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CASE STUDY

Recovery of Pyridine Saves $1.5 Million Per Year

by Chuck Crew and Tom Schafer

This case study highlights how one pharmaceutical manufacturer designed, installed, and implemented a continuous pyridine recovery system that will save the company an estimated $1.5 million per year.

Introduction

At 57 percent pyridine and 43 percent water, pyridine and water form an azeotrope which makes recovery of pyridine solvent a complex task. Further complicating pyridine recovery was the presence of multiple streams of pyridine, in varying concentrations and forms. One stream contained pyridine at or near the azeotrope. The other mother liquor streams contained mostly water with pyridine bound as an organic salt, such a pyridinium acetate.

Despite the complexity, it was considered prudent to design, install and implement a continuous pyridine recovery system for two reasons. First, virgin pyridine costs nearly $2.00/lb., and if the recovered pyridine met purity specifications, purchases of virgin pyridine could be significantly reduced. In addition, 100 percent of the process wastes previously had been incinerated on-site, and re-use of the recovered pyridine would reduce those disposal costs. Based on a cost of $1.00/gallon to recover pyridine, and a $5.00/gallon disposal cost, Burroughs Wellcome Co. (the manufacturer) estimated a savings of approximately $1.5 million a year after the installation of this recovery system.

Second, the recovery system coincided with the manufacturer's on-going corporate program of recycling, where the goal is to eliminate all unnecessary waste disposal.

Glitsch Package Plants (the design firm) was asked to conduct the initial process recovery study for Burroughs Wellcome involving the examination of nine pyridine recovery methods. Subsequently, bench scale and laboratory testing led to the design firm's recommendation of a continuous liquid-liquid extraction system using a strong caustic solution to remove the bulk of the water from the azeotrope.

The final design called for a modular extraction system that included a distillation column for removal of water, followed by a Karr liquid-liquid extraction column and, fi-

FIGURE 1

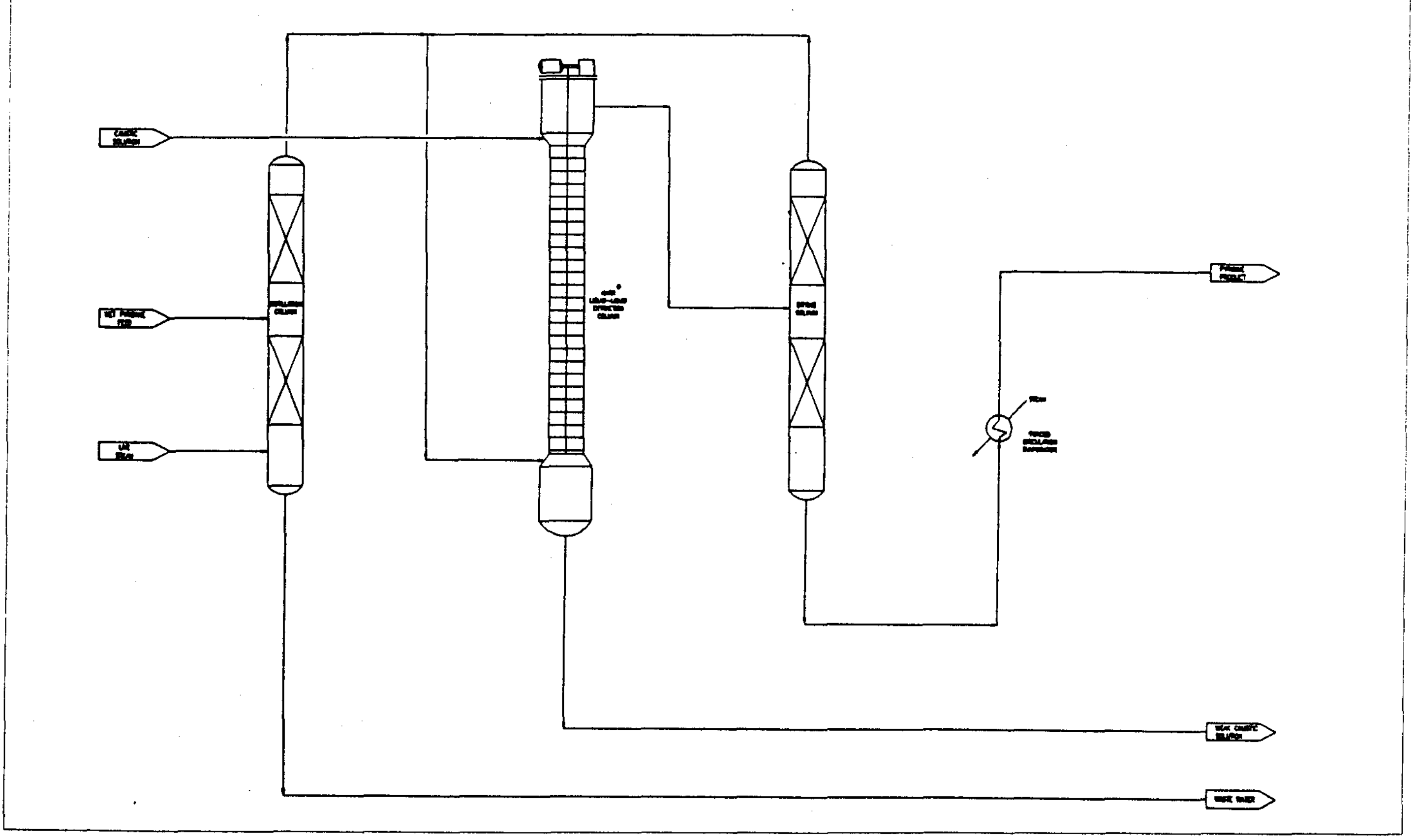

Figure 1. A modular extraction system.

nally, a drying tower and a forced circulation evaporator (Figure 1). At the time of the study, the manufacturer had no first-hand experience with continuous solvent recovery systems on-site, but approved its use based on the design firm's process guarantee.

Now completed, the results of the recovery system are evident. Burroughs Wellcome is recovering nearly 99 percent of the pyridine from the waste stream process, at less than 0.1 percent moisture content and meeting the required quality specifications. Burroughs Wellcome was able to re-use the recovered pyridine in the process from which it is recovered.

Process Development

The thought behind the development of a process for separating pyridine/water will be illustrated with a brief background on the theory of liquid-liquid extraction, with more detail on the practical application of this lesser-known technology to solvent recovery.

Step 1: Mix & Neutralize Waste Streams

This solvent recovery project centered around two primary water/pyridine streams. One was a dilute stream with pyridine bound as an organic salt. The other was a more concentrated stream, a result of crystallization. The solutions were stored separately in a tank farm and mixed just prior to recovery processing. At this point, the waste streams were neutralized (basified), as discussed later.

Step 2: Still Distillation

In general, distillation is the preferred method for the separation of liquid mixtures. In this project, the initial distillation column was packed with Gempak® structured packing to remove the bulk of the water. (Figure 2)

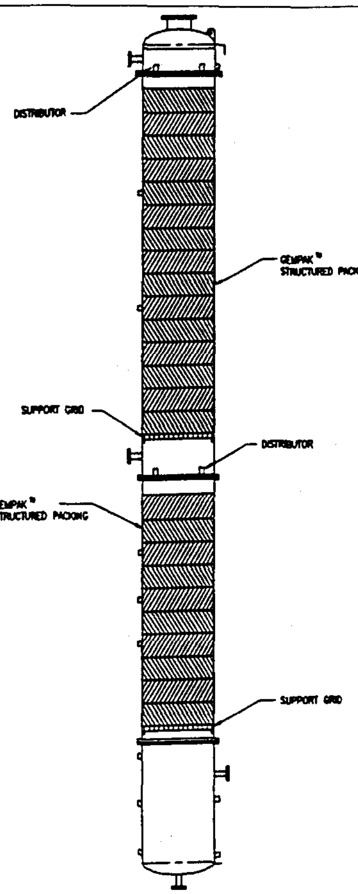

Figure 2. Distillation column with packing and internals.

Step 3: Many Options

There were many plausible ways to approach the problem of separating a pyridine and water azeotrope. Through in-house experience, a literature search and limited bench scale testing (shake testing), nine processes were identified as possible candidates. Six of the processes involved liquid-liquid extraction using one of the following chemicals: benzene, methylene chloride, chloroform, xylene, nitrobenzene, and caustic soda. Other options were azeotropic distillation with benzene, extractive distillation with a caustic solution, and pressure swing shifting of azeotrope.

This stage of the project included the preparation of preliminary process flow diagrams and budgets. Also examined were operating and capital costs and environmental liabilities. Ultimately, seven of these options were eliminated from consideration. Although all of these options were theoretically feasible, pressure swing shifting, for example, had never or rarely, been used commercially. After a preliminary presentation, bench scale testing with two of the liquid-liquid extraction options proceeded: extraction of pyridine with chloroform and extraction of water with caustic.

Why Liquid-Liquid Extraction (LLE)?

The Equations

Liquid-liquid extraction is an ideal technology for separating components that are either difficult or impossible to separate using ordinary distillation. LLE introduces the liquid feed to an immiscible or nearly immiscible liquid (the solvent), to preferentially extract the desired component, (the solute). The solvent must be carefully chosen based on a number of factors, the most important of which is its selectivity. Selectivity can be defined as:

$$B\,a/b = \frac{m(a)}{m(b)} \qquad \text{Equation 1}$$

where B is the selectivity of the solvent with regard to a solution of liquids a and b. m(a) and m(b) are called the distribution coefficients, and are calculated as a ratio of the concentration of the component a (or b) in the extract liquid to its concentration in the raffinate liquid at equilibrium, i.e. the *distribution* coefficient describes how the liquid a or b is *distributed* between the desirable extract liquid, made up of solvent and the desired component, the solute, and the raffinate, made up primarily of the "undesirable" component.

Usually, component a is considered the solute (the desired component), and component b the substance remaining behind, although we will see in the manufacturer's design that caustic soda is used to extract the water, leaving behind the desired component, pyridine, in the raffinate. A solvent with higher selectivity is usually the optimum choice, unless that solvent introduces undesirable side effects into the process. Selectivity must be greater than 1.0 for the separation to be possible at all.

Driving Force

When two liquid phases are brought into contact, the resulting deviation from chemical equilibrium provides the impetus for liquid-liquid extraction, as the two liquid phases struggle to regain equilibrium. There are resisting forces as well, and the goal of extraction equipment is to minimize this resistance. Slight resistance occurs at the interface of the contacting solvent and liquid feed, but it is small compared to the resistance exhibited by the two phases themselves. In its attempt to reach that state of equilibrium, the desired component, the solute, diffuses through the films (heavy resistance) adjacent to the interface of the feed plate, then *through the interface* (little resistance) from the feed phase into the solvent phase. (Figure 3)

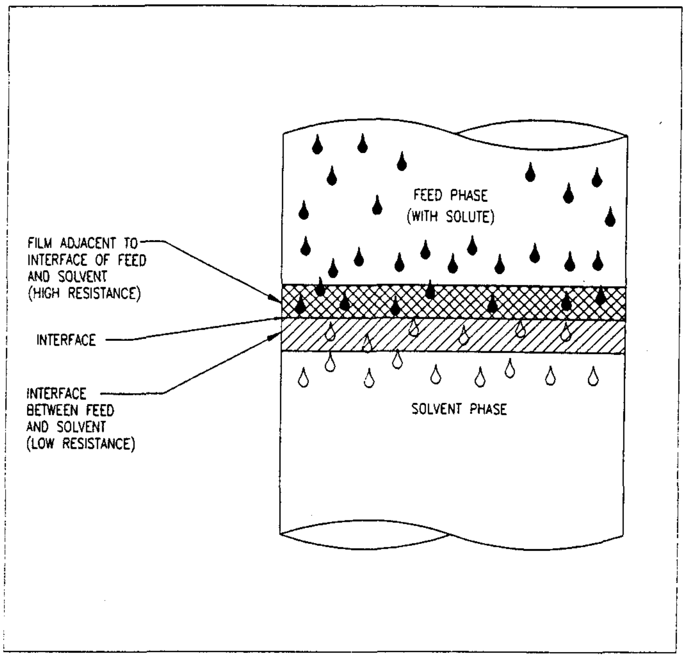

Figure 3. Liquid-liquid extraction.

Thus, all types of extraction equipment attempt to produce very small drops to maximize interfacial area, where resistance is low, and to minimize film thickness, where resistance is higher. The key to LLE is the large production of very small drops, drops that maintain their droplet form and do not coalesce or emulsify. It is easy to see how other parameters such as viscosity, temperature, density differences, interfacial tension could be critical to the proper formation of these drops. The Karr column used in this recovery system produces these very small drops for extraction, where the single feed is contacted by a single solvent in a countercurrent multistage process. (Figure 4).

Liquid-Liquid Extraction of Pyridine/Water

The two LLE solvents, chloroform and caustic, chosen for bench scale testing on the Burroughs Wellcome pyridine/water system differed slightly in their method of solvent recovery. The chloroform solvent system is conventional;

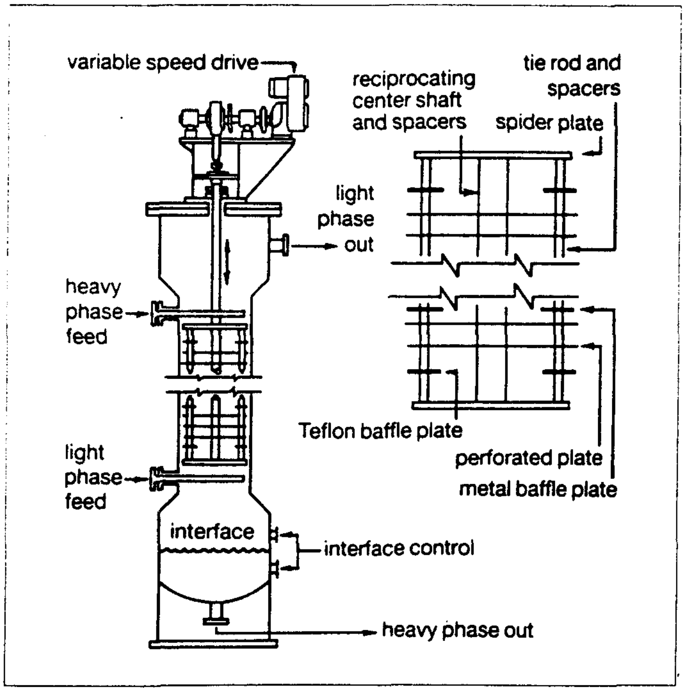

Figure 4. Karr reciprocating plate extraction column.

chloroform is used to extract pyridine. The caustic extraction system is less conventional. In this system, a 50 percent sodium hydroxide solution would be used to extract the majority of the water left behind in the azeotrope after the initial distillation step, leaving dry pyridine as the raffinate. (It is less conventional to have the desired product as the raffinate.)

Salt solutions reduce the solubility of water in organic solvents. On an ionic level, with a salt present, water breaks down into its ions, and binds with salt ions, allowing, in this case, removal of 99.4 percent water from the pyridine/water azeotropic mixture, thus "breaking" the azeotrope. In effect, the caustic acts as a drying system.

Furthermore, the caustic extraction system provided three significant advantages. By using 50 percent caustic soda (actually 50 percent sodium hydroxide/50 percent water) in the extraction column, the weak sodium hydroxide solution generated from the extraction step could be retained and used to liberate pyridine bound as organic salts in one of the feed streams to the recovery system. Since this dilute stream contained pyridine primarily in the form of organic salts, such as pyridinium acetate, the pyridine bound in the salt form would have to be liberated, by raising the pH with a strong base, in any process chosen, causing the pyridine to be in free form, with the base forming another salt species of the chloride or acetate group. The fact that the weak caustic generated from the extraction could perform this duty as a base was a distinct advantage.

Secondly, the one downside of LLE, specifically its production of a new solution of solvent and solute which usually requires further separation, was not a problem if caustic was chosen as the solvent. In other LLE processes, including the chloroform extraction process studied here, a new solution composed of chloroform/pyridine would be formed as a result of the extraction, requiring separation in an additional distillation step. However, by using a caustic soda system, the need for additional separation, and additional equipment investment and operational expense, was avoided, since the caustic, weakened by the addition of water, could be re-used to raise the pH of the salt-bound pyridine.

Finally, although chloroform has a high selectivity for pyridine, using it would introduce an additional and foreign solvent into the manufacturer's process, which was considered avoidable since caustic soda worked so well during the bench scale and pilot plant testing phase of the project.

Bench Scale Testing/Pilot Plant Testing

Vital for LLE Scale-Up

Once the team decided to pursue the examination of both chloroform extraction of pyridine and caustic soda extraction of water, bench scale and pilot plant testing were performed in the design firm's pilot plant. Laboratory and bench scale testing are of particular importance when designing liquid-liquid extraction systems. Bench scale testing refers here to the analysis performed to determine equilibrium concentrations, using techniques often called "shake tests", while pilot plant tests refer to the use of actual small scale, X in. and Y in., distillation and extraction columns.

Within a distillation system, physical properties remain relatively constant at all points in the tower and performance can be reliably predicted using well understood theoretical equations. With LLE, the behavior of a chosen extraction solvent on its target solute can be predicted theoretically to some extent, using the distribution coefficient to determine the selectivity. However, even a slight variation in any of a number of factors can affect the behavior of a liquid-liquid extraction system, which makes pilot testing the only way to ensure the final performance of the scaleup system.

For example, physical property changes can occur as extraction proceeds, especially when the percentage of solute, or desired component to be extracted, occurs in high concentrations in the feed, as it is in this pyridine/water system (43 percent water). These physical property changes can cause sufficient variations in interfacial tension, viscosity and density along the column to directly affect LLE performance. Also, when large concentrations of solute are present, flowrate changes may occur along the extraction column.

Although an experienced extraction engineer can anticipate coalescence and emulsion behavior, wetting characteristics, solids handling, the effect of contamination, and interfacial and droplet turbulence effects in a theoretical design, there are so many possible complex interactions between these factors that tests must be run in the pilot plant to fully characterize actual process conditions. Usually this is done to optimize the performance of an extraction column, i.e. to maximize the drive speed so that the smallest droplets can be formed which will still phase separate from stage to stage. The point where density difference is minimized can be a column limit point.

Use Actual Stream Material

It is important to note that because liquid-liquid extraction can be affected by slight variations in so many factors, actual stream material is always preferred for testing. In this project, the manufacturer arranged to have its pyridine/water waste streams shipped to the pilot plant in 55 gallon drums for the tests.

Dual Purpose for Pilot Testing

Pilot plant testing was conducted for two primary purposes: to verify the conceptual design of both the caustic soda and the chloroform extraction systems, and to make enough dry recovered pyridine to allow the manufacturer to conduct a "use test" as required by the FDA whenever anything other than virgin solvent is used. In a "use test" the recovered solvent is used to make the final drug product, then extensively tested by the company's Quality Assurance Group which must document any variation from the original before submitting the results to the FDA.

Besides producing a few kilograms of recovered pyridine for the use test, pilot plant testing uncovered two problem areas. The first problem, extensive fouling and foaming in the bottom still pot of the pilot system, was caused by a small and very dilute waste stream containing alcohols and organics. The solution was to eliminate this waste stream from the recovery process.

The second problem, however, prompted some design changes. In the original design, the final piece of equipment in the original design was a drying column containing two beds of structured packing. This distillation column was designed to remove the final <1 percent of the water remaining after extraction. Although the drying column was producing high purity, low moisture pyridine, the recovered pyridine had some undesirable colorbodies that failed to meet a Burroughs Wellcome color specification. After identifying some high boiling organics which were causing the color problem, the design firm added a forced circulation evaporator into the system, downstream of the drying column. This additional process step evaporated the pyridine out of the dry mixture, leaving the colorbodies behind and yielded a colorless pyridine which met color specifications. The periodic purging of this evaporator presently represents the only pyridine (less than 1 percent of the original waste stream) that still must be incinerated.

Caustic Process Chosen

During a formal presentation of pilot test results, the advantages of the caustic system became clear, and the final project proceeded with caustic soda extraction of water as the sole design. Within a few months, the design firm proceeded to Phase III of the project - a scaled up system design.

The final design proposal differed from the norm in one significant way. Because of possible variations in the feedstock stream (as is typical in a system which is batch upstream), three designs were actually prepared. The material balances and PFDs for minimum concentration, maximum concentration and average concentration were prepared, and equipment was sized to perform to specification, regardless of the scenario that was flowing at any time.

Modular System

Modular construction offered the manufacturer many benefits. Besides being a lower cost solution which still met the strictest criteria for quality, single source vendor responsibility is a key advantage. The compressed construction schedule of a modular unit also may offer some economic advantages, as the process is on-line more quickly. Because the modules are fabricated off-site, the bulk of the construction can occur simultaneous to the environmental application/approval process, whereas on-site construction may not begin until permits are obtained. With modular construction, permits do not affect the overall project schedule.

The manufacturer was assured the system would meet design requirements, including guarantees on moisture content and color quality, before it was shipped, because the supplier was responsible for verifying and checking that all the piping, instrumentation, columns, column internals, pumps, and the evaporator were connected and in good working order.

Automation and Start-Up

Once the manufacturer decided to proceed with a continuous system, it was also decided to automate the recovery process with a Fisher DCS system, a highly automated process control system which provides pictorial views of tank levels and historical data. This system operates the process from start-up to shutdown, with operators monitoring only the control board. The system included a pH analyzer on the feedstock tank, with level indicators for each of the surge tanks.

The complexity and necessary interaction between so many pieces of equipment directly influenced the decision to use the advanced Fisher DCS system. Consistent purity was a critical criteria, as well, and further influenced the decision to automate the system. In addition, the senior engineering management at the manufacturer supports the notion that technology is one of the key ways to maintain a competitive edge.

The manufacturer's process engineers, working closely with the design firm's process engineers, developed the algorithms for every aspect of the process control system. Sensors, controls and computer hardware were chosen to permit the algorithms to be processed in real time.

The process units started-up without a hitch, while the computer logic took another two months after start-up to debug, which is considered a standard time period for debugging complex software control.

Daily Operation and Results

The system has run to design specifications; with no corrosion or other problems and has met or exceeded the design firm's process guarantee. The manufacturer now recovers nearly 99 percent of the pyridine from the waste stream process, yielding 99.9 percent purity on a regular basis, because of the continuous nature of the process. There is less than 0.1 percent moisture in the recovered material. Furthermore, the quality of the recovered pyridine is such that the manufacturer is able to purchase 30 percent less virgin pyridine. Varying slightly with the amount of production, the manufacturer has been able to achieve the original goal of $1.5 million per year in total savings through the implementation of a continuous modular pyridine recovery process.