M1130-11-60 EFFECT OF MEDIUM VISCOSITY ON SWELLING AND DISINTEGRATION OF IMMEDIATE RELEASE SOLID ORAL TABLET

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PURPOSE

To develop biorelevant testing protocols to simulate fed conditions, the mechanism of disintegration in viscous media needs to be understood. This study aims to investigate swelling behavior of an immediate release midodrine hydrochloride, a BCS I drug product under different viscous Hydroxypropyl Methylcellulose (HPMC) media. Such investigation offers valuable insights into how tablets may swell and disintegrate under simulated fed conditions, thereby advancing our understanding of drug dissolution kinetics in physiologically relevant settings.

METHOD(S)

- Studies have shown that an increase in viscosity of dissolution medium, simulating the ingestion of a solid meal, may impact tablet disintegration and dissolution.
- Texture analyzer was used to investigate the swelling behavior of the tablet in viscous media.
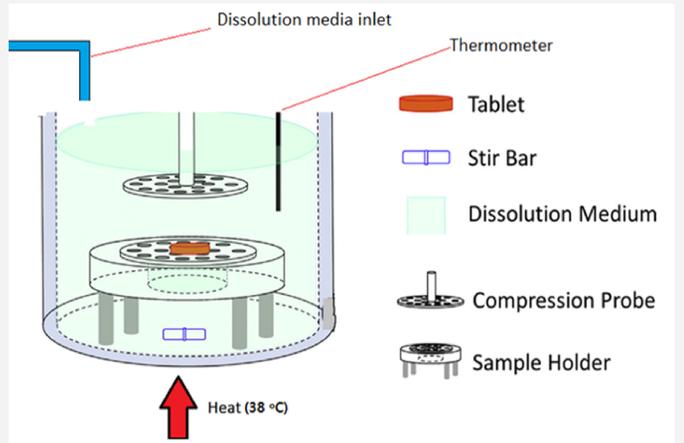
Schematic diagram of media reservoir method used to monitor the swelling behavior in viscous media.

Modified Method

The method was modified to simulate drug dissolution when co-administered with water, allowing us to investigate how the initial contact with water affects the dissolution process.

Tablets in 50 mL of USP media for 2 min
↓
Addition of 250 mL of 1% HPMC media at 2 minutes
↓
Addition of 600 mL of 1% HPMC media after 10 minutes

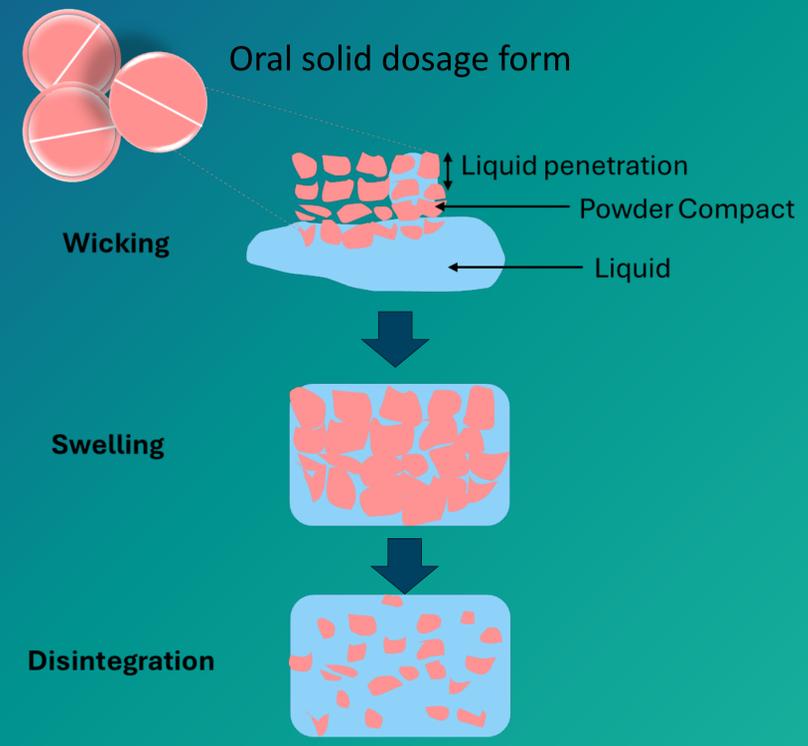- **Swelling** is one of the mechanisms of **drug disintegration[1]**.

- Initial **tablet swelling** is crucial in the **extent of drug release.**

- Stokes-Einstein equation:

$$D = \frac{k_B T}{6\pi\eta r_h}$$

- **Diffusion coefficient** (D) depends on **Viscosity** (η).

- Higher the viscosity, **poor diffusion of water** into the drug.

Oral solid dosage form

Wicking — Liquid penetration, Powder Compact, Liquid

Swelling

Disintegration

FDA U.S. FOOD & DRUG ADMINISTRATION
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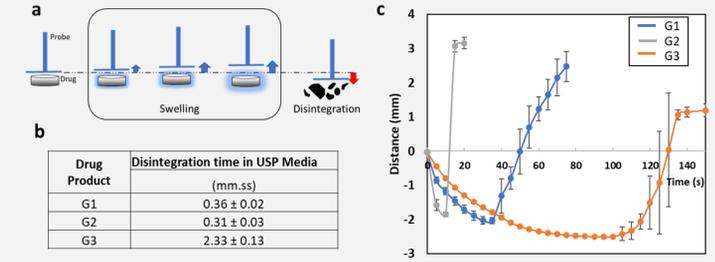
DISCLAIMER

RESULT(S)

Figure 1. a) Schematic diagram of tablet swelling and probe displacement b) disintegration time in USP media of the generic tablets G1-G3 and c) tablet swelling data of generic tablets G1-G3 acquired with Flowthrough Method in USP media (*n=3 and the error bars indicate the ± SD) and

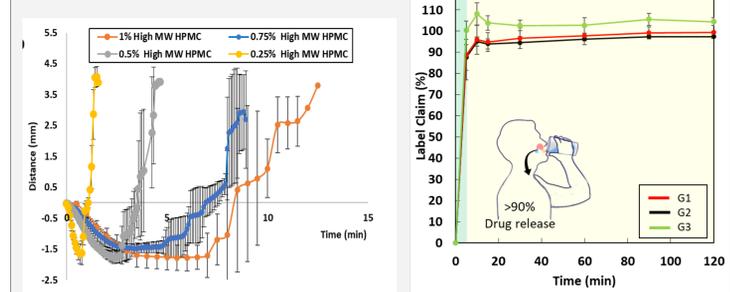| Drug Product	Disintegration time in USP Media (mm.ss)
G1	0.36 ± 0.02
G2	0.31 ± 0.03
G3	2.33 ± 0.13

Figure 2. Tablet swelling data of G2 acquired with Media Reservoir Method in different compositions of high MW HPMC media (*n=3 and the error bars indicate the ± SD)

Figure 3. Dissolution Profiles of 5 mg midodrine hydrochloride tablets (G1-G3) (*Each data point is the average of 3 and the error bars indicate the ± SD)

CONCLUSION(S)

- Swelling results agree with observations from disintegration tests in various viscous media.

- High viscosity dissolution media slows down the tablet swelling rates while increasing the swelling time, thus delaying tablet disintegration and dissolution.

- A small volume of free water is sufficient to facilitate the tablet swelling and disintegration, potentially reducing the impact of food induced viscosity on drug dissolution.

- This study shed insight into possible food-induced viscosity effect on the dissolution of BCS class I solid dosage forms.

[1] Markl et al., A Review of Disintegration Mechanisms and Measurement Techniques. Pharm Res. 2017, 34(5):890-917. https://doi.org/10.1007/s11095-017-2129-z.