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Formulation and Evaluation of Extended Release Tablets of Guaifenesin by using Natural Polymers

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A B S T R A C T

Exdended release drug delivery has become the standards in the modern pharmaceutical design and intensive research has been undertaken in achieving much better drug product effectiveness, reliability and safety. Guaifenesin Extended release tablets were formulated and optimized at the polymer concentration ratio of 30:20 (HPMC: EC) at the coating percentage of an average weight build-up of 7.36%w/w. *In vitro* release studies complied with the innovator and the formulation was found to be equal. It was increased. Similarity factor (f_2) value was calculated for all formulations. The similarity factor (f2) of all the formulations ranged from 30 to 68.7. The similarity factor of is high when comparing to other formulations so, it is more similar to that of marketed formulation.

Keywords: Guaifenesin Tablet, Manufacturing Methods, Excipients, Evaluation Methods.

A R T I C L E I N F O

CONTENTS

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1. Introduction

Recently, Exdended release drug delivery has become the standards in the moder pharmaceutical design and intensive research has been undertaken in achieving much better drug product effectiveness, reliability and safety[2]. Hence, in this work to formulate tablets in order to avoid the first pass metabolism and increase the bioavailability. Hence in this work an attempt was made to formulate extended release system in order to achieve plasma concentration profile up to 24 hrs[2]. Extended release drug delivery system achieves a slow release of the drug over an extended period of time or the drug is absorbed over a longer period of time. Extended release drug delivery system (ERDDS) have emerged as an effective mean of enhancing the bioavailability and controlled delivery of many drugs. ERDDS play an important role in reducing the dosing frequency as well as by enhancing the biological half- life of specific certain drugs[4]. The extended release tablet is the most widely used dosage form because of its convenience in terms of self-administration, com-pactness, and ease in manufacturing. The first approach has many disadvantages which therefore resulted in increased interest in the second approach[2]. An ideal controlled drug delivery system is the one which delivers the drug at a predetermined rate, locally or systemically, for specific period of time.

Objectives of Extended Release Drug Delivery System:

Suitable Drug Candidate for Extended Release Drug Delivery System:

- It should be orally effective and stable in GIT medium.
- Drugs that have short half-life, ideally a drug with half-life in the range of 1 – 5 hrs makes a good candidate for formulation into ER dosage forms eg. Captopril, Salbutamol sulphate.

Tablet Manufacturing Methods:

a) Direct Compression
b) Wet Granulation
c) Dry Granulation

Drugs, which are suitable for Extended release formulation:

I. Physiochemical Properties
II. Biological Properties

2. Materials and Methods

Materials: Guaifenesin Tablets, Chemicals and reagents used for the preparation of buffers, analytical solutions (HPMC K_4M, Xanthane gum, Ethyl Cellulose, Guargum etc.

Excipients Profile: Hydroxy Propyl Methyl Cellulose, Xanthane Gum, Guar Gum, Ethyl Cellulose

Methodology:

A) Preformulation Studies:.

a) Organoleptic Properties: We are observing the Colour, Tasteandodor

b) Physical Characteristics: Solubility, Loss on Drying, Flow properties:

a. Angle of Repose: The radius was measured and the angle of repose was determined. This was repeated three times for a sample.
b. Bulk density (ρ): It is ratio of given mass of powder and its bulk volume.
c. Hausner'sratio

B) Calibration Curve:

Objective: To Establish documented evidence that provides the data of pH solubility of Guaifenesin.

Instruments used: Analytical balance, sonicator, uv-visible spectrophotometer, pH-meter.

Buffers: Preparation of pH 1.2 , pH 4.5, pH 6.8, pH 7.4 Buffers**.**

Construction of Standard Graph of Guiafenesin in 0.1 N HCL:

a. Preparation of 0.1N HCl
b. Construction of Standard Graph of Guaifenesin in 0.1N HCl
c. Standard preparation
d. Preparation of serial dilutions for standard calibration curve

Construction of Standard Graph of Guaifenesin in 6.8P^H Phosphate Buffer:

Sample preparation

Standard preparation

Preparation of serial dilutions for standard calibration curve:

Necessary dilutions were made by using this second solution to give the different concentrations of Guaifenesin (5-50 mcg/mL) solutions.

$$\%\,\text{Drug dissolved} = \frac{\text{Sample area}}{\text{Standard area}} \times \frac{\text{Standard dilution}}{\text{Sample dilution}} \times \%\,\text{potency} \times 100$$

C) Formulation of Guaifenesinertablets using Different Ratios of Polymers

Direct compression technique

1. Sieving
2. Dry mixing
3. Lubrication
4. Compression

D) Drug-Excipient compatibility studies by FTIR:

FTIR studies were performed on pure drugs and bilayer tablet formulation using Shimadzu FTIR (Shimadzu Corp., India). The samples were analyzed between wave numbers 4000 and 400 cm^{-1}.

G) *In-vitro* dissolution studies:

Instruments used: Analytical balance, sonicator, PH-meter, HPLC

Acid and Buffer Stages are using preparing of Buffer, mobile phase, standard solutions, sample solutions

H) Comparison of dissolution profiles:

F) Evaluation of Tablets:

The quantitative evaluation and assessment of a tablets chemical, physical and bioavailability properties are important in the design of tablets and to monitor product quality. Thickness and diameter, Hardness test, Weight variation test, Friability test, Invitro dissolution characters

3. Results and Discussion

A) Preformulationstudies of Guaifenesin Er Tablets:

a) Organoleptic characters: It is white powder and Taste is Bitterm Odourless colour

b) Physical Characteristics:

i) Solubility:

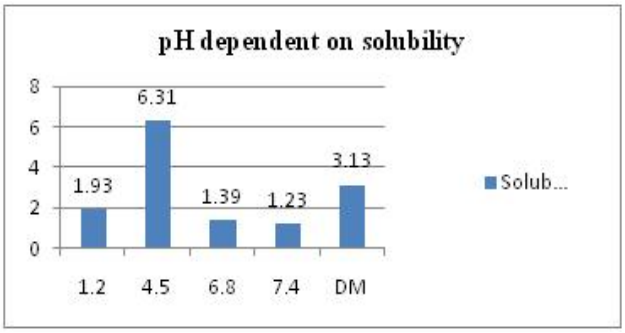

Figure 6: Solubility of Guaifenesin in different pH conditions

Table 1: Formulation of Guaifenesin ER tablets using different ratios of polymers (F1-F6)

S.No	Ingredient (in mg)	Formulation					
		F1	F2	F3	F4	F5	F6
1	Guaifenesin	42.66	42.66	42.66	42.66	42.66	42.66
2	HPMC K4M	30.00	40.00	50.00	40.00	40.00	30.00
3	Xanthan gum	-	-	-	10.00	-	10.00
4	Ethyl Cellulose	-	-	-	-	10.00	10.00
5	Gaur gum	10.00	10.00	10.00	10.00	10.00	10.00
6	Spray Dried Lactose	141.34	131.34	121.34	121.78	121.78	121.78
7	Aerosil	2.00	2.00	2.00	2.00	2.00	2.00
8	Magnesium steareate	4.00	4.00	4.00	4.00	4.00	4.00
9	Total Weight	230	230	230	230	230	230

ii) Loss on Drying: The Drug is found to be 0.53%, it is Not more than 1% W/W

iii) Flow properties:

Table 2: Flow properties of Guaifenesin

S. No	Formulations	Bulk density	Tapped density	Carr's index	Haussler's ratio	Angle of repose
1	Guaifenesin(F1)	0.206±0.02	0.466±0.009	55.682%	2.256	No flow through funnel
2	Guaifenesin(F2)	0.209±0.05	0.463±0.014	55.731%	2.283	No flow through funnel
3	Guaifenesin(F3)	0.212±0.03	0.471±0.015	55.802%	2.309	No flow through funnel
4	Guaifenesin(F4)	0.211±0.08	0.469±0.017	56.112%	2.333	No flow through funnel
5	Guaifenesin(F5)	0.217±0.10	0.473±0.011	56.210%	2.507	No flow through funnel
6	Guaifenesin(F6)	0.214±0.13	0.475±0.019	56.244%	2.601	No flow through funnel

c) Particle Size:

Table 3: Particle size analysis

Sieve No	Microns (μ)	Wt of drug + sieve (g)	Wt of the drug retained (g)	% of drug retained	Cumulative % of drug retained
#18	1000	381.4	0.4	1.9	1.9
# 50	297	374	20	95.24	97.14
#70	210	335.6	0.6	2.86	100
#120	125	329	0	0	0
#140	105	323	0	0	0
#170	88	321	0	0	0
#200	74	322	0	0	0
#200 pass		502	0	0	0
			21	100	

d) Drug Excipient Compatibility Studies:

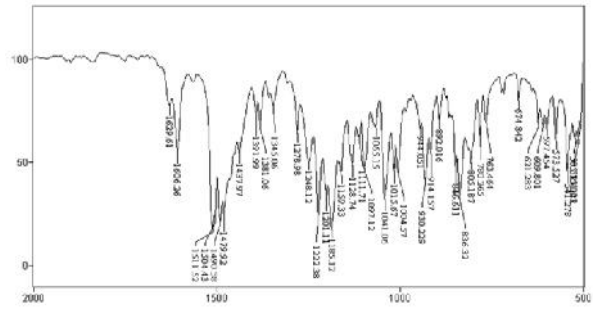

Figure 7:FTIR of API(Guaifenesin)

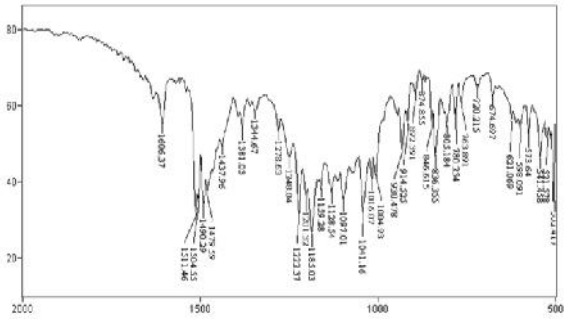

Figure 9: IR of API + Excipients

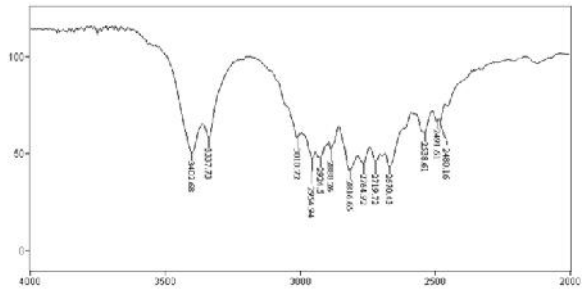

Figure 8: IR of API (Guaifenesin)

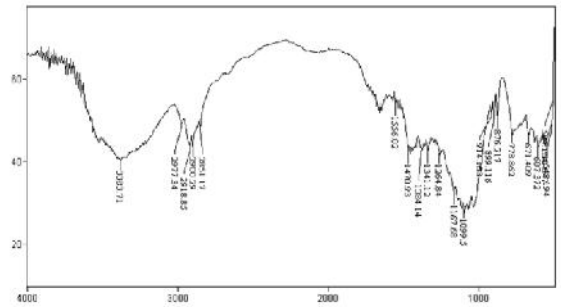

Figure 10: IR of Placebo

B) Characterization of Guaifenesinerblends:

a) PRE Compression Parameters:

Angle of repose:

Table 4: Characterization of Guaifenesin Blends (Pre Compression Tests)

Batch		Angle of repose (θ)	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index
UNCOATED TABLETS					
F1		26.07 ± 0.8	0.62± 0.01	0.72 ± 0.01	14.28 ± 0.3
F 2		25.25 ± 0.6	0.65± 0.0	0.71 ± 0.01	13.88 ± 0.6
F 3		28.45± 0.47	0.64± 0.01	0.74 ± 0.02	15.14 ± 0.6
F 4		25.12 ± 0.6	0.66± 0.02	0.74 ± 0.01	15.31 ± 0.08
F 5		26.10 ± 0.5	0.67± 0.03	0.74 ± 0.03	14.46 ± 0.4
F 6		26.91 ± 0.4	0.64± 0.02	0.73 ± 0.03	14.34 ± 0.02
ENTERIC COATED TABLETS					
F7	4.378%	27.46 ± 0.5	0.65± 0.01	0.75 ± 0.04	14.60 ± 0.24
	5%	26.20 ± 0.2	0.64± 0.01	0.73 ± 0.03	14.57 ± 0.54
	6.76%	25.45 ± 0.4	0.63± 0.01	0.71 ± 0.05	14.48 ± 0.21
F8	6.8%	27.01 ± 0.7	0.67± 0.03	0.72 ± 0.01	15.56 ± 0.36
F9	6.9%	25.92 ± 0.8	0.62± 0.03	0.74 ± 0.03	15.57 ± 0.24
	7.2%	26.23 ± 0.5	0.594± 0.01	0.76 ±0.01	14.08 ± 0.20
F10	6.4%	27.21 ± 0.4	0.56± 0.01	0.74 ± 0.01	15.39 ± 0.21
	7.36%	24.91 ± 0.45	0.487± 0.01	0.74 ± 0.03	15.39 ± 0.21
F11	6.8%	27.81±0.6	0.62± 0.01	0.72 ± 0.01	13.31 ± 0.08
	7.66%	26.07±0.7	0.61± 0.02	0.76 ±0.01	14.34 ± 0.02

b) Post Compression Parameters (Evalution Tests):

Table 5: Characterization of Guaifenesin ER tablets (Post Compression Tests)

Batch	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Weight Variation (mg)	Content Uniformity (%)
UNCOATED TABLETS					
F1	4.02 ± .012	6.2 ± 0.5	0.45± 0.005	225 ± 2	100.2 ±2.4
F 2	4.01 ± 0.09	6.6 ± 0.3	0.32± 0.0041	227 ± 2	98.2 ± 1.6
F 3	4.05 ± 0.16	6.4 ± 0.5	0.19± 0.003	226 ± 4	98.7 ±2.2
F 4	4.09 ± 0.07	6.6 ± 0.2	0.21± 0.002	220 ± 2	101.2 ±2.4
F 5	4.11 ± 0.05	7.1 ± 0.3	0.54± 0.004	228 ± 4	102.3 ±1.3
F 6	4.02 ± 0.19	6.8 ± 0.2	0.49± 0.011	232 ± 2	101.5 ±1.6
Enteric Coated Tablets					

F7	4.378%	4.28± 0.12	7.4±0.05	0.502±0.01	228± 2	98.2 ±1.2
	5%	4.21± 0.08	7.2±0.04	0.408±0.027	232± 2	99.2 ±1.8
	6.76%	429.± 0.09	6.8±0.11	0.418±0.012	226± 2	98.23±1.4
F8	6.8%	4.24± 0.01	6.4 ± 0.5	0.501±0.010	231± 2	98.4 ± 1.6
F9	6.9%	4.26± 0.13	7.1±0.04	0.41± 0.011	229± 2	102.3 ±1.3
	7.2%	4.28± 0.09	6.6 ± 0.2	0.538±0.013	230± 2	101.5 ±1.6
F10	6.4%	4.28± 0.12	7.4 ± 0.5	0.11± 0.003	227± 2	98.8± 1.6
	7.36%	4.27± 0.08	7.0 ± 0.2	0.034±0.012	229± 2	101.1±1.4
F11	6.8%	4.29± 0.13	6.8 ± 0.5	0.05± 0.005	228± 2	101.5 ±2.4
	7.66%	4.30± 0.09	6.6 ± 0.2	0.32± 0.004	226± 2	100.2 ±2.4

C) Calibration Curves:

a) Construction of standard graph of Guaifenesinin 0.1N HCl:

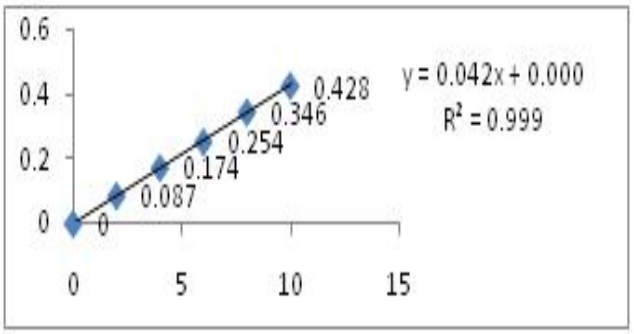

Figure 11: Standard graph of Guaifenesinin 0.1N HCl

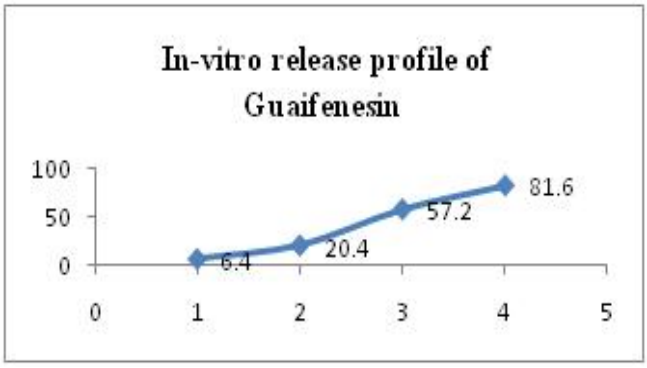

Fig.13*: In-vitro* dissolution profile of Guaifenesin

b) Construction of standard graph of Guaifenesin in 6.8P^{H} phosphate buffer:

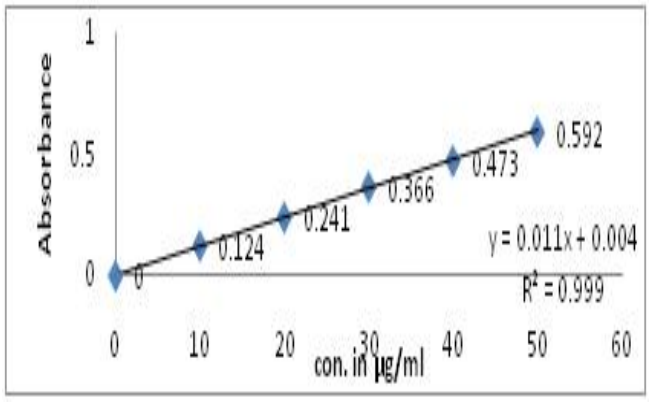

Figure 12: Calibration curve of Guaifenesin in 6.8 PH Phosphate buffer

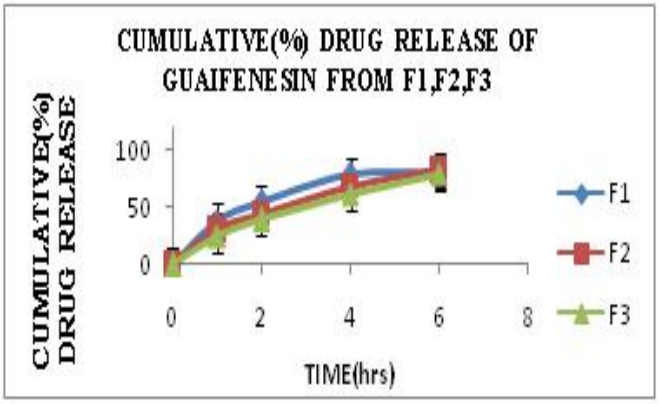

Figure 14: *In-vitro* dissolution profile - F1, F2, F3 batch's

D) *In-vitro* dissolution studies:

Table 6*: In-vitro* dissolution profile - F1, F2, F3 batch's

Batch No	**F1**	**F2**	**F3**
% Drug release in acid stage	0.0	0.0	0.0
% Drug release in buffer stage			
1 Hr	38±0.90	30.3±0.64	25±0.93
2 Hr	53.5±1.23	44.1±1.21	38.4±1.63
4 Hr	77.8±0.92	67.5±2.12	60.9±1.23
6 Hr	79.2±2.2	82.1±1.68	79.2±0.52

Table 7: *In-vitro* dissolution profile – F4, F5, F6 batch's

Batch No.	**F4**	**F5**	**F6**
%Drug release in acid stage	0.0	0.0	0.0
% Drug release in buffer stage			
1 Hr	11.4 ± 1.62	37.7±0.82	31.9±1.21
2 Hr	29.2±0.52	45.2±0.42	52.8±0.63
4 Hr	48.5±1.21	76.3±1.62	68.2±2.12
6 Hr	68.0±0.85	91.0±2.12	83.2± 0.21

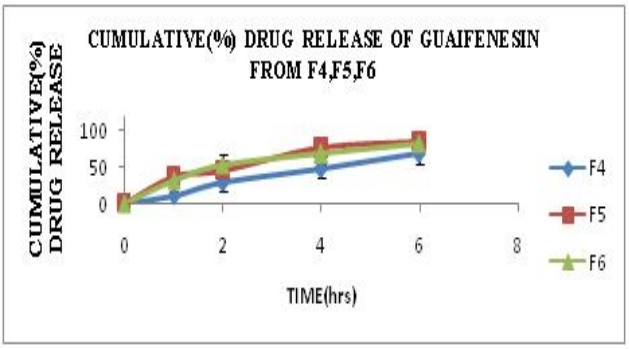

Figure 15: *In-vitro* dissolution profile – F4, F5, F6 batch's

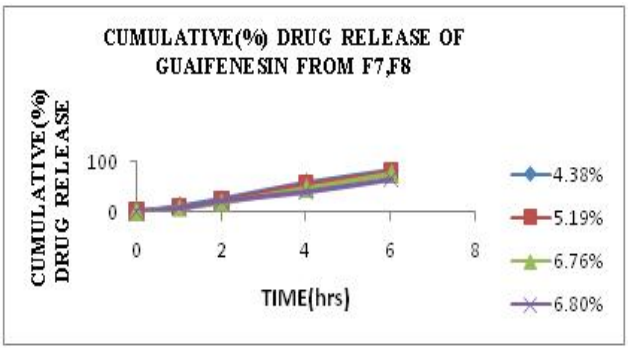

Fig 16*: In-vitro* dissolution profile – F7, F8 batch's

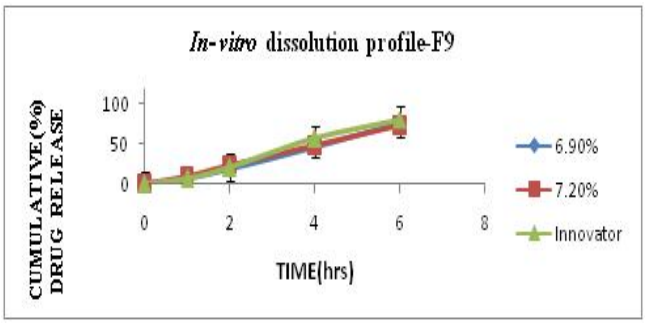

Figure 17*: In-vitro* dissolution profile – F9 batch

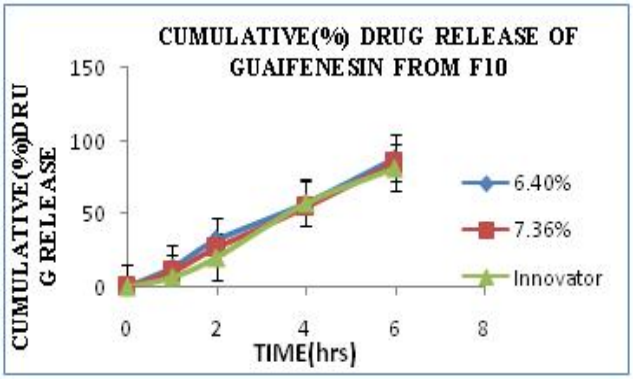

Fig 18: *In-vitro* dissolution profile – F10batch

Table 8 : *In-vitro* dissolution profile – F7, F8 batch's

Batch No	**F7**			**F8**
	4.378%	**5.19%**	**6.76%**	**6.8%**
% Drug release in acid stage	0.0	0.0	0.0	0.0
% Drug release in buffer stage				
1 Hr	10.3±0.42	9.0±0.96	7.6±0.56	7.9±0.65
2 Hr	25.6±1.21	24.2±1.61	19.4±0.78	21.1±0.32
4 Hr	57.3±0.56	54.1±1.22	46.6±1.23	40.8±0.98
6 Hr	83.1±1.21	78.7±0.41	75.0±1.56	66.7±1.23

Table 9: *In- vitro* dissolution profile – F9 batch

Batch No.	**F9**	
	6.9%	**7.2%**
% Drug release in acid stage	0.0	0.0
% Drug release in buffer stage		
1 Hr	6.9±1.23	9.7±2.12
2 Hr	19.2±1.24	24.1±1.78
4 Hr	46.6±0.89	48.1±0.99
6 Hr	75.6±0.99	72.8±0.67

Table 10: *In-vitro* dissolution profile – F10batch

Batch No.	**F10**	
	6.4%	**7.36%**
% Drug release in acid stage	0.0	0.0
% Drug release in buffer stage		
1 Hr	13.2±0.55	10.2±0.93
2 Hr	31.5±3.01	26.3±1.69
4 Hr	57.8±3.78	54.8±1.05
6 Hr	88.1±2.08	84.9±0.65

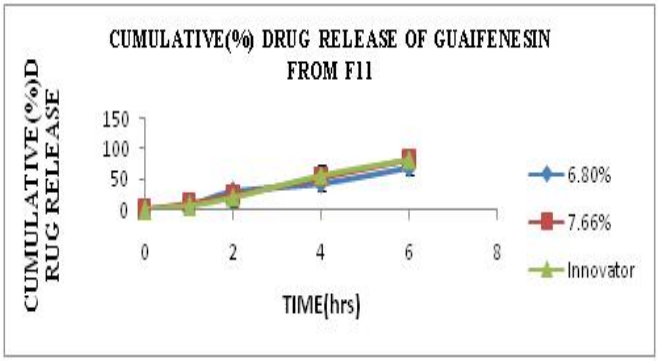

Fig 19: *In-vitro* dissolution profile – F11batch

Table 11: *In-vitro* dissolution profile – F11batch

	F11	
Batch No	**6.8%**	**7.66%**
% Drug release in acid stage	0.0	0.0
% Drug release in buffer stage		
1 Hr	8.6±1.22	10.2±1.25
2 Hr	29.4±1.26	24.6±0.96
4 Hr	43.7±0.59	53.7±1.25
6 Hr	69.6±2.23	82.7±3.23

Comparision of Formulations with Marketed formulation Guaifenesin using Similarity Factor (F2)

Table 12: Similarity factor (f2)

Formulations		**Similarity Factor (f_2)**
F1		30
F2		37.4
F3		44
F4		50
F5		32
F6		33.5
F7	A	64.7
	B	64.2
	C	49.6
F8	A	47.6
F9	A	60.4
	B	58.1
F10	A	56.7
	B	**68.7**
F11	A	49.6
	B	67.2

4. Summary

The present study was under taken to formulate and evaluate the extended release tablets of Guaifenesin by using direct compression. The study involved preformulation of drug and excipients, formulation, evaluation. Matrix tablets of Guaifenesin were prepared by using combination of hydrophobic and hydrophilic polymer consisting of, HPMCK4M, Xanthan gum and Ethyl Cellulose. The polymeric concentration of hydrophobic and hydrophilic polymer was optimized and was found that drug to polymeric ratio (hydrophic and hydrophobic) of 30:20 was appropriate for the formulation of Guaifenesin tablet.

5. Conclusion

Guaifenesin Extended release tablets were formulated and optimized at the polymer concentration ratio of 30:20 (HPMC: EC) at the coating percentage of an average weight build-up of 7.36%w/w. *In vitro* release studies complied with the innovator and the formulation was found to be equal. In the formulations are $HPMCK_4M$ concentration was decreased and ethyl cellulose was increased .The drug release was found to be increased when compared to F8.The formulation F10 contained with an average weight build-up of 7.36% complied with the innovator.

6. References

1. Chein YW, James Swarbrick, editors. Novel Drug Delivery System. 2nd ed. Marcel Dekker: New York; **1992**, pp.139-196.
2. Brahmankar DM, Sunil B Jaiswal, editors. Biopharmaceutics and pharmacokinetics a treatise. 1st Edn., Vallabh Prakashan Publications, Delhi **2001**, pp. 348-35.
3. Khan M G, Controlled release oral dosage forms: Some recent advances in matrix type drug delivery systems, The sciences, **2001**, 1(5): 350-354.
4. Murthy P N V N, Shafiullah D, Datta M, Formulation, development and evaluation of controlled release matrix tablets of guaiphenesin and salbutamol sulphate, Der pharmacia letter, **2011**, 3(4), 325-334.
5. Peter G Welling, Michael R Dobrinska, Robinson JR, Lee VHL, editors.Controlled Drug Delivery: Fundamentals and Applications. 2nd ed. Marcel Dekker: New York; **1987**. pp. 255-259.
6. Lippincott Williams, Wilkins, Thomas Wai- Yip Lee, Joseph R Robinson, editors. Remington's The

Science and Practice of Pharmacy. 20th ed. Maryland, **2000**. pp. 903-914.

7. Jayanthi B, Manna P M, Madhusudhan S, Mohanta G P, Manavalan R, Per oral extended release products-A overview, Journal of applied pharmaceutical science, **2011**, 01(02): 50-55.
8. Pogula M, Nazeer S, Extended release formulation, International journal of pharmacy and technology, **2010**, 02(04): 625-84.
9. Arora V, Gupta VB, Singha lR. Advance in direct compression technologies. Pharma Times, **2007**, 39(2): 26-27.
10. HerbertAL, LeonL, JosephBS. Pharmaceutical Dosageforms-Tablets. 2nd Ed. New York: Vol. I, II and III Marcel Dekker; **1989**.
11. WellJ, Aulton ME. The science of dosage form design-pre formulationin pharmaceutics. International student edition; **1998**.
12. Tousey MD. The granulation process 101. Pharm Tech, **2002**, 8-13.
13. Mahammed Athar A. Saikh. A Technical Note on Granulation Technology: International Journal of Pharamaceutical Sciences and Research. **2012**; 4(1): 55-67.
14. LeonL, HerbertAL, JosephLK. The theory and practiceofindustrial pharmacy. 3rd Edition. Varghese Publishing House; **1991**.