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Review

Solid-State Fermentation from Organic Wastes: A New Generation of Bioproducts

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Abstract: Solid-state fermentation (SSF) is part of the pathway to consolidate waste as a relevant alternative for the valorization of organic waste. The objective of SSF is to produce one or several bioproducts of added value from solid substrates. Solid-state fermentation can use a wide variety of organic waste as substrates thus, it is an excellent candidate in the framework of the circular bioeconomy to change the status of waste from feedstock. The development of SSF was boosted in the previous decade by scientific efforts devoted to the production of hydrolytic enzymes. Nowadays, SSF has expanded to other valuable products: biosurfactants, biopesticides, aromas, pigments, and bio-flocculants, among others. This review explores the conditions to obtain the main emerging SSF products and highlight and discuss the challenges related to the scale-up of these processes and the bioproducts downstream, which hamper their further commercialization.

Keywords: solid-state fermentation; organic waste; bioproducts; circular bioeconomy; biosurfactant; biopesticide

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1. Introduction

With the increasing implementation of biological treatments applied to organic waste due to a stringent worldwide legislation against landfill and incineration, anaerobic digestion (AD) [1] and composting [2] have become the main accepted ways to treat organic waste in the framework of the Circular Economy as they permit the recovery of energy and materials [3]. However, a new emerging field of research has been raised in recent years: solid-state fermentation (SSF). Although solid-state fermentation (SSF) has been known for decades, the use of organic waste as a substrate has made SSF a technology in which circularity goes one further step. Therefore, the main goal of SSF would be to produce a valuable/marketable product from renewable materials in a sustainable way, substituting for current highly impacting chemicals. In addition, nutrients in the spent solids could be further recovered through composting or AD [4]. Usually, this bioproduct obtained by SSF is also substituting a non-biodegradable chemical with similar properties and lower cost [3].

Solid-state fermentation is, by definition, the cultivation process in which microorganisms grow on solid materials without the presence of a free liquid phase [5]. In practical terms, a bioreactor, typically aerobic, is filled with the solid substrate and inoculated with the strain of interest to produce the desired bioproduct. Once produced, this bioproduct can be recovered, although in some cases the final fermented solid can be used as the end-product [6]. Several types of reactors have been used in SSF development: packed bed reactors, mechanically stirred reactors, tray reactors, and even plug flow configurations [7,8]. All these configurations have one common objective in the scale-up process: to overcome the mass and heat transfer limitations of organic matter in solid state, which can result in high temperatures that harm the strain of interest [9]. These problems typically appear when SSF is scaled up, and it is one of the main problems for a full SSF use and commercialization [10,11]. Recently, some models have been published to monitor the mass behavior in SSF reactors, using traditional techniques such as residence time distributions [12], or more complex approaches, such as computer fluid dynamics [13].

Solid-state fermentation is not a new idea and has been traditionally used for some food processes, especially in Asia. Moreover, composting is a very specific type of SSF. However, it is in the last two decades that the technology has arisen as a promising biotechnological tool. Regarding the bioproducts of interest, researchers first approached the production of hydrolytic enzymes by SSF [14]. A wide variety of enzyme families have been produced by SSF: proteases, lipases, cellulases, among others. Beyond these, SSF is being explored to produce materials to substitute chemicals for biodegradable products that offer the same benefits. This is the case of biopesticides [15], biosurfactants [16], aromas [17], and bioplastics [18], among others.

The objective of this review is to compile information about the production of these emerging bioproducts by SSF from organic waste, highlighting the SSF process conditions, substrates used, and the main challenges observed in the scale-up of these processes. The aim of this study was also to reveal some of the biggest drawbacks of most SSF studies, which are the scale of the fermentations, limiting the scope of experiments to the fermentation process, and the characterization of the bio-compounds. Not considering the process as a whole nor trying to integrate it into a zero waste or circular economy approach is another important disadvantage where SSF has the potential to improve things and as a result is highly relevant. Enzymes and biofuel produced by SSF will not be considered in this study, as several reviews are available in the literature [4,14,19,20]. This review will deal with SSF and its challenges rather than comparing it with submerged fermentation (SmF) in order not to confuse the focus of this study. There is extensive literature on the difference between these technologies [21,22].

2. Organic Waste as Substrate for SSF

Lignocellulosic agricultural waste types are the most used substrates and support materials in SSF [23]. However, other organic wastes have been recently used to create specific biochemical compositions as substrates to obtain a defined bioproduct. This is the typical case of glycolipid biosurfactants, for instance, where lipids are essential [24], whereas other materials can be produced from complex mixtures such as the organic fraction of municipal solid waste or digestate from biowaste [6,25]. Organic wastes are cheap and accessible resources that have a huge potential to be revalorized, and SSF can take advantage of these resources that have no other use. This poses some drawbacks because of the inherent characteristics of these wastes, such as their heterogeneity, complexity, and their changing nature.

Table 1 summarizes a compilation of some substrates used in SSF to produce specific metabolites. Table 1 does not intend to be exhaustive but rather shows recent and representative organic waste types used in SSF.

Table 1. Compilation of the nexus organic waste(substrate)/strain/bioproduct used recently in SSF.

SSF Objectives and Waste Description	Bioproduct	Strain	Reference
Degrade lignin and enhance the nutritive value of grape stalks. Lab scale incubators.	Animal feed	White rot fungi	[26]
Sargassum spp. macroalgae biomass subjected to hydrothermal pretreatments. Packed bed bioreactors.	Fungal proteins	*Aspergillus oryzae*	[27]

Table 1. *Cont.*

SSF Objectives and Waste Description	Bioproduct	Strain	Reference
Rice bran and soybean residue. Radio frequency rapid heating technology is used to dry the solid-state fermented product. Lab scale incubators.	Antioxidants	*Wolfiporia cocos*	[28]
Winterization oil cake and molasses to produce sophorolipids. Techno-Economic Analysis is presented at bench scale.	Sophorolipids	*Starmerella bombicola*	[29]
SSF of brewers' spent grain, after two pretreatments: extrusion and blade milling. Lab scale incubators.	Phenolic acids with antioxidant capacity	*Fusarium oxysporum*	[30]
Various agricultural lignocellulosic by-products (sugarcane bagasse, wheat straw, rice straw, rice bran, and corn cob). Lab scale incubators.	Biovanillin	*Enterobacter hormaechei*	[31]
Combined continuous solid-state distillation and vapor permeation to extract ethanol from fermented sweet sorghum bagasse. Rotary drum fermenter. Full scale (cubic meters).	Bioethanol	*Saccharomyces cerevisiae*	[32]
Wheat bran and white rice in SSF optimized by an experimental design to build a mathematical model. Lab scale incubators.	Fungicide	*Trichoderma* species	[33]
Food processing industry by-products (apple, pomegranate, black carrot, and red beet pulps) as raw materials for SSF. Lab scale incubators.	Pigments	*Aspergillus carbonarius*	[34]
Sequential batch operational strategy for fungal conidia production at bench scale using rice husk and beer draff as substrates. 22 L packed bed bioreactors.	Biopesticide	*Trichoderma harzianum*	[22]
SSF of the mixture sugarcane bagasse/sugar beet molasses used for producing a mixture of value-added fruit-like compounds. Fed-batch, static-batch and intermittent mixing at bench scale.	Fruit-like aromas	*Kluyveromyces marxianus*	[35]
Soybean cake hydrolysate as substrate in SSF and compared to submerged fermentation. Lab scale incubators.	Fumaric acid	*Rhizopus arrhizus*	[36]
Corymbia maculata leaves used as substrate in SSF for high added value product. Lab scale incubators.	Lovastatin	*Aspergillus terreus*	[37]
Soybean residues were used in SSF. SSF carried out in 4.5 L near-to-adiabatic packed bed bioreactors	Bio-flocculants	*Bacillus subtilis*	[38]

Table 1 shows the wide variety of combinations used in SSF to produce selected bioproducts. An important issue that will be treated later in this review is that most studies are performed at a laboratory scale under well-controlled conditions, and there is a lack of studies at larger scales. It can also be observed that fungi have a predominant role in SSF because the solid substrates and lower humidity conditions are more like their natural habitat when compared to SmF. For instance, aerial conidia, which is the primary compound in most fungal biopesticides, can only be produced by SSF [15,22]. Finally, it is expected that there will be an increase in the number of strains and bioproducts and the range of wastes as substrates in the following years, as new strains are isolated that are suitable for SSF systems [39].

3. Emerging Bioproducts from SSF

3.1. Biosurfactants

Biosurfactants refers to surfactants of microbial origin. Like synthetic surfactants, they are composed of a hydrophilic moiety made up of amino acids, peptides, (poly)saccharides, or sugar alcohols, and a hydrophobic moiety consisting of fatty acids. Correspondingly, the significant classes of biosurfactants include glycolipids, lipopeptides and lipoproteins, and polymeric surfactants. In the case of SSF and in submerged fermentation (SmF), this chemical duality is often achieved by the combination of two substrates, the most typical ones being industrial waste lipids (for instance, waste cooking oil or cakes resulting from oil refining) and sugars in different forms [40,41].

Low molecular weight biosurfactants stand out among the large number of biosurfactants recently synthetized and characterized. Consequently, glycolipids, which are conformed by mono-, di-, tri-, and tetra-saccharides in combination with one or more chains of aliphatic acids or hydroxyaliphatic acids, are the most common. They are classified into trehalolipids, mannosylerythritol lipids (MEL), rhamnolipids, and sophorolipids (SL) [42]. Among them, SL, which consist of a hydrophobic fatty acid tail of 16 or 18 carbon atoms and a hydrophilic carbohydrate head sophorose, have been recently reported as biosurfactants that can be produced using SSF in several conditions and in a viable economic way [29], and they are even supplied by several companies, although normally produced by SmF. The use of SL is increasing according to the literature, where the yeast *Starmerella bombicola* is the main reported producer [43]. Sophorolipids, in nature, are produced as extracellular storage and antimicrobial agents. From the industrial point of view, SL can be applied as active components and formulating agents in a wide variety of high-end and bulk applications. Probably, the most reported use is as detergent, although applications in personal care have also been published. Other applications in crop protection, food, biohydrometallurgy, and medical fields are being extensively researched [44].

However, SSF presents some limitations as it involves a three-phase heterogeneous system. Drawbacks related to poor homogeneity and energy and mass transfer may affect the process yield and become more complex downstream [45,46]. Therefore, reactor design and process conditions must be defined taking these limitations into account. In this sense, some models have been suggested for SSF systems, from simplified approaches based on oxygen uptake rate (OUR) to complex 2-D models [47,48]. However, to our knowledge, no specific model for SL production by SSF has been published, as has happened with other bioproducts. Production strategies assayed in submerged fermentation can be adapted to SSF processes using waste as substrate to increase the SL yield [49]. In this sense, Jiménez-Peñalver et al. [41] performed several experiments to produce SL by SSF of oil cake, molasses, and straw (used as bulking agent) inoculated with *S. bombicola*. The maximum yield was higher than 0.2 g of SL per g dry matter in 10 days, when intermittent mixing was applied to aerated packed bed reactors. The authors also observed that the SL yield correlated well with oxygen consumption, which is often observed in solid-state fermentation and composting of organic wastes [50].

Mannosylerythritol lipids (MEL) are other interesting glycolipids that are also produced by yeasts and show excellent interfacial properties and are also being studied for their possible applications in medicine [51]. In a similar way as SL, MEL-producers use oils and sugars as substrates [52]; however, to our knowledge, there are no publications on the production of MEL by SSF.

3.2. Biopesticides

Many microorganisms can produce compounds that are lethal for some typical plagues that are a problem for the cultivation of certain crops. Biopesticides have gained importance in recent years in comparison to traditional chemical products, because of their selective action, biodegradability, and in general, their innocuousness to the environment and food chain. Biopesticides are a group that includes biological control agents for plagues of mainly insects and fungi, and they are produced from a wide number of strains. In the case of SSF using waste as substrate, their development is relatively recent [15]. The reason for this is that not all the biopesticide producing strains are able to thrive in a non-sterile solid-state media. This is the typical case of bacteria, which often grow in synthetic media to produce biopesticides [53]. One of the most worldwide commercialized biopesticides are those produced from *Bacillus thuringiensis* (Bt), which has demonstrated rapid growth and effective sporulation that are key to be predominant in organic waste [21]. *Bacillus thuringiensis* is a gram-positive bacterium consisting of several species that, during sporulation, produce crystal proteins, called delta endotoxins, that have insecticidal action against many plagues [25]. The SSF process to make Bt to produce endotoxins is under study. Recently, it has been demonstrated that, as Bt is a facultative microorganism, it is convenient to include a limiting oxygen step to favor the production of these compounds under SSF conditions using a complex substrate as biowaste digestate as substrate [54,55]. This opens a new line of research to use different SSF conditions to enhance the behavior of bacteria in terms of biopesticide production.

Contrarily to bacteria, fungi are well-known producers of biopesticides, due to their ability to grow under solid-state conditions. In this case, SSF is an optimal environment for the growth and sporulation of biopesticide producer fungi strains. It is also worthwhile to mention that agricultural waste has been also referred as suitable substrates to promote fungi development [56]. In this case, it is also important to note that some strategies to overcome some batch reactors restrictions, such as mass and heat transfer limitations and the continuous production of biopesticide have been already published [22]. As the pure continuous mode of operation is highly complicated in SSF, these strategies consist of sequential batch operation, where other problems such as the need for inoculation and the decrease of porosity are also overcome [22]. Although these results are published for *Trichoderma harzianum*, a well-known fungus for producing biopesticides [57], it is evident that they can be extrapolated to other fungi and toxins of interest. This is the case of other strains, such as *Beauveria bassiana*, *Trichoderma koningiopsis*, or *Metarhizium novozealandicum*, which have been reported as biopesticide producers using solid substrates [58–60], an open field of research to have commercial products.

Another main challenge of biopesticide production from SSF is the downstream process. In this case, a singularity is worthwhile to mention. When the biopesticide has a foliar application, a complex downstream is typically necessary [61]. However, sometimes a compost-like product with biopesticide products is required, whose action mainly occurs in soil, which makes the resulting SSF solid an end product ready to use, given that sufficient stability and maturity is achieved [62].

3.3. Antibiotics

Antibiotics are essential for current health care and food production systems. Antibiotic is a very general term that includes different types of molecules with biocide activity, such as some biosurfactants or biopesticides (described above). The production of antibiotics through SSF has been successfully explored allowing for the use of different solid side streams as substrates and targeting diverse applications. This has been recently reviewed in two excellent works [63,64]. Kumar et al. [63] reviewed the production by SSF of antibiotics, among other secondary metabolites, including natamycin, sambacide, neomycin, and the biosurfactant surfactin. They reported successful SSF processes based on agro-industrial or food wastes. Barrios et al. [64] reviewed lovastatin biosynthesis. Although the mechanism that regulate secondary metabolism is often the same under either submerged or solid-state fermentation, some specific microorganisms display a different physiology in each environment. This is the case for *Aspergillus terreus* that produces lovastatin and shows a superior performance under solid-state fermentation [64]. Fermented oat straw was used as a lovastatin carrier to inhibit methanogenic archaea in the rumen. This allowed for a 38% reduction of methane emissions from beef cattle in in vitro trials [65].

Works on SSF often screen different materials as a substrate as per selection purposes. Al Farraj et al. [66] assessed the antibiotic production by *Streptomyces* sp. AS4 using different wastes, such as wheat and rice bran, apple pomace, or pine and orange peels. Antibiotic production ranged from 43 to 209 U/g influenced by the type of substrate. Wheat bran was the most suitable of the tested materials. In contrast, in a work by Vastrad and Neelagund as reported in [63], *Streptomyces fradiae* preferred apple pomace over cotton seed meal, soybean powder or wheat bran, the last showing the lowest yields for neomycin production. El-Housseiny et al., (2021) [67] assessed paromomycin production with *Streptomyces rimosus* through SSF and compared six different substrates. Corn bran outperformed sugarcane bagasse, sunflower seed meal, soybean meal, barley, and wheat bran. In this case paromomycin production was similar by both SSF and SmF; however, the authors highlighted some advantages of SSF over SmF, such as lower costs, energy consumption, and wastewater discharge.

Beyond nutrient composition, substrates often play the role of support for microbial growth. In this sense, physical properties such as water holding capacity, air porosity, particle size, surface area or rugosity play a key role in biosynthesis. An in-depth analysis of the effect of substrate characteristics including nutrients and physical characterization is required to establish robust industrial production systems for antibiotics or any other secondary metabolite.

3.4. Other Products

The recent boost of SSF research has provoked a proliferation of works published on the use of different typologies of bioproducts. Some of these compounds are still in a development stage and usually the main challenges to solve are scale-up and purification. However, they are of interest in the framework of this review as they intend to substitute for highly impacting chemical process or non-biodegradable products that can remain in the environment with harmful effects.

They are compiled and grouped according to their properties, although each month, the reader can find new products obtained by SSF:

(a) **Aromas and flavors**: this field is especially interesting, as typically synthetic products or natural products (after a costly extraction) are being used in food and other industries. Recently, some works have been published on the synthesis of molecules with aroma properties. This is the case of 2-phenylethanol, widely used in industry due to its rose-like odor and antibacterial properties, which has been produced via SSF using several agro-industrial wastes (mainly bagasses and molasses) inoculated by *Pichia kudriavzevii* and *Kluyveromyces marxianus* [68]. This latter strain and its related SSF process for aroma production has been scaled up to pilot scale using different operation strategies (fed-batch, static-batch, and intermittent mixing) with different productivities, which makes it especially interesting [32]. Other similar products have been focused on the production of fruit-like odor compounds constituted by a mixture of volatile esters [17].

(b) **Bioplastics**: this field has been traditionally related to wastewater research, especially in the case of PHA (polyhydroxyalkanoates) and PHB (polyhydroxybutyrate), which are synthetized from organic components of wastewater as volatile fatty acids generated in the first stage of anaerobic digestion [69,70]. In the case of SSF, several recent references report how to produce these novel materials by SSF, although this is again an emerging technology. For instance, Llimós et al. [18] used lignocellulosic-derived residues to produce lignocellulolytic enzymes from fungal strains through SSF to hydrolyze the same residue to be used for obtaining sugar-rich hydrolysates that serve as an alternative carbon source for PHA production. The same authors provide some interesting issues to consider when scaling up the SSF process using not-isolated and near-adiabatic bioreactors [71]. Other authors have proposed alternative ways of using agrifood by-products in the SSF process, e.g., using dairy processing waste [72] and other materials [73].

(c) **Antioxidants**: this is a property of certain chemicals that is of high value for the food and cosmetics industry, among others. There are different compounds with antioxidant properties, but the most typical ones biologically produced are the family of phenolic compounds [74]. In the case of SSF, there are several publications showing the suitability of certain wastes as a substrate to produce antioxidant phenolic compounds, with waste from olive oil production the most referred [75,76]. Other agricultural wastes, such as fruits- and cereals-derived waste have also been reported in the production of phenolic compounds by SSF [77,78]. The main problem of these publications is that they were normally focused on the characterization and properties of the product, whereas SSF is performed with a few grams in lab scale-controlled conditions, which again hampers its commercial development [79].

(d) Recent literature is full of other specific bioproducts obtained from SSF of selected organic waste (Table 1). This is the case of bio-flocculants [38], pigments [34], or specific compounds [31,36,37]. Although interesting, most of these studies have again been performed at a very small scale.

4. SSF Main Challenges

4.1. Mass and Heat Transfer

Solid-state fermentation presents a principal challenge regarding mass and heat transfer due to the limitations of these two factors in solid organic matter. Both issues are interconnected and cannot be entirely separated for their study and consideration. There are several variables in the process that have an influence on these transfer operations. For instance, temperature of the process has a key role in the heat transfer processes in two main directions: (1) microbial strains often need very specific temperature conditions for their growth and development, hence it is very important to control this parameter efficiently; and (2) the fermentation process produces temperature increases that need to be regulated for a satisfactory process [80]. Heat transmission by conduction in SSF is hindered due to low conductivity of organic solids and the presence of void areas in the reactor. Consequently, convection becomes the most interesting strategy for heat dissipation to avoid heat accumulation in the solid matrix leading to undesired temperature gradients. However, convection through aeration processes entails other problems, like moisture losses and drying of the solid substrate, therefore this method requires to be controlled, and low levels of aeration may be beneficial if compared to strong aerations [81]. There exist other cooling strategies, such as adding water during fermentation, but it requires a mixing device which may not be convenient for some SSF processes using filamentous fungi [82]. Therefore, it is necessary to study the heat dissipation methods which are more convenient in every SSF case and use a proper bioreactor accordingly.

Heat transfer limitations can cause problems in the moisture content of the reactor, which is important for the microorganisms' growth and nutrient diffusion, also related to mass transfer problems [83]. Inefficient sterilization is also a major problem caused by poor heat transfer. It is necessary to avoid the presence of microbes that may become harmful to the process of interest. It is important to mention that not all the sterilization procedures involve the application of heat, for instance the use of chemicals, vapor gas or chlorine gas streams also must deal with mass transfer problems, hence including both transfer operational problems when dealing with sterilization [23].

Several factors can provoke mass transfer problems or vice versa, besides the ones already mentioned. Access to oxygen is essential for the satisfactory development of the microorganisms, hence a proper aeration system becomes very important, including for the removal of carbon dioxide and other volatile substances [54]. Agitation is another useful strategy to address mass transfer issues, and even heat transfer, as it can help to keep more uniform conditions of temperature and gaseous conditions and enhance gas or liquid interface transfer [84]. Mass transfer limitations could hinder another crucial factor regarding microbial growth, the access to nutrients, which can experience a significant improvement by applying aeration and agitation [85]. On the other hand, agitation can harm filamentous fungi as mentioned before, and release nutrients which may cause an increase in microbe activity and hence a heat release [46]. It can also have a negative impact on porosity or deteriorate microorganisms' attachment to the substrate. To solve these issues, both strategies have to be applied, in some cases in an intermittent way [23]. Recent studies claim that new parameters like high granulometry and a low compressibility index of the reactor allow an efficient air flow, which facilitates heat transfer [86].

All the mentioned issues represent an important problem when working at a lab or pilot scale, but they can become the biggest problem when scaling up the process for increased production, which makes it essential to perform an adequate modelling for a proper design and study of a reactor of a bigger dimension [46]. Several attempts to find an adequate model for scaling up SSF reactors can be found in the literature, some of them very recent [80,86]. There are works focusing on the modelling of the economic aspects of the process [29]. However, most of them deal with several parameters to adjust to optimize the production, such as microbial growth or the behavior of the substrate [87]. It is usual to find models performed for a specific type of reactor, as geometry, mass distribution and the type of agitation or aeration directly shape heat and mass transfer. In this sense, tray and packed bed reactors are amongst the most used configurations for SSF processes, and several works have been published on the topic [9,11,88].

Figure 1 shows the main importance and allocation of heat and mass transfer within an entire SSF process in the circular bioeconomy framework.

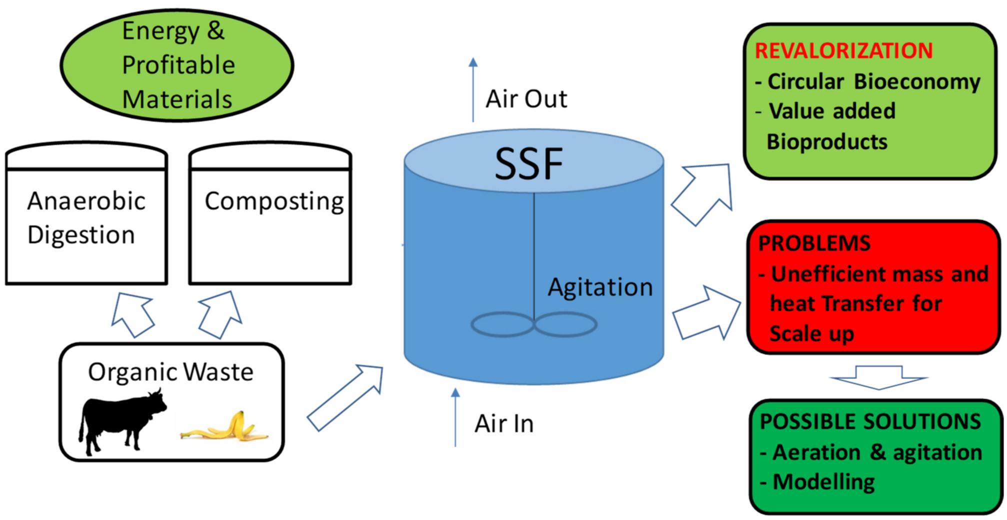

Figure 1. General overview of organic waste revalorization, with a special emphasis on SSF, its problems and possible solutions.

4.2. Bioproducts Recovery and Downstream

In processes based on solid-state fermentation, there is an intrinsic challenge due to the heterogeneity of the materials that implies a complex downstream process [89]. The main challenges of the downstream processes are the related high costs, around 70% of the total cost, jointly with the use of non-environmentally friendly solvents [90]. Documentation of downstream processes of bioproducts others than enzymes obtained by SSF is very limited. Searching in the Scopus® database using the key words "solid state fermentation" AND "downstream" but not including enzymes, resulted in only 37 articles from more than the last 20 years. Even then, most of these articles either just mention downstream but do not deal with it [20] or they focus on the optimization of the extraction method on a small scale [91,92]. For these reasons, this review will be focused on the most common recovery strategies independently of the scale.

The first question that needs to be answered is if the extraction of the bioproducts is necessary. In some applications, the fermented solid can be used as the final product [93]. This way, the need of a costly and environmentally impacting process is avoided. When this approach is not possible, after the extraction of the bioproducts, the exhaust solid becomes a new waste that must be managed. The handling and management of this waste can add costs to the process. Some of the most beneficial strategies are the reutilization of the final solid as animal feed, as substrate for anaerobic digestion, or for composting. This can be also complemented by the coproduction of other low value compounds like proteins and fatty acids from the exhaust solid that make it more valuable [93–95].

When compared to submerged fermentation (SmF), product recovery may become more difficult in SSF as the metabolites diffuse within the solid matrix. The extraction of secondary metabolites, in SSF, mostly implies the use of organic solvents as can be seen in Table 2 [96]. This is because it is an easy technique that has a long history as an extraction method for a wide range of products. However, this method comes with some disadvantages: high cost, due to the use of large volumes of organic solvents, time constraints, solvents remaining in exhaust solid that can cause disposal problems, and toxicity affecting the reusability of the exhaust solid waste [97]. This method also comes with some incompatibilities with health regulations, which can prevent the commercialization of bioproducts destined for human or animal consumption. For this reason, as the knowledge of SSF production for these bioproducts has increased, new techniques that can help reducing the economic and environmental impacts of the extraction process have arisen, such as ultrasound-assisted extraction, microwave-assisted extraction, supercritical fluid extraction, solid-liquid extraction, pressurized liquid extraction, subcritical water extraction, solid-solid extraction, or enzyme-assisted extraction [98]. As most of these new techniques need high power consumption compared to the common solvent extraction, it is necessary to balance performance and power consumption.

For the recovery of bioproducts, the benefits of SSF technology should be preserved during the extraction phase. The selection of an extraction method mostly depends on the characteristics of the product to extract. For example, its thermostability or pH resistance can be factors that reduce some possible options [98]. These restrictions are shared with other downstream processes, but in SSF production the presence of waste materials that introduce a huge variability and heterogeneity to the system must be considered. These wastes can significantly impact the downstream process and reduce the economic benefits of SSF [98,99].

Table 2. Compilation of extraction methods for different bioproducts produced by SSF.

	Bioproduct	Extraction Method	Details	Reference
Biosurfactants	Sophorolipids	Organic solvent extraction	Ethyl Acetate	[100]
	Rhamnolipids	Water extraction	n-Hexane	[101]
	Biosurfactants	Direct use of fermented solid	Also produced lipases	[102]
	Sophorolipids	Organic solvent extraction	Ethyl Acetate	[46]
Biopesticides	*Bacillus thuringiensis*	Enhanced compost		[62]
	Trichoderma Brev	Enhanced soil		[103]
	Trichoderma harzianum	-	Conidia were produced, could be used directly as pesticide	[58]
	Beauveria bassiana	-	Conidia were produced, could be used directly as pesticide	[58]
	Trichoderma asperellum	-	Conidia were produced, could be used directly as pesticide	[10]
	Lysinibacillus sphaericus	Water extraction		[104]
	Bacillus thuringiensis israelensis	Water extraction		[104]

Table 2. *Cont.*

	Bioproduct	Extraction Method	Details	Reference
Bioplastics	Polyhydroxybutyrate	Organic solvent extraction	Multi solvent	[92]
	Polyhydroxybutyrate	Organic solvent extraction	Multi solvent	[105]
	Polyhydroxyalkanoates	Organic solvent extraction		[71]
Aroma	2-Phenylethanol	Water extraction	Filtration	[39]
	2-phenethyl acetate	Organic solvent extraction	Methanol	[39]
	Coconut aroma	Water extraction	Dichloromethane	[106]
	Esters	Organic solvent extraction	Dichloromethane	[107]
	ε-Pinene	Organic solvent extraction	Co-enrichment of spent solid as animal feed	[20]
	Biovanillin	Water extraction	2-Thiobarbituric acid	[31]
	Aroma compounds	Supercritical fluid extraction		[108]
Antioxidants	β-Carotene	Organic solvent extraction	Petroleum ether	[109]
	Antioxidants	Microwave assisted	Water or ethanol	[28]
	Phenolic compounds	Supercritical fluid extraction	Ethanol and water as cosolvents	[110]
	Phenolic compounds	Supercritical fluid extraction		[110]
Other bioproducts	Cordycepin	Solvent extraction	Ethanol, Cellulase assisted	[111]
	Palmitate	Organic solvent extraction	Co-enrichment of spent solid as animal feed	[19]
	Red pigment	Organic solvent extraction	Ethanol	[112]
	Gallic acid	Water		[113]
	Pullulan	Organic solvent extraction	Ethanol	[114]
	Biopigments	Organic solvent extraction	Ethanol	[115]
	6-Pentyl-a-pyrone	Soxhlet	Hexane	[10]
	Phenalenones	Solid-solid extraction	Ethyl acetate	[116]
	Mosquitocidal toxins	Water		[61]
	Secondary metabolites	Organic solvent extraction	Ethyl acetate	[117]
	Bio-flocculant	Water		[38]
	Animal feed	Enhanced properties of feed		[26]
	Arabinoxylans	Water and enzyme assisted	Solvents used to separate compounds.	[30]
	Bioethanol	Dual Vapor Permeation		[32]
	Isoliquiritigenin	Ultrasound extraction	Ethanol	[118]

The purification step is less developed for most of these bioproducts [119]; however, isolating pure natural products from a solid matrix is a demanding process. The typically used silica-packed columns in contact with complex samples of natural origin are problematic due to the possibility of blockage, damage, or irreversible adsorption [100]. The cost of purification depends mostly on the degree of purity required and, while for secondary metabolites, usually a high degree of purity [63,89] is required for their use in the pharmaceutical and health industry, the use of wastes as feedstock may be affected by regulatory issues and public perception.

The stability of bioproducts generated by SSF is an important factor to consider when evaluating the potential of SSF for industrial applications. The stability of bioproducts generated by SSF can be evaluated by measuring the shelf-life, storage stability, and thermal stability of the bioproducts. Additionally, the effects of pH, temperature, and water activity on the stability of bioproducts should also be considered. Studies on enzyme production have shown that SSF can produce bioproducts with high stability and shelf-life [120]. Unfortunately, very little information can be found on less common products.

The last question to be answered on the downstream process is what to do with the consumed solid once the bio-compounds of interest have been extracted. As SSF is usually included in a circular economy mindset, a zero-waste approach is the most logical step. Some of the strategies are presented in Table 2, in which the solid as a whole is used as the product, or the consumed solid is utilized as a feed for composting material or for biogas production [121]. For this to be possible, the extraction method requires various characteristics depending on the use. That is why we think that more focus must be placed on the extraction methods and the compatibility they have with some of the uses formerly addressed.

5. Conclusions and Future Perspectives

This review highlights the most novel and recent applications of SSF to obtain bioproducts using practically all types of organic waste as a substrate. Bioproducts from SSF are of a wide variety and some of them are required to play a key role in the full development of the Circular Bioeconomy. However, given that SSF research is emerging, there is an important lack of studies that, for many presented bench-scale SSF experiments, address and overcome the main challenges for scaled-up production and downstream processes. It is the opinion of the authors that SSF cannot be the name to catalogue experiments carried out in petri dishes using a few grams of substrate and that in order for SSF to become a reliable technology, larger-scale studies have to be conducted to address the issues that have been discussed in this review, and which do not appear at smaller scales, where productivity and yield are the only factors considered.

In the case of organic waste or, in general, solid matrices, its heterogeneity, the need for a proper diffusion of oxygen inside the solid matrix and to avoid the existence of heat accumulation are inherent of any process of SSF.

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