



# Agro-Industrial Residues: Eco-Friendly and Inexpensive Substrates for Microbial Pigments Production

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#### **OPEN ACCESS**

#### Edited by:

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#### Reviewed by:

Samuel Bernardo, Autonomous University of Chihuahua, Mexico Mireille Fouillaud, Université de la Réunion, France

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#### Specialty section:

This article was submitted to Sustainable Food Processing, a section of the journal Frontiers in Sustainable Food Systems

> Received: 30 July 2020 Accepted: 17 February 2021 Published: 18 March 2021

#### Citation:

Lopes FC and Ligabue-Braun R (2021) Agro-Industrial Residues: Eco-Friendly and Inexpensive Substrates for Microbial Pigments Production. Front. Sustain. Food Syst. 5:589414. doi: 10.3389/fsufs.2021.589414 Many commodities are abundantly produced around the world, including soybean, corn, rice sugarcane, cassava, coffee, fruits, and many others. These productions are responsible for the generation of enormous amounts of daily residues, such as cassava and sugarcane bagasses, rice husk, and coffee peel. These residues are rich sources for renewable energy and can be used as substrates for industrial interest products. Microorganisms are useful biofactories, capable of producing important primary and secondary metabolites, including alcohol, enzymes, antibiotics, pigments, and many other molecules. The production of pigments was reported in bacteria, filamentous fungi, yeasts, and algae. These natural microbial pigments are very promising because synthetic colorants present a long history of allergies and toxicity. In addition, many natural pigments present other biological activities, such as antioxidant and antimicrobial activities, that are interesting for industrial applications. The use of inexpensive substrates for the production of these metabolites is very attractive, considering that agro-industrial residues are generated in high amounts and usually are a problem to the industry. Therefore, in this article we review the production of microbial pigments using agro-industrial residues during the current decade (2010-2020), considering both submerged and solid state fermentations, wild-type and genetically modified microorganisms, laboratorial to large-scale bioprocesses, and other possible biological activities related to these pigments.

Keywords: microbial pigments, biopigments, agro-industrial residues, biological activities, antimicrobial activity, antioxidant activity

# INTRODUCTION

Color has major importance in human activities. From traffic signals to arts and clothing, color has multiple cultural meanings. It is also central in interpreting edible items regarding their ingestion suitability, that is, if some food or beverage is fresh, ripe, safe, nutritional, or rotten (for instance, red vs. gray beef, green vs. yellow banana) (Sen et al., 2019).

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In this sense, molecules capable of bestowing color to products (food products, in particular) are especially interesting from a technological standpoint. Such molecules are generally called pigments and comprise a variety of chemical structures able to absorb light in the visible range (400–700 nm wavelengths). By chemical definitions, soluble colored substances are called colorants, while insoluble colored substances are called pigments. Nevertheless, under a biological perspective, the colored substances are called pigments, irrespective of their solubility (De Carvalho et al., 2014).

Synthetic colorants have been facing market resistance starting from 1960s due to multiple reasons, including allergenicity, toxicity, teratogenicity, and carcinogenicity problems (Sen et al., 2019). In addition to that, multiple synthetic colorants depend on precursors that are petroleum-based, a non-renewable resource (Kumar et al., 2015). These restrictions, combined with an increased advertising desire to label products (majorly food) as natural, ecological, biological, or eco-friendly have sparked the study of biopigments (Babitha, 2009). Biological pigments are considered safe if they are non-toxic, non-allergenic, non-carcinogenic, and biodegradable (Sen et al., 2019).

Among biological pigment sources, microbes like bacteria, yeasts, molds, and algae are being targeted as ideal resources to be tapped. Microbial pigments are forefront in colorant development due to their independence from weather conditions, considerable assortment of shades, fast growth, and substrate-dependent cost effectiveness, characteristics considered to be superior in comparison to plant and animal-sourced pigments (Lopes et al., 2013; Panesar et al., 2015). Such advantages, combined with shifts in consumer preferences, have been responsible for a steep rise in the biopigment market, with natural colors expected to grow 7% annually as a category (De Carvalho et al., 2014; Sen et al., 2019).

Microbial pigments are especially interesting when one considers that the major cost regarding their production is related to microbes growth media. Thus, as a rule of thumb, low-cost medium translates into low-cost pigment (Panesar et al., 2015; Sen et al., 2019). Among such low-cost media, agro-industrial residues are being regarded as ideal substrates for microbial pigment production, serving as sources of carbon, nitrogen, and minerals (Lopes et al., 2013; Panesar et al., 2015; Sen et al., 2019).

The agro-industrial residues are defined as many different wastes from the food and agriculture industry. These residues include multiple plant-based materials, such as straws, stems, stalks, leaves, husks, shells, peels, lint, seeds, pulps, stubbles, bagasse, spent coffee grounds, brewer's spent grains, and some animal byproducts, including feathers and whey (Madeira et al., 2017; Venil et al., 2020a). The efficient transformation of these residues has become a central environmental issue in recent years, with great attention being given to energy generation (e.g., biodiesel production) (Vandamme, 2009). However, new materials, chemicals and valuable products in general are being obtained from agro-industrial waste, including pigments (Madeira et al., 2017). These added-value products are obtained from cheaper materials that otherwise would cause environmental damage, either directly (phenolic or via other toxic compounds) or indirectly (by changing nutritional aspects of the ecosystem, normally causing eutrophication).

Microbial pigments are already used for food and textile coloring, with proposed uses in candles, soaps, ballpoint, salmon, yogurt, and highlighter pens (Venil et al., 2013; Sen et al., 2019). The applications of microbial-derived pigments, however, are not restricted to coloring. Some of these compounds have additional properties, such as antioxidant, antiparasitic, antimicrobial, and anticancer (Venil et al., 2013, 2020a; Sen et al., 2019).

In this article, we review the current literature on microbial pigment production using agro-industrial residues as substrates, encompassing the last decade (2010–2020). Exceptions were made for cornerstone articles and chapters that were considered of major interest for the reader but were outside the selected timeframe.

# PIGMENT-PRODUCING MICROORGANISMS

Microorganisms used in the production of biopigments include bacteria, yeasts, molds, and algae. The term "microbial pigments" is somewhat vague and can include some species that would not be considered *de facto* microorganisms (such as some filamentous fungi). In general, microbial pigment defines any non-plant, non-animal sourced biological pigment.

The microorganisms targeted for pigment production must satisfy a series of criteria: they should be non-pathogenic, nontoxic, able to use a wide range of carbon and nitrogen sources, able to give reasonable color yield, be tolerant to high salt concentration, be tolerant to variable temperatures and pH. They must also produce pigments that are easy to extract (Babitha, 2009; Kumar et al., 2015; Panesar et al., 2015; Venil et al., 2020a).

Biopigments can be classified based on chemical structure, with the main representatives being canthaxanthin, astaxanthin, prodigiosin, phycocyanin, violacein, riboflavin,  $\beta$ -carotene, melanin, and lycopene (Malik et al., 2012; Sen et al., 2019). All of them are currently used in the food industry (Sen et al., 2019). A variety of microbial pigments for which molecular identities were determined are shown in **Table 1**, along with synthesizing organism and pigment color. The molecular structure for some of the listed pigments is shown in **Figure 1**. For an updated list of macroscopic fungal pigments, please refer to Lagashetti et al. (2019).

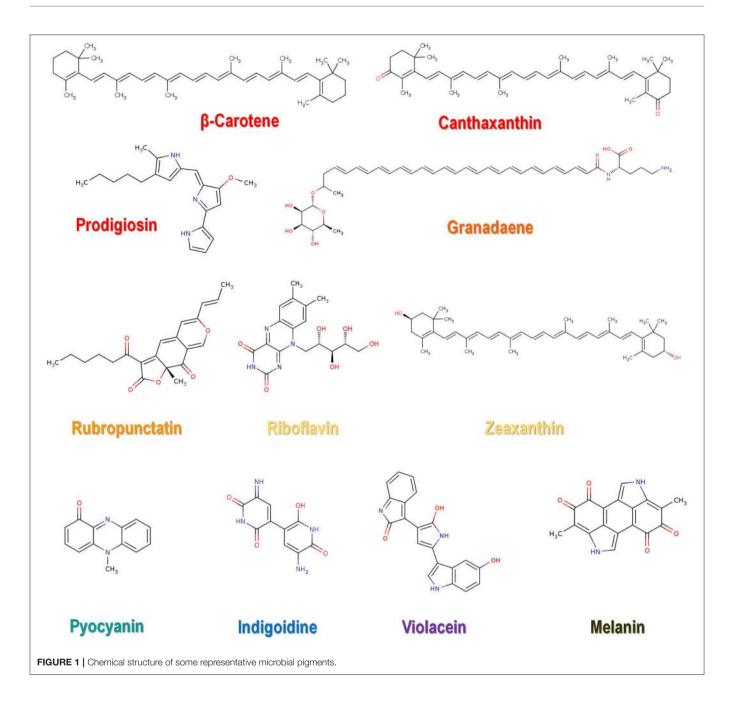
### AGRO-INDUSTRIAL RESIDUES USED FOR THE PRODUCTION OF MICROBIAL PIGMENTS

There is a need to explore novel strains of microorganisms and appropriate strategies for commercial production of microbial pigments (Nigam and Luke, 2016). Since synthetic culture media are usually expensive, the use of agro-industrial waste would be a profitable mean of reducing the production cost (Panesar et al., 2015). The Food and Agriculture Organization (FAO), in 2013, reported that 250 million tons of agro-industrial wastes are generated globally per year, during processing of different plant TABLE 1 | Microbial pigments and their source organisms [based on data from Malik et al. (2012), Panesar et al. (2015), Lagashetti et al. (2019), and Sen et al. (2019)].

Pigment (class)	Color	Microorganisms
Ankaflavin	Orange	Monascus purpureus
Anthraquinone	Red	Pacilomyces farinosus, Penicillium oxalicum,
Arpink Red	Dark red	Penicillium oxalicum
Astaxanthin	Pink red	Agrobacterium aurantiacum, Haematococcus pluvialis, Paracoccus carotinifaciens, Xanthophyllomyces dendrorhous (formerly Phaffia rhodozyma)
Atrovenetin	Yellow	Penicillium melinii
Azaphilones	Red	Penicillium purpurogenum, Talaromyces atroroseus
Canthaxanthin	Red	Bradyrhizobium sp., Brevibacterium sp., Dietzia maris, Haloferax alexandrinus, Lactobacillus pluvialis, Monascus roseus
Carotenoids	Red	Blakeslea trispora, Dunaliella salina, Fusarium sporotrichioides, Mucor circinelloides, Neurospora crassa, Phycomyces blakesleeanus, Rhodotorula rubra
Cycloprodigiosin	Red	Pseudoalteromonas denitrificans
Granadaene	Orange red	Streptococcus agalactiae
Indigoidine	Blue	Corynebacterium insidiosum
Lutein	Yellow	Chlorella spp.
Lycopene	Red	Blakslea trispora, Fusarium sporotrichioides
Melanin	Dark brown, Black	Bacillus thuringiensis H-14, Cryptococcus sp., Saccharomyces neoformans var. nigricans, Streptomyces virginiae, Yarrowia lipolytica
Monascin	Yellow	Monascus sp.
Monascorubramine	Red	Monascus sp.
Naphthoquinone	Brownish yellow	Fusarium sp.
Naphtoquinone	Dark red	Cordyceps unilateralis
Phycocyanin	Blue	Arthrospira sp. (formerly Spirulina sp.), Pseudomonas spp.,
Phycoerythrin	Red	Porphyridium cruentum
Physcion	Yellow	Aspergillus ruber
Prodigiosin	Red	Alteromonas rubra, Pseudoalteromonas rubra, Rugamonas rubra, Serratia sp., Streptomyces sp., Streptoverticillium rubrireticuli, Vibrio gaogenes
Prodoginine	Red	Streptoverticillium rubrireticuli
Pyocyanin	Blue green	Pseudomonas aeruginosa
Riboflavin	Yellow	Ashbya gossypi, Bacillus subtilis
Rubrolone	Red	Streptomyces echinoruber
Rubropunctatin	Orange	Monascus sp.
Staphyloxanthin	Golden yellow	Staphylococcus aureus
Torularhodin	Orange red	Rhodotorula glutinis
Violacein	Violet	Chromobacter violaceum, Janthinobacterium lividum, Pseudoalteromonas spp.
Xanthomonadin	Yellow	Xanthomonas oryzae
Zeaxanthin	Yellow	Flavobacterium sp., Paracoccus zeaxanthinifaciens, Sphingobacterium multivorum, Staphylococcus aureus

crops, mainly cereals, starchy roots, fruits, and other vegetables (Heredia-Guerrero et al., 2017).

Natural raw materials and by-products generated by industry are widely used as culture medium due to their low cost, once the components of the medium can represent from 38 to 73% of the total production cost (Panesar et al., 2015). Agro-industrial residues are untreated and underutilized, while being rich in nutrient components, such as carbohydrates, proteins, fibers, minerals, and vitamins. The utilization of this waste not only eliminates the disposal problems, but also the environment pollution (toxicity to aquatic life, pollution of surface and ground waters, altered soil quality, phyto-toxicity, odorous, and colored natural waters) and negative impact on human and animal health (Panesar et al., 2015; Zihare et al., 2018; Nayak and Bhushan, 2019). The environmental concern is related to the content of these wastes, since most of them include phenolic compounds that have toxic potential, in addition these wastes exhibit high value of biological oxygen demand, chemical oxygen demand, and other suspended solids that can be considered pollutant to the environment (Sadh et al., 2018; Venil et al., 2020a). Furthermore, plant cell walls found in the agro-industrial residues are composed of lignocellulose, a recalcitrant component, consisting of cellulose, hemicellulose and lignin, that can also be an environment pollutant (Sánchez, 2009). Recovery of high value-added components from the waste and their re-utilization as food additives or therapeutics are another interesting aspect to valorize these agro-industrial residues, we will not focus on

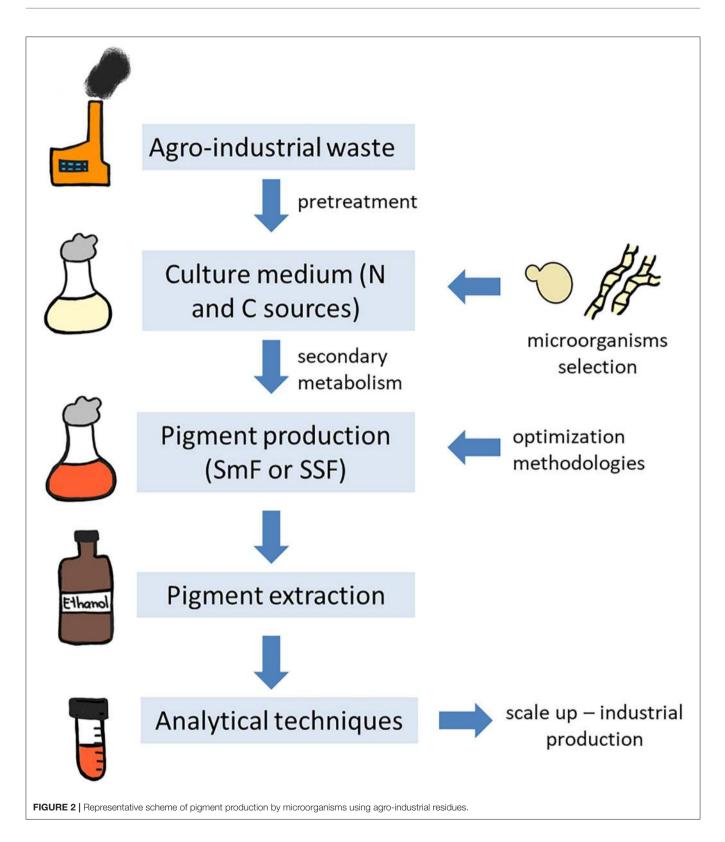


this approach in the present review. For more information about this strategy, please refer to Nayak and Bhushan (2019). A representative scheme of the different steps for microbial pigment production using agro-industrial waste is proposed in **Figure 2**.

In this work we reviewed the literature from 2010 to 2020 and selected studies with the production of microbial pigments using agro-industrial residues (Table 2). We restricted our selection to focus on the microorganisms that can produce pigments in an inexpensive manner using agro-industrial residues that are alternatives to decrease the costs of production. During this decade, there were

several works using waste as substrate, the sole substrate or supplemented with nutrients. The microorganisms more commonly used were fungi, both molds and yeasts. It is important to highlight some genera such as *Monascus* and *Rhodotorula* that were the most prevalent in these studies, especially *Monascus purpureus*, *Rhodotorula glutinis*, and *R. mucilaginosa*. Furthermore, carotenoids and *Monascus*polyketides were thus the pigments commonly produced by these microorganisms.

Yeasts are unicellular and have high growth rates, which favor these microorganisms in the production of biopigments (Bhosale and Gadre, 2001). Yeasts are pigment producers



considered as safer in comparison to filamentous fungi, due to the concerns about mycotoxin production by some of the latter. For instance, *Monascus* spp. is well-known for the production of citrinin, a nephrotoxic and hepatotoxic mycotoxin (Blanc et al., 1995). However, some genetic studies were published, currently modifying genes, eliminating non-essential genes of filamentous

#### TABLE 2 | Microbial pigments produced with agro-industrial waste and fermentation conditions (2010–2020).

Agro-industrial residues	Microorganisms	Туре	Pigment	Fermentation	Scale	Additional information	References
Petiole oil palm fronds	Monascus purpureus FTC 5357	Filamentous fungus	Red pigments	SSF	Laboratory	Peptone to supplement, 30°C, 8 days, 75% moisture, yield: 207 AU/g.d	Daud et al., 2020
High test molasses/sweet whey/corn steep liquor	Erwinia uredovora DSMZ 30080 and Rhodotorula glutinis number 32	Bacterium and yeast	Carotenoids	SmF	Laboratory (100 ml)	150 rpm, 4 days, 30°C, dark improved carotenoid production, yield: 1.46 $\pm$ 0.02 mg/L	Galal and Ahmed, 202
Peanut seed oil	<i>Serratia marcescens</i> 11E	Bacterium	Prodigiosin	SmF	Laboratory (100 ml)	28°C, 150 rpm, 36 h, yield: 2 g/L	Hernández-Velasco et al., 2020
Paper mill sludge/sugarcane bagasse	Planococcus sp. TRC1	Bacterium	β-carotene	SSF	Laboratory (100 g)	Supplemented with minimal salt media and yeast extract, 30°C, 120 h, mixing every 12 h, 80% moisture, yields: $38.54 \pm 1.4$ mg/g and $47.13 \pm 1.9$ mg/g	Majumdar et al., 2020
Onion peels/mung bean husk	Rhodotorula mucilaginosa MTCC-1403	Yeast	β-carotene, phytoene, torulene and Torularhodin	SmF	3 L bioreactor stirred tank	pH 6.1, 25.8°C, 119.6 rpm, 84 h, 1.0 vvm, yield: 719.69μg/g	Sharma and Ghoshal, 2020
Maltose syrup	<i>Monascus ruber</i> CCT 3802	Filamentous fungus	Orange, yellow and red pigments	SmF and SSF	Laboratory (petri dishes and 120 ml)	pH influenced the pigment production, 30°C, 120 rpm, 192 h	De Oliveira et al., 2019
Fruits and vegetable waste	<i>Blakeslea trispora</i> MTCC884	Filamentous fungus	Carotenoids	SSF	Laboratory	28°C, 4 days, 200 rpm, yield: 0.127 mg/mL	Kaur et al., 2019
Bengal gram husk	Talaromyces purpureogenus CFRM02	fungus	Red pigments	SmF	Laboratory (100 ml)	pH 5.5, 12 h day and night, 30°C, 10 days, 110 rpm, yield: 0.565 $\pm$ 0.05 AU/mL	Pandit et al., 2019
Oil palm frond	Monascus purpureus FTC 5356	fungus	Red pigments	SSF	Laboratory	50% moisture, pH 6, 2% peptone, 100% petiole, and 10 <sup>8</sup> spores/mL, 8 days, 30°C, yield: 2.93 AU/g	Said and Hamid, 2019
Cassava wastewater	Rhodotorula glutinis CTT 2182	Yeast	Carotenoids	SmF	Laboratory (150 ml)	30°C, 200 rpm, 120 h, darkness, yield: 0.98 mg/L	Santos Ribeiro et al., 2019
Mesquite pods/corn steep liquor	Xanthophyllomyces dendrorhous ATCC 24202	Yeast	Carotenoids	SmF	Laboratory (25 ml)	Mesquite pods extract (2%), corn steep liquor (0.3%) and yeast extract (0.3%), pH 5.5, 120 h, 200 rpm, 20°C, yield: 293.41 $\pm$ 31.12 µg/g	Villegas-Méndez et al., 2019
Sugarcane juice	Rhodotorula rubra 102	Yeast	Carotenoids	SmF	Laboratory (250 ml)	1.9% reducing sugar, 2% sucrose-and maltose-based media, Mg <sup>2+</sup> (0.16 % and 0.196 %), 30°C, 200 rpm and 1,600 lm of fluorescent lighting for 72 h, yield: 30.39 mg/g	Bonadio et al., 2018
Corn cob	<i>Monascus purpureus</i> ATCC 16436	Filamentous fungus	Orange and red pigments	SSF	Laboratory	24 g corn cobs, 2.17 M glycerol, pH 4.5, 30°C, 10 days, 150 rpm, 12 $\times$ 10 <sup>11</sup> spores/mL, yield: 133.77 UA/mL and 108.02 UA/mL	Embaby et al., 2018
Sugarcane bagasse hydrolysate	<i>Monascus ruber</i> Tieghem IOC 2225	Filamentous fungus	Red pigment	SmF	Laboratory (50 ml)	30°C, 150 rpm, 12 days, supplementation with glucose and cellobiose, darkness, yield: 18.71 AU	Hilares et al., 2018

(Continued)

Agro-Industrial Residues for Biopigments Production

#### TABLE 2 | Continued

Agro-industrial residues	Microorganisms	Туре	Pigment	Fermentation	Scale	Additional information	References
Waste orange peels	Monascus purpureus ATCC 16365 and Penicillium purpurogenum CBS 113139	Filamentous fungi	Yellow, orange and red pigments	SSF, Semi-SSF and SmF	Laboratory	5 g orange peels, 65% moisture, 25°C and 30°C, yields: 9 AU/g, 0.95 AU/mL, 0.58 AU/mL	Kantifedaki et al., 2018
Coffee husk/pulp extract	Rhodotorula mucilaginosa CCMA 0156	Yeast	Carotenoids	SmF	Laboratory (300 ml)	8.36% coffee husk extract, 0.636% glucose, 0.368% peptone and 0.5% tween 80, $10^7$ cell/mL, 28°C, 160 rpm, 5 days, dark, yields: 16.36 $\pm$ 0073 mg/L and 21.35 $\pm$ 0067 mg/L	Moreira et al., 2018
Crude glycerol/Corn maceration water/rice parboiling water	Sporidiobolus salmonicolor CBS 2636	Yeast	Carotenoids	SmF	2 L bioreactor Stirred tank (semi- continuous process)	8% crude glycerol, 8% corn maceration water, and 2% rice parboiling water, 25°C, pH 4.0, 180 rpm, 1.5 vvm, 50% working volume, yields: 34.8 g/L/h and 41.4 g/L/h	Colet et al., 2017
Cassava bagasse	Rhodotorula mucilaginosa	Yeast	Carotenoids	SmF	Laboratory (100 ml)	2% cassava bagasse, pH 6.0, 25°C, 4 days, yield: 12.0–12.5 mg/L.	Manimala and Murugesan, 2017
Wastes of potato chips manufacturing	<i>Monascus purpureus</i> Went NRRL 1992	fungus	Red, orange and yellow pigments	SSF	Laboratory (10 g)	67% moisture, pH 6.5, 1.5 mm particle size and 2% ammonium sulfate, $140 \times 10^3$ spores/10 g dry substrate, 15 days, $30^{\circ}$ C, darkness, yields: 126.5, 204.7, and 322.9 AU/g	Abdel-Raheam et al., 2016
Liquid pineapple waste	Chryseobacterium artocarpi CECT 8497	Bacterium	Yellowish-orange pigment	SmF	50 L- Bioreactor stirred tank	20% liquid pineapple waste, 12.5 % L-tryptophan 1.25 % KH <sub>2</sub> PO <sub>4</sub> , 30°C, 200 rpm, a. r. 10 L/min, pH 7.0, yield: 152 mg/L	Aruldass et al., 2016
Olive pomace	Xanthophyllomyces dendrorhous ATCC24202 and Sporidiobolus salmonicolor ATCC24259	Yeasts	Astaxanthin	SSF	Laboratory (100 g)	15°C, pH 4.5, 90% moisture, 10 <sup>6</sup> cells/mL, 12 days, yield: 220.24717.47 mg/gdp	Eryilmaz et al., 2016
Bakery waste	Monascus purpureus ATCC 16365	Filamentous fungus	Orange, yellow and red pigments	SSF and SmF	Laboratory	5 g bread waste, moisture 60%, 30°C, 100 mL, 250 rpm (SmF), yield: 24 AU/g glucose	Haque et al., 2016
Glycerol and soy peptone bagasses	<i>Serratia marcescens</i> Xd-1	Bacterium	Prodigiosin	SSF	Laboratory (2 g)	0.17% glycerol bagasse, 033% soy peptone bagasse, moisture 83.5%, 1 mm particles of bagasse, 28°C, 48 h with mixing every 12 h, yield: 40.86 g/kg	Xia et al., 2016
Liquid pineapple waste	Chromobacterium violaceum UTM5	Bacterium	Violacein and deoxyviolacein	SmF	50 L -Bioreactor stirred tank	10% pineapple waste, 24 h, 30°C, 200 rpm, a.r. 10 L/min, pH 7.0, yield: 16256 $\pm$ 440 mg/L	Aruldass et al., 2015
Sugarcane bagasse hydrolysate	<i>Dietzia maris</i> NIT-D	Bacterium	Trans- canthaxanthin (carotenoid)	SmF	Laboratory (50 ml)	1.5% of total reducing sugars, 2% peptone, 0.5% yeast extract, 0.25% NaCl and 1 mg/100 mL of glutamic acid, pH 5.5, 25°C, 5 days, 120 rpm, 2% inoculum	Goswami et al., 2015

(Continued)

Agro-Industrial Residues for Biopigments Production

#### TABLE 2 | Continued

Agro-industrial residues	Microorganisms	Туре	Pigment	Fermentation	Scale	Additional information	References
Raw glycerol/corn steep liquor/sugarcane molasses	Sporodiobolus pararoseus CCT 7689	Yeast	Carotenoids	SmF	Laboratory (250 ml)	3% raw glycerol and 5.29% corn steep liquor or 4% sugar cane molasses, 0.65% corn steep liquor, 25°C, 180 rpm, 1 $\times$ 10 <sup>7</sup> cell/mL 168 h darkness, yield: 520.94 $\mu$ g/L	Machado and de Medeiros Burkert, 2015
Carob pulp syrup/sugarcane molasses	Rhodosporidium toruloides NCYC 921	Yeast	Carotenoids	SmF	Laboratory (200 ml)	7.5% sugarcane molasses, 10% carob pulp syrup, pH 5.5, 30°C, 150 rpm, yield: 9.79 μg/L/h	Freitas et al., 2014
Slaughterhouse wastewater	Phormidium autumnale	Microalgae	Carotenoids	SmF	Bubble column bioreactor (2 L)	26°C, pH 7.6, C/N ratio of 30, 1 vvm, darkness, residence time of 168 h, yield: 107,902.5 kg/year	Rodrigues et al., 2014
Raw glycerol/corn steep liquor/parboiled rice water	Sporidiobolus pararoseus	Yeast	Carotenoids	SmF	Laboratory (100 ml)	4% glycerol, 4% corn steep water, 2% parboiled rice water, 25°C, pH 4.0, 180 rpm, yield: 843 μg/L	Valduga et al., 2014
Raw glycerol	<i>Monascus ruber</i> CCT 3802	Filamentous fungus	Yellow, orange and red pigments	SmF	Bioreactor stirred tank (4 L)	1% glucose, 1% glycerin, 0.5% glycine, 0.5% $K_2$ HPO <sub>4</sub> , 0.5% KH <sub>2</sub> PO <sub>4</sub> and micronutrients, 30°C, 350 rpm, 1 vvm, pH 6.5, yield: 8.28 UA	Bühler et al., 2013
Grape waste/cheese whey/soybean meal/feather meal/soy protein/rice husk	Penicillium chrysogenum IFL1 and IFL2, Fusarium graminearum IFL3, Monascus purpureus NRRL 1992, P. vasconiae IFL4	Filamentous fungi	Yellow, orange and red pigments	SmF	Laboratory (50 ml)	1% of each waste, pH 6.5, 7 days, 30°C, 125 rpm, 10 <sup>6</sup> spores/mL	Lopes et al., 2013
Brewery wastewater	Rhodotorula glutinis ATCC 15125	Yeast	Carotenoids	SmF	Laboratory (500 ml)	115 rpm, 25°C, 168 h, yields: 0.6 and 1.2 mg/L $$	Schneider et al., 2013
corn cob waste stream cellulose	Penicillium resticulosum	Filamentous fungus	Red pigments	SmF	Laboratory (50 ml)	12 days, 25°C, 60–70%, relative humidity, dark, yield: 497.03 $\pm$ 55.13 mg/L	Sopandi et al., 2013
Vegetable cabbage waste	Pseudomonas sp.	Bacterium	Melanin	SmF	Laboratory (50 ml)	25°C, 200 rpm, 48–72 h, 2.79 mg/mL	Tarangini and Mishra, 2013
Sugarcane bagasse	Chromobacterium violaceum	Bacterium	Violacein	SmF	Laboratory (50 ml)	3 g sugarcane bagasse, 10% L-tryptophan, 200 rpm, 30°C, 24 h, yield: 0.82 g/L	Ahmad et al., 2012
Corn meal	<i>Monascus purpureus</i> CMU001	Filamentous fungus	Red pigments	SSF	6 × 10-in. plastic bags	5 g of waste, salt solution, 8% glucose, 30°C for 14 days, 1 $\times$ 10 $6$ spores/mL, yield: 129.63 U/gds	Nimnoi and Lumyong, 2011
Waste chicken feathers	Rhodotorula glutinis MT-5	Yeast	Carotenoids	SmF	Laboratory (100 mL)	0.8% peptone of chicken feather, 4% glucose, 0.4% yeast extract, pH 6.0, 30°C, 200 rpm, yield: 6.47 mg/g	Taskin et al., 2011
Corn cob powder	Monascus purpureus KACC 42430	Filamentous fungus	Yellow and red pigments	SSF	Laboratory (5 g)	60% moisture, 30°C, 4 mL of spores/gram of dry substrate, 7 days, yield: 25.42 OD Units/gram	Velmurugan et al., 2011
Rice bran	Rhodotorula glutinis	Yeast	β-carotene	SSF	Laboratory (5 g)	pH 5, 70% moisture,C:N ratio 4, yield: 2.12 mg/kg rice bran	Roadjanakamolson and Suntornsuk, 2010

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SSF, Solid State Fermentation; SmF, Submerged Fermentation; vvm, volume of air per volume of liquid per minute; a.r., aeration rate; C:N ratio, carbon:nitrogen ratio.

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fungi in order to increase the production of pigment and decrease mycotoxin secretion (Lagashetti et al., 2019). In the case of *Monascus*, several techniques were performed to decrease the production of citrinin: changes in the nitrogen composition of the medium, the dissolved oxygen or the pH, as well as genetic alterations of the strains (Sen et al., 2019).

In the reviewed studies, some investigated the production of citrinin by Monascus strains. M. purpureus Went NRRL 1992 did not produce citrinin using potato waste in a solidstate fermentation. The mycotoxin detection was performed by thin layer chromatography (Abdel-Raheam et al., 2016). M. purpureus NRRL 1992 produced citrinin in potato dextrose agar, with mycotoxin production being evaluated by ESI-MS/MS (electrospray ionization tandem mass spectrometry). Nevertheless, the authors did not evaluate its production in the agro-industrial residues (Lopes et al., 2013). M. purpureus ATCC 16365 also produced citrinin in orange processing waste, however the authors did not demonstrate the methodology used in this study to detect citrinin (Kantifedaki et al., 2018). The detection of mycotoxin production by filamentous fungi is very important, considering the industrial production of pigments and it is a fundamental step to guarantee the safety of the final product.

Microorganisms from these studies were wild-type, and many of them were purchased from collection cultures or isolates. This fact is surprising due to the great advances regarding mutation techniques and heterologous expression with the purpose of obtaining strain improvement. Strain development is important because pigments produced by wild type strains are usually too low in quantity and take longer fermentation periods, making the process uneconomical (Sen et al., 2019). Due to the recent application of molecular techniques to improve pigment production, more studies will be probably published in a near future with recombinant strains grown on agroindustrial residues.

Regarding the wastes, pre-treatment is important for promoting breakdown of these residues, mainly formed by cellulose, hemicellulose and lignin. This breakdown will increase the availability of the nutrients from the substrate to the microorganisms. Various pre-treatment methods such as physical, chemical, biological (enzymatic), and combined are available (nee'Nigam et al., 2009). In the selected studies, the agro-industrial wastes were pre-treated (treated prior to use). Some examples of physical pre-treatment deal with paper mill sludge and sugarcane bagasse that are milled and sieved to achieve an uniform size of particles (Majumdar et al., 2020), as well as onion peels and mung bean husk (Sharma and Ghoshal, 2020), petiole oil palm fronds (Daud et al., 2020) and fruits and vegetable wastes (Kaur et al., 2019). Chemical treatments of the waste were performed in some studies. Bengal gram husk was pre-treated with hydrochloride acid, promoting an acid hydrolysis to improve the availability of the substrate (Pandit et al., 2019). Sugarcane bagasse was pre-treated under alkaline condition with sodium hydroxide and afterwards hydrolyzed with a commercial cellulase complex (Hilares et al., 2018). In this case there was the combination of a biological treatment. Bakery waste was also hydrolyzed with enzymes produced by Aspergillus awamori and Aspergillus oryzae before its use (Haque et al., 2016). In the majority of the studies, the agro-industrial wastes are used as carbon, nitrogen, and micronutrient sources by microorganisms. However, in some cases, the residues can be added as an inert support for the fermentation process, such as the bagasse used in the prodigiosin production by *Serratia marcescens* (Xia et al., 2016).

Brazil is one of the biggest agricultural commodity producers, since it is considered as the world's biggest producer of sugar, coffee, orange juice, and soybeans (Da Silva Vilar et al., 2019). In this review, 11 studies were performed in Brazil, due to the great availability of such residues in this country. Wastes used in these works were maltose syrup, cassava wastewater, sugarcane (juice, molasses, and hydrolyzed bagasse), solid coffee waste, crude glycerol, rice parboiling water, slaughterhouse wastewater, corn steep liquor (or corn maceration water), grape waste, cheese whey, soybean meal, feather meal, soy protein, and rice husk) (Table 2). In order to evaluate each residue as carbon and/or nitrogen source, Table 3 brings an average composition of the agro-industrial residues regarding carbon and nitrogen composition, according either to the works cited in this review or, in some cases to the composition obtained from other works, when this information was not available. It is important to highlight that this composition is variable, depending on the source of the waste; however, an average composition can be useful for planning new projects in this area.

### MODES OF FERMENTATION AND SCALE OF PRODUCTION

Traditional methods of microorganism isolation, culture and products extraction are now substituted by novel biotechnological techniques and strategies, via the advent of genetic engineering and fermentation technologies (Nigam and Luke, 2016). Different types of fermentation are used to produce pigments depending on the chosen strain and the type of pigment that will be extracted. Production of pigments by fermentation has a great number of advantages, including abundance of raw materials, absence of seasonal variation, cheaper production, easier extraction, perfectible yields, and procurement of biodegradable pigments (Venil et al., 2013; Charalampia et al., 2017). In addition, pigments produced by microorganisms through fermentation present higher stability to heat, to light exposure and pH variations, and are highly soluble in water (when compared to plant pigments) (Nigam and Luke, 2016). Some types of pigments are only produced by microorganisms (Dufossé, 2006) and the possibily of using industrially important species, such as Escherichia coli and Saccharomyces cerevisiae, to express these pigments heterologously are excellent alternatives (Venil et al., 2013).

Microorganisms produce pigments mainly by two types of fermentations processes: solid state fermentation (SSF) and submerged fermentation (SmF). In the SSF technique, the substrates are used by the microorganisms very slowly, and then the same substrate can be used for longer periods. This technique provides controlled release of nutrients during the process (Subramaniyam and Vimala, 2012). This type of TABLE 3 | Average carbon and nitrogen composition of the agro-industrial residues.

Agro-industrial residue	Carbon-composition	Nitrogen-composition	References	
Bakery waste	Starch (37.42 $\pm$ 0.032 g)	Proteins (14.72 $\pm$ 0.55 g) and other nitrogen sources (2.58 $\pm$ 0.97 g)	Haque et al., 2016	
Carob pulp syrup	Sugar (75 g $L^{-1}$ reducing sugar)	ni	Freitas et al., 2014	
Carrot peel	Carbohydrates (2.98 $\pm$ 0.75 g)	Proteins (9.70 $\pm$ 0.25 g)	Chantaro et al., 2008	
Cassava wastewater	Carbohydrates (58.11 $\pm$ 2.13 g)	Total nitrogen (1.94 $\pm$ 0.08 g)	Santos Ribeiro et al., 2019	
Cheese whey	Lactose (77%)	Proteins (13%)	Lopes et al., 2013	
Coffee pulp and husk	Carbohydrates (17.10–13.38%)	Proteins (24.21–30.50%)	Moreira et al., 2018	
Corn cob	Cellulose (32.3–45.6 %), hemicellulose (39.8 %)	ni	Embaby et al., 2018	
Corn steep liquor	Sugar (0.1–11.0% glucose)	Total nitrogen (2.7–4.5%)	Liggett and Koffler, 1948	
Feather meal	ni	Protein (83.7%)	Lopes et al., 2013	
Grape waste	Carbohydrates (21%)	Proteins (10%)	Lopes et al., 2013	
High test molasses	Sugar (74–79%)	Low amounts (0.1%)	Murphy, 1984	
Liquid pineapple waste	Sugars (reducing sugar, glucose, sucrose, fructose)	ni	Aruldass et al., 2016	
Maltose syrup	Maltose and glucose (70.0 g L <sup><math>-1</math></sup> maltose and 2.23 g L <sup><math>-1</math></sup> glucose)	ni	De Oliveira et al., 2019	
Mesquite pods	Sucrose, glucose, fructose	ni	Villegas-Méndez et al., 2019	
Mung bean husk	Sugar (327.78 $\pm$ 2.08 mg/g)	Proteins (262.23 $\pm$ 3.59 mg/g)	Sharma and Ghoshal, 2020	
Olive pomace	Fatty acids (59.03% and 63.81%)	Proteins (2.43 $\pm$ 0.00%) to (3.87 $\pm$ 0.17%) and other nitrogen sources (0.39 $\pm$ 0.0%) to (0.62 $\pm$ 0.02%)	Wedyan et al., 2017	
Onion peels	Sugar (851.33 $\pm$ 4.62 mg/g)	Proteins 165.10 $\pm$ 5.13 mg/g)	lfesan, 2017; Sharma and Ghoshal, 2020	
Orange peel	Cellulose (71.2 g/kg), hemicellulose (128 g/kg)	Crude protein (57.2 g/kg)	Ahmadi et al., 2015	
Papel mill sludge	Cellulose (62%), hemicellulose (15%) and lignin (20%)	ni	Majumdar et al., 2020	
Parboiled rice water	Present	Present	Valduga et al., 2014	
Peanut seed oil	Fatty acids (80% of these fatty acids are either oleic acid or linoleic acid)	ni	Rachaputi and Wright, 2015	
Petiole oil palm fronds	Cellulose (44%), hemicellulose (27.3%) and lignin (10.1%)	ni	lkubar et al., 2018	
Rice bran	ni	Protein (114.2 g/kg)	Roadjanakamolson and Suntornsuk, 2010	
Rice husk	Cellulose (31.12%), hemicellulose (22.48%) and lignin (22.34%)	ni	Kumar et al., 2010	
Slaughterhouse wastewater	ni	Total nitrogen (128.5 $\pm$ 12.1 mg/L)	Rodrigues et al., 2014	
Soybean meal	Carbohydrates (35%)	Proteins (50%)	Lopes et al., 2013	
Soybean protein	Carbohydrates (12%)	Proteins (79%)	Lopes et al., 2013	
Sugarcane bagasse	Cellulose (32–34%), hemicellulose (19–24%) and lignin (25–32%)	ni	Haghdan et al., 2016	
Sugarcane juice	Sugar (19 g reducing sugar)	ni	Bonadio et al., 2018	
Sweet whey	Lactose (4.5%)	Proteins (0.8%)	Morr, 1989	
Wastes of potato chips	Starch (61.49%)	Low amounts of protein	Korish and El-Sanat, 2007	

ni, not informed.

fermentation is suitable to filamentous fungi and microorganisms that require low moisture content for their growth. Their growth as SSF mimic (Joshi and Attri, 2006). This technique is very effective in waste valorization due to the microorganism conversion of waste into value-added products with low power supply and high yield. Arikan and co-authors observed higher production of a yellow pigment by *Aspergillus carbonarius* using pomegranate pulp through SSF than SmF (Arikan et al., 2020). According to Carvalho et al. (2005), the majority of *Monascus* researchers observed pigment production varying from hundreds of absorbance units per mL culture medium, in SmF; in contrast thousands of absorbance units/g dry substrate was observed

in SSF (Carvalho et al., 2005). In some cases, however, the higher production using SSF requires longer times of culture in comparison with SmF. The low energy to perform a SSF is due to the simplified bioreactors used in this type of fermentation, mainly when we compare some types of SmF bioreactors, such as stirred tank, that requires high energy consumption to maintain constant agitation during the process. In addition, it is considered an easy process, with minimal pretreatment of the waste being necessary (sometimes not needed at all) and generating less wastewater (Wang and Yang, 2007; Arun et al., 2020). Some of the common substrates used in SSF are wheat bran, rice and rice straw, fruit and vegetable waste, paper pulp, bagasse, and coconut coir (Panesar et al., 2015).

On the other hand, in SmF the substrates are consumed very rapidly, then it is possible to replace or supplement the culture media (fed batch or continuous culture strategies are necessary in some cases), or to use fast-growing microorganisms during the process (Subramaniyam and Vimala, 2012). It is important to highlight that in some cases supplementation of the medium in SSF is also needed, because of the poor nature of the substrate or low availability of the nutrients in the beginning of the bioprocess (substrates that are not pretreated, for example). This type of fermentation is commonly used for bacteria, due to their necessity of higher moisture in the fermentation process (Subramaniyam and Vimala, 2012). Some common substrates used in SmF are soluble sugars, molasses, fruit and vegetable juices, and sewage/wastewater (Panesar et al., 2015). Based on the data of this review (Table 2), the majority of the studies use SmF to produce pigments instead of using SSF. Solid-state fermentation systems could present some advantages because of the potential with natural substrates. Nonetheless, pigment production is performed commercially almost entirely in SmF (Sánchez-Muñoz et al., 2020). The main obstacles to SSF are the low amenability of the process to regulation, the heterogeneous fermentation conditions and the low reproducibility of the results. Moreover, some difficulties to scale-up may also appear, as well as often unfeasible determination of biomass or complicated product purification by downstream processes (Hölker and Lenz, 2005).

Agro-industrial residues decrease the costs of the fermentation process. Maximization of the pigment production while decreasing the production costs has been the goal of current techniques applied to produce microbial pigments at large scale. Medium optimization is especially important to maximize the production. Optimizing the medium includes controlling the conditions of the fermentation, such as temperature, pH, aeration, agitation, and media components. Process optimization techniques have used statistical experimental designs and response surface analysis with limited use of artificial intelligence (like genetic algorithms). Response surface methodology (RSM) is an effective approach for the process optimization in pigment production (Gharibzahedi et al., 2012; Sen et al., 2019).

Some studies reported in this review used statistical methodologies to optimize the production of pigments, with RSM being by far the most used. Sharma and Goshal optimized pH, temperature, and agitation conditions in the production of carotenoids by *R. mucilaginosa* (Sharma and Ghoshal,

2020). Embaby and co-authors used a three-step optimization, including RSM, to study the concentration of glycerol and inoculum size in the production of orange and red pigments by M. purpureus using corn cobs (Embaby et al., 2018). Aruldass and co-authors used RSM to optimize the production of yellowishorange pigments by Chryseobacterium artocarpi. The authors used three independent variables: concentrations of liquid pineapple waste, L-tryptophan, and KH<sub>2</sub>PO<sub>4</sub> (Aruldass et al., 2016). The production of astaxanthin by Xanthophyllomyces dendrorhous in olive pomace was optimized with RSM, testing temperature, moisture content and pH condition (Ervilmaz et al., 2016). Prodigiosin production by S. marcescens was optimized by RSM with three variables: glycerol bagasse, soybean peptone bagasse, and initial moisture content (Xia et al., 2016). Raw glycerol, steep liquor, and sugarcane molasses concentrations were tested in the optimization experiments of carotenoids production by Sporidiobolus pararoseus, as well as glycerol, corn steep liquor and parboiled rice water concentrations (Valduga et al., 2014; Machado and de Medeiros Burkert, 2015). Moisture, pH, and carbon-to-nitrogen ratio were evaluated in the carotenoids production by R. glutinis using rice bran (Roadjanakamolson and Suntornsuk, 2010). The Taguchi methodology was applied to optimize the production of carotenoids by Xanthophyllomyces dendrorhous, using four variables: concentrations of mesquite pods extract, corn steep liquor, yeast extract, and malt extract (Villegas-Méndez et al., 2019).

Another approach used in some studies is the optimization of one factor at a time (OVAT). For instance, the authors evaluated pH, temperature, and light on the carotenoids production by Planococcus sp. (Majumdar et al., 2020). Optimization of various factors such as pH, growth temperature, incubation time and the addition of nitrogen components was evaluated on the production of  $\beta$ -carotene by *Blakeslea trispora* (Kaur et al., 2019). Five operational factors such as the initial moisture content of oil palm frond, initial pH, supplementation of nitrogen source, the percentage of petiole to leaflet, and inoculum size were investigated on the red pigments production by M. purpureus (Said and Hamid, 2019). In the conventional approach OVAT, the conditions are optimized by changing one factor at a time while maintaining the other variables constant. This is a simple approach to implement and helps to choose the main variables. However, this methodology is time-consuming, because several experiments are necessary to study all the relevant conditions and also ignores the combined interaction(s) among the variables (Vishwanatha et al., 2010).

Variables that were most frequently evaluated in the optimization studies were pH, substrate concentration, and initial moisture. The pH is particularly important in the pigments production. pH of the medium plays an important role in activating key enzymes involved in pigment production and excretion by *M. pupureus* CCT3802, according to Orozco and Kilikian (2008). In addition, pH influences the color of the pigments. According to De Oliveira and co-authors, pH values close to neutrality lead to the formation of red pigments by *Monascus* sp. (De Oliveira et al., 2019). On the other hand, medium pH around 3 results in the production of

yellow pigments by Monascus anka (Shi et al., 2015). Substrate concentration is considered as an important variable to study, in particular the nitrogen source is a key regulation factor. It has been consistently shown that selective nitrogen sources largely influence the composition of Monascus pigments and this variable correlates with pH of the medium (Shi et al., 2015), highlighting the importance of the statistical methodologies to study the interactions among variables. Moisture is also a significant variable in SSF systems. Adequate water content of the substrate facilitates the oxygen transport, promoting microorganism growth. Nevertheless, excessive water content may lead to the reduction of oxygen transfer and diffusion because of substrate agglomeration, lowering the porosity of the substrate and increasing the risk of contamination, since an advantage of SSF is to select microorganisms that grow under low water content (Said and Hamid, 2019). Indeed, some filamentous fungi and yeasts are capable to grow at a water activity  $(a_w)$  of 0.61, the lowest  $a_w$  value for growth of microorganisms (Grant, 2004).

Large scale production with high yields and low costs of production are the biggest challenges faced by industry. Recent developments in molecular biology could be crucial. The genes responsible for the synthesis of several pigments have been cloned and recombinant DNA technology would be an alternative to overproduction of pigments. With the advances in the gene technology, the scientists intend to create cell factories for the production of pigments using the heterologous expression of biosynthetic pathways from already known or novel pigment producers (Malpartida and Hopwood, 1984; Pfeifer and Khosla, 2001; Venil et al., 2013). Martínez and co-authors reviewed the recombinant production of melanin by Escherichia coli, Pseudomonas putida, and Streptomyces kathirae (Martínez et al., 2019). In another work, the authors deleted the 15-kb citrinin biosynthetic gene cluster in M. purpureus industrial strain KL-001, using CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)-Cas system, obtaining a mutant strain that did not produce the mycotoxin and also increased red pigment production in 2–5% (Liu et al., 2020). From a technical point of view, the vast majority of the studies reported in the present review, were at a laboratory scale. Nevertheless, certain pigments are in a more advanced stage of scaling up. Some studies used SmF bioreactors, such as stirred tank and bubble column (Bühler et al., 2013; Rodrigues et al., 2014; Aruldass et al., 2015, 2016; Colet et al., 2017; Sharma and Ghoshal, 2020). These more advanced studies are interesting, since they show the high potentialities of scaling up microbial pigments targeting a future industrial application.

Industrial scale synthesis of microbial pigments is mainly limited by the high costs of production, the co-production of toxins in some of these processes, and the resistance of the final product to extreme processes conditions, such as high temperature and extreme pHs (conditions that are found in industrial processes) (Narsing Rao et al., 2017). Some microbial pigments are produced industrially, such as  $\beta$ -carotene (*Blakeslea trispora* and *Dunaliella salina*) and lycopene (*Blakeslea trispora*), *Monascus*-derived pigments in Natural Red<sup>TM</sup> (*Penicillium oxalicum*), riboflavin (*Aspergillus*) gossypii), phycocianin (Spirulina platensis), and astaxanthin (Paracoccus carotinifasciens and Haematococcus pluvialis) (Dufosse et al., 2014). The estimation of the universal food colorant market is anticipated to achieve 3.75 billion USD by 2022 (Venil et al., 2020b). Besides, the carotenoids (astaxanthin, betacarotene, canthaxanthin, lutein, lycopene, zeaxanthin) market in 2019/2020 is supposed to reach \$1.5–1.8 billion with annual growth rate of 3.9% (Barredo et al., 2017; Venil et al., 2020a). The global demand for natural pigments, including microbial pigments is high and tends to grow exponentially in the next years.

# OTHER BIOLOGICAL ACTIVITIES OF MICROBIAL PIGMENTS PRODUCED WITH AGRO-INDUSTRIAL WASTE

Microbial pigments not only add color, but they also have interesting biological properties such as antioxidant, antimicrobial, anticancer, immunoregulation, antiinflammatory, antiproliferative, and immunosuppressive activities (among others) (Kirti et al., 2014; Manimala and Murugesan, 2014; Kumar et al., 2015; Sen et al., 2019; Muthusamy et al., 2020). Because of these pharmacological properties, there are many more advantages of using natural pigments over synthetic colorants (Venil et al., 2013).

The most common biological activities were antibacterial and antioxidant in the reviewed studies (Table 2). The antimicrobial activity of pigments can be a strategy to improve the source microbe ability of competing with other microorganisms (De Carvalho et al., 2014). The violet crude extract produced by Chromobacterium violaceum using liquid pineapple waste contains the pigments violacein and deoxyviolacein. This extract has antibacterial activity against Staphylococcus aureus ATCC 29213 and methicillin-resistant S. aureus (MRSA) (Aruldass et al., 2015). The extracted  $\beta$ -carotene produced by *Planococcus* sp. TRC1 using paper mill sludge and sugarcane bagasse was active against Bacillus subtilis, Salmonella enterica, Escherichia coli, and Proteus vulgaris. In addition, this pigment had antioxidant activity (Majumdar et al., 2020). Red pigment produced by Talaromyces purpureogenus using Bengal gram husk was active against B. cereus, B. subtilis, S. aureus, Micrococcus luteus, E. coli, Klebsiella pneumoniae, Listeria monocytogenes, and Salmonella typhimurium. The extracted pigment presented antioxidant activity and was non-toxic to the crustacean Artemia franciscana (Pandit et al., 2019). Carotenoids produced by R. mucilaginosa using solid coffee waste exhibited antioxidant and antimicrobial activities against pathogenic bacteria: Salmonella cholerasus, E. coli, S. aureus, and L. monocytogenes, as well as against toxigenic fungi like Aspergillus flavus, A. parasiticus, A. carbonarius, and A. ochraceus (Moreira et al., 2018).  $\beta$ -carotene produced by Blakeslea trispora using fruit and vegetable waste, astaxanthin produced by Xanthophyllomyces dendrorhous in olive pomace, and melanin produced by Pseudomonas sp. using cabbage waste, also presented antioxidant activity (Tarangini and Mishra, 2013; Eryilmaz et al., 2016; Kaur et al., 2019).

## **CONCLUSIONS AND CHALLENGES**

The use of agro-industrial residues as substrate for microbial pigment synthesis is a green, sustainable way of solving a pollution problem while cutting costs in the production of added value assets. Besides reducing the carbon footprint, microbial pigments also satisfy a growing demand for natural colorants. The majority of these pigments are also vegan, circumventing the need for animal-based colors (dairy and poultry-waste based microbe production would not be vegan, however).

Considering the advantages of using microorganisms as pigment factories, there is a growing need for biodiversity sampling, in search for new molecular entities (including greater color variety). Not only that, but genetic engineering and synthetic biology approaches are expected to provide strains with increased productivity and tolerance to cultivation conditions. Brazil is an interesting place to bioprospect new microorganisms, due to its great natural biodiversity and its agriculture-based economy, providing a large variety of agro-industrial waste to be studied.

Besides the use of a strain that produces high yields of pigments in an inexpensive medium, the current and future challenges in this area are related to the safety of the final products, due to the mycotoxin co-produced by some of the microorganisms. Technologies to produce microorganisms with these characteristic are available and in some cases, they are not expensive, such as the new genome- editing methodology

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CRISPR. Another important approach is the stability of the natural pigments that are in some cases a problem for the final product. More studies about different modes of production are needed in order to find new pigments with high stability to be applied in different industries. Lastly, the use of agro-industrial residues needs to be more implemented in industries not only to decrease the costs of the production but also to execute a circular economy, that is an eco-friendly approach, extremely necessary in the current days.

The road is still long and largely unpaved for microbe-based biopigments, and as their use expands, so will the development of associated technologies with proportional cost reduction. In summary, the microbial pigment production using agroindustrial residues is a rare win-win scenario, in which "One man's trash is another man's treasure."

# AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

### ACKNOWLEDGMENTS

We would like to thank the Brazilian agency Conselho de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) by the postdoctoral fellowship (FCL).

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**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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