Stability Studies On Analytical Solutions In A Pharmaceutical Laboratory

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Introduction

Quality of pharmaceutical products, as defined by the ICH, is the suitability of either the drug product or the active pharmaceutical ingredient (API) for its intended application.[1] In achieving quality, appropriate monitoring of products, systems and processes is put into practice during manufacture to establish satisfactory conformity to the finished product specifications prior to release. Method validation is carried out in order to demonstrate that analytical procedures are scientifically sound and suitable for their intended applications.[2] Validation and suitability of the analytical procedures utilised in monitoring of the various stages of the production system are thus important in assuring accuracy and reliability of analytical results. Robustness, which is one of the validation characteristics tested during method validation, is a measure of the ability of an analytical procedure to remain unchanged by small but deliberate changes in the analytical parameters and provides an indication of the reliability of the procedure during routine application. In the case of liquid chromatography analytical procedures, one of the analytical parameters identified as subject to variation is the stability of analytical solutions. The data gathered from the determination of the stability of analytical solutions serves to set the range of analytical conditions under which the validity of the analytical procedure is maintained. These analytical conditions include the time between solution preparation and analysis and the conditions of storage.

Methodology

The robustness of the reversed-phase HPLC assay procedures for the determination of ramipril and amlodipine besilate in the finished product and the API terbinafine hydrochloride was tested with respect to the stability of analytical solutions. Stability testing of the pharmaceutical compounds in solution was carried out by monitoring the change in the content of the active substance over time. The concentration of active was determined chromatographically, by analysing the test solutions against freshly prepared standard solutions. The stability of the active compounds in solution was monitored under three conditions:

1. Ambient temperatures, exposed to light in amber glassware
2. Ambient temperatures, protected from light
3. Reduced temperatures.

The effect of the concentration of the active on the stability of solution was studied by performing stability studies on both the stock and working solutions. In addition, the difference between the stability of standard and sample solutions was also investigate during the study. Solutions were considered to be stable over the time period studied if there was no statistically significant difference at the 95% confidence level in the mean percentage assay between the initial time point and that under consideration or the mean difference between the two sets of results was less than 2.0%.

Results

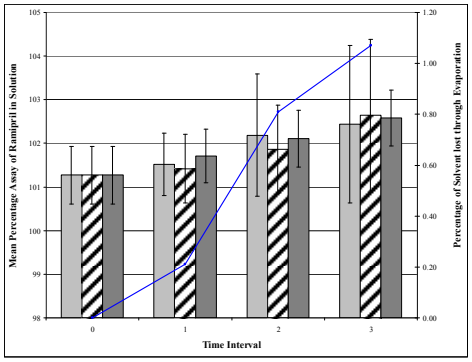

Fig 1: Variation in the Mean Percentage Assay of Ramipril with time as observed for sample working solutions

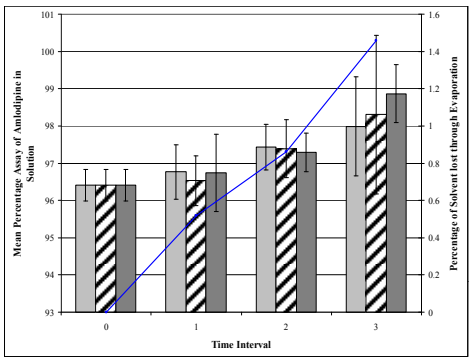

Fig 2: Variation in the Mean Percentage Assay of Amlodipine with time as observed for sample solutions

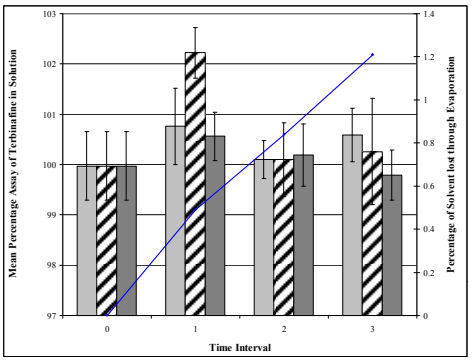

Fig 3: Variation in the Mean Percentage Assay of Terbinafine with time as observed for sample working solutions

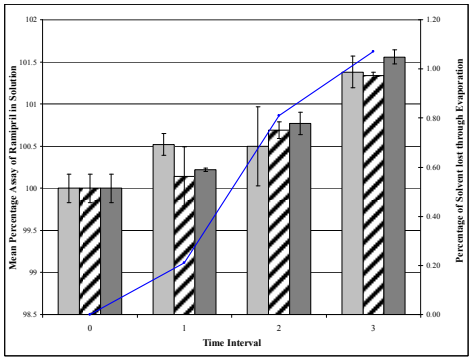

Fig 4: Variation in the Mean Percentage Assay of Ramipril with time as observed for standard working solutions

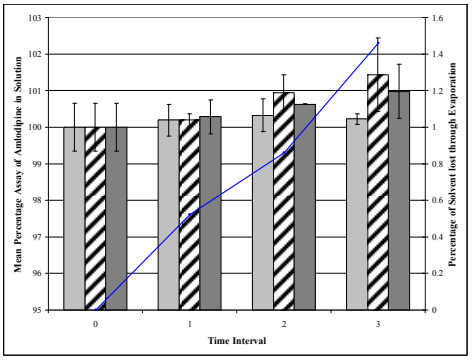

Fig 4: Variation in the Mean Percentage Assay of Amlodipine time as observed for standard solutions

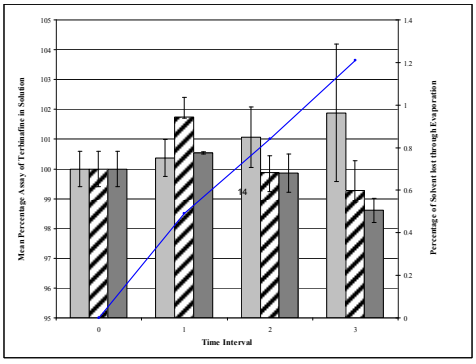

Fig 4: Variation in the Mean Percentage Assay of Terbinafine with time as observed for standard working solutions

Conclusions

The study revealed that there was no apparent degradation of ramipril and amlodipine in both sample and standard solutions of the two drug products over the time interval for which the analytical solutions were tested. On the other hand, due to significant evaporation of solvent, the time allowed between solution preparation and analysis cannot be extended to twenty-four days during routine application. Conversely, terbinafine hydrochloride was found to undergo degradation when present in solution. Stability data has been shown to be a good source for the reliable determination of variability associated with HPLC assay procedures.[3] The precision of the assay procedures was found to be dependant on the type of drug being analysed ,where the intermediate precision values associated with the assay procedures for the determination of the active in the finished product were higher than those associated with the assay procedure for the determination of the API.

References

1. International Conference on Harmonisation, ICH Harmonised Tripartite Guideline, 1999
2. R. Kellner *et al.*, '*Analytical Chemistry*', 2nd Ed., (2004), Wiley-VCH
3. J. Ermer *et al.*, *J. Pharm. Biomed. Anal.*, **38** (2005) 653.