01R0930

Evaluation of the gelatin and the enteric coating formulation for a hydrophilic soft gelatin capsule applying the QbD approach

C. Silva, D. Monterroza, J. Acosta, R. Gutierrez
PROCAPS S.A.

2016 AAPS ANNUAL MEETING AND EXPOSITION
NOVEMBER 13–17, 2016
COLORADO CONVENTION CENTER, DENVER
aaps

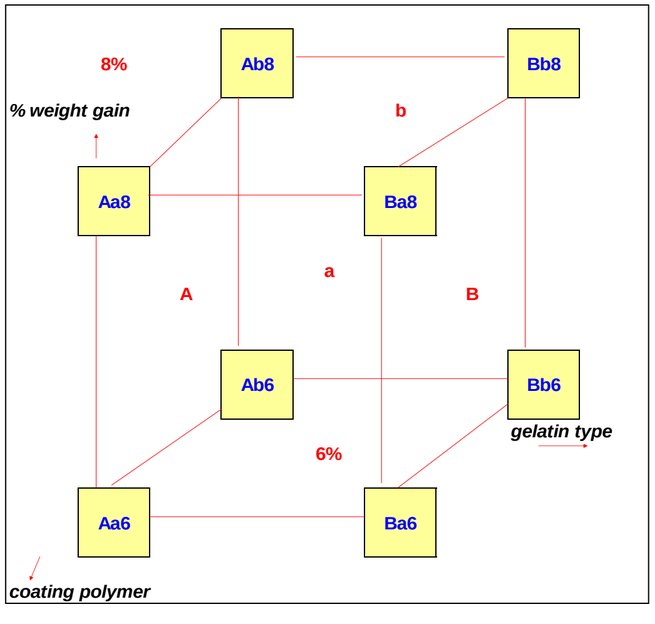
PURPOSE

This study is aimed to present an experimental design for developing the gelatin and the coating formulation of a pharmaceutical soft gelatin capsule under the Quality by Design framework.

METHOD

The tested softgels contained two active pharmaceutical ingredients in hydrophilic fill formulation. The experimental design considered different enteric coatings (methacrylic acid copolymers (a), polyvinyl acetate phthalate (b) and sodium alginate and ethylcellulose (c)). For each polymer, the gelatin formulation was tested using type A and B gelatins at the same level of plasticizer; and the coating formulation was tested at two levels of weight gain (6 and 8%).

Softgels were analyzed for gastro resistance (Q 10% max., 120 min), dissolution (Q 70% min., 45 min), assay (90-110%) and impurity levels according to the current USP monograph. Stability of the coated softgels was tested at 40°C/75 RH using two different packing materials (PVDC/foil and aclar) for three months. Statistical treatment (Unscrambler v.10.3) was applied in order to evaluate the effect on the critical quality attributes.



RESULTS

From the tested polymers, the methacrylic acid copolymers and the polyvinyl acetate phthalate met the gastroresistance and the dissolution tests for both gelatin types at both tested weight gain levels, except the type A using the polyvinyl acetate phthalate coating because of the pH incompatibility. According to these results, the gelatin formulation as well as the polymer weight gain were evaluated using the methacrylic acid copolymers. ANOVA treatment showed that the effect of the gelatin type is significant on dissolution for both APIs at 95% of confidence level. The corresponding contour plot (Fig.1) showed that the highest dissolution results were obtained for the type B gelatin in the tested range of coating weight gain.

In addition, the coating formulation (A and B) and the polymer weight gain were evaluated using the type B gelatin. ANOVA treatment showed that the effect of the coating polymer as well as the weight gain is significant on the dissolution for both APIs. The contour plot (Fig.2) showed that the highest dissolution results were obtained for the methacrylic acid copolymers coating at the 6% of weight gain.

Softgels at the highest tested weight gain met the criteria at accelerated stability conditions 40°C/75%RH at three months using aclar as packing material. In contrast, softgels at the lowest tested weight gain as well as softgels packed in PVDC/foil failed the physical stability due to the high moisture and temperature at accelerated conditions.

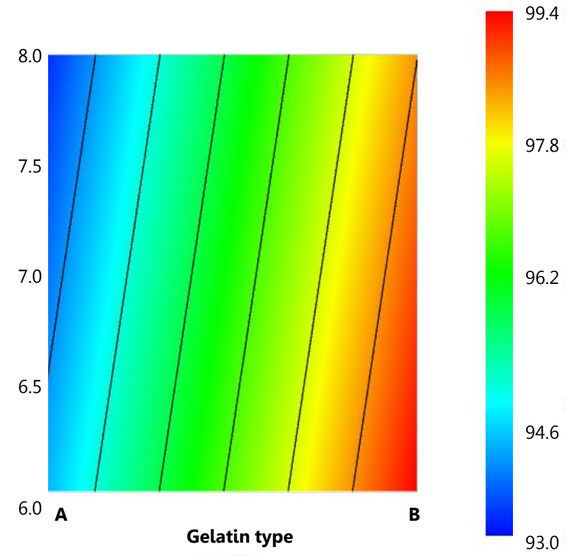


Fig. 1. Contour plot of dissolution (API A, coating a): Effect of gelatin type and weight gain

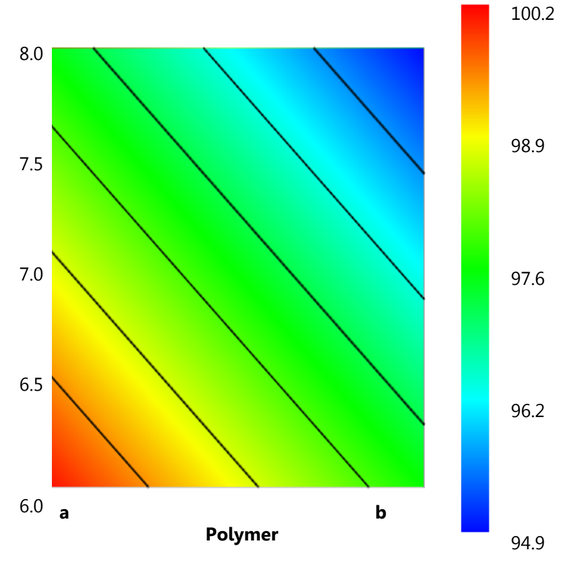


Fig. 2. Contour plot of dissolution (API A, gelatin type B): Effect of polymer and weight gain

CONCLUSION

As conclusion of the study, the results showed that the gelatin type B formulation and the methacrylic acid copolymers or the polyvinyl acetate phthalate coating systems at 8% weight gain had a comparable performance to meet the critical quality attributes of gastroresistance, dissolution, assay and impurities at stability conditions after three months when the aclar material was used.

REFERENCES

ICH, "(Q8R2) "Pharmaceutical Development," Harmonised Tripartite Guideline, Geneva, Switzerland, 2009

United States Pharmacopeial Convention. "U.S. Pharmacopoeia-National Formulary [USP 39 NF 34]". Rockville, Md, 2016