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THE EFFECT OF SUPERDISINTEGRANTS ON THE DISSOLUTION OF CALCIUM CARBONATE FAST DISSOLVING TABLETS

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ABSTRACT

The objective of the present study is to design and evaluate the effect of disintegrating agents such as Starch, Cross Caramellose Sodium, Sodium starch glycolate and crosprovidone Calcium carbonate conventional tablets simultaneously. The nature of calcium carbonate which forms cake on standing which affects the drug disintegration process there by inhibits the drug release from the Conventional Tablet. Hence in the present study the effect of disintegrating agents at different concentrations is carried out on both the drugs simultaneously and finding out the best concentration followed by stability studies for a period of 3 months.

Key words-Calcium Carbonate, Disintegrating agent, fast dissolving Tablets

INTRODUCTION

Despite increasing interest in controlled-release drug delivery systems, the most common tablets are those intended to be swallowed whole and to disintegrate and release their medicaments rapidly in the gastrointestinal tract (GIT). The proper choice of disintegrant or superdisintegrant and its consistency of performance are of critical importance to the formulation development of such tablets. Drug release from a solid dosage form can be enhanced by addition of suitable disintegrants. In more recent years, increasing attention has been paid to formulating fast dissolving and/or disintegrating tablets that are swallowed, but also orally disintegrating tablets that are intended to dissolve and/or disintegrate rapidly in the mouthThe present study is an attempt to select best possible combination of drug and disintegrating agent to formulate rapidly disintegrating tablet of calcium carbonate conventional tablets which disintegrates faster thereby reducing the time of onset of action. Lactose is selected as diluents, Starch, Sodium starch glycolate, CCS and crospovidone were selected as disintegrants. PVP K 30M paste was used as a binder in all formulations, Magnesium stearate and Talc as a Lubricant, Aerosil as a Glidant.

MATERIALS AND METHODS

Calcium carbonate Procured from MicroLabs,Bangalore , Cross Caramellose Sodium, Sodium Starch Glycolate Procured from Signet chemicals,Mumbai, Anhydrous lactose Procured from Jain Enterprises,Chennai,Aerosil ,Talc from Nice Chemicals Ltd, Chennai

Table 1(a): Formulation Tablet of Calcium carbonate conventional tablet

Formulation	FA1	FA2	FA3	FB1	FB2	FB3	FC1	FC2	FC3	FD1	FD2	FE1	FE2
Calcium Carbonate (mg)	250	250	250	250	250	250	250	250	250	250	250	500	500
Starch	50	100	150	-	-	-	-	-	-	-	-	-	-
CCS	-	-	-	10	20	30	-	-	-	-	-	-	-
SSG	-	-	-	-	-	-	40	50	60	-	-	-	-
CP	-	-	-	-	-	-	-	-	-	40	80	40	80
Lactose	570	520	470	610	600	590	580	570	560	580	540	340	300
PVP	50	50	50	50	50	50	50	50	50	50	50	20	20
Talc	50	50	50	50	50	50	50	50	50	50	50	50	50
Magnesium Sterate	30	30	30	30	30	30	30	30	30	30	30	50	50
Total Weight	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000

FA- Starch, FB- Croscarmelose Sodium, FC-Sodium starch glycolate, FD & FE- Crospovidone

EVALUATION OF FORMULATED CALCIUM CARBONATE TABLETS

Evaluation of blend characteristics: The Calcium carbonate granules were prepared using wet granulation method. Various formulations were made as shown in table: 1(a). The Formulated calcium carbonate granules were evaluated for Pre-formulation parameters like angle of repose, bulk density, tapped density, Compressibility index and Hausner's Ratio.

Using FA (Starch) as Disintegrant: The angle of repose of formulated calcium carbonate tablet was in the range of 20°-30°. Normally if the value falls between 20°-30°, it shows good flow property. The bulk density and tapped density were found to be in the range of 0.37 to 0.38 g/cm^3 and 0.44 to 0.45g/cm^3 respectively. A Hausner ratio was within the range of 1.16 to 1.17, lesser than 1.25 is considered to be an indication of good flow property. The compressibility index was within the range of 5-15 hence falls within the excellent range.

Using FB (Croscarmelose Sodium) as Disintegrant: The angle of repose of prepared calcium carbonate tablet was in the range of 20°-30°. Normally if the value falls between 20°-30°, it shows good flow property. The bulk density and tapped density were found to be in the range of 0.34 to 0.36 g/cm^3 and 0.39 to 0.40g/cm^3 respectively. The Hausner's ratio was within the range of 1.07 to 1.18, lesser than 1.25 is considered to be an indication of good flow property. The compressibility index was within the range of 5-15 hence falls within the excellent range.

Using FC (Sodium Starch Glycolate) as Disintegrant: The angle of repose of prepared calcium carbonate tablet was in the range of 20°-30°. Normally if the value falls between 20°-30°, it shows good flow property. The bulk density and tapped density were found to be in the range of 0.35 to 0.36 g/cm^3 and 0.39to 0.41g/cm^3 respectively. The Hausner's ratio was within the range of 1.08 to 1.18, lesser than 1.25 is considered to be an indication of good flow property. The compressibility index was within the range of 5-15 hence falls within the excellent range.

Using FD (Crospovidone- Internal) as Disintegrant: The angle of repose of prepared calcium carbonate tablet was in the range of 20°-30°. Normally if the value falls between 20°-30°, it shows good flow property. The bulk density and tapped density were found to be in the range of 0.36 to 0.38 g/cm^3 and 0.40 to 0.41g/cm^3 respectively. The Hausner's ratio was within the range of 1.07 to 1.15, lesser than 1.25 is considered to be an indication of good flow property. The compressibility index was within the range of 5-15 hence falls within the excellent range.

Using FE (Crospovidone- Internal& External)) as Disintegrant: The angle of repose of prepared calcium carbonate tablet was in the range of 20°-30°. Normally if the value falls between 20°-30°, it shows good flow property. The bulk density and tapped density were found to be in the range of 0.36 to 0.37 g/cm^3 and 0.40 to 0.41g/cm^3 respectively. The Hausner ratio was within the range of 1.10 to 1.11, lesser than 1.25 is considered to be an indication of good flow property. The compressibility index was within the range of 5-15 hence falls within the excellent range.

Post- Compressional Characteristic: The post compressional characteristic for all the formulated batches was found to be within the limits as per Indian pharmacopeia 2007. The hardness was found to be within the range of 3.5 to 5.5 Kg/cm^2 in all the formulations indicating good mechanical strength with an ability indicating physical and mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. In all the formulations, the friability value is less than 1% giving an indication that tablets formulated are mechanically stable. All the tablet formulations passed the weight variation test. The weight of all the formulations was found to be within the limits. The assay of all the formulations was found to be with in the 98% to 100.5% acceptable limits. The results of disintegration time of all the tablets prepared by wet granulation found to be varied with change in concentration of disintegrating agents from few seconds to several minutes. Formulations FD 1 and FE1 disintegrated within 3min and found to be more effective. The disintegration time of the tablets using different disintegrants decreases in the following order CP > Croscarmellose sodium > SSG > Starch. It is observed that, when CP is used as disintegrant, tablets disintegrate rapidly with in less time compared to other tablets prepared using croscarmellose sodium, starch and sodium starch glycolate disintegrants. Though tablets prepared by intra and extra granulation method found to be more effective in comparison with formulation prepared by only extra granulation. When concentration of Starch, SSG, CCS and BC is increased, the disintegration time was reduced significantly.

STABILITY STUDIES

Drug molecules are of reactive naturally, the additives are considered to be inert substance but this may not be true for all additives in a formulations. Hence, in developing any formulation, when additive are selected the same must be super imposed on to drugs and with other additives present in the formulation, to see how

compatible they are with the other formulation ingredients. Real time study of ICH guidelines involves storage of products at 30°C & 65% RH for the complete proposed shelf life period, and analyzing the product sample every month in the first 3 months, every 3 months from 4th month onwards up to one year, every 6 month in the second year of storage, afterwards once in a year till shelf life is completed. ICH guidelines also demands for storing samples at 40 ° c and 75 % RH (stress condition or accelerated stability studys) for relatively short period of time (3-6 months) which depends on claimed shelf life period as well as the zone (zone 1/2/3/4 of the world) to which the product is meant to be exported. This later study (with stress conditions) is to mine the alternating climates condition during the shelf life of the product. The stability parameter for all the formulation were evaluated after 15, 30, 45, 60, and 90 days for 40 °C at 75% RH and the values were been tabulated in table given in Table 11.

CONCLUSION

Selecting appropriate formulation excipients and manufacturing technology can obtain the design feature of fast disintegrating tablet. The disintegrants have the major function to oppose the efficiency of the tablet binder and the physical forces that act under compression to form the tablet. The stronger the binder, the more effective must be the disintegrating agents in order for the tablet to release its medication. Ideally, it should cause the tablet to disrupt, not only into the granules from which it was compressed, but also into powder particles from which the granulation was prepared. From this study, it is concluded that the disintegrants such as Starch, SSG, CCS was compared with crospovidone disintegrants and in this study calcium carbonate tablet using crospovidone as disintegrant prepared by intra and extra granulation method was found to be the most effective as they disintegrate rapidly when compared to other disintegrants, and the percentage drug release also shows a higher dissolution profile.

Table 1: Post-compressional characteristic of Calcium carbonate Tablets Using FA as disintegrant

Formulation	Weight variation(mg)	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm^2)	Friability (%)	Assay (%)
FA1	Compiles	7.194	18.99	3.5-5.5	0.291	91.8263
FA2	Compiles	7.29	19.06	3.5-5.5	0.386	93.1792
FA3	Compiles	7.39	18.97	3.5-5.5	0.254	99.9458

Table 2: Post-compressional characteristic of Calcium carbonate Tablets Using FB as disintegrant

Formulation	Weight variation (mg)	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm^2)	Friability (%)	Assay (%)
FB1	Compiles	7.31	18.91	3.5-5.5	0.355	99.2762
FB2	Compiles	7.46	19.03	3.5-5.5	0.318	98.4949
FB3	Compiles	7.27	19.11	3.5-5.5	0.347	99.5952

Table 3: Post-compressional characteristic of Calcium carbonate Tablets Using FC as disintegrant

Formulation	Weight variation (mg)	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm^2)	Friability (%)	Assay (%)
FC1	Compiles	7.251	17.96	3.5-5.5	0.314	99.6604
FC2	Compiles	7.564	18.42	3.5-5.5	0.389	98.8846
FC3	Compiles	7.387	18.55	3.5-5.5	0.296	98.8863

Table 4: Post-compressional characteristic of Calcium carbonate Tablets Using FD as disintegrant

Formulation	Weight variation (mg)	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm^2)	Friability (%)	Assay (%)
FD1	Compiles	7.27	19.11	3.5-5.5	0.214	98.4771
FD2	Compiles	7.39	19.27	3.5-5.5	0.296	99.2737

Table 5: Post-compressional characteristic of Calcium carbonate Tablets Using FE as disintegrant

Formulation	Weight variation (mg)	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm^2)	Friability (%)	Assay (%)
FE1	Compiles	6.94	18.72	3.5-5.5	0.184	98.2401
FE2	Compiles	7.05	18.92	3.5-5.5	0.213	99.1880

Table 6: Disintegration profile of Calcium carbonate tablets using FA as disintegrant

Formulation	With Disk			Without Disk		
	I	II	I	II	I	II
FA1	11min 43 sec	10 min 30 sec	10min 52sec	14min 32 sec	15min 11sec	15min 48 sec
FA2	8min 2sec	9min 33 sec	8min 18 sec	11min 14sec	12min 31 sec	11min 56 sec
FA3	4min 41 sec	5min 8 sec	4min 55sec	9min 23sec	9min 51 sec	8min 50sec

Table 7: Disintegration profile of Calcium carbonate tablets using FB as disintegrant

Formulation	With Disk			Without Disk		
	I	II	I	II	I	II
FB1	9min 21sec	8min 55 sec	10min 05sec	11min 15 sec	11min 24 sec	10min 55min
FB2	7min 43sec	8min 11 sec	8 min 5sec	9min 22 sec	9min 17 sec	10 min 31 sec
FB3	5min 22 sec	5min 42sec	6min 31sec	6 min 4 sec	7min 41sec	7min 18sec

Tab 8: Disintegration profile of Calcium carbonate tablets using FC as disintegrant

Formulation	With Disk			Without Disk		
	I	II	I	II	I	II
FC1	11min 41 sec	10min 21 sec	10min 54 sec	14min 11sec	14min 56sec	13min 34sec
FC2	8min 43sec	9min 21sec	9min 5sec	12min 37sec	14min 12sec	12min 44sec
FC3	4min 21sec	5min 32 sec	4min 13sec	6min 23sec	6min 47 sec	6min 43sec

Tab 9: Disintegration profile of Calcium carbonate tablets using FD as disintegrant

Formulation	With Disk			Without Disk		
	I	II	I	II	I	II
FD1	5 min 51 sec	6min 11 sec	5min 33sec	9min 46sec	8min 23 sec	9min 11sec
FD2	3min 11 sec	2 min 47 sec	2min 17sec	5min 25 sec	4min 21 sec	5 min 41 sec

Tab 10: Disintegration profile of Calcium carbonate tablets using FE as disintegrant

Formulation	With Disk			Without Disk		
	I	II	I	II	I	II
FE1	6min 19 sec	6min 5sec	5min 54sec	11min 19 sec	10min 47 sec	11min 14 sec
FE2	4min 45 sec	3min 52 sec	4min 32sec	9min 11sec	9min 42sec	8 min 4 sec

Stability studies:

Tab 11: Stability studies of calcium carbonate Optimized batch

Characteristics	$40^0C \pm 2^0C$, 75% ± 5%RH						
	Initial	15days	30days	45days	60days	75days	90days
Description	White	compiles	compiles	compiles	compiles	compiles	compiles
Weight variation (mg)	compiles	compiles	compiles	compiles	compiles	compiles	compiles
Thickness (mm)	6.31	6.27	6.24	6.28	6.23	6.22	6.24
Diameter (mm)	19.07	19.01	18.89	18.97	18.84	19.84	19.89
Hardness(kg/cm^2)	3	3	3	3	3	3	3
Friability (%)	0.09	0.04	0.01	0.01	0.01	0.01	0.01
Assay (%)	98.32	98.30	99.74	98.74	98.56	98.25	98.73
Disintegration (With disk)	4min 5sec	5min 19 sec	4min 34sec	4min 55sec	4min 5sec	4min 33sec	4min 56sec
Disintegration (Without disk)	8min 15 sec	8min40 sec	9min23 sec	8min 54sec	8min19 sec	7min 55sec	7min 49sec

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