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X-Ray Tomography to Determine Seal Integrity of Filled Capsules Sealed on Capsugel LEMS®70 and CFS 1200™ Equipments

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Key words: hard gelatin capsules, sealing, integrity, X-Ray Tomography, liquid formulation, encapsulation.

PURPOSE

The work presented hereafter demonstrates the effective fusion between the two parts of Capsugel hard capsules after sealing them on Capsugel LEMS®70 and CFS1200™ equipments.

Photo 1: LEMS®70 machine

CFS1200TM and LEMS®70 are equipments for respectively laboratory and production scales, equipped with the exclusive micro-spray technology patented by Capsugel.

The sealing process consists of spraying a solution of alcohol and water below cap edge that fills the overlap between the two parts of the filled capsule in closed position, then applying a gentle heating to fuse the two walls together (Photo 2).

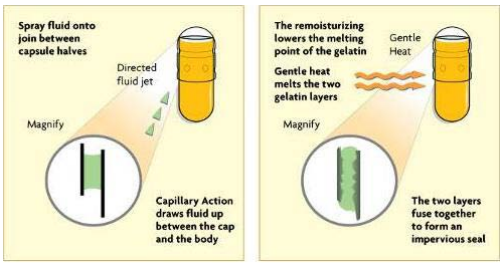

Photo 2: micro-spray technology

The sealing evidence is easily observed in case of transparent capsule, whereas it is very difficult to demonstrate in case of pharmaceutical product usually encapsulated in opaque capsules. The purpose of this study is to confirm the efficiency of the sealing process in opaque Licaps® using X-Ray Tomography non-destructive technique.

METHODS

Product description

- The capsules considered are Licaps® capsules size #00, #0 and #3 with different opaque colors from white to brown, filled with various formulations from very fluid to viscous (from 50 to 1000cP viscosity

at room temperature) and sealed either on CFS1200™ or on LEMS®70 in the presence of sealing fluid composed of ethanol and water 50/50.

Scanning using X-Ray Tomography

- The apparatus used is Skyscan1172 (Skyscan Belgium) able to provide X-Ray pictures with high resolution (4µm/pixel).
- One capsule is introduced in the observation chamber, placed on X-Ray-transparent holder in upright position and scanned rapidly to determine the best parameters for analysis: the size of the zone selected is linked to resolution to be reached, the quality of the pictures and the acquisition time.
- During the scanning session itself, capsule turns of 0.8° between scans, till 360° is covered. Multiple X-Ray pictures taken are treated by computed tomography to reconstruct to full picture of the object in three dimensions using inverse colors: density decreases with darkening. The virtual object is observed via numerous horizontal slices along vertical axis for easier interpretation (Photo 5).

Photo 3: Skyscan 1172 apparatus

RESULTS

Reference:
Natural transparent Licaps® size #0

- The formulation appears in grey and gelatin shell in dark grey, whereas air stands in white or light grey inside the capsule (Photo 4).
- The two layers of gelatin from cap and from body are fused together all along the seal zone.

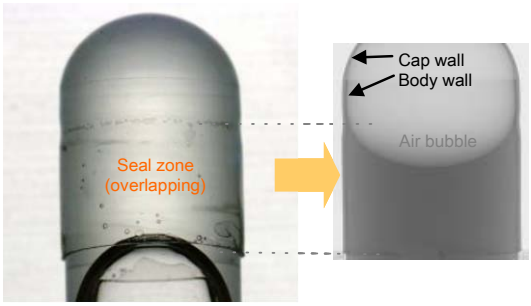

Photo 4: Transparent Licaps® capsule sealed on CFS1200 and observed under macroscope (left) and using X-Ray (right)

Opaque Licaps® size #0

As for our reference, the rapid scan shows that opaque capsule is filled with fluid formulation and sealed on both sides (Photo 5, top right). The three dimension pictures shows that sealing occurred all around the seal zone (Photo 5, bottom left).

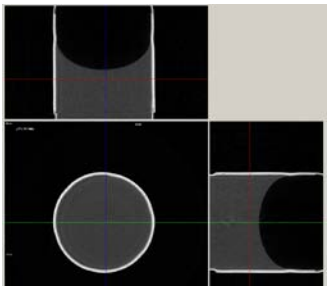

Photo 5: Opaque Licaps® size #0 sealed on LEMS®70 and scanned by X-Ray tomography

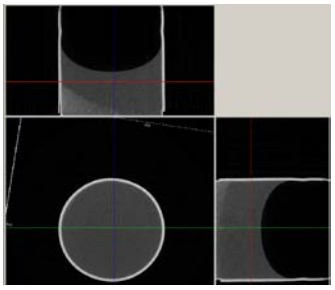

Photo 6: Opaque Licaps® size #00 sealed on LEMS®70 and scanned by X-Ray tomography

As gelatin wall is loaded with pigments for opacity purpose, cap and body walls appear in white (high density) compared to oil formulation in grey and air bubble in black. The cross section presented here is taken in the middle of the seal zone; it shows that cap and body are fused all around the capsule (Photo 5, bottom left). Very small defects in fusion at cap edge (top left and bottom right) are not at risk for leak.
This technique is also suitable for larger and smaller capsules:

Opaque Licaps® size #00
As in the previous sample, opaque gelatin shells are white (intensity is lower than in the previous sample because pigment content is inferior), the formulation separated into two phases with different densities, which make us suspect instability of the solids in this formulation, and air bubble entrapped stands in black (Photo 6).
The seal zone of this capsule is also well fused all around the capsule in the middle of the overlap. The bottom of cap part appears not perfectly fused to body wall, but it is not at risk for leakers.

Opaque Licaps® size #3
As the object is smaller, the resolution of scanning is better and we can see the different density of fused layer between cap and body wall (Photo 7, top left).
Here, the intensity of the cap wall is lower than the body's because of different colors and different pigment contents in both parts of the capsule. Moreover, this capsule was filled with very small quantity of fluid product, which is not visible here on the X-Ray pictures (it stands at body bottom).
The sealing occurred all around the capsule in the middle of the seal zone (Photo 7, bottom left); the small part not sealed located at cap edge (Photo 7, top left) does not affect the tightness of the Licaps® with regards to the product.

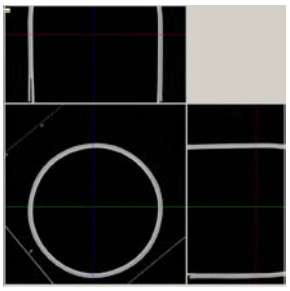

Photo 7: Opaque Licaps® size #3 sealed on LEMS®70 and scanned by X-Ray tomography.

CONCLUSION

The X-Ray Tomography is a powerful non-destructive technique to demonstrate that natural and opaque capsules sealed by Capsugel sealing equipments are *tamper resistant* tight. It is also successful in determining the reasons for defects generated on high-speed machines.

REFERENCES

- E.Cole et al "Challenges and opportunities in the encapsulation of liquid and semi-solid formulations into Drug Del. Review (2008) vol.60, 747-756 capsules for oral administration", Adv.

ACKNOWLEDGEMENT

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