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# EVALUATION OF EMCOCEL® 50 AND EMCOCEL® 90, A NEW EXCIPIENT IN DIRECT COMPRESSION

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## ABSTRACT

The tabletting properties of a new microcrystalline cellulose product, Emcocel® 50 and Emcocel® 90 were evaluated and compared with the tabletting properties of Avicel® PH 101. The evaluation of placebo tablets, of the dilution potential, of formulations with active compounds as Aspirin, Phenobarbital and a spraydried extract in high concentrations showed that Emcocel® has comparative tabletting properties in regard of Avicel® PH 101.

## INTRODUCTION

The excellent binding properties of microcrystalline cellulose (Avicel® PH 101) are well documented (1-5). Recently new tablet binders, also microcrystalline cellulose, are introduced on the market, under the name of Emcocel® 50 and 90.

The purpose of this work was to evaluate the tabletting properties of these new products in comparison with Avicel® PH 101 in direct compression. For that purpose, active compounds, different in their physical properties were evaluated : an active product, special treated for direct compression (Asagran®), an active compound (Phenobarbital) without special treatments and a spraydried extract (Equisetum Arvense).

## EXPERIMENTAL

### Materials

The directly compressible binders used were : microcrystalline cellulose (Emcocel® 90[1], Emcocel® 50[1] and Avicel® PH 101[2]). As filler Lactose (Tablettose®[1]) and dicalciumphosphate dihydrate unmilled (Emcompress®[3] were used, Sodium Starch Glycolate (Explotab®[1]), Crosspovidone (Kollidon® Cl[4]) and cross-linked Sodium Carboxymethylcellulose (Ac-Di-Sol®[2] , as disintegrants, Magnesium Stearate[5] as lubricant. As active compounds, Aspirin (Asagran®[6], Phenobarbital[7] and Equisetum Arvense spraydried extract[8] were employed.

### Methods

Preparation of Placebo Tablets. To 100 % binder, glidant was added, mixed[9] for 1 minute and compressed. The compression forces used were 0.5, 1, 1.5, 2 and 4 kN respectively.

Effect of Blending Time of Glidant on Tabletting Properties. Binder and glidant were blended for 1, 2, 3, 10 and 20 minutes respectively. The compression force was maintained at 1.5 kN. Magnesium Stearate was added in a concentration of 1 and 2 %.

The Dilution Potential. For testing the dilution potential, 30 % and 70 % Phenobarbital or Asagran® were mixed with 70 or 30 % binder for 5 minutes, 1 % Magnesium Stearate was added and the mixture blended for 1 minute. The blend was compressed at 3 kN.

Preparation of Tablets Containing Active Compounds. All the tablet ingredients, except Magnesium Stearate were mixed for 5 minutes, the glidant added and mixing continued for 1 minute. Different compression forces were used.

Tablet Compression. Tablets were compressed on a single punch tabletting machine[10] fitted with flat punches 12 mm in diameter. The compression forces were measured with a piezoelectric cell[11].

Average Tablet Weight, Standard Deviation (S.D.) and Coefficient of Variation (C.V. %)

The uniformity of weight was tested ; 20 tablets were weighed individually, the average weight, standard deviation (S.D.) and coefficient of variation (C.V. %) were calculated.

Friability. Friability was measured with an Erweka friabilator[12]. Ten tablets were weighed, rotated for five minutes at 20r/min and reweighed after careful dusting. The percentage of tablet weight loss was calculated.

Crushing Strength. Crushing strength was measured with a Monsanto tablet hardness tester[13]. The data given are the mean of at least 10 tablets.

Disintegration Time. Disintegration time was done according the European Pharmacopoeia with an Erweka ZT 3 apparatus[12] in water at 37 °C without disks. The data are the mean of the disintegration times of 6 individual tablets.

Dissolution. Dissolution of tablets with active compounds was performed according to the USP XXI, using the paddle method. A buffer solution of pH 4.5, composed of Sodium Acetate.$3H_2O$[14] and Glacial Acetic Acid[14] (USP XXI) was used for the tablets containing Asagran®, a buffer of pH 7.6 composed of $Na_2HPO_4.2H_2O$[14], citric acid.$1H_2O$[14] for tablets containing Phenobarbital. The dissolution was determined at 37 °C and 50 rpm. At several time intervals samples were taken and analyzed spectrophotometrically[15], after appropriate dilution, at 239.5 nm for Phenobarbital, at 270 nm for Asagran®. The data given are the mean of at least two experiments.
Evaluation of tablets. Tablets were evaluated as follows: disintegration time : < 5 min., good, 5 - 10 min. sufficient, > 10 min. poor, friability maximum 1 %, crushing strength > 6 kg good, 3 - 6 kg sufficient, < 3 kg poor.
Infrared analysis. The infrared spectra were produced using a Perkin-Elmer[15] I.R.-spectrophotometer, mode 983, equipped with a F4.A monochromator with 4 gratings and 9 filters (abscissa range : 5000 - 180 $cm^{-1}$) and connected with a computer Perkin-Elmer Data Station, model 3600 and an alpha numeric/graphic printer, mode PR-100. The samples were prepared as KBr-pellets and scanned in the region between 4000 - 300 $cm^{-1}$, resolution 7.0.

## RESULTS

### Placebo Tablets

The results of the placebo tablets were given in Fig. 1 - 2 . For the three binders the crushing strength was, at a same compression force, approximately the same (Fig. 1). The compression force necessary to obtain tablets with crushing strengths of more than 6 kg was low: 1.5 kN was sufficient. The crushing strenght as a function of compression force was almost linear (Fig. 1).
Disintegration times of tablets prepared with Emcocel® 50 and Avicel® PH 101 were nearly the same, with Emcocel® 90 were less (Fig. 2). With Emcocel® 90 tablets, the increase of disintegration time as a function of compression force was less pronounced from 0.5 up to 2 kN. For the three binders, disintegration times were less than 3 minutes, excepted for the tablets at a compression force of 4 kN (> 30 minutes). At all the compression forces used, friability was good, (less than 1 % ) excepted with Avicel® PH 101 tablets at 0.5 kN: a friability of 1.2 % was determined.

### Effect of Mixing Time of Glidant on Tablet Properties

The results are given in Table 1. Crushing strength was diminished as a function of mixing time, most pronounced in the first three minutes of mixing time.

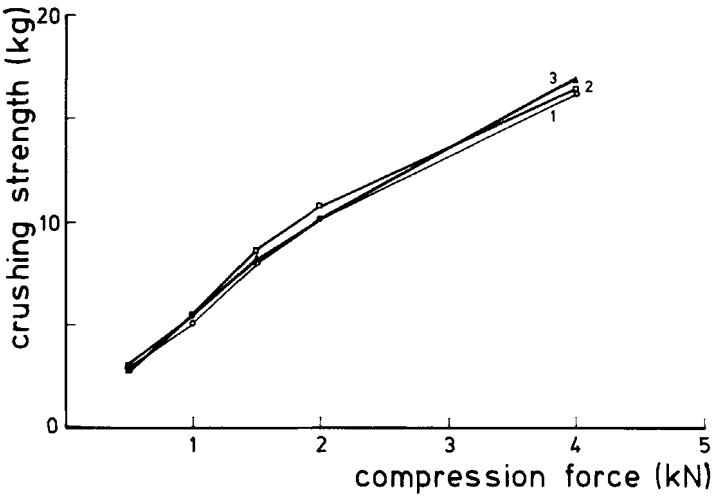


FIG. 1
Crushing Strength as a Function of Compression Force
1 = EMCOCEL® 50, 2 = EMCOCEL® 90, 3 = AVICEL® PH 101

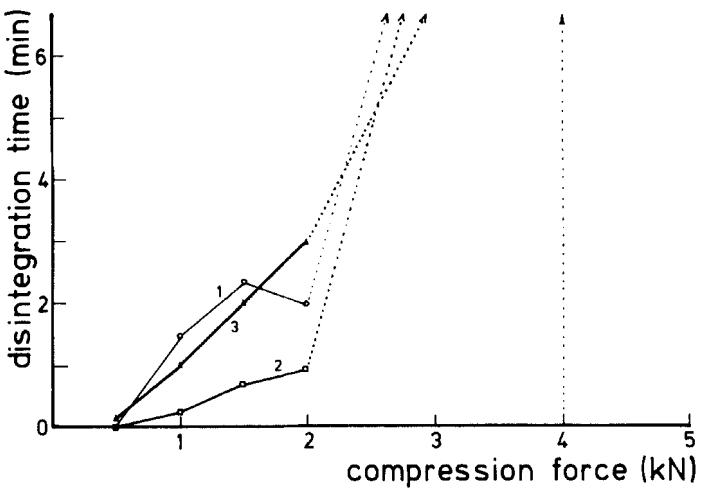


FIG. 2
Disintegration Time as a Function of Compression Force
1 = EMCOCEL® 50, 2 = EMCOCEL® 90, 3 = AVICEL® PH 101

TABLE 1
Effect of Mixing Time of Glidant on Tablet Properties

| Tablet Composition | | Mixing Time | Crush. Strength | Disintegr. Time | Friability | Weight | | |
|---|---|---|---|---|---|---|---|---|
| Binder | % Magn. Stearate | | (kg) | (min. sec) | (% ) | Mean (g) | S.D. (g) | C.V. (%) |
| Emcocel® 50 | 1 | 1 | 6.2 | 50" | 0.35 | .2901 | .0028 | 1.0 |
| | | 2 | 4.1 | 47" | 0.62 | .3214 | .0058 | 1.8 |
| | | 3 | 3.5 | 47" | 0.62 | .3316 | .0033 | 1.0 |
| | | 10 | 2.1 | 20" | 3.10 | .3525 | .0029 | 0.8 |
| | | 20 | 0.8 | 17" | 58.80 | .3499 | .0051 | 1.5 |
| Emcocel® 50 | 2 | 1 | 6.0 | 3' 11" | 0.70 | .2873 | .0035 | 1.2 |
| | | 2 | 4.1 | 54" | 1.59 | .3146 | .0026 | 0.8 |
| | | 3 | 2.9 | 28" | 1.24 | .3243 | .0017 | 0.5 |
| | | 10 | 1.3 | 1' 5" | 7.21 | .3459 | .0028 | 0.8 |
| | | 20 | 0.5 | 1' 37" | 86.18 | .3469 | .0045 | 1.3 |
| Emcocel® 90 | 1 | 1 | 6.0 | 1' 0" | 0.00 | .3045 | .0028 | 0.9 |
| | | 2 | 4.3 | 19" | 0.64 | .3123 | .0025 | 0.8 |
| | | 3 | 3.0 | 14" | 0.64 | .3169 | .0020 | 0.6 |
| | | 10 | 2.3 | 53" | 0.91 | .3301 | .0020 | 0.6 |
| | | 20 | 1.4 | 22' | 4.52 | .3312 | .0089 | 2.7 |
| Emcocel® 90 | 2 | 1 | 5.9 | 1' 20" | 0.65 | .3062 | .0015 | 0.5 |
| | | 2 | 3.9 | 1' 12" | 0.94 | .3189 | .0021 | 0.7 |
| | | 3 | 3.3 | 4' 51" | 0.00 | .3223 | .0027 | 0.8 |
| | | 10 | 3.0 | > 25' | 0.61 | .3304 | .0022 | 0.7 |
| | | 20 | 2.3 | > 30' | 1.22 | .3304 | .0037 | 1.1 |
| Avicel® PH 101 | 1 | 1 | 5.7 | 1' 40" | 0.00 | .2748 | .0034 | 1.2 |
| | | 2 | 5.1 | 2' | 0.35 | .2896 | .0042 | 1.5 |
| | | 3 | 4.2 | 1' 29" | 1.00 | .3049 | .0038 | 1.2 |
| | | 10 | 1.8 | 15" | 5.31 | .3400 | .0035 | 1.0 |
| | | 20 | 0.6 | 15" | 83.20 | .3343 | .0073 | 2.1 |
| Avicel® PH 101 | 2 | 1 | 5.6 | 1' 40" | 0.36 | .2752 | .0047 | 1.7 |
| | | 2 | 4.1 | 2' 20" | 0.67 | .2950 | .0032 | 1.1 |
| | | 3 | 3.3 | 1' 32" | 1.00 | .3054 | .0043 | 1.4 |
| | | 10 | 1.0 | 59" | 43.30 | .3335 | .0027 | 0.8 |
| | | 20 | 0.5 | > 30' | 92.20 | .3264 | .0147 | 4.5 |

TABLE 2
Properties of Tablets Containing 30 or 70 % Asagran®

| Concentr. Asagran® (%) | Binder Type | Conc. (%) | Crush. Strength (kg) | Disintegr. Time (min. sec) | Friability (%) | Weight Mean (g) | S.D. (g) | C.V. (%) |
|---|---|---|---|---|---|---|---|---|
| 30 | Emcocel® 50 | 70 | 14.7 | 14' | 0.00 | .3808 | .0086 | 2.3 |
| 30 | Emcocel® 90 | 70 | 12.7 | 2' 30" | 0.00 | .4071 | .0053 | 1.3 |
| 30 | Avicel® PH 101 | 70 | 10.7 | 10' | 0.00 | .3639 | .0136 | 3.7 |
| 70 | Emcocel® 50 | 30 | 14.5 | 3' 10" | 0.51 | .5955 | .0108 | 1.8 |
| 70 | Emcocel® 90 | 30 | 15.7 | 11' 55" | 0.36 | .5606 | .0079 | 1.4 |
| 70 | Avicel® PH 101 | 30 | 16.3 | 5' 40" | 0.33 | .6152 | .0169 | 2.7 |

The phenomenon of decreasing crushing strength with increasing mixing time of glidant was reported by some authors (6-9), the effect varying however with the physical nature of the base material (6).

With the three binders, crushing strength was diminished as a function of the concentration of Magnesium Stearate at all mixing times, only in the first minutes with Emcocel® 90. Generally disintegration times were small. With the three binders, disintegration time was increased with increasing Magnesium Stearate, very pronounced when the blends were mixed for 20 minutes: more than 30 minutes of disintegration time were noted with Emcocel® 90 and Avicel® PH 101. The small increase in disintegrating times noted with some tablets, mixed for 1 - 3 minutes with glidant, was due to flotation of the tablets by the incorporation of air, resulting in longer disintegration times.

Nor the weight of tablets nor the C.V. % was influenced by the per cent Magnesium Stearate. Friability was increased as a function of mixing time, very pronounced with Emcocel® 50 and Avicel® PH 101, less with Emcocel® 90 (Table 1). With Emcocel® 50 and Avicel® PH 101, friability was increased with increasing Magnesium Stearate concentration, not with Emcocel® 90: with this binder, longer mixing times, up to 10 minutes, resulted still in tablets with good friability.

As a conclusion good tablets could be obtained with the three binders when 1 % glidant was blended for 1 minute and the blend compressed at 3 kN.

Dilution Potential of the Binders The results are summarized in Table 2. Tablets were compressed without difficulty.

TABLE 3
Formulation of Tablets with 60 % Asagran®, 30 % Filler, 10 % Binder and 1 % Magnesium Stearate

| Binder | Compr. Force (kN) | Crush. Strength (kg) | Disintegr. Time (min.sec) | Friability (%) | Weight (g) | S.D. (g) | C.V. (%) |
|---|---|---|---|---|---|---|---|
| FILLER = TABLETTOSE® | | | | | | | |
| Emcocel® 90 | 1.5 | 3.5 | 2' 27" | 3.55 | .6474 | .0079 | 1.2 |
| | 2.0 | 5.8 | 1' 37" | 0.46 | .6522 | .0088 | 1.3 |
| | 3.0 | 14.2 | 8' 18" | 0.00 | .6391 | .0065 | 1.0 |
| Avicel® | 1.5 | 3.7 | 1' 6" | 2.80 | .6780 | .0040 | 0.6 |
| PH 101 | 2.0 | 8.2 | 1' 48" | 0.60 | .6702 | .0034 | 0.5 |
| | 3.0 | 15.1 | 20' 36" | 0.00 | .6633 | .0046 | 0.7 |
| FILLER = EMCOMPRESS® | | | | | | | |
| Avicel® | 1.0 | 1.3 | > 15' | 16.85 | .4964 | .0146 | 3.0 |
| PH 101 | 1.5 | 3.3 | > 15' | 1.05 | .5105 | .0043 | 0.8 |
| | 2.0 | 4.5 | > 15' | 0.57 | .5089 | .0050 | 1.0 |
| | 2.5 | 9.0 | > 15' | 0.23 | .5110 | .0065 | 1.3 |
| Emcocel® 50 | 1.0 | 1.3 | > 15' | 5.38 | .5178 | .0043 | 0.8 |
| | 1.5 | 2.2 | > 15' | 2.53 | .5122 | .0056 | 1.1 |
| | 2.0 | 4.2 | > 15' | 1.61 | .5167 | .0033 | 0.6 |
| | 2.5 | 6.3 | > 15' | 0.28 | .5193 | .0019 | 0.4 |
| Emcocel® 90 | 1.0 | 1.0 | > 15' | 32.33 | .4887 | .0033 | 0.7 |
| | 1.5 | 3.3 | > 15' | 1.17 | .4956 | .0034 | 0.7 |
| | 2.0 | 4.7 | > 15' | 0.41 | .4977 | .0030 | 0.6 |
| | 2.5 | 6.5 | > 15' | 0.28 | .4942 | .0057 | 1.2 |

The results were influenced by the percentage active product: with 30 % active compound, the crushing strength was most important with Emcocel® 50, with 70 % active compound, with Avicel® PH 101. Disintegration times were most increased with Emcocel® 50, containing 30 % Asagran®, with Emcocel® 90 containing 70 % Asagran®.

For the three binders friability was enhanced with increasing amount of Asagran®. This was expected as the amount of binder was diminished. The C.V. % was smallest with Emcocel® 90.

Tablets Containing Asagran® as Active Compound

From Table 3, it was noted that, with Tablettose® as filler, disintegration times were nearly the same for tablets prepared at compression forces of 1.5 and 2 kN; at 3 kN however, disintegration times were much higher with the Avicel® PH 101 tablets in comparison with the Emcocel® 90

TABLE 4
Formulation of Tablets Containing 60 % Asagran®, 10 % Binder, Disintegrant and 1 % Magnesium Stearate

| Tablet Composition | | Compr. Force | Crush. Strength | Disintegr. Time | Fria-bility | Weight Mean | S.D. | C.V. |
|---|---|---|---|---|---|---|---|---|
| Binder | Disintegr. | (kN) | (kg) | (min. sec) | (% ) | (g) | (g) | (%) |
| FILLER = TABLETTOSE® | | | | | | | | |
| Emcocel® 90 | Explotab® 4% | 2.0 | 5.9 | 35" | 0.94 | .6420 | .0051 | 0.8 |
| | | 2.5 | 14.1 | 3' 57" | 0.15 | .6590 | .0062 | 0.9 |
| | | 3.0 | 14.2 | 4' 46" | 0.15 | .6563 | .0099 | 1.5 |
| Avicel® PH 101 | Explotab® 4% | 2.0 | 10.4 | 1' 34" | 0.31 | .6283 | .0045 | 0.7 |
| | | 2.5 | 14.1 | 4' 17" | 0.15 | .6109 | .0072 | 1.2 |
| | | 3.0 | 16.0 | 6' 32" | 0.31 | .6258 | .0052 | 0.8 |
| Emcocel® 90 | Kollidon® Cl 2% | 2.0 | 6.9 | 23" | 0.95 | .6323 | .0061 | 1.0 |
| | | 2.5 | 14.5 | 1' 45" | 0.49 | .6535 | .0053 | 0.8 |
| | | 3.0 | 15.6 | 2' 7" | 0.00 | .6450 | .0040 | 0.6 |
| Avicel® PH 101 | Kollidon® Cl 2% | 2.0 | 8.9 | 20" | 0.61 | .6571 | .0055 | 0.8 |
| | | 2.5 | 11.8 | 1' 12" | 0.15 | .6660 | .0061 | 0.9 |
| | | 3.0 | 15.5 | 2' 7" | 0.46 | .6437 | .0070 | 1.1 |
| FILLER = EMCOMPRESS® | | | | | | | | |
| Avicel® PH 101 | Explotab® 4 % | 2.5 | 10.4 | 5' 33" | 0.25 | .4799 | .0072 | 1.5 |
| Emcocel® 90 | Explotab® 4 % | 2.5 | 10.0 | 8' 30" | 0.19 | .4711 | .0024 | 0.51 |

tablets. The crushing strength was somewhat smaller with the Emcocel® 90 tablets, the friability nearly the same for both tablets. Friability was to a large extent decreased from 1.5 up to 2 kN and became zero at a compression force of 3 kN.

With Emcompress® as filler, crushing strength was also increased as a function of the compression force. However, only at a compression force of 2.5 kN, crushing strength was sufficient (> 6 kg) and friability was low enough (< 1 %). For all compression forces, disintegration times of more than 15 minutes were noted.

Comparing the two fillers, at the same compression forces, far better tablet properties were obtained with Tablettose® in comparison with Emcompress®, especially for disintegration times.

Asagran® Tablets Containing Disintegrants

To improve the tablet properties, especially the disintegration time, disintegrants i.e. Explotab® or Kollidon® Cl were

TABLE 5
Formulation of Tablets with 30 % Phenobarbital, with and without disintegrant

| Binder + | Conc. (%) | Glidant (%) | Compr. Force (kN) | Crush. Strength (kg) | Disint. Time (min. s.) | Friability (%) | Weight (g) | S.D. (g) | C.V. (%) |
|---|---|---|---|---|---|---|---|---|---|
| WITHOUT DISINTEGRANT | | | | | | | | | |
| Emcocel® 90 | 10 | 2.0 | 2.5 | 7.9 | > 15' | .33 | .3369 | .0014 | 0.4 |
| Avicel® PH 101 | 10 | 2.0 | 2.5 | 7.6 | > 15' | .46 | .3364 | .0022 | 0.7 |
| + 4 % EXPLOTAB | | | | | | | | | |
| Avicel® PH 101 | 5 | 1.0 | 2.0 | 5.5 | 2' 5" | .52 | .3891 | .0150 | 3.9 |
| | 5 | 1.0 | 2.5 | 7.8 | 2' 5" | .32 | .3857 | .0110 | 2.9 |
| Avicel® PH 101 | 10 | 1.0 | 2.0 | 5.2 | 1' 17" | .60 | .3444 | .0158 | 4.6 |
| | 10 | 1.0 | 2.5 | 6.3 | 1' 18" | .23 | .3477 | .0157 | 4.5 |
| | 10 | 1.5 | 2.5 | 6.4 | 1' 27" | .23 | .3651 | .0035 | 1.0 |
| | 10 | 2.0 | 2.5 | 5.9 | 2' 9" | .35 | .3585 | .0028 | 0.8 |
| Emcocel® 90 | 10 | 2.0 | 2.5 | 5.5 | 1' | .31 | .3540 | .0033 | 0.9 |
| Emcocel® 50 | 10 | 2.0 | 2.5 | 6.5 | 1' 36" | .31 | .3588 | .0045 | 1.2 |

added. The compression forces were maintained at 2, 2.5 and 3 kN. The results are given in Table 4.

The crushing strength of the Avicel® PH 101/Tablettose® tablets (Table 4) containing 4 % Explotab® as disintegrant and compressed at 2 kN was nearly twice as much than those of the tablets containing Emcocel® 90. At higher compression forces, the crushing strengths were nearly the same with both binders. With 2 % Kollidon® Cl the tablets containing Avicel® PH 101 showed also higher crushing strength at the lowest compression force, the same values at 3 kN.

Friability was highest with Emcocel® 90 tablets at 2 kN compression force, at higher compression forces all tablets give values less than 1 % . With tablets, containing Explotab® as disintegrant, disintegration times were poorest with Avicel® PH 101 as binder; this was attributed to the observed flotation of these tablets during the disintegration test. With Kollidon® Cl as disintegrant, no differences were noted in disintegration times with the two binders. With Emcompress® as filler, all the tablet properties were poorer in comparison with Tablettose® as filler.

Comparing the results of tablets containing Tablettose® with and without disintegrants (Table 3-4), disintegration times were always diminished in the presence of a disintegrant, most with Kollidon® Cl. The friability had not much changed, the

crushing strength somewhat increased with Avicel® PH 101/Explotab® and Emcocel® 90/Kollidon® Cl tablets, unchanged with the two other tablets. With Emcompress® as filler, especially disintegration times and crushing strength were improved in the presence of Explotab® as disintegrant. With Emcompress®, some abrasion of the punches was also observed, so no further work was done with this product as the only diluent.

Tablets Containing Phenobarbital as Active Compound

The results are summarized in Table 5.
Practically no difference was noted between the two binders. Disintegration times were > 15' and were improved by adding Explotab® as disintegrant. (Table 5).
With 1 % Magnesium Stearate, filling of the die was very unregularly, observed also on the great variations of the crushing strengths (values obtained from 3.0 up to 8.8 kg) and the high C.V. % . No great difference was noted between the two Avicel® PH 101 concentrations. When increasing the glidant up to 2 % , the S.D. and C.V. % were improved, the other tablet properties had not much changed.

Comparing the three binders, compressed at 2.5 kN, no great differences of the tablet properties were noted. The C.V. % is somewhat higher with Emcocel® 50 than with the two other binders.

Tablets Containing the Spray Dried Extract Equisetum Arvense

With a blend of 36 % Equisetum Arvense spraydried extract, 5 % Avicel® PH 101, 59 % Tablettose® and 1 % Magnesium Stearate, severe segregation was observed, visually, but also from the great variations of the tablet weights. The segregated product, appearing on the surface of the blend, was analyzed with IR spectroscopy and compared with Avicel® PH 101 and Tablettose®. From the IR spectrum, it was already obvious that Tablettose® caused the segregation, probably due to the differencies in densities. Tablets were then tried without the addition of Tablettose®. The results are given in Table 6.

From Table 6 it was noted that the crushing strength without filler was high for the three binders, reaching > 6 kg from 1.5 kN compression force. In the presence of Emcompress®, best results were obtained with Avicel® PH 101 as binder. Friability was good from 1 kN compression force in the presence of Avicel® PH 101 and Emcocel® 50, from 1.5 kN for Emcocel® 90. By adding Emcompress®, friability was increased, especially at the low compression forces. Disintegration times were increased as a function of compression force, generally the addition of Emcompress® diminishing the disintegration times.
With these formulations, tablets could be produced, without segregation of the products, possessing good tablet properties even at low compression forces.

TABLE 6
Evaluation of Tablets Containing 36 % Equisetum Arvense Spraydried Extract, 59 % Binder (and) Filler, 5 % Ac-Di-Sol and 1 % Magnesium Stearate

| Binder (and) Filler | Compression Force (kN) | Crushing Strength (kg) | Disintegr. Time (min. s) | Friability (%) | Weight (g) | Standard Deviation (g) | C.V. (%) |
|---|---|---|---|---|---|---|---|
| Avicel® PH 101 | 0.5 | 3.1 | 1' 2" | 1.04 | .2940 | .0043 | 1.5 |
| | 1.0 | 7.2 | 2' 47" | 0.04 | .2872 | .0127 | 4.1 |
| | 1.5 | 8.6 | 7' 10" | 0.03 | .2795 | .0075 | 2.7 |
| | 2.0 | 16.6 | 8' 48" | 0.03 | .2811 | .0111 | 3.9 |
| | 3.0 | 17.0 | 14' 22" | 0.04 | .2909 | .0082 | 2.8 |
| Emcocel® 50 | 0.5 | 3.8 | 56" | 1.87 | .3237 | .0091 | 2.8 |
| | 1.0 | 6.2 | 1' 25" | 0.40 | .3218 | .0128 | 3.9 |
| | 1.5 | 11.3 | 7' 26" | 0.00 | .3255 | .0099 | 3.0 |
| | 2.0 | 15.6 | 11' 52" | 0.01 | .3283 | .0078 | 2.4 |
| Emcocel® 90 | 1.0 | 3.0 | 36" | 1.13 | .3625 | .0019 | 0.5 |
| | 1.5 | 7.7 | 6' 54" | 0.01 | .3592 | .0059 | 1.6 |
| | 2.0 | 12.9 | 10' 51" | 0.00 | .3596 | .0061 | 1.7 |
| | 2.5 | 16.2 | 14' 56" | 0.00 | .3622 | .0025 | 0.7 |
| BINDER AND FILLER (1:1) | | | | | | | |
| Avicel® PH 101 / Emcompress® | 0.5 | 4.24 | 0 50" | 1.21 | .3963 | .0112 | 2.9 |
| | 1.0 | 6.94 | 1' 15" | 0.76 | .4039 | .0135 | 3.3 |
| | 1.5 | 9.58 | 2' 40" | 0.06 | .4115 | .0058 | 1.3 |
| | 2.0 | 11.68 | 7' 48" | 0.01 | .4068 | .0071 | 1.7 |
| Emcocel® 50 / Emcompress® | 1.0 | 1.7 | 36" | 8.30 | .4877 | .0050 | 1.0 |
| | 1.5 | 5.0 | 4' 13" | 0.75 | .4825 | .0091 | 1.9 |
| | 2.0 | 7.5 | 7' 55" | 0.22 | .4821 | .0038 | 0.8 |
| | 2.5 | 14.9 | 14' 16" | 0.00 | .4785 | .0027 | 0.6 |
| Emcocel® 90 / Emcompress® | 1.0 | 2.1 | 33" | 8.99 | .4982 | .0066 | 1.3 |
| | 1.5 | 4.1 | 3' 20" | 2.45 | .4927 | .0137 | 2.8 |
| | 2.0 | 8.7 | 7' 25" | 0.47 | .4935 | .0090 | 1.8 |
| | 2.5 | 11.2 | 8' 54" | 0.22 | .4885 | .0068 | 1.4 |

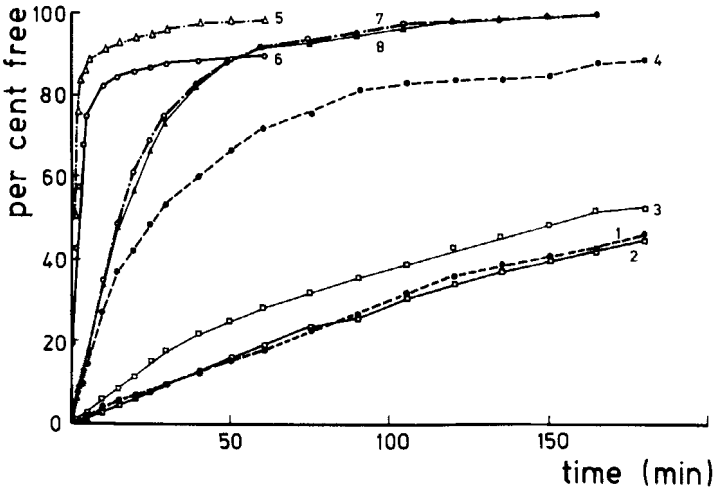


FIG. 3

Per Cent Release of Asagran as a Function of Time

1 = Asagran® 60 % , Avicel® PH 101 10 % , Emcompress® 30 % , Magnesium Stearate 1 % , Crushing Strength 3.3 kg

2 = Asagran® 60 % , Emcocel® 90 10 % , Emcompress® 30 % , Magnesium Stearate 1 % , Crushing Strength 3.3 kg

7 = Asagran® 60 % , Avicel® PH 101 10 % , Emcompress® 26 % , Explotab® 4 % , Magnesium Stearate 1 % , Crushing Strength 10.4 kg

8 = Asagran® 60 % , Emcocel® 90 10 % , Emcompress® 26 % , Explotab® 4 % , Magnesium Stearate 1 % , Crushing Strength 10.0 kg

4 = Phenobarbital 30 % , Emcocel® 90 10 % , Tablettose® 60 % , Magnesium Stearate 2 % , Crushing Strength 7.9 kg

3 = Phenobarbital 30 % , Avicel® PH 101 10 % , Tablettose® 60 % , Magnesium Stearate 2 % , Crushing Strength 7.6 kg

6 = Phenobarbital 30 % , Avicel® PH 101 10 % , Tablettose® 56 % , Explotab®4 % , Magnesium Stearate 2 % , Crushing Strength 5.9 kg

5 = Phenobarbital 30 % , Emcocel®0 10 % , Tablettose®56 % , Explotab®4 %, Magnesium Stearate 2 % , Crushing Strength 6.5

Dissolution Properties of Tablets Prepared with Avicel® PH 101 and Emcocel® 90

Tablets without and with disintegrant were used. The composition of the tablets and the results are given in Fig. 3. To compare the two binders, nearly the same crushing strenghts were used with each pair of formulations.

With tablets, containing Asagran® and Emcompress®, no differences in dissolution pattern were noted between the two binders. Addition of Explotab® as disintegrant enhances to a great extent the dissolution rate and was attributed to the fast disintegration of the tablets into powder.

With tablets containing Phenobarbital and Tablettose®, and no disintegrant, a great difference was noted in dissolution rates with Avicel® PH 101 or Emcocel® 90 as binder. Release rate was slower from Avicel® PH 101 tablets with regard to Emcocel® 90 tablets. After 1 and 3 hours respectively, 29 and 50 % released drug was determined with Avicel® PH 101 tablets, 73 and 90 % with Emcocel® 90 tablets.
In the presence of disintegrant, the release rate was very fast for both binders: after 5 minutes 75 % per cent release was noted with tablets containing Avicel® PH 101 , 90 % containing Emcocel® 90 as binder. Emcocel® 90 seems to be more convenient than Avicel® PH 101 as binder for the dissolution of Phenobarbital.

## CONCLUSIONS

The recently developed Emcocel® derivatives show comparable tablet properties in regard to Avicel PH 101®.

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## FOOTNOTES

1 Edward Mendell, New York, U.S.A.
2 FMC Europe, Brussels, Belgium
3 C.N. Schmidt, Amsterdam, Netherlands
4 BASF , Brussels (Belgium)
5 Federa, Brussels, Belgium
6 Monsanto, Brussels, Belgium
7 Flandria, Ghent, Belgium
8 Synthelabo, Brussels, Belgium
9 Chimexport, Wilrijk, Belgium
10 Courtoy Model NR 7 N, Courtoy, Halle, Belgium
11 Kistler, Winterthur, Switzerland
12 Erweka, Offenbach a/Main, West Germany
13 Manesty, Liverpool, U.K.
14 Merck, Darmstadt, W-Germany
15 Perkin Elmer, Van der Heyden, Brussels, Belgium

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