

Modern Tablet Film Coatings and Influence on Ease of Swallowing

OBJECTIVE

To investigate whether film coated tablets have shorter mean esophageal transit times and lower incidences of transit delays than those of uncoated tablets, or comparably sized hard gelatin or soft gelatin capsules. A pilot scintigraphic study was undertaken to investigate the esophageal transit of tablets and capsules in healthy volunteers.

STUDY DESIGN

Design

Oral dosage forms can be readily radiolabelled with a non-absorbed marker by drill and fill (tablets) or puncture and seal (capsules). The technique does not destroy the integrity of the tablets or capsules and does not interfere with the contact surface.

The study was carried out with the subject seated as (Figure 1). The administration with a minimum amount of water has been previously shown to discriminate between ease of swallowing for different capsules.¹ It is not permissible or desirable to repeatedly dose subjects with radioactivity and therefore the study was divided into two cohorts.

Shape

There is clinical evidence that the surface to mass ratio of a tablet may be an important risk factor in esophageal adhesion. One of the first bisphosphonates, alendronate 10mg, which was a round shallow convex tablet was associated with a high incidence of esophagitis. It is presumed that the larger surface area contributed to bioadhesion.² To our knowledge; there have been no reported comparison of the larger dosage forms featuring quite modest changes in geometry. It is therefore of interest to compare caplet and capsule shapes and the effect of coatings.

METHODOLOGY

Measurement of Esophageal Transit Using Gamma Scintigraphy

- Capsules vs. caplets; and uncoated vs. coated caplets and oval tablets.
- 48 volunteers
- ODFs were radio labelled with ⁹⁹Tc taken with 30 ml water.
- Dynamic scanning was conducted for 10 minutes.
- Images were taken every 0.5 sec for the first 30 seconds and every 15 sec thereafter.
- 30 sec. static image was taken at 30 min. post-dose to confirm formulation was in the stomach.

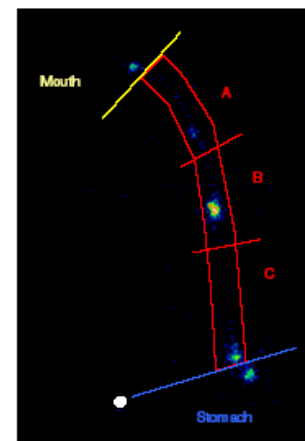
Figure 1



Angle 80°

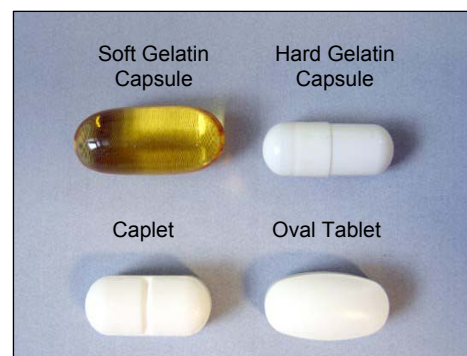
Scintigraphic Analysis

- The total dynamic scan was used to present an overview of the transit time, plus specific areas were noted to show the mouth, esophagus and stomach.
- The esophagus was further divided into 3 Regions of Interest - each representing one third of the esophagus. This was used for further analysis of the dynamic scan.
- Median transit time and the incidence of slow transit (> 15 sec) across evaluable subjects were determined.



Oral Dosage Forms Studied

- Hard gelatin capsule: White, opaque, size 0 filled with poloxamer 188.
- Soft gelatin capsule: Commercially available cod liver oil capsules.
- Caplet: placebo
- Oval tablet: placebo
- All dosages weighed ~ 1,000 mg

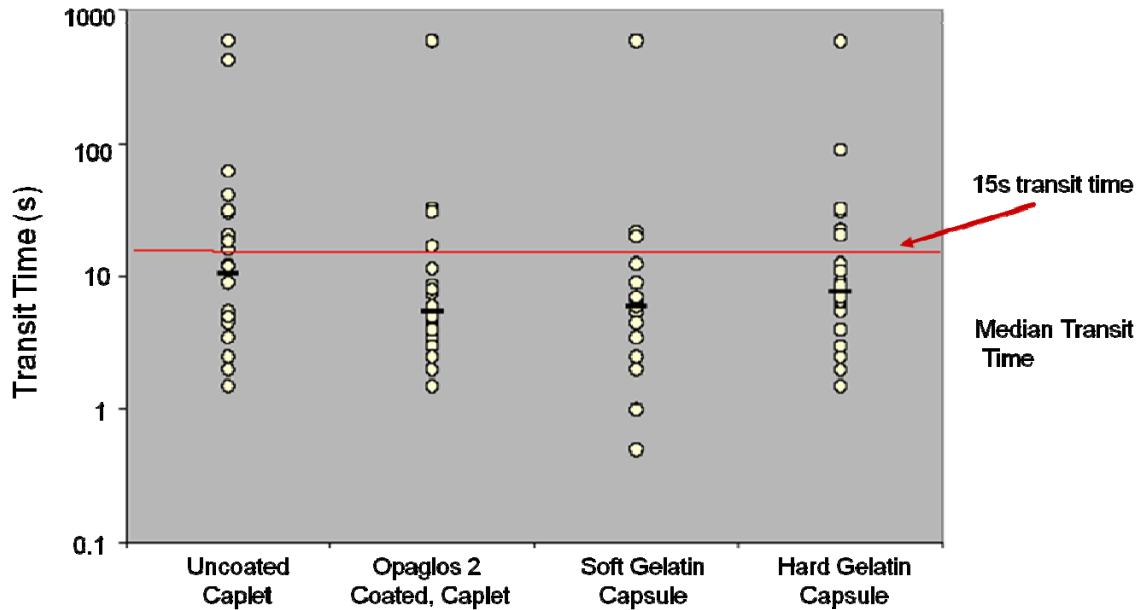


Oval tablets and caplets were either uncoated or coated with one of three clear film coatings (Opadry® 03B19222, Opadry II 85F19250 or Opaglos® 2 97W19196).

RESULTS

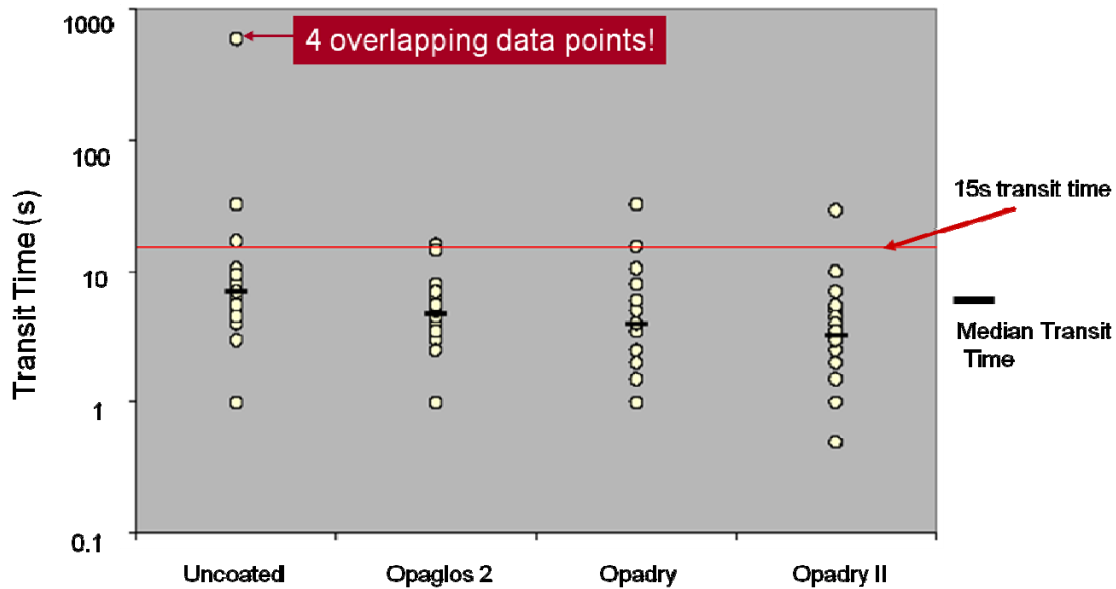
| Group | Formulation | Shape | n | Mean Transit (sec.) | Slow Transit (#) (i.e. ≥ 15 sec.) |
|-------|--------------|---------|----|---------------------|-----------------------------------|
| A | Hard Gelatin | Capsule | 23 | 13.7 ± 18.6 | 6 |
| A | Soft Gelatin | Capsule | 18 | 6.8 ± 5.8 | 4 |
| A | Uncoated | Caplet | 21 | 14.7 ± 16.2 | 9 |
| A | Opaglos® 2 | Caplet | 19 | 5.2 ± 3.6 | 6 |
| B | Uncoated | Oval | 19 | 7.6 ± 6.9 | 6 |
| B | Opaglos 2 | Oval | 24 | 8.1 ± 8.6 | 1 |
| B | Opadry® | Oval | 24 | 5.8 ± 6.5 | 2 |
| B | Opadry® II | Oval | 24 | 4.5 ± 5.7 | 1 |

Transit Times for Part A: Capsules and Caplets



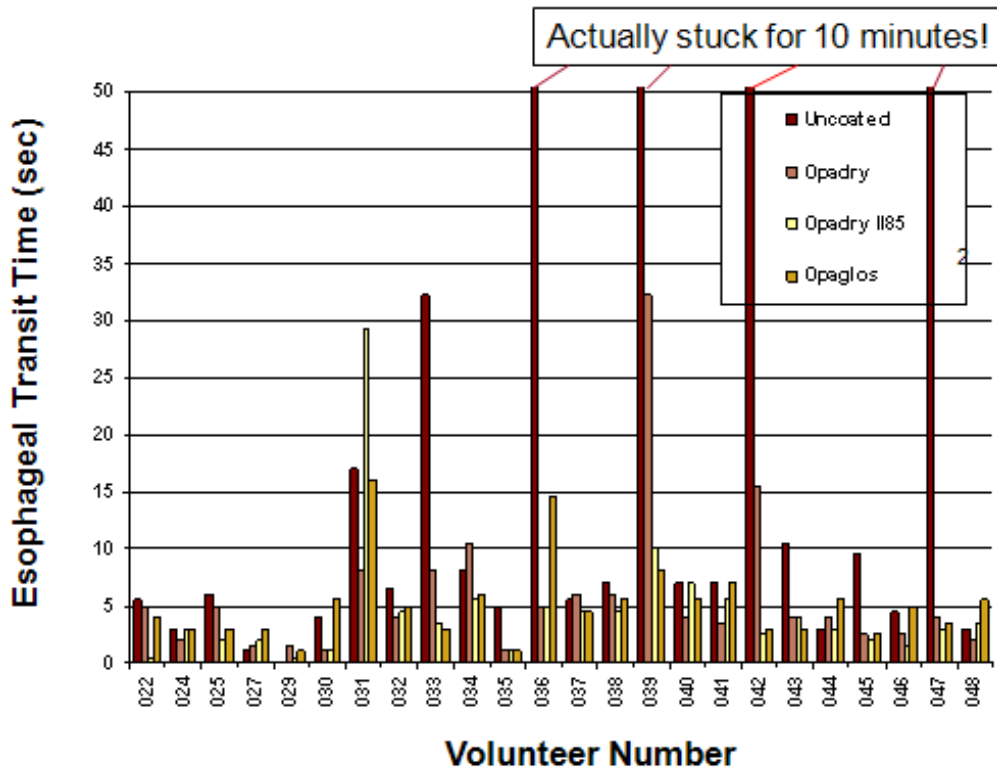
Non-parametric ANOVA showed no significant difference in transit times.

Transit Times for Part B: Coated and Uncoated Oval Tablets

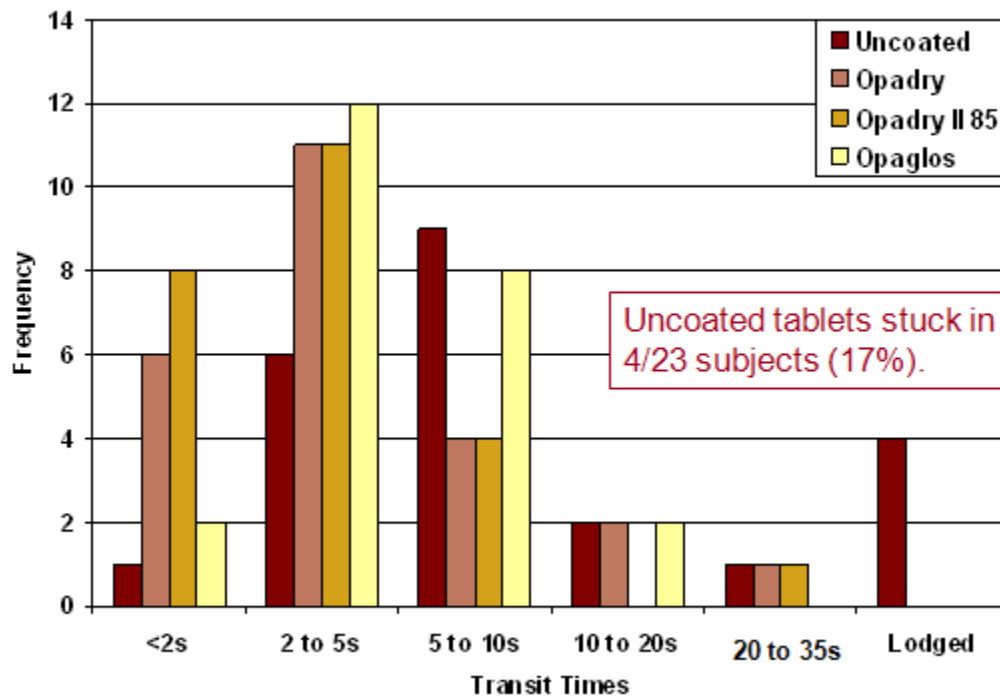


Non-parametric ANOVA showed a significant difference in transit times between uncoated and coated oval tablets as a group.

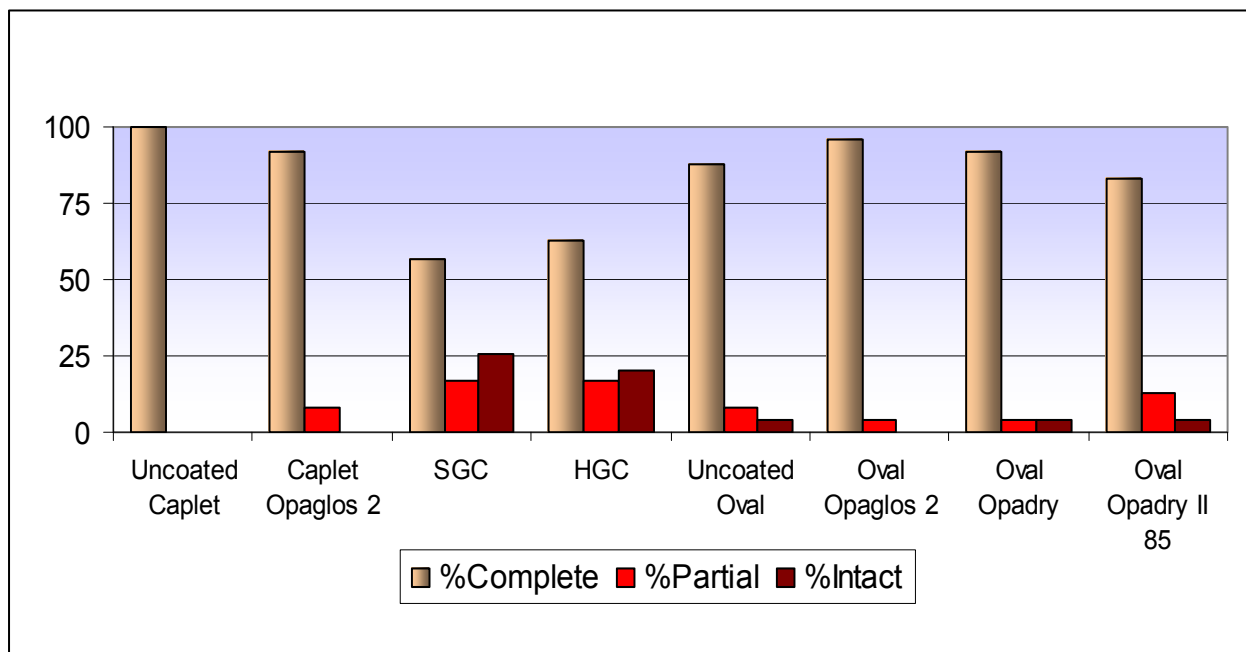
Part B: Individual Subject Data



Part B: Distribution of Total Transit Time



Extent of Disintegration of Dosage Forms in Stomach, 30 min after Swallowing



CONCLUSIONS & IMPLICATIONS

Coatings improve the ease of esophageal transit of oval tablets and prevent lodging of oval tablets in the esophagus. Uncoated, oval tablets arrested in the esophagus in 17% of the subjects; whereas, there was no significant sticking of coated, oval tablets in any of the subjects.

- Shape is also a key determinant of transit time: oval shaped tablets had faster transit times and a lower incidence of slow transit (> 15 s) than caplets. It is suggested that caplets have a greater surface area in contact with the esophagus than comparably sized oval tablets, which increases the propensity for caplets to stick.
- Capsules have a greater incidence of disintegration delays. Although the majority of caplets and oval tablets had completely disintegrated at 30 minutes, a significant number of hard gelatin capsules (5 out of 24) and soft gelatin capsules (6 out of 21) were still intact. Dysphagia (or difficulty in swallowing) is associated with many medical conditions including stroke, Parkinson's, AIDS, thyroidectomy, head and neck radiation therapy, and other neurological disorders. This condition is prevalent, and the reported incidence is (3):
 - 35% of the general population
 - 30–40% of elderly institutionalized patients and 18–22% of all persons in long-term care facilities.

In the dysphagic patient who has difficulty swallowing medication, the differences we have observed may be amplified, since dysphagia increases the likelihood of solid oral dosage forms lodging in the esophagus. The adhesion can lead to inflammation and stricture if the drug is a local irritant.

*Reprint of poster presented at American Association of Pharmaceutical Scientists Meeting, 2003.
Authors, C. Wilson, B. O'Mahony (Bio-Images Research, Ltd.) and T. Farrell, B. Friend, D. Taylor (Colorcon, Inc.)*

REFERENCES

1. Perkins AC, et. al. 2001. Int. J. Pharm. 222:295-303.
2. DeGroen, et. al. 1999. N. Eng. J. Med. 335:1016-1021.
3. Sastry S, Nyshadham J and Fix J. 2000. PharmaceuticalScience & Technology Today (Vol. 3, No. 4).

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
+1-215-699-7733

Europe/Middle East/Africa
+44-(0)-1322-293000

Asia Pacific
+65-6438-0318

Latin America
+54-11-5556-7700

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



© BPSI Holdings LLC, 2011. The information contained in this document is proprietary to Colorcon, Inc. and may not be used or disseminated inappropriately.

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

ads_ease_of_swallowing_ver2_02_2011.