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Short communication

Influence of lubricant glycerol dibehenate concentration on dissolution stability and tablet properties

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Introduction

One of the main challenges in oral solid formulations is achieving the right percentage of released API in a specified time span – dissolution. Whilst choosing the right excipients is the essence of a formulation, their concentrations need to be further optimized in order to have the desired effect *in vivo*.

Lubricants are one of the essential components in a formulation. Pharmaceutical lubricants are added to tablet and capsule formulations in a very small quantity (usually 0.25%–5.0% w/w) to improve the powder processing properties of formulations. Regardless of the small amount, lubricants play important roles in manufacturing; they decrease friction at the interface between a tablet's surface and the die wall during ejection so that the wear on punches and dies are reduced, and problems such as sticking and picking are reduced to a minimum level.

Glycerol dibehenate (Compritol® 888ATO) is a less commonly used lubricant in comparison with other lubricants such as magnesium stearate. In particular, glycerol dibehenate is an effective lubricant to replace magnesium stearate when the latter causes delay of dissolution and other compatibility issues. Relative to magnesium stearate, it is expected from glycerol dibehenate to have similar lubrication efficiency with a higher concentration. In addition, the usage of it should not affect compressibility.

Identified as one of the most challenging excipients for concentration optimizing in our formulation, the aim of this study was to compare the effect of different lubricant concentrations on the dissolution, the efficacy of the lubricant during tablet compression process and the final tablet characteristics.

Materials and methods

Materials

For preparing the analyzed formulations the following excipients were used: povidone (Kollidon K 25); lactose monohydrate (Lactose M 100 and Lactose M 200); crospovidone (Polyplasdone XL-10), colloidal anhydrous silica (Aerosil 200) and glycerol dibehenate (Compritol ATO 888).

Reagents, solvents and reference standards used for the dissolution test were: 0.1 M EDTA disodium; Eriochrome black T (indicator); ammonium hydroxide 10%; 0.1 M hydrochloric acid, ammonium chloride and purified water.

Methods

Three formulations with high percentage of API (>80%) were prepared with difference only in lubricant concentration. The preparation process includes fluid bed granulation, followed by tableting. The lubricant used was glycerol dibehenate (Compritol ATO888) in concentrations of 0.5%; 1% and 1.5%. The effects were observed during the tableting process (with the negative outcome being the sticking of granulate to tablet press punches) and also further analyses of the physical tablet characteristics were made, including hardness, disintegration and friability.

The main observed effect was the dissolution of tablets with a previously set limit: not less than 70% release of API for the time span of 30 minutes. The used dissolution method was a complexometric titration on apparatus 2 with paddle (according to Ph. Eur. 2.9.3). The dissolution test was repeated in order to evaluate the stability of the formulation after 3 and 6 weeks and 3

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months at conditions 25°C/60% RH (Petri dish); 40°C/75% RH (Petri dish and in dark glass jar) and 60°C (Petri dish).

Results and discussion

From the obtained results it can be seen that at the initial dissolution analysis in all three formulations (containing 0.5%; 1.0% and 1.5% glycerol dibehenate) the active ingredient dissolved completely for a period of 30 minutes with dissolution results being the following:

- Formulation 1 (0.5% lubricant) – 100.49% (SD=0.19%)
- Formulation 2 (1.0% lubricant) – 99.89% (SD=0.32%)
- Formulation 3 (1.5% lubricant) – 99.89% (SD=0.24%)

The stability results showed a different type of behavior, resulting in dissolution decrease of API, for formulation 1 stored in conditions 60°C - Petri dish (23.02%; SD=2.77% after 3 weeks and 16.44%; SD=1.33% after 6 weeks); formulation 2 held in conditions 60°C - Petri dish (9.43%; SD=1.12% after 3 weeks and 7.16%; SD=0.67% after 6 weeks) and formulation 3 held in conditions 60°C - Petri dish (23.38%; SD=3.42% after 3 weeks and 18.18%; SD=2.65% after 6 weeks). Tablets stored at 60°C - Petri dish stability testing have been discontinued after 6 weeks due to the significant dissolution decrease. The tablets stored at 25°/60% RH showed insignificant dissolution decrease after 3 weeks, 6 weeks and 3 months. The tablets for formulation 2 (1.0% lubricant) stored at 40°C/75% RH (dark glass jar) showed API dissolution decrease after 3 months - 81.54%; SD=1.80%. Formulation 1 (0.5% lubricant) and formulation 3 (1.5% lubricant) showed insignificant API dissolution decrease - 97.30%; SD=2.90% and 97.60%; SD=1.78% at 40°C/75% RH (dark glass jar) after 3 months.

The difference in lubricant concentration affected the tableting process in a way that manifested as sticking to the tablet press punches. Sticking was visible for formulations 1 and 2, and did not occur for formulation 3 due to the highest concentration of lubricant.

Conclusion

All three concentrations of glycerol dibehenate resulted with a dissolution within acceptance criteria (API dissolved above 70% within a time span of 30 minutes).

Stability results indicated that a concentration of 1.5% glycerol dibehenate results with the smallest decrease of API dissolution after 3 and 6 weeks on temperature of 60°C. Tablets stored at 25°/60% RH and 40°/75%RH did not show any changes in dissolution after 3 and 6 weeks.

Concentration of glycerol dibehenate affects the compression process and concentrations lower than 1.5% of glycerol dibehenate manifested with a sticking problem.

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