AFT 2026
Advanced Fermentation Technology

URD ABI
by AgroParisTech

Enhanced *de novo* Ferulic Acid Production in Biphasic Yeast Fermentation

IMATOUKENE Nabila

Research Scientist in Biotechnology

30 June – 1st July, 2026 Lille, France

GRAND REIMS COMMUNAUTÉ URBAINE
Marne LE DÉPARTEMENT
La Région Grand Est
CEBB Centre Européen de Biotechnologie et de Bioéconomie
l'Europe s'engage en France

ABI: A laboratory of AgroParisTech

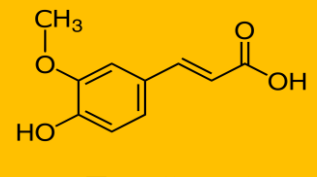
- R&D Unit of AgroParisTech
- Founded in 2012
- Led by Pr. Florent Allais
- Funded by local authorities:

Ferulic acid – a *p*-hydroxycinnamic acid

- **Ferulic acid (FA)**: a secondary metabolite
- **Present in plants**: free form and cross linked to plant cell wall
- **Precursor of chemicals**: coniferyl alcohol, vanillin, sinapic acid, and curcumin
- **Building blocks**
  - Food/feed
  - Cosmetic
  - Pharmaceutical
- **Numerous biological activities**
  - Antioxidant
  - Anti-UV
  - Antiallergic,…

Kumar et al.2014

Structure



Ferulic acid

***p*-hydroxycinnamic acid**

Table 1. Price and market for *p*-HCA or precursors.

Compound	Price range[a][27] [$ kg^{-1}]	Market [M$]	Estimated volume [t year^{-1}]
p-coumaric acid[28,29]	115–330	39.2 (2016)	118–340
caffeic acid	450–900	N.A.	N.A.
chlorogenic acid[30]	3000–7900	130 (2017)	16–43
ferulic acid[31–33]	180–380	53 (2019)	139–294
sinapic acid	370–1200	N.A.	N.A.

[a] For purity > 95 %. N.A. not available.

Flourat et al. 2021

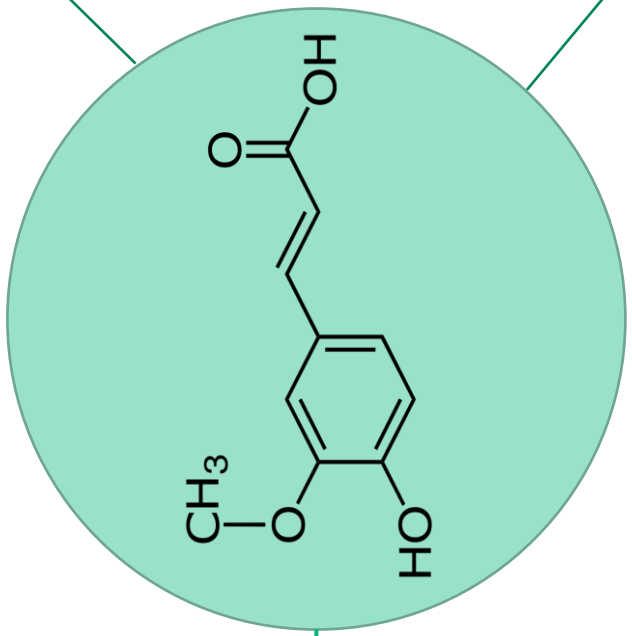
URD ABI by AgroParisTech

How to access this molecule?

Extraction

p-HCAs	Source	%
Ferulic acid	Wheat bran	1.5
Sinapic acid	Mustard bran	0.8
Caffeic acid	Sunflower meal	0.3

Difficult challenges for enzymatic extraction and use of hazardous solvents



Biosynthesis

Liquid fermentation using modified strains

Promising alternative:
Classification as a natural product
Challenges: Expression tuning, cofactor optimization

Chemical Synthesis

Knoevenagel-Doebner condensation from *p*-hydroxybenzaldehydes

URD ABI by AgroParisTech

Engineered microorganisms for FA production

Metabolic Engineering

Pathway of interest insertion in a microorganism. Enabling production of *FA* from simple sugar (e.g. glucose)

ΔFdc1 + paHpaB-SeHpaC(URA) + TAL4mopti-palev-C4Hev(TRP) Cpr1(LEU) + COMT1(HIS)

***S. cerevisiae* ABG20**

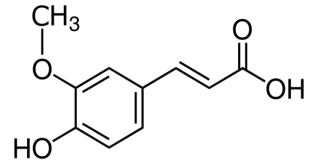
ABOLiS BIO-SYNTHESIS ARCHITECTS

Many researches on biotechnological production of FA using *E. coli* as host

Lack of work in fermentation process optimisation and downstream processing

Kang et al. 2012; Choi et al. 2011; Ni et al. 2015; Lv et al. 2017

FA properties



- Antimicrobial
- Degradation of FA by decarboxylases
- $Log(K_{o/w}) > 1$ → Lipophilic
  → Low solubility in water

Hydrophilic-lipophilic features: Partition coefficient between octanol and water

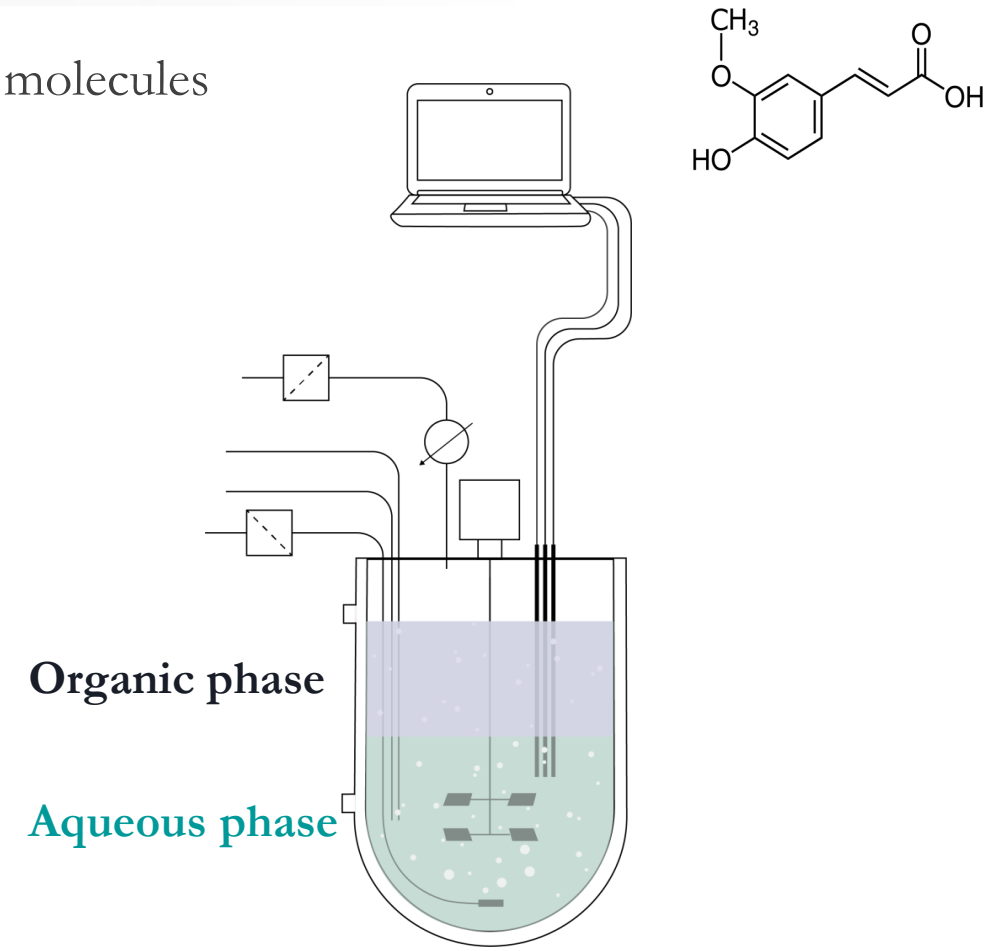
(Galanakis et al. 2013)

FERMENTATION
Use of microorganisms
Aqueous medium

URD ABI by AgroParisTech

Extractive fermentation

- **Extractive fermentation:** a mean of intensifying the production of molecules
  - Biphasic fermentation
  - Extraction assisted by membrane contactor
- **Creteria:**
  - Choice of solvent
  - Extraction performance
  - Biocompatibility of the solvent towards microorganisms
- **Advantages:**
  - Medium detoxification
  - Prevent product degradation and overcome the solubility limit
  - Improving yield and productivity and simplifiying product recovery

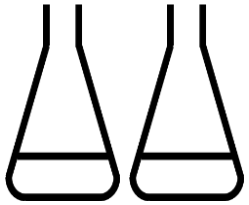


Biphasic fermentation

URD ABI by AgroParisTech

Biphasic fermentation for ferulic acid production

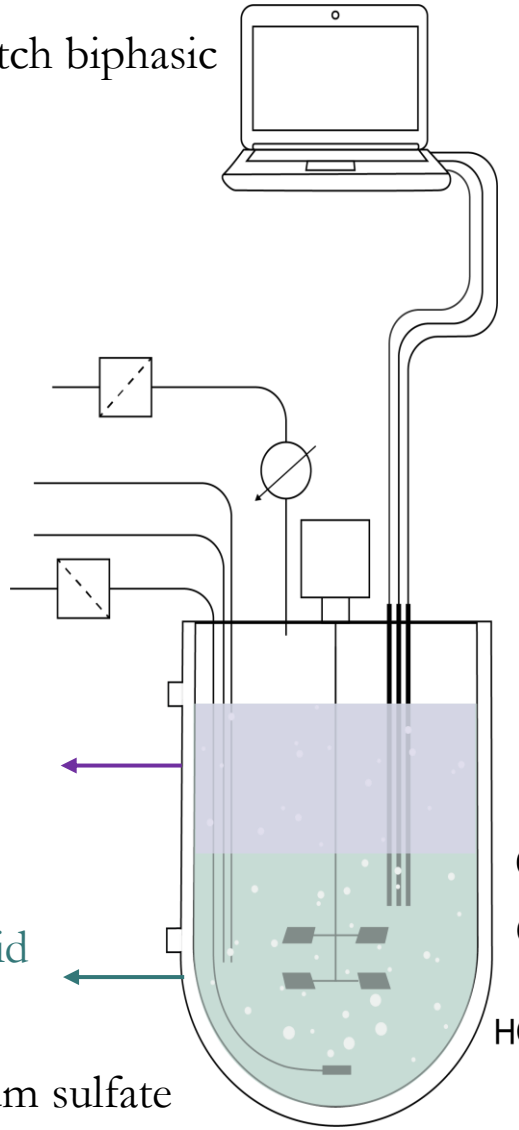
1



Ferulic acid (FA) production in YNB and YEPD media

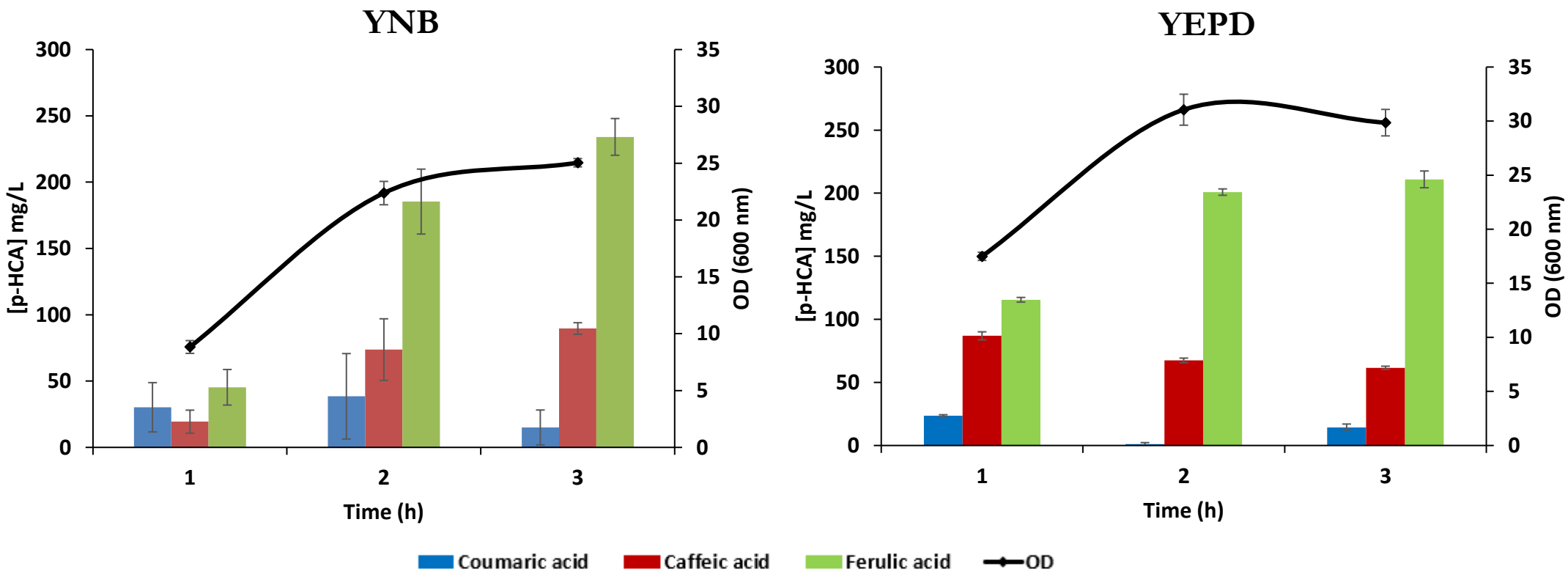
2

Batch and fed-batch biphasic fermentation



URD ABI by AgroParisTech

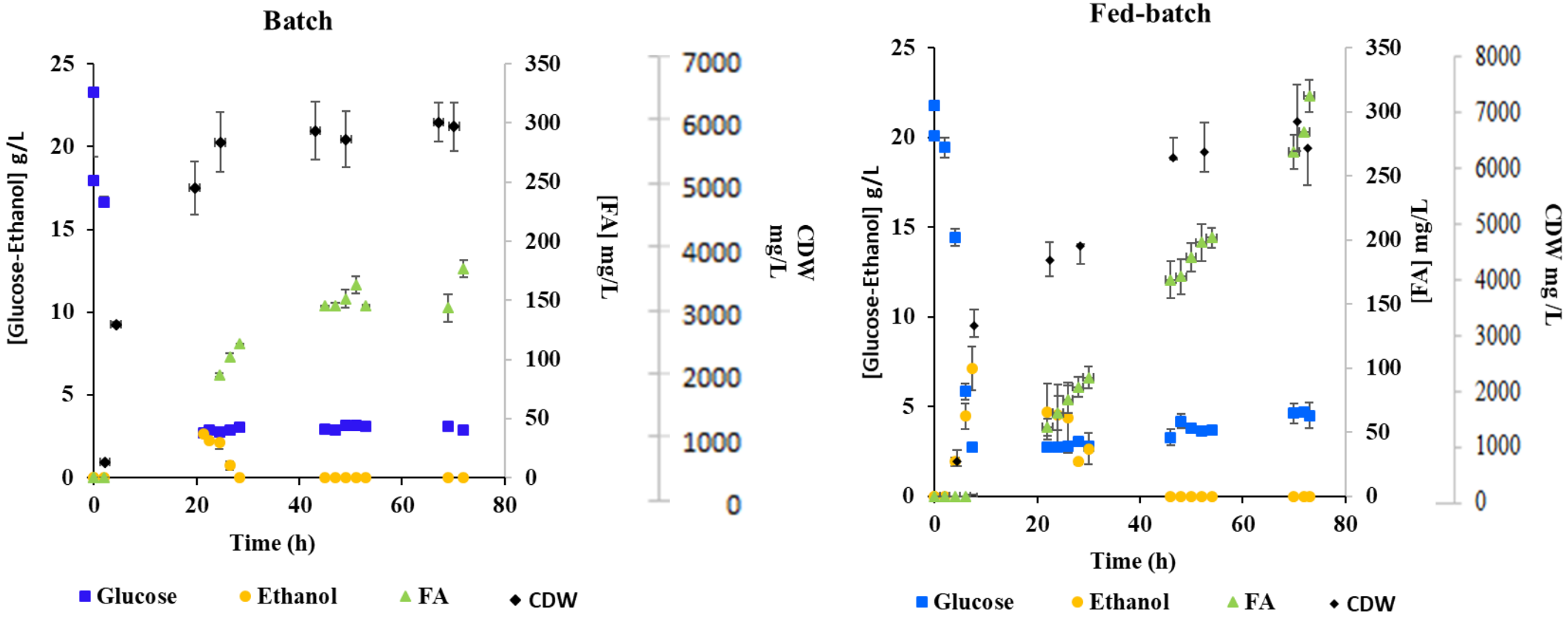
FA production in YNB and YEPD media



- Better productivity of FA in YEPD medium compared to YNB: 4.2 vs 3.2 $mg.L^{-1}.h^{-1}$
- Incomplete conversion of caffeic acid

URD ABI by AgroParisTech

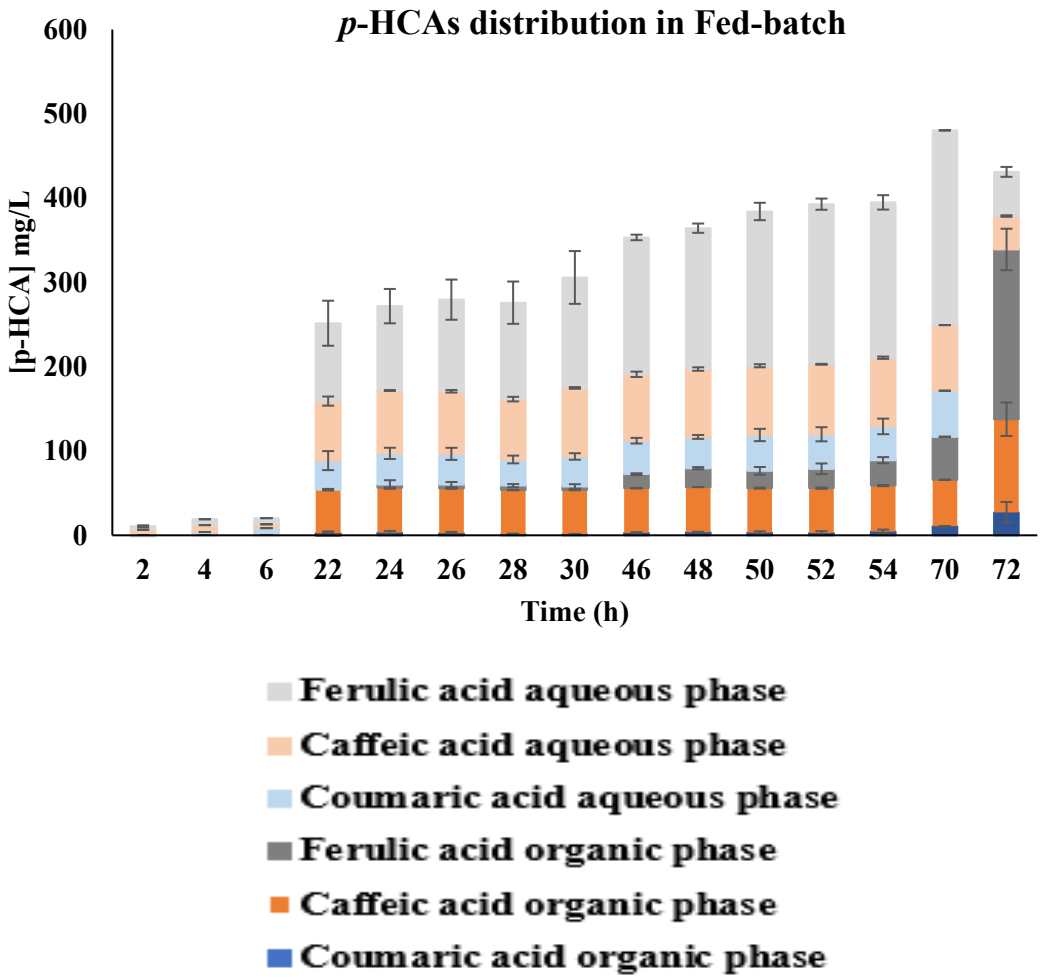
Batch and fed-batch biphasic fermentation



- FA production in fed-batch biphasic fermentation: 2 times higher than batch one
- Fed-batch biphasic fermentation: a production of 312.6 $mg.L^{-1}$ of FA in yeast

URD ABI by AgroParisTech

FA distribution in fed-batch biphasic fermentation



- **First 70h:** *p*-HCAs detected in the aqueous phase
- **After 70h:** At pH 4.5, the concentrations of *p*-HCAs in the broth decreased markedly

URD ABI by AgroParisTech

Conclusion

- Feasibility of *de novo* microbial production of FA using *S. cerevisiae*
- Better productivity of FA in YEPD medium compared to YNB one
- Importance of fed-batch fermentation and medium detoxification

Acknowlegments

Blandine Godon

Julien Couvreur

Fanny Brunissen

Fanny Brunois

Clémentine Fojcik

Florent Allais

Michel Lopez

Arnaud Haudrechy

References

- Flourat, Amandine L., Jeanne Combes, Claire Bailly-Maitre-Grand, Kévin Magnien, Arnaud Haudrechy, Jean-Hugues Renault, et Florent Allais. 2020. « Accessing p -Hydroxycinnamic Acids: Chemical Synthesis, Biomass Recovery, or Engineered Microbial Production? » ChemSusChem, octobre, cssc.202002141. https://doi.org/10.1002/cssc.202002141.
- Galanakis, C.M., V. Goulas, S. Tsakona, G.A. Manganaris, et V. Gekas. 2013. « A Knowledge Base for The Recovery of Natural Phenols with Different Solvents ». International Journal of Food Properties 16 (2): 382-96. https://doi.org/10.1080/10942912.2010.522750
- Kumar N, Pruthi V. Potential Applications of Ferulic Acid from Natural Sources. Biotechnol. Rep. 2014, 4, 86–93. doi:10.1016/j.btre.2014.09.002
- Choi O, Wu CZ, Kang SY, Ahn JS, Uhm TB, Hong YS. Biosynthesis of Plant-Specific Phenylpropanoids by Construction of an Artificial Biosynthetic Pathway in Escherichia coli. J. Ind. Microbiol. Biotechnol. 2011, 38, 1657–1665. doi:10.1007/s10295-011-0954-3.
- Kang SY, Choi O, Lee JK, Hwang BY, Uhm TB, Hong YS. Artificial Biosynthesis of Phenylpropanoic Acids in a Tyrosine Overproducing Escherichia coli Strain. Microb. Cell Fact. 2012, 11, 1–9. doi:10.1186/1475-2859-11-153.
- Lv H, Zhang Y, Shao J, Liu H, Wang Y. Ferulic Acid Production by Metabolically Engineered Escherichia coli. Bioresour. Bioprocess. 2021, 8, 70. doi:10.1186/s40643-021-00423-0.

URD ABI
by AgroParisTech

Thank you for your attention

IMATOUKENE Nabila

Research Scientist in Biotechnology

July 2, 2026

GRAND REIMS COMMUNAUTÉ URBAINE

Marne LE DÉPARTEMENT

La Région Grand Est

CEBB Centre Européen de Biotechnologie et de Bioéconomie

l'Europe s'engage en France