
Improving Patient Experience & Adherence

A Colorcon Whitepaper
2019

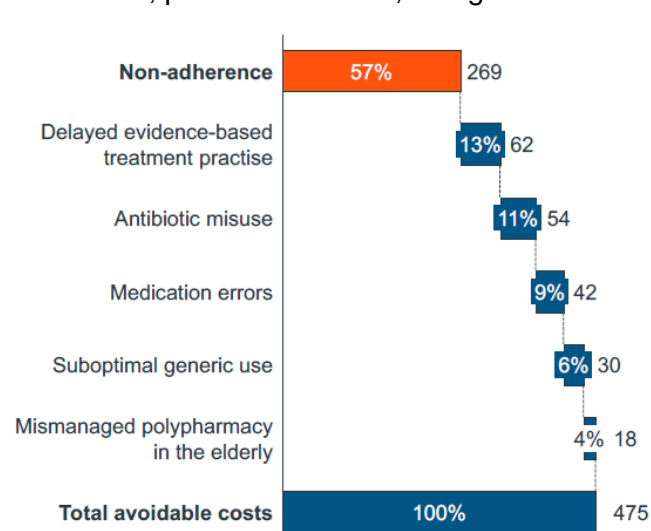


Patient Centricity

Difficulty swallowing medication is a significant contributor to patient non-adherence to prescribed medication.

Consider your own experience when taking medication. Most likely, we have all experienced some type of difficulty in taking medications or dietary supplements; or watched family members such as children or elderly parents struggle to take their medications.

According to a study¹, 4 in 10 adults report difficulty in swallowing tablets. An FDA guidance document², published in 2015, recognized that size, shape and coating are all contributory factors in



the swallowing process, and these factors can impact adherence to prescription regimens. If a person has trouble swallowing, they may delay taking, skip a dose or discontinue use altogether. Any of these actions can pose a serious health threat and lead to unnecessary medical costs.

Medical costs associated with skipping or discontinuing a medication is estimated at \$269 billion in the United States alone³. Imagine the size of this if it were to be applied globally. Every discontinued use of medication also equals lost revenue for the drug manufacturer.

Figure 1 Avoidable Medical Costs (USA, 2012)

Understanding the Impact of Tablet Coating

Colorcon has been working for over a decade to qualify and quantify the effect of film coating on swallowability. Early research used gamma scintigraphy to measure the influence film coatings have on the transit times of solid oral dosage forms from the mouth to the stomach. In this study, subjects were given four equal sized tablets to swallow; with three tablets finished using different film coatings and the fourth uncoated.⁴ Most of the tablets had an overall transit time of less than 30 seconds, but four tablets took more than 10 minutes to transit and were all uncoated. The coated tablets all passed the stomach without issue, and 92% of the coated tablets took less than 20 seconds to complete their journey to the stomach. **This work indicated that coated tablets are better in terms of ease of swallowability.**

Market Demand for Improved Swallowability

Guidance papers published by the U.S Food & Drug Administration^{2,5} (FDA) and the European Medicines Agency⁶ (EMA) address concerns related to the size, shape and coating of solid oral dosages and give guidance aimed at improving the patient experience and adherence to medication regimens. This patient-centric focus supports Colorcon's goal of enhancing tablet design to improve patient recognition and aid swallowability. To validate the earlier results showing that a coated tablet is much better than uncoated; further work was undertaken to **enhance the coating formulation and look at other attributes that can positively impact the swallowing experience for patients.**

Factors that Affect Swallowability

An important factor that contributes to the swallowability of a tablet is that of the **motivation of the patient**. If the medicine provides an essential clinical need that is important to the health and well-being of the patient, then they will be much more likely to take it. If the medication is discretionary and taken only to support lifestyle or general health, then the patient may choose to skip a dose or not take the tablet at all. Everyone will have their own unique experience with swallowing tablets. These may be impacted by their age, other medications taken, or whether they have underlying health issues such as stroke, Parkinson's disease, or other neurological disorders that can lead to dysphagia.

There are essentially four phases of swallowing with the first two being the most important when it comes to the patient deciding to swallow the tablet. First, they will look at the tablet and decide if it is something they could easily swallow. At this stage, factors around the appearance of the tablet are important. If the visual perception of the tablet is large and rough and, therefore, perceived as difficult to swallow, this will impact whether the patient decides to put the tablet in their mouth. Next, is how the tablet feels in the mouth/on the tongue. What is the texture like? Does it feel rough or smooth? Does it have a bad taste? The last two phases of swallowing revolve around avoiding choking and the tablet sticking in the esophagus.

Each of these phases constitutes the patient's perception of whether a tablet is easy or hard to swallow. In all cases, taking water with the tablet is important, this provides lubrication to improve transit times to the stomach and aids the disintegration process of the tablet itself.

Understanding Slip and the Science of Lubrication

Tribology is the field of science that helps to describe how surfaces interact with each other at a microscopic scale. In the case of oral dosage forms, the frictional interaction between surfaces and how fluids can help act as a lubricant is important to understand.

At a microscopic scale, surfaces in contact will interact with each other, and depending on how flat they are, will have more or less contact points. When these surfaces have no lubricant present and are dry, the friction between them will be high and the surfaces will be difficult to move over each other.

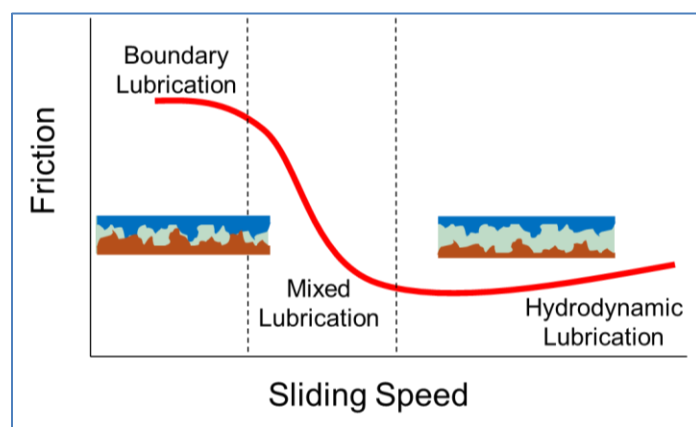


Figure 2 Modes of Lubrication

As an example, if you were to run your finger over a clean plate, you hear a squeaking sound indicating high friction between your finger and the plate. This is described as *boundary lubrication*. If a small amount of liquid is added to the surface of the plate it would slide much easier because the liquid is helping to keep the two surfaces apart. This is called *mixed lubrication*, where there is still some physical contact between the surfaces, but the liquid is helping to reduce the overall friction. By increasing the level of liquid between the surfaces further, they are separated and glide over each other easily, with minimal friction. This is called *hydrodynamic lubrication*.

With this understanding of tribology, the incorporation of hydrophilic polymers into film coatings to lubricate the tablet surface when wet, either by contact with saliva or through taking a glass of water with the tablet, can be investigated.

Evaluating Slip Behavior

Colorcon developed a single test to characterize how different coating materials behave and rank their slip performance. In this case, the slip was determined by measuring the force necessary to move tablets held in a weighted sled across a wet surface. The force necessary to start the sled moving, static friction, and the load necessary to keep the sled in motion, the dynamic friction was measured.

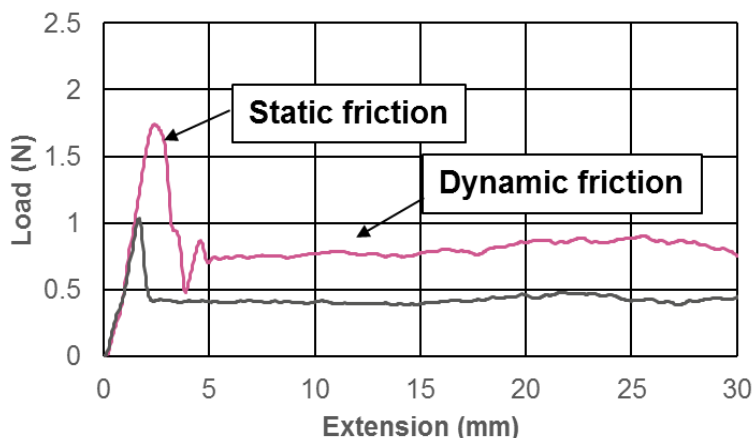


Figure 3 In Vitro Measurement of Slip Behavior

Using this test different materials and film coating formulations were evaluated to identify good slip behavior. The red line in Figure 3 represents a traditional HPMC-based film coating, while the black line represents a developmental slippery coating. Both the static friction and dynamic friction of the developmental coating are significantly lower than the traditional coating, indicating enhanced slip in the test.

As a result of this work, Opadry® EZ, Easy Swallow Film Coating was launched. This innovative film coating dramatically improves the swallowability of any tablet that the coating is applied to. Once wet, the slip performance is enhanced, significantly reducing the probably if sticking in the throat or esophagus.

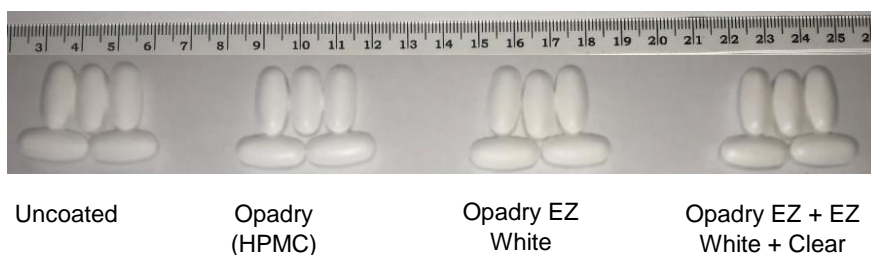
Human Swallowability Study

A study conducted by the University of Birmingham⁷ tested whether the enhanced slip of Opadry EZ, measured by in vivo methods resulted in a better swallowing experience for consumers, compared with uncoated and HPMC-based coated tablets.

The participant population included 84 healthy volunteers with a wide age and gender distribution. Factors evaluated included the amount of water required and time to swallow 4 placebo tablets. The study assessed overall experience, including ease of swallowing and mouthfeel.

Figure 4 shows the four variations of tablets used in the study; each participant was given these in a randomized order.

Figure 4 Placebo tablets (950 mg, 19.3 X 9.2)



Ease of swallowing was measured by evaluating the amount of water needed to take the tablet and the time taken to swallow. In the mouthfeel assessment, participants were asked to hold the tablet in their mouth for about 10 seconds and move it around with their tongue to see how easily it moved around. Participants scored using a Visual Analogue Scale (VAS) and the responses converted into a number that allowed for statistical analysis.

All coated tablets had 3% WG of coating applied. Opadry EZ+EZ had an additional 1% WG of clear Opadry EZ top-coat. The Opadry coated tablets were considered easier to swallow than uncoated tablets, but the mouthfeel parameters further discriminated between the coated tablets with Opadry EZ+EZ, outperforming Opadry HPMC-based coating and the single coated Opadry EZ tablet. Opadry EZ+EZ gave the most positive overall mouthfeel relating to stickiness, slipperiness, and smoothness.

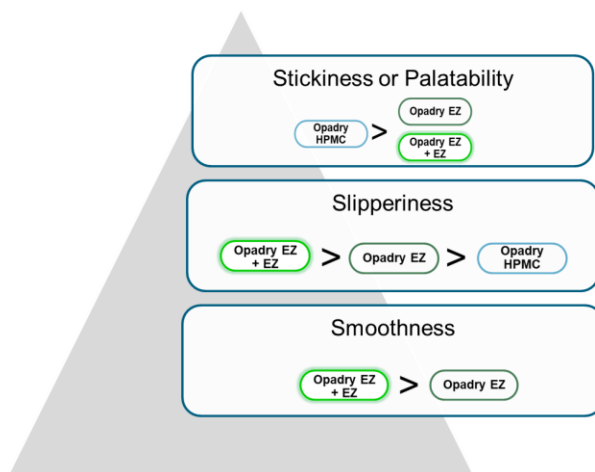
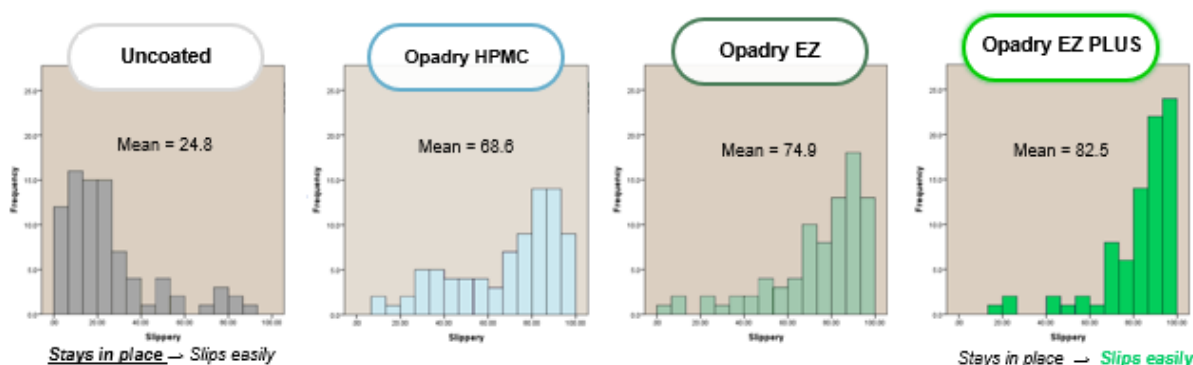


Figure 5 Mouthfeel assessments resulted in distinguishing coated tablets

Slipperiness is part of the mouthfeel parameters that participants were asked to evaluate using the Visual Analog Scale, with results calculated to a numerical score (Figure 6). Most participants gave the uncoated tablet a low score indicating that the tablet stayed in place or stuck in the mouth. The Opadry EZ tablets had a higher proportion of people reporting high levels of slipperiness, with Opadry EZ+EZ showing the highest number of participants scoring easy slip.

Figure 6 Scores of slipperiness vs. frequency of score used



In addition, each participant provided three words to describe their experience of swallowing the tablets to explore how participants felt and perception in the mouth. The results are shown using word clouds; with the highest occurrence appearing as large and those with only a few occurrences as small, or very small.

Color is used to differentiate, with orange words depicting undesirable characteristics and green as desirable characteristics.



Positive Patient Experience with Opadry EZ

Study results demonstrate that coated tablets are preferred to uncoated, but not all coatings are created equal. Opadry EZ demonstrates differentiated performance for swallowability. The results for the in vivo human swallowability study show that Opadry EZ coating is preferred for mouthfeel, palatability, and overall tablet acceptance, thereby providing the most positive patient experience.

For more information on Opadry EZ, visit www.colorcon.com

References

1. Harris interactive, 2004 study
2. Kux, L. Food and Drug Administration (2015). *Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules; Guidance for Industry; Availability* (Docket No. FDA-2013-N-1434). United States.
3. IQVIA European Thought Leadership; IQVIA Institute 2012 "Responsible use of Medicine"
4. C. Wilson, et al. Modern Tablet Film Coatings and Influence on Ease of Swallowing. AAPS Annual Meeting, 2003.
5. Kux, L. Food and Drug Administration (2015). *Safety Considerations for Product Design To Minimize Medication Errors; Guidance for Industry; Availability* (Docket No. FDA-2012-D-105). United States
6. Steffenino, Rita M. "Is Your Tablet Hard to Swallow? Guidance Addresses Drug Tablet Design." *Pharmaceutical Technology*, 9 May 2018, www.pharmtech.com/your-tablet-hard-swallow-guidance-addresses-drug-tablet-design.
7. Hofmanová, J.k., et al. "Developing Methodology to Evaluate the Oral Sensory Features of Pharmaceutical Tablet Coatings." *International Journal of Pharmaceutics*, vol. 562, 1 May 2019, pp. 212–217., doi:10.1016/j.ijpharm.2019.03.046.

The information contained herein, to the best of Colorcon, Inc.'s knowledge is true and accurate. Any recommendations or suggestions of Colorcon, Inc. with regard to the products provided by Colorcon, Inc. are made without warranty, either implied or expressed, because of the variations in methods, conditions and equipment which may be used in commercially processing the products, and no such warranties are made for the suitability of the products for any applications that you may have disclosed. Colorcon, Inc. shall not be liable for loss of profit or for incidental, special or consequential loss or damages.

Colorcon, Inc. makes no warranty, either expressed or implied, that the use of the products provided by Colorcon, Inc., will not infringe any trademark, trade name, copyright, patent or other rights held by any third person or entity when used in the customer's application.

For more information, contact your Colorcon representative or call:

North America	Europe/Middle East/Africa	Latin America	India	China
+1-215-699-7733	+44-(0)-1322-293000	+54-1-5556-7700	+91-832-6727373	+86-21-61982300

You can also visit our website at www.colorcon.com



© BPSI Holdings LLC, 2019.

The information contained in this document is proprietary to Colorcon and may not be used or disseminated inappropriately.

All trademarks, except where noted, are property of BPSI Holdings, LLC.

Swallowability_Whitepaper_OpadryEZ