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Advantages of Film Coating with a Novel Modified Starch vs. HPMC on the Disintegration Time and Dissolution Profile of Tablets Containing Polyphenolic Actives

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INTRODUCTION

Antioxidant supplements are gaining popularity due to their various health benefits such as anticancer effects, reducing cardiovascular and stroke risk, lowering LDL cholesterol as well as increasing metabolism and weight reduction. Many of these antioxidants are available as conventional film-coated tablets. Cellulosic polymers such as HPMC are widely used in film coating of these tablets, but suffer from drawbacks such as:

- Strong unwanted taste/odor and yellowish color to the solution,
- Difficulty in solubilization due to lumping and foam formation,
- "Bearding" on spray nozzles causing frequent production stops for cleaning,
- High coating cost per tablet due to longer coating times.

HPMC has a strong tendency to interact with antioxidant polyphenolic actives, resulting in formation of a sticky gel, which significantly increases tablet disintegration time (DT). A novel pregelatinized, hydroxypropyl starch polymer (LYCOAT®), ensures minimal interaction with polyphenolic actives and does not prolong DT of coated tablets. This study presents data supporting the superior compatibility of LYCOAT® in aqueous film coating of tablets with polyphenolic actives, resulting in minimal changes in DT of LYCOAT® coated tablets and significantly faster polyphenol dissolution profiles compared to HPMC.

MATERIALS & METHODS

Preparation of Dispersions: HPMC and LYCOAT® based ready to use film-coating formulations were dispersed in water at room temperature using a paddle stirrer. Viscosity measurements were performed using a Physica MCR 301 Anton Paar rheometer.

Tableting and Coating: Tablets (300mg, 10mm concave, 110N, 0.01% friability) containing 40% green tea extract were prepared on a Fette exacta 21 tablet press using MCC and pregelatinized starch. Tablets were film coated (3.2% weight gain) in a RWKA coating equipment with Binks 460 spray-gun. Tablet hardness, friability, and in-vitro DT were measured using appropriate Erweka equipment and USP/EP methods.

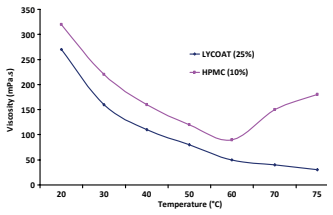
Polymer-Polyphenol Interaction studies: SOTAX equipment with paddles was used to study tablet dissolution profile in 900 ml water at 37°C. The level of dissolved polyphenols was quantified using the Folin-Ciocalteu colorimetric assay at 780nm. Physical interaction between polyphenols and polymers was studied by adding 1.5ml green tea extract (10%) to 10mL aqueous polymeric solutions (10%) and visually observing the precipitate before and after mixing. Free polyphenol levels in the supernatant were quantified colorimetrically after adding 1.5ml of 5% green tea extract to 1% and 2.5% solutions of HPMC or LYCOAT®.

RESULTS & DISCUSSION

Ease of Dispersion & Low Viscosity

Figure 1. Ease of Dispersing LYCOAT® vs. HPMC.

Figure 2. Viscosity of LYCOAT® vs. HPMC.



Despite higher solids level, the low viscosity and granular nature of LYCOAT® enables fast dispersion in water within 10 min at room temp using only a magnetic stirrer, without any lumps or foam formation (**Fig. 1**). Previous stability studies (6 months) on coated placebo tablets showed DT of 102 sec (68% increase) of HPMC coated tablets vs. only 50 sec (29% increase) with LYCOAT® compared to the uncoated cores.
The higher viscosity of HPMC even at low solids level and tendency to swell may result in delay of tablet DT upon storage (**Fig. 2**).

Green-Tea Tablet Formulation

Table 1. Core Tablet Formulation & Parameters.

Microcrystalline Cellulose	48.5%
Green Tea Extract (80% polyphenols)	40.0%
Partially Pregel Starch	9.5%
Fumed Silica	1.0%
Magnesium Stearate	1.0%
Tablet Shape	Concave
Tablet Diameter	10 mm
Tablet Thickness	4.61 ± 0.08 mm
Compression Force	9.3kN
Tablet weight (uncoated)	300 ± 10 mg
Tablet Hardness (uncoated)	108 ± 20 N
Friability	0.01 %
Disintegration Time	27 min

Core tablets containing 95.17mg theoretical polyphenol content were prepared on a FETTE® Exacta 21 single punch tabletting machine and parameters evaluated using standardized tests.

LYCOAT® Coating Does NOT Increase Green Tea Tablet Disintegration Time

Table 2. Coating Parameters For Ready to Use LYCOAT® & HPMC Coatings.

Parameters	LYCOAT®	HPMC
Solids content	20%	20%
Inlet Air temp	50°C	52°C
Tablet bed temp	37°C	42°C
Atomization pressure	2 bars	2 bars
Mean % weight gain	3.2 %	3.2 %

Ready to use aqueous film coating products containing LYCOAT® or HPMC were used in a RWKA conventional coating equipment with Binks 460 spray-gun.

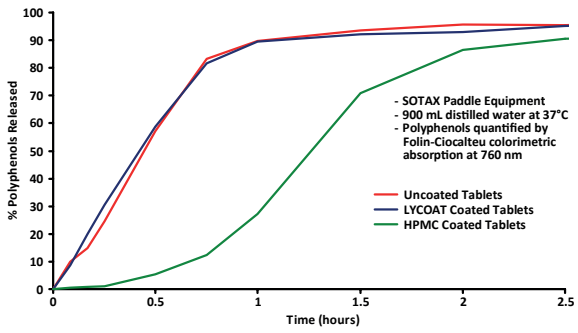
Table 3: Evaluation of Film Coated Tablets

	Weight (mg)	Hardness (N)	Disintegration Time (DT) minutes
Uncoated Tablets	298	108	27
LYCOAT® coated tablets	310	117	29
HPMC coated tablets	311	137	68

Unlike HPMC film-coating, LYCOAT® does NOT increase DT of green-tea tablets.

LYCOAT® Coating Does Not Delay Polyphenol Release from Tablets

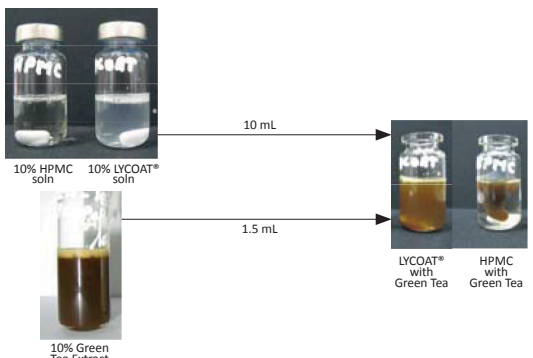
Figure 3. Comparative Dissolution Profiles of LYCOAT® vs. HPMC coated Green Tea Tablets.



LYCOAT® coating allows 60% polyphenol release in 30 min vs. only 5% with HPMC coating.

HPMC Forms a Sticky Gel with Polyphenols

Figure 4. Interaction of HPMC & LYCOAT® Solutions with Green Tea Extract.



HPMC forms a sticky gel on addition of Green Tea Extract.
LYCOAT® exhibits instant mixing and complete solubilization.

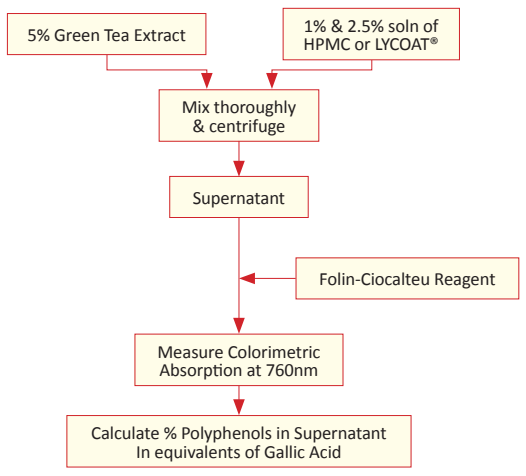
HPMC is Incompatible with Polyphenols

Figure 5. Qualitative Demonstration of Gel Formation with HPMC & Green Tea Extract.

10 mL HPMC soln (10%) + 1.5 mL Green Tea Extract (10%)

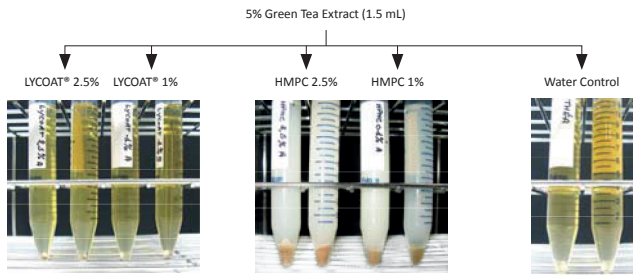
HPMC significantly increases tablet hardness after film coating (Table 3).
HPMC & Green Tea form a Sticky gel-like precipitate despite thorough mixing.
This gel layer significantly increases tablet DT and release of polyphenol actives.

Polyphenol Quantitative Analysis Method



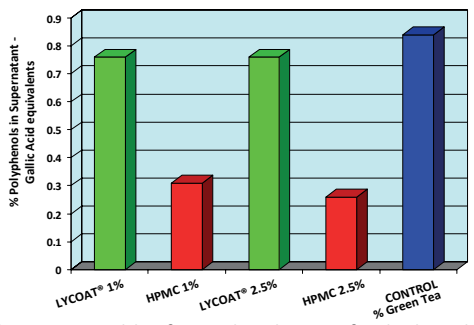
HPMC – Polyphenol Interaction

Figure 6. Quantitative Precipitate Formation with HPMC and Green Tea Extract.



Green Tea extract generates visible precipitate with 2.5% or 1% HPMC compared to LYCOAT®.

HPMC Quantitatively Reduces Solubilization of Polyphenolic Actives



LYCOAT® coating enables faster dissolution of polyphenols vs. HPMC:
- Complete miscibility of LYCOAT® with green tea extract without precipitation or gelling,
- Minimal binding of polyphenols by LYCOAT®.

CONCLUSION

By definition, an excipient is an inert and inactive substance used as a carrier for the active ingredients of a medication. This study shows that HPMC coating excipient interacts with polyphenolic actives. The gel-like precipitate with HPMC acts as a barrier, resulting in prolongation of the tablet disintegration and active dissolution time. A novel hydroxypropyl starch coating excipient (LYCOAT®) exhibits inertness with a broad range of actives with polyphenolic moieties (e.g. phytosterols) and does not increase the DT of tablets or prolong dissolution of actives. The inertness of LYCOAT® along with additional benefits related to the ease of use, high solids content coating solution and quicker coating process, makes it an ideal excipient for tablet coating (Ref. 1).

ACKNOWLEDGEMENTS
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REFERENCE

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