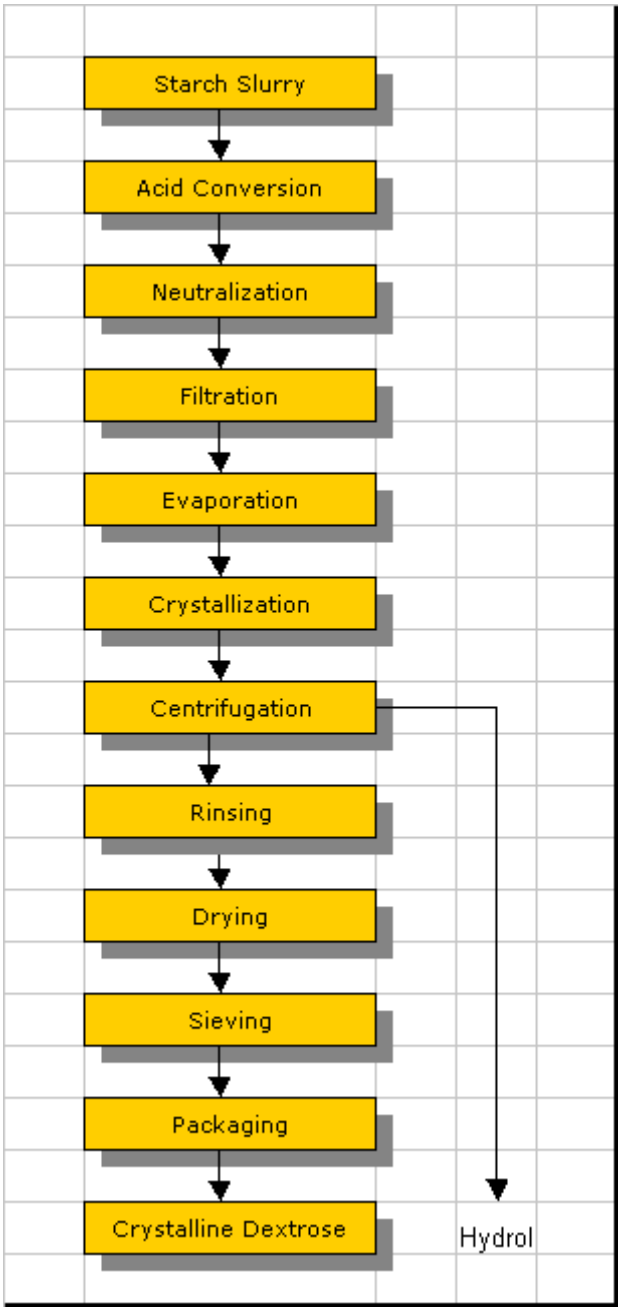
International Starch Institute

DEXTROSE PROCESS DEVELOPMENTS TM32-2e



In 1811 **Constantine Kirchoff** discovered that sugar could be produced by the acid hydrolysis of starch.

The commercial manufacture of glucose sugars from starch began during the Napoleonic Wars with England, when suppliers of sucrose sugar were cut off from France by sea blockade.

THE BATCH PROCESS

Until mid 20th century the process of making glucose syrup and crystalline dextrose was a batch process. It was an all-acid conversion. Starch was boiled in acidified water at moderate temperature and pressure. Both hydrochloric acid and sulphuric acid have been used.

The dextrose equivalent (DE) of the hydrolysate was not impressive.

← Typical pre-war batch process

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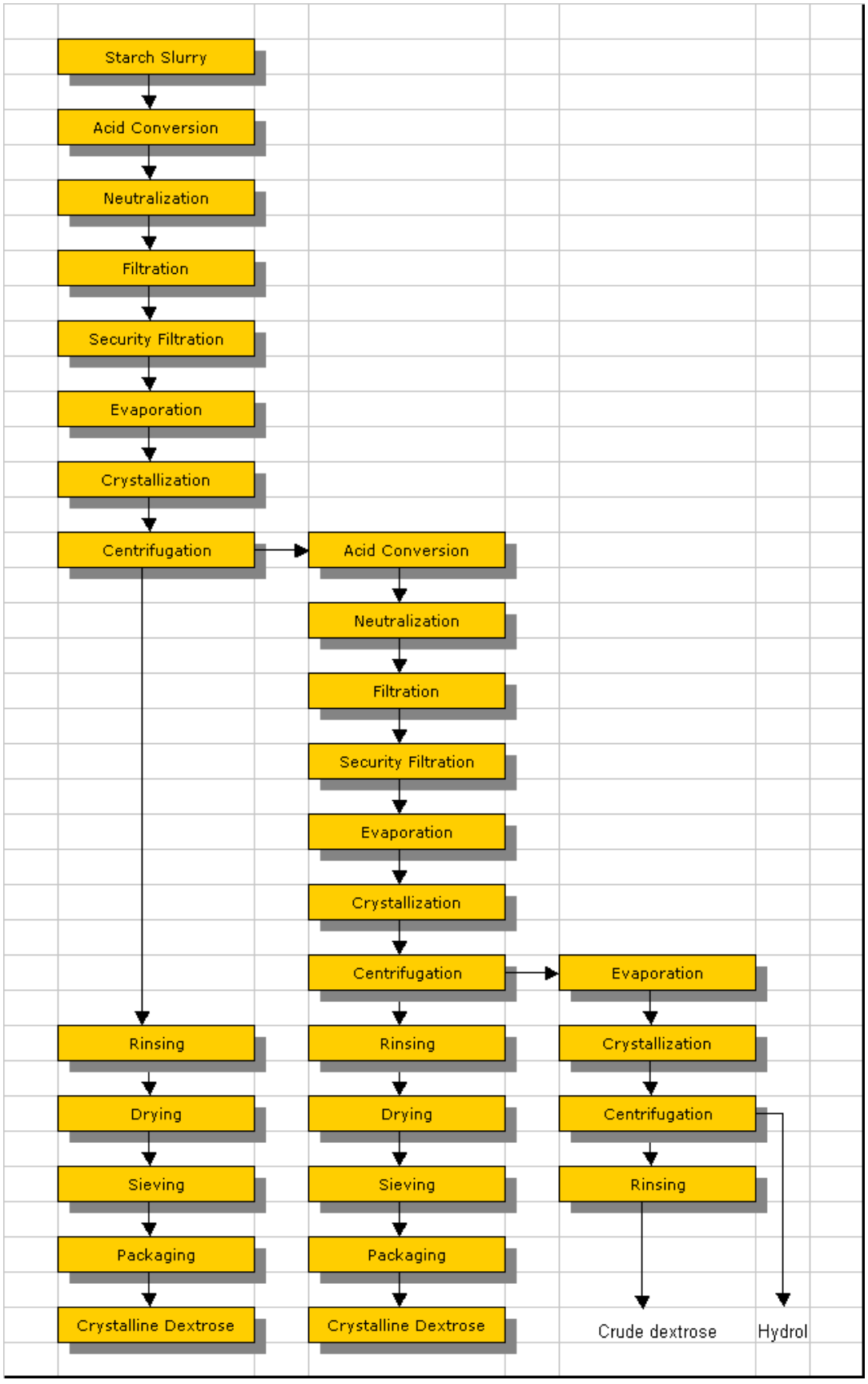

THE CONTINUOUS ALL-ACID PROCESS

Mid 20th century the Danish inventor Karl Kroyer made a breakthrough with his continuous glucose syrup process.

It was tempting to transfer the technology to the manufacturing of crystalline dextrose.

The Lomza project was, however, the only one implemented as an all-acid conversion.

← The process applied in Lomza.

The crude dextrose was re-dissolved and re-cycled; the hydrol was disposed of as pig-feed.

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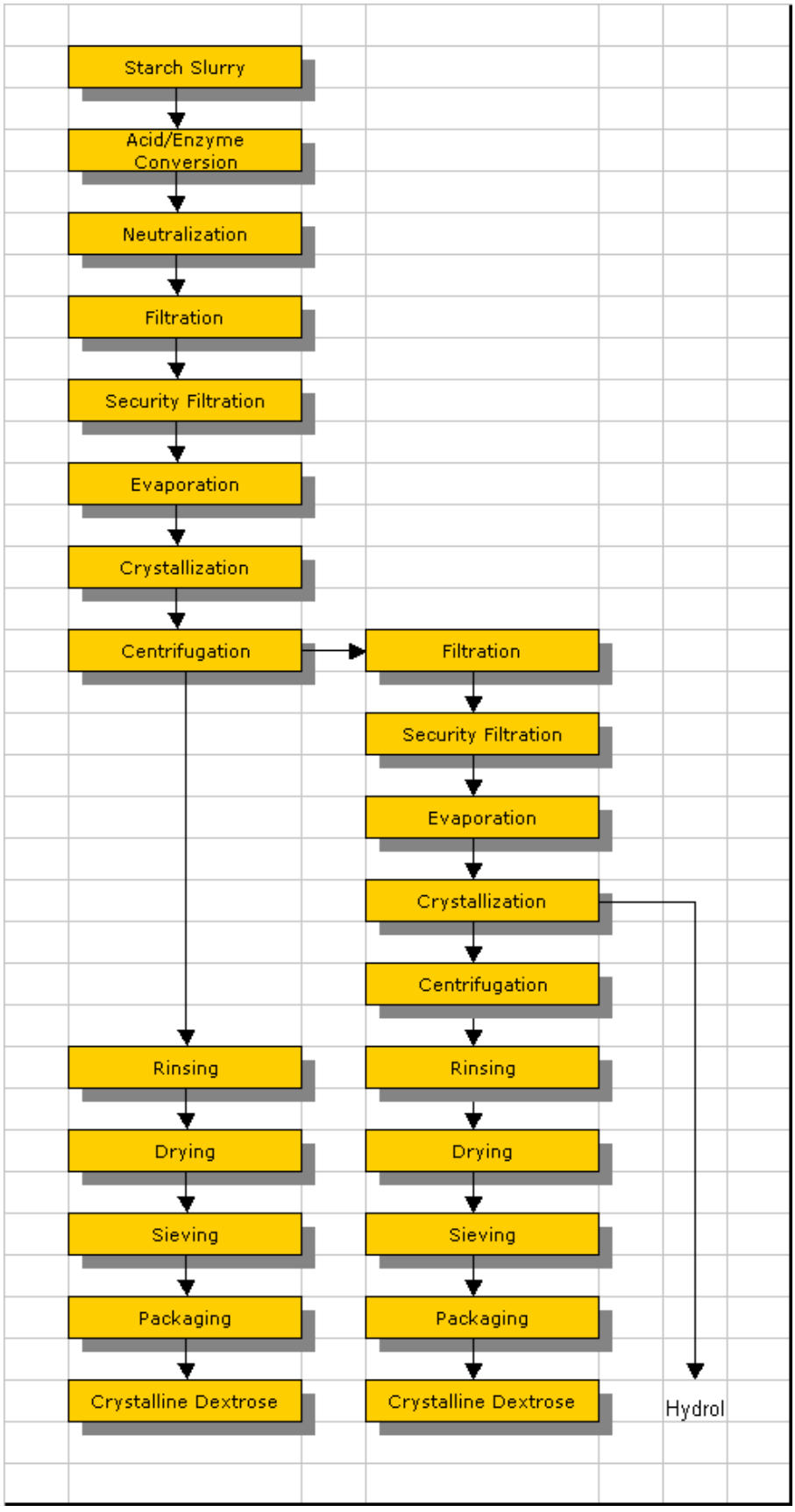

THE CONTINUOUS ACID / ENZYME PROCESS

Lomza represented a midstream situation and plans for switching to enzymes were worked out even before the Lomza factory was put in operation.

In crystalline dextrose manufacturing the enzyme technology in particular was a great step ahead. With enzymes the upper limit of saccharification moved well above 90 DE.

The purity of the hydrol after first crystallization obviously called for a second crystallization.

The Györ cornstarch and dextrose factory

← The process applied in Györ

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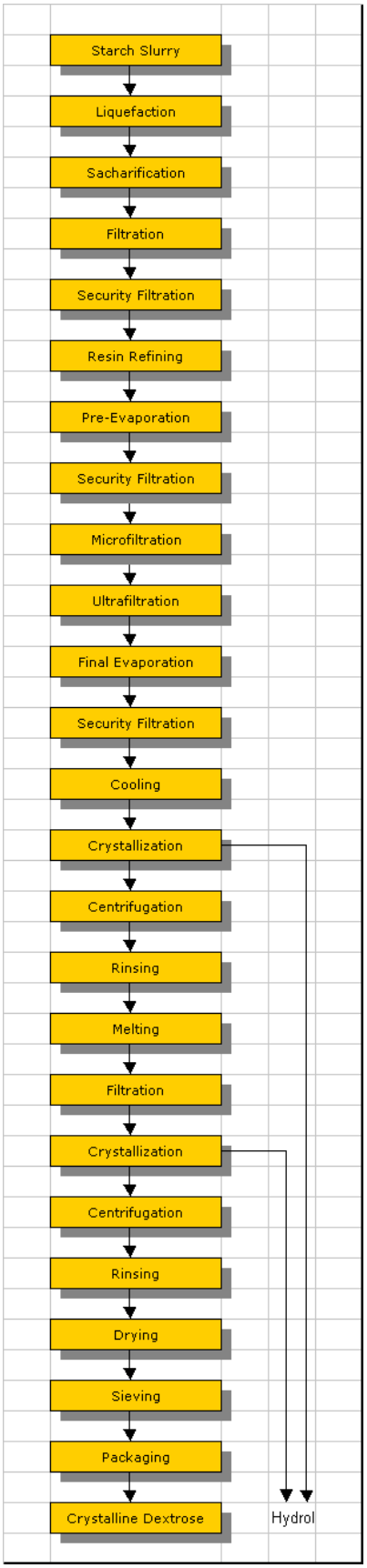

← Traditional dual crystallization of pharmaceutical grade dextrose.

THE ALL- ENZYME PROCESS

Both enzymatic liquefaction and enzymatic saccharification bring about DE values close to equilibrium and this is the state of art.

The hydrol benefits the most. It is not discarded anymore. The purity allows feeding an increased share of the hydrol back into the process and only a fraction has to be drawn off to maintain the sufficient purity in the system. The hydrol contains dextrose and higher sugars. Excess hydrol is typical mixed into syrups produced in an adjacent glucose syrup line.

Demineralization of the hydrolysate does also contribute to purity by removing salts otherwise hampering the crystallization.

DUAL CRYSTALLIZATION of PHARMACEUTICAL DEXTROSE.

If intended for use in large-volume preparations for parenteral use a competent pharmaceutical authority may require that dextrose comply with a test for pyrogens. Careful sanitary preparation and aseptic handling is a prerequisite which in combination with depyrogenation by membrane filtering secures that quality.

In general the European Pharmaco-poeia and others stipulate a set of quality parameters. A most traditional way to cope is by dual crystallization. Even with an all-enzyme process the first crystallization is not considered sufficient. Re-melting (re-dissolving) the crystal and re-crystallizing does the trick and very pure dextrose is achieved.

The purity of the second feed is so high that all second hydrol may be recycled together with a large fraction of first hydrol.

Payen, A., Persoz, J.F. (1833). Mémoire sur la diastase, les principaux produits de ses réactions, et leurs applications aux arts industriels. *Ann. Chim. (Phys.)* **53**: 73-92.

Payen, A., Persoz, J.F. were the first to become aware of enzymatic starch hydrolysis: they found that malt extract converted starch to sugar.

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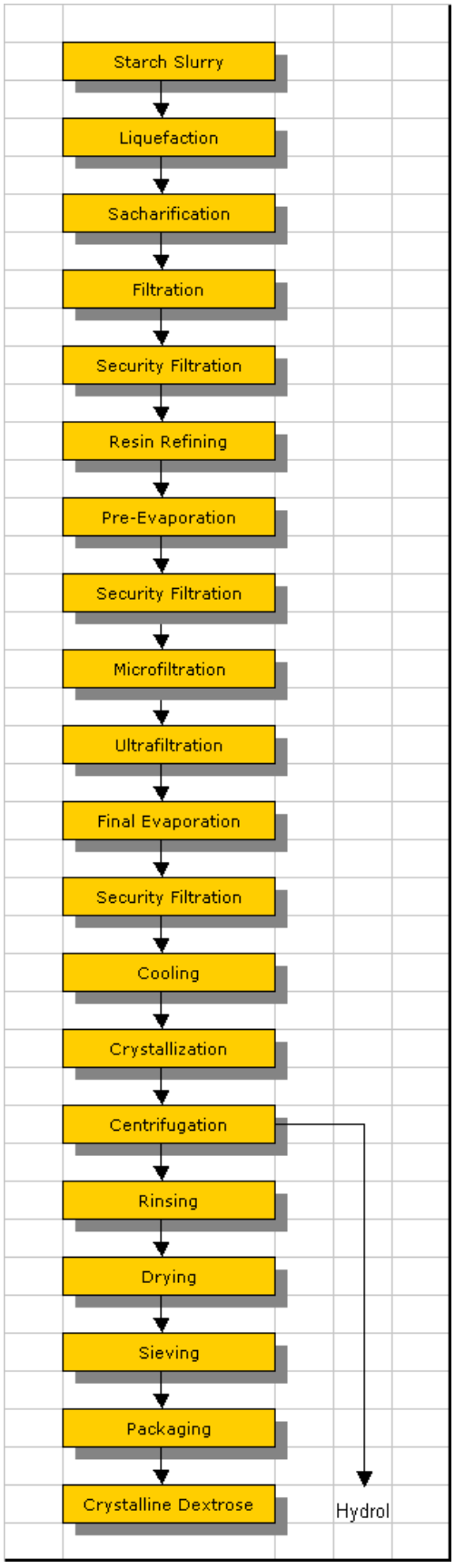

SINGLE CRYSTALLIZATION of PHARMACEUTICAL DEXTROSE.

Replacing the second crystallization with modern membrane and resin technique is a most elegant process for pharmaceutical dextrose. It limits direct recycling of hydrol and an adjacent large-scale glucose syrup production is therefore of particular advantage.

← The Cerestar single crystallization process for pharmaceutical grade dextrose.

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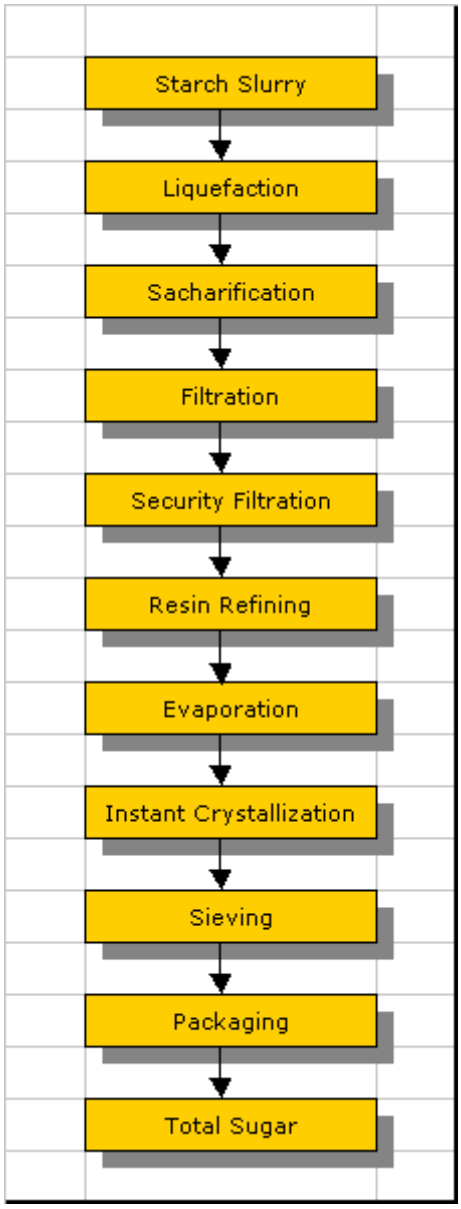


↑ Total Sugar Process.

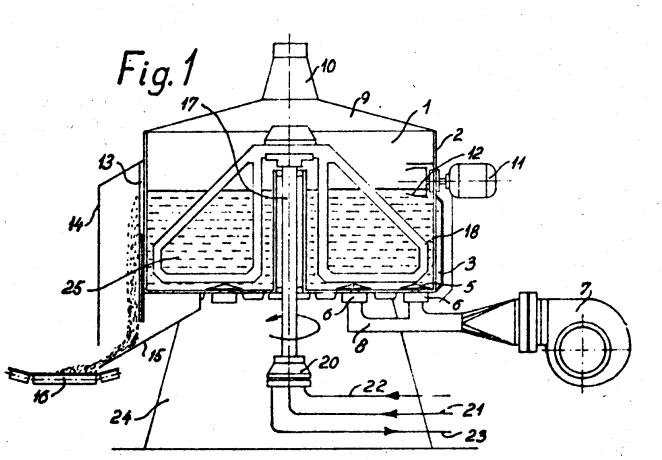
TOTAL SUGAR

The most elegant process of all is the total sugar process. It is fast, direct and leaves no hydrol.

With new modern membrane and resin techniques it definitely deserves a renaissance.

All-enzyme hydrolysis is a pre-requisite. The trick is to remove practical all excess water in the evaporator and chock crystallize the supersaturated syrup in one go. A spray crystallizer or an agitated crystallizer will do. The product is in the form of agglomerated microcrystals.

Duintjer, Wilkens Meihuizen & Co.
The total sugar spray crystallizer tower in background.
Commissioned by a member of the International Starch Group.



Total Sugar Agitated Instant Crystallizer.
Invented by a member of the International Starch Group.
U.S. Patent 3,743,539

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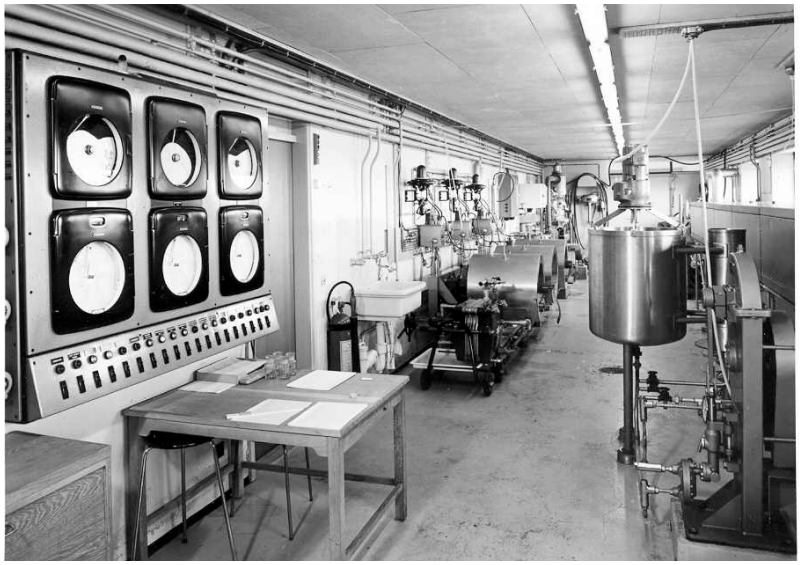
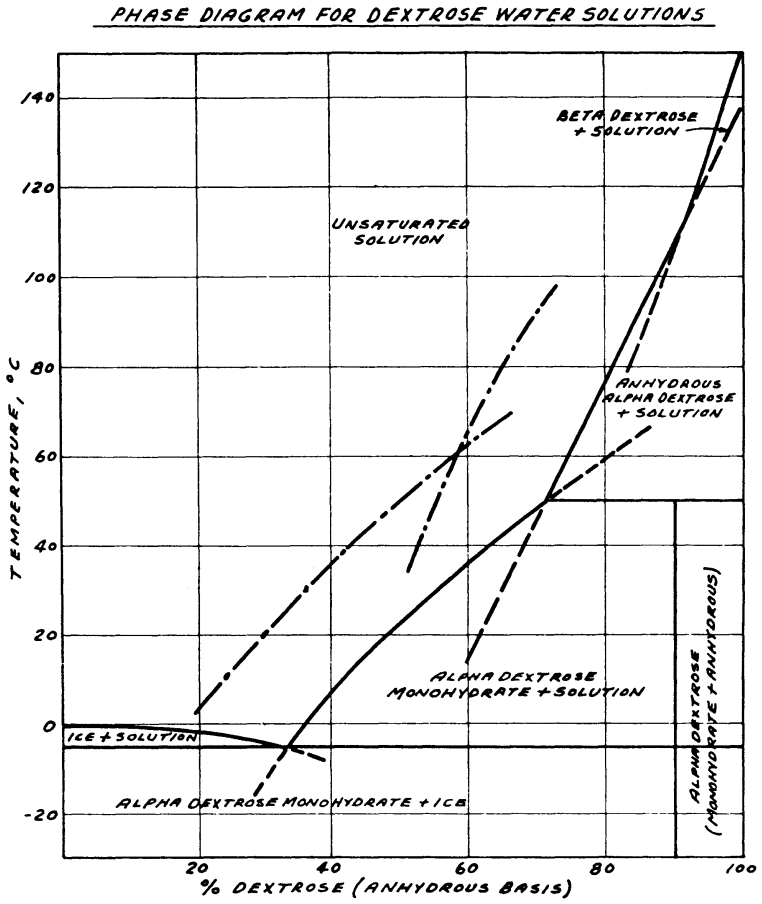


The Kroyer pilot plant - the cradle of the continuous starch conversion.

CRYSTALLIZATION TECHNIQUES.

The invention of the continuous starch-to-glucose conversion implied a quantum leap to the sweetener industry.

Enzymes and demineralization brought about an unprecedented purity of the hydrolysate with drastic reduction in crystallization time.

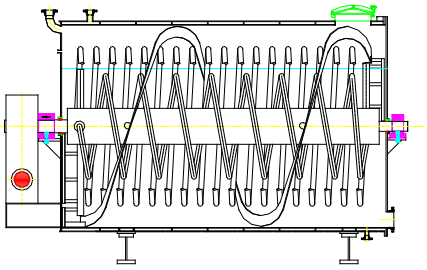


Ref.: Corn Products Refining Co. 1950

All dextrose crystallizing techniques have to obey the rules laid down in the dextrose phase diagram.

The phase diagram dictates a cooling crystallizer to get the monohydrate and an evaporative crystallizer for anhydrous dextrose.

The batch cooling crystallizer below has retained its popularity since its first use in the Lomza project. A continuous operation with three in series was soon adopted. Now the continuous vertical crystallizer is an preferred option.



Batch crystallizer with rotating cooling coils

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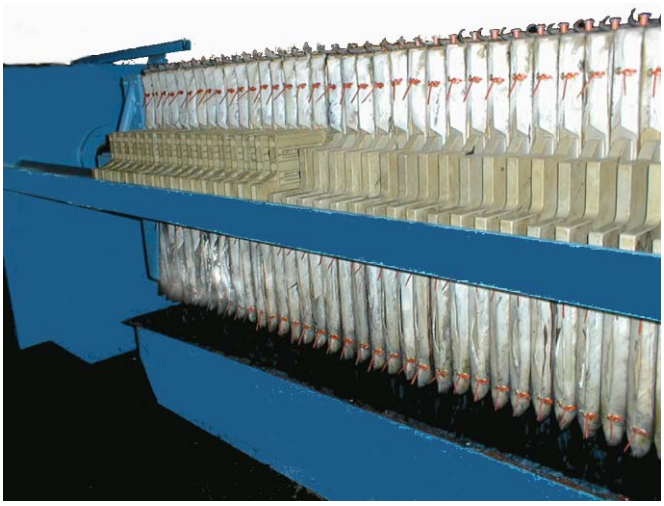
Outdoor vertical cooled crystallizers

For economical reasons and simplicity the all-in-one-column vertical crystallizer with separate stationary cooling coils most often replaces the three in a row batch machines in continuous crystallization.

More vacuum pans in a row may form an approximation to a similar continuous operation, but the vacuum condition impedes a similar simplicity in the manufacturer of anhydrous dextrose. Therefore the batch pan is often the obvious choice determined by the physical parameters.



Classic Filter Press

Filter presses and rotating vacuum filters are of well-proven efficiency. The rapid development of industrial membrane technology means that this process option is becoming increasingly attractive.

Cation and Anion Resin Columns

Demineralization using anion and cation exchangers is a standard procedure. Uninterrupted operation may be achieved in "merry go round" arrangement with two columns on duty, two on stand-by and two in regeneration.

When hydrolysate composition is to be corrected beyond demineralisation membranes and / or chromatographic resins may be applied to achieve specific saccharide profiles.

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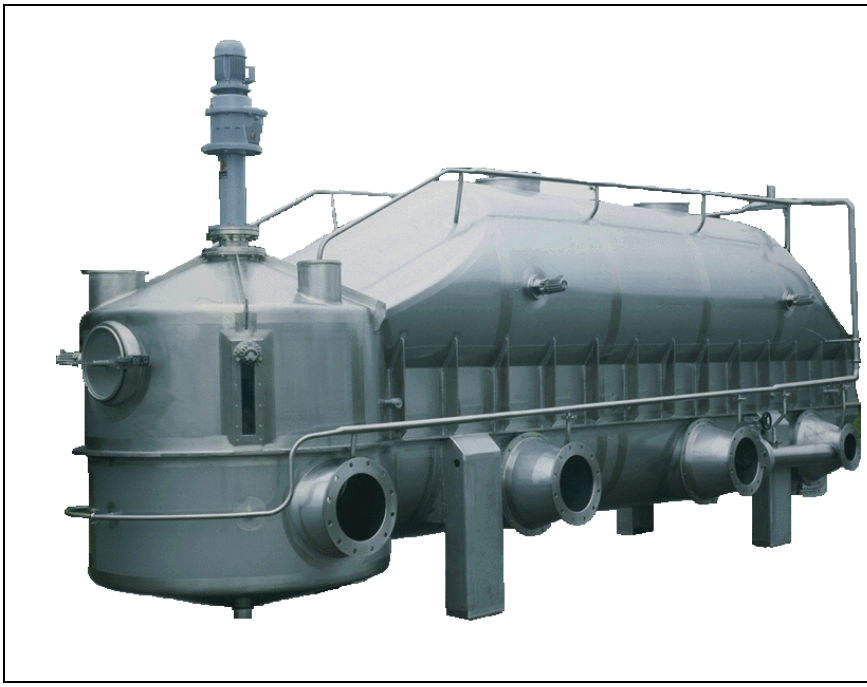
Batch Separators

CENTRIFUGATION

The massecuite leaving the crystallisers is separated in crystals and hydrol (mother liquor) by centrifugation.

Both batch type and continuous separators are used. The batch type is still the workhorse in the industry due to its simplicity, easy control and the easy in-centrifuge rinsing with water or steam.



Fluid Bed

DRYING

Previous rotating drum dryers / bundle dryers are today replaced by more gentle fluid beds.

Special design is a demand to handle the wet crystals.

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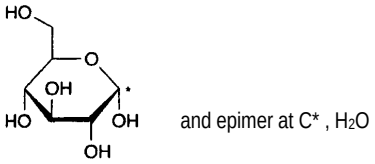
European Pharmacopoeia, Fourth Edition (2002)

01/2002:0178

GLUCOSE MONOHYDRATE

Glucosum monohydricum



$C_6H_{12}O_6,H_2$ M_r198.2

DEFINITION
Glucose monohydrate is the monohydrate of (+)-D-glucopyranose.

CHARACTERS
A white, crystalline powder, with a sweet taste, freely soluble in water, sparingly soluble in alcohol.

IDENTIFICATION
A. Specific optical rotation (see Tests): + 52.5 to + 53.3.
B. Examine by thin-layer chromatography (2.2.27), using *silica gel G R* as the coating substance.

Test solution. Dissolve 10 mg of the substance to be examined in a mixture of 2 volumes of *water R* and 3 volumes of *methanol R* and dilute to 20 ml with the same mixture of solvents.

Reference solution (a). Dissolve 10 mg of *glucose CRS* in a mixture of 2 volumes of *water R* and 3 volumes of *methanol R* and dilute to 20 ml with the same mixture of solvents.

Reference solution (b). Dissolve 10 mg each of *fructose CRS, glucose CRS, lactose CRS* and *sucrose CRS* in a mixture of 2 volumes of *water R* and 3 volumes of *methanol R* and dilute to 20 ml with the same mixture of solvents.

Apply separately to the plate 2 ml of each solution and thoroughly dry the starting points. Develop over a path of 15 cm using a mixture of 10 volumes of *water R,* 15 volumes of *methanol R,* 25 volumes of *anhydrous acetic acid R* and 50 volumes of *ethylene chloride R.* The solvents should be measured accurately since a slight excess of water produces cloudiness. Dry the plate in a current of warm air. Repeat the development immediately, after renewing the mobile phase. Dry the plate in a current of warm air and spray evenly with a solution of 0.5 g of *thymol R* in a mixture of 5 ml of *sulphuric acid R* and 95 ml of *alcohol R.* Heat at 130 °C for 10 min. The principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a). The test is not valid unless the chromatogram obtained with reference solution (b) shows 4 clearly separated spots.

C. Dissolve 0.1 g in 10 ml of *water R.* Add 3 ml of *cupri-tartaric solution R* and heat. A red precipitate is formed.

TESTS
Solution S. Dissolve 10.0 g in *distilled water R* and dilute to 100 ml with the same solvent.

Appearance of solution. Dissolve 10.0 g in 15 ml of *water R.* The solution is clear (2.2.1), odourless, and not more intensely coloured than reference solution BY, (2.2.2, *Method II).*

Acidity or alkalinity. Dissolve 6.0 g in 25 ml of *carbon dioxide-free water R* and add 0.3 ml of *phenolphthalein solution R.* The solution is colourless. Not more than 0.15 ml of 0.1 M *sodium hydroxide* is required to change the colour of the indicator to pink.

Specific optical rotation (2.2. 7). Dissolve 10.0 g in 80 ml of *water R,* add 0.2 ml of *dilute ammonia RI,* allow to stand for 30 min and dilute to 100.0 ml with *water R.* The specific optical rotation is + 52.5 to + 53.3, calculated with reference to the anhydrous substance.

Foreign sugars, soluble starch, dextrins. Dissolve 1.0 g by boiling in 30 ml of *alcohol (90 per cent VW) R. Cool;* the appearance of the solution shows no change.

Sulphites. Dissolve 5.0 g in 40 ml of *water R,* add 2.0 ml of 0.1 M *sodium hydroxide* and dilute to 50.0 ml with *water R. To 10.0* m1 of the solution, add 1 ml of a 310 g/1 solution of *hydrochloric acid R,* 2.0 m1 of *decolorised fuchsin solution RI* and 2.0 ml of a 0.5 per cent V/V solution of *formaldehyde R.* Allow to stand for 30 min and measure the absorbance (2.2.25) at the maximum at 583 nm. Prepare a standard as follows. Dissolve 76 mg of *sodium metabisulphite R* in *water R* and dilute to 50.0 mi with the same solvent. Dilute 5.0 ml of this solution to 100.0 ml with *water R. To* 3.0 ml of this solution add 4.0 ml of 0.1 M *sodium hydroxide* and dilute to 100.0 ml with *water R.* Immediately add to 10.0 ml of this solution 1 ml of a 310 g/1 solution of *hydrochloric acid R,* 2.0 ml of *decolorised fuchsin solution R1* and 2.0 ml of a 0.5 per cent V/V solution of *formaldehyde R.* Allow to stand for 30 min and measure the absorbance at the maximum at 583 nm. Use as compensation liquid for both measurements a solution prepared in the same manner using 10.0 ml of *water R.* The absorbance of the test solution is not greater than that of the standard (15 ppm of SO_2).

Chlorides (2.4.4).4 ml of solution S diluted to 15 ml with *water R* complies with the limit test for chlorides (125 ppm).

Sulphates (2.4.13). 7.5 ml of solution S diluted to 15 ml with *distilled water R* complies with the limit test for sulphates (200 ppm).

Arsenic (2.4.2). 1.0 g complies with limit test A for arsenic (1 ppm).

Barium. To 10 m1 of solution S add 1 ml of *dilute sulphuric acid R.* When examined immediately and after 1 h, any opalescence in the solution is not more intense than that in a mixture of 1 ml of *distilled water R* and 10 m1 of solution S.

Calcium (2.4.3).5 ml of solution S diluted to 15 ml with *distilled water R* complies with the limit test for calcium (200 ppm).

Lead in sugars (2.4.10). It complies with the limit test for lead in sugars (0.5 ppm).

Water (2.5.12). 7.0 per cent to 9.5 per cent, determined on 0.50 g by the semi-micro determination of water.

Sulphated ash (2.4.14). Not more than 0.1 per cent. Dissolve 5.0 g in 5 ml of *water R,* add 2 ml of *sulphuric acid R,* evaporate to dryness on a water-bath and ignite to constant mass. If necessary, repeat the heating with *sulphuric acid R.*

Pyrogens (2.6.8). If intended for use in large-volume preparations for parenteral use, the competent authority may require that it comply with the test for pyrogens carried out as follows. Inject per kilogram of the rabbit's mass 10 ml of a solution containing 55 mg per milliliter of the substance to be examined in *water for injections R.*

LABELLING
The label states where applicable, that the substance is apyrogenic.