SCREENING FOR INDOMETHACIN-GLUCOSAMINE HCl
CO-GROUND FORMULATIONS TO OBTAIN SYNERGIC
ANTI-INFLAMMATORY EFFECT

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Introduction
Indomethacin is a NSAID that is characterized by low solubility and high permeability. In order to improve the drug dissolution rate, the co-grinding method was used as an approach to prepare indomethacin co-ground in the carriers such as glucosamine hydrochloride. This amino sugar has been shown to decrease pain and improve mobility in osteoarthritis joints. Therefore, the incorporation of glucosamine in indomethacin formulations will offer additional benefits to patients. The present work is an attempt to use D-glucosamine HCl as a potential excipient to improve dissolution rate of indomethacin using the co-grinding approach. The effect of the order of grinding on the dissolution of indomethacin was also investigated. The physicochemical characteristics of prepared cогround systems, morphology of particles, and their solid state were also studied.

Methodology
Co-ground of different ratios of drug to carrier (2:1, 1:3, 1:5; and 1:10 w/w) were prepared using ball mill (Fritsch, Germany). Eight steel balls were used with diameter of 20 mm. The vibration rate was set to 400 rpm. The samples were subjected different grinding times (5, 20, and 60 min). In order to investigate the effect of grinding process on dissolution behaviour of indomethacin, the drug was ground separately in absence of glucosamine. Then the mixture of ground indomethacin and un-ground D-glucosamine HCl were prepared by mixing them in a tubular blender for 10 min. Different ratios of drug:carrier (4:1, 2:1, 1:1, 1:2 and 1:4) were prepared for comparison purposes. Physical mixtures of indomethacin and glucosamine were also prepared for comparison purposes.

Dissolution studies: A USP dissolution apparatus no. 1 was used to monitor the dissolution profiles of indomethacin co-ground powders and physical mixtures. The dissolution medium was 900 mL phosphate buffer (pH 7.2); equilibrated to 37 °C and the baskets were rotated at 100 rpm. The concentrations of indomethacin within the samples were determined by UV spectrophotometer at 318 nm.

Dissolution parameters: DE10min, MDT, and MDR were used to represent the dissolution rate from various preparations.

Solid state characterization: Properties of all Formulations were studied using FTIR, SEM, XRPD, and DSC.

RESULTS AND DISCUSSION

Dissolution studies
• Pure indomethacin has the lowest dissolution rate.
• All grinding techniques showed a general improvement in the dissolution rate of indomethacin.
• All dissolution profiles showed that the fastest dissolution was obtained when indomethacin was co-ground with glucosamine HCl for 5 min (Fig 1a). This was closely followed by mixing ground indomethacin with un-ground glucosamine HCl where higher grinding times (20 min) showed the fastest dissolution (Fig 1b). This case was the case for the mixed samples of ground indomethacin with ground glucosamine HCl at grinding time of 60 min. However, these samples demonstrated poorer dissolution than co-ground samples.

FT-IR results showed that samples ground for 60 min is the mixture of α and γ forms (Fig 3). When Indomethacin was mixed with glucosamine HCl (2:1or 1:10) and subjected to various grinding times from 5 to 60 min no changes were observed in their FT-IR spectra (Fig 4). This indicates that the presence of glucosamine HCl prevented the conversion of γ-form to α-form when the mixture was ground for 60 min.

Conclusion
This study demonstrated that glucosamine HCl can be used as an efficient hydrophilic carrier to improve the dissolution rate of ground indomethacin formulations. Also, the study showed that the dissolution of indomethacin is influenced by process used to formulate indomethacin samples, the ratio of drug: carrier, and grinding time. Indomethacin has converted from γ-form to α-form when grinding time has increased for 60 min. However, the presence of glucosamine HCl prevented such conversion.

References

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