REVIEW

Recovery of succinic acid from fermentation broth

Tanja Kurzrock · Dirk Weuster-Botz

Abstract Succinic acid is of high interest as bio-feedstock for the chemical industry. It is a precursor for a variety of many other chemicals, e.g. 1,4-butan-diol, tetrahydrofuran, biodegradable polymers and fumaric acid. Besides optimized production strains and fermentation processes it is indispensable to develop cost-saving and energy-effective downstream processes to compete with the current petrochemical production process. Various methods such as precipitation, sorption and ion exchange, electrodialysis, and liquid–liquid extraction have been investigated for the recovery of succinic acid from fermentation broth and are reviewed critically here.

Keywords Electrodialysis · Ion exchange · Precipitation · Reactive extraction · Succinic acid

Introduction

Succinic acid, a dicarboxylic acid with four carbon atoms, plays an important role as a precursor molecule for the synthesis of biodegradable polyester resins, dyestuffs, and pharmaceuticals and as additive in the food industry (Cornils et al. 2005).

Nowadays, succinic acid is exclusively produced from crude oil by catalytic hydrogenation of maleic anhydride to succinic anhydride and subsequent hydration or by direct catalytic hydrogenation of maleic acid (Cornils and Lappe 2002). The market price of petrochemically produced succinic acid is about US $ 5.9–8.8 kg^{-1} depending on its purity whereas the raw material costs based on production from maleic anhydride are about US $ 1 kg^{-1} succinic acid (Song and Lee 2005).

The current production of chemicals based on succinic acid accounts to about 16.000 t/y (Patel 2006). However the market potential is estimated to be about 270,000 t/y if succinic acid replaced maleic anhydride for all uses of the latter (Delhomme et al. 2009, Wilke and Vorlop 2004, Zeikus et al. 1999). Because of these predictions and the rising oil price interest in succinic acid production by fermentation processes is increasing.

Various working groups are dealing with the fermentation of succinic acid with strains of *Anaerobiospirillum succiniciproducens*, *Actinobacillus succinogenes*, *Mannheimia succinici-producens*, recombinant *Escherichia coli* strains and *Corynebacterium glutamicum* (Bechthold et al. 2008, Okino et al. 2008), which all are able to generate succinic acid under physiological conditions in the presence of glucose and CO_2. Succinic acid concentrations in the fermentation broth are reported to be up to 146 g succinic acid l^{-1} (Okino et al. 2008).

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The raw material costs based on succinic acid production via fermentation with glucose as carbon source are about US $ 0.43 kg^{-1} succinic acid (Song and Lee 2005).

For the biotechnological process to be competitive with petrochemical production it is necessary to minimize the production costs. About 60% of the total production costs are generated by downstream processing, e.g. the isolation and the purification of the product in the fermentation broth (Bechthold et al. 2008). For this reason, some new as well as some well known methods have been investigated for the recovery of succinic acid.

The first downstream processing step is cell separation by centrifugal separation or microfiltration, usually followed by ultrafiltration to separate cell debris, proteins and other polymers from the fermentation supernatant. For the isolation and concentration of succinic acid many unit operations have been suggested: precipitation with ammonia or calcium hydroxide, membrane processes such as electrodialysis, liquid–liquid extraction such as predispersed solvent extraction with colloidal liquid aphrons or reactive extraction. Different sorption/ion exchange methods and crystallization are the methods of choice for the final purification of the isolated acid.

All of these unit operations are presented below and their advantages and disadvantages will be discussed briefly with respect to their possible application for the industrial recovery of succinic acid from fermentation broth.

Ultrafiltration

Most unit-operations for the isolation of succinic acid require ultrafiltration for the separation of cell-debris and proteins as a first step. The fermentation broth is directed through a bypass crossflow, hollow-fiber ultrafiltration unit and recirculated into the bioreactor (Rüffer et al. 2004).

Precipitation

Precipitation with calcium hydroxide

The classical industrial method for the isolation of carboxylic acids from an aqueous fermentation broth is a precipitation with calcium hydroxide or calcium oxide. Lactic and citric acid have been recovered industrially with this method (Vickroy 1985; Kirk–Othmer 1979). Moreover, some patents are concerned specifically with the precipitation of succinic acid with calcium hydroxide although these processes are only at laboratory scale (Datta 1992; Datta et al. 1992; Berglund et al. 1991).

After addition of calcium hydroxide or calcium oxide, the calcium salt of succinic acid is filtered off from the fermentation broth and then treated with concentrated sulfuric acid. In this way, the by-product calcium sulfate (CaSO$_4$), gypsum, is generated in an equimolar amount. The free succinic acid is purified by some commonly applied methods, e.g. active carbon or ion exchange and then the product is further concentrated and crystallized by evaporation. With this approach, the crystallization of the acid is reported to be difficult and yields are low (Kertes and King 1985) (Fig. 1).

A fermentation process with *Anaerobiospirillum succiniciproducens* yields 1.4 mol succinic acid per mol glucose. After precipitation with calcium hydroxide the yield of succinic acid is 1.2 mol per mol glucose, which already means a loss of nearly 15% of the acid has occurred (Datta 1992; Datta et al. 1992). The complete process is depicted in Fig. 2.

Besides this, the main disadvantage of precipitation with calcium hydroxide or calcium oxide is the high amount of the by-product calcium sulfate which cannot be used commercially because of smell and colour impurities. Disposal of this by-product is required. Another negative issue is the high consumption of calcium hydroxide, calcium oxide and sulfuric acid. These additives cannot be regenerated or recycled, which results in high process costs (Datta 1992; Datta et al. 1992). These are the reasons why precipitation with calcium hydroxide or calcium oxide is unlikely to be applied on an industrial scale for recovery of bio-succinic acid and is generally not considered viable for large-scale production (Hermann and Patel 2007).

Precipitation with ammonia

Precipitation with ammonia is possible but so far has only been described on a laboratory scale (Berglund et al. 1999; Yedur et al. 2001). In this case diammonium succinate is generated by controlling the pH of the fermentation broth with an ammonia-based
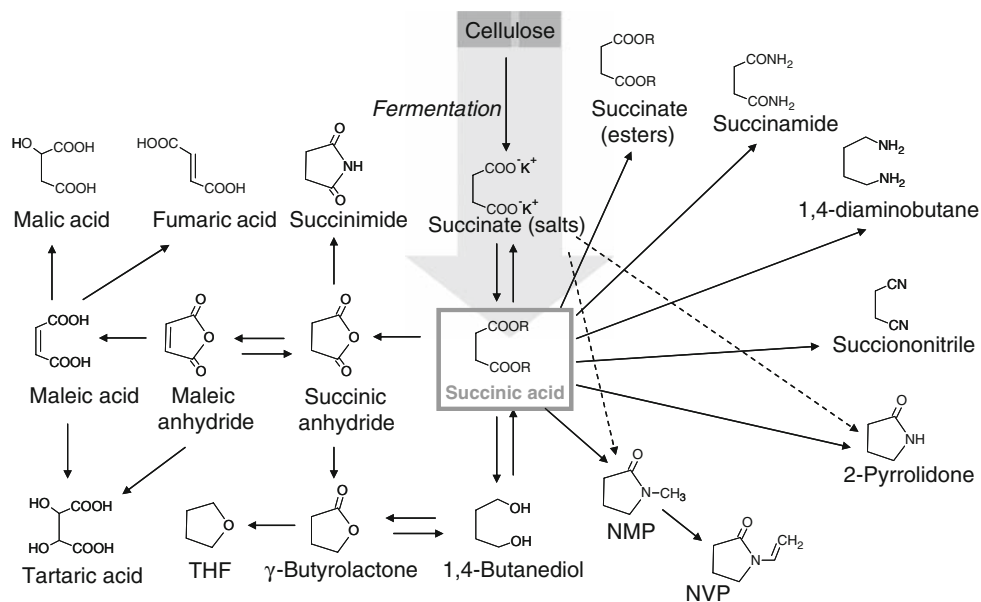
Fig. 1 Map of routes to succinic based products

titration agent or by substituting the cation in the succinate salt with ammonia after fermentation. The diammonium salt of succinic acid in the ultrafiltrated fermentation broth is then treated with sulfate ions or by combining it with ammonium bisulfate and/or sulfuric acid at low pH to yield the succinic acid precipitate and ammonium sulfate. The by-product ammonium sulfate can be cracked thermally into ammonia and ammonium bisulfate. The precipitated succinic acid is separated and purified after dissolution in methanol and re-crystallisation. With this approach, succinic acid can be refined with a yield of 93.3% based on the diammonium succinate available in the fermentation broth (Yedur et al. 2001).

The advantages of the integrated precipitation with ammonia are the lower amount of waste by-products and the possibility of recycling base and acid. The main disadvantage is the low selectivity of the precipitation with ammonia. Other organic acids present in the fermentation broth will be precipitated together with succinic acid at the same time (Yedur et al. 2001).

Electrodialysis

Electrodialysis is a well known method in the food industry for the separation of citric acid from citric juices (Zang et al. 1966). The application of electrodialysis for downstream processing of succinic acid has been studied on a laboratory scale in recent years. Glassner et al. (1992) proposed a desalting electrodialysis combined with a water-splitting electrodialysis to achieve succinic acid with high purity (Fig. 3). In a first purification step, the desalting electrodialysis separates the ionic species, such as acids, from the non-ionic species, e.g. sugars, saccharides or proteins under an electric potential. The desalting membranes are charged either with positive or negative groups and selectively allow the cations or anions to pass through the membranes, e.g. the positively charged membranes allow the passage of succinate anions and repel sodium cations. By this mechanism all charged molecules pass through the membrane whereas the uncharged molecules are not influenced by the charge and the electric field. A yield of 77% of succinic acid was achieved after electrodialysis.

In the next step the concentrated ionic stream with succinate and other ions is pumped across a set of chelating ion-exchange columns to replace the divalent cations of the succinate salt with sodium ions. The concentrated sodium succinate solution with the undesired ions is then fed to a bipolar membrane water-splitting dialysis to obtain succinic acid from succinate. This bipolar membrane is able to split water into protons and
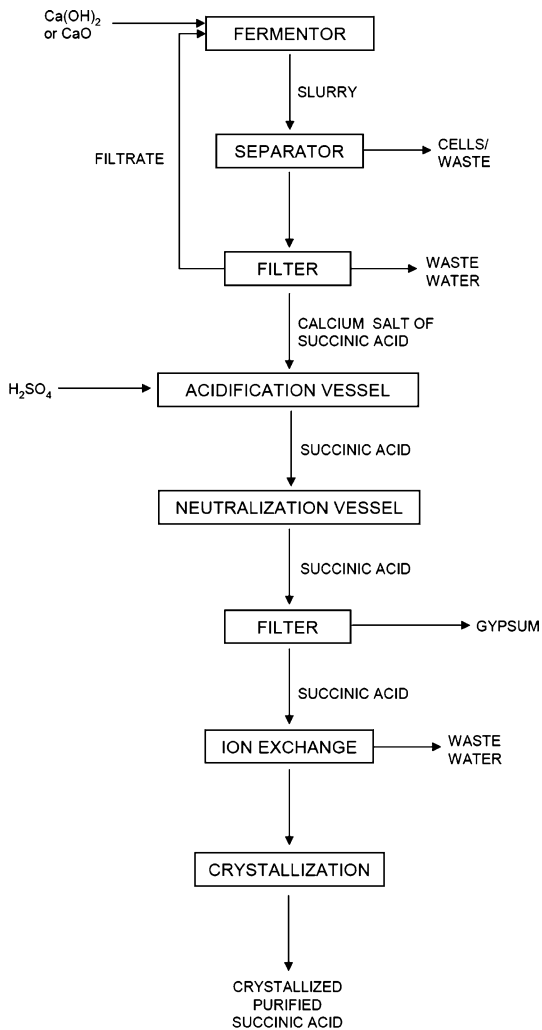
Fig. 2 Precipitation process with calcium hydroxide

Fig. 3 Process with electrodialysis and water-splitting electrodialysis

hydroxyl ions. Under an electric potential the succinate anions migrate to the anode and the sodium ions to the cathode. The sodium ions react with the hydroxyl ions to sodium hydroxide and succinate reacts with the protons to succinic acid. After water-splitting electrodialysis a total purification yield of 60% was achieved; this means a loss of 40% of the initial succinic acid. To yield a higher purity (>99%) of succinic acid the aqueous solution is subjected to anionic and cationic ion exchangers to remove ionic impurities.

The last step after electrodialysis and ion exchange is evaporation of water and thereby crystallization of the succinic acid (Zeikus et al. 1999; Glassner et al. 1992; Berglund et al. 1991).
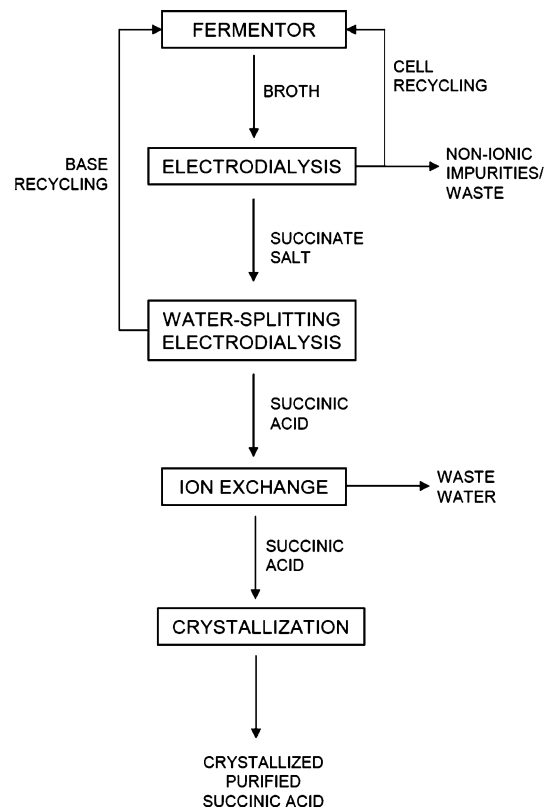
Disadvantages of electrodialysis are the high energy consumption, the material costs of the membranes and the low selectivity for succinic acid. Other organic acids, e.g. acetic acid, are indeed isolated together with succinic acid (McKinlay et al. 2007). Another problem is the presence of binary ions, which cannot be handled with electrodialysis membranes. For this reason, fermentations neutralized with magnesium or calcium hydroxide cannot be acidified and purified (Zeikus et al. 1999). Fouling is another hitherto unsolved problem (Jaquet et al. 1999).

Liquid–liquid extraction

Liquid–liquid extraction itself is a well and extensively used method in the chemical industry. There has been a lot of research in the last 30 years on its application for the separation of fermentation-based products, e.g. carboxylic acids (King and Dtarr 1990;

King and Sanchez 1985; King and Poole 1993). But in spite of these efforts liquid–liquid extraction is not usually applied in industrial production processes because most conventional extraction agents show very unfavourable distribution coefficients for organic acids.

Reactive extraction

To increase the extraction yield and the selectivity of the liquid–liquid extraction of organic acids from an aqueous phase, many authors propose the use of amines as reactive components, dissolved in non-water miscible organic solvents. Amines offer a high affinity to react with negatively charged molecules because of their high basicity (electron donor). Therefore they are suitable for the extraction of organic acids such as succinic acid (Pazouki and Panda 1998). The amine reacts with the succinic acid molecules at the interface between the aqueous and the organic phase leading to the formation of amine-acid–complexes. These complexes are solubilized into the organic phase. The mechanism consists in proton transfer or ion pair formation depending on the type of amine and the organic solvent (Kertes and King 1985; Hong et al. 2001).

Tamada et al. (1990; Tamada and King 1990a, b) studied the reaction mechanism of reactive extraction of various carboxylic acids with Alamine 336—a mixture of trioctylamine and tridecylamine—in various solvents. They distinguished 1,1-complexes (generated in active solvents like alcohol) and 2,1- or 3,1-acid–amine-complexes (generated in inactive solvents like alkanes or ketones).

For the reactive extraction of succinic acid from an aqueous phase, long-chain aliphatic primary, secondary and tertiary amines are proposed (Tung and King 1994a; Hong and Hong 2000a, b, c; Hong et al. 2002, Hong et al. 2004; Song et al. 2007).

Primary amines are characterized by a high solubility in the aqueous phase. Secondary amines have the highest distribution coefficients but tend to form amides in the downstream regeneration by distillation. Only the undissociated acid can be extracted by primary, secondary and tertiary amines. In contrast, quaternary amines can extract the dissociated and the undissociated form of the acid, but they are difficult to regenerate by back extraction. Consequently, tertiary amines are the most attractive

agents for the extraction of carboxylic acids (Lee et al. 2008; Yang et al. 1991; Kertes and King 1985).

In the literature mostly simple reactive extraction systems with tertiary amines in alcohol, xylene, heptane, kerosene, methylenchloride or nitrobenzene are described for the extraction of succinic acid from an aqueous solution (Hong and Hong 2000a, b, c; Juang et al. 1997; Tung and King 1994a; Yang et al. 1991, Song et al. 2007). For example, Song et al. (2007) proposed a simple process of reactive extraction with trioctylamine in 1-octanol, vacuum distillation and crystallization. In this approach, succinic acid has been isolated via reactive extraction with an extraction yield of more than 99% of the microbially produced acid.

A few complex systems have also been described: a mixture of amines in a mixture of solvents, e.g. tripropylamine/trioctylamine or trialkylamines in 1-octanol or chloroform and heptane (Hong and Hong 2000c; Heyberger et al. 1997). Matsumoto studied the extraction of organic acids using a combination of amine-based extractants and phosphorus-based extractants (Matsumoto et al. 2001).

Reactive extraction with aliphatic amines depends on the pH in the aqueous phase, the temperature, the type and properties of the organic solvent and the amine, the distribution coefficient, the loading ratio, the complexation equilibrium constant and the acid concentration (Huh et al. 2004; Kahya et al. 2001).

Most of the studies published so far on reactive extraction were performed with pure aqueous phases and the organic acid apart from the study of Jun et al. (2007). Jun et al. claimed that for an efficient reactive extraction of succinic acid with tertiary amines the pH of the fermentation broth should be far below $pKa_1 = 4.2$ so that most of the acid molecules are in the undissociated form. Impurities like other organic acids and salts (HPO_4^{2-}, PO_4^{3-}, CO_3^{2-}, SO_4^{2-}) cause a decrease in extraction yield because of their ionic strength. Their concentration should be minimized in the upstream process. Therefore, an opposite approach was investigated by Huh et al. (2006). By-product acids and impurities like acetic acid, pyruvic acid and salts are removed from fermentation broth in a pre-treatment step of reactive extraction with trioctylamine. Residual glucose is removed by crystallization at low pH. After the reactive extraction step, succinic acid remains in the fermentation supernatant with a yield of 97.1% related to the

initial amount. The final purification with an evapo-
rative crystallizer leads to a purity of 99.8% of the
acid and an overall yield of 71.3%. This has been
shown in an experiment with *Mannheimia succinic-
iproducens* fermentation broth (Huh et al. 2006).

Reactive extraction on a laboratory scale is usually
performed with simple mixer-settler setups such as
liquid–liquid centrifuges. Liquid–liquid centrifugal
extractors are well established for phase separation in
industry and they can easily be scaled up. In general
the amine solvent mixture can be recycled after back-
extraction with trimethylamine or pH-swing-, dilu-
ent-swing-, or temperature-swing-regeneration meth-
ods of the organic acid (Tung and King 1994b; Poole
and King 1991; Hong et al. 2001). The complete
process scheme, not yet realized on an industrial
scale, is shown in Fig. 4.

Reactive extraction is generally considered to be
an effective primary separation step for the recovery
of carboxylic acids from aqueous solutions (Cascaval
and Balaction 2004). Furthermore reactive extraction
enables the integrated product recovery of carboxylic
acids during fermentation (Rüffer et al. 2004). If the
separation process enables the recycling of the costly
amines efficiently, it is very likely that optimized
reactive extraction processes may be applied in the
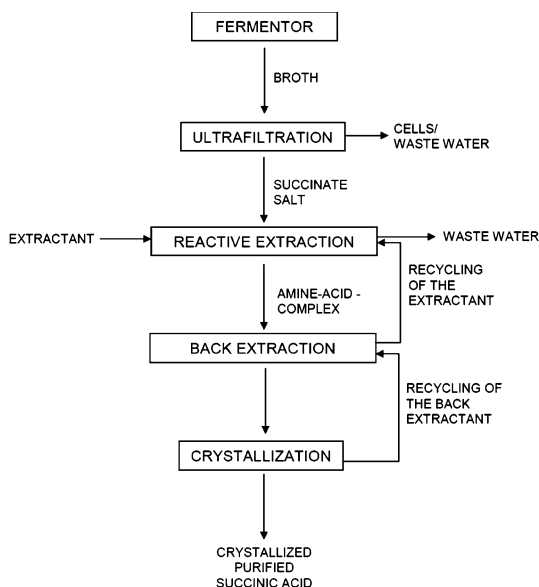near future for industrial production of bio-succinic
acid.

Fig. 4 Reactive extraction process for succinic acid

Predispersed solvent extraction (PDSE)

Conventional solvent extraction processes, such
as reactive extraction and back-extraction require
energy consuming mixer-settler setups for mechani-
cal mixing and separation of the phases.

Predispersed solvent extraction (PDSE) using col-
loidal liquid aphrons (CLAs) may be a new and more
energy-saving way for solvent extraction. The advan-
tage of this approach is that less energy is necessary for
phase mixing and separation. The extraction only
depends on the dispersion of the CLAs in the aqueous
fermentation broth. CLAs are defined as liquid glob-
ules with colloidal dimension encapsulated by an
aqueous soapy shell and dispersed in a continuous
aqueous phase. The liquid core contains a small
amount of oil soluble surfactant. An organic phase
(solvent with amine) is placed inside. Continuous
operation with PDSE is carried out with succinic acid
aqueous solution as continuous phase and the CLAs as
dispersed phase in the column. The principle is a
counter current extraction in which the continuous
phase is supplied from the top of the column and the
dispersed phase from the bottom – both with the same
flow rate. The stripping of the extracted succinic acid
from the organic phase is performed by temperature-
swing, pH-swing or diluent-swing.

There should be no difference in extraction
capabilities between a PDSE process with CLAs
and a conventional mixer-settler extraction. The
extractability of the acid with CLAs and the stability
of the CLAs depend on the presence of salts, the
concentration of amines and solvents and the pH.
However, PDSE is less energy-consuming and for
this reason may be more cost-saving compared to a
standard reactive extraction process with centrifugal
extractors and has already been applied successfully
to real fermentation broth on a laboratory scale (Kim
et al. 2002; 2004a, b).

Sorption and ion exchange

After the separation of cells and proteins and the
isolation and concentration of the product some more
purification steps are necessary. Ion exchange is a well
established unit operation for the final purification of
succinic acid from an aqueous solution. Ion exchange
is mainly applied for the removal of residual cations

and anions. Kushiku proposes H-type strongly acidic cation-exchange resins to produce succinic acid from succinate. The concentration of hydrogen ions has to be 1–10% higher than the equivalent concentration of the cations in the fermentation broth. Finally crystallization is applied to produce the pure succinic acid (Kushiku et al. 2006).

Li et al. (2008) investigated an alkaline anion-exchange resin (NERCB 04) for in situ separation of succinic acid from fermentation broth. The hydroxyl group of the acid reacts with the alkaline anion-exchange resin whereas the resin acts as in situ base producer at the same time. Thus base addition for pH-control was reduced during the fermentation process. The elution of the acid and the regeneration of the resin are carried out by adding 0.5 M NaOH.

A new approach was published by Jun et al. (2007). They suggested the use of mesoporous silica (SBA-15) functionalized with primary, secondary and tertiary amino-functional silanes for the isolation of pyruvic and succinic acid from fermentation broth. The amino-functionalized silanes are covalently bound to the active layer of pore walls. The amine-acid-complex is coupled via hydrogen bonding. Pyruvic acid was adsorbed threefold better than succinic acid. Therefore, amino-functionalized SBA-15 silica seems to be more useful for the removal of contaminant acids from fermentation broth than for the separation of succinic acid itself (Jun et al. 2007).

In general, ion-exchange may be only applied as an additional purification step for succinic acid recovery, because selectivity is not high enough and yields remain low (Pai et al. 2002).

Conclusions

There have been a lot of investigations and efforts on designing an adequate downstream process for the recovery of succinic acid from fermentation broth. Most of these approaches are principally functional, but industrial realisation will depend on scalability, robustness, overall separation yield and costs.

Most of the so far proposed process schemes for the separation of succinic acid from fermentation broth do not result in high selectivity with respect to other carboxylic acids which may be present in the fermentation broth. As the final purification accounts for a significant cost factor, the production of these

byproducts (acetic acid, pyruvic acid and others) in the fermentation should be reduced to a minimum by metabolic design of the microbial producers and optimization of the fermentation processes.

Separation processes based on reactive extraction have been presented in a number of studies and patents as a cost-saving and environmentally friendly approach for the recovery of succinic acid if all additives, e.g. amines and solvents can be recycled. A fermentation process integrated reactive extraction of succinic acid seems feasible. The efficiency of the extraction depends on the type of amine and solvent, the pH in the fermentation broth, other acids and ions and the concentration of succinic acid itself. The extraction conditions and amine-solvent mixtures have to be adapted to the different fermentation processes.

To compete with the present petrochemical production of succinic acid it is necessary to minimize the total production costs. Hermann and Patel (2007) estimated the production costs plus profit of bio-succinic acid as function of the sugar price to 1.1–1.6 € kg^{-1} succinic acid (about US $ 1.6–2.4 kg^{-1} succinic acid) on 100,000 tons per year basis without giving further details on the downstream processing. They expect that "in the future" these biotechnological production costs plus profit can be reduced to 0.45–0.92 € kg^{-1} succinic acid (about US $ 0.7–1.4 kg^{-1} succinic acid). This challenging objective can only be fulfilled with high-volume production plants (economy of scale) and if (i) inexpensive cellulosic raw materials can be applied as carbon source, (ii) a molar succinic acid yield based on carbon source of more than 1 can be achieved during fermentation (additional fixation of CO_2) with a mimimum of byproduct formation (organic acids) and (iii) the high downstream processing yields reported so far on a laboratory scale will be realised on an industrial scale, with the consequential lower processing costs.

As an alternative to the complex and difficult isolation and purification of succinic acid from fermentation broth, Delhomme et al. (2009) reviewed the catalytic possibilities of using succinic acid as a C$_4$ building block in aqueous fermentation media. They came to the conclusion that the efforts and costs for purification of succinic acid from fermentation broth may be reduced in the near future, if more water-stable and highly active catalysts (metal containing ones or organo-metallic complexes) become

available for the selective and direct aqueous hydrogenation of succinic acid.

References

Baniel AM, Eyal AM (1995) Citric acid extraction. US patent 5,426,220

Bechthold I, Bretz K, Kabasci S, Kopitzky R, Springer A (2008) Succinic acid: a new platform chemical for bio-based polymers from renewable resources. Chem Eng Technol 5:647–654

Berglund KA, Elankovan P, Glassner DA (1991) Carboxylic acid purification and crystallization process. US patent 5,034,105

Berglund KA, Yedur S, Dunuwila D (1999) Succinic acid production and purification. US patent 5,958,744

Cascaval D, Balaction AI (2004) New separation techniques on bioseparations 1. Reactive extraction. Chem Ind 58(9): 375–386

Cornils B, Lappe P (2002) Dicarboxylic acids, aliphatic Ullmann's Enzyklopedia of industrial chemistry. Wiley-VCH Verlag, Weinheim

Datta R (1992) Process for the production of succinic acid by anaerobic fermentation. US patent 5,143,833

Datta R, Glassner DA, Jain MK, Vicky Roy JR (1992) Fermentation and purification process for succinic acid. US patent 5,168,055

Delhomme C, Weuster-Botz D, Kühn F (2009) Succinic acid from renewable resources as a C4 building-block chemical–a review of the catalytic possibilities in aqueous media. Green Chem 11:13–26

Glassner DA, Satinwood RD, Datta R (1992) Process for the production and purification of succinic acid. US patent 5,143,834

Hermann BG, Patel M (2007) Today's and tomorrow's bio-based bulk chemicals from white biotechnology–a techno-economic analysis. Appl Biochem Biotechnol 136: 361–388

Heyberger A, Prochazka J, Volaufova E (1997) Extraction of citric acid with tertiary amine–third phase formation. Chem Eng Sci 97:00321–00327

Hong YK, Hong WH (2000a) Equilibrium studies on reactive extraction of succinic acid from aqueous solutions with tertiary amines. Bioproc Eng 22:477–481

Hong YK, Hong WH (2000b) Reactive extraction of succinic acid with tripropylamine (TPA) in various diluents. Bioproc Eng 22:281–284

Hong YK, Hong WH (2000c) Extraction of succinic acid with 1-octanol/n-heptane solutions of mixed tertiary amine. Bioproc Eng 23:535–538

Hong YK, Hong WH (2004) Influence of chain length of tertiary amines on extractability and chemical interactions in reactive extraction of succinic acid. Korean J Chem Eng 21:488–493

Hong SH, Lee SY (2001) Metabolic flux analysis for succinic acid production by recombinant *Escherichia coli* with amplified malic enzyme activity. Biotechnol Bioeng 74:89–95

Hong YK, Hong WH, Han DH (2001) Application of reactive extraction to recovery of carboxylic acids. Biotechnol Bioproc Eng 6:386–394

Hong YK, Han DH, Hong WH (2002) Water enhanced solubilities of succinic acid in reactive extraction using tertiary amines/alcohol systems. Korean J Chem Eng 19:83–86

Huh YS, Hong YK, Hong WH, Chang HN (2004) Selective extraction of acetic acid from the fermentation broth produced by *Mannheimia succiniciproducens*. Biotechnol Lett 26:1581–1584

Huh YS, Jun Y-S, Kong YK, Song H, Lee SY, Hong WH (2006) Effective purification of succinic acid from fermentation broth produced by *Mannheimia succiniciproducens*. Proc Biochem 41:1461–1465

Jaquet A, Quan R, Marison W, vain Stockar U (1999) Factors influenceing in potentioluse of aliquat 336 for the in situ extraction of carboxylic acids from cultures of *Pseudomonas putida*. J Biotechnol 68:185

Juang RS, Huang RH (1997) Equilibrium studies on reactive extraction of lactic acid with an amine extractant. Chem Eng J 65:47–53

Jun YS, Huh YS, Park HS, Thomas A, Jeon SJ, Lee EZ, Won HJ, Hong WH, Lee SY, Hong YK (2007) Adsorption of pyruvic and succinic acid by amine-functionalized SBA-15 for the purification of succinic acid from fermentation broth. J Phys Chem C 200(111):13076–13086

Kahya E, Bayraktar E, Mehmetoglu Ü (2001) Optimization of process parameters for reactive lactic acid extraction. Turk J Chem 25:223–230

Kertes AS, King CJ (1985) Extraction chemistry of fermentation product carboxylic acids. Biotechnol Bioeng 28:269

Kim BS, Hong YK, Hong WH (2002) Effect of pH on the extraction characteristics of succinic acid and the stability of colloidal liquid aphrons. Korean J Chem Eng 19: 669–672

Kim BS, Hong YK, Hong WH (2004a) Effect of salts on the extraction characteristics of succinic acid by predispersed solvent extraction. Biotechnol Bioproc Eng 9:207–211

Kim BS, Hong YK, Huh YS, Hong WH (2004b) Predispersed solvent extraction of succinic acid aqueous solution by colloidal liquid aphrons in column. Biotechnol Bioproc Eng 9:454–458

King CJ, Dtarr J (1990) Recovery of carboxylic acids from water by precipitation from organic solutions. US patent 5,104,492

King CJ, Poole LJ (1993) Craboxylic acid sorption regeneration process. US patent 5,412,126

King CJ, Sanchez PA (1985) Process for sorption solute recovery. US patent 4,670,155

Kirk-Othmer (1979) Encyclopedia of chemical technology, 3rd edn. Wiley, New York. Citric acid, vol 6; Hxdroxycarboxylic acids, vol 13

Kushiku T, Fujiwara K, Satou T, Sano (2006) Method for purifying succinic acid from fermentation broth. US patent 2006/0276674A1

Lee SY, Kim JM, Song H, Lee JW, Kim TY, Yang YS (2008) From genome sequence to integrated bioprocess for

succinic acid production by *Mannheimia succiniciproducens*. Appl Microbiol Biotechnol 79:11–22

Li Q, Li WL, Wang D, Liu BB, Tang H, Yang MH, Liu Q, Xing JM, Su ZG (2008) pH neutralization while succinic acid adsorption onto anion-exchange resins. Appl Biochem Biotechnol. doi:10.1007/s12010-008-8355-4

Likidis Z, Schügerl K (1987) Recovery of penicillin by reactive extraction in centrifugal extractors. Biotechnol Bioeng 30:1032–1040

Matsumoto M, Otono T, Kondo K (2001) Synergistic extraction of organic acids with tri-n-octylamine ant tri-n-butylphosphate. Sep Purif Technol 24:337–342

McKinlay JB, Vieille C, Zeikus JG (2007) Prospects for a bio-based succinate industry. Appl Microbiol Biotechnol. doi:10.1007/s00253-007-1057-y

Meynial-Salles I, Dorotyn S, Soucaille P (2007) A new process for the continuous production of succinic acid from glucose at high yield, titer, an productivity. Biotechnol Bioeng 99(1) Jan 1, 2008

Okino SH, Noburyu R, Suda M, Jojima T, Inui M, Yukawa H (2008) An efficient succinic acid production process in a metabolically engineered Corynebacterium glutamicum strain. Appl Microbiol Biotechnol 81:459–464

Pai RA, Doherty MF, Malone MF (2002) Design of reactive extraction systems for bioproduct recovery. AIChE J 48:514–526

Patel MA (2006) Medium and long-term opportunities and risks of the biotechnological production of bulk chemicals from renewable resources—the potential of white biotechnology. The BREW Project (http:www.chem.uu.nl/brew/)

Pazouki M, Panda T (1998) Recovery of citric acid—a review. Bioproc Eng 19:435–439

Poole LJ, King CJ (1991) Regeneration of carboxylic acid-amine extracts by back-extraction with an aqueous solution of a volatile amine. Ind Eng Chem Res 30:923–929

Rüffer N, Heidersdorf U, Kretzers I, Sprenger GA, Raeven L, Takors R (2004) Fully integrated L-phenylalanine separation and concentration using reactive-extraction with liquid-liquid centrifuges in a fed-batch process with E. coli. Bioprocess Biosyst Eng 26:239–248

Schlichting E, Halwachst W, Schügerl K (1987) Reactive extraction of salicylic acid and D/L phenylalanine in a stirred cell. Chem Eng Com 51:193–205

Song H, Lee SY (2005) Production of succinic acid by bacterial fermentation. Enzym Microbial Technol 39: 352–361

Song H, Huh YS, Lee SY, Hong WH, Hong YK (2007) Recovery of succinic acid produced by fermentation of a metabolomically engineered *Mannheimia succiniciproducens* strain. J Biotechnnol 132:445–452

Tamada JA, King CJ (1990a) Extraction of carboxylic acids with amine extractants: 2. Chemical interactions and interpretation of data. Ind Eng Chem Res 29:1327–1333

Tamada JA, King CJ (1990b) Extraction of carboxylic acids with amine extractants: 3. Effects of temperature, water coextraction and process considerations. Ind Eng Chem Res 29:1333–1338

Tamada JA, Kertes AS, King CJ (1990) Extraction of carboxylic acids with amine extractants: 1. Equilibria and law of mass action modeling. Ind Eng Chem Res 29:1319–1326

Tung LA, King CJ (1994a) Sorption and extraction of lactic and succinic acids at pH > pK_{a1}. 1. Factors governing equilibria. Ind Eng Chem Res 33:3217–3223

Tung LA, King CJ (1994b) Sorption and extraction of lactic and succinic acids at pH > pK_{a1}. 2. Regeneration and process considerations. Ind Eng Chem Res 33:3224–3229

Vickroy TB (1985) Lactic acid. In: Comprehensive Biotechnology, Blanch HW, Drew S, Wang DIC (eds) Comprehensive biotechnology, vol 3, pp 761–776. Pergamon Press, New York

Wieczorek S, Bauer H (1998) Continuous production of citric acid with recirculation of the fermentation broth after product recovery. Bioprocess Eng 18:1–5

Wilke T, Vorlop K-D (2004) Industrial bioconversion of renewable resources as an alternative to conventional chemistry. Appl Microbiol Biotechnol 66:131–142

Yedur S, Berglung KS, Dunuwila DD (2001) Succinic acid production and purification. US patent 6,265,190

Zang JA, Moshy RJ, Smith RN (1966) Electrodialysis in food processing. Chem Eng Progress Symp Ser 62:105–110

Zeikus JG, Jain MK, Elankovan P (1999) Biotechnology of succinic acid production and markets for derived industrial products. Appl Microbiol Biotechnol 51:545–552