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Formulation and Evaluation of Ambroxol HCL Microsphere Suspension

Ch. Saibabu, Bommala Himabindu* and Karavadi Thejomoorthy

Department of Pharmaceutics, Malineni Lakshmaiah College of Pharmacy, Kanumalla, Singarayakonda-523101

ABSTRACT

For the treatment of asthma, various conventional oral dosage forms like tablets, capsules, suspensions, syrups etc., are available in market. The difficulty experienced in frequent medication and unpleasant taste. For this reason microencapsulated suspensions have attracted great deal of attention. This microencapsulated suspension achieved long half life to the formulation with masked taste. The Aim of the study is related to the formulation and evaluation of Ambroxol Hcl 25ml of microencapsulated suspension by solvent evaporation method by using Indion resin 204, HPMC, Carbapol 934 Pluronic F 68, Glycerinn, xanthum gum and sorbitol solution as an excipients. Total six formulations were formulated, among which F3 formulation containing HPMC showed controlled drug release when compared to other formulations. Studies like FTIR, SEM analysis and raman analysis indicated that all the formulations were stable without any interactions.

Key words: Ambroxol HCL Eudragit RS Indion Resin 244, HPMC K15M.

Introduction

Asthma is a disease affecting the airways that carry air to and from your lungs. People who suffer from this chronic condition (long-lasting or recurrent) are said to be asthmatic.According to World Health Organization (WHO) estimates 235 million people worldwide suffer from asthma.Asthma is the most common chronic disease among children.Asthma is not just a public health problem for high income countries: it occurs in all countries regardless of level of development. Over 80% of asthma deaths occurs in low- and lower-middle income countries. Asthma is under-diagnosed and under-treated, creating asubstantial burden to individuals and families and possibly restricting individuals' activities for a lifetime1-5 The muscles around the airways tighten up, narrowing the airway.Less air is able to flow through the Inflammation of the airways increases, further narrowing the airway.More mucus is produced in the airways, undermining the flow of air even more.Primary cause for narrowing of airways Excess production of mucus causes accumulation in airways which obstructs the free passage of air due to narrowing of airways(fig:1). Difficulty in breathing occurs which leads to respiratory problem 6-9. So to prevent this problem accumulation shouldbeavoided2 Ambroxol HCL is belongs to mucokinetic. This agent is thought to stimulate surfactant and mucous secretion, yet promoting normalization of mucous viscosity in viscid secretions. A recent systematic review towards evidence of generalized benefit using ambroxol for a range of parameters including secretolytic activity(promoting mucous clearance),anti inflammatory and anti oxidant activity and exerts local anesthetic effect10-12.

MATERIALS AND METHODS

Ambroxol Hcl were obtained from Karnataka fine chem .Banglore. Eudragit RS INDION RESIN 244, HPMC K15M were obtained from Qualigenes fine chemicals.

Formulation of suspension

The different batches of sustained release suspension were developed by using microencapsulated resinate of Ambroxol Hcl. To prepare reconstituble suspension xanthan gum were used as suspending agent. 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 adjust pH sodium citrate used.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 and for preservation methyl paraben and propyl paraben is used.

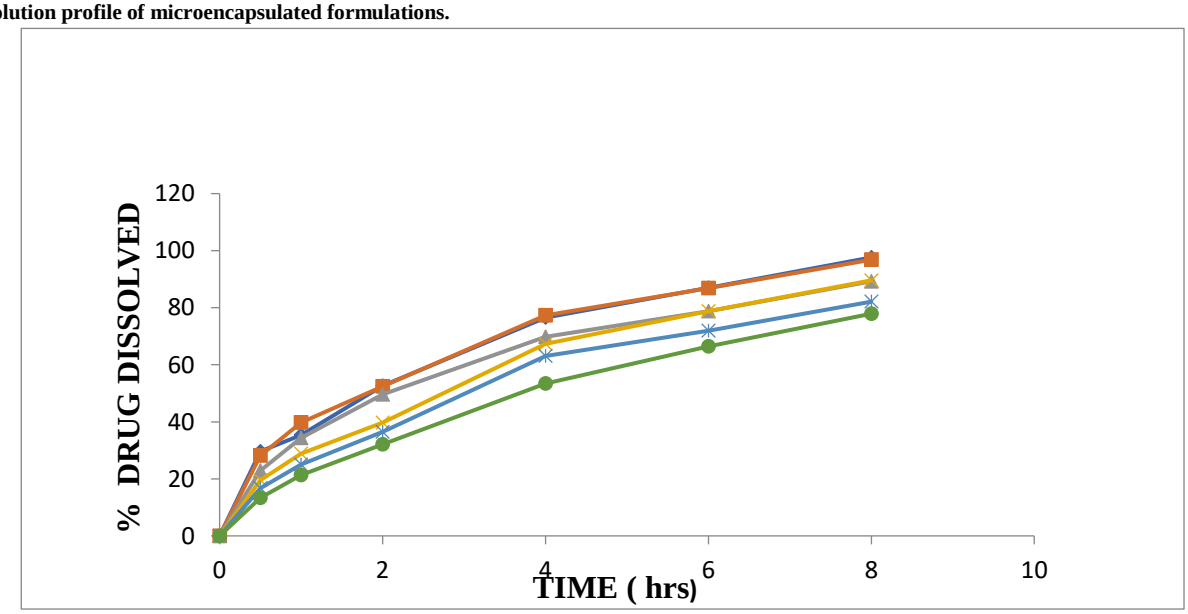
Formulation of Ambroxol hcl microsphere suspension

Ingredients	Quantity of Ingredients (mg)					
	F-1	F-2	F-3	F-4	F-5	F-6
Ambroxol hcl(mg)	75	75	75	75	75	75
Indionresin 244(mg)	75	75	75	75	75	75
HPMC(mg)	20	25	30	---	---	---
Eudragit rs 100(mg)	--	--	--	20	25	30
Sucrose(mg)	15	15	15	15	15	15
Xanthan gum(%w/v)	0.6	0.6	0.6	0.6	0.6	0.6
Sorbitol(%w/v)	20	20	20	20	20	20
ppermintoil, sunset yellow(ml)	0.2	0.2	0.2	0.2	0.2	0.2
thylparaben&propyl raben(ml)	0.02	0.02	0.02	0.02	0.02	0.02

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 6hrs.) the temperature and speed were maintained at 37Oc 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.

Dissolution profile of microencapsulated formulations.



Correlation coefficients according to different kinetic equations

Formulation Code	Mathematical Models (Kinetics)					
	Zero	First Order	Higuchi Matrix	Peppas	Hixson Crowell	Best fit Mode
F1	K0=16.4 R2=0.86	K=0.30 R2=0.996	K=32.5 R2=0.99	n=0.242 R2=0.97	K=-0.05 R2=0.92	First order
F2	K0=15.6 R2=0.87	K=0.25 R2=0.99	K=31.8 R2=0.99	n=0.237 R2=0.97	K=-0.06 R2=0.91	First order
F3	Ko=15.2 R2=0.93	K=0.23 R2=0.994	K=33.47 R2=0.99	n=0.277 R2=0.98	K=-0.08 R2=0.93	First order
F4	K0=14.7 R2=0.98	K=0.195 R2=0.968	K=33.04 R2=0.97	n=0.297 R2=0.97	K=-0.08 R2=0.85	First Order
F5	K0=14.5 R2=0.98	K=0.195 R2=0.986	K=33.58 R2=0.970	n=0.349 R2=0.981	K=-0.13 R2=0.98	First order
F6	K0=13.0 R2=0.98	K=0.168 R2=0.998	K=31.85 R2=0.98	n=0.404 R2=0.99	K=-0.23 R2=0.95	First order

DISCUSSION OF RESULTS

The treatment of asthma can be made successful only by clearing mucus and to achieve this,constant and uniform supply of drug is desired.administration of multiple doses at intervals of 2 to 4hrs is difficult for a patient which can lead to noncompliance.Ambroxol Hcl is a good mucolytic used in treatment of Asthma and COPD.And are suitable candidates for the development sustained release dosage forms.In the present study ,HPMC and EUDRAGIT RSPO are employed to formulate sustained release microsphere suspension of AH.All the formulations were prepared according to the formula given in tables.The microcapsules were evaluated for particle size drug content,SEM analysis,FTIR analysis,invitro release studies including stability studies.From the data in table the particle size of microcapsules prepared with eudragit RSPO were quite smaller than microcapsules prepared with HPMC.From the IR spectral analysis it indicated that drug is compatible with high proportion of both polymersFrom the data of curve fitting analysis all the formulations showed higher r2 values for first order plot indicating that release of drug follows first order kinetic, further Korsmeyer and peppas equation resulted into the value of n in the range of 0.980 to 0.995 indicating a non-fickian diffusion mechanism and may indicate that the drug release is controlled by more than one process.Stability studies were subjected to accelerated stability studies where the representative samples were stored at various temperatures. i.e. room temperature, 37oC,45oC and 60oC. 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

Novel lung-targeting sustained-release AH microspheres were prepared and characterized. The AH microsphere's particle size was appropriate for a lung-targeting purpose.Sustained release ambroxol hcl microsphere suspension was formulated by using HPMC and EUDRAGIT RSPO as release retartdant by solvent evaporation technique.by increasing polymer concentration there is decrease in rate of drugrelease.by comparing two polymers formulations with eudragit rspo showed more sustained release behavior.The microspheres had a sustained-release profile in-vitro without the burst release phenomenon. These microspheres containing AH thus demonstrated a great potential therapy option with appropriate biocompatility, sustained release profiles and appropriate particle size for lung targetingIon exchange resinate of Ambroxol Hcl coated with Eudragit RSP0 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 and pediatric use

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