Journal of Pharmacreations

PharmaCreations

ISSN: 2348-6295

*Pharmacreations* | *Vol.10* | *Issue 1* | *Jan- Mar- 2023*

*Journal Home page: www.pharmacreations.com*

*Research article* *Open Access*

# Design, formulation and *in vitro* evaluation of extended-release tablets of guaifenesin

**V. Anusha*, Y. Ganesh Kumar, Deshmukh Harshal, Gudepu Jhansi.**

**Assistant professor, Department of Pharmaceutics, KVK College of Pharmacy, Hyderabad, Telangana, India. Department of Pharmaceutics, KVK College of Pharmacy, Surmaiguda (V), Lashkarguda (G.P), Abdullapurmet (M), R.R Dist., Telangana, India - 501512*

**Corresponding Author: V. Anusha**

## ABSTRACT

The objective of the present study was to develop extended-release matrix tablets of Guaifenesin. Guaifenesin is used to help clear mucus or phlegm (pronounced flem) from the chest when you have congestion from a cold or fly. The extended-release tablets were prepared by direct compression method using Ethyl cellulose, Sodium alginate in various concentrations. The powder showed satisfactory flow properties and compressibility. The powders for tableting were evaluated for angle of repose, loose bulk density, tapped bulk density, compressibility index and Hausner's ratio etc. The powder blend showed satisfactory flow properties. The tablets were subjected to thickness, weight variation test, drug content, hardness, friability and in-vitro release studies. All the formulations showed good results which were compliance with Pharmacopoeia standards. All the eight formulations showed acceptable pharmacopoeia standards. The result of formulation F4 extended the release of Guaifenesin up to 8 hrs.

**Keywords:** Guaifenesin, extended release, natural and synthetic polymers, direct compression technique, FTIR studies, in vitro rug release.

## INTRODUCTION

The vital role of novel drug delivery system that improve the therapeutic effectiveness of integrated drugs by providing extended, controlled delivery and or targeting the drug to desired site. Extended-release formulations make the drug available over extended time period after oral administration. The extended-release product will optimize therapeutic effect and safety of a drug at the same time improving the patient convenience and compliance[1]. By incorporating the dose for 24 hrs into one tablet/capsule from which the drug is released slowly. This formulation helps to avoid the side effects associated with low and high concentrations. The ideal drug delivery system should show a constant zero-order release rate and maintain the constant plasma concentrations[2]. The design of oral extended release delivery systems is subjected to several interrelated variables of considerable importance such as the type of delivery system, the disease being treated, the patient, the length of therapy and the properties of the drug[3]. Matrix tablets are considered to be the commercially feasible extended action dosage forms that involve the least processing variables, utilize the conventional facilities and accommodate large doses of drug. These remains an interest in developing novel formulations that allow for extended the drug release using readily available, inexpensive excipient by matrix-based formulation.[4,5] During the last two decades there has been remarkable increase in interest in extended-release drug delivery system. This has been due to various factors like the prohibitive cost of developing new drug entities, expiration of existing international patients, discovery of new polymeric materials suitable for prolonging the drug release, and the improvement in therapeutic efficiency and safety achieved by these delivery systems. The basic goal is to achieve a steady state blood level that is therapeutically effective and non-toxic for an extended period of time. The design of proper dosage form is an important element to accomplish this goal.[6,7] In the case of oral extended released dosage form, an effect is for several hours depending upon residence time of formulation in the GIT. The aim of the study Guaifenesin has to be released in a Extended manner, so that therapeutic concentration can be maintained. Guaifenesin is most widely used drugs Guaifenesin is used to relieve chest congestion[8]. To develop the Guaifenesin extended-release matrix tablets using natural and synthetic polymers by using direct compression method and evaluated. The main objective of the present study is to

formulate and evaluate an extended-release matrix drug delivery system for Development of suitable analytical method for the estimation of the drug.Pre-formulation studies, Drug- excipients compatibility studies for selection of excipients. Formulation of tablet using various polymers for drug delivery. To evaluate pre compression and post compression parameters of the formulated tablets.Stability study of the most satisfactory formulation.

## MATERIALS AND METHODS

### MATERIALS

Guaifenesin was collected as a gift sample from Hetero Drugs Ltd, Hyd, polymers and various excipients were purchased from AR chemicals, HYD.

## METHODOLOGY

### Drug - excipient compatibility studies

Infrared spectroscopy is a useful analytical technique utilized to check the chemical interaction between the drug and excipients used in the formulation. By ensuring the crystalis clean,1e2 mg of solid fine powder of SVD was placed over on the window (which is made up of diamond crystal) and turning the dial path to required path-length (4000-400 cm1) to get the sample tobe analyzed through Micro Lab FTIR software. The FTIR (ShimadzuAUX 220, Japan) spectrum of the pure SVD and its physical mixture were compared to check the possibility of drug polymer interactions[9].

**Table 1: Development of Guaifenesin Extended release tablets**

| S.NO. | INGREDIENTS | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Guaifenesin | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| 2 | Ethylcellulose | 50 | 100 | 150 | 200 | - | - | - | - |
| 4 | Sodium alginate | - | - | - | - | 50 | 100 | 150 | 200 |
| 6 | Micro crystalline cellulose | 245 | 195 | 145 | 95 | 245 | 195 | 145 | 95 |
| 7 | Magnesium stearate | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| 8 | Talc | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| **9** | **Total weight** | **500** | **500** | **500** | **500** | **500** | **500** | **500** | **500** |

### Direct compression method [10]

Pre weighed ingredients were passed through Sieve no. 40 mesh separately and collected. Ingredients were mixed in geometrical order and thoroughly mixed in a polythene bag for 15 minutes to get a uniform mixture. Talc and magnesium stearate were added to the powder mixture and compressed on a 16- station rotary tablet compression machine using 10mm round flat face punch.

### Evaluation studies [11,12]

### Bulk Density

Bulk densities of all types of granules were determined by pouring gently some amount of sample through a glass funnel into a 10 ml graduated cylinder. The volumes occupied by the sample were recorded. Bulk density was calculated:

**Bulk density = weight of sample taken /volume noted**

### Tap density

Tapped densities of all types of granules were determined by pouring gently some amount of sample through a glass funnel into a 10 ml graduated cylinder. The cylinder was tapped from a height of 2 inches until a constant volume was obtained. Volumes occupied by the sample after tapping were recorded, and tapped density was calculated

**Tapped density = weight of sample taken / tapped volume**

Where,

$V_o$ = initial volume

$V_f$ = final volume.

### Compressibility index

% compressibility was determined by the Carr's compressibility index

**Carr's index = Tapped density - Bulk density / Tapped density X 100**

### Hausner's ratio

**Hausner's ratio = Tapped density / Bulk density**

### Angle of repose

The angle of repose of granules was determined by funnel method. A funnel with 10 mm inner diameter of stem was fixed at a height of 2 cm. over the platform. About 10 g of sample was slowly passed along the wall of the funnel till the tip of the pile formed and touches the steam of the funnel. A rough circle was drawn around the pile base, and the radius of the powder cone was measured.

$$\tan\theta = h/r$$

$$\theta = \tan^{-1} h/r$$

Where

*h* = height of pile

r = radius of the base of the pile

θ = angle of repose

## Evaluation of tablet[13,14,15]

### Weight variation

To find out weight variation 20 tablets of each formulation were weighed individually using an electronic balance, average weight was calculated and individual tablet weight was then compared with average value to find the deviation in weight. The test was performed according to the official method

### Thickness

The thickness and diameter of tablets were important for uniformity of tablet size. The thickness and diameter of the tablets was determined using a Vernier caliper. Ten tablets from each type of formulation were used and average values were calculated.

### Hardness

For each formulation, the hardness of 10 tablets was determined using the Monsanto hardness tester. The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading should be zero kg/cm2 . Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted in $kg/cm^2$.

### Friability

Friability is the measure of tablet strength. This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of preweighed tablets was placed in Roche friabilator which was then operated for 100 revolutions. The tablets were then dedusted and reweighed. A loss of less than 1 % in weight is generally. The percentage friability was measured using the formula,

$$\% F = \{1-(Wo/W)\} \times 100$$

Where,

% F = friability in percentage
Wo = Initial weight of tablet
W = weight of tablets after revolution

### Content Uniformity

Twenty tablets were powdered in a mortar. An accurately weighed quantity of powdered tablets equivalent to100 mg of guaifenesin was extracted with pH 6.8 phosphate buffer and the solution was filtered through whatmann filter paper. The absorbance was measured at 274 nm after suitable dilution.

### In- Vitro Release study

Drug release was assessed by dissolution test under the following conditions: n = 3, USP type I dissolution apparatus (Basket method) at 100 rpm in 900 mL of phosphate buffer pH 6.8 throughout the dissolution up to 12 hours, maintained at 37°C ± 0.5°C. 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 and drug content in each sample was analyzed by UV-Visible spectrophotometer at 274 nm

### Stability studies

To assess the drug and formulation stability, stability studies were done according to ICH guidelines. The optimized formulation was subjected to stability study at 40±2ºC and 75±5% RH for 90days. The samples were evaluated for physical changes, hardness, friability, drug content and percentage drug release during the stability studies[16].

## RESULTS AND DISCUSSION

Extended release tablets of Guaifenesin were prepared and evaluated.

### Drug - excipient compatibility studies (FT-IR)

The compatibility between the drug and other excipients was evaluated using FTIR peak matching method. There was no appearance or disappearance of peaks in the drug-lipid mixture, which confirmed the absence of any chemical interaction between the drug, lipid and other chemicals.

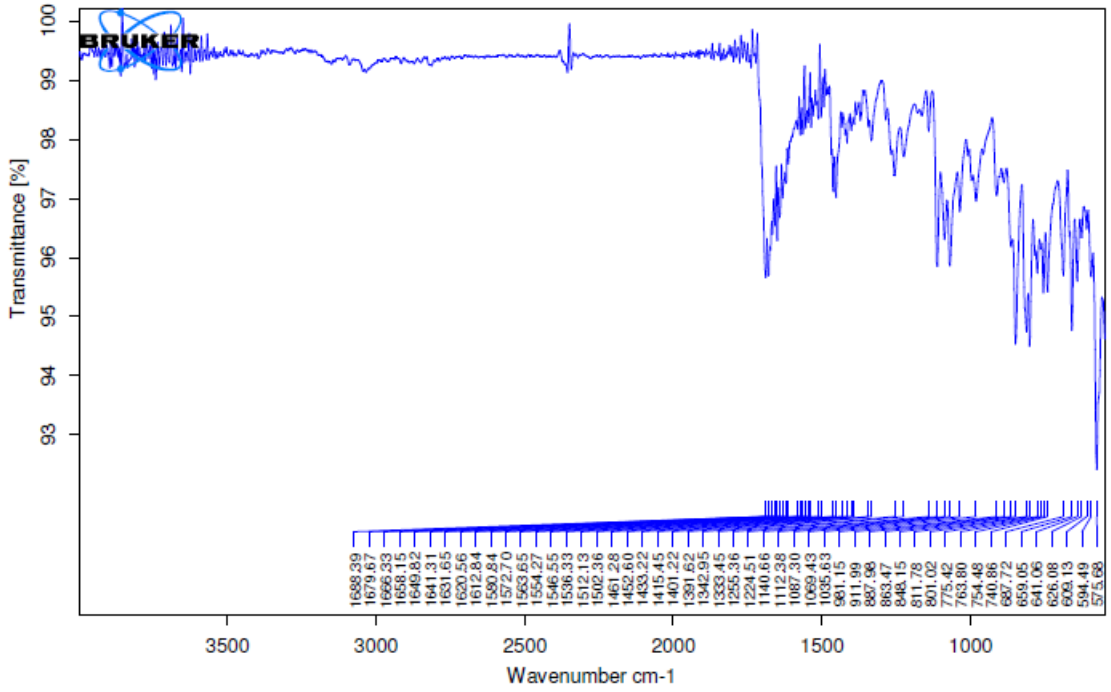


**Fig 1: FTIR Studies of Pure Drug**

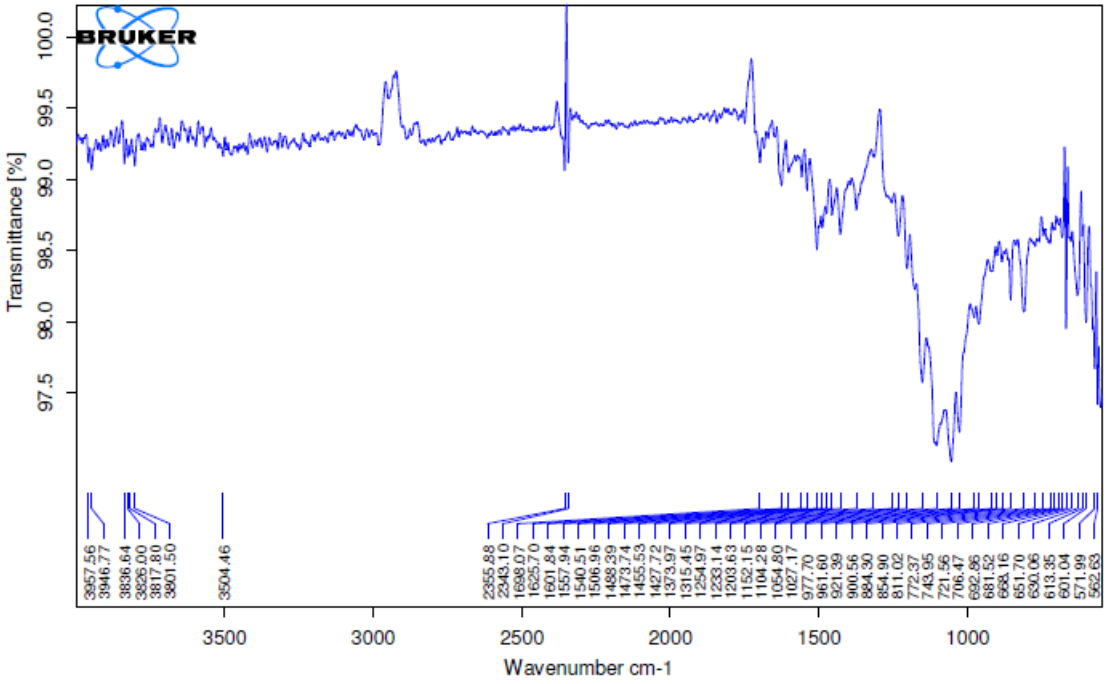


**Fig 2: FTIR Studies of physical mixture of drug and excipients**

## Evaluation studies

### Pre compression parameters

**Bulk Density:** The bulk density for the formulated blend was carried out for all formulation and found in the range of 0.419-0.432.

**Tapped density:** The tapped density for the formulated blend was carried out for all formulation and found in the range of 0.521-0.543.

**Angle of repose:** The angle of repose for the formulated blend was carried out. It concludes that all the formulations blend was found to be in the range of 27 $^0$ to 31 $^0$

**Compressibility index:** Compressibility index was carried out, it found between 10% to 20.70% indicating the powder blend have the required flow property for compression.

**Table 2: Results for pre compression parameters**

| F. no | Bulk density | Tapped density | Compressibility index | Hausner ratio | ANGLE OF REPOSE(0) |
|---|---|---|---|---|---|
| F1 | 0.419 | 0.529 | 20.79 | 1.26 | $31^0$ |
| F2 | 0.426 | 0.530 | 19.62 | 1.24 | $29^0$ |
| F3 | 0.430 | 0.540 | 20.37 | 1.25 | $30^0$ |
| F4 | 0.429 | 0.535 | 19.81 | 1.24 | $31^0$ |

## Post compression parameters

### Weight variation

All the formulated (F1 to F8) tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits of ±7.5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values.

### Thickness

Tablets mean thickness were uniform in F1 to F8 formulations and were found to be in the range of 4.26 mm to 4.55 mm.

### Hardness

The measured hardness of tablets of each batch ranged between 5.15 to 5.27 kg/cm$^2$ .This ensures good handling characteristics of all batches.

### Friability

The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

### Content Uniformity

The percentage of drug content for F1 to F8 was found to be between 95.90% and 98.55 % of Guaifenesin, it complies with official specifications.

**Table 3: Physical parameters of tablets of each formulation**

| F. No. | Weight variation (mg) | Thickness (mm) | Hardness (kg/cm$^2$) | Friability (%) | Drug content (%) |
|---|---|---|---|---|---|
| F1 | 500 | 4.26 | 5.15 | 0.39 | 88.92 |
| F2 | 499 | 4.55 | 5.21 | 0.42 | 91.55 |
| F3 | 501 | 4.51 | 5.28 | 0.47 | 94.62 |
| F4 | 500 | 4.48 | 5.22 | 0.48 | 97.29 |
| F5 | 498 | 4.42 | 5.32 | 0.34 | 87.28 |
| F6 | 499 | 4.50 | 5.12 | 0.44 | 90.56 |
| F7 | 500 | 4.54 | 5.36 | 0.40 | 92.42 |
| F8 | 498 | 4.42 | 5.16 | 0.32 | 93.16 |

## In-vitro Dissolution Study

All the 8 formulation of prepared matrix tablets of Guaifenesin were subjected to in-vitro release studies these studies were carried out using dissolution apparatus. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for the 8 hrs.

**Table 4: Dissolution Profile of F1 to F4**

| Time (hrs.) | $F_1$ | $F_2$ | $F_3$ | $F_4$ |
|---|---|---|---|---|
| **0** | 0 | 0 | 0 | 0 |
| **1** | 19.12 | 18.20 | 17.11 | 28.22 |
| **2** | 22.45 | 25.30 | 23.11 | 33.60 |
| **3** | 32.80 | 35.32 | 33.76 | 46.82 |
| **4** | 42.63 | 44.65 | 43.23 | 53.48 |
| **5** | 58.21 | 59.28 | 52.11 | 67.17 |
| **6** | 63.35 | 68.55 | 65.22 | 79.81 |
| **7** | 78.26 | 80.10 | 75.16 | 86.22 |
| **8** | 88.25 | 92.11 | 95.12 | 98.12 |

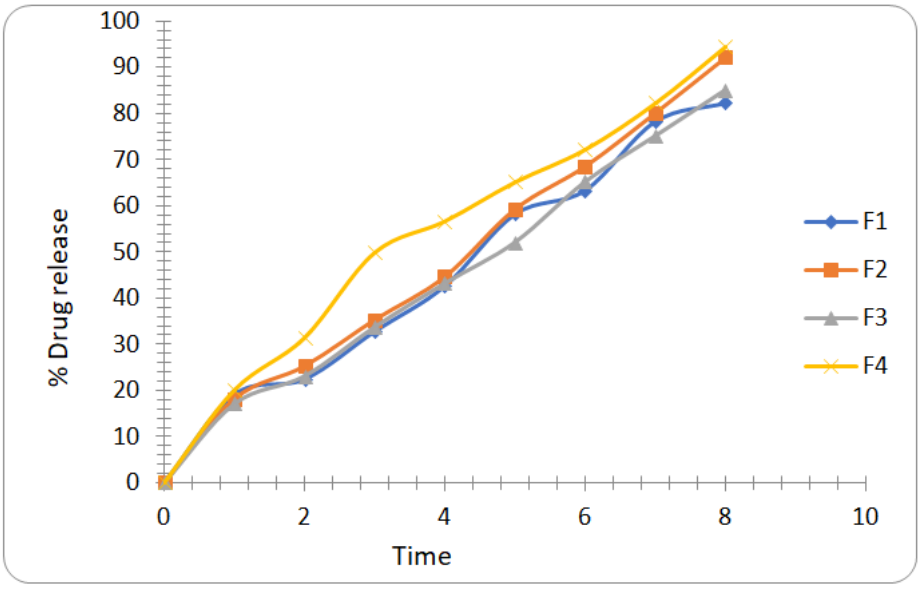


**Fig 3: Dissolution profile of (F1-F4) Formulations**

**Table 5: Dissolution Profile of F1 to F4**

| Time (hrs.) | F5 | F6 | F7 | F8 |
|---|---|---|---|---|
| **0** | 0 | 0 | 0 | 0 |
| **1** | 23.35 | 25.50 | 20.41 | 22.30 |
| **2** | 34.62 | 31.15 | 32.81 | 32.42 |
| **3** | 40.92 | 38.65 | 39.90 | 41.18 |
| **4** | 52.65 | 48.23 | 53.41 | 50.90 |
| **5** | 61.25 | 59.95 | 65.50 | 63.82 |
| **6** | 73.12 | 72.82 | 74.84 | 73.86 |
| **7** | 80.19 | 81.84 | 83.90 | 84.82 |
| **8** | 91.16 | 92.32 | 93.25 | 94.12 |

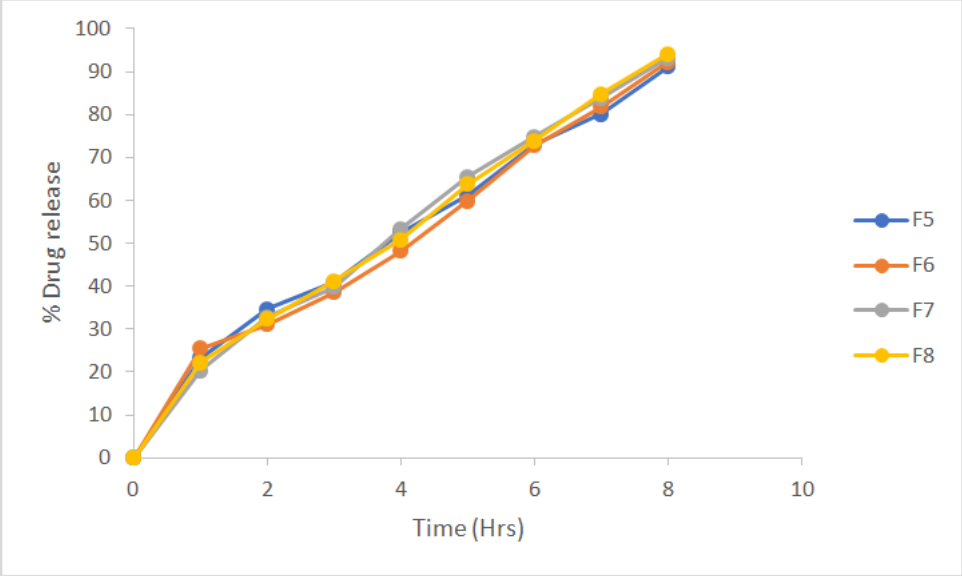


**Fig 4: Dissolution profile of (F5-F8) Formulations**

## Stability studies

Extended-release tablets of Guaifenesin formulated in the present study were subjected to accelerated stability studies. Stability studies of the prepared formulations were performed at ambient humidity conditions, at room temperature, at 40°c and 2-8°c for a period up to 90 days. The results revealed that no significant changes in appearance, drug content, hardness, friability, and in vitro release for F4 formulation. When it was stored at the three storage conditions. How ever there was slight variation in invitro release when it is stored at 2-8°c, there was no change when it is stored at 40°c and room temperature.

**Table 6: Results of stability studies of optimized formulation F-4**

| Formulation Code | Parameters | Initial | 1st Month | 2nd Month | 3 rd Month | Limits as per Specifications |
|---|---|---|---|---|---|---|
| F-4 | $25^0$C/60%RH % Release | 98.12 | 98.08 | 97.82 | 97.03 | Not less than 85 % |
| F-4 | $30^0$C/75% RH % Release | 98.12 | 98.02 | 97.15 | 96.99 | Not less than 85 % |
| F-4 | $40^0$C/75% RH % Release | 98.12 | 97.99 | 97.05 | 96.73 | Not less than 85 % |

## CONCLUSION

This study deals with the investigation carried out with the objective of developing oral Extended-release formulation of Guaifenesin using natural and synthetic polymers. Preparation of matrix tablet by direct compression technique was found to be more effective in sustaining the release of drug. Drug content for all formulations were found to be complies with pharmacopeial standards. Formulation F4 containing Ethyl cellulose with drug release 98.12% for 8 hrs. The controlled and efficient drug delivery system developed in the present study will maintain the plasma Guaifenesin levels better, which will overcome the drawbacks associated with the conventional therapy. Based on the in-vitro drug release data, the formulation F4 it was concluded as best formulation. In conclusion the present study demonstrated the successful preparation of Extended-release tablet of Guaifenesin.

## REFERENCES


1. Chien YW. Novel drug Delivery system. 2nd ed, Revised and expanded; 1992,p.no.139-140.
2. Remington. The Science and Practice of pharmacy. 20th ed. Vol. I, p.no.903-913.
3. Brahmankar DM, Jaiswal SB. 'Vallabh Prakashan, 1st edn, 1995,p.no.347- 352.
4. Lee V.H., Robinson J.R. in,'Sustained and Controlled Release Drug Delivery System. Vol 6. Dekker, 270 Madison Ave., New York, NY 10016. https://doi.org/10.1002/jps.2600690444
5. Lachman Leon LHA, Kanig JL, editors, "The Theory and Practice of industrial pharmacy".
6. Biopharmaceutics and pharmacokinetics, "A Treatise. 3rd ed. Vol. 5. New York: Marcel Dekker, p.no. 71-121.,138-171, Varghese publishing House Bombay, p.no.430.
7. Ruggero Bettini, www.medfarm uniforit/pharmaco/itcis/Erasmus/erasm13. html[7k.
8. Lapidus J, Lordi NG. J Pharm Sci. 1991-1992;8, p.p 86.
9. Liberman HA. Pharmaceutical dosage form; tablets. 2nd ed. Vol. I, p.no. 136.
10. Aulton ME. Hand Book of pharmaceutics Edition 2001, p.no.291-295.
11. Howard C. Ansel "Pharmaceutical Dosage Form and Drug Delivery Systems". 7th ed p.no.229-243.
12. Jain NK. 'Controlled And Novel Drug Delivery' CBS. Vols. 1-2; 2002, p.no.676-698.
13. Ghirnikar RS. Yuen L. lee and Lawrence F. Eng, Spinal Cord Injury:Hope for a cure. Indian J Pharm Sci. 2001;63(5), p.no. 349-363.
14. Qui Y, Cheskin H," sustained release hydrophilic matrix tablets of zileuton : formulation and in vitro/ in vivo studies". J Control Rel. 1997;45, p.no.249-256.
15. Indiran Pather S, Tussell I, Syce JA,"sustained release theophylline by direct compression formulation and in vitro evaluation," Int. J Pharmacol. 1998;168, p.No. 1-10.
16. Baveja SK. A.V. Hassan and Amarjit Sinhg in. Ind J Pharm Sci. 1989;55, 249-250.
17. P J Cox, K A Khan, D L Munday, J Sujja-areevath. Development and evaluation of a multiple-unit oral sustained release dosage form for S(+)-ibuprofen: preparation and release kinetics. Int J Pharm. 1999 Dec 20;193(1):73-84. doi: 10.1016/s0378-5173(99)00320-8.