# Orally Disintegrating Tablet Formulation Development Through Functional Excipients

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## PURPOSE

In this study, a practical solution was provided to formulate a direct compression orally disintegrating tablet (ODT) formulation by selecting a functional superdisintegrant to achieve fast disintegration and utilizing ion exchange technology to properly mask the bitter taste of the active pharmaceutical ingredient (API). The superdisintegrant that is used in this study was Ac-Di-Sol® SD-711 NF, a very well established material widely used to accelerate disintegration rate of tablets. AMBERLITE™ IRP88 ion exchange resin (IER) was selected as a taste masking agent.

## OBJECTIVE(S)

The objectives of this study were to evaluate the effectiveness of superdisintegrant Ac-Di-Sol® SD-711 and masking agent IER AMBERLITE™ IRP88 on ODT formulation development.

## METHOD(S)

Four formulations were prepared using dextromethorphan (Dex) as a model drug (Table 1). Formulations F1 and F2 were prepared through simple blending of all dry ingredients. Formulations F3 and F4 had a resinate synthesis first step. The resinates were synthesized using aqueous solutions of drugs with resin added at room temperature. The resinates with 50% drug loading were then isolated by filtration, followed by washing and drying. To prepare the final formulation, dried AMBERLITE™ IRP88 resinates were blended uniformly with the other dry ingredients.

For each formulation, all ingredients were weighed and blended in a V-blender for 15 minutes. Tablets were compressed using a Stokes 512 tablet press with four stations. Standard 7/16" concave punches and corresponding dies were used.

Disintegration times of tablets were determined using Distek 3100 disintegration tester. The test was conducted at 37°C in a medium of Simulated Intestinal Fluid (SIF). Six tablets per sample were analyzed and the mean is reported.

Buccal dissolution experiments were run using a novel patented flow-through buccal dissolution test with Simulated Saliva (SS) at pH 6.2 as the dissolution medium. The residence time in the cell was determined by the flow rate and volume of the cell. The flow stream was split 2:1 to allow solids to be removed from the cell via a dip tube and to be analyzed either by flow through UV or fractions for HPLC. The results are reported as a time concentration curve.

*Table 1. Formulation details*

| Ingredients | F1 2%ADS (mg) | F2 2%ADS-10%IRP88 (mg) | F3 0%ADS-10%IRP88 resinate (mg) | F4 2%ADS-10%IRP88 resinate (mg) |
|---|---|---|---|---|
| Mannitol | 261 | 231 | 237 | 231 |
| Ac-Di-Sol® SD-711 (ADS) | 6 | 6 | | 6 |
| Alubra™ PG-100 | 3 | 3 | 3 | 3 |
| Dextromethorphan | 30 | 30 | | |
| AMBERLITE™ IRP88 (IRP88) | | 30 | | |
| IRP88 resinates | | | 60 | 60 |
| Total weight | 300 | 300 | 300 | 300 |

## RESULT(S)

Figure 1 shows the disintegration times of tablets made from different formulations. The use of 2% Ac-Di-Sol® SD-711 (formulation F1) enables Dex tablets to disintegrate in less than 26 seconds, achieving the physical property requirement for being ODTs. However, the buccal dissolution in Figure 2 showed a $C_{max}$ of 2137mg/L which indicates the unpleasant taste of Dex would burst into full effect in seconds. The addition of AMBERLITE™ IRP88 as a taste masking IER directly into the dry blend, no pre-resination, (formulation F2) showed improvement in taste masking, e.g., a reduction of $C_{max}$ by 29.4% due to in situ loading, and the F2 tablets still showed comparable disintegration time to that of F1 from the contribution of Ac-Di-Sol® SD-711. To further optimize the taste masking, resinates were used in formulation F3 and F4, both formulations showed significant reduction in $C_{max}$, a clear indication of 79% and 72% taste masking for both formulations. However, F3 tablets without Ac-Di-Sol® SD-711 can't achieve the desired disintegration time. Formulation F4 showed a more optimized ODT formulation, achieving quick disintegration time at typical ODT tablet hardness range due to the use of Ac-Di-Sol® SD-711 and taste masking from the AMBERLITE™ IRP88 resinates.

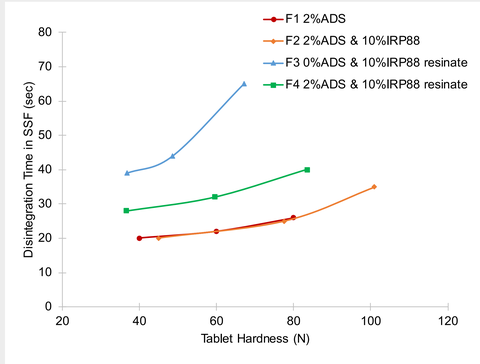


*Figure 1. Tablet disintegration time in SIF*

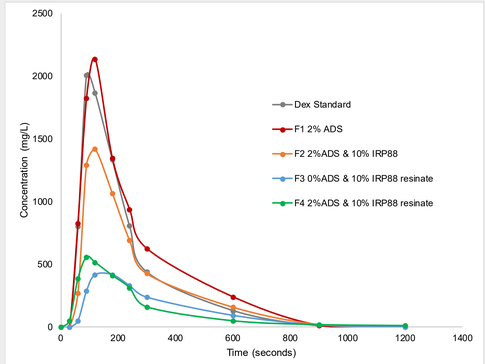


*Figure 2. Buccal Dissolution Profile in SS*

## CONCLUSION(S)

Ac-Di-Sol® SD-711 can be used to formulate ODTs and promote effective tablet disintegration within seconds. The formation of complexation between AMBERLITE™ IRP88 and dextromethorphan achieved significant taste masking. The combination of Ac-Di-Sol® SD-711 and AMBERLITE™ IRP88 enables the successful formulation of ODT to be produced via traditional direct compression tableting process.

## REFERENCE


- Hughes, Lyn, Buccal Dissolution of active substances, US Patent No. 7470545, B2, Dec 8, 2008.
- Hughes, Lyn, Dissolution Test Equipment and Method. US Patent No. 2003/0088369 A1, May 8th, 2003.


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