Bioprocess design to produce resveratrol

Part 3: Downstream

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INTRODUCTION: Resveratrol is an interesting molecule because of its benefits and growing demand. That is the reason why a biotechnological process is designed with the aim to produce this substance. Resveratrol can be obtainend by cultivating an engineerized *Escherichia coli* in a medium that contains p-coumaric, which is a resveratrol precursor. When the reaction is finished , resveratrol has been separated from the other components. A downstream separation and purification process is designed with a yield of 89.8% and a purity of 99.99% to prepare pills as a final product. This downstream process consists in two extractions with its solvent recovery and a packaging step.
A gel filtration chromatography can also be used as a downstream process, but this has been rejected because of its yield (61%) and purity (96%).

1. EXTRACTION PROCESS

First extraction:

-Solvent: ETBE (ethyl tert-butyl ether)

-Resveratrol passes from fermentation broth to ETBE because it has higher solubility in this solvent.

-Three extraction steps with ETBE are needed to optimize resveratrol recovery.

Some other contaminants passes to ETBE solvent, so a second extraction is needed.

Second extraction:

-Solvent: NaOH solution (pH=9)

-Contaminants pass from ETBE to NaOH solution.

-Two extraction steps with ETBE are needed to optimize resveratrol recovery.

Final yield: 89.8%

Resveratrol purity: 99.9%

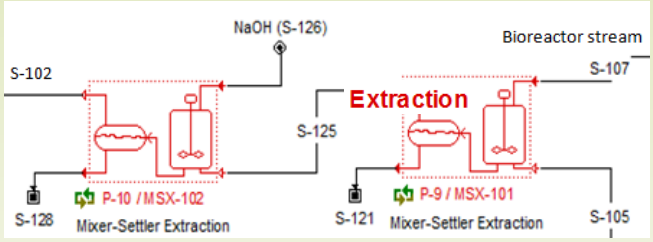

Figure 1. Two extractions flow diagram designed using SuperPro Designer software. S-107: resveratrol and contaminant components, S-105: ETBE, S-125: resveratrol, ETBE and contaminant components; S-121: other contaminant components, S-126: NaOH, S-128: NaOH and contaminants components, S-102: resveratrol ETBE.

2. FORMULATION AND PACKAGING

- Evaporation: ETBE and water are evaporated to purify resveratrol.
- Tray Drying: eliminates residual water from resveratrol.
- Mixing: mixes starch and resveratrol
- Tablet press: manufactures pills

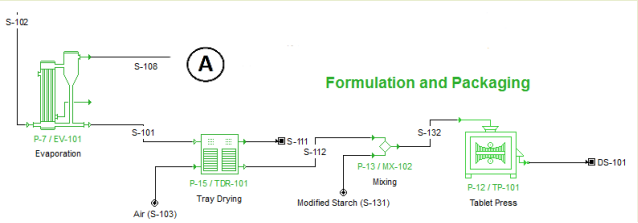

Figure 2. Formulation and packaging flow diagram designed using SuperPro Designer software. S-102: ETBE and resveratrol mix, S-108: ETBE and water steam, S-101: moist resveratrol, S-103: air, S-111: air, S-112: dryed resveratrol, S-131: modified starch, S-132: resveratrol and starch, DS-101: resveratrol pills.

3. ETBE RECOVERY

ETBE recovery is necessary because of economic and environmental needs.

-After evaporation and condensation, a mixture of ETBE and water is obtained.

-Destillation is used to purify ETBE.

-A small part of ETBE is lost, so fresh ETBE has to be added to the following process.

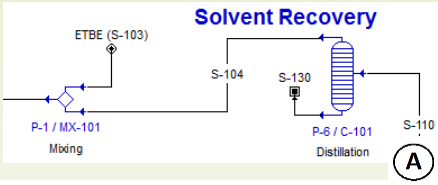

Figure 3. Solvent recovery flow diagram designed using SuperPro Designer software. S-110: ETBE and water, S-130: ETBE and water, S-104: ETBE, S-103: new ETBE.

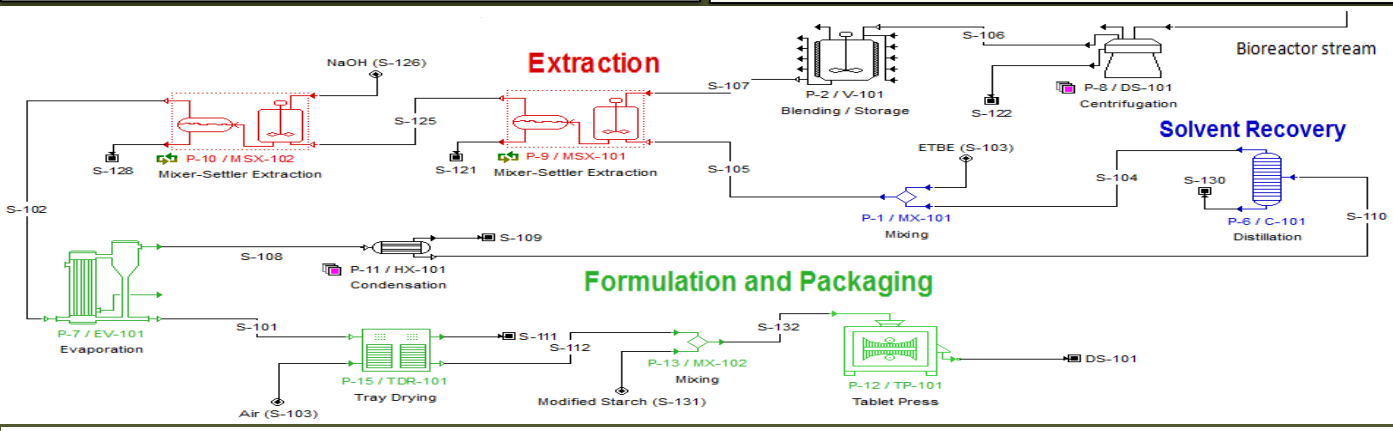

Figure 4. Complete flow diagram designed using SuperPro Designer software, showing the three parts described before. (extraction, purification and packaging and solvent recovery). In addition, there are some equipment also used in this downstream process: centrifugation, storage tank and condensation (in black). All data of equipment and streams are in SuperPro flowsheet.

REFERENCES

1- Ferrer, J.-L., Austin, M. B., Stewart, C. & Noel, J. P. Structure and function of enzymes involved in the biosynthesis of phenylpropanoids. *Plant Physiol. Biochem.* 46, 356–70 (2008).

2- Gu, M., Su, Z.-G. & Janson, J.-C. One-Step Purification of Resveratrol and Polydatin from *Polygonum cuspidatum* (Sieb. & Zucc.) by Isocratic Hydrogen Bond Adsorption Chromatography on Cross-Linked 12% Agarose. *Chromatographia* 64, 701–704 (2006).