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Separation and purification of bromelain from pineapple residue using ultrafiltration membranes: a review

Separação e purificação da bromelina do resíduo de abacaxi utilizando ultrafiltração com membranas: uma revisão

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Abstract
Pineapple is the most popular fruit globally, whose production increased in the last years, raising concerns about the reuse of the waste. Bromelain constitutes an attractive byproduct for various industrial sectors. Ultrafiltration (UF), widely applied in macromolecule retention processes, faces significant challenges such as fouling, which limits its effectiveness. This article reviews strategies to improve permeate flow and control fouling during bromelain recovery from pineapple residues. Prominent strategies for improving UF performance include gas sparging, vibratory or rotational modules, and pre-treatment processes like diafiltration or enzymatic treatment. While gas sparging enhances turbulence and flow, its energy efficiency is limited. Integrated approaches, such as combining MF and UF or utilizing two-stage UF systems, achieve high bromelain recovery (over 94%) and effective fouling control. Strategies involving turbulence promoters enhanced permeate flux by over 40%, while fouling mitigation techniques reduced fouling rates by up to 80%, preserving enzyme activity. These findings suggest that advancements in module design, pre-treatment processes, and turbulence-inducing systems can significantly enhance UF performance, offering promising directions for industrial bromelain recovery.
Keywords: Activated carbon. Bromelain. Membrane. Pineapple waste. Ultrafiltration.

Resumo
O abacaxi é a fruta mais popular globalmente, cuja produção aumentou nos últimos anos, levantando preocupações sobre o reaproveitamento dos resíduos. A bromelina constitui um subproduto atrativo para diversos setores industriais. A ultrafiltração (UF), embora amplamente utilizada para a retenção de macromoléculas, enfrenta desafios significativos, como a incrustação, que limita sua eficácia. Este artigo revisa estratégias para melhorar o fluxo de permeado e controlar a incrustação durante a recuperação de bromelina a partir de resíduos de abacaxi. Estratégias proeminentes para melhorar o desempenho da UF incluem aeração com gás, módulos vibratórios ou rotacionais e processos de pré-tratamento, como diafiltração ou tratamento enzimático. Embora a aeração com gás aumente a

turbulência e o fluxo, sua eficiência energética é limitada. Abordagens integradas, como a combinação de microfiltração (MF) e UF ou o uso de sistemas de UF em duas etapas, alcançam altas taxas de recuperação de bromelina (acima de 94%) e controle eficaz da incrustação. Estratégias envolvendo promotores de turbulência aumentaram o fluxo de permeado em mais de 40%, enquanto técnicas de mitigação de incrustações reduziram as taxas de incrustação em até 80%, preservando a atividade enzimática. Esses resultados sugerem que avanços no projeto de módulos, nos processos de pré-tratamento e em sistemas que induzem turbulência podem melhorar significativamente o desempenho da UF, oferecendo direções promissoras para a recuperação industrial de bromelina.
Palavras-chave: Carvão ativado. Bromelina. Membrana. Resíduo de abacaxi. Ultrafiltração.

*On behalf of all authors, the corresponding author states that there is no conflict of interest.

Nomenclature
UF Ultrafiltration
MF Microfiltration
RME Reverse Micellar Extraction
MWCO Molecular Weight Cut Off
ATPS Aqueous Two-Phase System
PEG Polyethylene Glycol
PVDF Polyvinylidene Fluoride
GO Graphene Oxide
BSA Bovine Serum Albumin
NIPS Nonsolvent-Induced Phase Separation
PES Polyethersulfone
PANI Polyaniline
FRR Flux Recovery Ratio
IFR Irreversible Fouling Ratio
SCH-NPs Sulfonated Nanoparticles
PVC Polyvinyl Chloride

1. Introduction

In September 2015, the United Nations introduced the 2030 Agenda for Sustainable Development, which delineated 17 objectives covering a total of 169 targets aimed at poverty eradication and the establishment of an environment conducive to societal well-being while respecting the limits of the planet. Among these objectives, particular emphasis is placed on Goals "Industry, Innovation, and Infrastructure" and "Sustainable Consumption and Production". The global goal by 2030 is to instigate a transition to more sustainable industries, enhancing resource efficiency, fostering innovation, adopting environmentally friendly industrial technologies and processes, and substantially curtailing waste generation through intricately interwoven measures of prevention, reduction, recycling, and reuse (ONU, 2024). Previously underutilized agroindustrial waste, traditionally relegated to applications like animal feed and fertilizers, is now recognized as a reservoir of valuable constituents. In the realm of food processing, these residues comprise trimmings of fruits and vegetables, peels, stalks, seeds, and assorted materials (Seguí and Maupoey, 2018).

In this context, pineapples emerge as a compelling subject of study owing to their status as among the most prolific generators of solid waste in the production spectrum—whether from fresh cutting or fruit juice extraction. It is estimated that approximately 50% of the pineapple constitutes what is commonly termed industrial waste, encompassing the stem, crown, leaves, and peel (Roda *et al.*, 2016). This waste reservoir harbors within a diverse array of high-value substances with significant exploitative potential, including cellulose (insoluble fiber), simple sugars, and foremost among them, bromelain.

Pineapples (*Ananas comosus*), belonging to the Bromeliaceae family, represent a globally favored fruit, characterized by continual production growth over successive years, a trend that engenders escalating concerns regarding waste management (Nor *et al*., 2015). Bromelain, a proteolytic enzyme extracted from pineapples, has diverse industrial applications, including cosmetics, food, and pharmaceuticals. Its potential arises from its pharmacological and functional properties. Despite its initial characterization as an enzyme blend, bromelain scope now extends to encompass any protease extracted from Bromeliaceae family members.

Bromelain intrinsic proteases - cysteine endopeptidases that catalyze the hydrolysis of the N-terminal amino acid peptide bond with an amino group at one terminus - incorporate a diverse range of compounds encompassing glycosidases, phosphatases, ribonucleases, cellulases, peroxidases, and glycoproteases primarily targeting alanyl, leucyl, and glycyl bonds (Colletti *et al*., 2021). The dynamic composition of these enzymes is subject to numerous influencing factors, including fruit geographic origin, soil type, cultivation practices, extraction methodologies, and notably, the specific plant part subjected to extraction. Consequently, bromelain enzymatic activity is inherently contingent upon the botanical source within the pineapple plant, with molecular weights spanning 20 to 31 kDa and isoelectric points ranging from 4.6 to 10 (Novaes *et al*., 2016). Noteworthy studies reveal that the predominance of bromelain in pineapple stems (EC 3.4.22.32) contrasted against other fruit components, harbors an isoelectric point of 9.5, as opposed to the comparatively scarce distribution of bromelain in the fruit pulp (EC 3.4.22.33) characterized by an isoelectric point of 4.6 (Novaes *et al*, 2016; Arshad *et al*., 2014).

The escalating interest in bromelain stems predominantly from its pharmacological applications, manifesting in anti-inflammatory, anti-edematous, anticoagulant, anticancer properties, and diverse utilizations across cosmetic, meat processing, meat tenderization, and beer clarification industries (Colletti *et al*., 2021; Arshad *et al*., 2014). Commercial bromelain production entails a multistep process spanning extraction, purification, drying, and powder packaging. Of these stages, purification emerges as a pivotal juncture significantly influencing the enzymatic activity of the final product. Consequently, after extraction, purification stands as the most labor-intensive and cost-consuming facet of bromelain processing, prompting the development of multifaceted methodologies such as ion exchange chromatography, reverse micellar extraction, ammonium sulfate fractionation, aqueous biphasic systems, and membrane filtration techniques (Nor *et al*., 2015; Abreu *et al*., 2019). Among these, membrane filtration methodologies spotlight ultrafiltration as a recurrent theme within the academic discourse, owing to its scalable attributes. Nevertheless, challenges persist in the form of permeate flow instability and fouling susceptibility, hindering the widespread implementation viability of this technique (Simões *et al*., 2022).

Although significant advances in ultrafiltration (UF) for bromelain purification have been extensively studied, critical gaps remain, particularly in understanding the interactions between membrane types, modular configurations, and fouling control strategies for large-scale applications. Current literature often focuses on isolated studies that fail to comprehensively address the combined impacts of different pre-treatment methods and emerging technologies on permeate flux efficiency and enzyme recovery. Furthermore, few works assess the economic feasibility and scalability of proposed solutions, limiting their industrial adoption. This review aims to address these gaps by providing an in-depth analysis of UF configurations used for bromelain purification, emphasizing strategies to enhance permeate flux, mitigate fouling, and evaluate the scalability and integration potential of these approaches.

2. Strategies for improving flow and fouling control for ultrafiltration applied in the dairy industry and water treatment

Ultrafiltration (UF) is one of the membrane filtration methods commonly used to concentrate proteins, yielding favorable outcomes both at the laboratory and industrial scales. These membranes have an average pore diameter ranging from 10 to 100 Å, with protein, colloid, and macromolecule retention being governed by the differences in their respective molecular weights, resulting in a Molecular Weight Cut-Off ranging from 3 to 100 kDa (Novaes *et al*., 2016; Baker, 2004). While this process finds widespread application in the dairy industry and water treatment, various physicochemical properties can influence the separation efficiency, such as the isoelectric point of components in the feed, membrane characteristics like hydrophobicity and roughness, and the ionization constant itself (Novaes *et al*., 2016).

Fouling susceptibility is a significant issue affecting the implementation of UF in various purification processes. Concentration polarization, and subsequent fouling, prolonged operation times, and frequent halts for physical or chemical cleaning are commonly cited drawbacks in the literature (Arshad *et al*., 2014). The pressure difference applied to the process itself can lead to the agglomeration of sugars, polysaccharides, and proteins present in the feed, resulting in concentration polarization, potential membrane fouling, pore constriction, and blockages leading to a reduction in permeate flow (Abreu *et al*., 2019; Polyakov and Zydney, 2013).

In this regard, several strategies have been explored to alleviate these challenges, including additional steps prior to UF processing, such as diafiltration, enzymatic treatments, coagulation, addition of nanoparticles to the feed, integrated processes with UF like reverse micellar extraction (RME), aqueous two-phase system (ATPS), as well as modifications to the membrane itself by incorporating nanomaterials and utilizing turbulence promoters in the feed. Table 1 succinctly summarizes these studies and the key strategies identified in the literature.

It is important to emphasize that most of the strategies mentioned may result in increased energy consumption for the plant and may even decrease the lifespan of the membranes. Among the pre-treatments commonly used in UF processes, coagulation is the most practical and successful, offering low cost and ease of application. This pre-treatment promotes the adhesion of suspended particles, colloids, and high molecular weight foulants, forming large flocs that will reduce the deposition of matter on the membrane surface (He *et al*., 2022; Ruígomez *et al*., 2022). This strategy is primarily used in water treatment, as once the organic content adheres to the floc, it becomes difficult to recover. Furthermore, depending on the coagulant used, there may be denaturation of organic matter, impeding its recovery and reuse in other industrial sectors.

Regarding the physical and chemical cleaning methods of the modules, membrane relaxation and backwashing are simple and effective methods to eliminate loosely adhered foulants on the surface or even inside the membrane pores. However, in recent studies, these strategies have been combined with turbulence promoters, such as air/gas spraying or dynamic shear improvement membranes, aiming to enhance module cleaning and reduce external residual fouling caused by foulants that are more strongly adhered to the membrane (Dattabanik *et al*., 2022; Ruígomez *et al*., 2022). The addition of chemicals during backwashing can also prevent the consolidation of organic and inorganic matter on the membrane surface, particularly recommended for long-duration operations and in the presence of foulants that form strong chemical bonds with the membrane structure.

The use of turbulence promoters, such as dynamic shear improvement membranes, is increasingly being explored in ultrafiltration processes. The incorporation of these systems creates high shear rates that help control fouling in the module. Unlike air/gas spraying, where a large part of the energy is dissipated in bubble formation, in rotation and vibration systems, shear forces are specifically formed in the vicinity of the membrane, enhancing the physical cleaning of the module (Ruígomez *et al*., 2022).

Table 1: Summary of the strategies, membrane polymer and module configuration to address membrane fouling related to milk processing and water reclamation by means of ultrafiltration.

Strategy	Membrane	Module configuration	Feed	Reference
Incorporation of nanobubbles into the feed	Polyethersulfone with MWCO of 10 kDa	Flat membrane with cross-flow filtration	Milk concentrate dispersion	Babu and Amamcharla (2023)
Addition of turbulence promoter "wire-type"	Polyvinylidene fluoride with MWCO of 50 kDa	Dynamic shear enhancement (DSE) module, using rotating basket filtration	Eluent from the dairy industry and synthetic solution of bovine serum albumin	Dattabanik *et al.* (2022)
Coagulation followed by Ultrafiltration	Polyvinylidene fluoride with MWCO of 100 kDa	Flat membrane with dead-end filtration	Synthetic solution of humic acid	He *et al.* (2022)
Addition of g-C_3N_4 and Bi_2MoO_6 nanoparticles to the membrane	Polysulfone with MWCO of 84.4 kDa	Flat membrane with cross-flow filtration	Synthetic solution of bovine serum albumin	Meng *et al.* (2021)
Use of rotating hollow fiber ultrafiltration modules combined with a coagulation step as pre-treatment and membrane relaxation during the backwash step	Commercial Hollow fiber	Hollow fiber membranes in dead-end configuration	Wastewater effluent with high colloidal content and non-biodegradable organic matter	Ruígomez *et al.* (2022)
Addition of iron oxide nanoparticles decorated with functionalized graphene oxide nanosheets with carboxyl groups	Polysulfone	Hollow fiber module	Synthetic solution of lysozyme, trypsin, pepsin, human serum albumin, γ-globulin, and human fibrinogen	Modi and Bellare (2019)

Ruígomez *et al*. (2022) studied a dynamic membrane system with improved shear using a rotating hollow fiber module consisting of 97 fibers with a surface area of 0.047 m2, in the treatment of wastewater for domestic water consumption. The authors also evaluated the best configuration for applying coagulation as a pre-treatment (in-situ ex-situ), as well as analyzing the appropriate rotation speed and the best relaxation time to increase module cleaning efficiency. Authors concluded that performing the coagulation pre-treatment ex-situ in an external chamber was the best way to carry out the pre-treatment, as it prevented the breakage of generated flocs and the release of foulants during the UF process. Moreover, increasing the rotation during the physical backwashing step to 260 rpm was effective in eroding and redistributing external fouling residues on the membrane surface. As for the relaxation step, using a 180-second break allowed for relaxation and reduction of shear caused by module rotation, improving foulant redistribution. Overall, the authors obtained good results for moderate concentrations of organics in the feed, achieving a permeate flow of 24 L.h-1.m-2.

He *et al*. (2022) adopted a dead-end configuration in UF with a transmembrane pressure of 0.1 MPa, also applying a coagulation step prior to filtration to retain humic acid present in natural waters and reduce fouling risk. The study evaluated the application of the technique in water treatment, where the aluminum hydrolysis on the floc surface formed during coagulation reduced the interaction between the foulant and the membrane, contributing to fouling control. It is worth noting that although this strategy significantly reduced fouling and increased permeate flow, if applied for bromelain recovery, it could result in protein denaturation and loss of activity.

Babu and Amamcharla (2023) further studied the effects of introducing nanobubbles into the milk concentrate feed to improve flow and reduce fouling. Authors compared the results with a control feed without nanobubbles. By incorporating nanobubbles, there was an improvement in permeate flow, using a flat membrane module with a constant transmembrane pressure of 0.2 MPa, achieving a maximum of 14.57 kg.m-2h-1 and a minimum of 9.59 kg.m-2.h-1, while in the control feed, the maximum flow was 9.27 kg.m-2.h-1 and 6.89 kg.m-2.h-1. Images of the membrane surface after processing in the control system showed an accumulation of encrusted particles on the membrane and the formation of a thick, dense layer on its surface, indicating that the incorporation of nanobubbles in the feed is a valid strategy in UF systems aiming for protein retention and contributing to reducing the system apparent viscosity. Regarding pump energy consumption, incorporating nanobubbles into the feed significantly reduced energy requirements, showing a 20% reduction after 1 hour of operation compared to the control system. The difference in energy consumption can be explained by the decreased apparent viscosity of the system caused by the insertion of nanobubbles, reducing the energy demand for pumping the system.

Dattabanik *et al*. (2022) tested a dynamic shear enhancement module using flat UF membranes in a rotating basket for treating dairy industry effluents. A simple "wire-type" turbulence promoter was used in both real effluent and a synthetic aqueous solution containing bovine serum albumin. In the real effluent, there was a 204% improvement in permeate flow, although fouling was still pronounced due to the presence of casein micelles in the feed. In the synthetic solution, on the other hand, the permeate flow increased by 445% and fouling was significantly reduced. Regarding energy consumption, adding turbulence promoters to the system only increased total energy expenditure by 9% while bringing significant improvements in flow and fouling, increasing shear and kinetic energy on the membrane surface and contributing to fouling reduction.

Continuing efforts to reduce fouling inherent in ultrafiltration processes, Meng *et al*. (2021) introduced graphene-like g-C3N4 carbon nitride nanoparticles and bismuth molybdate (Bi2MoO6) nanoparticles into polysulfone membranes, aiming for a self-cleaning functionalization on the UF membrane surface to alleviate possible irreversible fouling. In this case, the g-C3N4 nanosheets decorating the Bi2MoO6 surface improved the photocatalytic performance in the degradation of bovine serum albumin under visible light, removing irreversible fouling. Additionally, the permeate flow recovery obtained by the authors was 82.53% with 95% rejection of albumin, indicating good results in applying wastewater treatment for effluents with high organic matter concentrations.

Modi and Bellare (2019) evaluated the addition of iron oxide nanoparticles decorated with carboxylated graphene oxide nanosheets in hollow fiber polysulfone membranes for the separation of proteins - lysozyme, trypsin, pepsin, human serum albumin, γ-globulin, and human fibrinogen. The composite membranes obtained showed high pure water flux, approximately 110 L.m-2.h-1, and high flow recovery (above 97.8%). The proteins considered had rejection rates above 94%, indicating effective performance of the modified hollow fiber UF membranes with nanoparticles and the feasibility of application in the separation of biomolecules in food and pharmaceutical industrial sectors.

3. Strategies for improving flow and fouling control for ultrafiltration applied to the recovery of bromelain

Regarding the use of ultrafiltration applied to the purification of bromelain, it is important to emphasize that a direct comparison between the results obtained in each study is not an easy task, due to the divergences between the initial feeding and operating conditions. In this context, the present work will explore a qualitative comparison of the effectiveness of each strategy adopted by each author to increase permeate flux and reduce fouling, evaluating the percentage of bromelain activity recovery. Discrepancies between the results can be found, mainly due to the variations between the pineapples used in the studies, such as the geographical location of each plant and its agricultural management, which is influenced by climate, soil, and lighting levels that affect the metabolism of the plant (Nor *et al*., 2016).

Regarding the application of UF for bromelain purification, some restrictions on operating conditions are found in the literature, such as differences in transmembrane pressure ranging from 0.5 to 4 bar, temperature and pH ranges between 10 and 30°C and 4 and 8.5, respectively, and the absence of corrosive components involved in the process (Nor *et al*., 2018). Table 2 briefly presents which strategies are commonly found in the literature for bromelain purification, maintaining adequate activity levels and high protein recovery.

Table 2: Summary of the strategies, membrane polymer and module configuration to recover bromelain from pineapple juice and residues by means of membranes.

Strategy	Membrane	Module configuration	Feed	Reference
Microfiltration followed by Ultrafiltration	Millipore Amicon with MWCO of 10 kDa	Flat membrane with cross-flow filtration	Pineapple juice	Gamarra *et al*. (2022)
Two stages Ultrafiltration	ZrO ceramic membrane with MWCO of 75 kDa (1st stage) and 10 kDa (2nd stage)	Tubular membranes with cross-flow filtration	Crude pineapple residue	Nor *et al*. (2016)
Diafiltration and enzymatic pre-treatment	ZrO ceramic membrane with MWCO of 75 kDa (1st stage) and 10 kDa (2nd stage)	Tubular membranes with cross-flow filtration	Crude pineapple residue	Nor *et al*. (2018)
Reverse Micellar Extraction integrated with ultrafiltration	Cellulose acetate with MWCO of 5 kDa	Flat membrane with cross-flow filtration	Pineapple juice	Hebbar *et al*. (2012)
Ultrafiltration, aqueous two-phase system, and ultrafiltration integrated with aqueous two-phase system	Millipore Amicon with MWCO of 100 and 3 kDa	Flat membrane with cross-flow filtration	Pineapple residue	Simões *et al*. (2022)

Gamarra *et al.* (2022) evaluated the influence of pH and transmembrane pressure difference on the recovery of bromelain obtained from pineapple juice using a microfiltration (MF) system followed by ultrafiltration, considering two different configurations in the MF: flat membrane and hollow fiber in cross-flow. A lower permeate flux was obtained for low pressure values due to concentration polarization and consequent fouling, which decreased the diffusion coefficient through the membrane. The system using flat MF and UF membranes yielded the best result, with a recovery of 85-87% of bromelain in the MF and 100% in the UF.

The addition of a prior RME step to UF carried out by Hebbar *et al.* (2012) in the purification of bromelain from pineapple juice using a flat membrane model with a transmembrane pressure of 1 bar, contributed to increasing the recovery and purification factor of the protein, obtaining at the end of RME a recovery of activity of 95.8% and a purification factor of 5.9, after UF the purification factor increased to 8.69. Comparing the results of RME with ATPS (activity recovery of 93.1% and purification factor of 3.2) and conventional precipitation with ammonium sulfate (activity recovery of 82.1% and purification factor of 2.5) indicated the superior performance of RME as a prior step to UF.

On the other hand, Simões *et al.* (2022) further explored the performance of bromelain purification from pineapple residue through UF, ATPS, and the integration of both techniques, using a flat membrane module. ATPS achieved a bromelain recovery of 18.5% using PEG at a pH of 7.5 as extractant, while UF revealed a recovery of 93.2% at pH 6.5, whereas the integration of processes achieved a recovery of only 14.1%, demonstrating poor performance for bromelain recovery using a biphasic aqueous system prior to UF.

Nor *et al.* (2016) used a two-stage ultrafiltration system with ceramic tubular membranes for the purification of bromelain from crude pineapple residue, mainly evaluating the permeate flux. In the first stage, a recovery of 96.8% of bromelain and a permeate flux of 11.6 kg.m-2.h-1 were obtained, while in the second stage, the enzyme purity could be increased by 2.5 times and the permeate flux obtained was 6.2 kg.m-2.h-1. It was also determined that high VRF (volume reduction factor) values in stage 2 lead to higher enzyme purity retention, however, there was a greater loss of protein activity under these conditions, suggesting a cross-flow velocity lower than 7.5 m.s-1 during the process or changing the MWCO of the membrane to a value lower than 10 kDa.

In a subsequent work, Nor *et al.* (2018) evaluated the use of enzymatic pretreatment, with pectinase, cellulase, and a combination of both, combined with a diafiltration step between stages 1 and 2 of ultrafiltration to reduce the apparent viscosity of the system and thus decrease fouling risk, increasing permeate flux. The authors obtained a 12% reduction in the apparent viscosity of the feed using pectinase in the enzymatic treatment, while the flux increased by 37-38% in both UF stages. The pretreatment likely prevented the formation of a thick fouling layer on the membrane surface, resulting in higher enzymatic recovery in stage 1. Meanwhile, the introduction of diafiltration in stage 2 of UF helped maintain high flux values while increasing the bromelain purification factor by 4.4 times, higher than the purity achieved in Nor *et al.* (2016). However, a large volume of diluent was needed to achieve these results.

4. Emerging Technologies and Scalability

Emerging technologies, such as bio-based membranes and nanocomposites, are promising alternatives for enhancing ultrafiltration processes, particularly in fouling control and protein recovery. Bio-based membranes offer advantages like biodegradability and higher environmental compatibility, while nanocomposites provide specific properties such as enhanced mechanical strength, antimicrobial activity, and mitigation of irreversible fouling (Lau *et al.*, 2018; Muqeet *et al.*, 2020; Amiri *et al.*, 2022; Rhimi *et al.*, 2021; Radoor *et al.*, 2024).

The use of nanomaterials, including graphene oxide, carbon nanotubes, and metallic nanoparticles, has been extensively explored in membrane modifications, achieving significant advancements in selectivity and transport efficiency (Petukhov & Johnson, 2024). Additionally, hybrid membranes that combine conventional polymers with inorganic additives represent an effective strategy to extend membrane lifespan and reduce operational costs, offering high-performance solutions for industrial applications (Tanudjaja *et al*., 2022).

Assessing the scalability of these technologies requires not only evaluating their technical performance but also considering economic and environmental factors (Amiri *et al*., 2022; Radoor *et al*., 2024). Studies integrating these analyses can provide valuable insights for industrial adoption. Thus, emerging technologies present a fertile ground for advancements, contributing to the sustainable evolution of ultrafiltration processes (Amiri *et al*., 2022; Radoor *et al*., 2024).

In a study by Ma *et al*. (2024), polyvinylidene fluoride (PVDF) ultrafiltration membranes modified with graphene oxide (GO) and cerium-doped titanium dioxide (Ce-TiO_2) demonstrated significant improvements in hydrophilicity, fouling resistance, and self-cleaning properties under UV light activation. Compared to unmodified PVDF membranes, the pure water flux of GO/Ce-TiO_2-PVDF membranes increased to 119.64 $L \cdot m^{-2} \cdot h^{-1}$, representing a 249.42% improvement. The bovine serum albumin (BSA) rejection rate also rose to 95.3%, surpassing the 88.6% of conventional membranes. After water washing and UV irradiation, the fouled membrane recovered 91.54% of its flux, achieving a maximum flux of 110.62 $L \cdot m^{-2} \cdot h^{-1}$, a 379.5% increase compared to the original membrane. During cyclic self-cleaning experiments, the membrane's flux was restored from 78.45 $L \cdot m^{-2} \cdot h^{-1}$ to 76.95 $L \cdot m^{-2} \cdot h^{-1}$, maintaining a BSA rejection rate of approximately 95%.

Despite these advancements, Ma *et al*. (2024) highlighted that the scalability of the methodology involving GO and Ce-TiO_2 incorporation into PVDF membranes is feasible using relatively simple modification techniques, such as nonsolvent-induced phase separation (NIPS). Additionally, the accessibility of UV light activation reinforces its potential for industrial applications. However, the authors noted that achieving uniform dispersion of nanomaterials and addressing the associated costs of specific modifications remain significant challenges for large-scale production, consistent with findings by Khraisheh *et al*. (2021) and Xing *et al*. (2024).

Similarly, Li *et al*. (2023) reported significant advances in water flux, pollutant rejection, and antifouling properties with $Ti_3C_2T_x$ (MXene) and polyaniline (PANI) incorporated into polyethersulfone (PES) ultrafiltration membranes. The composite membrane M2 (containing 0.04 wt% MXene and 0.5 wt% PANI) achieved a pure water flux of 227 $L \cdot m^{-2} \cdot h^{-1}$, approximately twice that of conventional membranes. The BSA rejection rate remained above 99%, while Congo Red and Methylene Blue dye rejections were 99.1% and 98.4%, respectively. Furthermore, the membrane's electrical conductivity increased to 0.5 $S \cdot m^{-1}$, significantly higher than the 0.02 $S \cdot m^{-1}$ of conventional membranes, enabling the application of a negative electric field to reduce contaminant deposition and improve flux recovery to 93.7% after cleaning. These results underscore the potential of MXene-PANI/PES membranes as effective and multifunctional solutions for wastewater treatment, combining high permeability, selectivity, and fouling resistance.

Regarding scalability, Li *et al*. (2023) emphasized that MXene-PANI/PES composite membranes face challenges related to manufacturing uniformity and stability. However, the nonsolvent-induced phase separation (NIPS) method used in their production is widely adopted in industry, indicating strong potential for large-scale production. Moreover, the electrostatic assembly process employed to combine MXene and PANI is described as simple and efficient, requiring moderate operational conditions, which enhances the scalability of the process. Nonetheless, achieving uniform dispersion of MXene and PANI within the polymer matrix remains a critical step to ensure consistent performance and competitive costs in industrial-scale production.

For bio-based membranes, Shirdast and Sharif (2025) investigated ultrafiltration membranes based on polyvinyl chloride (PVC) modified with functionalized chitosan nanoparticles containing carboxyl, sulfonate, and phosphate groups. Adding 0.2 wt% sulfonated nanoparticles (SCH-NPs) resulted in a 300% increase in pure water flux (370 $L \cdot m^{-2} \cdot h^{-1}$) and a 13% increase in alginate rejection compared to unmodified PVC membranes. Additionally, the SCH-NP-modified membranes exhibited superior antifouling properties, with a flux recovery ratio (FRR) of 87.5% and a significant reduction in the irreversible fouling ratio (IFR) to 12.5%, compared to 76.3% in conventional membranes. In terms of scalability, the NIPS method used in their fabrication is considered industrially viable. However, the authors emphasized the importance of fine-tuning surface chemistry and nanoparticle size to optimize interfacial segregation and minimize leaching, ensuring consistent performance at large scales.

5. Economic Feasibility and Energy Efficiency

The evaluation of economic feasibility and energy efficiency plays a critical role in the development and application of ultrafiltration (UF) strategies for protein purification. These factors are essential to ensuring the competitiveness and sustainability of processes at an industrial scale, particularly in sectors where reducing operational costs is paramount (Tanudjaja *et al*., 2022).

Techniques such as turbulence promoters, enzymatic pre-treatments, and modified membranes have demonstrated promising performance improvements but often require significant initial investments in equipment and energy. For instance, turbulence promoters effectively control fouling but necessitate increased energy consumption due to higher shear rates (Ruígomez *et al*., 2022; Dattabanik *et al*., 2022; Babu and Amamcharla, 2023; Jiang *et al*., 2021). Similarly, integrated processes, such as combining microfiltration and ultrafiltration, may require higher energy consumption and material inputs but offer substantial improvements in separation efficiency (He *et al*., 2022; Gamarra *et al*., 2022; Nor *et al*., 2018).

Recent advancements in module design and the integration of nanocomposites present opportunities to lower operational costs, enhance efficiency, and extend membrane lifespan (Kolya & Kang, 2023; Khraisheh *et al*., 2021; Kertész *et al*., 2023). Additionally, life cycle analyses and cost-benefit studies provide a robust foundation for strategic decisions, considering the economic and environmental impacts of each technology (Hamid *et al*., 2019; Kehrein *et al*., 2021).

These approaches offer valuable insights for adopting more accessible and sustainable technological solutions, facilitating large-scale application in an economically viable and environmentally responsible manner.

A quantitative study by Jafari *et al*. (2021) in reverse osmosis systems revealed that fouling costs could account for up to 24% of total operational expenses. Integrating turbulence promoters into the system mitigated fouling, improved productivity, and reduced cleaning downtime. However, this improvement came at the expense of increased energy costs for the plant. This underscores the energy efficiency challenges in membrane separation processes, where trade-offs often occur between fouling mitigation and energy costs for maintaining optimal performance. Although this study focuses on reverse osmosis, it provides insights into the potential scale of operational costs relevant to ultrafiltration.

Tanudjaja *et al*. (2022) proposed designing low-resistance hydraulic modules and utilizing optimized spacers to achieve a balance between energy consumption and process efficiency. This highlights the need for integrated energy efficiency analyses in UF operations, an emerging area of research aimed at mitigating costs without compromising performance.

6. Perspectives on the use of UF for the purification of bromelain obtained from pineapple residue

In general, UF membranes are a promising alternative for the purification of bromelain, as it is a separation technique widely used for obtaining protein-rich products. However, fouling inherent to this process remains an obstacle to be overcome. There is a general trend in the literature to associate UF processes with pretreatments or cleaning strategies that reduce fouling while maintaining the enzyme structure intact, especially when the protein is the target product in the process. Additionally, mild turbulence promoters, including vibratory modules or air sparging, can further enhance efficiency without compromising enzyme structure. Future studies should explore the impact of turbulence-induced shear rates on enzyme activity and membrane lifespan, alongside economic feasibility, to ensure industrial scalability.

On the other hand, the use of integrated processes, such as two consecutive UF stages gradually decreasing the Molecular Weight Cut-Off of the membrane used, can be efficient in controlling fouling within the modules and maintaining a constant permeate flow (Nor *et al*., 2016; Gamarra *et al*., 2022). In addition, it may be interesting to combine mild turbulence promoters with these integrated processes to avoid protein structure breakdown. The introduction of baffles inside UF modules, air/gas sparging, or even the use of vibratory/rotary modules are attractive alternatives for improving flow and fouling control (Babu and Amamcharla, 2023; Dattabanik *et al*., 2022; Ruígomez *et al*., 2022).

7. Conclusion

This review consolidates key strategies for enhancing UF performance in bromelain recovery, emphasizing the importance of integrated approaches and process optimizations. While turbulence promoters and pre-treatment steps can reduce fouling and improve flow, balancing operational efficiency with enzyme preservation remains essential. Turbulence promoters can also deliver good results at the expense of higher energy consumption. Furthermore, modifications to membrane structure have shown great potential for exploration, as they contribute both to reducing fouling and recovering permeate flow, removing irreversible fouling, although tests involving specific bromelain recovery are still needed to evaluate if protein activity may be lost in these cases. Regarding module configuration, a deterministic conclusion could not be reached due to the divergences in the composition of the feed in each study. Overall, flat UF membranes are more commonly used and, therefore, deliver good protein recovery results. In addition, the adoption of a cross-flow configuration over dead-end becomes the most intelligent alternative, as it helps to increase turbulence in the module and avoid concentration polarization, which, in turn, leads to fouling. Future research should prioritize scalable and economically viable solutions to advance UF applications in the enzyme recovery industry.

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