SOLID STATE INTERACTIONS OF DAFLAMPRIDINE AND EXCIPIENTS

Stefani Fertaki[*,**], Malvina Orkoula[*,**] and Christos Kontoyannis [*,**]

[*]Department of Pharmacy, University of Patras, Greece
[**]ICE/HT-FORTH

The successful formulation of a stable solid dosage form depends on the careful choice of the excipients. The literature data has revealed that several excipients can interact with some APIs. Such interactions may involve intermolecular hydrogen bonds or van der Waals contacts [1, 2]. The existence of a drug–excipient interaction should be considered for the preparation of effective controlled release formulations [1].

In the present study, the possible interaction between Daflampridine and excipients (Hydroxypropyl methylcellulose (HPMC), microscrystalline cellulose (MCC), magnesium stearate and Aerosil 200) used in Fampyra® 10mg Fc Tabs was investigated through Raman Spectroscopy, Optical Microscopy, Differential Scanning Calorimetry (DSC) and X-Ray Powder Diffraction (XRPD). Binary physical mixtures of API and each of the excipients were prepared by a gentle mixing of ingredients

The diffractograms of the freshly prepared (zero time) mixtures were the sum of the API and each excipient. The same was valid for Raman spectra and DSC patterns . During time (aged mixtures), though, remarkable changes were revealed. In the diffractograms of the binary mixtures of API with each of HPMC, MCC and Aerosil 200 excipients, amorphization of the API was observed. Furthermore, the crystalline API particles were no longer visible through the optical microscopy. In Raman spectra, some new bands emerged while other were shifted or disappeared completely. The melting endotherm of pure API was missing in the thermographs of the aged mixtures. Moreover, the Tg of the HPMC was shifted to lower temperature.

All these suggest that a chemical interaction occur between API and excipients resulting in loss of API crystallinity as observed in the XRPD patterns. A working hypothesis is that solid solution is formed when API is dispersed in the excipient’s matrix in its neutral state through H-bonding. The effect of temperature and humidity on this interaction, was studied. The maximum API quantity that could interact with each excipient was also calculated.

REFERENCES

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