Evaluation of the properties of HPMC capsules manufactured using different methods

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OBJECTIVES

Two-piece hard capsules are popular for pharmaceutical products with many active ingredients. Hypromellose (HPMC) capsules are regarded as the one of best choices because of their low moisture content, lack of brittleness and good chemical stability.

HPMC capsules are commonly prepared by two different methods: **cold gelling using a gelling agent** and **thermal gelling**. The physicochemical properties of the capsules prepared by these methods could be different due to different thermal histories, additives and HPMC grades.

In preparing capsule formulations, it is important for capsules to meet customer requirements such as robust processability, with no damage during encapsulation, and fast dissolution with less variability irrespective of the test media pH.

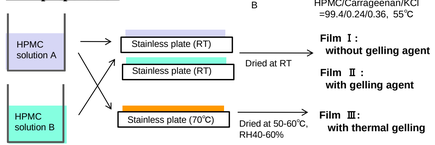
In this study, the factors important for capsule performance, dissolution, brittleness and moisture content were evaluated on films and commercially available HPMC capsules manufactured by these 2 methods.

FILM PROPERTIES

HPMC

- HPMC 2910 (Shin-etsu, TC-5M)
- HPMC 2906 (Dow, F5)

Film preparation



Tensile test for films

Cast films were attached to the device and stretched at constant speed of separation (10 mm/min) using an Autograph (AGS-J System, SHIMADZU, Japan) .

Mechanical property of Films

		Tensile strength [N]	Elongation at break [%]
HPMC 2910	Ⅰ	105±5	26.5±8.0
	Ⅱ	102±6	21.5±8.5
	Ⅲ	93±14	9.5±3.0
HPMC 2906	Ⅰ	104±4	18.0±4.0
	Ⅱ	103±2	20.0±3.5
	Ⅲ	104±2	12.5±3.5

(N=6, Average±SD)

- HPMC films by thermal gelling were torn more easily than HPMC films dried at room temperature irrespective of the addition of a gelling agent (Carrageenan) for both HPMC 2910 and HPMC 2906.

CAPSULE PROPERTIES

HPMC Capsules

- **Capsule A (Quali-V®, made by cold gelling using a gelling agent)**
- **Capsule B (Vcaps Plus®, made by thermal gelling, samples obtained in US and Japan)**

Impact test

A capsule was placed on the holder. A fifty gram weight was dropped from 10 cm onto the capsule. The percentage of capsules that split or shattered was recorded. (A)

Capsule product test

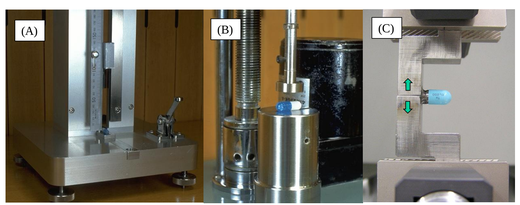
A filled capsule was placed on the holder and a 5Kg force was applied with a platen. The percentage of capsules that broke was recorded.
[Simulated "de-blistering"] (B)

Capsule tensile strength test

The cap of a capsule was mounted onto a pair of probes. The upper probe was raised at constant speed of separation (10 mm/min) until the cap split. (C)

Dissolution Test

- Model drug : Acetaminophen (AC)/Lactose/Disintegrant=20/70/10
- Paddle, 50 rpm, with sinker, N=6
- Test medium:
  - Purified Water
  - pH 1.2 (77.8 mM HCl, 34.2 mM NaCl)
  - pH 6.8 (50.0 mM KH_2PO_4, 23.6 mM)
  - pH 4.0 (0.1M Acetic acid buffer solution)



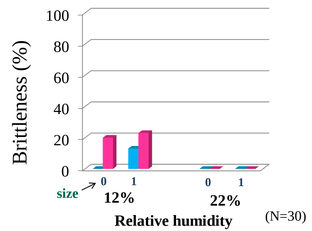
Mechanical property of Capsules

	Capsule	Tensile strength [N]	Elongation at break [%]
RH45-50% (Ambient humidity)	A	165±16	14.6±2.4
	B	153±15	9.7±0.8
RH12% (Low humidity)	A	172±21	11.1±2.0
	B	119±40	8.5±1.2

(size 1, N=10, Average±SD)

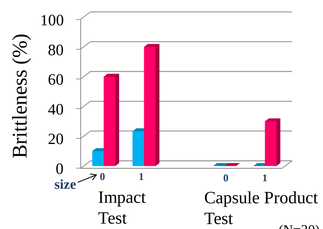
- Capsule B was more susceptible to splitting.

Capsule brittleness



(N=30)

Product brittleness : Dry corn starch filled capsules



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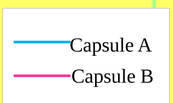
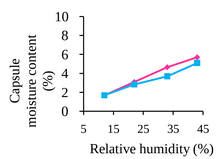
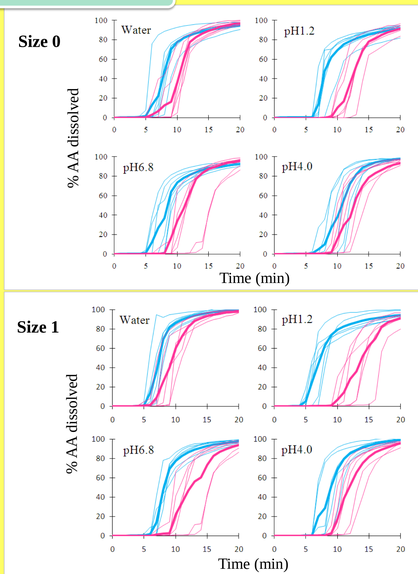


Moisture contents of Capsules



- At low humidity (RH12%), Capsule A did not fracture unlike capsule B where about 20% fractured.
- When filled with dry corn starch, only Capsule B had a high fracture rate using both the Impact Tester and the Capsule Product Tester.
- Moisture content of both capsules was similar.

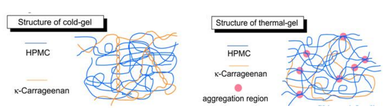
Dissolution profiles



- Drug release from Capsule A was more rapid in all test fluids.
- Drug release from Capsule B was more variable.
- Capsule A released 75% of the drug within 10 minutes irrespective of its size and test media.

DISCUSSION

The ordered structure of HPMC molecules in solution is retained during the drying process. HPMC molecules in solution form a rigid thermal gel above the gelling temperature. In the thermal gel state, HPMC molecules are likely to aggregate in groups to form a gel structure.



In addition, it is possible that drying temperature affects the structure of the film. By using SEM, micro-pores and non-homogeneous lamellar-like structures were detected in HPMC cast films dried at high temperatures (55, 75℃) (*G. Perfetti* et al 2010). This was probably due to trapped water in the structure causing the formation of small holes owing to a faster drying rate of the surface than the rest of the film.

It was demonstrated that the addition of a gelling agent, Carrageenan, did not affect the mechanical properties of the film and it was thought to work as a dissolution promoter in HPMC films probably by getting into HPMC tight structures.

These results show that capsule A, which was prepared by cold gelling using Carrageenan, had fast and pH-independent dissolution with good mechanical strength.

CONCLUSIONS

This study indicates that HPMC films show excellent physical properties when prepared by the 'cold gelling method' using a gelling agent. These capsules are less brittle and their rate of dissolution is faster than Capsule B manufactured by thermal gelling.

It is suggested that Capsule A would be preferred for pharmaceutical products because of its mechanical and dissolution properties.

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