XPURE
innovative continuous chromatography

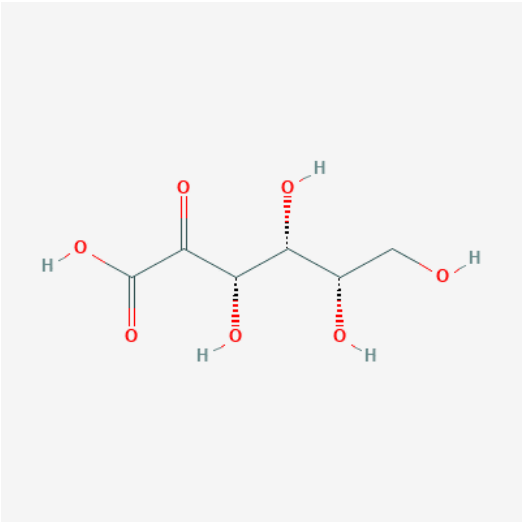
July 3, 2020 CASE STUDY

#Application Note: Vitamin C Production and Purification

Ascorbic acid was discovered in 1928 by Szent-Györgi. Commercially, ascorbic acid is mainly produced by a combination of synthetic organic steps and biotransformation. A well-known intermediate product is 2-keto-L-gulonic acid. This is produced from the sodium salt of the L-gulonic acid and has been acidified according to exactly the same ion exchange route, as presented below for vitamin C.

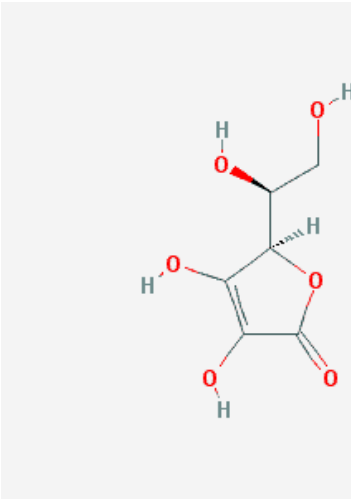
In order to obtain the pure product, ion exchange is an attractive method for removing the salts.

The objective of this application note is to demonstrate the feasibility of the continuous ion exchange for removing Na^+ from the sodium ascorbate. The feed flow consists of an aqueous solution containing Na-ascorbate. The sodium is exchanged by H^+ on a strong cation resin in the H^+ form. The resin is regenerated with HCl.



2-keto-L-gulonic acid

(precursor to vit. C or ascorbic acid)



Ascorbic acid

(vitamin C)

Design Considerations

The sodium form associated with the Asc (ascorbic acid) would be exchanged for an H^+ thus forming ascorbic acid on a strong acid cation resin with 1,8 eq/l (expressed in terms of equivalents per unit volume of packed bed) maximum capacity.

The entire operation is executed in an XPure carrousel system with 20 to 30 columns.

Process Description

The overall manufacturing process is schematically summarized in the next diagram **(Figure 1).**

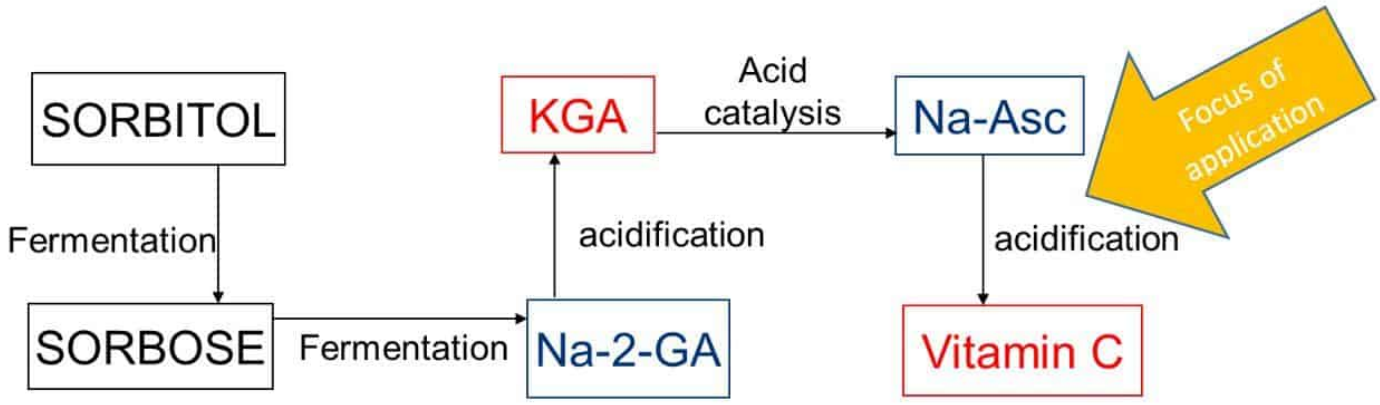


Figure 1. Flow diagram for vitamin C manufacturing

For the ion exchange step we focus on the acidification step to vitamin C. This is in fact a purification step; see below **Figure 2**.

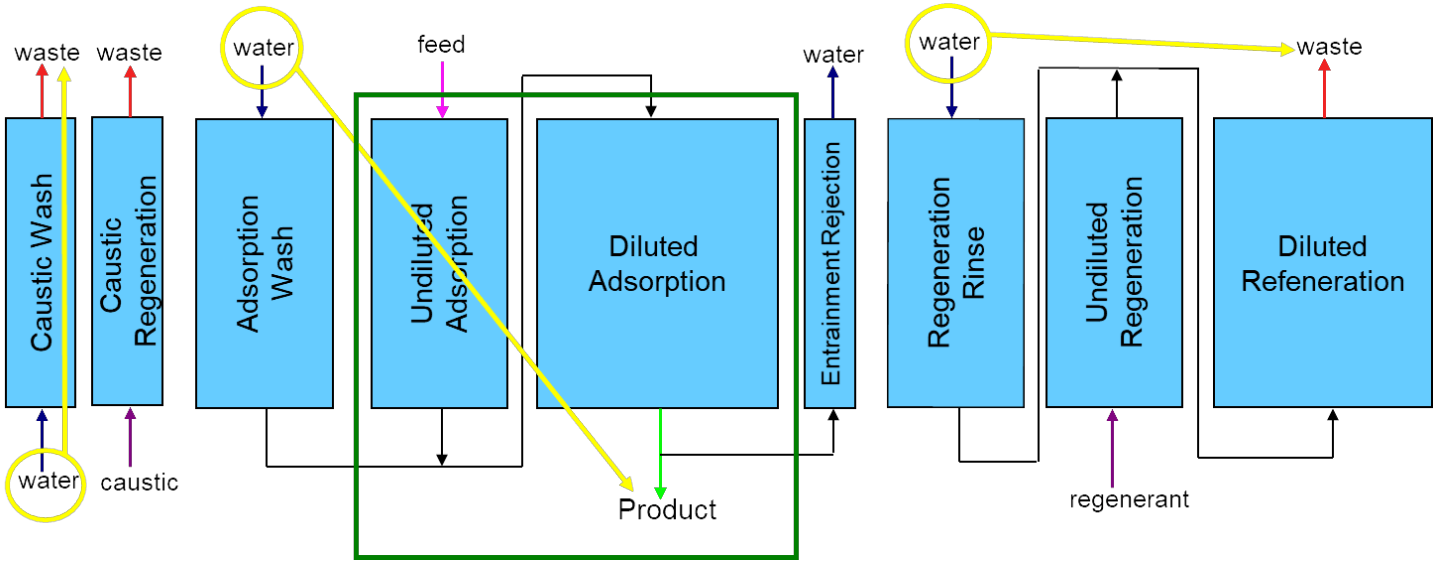


Figure 2. Conceptual design of continuous IX purification for (Product) vitamin C. Each block may contain multiple columns. Total number of columns typically 20-30.

Note: yellow lines indicate water flows within the system

The regenerant involves hydrochloric acid implying that NaCl is the target compound to remove in the subsequent wash steps. Caustic is applied for intermittent regeneration and protein removal.

In an experimental study it has been found that residual Na-ascorbate is more difficult to remove (ads wash) than NaCl (regen rinse); the ascorbate obviously shows affinity to the resin surface.

Water consumption is an important process parameter. In order to save on water, a counter-current contact concept has been applied. This can be accomplished by assigning multiple columns to the wash & rinse zones. The next **Figure 3** shows the effect on water consumption – expressed in BedVolumes – for 4 different configurations. Please note ideally 0.3-0.5 BV ("interstitial volume" or void fraction) would be sufficient for 1 column displacement.

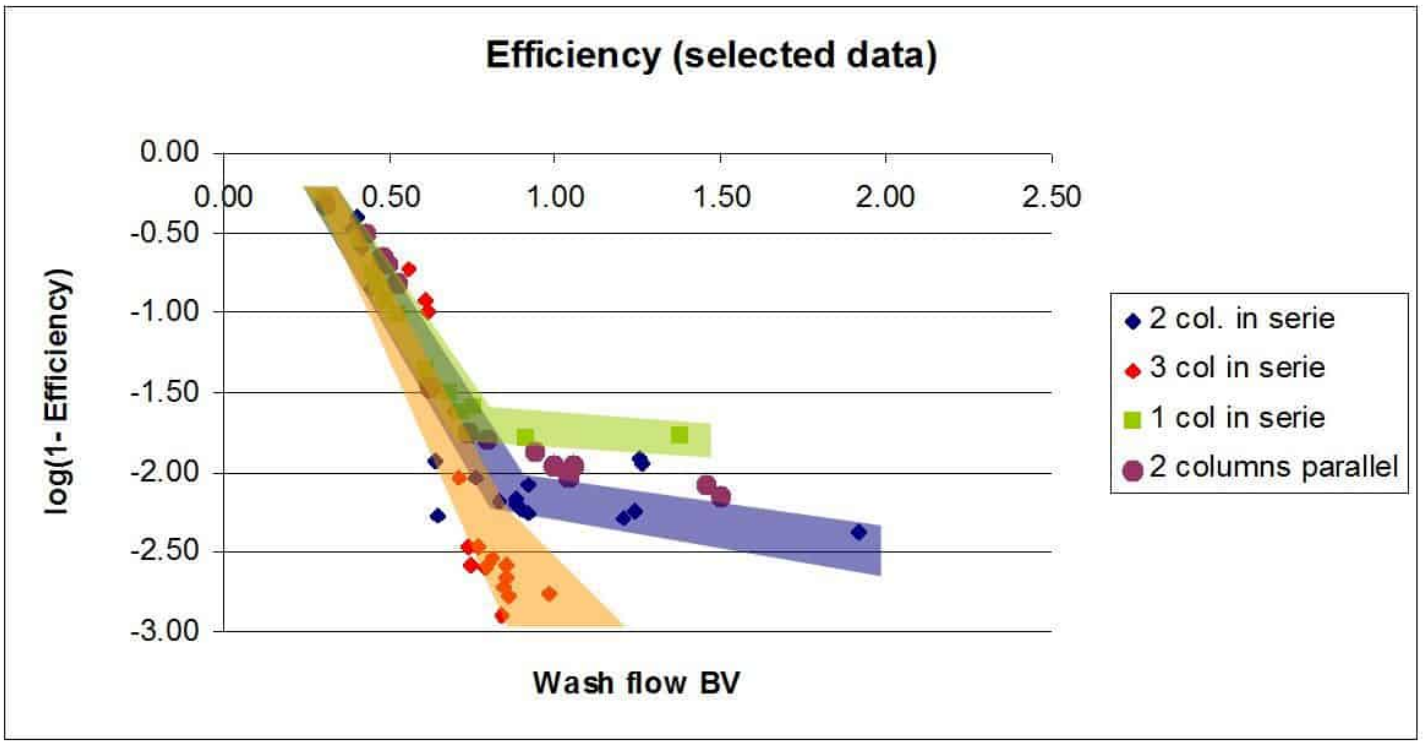


Figure 3. Wash efficiency with growing number of counter-current connected columns

A multi-column carrousel system can easily, and relatively cost-effectively, accommodate a counter-current contact zone.

The dilution in the vitamin C process typically is 20%-35%. This is significantly lower than fixed bed processes in which two-fold dilutions are not exceptional.

The conversion of Na-ascorbate is at least 99.5%. The water consumption, without using the possibilities to re-use water in the process, is about 15 liter per kg Vitamin C. The hydrochloric acid (7 wt%) consumption is 5.4 liter per kg vitamin C, taking into account excessive use of 20%. The caustic consumption should be fine-tuned to the protein content of the feed solution and can be minimized by optimizing the intermittent caustic

wash. Losses of product in the caustic wash and contamination of the product stream with chloride are minimized by carefully designing the adsorption wash and elution wash sections. Product dilution is minimized by applying an entrainment rejection zone.

One of the dominant factors in the operating expenses for ascorbate (and Na-2-KLG) acidification is related to the costs of the ion exchange resin. This can be related to the specific productivity of the system, which expresses the annual amount of product that can be purified per unit volume of resin. The productivity of a carrousel system for the purification of KGA and vitamin C typically is higher than 800 tpa/m^3. Productivities in fixed bed processes may be a factor 5-10 lower.