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EVALUATION OF POWDERED CELLULOSE AS A DIRECT COMPRESSION CARRIER

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ABSTRACT

The feasibility of the use of Solka Floc® as a direct compression carrier was investigated. The powder characteristics of the six grades of Solka Floc were evaluated and compared to Avicel®. Various parameters studied, include, particle size, bulk density, moisture content, and flow characteristics. The compressional characteristics were investigated for Solka Floc. The particulate grade of Solka Floc in combination with Avicel had an adequate compressional characteristics. Tablets were made with acetaminophen from combination of Solka Floc and Avicel and from Avicel alone. The tablets from both formulations were comparable with respect to weight variation, hardness variation, thickness variation, friability, and disintegration time.

The dissolution of acetaminophen from the formulation with Solka Floc was faster than from tablets with Avicel alone.

INTRODUCTION

Direct compression is the most advanced and economical process for the production of tablets (1). Some of the advantages offered by direct compression are its simplicity, reduction in production cost, in terms of labor, equipment and personnel requirement. One of the greatest advantage is the unique "biologic availability" potential, since there is essentially no change in the physical or chemical form of the drug incorporated (2).

A direct compression carrier is an inert substance possessing adequate flow and compressional characteristics. Direct compression carriers recently available include mannitol, sorbitol, spray dried lactose and microcrystalline cellulose. Solka Floc[1] is a powdered cellulose product which is primarily used in processed food, food products and some pharmaceutical products. Although some reports indicate that Solka Floc possibly may be used as a direct compression carrier, a diluent or as a disintegrant (3,4) the experimental data is scanty. Therefore, the present study is concerned with the investigation of the feasibility of Solka Floc as a potential direct compression carrier.

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1 A powdered cellulose product manufactured by Brown Co., Berlin, N.H.

EXPERIMENTAL

Particle Size Determination:

Particle size of the six grades[1] of Solka Floc and Avicel[2] was determined by the conventional seive shaker[3] method comprising of the seives ranging from 840-37 μm. From the data obtained the arithmatic mean of the particle size of each grade was computed.

Bulk Density:

Bulk density was determined by the method suggested by Butler and Ransey (5). From the bulk density of the bulk (ml/gm) was calculated.

Moisture Content:

The moisture content (expressed as loss on drying) was determined on the Ohaus Moisture Determination Balance[4]. The settings on the appartus were adjusted so as to acquire a temperature of 104°C for drying.

Flow Characteristics:

a) Angle of Flow: Dry angle flowmeter[5] was used for the determination of angle of flow. The method essentially involved developing an angle on a fixed base just enough to make the powder flow.

1 Solka Floc pharmaceutical grades BW40,BW60,BW200,BW300,BW2030 and Particulate (granular).
2 Avicel PH101 manufactured by F.M.C. Corporation.
3 Erewka Sieve Shaker, Erweka Apparatebau G.m.b.H.
4 Ohaus Moisture Determination Balance, Ohaus Scale Corporation,N.J.
5 Dry Angle Flowmeter, Bolar Incorporated, Derry,N.H.

b) Angle of Repose: The angle of repose was determined by the method described by Train (6). A fixed weight of the powder was allowed to flow through the funnel so as to form a heap. From the height and the diameter of the heap the angle of repose was determined.

Evaluation of the Compressional Characteristics:

The study of the compressional characteristics was accomplished on an instrumented rotary tablet press[1] at five levels of compressional forces using 1.111 cm (7/16 in) circular standard concave punches.

The compressional characteristics was evaluated for the six grades of Solka Floc and Avicel was used as control. Since the finer grades (BW40, BW60, BW200, BW300, and BW2030) of Solka Floc had a poor flow characteristics, further study was restricted to the particulate (granular) Solka Floc. Due to the inadequate compressional characteristics of the particulate floc, alone, various combinations of this grade with a direct compression carrier (Avicel) and co-dried binder was evaluated. Based on the preliminary findings a complete pressure-hardness and pressure-disintegration time profiles were generated on the five formulations summarized in Table I.

Tabletting with Test Drug:

For further studies Acetaminophen was used as a test drug to produce tablets formulated with the combination of Solka Floc

1 Stokes Rotary Tablet Press Model B2 equipped with strain guages and Dual Beam Tektronix Oscilloscope.

TABLE I

PRELIMINARY FORMULATION FOR THE EVALUATION OF COMPRESSIONAL CHARACTERISTICS

Formulation A	Particulate Solka Floc alone	
Formulation B	Particulate Solka Floc with 1% Carbowax 6000	
Formulation C	Particulate Solka Floc	89%
	Co-dried binder*	10%
	Carbowax® 6000	1%
Formulation D	Particulate Solka Floc	49.75%
	Avicel PH101	49.75%
	Magnesium Stearate	0.50%
Formulation E	Avicel PH101 with 0.5% magnesium stearate	

• Corn Starch	24.4%
Sucrose	73.1%
Agar	2.5%

and Avicel as well as with Avicel alone. The composition of the formulations are summarized in Table II.

Evaluation of The Tablets:

The tablets were physically evaluated on the basis of weight variation, hardness variation, thickness variation, friability and disintegration time. The tablets were also evaluated for the content uniformity. Acetaminophen was assayed according to the U.S.P. XIX (7).

The two formulations were evaluated for the dissolution rate using the U.S.P. XIX procedure. The dissolution medium consisted of 900 ml of modified gastric fluid or water, maintained at 37°C in a constant temperature bath. The baskets were ro-

TABLE II

COMPOSITION OF ACETAMINOPHEN TABLET FORMULATION

Formulations	Ingredients (%)			
	D	C1	C2	L
I	65.0	13.2	19.8	2.0
II	65.0	---	33.0	2.0
III	----	39.2	58.8	2.0

D = Acetaminophen Granular U.S.P.
C1 = Solka Floc (Particulate)
C2 = Avicel PH 101
L = Polyethylene Glycol 6000

tated at 50 rpm. Samples of 2 ml were collected at 2, 4, 6, 8, 10, 15, 20, 30, 45 and 60 minutes. Each sample withdrawn was replaced by an equivalent amount of the dissolution medium. The samples after dilution were assayed by the method described in U.S.P. XIX. The dissolution rate was then computed for each formulation.

The formulations were also evaluated for their stability at elevated conditions of temperature and humidity. Tablets made from the combination of particulate Solka Floc and Avicel without acetaminophen were also kept under identical storage conditions to serve as control.

RESULTS AND DISCUSSIONS

The parameters evaluated and the results obtained are summarized in Table III.The average particle size of the fine

TABLE III

RESULTS OF THE POWDER CHARACTERISTICS OF SOLKA FLOC AND AVICEL

Physical Characters	Finer Grades BW 40	BW 60	BW 200	BW300	BW2030	Particulate (Granular)	Avicel PH 101
Avg. Part. size (um)	84.47	64.74	70.04	68.77	69.47	239.18	60.97
Bulk Dens. (gm/ml)	0.273	0.341	0.439	0.402	0.476	0.547	0.435
Bulk(ml/gm)	3.663	2.929	2.278	2.488	2.101	1.828	2.299
Angle of flow (°)	31.40	25.70	25.50	24.80	25.10	22.00	22.20
Angle of repose (°)	60.62	48.67	48.90	50.60	46.63	44.60	45.53
Loss on drying (%)	5.34	6.52	6.36	5.87	6.78	7.22	4.89

grades of Solka Floc was between 70 and 90 μm, which did not differ from that of Avicel (average size 61 μm). The average particle size of particulate floc was 239 μm, approximately 4 times larger than the particles of Avicel.

The bulk density of the finer grades was comparable to that of Avicel. The particulate floc was slightly denser than the other grades.

The moisture content of the finer grades was found to be between 5 and 7% (expressed as loss on drying), while that of Avicel was 4.9%. The maximum moisture content in the particulate floc was 7.2%.

Although the angle of flow for the finer grades of Solka Floc appear to be closer to that of Avicel the flow characteristics were not identical. Erroneous results were obtained due to the extensive electrostatic cohesiveness of the finer grades. Better evaluation could be made from the results of the angle of repose. Only particulate Solka Floc possessed the angle of repose close to that of Avicel. The better flow property of the particulate floc in comparison to the other grades could be attributed to relatively larger particle size.

The finer grades of Solka Floc, due to poor flow characteristics, were found unsuitable as direct compression carrier. The particulate Solka Floc, although having excellent flow property, did not possess the adequate compressional characteristics. One of the striking features observed was the loss of compressibility of particulate floc in the presence of magnesium stearate. For

this reason all further studies conducted on particulate floc were using Carbowax (Polyethylene Glycol) 6000 as lubricant.

From the pressure-hardness profile (Figure 1) it is evident that the particulate Solka Floc by itself is not a suitable direct compression carrier. The combination of particulate floc and avicel appeared a promising direct compression carrier. Even though a hardness of 23 SCU could be attained with Avicel (which is approximately 2.3 times greater than the blend*), at compressional force of 1000 kgs appears fascinating, however, in actual practice such high hardness are rarely desirable. The added advantage offered by the combination of floc and avicel is the rapid disintegration (which may lead to faster dissolution and hence absorption). Formulation C containing 10% co-dried gum also appears to be promising except for the delayed disintegration.

The results of the preliminary evaluation of the three formulations are summarized in Table IV. The weight variation of the three formulations were well within the compendial limits (i.e., 5%). The weight variation for the tablets made with the combination of floc and avicel were better than those made with avicel alone. This less weight variation was probably due to the better flowability of the particulate floc. The tablet hardness were 6-7 SCU. The compressional forces required to compress the tablets for this hardness was higher

* Blend of Particulate Solka Floc and Avicel

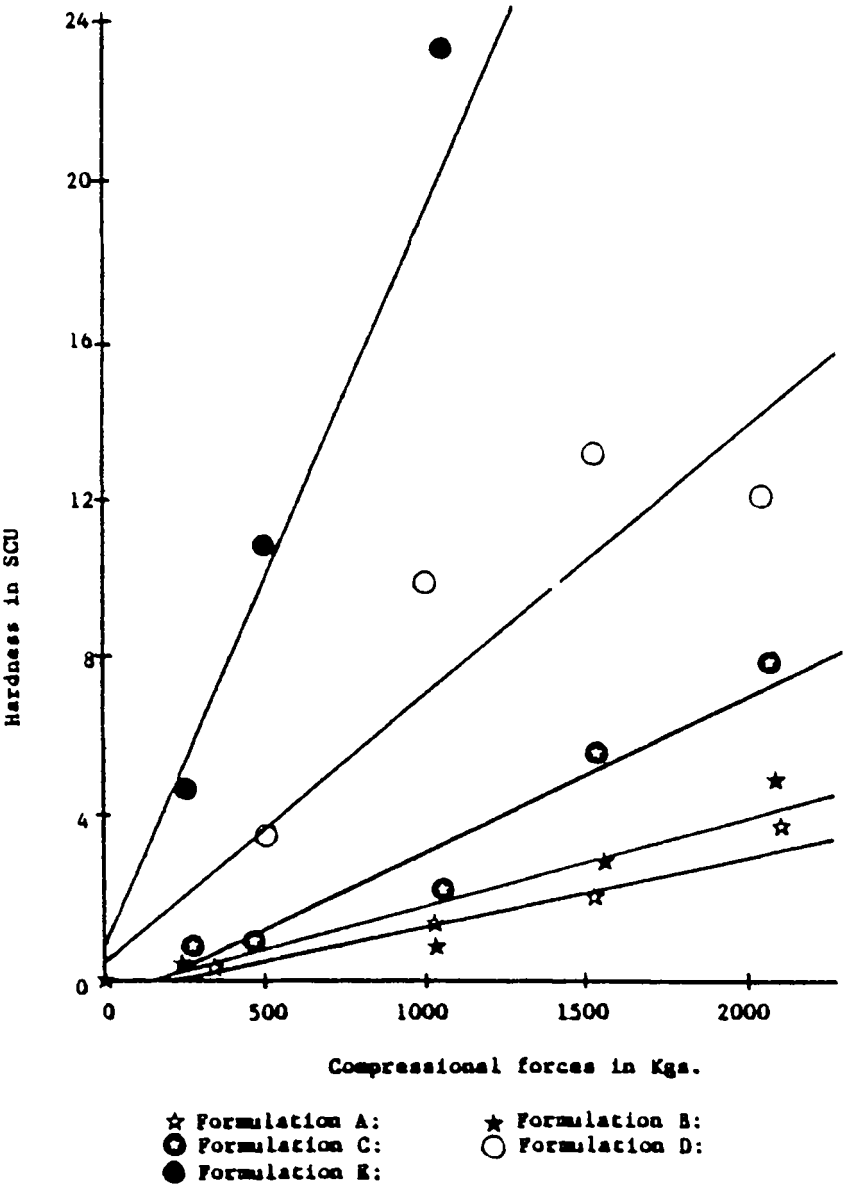

FIGURE 1
Pressure - Hardness Profile for Five Preliminary Formulations

TABLE IV

SUMMARY OF THE EVALUATION OF ACETAMINOPHEN TABLET FORMULATIONS

Parameters	Formulations		
	I	II	III
Comp. Force (Kgs)	1920	1570	1180
Ejection Force (kgs)	60	60	40
Avg.Weight*(mg) S.D.	504±5	512±9	496± 3
Avg. Hardness*(SCU) S.D.	6 ± 1	7 ± 1	6 ± 0
Avg.Thickness*(mm) S.D.	5.35 ± .03	5.43 ± .05	6.47 ± .03
Friability (%)	0.59	0.77	0.29
Disintegration Time (secs)	4	5	10
Content uniformity@ (%) S.D.	98.8 ± 1.4	103.3 ± 2.4	-----
Dissolution rate (mg/min)	0.191	0.109	-----

* Average of twenty determinations

@ Average of ten determinations

for formulation I than formulation II. Friability of the two formulations was within the range of 0.3 to 0.8%. The disintegration was extremely rapid for all the three formulations. Content uniformity, in either case, ranged from 98.8% to 103.3%, which were well within the compendial limits

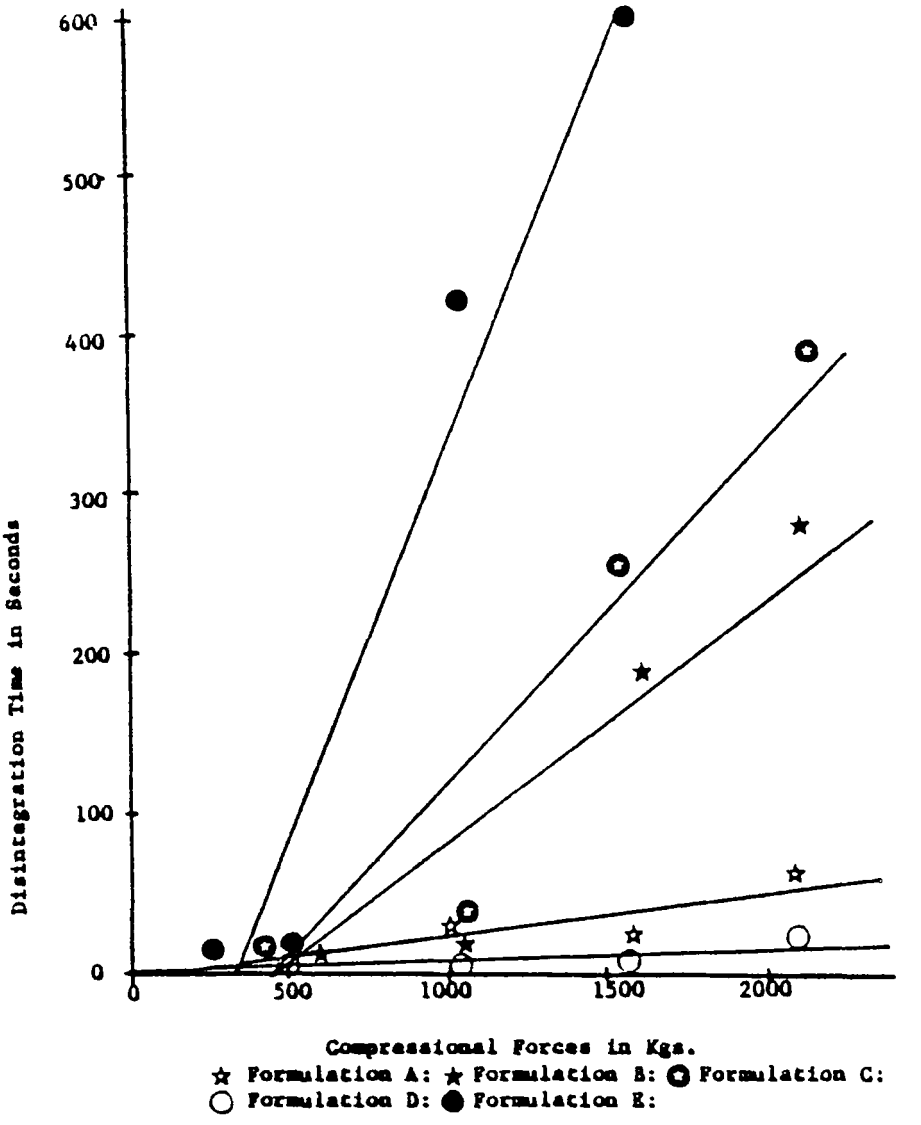

FIGURE 2
Pressure - Disintegration Time Profile for Five Preliminary Formulations

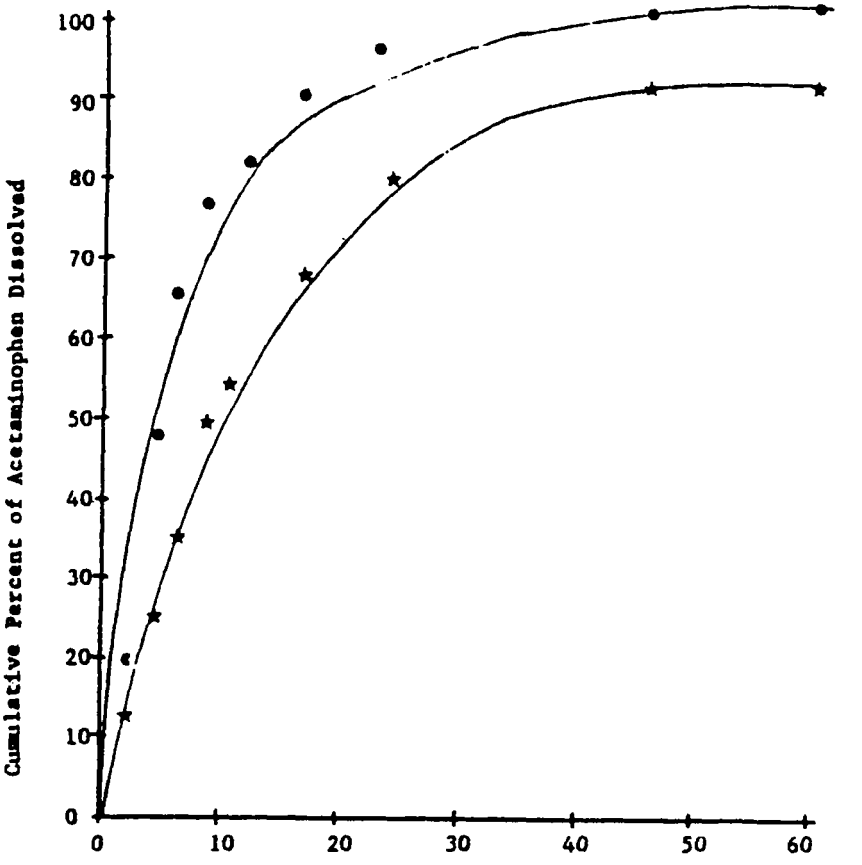

FIGURE 3

Mean Cumulative Percent Acetaminophen Dissolved vs. Time Plot

of 85-115%. The dissolution rate constant for the two formulations were found to be different. The formulation containing the combination of Solka Floc and Avicel was found to have a dissolution rate constant of 0.191 $min.^{-1}$, whereas,

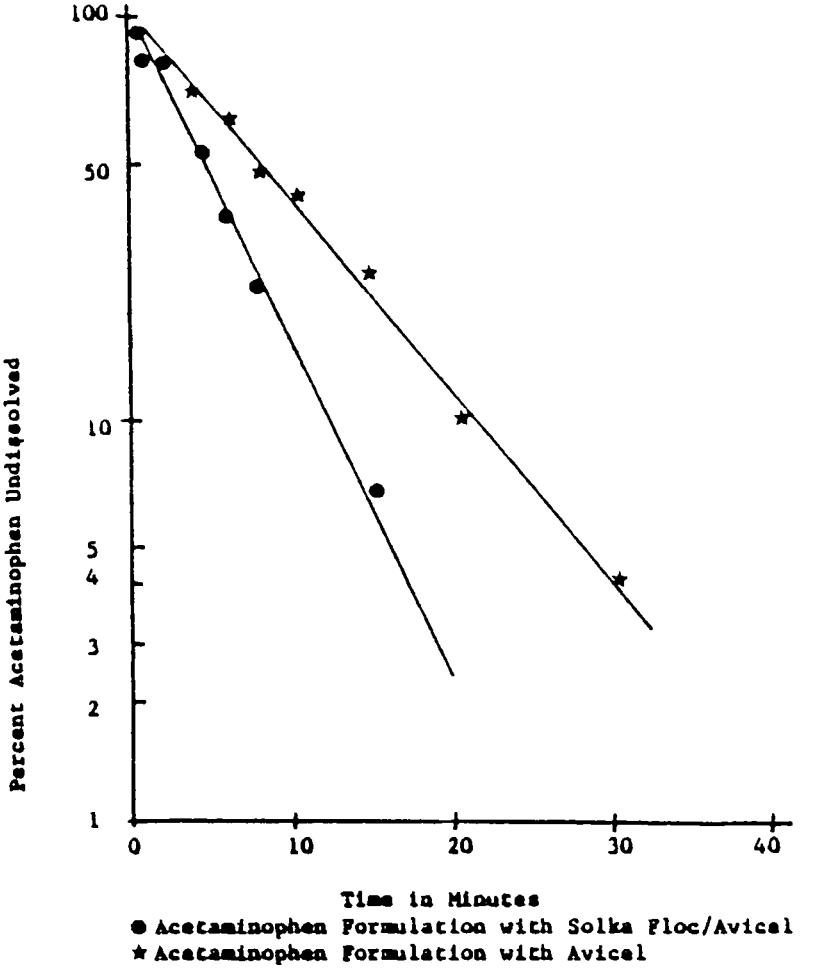

FIGURE 4

Plot of Log Percent Acetaminophen Undissolved Against Time

the formulation with only Avicel had a dissolution rate constant of 0.109 min.$^{-1}$. Similar results were observed when the dissolution study was performed with distilled water as the dissolution medium. The faster dissolution rate constant of the former might indicate a faster *in vivo* absorption.

CONCLUSIONS

The finer grades of Solka Floc are unsuitable as a direct compression carrier when used alone, due to their poor flow characteristics but could be used in combination with other direct compression carrier.

Combination of particulate Solka Floc and Avicel turned out to be an acceptable direct compression carrier. Tablet formulations made with this combination and avicel alone were comparable with respect to their physical evaluation such as weight variation, hardness variation, thickness variation, friability, disintegration time and content uniformity tests. The dissolution rate constant of APAP from tablets prepared with the Solka Floc-Avicel combination was better than that from tablets prepared with Avicel alone.

Replacement of 40% of Avicel with Solka Floc in a formulation may offer economic advantage. If the combination of Solka Floc and Avicel is used as a direct compression carrier, the dissolution medium used in the routine quality control, could be distilled water.

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