Formulation and Evaluation Non-Gelatinous Hard Capsule Shells Prepared From Films of Starches Obtained From Different Plant Sources

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Abstract

Polysaccharide films were developed using red lentil, water chestnut, and tamarind seed powder starches as the basic raw materials. The same starches were used to develop hard capsules to be used in the pharmaceutical industry as substitutes for gelatin or animal-based products. High amylose starches exhibited hard capsule forming capabilities and properties compared to low amylase starches. Physical (viscosity) characterization of the vegetable starches showed that the high amylose starches formed better capsules compared to the low amylose and high amylopectin starches. Polysaccharide films and hard capsules for pharmaceutical applications could be developed from plant starches with similar physical and mechanical properties to synthetic and gelatin products.

Keywords: Starch, Gelatin, Animal Base Film, Hard Capsule Shell, Amylose

Introduction:

CAPSULE

Capsule shells and contents may contain excipients such as diluents, solvents, surfactants, opaque fillers, antimicrobial agents, sweeteners, colourants approved by the competent national or regional authority, flavouring agents, disintegrants, lubricants, and substances that may alter the behaviour of the active ingredient(s) in the gastrointestinal tract. The ingredients must not cause shell deterioration. If excipients are used, it must be ensured that they do not affect the stability, dissolution rate, bioavailability, safety or efficacy of the active ingredient(s); there must be no incompatibility between the components of the dosage form.[1]

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Size	Volume in ml	Size in mm
000	1.37	26.3
00	0.95	23.7
0	0.68	21.8
1	0.50	19.2
2	0.37	18.3
3	0.30	15.3
4	0.21	14.7
5	0.15	11.9

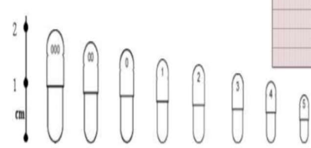

Figure 1 Different Sizes of Capsules Shell

- **The Different Categories of Capsule Shell Include:** [2]
  - Hard capsules
  - Soft Capsules
  - Modified-Release Capsules

- **Steps Involved in Manufacturing of Hard Gelatine Capsule Shell** [3, 4]

- Dipping
- Spinning
- Drying
- Stripping
- Trimming and Joining
- Polishing

- **Evaluation parameter for Capsule Shell [5]**

- Weight Variation Test
- Disintegration Test
- Shape, size & Color
- Thickness of capsule shell
- Permeation Test
- Uniformity of content
- Melting Point
- Stability Tests.
- Moisture

- **Selection of the capsule size:**

The volume of material that was to be filled into the capsule determined the size of the capsule that was needed. Generally, capsules of sizes "0" to "4" were readily available in the market and the relationship between the capsule size and related body volume. For pharmaceutical products it is unusual to use a size larger than "0" because of the difficulty in swallowing larger size capsules, whilst size "5" is rarely used due to difficulties in the automatic filling process. [6]

- **Evaluation Parameters for Hard Capsules Shell.[7]**

- **Visual Inspection (Shape, size & Colour Texture)**

Check Shape, Size, Colour & Texture of the final Film prepare by visual inspection.[8]

- **Thickness of capsule shell**
- **Melting Point:**
- **Starch content**
- **Disintegration Test**
- **Accelerated Stability study:**
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- **<u>Result and Discussion:</u>**

- **Preparation of Capsule Shell:**

The Size '0' of capsule shell is prepare by dipping method by using following formulas

Table 1. Detail of Capsule Shell Formulation from Film Solution

Ingredient mg	F1	F2	F3	F4	F5	F6	F7	F8	**F9**	**F10**
RL	100	150	200	---	---	---	---	---	**---**	**---**
WCS	---	---	---	100	150	200	---	---	**---**	**---**
TSP	---	---	---	---	---	---	100	150	**200**	**200**
HEC	---	---	---	---	---	---	---	---	**---**	**200**
Titanium dioxide	1	1.50	2	1	1.50	2	1	1.50	**2**	**4**
Tween 80	1	1	1	1	1	1	1	1	**1**	**1**
Polyethylene Glycol (PEG400)	5	7.50	10	5	7.50	10	5	7.50	**10**	**20**
Benzalkonium Chloride	0.10	0.15	0.20	0.10	0.15	0.20	0.10	0.15	**0.20**	**0.40**

Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	**q.s**	**q.s**

Discussion:

The Capsule shell of size '0' of F9 and F10 (table 1) was prepare by using the Diping method

- **Evaluation of capsule Shell**

Take 10 random sample of capsule of both formulation batches for further evaluation

➢ **Visual Inspection (Weight, Shape, size, Colour & Texture)**

Table2. Results of Visual Inspection of Polysaccharide Capsule Shell

Capsule Shell	Weight		Colour	
	F9 (gm)	F10 (gm)	F9	F10
1	0.411	0.439	Transparent yellowish brown	Transparent yellowish brown
2	0.411	0.439	Transparent yellowish brown	Transparent yellowish brown
3	0.401	0.429	Transparent yellowish brown	Transparent yellowish brown
4	0.400	0.428	Transparent yellowish brown	Transparent yellowish brown
5	0.400	0.428	Transparent yellowish brown	Transparent yellowish brown
6	0.402	0.430	Transparent yellowish brown	Transparent yellowish brown
7	0.410	0.438	Transparent yellowish brown	Transparent yellowish brown
8	0.400	0.428	Transparent yellowish brown	Transparent yellowish brown
9	0.400	0.428	Transparent yellowish brown	Transparent yellowish brown
10	0.400	0.428	Transparent yellowish brown	Transparent yellowish brown
Average Weight	0.403	0.432	-----	-----

Discussion:

Results of Visual Inspection of 10 sample of both batch of Polysaccharide Capsule Shell was done and the results shows in table 2

➢ **Thickness of capsule shell**

Table 3. Thickness of capsule shell

Capsule Shell	Thickness (mm) F9	Thickness (mm) F10
1	1.1	1.3
2	0.7	1.1
3	1.0	1.2
4	0.9	1.0
5	0.7	1.1
6	1.3	0.9
7	1.1	0.9
8	0.9	0.8
9	1.1	1.0
10	1.1	1.3
Average Thickness	0.99=1.0	1.06=1.1

Discussion: The thickness of 10 sample of both batch of Polysaccharide Capsule Shell was done and the results shows in table 3

➢ **Melting Point:**

Table 4. Melting Point of Capsules Shell

Capsule Shell	Melting Point (^{0}c) F9	Melting Point (^{0}c) F10
1	41	51
2	40	50
3	45	52
4	42	49
5	43	53
6	47	47
7	44	54
8	44	51
9	42	52
10	46	46

Discussion:
The melting point of 10 sample of both batch of Polysaccharide Capsule Shell was done and the results shows in table 4 the average weight of are 43.5 for F9 & 50.5 for F10

➢ **Disintegration test of capsule shell**

Table 5. Times to Disintegration

Formulation	Disintegration Time (Min)
F9	47$\pm$1.5
F10	48$\pm$1.5

n=6 (Mean $\pm$ SD)

Discussion:
The disintegration time study was performed by regular method of 6 capsule Shell of each batch of formulation and mean was noted in the table 5

7.5.5 Accelerated Stability study

Table 6. Comparison study Before and After Stability Study Test

Formulation	Disintegration Time (Min)		Melting Point(^{0}c)		Color		Texture	
	Before	After	Before	After	Before	After	Before	After
F9	47$\pm$1.5	49$\pm$1.5	43$\pm$0.5	41$\pm$0.5	Transparent yellowish brown	Transparent yellowish brown	Smooth	Smooth

F10	48±1.5	49±1.5	50±0.5	49±0.5	Transparent yellowish brown	Transparent yellowish brown	Smooth	Smooth

n=6 (Mean ± SD) n=3 (Mean ± SD)

Discussion:

The capsules are store in the said condition for said time and the stability was check by checking the Disintegration time, melting point, colour, texture, size was check there is no significance change occur in both formulation but the Very Good results occur in F10 due to addition of HEC in the formulation as compare to the Formulation F9

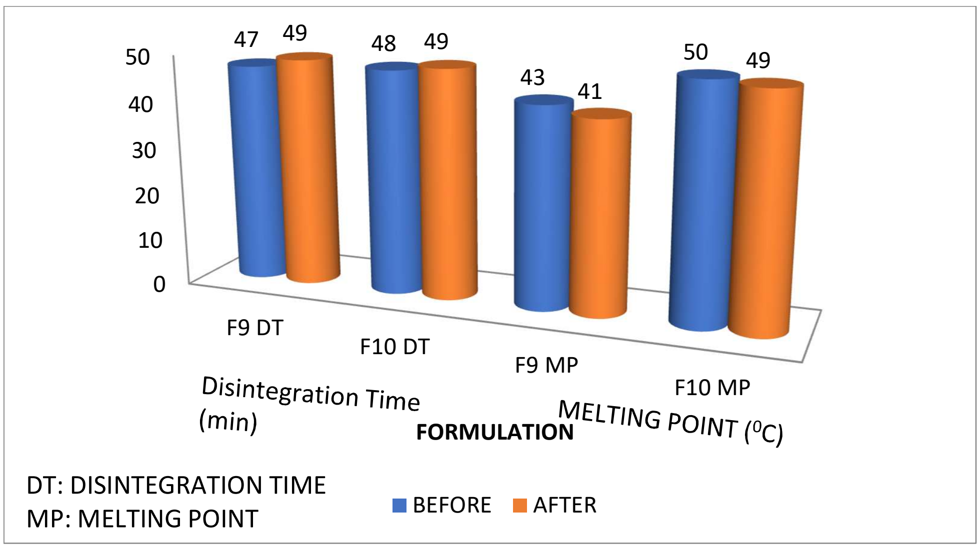

Figure 2 Comparisons of Disintegration and Melting Point Before and After Stability Study

Conclusion:

The developed capsules had good molding properties and formed high quality hard capsules with the conventional dip coating technique. The developed starch capsules were clear, had a smooth surface, and were flexible. Starches with high amylose content produced better films and capsules than those with low amylose content and high amylopectin content. With high amylose starches (tamarind seed), it was possible to develop hard capsules without gelling agents. The developed starch capsules did not dissolve completely and had some fragments in water or HCl solution. Starch-based hard capsules have the potential to be used in the pharmaceutical industry as a substitute for gelatin or animal protein-based products.

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