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White Paper

Enhancement of Tablet Coating using an Innovative Functional Excipient

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During formulation of solid dosage forms, film coating is used to improve the appearance and stability of tablets, make them easier to swallow, mask the taste, modify or sustain release, protect the drug from the harsh gastric environment, protect from moisture and/or oxidation and, as a result, to improve the stability and overall therapeutic effect of the final drug product. Depending on the individual needs, a polymer with appropriate properties is chosen during formulation development to serve as film-coating matrix. In addition to the polymer which is solubilized in a solvent, the coating formulation typically includes additives such as plasticizers, anti-tacking agents and pigments. This solution is sprayed onto a rotating or fluidized tablet bed and subsequent drying leads to removal of the solvent, resulting in a deposition of coating material around each tablet core.

Pre-mixed solutions are commonly used for tablet film coating. These solutions offer ease-of-use as no additional formulation is required and can reduce the time needed for designing compounds and sourcing ingredients. While a pre-mixed solution can offer greater convenience, they increase dependence on an individual supplier and reduce flexibility in the formulation which can prolong the response time to regulatory requests if an ingredient needs to be changed. In addition, there will be limited ability to adapt the formulation if incompatibilities arise. Instead, many formulators prefer to design the coating composition themselves to tailor it to their specific needs.

This white paper describes key considerations and provides guidance on the preparation of a coating formulation. Parteck® COAT, a functional excipient designed for immediate release coating/protective coating for individual mixtures is highlighted along with a process analytical technology (PAT) tool that can be implemented to enhance formulation development. Screening of a range of plasticizers for compatibility with the Parteck® COAT excipient is also described; plasticizers are an important component when optimizing tablet coating formulations.

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Key Considerations for Tablet Coating

Several factors must be considered for successful tablet film coating. For the polymer, the required functionality must be determined; it must offer robust film forming ability and have the appropriate viscosity in solution as this affects the loading rate of the solution. In case of protective coatings the polymer must also provide enough protection against oxidation or moisture. Plasticizers are frequently needed to support film forming ability by reducing the glass transition temperature. For this, the right concentration and structure of the plasticizer are critical. The ratio of the polymer and plasticizer is also important to ensure film flexibility and avoid cracking. Anti-tacking agents ensure a robust process by preventing the sticking of tablets during the coating process itself which can damage the coating surface. A final consideration is the finishing which is used to enhance the look of the tablets though colorants or pigments.

Parteck® COAT Excipient for Immediate Release and Protective Coating

Parteck® COAT excipient is a particle engineered polyvinyl alcohol (PVA) with a unique structure specifically designed for immediate release film coating applications. Due to the optimized particle size, it helps to reduce dissolving times in coating solution preparation, thus increasing process efficiency. It is a polyvinyl alcohol 5-88 milled to a medium particle size that facilitates rapid development of coating solutions (the “5” refers to the viscosity in solution – approximately 5 mPas of a 4% solution in water at 20 °C – which is a relative indication for the molecular mass while the “88” refers to the approximate degree of hydrolysis of polyvinyl acetate groups). This multi-compendial, pharmaceutical-grade PVA is compliant with and surpasses the requirements of all major pharmacopoeias, including United States Pharmacopoeia (USP), European Pharmacopoeia (Ph. Eur.), Chinese Pharmacopoeia (ChP) and Japanese Pharmaceutical Excipients (JPE). In addition, it is an Emprove® qualified product and has a very high purity, with low sulfated ash.

Figure 1 summarizes the product characteristics of Parteck® COAT excipient, provides SEM images of the particles and the particle size distribution of three exemplary batches showing a high level of batch-to-batch consistency. In developing this excipient, it was essential to control the particle size as this parameter strongly affects the angle of repose, the flowability of the powder, and how quickly the polymer can go into solution.

Parameters	Ranges
Angle of repose [°]	30–35
Bulk density [g/mL]	0.6–0.7
Tapped density [g/mL]	0.8–0.9
Particle size $d_v(0.10)$ [m]	30–120
Particle size $d_v(0.50)$ [m]	180–260
Particle size $d_v(0.90)$ [m]	300–700
pH value of 4% solution	5.0–6.5
Hydrolysis degree [%]	85–89
Mass Average Molar Mass Mw [g/mol]	40,000

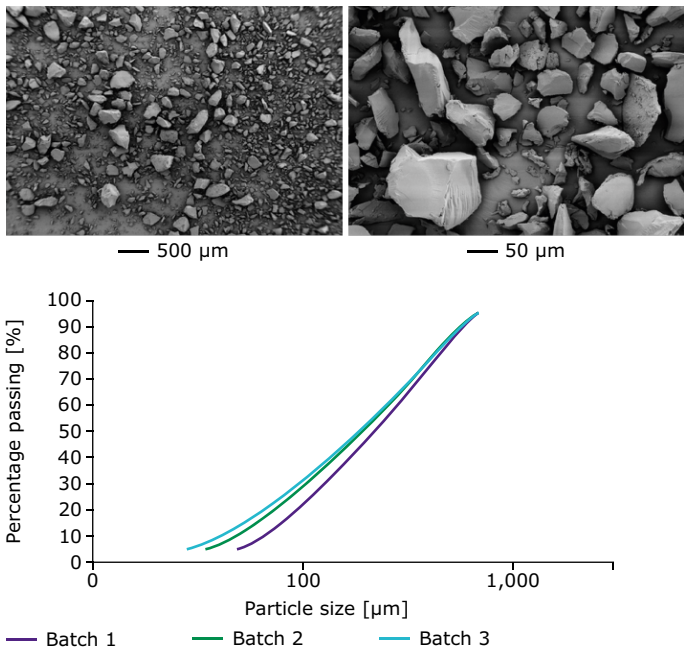

Figure 1.

Parteck® COAT excipient characteristics, SEM images and particle size distribution.

Comparison of Commonly Used Polymers in Film Coating Application

The following studies were performed on the most critical properties of polymer and final film coating to assess suitability of Parteck® COAT excipient in comparison to other commonly used polymers.

- To assess process efficiency, polymer dissolution time, effect of polymer concentration on coating solution viscosity and thermal properties were evaluated.
- To assess final formulation performance and stability, tablet dissolution behavior, moisture and oxygen permeability were evaluated.

Table 1 summarizes the dissolution time of Parteck® COAT excipient at different temperatures compared to a standard PVA 5-88 and hydroxypropyl methylcellulose (HPMC)-based polymers. The water-soluble and rapidly dissolving Parteck® COAT particles enable rapid preparation of coating liquids even at room temperatures. Compared to the standard PVA 5-88 and HPMC-based polymers, Parteck® COAT excipient can reduce the preparation time from 4 h to 1 h.

		Parteck® COAT	Standard PVA 5-88	HPMC based polymer 1	HPMC based polymer 2
Time to dissolve [min]	20 °C	60	>240	>240	>240
	40 °C	35	>240	>240	>240
	60 °C	20	30	>240	>240

Table 1.

Comparison of dissolution time for Parteck® COAT and other PVA or HPMC-based excipients.

Figure 2 shows the effect of the polymer concentration on viscosity which dictates the ability to spray the solution through very fine nozzles and evenly distribute the coating. Even at a high concentration of Parteck® COAT excipient, the viscosity remains quite low, whereas viscosity of the cellulose-based polymers is drastically increased with higher concentration. The ability to maintain low viscosity leads to faster processes and very high efficiency during the spraying process, which provides flexibility to formulators.

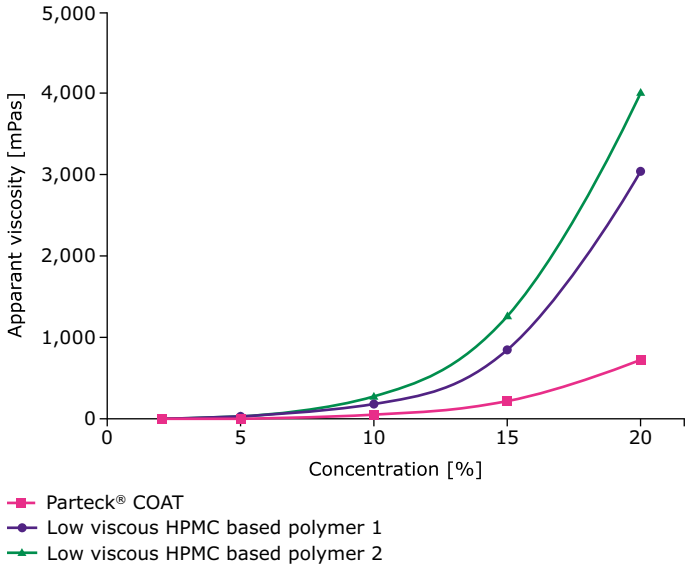

Figure 2.

Comparison of the effect of polymer concentration on solution viscosity.

Characterization of the thermal behavior of Parteck® COAT excipient using differential scanning calorimetry (DSC) is shown in Figure 3. The glass transition temperature (T_g) is an important indicator for the processability and subsequent film formation; here, in its pure form, the T_g of Parteck® COAT excipient is approximately 60 to 70 °C which is a very good processing range for the coating. Depending on the process characteristics, plasticizer can be added to further reduce the T_g and fine-tune the process.

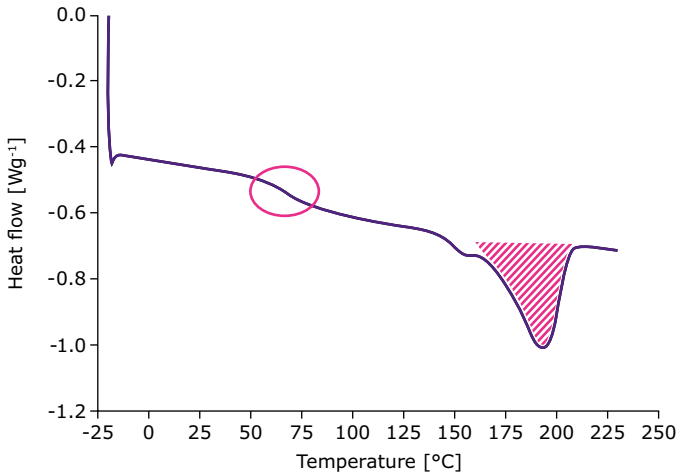

Figure 3.

Characterization of the thermal behavior of Parteck® COAT excipient.

Another important characteristic of Parteck® COAT excipient is the impact on the dissolution behavior of the tablet. To evaluate a potential influence of the coating on the release kinetics, a model compound (ascorbic acid, water soluble) was integrated into the tablet core formulation. The tablet core and coating formulations are shown in Table 2 and the release kinetics in Figures 4 and 5.

The uncoated tablet core dissolved within six to eight minutes. With the Parteck® COAT excipient layer, only a minor effect on release kinetics was observed; similarity in kinetics is desirable as the coating should not affect release rate. In contrast, cellulose-based polymers delayed release to a greater extent.

Tablet core formulation:

Ingredient	Amount [%]
Ascorbic acid	10
Parteck® M 200 (DC mannitol)	87
Silicium dioxide	1
Sodium stearyl fumarate	2

Coating formulation:

Ingredient	Amount [%]
Polymer	70
Triethyl citrate	20
Talcum	10

Table 2.

Tablet core and coating formulations.

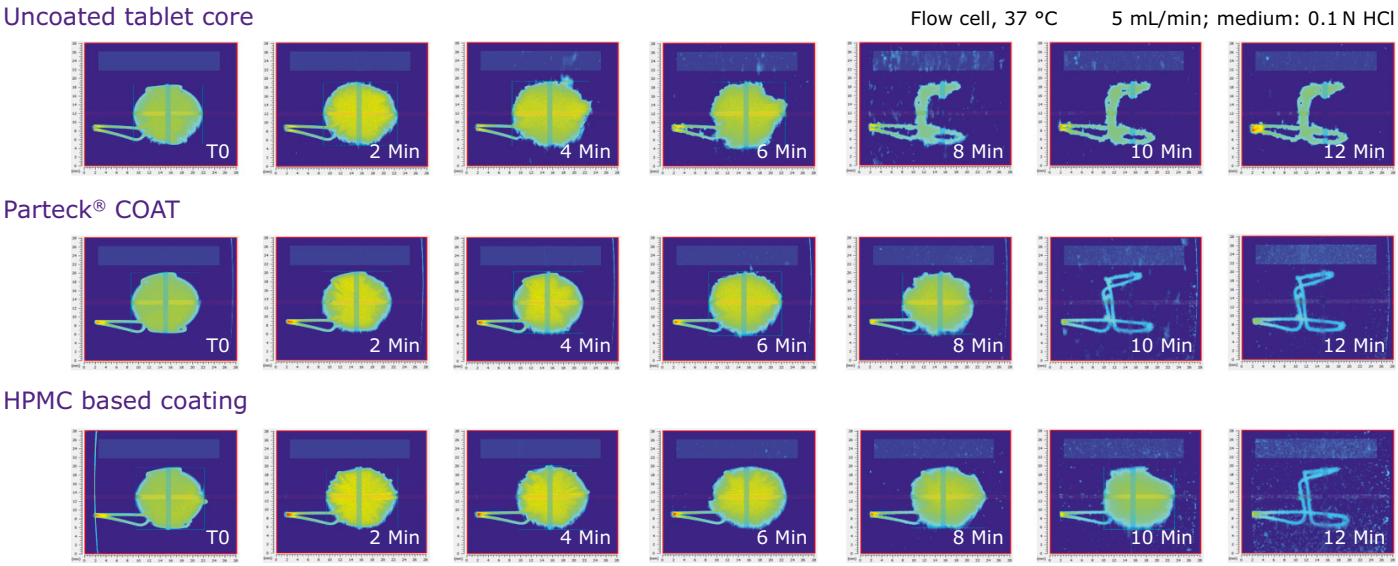

Figure 4.

Effect of PVA-based coatings on release kinetics compared to cellulose-based polymers. Visualization of the tablet disintegration in a flow cell model using an IDAS SDi2 system from Pion Inc. (UK).

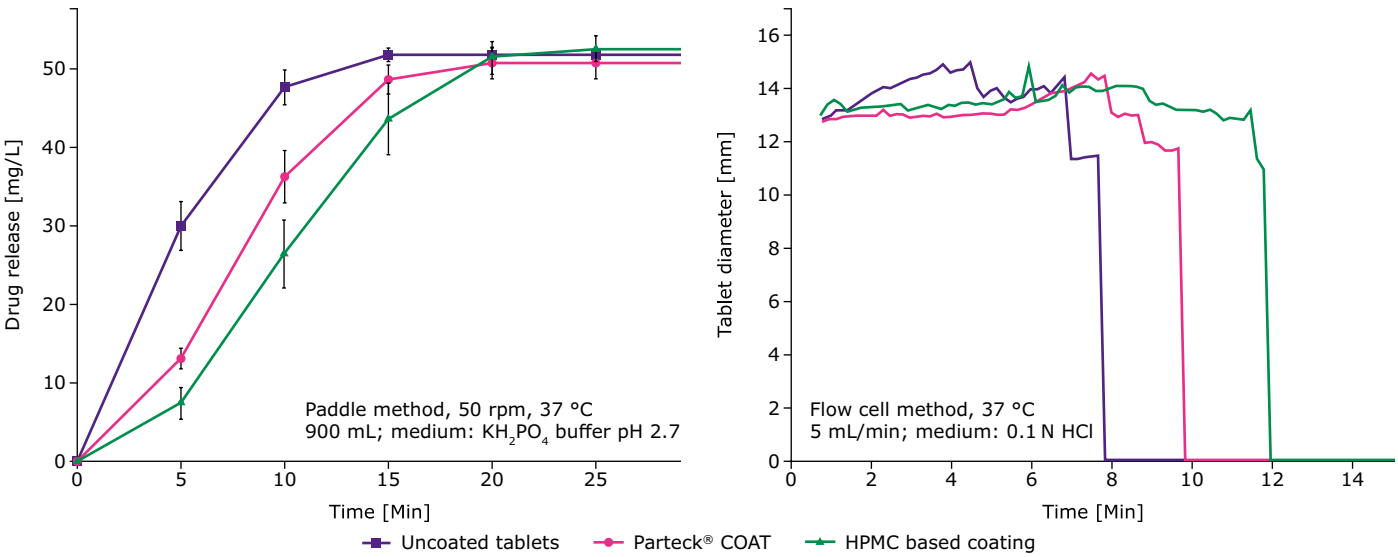

Figure 5.

Release profiles of ascorbic acid tablets coated using Parteck® COAT, a cellulose-based polymer or without a coating.

Coatings with Parteck® COAT provide a stable moisture barrier even under accelerated storage conditions. This is especially relevant for active pharmaceutical ingredients (APIs) susceptible to instabilities or degradation induced by moisture. Figure 6 shows how Parteck® COAT excipient can provide protection of moisture-sensitive or oxygen-sensitive drug substances. Films were created based on different polymers and HPMC grades and the water permeation rate determined. The Parteck® COAT excipient created a highly effective barrier that can protect a drug from outside water and humidity; water permeation was much lower compared to the other polymers. Similar results were observed for oxygen which confirms this excipient provides very reliable protection for sensitive drug substances.

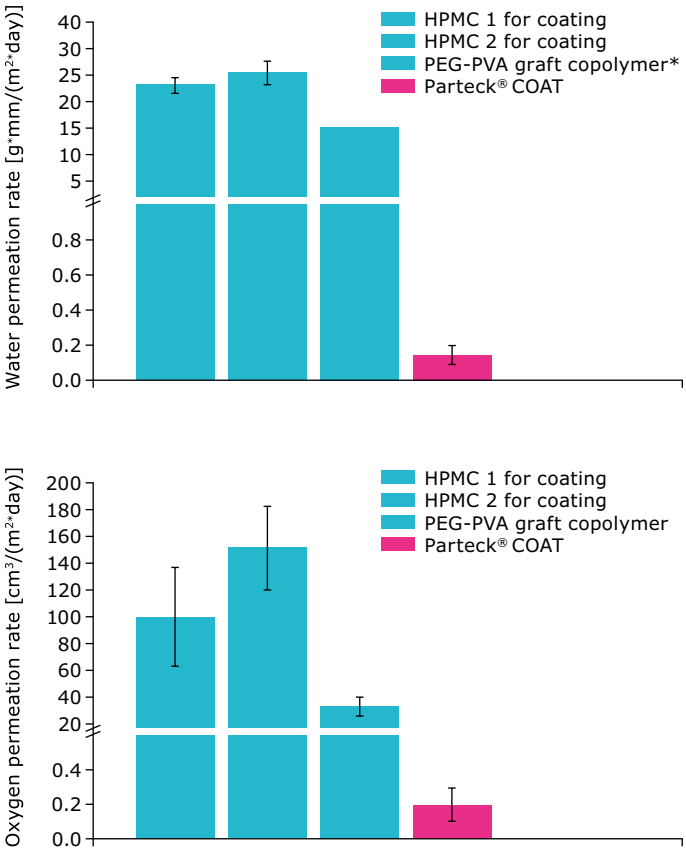

Figure 6.

Assessment of polymer films for their water and oxygen permeability: Polymer films prepared via film casting (evaluated film thickness: ~ 200 µm); water transmission rate measured in relation to DIN 53380-1, gravimetric method; oxygen transmission rate measured using an Oxtran 2/21 oxygen permeability instrument; samples masked to 20 cm^2.

**PEG-PVA graft copolymer: Single data point only due to low physical stability of the films.*

Application of Process Analytical Technology (PAT) for Film Coating

In the context of automated coating processes and efforts to establish continuous processes, application of process analytical technology (PAT) becomes increasingly important to pharmaceutical industry.

Optical coherence tomography (OCT) is a promising technology for use in formulation development to monitor how the film coating evolves during a coating process. Figure 7 shows a cross-sectional image of a tablet in which the tablet core and coating layer are visible. OCT enables real-time measurement of coating thickness, surface roughness and coating structure to assess reliability and reproducibility of the process, which is a key consideration for further continuous coating operations.

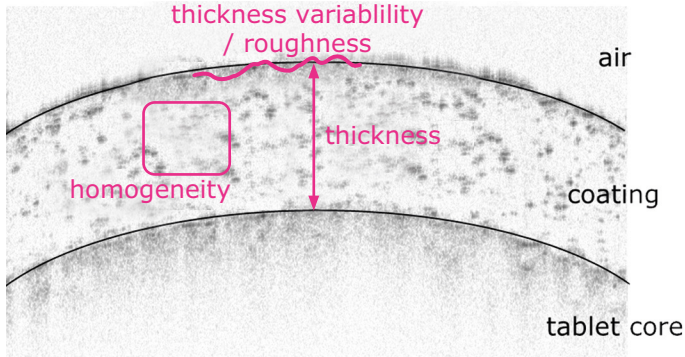

Figure 7.

OCT enables visualization of the coating process and quality.

Image courtesy of Research Center Pharmaceutical Engineering and Phyllon GmbH

Plasticizer Screening

Plasticizers are used to increase the distance between individual polymer chains and influence glass transition temperature and film formation. A range of plasticizers were evaluated to combine with Parteck® COAT excipient (Table 3). The sample preparation was as follows:

- Prepare stock solutions of PVA and plasticizer
- Add 50 µL of the coating solution to the DSC pan
- Dry 10 h
- Measure the weight of the dried material
- Close the pan
- Begin the DSC measurements

Polymer	Plasticizer	Glass transition temperature T_g [°C]	Enthalpy T_g [J/g]	Melting point [°C]	Melting enthalpy [J/g]
Parteck® COAT	No plasticizer	47.63	0.672	169.06	33.66
	Triethyl citrate	16.47	0.607	157.79	33.04
	Triacetin	13.83	0.628	156.24	56.28
	PEG 300	40.04	0.120	165.84	26.97
	PEG 1000	21.49	1.159	204.35	86.17
	PEG 3000	n.a.[a]	n.a.[a]	172.96	20.77
	PEG 6000	n.a.[b]	n.a.[b]	175.24	17.15
	Glycerol	24.96	0.216	n.a.	n.a.
	Parteck® SI 150 (sorbitol)	45.34	0.232	152.81	14.47
	Parteck® M 200 (mannitol)	27.41	0.829	159.23	9.33

T_g overlaps with melting point: [a] PEG 3000: 50.96 °C; 28.53 J/g [b] PEG 6000: 50.74 °C; 27.77 J/g

Table 3.

Plasticizers evaluated for use with Parteck® COAT excipient.

As shown in Table 3, use of triethyl citrate and triacetin as plasticizers resulted in a strong decrease in the glass transition temperature into ranges that are much easier to process with the coating itself. Polyethylene glycol (PEG) 300 did not have a strong influence while PEG 1000 resulted in a very strong decrease which indicates a robust plasticizing effect. For the PEG grades with higher molecular weight there were good effects observed during film forming tests, but in the DSC screening, the signals could not be differentiated from the melting peaks which prevented determination of glass transition temperatures. Glycerol also worked as a good plasticizer as well as other investigated polyols.

The effect of the plasticizer on the surface finishing of the tablet was then examined using laser scanning microscopy using a defined raster pattern to ensure a representative dataset. The box plot diagrams in Figure 8 shows the surface roughness versus the different type of plasticizers and concentrations. Roughness was strongly decreased for triethyl citrate but not for glycerol, despite what was assumed based on T_g reduction results shown in table 3. Triacetin had a very strong influence, as did sorbitol (Parteck® SI 150). Figure 9 shows the height maps for the tablet surfaces and highlights how plasticizer concentration enhanced surface smoothness.

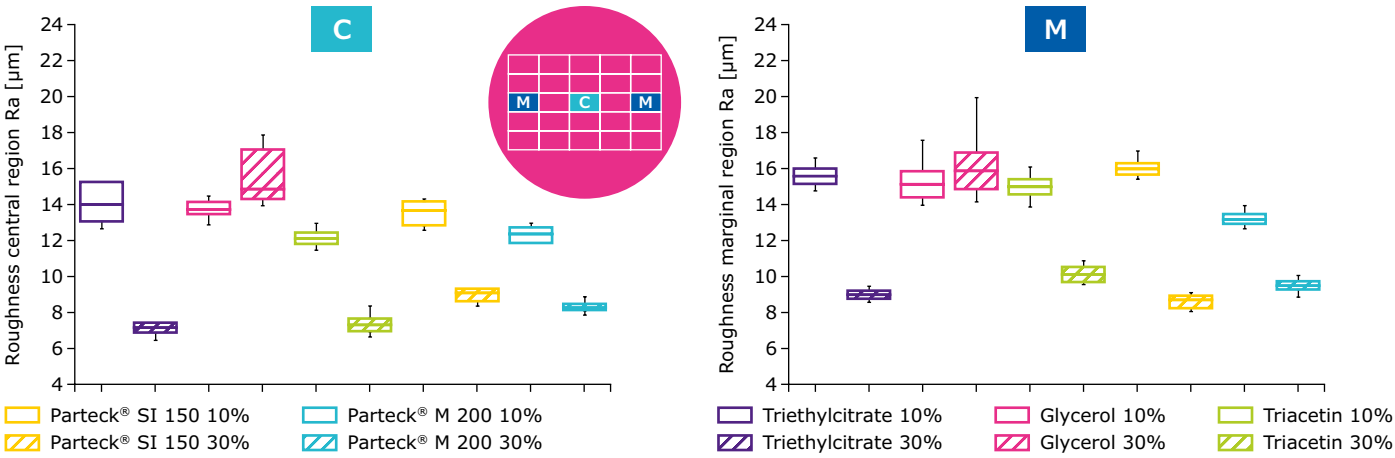

Figure 8.

Influence of different plasticizers on the roughness of the tablet surface measured in the center (C) and margin region (M) of the tablet.

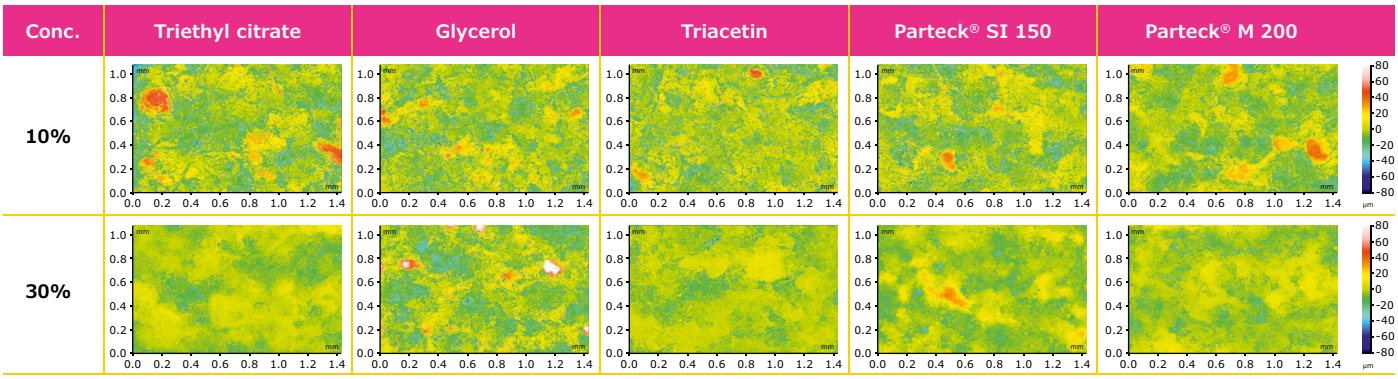

Figure 9.

Effect of different types and concentrations of plasticizers on tablet surface roughness.

Figures 10 and 11 show the same assessment of surface roughness but this time with PEG grades with different molecular weights at the same concentration. PEG 1000 offered the lowest surface roughness. Surface roughness slightly increases depending on the molecular weight of the PEG grade. These results indicated that use of PEGs of different molecular weights offers the possibility to fine-tune the surface as needed in applications that require dedicated surface structure.

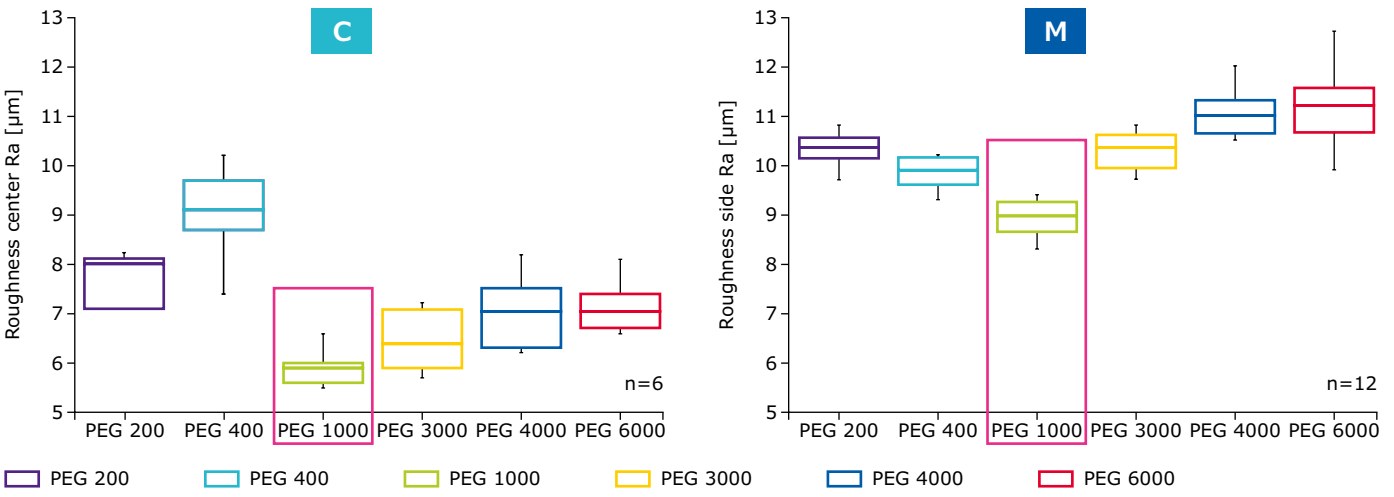

Figure 10.

Comparison of the effect of different PEG plasticizers on tablet surface roughness.

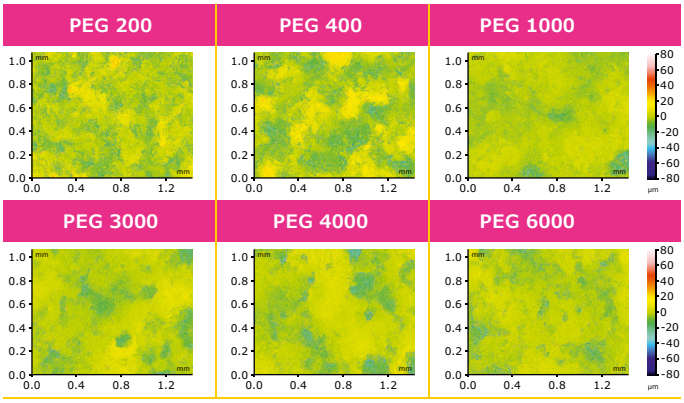

Figure 11.

Effect of different types and concentrations of PEG plasticizers on tablet surface roughness.

Suitability for Titanium dioxide (TiO_2) Free Film Coatings

The European Food Safety Authority (EFSA) evaluated titanium dioxide as a food additive in 2020 as a result of safety concerns; the organization's 2021 statement that it is no longer safe to be used as a food additive due to potential carcinogenic and genotoxic effects has led formulators in the pharmaceutical sector to identify alternative pigments which yield white tablets.[1] Given this situation, suitability of Parteck® COAT-based film coatings with calcium carbonate was investigated. Results showed an excellent surface finishing using calcium carbonate, similar to that provided by titanium dioxide. This combination of Parteck® COAT excipient and calcium carbonate represents a viable alternative to titanium dioxide, offering formulators an easy solution when anticipating potential future regulatory developments.

Conclusion

Parteck® COAT excipient is an innovative solution for tablet coating that offers distinct advantages over pre-mixed solutions and conventional PVA excipients. Key benefits include:

- Rapid preparation time – the particles are optimized to enable rapid dissolution, even at room temperature.
- Formulation flexibility – as part of the formulation toolbox, this excipient offers flexibility for process development.
- Excellent surface finishing – enables the appearance of the formulation to be enhanced.
- Stable moisture and oxygen barrier – moisture-sensitive APIs can be effectively protected.
- Reliable batch-to-batch consistency – ensures reproducible quality and performance.
- High concentration of the spraying liquid with low viscosity at high concentration – enables a reduction in process time and enhanced efficacy.
- Multi-compendial – compliant with Ph Eur, ChP, JPE and USP.
- Comprehensive ready-to-use Emprove® documentation – facilitates qualification, risk assessment, and process optimization.

In addition to Parteck® COAT excipient as the matrix polymer, a range of plasticizers, anti-tacking agents and pigments and application support are available to assist formulators with coating compound design and feasibility studies by Merck.

References

1. EFSA Panel on Food Additives and Flavourings, Younes M, Aquilina G, Castle L, Engel K-H, Fowler P, et al. Safety assessment of titanium dioxide (E171) as a food additive. EFSA Journal. 2021;19(5):6585.

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