Recovery of 2,3-Butanediol from Fermentation Broth: A Review

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Abstract: 2,3-Butanediol (2,3-BDO) is a key bio-based platform chemical with wide-ranging applications in fuels, synthetic rubber, pharmaceuticals, and polymer industries. The sustainable production of 2,3-BDO via microbial fermentation of renewable biomass has gained significant attention as an alternative to fossil-based routes. However, the efficient recovery of 2,3-BDO from fermentation broth remains a critical challenge, primarily due to its high boiling point, strong hydrophilicity, and relatively low concentration in aqueous systems. These characteristics render conventional separation processes, particularly distillation, highly energy-intensive and economically unfavorable. This review systematically summarizes the current advances in downstream processing technologies for 2,3-BDO recovery, including distillation, liquid–liquid extraction, gas stripping, adsorption, membrane-based separation, and the emerging salting-out extraction method. The fundamental principles, advantages, limitations, and recent developments of each technique are critically analyzed. In particular, salting-out extraction is highlighted as an effective strategy for enhancing the partitioning of hydrophilic compounds and reducing energy consumption. Furthermore, hybrid separation processes that integrate multiple techniques, as well as in situ product recovery (ISPR) approaches, are discussed for their potential to improve process efficiency and alleviate product inhibition during fermentation. Finally, future perspectives are proposed, focusing on the development of green solvents, advanced membrane materials, and intensified hybrid systems. These innovations are expected to enable more efficient, cost-effective, and sustainable recovery of 2,3-BDO, thereby facilitating its large-scale industrial application within emerging biorefinery frameworks.

Keywords: 2,3-butanediol; Fermentation Broth; Downstream Processing; Salting-out Extraction; Membrane Separation; Biorefinery

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1 Introduction

The growing demand for sustainable chemicals and fuels has accelerated the transition from fossil-based resources to renewable biomass as a feedstock for chemical manufacturing [1–3]. Among various bio-based platform molecules, 2,3-butanediol (2,3-BDO) has emerged as a highly versatile intermediate with broad industrial applications [4]. This diol is widely used as a precursor for the production of hydrogen [5], methyl ethyl ketone (MEK) [6, 7], 1,3-butadiene [8], and various oxygenated fuels and polymers [9, 10]. In addition, 2,3-BDO can serve directly as an anti-freeze agen, liquid fuel additive, solvent, and precursor for synthetic rubber and plasticizers [11]. Because of its structural versatility and multiple downstream conversion routes [12–14], 2,3-BDO is considered an important building block in the development of sustainable biorefineries [15].

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Traditionally, 2,3-BDO was produced through petrochemical pathways; however, increasing concerns over fossil resource depletion and greenhouse gas emissions have stimulated interest in bio-based production routes [16]. Microbial fermentation has become the most promising approach for producing 2,3-BDO from renewable resources [17]. Various microorganisms—including Klebsiella [18], Enterobacter [11], Bacillus [19], and Paenibacillus [20] species—are capable of converting sugars derived from lignocellulosic biomass, starch, or industrial waste streams into 2,3-BDO through well-established metabolic pathways [21]. Advances in metabolic engineering, synthetic biology, and fermentation optimization have significantly improved fermentation performance [22]. In recent years, titers exceeding 100–150 gL^{-1}, yields approaching theoretical limits [23], and productivities above 2–4 g L^{-1} h^{-1} have been reported in laboratory and pilot-scale fermentations. These technological improvements have brought bio-based 2,3-BDO production closer to commercial viability [24].

Despite these significant advances in upstream fermentation technology, downstream recovery and purification remain one of the most challenging and costly steps in the overall production process [25]. The recovery of 2,3-BDO from fermentation broth is particularly difficult due to several intrinsic physicochemical properties of the molecule. First, 2,3-BDO possesses a relatively high boiling point (approximately 180 ℃), which leads to high energy consumption during thermal separation processes such as distillation [26, 27]. Second, the presence of two hydroxyl groups enables strong hydrogen bonding with water molecules, resulting in high miscibility with water and poor volatility. Third, the concentration of 2,3-BDO in fermentation broth is typically limited to tens of grams per liter, meaning that large volumes of water must be processed to recover the product [28]. In addition, fermentation broths contain a variety of impurities—including microbial cells, proteins, organic acids, residual sugars, and metabolic byproducts such as acetoin and ethanol—which further complicate separation and purification processes [29, 30].

As a result of these challenges, downstream processing can account for up to 50–70% of the total production cost of bio-based 2,3-BDO [31]. Conventional recovery methods such as distillation are often energy-intensive and economically unattractive when applied directly to dilute fermentation broths [32, 33]. Consequently, significant research efforts have been devoted to developing alternative separation technologies that can improve energy efficiency and reduce operational costs [34–36]. Various approaches have been investigated, including liquid–liquid extraction [37], gas stripping [38], adsorption [39], membrane-based separations [40, 41], salting-out extraction [42], and integrated hybrid processes [43]. Each of these technologies offers unique advantages and limitations in terms of selectivity, energy consumption, scalability, and compatibility with fermentation systems.

In recent years, particular attention has been directed toward process intensification strategies that combine fermentation and separation steps [44, 45]. In situ product recovery (ISPR) techniques, for example, can continuously remove 2,3-BDO from fermentation broth, thereby alleviating product inhibition and enhancing microbial productivity [24]. Meanwhile, emerging separation technologies such as membrane distillation [46], pervaporation [47], and salting-out extraction [48, 49] have demonstrated promising potential for improving the efficiency of 2,3-BDO recovery.

In this context, a comprehensive understanding of downstream separation technologies is essential for advancing the commercialization of bio-based 2,3-BDO production. This review provides a systematic overview of the current progress in recovery and purification strategies for 2,3-butanediol from fermentation broth. The physicochemical characteristics of fermentation systems and the associated separation challenges are first discussed. Subsequently, conventional and emerging separation technologies—including distillation, solvent extraction, adsorption, membrane processes, and salting-out extraction—are critically evaluated. Finally, future perspectives are proposed regarding process integration, advanced materials, and sustainable separation strategies for efficient recovery of 2,3-BDO within next-generation biorefineries.

2 Characteristics of Fermentation Broth and Separation Challenges

The composition of fermentation broth significantly influences the design of downstream separation processes [25]. Typical fermentation systems contain microbial cells, nutrients, residual sugars, organic acids, and metabolic byproducts such as acetoin and ethanol [50–52]. In addition, fermentation media often contain salts and proteins that can interfere with separation processes.

The concentration of 2,3-BDO in fermentation broth generally ranges from 40 to 120 g L^{-1}, depending on microbial strains and fermentation conditions [53]. Although this concentration is relatively high compared with other bio-based chemicals, it is still far below the level required for direct purification through simple distillation.

Another key challenge arises from the high boiling point and strong hydrophilicity of 2,3-BDO. Due to the presence of two hydroxyl groups, 2,3-BDO forms extensive hydrogen bonds with water molecules. This strong interaction significantly increases the energy demand for evaporation and distillation.

Moreover, fermentation broth contains various impurities that may cause foaming, fouling, and catalyst poisoning during separation and downstream upgrading processes. Therefore, an effective recovery strategy must consider both product separation and impurity removal.

3 Separation Techniques for 2,3-BDO

3.1 Distillation-Based Separation

Distillation is one of the most widely used industrial separation technologies [54–56]. In early industrial processes, 2,3-BDO was primarily recovered by multi-stage vacuum distillation following removal of cells and proteins from fermentation broth [24, 57].

The typical process involves several steps [58]. First, microbial cells and suspended solids are removed by filtration or centrifugation. The clarified broth is then concentrated by evaporation to reduce the water content. Subsequently, vacuum distillation is applied to separate 2,3-BDO from remaining impurities [58, 59].

Although distillation is a mature technology, it suffers from extremely high energy consumption when applied to 2,3-BDO recovery [46]. The high boiling point of 2,3-BDO requires elevated temperatures or deep vacuum conditions, which significantly increases operational costs. Furthermore, thermal degradation of fermentation components may occur during prolonged heating.

To improve efficiency, researchers have explored extractive distillation and reactive distillation [60, 61]. These processes introduce a solvent or reactant to modify the volatility of 2,3-BDO and facilitate separation [62]. However, additional solvent recovery steps are required, which may complicate the process [63–66].

Overall, while distillation remains important for final purification, it is generally combined with other pre-concentration methods to reduce energy demand.

3.2 Liquid–Liquid Extraction

Liquid–liquid extraction (LLE) has been extensively investigated as an alternative method for recovering 2,3-BDO [67]. In this approach, an organic solvent selectively extracts 2,3-BDO from aqueous fermentation broth [68, 69].

The efficiency of LLE depends largely on the distribution coefficient and selectivity of the solvent [70]. Various solvents have been studied, including higher alcohols [71], esters [72], ethers [73], and ionic liquids [74, 75]. Among them, solvents containing polar functional groups tend to exhibit stronger affinity toward 2,3-BDO due to hydrogen-bond interactions [76].

Despite its advantages, traditional solvent extraction faces several limitations. Many organic solvents exhibit low partition coefficients for 2,3-BDO [72], requiring large solvent volumes. In addition, solvent toxicity may inhibit microbial activity if extraction is conducted in situ during fermentation.

3.3 Gas Stripping and Vacuum Evaporation

Gas stripping is another technique used to remove volatile fermentation products from broth [77]. In this process, an inert gas such as nitrogen [78] or carbon dioxide [79, 80] is bubbled through the fermentation medium, carrying volatile compounds into a condenser.

However, 2,3-BDO exhibits low volatility, which limits the effectiveness of gas stripping. As a result, this method is more suitable for removing by-products such as acetoin and ethanol rather than directly recovering 2,3-BDO [81].

Vacuum evaporation has also been explored for concentrating fermentation broth [58]. By lowering the operating pressure, water can be selectively evaporated while retaining most of the 2,3-BDO in the liquid phase. This method can reduce the volume of broth prior to further purification steps.

3.4 Adsorption-Based Separation

Adsorption processes employ porous materials to selectively capture target molecules from aqueous solutions [82]. Various adsorbents, including activated carbon [83–85], polymeric resins [86], and zeolites [87, 88], have been investigated for 2,3-BDO recovery.

Polymeric adsorption resins are particularly attractive due to their high surface area and tunable surface chemistry. Hydrophobic resins can selectively adsorb 2,3-BDO while excluding water molecules [89]. After adsorption, the product can be recovered by solvent desorption or thermal regeneration.

The main advantages of adsorption include low energy consumption and mild operating conditions. However, adsorption capacity and selectivity may decrease in complex fermentation broths due to competitive adsorption of other organic compounds and reactions [6].

3.5 Membrane-Based Separation

Membrane technologies have emerged as promising alternatives for bio-product recovery due to their energy efficiency and scalability [68]. Several membrane processes have been applied to 2,3-BDO separation, including ultrafiltration [90], nanofiltration [53], pervaporation [68], and membrane distillation [46].

Ultrafiltration and microfiltration are commonly used as pretreatment steps to remove microbial cells and macromolecules from fermentation broth. This reduces fouling in downstream separation processes.

Pervaporation has been widely investigated for recovering organic compounds from aqueous solutions [47]. In this process, a selective membrane allows 2,3-BDO to permeate and vaporize on the permeate side under reduced pressure. Polymeric membranes such as polydimethylsiloxane (PDMS) and composite membranes have shown promising separation performance [91].

Nevertheless, membrane fouling and limited flux remain major challenges for large-scale applications [92].

3.6 Salting-Out Extraction

Salting-out extraction has recently emerged as an effective method for recovering highly water-soluble bioalcohols from fermentation broths [93]. This technique is based on the salting-out effect [94–96], a phenomenon in which the addition of inorganic or organic salts decreases the solubility of organic compounds in water, thereby promoting their transfer into a separate organic phase [97]. The effect originates from the strong hydration interactions between salt ions and water molecules [98]. When salts dissolve in water, they compete with organic solutes for water molecules, reducing the ability of water to solvate polar organic compounds such as 2,3-butanediol [99].

For the recovery of 2,3-butanediol, salting-out extraction typically involves the addition of an inorganic salt together with an organic solvent to the fermentation broth [100]. The presence of salt significantly increases the distribution coefficient of 2,3-butanediol between the aqueous and organic phases, resulting in enhanced extraction efficiency [101]. Commonly used salts include potassium carbonate [100, 102], sodium sulfate [69], ammonium sulfate [103–105], and potassium phosphate [100], all of which exhibit strong hydration capacity and pronounced salting-out effects. The organic solvents used in this process are generally moderately polar solvents capable of interacting with 2,3-butanediol through hydrogen bonding or dipole–dipole interactions [30, 106, 107].

One of the major advantages of salting-out extraction is its high extraction efficiency for hydrophilic compounds [108]. Compared with conventional liquid–liquid extraction, the addition of salt can dramatically increase the partition coefficient of 2,3-butanediol [19], thereby reducing the required solvent volume. Moreover, the salting-out process often facilitates rapid phase separation, which simplifies downstream processing and improves operational stability.

Another important benefit of this method is that it operates under mild temperature and pressure conditions [109], making it compatible with fermentation systems and sensitive biomolecules. In some cases, salting-out extraction can even be applied as part of an in situ product recovery strategy, where the product is continuously removed from the fermentation broth to alleviate product inhibition and enhance fermentation productivity.

However, several challenges must be addressed for practical implementation of salting-out extraction [110]. The accumulation of salts in the process stream may lead to increased operational costs and environmental concerns if salt recovery and recycling are not properly managed [111]. In addition, the choice of solvent must consider not only extraction efficiency but also solvent toxicity [33], recyclability [48], and environmental impact. Therefore, future research should focus on optimizing salt–solvent combinations, improving solvent recovery methods, and developing sustainable process configurations.

Despite these challenges, salting-out extraction represents a promising and energy-efficient approach for the recovery of 2,3-butanediol from fermentation broths. When combined with other separation technologies such as distillation or membrane processes, it can serve as an effective pre-concentration step that significantly reduces the energy demand of downstream purification.

3.7 Hybrid and Integrated Separation Processes

Given the inherent limitations of individual separation techniques, hybrid and integrated separation processes have increasingly attracted attention for the recovery of 2,3-butanediol from fermentation broths [4]. In practical systems, no single technology can simultaneously achieve high selectivity, low energy consumption, and economic feasibility. Hybrid strategies combine two or more separation methods to exploit their complementary advantages, thereby improving overall process efficiency and reducing operational costs. Typical integrated schemes involve combinations such as membrane filtration–distillation, extraction–distillation [29], adsorption–desorption, or salting-out extraction coupled with thermal separation.

One promising approach is the integration of solvent extraction with distillation [112]. In such systems, organic solvents selectively extract 2,3-butanediol from the aqueous phase, thereby concentrating the product and reducing the volume of water that must be processed during distillation. After extraction, the organic phase containing 2,3-butanediol is subjected to solvent recovery through distillation or back-extraction. This integrated process can significantly reduce the energy demand associated with direct distillation of dilute fermentation broths.

Overall, hybrid separation systems represent a promising direction for improving the efficiency and economic viability of 2,3-butanediol recovery. By strategically combining complementary technologies [113], it is possible to overcome the limitations of individual methods and develop scalable downstream processes suitable for industrial biorefineries.

4 Conclusion and Outlook

The sustainable production of 2,3-butanediol from renewable biomass has attracted considerable attention as part of the global transition toward bio-based chemical manufacturing. While significant progress has been achieved in microbial fermentation technologies, the efficient recovery of 2,3-butanediol from fermentation broths remains a major challenge due to its high boiling point, strong hydrophilicity, and relatively low concentration in aqueous media. These physicochemical characteristics make conventional separation methods, particularly distillation, highly energy-intensive and economically demanding.

A variety of separation technologies have been explored to address these challenges. Traditional approaches such as distillation remain important for final purification but are generally unsuitable for direct processing of dilute fermentation broths. Alternative techniques—including solvent extraction, adsorption, gas stripping, and membrane-based separations—have demonstrated potential for improving energy efficiency and reducing operational costs. Among these methods, membrane technologies offer advantages in terms of modularity and low energy consumption, while adsorption processes provide selective capture of target molecules under mild conditions.

More recently, salting-out extraction has emerged as a particularly promising strategy for recovering water-soluble bioalcohols such as 2,3-butanediol. By introducing inorganic salts that strongly hydrate with water molecules, the solubility of organic compounds in the aqueous phase is significantly reduced, promoting their transfer into an organic solvent phase. This method can dramatically enhance extraction efficiency while maintaining relatively low energy requirements. When combined with solvent recovery or distillation, salting-out extraction provides an effective route for pre-concentrating 2,3-butanediol prior to final purification.

Despite these advances, several challenges remain before large-scale industrial implementation can be realized. First, the development of highly selective and environmentally benign solvents is essential for improving extraction performance while minimizing toxicity and environmental impact. Second, advanced membrane materials with improved permeability and antifouling properties are needed to enhance the stability and long-term performance of membrane-based separation processes. Third, effective strategies for salt recovery and recycling must be established in salting-out systems to reduce operational costs and environmental burdens.

Another promising direction lies in the integration of fermentation and downstream separation through process intensification strategies. In situ product recovery technologies can continuously remove 2,3-butanediol during fermentation, alleviating product inhibition and increasing productivity. Coupling fermentation with advanced separation processes such as membrane extraction, adsorption, or salting-out extraction could significantly improve the overall efficiency of the production process.

Looking forward, the future development of 2,3-butanediol recovery technologies will likely focus on hybrid separation systems, advanced functional materials, and integrated biorefinery concepts. By combining innovations in fermentation engineering, separation science, and process design, it will be possible to establish economically viable and environmentally sustainable production pathways for bio-based 2,3-butanediol. Such advancements will play an important role in enabling the large-scale deployment of renewable chemicals and fuels in the emerging bioeconomy.

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