review summarizes the structural variations in carotenoids and all perspectives on the positioning of carotenoid in the membranes of thermophiles that help them to survive extreme temperatures with enhanced biological potential. To the best of our knowlege this approach with respect to carotenoids from thermophiles has not yet been reported.

2. MICROBIAL CAROTENOIDS: GENERAL STRUCTURE & STRUCTURAL FEATURES IN CAROTENOIDS FROM THERMOPHILES

2.1. General structure of Microbial Carotenoids

Carotenoids are generally tetraterpenoids, built over a basic unit called an isoprene unit, that comprises of 5 carbons and 2 conjugated double bonds [7]. They are classified into two main groups:carotenes and xanthophylls. Carotenes are carotenoids which have only hydrogen and carbon whereas xanthophylls are oxygenated carotenes.

Microbial carotenes are derivatives of a red colored water insoluble tetra-terpene hydrocarbon called all trans-lycopenewhich undergoes cyclization either at one or both the ends of the hydrocarbon chain to form monocyclic (i.e Υ/δ) or dicyclic (i.e α/β) carotenes (Fig. 1). Further, the cyclic carotenes by the process of

hydroxylation can be converted to relatively polar class of carotenoids called xanthophylls. The structural modifications in the tetraterpenoids, in terms of presence and absence of oxygen moiety localized at the linear or cyclic ends, renders carotenoids exhibiting lipophilic to amphipathic nature. Apart from the presence or absence of polar groups, centrally positioned conjugated double bond system, E- or Z-configuration and presence or absence of esterification in a carotenoid are important characteristics which affects its properties and biological functions [8].

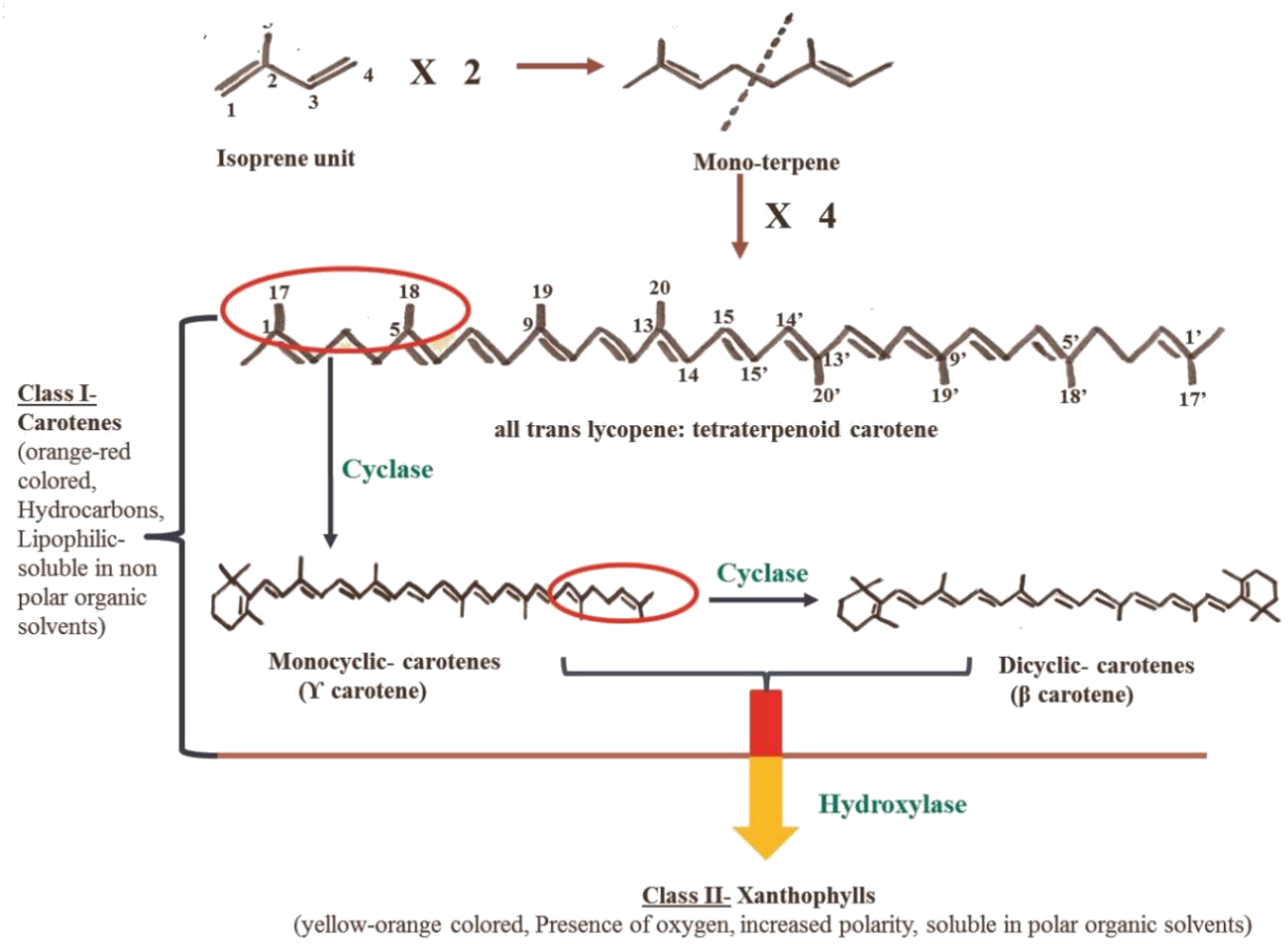


Fig. 1: Concept of carotenoid structure, classes and properties

2.2. Structural Features of Carotenoids from Thermophiles

Thermophilic bacteria are used for plethora of applications, such as bioconversion of wastes, enzyme technology or fuel production [9]; however, their potential in terms of carotenoid production is not explored. The thermophilic bacteria have amended to high temperature by producing unique carotenoids with distinct structural modifications (Table 1) that stabilizes their membranes. The mono or dicyclic carotenes (Fig. 1) form the basic skeleton which undergoes modifications resulting in structurally diverse and unique carotenoids.

The structural features observed in the thermophilic carotenoids can be categorized into 4 types as mentioned below;

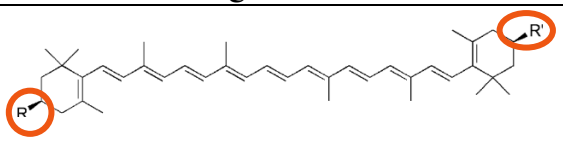
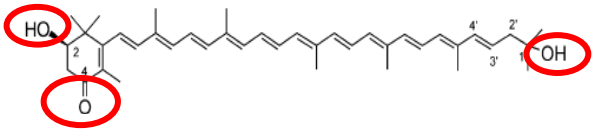
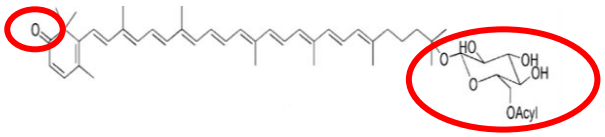
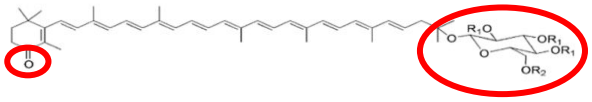
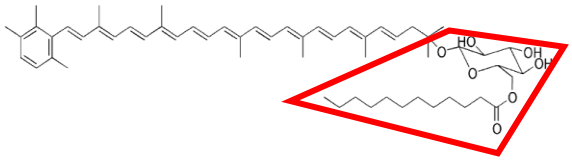
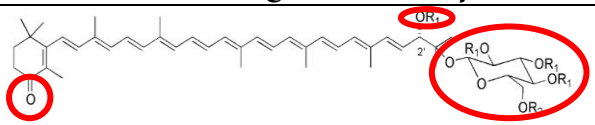
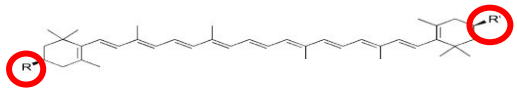
Type I. Number of carbons

Type II. Presence of polar groups such as hydroxyl, keto etc.

Type III. Modifications such as desaturation, glycol-sylation, acylation at the ring/C-end

Type IV. Presence of glycosyl fatty acid esters

Table 1: Structural features of Carotenoids from Thermophiles

Micro-organism	Structural Modifications in Basic Carotenoid skeleton	Name & structure of carotenoid with area/region of modification.	Ref.
Thermus. thermophilus	Type I. Number of carbons **(>C50)** Type II. Dicyclic ring - hydroxylation **(Thermozeaxanthin)** Type IV. Presence of glucosyl fatty acid esters	 **1.Thermozeaxanthin R= OGlucAcyl, R' =OH)** **2. Thermo-(bis)zeaxanthin (R=R' = OGlucAcyl)** **3.Thermocryptoxanthin (R= OGlucAcyl, R' =H)**	10,11
Deinococcus radiodurans	Type II. Hydroxyl group at C-end Type II. Monocyclic ring with hydroxylation at 2nd position &ketolation at 4th position	 **Deinoxanthin**	12
Meiothermus ruber	Type II. Monocyclic ring with Ketolation at 2nd position, desaturation of the ring Type III. Acylation, glycosylation at C-end	 **10-(6-O-acyl-b-D-glucopyranosyloxy)-3,4,30,40-tetradehydro-10,20-dihydro-b,C-caroten-2-one**	13
Roseiflexus castenholzii	Type II. Monocyclic ring with ketolation at 4th position Type III. Acylation, Glycosylation at C-end.	 **Acylated ketomyxocoxan..... glucoside(R_1=R_2=H)**	14
Chlorobium. tepidum	Type III. Desaturation at the ring end. Type IV. Glycosyl fatty acid ester at C- end	 **OH-chlorobactene glucoside lauryl ester**	15
Rhodothermus marinus	Type II. Hydroxyl group at the C-end, keto group at ring end Type III. glucosylationacytelation the C-end	 **(all-E, 20S)-20-hydroxy-10-(b-d-glucopyranosyloxy)-30,40-didehydro- 10,20-dihydro-b,w-caroten-4-one (R_1=R_2=H/R_1=R_2=Ac)**	16
Sulfolobus shibatae	Type IV. Dicyclic ring with Glucose or Rhamnose ester.	 **β-d-glucosides and α-l-rhamnosides of zeaxanthin (R=R'=OGluc/ R=R'=ORham)**	17

3. BIOLOGICAL ADVANTAGES ATTRIBUTABLE TO STRUCTURAL FEATURES

3.1. Improved Membrane Stability

High temperature increases the fluidity of the membrane due to loss of rigidity of membrane phospholipids [18]. This results in increased membrane permeability which makes the cell more susceptible to oxidative damage; therefore membrane stability is a key requisite in order to survive at these temperatures and pressure [19]. Active oxygen species attack the bio-membranes at the hydrophobic core which is composed of polyunsaturated fatty acids that may directly degrade the membrane [20]. In most of the cases, it has been observed that, the thermophilic carotenoids span the entire length of lipid bilayer and have their polar groups anchored in the opposite polar zones of the membrane [21]. The Van der Waals interactions between the carotenoids and acyl chains of lipids, rigidifies the fluid phase of the membranes and limit oxygen penetration to the hydrophobic membrane [22]. Thus, the presence of polar carotenoids in the lipid phase modifies the membrane fluidity and alters permeability for small molecules, including oxygen [20, 23]. Studies revealed that purified deinoxanthin from thermophilic *Deinococcus radiodurans* showed approximately 1-fold more inhibition of oxidative damage in bovine serum albumin as compared to lutein [24]. This suggests potential use of carotenoids from thermophiles as membrane stabilizers in drug delivery systems.

3.2. Enhanced Bioavailability

Carotenoids are widely utilized in animal feed products meant for poultry, fish or shrimp due to their coloring properties. For acquiring the beneficial effects of dietary carotenoids, their bioavailability is very essential. During the process of digestion, the dietary fats are emulsified to form micelles in the small intestine which aids in the transport of carotenoids to the surface of enterocytes [25,26].Although the absorption efficacy of dietary carotenoids by fatty acids is fairly high, but their bioavailabilityin general is very low and relies on multiple factors which includes carotenoid speciation [27]. In terms of carotenoid speciation, xanthophyllsare-reported to have reasonably higher bioavailability than carotenes [28]. One of the reason for this is hydrophilic nature of xanthophylls due to which they are positioned at the surface of oil droplets with better access to mixed micelles and thus they are more freely partitioned into micelles as compared to carotenes [29, 30]. Other reason for better bioavailability of xanthophylls is that, they often are present as esters in fruits and vegetables. The esters are very hydrophobic and require hydrolysis to the free form during digestion for efficient micellarization and uptake by enterocytes [31]. Carotenoids from thermophiles have both hydrophilic nature and presence of glucosyl fatty acid esters (Table1: Type II and Type IV modification) which imparts them with an additional advantage of enhanced bioavailability as compared to carotenoids from non-thermophilic sources.

3.3. Augmented Functionality

Carotenoids are known for their role as antioxidants and studies have suggested that carotenoids from thermophiles have better antioxidant activity as compared to those obtained from non-thermophilic counterparts [32-34]. The carotenoid extract containing deinoxanthin as a major carotenoid from thermophilic *Deinococcus radiodurans* was capable of scavenging superoxide anion generated by the irradiated riboflavin/EDTA system which was validated using electron spin resonance and spin trapping techniques [33]. Chemiluminescence analysis have revealed that at a concentration of 0.03 mM deinoxanthin exhibited 20% more H_2O_2 scavenging as compared to carotenes (lycopene and β-carotene) and xanthophylls (zeaxanthin and lutein) from non-thermophilic sources [32]. A 4-fold higher protection of DNA was shown by deinoxanthin upon *in vitro* treatment with hydroxyl radical as compared with β-carotene [24]. Deinoxanthin was found to possess lower lowest triplet excitation energy for its unique structure than other carotenoids, such as β-carotene and zeaxanthin, which confers it a strong potential in the energy transfer-based ROS-scavenging process. Moreover, the reduction potential in terms of H-atom of deinoxanthin is comparable to zeaxanthin according to the theoretical homolytic O-H bond dissociation enthalpy,which is contributed by presence of large number of conjugated double bonds [34].

Above reports supports the fact that carotenoids from thermophiles not only possess better functionality in terms of their antioxidant potential but also provide better bioassessibility and membrane stability.

4. CONCLUSION

In this era of white biotechnology, there is an increasing interest in carotenoids obtained naturally by biotechnological processes. Worldwide market size of carotenoids have abundant scope for innovative

pigments that are sustainably sourced and offer better functionality. Carotenoids from thermophilic bacteria have modifications in their structures that could contribute towards maintaining stability and bioactivity during processing and storage and thus can be explored for wide industrial usage. Considering their huge potential, systematic studies on development of high yielding new strains needs to be carried out. There is tremendous scope of research in this area and efforts are needed to evaluate their safety and efficacy in comparison with the presently used synthetic carotenoids.

Conflict of interest

None declared

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