Interactions Between Daflampridine and Excipients in the Solid State

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ABSTRACT

The successful formulation of a stable solid dosage form depends on the careful choice of the excipients. Hydroxypropyl methylcellulose (hypromellose) and Aerosil are widely known excipients and are most commonly used in the preparation of drug formulations. They can serve either as a solvent for an active pharmaceutical ingredient (API) or to form stable dispersion with no tendency to aggregation etc. However, the evaluation of possible drug–excipient interactions is of the utmost importance for the preparation of effective controlled release formulations [1, 2]. The literature data has revealed that several excipients can interact with some APIs. Drug–excipient interactions may involve intermolecular hydrogen bonds or subtler intermolecular interactions, e.g., van der Waals contacts [1, 2, 3].

In the present study, the possible interactions between daflampridine and its excipients were investigated through Raman Spectroscopy (RS) and X-Ray Powder Diffraction (XRPD). Binary physical mixtures of API and each of the excipients at various percentages were prepared by a gentle mixing of ingredients in order to minimize the influence of sample preparation on the possible interactions between the components.

The diffractograms and spectra of the fresh mixtures were the sum of the API and of the respective excipient pattern and spectrum. The Raman spectra and XRPD patterns of the mixtures of the API with hypromellose and Aerosil that were recorded after 48 h revealed remarkable changes. Some new Raman bands emerged while others disappeared or were shifted. Raman spectra suggested that a physical interaction or chemical reaction occurred between ingredients. From the XRPD patterns of mixtures with low API percentage no crystalline API was found i.e. significant crystallinity reduction was observed, while the XRPD patterns of mixtures with higher API content have shown the presence of both pure crystalline API and non-crystalline form.

From the above it is apparent that there are interactions between the two excipients and the API. A plausible explanation, which at the moment is under investigation, is that there is intermolecular hydrogen bonding between API and each of these two excipients leading to a complex non crystalline formation.

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