The Effect of Superdisintegrant on Acid Resistance of Enteric Coated Tablets

INTRODUCTION

Superdisintegrants are frequently used in tablet core formulations intended for enteric coating. The influence of superdisintegrant types and levels on the performance of two enteric coated tablet formulations have been investigated.

METHODS AND MATERIALS

A soluble filler [91-98% (w/w) lactose, FastFlo] or insoluble filler (91-98% (w/w) microcrystalline cellulose, (MCC), Emcocel 90M) was blended with a flow aid [0.5% (w/w) colloidal silicon dioxide, Cab-O-Sil] and varied levels of superdisintegrant [1-6% (w/w) croscarmellose sodium, Ac-Di-Sol] or [1-8% (w/w) sodium starch glycolate, Explotab], in a V-blender for 10 minutes. Lubricant (0.5% (w/w) magnesium stearate, Mallinckrodt) was added and blended for an additional 3 minutes.

Placebo tablets were manufactured by direct compression on a Piccola 10 station rotary tablet press using 2 stations of 9/32" (7.144mm) standard concave tooling. The tablets' physical characteristics including weight, thickness, hardness, and friability were measured. Tablets were coated in 1.2kg batches using a Thomas Compu-Lab fully perforated 15" pan. Tablets were coated with Acryl-EZE®, aqueous acrylic enteric system, 93F19255, fully formulated enteric film coating system, with or without a seal coat (3% theoretical weight gain of Opadry®, high performance film coating system, 03K19229), to theoretical weight gains of 8-14%.

Acid uptake was determined after two hours in a USP disintegration apparatus containing 900ml of 0.1N HCl at 37±2°C. Six tablets were individually weighed prior to testing. After two hours in 0.1N HCl, the excess medium was removed from the tablets and the tablets were individually weighed again. The difference between the weights, expressed in percent, was reported as acid uptake, defined as the (w/w) % of acid medium taken up by the dosage form. Following the acid phase, disintegration time in pH 6.8 phosphate buffer was recorded.

RESULTS AND DISCUSSION

Tablets were similar in weight (221mg±5.6), diameter (7.05mm±0.1), thickness (5.00mm±0.5) and friability (0.11%±0.17). The MCC/Explotab tablet cores were harder (36.7-40.5kp) than the MCC/AcDiSol or lactose formulation cores (19.2-28.9kp). No other physical differences were observed between the formulations. The hardness and disintegration (in 0.1N HCl) data for the cores is listed in Tables 1 and 2.

Table 1. Lactose Cores: Disintegration Time (DT) in 0.1N HCl, n=6

Formula No.	Explotab (% w/w)	AcDiSol (% w/w)	Hardness (kp)	D.T. (min)
1	0	0	22.6	17
2	1	0	22.9	11
3	4	0	20.6	7
4	8	0	23.6	4
5	0	1	24.1	11
6	0	3	22.4	7
7	0	6	19.2	4

Table 2. MCC Cores: Disintegration time (DT) in 0.1N HCl, n=6

Formula No.	Explotab (% w/w)	AcDiSol (% w/w)	Hardness (kp)	D.T. (min)
8	0	0	28.5	> 180
9	1	0	36.7	4
10	4	0	37.4	2
11	8	0	40.5	2
12	0	1	26.7	4
13	0	3	28.9	2
14	0	6	26.6	2

The physical characteristics of the tablets (i.e. size, shape, hardness) remained unchanged when acid uptake was less than or equal to 10%. Tablets showed evidence of disintegration, cracking or softening, when acid uptake was greater than 10%. Therefore, acid uptake of less than 10% was considered acceptable.

Adding superdisintegrant to tablets with a soluble filler (lactose) resulted in high acid uptake (>12%) across all superdisintegrant levels and all theoretical enteric weight gains (8-14%). However, the application of a 3% theoretical seal coat reduced acid uptake (<9%) across all superdisintegrant levels and all enteric weight gains (Figures 1 and 2). Superdisintegrant decreased the mean disintegration time in pH 6.8 buffer from 25 to 7 minutes.

Figure 1. Acid Uptake, Lactose and Explotab

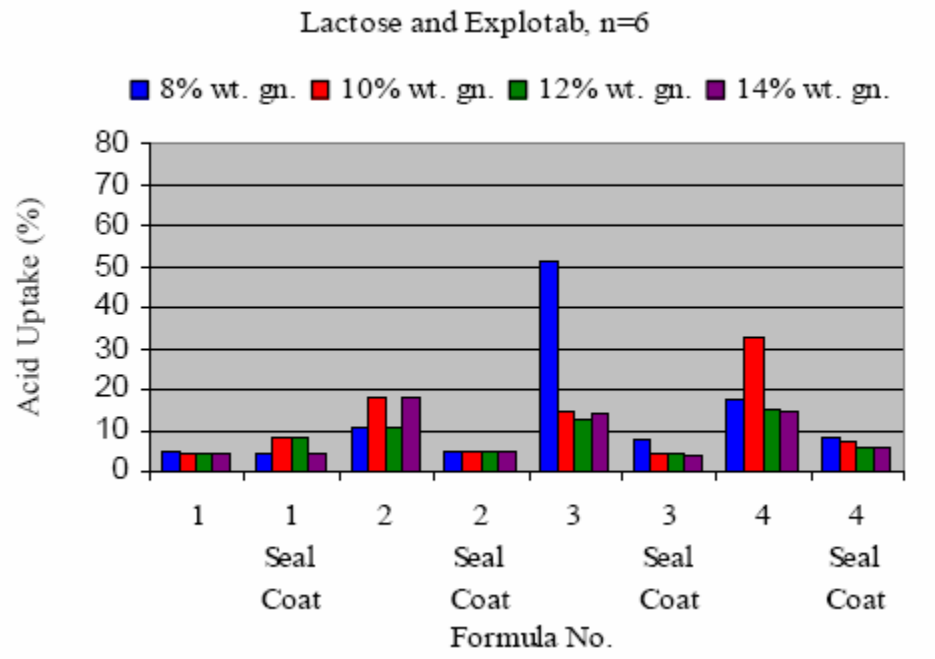
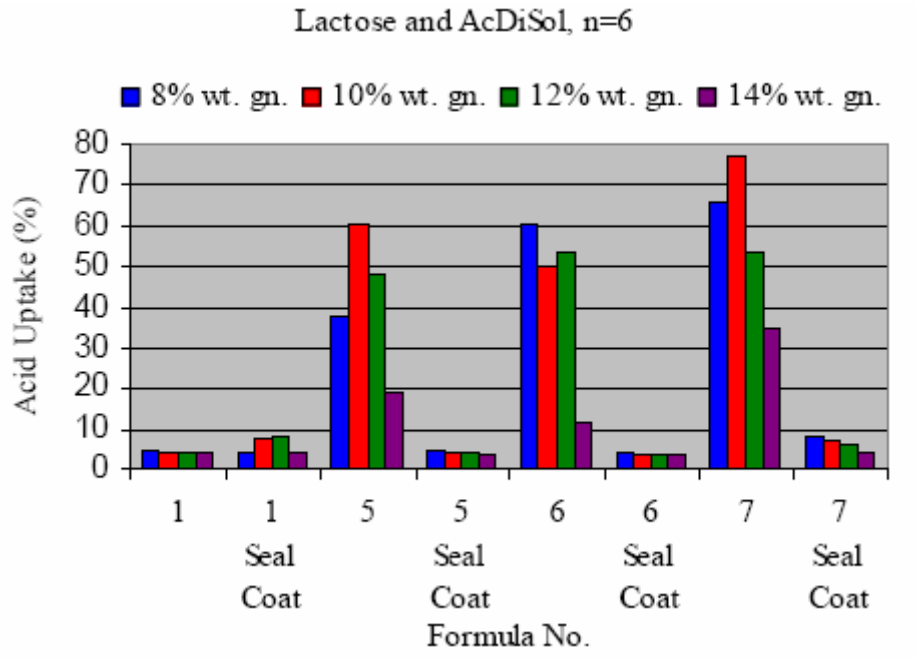


Figure 2. Acid Uptake, Lactose and Ac-Di-Sol



Adding superdisintegrant to tablets with an insoluble filler (MCC) resulted in low acid uptake (<10%) across all superdisintegrant levels and all theoretical enteric weight gains (8-14%). No differences were observed between seal coated and non-seal coated tablets (Figures 3 and 4). Superdisintegrant decreased the mean disintegration time in pH 6.8 buffer from 3 hours to 17 minutes.

Figure 3. Acid Uptake, MCC and Explotab

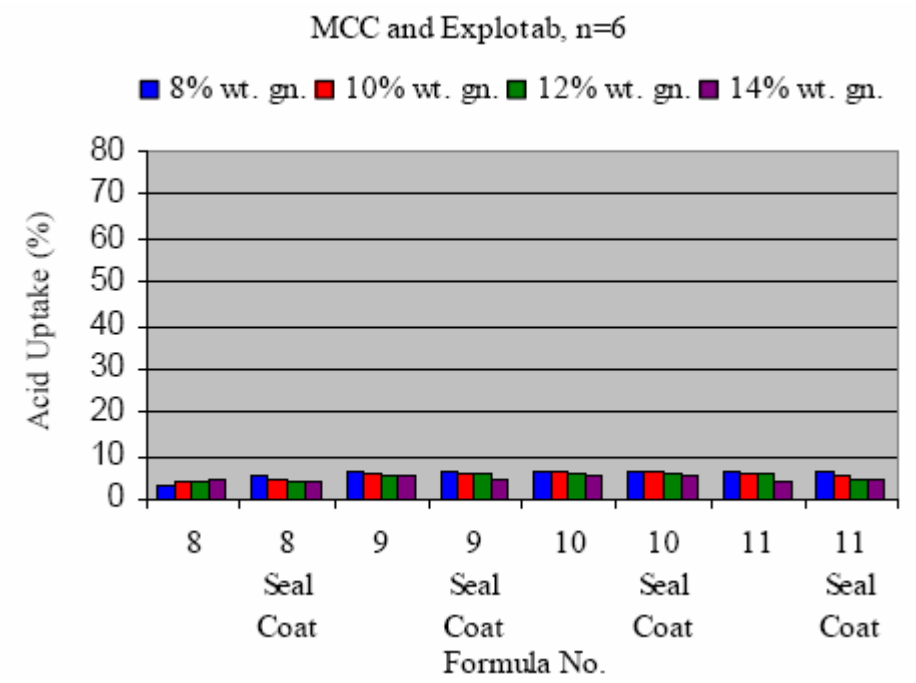
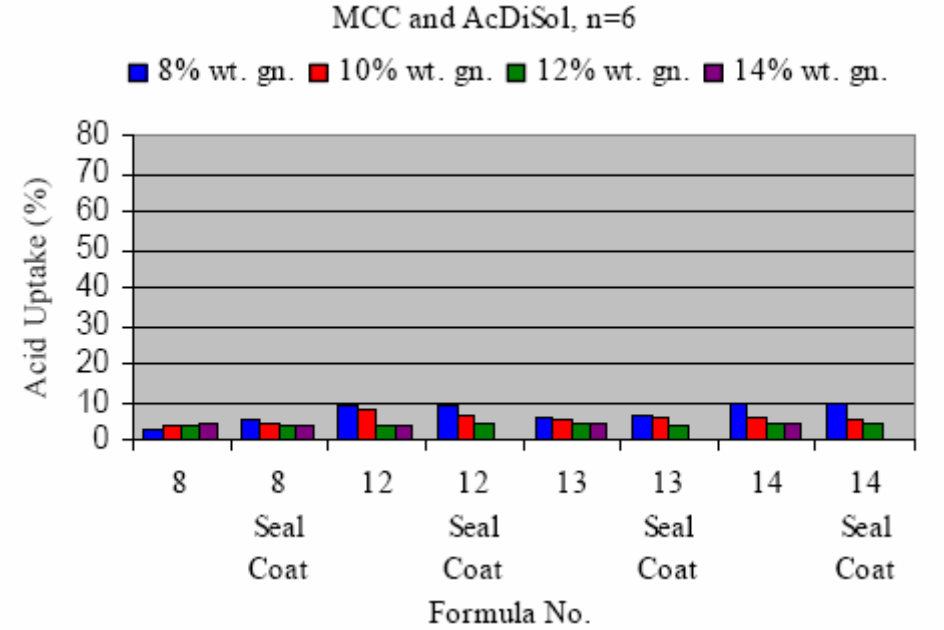


Figure 4. Acid Uptake, MCC and Ac-Di-Sol



CONCLUSIONS

Superdisintegrants reduced the acid resistance of cores containing a soluble filler (lactose) unless a seal coat was applied. Superdisintegrants do not affect acid resistance of cores containing an insoluble filler (MCC), with or without a seal coat. Tablets containing Explotab had better acid resistance than those containing Ac-Di-Sol. Increasing the weight gain of the enteric coating improved acid resistance regardless of filler type or superdisintegrant level

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