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Sustainable Biosynthesis of Astaxanthin: A Strategy to Address Global Food Challenges

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Abstract. With the continuous growth of the global population, today's food system is facing severe challenges. Researchers have begun to explore how to maximize possible yield while minimizing environmental pollution. During the last few years, there has been extraordinary research in biosynthesis of astaxanthin, a ketocarotenoid that offers numerous properties such as antioxidant, anticancer, and eye-protective function. This study focuses on discovery of the best possible pathway, gene editing strategies, host organism, and feedstock for biosynthesis of astaxanthin. Ultimately, we concluded the final biosynthetic pathway with specially focused gene modification, chosen the host organism as Saccharomyces cerevisiae, and sweet potato juice as the feed. Through genetic engineering methodology, this study demonstrates that astaxanthin can be efficiently produced by microorganisms, reducing the environmental impact of traditional extraction from aquatic organisms and addressing the safety concerns of chemical synthesis. These findings thereby have profound implications for the food system.

Keywords: Astaxanthin, genetic modification, metabolic engineering, synthetic biology

1. Introduction

Humanity is facing – and will continue to face a severe food security crisis. By 2025, the global population is expected to come to 10 billion in 2050, and this phenomenon may likely persist for decades [1]. According to the Global Report on Food Crises (2025), more than 295 million people across 53 countries and regions suffered from critical hunger in 2024 [2]. With this precondition, finding innovative food solutions to feed an increasing number of people is demanding. However, the current state of the food system is far from ideal, with problems such as climate stress, food waste, environmental footprint, and pollution of materials.

Two problems arise due to these realities: environmentally and economically. For the former one, agriculture and other food production activities are among the largest emitters of greenhouse gases [3]. Recent study showed that people produced 16.5 Gt CO_2 eq annually, which counted for approximately one third of global emission [4]. There are three major pathways for this great emission: crop and livestock production, deforestation, and production of fertilizers plus

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transportation [4]. For the latter one, though people used vast areas of land for cultivation, there is still price volatility and unequal access to nutritious food. An example from Spain shows that 16.2% of adolescents faced food insecurity, and such rates were higher in nontraditional families and immigrant families [5].

Therefore, we need to search for solutions to reduce emission of greenhouse gases, reduce environmental impacts, and try to make as many people as possible have adequate and affordable food. The solutions for such matters are building a sustainable agricultural system, using advanced technologies such as gene editing and targeted expression of enzymes, and generalizing circular use. Therefore, our group is interested in the exploration of the application of genetic engineering in microorganisms to enable sustainable and efficient production of targeted product, which is astaxanthin. Compared to chemical synthesis and directly extracting from the shrimp shells, such biosynthesis production not only can be safely used in the human body but also reduces overharvesting of biological assets and discharging production of additional waste. Therefore, our biosynthesis application inhibits disruption of the ecosystems as well as disruption of the food cycle as an entirety.

2. Results and discussion

2.1. Product selection

Astaxanthin, classified as a natural ketocarotenoid, occurs in diverse species, notably in microalgae (Haematococcus pluvialis), yeast, shrimp, and salmon. We have selected astaxanthin as our targeted product for several health, environmental, and economic reasons. From a healthcare perspective, it exhibits very strong antioxidant properties. Astaxanthin antioxidant activity stands out among any other available antioxidants involving β-carotene, canthaxanthin, lutein, zeaxanthin, vitamin C and vitamin E [6]. Many studies have shown extraordinary protective functions of astaxanthin against age-related physiological and pathological processes. In experiments, astaxanthin has proved to have the ability to reduce oxidative stress, inflammatory reactions, apoptosis, and faulty autophagy via the adjustment of key cellular signaling events [7]. Hence, astaxanthin has already been exploited in nutraceuticals and functional food applications.

Second, from a sustainability standpoint, the choice of biosynthesis of astaxanthin ensures sustainability. Conventional production methods, such as extraction from crustacean derivatives, are limited with low production and high cost [8]. Chemical synthesis, though holds 95% of the market share because of its relatively lower production costs and prices, is dangerous in safety and produces a racemic mixture not safe for direct human consumption [9]. Relatively, application of engineered microbes or microalgae in a biosynthetic process presents a renewable option, minimizing the environmental footprint and resource-intensive dependency.

Third, from a market perspective, natural astaxanthin demand worldwide is still growing at a rapid rate. Its market was forecasted to reach $2.83 billion in 2025 and to reach $7.57 billion in 2035, at a 10.3% compound annual growth [10]. Such growth indicates increased consumer desire for environmental-friendly, safe, and sustainable products. Therefore, astaxanthin was highlighted for promotion as a targeted product because it combines health, environmental, and high commercial potential perfectly, with a promising prospect for the markets.

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2.2. Approach and pathway

The biosynthesis of astaxanthin was divided into three modules to enable precise metabolic control and optimization, which are IPP Synthesis Module, β-carotene Synthesis Module, and Astaxanthin Synthesis Module (Fig 1).

The main goal of the first module is to enhance the supply of isopentenyl diphosphate and dimethylallyl diphosphate, which are basic precursors for terpenoid biosynthesis. This could be achieved by overexpression of the important rate-controlling enzymes, for example, DXS and IDI. For DXS, it would carry out the condensation between glyceraldehyde-3-phosphate and pyruvate to produce the DXP. And for IDI, it would enable IPP and DMAPP interconversion. Therefore, we can introduce additional copies of DXS and IDI genes into the host genome under strong inducible promoters such as T7 or trc so that we can increase precursor availability.

The second module is to maximize β-carotene production from geranylgeranyl diphosphate. The key enzymes in this module are CrtB, CrtE, CrtI, and CrtY, which are phytoene sunthase, GGPP synthase, phytoene desaturase, and lycopene cyclase, respectively. To optimize flux toward β-carotene and prevent intermediate accumulation, we can employ some strategies such as promoter engineering, gene order rearrangement, copy number control, and fusion protein design.

The third module is to synthesize Astaxanthin from β-carotene through two main pathways. In the first pathway, the ketolation-first pathway involves the enzyme CrtW introducing keto groups to form echinenone and canthaxanthin. And then, a CrtZ-mediated hydroxylation yields Astaxanthin. In the second pathway, the hydroxylation-first pathway can utilize CrtZ to convert β-carotene into zeaxanthin, which is subsequently ketolated by CrtW to produce Astaxanthin. To optimize yield, we can upregulate CrtW and CrtZ expression and inhibit competing enzymes such as CrtU and CrtX, thereby leading metabolic flux toward astaxanthin accumulation.

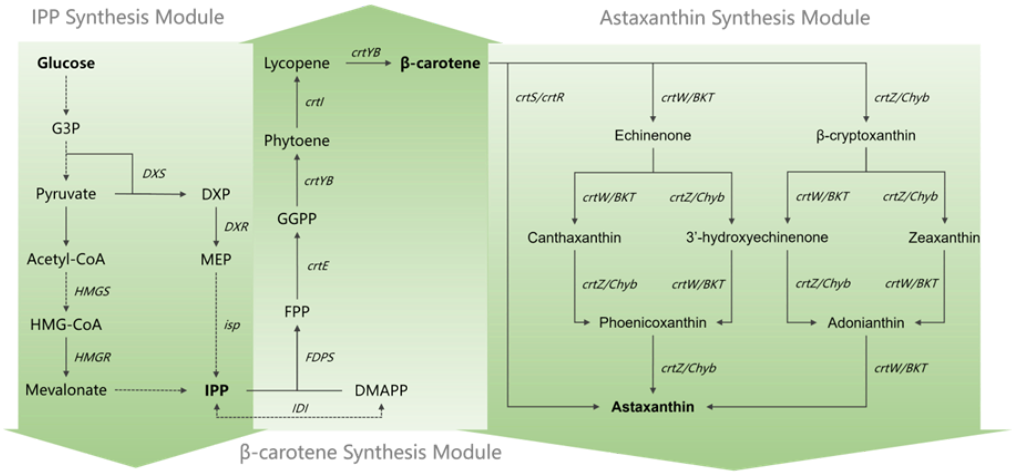

Figure 1. Astaxanthin biosynthetic pathway overview

2.3. Host selection

A variety of host organisms have been engineered for astaxanthin production, each with distinct advantages and modifications.

While chloroplast engineering—specifically, overexpressing phytoene desaturase (PDS) via the psbA promoter/UTR system—successfully enhanced astaxanthin accumulation in H. pluvialis under stress conditions (high light & nitrogen deprivation), the commercial potential of this approach is

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hampered by the organism's inherent limitations [11]. Its notoriously slow growth rate and high sensitivity to cultivation parameters present significant challenges for industrial scalability [12].

Chlamydomonas reinhardtii was engineered by knocking out LCYE to block the α-branch of carotenoid pathway, reducing lutein synthesis, and deleting ZEP to prevent zeaxanthin conversion to violaxanthin. A synthetic, codon-optimized BKT gene was introduced to enhance ketolation activity [13].

In the yeast Rhodotorula rubra, the mevalonate pathway was strengthened by overexpressing rate-limiting enzymes, and GGPP synthase (CrtE) was amplified to enhance precursor supply. Lipid droplet formation was promoted via overexpression of DGA1 to improve astaxanthin storage.

Yarrowia lipolytica presents several advantages, including its innate capacity for high lipid accumulation and strong flux through acetyl-CoA. However, its application for astaxanthin production is constrained by the absence of a complete native pathway.So we should introduce the critical heterologous enzymes β-carotene ketolase and hydroxylase from organisms such as Haematococcus pluvialis to enable the conversion of β-carotene into astaxanthin. Despite these modifications, achieving high yields in Y. lipolytica remains challenging due to relatively lower transformation efficiency [8].

Escherichia coli was also employed due to its well-characterized genetics and rapid growth. Strategies included overexpressing DXS and IDI to enhance IPP/DMAPP supply, deleting ldhA and ackA to reduce carbon loss to byproducts, and modulating ispG and ispH to avoid toxic intermediate accumulation. Nevertheless, E. coli lacks native carotenoid storage mechanisms and often suffers from cytotoxicity upon high-level terpenoid production.

Saccharomyces cerevisiae emerged as the most promising host due to its exceptional genetic tractability, well-characterized mevalonate pathway, and robust performance in industrial fermentation. For the engineering strategies, we can implement a fused CrtZ–CrtW module to enhance catalytic efficiency and substrate channeling, along with atmospheric and room temperature plasma mutagenesis to uncover novel molecular targets such as CSS1 that significantly improve astaxanthin yield. Furthermore, S. cerevisiae has innate ability to accumulate lipids in intracellular droplets, which provides ideal storage compartments for hydrophobic astaxanthin, enhancing product stability and final titter. Also, the extensive synthetic biology toolbox available for this yeast enabled precise regulation of pathway enzymes and redirection of metabolic flux toward astaxanthin biosynthesis [14].

S. cerevisiae proved to be the superior host for our astaxanthin production aims. We prioritized it not only for its well-known genetic tractability and precursor pools but also for its resilience in storage. Crucially, the extensive groundwork laid by previous metabolic engineering studies using yeast significantly de-risked our scaling efforts [15]. This combination of traits is essential for a viable production platform.

Table 1. Comparison and summary of a variety of host organisms

	H. pluvialis	Chlamydomonas reinhardtii	Rhodotorula rubra	Yarrowia lipolytica	E. Coli	S. cerevisiae
Intracellular compartmentalisation	Yes	Yes	Yes	Yes	No	Yes
GRAS	Yes	Partial/Strain-dependent	Yes	Yes	No	Yes
Glycosylation system	Yes	Yes	Yes	Yes	No	Yes
Growth rate	Low	Low	Good	Fast	Fast	Good

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Table 1. (continued)

Top titer	34.3 ± 1.4 mg/L	2.84 mg/L	120mg/L	285mg/L	432.82 mg/L	217.9 mg/L
Top yield	11.4 mg/g DCW	0.22 mg/g DCW	10.1mg/g DCW	6mg/g DCW	7.12mg/g DCW	13.8mg/g DCW
Genetic background	+	++	+	++	+++	++
Geonome editing tools	+	++	+	+++	+++	++
Gene expression regulatory elements	++	++	++	++	+++	+++
Cheap substrate utilisation	+	+	+++	+++	+++	+++
Secretion ability	+	+	+	+++	+	++

2.4. Feedstock and process

The selection of a low cost and sustainable feedstock is paramount to the commercial viability of astaxanthin biosynthesis [16]. Instead of using purified expensive sucrose or glucose, we employ sweet potato juice (SPJ), a wastewater byproduct generated in large volumes during the extraction of starch from sweet potatoes. It is a waste that is available abundantly, is inexpensive, and its use solves pollution disposal problem. SPJ is rich in fermentable sugars (3-4% w/v), which are sucrose, glucose, and fructose, and they together make up around 60% of the total soluble solids [17]. The SPJ has traces of protein, vitamins, and minerals that provide essential nutrition for yeast growth and, in effect, are a complete culture medium.

The process begins with the harvest of raw SPJ (SPJ-A). A critical pre-treatment step consists of deproteinization to remove compounds that can inhibit microbial growth. This is achieved by adjusting the pH of SPJ-A to 4.0 using hydrochloric acid (HCl) at 50°C, causing precipitation of native sweet potato proteins. The supernatant (SPJ-B) recovered through centrifugation. The HCl-deproteinized juice stood out to alternatives, such as citric acid treatment, for supporting high-density yeast growth. SPJ-B can be vacuum-concentrated to obtain a syrup (SPJ-C) with ~50% soluble solids, providing higher sugar concentrations in the fermenter without increasing the volume [16]. As a carbon substrate for use with Saccharomyces cerevisiae, this feedstock and process strategy drastically reduces raw material costs and contributes to a circular bioeconomy by converting agricultural waste into a high-value product. With proper pre-treatment to remove inhibitory compounds and concentration to achieve suitable sugar levels, SPJ can serve as an effective feedstock for large-scale fermentation.

3. Conclusion

The global food system faces challenges of climate change, resource depletion, and safety concerns. These challenges should raise humankind's attention, and we should call for a more innovative way to prevent further damage. It is illustrated in this article that biosynthesis of astaxanthin replaces chemical synthesis and traditional extraction since this method stands out for its safety and sustainability concerns. Our research group designed a three-module metabolic pathway for biosynthesis of astaxanthin, selected host Saccharomyces cerevisiae, and determined sweet potato juice as a low-cost feedstock. These strategies make possible a promising platform for efficient and green production. Future studies should focus more on optimizing pathway regulation, high-yield production, and scaling up promises for redirecting the food system with biotechnology.

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Danlin Zhang and Ruguo Deng contributed equally to this work and should be considered co-first authors.

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