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Impact of Polymer Concentration on Metformin HCl Tablet Properties and Extended Release Profiles

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INTRODUCTION

- The formulation of **extended-release (ER) tablets** is a critical aspect of pharmaceutical development for a **highly water-soluble drug like metformin HCl**, primarily due to their propensity for rapid dissolution in gastrointestinal fluids, which can lead to dose dumping and compromised therapeutic efficacy.
- This study explores the use of **high viscosity hypromellose (HPMC, AnyCoat® CN10T)** in a direct compression (DC) metformin HCl 500 mg ER formulation to characterize tablet properties and the impact of polymer levels on the drug release profile of a highly water-soluble drug.

METHODS

- A high viscosity hypromellose, HPMC 2208 and 100,000 cP (AnyCoat CN10T, Lotte Fine Chemical, Korea) was evaluated for morphology using a scanning electron microscope (SEM). **Powder properties** of individual ingredients of the formulation were evaluated for moisture content, bulk density, tapped density, compressibility index and particle size distribution.
- **Tabletability of the hypromellose** was determined at different compression forces to evaluate its compaction profile. Tablets of polymer alone were prepared by blending AnyCoat CN10T with 0.25% magnesium stearate for 2 minutes in a V-blender, followed by compression using 10 mm round standard concave tooling. The formulations of metformin HCl ER are shown in Table 1.
- For the **ER tablets**, powder blends were prepared by mixing API, microcrystalline cellulose (MCC PH-102), and HPMC in a V-blender for 5 minutes. Magnesium stearate was then added to the V-blender and mixed for an additional 2 minutes. Tablets (1000 mg) were prepared using 8.38 x 18.9 mm oblong tooling.
- All tablets were prepared in a Piccola rotary tablet press operated at 50 rpm and evaluated for tensile strength, ejection pressure and in-vitro dissolution.

SEM Image of AnyCoat CN10T.

RESULTS

- The results of powder properties of polymer and MCC (Table 2) showed acceptable compressibility index but “very poor” and “passable” powder flow, respectively, according to the USP flow definition. Conversely, metformin HCl granules demonstrated “good” flow properties (as per USP flow definition) but a poor compressibility index.
- The **polymer demonstrated excellent tabletability** with lower ejection pressure when compressed at a wide range of compaction pressures (Figure 1). The ejection pressure results of the ER formulations showed that an increase in polymer level in the formulation led to a reduction in ejection pressure (Figure 2A). Tensile strengths greater than 1.5 MPa were observed for all formulations when compressed at compaction pressures exceeding 150 MPa (Figure 2B), indicating **acceptable mechanical integrity** of the tablets. The tensile strength of the tablets decreased with reduced levels of MCC in the formulation.
- Drug release profiles for **tablets prepared at 250 MPa compaction pressure** for all batches were evaluated in 900 mL of 6.8 pH phosphate buffer using USP II dissolution apparatus at 100 rpm paddle speed. The results demonstrated that **similar drug release profiles observed from all formulations**, regardless of polymer concentration in formulation (Figure 3). The similarity factor results **confirmed no significant difference between formulations** prepared using 20% and 40% AnyCoat CN10T (f_2 **= 67.9**).
- Drug release from metformin ER tablets followed **both Higuchi and first-order kinetics** (Table 3) where Fickian diffusion was the main mechanism of drug release. The combination of these two release mechanisms can be attributed to the nature of the HPMC matrix. The drug release is primarily governed by diffusion of the drug through the gel layer (Higuchi model). As the drug concentration within the matrix decreases over time, the release rate becomes more dependent on the remaining drug concentration, fitting the first-order kinetic model.

Table 1: Metformin HCl 500 mg ER Tablet Formulations

Ingredients	Application	Quantity %w/w		
		A	B	C
Metformin HCl DC Granules	API	55.56	55.56	55.56
Hypromellose K100M (AnyCoat CN10T)	Release rate controlling polymer	20.00	30.00	40.00
Microcrystalline Cellulose (MCC) (PH-102)	Diluent	23.94	13.94	3.94
Magnesium Stearate	Lubricant	0.50	0.50	0.50
Total		100.0	100.0	100.0

Table 2: Powder Properties of Metformin HCl DC Granules, AnyCoat CN10T and MCC.

Formulation	% LOD	Bulk Density (g/mL)	Tapped Density (g/mL)	Compressibility Index (%)	Particle size distribution (µm)			
					D10	D50	D90	D (4,3)
Metformin HCl DC Granules	1.76 ± 0.1	0.64 ± 0.0	0.76 ± 0.0	15.92 ± 0.1	26	278	806	357
AnyCoat CN10T	3.87 ± 0.2	0.31 ± 0.0	0.46 ± 0.0	32.58 ± 0.6	34	100	219	115
Microcrystalline Cellulose (MCC) PH-102	4.94 ± 0.0	0.33 ± 0.0	0.44 ± 0.0	24.13 ± 0.6	37	119	236	129

Table 3: Drug Release Kinetic for Metformin HCl Tablets.

Formulation with:	R Square Value for different mathematical model				
	Zero Order	First Order	Higuchi	Hixson-Crowell	Korsmeyer-Peppas
20% AnyCoat CN10T	0.9550	0.9995	0.9962	0.9525	0.9766
30% AnyCoat CN10T	0.9652	0.9990	0.9987	0.9594	0.9794
40% AnyCoat CN10T	0.9669	0.9989	0.9997	0.9594	0.9799

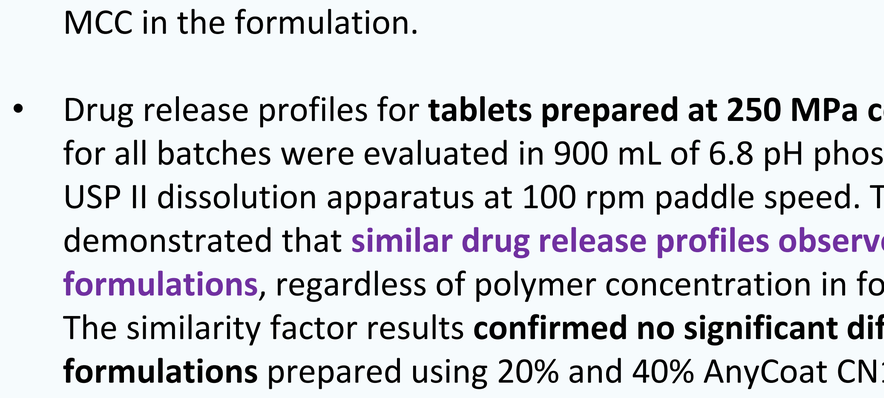

Figure 2: Tablet Properties of AnyCoat CN10T

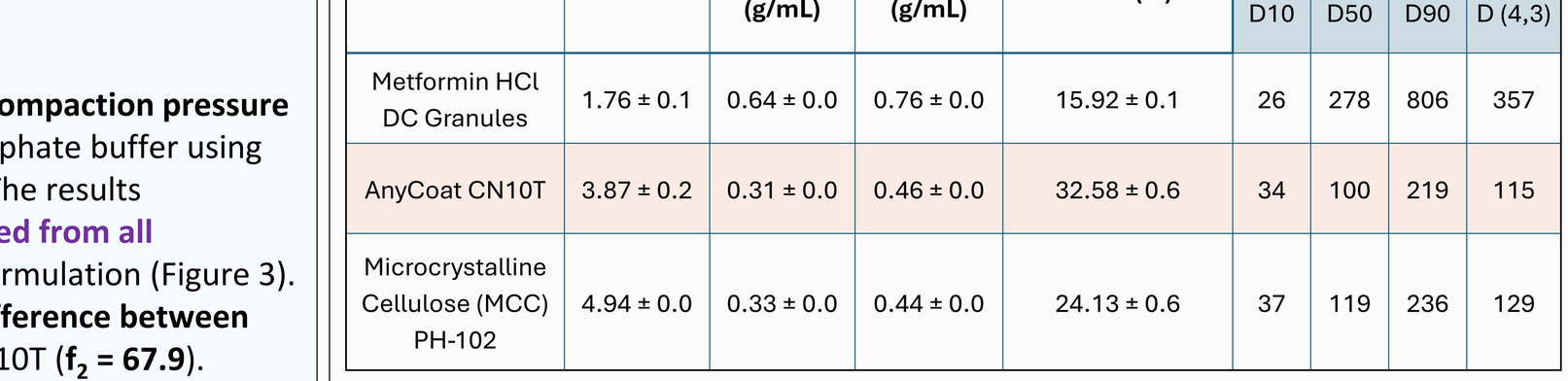

Figure 3: Tablet Properties of Metformin HCl ER Tablets
A) Ejection pressure profile, B) Tabletability Profile

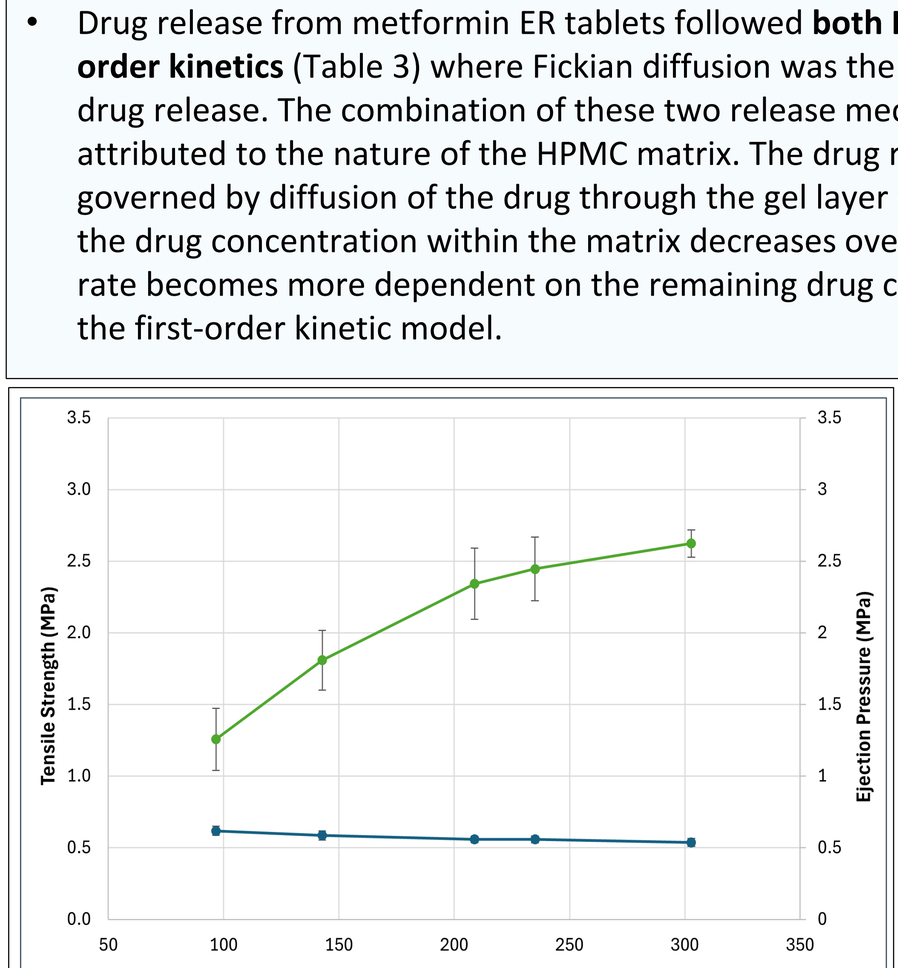

Figure 4: *In-Vitro* Drug Dissolution Profile for Metformin HCl ER Tablets

CONCLUSION

- For the highly soluble drug metformin HCl, the **release profile was unaffected** by concentration of the polymer above a threshold of 20% inclusion level.
- The polymer level, however, affected the mechanical properties of tablets with a reduction in ejection pressure and tablet tensile strength.
- The formulations with different levels of AnyCoat CN10T demonstrated **good tabletability with robust drug release profiles.**

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