



Solubility Enhancement of Ticagrelor by Co-Crystal Technology: Preparation, Solid State Characterization and Solubility Studies

Nazare L.J. SHANE ¹, Aravind PAI ², Girish PAI ³, Vasudev PAI ⁴,
Vasanthraju SG ¹ & Muddukrishna B. SATHYANARAYANA * ¹

¹ Department of Pharmaceutical Quality Assurance,

² Department of Pharmaceutical Chemistry,

³ Department of Pharmaceutics, ⁴ Department of Pharmacognosy,

Manipal College of Pharmaceutical Sciences(MCOPS), MAHE, Manipal, Karnataka, India.

SUMMARY. In this study a new co-crystal of ticagrelor with quercetin has been fabricated with improved solubility. Ticagrelor is a class VI drug with poor solubility and permeability; hence an attempt has been made to improve its solubility by co-crystallization technology. A co-crystal is a structurally homogeneous crystalline material containing an active pharmaceutical ingredient and the co-former in definite stoichiometric amounts. In this study the conformer selected was quercetin based on ease of hydrogen bond formation and also as quercetin will provide a synergistic effect with ticagrelor. The co-crystal of ticagrelor with quercetin was prepared in two ratios (1:1, 2:1). Ticagrelor formed stable co-crystals in the ratios 1:1 and 2:1. The formation of co-crystal was confirmed by PXRD, DSC, and FTIR. The dynamic solubility of co-crystals in the ratios 1:1 and 2:1 increased by approximately 1.6 fold as compared to pure drug.

RESUMEN. En este estudio se fabricó un nuevo co-cristal de ticagrelor con quercetina con solubilidad mejorada. El ticagrelor es un fármaco de clase VI con poca solubilidad y permeabilidad; por lo tanto, se ha intentado mejorar su solubilidad mediante la tecnología de co-cristalización. Un co-cristal es un material cristalino estructuralmente homogéneo que contiene un ingrediente farmacéutico activo y el co-formador en cantidades estequiométricas definidas. En este estudio, el conformador seleccionado fue la quercetina basada en la facilidad de formación de enlaces de hidrógeno y también porque la quercetina proporciona un efecto sinérgico con ticagrelor. El cocristal de ticagrelor con quercetina se preparó en dos proporciones (1:1, 2:1). El ticagrelor formó co-cristales estables en ambas proporciones. La formación de co-cristal fue confirmada por PXRD, DSC y FTIR. La solubilidad dinámica de los co-cristales en las proporciones 1:1 y 2:1 aumentó aproximadamente 1,6 veces en comparación con el fármaco puro.

KEY WORDS: co-crystal, ticagrelor, dynamic solubility, quercetin, slow evaporation method.

* Author to whom correspondence should be addressed. E-mail: krishna.mbs@manipal.edu