



AN EASY PILL TO SWALLOW

In this article, Kelly Boyer, Vice-President, Film Coating, and Ali Rajabi-Siahboomi, PhD, Chief Scientific Officer, both of Colorcon, explore the role of different tablet coating materials in improving the patient experience and adherence to prescription regimens.

Around four in 10 adults report difficulty in swallowing tablets.¹ Recent guidance documents published by the US FDA and the EMA recognise that size, shape and coating are all contributory factors in the swallowing process and can impact adherence to prescription regimens.²

If a person has trouble swallowing, they may delay taking a tablet, skip a dose or discontinue the medication. Any of these actions can pose a serious health threat and, in the case of antibiotics, may contribute to antimicrobial resistance. Poor swallowability also leads to unnecessary medical costs and lost revenue for the drug manufacturer. Medical costs associated with skipping or discontinuing a medication are estimated at US\$269 billion (£215 billion) in the US alone.³

Colorcon, a leader in the development and supply of specialty excipients, is incorporating the results of recent patient studies on swallowability to reinforce the benefits of tablet coating. The company anticipates that this approach will support the pharmaceutical industry in the creation of products that overcome both the perceived and real problems associated with swallowability, for all ages, mitigating adverse events such as pain, gagging and choking, whilst also providing a means of clear drug product differentiation.

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FACTORS THAT AFFECT SWALLOWABILITY

Perception of medicines and a willingness to take tablets may be as important as physical difficulties in swallowing or dysphagia. If the medicine is crucial to the health and well-being of the patient, they will be much more likely to take it. If the medication is discretionary and taken only to support lifestyle or general health, the patient may choose to skip a dose or stop taking the tablets altogether.

A patient’s experience and ability to swallow medications may be impacted by age and whether they have underlying health issues such as stroke, Parkinson’s disease or other neurological disorders that can lead to dysphagia. In the case of children, the elderly and psychiatric patients, their physiological and cognitive responses may be different from those of the general population.

There are essentially four phases of swallowing, the first two of which are the most important when it comes to the patient deciding to take the dose. Firstly, factors around the appearance of the tablet are important. If the visual perception of the tablet is large and rough, it will be perceived as difficult to swallow and the patient will be less likely to put it in their mouth. Next is how the tablet feels in the mouth/ on the tongue – does it have an unpleasant taste, what is the texture like? The last two phases of swallowing revolve around avoiding choking and the tablet sticking in the oesophagus.

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



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as this provides lubrication to improve transit times to the stomach and aids the disintegration process of the tablet itself.

REGULATORY GUIDANCE

In the past few years, both the FDA and the EMA have issued guidance encouraging pharmaceutical companies to design products that promote patient compliance and reduce medication errors. In practice, this means tablets should be of an appropriate size and shape to enhance swallowability and palatability of the drug. Tablet weight, surface area, disintegration time and propensity for swelling should all be considered when designing products.

Regulatory agencies around the world have acknowledged the advantages of film coatings applied to tablets and multiparticulate dosage forms. Benefits include:

- Easing swallowability by increasing mobility compared with an uncoated tablet of the same size and shape
- Improving the palatability of tablets by masking unpleasant tastes and odours
- Improving the aesthetic appeal of tablets
- Achieving the desired immediate- or modified-release profile
- Allowing easy identification, thereby minimising the risk of medication errors
- Enhancing the performance of the drug, protecting it from the environment, reducing friability and dusting issues, and ensuring better stability of the overall formulations.

SAFETY BY DESIGN

As the number and variety of medicines available increases and people are living longer, many patients are taking multiple medications and supplements. Pharmaceutical companies recognise that their products must meet the needs of target populations. While managing taste, smell and palatability are especially important for

paediatric formulations, in the case of elderly patients it is crucial to support safe swallowing and reduce the risk of choking.

Focusing on the specific needs of patients ensures ‘safety by design’ and has an impact on a drug’s success in the marketplace. This may include formulating drugs with extended-release profiles to reduce dosing frequency or using combination drugs. However, this approach can lead to larger tablets, which can negatively impact the ability to swallow.

Colorcon has conducted research into swallowability in order to improve the patient experience and safety. Studies have considered the impact of tablet size, weight, shape, surface area, disintegration time, palatability and propensity for swelling. Recent research focused on the development and application of film coatings to provide enhanced formulations that can positively impact the swallowing experience for patients.

SWALLOWABILITY AND UNDERSTANDING SLIP

Tribology is the field of science that describes 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 act as a lubricant are important. Mixed lubrication is where there is still some physical contact between the surfaces, but a liquid is helping to reduce the overall friction. Hydrodynamic lubrication is achieved by increasing the amount of liquid between the surfaces, so they are separated and glide over each other more easily, with minimal friction.

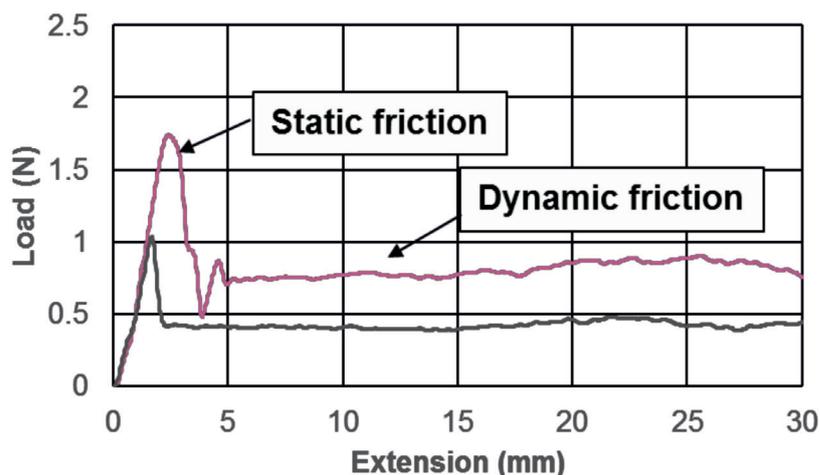


Figure 1: *In vitro* measurement of slip behaviour. Red line: hydroxypropyl methycellulose (HPMC)-based film coating. Black line: developmental slippery coating.

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Uncoated tablets can take 10 minutes or longer to move from the mouth to the stomach. Early research used gamma scintigraphy to measure the influence of film coatings on reducing transit times and demonstrated that the most effective coatings can reduce transit times to around 20–30 seconds.⁴

To investigate 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 – Colorcon developed a single test to characterise how different coating materials behave and to rank their slip performance. 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 (dynamic friction) were measured.

Using this test, different materials and film coating formulations were evaluated to identify good slip behaviour. The red line in Figure 1 represents a traditional hydroxypropyl methycellulose (HPMC)-based film coating, while the black line represents a developmental slippery coating, later launched as Opadry EZ, easy-swallow coating. Both the static friction and dynamic friction of the developmental coating are significantly lower than the traditional coating, indicating enhanced slip.

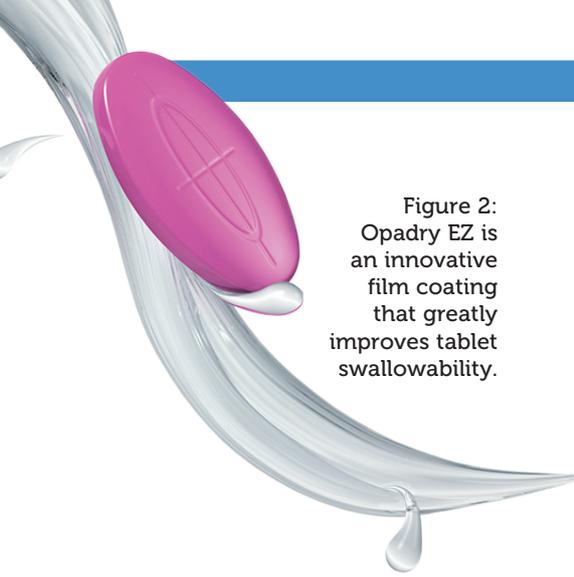


Figure 2: Opadry EZ is an innovative film coating that greatly improves tablet swallowability.

	Tablet specification	Short name
1	Uncoated placebo tablet	Uncoated
2	Opadry (Complete Film Coating System) 03F white coated placebo tablet	Opadry
3	Opadry EZ (Easy Swallow Film Coating System) white coated placebo tablet	EZ
4	Opadry EZ-EZ (Easy Swallow Film Coating System) white and clear top-coated placebo tablet	EZ-EZ

Table 1: Four variations of tablets used in the study.

As a result of this work, Opadry EZ easy swallow film coating was launched in February 2018. This innovative film coating greatly improves the swallowability of any tablet to which the coating is applied (Figure 2). Once wet, the slip performance is enhanced, significantly reducing the probability of the tablet sticking in the throat or oesophagus.

HUMAN SWALLOWABILITY STUDY

To test whether the enhanced slip of Opadry EZ, as shown by this *in vitro* method, resulted in a better swallowing experience for patients, an investigation was carried out in association with the University of Birmingham in the UK.⁵ The study involved 84 healthy volunteers with a wide age and gender distribution. A single centre

crossover study was used to measure the mouthfeel and swallowing experience of four 19 mm placebo tablets, taken in randomised order. One tablet was uncoated and the other three were coated as detailed in Table 1. Each participant was given four tablets in a randomised order.

Participants were asked to score the mouthfeel after holding the tablet in their mouth for 10 seconds based on the following parameters: smoothness, stickiness, slipperiness and palatability, using visual analogue scales (VAS). They were asked to rank the tablets in order of preference for ease of swallowing. The time taken to swallow the tablet and the volume of water used to aid swallowing were also recorded.

When the tablets were ranked in order of preference based on overall swallowing

experience, the favoured sample was Opadry EZ-EZ, which was the first choice for 37.8% of participants (Figure 3). The tablet finish that was preferred by volunteers was the Opadry EZ film coating, either pigmented or with additional top coat for extra gloss. This reportedly increased mobility during the swallowing process.

The slipperiness of the tablet was found to be the best predictor of the ease of swallowing. VAS results for slipperiness were converted to a numerical score (Figure 4). 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 EZ-EZ showing the highest number of participants scoring easy slip.

In addition, participants provided three words to describe their experience of swallowing each of the tablets in order to explore their perception of the tablet in their mouth. The results are shown in Figure 5 using word clouds – responses with the highest occurrence appearing in large font and those with only a few occurrences in small or very small font. Colour is used to differentiate, with orange words depicting undesirable characteristics and green showing desirable characteristics.

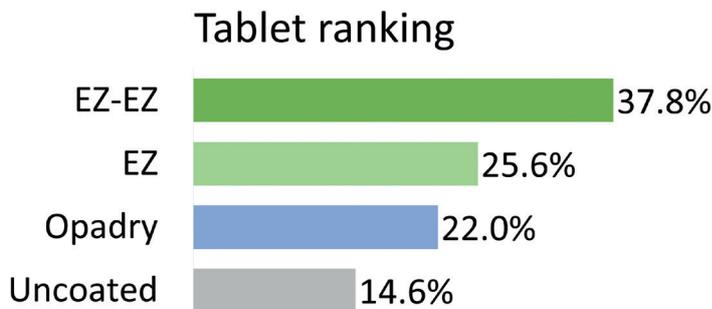


Figure 3: Study participant preference ranking of tablets.

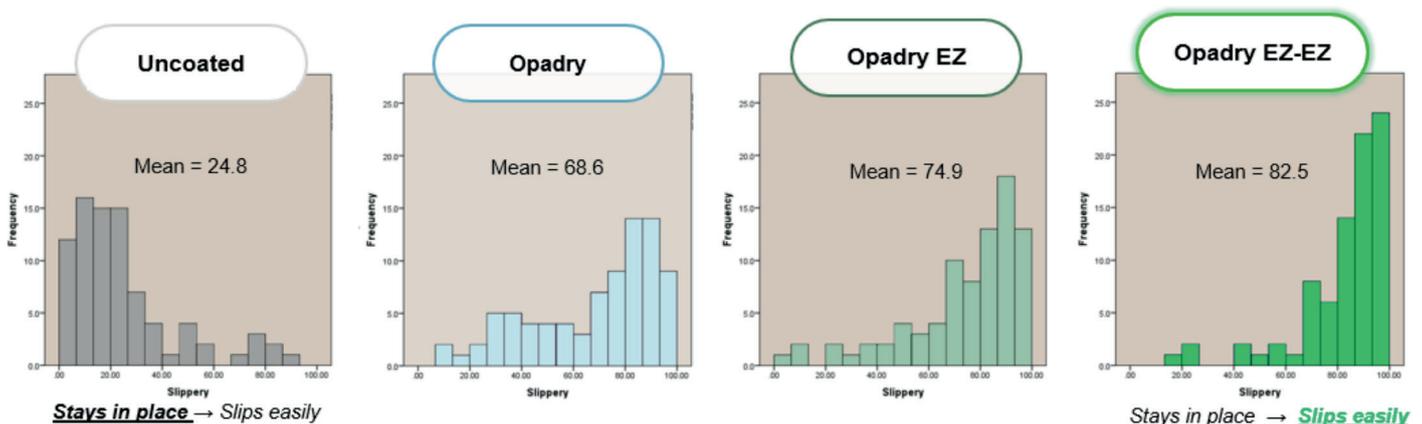


Figure 4: Scores of slipperiness versus frequency of score used.

