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Formulation and Evaluation of Guaifenesin Gastro Retentive Tablets

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Abstract

Guaifenesin is an expectorant and belongs to BCS class I which exhibits high solubility and high permeability. Guaifenesin has a half-life of 1 hour; in order to increase its duration of action gastroretentive tablets are formulated. Guaifenesin shows poor flow properties so the method opted for the preparation of this tablets is Top spray granulation. In which HPMC K100LV/HPMC E6LV/HPMC K100M/HPMC K15MPCR is used as swelling matrix polymer, Povidone is used as binder, Magnesium stearate is used as lubricant and MCC is used as diluent. Tablets are evaluated for floating lag time, total floating time, thickness, hardness, friability and invitro drug release studies were performed. The optimized formulation showed less floating lag time, sufficient floating time and with maximum drug release of 88.9% at the end of 12 hours.

Keywords: Gastroretentive, Top spray granulation, Guaifenesin, Floating lag time.

INTRODUCTION

Drug: Drug is any substance which intended to be used of mitigation, space prevention, space cure and diagnosis of disease and disorder and maintains the good quality of health [1].

Dosage form: dosage forms are the means by which drug substances are delivered to sites of action within the body [1].

Drug= Active pharmaceutical ingredient + excipients

Drug Delivery Systems

The system to lever the drug to the body to produce desired therapeutic action against diseases and disorders is known as drug delivery systems.

Types of Drug Delivery Systems [2]

1. Conventional drug delivery system.
2. Oral drug delivery system.
3. Sustained drug delivery system.
4. Controlled drug delivery system.
5. Targeted drug delivery system.

Gastroretentive Drug Delivery system [2]

Definition: these are the drug delivery system in which can specifically targeted at the site of GI tract is known as gastroretentive drug delivery system.

Mechanism: releases the drug at the site of abdomen/stomach. This type of drug delivery is an approach used to prolong gastric residence time so that the drug remains in the stomach for prolonged time and shows required pharmaceutical action.

Drugs Suitable for Gastroretention [3]

- Drugs having local activity in the stomach.
- Drugs which are unstable in alkaline environment.
- Drugs having maximum absorption in the stomach.
- Drugs having shorter half-life.

Advantages

- Improves the bio availability of drugs thereby possible reduction of dose
- Maintains constant therapeutic levels over prolonged period of time

Disadvantages

- Stomach may faded with water
- The absorption of drug may hindered in absence of food

Guaifenesin

Guaifenesin is an expectorant belongs to class I of BCS classification. Guaifenesin is used to clear mucus or phlegm from the chest when there is congestion from cold or flu. It works by thinning the mucus or sputum in the lungs. Guaifenesin is available

both over the counter (OTC) and with registered medical practitioner prescription. Guaifenesin has shorter half-life; it was approximately one hour so guaifenesin is mostly formulated as controlled drug delivery system. [6]

MATERIALS AND METHODS

Materials

Guaifenesin from Sigma-Aldrich Company, different grades of HPMC from DFE pharma, Magnesium stearate from Peter Greven and colloidal silicon Dioxide is purchased from S Zaveri supplier.

DETERMINATION OF ANALYTICAL METHODS

There are misshapen analytical methods worn in current swot are UV-Visible spectroscopy and HPLC. Guaifenesin was analyzed via Shimadzu UV-Visible 1800 twofold beam spectro photometer through way of data acquisition system UV probe and aid in determination of solubility [8].

UV SPECTROPHOTOMETRIC METHOD FOR ANALYSIS OF GUAIFENESIN

Preparation of Standard Stock Solution

Weigh and transfer about 100mg of Guaifenesin standard into 100ml volumetric flask, add about 60ml of methanol sonicate for 20 minutes and make up the volume to 100ml with methanol.

Preparation of Test Solution

From the stock solution take 1ml and dilute to 100ml with methanol, 10ppm solution is prepared. λ_{max} is calculated by using 10ppm concentration in the range of 200-700nm.

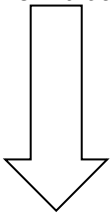
Standard Graph of Guaifenesin

Weigh and transfer about 100mg of Guaifenesin standard into 100ml volumetric flask, add about 60ml of methanol, sonicate for 20 minutes and make up the volume to 100ml with methanol. From the stock solution take 1ml and dilute to 100ml with methanol, 10ppm solution is prepared. From the stock solution 6, 8, 10, 12, 14 µg/ml were prepared and the absorbance was measured at 273nm.

Drug Excipient Compatibility Studies Using HPLC

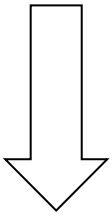
Drug excipient compatibility swot is imperative stage in this study for dosage stage development. These studies mainly conducted to prophesy the chemical reaction flanked by active pharmaceutical ingredient and excipients, excipient role in drug destabilization and chemical amend and it helps in optimization of formulation premeditated. This affords information to plump for the excipients indispensable for formulation [10].

Formulation of Guaifenesin Gastroretentive Tablets



Method of Preparation – Top spray granulation

Sifted API was transferred into FBP and fluidized for 5min, after obtaining product temperature 36^0C spray was started, after complete of spray solution; the granulated material was allowed to dry for about 15 minutes.



Other extra granulated material was added prelubricated for 10 minutes, then lubricated for 5 minutes with Magnesium stearate and compressed into tablets.

Table no 1: Formulation of Guaifenesin Gastroretentive Tablets

Ingredient	F1	F2	F3	F4
Guaifenesin	1000	1000	1000	1000
HPMC K100 LV	100	-	-	-
HPMC E6 LV	-	100	-	-
HPMC K100 M	-	-	100	-
HPMC K15 MPCR	-	-	-	100
Povidone	30	30	30	30
MCC ph 102	50	40	30	20
Magnesium stearate	10	6.5	0	6.5
Colloidal silicon oxide	10	20	20	28
Purified water	q.s	q.s	q.s	q.s

EVALUATION OF GUAIFENESIN GASTRORETENTIVE TABLETS

Evaluation of Pre-Compression Parameters

Angle of Repose

The maximum angle possible between the surface of the pile of the powder and the horizontal plane."Lower the angle of repose, better the flow properties.

Bulk Density

Bulk density denotes the total density of the material. It includes the true volume of the interparticle spaces and intraparticle pores.

Hausner Ratio

The ratio of tapped density to bulk density is known as Hausner ratio.

Compressibility Index

The compressibility index of the granules was determined by Carr's index:

Carr's Index (%) = [(TD-BD)/TD] × 100

Evaluation of Post Compression Parameters

Hardness

The application of hardness testing enables to evaluate whether produced dosage form meets the defined specifications. The hardness of the tablet is tested by LAB INDIA hardness tester.

Thickness

The uniformity in diameter of tablets is very important in increasing patient compliance. Thickness is measured by vernier callipers.

Friability

Friability testing determines how much mechanical stress tablets are able to withstand during their transportation and handling by customers. Friability of the tablet measured by Roche friabilator

Weight Variation

Weight variation evaluation is used to confirm uniformity of the dosage unit and supports product safety, identity, and quality.

Dissolution Test

Objective

A drug must be in solution in relevant body fluid before absorption can takes place. It ensures that minimum amount of drug will be released and dissolved from that dosage form with in specified time.

Apparatus: USP Dissolution Apparatus I.
Dissolution Medium: Phosphate Buffer.
Temperature: 37 degrees Celsius.
Rotational Speed: 100 rpm.

CHARACTERIZATION OF GUAIFENESIN GASTRORETENTIVE FLOATING TABLETS

Floating Lag Time

Time required for the tablet to float rise on the surface of the medium was considered as floating lag time.

Floating Time

Total duration of the tablet floating on the medium was considered as floating time.

RESULTS AND DISCUSSION

Calibration Curve of Guaifenesin in Methanol

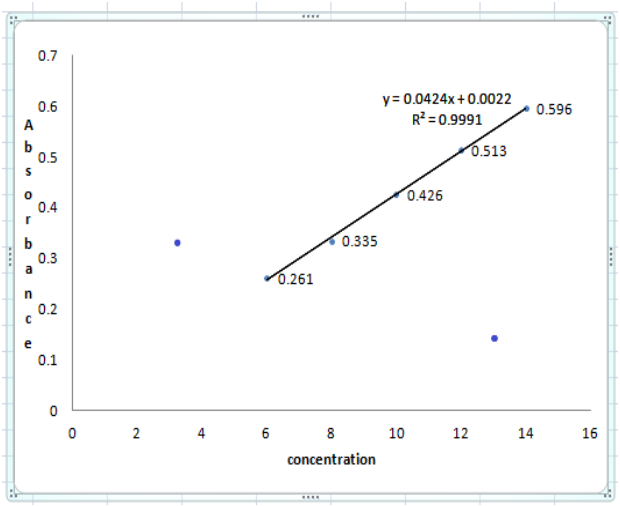


Fig. no 1: Standard calibration graph of Guaifenesin

Table no 2: calibration curve of Guaifenesin

S.NO	Sample ID	Concentration (µg/ml)	Absorbance
6	6ppm	6	0.261
8	8ppm	8	0.335
10	10ppm	10	0.426
12	12ppm	12	0.513
14	14ppm	14	0.596

Assay and Related Substances by HPLC

The compatibility between drug and excipients was determined by using HPLC through the detection of Assay and Related substances. There is no significant change in the amount of related substances indicates the compatibility between drug and excipients.

Table no 3: Drug Excipient Compatibility Studies

Drug excipient compatibility studies			
Guaifenesin	Assay	Related Substances	Max Unknown impurities
Guaifenesin	101.4	0.28	Nil
API+MCC	101.4	0.38	Nil
API+HPMC E6 LV	100.4	0.28	Nil
API+HPMC K100M	102.8	0.27	Nil
API+HPMC K100 LV	97.9	0.28	Nil
API+HPMC K15 MPCR	98.8	0.38	Nil
API+All Excipients	95	1.47	0.056

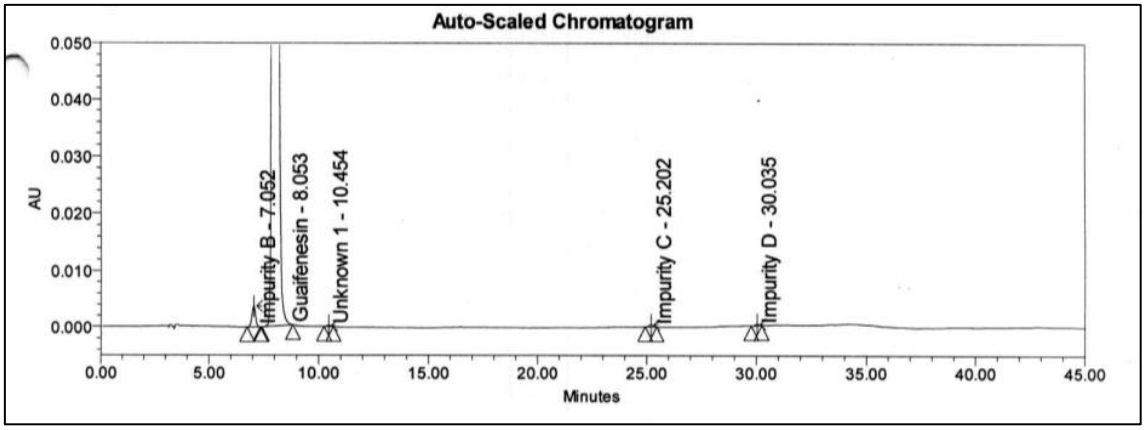


Fig. no 2: Auto scaled chromatogram of Guaifenesin

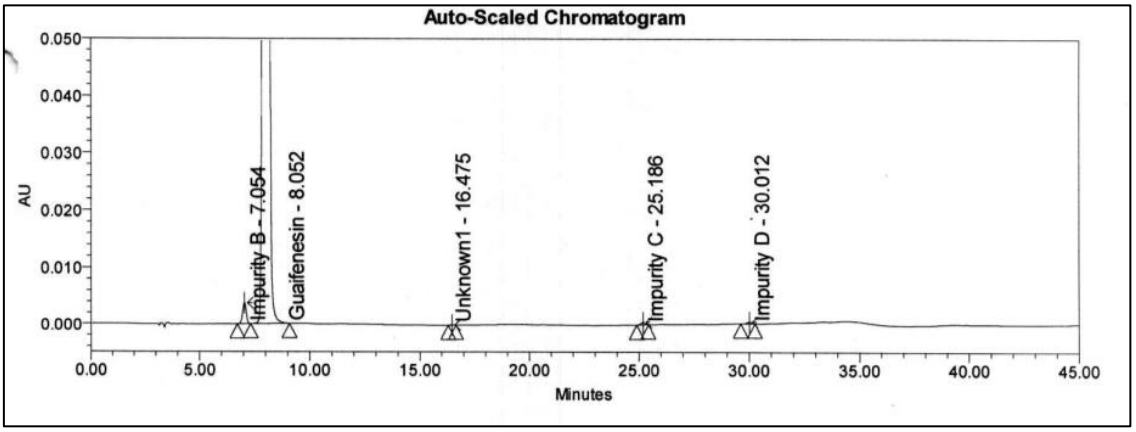


Fig. no 3: Auto Scaled chromatogram of Guaifenesin+MCC

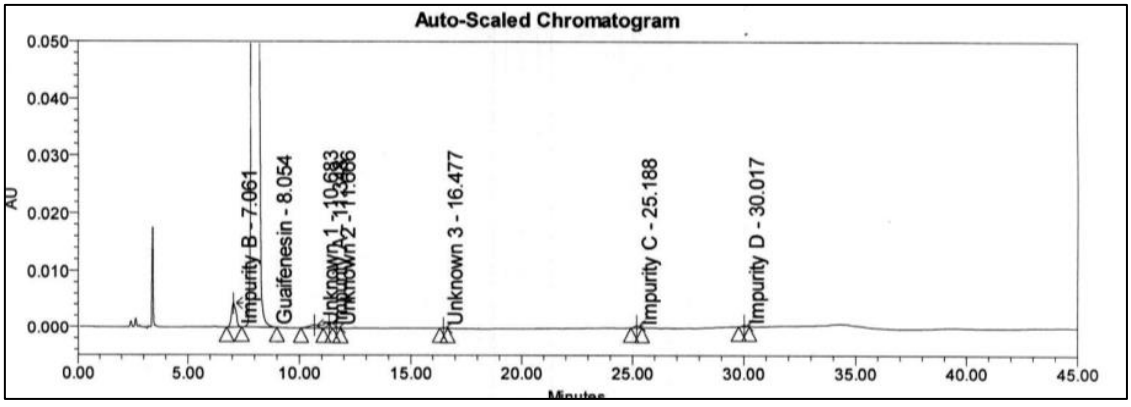


Fig. no 4: Auto scaled chromatogram Guaifenesin+HPMC K100LV

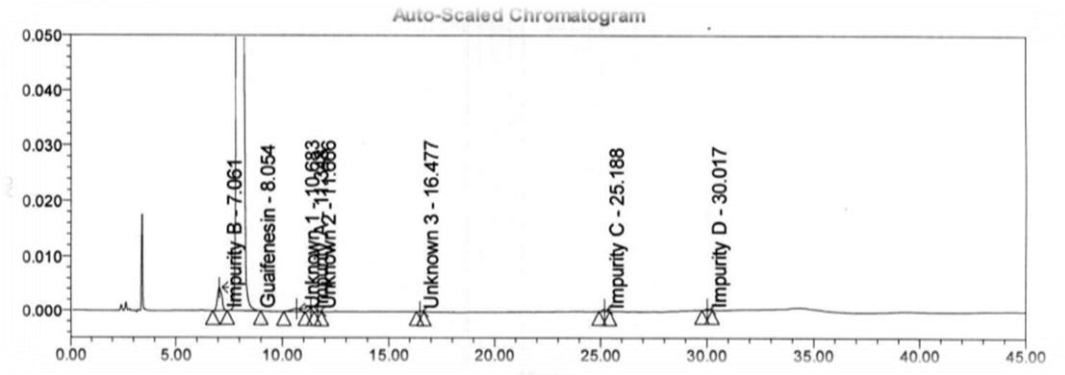


Fig no 5: Auto scaled chromatogram of Guaifenesin+All excipients

Pre Compression Parameters

Table no 4: pre compression parameters

Formulation Trial	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio
F1	0.50	0.63	23	1.3
F2	0.49	0.54	12.3	1.12
F3	0.43	0.49	8.3	1.089
FF	0.41	0.54	25	1.132

In Process Parameters

Table no 5: In process parameters

Formulation Trial	Weight variation	Hardness	Thickness	Friability
F1	1189-1192	9.3-11.9	9.5-9.7	0.27
F2	1193-1196	9.4-12.5	9.5-9.8	0.28
F3	1208-1211	9.3-12.2	9.3-9.5	0.32
F4	1198-1208	9.4-12.5	9.4-9.6	0.27

Floating Lag Time

Table No 6: floating lag time

Formulation trial	Floating lag time
F1	Immediately
F2	Immediately
F3	Immediately
F4	Immediately

Invitro Drug Release Study of Guaifenesin Floating Tablets

Table no 7: dissolution profile in 0.1N HCl

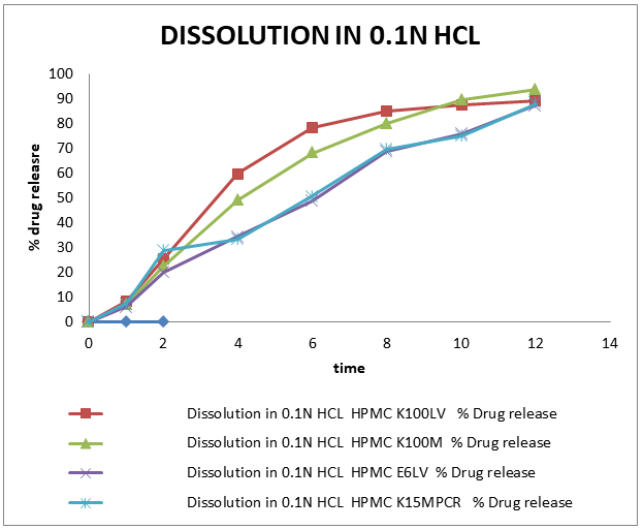
Time (Hrs)	F1	F2	F3	F4
0	0	0	0	0
1	8.4±1.2	7.3±0.7	6.2±1.1	7.5±0.7
2	25.5±0.9	22.7±1.1	20.1±0.8	28.9±1.1
4	59.8±0.6	49.3±0.9	34.5±0.5	33.6±0.6
6	78.2±1.3	68.0±0.4	48.7±1.2	50.8±0.5
8	85.1±1.4	79.7±1.2	68.6±1.7	69.5±1.4
10	87.4±1.1	89.3±1.2	75.9±0.5	74.8±1.7
12	88.9±0.6	93±0.6	87.3±0.3	88.0±0.6

The cumulative % of drug release from tablets at the end of 12hrs is found to be 88.9% in formulation F1.

The cumulative % of drug release from the tablets at the end of 12hrs is found to be 93% in formulation F2.

The cumulative % of drug release from the tablets at the end of 12hrs was found to be 87.3% in formulation F3.

The cumulative % of drug release from the tablets at the end of 12hrs was found to be 88% in formulation F4.



CONCLUSION

In the present study by using top spray granulation method, floating gastroretentive tablets of Guaifenesin are developed. Guaifenesin along with other excipients which are selected for the formulation are compatible and were confirmed by drug excipient compatibility studies. Prepared blend was evaluated for pre compression parameters like bulk density, tapped density, Hausner's ratio and Carr's index. And then tablets are evaluated for post compression parameters like thickness, Hardness, friability and Dissolution. All the formulations were evaluated and formulation F2 was found to be the optimized formulation. Hence it was concluded that the formulation F2 had a better drug release profile.

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