

# Rapid Screening Method to Identify Suitable Resin Chemistry to Develop Drug-Resin Complexation of Dextromethorphan HBr and Characterization of Drug-Resin Complex

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CRS  
Poster Reprint 2021

## Purpose

Ion exchange resins (IER) are crosslinked water-insoluble polymers containing the ionizable functional groups. To successfully develop taste-masking applications using IER, the drug needs to form a reversible drug-resin complex by exchanging counter ions with IER. The drug-resin complexation occurs with the resin of favorable chemistry and the current process to identify suitable resin chemistry is time-consuming and complex. Hence, this investigation demonstrates the utility of a small volume dissolution bath to rapidly identify the suitable resin chemistry for the model drug, dextromethorphan HBr. The drug to resin ratio was optimized using this high throughput method and the drug resin complex characterized using X-ray diffraction.

## Methods

Dextromethorphan HBr (DM) drug solution (1% w/v) was dispensed into the small volume dissolution vessels (Figure 1). The dissolution bath was connected to the online UV spectrophotometer equipped with 0.2 mm UV cells. Strong cationic resin (DuPont™ AmberLite™ IRP 69), weak cationic resins (AmberLite™ IRP 88 and AmberLite™ IRP 64) and weak anionic resin DuPont™ Duolite™ AP143/1096) were added to different vessels at 1:1 w/w drug to resin ratio. Drug resin suspension was kept under stirring at 22°C for 20 h and unloaded drug concentration was measured at 278 nm by recirculating the suspension through UV cells.

Drug loading was further optimized for the favorable resin chemistry at 1:1, 1:2 and 1:3 w/w drug to resin ratio with help of a high throughput process. Drug loaded resins were filtered and dried in a vacuum oven at 60°C for 24 h. Drug-resin complexes were then analyzed using X-ray diffraction (ARL EQUINOX 100 X-ray Diffractometer, Thermo-Scientific, USA).

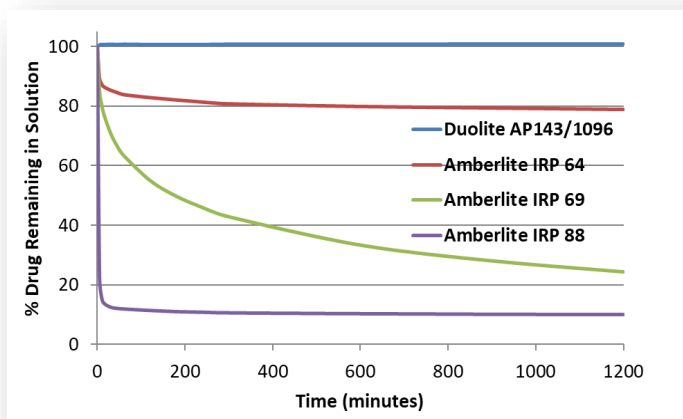
Figure 1. Small Volume Dissolution Set Up For High Throughput Screening



## Results

Figure 2 shows depleting DM concentration when mixed with different resin chemistries at a 1:1 w/w ratio. The lowest remaining drug concentration indicates that the drug was bound and efficiently complexed onto the resin. Anionic resin, Duolite™ AP143/1096, did not show drug loading since available drug concentration remained unchanged. Cationic resin chemistries, AmberLite™ IRP 69 and AmberLite™ IRP 88, showed a significant decline in the drug concentration, suggesting better drug loading. For Amberlite™ IRP 69, higher drug loading (98%) was achieved at 1:3 w/w drug to resin ratio (Figure 3).

**Figure 2. Depleting Dextromethorphan HBr Concentration Using Different Resin Chemistries**



**Figure 3. Depleting Dextromethorphan HBr Concentration Using Different Drug to Resin Ratio**

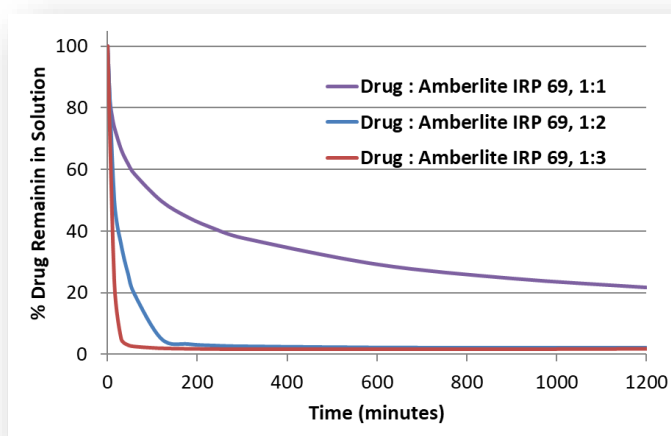
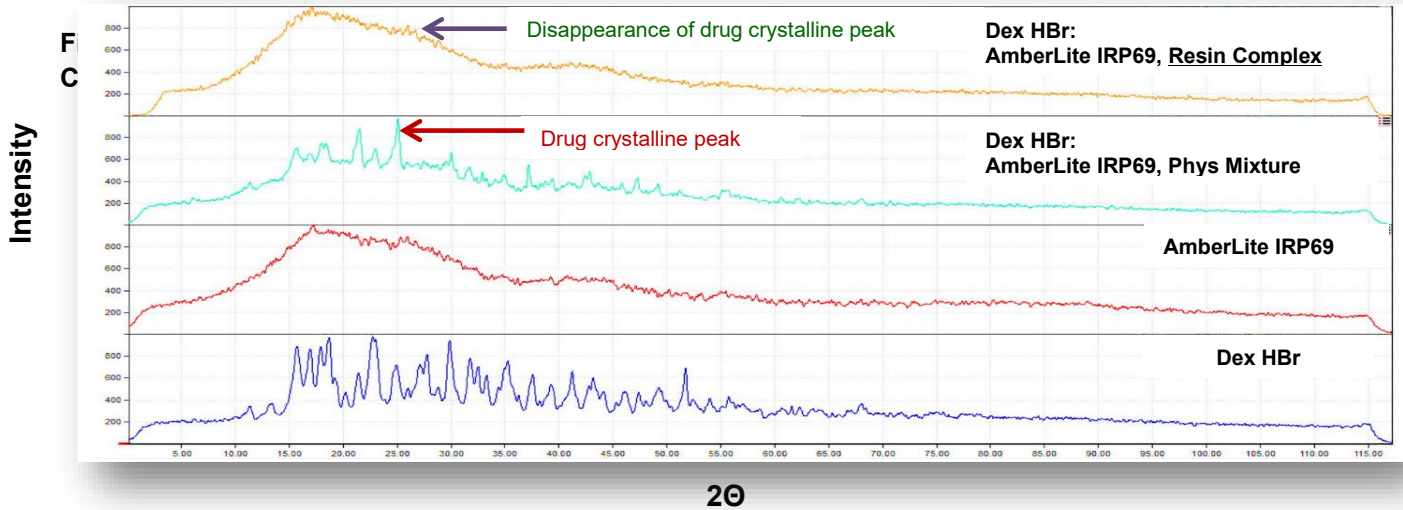


Figure 4 shows the X-ray diffraction pattern of drug and ion exchange resin pure components, physical mixture and drug-resin complex. Drug resin complexation resulted in the disappearance of crystalline drug peaks in X-ray diffraction, while physical mixture shows the presence of crystalline drug.



## Conclusions

The high throughput screening method was successfully developed using a small volume dissolution bath equipped with an autosampler to screen efficiency of drug-ion-exchange resins complexation. This method rapidly identified suitable resin chemistry and optimized drug loading for the model drug, dextromethorphan HBr. X-ray diffraction confirmed the drug resin complexation with help of the disappearance of crystalline drug peaks.

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