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PREPARATION AND *INVITRO* EVALUATION OF NANOCAPSULE BY USING GUAIFENESIN AN EXPECTORANT DRUG

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ABSTRACT

Guaifenesin is a drug of choice for treating common cold, chronic bronchitis. The prepared nano capsules of Guaifenesin aim to deliver the drug which passes through oral route as it provides controlled release of drug when compared to other route of administration. The Guaifenesin nano capsules was successfully prepared by using nanoprecipitation method by taking F01to F05 formulation by using different concentration of polymer ratio. And as a polymer Hydroxy propyl methyl cellulose is used and polyvinyl alcohol (PVA) as a stabilizer. The prepared formulations of nanocapsules were evaluated for various parameters. Guaifenesin in 1:5 (F05) shows better particle shape and size, SEM study of prepared nanocapsules were within the range of (1-1000µm). There is no drug excipients interactions in FTIR and DSC. FTIR results shows peaks at 3244 cm-1, 1455cm-1, 1376cm-1 and 1594cm-1The physical mixture on the other hand shows peaks at 3421cm-1, 1440cm-1, 1371cm-1, 1564cm-1. Thus, it is concluded that the physical mixture of the drug (Guaifenesin) does not show any major interactions with the formulation components like (HPMC, Sorbitan monostearate and PVA). This indicates that drug was compatible with the excipients. In DSC Results The pure Guaifenesin shows a sharp endothermic peak at 300ºC and some similar changes occurs in endothermic peak were observed at similar temperature in prepared formulations at 250.2ºC. Thus, it is concluded that there no drug excipients interactions. The formulation of F05 showed good particle size with good spherical shape and uniformly distributed without any lumps. The percent drug content was found to be in 8hrs showed anomalous mode of drug release, in F05 formulations.

Keywords: Guaifenesin, Nanocapsule, nanoparticles, common cold, chronic bronchitis.

1. INTRODUCTION

Nanotechnology is a branch of science that refers to small objects. The word nano comes from the Greek word "Nano," which meaning "dwarf." Nanotechnology development is done on a nanoscale scale, with sizes ranging from 0.1 to 100 nanometers. Nanomaterials have a wide range of uses in the medicinal, pharmacological, electrical, and molecular diagnostic domains. The polymeric nanoparticles (PNPs) are made of biocompatible and biodegradable polymers that range in size from 10 to 1000 nanometers. The medicine is dissolved, entrapped, encapsulated, or linked to the matrix of a nanoparticle[1].

Smart Drugs Made from Nano capsules[2]

Because nano capsules have specific chemical receptors and only bind to specific cells, they can also be used as smart drugs. This receptor assembles the smart' drug, allowing it to target cancer or disease.

• Higher dose filled with smaller dose volumes is one of the advantages of nano- encapsulation technologies for pharmaceutical applications.
• Long-term dose retention at a specific location
• Increased absorption of active drug substances at a faster rate
• The drug's bioavailability has been increased.
• Greater efficacy and protection
• Patient compliance has improved**.**

The Properties of Polymeric Nano capsules

Polymeric Nano capsules can be made in a variety of sizes and shapes, as well as in large quantities. Nano capsules can be designed to perform a variety of tasks. Monodisperse particles with clearly delineated biochemical, electrical, optical, and magnetic properties can be manufactured. They can be tailored to fit the complexity of whatever application they're intended for; for example, in targeted drug delivery systems, the contents can be released in response to a bi molecular triggering mechanisms.[3]

CHARACTERIZATION (OR) EVALUATION OF NANOCAPSULES[4]

1. DETERMINATION OF THE PH OF NANOCAPSULE: Nano capsules formulation pH was estimated utilizing an advanced computerized pH meter at room temperature. Nano capsules scattering pH values drop inside a scope of 3.0-7.5.

2. MEAN NANOCAPSULES: The mean molecular size of Nano capsules prepared from performed polymers are in general between 250-500nm. In double emulsification method has concluded that particle size depends on the internal and external surfactants that determine droplet size, the interaction at the interface and the structural conformation of the nano capsules wall.

3. DETERMINATION OF DRUG CONTENT: Drug content was controlled by dissolving 1ml of arranged Nano capsules in 20ml of acetonitrile. Appropriate amount of sample was then exposed to the UV Spectrophotometer at 232nm. The absorbance for each sample was estimated and contrasted with the standard.

4. PARTICLE SIZE DISTRIBUTATION AND PARTICLE CHARGE/ZETA POTENTIAL: Particle size appropriation is an important aspect during the formulations of nano systems. Nano capsules were characterized for their molecule size dissemination and zeta potential using Malvern zeta sizer.

5. STRUCTURAL CHARACTERISATION: Structural characterization should be possible by using field emission scanning electron microscopy (FE-SEM) and transmission electron microscopy (TEM) to determine the various attributes like shape, size, and surface morphology, micrographs of the nano capsules were obtained. utilizing a Phillips Cm 200 worked at 20-200 Kev while the Fe-SEM was done utilizing Hitachi S-4800 FE-SEM outfitted with Energy Dispersion Spectrometer (EDS).

IN-VITRO DRUG RELESE

In vitro drug discharge studies were done utilizing USP type II dissolution apparatus. The study was carried out in 100 ml of buffer (PH 3.0). The nano capsules suspension was putdown in dialysis membrane and immersed in dissolution medium which was kept inert thermostatically at 37±0.5°C. The stirring rate was maintained at 100 rpm. At predetermined time intervals 5ml of sample were withdrawn and assessed for drug release Spectro photo metrically. After each withdrawal 5 ml of fresh dissolution medium was added to dissolution jar.

2. MATERIALS AND METHODOLOGY

Table 1: LIST OF MATERIALS

S.NO.	NAME OF THE	NAME OF THE SUPPLIER
1.	Guaifenisin	MSN Organics Pvt Ltd. Bibinagar, Telangana,
2.	Hydroxy propyl methyl	TCI Chemical (India)Pvt. Ltd
3.	Sorbitan monostearate	Ankit Polymers Industries, Ahmedabad
4.	Oleic acid	Famous chemical Industries, Hyderabad.
5.	Ethanol	Taj Pharmaceuticals Ltd. Hyderabad
6.	PVA	Elbs pharma
7.	Water	Geethanjali college of Pharmacy.

METHODOLOGY

METHOD OF PREPARATION

Nanoprecipitation Method or Interfacial Deposition of Polymers.

MATERIALS AND FORMULATION

Compositions of Guaifenesin and LNC-blank yielding a final volume of 10 ml nanosuspension.

Table 2: Formulations of Guaifenesin nano capsules

Materials	LNC-	1:1	1:2	1:3	1:4	1:5
Guaifenesin(active	_	25mg	25mg	25mg	25mg	25mg
HPMC (polymer)	25 mg	25mg	50mg	75mg	100mg	125mg
Sorbitan monostearate	40 mg	40mg	40 mg	40 mg	40 mg	40 mg
Oleic acid	0.4 ml	0.4 ml	0.4 ml	0.4 ml	0.4 ml	0.4 ml
Ethanol	50 ml	50 ml	50 ml	50 ml	50 ml	50 ml
PVA	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg
Water	50 ml	50 ml	50 ml	50 ml	50 ml	50 ml

Preparation of Nano capsule[5-7]

Guaifenesin– loaded lipid core nano capsules were prepared by solvent displacement method or nanoprecipitation method. This method is also known as interfacial deposition of polymer. In this method nano capsules creating a colloidal suspension between two separate phases such as organic and aqueous phase. Organic phase consists of drug i.e. Guaifenesin(25mg) and polymers i.e. HPMC (25 mg,50 mg,75 mg,100mg,125 mg) in different ratios (1:1,1:2,1:3,1:4,1:5). polymer solubilized in oleic acid (oil-

0.4 ml) previously. Aqueous phase consists of PVA (stabilizing agent- 80 mg) with water (50 ml). Then organic phase injected slowly as dropwise into aqueous phase under constant speed of magnetic stirring for 10 min. Acetone is removed by vaporizing under low pressure to approximately 9ml. Closing volume was adjusted in a volumetric flask up to 10 ml. Blank nano capsules were prepared similarlybut without addition of guaifenesin to oleic acid. Size and shape of nanoparticles depends on rate of injection and agitation. Final results of nano particles are filled into core nano capsules.

EVALUATIONS OF NANOCAPSULES[8-11]

a) Scanning electron microscopy (SEM)

Scanning electron microscopy was used to determine surface topography, particle size, texture and by the SEM we can detect the size and morphology of broken or sectional surface. So, the dried Guaifenesin hydrochloride nano capsules were kept on the electron microscope stub which was covered with a black adhesive tape. Later, these nano capsules were coated with gold and examined under vaccum at room temperature. The nano capsules were observed at accelerated voltage of 1000 volts

b) Differential scanning calorimetry (DSC)

DSC is carried out by the physical state of Guaifenesin Hydrochloride on microspheres were analyzed by differential scanning colorimeter. Thermogram of pure drug, pure polymer and drug loaded microspheres were obtained at a scanning rate of over a temperature vary of 250.28˚C. DSC determines that the temperature range and heat rate. And by this DSC we can find quantitative and qualitative information on endothermic (heat absorption) exothermic (heat evolution process of materials) during physical transition

c) Drug and polymer interaction study (FTIR)

FTIR spectroscopy was performed on the Fourier transform infrared spectrophotometer and it is used to study and find out whether there are any physical and chemical interactions between the drug and polymer used in the formulation. And, to know the stability of the drug during encapsulation process.

d)*In vitro* dissolution drug release study

By using dissolution apparatus which is carried out in USP dissolution apparatus-II. 900ml of dissolution medium (distilled H_2O) was placed into each vessel and the apparatus was assembled. Then the medium was allowed to equilibrate to a temperature of 37±0.5. 100mg of all formulations was placed into each vessel and operated at 50rpm. After 1 hr, 5ml of dissolution medium is withdrawn and replaced with 5ml of dissolution medium into the same vessel. The same process was repeated for 4hrs, four concentrations were collected for each 1 hr. And then it was filtered and transferred into UV spectrophotometer were not ed at 272nm.

3. RESULTS AND DISCUSSIONS

INCOMPATIBILITY STUDIES

Drug Excipients interaction study: FTIR

'This is carried out using FTIR which is used to analysis the physicochemical interactions between the active substance and excipient used in the dosage form. Drug excipients interactions play an important function in the discharge of the drug from the formulation. The pure Guaifenesin and it's blended with each of different concentrations of hydroxyl propyl methyl cellulose were scanned by using FTIR instrument. The drug exhibits peak due to ketonic group, broad peak of alcohol group and C=C stretching which is shown in Fig 1. It was noticed that there were no changes in these main peaks in the IR spectra of a mixture o f drug and polymers [Fig 2]. The FTIR study revealed no physical or chemical interactions of Guaifenesin with hydroxypropyl methylcellulose as evident.

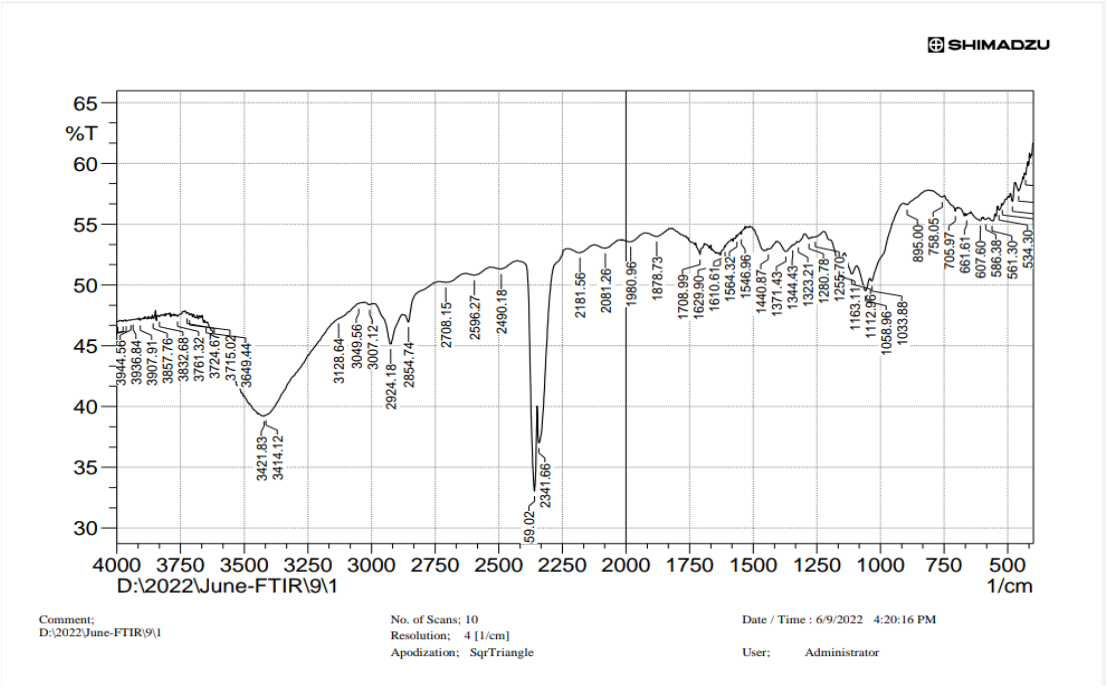
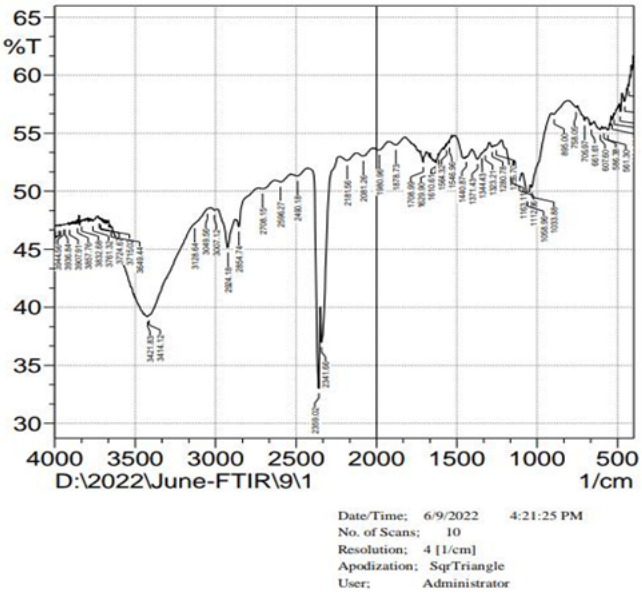


Fig 1: FTIR of Pure Guaifenesin



SHIMADZU

	Peak	Intensity	Corr. Inte	Base (H)	Base (L)	Area	Corr. Are
1	430.14	59.061	0.429	434	422.42	2.611	0.017
2	457.14	57.737	0.902	470.65	441.71	6.815	0.113
3	482.22	56.874	0.946	488.01	472.58	3.719	0.068
4	520.8	56.586	0.154	522.73	509.22	3.318	0.011
5	534.3	56.172	0.387	540.09	524.66	3.848	0.032
6	561.3	55.265	0.372	572.88	551.66	5.446	0.043
7	586.38	55.387	0.033	588.31	574.81	3.456	0.001
8	607.6	55.299	0.3	644.25	601.81	10.845	0.076
9	661.61	55.727	0.128	665.46	651.96	3.419	0.005
10	705.97	56.081	0.412	748.41	700.18	11.904	0.076
11	758.05	57.231	0.184	796.63	750.33	11.144	0.035
12	895	56.613	0.246	908.5	808.2	24.313	0.054
13	1033.88	50.327	0.596	1041.6	914.29	34.563	0.19
14	1058.96	49.526	1.323	1093.67	1043.52	14.928	0.275
15	1112.96	50.901	1.076	1139.97	1095.6	12.797	0.222
16	1163.11	51.558	1.544	1222.91	1141.9	22.373	0.366
17	1255.7	53.957	0.028	1257.63	1224.84	8.739	0.014
18	1280.78	53.799	0.257	1298.14	1267.27	8.272	0.029
19	1323.21	53.509	0.1	1325.14	1300.07	6.753	0.022
20	1344.43	53.255	0.072	1346.36	1327.07	5.255	0.008
21	1371.43	52.758	0.661	1404.22	1346.36	15.916	0.165
22	1440.87	52.94	0.086	1442.8	1410.01	8.989	0.032
23	1546.96	54.177	0.228	1548.89	1537.32	3.055	0.005
24	1564.32	53.967	0.139	1566.25	1550.82	4.11	0.006
25	1610.61	53.131	0.133	1612.54	1583.61	7.857	0.004
26	1629.9	52.443	0.282	1631.83	1612.54	5.343	0.02
27	1708.99	52.489	0.91	1726.35	1693.56	9.048	0.114
28	1878.73	53.979	0.474	1923.09	1830.51	24.621	0.189
29	1980.96	53.552	0.398	2013.75	1928.88	22.853	0.153
30	2081.26	53.031	0.073	2087.05	2025.32	16.848	0.029
31	2181.56	52.652	0.467	2224	2125.63	27.203	0.195
32	2341.66	36.996	2.742	2347.45	2225.93	39.163	0.629
33	2359.02	33.022	8.494	2426.53	2349.38	26.718	1.707
34	2490.18	51.315	0.116	2499.83	2428.46	20.493	0.035
35	2596.27	50.802	0.322	2627.13	2534.55	27.048	0.143
36	2708.15	50.215	0.109	2717.79	2629.06	26.301	0.065
37	2854.74	46.947	0.854	2868.24	2733.22	41.514	0.093
38	2924.18	45.133	2.806	2985.91	2879.82	34.914	1.098
39	3007.12	48.374	0.113	3026.41	2999.41	8.498	0.014
40	3049.56	48.465	0.013	3051.49	3037.99	4.241	0
41	3128.64	47.243	0.037	3130.57	3053.42	24.741	0.055

SHIMADZU

42	3414.12	39.301	0.054	3416.05	3130.57	103.713	0.108
43	3421.83	39.196	0.09	3429.55	3417.98	4.702	0.006
44	3649.44	46.885	0.124	3655.23	3645.58	3.169	0.007
45	3715.02	47.531	0.15	3718.88	3709.24	3.11	0.007
46	3724.67	47.659	0.125	3730.45	3720.81	3.1	0.007
47	3761.32	47.41	0.155	3767.1	3751.67	4.987	0.009
48	3832.68	47.395	0.136	3838.47	3824.97	4.369	0.008
49	3857.76	47.25	0.293	3859.69	3850.04	3.127	0.019
50	3907.91	47.081	0.204	3911.77	3898.27	4.405	0.011
51	3936.84	47.146	0.014	3938.77	3921.41	5.664	0.003
52	3944.56	47.1	0.04	3948.42	3938.77	3.152	0.002
53	3963.85	47.018	0.096	3967.71	3958.06	3.157	0.004
54	3975.42	47.006	0.071	3979.28	3969.64	3.157	0.003
55	3996.64	46.977	0.065	4000.5	3988.92	3.793	0.004

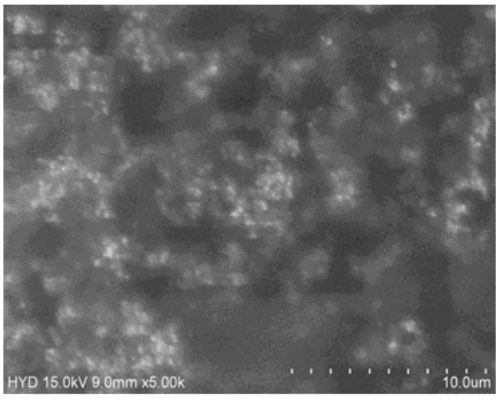
Fig 2: FTIR of Guaifenesin and Excipients

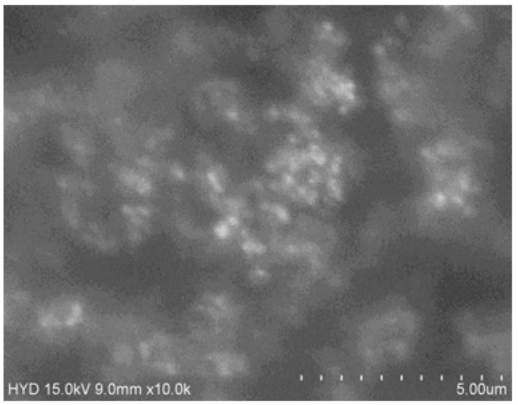
Differential Scanning Calorimeter (DSC)

The best formulation of Guaifenesin Nanocapsules were evaluated for DSC. The pure Guaifenesin shows a sharp endothermic peak at 300ºC and some similar changes occurs in endothermic peak were observed at similar temperature in prepared formulations at 250.2ºC. Thus it is concluded that there no drug excipients interactions. Thus it is concluded that no interactions between the drug and excipients.

Scanning Electron Microscope

Nanocapsules are in good spherical shape with smooth surface and also some of the rough space in its morphology and the particle were uniformly distributed without forming any lumps. The particle sizes observed in SEM photo microscopy are in the same line as determined by optical microscopic method. However SEM photographs of F5 formulations of (1:5) ratio was shown in fig 3. surface smoothness of Guaifenesin nanocapsules were discrete, large size and showed less aggregation with spherical and uniform free flowing which was confirmed by SEM.





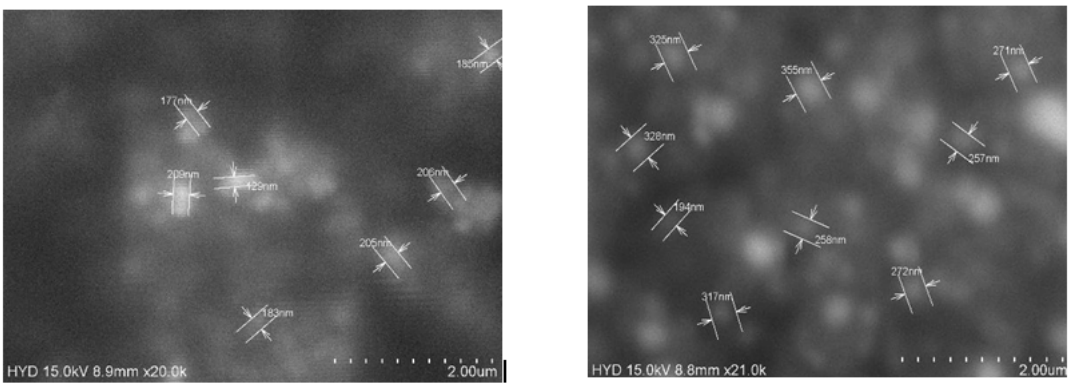


Fig 3: Scanning Electron Microscope of Guaifenesin Nanocapsules.

DRUG CONTENT

A) Drug Content

Table 4: % of drug content from F1-F4

S.No	formulations	Drug content (%)
1.	F1	70.2 ± 0.19
2.	F2	75.9 ± 0.35
3.	F3	80.4 ± 0.21
4.	F4	82.2 ± 0.23
5.	F5	85.2 ± 0.23

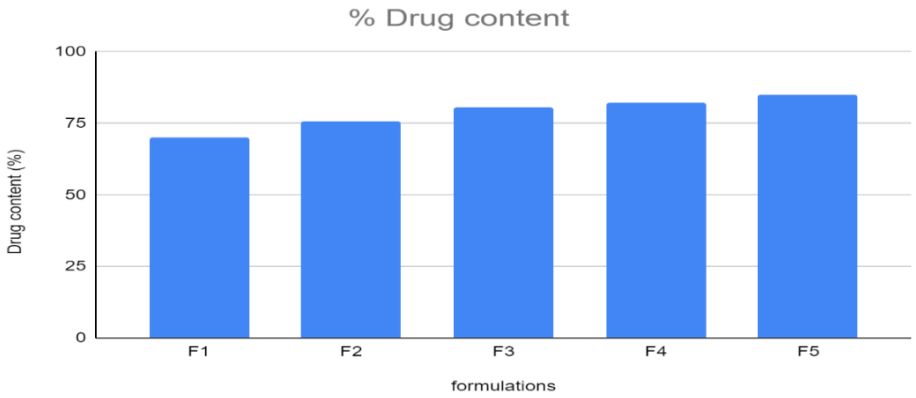


Fig 4: Graph of % Drug Content

B) Percent Entrapment Efficiency

Percent drug entrapment efficiency was used to determine the amount of drug entrapped into the prepared microspheres. The % Entrapment Efficiency of all the formulations ranges between 47.5±0.15 to 58.2±0.25. This indicates that increase in drug loading increase the percentage of drug entrapment efficiency. The %Entrapment efficiency values of all the Formulations were given in table 5 and graph representing the % Entrapment efficiency was given in Fig 5.

Table 5: % E.E value of formulations

S.No	formulations	% E.E ± S.D
1.	F1	47.5 ±0.15
2.	F2	48.3 ± 0.23
3.	F3	56.2 ± 0.23
4.	F4	58.5 ± 0.25
5.	F5	60.5 ± 0.25

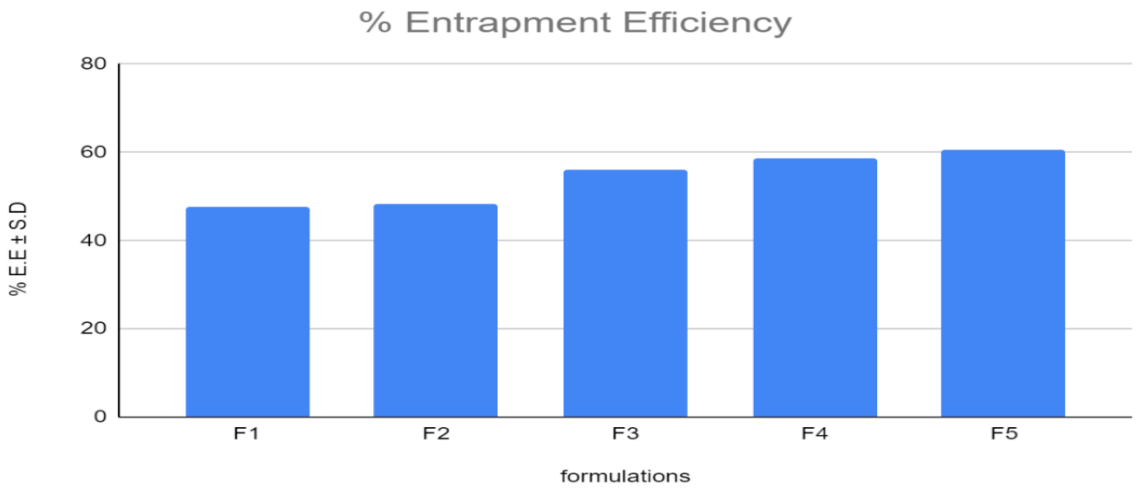


Fig 5: % Entrapment Efficiency graph

In-vitro drug release studies

The dissolution research been carried out in USP type II apparatus using 0.1N HCl as a medium, maintained at a temperature of 37 C for about 10 hours.

Drug release was calculated utilizing the next formulas

$$\% \text{ drug release} = \frac{\text{amount of sample (mg)}}{\text{dose (mg)}} \text{ x } 100$$

$$\% \text{ cumulative drug release} = \frac{\text{volume of sample withdrawn (ml)}}{\text{bath volume (ml)}} \text{ x } P(t-1) \text{x } Pt$$

Where

P (t-1) = percent drug release before time 't'

Pt = percent drug release at time 't'

Table 6: Cumulative percent drug release profile

Time	Formulation	Formulation	Formulation	Formulation	Formulation
1hr	10.26±0.12	11.79±0.38	12.6±0.54	14.4±0.65	**16.83±0.28**
2hr	14.46±0.91	15.26±0.68	16.88±0.22	18.85±0.63	**20.44±0.75**
3hr	21.13±0.51	23.75±0.42	24.64±0.75	25.35±0.85	**27.82±0.61**
4hr	29.55±0.54	31.16±0.61	32.88±0.84	34.61±0.31	**37.11±0.24**
5hr	36.25±0.43	37.56±0.12	38.76±0.35	42.09±0.62	**48.87±0.20**
6hr	40.50±0.24	45.46±0.32	46.35±0.43	48.00±0.62	**56.40±0.53**
7hr	44.65±0.21	49.72±0.12	51.35±0.19	56.69±0.53	**64.00±0.39**
8hr	58.12±0.01	60.65±0.22	63.19±0.29	64.53±0.18	**70.70±0.74**
10hr	64.82±0.71	65.61±0.56	69.04±0.46	73.52±0.82	**76.58±0.25**
12hr	68.17±0.73	69.62±0.92	73.22±0.72	76.59±0.64	**80.84±0.09**

Invitro drug release study for all the five formulations were carried out for12hrs and tabulated shown in table 6. The results obtained proved that the *invitro* release influenced by polymer ratios. The capsules containing hydroxypropyl methylcellulose at different ratios has shown drug release at various percentages as shown in above table 6. These variations in drug release were due to changes in polymer concentration on capsules. Formulations F 05 met the desired drug release profile in 12hr.Therefore, thought of one of the best formulations around all the formulations.

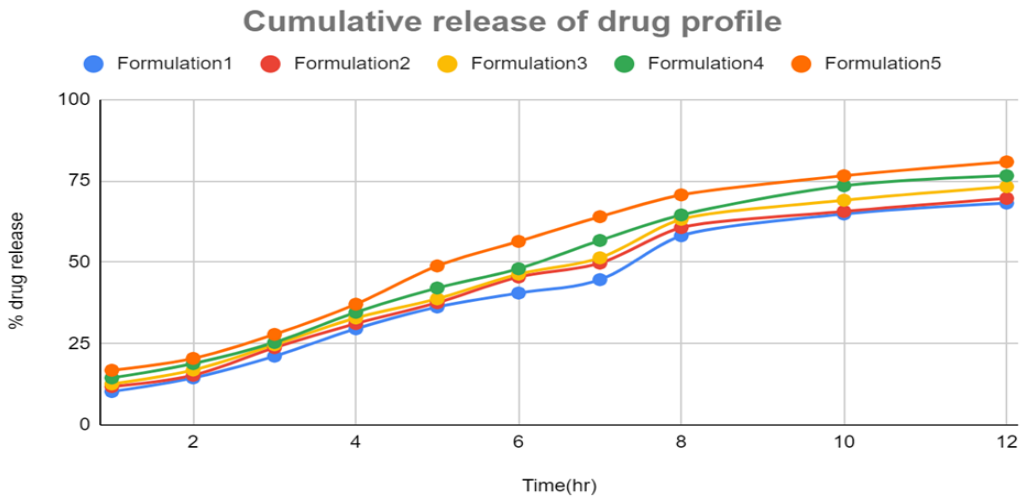


Fig 7: Cumulative percent of drug release profile

CONCLUSION

Guaifenesin is a drug of choice for treating common cold, chronic bronchitis. The prepared nano capsules of Guaifenesin aim to deliver the drug which passes through oral route as it provides controlled release of drug when compared to other route of administration. Formulate and characterize the formulation of Guaifenesin to minimize the side effects such as dizziness, rashes. The Guaifenesin nano capsules was successfully prepared by using nanoprecipitation method by taking F01to F05 formulation by using different concentration of polymer ratio. And as a polymer Hydroxy propyl methyl cellulose is used and polyvinyl alcohol (PVA) as a stabilizer. The prepared formulations of nanocapsules were evaluated for various parameters. Guaifenesin in 1:5 (F05) shows better particle shape and size, SEM study of prepared nanocapsules were within the range of (1-1000µm). There is no drug excipients interactions in FTIR and DSC. FTIR results shows peaks at 3244 cm-1, 1455cm-1, 1376cm-1 and 1594cm-1. The physical mixture on the other hand shows peaks at 3421cm-1, 1440cm-1, 1371cm-1, 1564cm-1. Thus, it is concluded that the physical mixture of the drug (Guaifenesin) does not show any major interactions with the formulation components like (HPMC, Sorbitan monostearate and PVA). This indicates that drug was compatible with the excipients. In DSC Results The pure Guaifenesin shows a sharp endothermic peak at 300ºC and some similar changes occurs in endothermic peak were observed at similar temperature in prepared formulations at 250.2ºC. Thus, it is concluded that there no drug excipients interactions. The formulation of F05 showed good particle size with good spherical shape and uniformly distributed without any lumps. The percent drug content was found to be in 8hrs showed anomalous mode of drug release, in F05 formulations.

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