DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 17(15), 2093-2102 (1991)

AN EVALUATION OF SMECTA AS A TABLET DISINTEGRANT AND DISSOLUTION AID

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ABSTRACT

Smecta is a nonfibrous Attapulgite (NFA), mostly composed of smectite. It was evaluated as a disintegrant in tablets made by direct compression as well as by wet granulation and using lactose and dicalcium phosphate as water soluble and water insoluble fillers, respectively. An inorganic clay, magnesium aluminum silicate (Veegum), a modified starch (Starch 1500), a cross-linked carboxymethyl cellulose (Ac-Di-Sol), and a cross-linked polyvinylpyrrolidone (Polyplasdone XL) were used for comparative evaluation. Smecta performed well as a disintegrant in tablets made by either method. It was superior to Veegum and Starch 1500, but inferior to Ac-Di-Sol and Polyplasdone XL. In tablets with Smecta, dissolution of hydrochlorothiazide (HCTZ) was superior to those with Ac-Di-Sol.

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INTRODUCTION

The increasing attention being given to bioavailability and generic equivalence has further emphasized the importance of rapid disintegration as a criterion for uninhibited drug dissolution of poorly soluble drugs. A review of various disintegrating agents was published by Shangraw et al (1) and disintegrant properties of modified starch (2), carboxylmethyl cellulose (3), and polyvinylpyrrolidone (4) have been described. Starch and modified starch improve disintegration but may create new set of physicochemical problems (5). Pharmaceutical grade clays, namely Bentonite, Kaolin and magnesium aluminum silicate have been evaluated as disintegrants in tablets and were found to be satisfactory disintegrants (6-9).

Smecta is a clay mostly composed of Smectite, a nonfibrous Attapulgite. It belongs to the mineral family of montmorillonite. It differs from Veegum in its chemical composition and leaf-like crystalline structure. Its layered leaf-like structure consists of an aluminum octahedral layer sandwiched between two tetrahedral silica layers. Silica tetrahedrons are linked together to form layers and aluminum octahedrons are organized in the same way (10). Smecta has a large specific area and high affinity for water. It is physiologically and chemically inert. Oza et al.(11) found Smecta more adsorptive than other antidiarrheal clays, namely fibrous Attapulgite and Kaolin. All these properties suggested Smecta's potential as a disintegrant and dissolution aid in pharmaceutical tablets.

The purpose of our research was to evaluate Smecta as a disintegrant and compare its disintegrant properties to Starch 1500, Ac-Di-Sol, Polyplasdone XL, and Veegum.

Further, Smecta was also evaluated as a dissolution aid in tablets.

EXPERIMENTAL

Materials:

Pharmaceutical grade Smecta[1] was used as received from the supplier. Other materials used were: anhydrous lactose (Lactose DT)[2], hydrous lactose USP[2], dicalcium phosphate dihydrate (Di-Tab)[3], magnesium stearate NF[4], cross-linked carboxymethyl cellulose (Ac-Di-Sol)[5], cross-linked polyvinylpyrrolidone (Polyplasdone XL)[6], modified starch (Starch 1500)[7], magnesium aluminum silicate (Veegum)[8], hydrochlorothiazide[9], 0.1N hydrochloric acid[10] and gelatin[11]. All materials were compendial grade, wherever applicable.

Formulations:

The formulations used to study the disintegrant properties of Smecta in tablets prepared by direct compression and wet granulation are listed in Tables I and II, respectively. Evaluation of 5% Smecta as a dissolution aid was performed using HCTZ as a model drug in tablets prepared by direct compression and containing Di-Tab as a insoluble filler. The dissolution profiles of these tablets were compared to those without any disintegrant, and to those prepared similarly and containing 5% Ac-Di-Sol.

Direct compression:

Batches of various formulations (500 gm) were prepared by mixing filler, disintegrant and HCTZ, wherever applicable, in a cube blender[12] at 25 rpm for 5 minutes.

TABLE I
Direct Compression Tablet Formulations of Smecta

Ingredients	Weight Percent			
1. Smecta	0.0	5.0	7.5	10.0
2. Filler (Lactose DT or Di-Tab)	99.5	94.5	92.0	89.5
3. Lubricant (Magnesium Stearate)	0.5	0.5	0.5	0.5

TABLE II
Wet Granulation Tablet Formulations of Smecta

Ingredients	Weight Percent		
1. Smecta	0.0	5.0	10.0
2. Filler (Hydrous Lactose[a] or Di-Tab[b])	99.5	94.5	89.5
3. Lubricant (Magnesium Stearate)	0.5	0.5	0.5

[a] Water was used as granulating agent.

[b] A 10% gelatin solution was used as granulating agent.

Wet granulation:

Smecta was incorporated intragranularly in all wet granulation formulations. In tablets containing dicalcium phosphate as filler, a 10% gelatin solution was used as granulating agent, while water was used to granulate hydrous lactose. The weighed quantities of Smecta and filler were mixed in a hobart blender[13] at 25 rpm for 5 minutes. The blend was granulated and the wet mass was passed through U.S. Sieve #10[14]. The granules were dried at 120°F for 12 hours in a tray dryer[15] and dry screened through U.S. Sieve #14[14].

Tableting:

Magnesium stearate was mixed with the blends obtained from either process in a cube blender[12] at 25 rpm for 3 minutes. The blend was compressed on a rotary tablet press[16] using 7/16" standard concave tooling to give a hardness of 8-10 kp and weight of 500 mg.

Test Procedures:

The weights of twenty tablets were determined using a top-loading balance[17]. The hardness of ten tablets was determined using a tablet hardness tester[18]. Friability was determined using a Roche friabilator[19]. Disintegration times were determined according to the test procedure of USP XXI for uncoated tablets in water (12). Dissolution studies[20] were conducted according to the specifications of the USP XXI monograph on HCTZ tablets (13). All tests were performed after allowing the tablets to age for at least 48 hours.

RESULTS AND DISCUSSION

In general, there were very few differences in the variability of tablet weight and hardness among

TABLE III

Comparative Disintegration Time of Tablets

Direct Compression :

Disintegrant	% w/w	Disintegration time (minutes)	
		Di-Tab	Lactose DT
Control	0.0	>30.00	19.50
Smecta	5.0	2.95	5.50
	7.5	1.12	3.25
	10.0	0.60	1.50
Veegum	5.0	7.16	7.50
Starch 1500	5.0	0.71	7.40
Ac-Di-Sol	5.0	0.15	0.52
Polyplasdone XL	5.0	0.10	0.35

TABLE IV

Comparative Disintegration Time of Tablets

Wet Granulation :

Disintegrant	% w/w	Disintegration time (minutes)	
		Di-Tab	Hydrous Lactose
Control	0.0	>30.00	15.60
Smecta	5.0	4.10	5.00
	10.0	3.18	5.00
Veegum	5.0	6.20	8.60
Starch 1500	5.0	5.20	6.00
Ac-Di-Sol	5.0	0.80	2.25
Polyplasdone XL	5.0	0.60	1.80

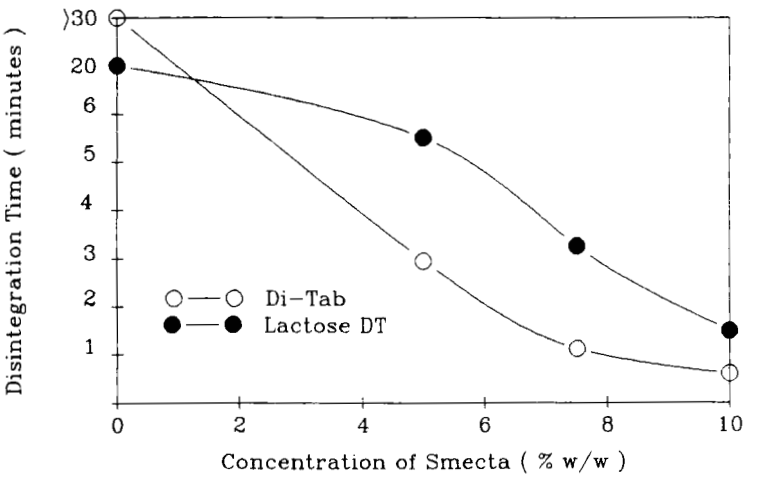

FIGURE 1

Plot of disintegration time versus concentration of Smecta in tablets made by direct compression using Di-Tab and Lactose DT as fillers.

formulations. For any given formulation, weight variation was less than 2%. The hardness value of all tablets remained within 1 kp of target value. The presence of Smecta did not have any significant effect on the hardness of tablets made by either method. In HCTZ formulations, the tablet hardness increased slightly for both disintegrants. The friability of tablets for all formulations was less than 1%.

Disintegration:

The effect of disintegrant types and their concentration on disintegration times of tablets is shown in Tables III and IV. Smecta gave significantly lower disintegration times compared to tablets made without a disintegrant. An increase in the concentration of Smecta resulted in decreased disintegration time as shown in Figure 1. Tablets with Di-Tab as filler exhibited slower

disintegration times than tablets with hydrous lactose or lactose DT. Smecta at 5% and 10% levels exhibited superior disintegrant properties compared to Veegum in tablets prepared by either method. Ac-Di-Sol and Polyplasdone XL exhibited superior disintegrant properties compared to Smecta. Smecta exhibited slightly superior disintegrant properties to Starch 1500 in tablets prepared by wet granulation, but not in tablets prepared by direct compression.

Dissolution:

The amount of HCTZ dissolved in 30 minutes was 100%, 84% and 29.5% from tablets containing Smecta, Ac-Di-Sol and no disintegrant,respectively. Smecta significantly increased the dissolution of HCTZ and was a superior dissolution aid than Ac-Di-Sol.

SUMMARY

Smecta appears to perform well as a disintegrant in tablets made by direct compression as well as wet granulation. It does not adversely affect the compressibility or the friability of tablets. Smecta was found to be a superior than Veegum in tablets prepared by either method. Smecta does not compare favorably with Ac-Di-Sol and Polyplasdone XL in its disintegration action. However, it significantly enhances the dissolution of HCTZ compared to Ac-Di-Sol.

ACKNOWLEDGEMENTS

The Authors are grateful to Ipsen Beaufour International, Paris, France for their generous financial support. This work was presented at the Japan-United States Congress of Pharmaceutical Sciences (JUC '87) in Honolulu, HI, December, 1987.

FOOTNOTES

1. Ipsen-Beaufour, Paris, France.
2. Humko Shefield, Lyndhurst NJ.
3. Stauffer Chemical Co., Westport, CT.
4. Mallinkrodt, Inc. St. Louis, MO.
5. FMC Corporation, Food & Pharmaceutical Division, Philadelphia, PA.
6. GAF Corporation, Wayne, NJ.
7. A.E.Stanley Co., Decatur, IL.
8. R.T.Vanderbilt & Co., Norwalk, CT.
9. Ciba Geigy, Inc., Summit, NJ.
10. Fisher Scientific Co., Malden MA.
11. Atlantic Pharmaceutical Co., Woburn, MA.
12. Erweka model KB-15 Cube Mixer, Erweka Apparatebau, G.M.B.H., W. Germany.
13. The Hobart Manufacturing Co., Troy, OH
14. Newark Wire Cloth Co., Newark, NJ.
15. Model #1330-2-T2, Lydon Brothers, Hackensack, NJ.
16. Model B-2, Stokes Division, Pennwalt Corp., Westminster, PA.
17. Model 7124A, Fisher Scientific Co., Malden, MA.
18. Schleuniger Hardness Tester, Model 2E, Dr. K. Schleuniger & Co., Solothurn, Switzerland.
19. Vankel Industries, Chattam, NJ.
20. Hansen Research Corp., Northridge, CA.

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13. United States Pharmacopeia XXI and National Formulary XVI, U.S. Pharmacopeial Convention, Inc., Rockville, MD, 1985, p.497.