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SCIENTIFIC CORRESPONDENCE

# Progress in Microbial Carotenoids Production

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**Abstract** Carotenoids are versatile isoprenoids pigments, play a vital role in the cellular system, starting from antioxidant to gene regulation. Carotenoids are widely used in food, nutraceuticals, and cosmetics owing to their vitamin A, antioxidant and anticancer activities. The demand of carotenoids in various sectors has triggered the research to explore a commercially viable and environmentally friendly production. This article presents a short review of progress in carotenoids production from microbial platforms.

**Keywords** β-carotene · Astaxanthin · *Blakeslea* · *Corynebacterium*

Carotenoids, a subfamily of isoprenoids (also called "terpenoids"), are one of the most diverse classes of secondary metabolites synthesized by plants, fungi, algae, and bacteria. In the last decade, the remarkable progress have witnessed in carotenoids production based on microbial platforms, which is in response to the great demands because of antioxidant and Vitamin A activity, widely applied in nutraceuticals, pharmaceuticals, poultry, food and cosmetics [1] The current commercial market value of these carotenoids is estimated $1.5 billion in 2014, with a chance to grow to $1.8 billion in 2019, with a compound annual growth rate of 2.3%. The astaxanthin, β-carotene, and lutein together share nearly 60% of total market value. Chemically-synthesized carotenoids account for 90% of the total market, although the demand for naturally produced carotenoids is growing rapidly due to the health concern of synthetic carotenoids. The carotenoid production using organic synthesis or extraction from plant based sources is limited owing to low yields that result in high product costs. Consequently, there is considerable interest in the microbial production of various carotenoids, such as astaxanthin, β-carotene, lutein, lycopene, and zeaxanthin, as an alternative that has shown better yields. Also, the microbial production of commercially used carotenoids could be a better alternative to produce novel $C_{50}$ carotenoids at low costs, by utilizing agro-industrials wastes as low-cost substrates [1].

Microalgae species belonging to genus *Chlorella, Dunaliella, Scenedesmus* and *Haematococcus* are considered as the key producers of commercially vital carotenoids. These organisms can produce astaxanthin, lutein, and β-carotene. *Dunaliella salina* can accumulate up to 10% of β-carotene on dry cell weight (DCW) at certain extreme environmental situation. Similarly, *Haematococcus pluvialis* is a commercially viable source of natural astaxanthin (80–99% of total carotenoids). Under specific culture conditions, *H. pluvialis* can naturally accumulate astaxanthin up to 3–5% of DCW [1, 2]. The production cost of astaxanthin using *H. pluvialis* has estimated as $ 552/Kg. Here, cost study indicated that natural production of carotenoids in economically feasible and competitive to synthetic carotenoids with a production cost of $ 1000/kg. Microbes such as *Corynebacterium glutamicum* (Gram-positive soil bacterium) are a unique source to produce novel $C_{50}$ carotenoids such as 4-decaprenoxanthin and its glycosylated forms. These are principally used in medical and cosmetic products owning to its UV light-protecting properties [3]. Interestingly, *C. glutamicum* commercially produced more than 3 million tons of amino acids,

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annually. The genetically engineered *C. glutamicum* showed red pigmentation with a more than 80 folds higher content of lycopene (2.4 mg/g DCW) [4].

*Blakeslea trispora*, a filamentous fungus, intensively used for the commercial production of β-carotene and lycopene. The carotenoids production from fungi is advantageous due to high mycelial growth rate and responsive to the metabolic stimulators and inhibitors in large-scale industrial production. Additionally, the use of agro-industrial wastes reduce the production costs and a suitable substitute to reduce environmental contamination. Shi et al. [5] recorded a maximum 578 mg/l lycopene production with supplementation of mevalonic acid as metabolic precursors by *B. trispora*. The production of carotenoid in microbes can be further improved by: (1) optimizations of native pathways, (2) introduction and expression of foreign genes to increase flux in metabolic pathways, and (3) by adaptive laboratory evolution [6]. In recent years, biotechnological production of carotenoids by heterologous production has become more attractive. For instance, *Saccharomyces cerevisiae* can turn into the β-carotene-producing organism (1.04 mg/g DCW and 2.24 mg/l broth), after successive transformation with carotenogenic genes and by inverse metabolic pathways engineering with supplementation of oleic acid and palmitoleic acid [7]. In bacteria, carotenoids are biosynthesized using isopentenyl pyrophosphate as a precursor, produced from methylerythritol phosphate (MEP) pathway. Zhao et al. [8] observed that engineering MEP module can result in a 3.5-fold increase of β-carotene yield in *E. coli*.

There are enormous microbes that can produce commercially vital carotenoids; however, information is lacking regarding approaches to yield within quality at industrial scale. There are various process parameters for enhanced accumulation of carotenoids in microbes, which is the important step toward the economically feasible production of carotenoids.

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