Florian Buchbender*
Martin Wiese

Efficient Concentration of an Amino Acid Using Reactive Extraction Coupled with Bipolar Electrodialysis

One intention of the PRODIAS (processing diluted aqueous systems) project is to develop and establish a toolbox of innovative and tailored separation technologies applicable to design energy-efficient water removal and product recovery techniques. Within this project, the recovery of γ-aminobutyric acid (GABA) was investigated. Using both synthetic as well as fermented solutions, reactive extraction of GABA with the solvent di-(2-ethylhexyl)phosphoric acid + isododecane was performed. For back extraction, different mineral acids were examined. Multistage countercurrent reactive extraction using pH adjustments along the stages to increase extraction efficiency as well as back extraction were then run on pilot-plant scale with fermented GABA solutions. The resulting GABA salt from back extraction was finally split by means of bipolar electrodialysis.

Keywords: Amino acids, γ-Aminobutyric acid, Bipolar membranes, Electrodialysis, Fermentation broth, Reactive extraction

Received: June 07, 2018; *revised:* July 27, 2018; *accepted:* August 30, 2018

DOI: 10.1002/ceat.201800286

1 Introduction

The main challenge for the economic production of chemicals based on renewable raw materials is to develop cost- and energy-efficient downstream processes. Within the European Community's Framework Programme for Research and Innovation Horizon 2020, the project PRODIAS (processing diluted aqueous systems) was established. One objective of the project is to develop and implement a toolbox of innovative and tailored (hybrid) separation technologies that can be applied to design energy-efficient water removal and product recovery techniques.

One exemplary system in the PRODIAS project is the amino acid γ-aminobutyric acid (GABA). GABA is a neutral amino acid, which occurs as a zwitterion at its isoelectric point (pH 7.3). Here, the acid group ($pK_{a,1}$ = 4.23)[1)] is completely deprotonated and the amino group ($pK_{a,2}$ = 10.23) is completely protonated. This zwitterion form of GABA, which is highly polar, is the one obtained from fermentations which are usually run at neutral pH conditions (Fig. 1). The concentration of GABA after fermentation is in the range of 10 g per 100 g. Since GABA exhibits a solubility in water of about 55 g per 100 g, vast amounts of water must be removed to obtain it in crystallized form.

An alternative to evaporating water is the application of reactive extraction. Since conventional organic solvents are not capable to dissolve the polar GABA zwitterion, a reactive agent dissolved in a suitable solvent is used. The recovery of amino acids by reactive extraction has been described by numerous authors. Bart et al. [1] and Pursell et al. [2] investigated the extraction of phenylalanine with the amine-based cation exchanger Aliquat 336, while Rüffer et al. [3], Rüffer [4], and Takors et al. [5] extracted phenylalanine in situ from a fermentation broth using the anion exchanger di-(2-ethylhexyl)phos-

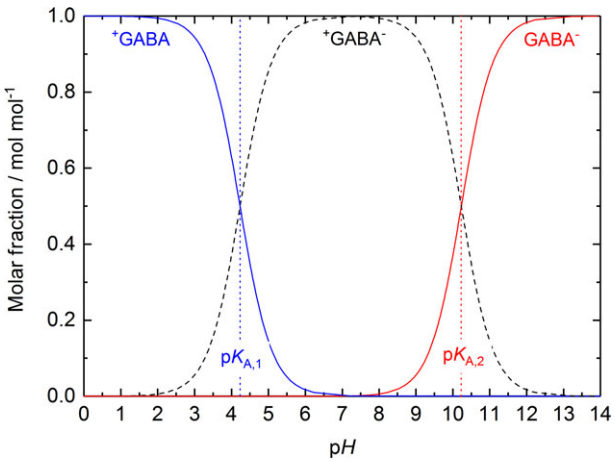

Figure 1. Charge of GABA as a function of the pH value.

1) List of symbols at the end of the paper.

Dr.-Ing. Florian Buchbender, Martin Wiese
florian.buchbender@basf.com
BASF SE, Carl-Bosch-Strasse 38, 67056 Ludwigshafen, Germany.

phoric acid (D2EHPA) dissolved in kerosin. Oniscu et al. [6], Cascaval et al. [7, 8], and Kloetzer et al. [9] investigated the extraction of acidic, neutral, and basic amino acids as a function of the pH by means of the solvent system D2EHPA + *n*-butyl acetate.

The extraction principle is to either extract the anionic species of the amino acid using an amine-based reactive extractant under basic pH conditions or the cationic species of the amino acid with an organic acid-based reactive extractant under acidic conditions. The simplified reactive extraction principle of the amino acid GABA using the reactive extractant D2EHPA dissolved in isododecane is illustrated in Fig. 2. Here, D2EHPA partitioned between the organic and the aqueous phase. The fraction of D2EHPA molecules in the aqueous phase deprotonated, and the inherent decrease of pH led to a protonation of GABAs acid group. As a result, GABA was transferred to its cationic state to form an ionic bond with the deprotonated D2EHPA that was then extracted into the organic solvent phase. A more detailed species distribution for the reactive extraction of amino acids with D2EHPA can be found in Zhang et al. [10].

A common way to regenerate the reactive extraction solvent is to back extract the amino acid into an aqueous phase by a pH shift [4, 10]. When using an organic acid for reactive extraction, a strong mineral acid is necessary for back extraction. In case of an amine-based reactive extractant, an alkaline solution such as NaOH is employed for back extraction. During the back extraction step, the concentration of the amino acid highly increases by using small phase ratios v(S/F). Here, the pH value is the driving force and not the concentration gradient.

A result of the back extraction step using mineral acids is the formation of an acid salt of the amino acid. If the pure form of the amino acid is desired, it must then be released from its salt form, e.g., by neutralization using an alkaline solution. This, however, is not desirable for several reasons: (i) the consumption of stoichiometric amounts of NaOH or KOH, (ii) the formation of a salt waste stream, and, from a process point of view, (iii) the unknown impact of salt ions on the crystallization of GABA.

Therefore, an alternative to neutralization of the back extract with caustic or KOH was developed and is depicted in Fig. 3. Here, in the reactive extraction step, GABA is extracted using an acidic reactive extractant, namely, D2EHPA dissolved in isododecane and then re-extracted from the extract of the reactive extraction step using a mineral acid. By doing this, GABA is concentrated by forming the corresponding mineral acid salt. This salt is then split using bipolar electrodialysis.

Electrodialysis (ED) is a membrane-based separation technique that enables the simultaneous purification and depletion of electrically charged ions and molecules in aqueous solutions [11]. Due to their high separation quality, ED processes are applied in biotechnology, e.g., purification of amino acids [12, 13], chemical industry, e.g., demineralization and recovery of dimethylsiopropylamin and EDTA, and wastewater treatment, e.g., recovery of Ni and Cu [11].

In ED, the direction of the electric field forces the charged ions to move towards the respective electrodes. In this way, anions are dragged to the positively charged anode, whereas cations move towards the cathode. To control the movement of these ions and to split the compartment into a diluted and concentrated stream, ion exchange membranes are integrated within a membrane stack [14]. These membranes either allow the anions (anion exchange membrane) or the cations (cation exchange membrane) to pass the membrane, thus, creating several compartments of dilute and concentrate.

When using bipolar membranes, the ED process further allows water splitting into H^+ and OH^- ions with less energy demand than in the electrolysis process [11, 15]. Bipolar membranes merge one anion exchange membrane (AEM) and one cation exchange membrane (CEM) into one membrane unit leaving an intermediate layer (smaller than a few micrometers [16]) of water in between. This water layer can dramatically increase the membrane resistance if the rate of water dissocia-

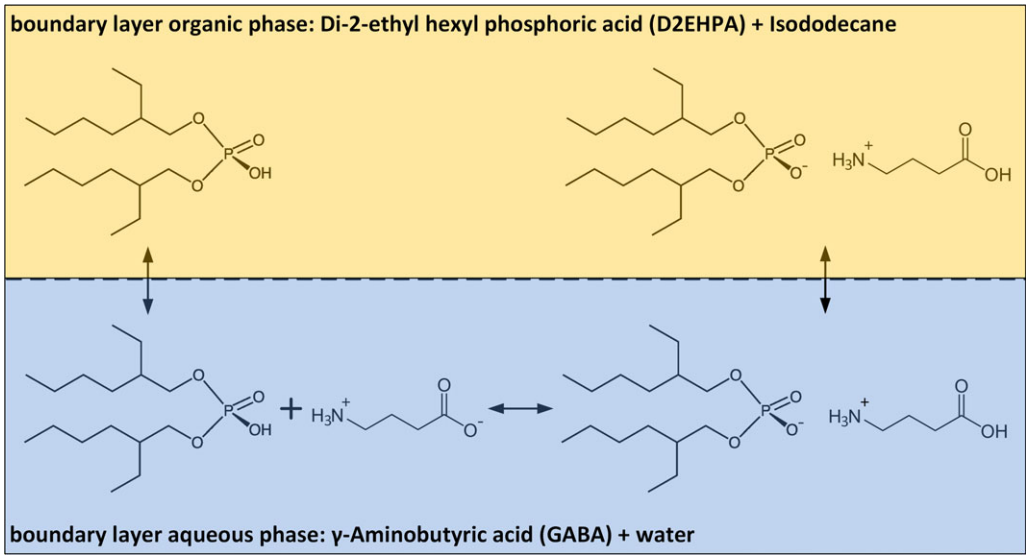

Figure 2. Simplified reactive extraction of GABA using D2EHPA + isododecane.

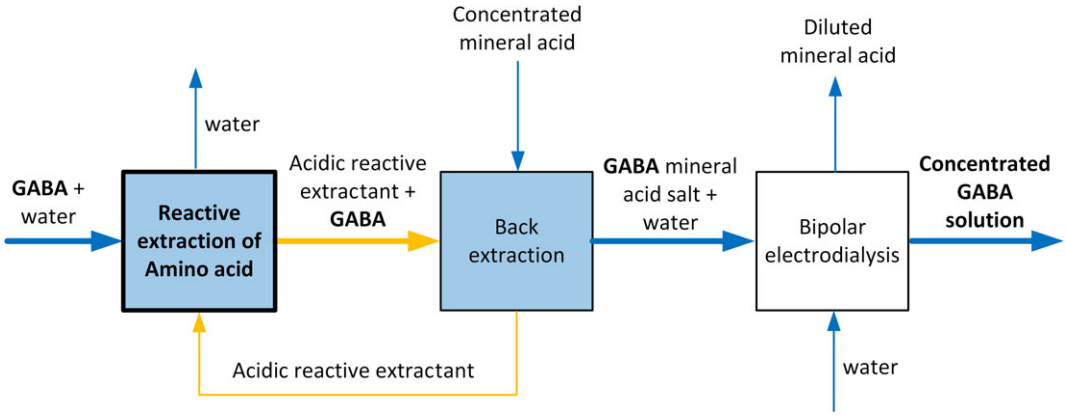

Figure 3. Concept for reactive extraction, back extraction, and bipolar electrodialysis hybrid for the purification and concentration of GABA.

tion is faster than the water transport into the bipolar membrane [17]. Strathmann et al. have intensively discussed the mechanisms of water splitting in bipolar membranes [18, 19].

Common fields, in which bipolar membranes are applied, include the generation of dilute acid and base solutions [20–22], desalination, and separation of alcohols in nonliquid media [11]. Due to the versatile usage of bipolar membranes combined with their ability to selectively separate ions, a bipolar membrane-based electrodialysis process was chosen for this study.

First, the focus was on the reactive extraction step of GABA. The extraction efficiency is defined as follows:

$$E = \frac{m^0_{\mathrm{GABA}} - m^{\mathrm{eq}}_{\mathrm{GABA}}}{m^0_{\mathrm{GABA}}} \quad (1)$$

where m^0_{GABA} is the initial and $m^{\mathrm{eq}}_{\mathrm{GABA}}$ the equilibrium weight fraction of GABA in the aqueous phase. The extraction efficiency was measured on lab scale with synthetic GABA feeds and ultrafiltrated GABA fermentation broths as a function of the phase ratio v(org/aq) and the solvent composition. Next, back extraction of GABA with different solvents was investigated on lab scale. Finally, continuous multistage GABA reactive extraction and back extraction was evaluated on pilot scale with subsequent salt split using bipolar electrodialysis (BPED).

2 Materials and Methods

Experiments with synthetic solutions were performed using GABA from Sigma Aldrich with a purity of ≥ 99 %. An amount of 150 mmol L^{-1} NaCl was added to improve phase separation [23]. For experiments specified with "fermented GABA", GABA produced by fermentation and subsequent ultrafiltration was employed. D2EHPA was purchased from Lanxess (Baysolvex) and isododecane (isomeric mixture > 80 % purity) from IMCD Deutschand; 30 % HCl, 96 % sulfuric acid, 80 % phosphoric acid, and 10 % NaOH solutions were of technical grade.

Equilibria were measured using a temperature-controlled 1-L lab-scale stirred vessel. Here, both phases were homogeneously dispersed for at least 10 min and then separated. In case of turbid phases after settling, the phases were then centrifuged.

The GABA content in both the organic and the aqueous phase from experiments with a synthetic GABA solution were determined by titration with KOH while for experiments using fermented GABA solutions HPLC was applied for the aqueous phase. To determine the GABA content of the organic phase, GABA was first extracted with an aqueous hydrochloric acid solution. The GABA content in the aqueous phase was then analyzed using HPLC whereas the GABA content in the organic phase was subsequently calculated by mass balance. Equilibrium measurements were conducted at room temperature if not specified otherwise.

The electrodialysis experiments were carried out in a BPED unit built in-house. Fig. 4 a presents the flowsheet of the experimental setup emphasizing the BPED unit, the acid concentration and deacidification loop as well as the electrode rinsing loop. The BPED unit that is a membrane stack consisted of two electrodes (anode and cathode) and an alternating arrangement of bipolar membrane, CEM, and AEM as exemplarily shown in Fig. 4 b. Within the separation process, chloride ions move into the acid concentration loop by passing the AEMs. In this way, these chloride ions then react with hydrogen coming from the bipolar membrane to form hydrochloric acid. Due to the formation of electrode gases and to avoid side reactions, the anode and cathode chambers were constantly flushed with an acidic electrolyte.

Analytically, the following streams and vessels were analyzed periodically over the time course of the hybrid experiment: the GABA inlet stream and GABA loop after the BPED unit, the acid concentration loop after the BPED unit, and the total volume of the de-acidification loop at the outlet. In this way, it was possible to determine the efficiency of the BPED process as well as product quality as a function of time. Apart from GABA, which was analyzed by HPLC, phosphoric acid, sulfate, and ammonia were determined with ion chromatography.

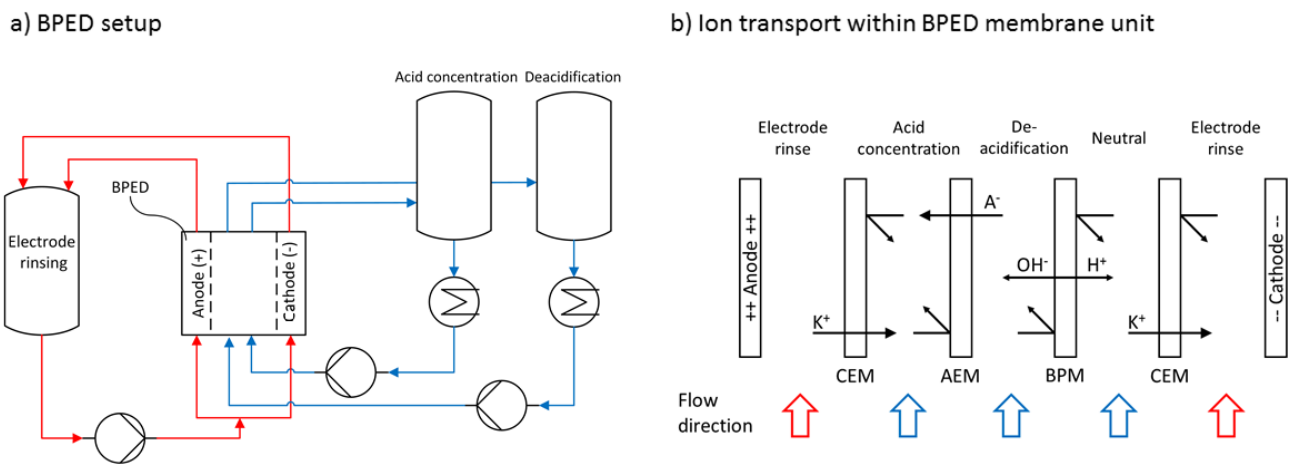

Figure 4. Flowsheet of the BPED apparatus showing the membrane unit and the loops for desalination and concentration of GABA chloride.

3 Results and Discussion

3.1 Equilibrium Measurements for Reactive Extraction

Equilibrium measurements were performed using the reactive extractant D2EHPA dissolved in isododecane. For a synthetic GABA solution, extraction efficiencies (single stage) higher than 90 % could be achieved for a solvent composition of 50 g per 100 g D2EHPA + 50 g per 100 g isododecane and a phase ratio of $\nu(S/F) = 2\,g\,g^{-1}$ (Fig. 5).

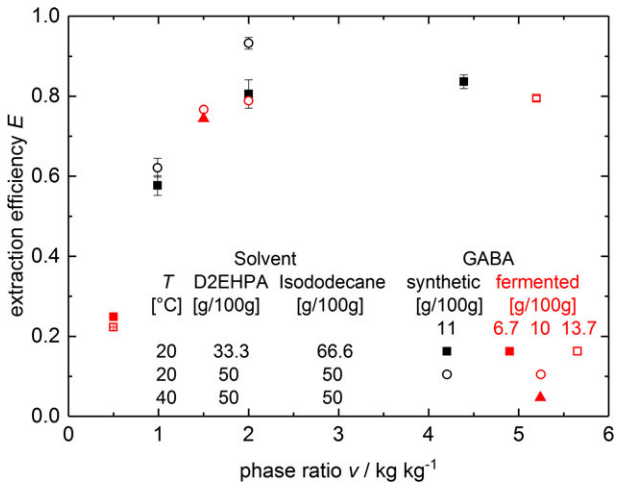

Figure 5. Extraction efficiency for synthetic GABA and GABA produced by fermentation using D2EHPA + isododecane as a function of the phase ratio and the solvent composition.

The use of fermented GABA feeds (pH ~ 7) showed slightly lower extraction efficiencies compared to those obtained with synthetic GABA solutions (Fig. 5), most likely due to the presence of ammonia in the fermentation broth, that is co-extracted, and the presence of other acidic side components such as acetic acid and succinic acid. When ammonia is co-extracted by D2EHPA, acetic acid and succinic acid lower the pH, which in turn hinders the deprotonation of D2EHPA, necessary for the extraction of GABA.

A higher D2EHPA content in the solvent improves the extraction efficiency; however, the viscosity of the solvent increases, which is disadvantageous for extraction kinetics and phase separation. A temperature increase from T = 20 °C to T = 40 °C significantly lowers the viscosity of the solvent phase (Tab. 1) and does not seem to have a significant impact on extraction efficiency (Fig. 5).

Table 1. Viscosities and densities of the solvent as a function of solvent composition and temperature.

	Density [kg m^{-3}]		Viscosity [mPa s]	
	T = 20 °C	T = 40 °C	T = 20 °C	T = 40 °C
50 g per 100 g D2EHPA + 50 g per 100 g isododecane	855	840	4.2	2.7
33.3 g per 100 g D2EHPA + 66.6 g per 100 g isododecane	822	807	2.8	2

The direction of dispersion has a strong effect on phase separation. Dispersing the aqueous phase in the solvent led to poor phase separation with a pronounced crud layer at the interphase (Fig. 6 a), whereas dispersing the organic phase in the aqueous phase improved phase separation significantly and only exhibited a very minor crud layer (cuticles) at the interphase (Fig. 6 b). It is believed that the crud is either formed by proteins that denaturate at low pH values or by precipitated phospholipids.

To investigate the concentration-dependent depletion of both synthetic GABA and GABA produced by fermentation,

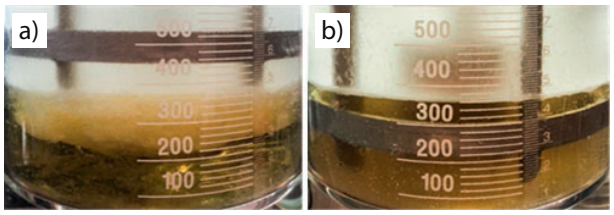

Figure 6. Phase separation of aqueous in organic phase dispersion (a) and organic in aqueous phase dispersion (b).

crosscurrent extraction of GABA using an unloaded solvent for each stage was performed (Fig. 7). Here, the equilibrium concentration of GABA in the aqueous phase is plotted for each stage (denoted by the number next to the symbol) as a function of the equilibrium pH in the aqueous phase.

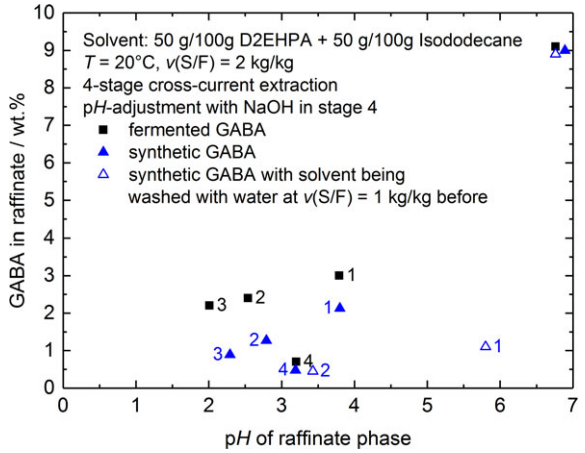

Figure 7. GABA content in the raffinate of a crosscurrent extraction as a function of the pH.

Like before (Fig. 5), the depletion of synthetic GABA in the aqueous phase is stronger than with GABA produced by fermentation. It becomes also evident that the degree of depletion decreases from stage 1 to stage 3 and this effect is even more pronounced with a feed produced by fermentation. The reasons for this behavior are explained as follows. First, during fermentation, acidic side components such as acetic acid and succinic acid are neutralized with ammonia. During the reactive extraction step, ammonia is co-extracted (0.1–0.2 g per 100 g in extract depending on the phase ratio) releasing the acidic side components that lower the pH of the raffinate. At low pH values, the deprotonation of D2EHPA (measured half neutralization point of 10 g per 100 g D2EHPA in a water (30 g per 100 g) isopropanol mixture (70 g per 100 g) was at about pH 3) is hindered and, thus, it becomes inactive for the extraction of GABA.

Titrating the extract raffinate of the third stage to GABAs isoelectric point of pH 7.3 with NaOH before extraction led to an equilibrium pH of 3.2 for stage 4 and showed that a further depletion of GABA in the raffinate phase is possible (Fig. 7). While for a GABA feed produced by fermentation in stage 3 without pH adjustment the depletion was only 8 %, it was almost eight times higher (68 %) in stage 4. Thus, adjusting the pH during multistage extraction should increase depletion of GABA in the raffinate.

Secondly, the reactive extractant D2EHPA contains very small amounts of mono-(2-ethylhexyl)phosphoric acid (M2EHPA) and phosphoric acid, which together with the released acidic side components form an unextractable salt of GABA in the raffinate phase. Washing the solvent with water before, thus, extracting phosphoric acid from it, increased the equilibrium pH and extraction efficiency (Fig. 7).

3.2 Equilibrium Measurements for Back Extraction

Back extraction of GABA was done by titration of the extract from the reactive extraction step with an aqueous mineral acid solution to pH^{eq} 0.1 in the case of 96 g per 100 g sulfuric and 36 g per 100 g hydrochloric acid and pH^{eq} 1.7 in the case of 85 g per 100 g phosphoric acid. Extraction efficiencies and GABA content in the re-extract for these three re-extraction solvents are compared in Fig. 8. Sulfuric and hydrochloric acid have similar extraction efficiencies (99 %), however, the concentration of GABA in the re-extract is the highest with sulfuric acid (34 g per 100 g), which, with 9 g per 100 g GABA in the fermentation feed, corresponds to a concentration factor of 3.8. For phosphoric acid, which is a weaker mineral acid compared to sulfuric acid and HCl, both the extraction efficiency and concentration factor is lowest.

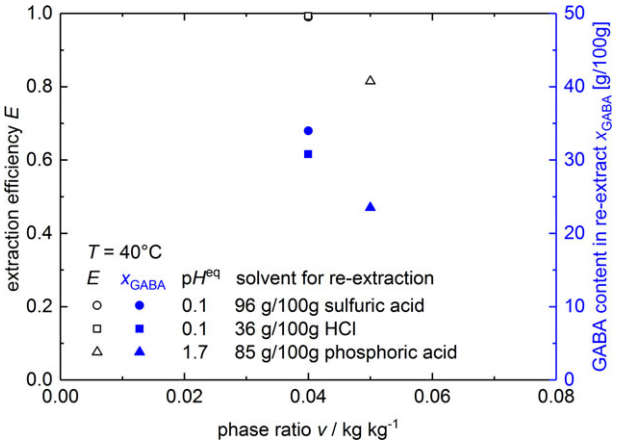

Figure 8. Extraction efficiencies and GABA content in the re-extract as a function of the phase ratio and different mineral acids as back extraction solvents.

Phase separation during back extraction was fast with all mineral acids; however, with sulfuric acid the formation of small crystals at the interface was observed. An XRD spectroscopy proved these crystals to be calcium sulfate (gypsum). Calcium sulfate is used during fermentations as mineral nutriment. During the reactive extraction step, the calcium ions are complexed by D2EHPA and thus extracted. During back extraction with sulfuric acid, calcium sulfate is again formed and concentrated. Here, due to the low solubility of gypsum in water ($\sim$1 g L^{-1}), gypsum crystals precipitate. During a continuous process, these gypsum crystals would accumulate in the

settler and eventually lead to blockage of the settler if not purged every now and again.

Preliminary bipolar electrodialysis experiments with clear-filtrated GABA sulfate re-extract even showed membrane fouling most likely with gypsum on the AEM which is also known as scaling [11]. Scaling on the AEM results from the locally high concentrations of sulfate or calcium exceeding their solubility limit. To avoid scaling and the subsequent formation of gypsum, hydrochloric acid was chosen for back extraction even though with sulfuric acid the highest concentration of GABA during back extraction is possible.

3.3 Continuous Multistage Extraction

Since a reasonable depletion (> 90 %) of GABA from the fermentation broth is not possible in one single stage, even when using high phase ratios (Fig. 5), GABA depletion using multistage extraction was evaluated. This extraction was done at T = 40 °C using a DN40 Kühni-type extraction column with an active height of 1.5 m and 48 compartments at a stirrer speed of N = 220 min^{-1}. One advantage of a Kühni-type extraction column is that the compartment geometry can be adjusted along the column in terms of energy input and throughput [24].

The reactive extractant containing 50 g per 100 g D2EHPA + 50 g per 100 g isododecane was dispersed at the bottom of the column while ultrafiltrated fermentation broth containing 9 g per 100 g GABA was fed at the top of the column. Preliminary experiments showed coalescence inhibition of drops at the GABA feed stage. Here, the previously mentioned cuticles (Fig. 6 b) formed around the drops. Furthermore, due to the -extraction of GABA, the mass flows of both phases decrease from top to bottom. Therefore, the geometry of the compartments, i.e., open area fractions of stator plates of the column, was adapted according to Fig. 9. The pH of the aqueous phase was adjusted to ~3.2 (see Sect. 3.1) by dosing 10 % NaOH at heights of 30, 50, and 70 cm above the inlet of the dispersed phase (Fig. 9) using a dosing pump (Ritmo R05-60, Fink CHEM+TEC, Bad Dürrheim, Germany).

The column was operated at loads between 6.8 and 9.1 $m^3m^{-2}h^{-1}$. Depletion of GABA was higher than 96 %. Increasing the phase ratio v(S/F) from 3 to 4 $kg\,kg^{-1}$ only slightly enhanced depletion to 98 % (Tab. 2).

Table 2. Depletion as a function of S/F ratio and pH at different heights of the column.

Phase ratio v(S/F) [$kg\,kg^{-1}$]	Load [$m^3m^{-2}h^{-1}$]	Depletion [%] $\frac{\dot{m}_{GABA,F} - \dot{m}_{GABA,R}}{\dot{m}_{GABA,F}} \times 100\%$
3	7.2	96
4	9.1	97
4	6.8	98

3.4 Continuous Back Extraction

Next, GABA was back extracted from the extract generated during the reactive extraction step (see Sect. 3.3) at T = 40 °C with a single-stage extraction with 30 % hydrochloric acid in a 750-mL mixer and DN40 settler. The phase ratio was adjusted manually to achieve a target pH in the re-extract (heavy GABA-chloride phase) of ~0.3. Depending on the actual phase ratio, the GABA content of the raffinate (D2EHPA + isododecane) was between 0.1 and 1.3 g per 100 g and the GABA content in the re-extract was between 22 g per 100 g and 25 g per 100 g.

During start-up, the chosen v(S/F) ratio was slightly too high which resulted in pH < 0 of the aqueous re-extract. As a result, the collected re-extract mixture had to be titrated with NaOH to a pH > 0 to match the boundary conditions of the bipolar ED membrane sheets regarding pH resistance. In

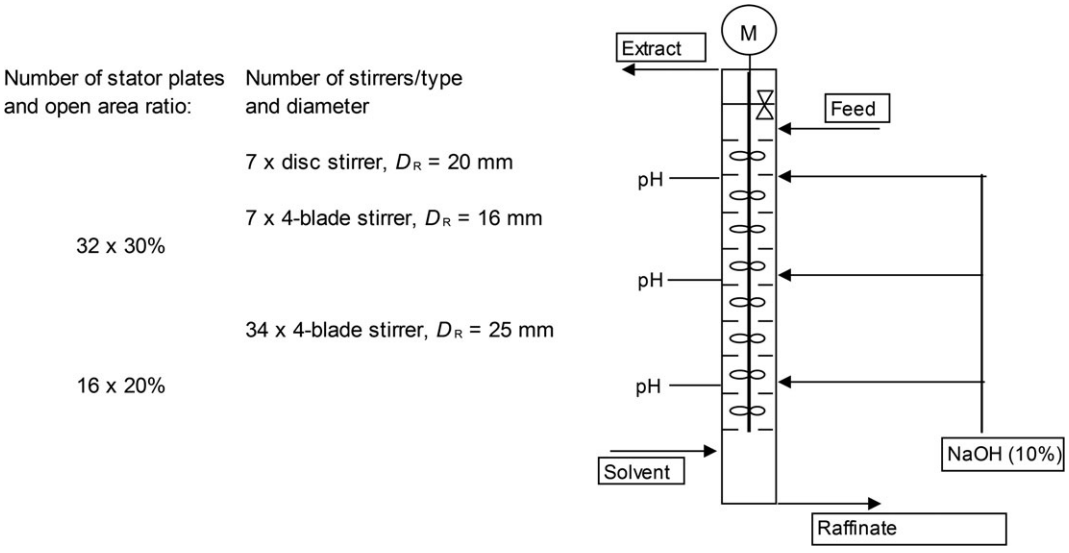

Figure 9. Extraction column setup with pH adjustment.

turn, GABA in the re-extract was slightly diluted to 21 g per 100 g.

3.5 Using BPED for Desalination of GABA Chloride

Bipolar ED salt-split tests were performed with re-extract from the back extraction experiment with hydrochloric acid. Fig. 10 presents the conductivity, pH, and current curves over time during the desalination of GABA chloride. The steady decrease in conductivity reflects the continued progress of desalination at a constant target current of 9.5 A. During 5 h of desalination, three regions were observed: (i) a fast desalination with high current resulting in a quick decrease of conductivity to a value of approx. 130 mS cm^{-1} and a pH of approx. 2.2; (ii) a slower desalination gradient in conductivity while the pH value increases due to lower current; and (iii) fast final desalination until the pH value reaches approx. 7.3 and the experiment was stopped. At this point, GABA is at its isoelectric point and its conductivity is negligible. However, the conductivity shows approximately 75 mS cm^{-1}. Since sodium hydroxide had to be added to match the boundary conditions of the BPED membrane sheets regarding pH resistance, sodium chloride was formed during the electrodialysis, therefore showing a higher conductivity level.

The pH behavior in the GABA loop resembles a typical trend of a weak acid with a strong base. GABA being a weak acid has its pK_a at 4.23 which is the inflection point indicated in Fig. 10. The pH value increases over the experimental time due to hydroxy ions that move into the deacidification loop.

Analytical values reflect that all chloride ions moved from the de-acidification loop into the acid concentration loop to form hydrochloric acid. After nearly 5 h of filtration, it was possible to concentrate GABA to 23 g per 100 g which results in a concentration factor of 2.6 related to the GABA content after fermentation (9 g per 100 g). Please note that the concentration of GABA also results from the decrease in product molar mass due to exchange of chloride ions with hydroxide. No GABA was found in the acid concentration loop.

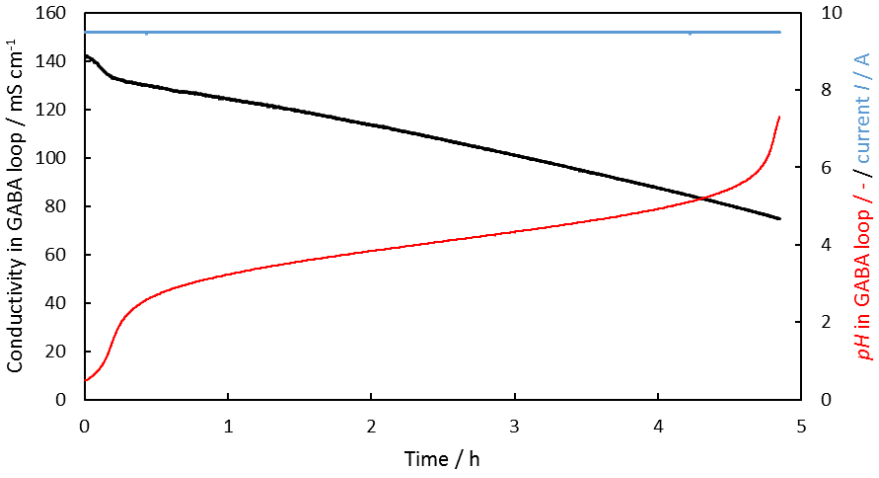

Figure 10. Conductivity and pH in the GABA desalination loop and current for desalination of GABA chloride over time.

3.6 Specific Energy Demand for Desalination Using BPED

Based on the average current, average voltage, and duration of the desalination, the energy consumption of the desalination can be calculated. The GABA-specific energy consumption during the desalination can be calculated by the following equation:

$$e_{spec} = \frac{I_{av} U_{av} t_{desal}}{m_{GABA}} \quad (2)$$

with I_{av} (A) as the average current that is applied during a desalination cycle, U_{av} (V) as the average voltage over the membrane stack, and t_{desal} as the time required for the desalination; m_{GABA} (kg) is the amount of GABA produced during desalination. By that, the specific energy consumption e_{spec} has the unit kWh kg_{GABA}^{-1}. Moreover, e_{desal} (kWh) can be calculated by multiplying e_{spec} with the total amount of produced GABA. For the desalination of GABA chloride, the specific energy demand limits to 0.95 kW kg_{GABA}^{-1} (Tab. 3). The reasons for this low energy demand are (i) the low specific resistance of the chloride ion and (ii) that only one chloride ion links to the GABA molecule.

Table 3. Characteristic values concerning energy demand during the GABA chloride desalination experiment.

Parameter	Value
Average current [A]	9.5
Average voltage [V]	15.8
Duration until pH 7.3 [h]	4.85
Energy consumption [kWh]	0.73
Specific energy consumption [kWh kg_{GABA}^{-1}]	0.95

4 Conclusions

It was demonstrated that GABA can be recovered from an ultrafiltrated fermentation broth and concentrated using a combination of reactive extraction, back extraction, and bipolar electrodialysis. Since the isoelectric point of GABA is at pH 7.3, the fermentation broth has an almost neutral pH. This allows the extraction of GABA when using a strong hydrophobic acid such as D2EHPA as it acidifies the GABA phase and transfers GABA into its cationic form, which, in turn, forms an ionic bound with D2EHPA and, thus, is extracted into the organic phase.

For back extraction, the use of sulfuric acid should be avoided since during the extraction step with D2EHPA calcium, which is usually present in fermentation broths, is co-extracted and then precipitates as calcium sulfate (gypsum) during back extraction. It then accumulates in the phase separator of

the back extraction step and in electrodialysis which leads to fouling of the membranes. Using, e.g., hydrochloric acid during back extraction avoids these issues.

The combination of reactive extraction, back extraction, and bipolar electrodialysis circumvents the usage of expensive NaOH after back extraction and, thus, irreversible salt formation. Instead, electricity (0.95 kWh kg_{GABA}^{-1}) is applied to release GABA from its salt form. During this process, GABA was concentrated by a factor of 2.6 which means that 2.6 times less water must be evaporated to crystallize GABA, e.g., by evaporation crystallization.

Setting up a reliable pH control for back extraction would avoid the mentioned dilution of the re-extract with NaOH which was necessary to match the boundary conditions of the bipolar ED membrane sheets regarding pH resistance and thus lead to a higher concentration factor of at least 3. The concentration factor could be even further increased by using 36 % HCl instead of 30 % HCl during back extraction.

Acknowledgment

The authors gratefully acknowledge financial support from the European Union's (EU's) framework program for research and innovation Horizon 2020 (2014–2020) under grant agreement no. 636077.

The authors have declared no conflict of interest.

Symbols used

D	[mm]	diameter
e	[kWh kg_{GABA}^{-1}]	energy consumption
E	[–]	extraction efficiency
I	[A]	applied current
m	[kg]	mass
$\dot{m}$	[kg h^{-1}]	mass flow
N	[min^{-1}]	stirrer speed
pK_a	[–]	dissociation exponent
t	[s]	time
T	[°C]	temperature
U	[V]	voltage
v	[kg kg^{-1}]	phase ratio
x	[g/100 g]	weight percent

Sub- and superscripts

0	at initial conditions
av	average
desal	desalination
eq	at equilibrium conditions
R	stirrer, raffinate
spec	specific

Abbreviations

AEM	anion exchange membrane
BPED	bipolar electrodialysis
CEM	cation exchange membrane
D2EHPA	di-(2-ethylhexyl)phosphoric acid
ED	electrodialysis
F	feed
GABA	γ-aminobutyric acid
M2EHPA	mono-(2-ethylhexyl)phosphoric acid
S	solvent

References

[1] H. J. Bart, R. Marr, U. Bauer, *Ber. Bunsen-Ges. Phys. Chem.* **1989**, *93*, 984–988.
[2] M. R. Pursell, M. A. Mendes-Tatsis, D. C. Stuckey, *Biotechnol. Bioeng.* **2003**, *82 (5)*, 533–542.
[3] N. Rüffer, U. Heidersdorf, I. Krezers, G. A. Sprenger, L. Raeven, R. Takors, *Bioprocess. Biosyst. Eng.* **2004**, *26 (4)*, 239–248.
[4] N. Rüffer, *Ph.D. Thesis*, Forschungszentrum Jülich **2004**.
[5] R. Takors, M. Gerigk, D. Maass, A. Kreutzer, J. Bongaers, K. Schmidt, G. Sprenger, M. Wubbolts, C. Wandrey, *IFAC Proc. Ser.* **1989**, *34 (5)*, 183–188.
[6] C. Oniscu, A.-I. Galaction, D. Cascaval, *Rom. Biotechnol. Lett.* **2000**, *5 (3)*, 171–178.
[7] D. Cascaval, C. Oniscu, A.-I. Galaction, *Biochem. Eng. J.* **2001**, *7 (3)*, 171–176.
[8] D. Cascaval, A.-I. Galaction, *Chem. Ind.* **2004**, *58 (9)*, 375–386.
[9] L. Kloezer, A. C. Blaga, M. Potaru, A. I. Galaction, D. Cascaval, *4th Int. Conf. on Food Engineering and Biotechnology*, Copenhagen, May **2013**.
[10] J. Zhang, S. Zhang, X. Yang, L. Qiu, B. Gao, R. Lia, J. Chen, *J. Chem. Technol. Biotechnol.* **2016**, *91 (2)*, 483–489.
[11] *Membranverfahren* (Eds: T. Melin, R. Rautenbach), Springer, Berlin **2007**.
[12] A. Fischer, C. Martin, J. Müller, *DE 199 52 961 A1*, **2001**.
[13] J. Stodollick, R. Femmer, M. Gloede, T. Melin, M. Wessling, *J. Membr. Sci.* **2014**, *453*, 275–281.
[14] T. Luo, S. Abdu, M. Wessling, *J. Membr. Sci.*, **2018**, *555*, 429–454.
[15] J. Ran, L. Wu, Y. He, Z. Yang, Y. Wang, C. Jiang, L. Ge, E. Bakangura, T. Xu, *J. Membr. Sci.* **2017**, *522*, 267–291.
[16] R. Baker, *Membrane Technology and Applications*, 3rd ed., John Wiley & Sons, New York **2012**.
[17] J. Balster, D. F. Stamatialis, M. Wessling, *Chem. Eng. Process.* **2004**, *43 (9)*, 1115–1127.
[18] R. Baker, E. Cussler, W. Eykamp, W. Koros, R. Riley, *Membrane Separation Systems: Recent Developments and Future Directions*, Noyes Data Corporation, Park Ridge, NJ **1991**, 396–448.
[19] H. Strathmann, J. J. Krol, H.-J. Rapp, G. Eigenberger, *J. Membr. Sci.* **1997**, *125 (1)*, 123–142.
[20] F. Ilhan, H. A. Kabuk, U. Kurt, Y. Avsar, M. T. Gonulla, *Desalin. Water Treat.* **2016**, *57 (11)*, 5165–5173.
[21] C. Jiang, Y. Wang, T. Xu, *Sep. Purif. Technol.* **2013**, *115*, 100–106.
[22] C. Jiang, Q. Wang, Y. Zhang, Y. Li, Y. Wang, T. Xu, *J. Membr. Sci.* **2016**, *498*, 48–56.
[23] A. Pfennig, A. Schwerin, *Ind. Eng. Chem. Res.* **1998**, *8 (3)*, 3180–3188.
[24] F. Buchbender, A. Fischer, A. Pfennig, *Chem. Eng. Sci.* **2013**, *104*, 701–716.

