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Liquid-filled hard gelatin capsules: excipient/capsule compatibility studies

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INTRODUCTION

Encapsulation of pharmaceutical formulations as liquids or semisolids, within hard gelatin capsules, presents an important oral dosage strategy for poorly water-soluble drugs, resulting in good bioavailability and reproducible drug absorption [1]. In addition, this technology offers an inherently safer process than powder filled capsules and tablets for highly potent or cytotoxic drugs by avoiding dust generation.

Gelatin is a mixture of water-soluble proteins and as such is chemically not inert. Crosslinking can occur as a result of elevated temperature, humidity, UV light and/or presence of aldehydes. Certain excipients used in the formulation of liquid filled capsules may have, or may generate during storage, low levels of aldehydes, which can potentially react with gelatin. Crosslinking can cause considerable changes in the dissolution profile of gelatin capsules.

Moisture within the gelatin capsules acts as a plasticiser for gelatin. Hygroscopic materials, when filled into the capsule, can extract moisture from the shell and thereby induce capsule brittleness, which in turn reduces the robustness of the capsule product.

Here we present a compatibility study of hard gelatin capsules with common excipients in absence of active pharmaceutical.

MATERIAL AND METHODS

Capsugel Licaps were filled with excipients and stored at 5°C, 25°C/60% relative humidity (%RH) and 40°C/75%RH. Mass increase of the filled capsules during storage was determined gravimetrically. Capsule dissolution behaviour in 0.1M HCl was assessed visually using a Caleva 10ST dissolution apparatus (37°C; paddle speed: 99 rpm).

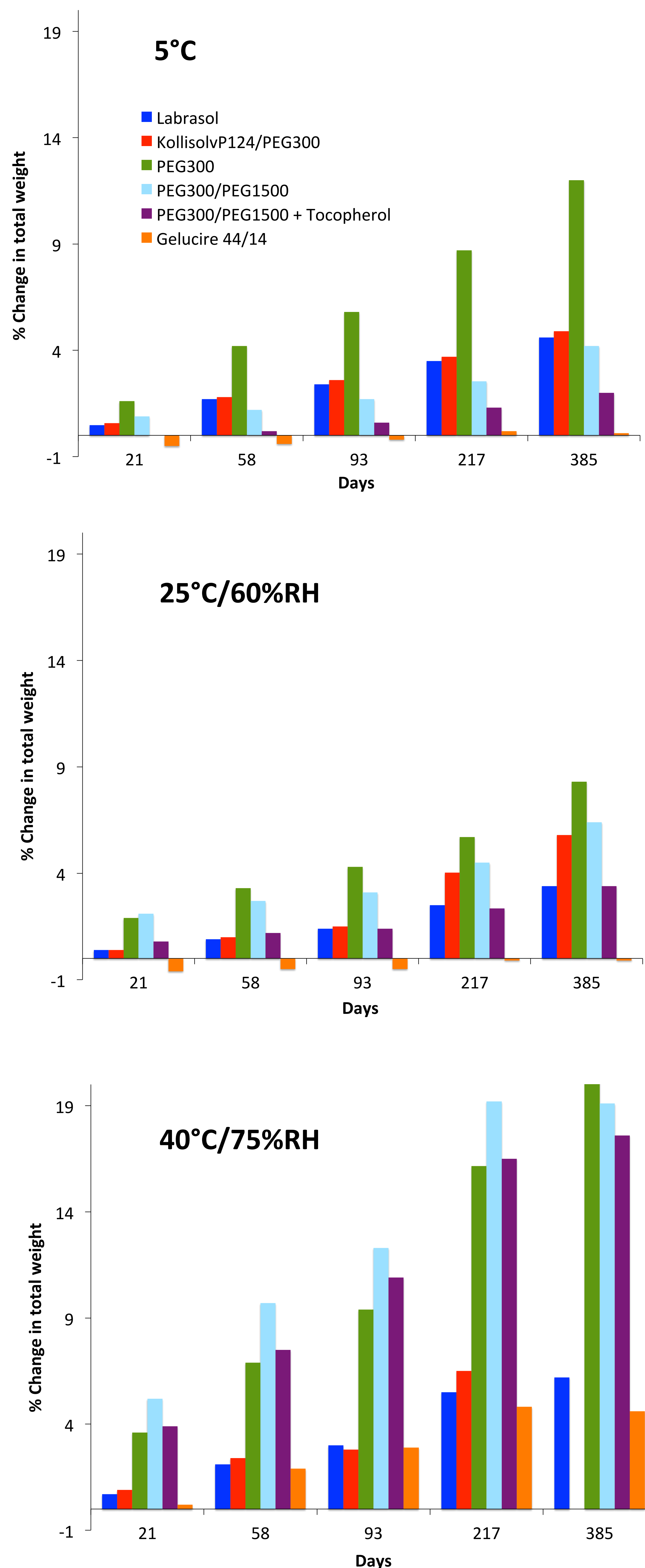


Figure 1:
Weight change of Licaps gelatin capsules filled with excipients in absence of drug stored at controlled conditions: 5°C, 25°C/60% RH, 40°C/75%RH.

RESULTS AND DISCUSSION

Weight increase of capsules containing excipients are displayed in Fig. 1. PEG 300, which is known to be hygroscopic, shows the highest weight increase at 5°C and 25°C. Addition of Tocopherol (Vitamin E) to the PEG300/1500 mixture reduced the weight increase. Weight increase was lowest for capsules filled with Gelucire 44/14.

After 6 month storage at 40°C/75%RH only the capsules containing Gelucire, Kollisolv/PEG300 and the PEG1500/300 mixture with Tocopherol had fully dissolved after 90 min in the dissolution vessel. Capsule shells were only partially dissolved when filled with Labrasol, PEG300 and the PEG mixture without Tocopherol, indicating gelatin crosslinking during storage.

CONCLUSIONS

- Simple weight checks under stressed conditions give useful insights into excipient/capsule compatibility.
- Presence of antioxidants can add to improved capsule excipient compatibility by preventing crosslinking of gelatin.

ACKNOWLEDGEMENTS

This work was funded by Cancer Research UK.

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