SOLUTIONS system

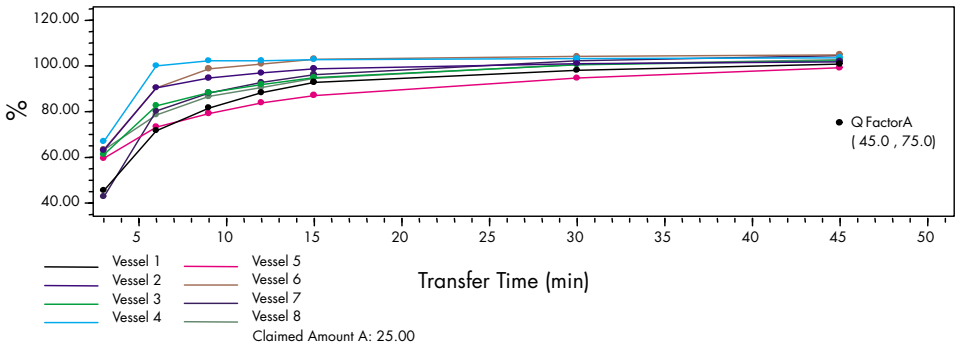
Automated Dissolution of Immediate and Extended Release Formulations

Waters Alliance® Dissolution System, the automated on-line solution to your dissolution testing needs, combines highly precise on-line sample acquisition and analysis, plus Millennium®32 data reduction and single keyboard control with the unmatched performance of Alliance technology. The Alliance Dissolution System incorporates: Waters® 2690D Separations Module, Hanson SR8-Plus™ Dissolution Bath, Waters Transfer Module, and Waters 2487 Dual Wavelength Absorbance Detector into a compact system that fits on a standard laboratory bench.

Powerful Dissolution Testing with Alliance® Technology

Dissolution testing is required by the United States Pharmacopoeia (USP) on most solid dosage forms and is also used extensively in formulation development. In recent years, there has been an increasing trend to develop extended release formulations using the same active ingredients as the immediate release formulation. The extended release product has the advantage of slowly releasing the active ingredient over a longer period of time. The effect of changing the formulation as well as changing the ratios of excipients in the product can be determined with dissolution testing. Most importantly, dissolution testing is used in the final evaluation of the new product formulation for quality control before it ever reaches the consumer.

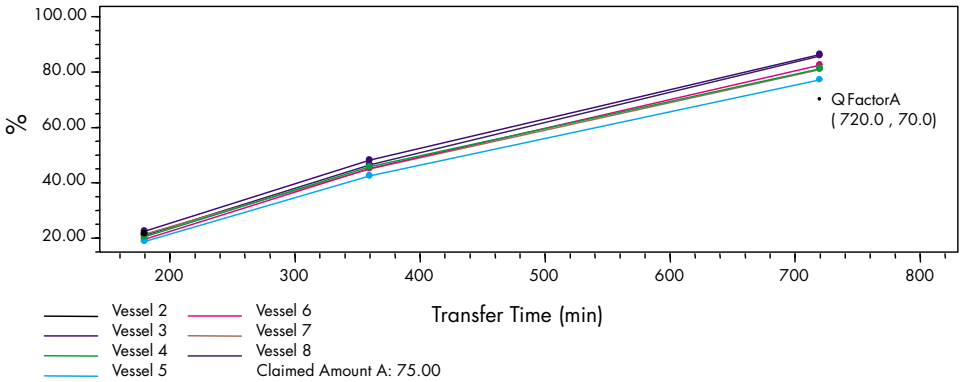
The extended release products release active ingredients over a 12- to 24-hour period. Dissolution sampling must be performed at various time intervals over this period of time. Waters Alliance Dissolution System can automatically perform this task without any intervention. Sample aliquots are automatically transferred from the temperature-controlled Hanson SR8-PLUS™ Dissolution Bath into vials archived inside the chilled sample compartment of the Waters 2690D Separations Module. The samples are analyzed by HPLC, the results are calculated, and a dissolution profile is automatically generated. The Alliance Dissolution System can be set up, run unattended overnight, and provide you with a comprehensive report at the completion of the dissolution test.



Conditions

Sample:	Phenylpropanolamine tablets	**Sample Temp.:**	4° C
USP Apparatus:	2 (paddle), Speed: 50 rpm, Media: Water (900 mL)	**Flow Rate:**	0.7 mL/min
HPLC Mobile Phase:	Hexanesulfonate/NaH_2PO_4/TEA/H_2O	**Injection Volume:**	20 µL
Column:	Symmetry® C_{18} 3.9 x 50 mm	**Runtime:**	3.0 minutes
Column Temp.:	25° C		

Figure 1 shows the Rate Release Profile of the immediate release tablet formulation of Phenylpropanolamine Hydrochloride, which is used as a decongestant for the temporary relief of symptoms from sinusitis, bronchitis, and the common cold. The dissolution results were calculated using algorithms in the Millennium^{32} software. The dissolution profile report was generated automatically at the completion of the dissolution test.



Conditions

Sample:	Phenylpropanolamine capsule	**Sample Temp.:**	4° C
USP Apparatus:	1 (basket), Speed: 100 rpm, Media: Water (1000 mL)	**Flow Rate:**	0.7 mL/min
HPLC Mobile Phase:	Hexanesulfonate/NaH_2PO_4/TEA/H_2O	**Injection Volume:**	10 µL
Column:	Symmetry® C_{18} 3.9 x 50 mm	**Runtime:**	3.0 minutes
Column Temp.:	25° C		

Figure 2 shows the Rate Release Profile of the extended release capsule formulation of Phenylpropanolamine Hydrochloride, which is used as a longer lasting decongestant medication and often used as an appetite suppressant. Note the last timed sample aliquot was taken after 720 minutes or 12 hours of elapsed time.

Summary

- An increasing trend is to develop extended release pharmaceutical products with the same active ingredients as contained in the immediate release form.
- The extended release dosage forms require sampling times over a much longer period of time.
- Dissolution testing can be used effectively to monitor changes in the development of a new fomulation and monitor the quality control of the product over extended periods of time.
- Use of a fully automated Alliance Dissolution System with Millennium®32 single keyboard control provides a solution for the extended release application.

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