Evaluation of Stability and Physical Parameters of Sitagliptin IR Tablets Coated with Different Titanium Dioxide Free Coating Systems

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Introduction

To address concerns around the use of titanium dioxide (TiO2) in certain markets and the potential impact on pharmaceutical products, Opadry® TF, TiO2 Free Formulated Film Coatings have been developed.[1] This range of coating formulations, though similar in functionality, may contain additional ingredients such as calcium carbonate or rice starch that are not present in existing TiO2 containing formulations to impart opacity to the film coatings. New best-in-class TiO2 free formulations such as Opadry TF 276U are designed to provide higher opacity at standard coating weight gains, while Opadry TF 277U, a calcium carbonate free coating, is suitable for pH sensitive APIs. The objective of this study was to evaluate the impact of various Opadry TF coating systems as shown in Table 1 on physicochemical properties such as assay, impurity, color difference, disintegration time (DT) and dissolution performance of immediate release (IR) tablets using a model drug, sitagliptin.

Table 1. TiO2 Free Coating Systems Evaluated

Trial No.	Coating Formulation	Key Characteristics
1	Opadry 03F	HPMC-based with TiO2
2	Opadry TF 276U	High Opacity, TiO2 Free
3	Opadry TF 277U	Calcium carbonate free, TiO2 Free
4	Opadry TF 269F	PVA-based, TiO2 Free
5	Opadry TF 265F	HPMC-based, TiO2 Free

Methods

Manufacturing of Sitagliptin Tablets: Sitagliptin IR tablets were produced by direct compression using StarTab®, directly compressible starch, and microcrystalline cellulose as diluents, silicon dioxide as the glidant, and magnesium stearate as the lubricant (Table 2). All ingredients including API (except magnesium stearate) were passed through ASTM #40 screen and accurately weighed, followed by blending in DCM-10 blender (Rimek Kalweka, India) for 10 minutes at 20 rpm. The lubrication of the blend was carried out with magnesium stearate previously passed through ASTM #60 screen for additional 2 minutes at 20 rpm. Powder blend properties were determined using tap density apparatus (Electrolab, India).

Tablets were compressed on a rotary tablet press (Rimek Minipress SF II, India) using 10.0 mm round plain, D-type standard concave tooling at target tablet weight of 381.7 mg.

Table 2: Composition of Sitagliptin Tablets (100 mg)

Ingredients	% w/w	mg/tablet
Sitagliptin phosphate monohydrate (equivalent to 100 mg of sitagliptin)	33.6	128.4
StarTab	36.2	138.0
Avicel pH 102	28.2	107.5
Cabosil	1.0	4.0
Magnesium Stearate	1.0	3.8
Total	100.00	381.7

Film Coating of Sitagliptin Tablets: Film coating was performed using an Opadry and Opadry TF coating systems (Table 3) in a 12.5" perforated coating pan (O'Hara Labcoat M5), using 900 g batch size.

Testing of Tablets: Coated tablets were evaluated for surface roughness, hardness, disintegration time (DT) in purified water, drug assay and impurity testing. Film coated sitagliptin tablets were tested for dissolution using 900 mL of 0.1N HCl in USP Apparatus II at 75 rpm. The coated tablets were stored in 75 cc HDPE containers at accelerated storage conditions of 40°C/75% RH and 30°C/65% RH for 3 months.

Table 3. Coating Process Parameters

Process Parameters	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
Pan load, Kg	0.9				
Coating machine	O'Hara Labcoat M5				
Pan size	12.5 inch				
Number of spray gun	1.0				
Nozzle diameter, mm	1.0				
% Weight gain	1.0				
Coating media	Purified water				
% Solids	15	20	20	20	15
Spray rate, g/min	4-5				
Pan speed, rpm	6-8				
Inlet air temperature, °C	59-64	58-65	58-60	59-62	60-62
Exhaust temperature, °C	42-47	40-45	41-43	42-43	41-44
Bed Temperature, °C	40-43	40-44	42-43	42-43	41-43
Atomization air pressure, bar	1.35	1.31-1.36	1.35-1.40	1.39	1.39
Pattern air pressure, psi	1.35	1.32-1.36	1.34-1.38	1.37-1.40	1.38-1.39
Air flow, m^3/hr	133-135	142-150	135-138	140-146	140-143

Results

Sitagliptin Tablet Physical Properties: The sitagliptin IR formulation powder blends showed satisfactory flow properties with good compressibility, resulting in good tablet hardness (~13-14kP), low friability (~0.3%) and no variation after film coating applications. Coated tablets with all Opadry systems showed good surface appearance (Figure 1) and disintegration of 1-2 minutes.

Figure 1: Surface Appearance for Uncoated vs Film Coated Tablets

Assay, Impurity Testing and Dissolution Testing for Sitagliptin: The sitagliptin content of the uncoated and film coated tablets (Trials 1-5) was within acceptable limits of 95-105% at both the initial and end of 3M accelerated stability storage (Figure 2). Impurity profile was NMT 0.2% (limit is 1%) up to 3M upon stability storage for all film coated tablets, indicating Opadry TF film coating system did not result in drug degradation. No significant difference in drug release was observed for all the film coated tablets at initial and accelerated stability conditions of 40°C/75% RH (Figure 3).

Figure 2: Assay Test Results for Sitagliptin Tablets at Initial and Accelerated Stability Conditions

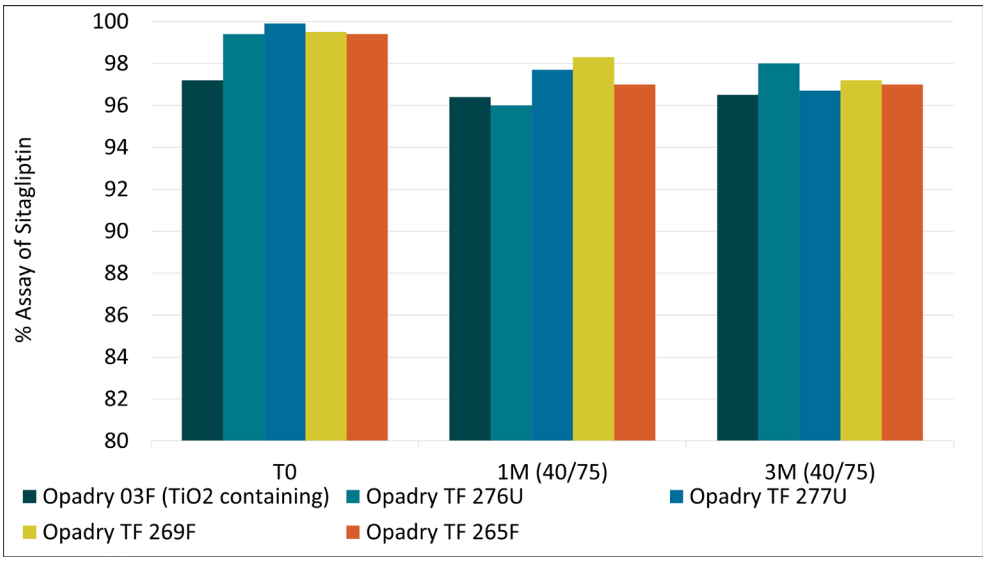
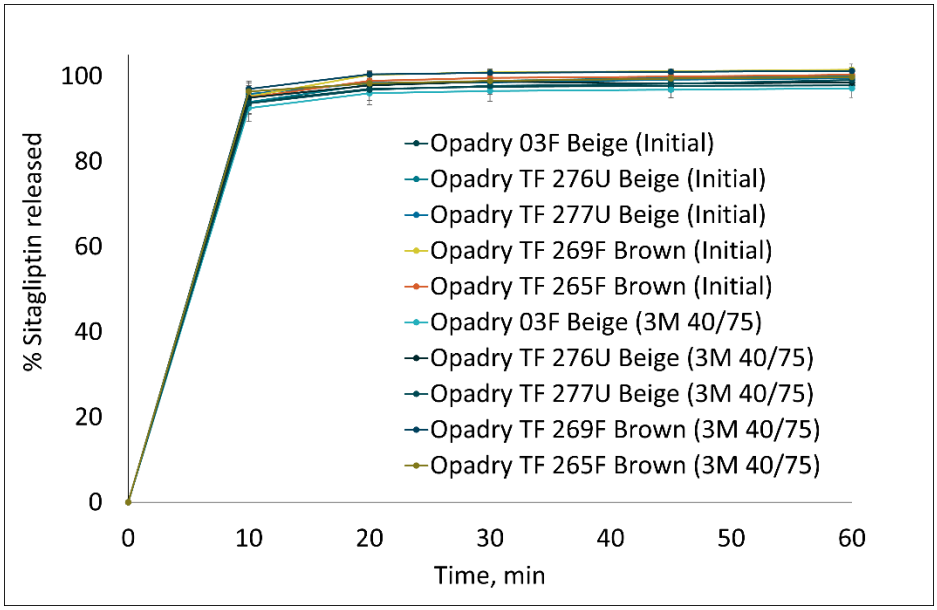


Figure 3: Drug Release Profiles of Sitagliptin Tablets at Initial and Accelerated Stability Condition



Conclusions

This study showed that sitagliptin tablets coated with Opadry TF had comparable physicochemical performance to those coated tablets containing TiO2, when applied at 4% WG. At the end of 3M accelerated stability studies, coated tablets complied with all the analytical tests showing that Opadry TF does not have any adverse impact on sitagliptin tablet formulation.

References

1. Opadry® TF, TiO2 Free Formulated Film Coatings. Accessed : 15 Aug 2023 https://www.colorcon.com/markets/pharmaceuticals/filmcoatings/immediate-release/opadry-tf