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A COMPARATIVE EVALUATION OF THE PROPERTIES OF SOME TABLET DISINTEGRANTS

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Abstract

The subject of the study is a comparative evaluation of the properties of different disintegrants : starches (corn, maize, potatoe, rice) and derivatives (STARX 1500, carboxymethylstarches as PRIMOJEL or EXPLOTAB) ; celluloses (AVICEL, ELCEMA) and derivated products as methylcellulose (METHOCEL), carboxymethylcellulose (sodium salt, NYMCEL, AC DI SOL), low substituted hydroxypropylcellulose (L-HPC) ; macromolecules (Alginic acid, AMBERLITE IRP 88, ESMA SPRENG, Pectins, a.s.o.) ; finely divided solids (AEROSIL, VEEGUM). To realize this comparative study, different methods of evaluation of disintegrants physical properties are choosen, and wettability (contact angle), water uptake and swelling of the products measured. The disintegrants are also included in a calcium phosphate based tablet formula, and the disintegration is studied. The mechanism of action of the disintegrants is shortly discussed, and an approximate price/efficiency ratio given.

The results of the work permit a better choice of an appropriated disintegrant.

Purpose of tablets formulation is now to obtain very short disintegrating times so that to the liberation of drug can begin without delay as soon as the tablet is in contact with gastric juice.

Therefore, it is now important to look for the more efficient disintegrants, and so, many materials are avalaible from industry.

Purpose of present study was to compare some physical properties of these different disintegrants.

MATERIALS

Studied disintegrants were classified in different groups - Tables 1 to 3 give the composition of these groups, as also particular detail and the name of the supplier of each disintegrant.

First group joins together standard disintegrants, starches and derivatives (Table 1). Different starches were studied : corn starch ; maize starch ; waxy maize starch, which is an hybrid plant of maize giving a starch containing a great amount of amylopectin and practicly no amylose ; potatoe starch and rice starch. Among starches derivatives, different carboxymethyl-starches obtained from potatoe starch were kept (EXPLOTAB, standard PRIMOJEL and PRIMOJEL LV which is different from previous by its low viscosity in solution) and a maize starch modified by milling with water to break the amyloplasts and agglomerating the fragments under pressure (STARX 1500).

The second group includes celluloses and derivatives of celluloses (Table 2) : microcrystalline cellulose (AVICEL), methylcellulose, different carboxymethylcelluloses with different degrees of substitution and water solubilities (CMC Na, NYMCEL), cross- linked carboxymethylcellulose (AC DI SOL) hydroxypropylcellulose (L-HPC), mixture of sodium carboxymethylcellulose and microcrystalline cellulose (AVICEL RC 591).

The third group includes various macromolecules which are different from the two others groups (table 3) : alginic acid, guar gum (VIDOGUM KL 175), casein formaldehyde (ESMA SPRENG),

TABLE 1

STARCHES AND DERIVATIVES

MATERIAL	NATURE OF THE DESINTEGRANT	SUPPLIER
Cornstarch		Roquette
Standard maize starch		Roquette
Waxy maize starch	starch without amylose (hybrid plant.)	Roquette
Potatoe starch		Roquette
Rice starch		Prolabo
PRIMOJEL Standard	Carboxymethylstarch	Doittau
PRIMOJEL LV	Carboxymethylstarch with low viscosity	Doittau
EXPLOTAB	Carboxymethylstarch	Ed. Mendell
STARX 1500	Maize starch milled and agglomerated with water	Staley

pectins, cation exchange resin (AMBERLITE IRP 88), cross linked polyvinylpyrrolidon (POLYPLASDONE XL).

In table 3, are also present two finely divided solids, which are the fourth group of disintegrants : one is composed with magnesium and aluminium silicates (VEEGUM F), the other one is a colloidal.silicon dioxide (AEROSIL 200).

METHODS

Tablets disintegration is depending on several factors, the relative importance of which is discussed [1-7]. In many cases, disintegration is caused by a water uptake in tablet. After this

TABLE 2

CELLULOSES AND DERIVATIVES

MATERIAL	NATURE OF THE DISINTEGRANT	SUPPLIER
ELCEMA P 050	αcellulose particle size from 1 to 50 µm	Degussa
ELCEMA P 100	αcellulose particle size 1 to 100 µm	Degussa
ELCEMA F 150	αcellulose, fibers from 1 to 150 µm	Degussa
ELCEMA G 250	αcellulose granulated from 90 to 250 µm	Degussa
AVICEL PH 101	αcellulose microcrystalline	F.M.C.
AVICEL PH 102	αcellulose microcrystalline granulated	F.M.C.
METHOCEL 50 cps	methylcellulose	Dow chemical
Sodium carboxymethylcellulose	CMC low substituted (soluble in water)	Prolabo
NYMCEL ZSB 10	CMC- degree of substitution from 0,20 to 0,26	Nyma
NYMCEL ZSB 16	CMC- degree of substitution from 0,34 to 0,40	Nyma
AC DI SOL	cross linked CMC (non soluble in water)	F.M.C.
L-HPC	Hydroxypropylcellulose low substitued	Shin Etsu
AVICEL RC 591	Mixture of microcrystalline cellulose (89%) and of CMCNa (11%)	F.M.C.

TABLE 3
MACROMOLECULES AND FINELY DIVIDIED SOLIDS

MATERIAL	NATURE OF THE DISINTEGRANT	SUPPLIER
Alginic Acid		Prolabo
VIDOGUM KL 175	Guar gum	Unipectine
ESMA SPRENG	Casein formaldehyde	Edelfettwerke
PECTIN BRUN PHAL	Citrus pectin high esterified	Unipectine
PECTIN BRUN NF	Orange pectin high esterified	Unipectine
AMBERLITE IRP 88	Cation exchange resin (potassium polymethacrylate)	Röhm and Haas
POLYPLASDONE XL	Cross linked polyvinylpyrrolidon	G.A.F.
VEEGUM F	Mixture of magnesium and aluminium silicon dioxyde	Degussa

absorption, there is a rupture of intraparticular cohesive forces, which may be increased by the swelling of disintegrant. The more important factors to account for the efficiency of a disintegrant are therefore wetting, water uptake which permits the penetration of gastric juice in tablet; and swelling which increases tablet disintegration. These are the different factors which were studied one several disintegrants.

Particle size

Particle size of the different disintegrants was determined by microscopy with a projection system and electronic analysis apparatus KONTRON-MOB. Results are the maximum diameter of the particles, because many materials are long fibers, and it seems that maximum lenght may be the most qualified measurement to take this particular form of the disintegrants in consideration.

Contact Angle

Wetting of the disintegrants was determined by contact angle measurement of a water drop with tablets of pure disintegrants, made by direct compression at a pressure of about 100 MPa. The measurement of this angle was made with a photographic technic which gives a good reproducibility of the measurements[8].

Water absorption

The rate of water absorption in the tablets was studied with an apparatus (figure 1) similar to that described by NOGAMI and al[9].

This rate of water uptake was studied on one hand on pure disintegrant tablets prepared by direct compression at a pressure of about 100 MPa. It was also studied on tablets prepared by direct compression of a mixture of dicalcium phosphate (EMCOMPRESS), magnesium stearate (1%) and disintegrant (2 or 5%) ;

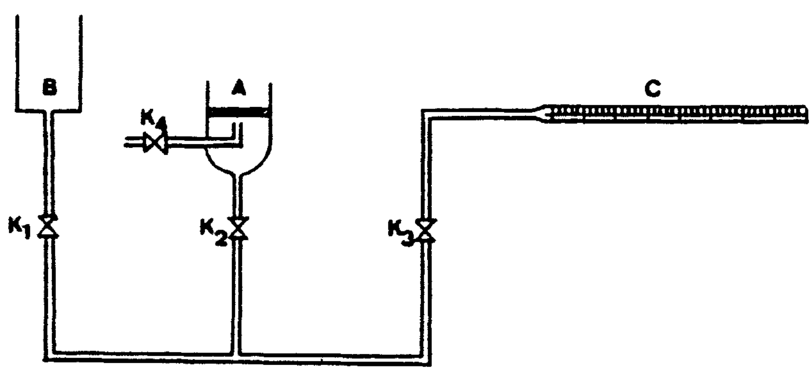

FIGURE 1
Water absorption apparatus (according to Nogami and al.[9])

these tablets were made under a pressure so as to the crushing strength was 6 ± 1 kg (measured with an ERWEKA TBT apparatus).

Swelling

During the water uptake measurement, the swelling of tablets of pure disintegrants was studied with a linear inductive transducer in contact with the tablets and connected with a recorder (figure 2).

The swelling of tablets was recorded during a maximum of 15 minutes (In few cases, it was not possible to carry on the measurement after some minuts because of a fast disintegration of the tablets). The swelling measured is given in percent, according to the relation :

$$G\% = \frac{h_t - h_o}{h_o} \times 100$$

where h_o is the height of the tablet at the beginning of the test and h_t the height of the tablet at the time t.

Disintegrating time

Disintegrating time of tablets was measured according to the technic described by the European Pharmacopea.

RESULTS

Results of particle size analysis are shown in table 4. This table indicates that the middle size of most disintegrants is between 9 and 60 µm ; however some of the studied materials are too fine to be analysed by microscopy (AEROSIL, VEEGUM) ; some others present a diameter smaller than 9 µm (corn starch, rice starch). ELCEMA G 250 and AVICEL PH 102 are special cases because they are materials resulting from dry granulation respectively of ELCEMA P 100 and AVICEL PH 101.

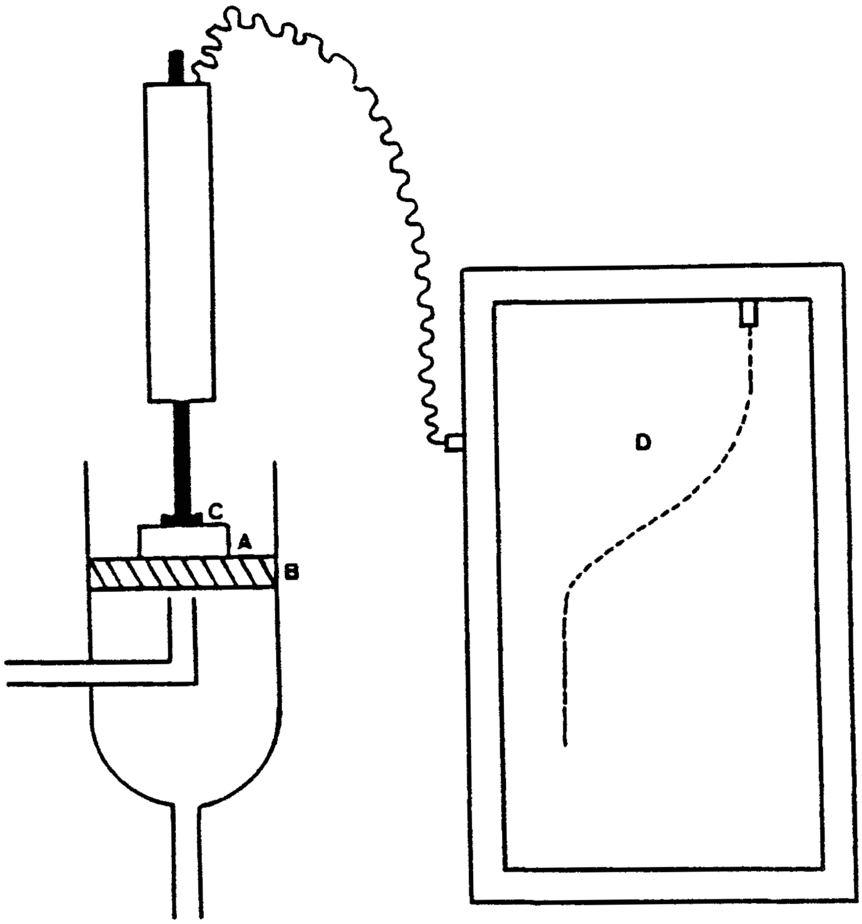

FIGURE 2

Swelling recorder A : Tablet ; E : Water penetration ;
C : Transducer ; D : Recorder

Table 5 shows the values of contact angle of pure disintegrant tablets with water.

Among starches, only maize starch shows a contact angle equal to zero, that is to say a perfect hydrophily ; starch derivatives are very hydrophilic - Celluloses as ELCEMA have a mean hydrophily, which is lower than this of AVICEL. Cellulose

TABLE 4

PARTICLE SIZE OF DISINTEGRANTS

Corn starch	5,3µm	ELCEMA P050	33,7µm	Alginic Acid	43,7µm
Standard Maize starch	9,9µm	ELCEMA P100	46,6µm	AMBERLITE IRP 88	20,8µm
Waxy Maize starch	9,7µm	ELCEMA F150	50,1µm	ESMA SPRENG	33 µm
Potatoe starch	17 µm	ELCEMA G250	108 µm	Pectin BRUN PHAL	58 µm
Rice starch	4,1µm	AVICEL PH 101	32,8µm	Pectin BRUN NF	47,2µm
STARX 1500	16,7µm	AVICEL PH 101	50,1µm	VIDOGUM KL 175	18,7µm
PRIMOJEL STD	23,7µm	METHOCEL 50 cps	32,2µm	POLYPLASDONE XL	19,1µm
PRIMOJEL LV	19,3µm	CMC Na	44,4µm	AEROSIL 200	very fine
EXPLOTAB	22,6µm	NYMCEL ZSB 10	26,7µm	VEEGUM F	very fine
		NYMCEL ZSB 16	36,9µm		
		AC DI SOL	20,9µm		
		L-HPC	22,2µm		
		AVICEL RC 591	10,6µm		

derivatives are not very hydrophilic except AC DI SOL which has a contact angle equal to zero. One can notice that METHOCEL is poorly hydrophilic.

Among macromolecules, it appears that ESMA SPRENG is not hydrophilic ; on the other hand the other materials are fairly or good hydrophilic. Contact angles of VIDOGUM KL 175 and AEROSIL were not achieved because it was not possible to make tablets of pure material with these two disintegrants. Water absorption of pure disintegrants or in mixture (2 or 5%) with dicalcium phosphate is shown in figures 3 to 7.

TABLE 5

CONTACT ANGLES OF DISINTEGRANTS

Cornstarch	15°	ELCEMA P050	57°	Alginic acid	19°
Standard maize starch	0°	ELCEMA P100	43°	AMBERLITE IPR88	35°
Waxy maize starch	0°	ELCEMA F150	40°	ESMA SPRENG	104°
Potatoe starch	18°	ELCEMA G250	52°	Pectin BRUN PHAL	0°
Rice starch	28°	AVICEL PH101	17°	Pectin BRUN NF	25°
STARX 1500	0°	AVICEL PH102	21°	VIDOGUM KL 175	?
PRIMOJEL STD	0°	METHOCEL 50 cps	82°	POLYPLASDONE XL	34°
PRIMOJEL LV	0°	CMC Na	40°	AEROSIL 200	?
EXPLOTAB	0°	NYMCEL ZSB 10	66°	VEEGUM F	26°
		NYMCEL ZSB 16	51°		
		AC DI SOL	0°		
		L-HPC	50°		
		AVICEL RC 591	46°		

Figure 3 shows the capacity of water absorption of starches ; corn starch sucks up much more water than other starches. Maize starch absorption is more gradual than other. These differencies disappear when disintegrants are not studied pure but in mixture with dicalcium phosphate in tablet.

Pure carboxymethylstarches (figure 4) produce very high water absorption ; in tablets formula with EMCOMPRESS, they keep the properties of increasing water absorption ; and PRIMOJEL seems more efficient than EXPLOTAB. On the other hand STARX 1500

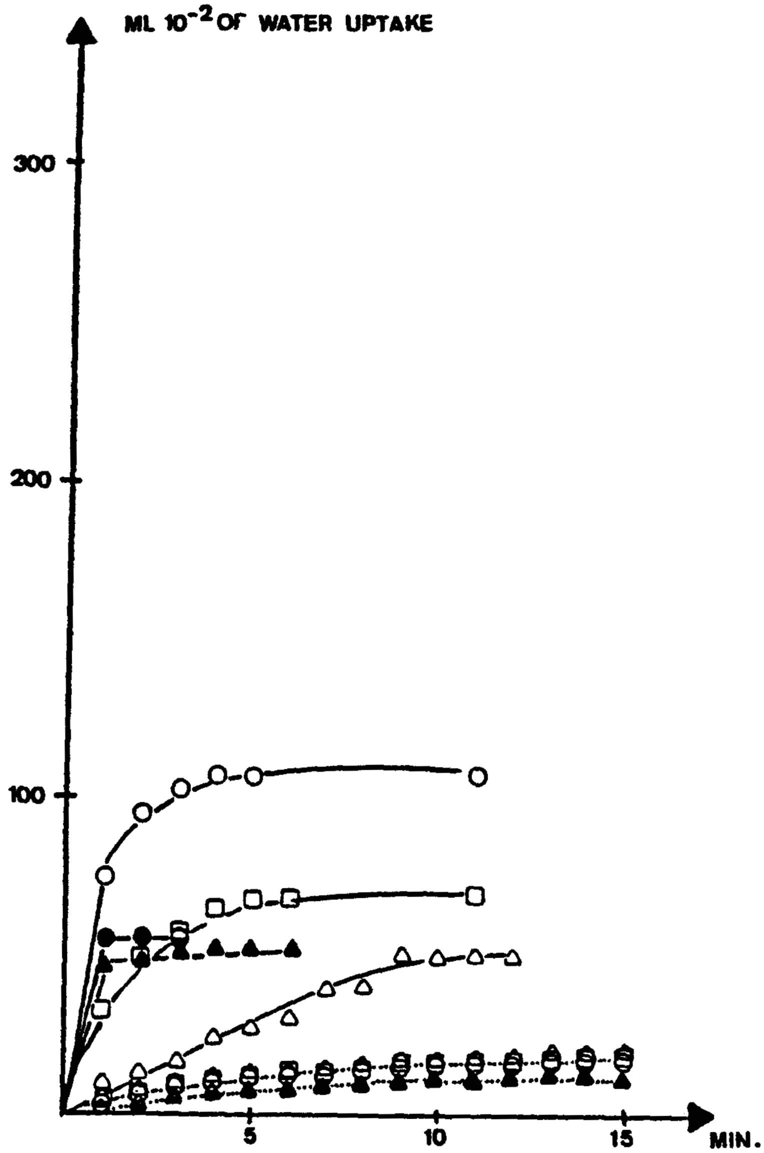

FIGURE 3

Water absorption of starches : —— pure materials, --- in a 5% mixture with EMCOMPRESS ○ corn starch △ standard maize starch □ waxy maize starch ● potatoe starch ▲ rice starch.

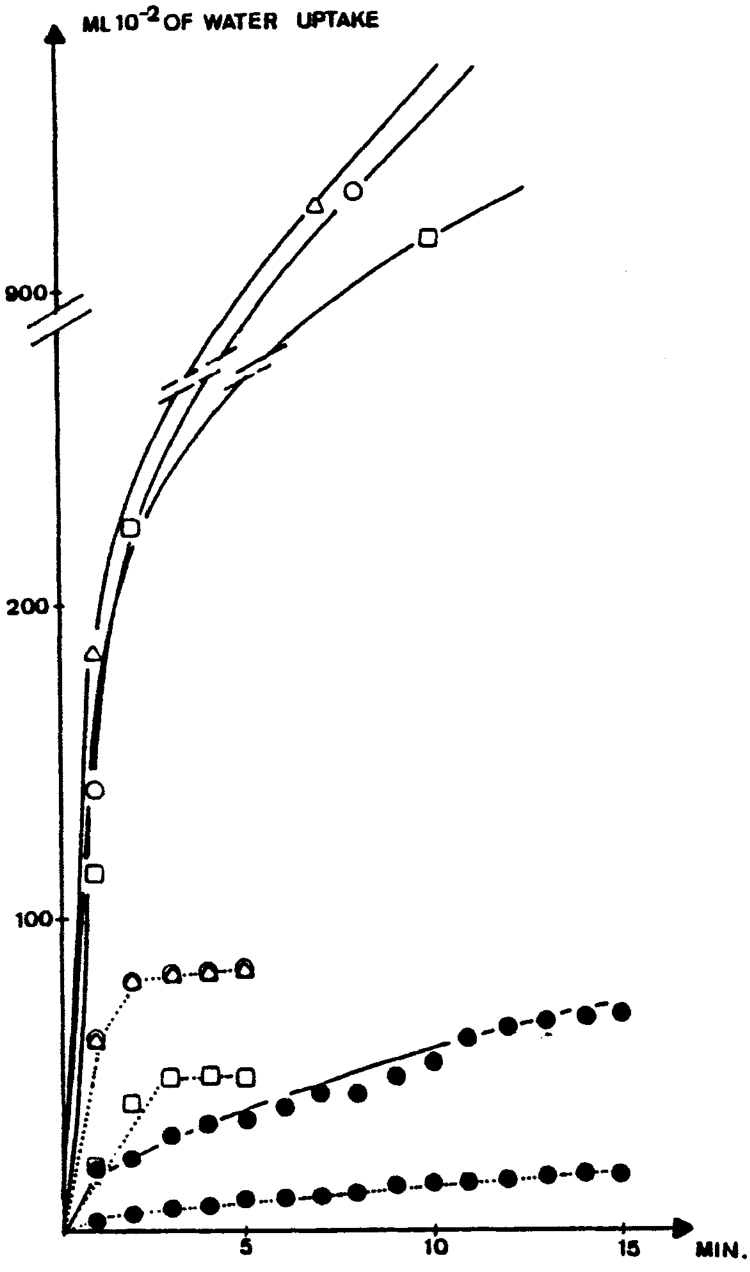

FIGURE 4

Water absorption of starch derivatives :—— pure materials,
--- in a 2% mixture with ENCOMPRESS △ PRIMOJEL LV, ○ PRIMOJEL
standard, □ EXPLOTAB, ● STARX 1500.

is not very hydrophilic and its behavior is similar to this of maize starch from which it proceeds.

Celluloses (figure 5) absorb more important quantities of water than starches, and among pure materials, one can see that ELCEMA G250 is particularly hydrophilic. In a tablet formula with EMCOMPRESS, no cellulose can promote water penetration.

Derivatives of celluloses (figure 6) have different behaviors : pure AC DI SOL and pure L-HPC absorb very fast great quantities of water ; NYMCEL absorbs a little more slowly water, but absorption is regular ; AVICEL RC 591 and SODIUM CMC absorb small quantities of water ; METHYLCELLULOSE absorbs scarcely water.

After compression with EMCOMPRESS, NYMCEL ZSB 16 is the most efficient of this group to improve water penetration in tablet.

In the group of macromolecules (figure 7) AMBERLITE IRP 18 absorbs smaller quantities of water, then POLYPLASDONE XL or alginic acid. The absortion of ESMA SPRENG is the smallest. These different materials are however not efficient to give a penetration of great quantities of water in EMCOMPRESS tablets.

Pure VEEGUM F absorbs water but does not improve water absorption of dicalcium phosphate tablets.

Swelling of pure disintegrants tablets is shown in table 6 ; in this table is also reported the maximum swelling and the time necessary to reach maximum swelling. When maximum swelling occurs at the 15th minute, the value is indicated in brackets because it is possible that this swelling carries on after that period which was the end of the test.

In the group of starches, one can notice that these materials are swelling very fast : during the first minute, the maximum swelling is reached ; swelling is very high for maize starch, then cornstarch and low for potatoe starch and rice starch. The effectiveness of these materials as disintegrant is however also dependent of particle size.

Among starch derivatives, one notice the low swelling of STARX 1500, and, on the opposite, the great swelling of carboxy-

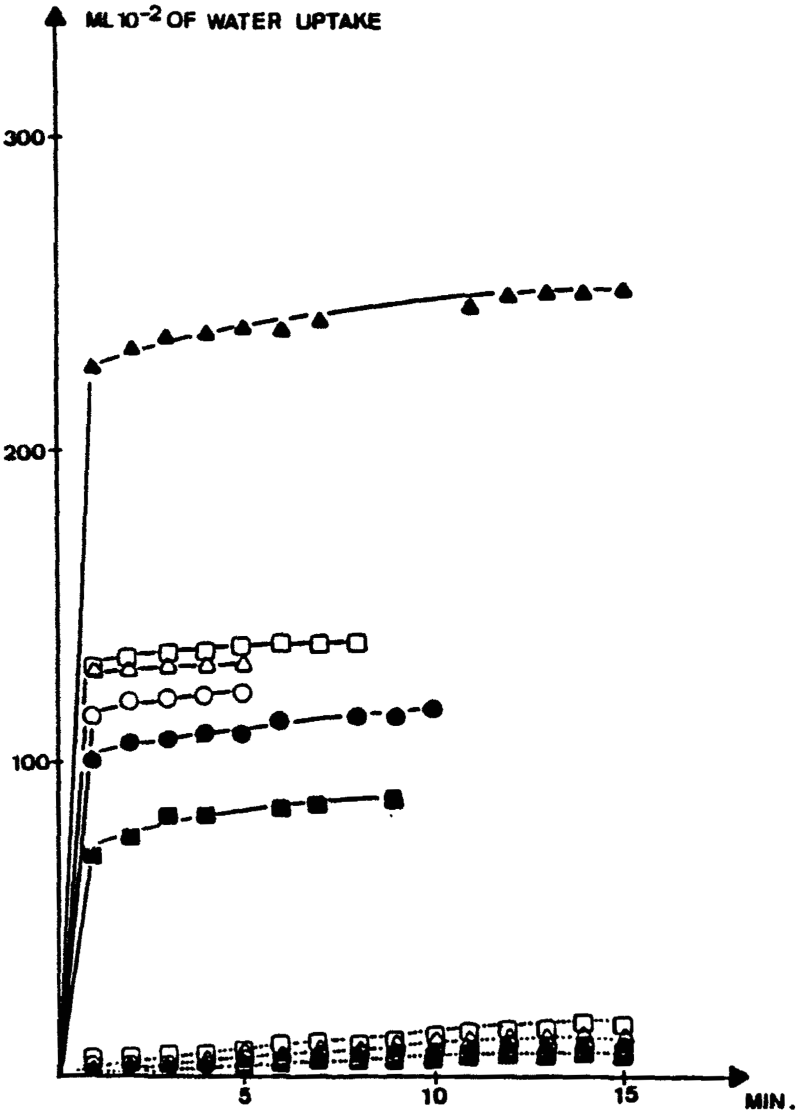

FIGURE 5

Water absorption fo celluloses : —pure materials, --- in mixture with EMCOMPRESS ; △ ELCEMA P050 (5%), ○ ELCEMA P100 (5%), □ ELCEMA F150 (5%), ▲ ELCEMA G250 (2%), ● AVICEL PH 101 (5%), ■ AVICEL PH 102 (5%).

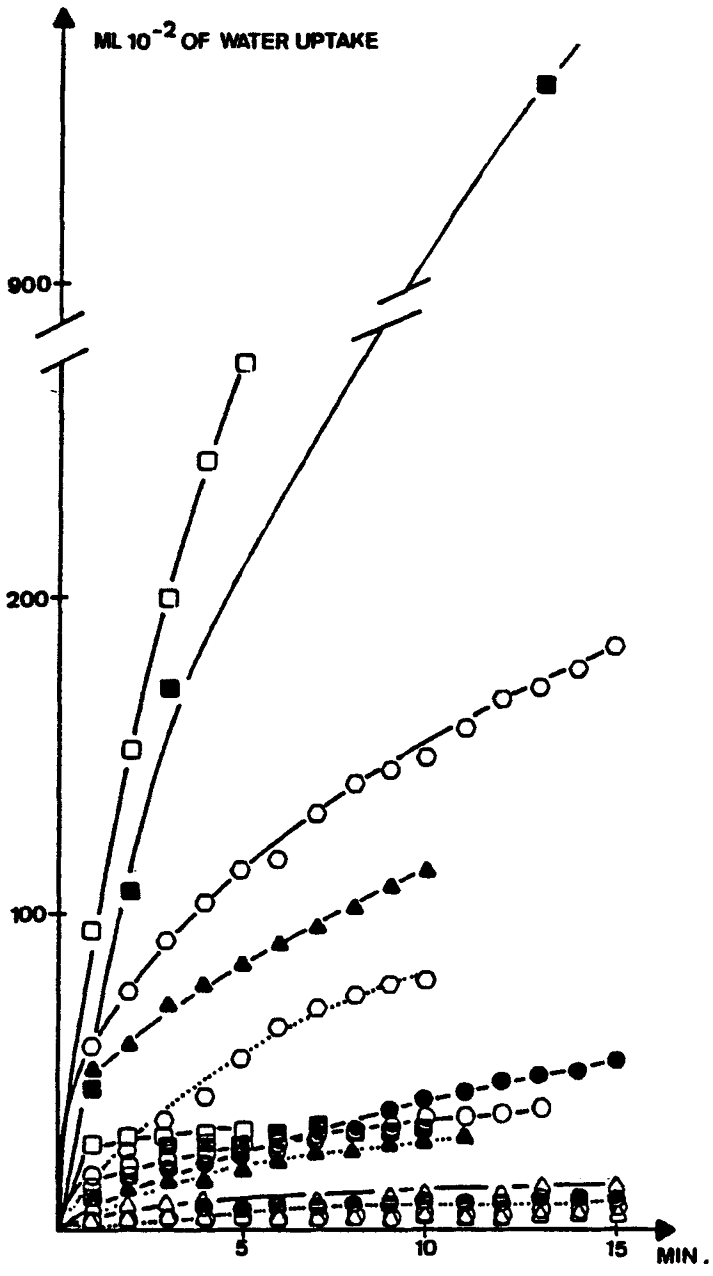

FIGURE 6

Water absorption of cellulose derivatives :—pure materials, --- in mixture with EMCOMPRESS ; △ METHOCEL (5%), ○ CMC Na (5%), ▲ NYMCEL ZSB10 (2%), ○ NYMCEL ZSB16 (2%), □ AC DI SOL (2%), ■ L-HPC (2%), ● AVICEL RC 591 (5%).

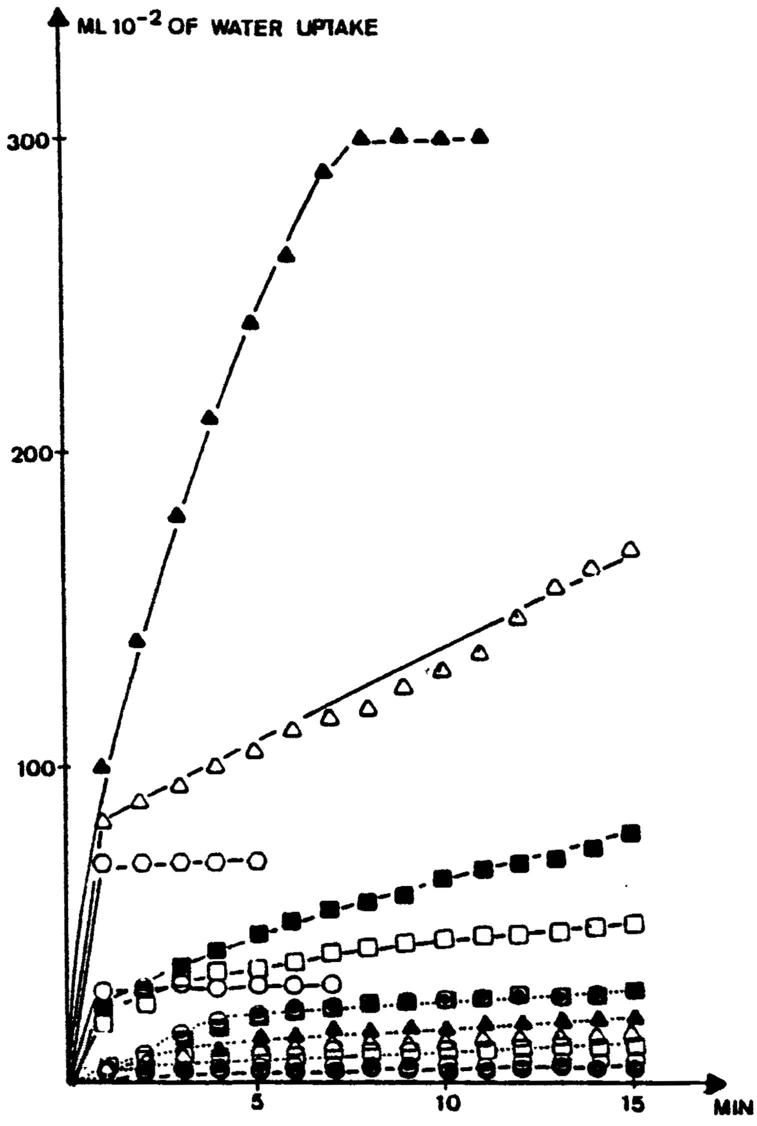

FIGURE 7

Water absorption of the other disintegrants : —— pure materials, ---- in a 2% mixture with EMCOMPRESS ; △ Alginic acid, ○ ESHA SPRENG, ⬡ pectin BRUN PHAL, ● pectin BRUN NF, □ AMBERLITE IRP 88, ▲ POLYPLASDONE XL, ■ VEEGUM F

TABLE 6

SWELLING OF PURE DISINTEGRANTS

DISINTEGRANT	SWELLING AFTER				MAXIMUM SWELLING	TIME FOR MAXIMUM SWELLING
	1 minute	2 minutes	3 minutes	5 minutes		
Corn Starch	17 %	9 %	-	-	17 %	1 minute
Standard maize starch	82 %	95 %	103 %	80 %	103 %	3 minutes
Waxy maize starch	88 %	73 %	54 %	-	88 %	1 minute
Potatoe starch	5 %	5 %	3 %	-	5 %	1 minute
Rice starch	5 %	2 %	-	-	5 %	1 minute
STARX 1500	4 %	5 %	6 %	7 %	(13 %)	15 minutes
PRIMOJEL STANDARD	53 %	79 %	95 %	110 %	110 %	5 minutes
PRIMOJEL LV	114 %	159 %	181 %	201 %	201 %	5 minutes
EXPLOTAB	60 %	69 %	80 %	93 %	93 %	5 minutes
ELCEMA P050	42 %	42 %	42 %	42 %	42 %	1 minute
ELCEMA P100	62 %	62 %	62 %	62 %	62 %	1 minute
ELCEMA F150	57 %	58 %	58 %	58 %	58 %	1 minute
ELCEMA G250	90 %	91 %	91 %	92 %	92 %	1 minute
AVICEL PH 101	39 %	40 %	42 %	43 %	43 %	1 minute
AVICEL PH 102	30 %	31 %	31 %	33 %	33 %	1 minute
Methocel 50 cps	-	-	-	1 %	(4 %)	15 minutes
Carboxymethyl-cellulose	1 %	4 %	7 %	12 %	26 %	14 minutes
NYMCEL ZSB 10	18 %	23 %	26 %	29 %	36 %	10 minutes
NYMCEL ZSB 16	34 %	44 %	51 %	64 %	98 %	14 minutes
AC DI SOL	48 %	95 %	116 %	151 %	210 %	10 minutes
L-HPC	26 %	53 %	82 %	137 %	(313 %)	15 minutes
AVICEL RC 591	1 %	2 %	4 %	11 %	(32 %	15 minutes
Alginic acid	6,5 %	9 %	13 %	18 %	(39 %)	15 minutes
AMBERLITE IRP 88	17 %	22 %	26 %	32 %	(57 %)	15 minutes
ESMA SPRENG	56 %	57 %	57 %	57 %	57 %	1 minute
Pectin BRUN PILAL	26 %	26 %	26 %	26 %	26 %	1 minute
Pectin BRUN NF	1 %	2 %	2 %	3 %	(5 %)	15 minutes
VIDOGUM	5 %	8 %	9 %	9 %	(10 %)	6 minutes
POLYPLASDONE XL	29 %	47 %	62 %	85 %	112 %	9 minutes
VEEGUM F	24 %	47 %	64 %	87 %	111 %	13 minutes

methylstarches ; among them, the material with low viscosity is more efficient : its volume is doubled in one minut and after 5 minutes the value of the swelling reaches 200%.

In the group of celluloses, the maximum swellings are reached during the first minut.

Derivatives of celluloses swell slower but their swelling can be very high (210% for AC DI SOL, 313% for L-HPC).

Macromolecules swell generaly a little, exept for POLYPLASDONE XL which doubles its volume in five minutes.

The study of the swelling of finely divided solids is limited to the VEEGUM because it was very difficult to produce tablets with pure AEROSIL. VEEGUM swells well, but, in consideration with its very fine particle size, it may be possible that swelling of this material is unable to promote tablets disintegration.

Disintegrating times of different tablets of EMCOMPRESS including different proportions of disintegrants are shown in table 7.

In the first group of disintegrants (starches and derivatives), one can notice that very short disintegrating times (shorter than 1 minute) can be obtained with high proportions (10%) of these usual disintegrants which are starches. A 5% proportion promotes a disintegrating time near by 2 minutes, except for rice starch, which disintegrating time reaches 6 minutes. With a 2% concentration, disintegrating times are very high : potatoe starch, which is the most efficient, promotes disintegration of tablets in 7 minutes : for the other, results present a wide range beetween 24 minutes and 1 hour. It is not possible to notice a clear difference between standard maize starch and "waxy" maize starch when these disintegrants are used in high concentration ; but with a 2% concentration, disintegrating times are respectively 35 minutes with waxy maize starch and one hour with standard maize starch.

Starch derivatives were not used in the same concentration because with a 2% concentration in formula, disintegration of tablets was achieved in less than one and a half minut. With 0,5% concentrations, carboxymethylstarches are still very efficient and it appears that PRIMOJEL are more efficient than EXPLOTAB. STARX 1500 gives a lower disintegration with this concentration but the time does not exceed 10 minutes.

TABLE 7

DISINTEGRATING TIME OF TABLETS OF A FORMULA WITH EMCOMPRESS AND VARIOUS PROPORTIONS OF DIFFERENT DISINTEGRANTS

Disintegrants	PERCENT OF DISINTEGRANT USED IN TABLETS FORMULA				
	10%	5%	2%	1%	0,5%
Cornstarch	35s	120s	1440s	-	-
Standard maize starch	27s	110s	3600s	-	-
Waxy maize starch	25s	100s	1980s	-	-
Potatoe starch	47s	130s	420s	-	-
Rice starch	60s	340s	2280s	-	-
EXPLOTAB	-	-	42s	90s	250s
STD PRIMOJEL	-	-	22s	32s	53s
PRIMOJEL LV	-	-	24s	27s	43s
STARX 1500	-	-	75s	360s	3620s
ELCEMA P050	660s	> 7200s	-	-	-
ELCEMA P100	240s	1920s	-	-	-
ELCEMA F150	690s	3180s	-	-	-
ELCEMA G 250	105s	270s	1020s	-	-
AVICEL PN 101	260s	840s	-	-	-
AVICEL PN 102	320s	3615s	-	-	-
METHOCEL 50 cps	> 7200s	-	-	-	-
CMC Na	6000s	4200s	-	-	-
NYMCEL ZSB 10	-	-	60s	70s	300s
NYMCEL ZSB 16	-	-	25s	75s	100s
AC DI SOL	-	-	12s	22s	32s
L-HPC	-	-	60s	195s	360s
AVICEL RC 591	-	-	195s	390s	-
Alginic acid	-	55s	160s	370s	-
VIDOGUM KL 175	-	225s	240s	90s	-
ESMA SPRENG	-	-	80s	225s	1080s
Pectin BRUN PHAL	>3600s	2640s	760s	-	-
Pectin BRUN NF	> 7200s	> 7200s	> 7200s	-	-
AMBERLITE IRP 88	-	42s	100s	240s	420s
POLYPLASDONE XL	-	-	120s	210s	180s
VEEGUM F	1680s	560s	-	-	-
AEROSIL 200	-	> 7200s	-	> 7200s	-

The group of cellulose derivatives shows that disintegrating times are included between 4 and 11 minutes with high concentrations (10%) of pure celluloses in tablets. These times are very long in comparison with these obtained with starches employed at the same concentration.

When celluloses are employed in a 5% concentration, their action on disintegration is unsatisfactory, exept for ELCEMA G250, which is relatively efficient with a 2% concentration (disintegrating time = 17 minutes).

Among cellulose derivatives, one can notice the non effectiveness of the studied methylcellulose and the slight efficiency of soluble carboxymethylcellulose ; on the other hand, the different poorly water solubles carboxymethylcelluloses were very efficient, since with 2% concentration, these disintegrants proceeded tablets disintegration in times lower or equal to 1 minut. Mixture of microcrystalline cellulose-sodium carboxymethylcellulose (AVICEL RC 591) is clearly more efficient than each of these agents used separately. The different disintegrants of this group, efficient in 2% concentration, can also be used at 1% or even 0,5% without higher disintegrating times. The most efficient material of this group is cross linked carboxymethylcellulose (AC DI SOL). The examination of the results obtained with the other macromolecular disintegrants, gives the information that this type of excipient must not be employed in high concentration under penalty of higher disintegrating times (pectins, and guar gum's examples) ; a 2% concentration promotes disintegration included between 1 and 4 minutes exept for pectins, which are not good disintegrants for dicalcium phosphate tablets. Employed in a 1% concentration, some of these disintegrants promote the disintegration within 7 minutes. POLYPLASDONE XL is the most efficient disintegrant of this groupe : in 0,5% concentration, disintegrating time is 3 minutes.

Disintegrants of the fourth group (finely divided materials) are not able to give a short disintegrating time to dicalcium phosphate tablets.

DISCUSSION

The most efficient disintegrants, which allow short disintegrating time in 0,5% concentration, are carboxymethylstarches (EXPLOTAB, PRIMOJEL standard and LV), some carboxymethylcelluloses (NYMCEL, AC DI SOL) hydroxypropylcellulose (L-HPC) cation exchange resin (AMBERLITE IRP 88) and cross linked polyvinylpyrrolidone (POLYPLASDONE XL).

Comparison of particle size of the most efficient disintegrants shows that they have a particle size included between 19,1 µm (POLYPLASDONE XL) and 26,7 µm (NYMCEL ZSB10) exept for one material (NYMCEL ZSB16) which particule size is 36,9 µm.

According to the theory of RINGARD and GUYOT-HERMANN[6], the optimum concentration of a disintegrant is that which corresponds to the formation of a porous capillary net-work around the particles of the tablets. The same authors indicated in a later paper[7] a method for calculation of the optimum concentration, which takes into consideration particle size of the disintegrants and elements of the tablets formula, as also porosity, and relative density of the components. According to these authors, the calculating method would be essentialy representative for spherical particles.

The method of RINGARD and GUYOT-HERMANN was applied to the mixtures of starches or starch derivatives - EMCOMPRESS because the form of these different components is approximately spherical.

If calculation was approximately possible with some starches, theory of porous capillary net-work presumes that higher the particle size, more important is the necessary quantity of disintegrant ; and so more quantity of carboxymethylstarch should be required (particle size near by 20 µm) than rice starch (particle size : 4.1 µm) ; this is in absolute contradiction with experimental results.

Therefore it seems that disintegration of a tablet cannot be explained only by the formation of a porous capillary net-work but must take into account several successive factors : wetting (contact angle), water absorption and then swelling : Figure 8

TABLE 8

COMPARISON BETWEEN OPTIMUM THEORICAL CONCENTRATION (according to 7) AND OPTIMUM EXPERIMENTAL CONCENTRATION FOR SOME STARCHES AND DERIVATIVES

DISINTEGRANTS	PARTICLES SIZE	OPTIMUM PERCENT ACCORDING TO(7)	PERCENT WHICH GIVES A DISINTEGRATION LOWER THAN 5 MINUTS.
Cornstarch	5,3 µm	2,1 %	5 %
Standard maize starch	9,9 µm	4,1 %	5 %
Waxy maize starch	9,7 µm	4,0 %	5 %
Potatoe starch	17 µm	7,3 %	5 %
Rice starch	4,1 µm	1,6 %	10 %
STARX 1500	16,7 µm	7,2 %	2 %
PRIMOJEL STD	23,7 µm	11,1 %	0,5 %
PRIMOJEL LV	19,6 µm	8,4 %	0,5 %
EXPLOTAB	22,6 µm	10,1 %	0,5 %
EMCOMPRESS	160 µm		

shows on four different scales, disintegrating times of tablets and three important physical properties (contact angle, quantities of water sucked after 1 minute, percent of maximum swelling after 15 minutes). A low disintegrating time is obtained when the three properties present favourable values (AC DI SOL, PRIMOJEL) and the higher disintegrating time were obtained when these properties are not favourable.

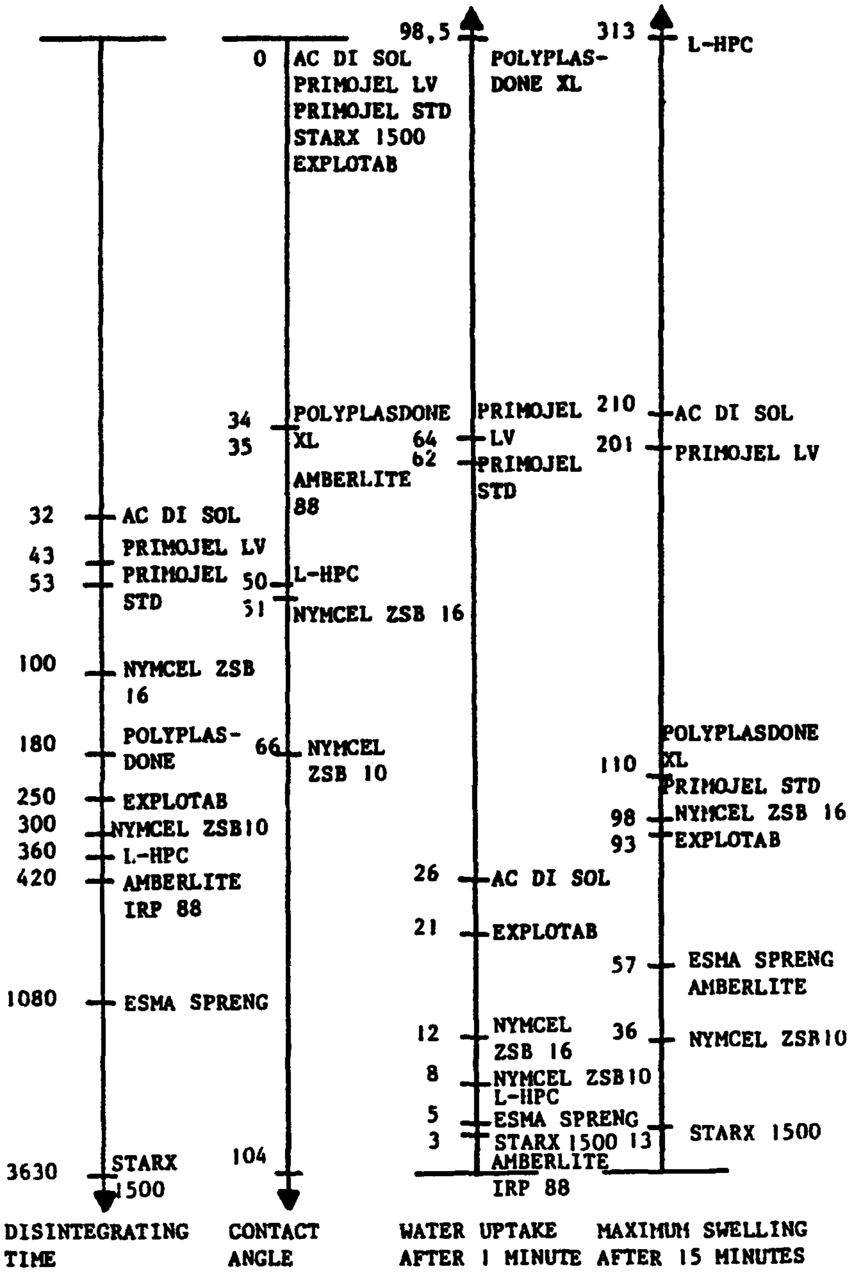

FIGURE 8

Comparative scales of physical properties of some disintegrants

Some disintegrants showed a high effectiveness to improve disintegration of dicalcium phosphate tablets, but one can examine what is the cost of this disintegration time reduction.

Although determination of prices is a difficult operation which depends of many factors, and is liable to many fluctuations, we tried to determine cost of disintegrants with a comparable way. It is evident that this cost has not an absolute value, but it is only a relative indication of prices used in one country (FRANCE) in a given period (January 1980) and for given quantities (between 50 and 100 kg) ; comparison was made with the price indicated by the suppliers who have provided the materials used for this study. In figure 9, are reported on one hand comparative prices of different disintegratns taking into account the necessary quantity to obtain a disintegration in less than 5 minutes, and on the other hand the same indications for a disintegration in less than 1 minute. Scales do not include numbered indications of price because large variations are possible around the given values.

For a disintegration in less than 5 minutes, the more interesting disintegrants are starches and carboxymethylstarches. For very short disintegrating times (less than 1 minute), the most efficient disintegrants are the most interesting (PRIMOJEL, AC DI SOL) because they promote with low concentration a fast disintegration and their cost is then less than this of starches ; furthermore with low concentrations, the influence of disintegrants on the compressibility is negligible.

CONCLUSION

The subject of this work was a comparative evaluation of the properties of many disintegrants (contact angle, water absorption, swelling). It showed that disintegration cannot be explained with only the formation of a porous capillary net-work in tablets, but many other factors must also be considered such as water absorption capacity, and swelling degree. A short study of cost indica-

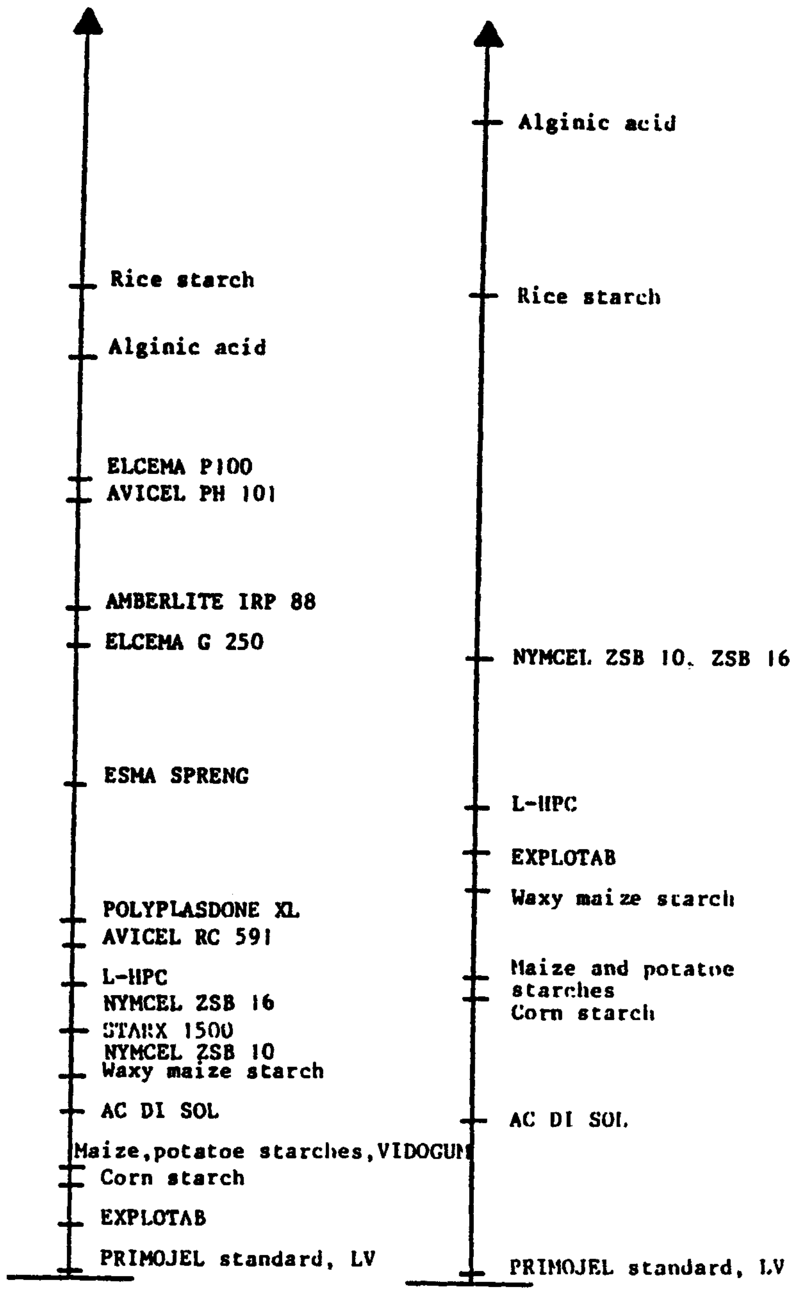

FIGURE 9

Comparative prices scales of different disintegrants used in dicalcium phosphate tablets.
Left : disintegration time less than 5 minutes
Rigth : disintegration time less than 1 minute

ted that for very short disintegration times some new agents are more interesting than usual disintegrants such as starches.

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