Evaluating the lubricant capacity of Compritol® HD5 ATO – a water dispersible pharmaceutical lubricant

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ABSTRACT:
Hydrophilic lubricants commonly used to reduce the frictional forces generated during tabletting impart a hydrophobic film on the surface of the powder or granules. This negatively impacts the performance properties of the resultant tablets by prolonging the disintegration time, slowing dissolution due to reduced water penetration rate and lowering tablet strength due to decreased interparticle bonding. These negative effects can become problematic, especially in the case of orally disintegrating tablets, which are required to disintegrate within 30 seconds when tested for DT by USP Disintegration Test Method <701>. For this reason, several new lubricants which are less hydrophobic such as ‘Compritol HD5 ATO’ (Behenoylpolyoxyl – 8 glycerides NF), a mixture of glycerol and polyethylene glycol behenate are proposed. As Compritol HD5 ATO is an amphiphilic substance, it can also be used to enhance the aqueous solubility or dissolution characteristics of poorly soluble compounds while making solid dispersions. In this study, the lubricant capacity of Compritol HD5 ATO is evaluated by studying the effect of its concentration and mixing time on material flow properties, tablet ejection force, hardness, disintegration time and rate of dissolution. A comparative evaluation with Sodium Stearyl Fumarate and PEG 6000 is also performed. This study would help establish Compritol HD5 ATO as an effective solution for formulations wherein an amphiphilic lubricant is desired.

INTRODUCTION:
- Lubrication is an essential step for pharmaceutical operations such as blending, roller compaction, tablet manufacturing, capsule filling etc. as it reduces the friction between the surfaces of manufacturing equipment and that of pharmaceutical solids, improves blend flowability and ensures the continuation of an operation.
- Unfortunately, the nature of lubricants induces two well-known negative effects due to their hydrophobic characteristics: the decrease of tablet tensile strength and the slowing of drug release, especially observed w.r.t. Magnesium Stearate.
- Hence several less hydrophobic lubricants s.a. Compritol HD5 ATO (Behenoylpolyoxyl – 8 glycerides NF) are proposed.
- The objective of this study was to perform comparative evaluation of lubricant capacity of Compritol HD5 ATO (hydrodispersible lubricant, HLB 5), Sodium Stearyl Fumarate and PEG 6000 by studying the effect of their concentration and mixing time on flow properties, tablet ejection force, hardness, disintegration time and rate of dissolution.

METHODS:
- Physical characterisation of the lubricants under study was performed w.r.t.
  - Specific surface area (BET technique),
  - % Crystallinity (ORI Technique),
  - Differential Scanning Calorimetry
  - Contact angle measurement.
- For evaluating the performance characteristics of the selected lubricants, placebo granules of Avicel PH 101 and Pharmatose 200M were prepared using Rapid Mixer Granulator (Sanuth, Mumbai).
- The effect of concentration and mixing time of each of the lubricants on the flow properties of the placebo granules was evaluated.
- The placebo granules were further compressed into tablets using tablet rotary press (KL 100 Korsch, Germany) and the impact of lubricant concentration and mixing time on the ejection force, main compression force, hardness and disintegration time of the tablets was evaluated.
- A comparative dissolution profile of a drug belonging to BCS Class II using the lubricants under study was plotted to evaluate the effect of each of the lubricants on the release profile of the drug.

DISCUSSION:
- PHYSICAL EVALUATION
  - Compritol HD 5 and PEG 6000 have a crystalline structure while SSF exhibited partial crystallinity.
  - Surface area: SSF > PEG 6000 = Compritol HD5
  - The thermograms for Compritol HD 5 and PEG 6000 showed a sharp endotherm at their respective melting point range while multiple endotherms are observed in case of SSF.
  - Wettability of the lubricants can be graded as: PEG 6000 > Compritol HD 5 > SSF
- PERFORMANCE EVALUATION
  - Flow Properties:
    - The flow properties of the granules after addition of Compritol HD 5, SSF and PEG 6000 were comparable and were found to be optimized at 20 % concentration level for Compritol HD 5.
    - Flow properties of the lubricated granules improved when the mixing time was increased from 3 min to 5 min, while not much impact was observed after increasing the mixing time to 10 min in case of Compritol HD5.
  - Force Monitoring:
    - The lubricants can be graded as follows for their ability to reduce the Ejection force:
      - Compritol HD 5 > SSF > PEG – 6000
    - The compaction behaviour for Compritol HD 5, SSF and PEG 6000 was comparable and can be graded as:
      - PEG 6000 > Compritol HD 5 > SSF
    - The desired hardness range of 80 – 120 N was very easily obtained with Compritol HD 5 & PEG – 6000, while with SSF the hardness range could not be achieved even at higher compression forces.
    - The disintegration time range for Compritol HD 5 & PEG – 6000 were comparable while with SSF delayed disintegration was observed even at lower concentration.
    - No impact of mixing time on ejection force, hardness and DT were observed w.r.t. Compritol HD 5 & PEG – 6000 while major impact was observed for SSF.
- Dissolution studies:
  - Compritol HD 5 marginally increased the release profile by aiding in enhancing the solubility of BCS Class II drug in comparison to SSF.

CONCLUSION:
- Compritol HD 5 ATO:
  - Has crystalline, hydrodispersible and thermostable properties.
  - Effectively reduced tablet ejection force in contrast to plain granules and PEG – 6000.
  - Desired hardness range was easily achieved at considerably low compression forces in contrast to SSF.
  - Hardness and DT values are not sensitive to mixing time and concentration of Compritol HD 5 in contrast to SSF.
  - Aids in enhancing the dissolution of poorly soluble drugs.
- Compritol HD 5 ATO was found to be very economical and effective hydrodispersible lubricant.

REFERENCE:

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