of these trial and error runs may be needed to obtain the desired separation, which may conceivably be time consuming.

In the last fifteen years or so, the use of software for method development in reversed-phased HPLC has increased dramatically, with the intended purpose of separating complex mixtures by shortening the development time and optimizing the resolution based on a limited amount of experimental retention data. A number of these computer systems are commercially available. Many reviews on the subject have been published (30), and many references to using the DryLab^{TM} have been reported (31). DryLab^{TM} is a widely used computer simulation program that after a limited number of actual injections at different conditions can predict an optimal condition or separation at other conditions.

13. OTHER APPLICATIONS

13.1. Analytical Method for Cleaning Assessment

Normally, production equipment is shared to manufacture different pharmaceutical products. Thus cleaning processes following production of pharmaceutical products are critical to prevent cross-contamination. The analytical method used to assess the effectiveness of the cleaning process is usually the same stability-indicating method used for product release and stability monitoring, with some adjustments to increase its sensitivity. How sensitive and specific the method has to be is commonly determined from a joint effort between the pharmaceutical engineer and the analytical chemist to establish the necessary cleaning limit. The method developed must be capable of being validated and rugged enough to meet predetermined specifications consistently. In addition to HPLC, total organic carbon (TOC) analysis has become a widely used method for analyzing cleaning residues, and the Compendia have dedicated General Chapter <643>, Total Organic Carbon, to the subject (32). TOC, however, is not as specific as HPLC. Conductivity has also been used. Generally HPLC is the most accurate, reliable, and specific of all the analytical cleaning methods.

13.2. Physicochemical Characterization Method (Dissolution Method)

A liquid chromatographic method developed for product release or stability monitoring can be adapted for use with a dissolution assay. An HPLC method for dissolution assay testing is optimized for speed and is not intended for determination of degradation products or process impurities. Instead, the real utility of this combination (dissolution with HPLC determination) is that it eliminates interferences from formulation excipients. Assuming that the HPLC method has been developed and validated, the development process is bridged over to developing the dissolution methodology. A preliminary dissolution test is developed very early in the pharmaceutical development process to support formulation development. Primary dissolution parameters for development include selection of the filter, the apparatus type, the rotation speed, and the dissolution medium. Once these parameters have been established, they are to be validated as part of the total validation effort for the HPLC dissolution methodology. The reader is referred to the article by Skoug et al. (33) for an overview of the subject.