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Integration of *Agave* plants into the polyhydroxybutyrate (PHB) production: A gift of the ancient Aztecs to the current bioworld

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A R T I C L E I N F O

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A B S T R A C T

Agave is a genus of succulent plants distributed throughout the American continent with an important epicenter in Mexico. Since ancient times, these plants have been cultivated and harvested by the Aztec population. Nowadays, *Agave* plants are considered an important income source due to the different applications directed to produce alcoholic beverages, foods, and natural fibers. Likewise, novel biotechnological approaches are investigated to explore the multiple benefits of these plants. In this sense, this review analyzed the incorporation of *Agave* plants derivatives (syrups, carbohydrates, lignocellulosic wastes, and vinasses) into the polyhydroxybutyrate (PHB) production, focusing on reports aimed to enhance the production of this bacterial biopolymer, the improvement of physical properties when PHB and PHBV are blended with *Agave* fibers, the potential benefits of circular economy strategies if were implemented by the rural communities dedicated to the production of this vegetal resource, and the challenges related to the implementation of this technology.

1. Introduction

Agave plants are distributed throughout the American continent, with a strong presence in Mexico (containing 75% of all species). These plants belong to the order Asparagales within the family Agavaceae and are commonly composed of a pine surrounded by large spiral leaves forming a succulent rosette. Some important species are *Agave lechuguilla* (Sonora and Chihuahua), *A. duragensis* (Durango), *A. salmiana* (San Luis Potosí and Zacatecas), *A. tequilana* (Jalisco and Tamaulipas), *A. cupreata* (Guerrero), and *A. angustifolia* (Oaxaca), which are used for the traditional production of alcoholic beverages in several Mexican states (López-Romero et al., 2018a; Nava-Cruz et al., 2015).

Since ancient times, *Agave* plants have been considered sacred by the Aztec population because they represented the goddess "Mayahuel", who brought joy to humanity with the sweet nectar obtained from these plants (López-Romero et al., 2018a; Nava-Cruz et al., 2015; Radding, 2011). Currently, *Agave* plants represent an important economic resource in Mexico due to their diverse applications (Fig. 1). They are used to produce alcoholic beverages (tequila, mezcal, henequén, sotol, and pulque), foods (sugars, syrups, and Mexican stews), and natural fibers (cordage, straw, and basketry). They also have attracted attention because of recent investigations about the extraction and production of novel bioactive compounds such as antioxidants and saponins (Ibarra-Cantún et al., 2020; López-Romero et al., 2018b; Narváez-Zapata and Sánchez-Teyer, 2009), the isolation of new bacterial and yeast strains for the food industry (Narváez-Zapata et al., 2010; Páez-Lerma et al., 2013), and the production of biofuels and biomaterials (Carrillo-Nieves et al., 2019; Palomo-Briones et al., 2017), which means the integration of this vegetal resource into the growing biotechnological industry.

Recently, biotechnological industry has increased the production of a wide variety of biopolymers such as cellulose acetate (CA), polycaprolactone (PCL), polylactic acid (PLA), bio-polyethylene (bio-PE), and polyhydroxyalkanoates (PHAs) (Robledo-Ortíz et al., 2020). The demand for these biomaterials is expected to grow up to 9.45 million tons by 2023, encouraging the population to reduce the use of synthetic polymers and produce biopolymers in a sustainable and circular manner (Reichert et al., 2020). In this case, PHAs have been highlighted because of their biodegradation (which is better than that presented by other biopolymers), the advantage of their production from waste materials (lignocellulosic wastes, dairy wastes, legumes, residual oils, molasses, syrups, and juices), and their potential to enter the global market of bioplastics (Akaraonye et al., 2010; Keshavarz and Roy, 2010; Marciniak

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and Możejko-Ciesielska, 2021; Policastro et al., 2021; Tokiwa et al., 2009).

The PHAs are produced as cytoplasmic granules by several bacterial strains under nutritional and incubation stresses (Mayet et al., 2013; Obruca et al., 2020, 2017). Structurally, they are classified into short-chain-length polyhydroxyalkanoates (scl-PHA), which have 3—5 carbon atoms, medium-chain-length polyhydroxyalkanoates (mcl-PHA), formed by 6—14 carbon atoms, and long-chain-length polyhydroxyalkanoates (lcl-PHA), containing more than 14 carbon atoms. Also, another classification divides PHAs into homopolymers which are composed of one type of monomer unit, and copolymers which are formed by more than one type of monomer unit (Kaur, 2015; Quillaguamán et al., 2010; Sudesh et al., 2000). Within the broad family of PHAs, polyhydroxybutyrate (PHB) is the most characterized scl-PHA. The importance of PHB lies in the fact that it is a versatile biopolymer with biodegradable, biocompatible, and non-toxic properties that can replace polypropylene (PP) and polyethylene (PE) in several areas of human development (Garcia Alcântara et al., 2020; McAdam et al., 2020; Możejko-Ciesielska and Kiewisz, 2016; Pillai et al., 2017). Also, this biopolymer is produced and commercialized by different international companies, such as Biomer (Germany), Bio-On (Italy), BluePHA (China), Tianjin GreenBio Materials (China), Biomatera (Canada), PolyFerm (Canada), Newlight Technologies LLC (USA), Metabolix (USA), and PHB Industrial S.A (Brazil) (González-García et al., 2019; Kourmentza et al., 2017). Notwithstanding, the major bottleneck is the commercialization of PHB due to their high production cost resulting in higher prices compared to petrochemical plastics. According to Mostafa et al. (2020), the universal manufacturing capacity of PHB is approximately 30,000 tons per year (less than 0.1% that PP). Likewise, is reported that the price of PHB is around US$2.25–2.75/lb, while PP and PE cost is ranging between US$0.60–0.87/lb (Flores-Sánchez et al., 2017; Kourmentza et al., 2017; Muhammadi et al., 2015; Nielsen et al., 2017; Saratale et al., 2019) Additionally, PHB applications are still limited because of their high stiffness and brittleness (Robledo-Ortíz et al., 2020).

One of the most promising alternatives to reduce production costs is the use of lignocellulosic biomass for the fermentation process due to its abundance and low-cost (Kumar et al., 2017; Saratale et al., 2021). Previous reports have demonstrated the production of PHB under the influence of non-food tree species (Bowers et al., 2013), kenaf biomass (*Hibiscus cannabinus* L.) (Saratale et al., 2019), and noxious weed water hyacinth biomass (Saratale et al., 2020). The use of lignocellulosic substrates would be a potential solution to economize the production of PHB by at least 25–40%. Also, this process could agree with zero waste

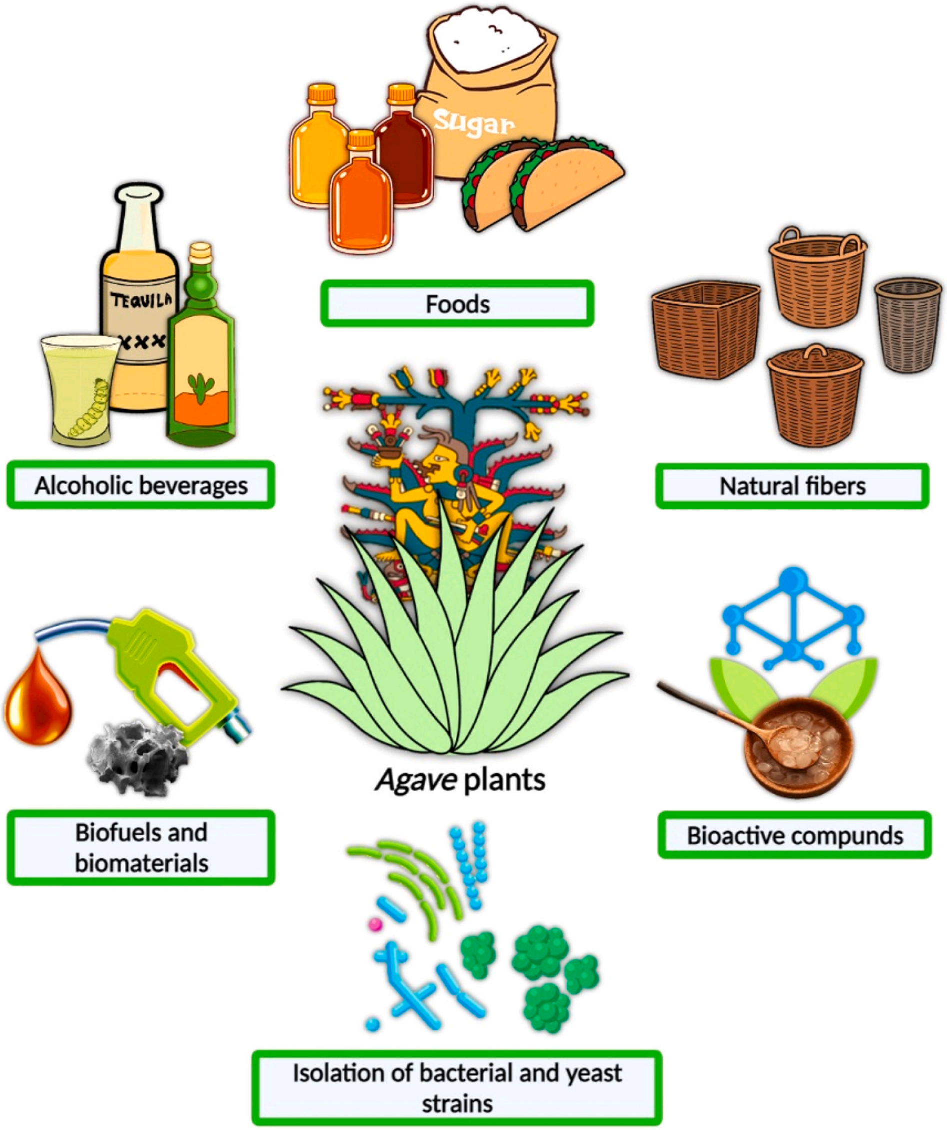

Fig. 1. Products obtained from *Agave* plants.

policies and stimulate the circular economy due to their conversion into value-added products (Saratale et al., 2020, 2019). Likewise, according to Vaidya et al. (2019), lignocellulosic biomass can be blended with PHB to obtain novel composites with better properties. Therefore, these reports demonstrate that the integration of lignocellulosic biomass into the production of PHB is a novel option that could help to reduce production costs.

Since 2015 there has been an accelerated growth in research focused on *Agave* biomass for PHB production. In Mexico, this feedstock is obtained in large quantities from the alcoholic beverage industry (300,000 to 1 million tons are wasted annually) and does not present a specific use. For this reason, *Agave* biomass can be directed as a novel and low-cost substrate for several biotechnological applications (Contreras-Hernández et al., 2018; González-García et al., 2019; Palomo-Briones et al., 2017). In this sense, the objective of this research review was to show the benefits of several *Agave* derivatives (syrups, carbohydrates, lignocellulosic wastes, and vinasses) as potential feedstocks directed to produce PHB and enhance its physical properties in a sustainable and eco-friendly way. In addition, this review analyzes the potential benefits of circular economy strategies if were implemented to improve the socio-economic development of several Mexican communities, and the biological, technological, economical, and social challenges to make this technology a reality in Mexico.

2. *Agave* derivatives for polyhydroxybutyrate (PHB) production

The relationship between *Agave* derivatives and PHB started in the years 2000–2004, but investigations that involve these derivatives for PHB production or physical improvement increased after 2015 (Table 1). For this reason, these investigations are considered novel, with a significant impact on the current development of PHB production. Some of these reports point out that products and by-products, such as fructose-rich syrups, complex carbohydrates, lignocellulosic wastes, and vinasses, obtained from alcoholic beverage and food industries can be used as low-cost substrates for the microbial biosynthesis of PHB (Table 2).

According to Alva and Riley (2008), *Saccharophagus degradans* can use *A. tequilana* bagasse as a lignocellulosic substrate for the microbial production of PHAs. However, it is indicated that an efficient protocol to extract this biopolymer is necessary due to the interference of cellulose remains on the final extract. Afterward, González-García et al. (2019) and Clifton-García et al. (2019) reported that *Burkholderia sacchari* and *Achromobacter mucicolens* can grow and produce PHB under the influence of Tequila *Agave* Bagasse Hydrolysate (TABH), a complex substrate obtained from the acid hydrolysis of lignocellulosic wastes of the tequila industry. This substrate is composed of reducing sugars (20.61 gL^{-1}); especially xylose and glucose, and phenolic compounds (1.70 gL^{-1}). However, it is known that requires a pre-treatment with activated charcoal to purify the presence of antimicrobial agents such as furfural, hydroxymethylfurfural (HMF), leuvinic acid, and formic acid (Bowers et al., 2013; González-García et al., 2019; Panagiotopoulos et al., 2011).

According to Martínez-Herrera et al. (2020), *Bacillus cereus* can efficiently grow and produce PHB under the influence of *Agave* syrup as a carbon source. This syrup stimulates the biosynthesis of PHB due to the high content of fructose ($>$ 60%) and other simple sugars (Velázquez Ríos et al., 2019). Furthermore, the high availability in Mexico (724,000 tons are produced annually) and low-cost (Montañez Soto et al., 2011) make it a potential substitute for glucose in this bioprocess. Likewise, the same authors point out that agavins (complex sugars obtained from *Agave* plants and biochemically characterized as a mixture of highly branched fructans) can be used by *B. cereus* for the biosynthesis of PHB suitable for biomedical applications due to its thermal and crystalline stability. It is important to point out that these products are rich in fermentable sugars and are easily used by the bacterial strain for PHB production. However, the utilization of non-edible substrates is a priority to integrate efficiently zero waste policies to this technology.

Table 1
Investigations that relate *Agave* derivatives and PHB*.

Years	*Agave* derivative used	Type of PHA used or produced	Objective	Reference
2000–2004	*Agave* fibers (*Agave fourcroydes*)	PHBV	Improve physical properties	Luo and Netravali (2001)
2005–2009	*Agave* bagasse (*Agave tequilana*)	PHA	Production	Alva and Riley (2008)
2010–2014	–	–	–	–
2015–2019	*Agave* fibers (*Agave tequilana*)	PHB PHBV	Improve physical properties	Torres-Tello et al. (2017)
	Agave fibers (*Agave sisalana*)	PHB	Improve physical properties	Hosokawa et al. (2017)
	Agave bagasse (*Agave tequilana*)	PHB	Production	González-García et al. (2019)
	Agave bagasse (*Agave tequilana*)	PHB PHBV	Production	Clifton-García et al. (2019)
2020–Present	Fructose-rich syrup and agavins (*Agave tequilana*)	PHB	Production and improve physical properties	Martínez-Herrera et al. (2020)
	Agave fibers (*Agave tequilana*)	PHB	Improve physical properties	Smith et al. (2020)
	Agave leaves (*Agave durangensis*)	PHB	Production	Martínez-Herrera et al. (2021)
	Agave fibers (*Agave tequilana*)	PHB PHBV	Improve physical properties	Gallardo-Cervantes et al. (2021)
	Vinasses (*Agave tequilana*)	PHB	Production	Franco-León et al. (2021)

[*] Original articles were searched through Google scholar, Pubmed, and PMC. PHB: polyhydroxybutyrate (homopolymer), PHBV: poly(hydroxybutyrate-co-hidroxyvalerate) (copolymer).

As we had mentioned above, in Mexico the lignocellulosic biomass obtained from *Agave* processing does not have a specific use and is discarded as agro-industrial waste. These residues are mainly composed of cellulose (42—50%), hemicellulose (11—32%), lignin (11—25%), as well as small amounts of extractive compounds (Contreras-Hernández et al., 2018; Palomo-Briones et al., 2017; Robles-García et al., 2018). This biomass can be pre-treated by physical, chemical, or biological techniques which break down the lignocellulosic structure and increase the release of several substances that triggers the enzymatic activity (Contreras-Hernández et al., 2018). In this sense, Martínez-Herrera et al. (2021) informed that *A. durangensis* leaves (ADL) (a lignocellulosic waste obtained from the artisanal mezcal industry) were physically pre-treated. In this case, was reported that ADL presents a high content of polysaccharides (49.78%), but when were submitted to ultrasound during 30 min or thermic pre-treatment the polysaccharides content was reduced by 31—38%, which makes the substrate flexible and digestible for PHB production. Furthermore, when ultrasonic pre-treatment for 60 min was used on ADL a significant reduction of 88% in the phenolic content was observed, and this allows an increase in the cellular biomass generation by *B. cereus*. These results are explained according to the physicochemical alteration that suffers ADL under the influence of these physical pre-treatments, which triggers a different metabolic response

Table 2
PHB production under the influence of *Agave* derivatives.

Agave derivative	Pre-treatment	Microorganism	Biomass (gL^{-1})	PHB (gL^{-1})	% PHB	Type of PHA produced	Reference
Agave tequilana bagasse	No	*Saccharophagus degradans*	–	1.50	–	PHA	Alva and Riley (2008)
Agave tequilana bagasse (TABH)	Acid hydrolysis and charcoal purification	*Burkholderia sacchari*	11.03	2.67	24.20	PHB	González-García et al. (2019)
Agave tequilana bagasse (TABH)	Acid hydrolysis and charcoal purification	*Achromobacter mucicolens*	2.60	0.23	20.40	PHB	Clifton-García et al. (2019)
Agave tequilana syrup	No	*Bacillus cereus*	5.25	2.96	56.39	PHB	Martínez-Herrera et al. (2020)
Agavins	No		2.57	0.67	25.85	PHB	
Agave durangensis leaves	No		1.68	0.34	20.48	PHB	Martínez-Herrera et al. (2021)
Agave durangensis leaves	Ultrasound for 30 min		1.65	0.66	39.99	PHB	
Agave durangensis leaves	Ultrasound for 60 min		2.18	0.50	22.99	PHB	
Agave durangensis leaves	Thermic pre-treatment		1.77	0.66	37.27	PHB	
Tequila vinasses	No	*Rhodopseudomonas pseudopalustris*	–	0.31	–	PHB	Franco-León et al. (2021)

by the microorganism employed during the fermentation process. It should be noted that the cavitation phenomenon produced by the ultrasonic pre-treatment is responsible for the generation of microbubbles that causes fragmentation in the surface of the lignocellulosic biomass. Moreover, thermal pre-treatments cause a delignification process that generates a reduction in the polysaccharides content (Contreras-Hernández et al., 2018). Therefore, physical pre-treatments are considered efficient for PHB production, highlighting that do not produce antimicrobial compounds.

The most recent study carried out by Franco-León et al. (2021), indicates that *Rhodopseudomonas pseudopalustris* (a purple non-sulfur bacteria) is capable to grow and produce PHB under the influence of a growth medium supplemented with tequila vinasses (a by-product obtained from the tequila industry and considered a pollutant), a low phosphate concentration, and the presence of an argon (Ar) headspace. This bacterial strain is capable to use the high organic acids content in tequila vinasses as a carbon source, which indicates that the metabolic robustness presented by this bacterial strain makes it tolerant to these inhibitory compounds. Hence, it is important to indicate that the *Agave* derivative used as a carbon source, pre-treatments employed, the bacterial strain used for the fermentation process, incubation conditions, and the recovery protocol employed are parameters that affect the production of PHB. Also, it is necessary to continue the research of novel factors that allow the optimal use of *Agave* derivatives to economize production costs and make this biopolymer more competitive in the global market of plastics.

3. Green composites

According to Zagho et al. (2018), a composite is defined as a material structure that consists of at least two macroscopically identifiable materials that work together to achieve a better result. These materials are classified according to the matrix and reinforcement materials that interact. Biocomposites (green composites) are defined as composites made from biodegradable polymers and natural fibers. As mentioned in Section 1, PHB is a natural biopolymer with biodegradable, biocompatible, and nontoxic properties that can replace the use of petrochemical plastics (PP and PE) due to similarities in terms of strength, modulus, and melting temperature (Smith et al., 2020). Nevertheless, its brittleness is considered a limitation, and recent investigations have aimed to propose the production of different PHB composites with lignocellulosic materials (wheat straw fiber, kenaf, coconut fiber, wood flour, bamboo, rice husks, coir husks, pineapple leaves, and hemp hurd) due to their low-costs, renewability, biodegradability, and good mechanical properties (Faruk et al., 2012; Reichert et al., 2020; Robledo-Ortíz et al., 2020).

In this sense, *Agave* bagasse is a lignocellulosic material that has attracted attention because the fibers obtained from this by-product can be blended with PHB and PHBV (principally by extrusion, injection molding, and solvent casting) to obtain green composites with interesting physical properties (Robledo-Ortíz et al., 2020). As shown in Table 3, these composites improve their mechanical and thermal properties due to the increase in flexural strength, impact strength, and degradation temperature (even flexural and impact strengths are higher compared to PHB-PE and PHB-PP blends). On the other hand, tensile strength is reduced because of a decrease in crystallinity (Smith et al., 2020). Moreover, it should be noted that the reports focused on the synthesis of PHB-*Agave* and PHBV-*Agave* composites indicate that biodegradability is not negatively affected, and these composites have the potential to be used and recycled for food packaging and textile applications (Gallardo-Cervantes et al., 2021; Reichert et al., 2020; Smith et al., 2020; Torres-Tello et al., 2017).

Although the PHB-*Agave* and PHBV-*Agave* composites have low stiffness, high flexibility, resistance, and thermal stability, it is necessary to consider the following for their synthesis: (**1**) the *Agave* species used as feedstock for fiber production. In this case, it is necessary to know the lignocellulosic composition of the *Agave* species employed, such as the case of *A. tequilana* which presents a high lignin composition (16—18%) that provides strength to the fiber. Likewise, *A. sisalana* and *A. fourcroydes* present a high content of cellulose (60—88%) and hemicellulose (28%), this composition provides a high mechanical strength to the fiber, but a high hydrophily that can affect the blend with a hydrophobic polymeric matrix (Espino et al., 2014; Sahu and Gupta, 2017); (**2**) the age of *Agave* plant and the extraction method used. These parameters cause a direct effect on the lignocellulosic composition of the fiber which can repercuss on the mechanical properties (Espino et al., 2014); and (**3**) processing technologies. Many manufacturing processes such as extrusion, injection molding, and solvent casting are utilized for the fabrication of PHB-*Agave* and PHBV-*Agave* composites. These methods are highly related to the enhancement of the flexural strength, impact strength, and thermo-resistance of the final biocomposite. However, it is necessary to consider the complexity of the design, the optimal ratio between biopolymer and natural fiber, and capital cost requirements (Mann et al., 2018).

Table 3
Effect of lignocellulosic fibers obtained from *Agave* bagasse as a reinforcement of PHB and PHBV[*].

Type of PHA used	Reinforcement	Composition of PHA: Synthetic polymer (%)	Tensile strength (MPa)	Flexural strength (MPa)	Impact strength (J/m)	Degradation temperature (°C)	Reference
PHB	Polyethylene (PE)	30:70	9.1	14.3	40	–	Rocha and Moraes (2015)
PHB	Polypropylene (PP)	50:50	27.5	–	26.5	–	Pachekoski et al. (2009)
Type of PHA used	**Reinforcement**	**Composition of PHA: Natural fibers (%)**	**Tensile strength (MPa)**	**Flexural strength (MPa)**	**Impact strength (J/m)**	**Degradation temperature (°C)**	**Reference**
PHB	–	100:0	20.5–28.5	29.2	25–30	260–275	Pachekoski et al. (2009) Hosokawa et al. (2017) Seoane et al. (2017) Robledo-Ortíz et al. (2020)
PHB	*Agave* fibers (*Agave tequilana*)	70:30	13.7	36.8	34.4	291	Torres-Tello et al. (2017)
PHB	*Agave* fibers (*Agave sisalana*)	85:15	18.2	38.3	–	281	Hosokawa et al. (2017)
PHB	*Agave* fibers (*Agave tequilana*)	75:25	19.2	39	38	275	Smith et al. (2020)
PHB	*Agave* fibers (*Agave tequilana*)	80:20	12	39	39	–	Gallardo-Cervantes et al. (2021)
PHBV	–	100:0	20.3	28.2	0.85	260–275	Persico et al. (2011) Li et al. (2020)
PHBV	*Agave* fibers (*Agave fourcroydes*)	–	5.24–6.97	–	–	–	Luo and Netravali (2001)
PHBV	*Agave* fibers (*Agave tequilana*)	70:30	15.7	32	41.3	291	Torres-Tello et al. (2017)
PHBV	*Agave* fibers (*Agave tequilana*)	80:20	15	34	56	–	Gallardo-Cervantes et al. (2021)

[*] PHB: polyhydroxybutyrate (homopolymer), PHBV: poly(hydroxybutyrate-co-hidroxyvalerate) (copolymer).

Nowadays, the interest in biocomposites is growing due to their biodegradability and physical properties that can direct them to package, biomedical, and automotive applications (Mann et al., 2018). However, it should be considered that biocomposites produced must certify their quality under the criteria of international and national organizations. According to Bhagwat et al. (2020), International Organization for Standardization (ISO) has established ISO 17088:2012 (specifications for compostable plastics), European Committee for Standardization (CEN) has established EN 14995:2006 (technical specification for the compostability of bioplastics) and CEN/TS 16137:2011 (determination of bio-based carbon content), while the American Society for Testing and Materials (ASTM) has established ATSM D6400-19 (standard specification for labeling of plastics designed to be aerobically composted) and ASTM D5338-15 (requirements for biodegradability). In the case of Mexico, Lara et al. (2020) reported the existence of voluntary guidelines (NMX) related to biomaterials. These rules are intended to serve as guidelines and compliance is generally voluntary rather than mandatory and are based on lineaments established by ISO and ASTM, some of these are NMX-e-232 (plastic identification symbols), NMX-e-233 (recycling terminology), NMX-e-260 (bioplastics terminology), and NMX-e-267 (methods of testing of bio-based plastics). In addition, after 2020 some regulations aimed to ban the commercial sale and use of synthetic plastics were established in several Mexican states. Therefore, policies are still being developed directed to open the door to the production and commercialization of biocomposites, which will be integrated into the Mexican market of plastics soon.

4. Circular economy and rural development

The circular economy is a concept that is gaining strength in the research around PHB production. It is based on applying the 3 R principles: Reduce, Reuse, and Recycle to exploit the waste generation of several industries for creating products in an economical and environmentally sustainable manner (Menon and Lyng, 2021; Tisserant et al., 2017). The dynamics of this concept are centered on three strategies: (**1**) policies for reuse, repair, and remanufacturing; (**2**) green innovation procurement; and (**3**) policies for improving the secondary material markets (Milios, 2017). If these strategies were focused on PHB production under the influence of *Agave* derivatives, we could stimulate the economy of several rural areas in Mexico (Fig. 2).

The cultivation and harvesting of *Agave* plants are carried out by diverse Mexican rural communities in a traditional way. These communities mainly provide their harvest to the industries of alcoholic beverages (tequila and mezcal) and foods (Nava-Cruz et al., 2015; Zizumbo-Villarreal et al., 2012). However, the incorporation of *Agave* plants into the PHB production and the circular economy strategies mentioned above can serve as an alternative to improve the productivity of traditional *Agave* farms, generate a greater availability of jobs, and enhance the socio-economic development of these communities (Osorio et al., 2021; Schroeder et al., 2018). According to Narváez-Zapata and Sánchez-Teyer (2009), if *Agave* plants were re-directed to the production of novel biotechnological products with added value, they could be positioned as an important resource, incorporating new economic benefits for rural communities dedicated to the production of this plant resource. Also, the revalorization of *Agave* by-products from alcoholic beverage and food industries can serve as an alternative to stimulate the production of PHB-based products and biocomposites in an economical way, with easy waste management (Masullo, 2017; Palomo-Briones et al., 2017; Smith et al., 2020; Tsang et al., 2019). Likewise, the search for new markets and the recycling properties of these products can trigger an economic benefit to PHB producer companies and would therefore have an indirect benefit for the alcoholic beverage and food industries as well as the traditional *Agave* producers. In addition, it is crucial to increase the awareness about the sustainable development of the communities dedicated to cultivating and harvesting *Agave* plants, a plant resource that could move the population to a system based on bioeconomy.

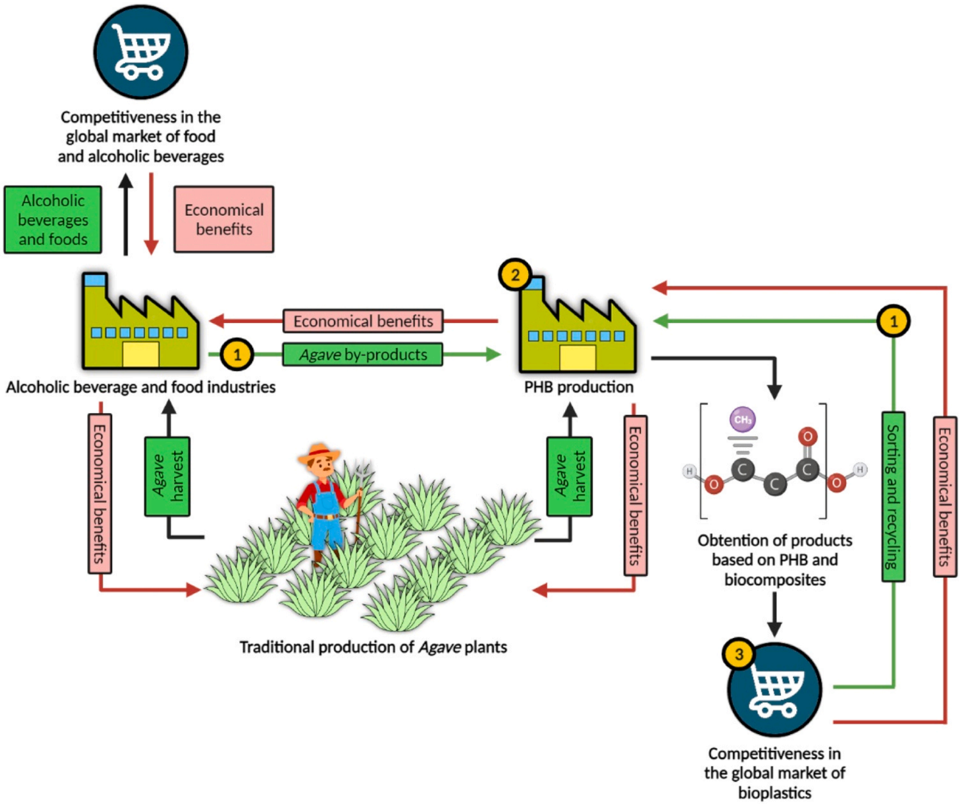

Fig. 2. Proposal of *Agave* plants integration into the PHB production and application of circular economy strategies: (1) Policies for reuse, repair, and remanufacturing; (2) Green innovation procurement; and (3) Policies for improving secondary material markets.

5. Technical challenges to overcome and future perspectives

For the successful integration of *Agave* plants into the PHB production, it is necessary to consider many challenges in different areas (Fig. 3). The first challenge is to consider the biological aspect of this process, since the isolation of novel bacterial strains (bioprospecting) with a metabolic versatility that allows them to uptake *Agave* lignocellulosic biomass as a substrate for PHB production in an efficient way and the use of synthetic biology as a tool directed to the optimal development of industrial strains with clear genomic information, efficient growth capacity on waste substrates, and systems not easily contaminated by other bacteria are an imperative need directed to increase the production of PHB (Saratale et al., 2021). The second challenge is the technological strategies directed to enhance the production of PHB through pre-treatments that allow a better use of *Agave* lignocellulosic biomass by the bacterial strain employed for the fermentation process (Martínez-Herrera et al., 2021). Likewise, optimization of the fermentation process through statistical analysis, improve PHB recovery with protocols that involve a low use of halogenated solvents, and increase the quality of biocomposites PHB-*Agave* and PHBV-*Agave* according to the criteria of international and national organizations (Bhagwat et al., 2020; Rodriguez-Perez et al., 2018). The third challenge is to carry out a techno-economic analysis aimed to analyze the feasibility to include *Agave* derivatives to produce PHB on an industrial scale. For this, it is necessary to contemplate direct costs (raw materials price, operating labor, and utility costs), fixed costs (plant depreciation, taxes, and insurances), and general costs (overheads for maintenance of the plant operations, administrative costs, and development funds) (Levett et al., 2016; Shahzad et al., 2017). Furthermore, a fourth challenge or social challenge is contemplated in this research review due to the ancestral knowledge about *Agave* plants that has been maintained by different Mexican communities. In this case, is necessary to protect the rural communities from “biopiracy”, which is the illegal appropriation of traditional knowledge and biological materials by different groups (Soria-López and Fuentes-Páramo, 2016). For this, it is imperative to encourage the participation of an academic, governmental, and business cluster for the creation of strict laws against “biopiracy” and legislative principles for social integration and technological-scientific development. Likewise, awareness of rural communities about the biotechnological potential and its economic benefits that can arise from the multiple uses of *Agave* plants. Highlighting bioeconomy as an alternative for the creation of biotechnological industries (biorefineries) in conjunction with local *Agave* farmers that could allow a greater availability of jobs and improve their quality of life.

6. Conclusions

Although Mexico and the world are understanding the importance of the biotechnological production of PHB under the influence of different *Agave* derivatives is still necessary to overcome several challenges in different areas before scaling up this technology. Therefore, this research review is a manifesto aimed at the scientific community, and the public and private sectors to encourage the cooperation directed to innovate the use of *Agave* derivatives (especially lignocellulosic biomass) as novel feedstocks with the potential to improve the production of PHB, its physical properties through the manufacture of biocomposites, and move the rural communities to a system based on bioeconomy.

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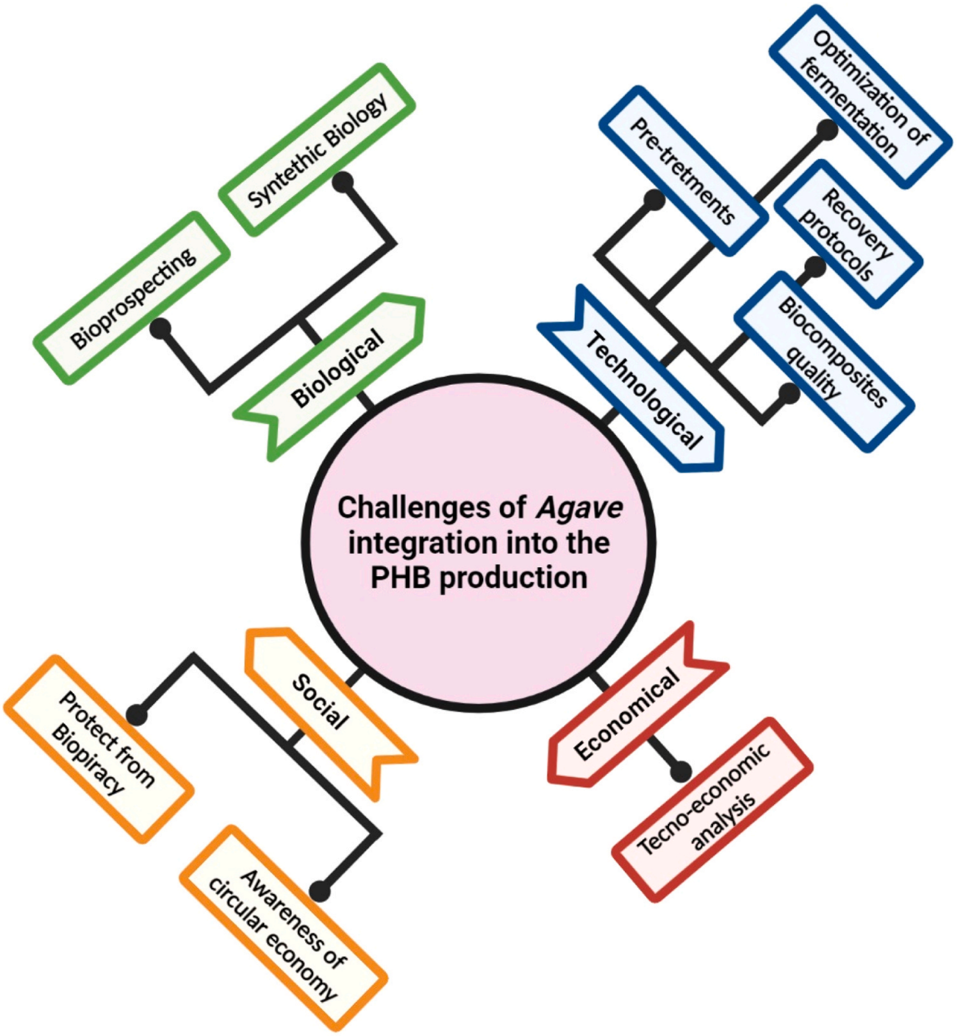

Fig. 3. Biological, technological, economical, and social challenges for the integration of *Agave* plants into the PHB production.

CRediT authorship contribution statement

Raul E. Martínez-Herrera: Conceptualization, Investigation, Writing – original draft, **O. Miriam Rutiaga-Quiñones:** Visualization, Writing – review & editing, **María E. Alemán-Huerta:** Visualization, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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