Milling and co-milling with various excipients for the improvement of intrinsic dissolution rate of ibuprofen

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AIM

The aim of this study was to improve the intrinsic dissolution rate of poor soluble drug ibuprofen.

INTRODUCTION

Ibuprofen is a poorly water soluble drug and co-milling with different hydrophilic excipients is one technique that can be employed for the improvement of solubility and dissolution rate of poorly soluble drugs (Garg et al., 2009). Soluplus is a relatively new solubilizer which has widely been used in making solid dispersion for the improvement of dissolution rate of poorly soluble drugs (Djuric and Kolter, 2010).

MATERIALS AND METHOD

Ibuprofen and excipients (Soluplus, HPMC, PVP, Avicel-102) in ratios of 1:1 were co-milled in a planetary ball mill. The mill was run at 25Hz for 15min. The co-milled mixtures were pressed into compacts by a 10 tons hydraulic press and coated with hard paraffin wax to cover its all side except one surface by pouring the molten wax in the plastic mould in which compacts were placed on glass slides. The wax plugged compacts were attached to the basket holder of the EU dissolution apparatus and dissolution was performed in buffer solution (pH 7.4) at 37°C±0.4 with the basket rotating at a speed of 50rpm. The intrinsic dissolution rate (IDR) was determined spectrophotometrically at 258 nm.

RESULTS AND DISCUSSION

The IDR of the un-milled ibuprofen compact was 0.08 mg/cm^2/min which increased to 0.30 mg/cm^2/min for milled drug. The co-milled formulations with soluplus, HPMC, PVP and Avicel-102 gave intrinsic dissolution rates of 0.26, 0.47, 0.06 and 0.14 mg/cm^2/min, respectively (Figure 1). The IDR was relatively slow for the co-milled formulations with PVP and Avicel-102 and similar to that for the un-milled drug, suggesting that a gelation of viscosity effect may be retarding the release of drug. On the other hand it was high for the milled drug and further high for the co-milled formulation with HPMC. These were probably due to increased surface area of the drug on milling and swelling and erosion action of HPMC (this was visible in micrograph pictures, not shown). The co-milled formulation with soluplus has fastest IDR (because of solubilization action of soluplus) with gradient of 0.58 in first 45min of dissolution which slow down afterward probably due to saturation of solubilization action.

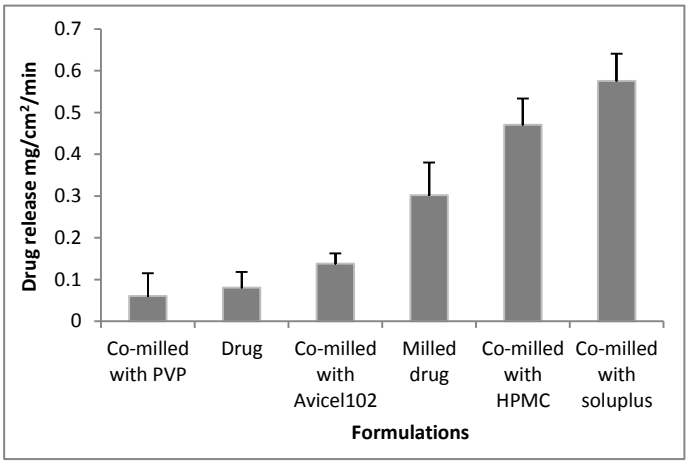

Figure 1: Drug release gradient per cm^2 for un-milled, milled drug and different co-milled formulations.

CONCLUSION

The co-milling with soluplus and HPMC significantly increased the intrinsic dissolution rate of ibuprofen.

REFERENCES

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