Project 1: The Effect of Processing on the Solid - State form of Selected Sulphonamides and their Sodium Salts, alone and as Drug - Excipient Composites.	Authors: Robert Ahern, Abina Crean and Katie Ryan
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Enhanced Dissolution Rate of Fenofibrate by Loading onto Mesoporous Silica

Objective

Enhance the dissolution rate of fenofibrate by loading onto a high-surface area carrier (mesoporous silica) using supercritical carbon dioxide as the solvent.

Method

Mesoporous silica – fenofibrate samples were prepared by processing in supercritical carbon dioxide. Various processing conditions were investigated to determine the optimum for drug loading. The ratio of fenofibrate to mesoporous silica was kept constant.
The XRD, DSC, Dissolution and Surface Area data of the processed samples were compared to the unprocessed fenofibrate and mesoporous silica. This allowed the alterations in fenofibrate's solid-state and mesoporous silica's surface area properties to be determined.

Results

Fenofibrate Crystalline Structure:

Unprocessed fenofibrate was in the crystalline state. The processed samples were in the amorphous state. During processing, fenofibrate was solubilised by the supercritical carbon dioxide. Upon depressurizing, fenofibrate was trapped in the pores of the mesoporous silica and could not re-crystallize. Crystalline structure was determined by XRD (fig.1).

DSC was also used to determined fenofibrate crystalline structure in the unprocessed and processed samples.
Unprocessed fenofibrate samples had the characteristic melting endotherm whereas in the processed samples; the endotherm had disappeared.

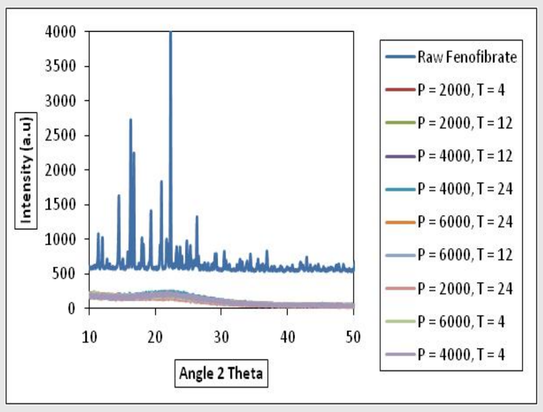

Fig.1. P-XRD data of unprocessed and processed fenofibrate.

Mesoporous Silica Surface Area Properties

The effect of drug-loading on the surface area properties of mesoporous silica was determined by BET analysis. There was a clear reduction in the surface area, cumulative pore area and cumulative pore volume of the mesoporous silica in the drug-loaded samples, (fig.2 and 3). This was because the fenofibrate had entered into the pores of the mesoporous silica. The larger pores contained the drug as there was a reduction in average pore width of the loaded samples, (fig.3).

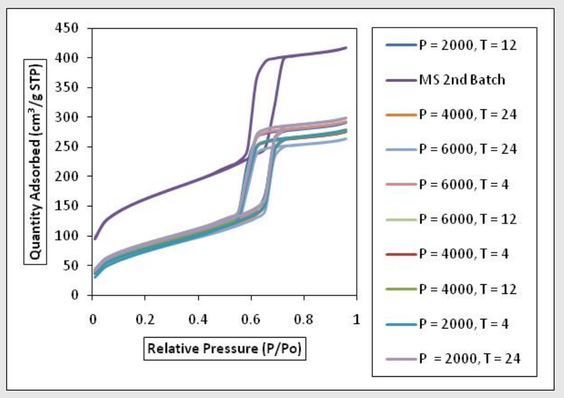

Fig.2. BET Nitrogen Adsorption Isotherm for the unloaded and drug-loaded mesoporous silica..

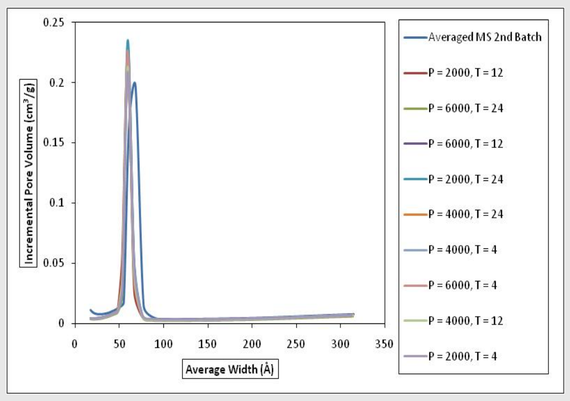

Fig.3. BET Pore Width Data for the unloaded and drug-loaded mesoporous silica.

Fenofibrate Dissolution Rate

The dissolution rate of unprocessed fenofibrate is quite slow. It takes two hours for 24 % of the drug to dissolve.
In the processed samples, there is rapid dissolution of fenofibrate. After 5 minutes, 50 % or more of fenofibrate has dissolved. The equivalent value for unprocessed fenofibrate is 0.25 %.

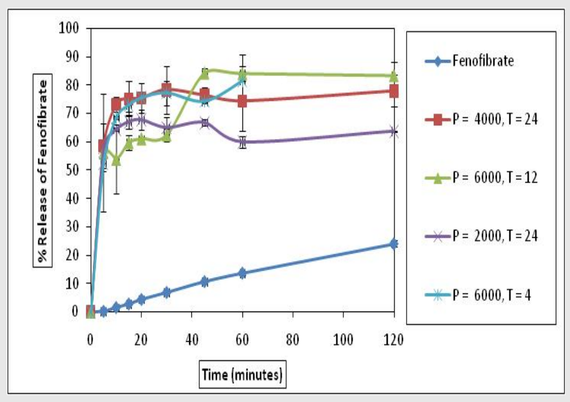

Fig.5. Fenofibrate Dissolution Rate Enhancement of Fenofibrate in the processed samples.