

PRODUCTION OF PHENOLIC COMPOUNDS WITH INDUSTRIAL RELEVANCE THROUGH BIOPROCESSING: LEVERAGING LIGNOCELLULOSIC BIOMASS AND BACTERIAL METABOLISM FOR SUSTAINABLE MANUFACTURING

Ana Luiza S. Zacaron^{1*}, Lara M. Biancheti¹ & Eleni Gomes¹.

¹ São Paulo State University (Unesp), Institute of Biosciences, Humanities and Exact Sciences, São José do Rio Preto, São Paulo, Brazil.

* ana.serantoni@unesp.br

ABSTRACT

The phenolic compounds are secondary metabolites of plants with antioxidant, anti-inflammatory, and antitumor properties. Their commercial production is carried out by biosynthesis or chemical synthesis, with advantages and limitations in both methods. The use of agricultural residues as substrates is economical and environmentally viable. Sugarcane bagasse, rich in lignin, can be a valuable source for the production of these compounds. Chemical treatments of biomass generate residues rich in phenolic compounds such as ferulic acid, p-coumaric, and caffeic acid. These compounds have diverse industrial applications, including the production of pharmaceuticals and food additives.

Keywords: Bioprocess. Phenolic compounds. Lignocellulosic biomass. Biosynthesis. Enzymes.

1. INTRODUCTION

Phenolic compounds encompass a wide range of secondary metabolites found in plants, categorized as polyphenols, phenolic acids, phenylpropanoids, flavonoids, stilbenes, coumarins and their derivatives. These compounds have aromatic rings accompanied by one or more hydroxyl groups, and exhibit several beneficial activities, including antioxidant, anti-inflammatory, antitumor, antiviral, antibacterial properties, among others¹.

Currently, the commercial production of these compounds is carried out through biosynthesis or chemical synthesis¹. Biosynthesis can occur via microbial conversion, in which microorganisms use a variety of natural substrates, such as lignin, eugenol, isoeugenol and glucose. Although it is easily applicable, this method often has limitations, such as low yield and microbial strains that tolerate high concentrations of the compounds involved².

On the other hand, commercial chemical synthesis uses several substrates, such as phenol, isoeugenol, glucose and ferulic acid. This method involves multiple steps of chemical reactions such as oxidation, decarboxylation and acidification. Compared to biosynthesis, chemical synthesis offers several advantages, such as higher yield, stability in the synthesis pathway, knowledge of the reaction mechanism and reduced reaction time. However, it can be inefficient, expensive and generate waste that is harmful to the environment³. In microbial synthesis, the choice of substrates directly influences the production cost. Substrates from agricultural or agro-industrial residues, such as sugarcane bagasse, fruit peels and grain residues, are economically viable and ecologically safe⁴.

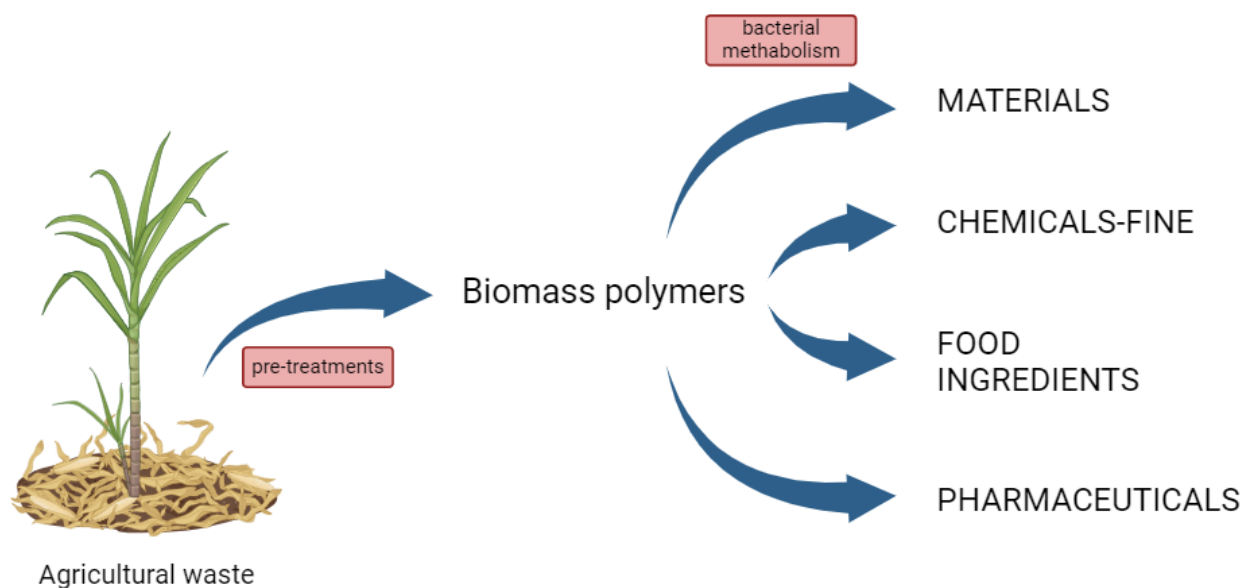


Figure 1 Model for the use of lignocellulosic biomass through bacterial metabolism. Created with Biorender.com

Sugarcane bagasse, the main agro-industrial co-product in Brazil, is composed, on average, of 25% lignin, 25% hemicellulose and 40 to 50% cellulose⁵. Although the carbohydrate fraction is already widely used as a substrate in the production of second-generation ethanol, lignin is underused due to its high recalcitrance and the complexity of the compounds resulting from its degradation⁶. Before being used, lignocellulosic biomass requires chemical and/or physical treatments to disrupt its complex organization, allowing microorganisms or enzymes access to its components⁷. These treatments generate liquid waste rich in lignin and its phenolic derivatives, including ferulic, *p*-coumaric and caffeic acids^{8,9}.

p-Coumaric acid, abundant in nature and recognized for its chemoprotective and antioxidant properties, is a valuable substrate for microbial transformation in the production of other phenolic products, such as 4-vinyl phenol, with diverse industrial applications¹⁰. Caffeic acid, released during lignin cleavage, is a potent antioxidant with increasing industrial applications in the food and pharmaceutical industries due to its antimicrobial, anticancer and antioxidant properties¹¹. 4-vinyl catechol, derived from caffeic acid, is a compound with similar properties and applications, being used as a polymerizer in several industrial syntheses¹². Ferulic acid, a natural precursor, plays a crucial role in the synthesis of aromatic compounds, including 4-vinyl guaiacol and other vinyl phenols. This acid is one of the main hydroxycinnamic components present in plant cell walls. Its abundance in nature has aroused the interest of researchers to explore it as a raw material in the production of valuable aromatic compounds through microbial or enzymatic processes. 4-vinyl guaiacol, a product derived from ferulic acid, stands out for its relevance in sectors such as medicine, food, perfumery and cosmetics, due to its notable biological activity and low toxicity¹³.

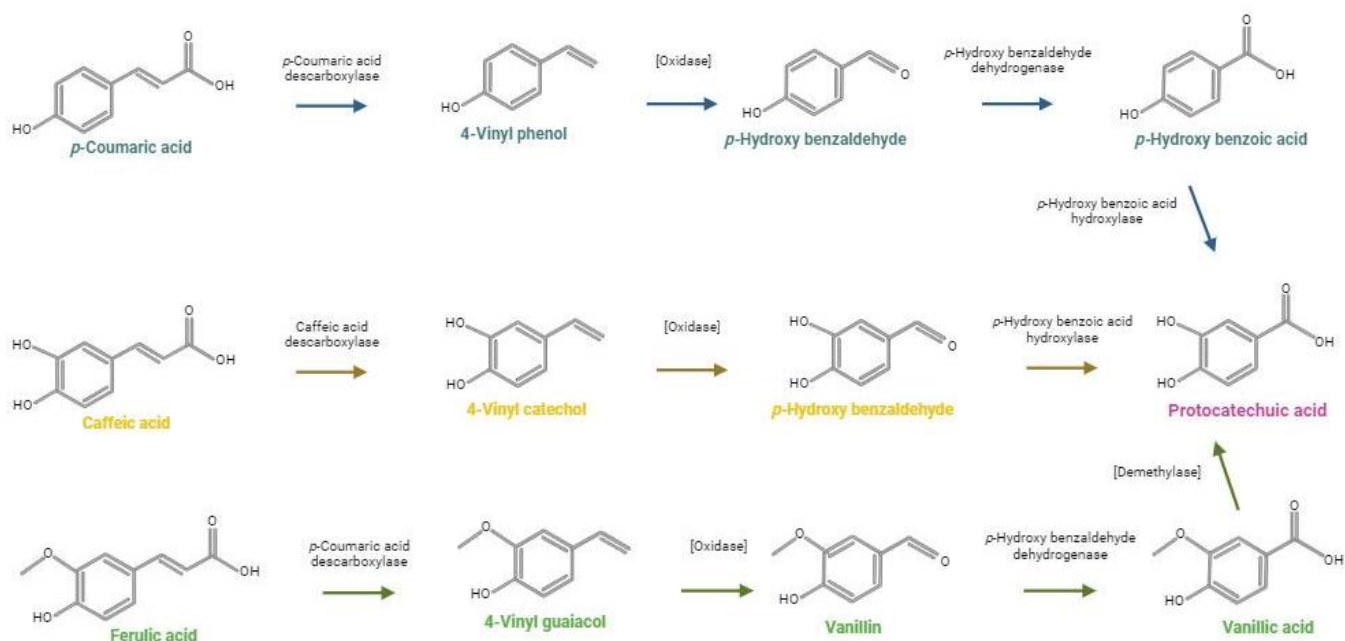


Figure 2 Described bacterial metabolism of conversion of ferulic acid, *p*-coumaric acid and caffeic acid into their derivative compounds. Created with Biorender.com

Bacterial metabolism of phenolic acids begins with side chain fragmentation. Cleavage at the C1 position of the aliphatic chain leads to the production of vinyl derivatives through non-oxidative decarboxylation, while cleavage at the C2 position results in the formation of aldehydes. The catabolism of these phenolic acids generally follows the C1 cleavage route, generating vinyl derivatives through the action of phenolic acid decarboxylase. The process begins with decarboxylation, forming products that are catalyzed by the enzyme decarboxylase. Then, the product undergoes oxidation to transform into its respective subsequent compound¹⁴.

As regulated by the FDA (United States Food and Drug Administration) and European legislation, products resulting from enzymatic or microbial processes are recognized as natural. Biotechnology methods are generally more environmentally friendly, causing less environmental impact than traditional chemical processes. Due to the growing consumer demand for aromatic compounds of natural origin, the commercial relevance of aromas obtained through biotechnology will certainly be even more valued in the near future¹³.

2. MATERIAL & METHODS

Taking into account the fact that it is an area of study on the rise and that there are not a large number of articles published on the subject, a bibliographical survey of the last 20 years was carried out, covering an important part of what has already been described in subject.

Three different databases were used: Google Scholar, Elsevier and SciELO. In which, articles were filtered according to the terms "bioprocesses", "lignin to phenolic acids", "biomass conversion through bacterial metabolism" and "bioconversion of phenolic acids by bacteria". Subsequently, the articles were selected for critical reading and evaluation of their potential for use in the review. After this stage, the process of writing and referencing began.

It is important to highlight that the access to the articles was provided by partnerships signed between UNESP and the magazines and database.

REFERENCES

1. SUN, X. et al. Recent advances in microbial production of phenolic compounds. **Chinese Journal of Chemical Engineering**, v. 30, p. 54–61, 2021.
2. XU, L. et al. Advances in the vanillin synthesis and biotransformation: A review. **Renewable and Sustainable Energy Reviews**, v. 189, n. PA, p. 113905, 2024.
3. ZHANG, S.; WANG, J.; JIANG, H. Microbial production of value-added bioproducts and enzymes from molasses, a by-product of sugar industry. **Food Chemistry**, v. 346, n. December 2020, p. 128860, 2021.
4. KÄMPF, A. N. (Coord.) Produção comercial de plantas ornamentais. 2. ed. Guaíba: **Agropecuária**, p. 254, 2005.
5. SAKDARONNARONG, C. K. et al. Improving enzymatic saccharification of sugarcane bagasse by biological/physico-chemical pretreatment using *trametes versicolor* and *Bacillus sp.* **BioResources**, v. 7, n. 3, p. 3935–3947, 2012.
6. SANTOS, M. B. C. DOS. Biotransformação bacteriana de ácido ferúlico obtido de resíduo lignocelulósico a 4-vinilguaicol. p. 56, 2018.
7. ROOPAN, S. M. An overview of natural renewable bio-polymer lignin towards nano and biotechnological applications. **International Journal of Biological Macromolecules**, v. 103, p. 508–514, 2017.
8. PAONE, E.; TABANELLI, T.; MAURIELLO, F. The rise of lignin biorefinery. **Current Opinion in Green and Sustainable Chemistry**, v. 24, n. Figure 1, p. 1–6, 2020.
9. SINGHANIA, R. R. et al. Lignin valorisation via enzymes: A sustainable approach. **Fuel**, v.311, n. November 2021, p. 122608, 2022.
10. ESTRADA ALVARADO, I. et al. Fungal biotransformation of p-coumaric acid into caffeic acid by *Pycnoporus cinnabarinus*: An alternative for producing a strong natural antioxidant. **World Journal of Microbiology and Biotechnology**, v. 19, n. 2, p. 157–160, 2003.
11. ANWAR, J. The Effects of Caffeic Acid and Caffeic Acid Phenethyl Ester on the Activities of Acetylcholinesterase and Ecto-Nucleotidases in Rats. 2013.
12. TERPINC, P. et al. Antioxidant properties of 4-vinyl derivatives of hydroxycinnamic acids. **Food Chemistry**, v. 128, n. 1, p. 62–69, 2011.
13. MISHRA, S. et al. Transformation of ferulic acid to 4-vinyl guaiacol as a major metabolite: a microbial approach. **Reviews in Environmental Science and Biotechnology**, v. 13, n. 4, p. 377–385, 2014.
14. MONISHA, T. R. et al. Utilization of Phenylpropanoids by Newly Isolated Bacterium *Pseudomonas sp.* TRMK1. **Applied Biochemistry and Biotechnology**, v. 182, n. 3, p. 1240–1255, 2017.

ACKNOWLEDGEMENTS

We thank CAPES and FAPESP for the resources and financial support. To the professor Dra Eleni Gomes for the opportunity and assistance during the research. Also thank UNESP, as well as the Institute of Bioscience, Humanities and Exact Sciences for the infrastructure.