

Formulation and Evaluation of Sustained release suspension of Ambroxol Hcl Using Ion Exchange Resin

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Abstract: Eudragit RS100 coated ion exchange resinate of Ambroxol Hcl were prepared using Indion-244 by Solvent evaporation method. Among the various formulation of microcapsule (drug resinate Eudragit ratio) prepared. An ideal formulation (drug resinate 1:1) and 10% eudragit coating was selected for the formulation of sustained release suspension. Three formulation of suspension were prepared using xanthan gum as suspending agent in three different concentration (0.2, 0.3, 0.4% w/v). This suspension was evaluated for physical stability, redispersibility and in vitro drug release pattern. The result showed that the suspension prepared with xanthan gum (0.3%w/v) as a suspending agent showed a optimum drug release and was found to be ideal for sustained release preparation.

Keywords: Sustained release suspension, Ambroxol Hcl, Ion exchange resinate

INTRODUCTION

Sustained release dosage forms aimed at controlling the rate of release as well as maintaining desire drug level in the blood for long duration. An oral suspension could be the best suitable dosage form for geriatric patients. Many therapeutic benefits could be gained by incorporating functions of sustained drug release in to suspension dosage form. They include improvement of rate and extent of drug absorption, higher patient compliance, reduction of side effects and taste masking for bitter drug^{1,2}. Ambroxol Hcl used in the treatment of respiratory disorders associated with viscid mucous. Its usual dose is 15-30 mg 3-4 times daily³. To improve the patients compliances and reduce the dose, different methods for sustaining the release of drugs are described by Ariens⁴. One of the methods to sustained the drug release is the use of ion exchange resins. In the present work, Ambroxol Hcl was absorbed on cationic exchange resin, Indion 244 and later a coating of Eudragit RS100 was given. Then, these resonates were formulated in to a suspension form, which can release the drug in a slow and controlled manner. The dissolution rate and bioavailability from suspensions are reported to be adversely affected by the suspending agents, which are used to increase the viscosity of the media to maintain uniform dispersion during storage^{5, 6}. Hence, in the

present study an attempt is made to evaluate different concentration of suspending agents for their suitability for the formulation of sustained release suspension containing Ambroxol Hcl microcapsules.

MATERIALS AND METHOD

Ambroxol Hcl, Eudragit RS100, Indion-244 was a gift sample from Indoco Remedies, Mumbai, and other chemicals used were analytical reagent grade.

EXPERIMENTAL:

Resin Pretreatment:

Indion 244 was given a pretreatment to remove the impurities associated with industrial scale manufacture. The resin was treated with 5-10 bed volumes of 2N NaOH solution and 1.5N Hcl solution prepared in distilled water. The resin in hydrogen form was evaluated for moisture content, particle size and cation exchange capacity and they were found to be 3.8%w/w, 14-100 um and 5.49 meq/gm drug resin respectively.

Sorption of drug on the resin:

Preparation of drug resinate was tried by both the column and batch method. Efficient elution of the drug solution was not possible from the column due to its small particle size hence batch method was preferred. Accurately weighed 1.0gm of Ambroxol Hcl was dissolved in 60 ml

solvent (mixture of methanol and water in the proportion of 1:1) and Indion 244, 1.0gm was added. The mixture was stirred on a magnetic stirrer till equilibrium was established; the process of drug sorption was optimized with respect to methodology drug resin proportion and time for sorption is carried out. The time for maximum drug loading was noted.

EVALUATION OF DRUG RESINATES

The resonates were allowed to dry and evaluated for physicochemical characterization like mixture content, flow properties, drug content and *In vitro* drug release kinetics.

Drug content:

It was determined by eluting the drug in 0.1M methanolic Hcl. 100mg of drug resinate was stirred with 100ml of 0.1M methanolic Hcl for six hrs. The solution was filtered and after suitable dissolution drug content was determined spectrophotometrically at 245nm.

In vitro drug release study:

The release characteristics were studied using USP dissolution rate test apparatus i.e basket type, in pH 1.2 buffer (for first 2 hrs.) pH 7.2 buffer (for remaining 6 hrs.) the temperature and speed were maintained at 37°C and 100 rpm respectively. The release patter was compared with that of conventional Ambroxol Hcl tablet.

Microencapsulation of drug resins:

To further retard the drug release, the resinate particles were coated with Eudragit RS100 (5-20% w/w). Microencapsulation was carried out by solvent evaporation techniques⁷.

Drug resinate (1.0gm) was stirred with polymer solution for 2 hrs. the solvent cyclohexane was evaporated by continuous stirring on a water bath. Stirring rate was gradually increase as the viscosity of the mixture was increased. The product was filtered and dried at 37°C and evaluated for drug content, particle size and *In vitro* drug release.

Determination of drug content in the microcapsules:

A known quantity of microcapsules was stirred with 100 ml of 0.2M Hcl for 6 hrs, filtered and the absorbance of filtrate was measured spectrophotometrically at 245nm. The drug content was calculated using the calibration curve.

Scanning electron microscopy:

The surface of microcapsules was examine by Scanning electron microscopy The samples were splutter coated with gold before scanning.

In vitro release from microcapsule:

The release characteristics were studied using USP dissolution rate test apparatus i.e basket type, in pH 1.2 buffer (for first 2 hrs.) pH 7.2 buffers (for remaining 6 hrs.) the temperature and speed were maintained at 37°C and 100 rpm respectively. Aliquots of 10ml were withdrawn at specific time intervals and equal amount of fresh medium was added to replace withdrawn aliquots after each sampling. The amount of drug dissolved was determine by diluting the samples suitably and measured the absorbance at 245 nm. using spectrophotometer.

FORMULATION OF SUSPENSION

Three different batches of sustained release suspension were developed by using microencapsulated resinate of Ambroxol Hcl. To study the different concentration of xanthan gum were used. The concentration of sucrose and sorbitol were kept constant. The concentration of microencapsulated resinate was taken such that each 10 ml of prepared suspension with deliver 60 mg of Ambroxol Hcl. To improve the aesthetic appeal of suspension peppermint oil in the concentration of 0.2 ml and sunset yellow in the concentration of 0.001% w/v are used as a flavoring agent and coloring agent respectively.

Study of physical stability and redispersibility of suspension:

The formulated suspensions were evaluated for physical stability by determining the sedimentation volume⁸.

Drug leaching in to the suspension:

The amount of drug leaching in to the vehicle after the storage of suspension at room temperature for one month was determined by filtering the suspension and measuring the absorbance at 245nm, using a suspension prepare without microcapsule as a blank. The drug leached in the vehicle was calculated using the calibration curve.

In vitro release study from suspension:

The release characteristics were studied using USP dissolution rate test apparatus i.e basket type, in pH 1.2 buffer (for first 2 hrs.) pH 7.2 buffers (for remaining 6 hrs.) the temperature and speed were maintained at 37°C and 100 rpm respectively. Aliquots of 10ml were withdrawn at specific time intervals and equal amount of fresh medium was added to replace withdrawn aliquots after each sampling. The amount of drug dissolved was determine by diluting the samples suitably and measured the absorbance at 245 nm. using spectrophotometer.

RESULT AND DISCUSSION

Five batches of microcapsule (FE1-FE5) of Ambroxol Hcl corresponding to drug polymer ratio (5-20% w/w) were evaluated for percentage yield, drug content, particle size and *in vitro* release profile. The drug loading capacity of the ion exchange resin was found to be 50%. Uniformity of drug contents were found to be satisfactory. These values are shown in (Table I). the average particle sizes for (FE1-FE5) were found to be suitable for the formulation of suspension. The *in vitro* drug release studies for different batches of microcapsules showed (Figure-I) that increase in eudragit RS100 proportion reduced the rate of release. The batch FE5 in which Maximum eudragit RS100 was used, showed minimum drug release (54.00%) at the end of 8 hrs. Batch FE1, in which minimum proportion of eudragit RS100 was used showed maximum drug release (102.00%). Among the five batches batch FE2 showed uniformity of drug release up to 8 hrs. and was considered as ideal formulation of sustained release suspension.

Three batches of suspension of Ambroxol Hcl were evaluated for aesthetic appeal, pH, particle size, wt/ml,

sedimentation rate, redispersibility, viscosity; drug content and in vitro drug release pattern are shown in (Table II).

The release data given (Figure-II) showed that the rate of drug release from the suspension was reduced with the increase in the concentration of suspending agent. This is because of the reason that an increase in concentration of suspending agent increases viscosity, which in turn reduces the rate of diffusion. The suspension prepared with 0.3 % of xanthan gum had good physical properties and redispersibility. The release was also suitable for a sustained release suspension. Hence, they were considered as an ideal.

Stability studies were subjected to accelerated stability studies where the representative samples were stored at various temperatures. i.e. room temperature, 37°C, 45°C and 60°C. and there was no considerable change in the formulation after one month. Thus the formulation containing microcapsule suspension was found to be more stable.

CONCLUSION

Ion exchange resinate of Ambroxol Hcl coated with Eudragit RS100 and formulated as oral suspension is an efficient system for sustained release of Ambroxol Hcl and this can be suitable dosage form for geriatric use.

Table I : Physical characteristic of microcapsule.

Batch no.	Drug resinate polymer ratio	Nature of microcapsule	Drug content (%)	Average particle size(um)
FE1	5	Free Flowing	94.99	62-142
FE2	10	Free Flowing	97.83	72-153
FE3	12	Free Flowing	95.88	85-167
FE4	15	Free Flowing	96.70	93-177
FE5	20	Free Flowing	94.21	97-179

Table II: Evaluation of suspension:

Parameter	Batch Number		
	FE1	FE2	FE3
Appearance	uniform	uniform	uniform
taste	Sweet, palatable	Sweet, palatable	Sweet, palatable
pH	6.09 ± 0.01	6.00 ± 0.02	5.99 ± 0.01
Viscosity(cps)	210	225	310
Sedimentation ratio	0.95	0.92	0.91
Particle size(um)	71-189	69-187	65-186
Redispersibility	+++	+++	+++
Drug content (% w/v)	94.99	97.83	95.88
<i>In vitro</i> dissolution (%)	92.52	90.64	89.16
Drug eluted in vehicle	0.33	0.31	0.25
wt./ ml	1.29	1.22	1.30

Figure I: *In vitro* drug release profile of Ambroxol Hcl microencapsulated resinate.

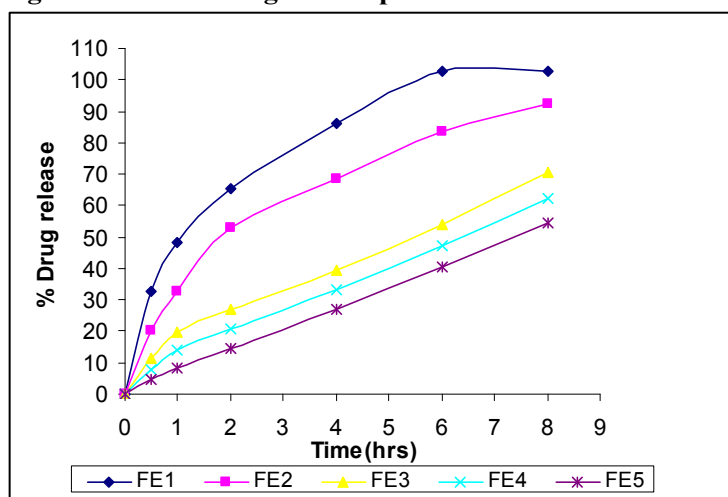
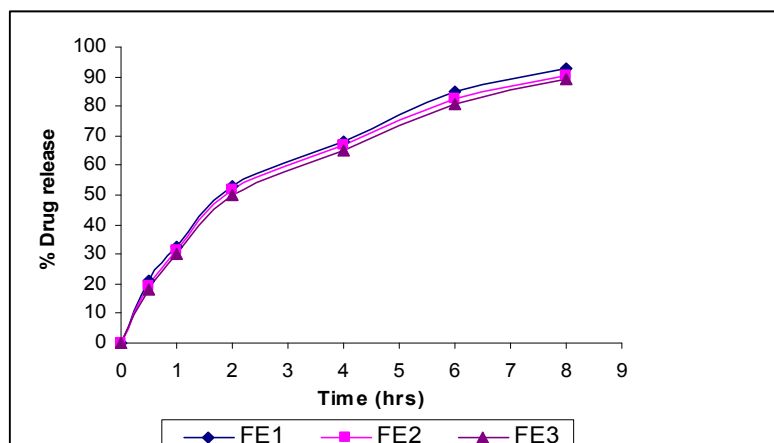
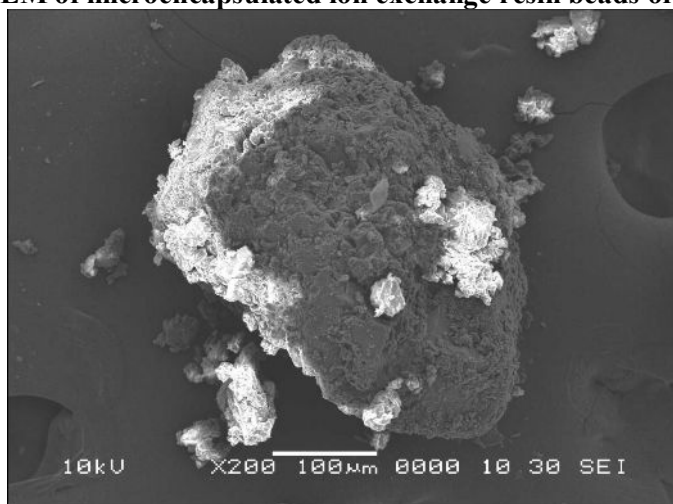


Figure II : *In vitro* drug release profile of Ambroxol Hcl microencapsulated Suspension.**Figure III: SEM of microencapsulated ion exchange resin beads of Ambroxol Hcl.****REFERENCES**

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