Permexa™ C10: An Engineered Sodium Caprate for Improved Flowability and Compressibility in Oral Peptide Tablets

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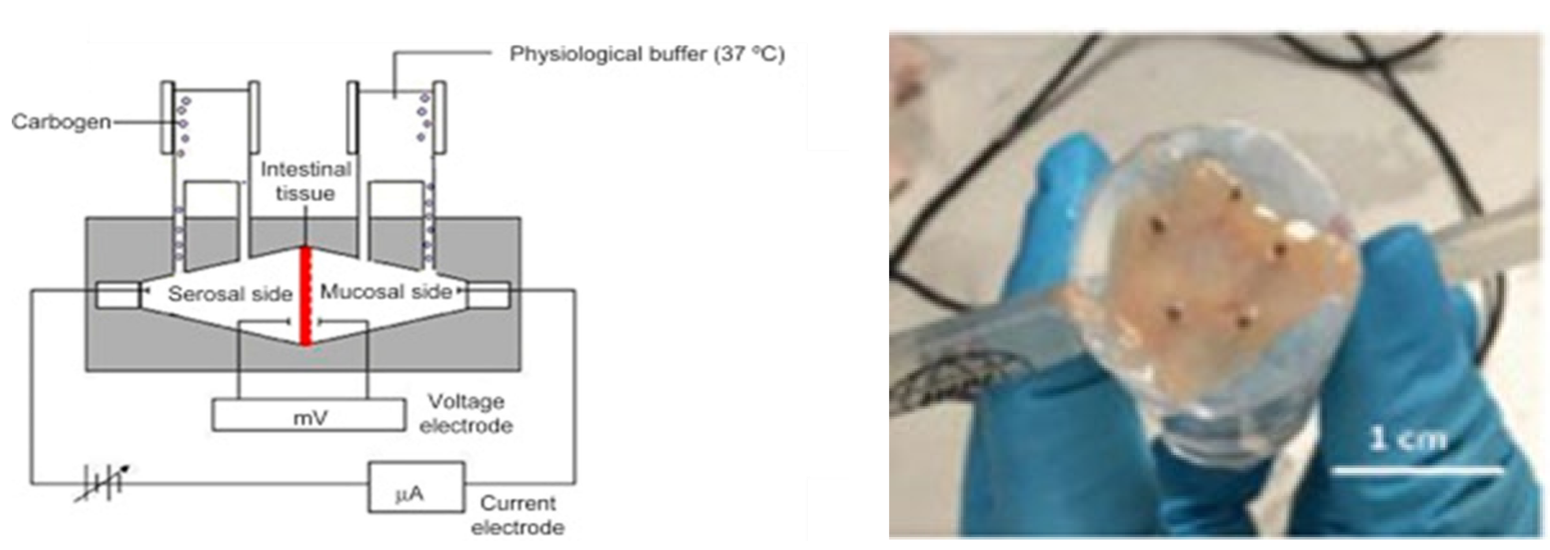
Introduction:

The oral administration of biologics presents significant challenges in pharmaceutical development. Permeation enhancers (PEs) such as sodium caprate (SC) facilitate the oral absorption of low-permeability drugs like peptides by enhancing intestinal uptake. Despite its effectiveness, sodium caprate's suboptimal flow and compression characteristics restrict its application in direct-compression tableting for biologics. Permexa™ is a process-engineered variant of SC, designed to improve flowability and compactibility, thereby enabling more robust tablet production. Evaluations compared peptide tablet formulations with Permexa™ to those made with commercially available SC.

Methods:

The potential of Permexa™ and other sodium caprate formulations to promote permeation across rat colonic mucosa was evaluated by measuring Trans-Epithelial Electrical Resistance (TEER) with the mounted tissue chamber method.

Figure 1: preparation of dissected rat intestinal tissue to evaluate sodium caprate intestinal permeability across using Ussing chambers.



Additionally, the flowability and flow characteristics of different grades of sodium caprate were analyzed using Flowdex™, a Brookfield shear cell, and a K Tron KSU-II LWF equipped with auger twin screws operating at a feed rate of 12 kg/h.

The influence of tableting speed on directly compressed peptide (collagen) tablets (Table 1) was measured with a Styl'One Evolution Compaction Simulator, which modeled a Fette 2090 press applying a compression force of compression force profiles at 10, 15, 20, and 25 kN and production run at 20 kN, at tablet press speeds of 20, 37, and 51 RPM.

Table 1: Bovin Collagen Peptide tablet formulation

No	Ingredients	Composition (%)	Tablet Weight (mg)
1	Bovine collagen Peptide	1.7	7.0
2	Sodium Caprate	75.0	300.6
3	Povidone K90	2.8	11.2
4	Avicel PH 102 MCC	19.5	78.0
5	Magnesium Stearate	1.0	4.0
	Total	100.0	400.8

Results:

Figure 1: Trans-Epithelial Electrical Resistance (TEER) values across rat colonic mucosae exposed to apical 10mM Sodium Caprate

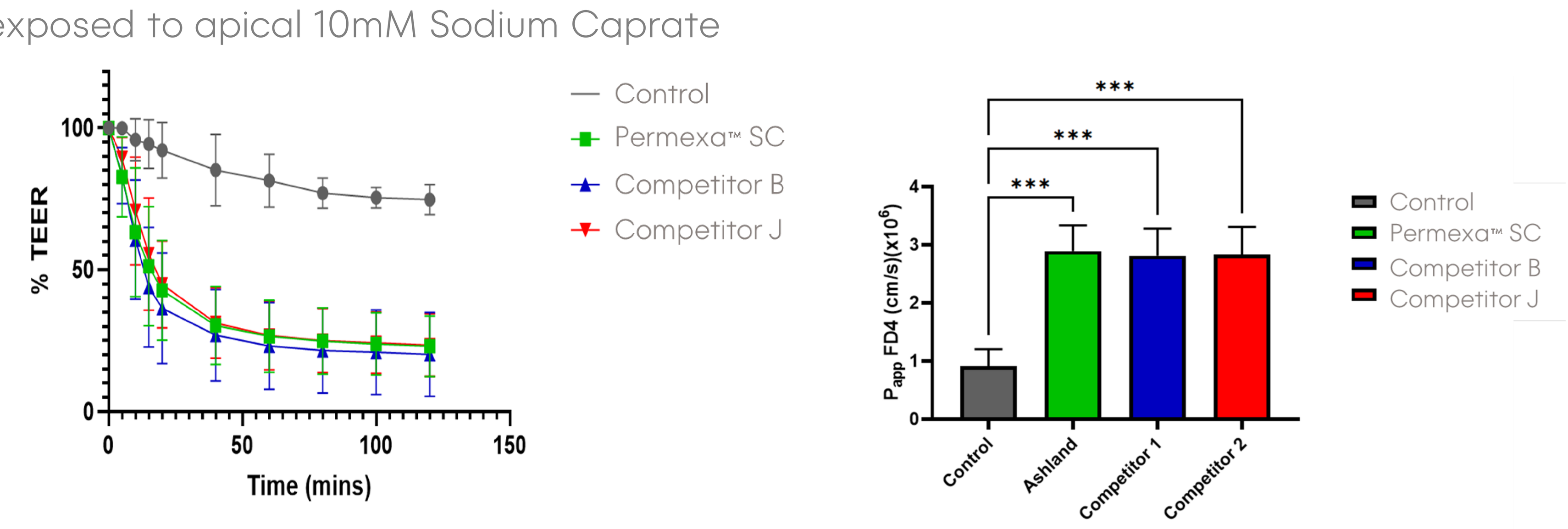
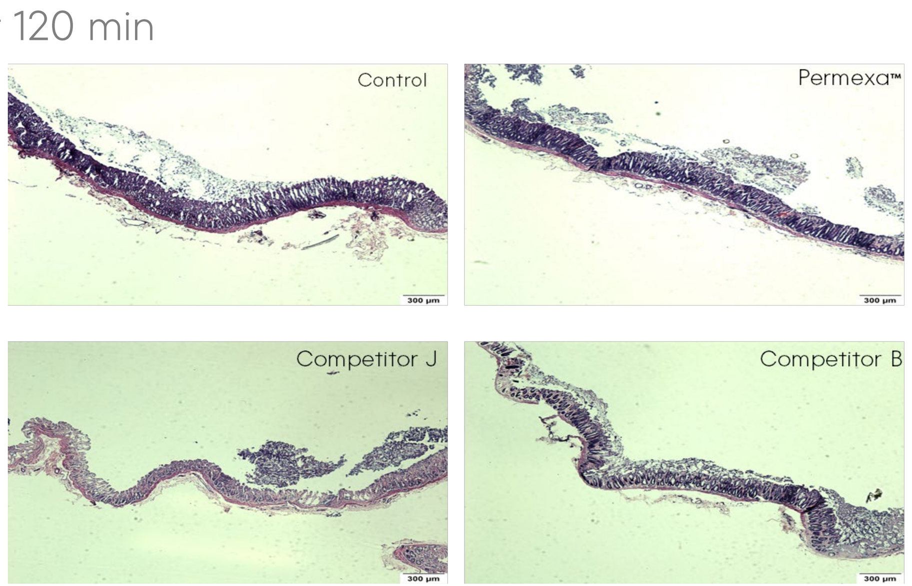
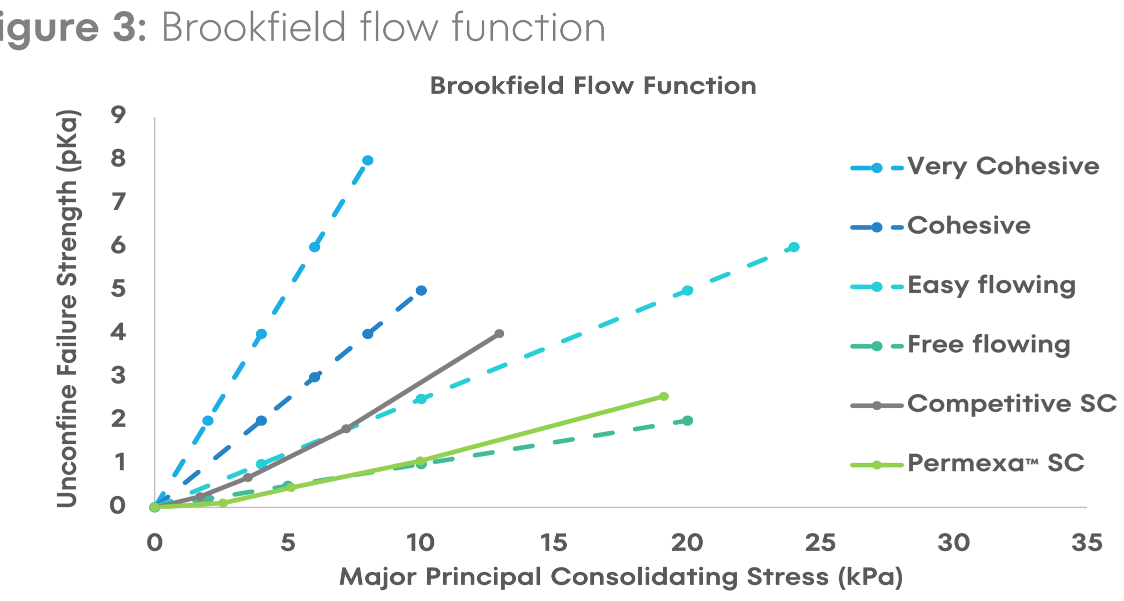


Figure 2: Hematoxylin and Eosin (H&E) staining of rat colonic mucosae in Ussing chambers at 120 min



In the permeability test, all products showed similar Trans-Epithelial Electrical Resistance (TEER) trends (Figure 1), indicating the Permexa™ Sodium caprate provides permeation enhancement similar to commercially available material with largely preserving tissue integrity (Figure 2).

Figure 3: Brookfield flow function



Flow Function: Sample is compressed under a load and then sheared against itself to measure the forces between particles of the powder samples

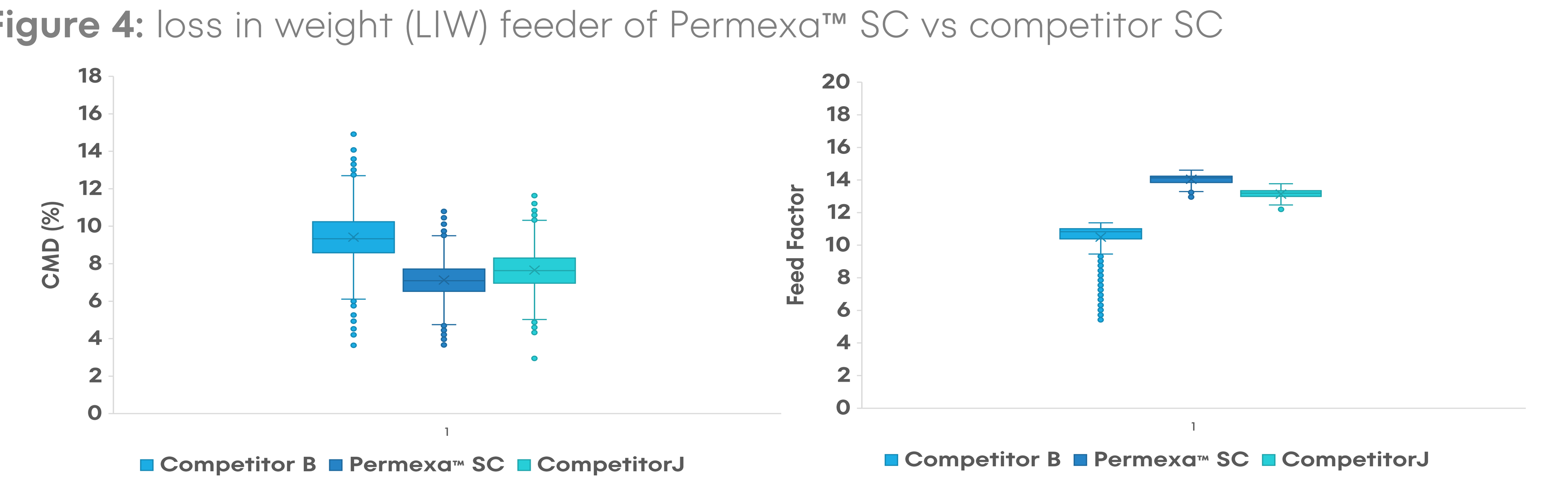
Higher ffc = better flow

Material characterization revealed that the Permexa™ sodium caprate has intrinsically superior powder properties, such as low cohesion and higher bulk density, leading to a better flow profile when tested on a shear cell.

Table 2: Flowability of different Sodium Caprate (SC)

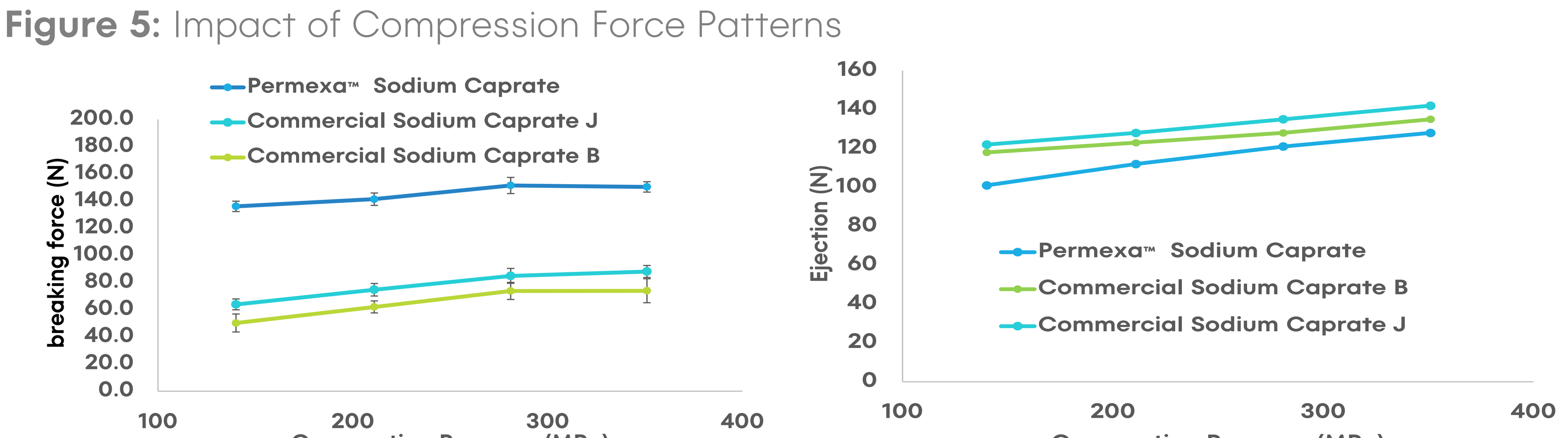
Test	Competitor B	Competitive J	Permexa™
aspect ratio	0.4	0.5	0.7
Flowdex flowability (mm)	22	22	16 Improved Flow

Figure 4: loss in weight (LIW) feeder of Permexa™ SC vs competitor SC



Permexa™ has intrinsically superior powder properties, such as better flow profiles, lower average CMD%, and higher feed factor than other sodium caprates. % RSD decreased by ~79% to competitor SC B and ~18% to competitor SC J

Figure 5: Impact of Compression Force Patterns



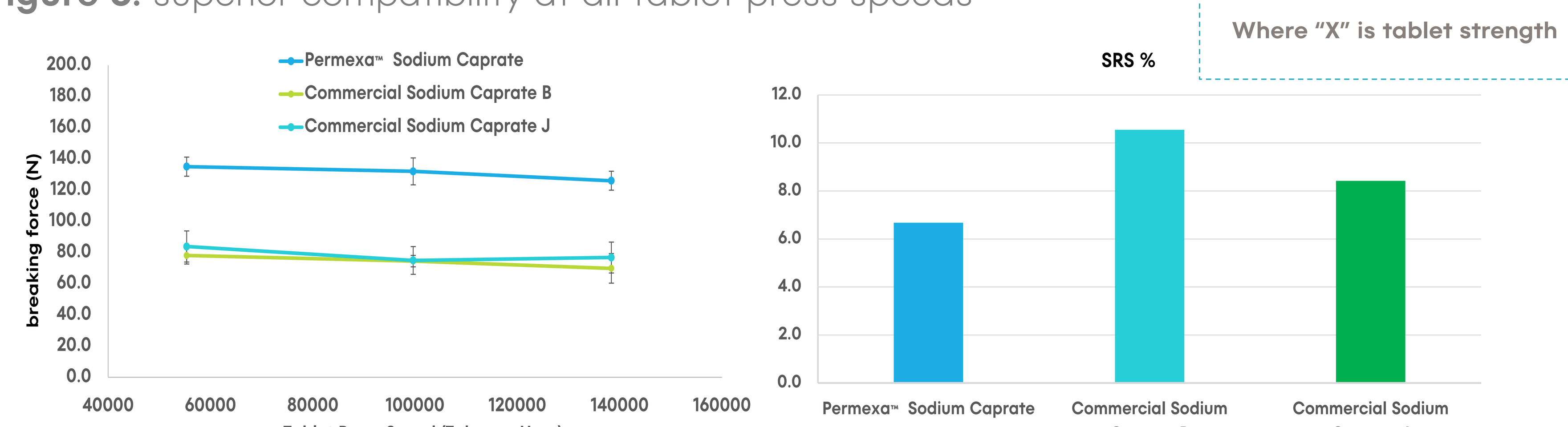
Tablets made with Permexa™ collagen demonstrate significantly higher tablet strength and reduced ejection force than those produced using Competitor SC.

Strain rate sensitivity index (SRS)

$$SRS = 100 \times \frac{X20rpm - X51rpm}{X20rpm}$$

Where "X" is tablet strength

Figure 6: superior compatibility at all tablet press speeds



The peptide tablet formulation with Permexa™ yielded stronger tablets and a lower Strain rate sensitivity index (SRS) than the standard material.

Conclusion:

SC is a widely used permeation enhancer for oral drugs, but its poor flow and compression properties have limited its use in dry granulation tableting. Permexa™ offers superior flow and compressibility at high speeds compared to other commercial grades, while maintaining similar permeation enhancement.

Reference:

Fattah, S., Salcaprozate sodium (SNAC) enhances permeability of octreotide across isolated rat and human intestinal epithelial mucosae in Ussing chambers. EJPS, 154, 105509

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