The influence of external lubrication on the puncturing properties of hard capsules for dry powder inhalations

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PURPOSE

After capsule production, external lubricants are applied to prevent the capsules from sticking together and to facilitate processing in a capsule filling machine[1]. When piercing capsules in a dry powder inhaler, the mechanical properties of the capsule materials play a major role in terms of elasticity, plasticity, stiffness and deformability, which can have a decisive influence on the opening of capsules and aerosolization properties[2-5]. In this study, we attempted to understand the effect of external lubrication on the piercing behaviour of gelatin and HPMC hard capsule shells, in relation to different working humidities (RH's) using automated and manual puncturing mechanisms.

METHOD(S)

Capsules

Hard capsules of size 3 (**gelatin** and **HPMC**) were externally lubricated with: **Magnesium stearate** (**MgSt**), **Sodium lauryl sulphate** (**SLS**) or **Carnauba wax** (**CW**). Additionally, one **unlubricated** (**wo**) capsule of each type was tested.

Capsules were stored over saturated salt solutions at **11% RH**, **22% RH** and **51% RH** for 7 days before measurement.

Puncturing

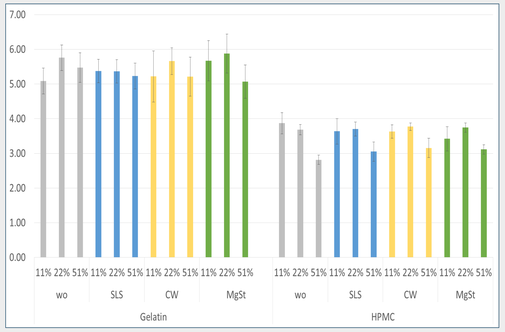
Capsules were punctured on their domed ends two ways:

- **Manually**: with **Plastiape RS01** device.
- **Automated**: with a piercing needle from the Plastiape RS01 device mounted on the force transmission arm of an **Instron 5943**.

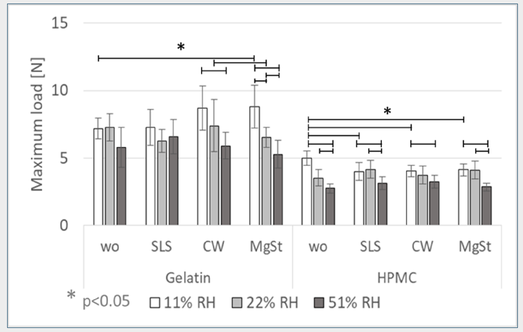
Analysis

Photos of the openings were evaluated using **ImageJ software**. The sizes of the openings were compared to the diameter of the Plastiape RS01 needle and expressed as a **percentage of the needle diameter**.

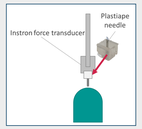
RESULT(S)



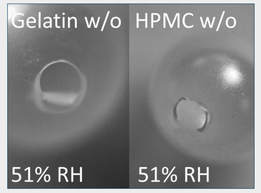
Young modulus of Gelatin and HPMC capsules at 11% RH, 22% RH and 51% RH (n=6).



Maximum load needed for the puncturing of the capsule with a needle mounted on an automated compression and tensile sensor (n=3).



Schematic setup of the maximum load measurement using Instron.



Openings of HPMC and gelatin at 51% RH. Gelatin reveals a more circular shape of the opening (n=3).

Mechanical properties

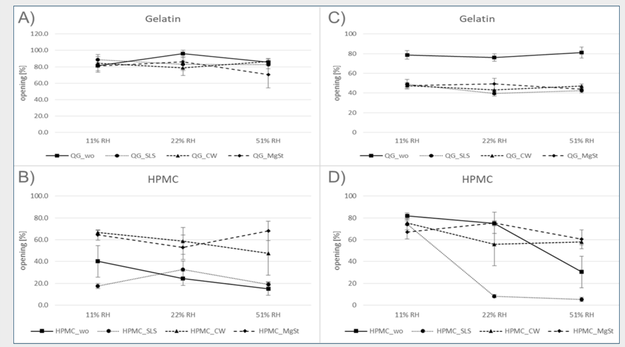
- The elasticity of the capsules increased with increased storage RH.
- Elasticity of HPMC at higher RH leads to a reclosure after puncturing, especially on HPMC capsules with SLS.

Maximum load

- The maximum load didn't change significantly ($p < 0.05$) as a consequence of different external lubricant. Exception was HPMC wo stored at 11% RH.
- Both capsule material required more force with lower humidity during storage.
- Less force was needed for puncturing HPMC capsules.

Opening formation

- Formation of the openings differed largely in automatic and manual puncturing.
- Opening size created by automated puncturing was less affected by the use of external lubricants in gelatin capsules, however, differently lubricated HPMC capsules exhibited large differences in opening sizes.
- Opening size of lubricated gelatin capsules was 20% reduced using manual puncturing compared to unlubricated capsules.
- Influence of RH on the opening size of gelatin capsules was not very dominant for both puncturing methods.
- In automated puncturing, HPMC capsules wo and SLS exhibited smaller openings compared to CW and MgSt at all RH conditions and no visible trends could be observed with increased RH.
- In manual puncturing, HPMC capsules exhibited a reduction in opening size with increasing RH, which is the most dominant for capsules lubricated with SLS.



Opening size in relation to needle diameter for capsules stored at different RH.
Automated puncturing of gelatin(A) and HPMC (B) capsules with Instron. Manual puncturing of gelatin (C) and HPMC (D) capsules with Plastiape RS01.

CONCLUSION(S)

- External lubrication decreases the opening size of manually punctured gelatin capsules.
- External lubrication and RH did not largely affect the opening sizes of automated punctured gelatin capsules.
- Manually punctured HPMC capsules revealed opening size decrease due to lubrication and RH.
- Lubrication did not impact automated HPMC puncturing.
- Opening sizes of capsules could have a possible effect on aerosolization performance and thus affect patient therapeutic outcome.

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