Bioprocess Design of an Astaxanthin Production Plant - I

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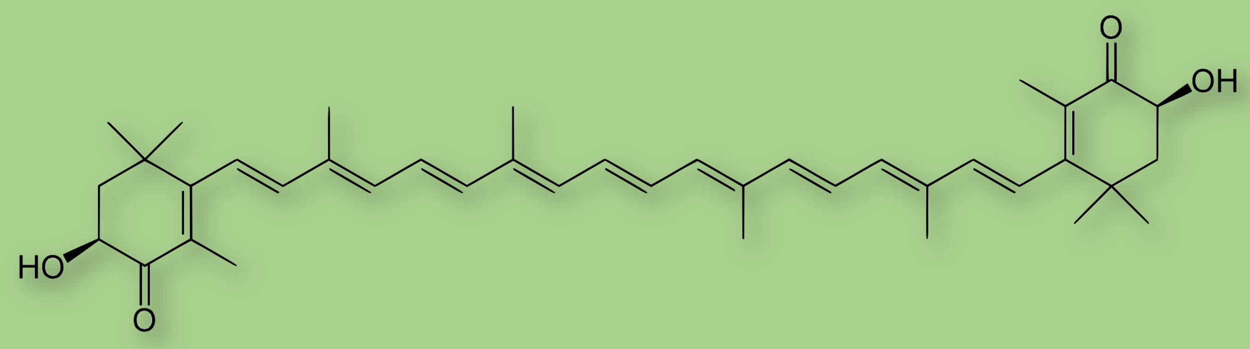
Introduction

What is Astaxanthin?

Astaxanthin (E-161j) is a **carotenoid** pigment from the xanthophyll family. Within its molecular structure it has a couple of hydroxyl and ketone groups which provide **antioxidant properties** and also it is commonly used in the food industry as a colorant and animal feeding. Those properties make astaxanthin industrially attractive.
It is a GRAS and FDA approved compound both for human and animal consumption as well as for its pharmacological applications.



Astaxanthin can be found in different organisms such as algae and crustaceans in tree different stereoisomers: (3R,3'R), (3R,3'S) and (3S,3'S). The last stereoisomer is the one with the best properties for human consumption and applications such as a **nutraceutical**.

Aim

The aim of this project is to simulate, using **SuperPro Designer®**, an **economical**, **environmental** and **social** astaxanthin production plant with its target in the pharmaceutical and the fine chemical market. Thus, its has to be a sole stereoisomer final product with the highest purity possible.

Organism and Strain

To accomplish this objective, the process has been simulated using ***Haematococcus pluvialis* NIE-144** mixotrophic strain. Which provides the best possible production yield among others and, what is more important, it synthetizes mainly the (3S,3'S) stereoisomer.

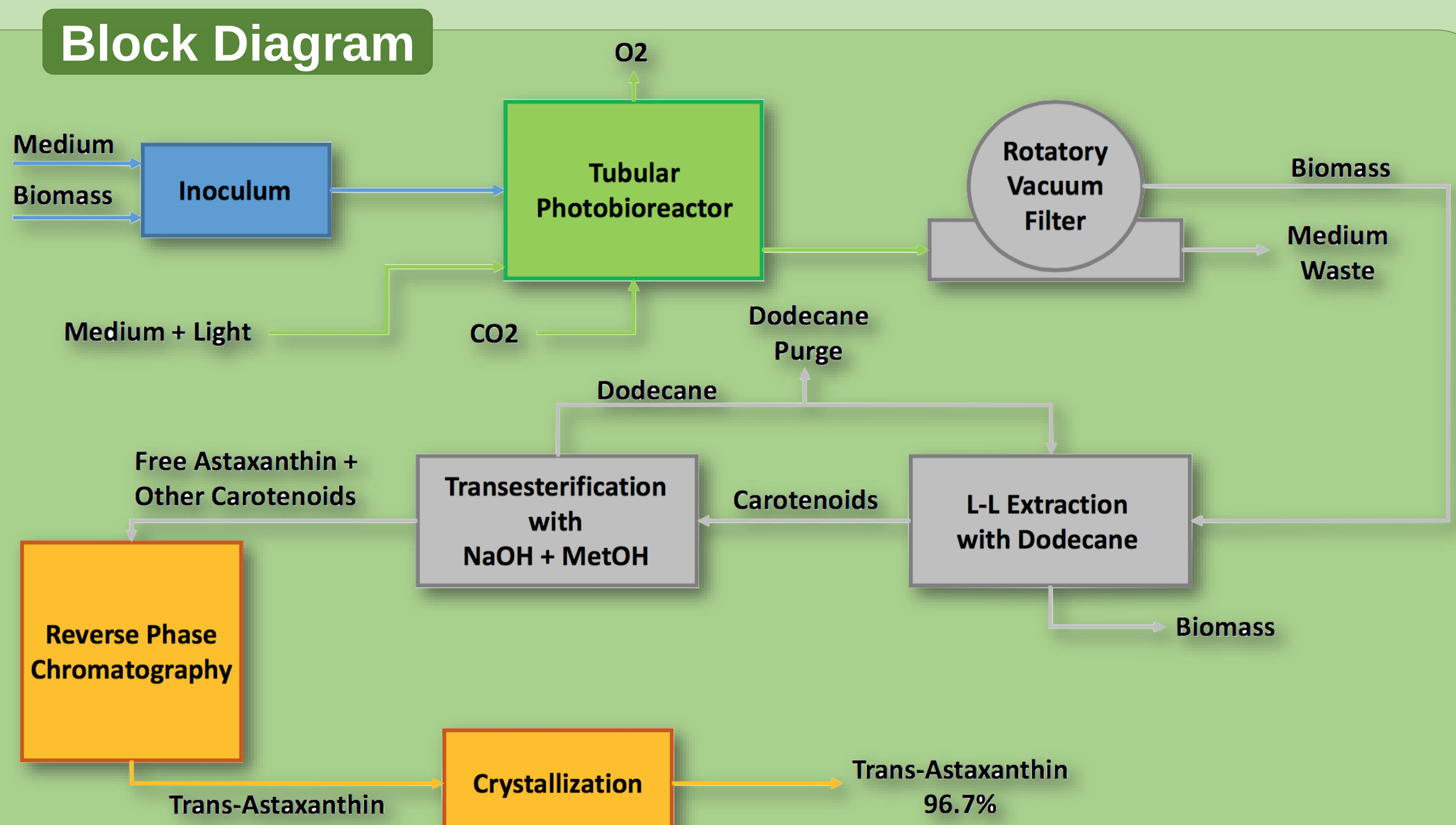
Others like *Xanthophyllomyces dendrorhous* offer better yields but produces other non-attractive stereoisomers in higher proportions.

Strain	Culture Conditions [a]	Cell Density ($g\ L^{-1}$)	Biomass Productivity ($g\ L^{-1}\ day^{-1}$)	Astaxanthin Content ($mg\ g^{-1}$ Dry Weight)	Astaxanthin Yield ($mg\ L^{-1}$)	Astaxanthin Productivity ($mg\ L^{-1}\ day^{-1}$)
H. pluvialis						
CCAP34/7	P, batch	1.6	0.02	27	43.2	0.44
UTEX16	M, batch	2.65	0.13	20.1	53.4	2.6
	M, fed-batch	2.74	0.14	23.5	64.4	3.2
CCAP34/7	P, batch	-	-	22.7	-	2.7
CCAP34/8	P, batch	7.0	0.41	11.0	77	4.4
CCAP34/8	P, continuous	-	0.6	8	-	5.6
NIES-144	P, fed-batch	6.7	0.2	36	390	7.2
CCAP34/8	P, continuous	1.5	0.7	10	15	7
X. dendrorhous						
ATCC24202	H, fed-batch	30	5.1	0.72	21.6	3.7
NRRL Y17268	H, Batch	23.2	3.4	0.45	10.4	1.5
ATCC24202	H, fed-batch	18.8	4.7	0.3	5.7	1.4
2A2N [b]	H, batch	36	7.2	1.1	39.6	7.9
ZJUT46 [b]	H, batch	15.7	2.85	1.74	27.1	5.0
	H, fed-batch	17.7	3.2	2.0	34.4	6.4
E5042 [b]	H, batch	30.7	5.4	2.5	76.8	13.5
VKPM Y2476 [b]	M, fed-batch	88	9.7	4.7	420	45.6

[a] P, photoautrophic, M, mixotrophic, H, heterotrophic; [b] mutants.

Plant Production

Block Diagram



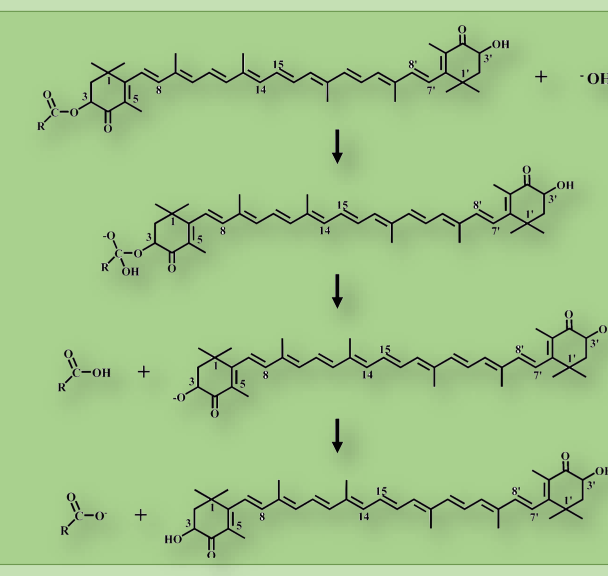
Block diagram of the whole process showing each stream and recirculation. It is a **Fed-Batch** process with three **16m3** staggered photobioreactors. The plant has been designed to achieve a **96.7% product purity.**

Process Characteristics

The production is carried out in a **tubular LED-lit photobioreactor** and, due to the long time it takes to finish a single batch, a huge scheduling work has been done behind in terms to reach an annual production around 200Kg. **Green and Red growth stages** of *H.pluvialis* has to be taken into account while programming the photobioreactor considering *H.pluvialis*' kinetics.

Free Astaxanthin

H.pluvialis anchor astaxanthin in its cell membrane in terms to protect itself from external agents such as light. Because of that, astaxanthin is produced in its ester form (mono and/or diester) and therefore removal of this ester is required by performing a **transesterification,** resulting in the commercial **free-astaxanthin** form.



Chromatography

By performing a reverse-phase chromatography, it allows the separation of **(3S,3'S)-*trans*-Astaxanthin** from the other unwanted forms of astaxanthin, non ester-free astaxanthin as well as the rest of carotenoids that might have been carried with the L-L extraction.

Layout

General View

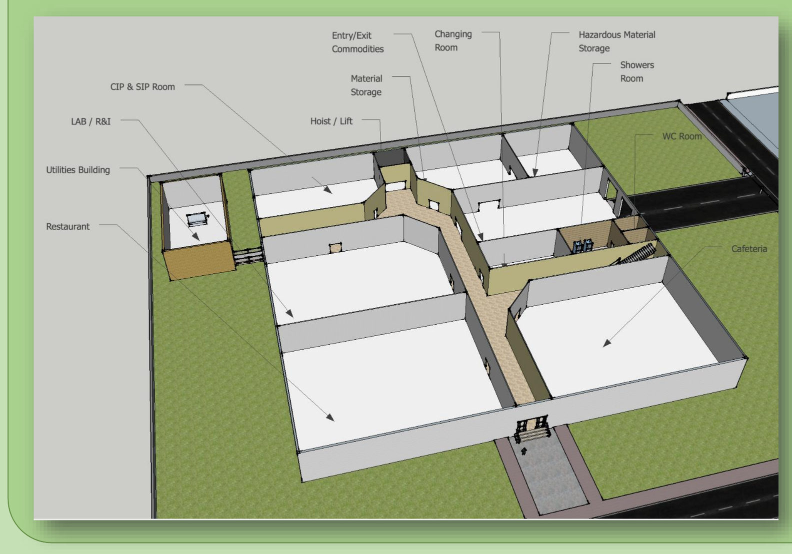
Entire **3D model** of the final production plant and the office building. **SketchUp Make®** designing software has been used to accomplish this 3D layout.

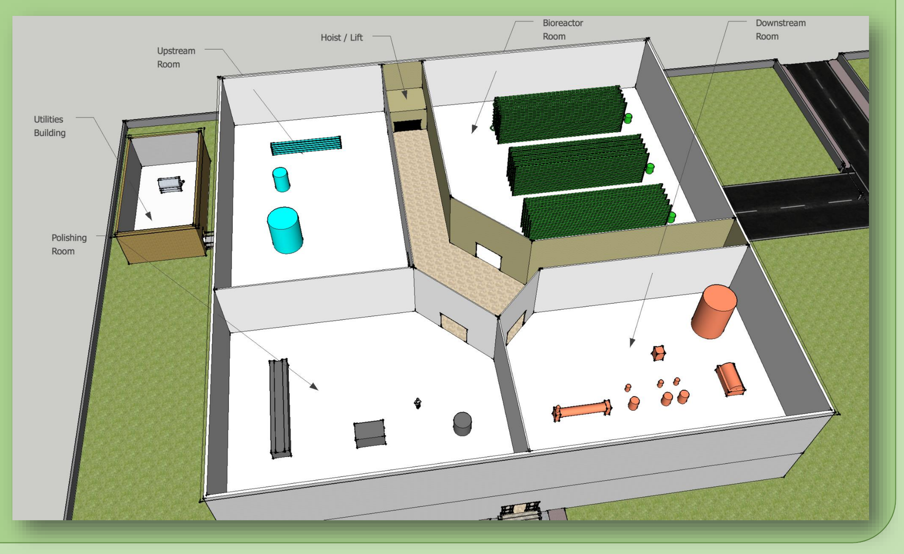
Facilities such as parking lots, cafeteria, roads, sidewalks, etc. has been taken into account in the model.

*Scan this QR code to watch a walkthrough video

Close-up View

Images showing a detailed look at the **1st** and **2nd floor** of the plant. All process-related equipment is located in the 2nd floor, maintaining a clean environment for the whole process there. Furthermore, the model contemplates in it all the facilities that an industrial plant would need.





Enhancements

The current plant described above has been designed accomplishing little **environmental considerations**. Therefore, enhancements in environmental facts must be taken into account in the next step of designing the final production plant. The main focus now is on exchanging the different organic solvents used in the **downstream** part as well as introducing the **formulation and packaging** in the simulation flow diagram. Hereunder are depicted the two main changes introduced in the plant but the whole final plant is described in depth in the second part "Bioprocess Design of an Astaxanthin Production Plant – II".

L-L Extraction

~~Dodecane~~ → Olive Oil

Differential Extraction

~~Dichloro-methane~~ → Hexane & Ethyl Acetate

Conclusions

H.Pluvialis is the best option to produce Astaxanthin in the industry but it is not perfect due to the low cell density algae reach in a photobioreactor. Bibliography shows alternatives such as expression in *E.coli* but they happen to be in very early stages for industrial applications.

Anyway, this project has resulted in a **very profitable** one with huge **revenues** (see "Bioprocess Design of an Astaxanthin Production Plant – III") and very attractive for investors. Although the initial designed plant is not environmentally friendly at all, due to the high revenues obtained a big investment towards improving this facet can be done.

References
Organism and Strain – Table 1 edited and extracted from: Liu J et al. *Chlorella zofingiensis as an alternative microalgal producer of astaxanthin: biology and industrial potential.* Mar Drugs. 2014;12(6):3487-3515. doi:10.3390/md12063487. Open Access Article licensed under CC Attribution-Share Alike v3.0 Unported.
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