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FABRICATION AND CHARACTERIZATION OF ANTITUSSIVE DISPERSIBLE TABLETS

Lakshmi Prasanna J.*, Supriya J., Sudhakar Babu AMS

Department of Pharmaceutics, AM Reddy Memorial College of Pharmacy, Petlurivaripalem, Narasaraopet, Guntur-522 601, Andhra Pradesh, India.

***Corresponding Author: Lakshmi Prasanna J.**
Department of Pharmaceutics, AM Reddy Memorial College of Pharmacy, Petlurivaripalem, Narasaraopet, Guntur- 522 601, Andhra Pradesh, India.

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ABSTRACT

The aim of the study was to fabricate and characterize antitussive disperisbe tablets using super disintegrants. Dispersible tablets of Guaiphenesin were prepared by direct compression method using Sodium starch glycollate(SSG), Croscarmellose sodium(CCS) and Crospovidone(CP). Different concentrations of super disintegrants SSG (5%, 10% and 15%), CCS (5%, 10% and15%) and CP (5%, 10% and15%) were examined to know their effect on *in vitro* drug release. Tablets were characterized for their pre compression and post compression parameters. The *in vitro drug* release studies were carried out in pH 6.8 phosphate buffer. Of all the formulations, tablets containing 15% of SSG, CCS and CP showed good drug release.

KEYWORDS: Guaiphenesin, SSG, CCS, CP, Dispersible tablets.

INTRODUCTION

Most widely accepted and used route of administration for drugs is an oral route of administration having a common drawback of swallowing especially in case of pediatric and geriatric patients. To overcome this pharma companies has been developing a variety of dispersible tablets with the potential to accommodate various physicochemical, pharmacokinetic and pharmacodynamics characteristics of drugs.[1,2] Oral Dispersible tablet is an innovative tablet technology where the dosage form containing active pharmaceutical ingredients disintegrates rapidly, usually in a matter of seconds, without the need for water, providing optimal convenience to the patient.[3] The proper choice of super disintegrant and its consistency of performance are of critical importance to the formulation development of antitussive dispersible tablets.

Guaiphenesin is an expectorant which increases respiratory tract fluid secretions and helps to loosen phelgm and bronchial secretions. By reducing the viscosity of secretions, guaifenesin increases the efficiency of the cough reflex and of ciliary action in removing accumulated secretions from the trachea and bronchi. Guaifenesin is readily absorbed from the gastrointestinal tract and is rapidly metabolized and excreted in the urine.[4] The main objective of present investigation is to fabricate and characterize antitussive dispersible tablets of guaiphenesin using super disintegrants in various concentrations in order to improve patient compliance and to decrease the side effects.

MATERIAL AND METHOD

Materials

Guaiphenesin, Sodium starch glycolate, Crospovidone and croscarmellose sodium are obtained from Hetero drugs Pvt. Ltd, Hyderabad, India. Other materials and solvents used were of analytical grade.

Preparation of tablets

Dispersible tablets containing 200 mg of Guaiphenesin were prepared by direct compression method. Drug is mixed with appropriate quantities of SSG (5%, 10%, 15%), CCS(5%, 10%, 15%), crospovidone (5%, 10%, 15%) and directly compressible lactose for 20min to ensure uniform mixing in geometrical ratio. The formulation of the tablets was given in Table 1. Powder mixture was evaluated for angle of repose bulk density (BD) and tapped density (TD). Carr's index (CI) and Hausner ratio were calculated using following equations. After evaluation this powder mixture was blended with lubricating agents (1% w/w magnesium stearate and 2% w/w talc) and compressed using 16 station rotary punching machine, equipped with flat-faced, round punches of 8-mm diameter.

Table 1: Composition of Guaiphenesin dispersible tablet formulations.

Ingredients	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Guaiphenesin(mg)	200	200	200	200	200	200	200	200	200
SSG (%)	10	20	30	-	-	-	-	-	-
CCS (%)	-	-	-	10	20	30	-	-	-
CP (%)	-	-	-	-	-	-	10	20	30
Lactose (mg)	34	24	14	34	24	14	34	24	14
Mg (%)	2	2	2	2	2	2	2	2	2
Talc (%)	4	4	4	4	4	4	4	4	4
Total weight(mg)	250	250	250	250	250	250	250	250	250

Characterization of powders[5]

Granules were evaluated for their characteristic parameters. Angle of repose was determined by funnel method, bulk density (BD) and tapped density (TD) were determined by cylinder method. Carr's index (CI) and Hausner ratio were calculated using following equations.

$$Hausner\ ratio = \frac{TD}{BD} \qquad \%CI = \frac{TD - BD}{TD} X\ 100$$

Evaluation of prepared tablets

The prepared dispersible tablets were evaluated for hardness, friability, thickness, uniformity of the weight, content uniformity, wetting time, uniformity of dispersion and drug release studies. Hardness was determined by using Pfizer hardness tester. Friability was determined using Roche friability testing apparatus. Thickness was measured using vernier calipers. Disintegration, uniformity of the weight and content uniformity were performed according to the I.P method. [6,7] Wetting time, uniformity of dispersion and *in vitro* drug release studies were performed by the following methods.

Wetting time[8]

A piece of tissue paper (12cmx10.75cm) folded twice was placed in a petri dish containing 6ml of water. A tablet was placed on the paper and the time taken for complete wetting of tablet was noted three tablets from each formulation were randomly selected and the average wetting time was noted.

Uniformity of dispersion

Two tablets were placed in 100ml of water and stirred gently until completely dispersed. A smooth dispersion was obtained which passes through a sieve screen with a nominal mesh aperture of 710µm (sieve no: 22).

***In vitro* drug release studies**

The *in vitro* drug release studies were carried out on a eight stationed USP type II dissolution apparatus (paddle method) at 37°C ± 0.5°C and 50 rpm for a period of 1h. The dissolution studies were carried in triplicate in 900 ml of the phosphate buffer pH 6.8 from 45min to 1hr. An aliquot (5ml) was withdrawn at specific time intervals and replaced with the same volume of pre warmed (37°C ± 0.5°C) fresh dissolution medium. The samples withdrawn were filtered through whatmann filter paper (No.1) and drug content in each sample was analyzed by UV-visible spectrophotometer at274 nm. The amount of drug present in the sample was calculated with the help of appropriate calibration curve constructed from reference standards.

RESULT AND DISCUSSION

For each designed formulation, blend of drug and excipients was prepared according to the formulae given in Table 1. The powders were characterized with respect to angle of repose, BD and TD. Bulk density was found to be between 0.42±0.02 and 0.53±0.03 gm/cm^3 and tapped density between 0.47±0.02 and 0.56±0.01 gm/cm^3 for all formulations. From density data carr's index was calculated and was found to be between 2.56±0.96 and 7.64±0.81. Angle of repose was found to be in the range of 26.54±0.15 and 29.03±0.06. Hausner ratio was found below 1.12. All the formulations show good micromeritic properties for direct compression and were given in Table 2.

Table 2: Pre compression parameters of formulation blends (mean ± S.D; n=3).

Formulation code	Angle of repose (°)	Bulk density (g/cc)	Tapped density(g/cc)	Carr's index (%)	Hausner's ratio
F_1	26.85±0.11	0.51 ± 0.01	0.50±0.01	2.56± 0.96	1.02±0.01
F_2	26.54±0.15	0.52± 0.01	0.56±0.01	7.64 ± 0.81	1.07±0.00
F_3	27.07±0.06	0.42 ± 0.02	0.47±0.02	11.2 ± 1.10	1.09 ± 0.05
F_4	27.20±0.14	0.48 ± 0.02	0.52±0.01	8.25 ± 1.10	1.12 ± 0.02
F_5	28.31±0.05	0.48 ± 0.02	0.51±0.02	4.58 ± 0.93	1.04 ± 0.01
F_6	28.49±0.05	0.51 ±0.02	0.54±0.02	4.91 ± 0.70	1.05 ± 0.00
F_7	27.80±0.43	0.53±0.03	0.55±0.03	3.62±0.24	1.03±0.00
F_8	29.03±0.06	0.49±0.02	0.52±0.02	5.12±0.88	1.05±0.00
F_9	28.82±0.02	0.51±0.02	0.53±0.01	6.20±0.776	1.05±0.01

As the tablet powder mixture was free flowing, the hardness of the tablets ranged from 4.43-4.73kg/cm^2 and the friability values were less than 1.0% indicating that the dispersible tablets were compact and hard. The thickness of the tablets depends on size of the punch and weight of the tablet and was between 248-250mg. Drug content of the formulations was found to be 97.47-99.81% of Guaiphenesin and good uniformity in drug content was observed. The wetting times of tablets was found to be between 37 – 45sec. Dispersion time of the prepared tablets were found to be in the range of 23-33 seconds. All the prepared tablets disintegrated within 1 minute time. Thus all the physical attributes of the prepared tablets were found be practically within control and were given in Table 3 and 4.

Table 3: Physical characteristics of the dispersible tablets (mean±S. D; n=3).

Formulation code	Hardness (Kg/cm^2)	Friability (%)	Tensile strength	Weight variation
F_1	4.46±0.16	0.51	8.68±0.3	250±0.001
F_2	4.60±0.28	0.52	9.15±0.6	248±0.001
F_3	4.43±0.20	0.61	8.81±0.4	252±0.001
F_4	4.63±0.07	0.81	9.21±0.0	249±0.001
F_5	4.46±0.30	0.75	8.88±0.61	250±0.001
F_6	4.73±0.12	0.7	9.41±0.24	250±0.001
F_7	4.53±0.16	0.82	9.01±0.33	248±0.001
F_8	4.46±0.30	0.81	8.88±0.61	249±0.001
F_9	4.46±0.12	0.79	8.88±0.24	250±0.001

Table 4: Drug Content, Wetting time, Dispersion time and Disintegration time of the dispersible tablets.

Formulation code	Drug content uniformity	Wetting time(sec)	Dispersion time(sec)	Disintegration time(sec)
F_1	98.05±0.58	37	23.44	43.83
F_2	99.8±1.33	41	28.31	35.33
F_3	97.4±0.68	44	33.47	29.33
F_4	99.5±0.78	39	29.41	31.16
F_5	98.8±0.91	42	31.57	35.83
F_6	99.1±0.89	45	35.42	43.16
F_7	99.78±0.75	41	31.78	37.5
F_8	98.79±0.82	39	32.24	30.5
F_9	98.55±0.87	44	33.35	26.83

From the *in vitro* dissolution studies, it was observed that among the three different superdisintegrant ratios used formulations with superdisintegrants ratio 5% showed higher drug release rates when compared to 10% and 15%. Figure 1 depicts the release profile guaiphenesin from the dispersable tablets having different concentration of cross caramellose sodium. The results indicated that the rate relase of guaiphenesin decreased by increasing the concentration of the superdisintegrant. The order of release was $F_1>F_2>F_3>$. Figure 2 depicts the release profile of guaiphenesin from the dispersable tablets having different concentration of sodium starch glycolate. The results indicated that the rate release of drug decreased by increasing the concentration of the superdisintegrant. The order of release was $F_4>F_5>F_6$. Figure 3 depicts the release profile guaiphenesin from the dispersable tablets having different concentration of crosspovidone. The results indicated that the rate relase of guaiphenesin decreased by increasing the concentration of the superdisintegrant. The order of release was $F_7>F_8>F_9$. The influence of super disintegrants on the dissolution of guaiphenesin from the tablets is given in Table 5 and 6 respectively. Figure 4 depicts the comparative release profile of guaiphenesin formulations having high concentration of superdisintegrants. Out of nine formulations F9 formulation shows drug release 99.99% in 45min.

Table 5: *In vitro* percent drug release data of Guaiphenesin dispersible tablets using CCS and SSG.

Time (min)	F_1	F_2	F_3	F_4	F_5	F_6
5.	28.35±0.06	23.4±0.05	22.05±0.04	31.5±0.07	25.2±0.05	26.55±0.05
10.	63±0.14	57.6±0.12	51.75±0.11	67.5±0.15	56.25±0.12	58.05±0.12
15.	98.01±0.21	77.4±0.17	69.3±0.15	98.55±0.21	78.3±0.17	67.5±0.15
20.	-	85.5±0.19	78.3±0.17	-	86.4±0.19	75.15±0.16
30.	-	98.55±0.21	86.4±0.19	-	99.45±0.22	86.85±0.19
45.	-	-	99±0.22	-	-	99±0.22

Table 6: *In vitro* percent drug release data of Guaiphenesin dispersible tablets using CP.

Time(min)	F_7	F_8	F_9
5.	32.4±0.07	25.2±0.05	26.55±0.05
10.	67.5±0.15	57.6±0.12	56.25±0.12
15.	99±0.22	68.85±0.15	69.75±0.15
20.	-	81.9±0.18	78.3±0.17
30.	-	99.45±0.22	85.95±0.19
45.	-	-	99.99±.0.22

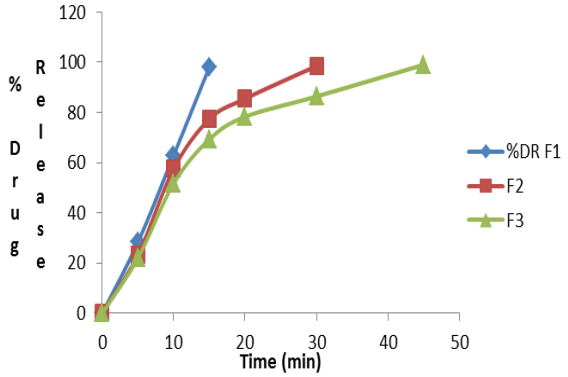

Fig 1: *In vitro* drug release profile of dispersible tablets using CCS.

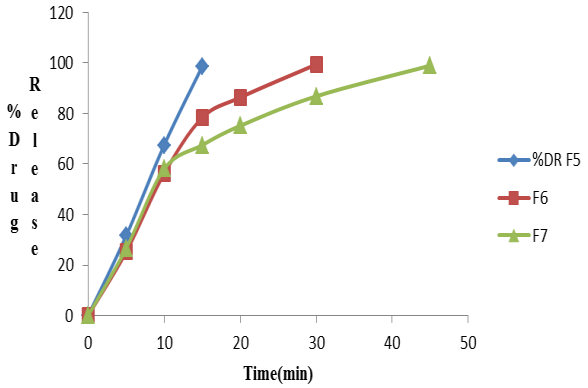

Fig 2: *In vitro* drug release profile of dispersible tablets using SSG.

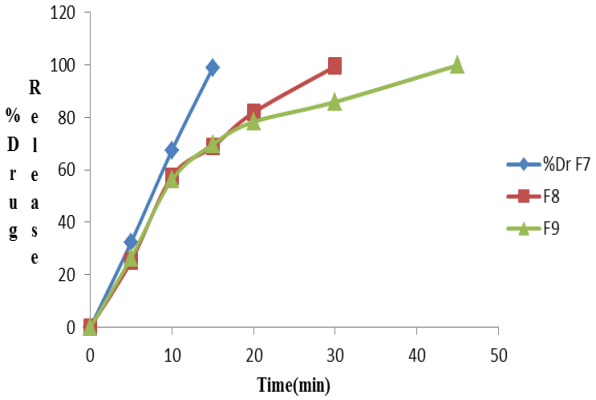

Fig. 3: *In vitro* drug release profile of dispersible tablets using CP.

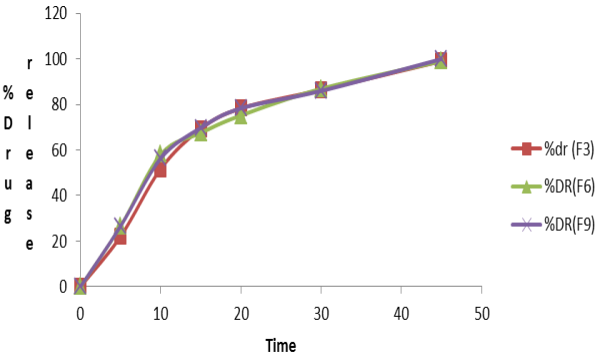

Fig 4: Comparative *in vitro* drug release profile of dispersible tablets using 15% of super disintegrants.

CONCLUSION

In the present study, Guaiphenesin dispersible tablets with satisfactory results were successfully prepared using super disintegrants namely Sodium starch glycolate, Croscarmellose sodium and Crospovidone by direct compression method. Study indicated that increase in the concentration of super disintegrants result in decrease in the release of drug and increase in the dispersion time and wetting time. It was concluded that SSG, CCS and CP with highest concentration were able to produce desired effects.

ABBREVIATIONS

CCS- Crosscaramellose sodium, CP- Crospovidone, SSG- Sodim starch glycolate.

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