DuPont™ AmberLite™ and Duolite™ Ion Exchange Resins

Guidelines for Resin Screening and Optimization of Drug to Resin Ratio

To automate and expedite the resination process, rapid screening of ion exchange resins (IER) and optimization of drug to resin ratio can be carried out using dissolution apparatus and online UV spectrophotometry. An alternative process is to mix drug solution and resin using a magnetic or overhead stirrer, and periodically sample the solution to determine drug loading.

1: Selection of Ion Exchange Resin

1.1 Identify an appropriate UV cell and drug concentration for the resination process

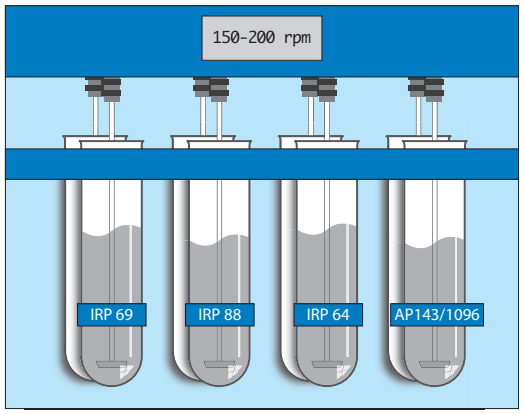
- Prepare 1% w/v drug solution and measure absorbance using 10 mm UV cell
- Achieve drug solution absorbance less than 1.5 au (absorbance unit) by either diluting the solution or reducing the UV cell path length
- In some cases, both dilution of drug solution and the use of shorter path length cell may be required

1.2 Set up online dissolution system with UV cell identified in Step 1.1

- Use manual sampling if online measurement is not available

1.3 Fill the dissolution vessels with drug solution concentration identified in Step 1.1

- Use of small volume vessels (150 mL) will reduce the quantity of drug needed for screening process
- Regular sized vessels can be used (500 mL or 1000 mL) if small volume vessels are not available

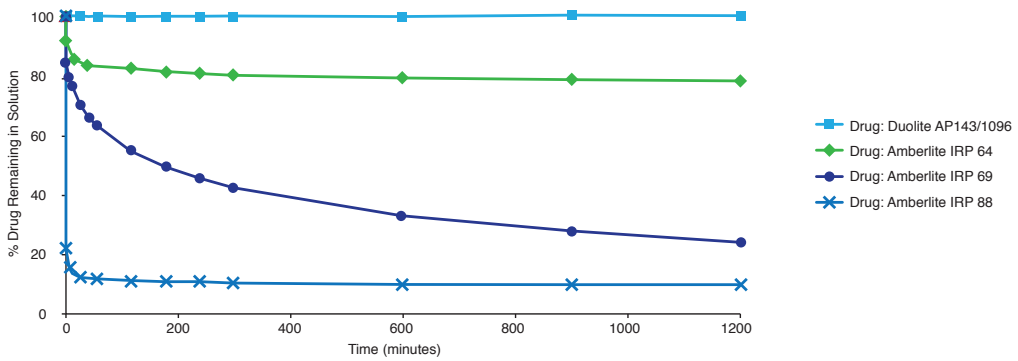


1.4 Add a different grade of resin to each vessel at 1:1 w/w ratio with drug, allow to mix for 20 hours

- Use sufficient stirring speed 150-200 rpm, to maintain resin suspended in drug solution

1.5 Identify preferred resin type

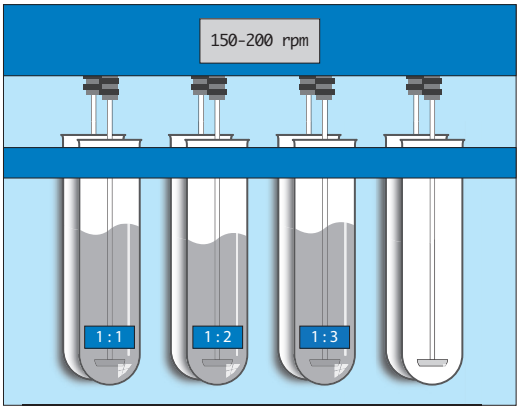
- Suitable resin types for the drug loading process are indicated by low concentrations of drug remaining in solution
- In this example, AmberLite™ IRP 88 and IRP 69 have low concentrations of remaining drug, indicating they are suitable resins for drug loading



2: Optimize Drug to Resin Ratio and Process Time

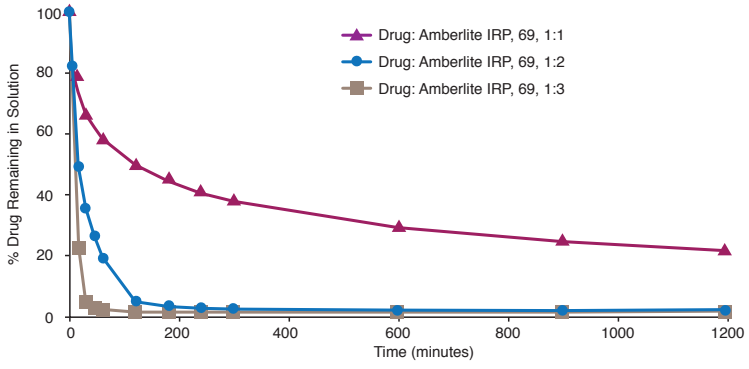
2.1 Set up dissolution system with UV cell, fill vessels with drug solution having the concentration as identified in Step 1.1

2.2 Add preferred resin type (identified in Step 1.5) to the vessels at Drug : Resin ratios of 1:1, 1:2 and 1:3 w/w



2.3 Mix the resin and solution until the drug loading curve reaches a steady state

- Identify suitable drug to resin ratio based on dose, tablet weight and release requirements
- Drug loading process time is defined as time to achieve equilibrium at selected drug to resin ratio



2.4 Filter the resinate using a filter paper, buchner funnel and vacuum pump assembly. Centrifugation may also be used.

- Wash the filter cake with DI water to remove residual drug and by-product salt from resinate
- Dry the resinate in vacuum oven at 60°C overnight
- Large quantity of resinate can also be dried in fluid bed drier
- Use the drug loaded resinate for further formulation development

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- DuPont™ polymer chemistry expertise and manufacturing capability
- Colorcon dedicated team provides formulation expertise
- Colorcon local technical support for trials, scale-up and troubleshooting
- Colorcon global supply and logistics

Contact your Colorcon representative or call:

North America
+1-215-699-7733

Europe/Middle East/Africa
+44-(0)-1322-193000

Latin America
+54-11-5556-7700

India
+91-832-6727373

China
+86-21-61982300

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